Public Health England

Protecting and improving the nation's health

Investigation of novel SARS-CoV-2 variant

Variant of Concern 202012/01

Technical briefing 5

This briefing provides an update on the briefing of 14 January 2021

Contents

Summary

SGTF detections indicate VOC202012/01 continues to predominate across all regions. S gene target failure remains a well correlated proxy measure of VOC 202012/01. An assessment of severity of disease has been conducted by NERVTAG. A limited number of B.1.1.7 VOC 202012/01 genomes with E484K mutation have been detected.

Nomenclature of variants in the UK

SARS-CoV-2 variants if considered to have concerning epidemiological, immunological or pathogenic properties are raised for formal investigation. At this point they are designated Variant Under Investigation (VUI) with a year, month, and number. Following risk assessment with the relevant expert committee, they may be designated Variant of Concern (VOC). This variant was designated VUI 202012/01 on detection and on review re-designated as VOC 202012/01 on 18 December 2020.

Severity of disease

A summary of the current data and analyses on severity of disease associated with B.1.1.7 is available at:
www.gov.uk/government/publications/nervtag-paper-on-covid-19-variant-of-concern-b117

Epidemiological findings

Updated 26 January 2021 to include new data. A matched cohort study was undertaken with SGTF and non-SGTF cases, with matching based on 10-year age bands, sex, week of test and lower-tier local authority. There were 92,207 SGTF cases and an equal number of corresponding comparators included in the matched cohort (n = 184,414). A 28 day case fatality risk was calculated for both SGTF and non-SGTF cases. Initial analysis was completed on 8 January 2021; of 14,939 SGTF cases and 15,555 comparators who had at least 28 days between specimen date and the study period end date. There were 25 deaths (0.17%) in SGTF cases and 26 deaths (0.17%) in comparators (RR 1.00, 95% CI 0.58 – 1.73). On 19/01/2021, updated linkage of deaths data to the same matched cohort provided increased time for follow-up and ascertainment of deaths identified there were 65 deaths among non-SGTF cases (0.1%) and 104 deaths among SGTF cases (0.2%), within 28 days of specimen date. With this, the risk ratio increased to 1.65 (95%CI 1.21-2.25).

S gene target failure/lineage correlation

Only a small fraction of all new cases of VOC 202012/01 are identified by whole-genome sequencing, and this data typically lags test date by approximately 2 weeks, therefore a proxy S gene target failure (SGTF) is used to monitor the VOC.

We previously observed that one of the S gene mutations in the VOC, which deletes amino acids 69 and 70 (Δ69-70), causes a reproducible S gene target failure (SGTF) in the ThermoFisher TaqPath assay used in 3 UK lighthouse laboratories (see Technical Briefing 1). These laboratories are referred to here as 'TaqPath laboratories.' The Lighthouse laboratories provide testing for samples from the community.
This coincidental occurrence provides a good proxy for monitoring trends in VOC 202012/01. SGTF correlates almost perfectly with presence of Δ69-70. Considering 31,284 tested pillar 2 samples where we know both the sequence and the SGTF status, 99.6% of Δ69-70 sequences (12,675 of 12,720) are SGTF, compared to 0.05% of sequences without the deletion (9 of 18,564).

Because Δ69-70 has arisen multiple times, and SGTF is a proxy for any lineage with that mutation, the utility of SGTF as a proxy for VOC 202012/01 varies over time and region. Table 1 shows, for all pillar 2 sequences, the weekly proportion of Δ69-70 sequences that were confirmed to be VOC 202012/01. Table 2 shows the proportion of Δ69-70 that is the VOC 202012/01 in England since December 21, broken down by region. It is now over 99% in all regions of England. The numbers in these tables are based on sequenced samples, some of which may have come from the same individual (this effect is likely to be small).

Table 1. Percentage of Pillar 2 Δ69-70 sequences that are VOC 202012/01, 12 October 2020 to 18 January 2021

Week beginning	Percentage VOC of all Δ69-70	Number of pillar 2 Δ69-70 sequences
2020-10-12	3%	116
2020-10-19	15%	220
2020-10-26	29%	156
2020-11-02	64%	399
2020-11-09	81%	711
2020-11-16	89%	771
2020-11-23	93%	387
2020-11-30	95%	423
2020-12-07	98%	2704
2020-12-14	99%	4301
2020-12-21	99%	2400
2020-12-28	99.7%	4766
2021-01-04	99.7%	4509
2021-01-11	99.9%	972

Table 2. Percentage Pillar 2 Δ69-70 sequences from that are VOC 202012/01, by region of England, 1 December 2020 to 18 January 2021

Region	Percentage VOC 202012/01 of all Δ69-70	Number of Pillar 2 Δ69-70 1 December 2020 to 18 January 2021
East Midlands	99.6%	282
East of England	99.7%	1567
London	99.7%	3845
North East	99.4%	470
North West	99.6%	1808
South East	99.5%	1908
South West	100%	329
West Midlands	99.2%	1320
Yorkshire and the Humber	100%	430

Figure 1 shows the weekly percentage of VOC202012/01 and STGF combinations, showing increasing proportion of VOC202012/01 with SGTF (Pillar 2 samples with CT <30).

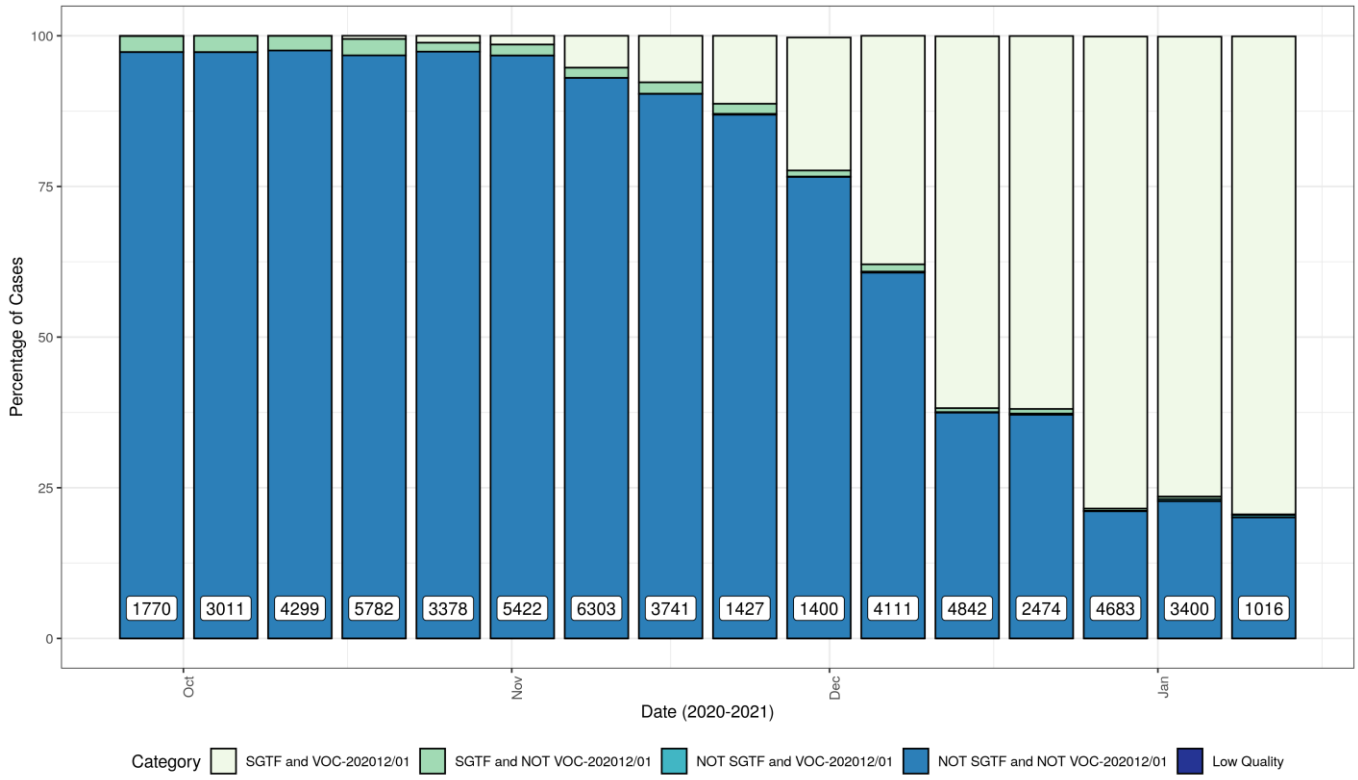


Figure 1. Weekly percentage of VOC202012/01 and SGTF combinations, 1 October 2020 to 16 January 2021 (Pillar 2 data, not deduplicated, England sample identifiers of Taqpath Tests carried out at Lighthouse laboratories with a CT<30, matched to COG-UK sequence IDs that had been assigned as VOC202012/01 confirmed or probable). Excludes samples not linked to a COG-UK ID and/or VOC classification.

In addition there is now a small amount of data from hospital settings (unpublished).

A study of 82 sequences was undertaken in a single hospital in January 2021. 100% (66/66) SGTF samples were confirmed as VOC 202012/01 by sequencing. 15/15 non VOC 202012/01 genomes had S gene ampification. A single VOC 202012/01 genome that was S gene positive demonstrated S gene amplifcation >5 CT compared to N and ORF1ab results on multiplex testing of the same sample (TaqPath PCR). Diagnostic labs should be aware of the possibility of late S gene amplification as another potential presentation of variant VOC 202012/01, although additional genomic confirmation studies are required.

A second study included 636 samples at two hospitals tested by the Thermofisher TaqPath PCR over weeks 44-53 2020. Those samples with a CT of <30 in at least one target were sequenced. Analysis by week shows that the VOC 202012/01 is the predominant cause of SGTF by week 50 and was the cause of almost all SGTF in week 52/53. Lineage B. 1.258 is noted as a cause of SGTF in earlier samples and individual hospitals may be affected by local

outbreaks, altering circulating lineages. A small number of 'late' S gene target positives in VOC 202012/01 samples, as highlighted above were also identified in this study.

Diagnostic labs should be aware of the possibility of late S gene amplification as another potential presentation of VOC 202012/01, although additional genomic confirmation studies are required.

Epidemiology of S gene target failure

Since 1 September 2020, the proportion of England specimens tested in TaqPath laboratories has remained at approximately 35% (Figure 2). This coverage is however lower in local authorities in the East and South West of England.

Descriptive analyses below are restricted to TaqPath lab Pillar 2 positive tests with CT values <=30 for non S gene targets. This restriction to CT values removes potential confounders around variable target performance at lower viral loads, and is consistent with the sample set for which genomic confirmation is available.

The following definitions apply (please note the **change from previous reports**):

- **confirmed SGTF**: Positive test with non-detectable S gene and <=30 CT values for N and ORF1ab genes
- **confirmed S gene positive**: Positive test with <=30 CT values for S, N, and ORF1ab genes

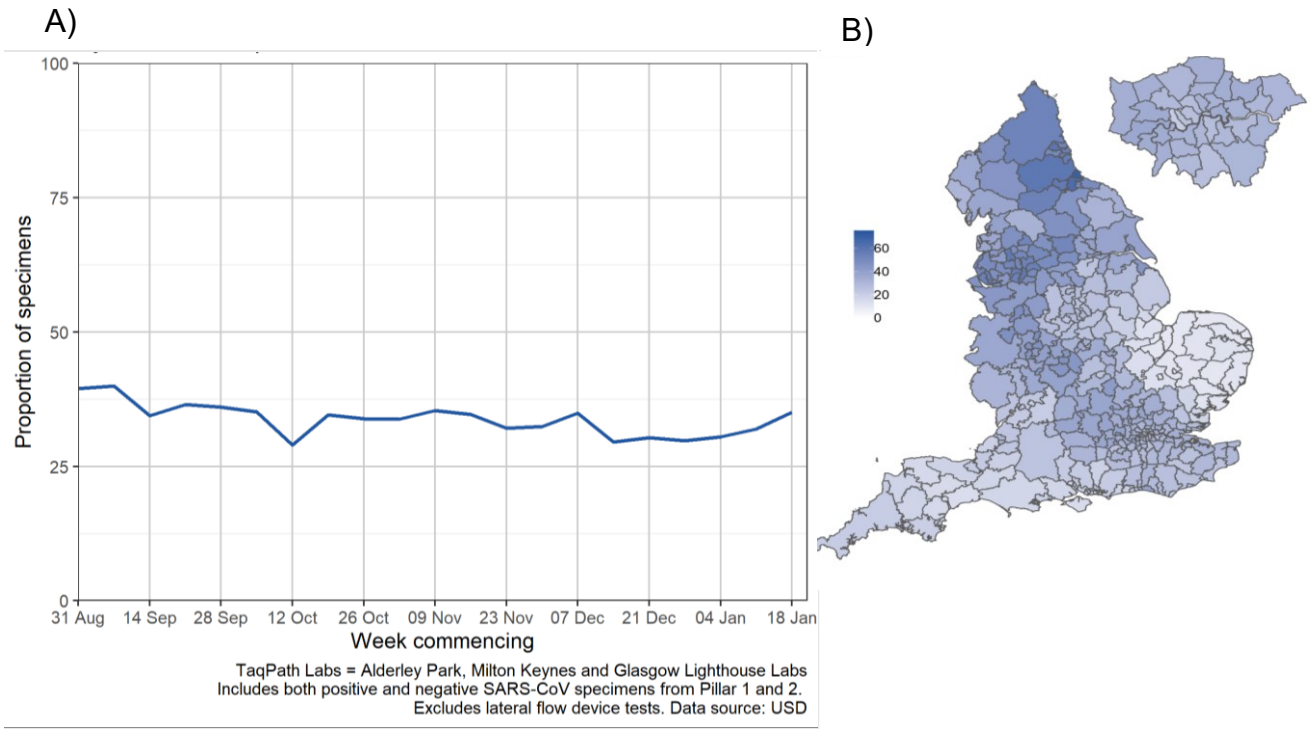
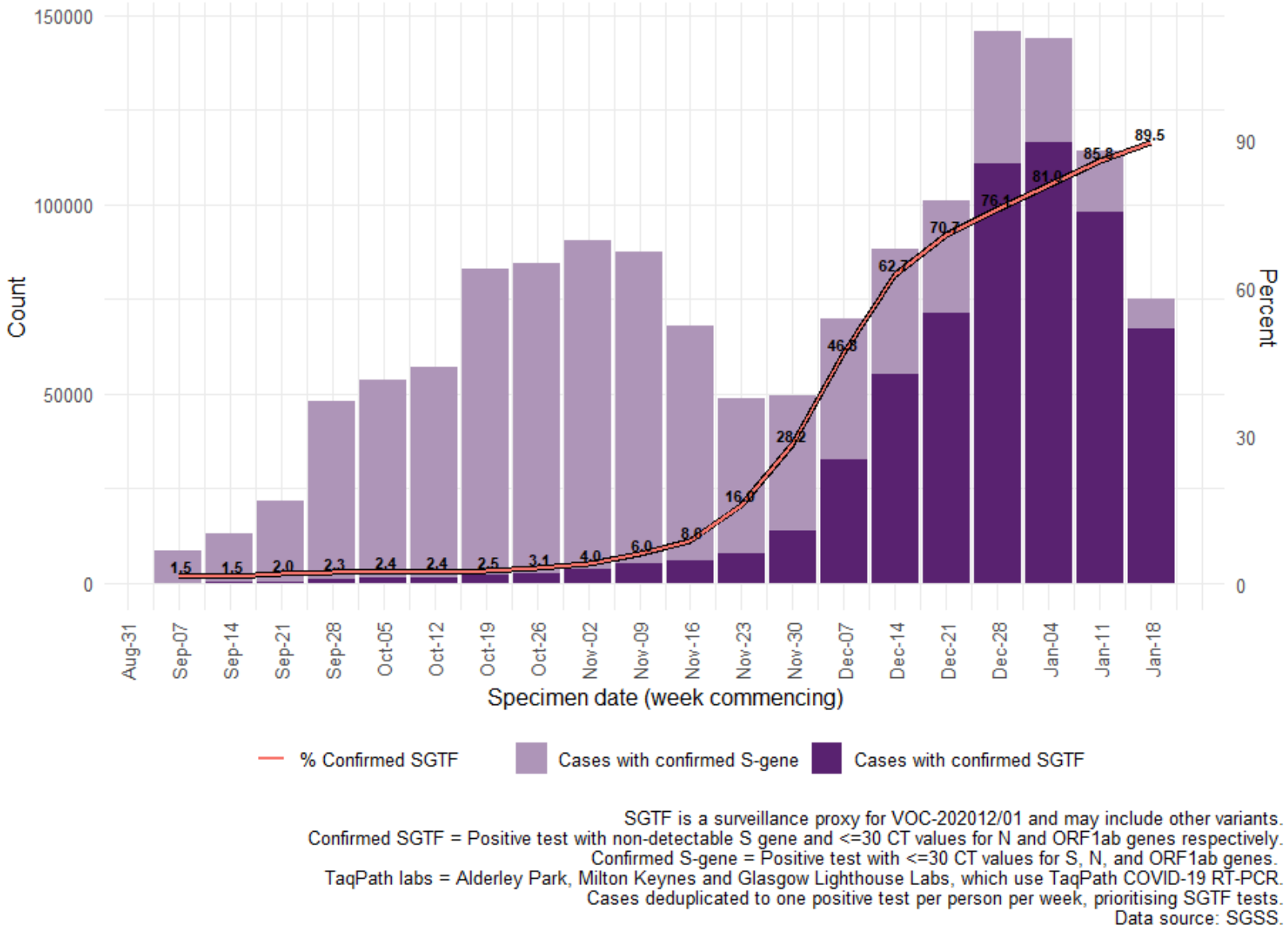


Figure 2. Proportion of England specimens tested in TaqPath laboratories by A) week and B) local authority (1 September 2020 to 24 January 2021)

In the most recent 7-day period (18 to 24 January 2021), 89.5% of 75,092 cases with S gene detection results had isolates with SGTF, compared to 85.8% in the prior seven day period and 28.2% in the seven day period starting November 30th (Figure 3). This increase coincides with the overall case number increase across England, however has persisted in recent weeks while case counts decrease.

By region, the proportion of cases with SGTF has reached nearly 100% in London, the South East, and East of England (Figure 4), whereas other areas see lower proportions that continue to rise. This geographic spread from these areas to the rest of England is evident in Figure 5, although higher proportions of SGTF were also detected earlier on in some local authorities of the North West.



SGTF is a surveillance proxy for VOC-202012/01 and may include other variants.
Confirmed SGTF = Positive test with non-detectable S gene and <=30 CT values for N and ORF1ab genes respectively.
Confirmed S-gene = Positive test with <=30 CT values for S, N, and ORF1ab genes.
TaqPath labs = Alderley Park, Milton Keynes and Glasgow Lighthouse Labs, which use TaqPath COVID-19 RT-PCR.
Cases deduplicated to one positive test per person per week, prioritising SGTF tests.
Data source: SGSS.

Figure 3. Weekly number (bars) and proportion (line) of England Pillar 2 COVID-19 cases with SGTF among those tested in TaqPath laboratories and with S gene detection results (7 September 2020 to 24 January 2021).

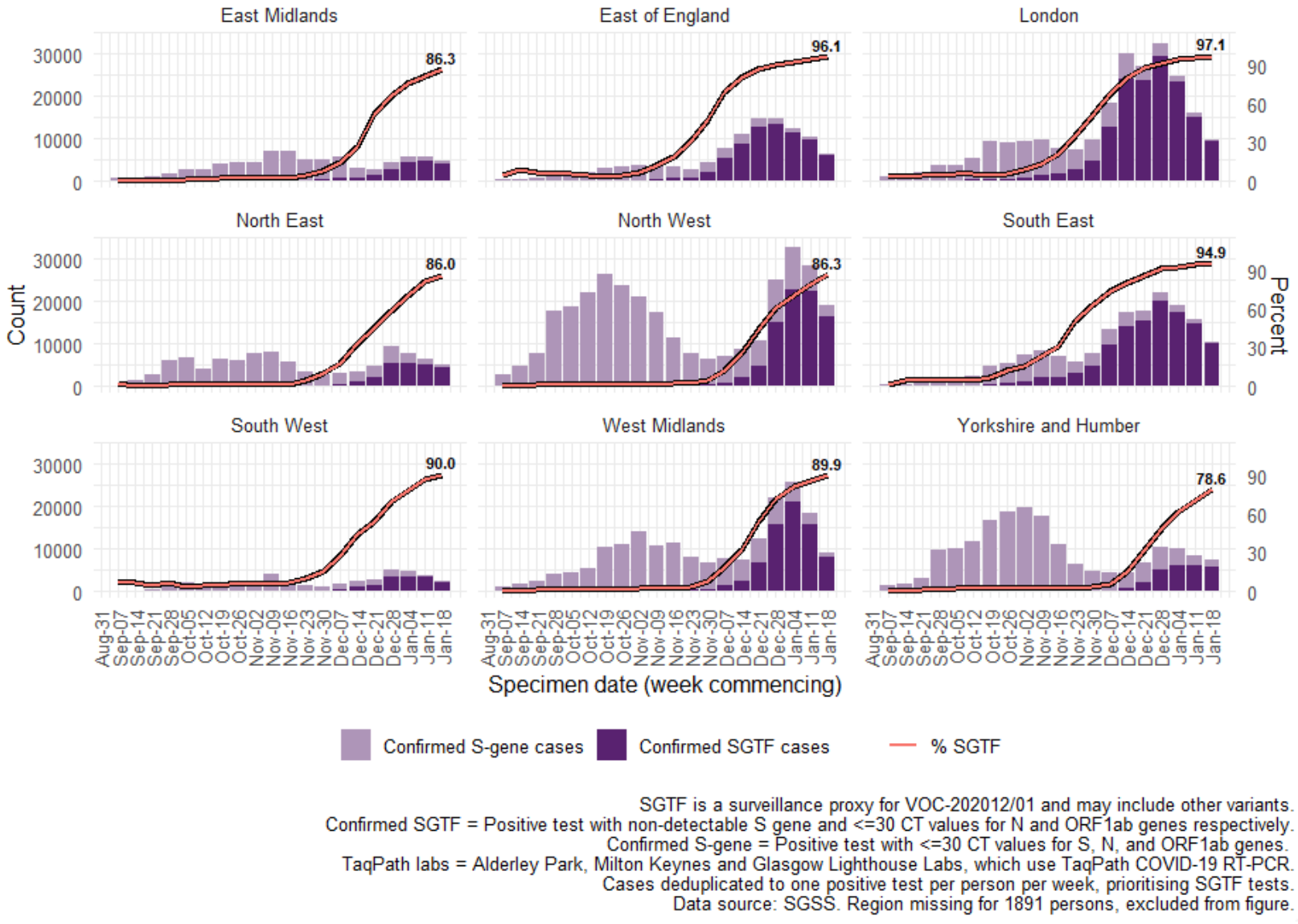
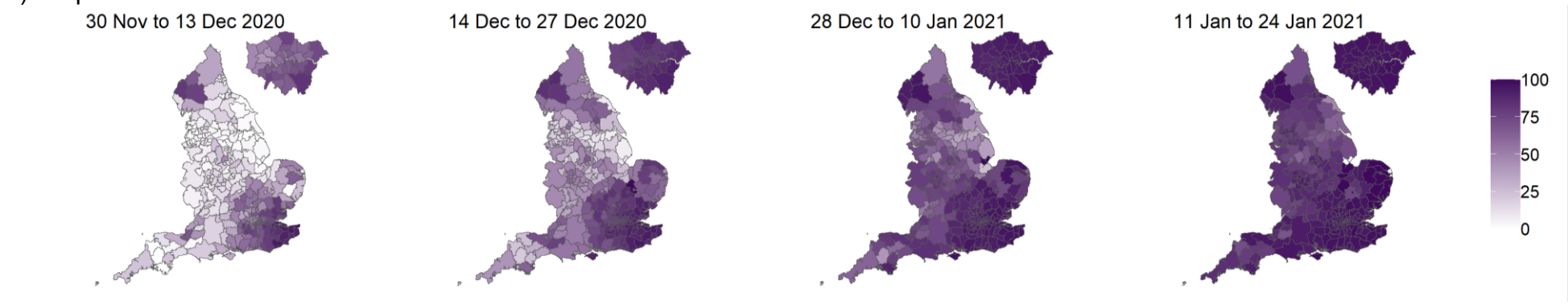


Figure 4. Weekly number (bars) and proportion (red lines) of Pillar 2 COVID-19 cases tested by TaqPath laboratories with SGTF among those with S gene detection results, by region of residence (7 September 2020 to 24 January 2021). Percent confirmed SGTF for most recent days annotated.

A) Proportion confirmed SGTF



B) TaqPath lab testing coverage

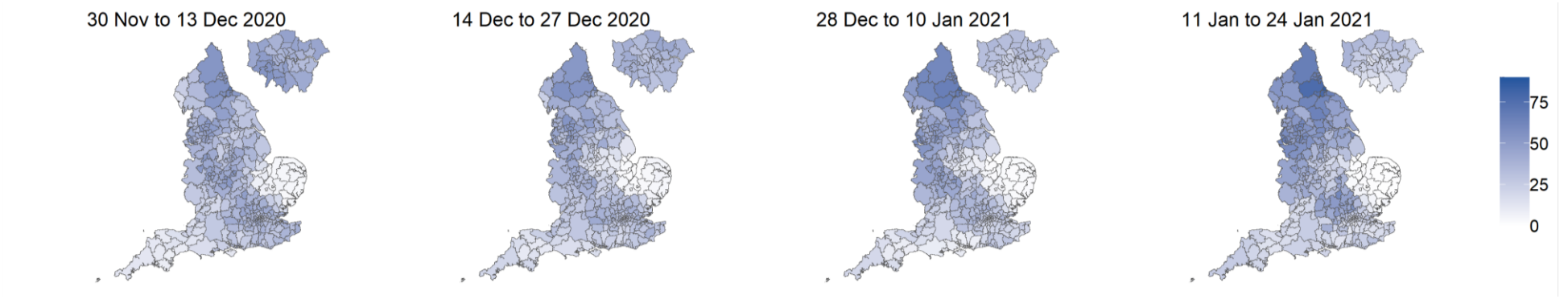


Figure 5. Local authority maps of A) proportion of Pillar 2 COVID-19 cases with SGTF among those tested in TaqPath laboratories and with S gene detection results, and B) Proportion of all specimens tested in TaqPath laboratories (30 November 2020 to 24 January 2021)

Cases by age and sex are displayed (Table 3). Proportions of cases with SGTF are highest in cases aged 10 or younger, at 74.1% of 44,627 cases between 1 December 2020 and 24 January 2021, and lowest in cases aged 75 or older, at 64.9% of 19,216 cases within the same period.

Table 3. Number and proportion of Pillar 2 COVID-19 cases tested by TaqPath laboratories among those with S gene detection results, by age group and sex (1 December 2020 to 14 January 2021). Unknown sex/age included in totals.

	Females			Males			Total		
Age group	Cases	SGTF cases	Percent SGTF	Cases	SGTF cases	Percent SGTF	Cases	SGTF cases	Percent SGTF
≤10 years	21716	16145	74.3	22911	16945	74.0	44627	33090	74.1
11-16 years	23872	16526	69.2	22686	15605	68.8	46558	32131	69.0
17-24 years	55307	40237	72.8	46199	34102	73.8	101507	74339	73.2
25-59 years	252278	182272	72.3	231789	170595	73.6	484071	352870	72.9
60-74 years	36215	25374	70.1	36811	26340	71.6	73026	51714	70.8
75+ years	11384	7381	64.8	7832	5096	65.1	19216	12477	64.9
Total	400796	287952	71.8	368261	268709	73.0	769062	556664	72.4

Data on coverage of TaqPath laboratories testing and numbers/proportions of cases with SGTF are shared daily with Local Authorities (Sunday-Friday) on the COVID-19 PHE Local Authorities Report Store (Sharepoint).

Analysis of secondary attack rates using routine contact tracing data

This data has been updated from the previous briefing to include cases reported up to the 10 January 2021 (analysed on 26 January 2021). Findings are similar to those previously reported (www.gov.uk/government/publications/investigation-of-novel-sars-cov-2-variant-variant-of-concern-20201201).

PHE have analysed secondary attack rates among contact tracing data (from NHS Test and Trace) for the variant of concern (VOC 202012/01) using both genomic sequence variant data and S gene target failure (SGTF) data for Pillar 2 cases with valid S gene detection results, as defined above.

Between 30 November 2020 and 10 January 2021, 1,364,301 cases were reported to NHS Test and Trace. 35,597 (2.6%) had genomic sequencing data included*; 18,160 (51%) of those cases had a result of confirmed VOC 202012/01. 572,356 (42%) had valid S gene detection results; 376,274 (65.7%) of those cases had SGTF.

2,722,845 contacts reported to NHS Test and Trace were identified between 30 November 2020 and 10 January 2021. 66,847 contacts were reported by cases with genomic sequencing data; 37,585 of those contacts were reported by cases with VOC 202012/01. In all, 46.5% (1,266,461) Pillar 2 contacts of cases who were tested for S gene; of which 68.4% (866,608) had SGTF.

308,038 (11.3%) of all contacts were infected (secondary attack rate)

- 12.9% among those whose index case with genomic data had confirmed VOC 202012/01. 12.9% among those whose index case had laboratory detections of SGTF.
- 9.7% among those whose index case had a genomic result of wild type. 9.9% among those whose index case had confirmed presence or absence of S gene and did not have SGTF.

Both when using genomic sequence data directly and SGTF as a proxy, the secondary attack rates estimated from contact tracing data were observed to be higher if the index case has the variant strain, from around 10% to 13% of named contacts. This increase was around 10%-55% across most age groups and regions where sufficient sequencing data is available. Using the SGTF proxy to give a more comprehensive overview the increase was consistently around 25%-40%.

Attack rate: contacts becoming cases
Table 4. Breakdown by contact characteristics using genomic sequencing data

Characteristic of contact		All contacts	Contacts of people with confirmed VOC 202012/01			Contacts of people with other variants/ lineages		
		Total contacts	All contacts	Contacts that became cases	%	All contacts	Contacts that became cases	%
	All	2,722,845	37,585	4,845	12.9	24,239	2,340	9.7
Region of residence	East Midlands	172,594	868	100	11.5	1,734	185	10.7
	East of England	406,849	6,801	876	12.9	2,358	243	10.3
	London	721,377	12,883	1,624	12.6	3,464	299	8.6
	North East	85,273	1,104	122	11.1	1,795	178	9.9
	North West	274,688	3,577	542	15.2	5,121	495	9.7
	South East	496,778	7,503	912	12.2	2,044	167	8.2
	South West	150,985	1,011	131	13.0	1,459	160	11.0
	West Midlands	259,729	2,806	392	14.0	2,891	279	9.7
	Yorkshire and Humber	146,304	949	130	13.7	3,301	329	10.0
Level of contact*	Direct	2,513,595	34,674	4,636	13.4	21,777	2,215	10.2
	Close	200,131	2,712	202	7.4	1,964	114	5.8
Age group	0 – 9	381,835	5,306	427	8.0	3,242	172	5.3
	10 – 19	455,374	6,463	668	10.3	4,064	349	8.6
	20 – 29	357,008	4,792	711	14.8	3,016	367	12.2
	30 – 39	317,666	4,393	754	17.2	2,820	309	11.0
	40 – 49	327,015	4,575	725	15.8	2,897	355	12.3
	50 – 59	304,303	4,149	740	17.8	2,691	358	13.3
	60 – 69	142,712	1,892	349	18.4	1,377	180	13.1
	70 – 79	55,456	708	157	22.2	550	111	20.2
	80+	23,102	273	55	20.1	250	36	14.4
	Not known	358,374	5,034	259	5.1	3,332	103	3.1

Table 5. Breakdown by contact characteristics by SGTF

Characteristic of contact		All contacts	Contacts of people with S gene target failure			Contacts of people other variants/ lineages (no S gene target failure)		
		Total contacts	All contacts	Contacts that became cases	%	All contacts	Contacts that became cases	%
	All	2,722,845	866,608	111,521	12.9	399,853	39,690	9.9
Region of residence	East Midlands	172,594	25,988	3,373	13.0	32,548	3,128	9.6
	East of England	406,849	117,176	15,113	12.9	23,471	2,376	10.1
	London	721,377	237,141	28,311	11.9	46,290	4,270	9.2
	North East	85,273	33,739	4,667	13.8	31,662	3,241	10.2
	North West	274,688	103,121	14,320	13.9	89,440	9,420	10.5
	South East	496,778	179,693	23,124	12.9	33,834	3,366	9.9
	South West	150,985	23,366	3,179	13.6	15,617	1,571	10.1
	West Midlands	259,729	110,585	14,662	13.3	72,559	7,031	9.7
	Yorkshire and Humber	146,304	33,208	4,477	13.5	53,341	5,198	9.7
Level of contact*	Direct	2,513,595	801,510	106,350	13.3	364,585	37,591	10.3
	Close	200,131	62,733	5,133	8.2	33,288	2,073	6.2
Age group	0 – 9	381,835	123,487	9,366	7.6	56,639	3,043	5.4
	10 – 19	455,374	147,357	15,843	10.8	68,885	5,941	8.6
	20 – 29	357,008	114,669	17,477	15.2	49,838	6,119	12.3
	30 – 39	317,666	100,478	16,396	16.3	46,773	5,910	12.6
	40 – 49	327,015	105,153	17,039	16.2	48,889	5,964	12.2
	50 – 59	304,303	97,345	16,946	17.4	45,493	5,990	13.2
	60 – 69	142,712	43,780	8,019	18.3	21,177	2,955	14.0
	70 – 79	55,456	15,933	3,142	19.7	8,037	1,212	15.1
	80+	23,102	6,259	1,173	18.7	3,317	542	16.3
	Not known	358,374	112,147	6,120	5.5	50,805	2,014	4.0

*Direct: face to face contact (e.g. a conversation within 1 metre); skin to skin contact (including sexual contact); coughed on, sneezed on or spat on. Close: within 1 metre for 1 min. or more (not necessarily face to face); within 1-2 metres for 15 mins. or more (could be total 15 mins. over 24 hours); travelling in a small vehicle; travelling in a large vehicle or plane (1 metre for 1 min. and 1-2 metres for 15 mins.).
Estimated attack rates for cases with VOC 202012/01 are 10%-55% higher than estimated attack rates with sequencing and other variants/ lineages for most regions and age groups, excepting the East Midlands (which has relatively small numbers of people with genomic results).

Estimated attack rates for cases with SGTF are 25% - 40% higher than estimated attack rates for cases with S gene detection results and no SGTF for most regions and age groups, excepting groups with few records such as the 80+ age group.

Detection of E484K mutation in B.1.1.7 VOC 202012/01

The COG-UK dataset (total sequences 214,159) was analysed on 26/01/2021. The spike protein mutation E484K (found in VOC 202012/02 B1.351 and VOC 202101/02 P1) has been detected in 11 B1.1.7 sequences. Preliminary information suggests more than one acquisition event.

Office of National Statistics data

Office National Statistics Coronavirus (COVID-19) Infection Survey data is regularly updated and available here including estimates of COVID-19 cases for England, regions of England and by cases compatible with the new variant (VOC 202012/01).
It includes new symptom comparison data:
www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19infectionsinthecommunityinengland/characteristicsofpeopletestingpositiveforcovid19inengland27january2021#symptoms-profile-by-cases-compatible-with-the-new-uk-variant-and-other-positive-cases

Data sources

Data used in this investigation is derived from the COG-UK dataset, the PHE Second Generation Surveillance System, NHS Test and Trace, the secondary uses service (SUS) dataset and Emergency Care Data Set (ECDS).

GISAID reference genome

Sequences from this VOC can be identified by searching for the B1.1.7 lineage on GISAID (gisaid.org). The canonical VOC genome is deposited with accession EPI_ISL_601443.

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Variant Technical Group

This group includes representation with the following organisaions:
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Imperial College London, London School of Hygiene & Tropical Medicine, University of Birmingham, University of Cambridge, University of Edinburgh, University of Liverpool.
Wellcome Sanger Institute

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The COG-UK-HOCI study, University College London: Judith Breuer
University Hospitals Birmingham NHS Foundation Trust

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