

Protecting and improving the nation's health

Investigation of novel SARS-CoV-2 variant

Variant of Concern 202012/01

Technical briefing 3

This briefing provides an update on the briefing of 28/12/2020

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 18/12/2020.

Current epidemiological findings

The specimen date for the first COVID-19 case with the VOC 202012/01 variant in England was 20 September 2020. As of 4 January 2021, a total of 6,008 cases with this variant have been identified in England, via routine genomic surveillance.

The following section describes demographic breakdowns of cases with the variant identified. As routine genomic surveillance may be non-random and not representative of all COVID-19 cases, similar breakdowns for the 68,246 cases with specimen dates between 20 September 2020 and 4 January 2021 that were routinely sequenced are provided for comparison¹.

Age group	VOC 202012/01		All sequenced	
0 0 .	n	%	n .	%
0-9	365	6.1	2,752	4.0
10-19	846	14.1	9,062	17.3
20-29	1,033	17.2	13,513	19.8
30-39	1,151	19.2	11,915	17.5
40-49	1,111	18.5	10,263	15.0
50-59	821	13.7	9,881	14.5
60-69	369	6.1	5,226	7.7
70-79	176	2.9	2,797	4.1
80+	136	2.3	2,821	4.1
Unknown	0	0.0	16	0.0
Total	6,008		68,246	

Table 1. Age breakdown of VOC 202012/01 cases in England compared to sequenced cases, 20 September 2020 to 4 January 2021.

Sex	VOC 202012/01	All sequenced	All sequenced			
	n	%	n ·	%		
Female	3,138	52.2	35,766	52.4		
Male	2,868	47.7	32,302	47.3		
Unknown	2	0.0	178	0.3		
Total	6,008		68,246			

Table 2. Sex breakdown of VOC 202012/01 cases in England compared to sequenced cases, 20 September 2020 to 4 January 2021.

¹ Please note that the 6,008 VOC-202012/01 cases are included in the 68,246 'all sequenced' samples

PHE Centre	VOC 202012/01	All sequenced					
	n	%	n	%			
East Midlands	94	1.6	4,292	6.3			
East of England	1,123	18.7	6,906	10.1			
London	2,200	36.6	12,687	18.6			
North East	104	1.7	5,024	7.4			
North West	211	3.5	13,858	20.3			
South East	1,929	32.1	7,193	10.5			
South West	118	2.0	2,263	3.3			
West Midlands	150	2.5	6,065	8.9			
Yorkshire and	61	1.0	9,548	14.0			
Humber							
Unknown	18	0.3	410	0.6			
Total	6,008		68,246				

Table 3. Regional breakdown of VOC 202012/01 cases in England compared to sequenced cases, 20 September 2020 to 4 January 2021.

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 two weeks, therefore a proxy S gene target failure (SGTF) is used to indicate carriage of the VOC.

We previously observed that one of the S gene mutations in the VOC, which deletes amino acids 69 and 70 (Δ 69-70), causes a reproducible S gene target failure (SGTF) in the Thermopath TaqPath assay used in three UK lighthouse laboratories (see <u>Technical Briefing 1</u>).

This coincidental occurrence provides a good proxy for monitoring trends in VOC 202012/01. SGTF correlates almost perfectly with presence of $\Delta 69$ -70. Considering 14,950 tested samples where we know both the sequence and the SGTF status, 99.5% of $\Delta 69$ -70 sequences (2190 of 2202) are SGTF, compared to 0.05% of sequences without the deletion (7 of 13278).

Because $\Delta 69$ -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 4 shows, for all pillar 2 sequences, the weekly proportion of $\Delta 69$ -70 sequences that were confirmed to be VOC 202012/01. Table 5 shows the proportion of $\Delta 69$ -70 that is the VOC 202012/01 in England during December, broken down by region. It is, as expected, highest in the areas where the VOC was first observed, but it has been a substantial majority in all areas of England during the month of December. 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).

Week beginning	Per cent VOC of all Δ69-70	Number of pillar 2 Δ69-70 sequences
2020-10-12	3%	116
2020-10-19	15%	219
2020-10-26	29%	156
2020-11-02	64%	398
2020-11-09	79%	632
2020-11-16	88%	605
2020-11-23	93%	372
2020-11-30	96%	379
2020-12-07	98%	2022
2020-12-14	99%	2168
2020-12-21	98%	150

Table 4. Percent of all Pillar 2 Δ 69-70 sequences that are VOC 202012/01, from 12 October 2020 to 27 December 2020.

Region	Percent VOC 202012/01 of all Δ69-70	Number of pillar 2 Δ69-70 December 1st-27th
East Midlands	88%	73
East of England	99%	786
London	99%	1848
North East	93%	111
North West	96%	217
South East	99%	1267
South West	100%	107
West Midlands	97%	172
Yorkshire and the Humber	90%	76

Table 5. Per cent of all Pillar 2 Δ 69-70 sequences from December 1-21 that are VOC 202012/01, by region of England, from 1 December 2020 to 27 December 2020.

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Epidemiology of S gene target failure

The proportion of England specimens tested in the lighthouse laboratories using the assay which produces the S gene target failure is substantial and has been relatively constant over time (Figure 1). This however varies by geography, with lower coverage between September 1st 2020 and January 4th 2021 in local authorities in the East and South West of England.

The proportion of cases tested by this assay which are SGTF has continued to rise in December (Figure 2 and 3) in all regions (Figure 4). In the most recent seven-day period (December 29 2020 to January 4 2021), 71.5% of 133,925 Pillar 2 cases detected in TaqPath laboratories had isolates with SGTF, compared to 27.7% of 57,919 in the seven-day period starting December 01 2021.

The spatial distribution of SGTF cases shows a relatively higher burden in the South of England but with clear evidence of spread since the last update (Figure 2).

Cases by age and sex are displayed (Figure 5 and 6). Cases that had isolates with SGTF display a similar age-sex profile to other Pillar 2 cases tested by the TaqPath laboratories. Proportions of cases with SGTF were also similar across those aged under 25, between 25 and 59, and over 60: 71.0%, 72.2%, and 68.9% respectively among those diagnosed by TaqPath laboratories in the most recent seven-day period.

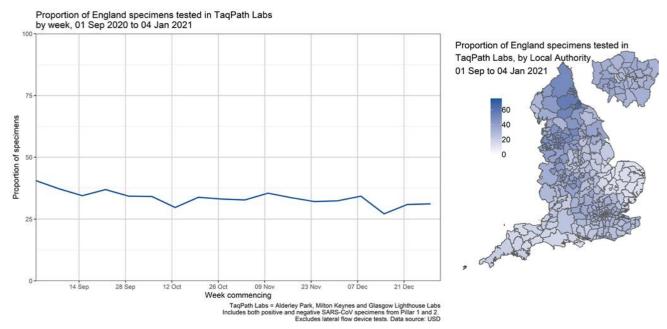


Figure 1. Proportion of England Specimens tested in TaqPath labs by week (2020-09-01 to 2021-01-04).

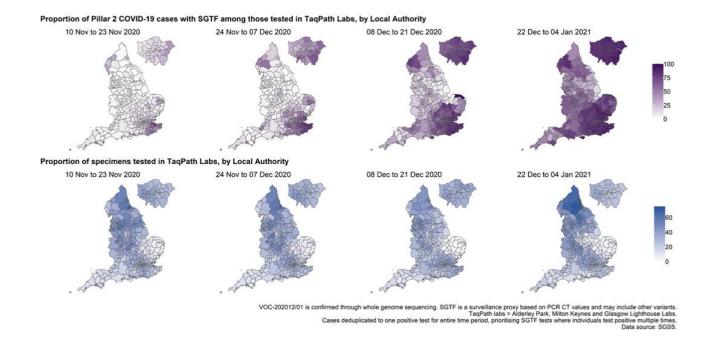
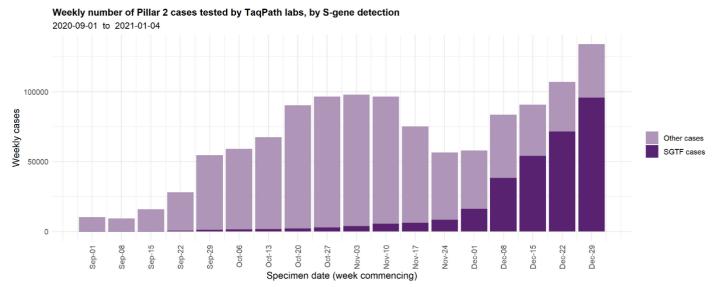


Figure 2. Proportion of Pillar 2 COVID-19 cases with SGTF among those tested in TaqPath Labs, by Local Authority (2020-11-10 to 2021-01-04).



VOC-202012/01 is confirmed through whole genome sequencing. SGTF is a surveillance proxy based on PCR CT values and may include other variants, particularly before December 2020.

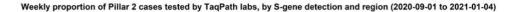
SGTF = Positive test with non-detectable S gene and <=30 CT values for N and ORF1ab genes respectively

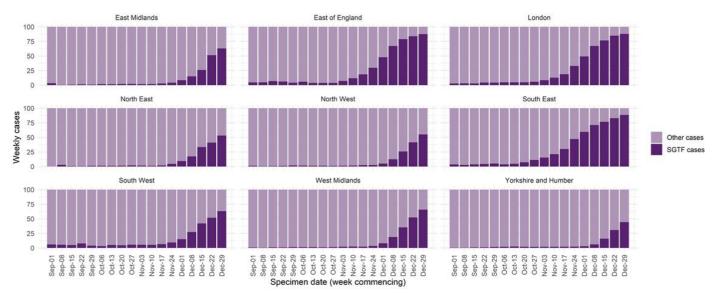
TaqPath labs = Alderley Park, Milton Keynes and Glasgow Lighthouse Labs.

Cases deduplicated to one positive test per person per week, prioritising SGTF tests. Complete 7-day periods shown with moving start days.

Data source: SGSS

Figure 3. Weekly number of Pillar 2 cases tested by TaqPath labs, by S-gene detection (2020-09-01 to 2021-01-04).





VOC-202012/01 is confirmed through whole genome sequencing. SGTF is a surveillance proxy based on PCR CT values and may include other variants, especially before Dec 2020.

SGTF = Positive test with non-detectable S gene and <=30 CT values for N and ORF1ab genes respectively

TapPath labs = Alderley Park, Milton Keynes and Glasgow Lighthouse Labs.

Cases deduplicated to one positive test per person per week, prioritising SGTF tests. Complete 7-day periods shown with moving start days.

Data source: SGSS. Region missing in 1626 persons, excluded from figure.

Figure 4. Weekly proportion of Pillar 2 cases tested by TaqPath labs, by S-gene detection and region (2020-09-01 to 2021-01-04).

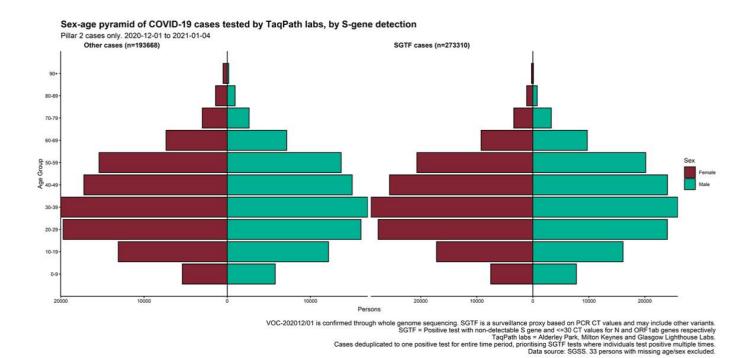
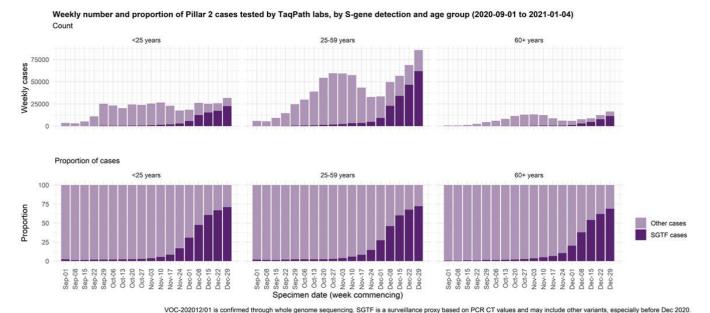


Figure 5. Sex-age pyramid of COVID-19 cases tested by TaqPath labs, S-gene detection, Pillar 2 cases only (2020-12-01 to 2021-01-04).



VOC-202012/01 is confirmed through whole genome sequencing. SGTF is a surveillance proxy based on PCR CT values and may include other variants, especially before Dec 2020.

SGTF = Positive test with non-detectable S gene and <=30 CT values for N and ORF1ab genes respectively

TaqPath labs = Alderley Park, Milton Keynes and Glasgow Lighthouse Labs.

Cases deduplicated to one positive test per person per week, prioritising SGTF tests. Complete 7-day periods shown with moving start days.

Data source: SGSS. Age missing in 49 persons, excluded from figure.

Figure 6. Weekly number and proportion of Pillar 2 cases tested by TaqPath labs, by S-gene detection and age group (2020-09-01 to 2021-01-04).

Analysis of secondary attack rates using routine contact tracing data

As of 2021-01-05, 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 tested by TaqPath labs.

Between 2020-11-30 and 2020-12-20, 386,805 cases were reported to NHS Test and Trace. 9,321 (2.4%) of these cases had genomic sequencing data included; 3,801 (40.8%) of those cases were VOC 202012/01. 212,943 (55.1%) cases had data from TaqPath; 90,401 (42.5%) of those cases were isolates with SGTF.

956,519 contacts reported to NHS Test and Trace were exposed between 2020-11-30 and 2020-12-20. 20,497 contacts were reported by cases with genomic sequencing data; 9,228 of those contacts were reported by cases with VOC 202012/01. 525,001 contacts were reported by pillar 2 cases tested by TaqPath labs; 262,769 of those contacts were reported by cases with SGTF.

121,072 (12.7%) of all contacts were known to become cases (secondary attack rate) ²

- 14.7% among those whose index case had VOC 202012/01. 14.9% among those whose index case had SGTF.
- 11% among those whose index case had a genomic result of wild type. 11% among those whose index case was tested by a TaqPath lab 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 are observed to be higher if the index case has the variant strain, from around 11% to 15% of named contacts. This increase is around 10%-70% across most age groups and regions where sufficient sequencing data is available. Using the SGTF proxy to give a more comprehensive overview the increase is consistently around 30%-50%.

Attack rate: contacts becoming cases

Characteristic of contact	All contacts	Contacts of people with VOC 202012/01		WIID TVDA (DOT VI)C.			Contacts of people without sequencing	
	Total contacts	All contacts	Contacts that became cases	%	All contacts	Contacts that became cases	%	%
All	956,519	9,228	1,361	14.7	11,269	1,244	11.0	12.7
East Midlands	60,153	150	15	10.0	1,008	117	11.6	11.2

² Data source and methods

Contacts with exposure dates within 2020-11-30 – 2020-12-20 were analysed for attack rate analyses.

Genomic data from 2020-10-01 to 2021-01-04 and SGTF data from 2020-10-01 to 2021-01-05 were linked on SGSS specimen request ID to NHS Test and Trace (CTAS) individuals. Records with multiple inconsistent variants were not successfully linked.

CTAS data contains information collected from individuals with a positive test for SARS-CoV-2 referred to NHS Test and Trace ("cases") and individuals named by them as having been in contact with them between two days prior to symptom onset or test date and the date of tracing ("contacts"). Persons can arise multiple times as cases and/or contacts in the data and are matched with themselves via combination of name, NHS number, date of birth, address and contact information. Transmission is defined to have occurred where a confirmed case (B) was previously reported as a contact by a case (A), where the date for case (A) interacting with case (B) is between 1 and 14 days inclusive prior to the onset of symptoms (or test date) for case (B). Where there was more than one contact event within the transmission window leading to a case, one event is counted per case who was previously a contact, with priority given to household contacts and to later interactions.

Sampling for variant breakdown in genomic and SGTF datasets is not random.

	East of England	154,144	1,869	263	14.1	1,199	153	12.8	13.5
	London	281,461	3,507	505	14.4	1,844	197	10.7	13.1
	North East	28,450	235	29	12.3	738	79	10.7	11.8
Region of	North West	71,002	400	65	16.2	2,182	223	10.2	11.7
residence	South East	186,311	2,419	377	15.6	1,155	107	9.3	13.5
	South West	41,465	230	43	18.7	380	50	13.2	11.8
	West Midlands	78,112	299	47	15.7	1,388	155	11.2	11.6
	Yorkshire and Humber	53,192	109	16	14.7	1,339	158	11.8	10.6
Level of	Direct	875,237	8,399	1,299	15.5	10,088	1,193	11.8	13.2
contact*	Close	79,867	829	62	7.5	863	45	5.2	6.9
	0 – 9	135,998	1,345	121	9.0	1,536	93	6.1	7.2
	10 – 19	172,506	1,659	196	11.8	1,943	186	9.6	10.4
	20 – 29	111,391	1,020	167	16.4	1,352	192	14.2	15.1
	30 - 39	111,712	1,145	229	20.0	1,361	175	12.9	16.7
Age	40 – 49	126,005	1,241	263	21.2	1,448	199	13.7	16.8
group	50 – 59	101,501	953	190	19.9	1,236	181	14.6	17.1
	60 – 69	44,985	366	74	20.2	610	92	15.1	17.7
	70 – 79	17,817	142	34	23.9	198	38	19.2	18.1
	80+	7,429	53	11	20.8	93	14	15.1	17.7
	Not known	127,175	1,304	76	5.8	1,492	74	5.0	5.3

Table 6. Breakdown by contact characteristics using genomic sequencing data.

Close: within 1 metre for 1 minute 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%-70% higher than estimated attack rates with sequencing and wild type virus for most regions and age groups, excepting the East Midlands (which has relatively small numbers of people with genomic results).

Characteristic of contact Contacts of Con				WIID TVDG (DO S-00D			Contacts of people without SGTF data		
_		Total contacts	All contacts	Contacts that became cases	%	All contacts	Contacts that became cases	%	%
	All	956,519	262,769	39,277	15.0	262,232	28,770	11.0	12.3
	East Midlands	60,153	5,421	782	14.4	26,750	2,899	10.8	11.0
	East of England	154,144	45,396	6,953	15.3	18,791	2,141	11.4	13.0
	London	281,461	101,056	14,638	14.5	41,365	4,392	10.6	12.8
	North East	28,450	5,860	897	15.3	17,454	1,948	11.2	10.0
Region of	North West	71,002	9,575	1,531	16.0	45,852	5,182	11.3	10.3
residence	South East	186,311	73,133	11,043	15.1	27,849	3,052	11.0	13.0
	South West	41,465	4,692	716	15.3	9,084	1,038	11.4	11.5
	West Midlands	78,112	13,588	2,099	15.5	43,848	4,751	10.8	10.6
	Yorkshire and Humber	53,192	3,448	533	15.5	30,616	3,310	10.8	9.5
Level of	Direct	875,237	239,922	37,362	15.6	240,491	27,495	11.4	12.8
contact*	Close	79,867	22,710	1,914	8.4	21,038	1,266	6.0	6.5

^{*}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

	0 – 9	135,998	37,512	3,343	8.9	38,537	2,401	6.2	6.8
	10 – 19	172,506	48,748	5,921	12.2	48,368	4,542	9.4	10.0
20 - 29 30 - 39 Age 40 - 49 group 50 - 59 60 - 69 70 - 79 80+ Not known	20 – 29	111,391	29,896	5,288	17.7	29,817	4,008	13.4	14.6
	30 - 39	111,712	30,693	6,070	19.8	30,873	4,409	14.3	16.2
	40 – 49	126,005	36,238	7,229	20.0	34,353	4,875	14.2	16.3
	50 – 59	101,501	27,749	5,640	20.3	27,609	4,042	14.6	16.7
	60 – 69	44,985	11,261	2,340	20.8	12,223	1,945	15.9	17.1
	70 – 79	17,817	4,116	891	21.7	4,617	748	16.2	17.7
	*************************************	7,429	1,535	299	19.5	1,941	334	17.2	17.2
	Not known	127,175	35,021	2,256	6.4	33,894	1,466	4.3	5.2

Table 7. Breakdown by contact characteristics by SGTF using TaqPath data:

Close: within 1 metre for 1 minute 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 SGTF are 30% - 50% higher than estimated attack rates for cases with TaqPath data without SGTF for most regions and age groups, excepting groups with few records such as the 80+ age group.

^{*}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

Virology

The workflow in process by PHE and partner laboratories is shown in Figure 7. Activities in grey are completed and in blue are underway.

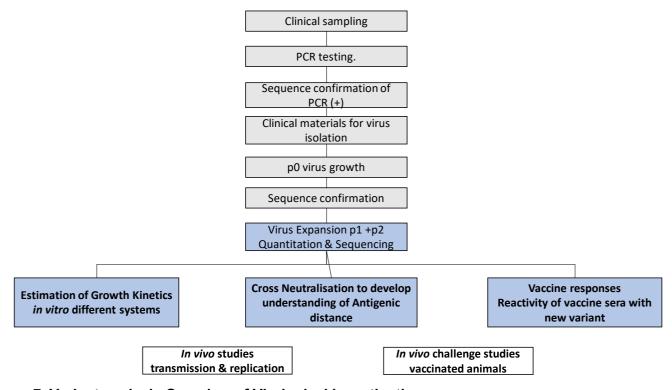


Figure 7. Variant analysis Overview of Virological Investigations

Summary

The proportion of VOC 202012/01 has increased in all areas.

Secondary attack rates estimated from contact tracing data are observed to be higher where the index case has the variant strain, from around 11% to 15% of named contacts.

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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