

Technical Brief: Viral Variant VOC-202012/01 (23 December 2020)

Key messages

- A new variant of SAR-COV-2, the coronavirus that causes Covid-19, has been identified and is circulating in the UK, with small numbers also being found overseas.
- The variant was called a VUI (Variant Under Investigation) when it was first identified, but it is now called a VOC (Variant of Concern). Its name refers to its status (VOC), year (2020), month (12) and number of variants investigated in that month (01).
- The new variant can only be confirmed by sequencing the full RNA of a sample, which is only done for a proportion of tests. 3,000 sequences of the new variant have now been completed, of which 49 were in Wales. However, several labs in the UK use a test which can infer when a positive test is a new variant, due to a blank area in the test results associated with the mutation.
- Transmission is increased in the new variant (high confidence)
- There is currently no evidence that the variant is different in severity, or differs by characteristics of sex and ethnicity. The SAGE subgroup NERVTAG stated that there are currently insufficient data to draw any conclusion on the age distribution of cases and the European Centre for Disease Control threat assessment from 20 December says the cases with the VOC-202012/01 variant are predominantly currently identified in people younger than 60 years.
- It is not clear if immunity to SARS-CoV-2 is affected by the variant. Early analysis in England and Wales has not found an increased frequency of repeat infections for this variant cases when compared to reinfections reported for other contemporaneously circulating variants. Immunity is raised to a number of different viral proteins/parts of viral proteins, so a small number of changes is unlikely to have a large impact on immunity.
- There is an ongoing investigation into the role of children in transmitting this variant.
- There is no evidence that shows that the vaccine will be less effective in people who are infected with this variant (medium confidence).

- The advice for avoiding infection remains the same. Don't mix. Get a test if you have symptoms and quarantine if you test positive.

About the variant

- A variant of SARS-CoV-2, VOC-202012/01, has been identified and is circulating in the UK – the variant was first identified on 20 September 2020, with a cluster recognised in December. Since then it has also been found in Denmark and Australia (small numbers). Recently the variant has been shown to be rapidly increasing in numbers.
- A recent technical briefing by Public Health England (PHE) provides an excellent summary of the new variant¹. An assessment of the new variant has also been published by the European Centre for Disease Control². A summary of the genomic characteristics of the VOC has been published by the COVID-19 Genomics UK Consortium (COG-UK)³.
- VOC-202012/01 means 'Variant of Concern' in December 2020 and is a common way of describing circulating viruses that have changed or adapted.
- The VOC-202012/01 variant includes 23 changes in the virus:
 - eight mutations (changes) in the outer "spike" protein;
 - nine changes that alter the amino acid sequence of proteins elsewhere in the virus genome, and
 - six changes that do not alter the amino acid sequence of proteins elsewhere in the virus genome.
- To date over 3,000 cases, confirmed by whole genome sequencing, have been identified in the UK, mainly in South East of England but also found in Wales (49 cases) and Scotland (9 cases)⁴. This is an underestimate as only a fraction of cases are fully sequenced, and this sample is not representative.

Public Health Wales analysis

- Of the 66,000 positive Pillar 1 and Pillar 2 COVID-19 samples collected in Wales since the 1 November, approximately 7% have been sequenced – of

¹https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/947048/Technical_Briefing_VOC_SH_NJL2_SH2.pdf

² <https://www.ecdc.europa.eu/sites/default/files/documents/SARS-CoV-2-variant-multiple-spike-protein-mutations-United-Kingdom.pdf>

³ <https://virological.org/t/preliminary-genomic-characterisation-of-an-emergent-sars-cov-2-lineage-in-the-uk-defined-by-a-novel-set-of-spike-mutations/563>

⁴ <https://beta.microreact.org/project/b1FRyhxAqTatsvNysxDU35-cog-uk-2020-12-19-sars-cov-2-in-the-uk>

which 49 cases were confirmed as the new variant by sequencing (all sequenced from Pillar 1). These variants were detected in several local authorities across Wales.

- Some laboratories testing for presence of virus in people using Polymerase Chain Reaction (PCR) can also detect the variant through failure of one part of the test – this is due to a phenomenon called S-gene drop-out. S-gene dropout is due to one of the mutations in the VOC, a two codon deletion at positions 69 and 70 of the Spike protein. This mutation, not widely present in other SARS-CoV-2 variants circulating in the UK, causes diagnostic primers targeting this region of the spike protein to fail. To identify SARS CoV-2 infection a PCR test targets several parts of the viral genome, and some diagnostic tests include a target in the S-gene as one of several used in the test. Failure of the S-gene in a test does not mean the test will not identify people who are COVID-19 positive as other parts of the virus genome are still detected. Based upon the low frequency of other mutations in this area of the spike protein circulating in the UK, the S-gene drop-out provides a reasonable proxy method for detecting the new viral variant. Some but not all Lighthouse Laboratories (LHLs) use the test that can detect the variant. Other laboratories, including Public Health Wales (PHW), cannot detect the variant on the majority of their platforms.
- In England, it has been shown that “S gene target failure” (or SGTF) correlate with the increase of confirmed, sequenced variants.
- Samples from Wales are sent to different LHLs for analysis with some of these samples going to laboratories that can detect the S-gene drop-out. Analysis of 8,788 samples sent to LHLs that can detect the S-gene from 26 November to 21 December found 1,259 cases of the variant (14.3%), of which a significant number will be a the new variant⁵.
- This 14.3% is also likely to be an underestimate and non-representative, as cases in the highest incidence areas in South Wales are the least likely to have this type of distinguishing test. As around 50% or more of English cases diagnosed in LHLs are SGTF variants, it is likely that the prevalence in Wales is higher than this estimate.
- PHW undertook preliminary analyses to estimate impact on re-infections. The data on S-gene drop-out/SGTFs from Wales residents tested in relevant LHLs was linked to DataStore (the data repository within PHW) data on positives authorised within the same date range (26/11/20 to 21/12/20 inclusive). Linkage of these two datasets did not find any evidence of a higher frequency of repeat infections in variant cases (0 of 5 repeats in the linked dataset were variant type).

⁵ As of 30 November 96% of samples in Milton Keynes LHL with S-gene drop-out have been shown to be the new variant

- This analysis does not support repeat infections being more likely in VOC cases, however it would be helpful to repeat this analysis with larger datasets.
- As the variation includes changes to the antigenic S-gene, which is also the target for current licensed vaccines, concerns have been raised that immunity to past infection or through vaccination might be lower for this variant. Based upon what we know about the way the immune system behaves this is not considered to be likely, as the immune response will recognise multiple viral protein locations. However, looking for evidence of an effect in a fast-spreading variant through experimental work is prudent in the context of ensuring that vaccines are not affected by any viral protein changes. The changes may also affect the performance of certain tests for SARS-CoV-2 that make use of antibodies that target specific parts of viral proteins. This may result in false negatives for some tests or parts of test sets. Further work is ongoing in PHE in order to provide further evidence of changes to the antigenicity of the new variant.
- Variations in seasonal coronaviruses do and have occurred in the usual evolution of these viruses, but there is concern for impact of this particular variant on prevalence (how common compared to previous strains), transmissibility (speed of spread), the ability to detect the virus through testing, and immunity through past infection or vaccination.
- Working with PHE and other partners, PHW is a member of the national Incident Management Team (IMT) for the variant SARS-CoV-2 incident (PHE.NICC34) which is currently meeting daily, with wider meetings twice a week. PHW has also convened an IMT for this variant. Wales is a core member of the COG-UK, through which this variant has been characterised, with direct involvement in current analyses.
- As can be seen below, the proportion of likely VOC cases in those cases tested has increased over time, now accounting for more than one in three cases tested. As above, **this is likely to be an under-estimate as areas with the highest case numbers have had the lowest percentage tested with the distinguishing test.**

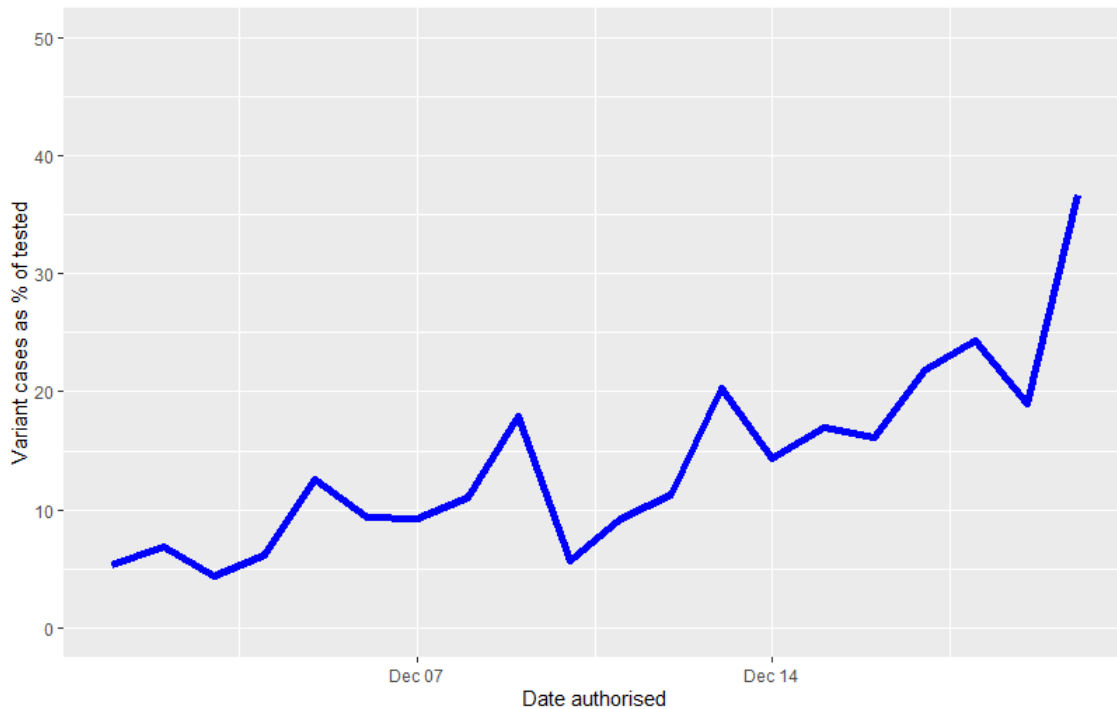


Figure 1. Change in S-gene drop-out presence from LHL tests (PHW data).

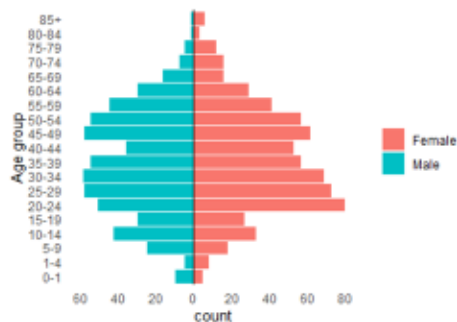
- The age distribution of cases with and without the VOC (using the proxy measure) are similar. This should be interpreted with caution as different areas have different age compositions.

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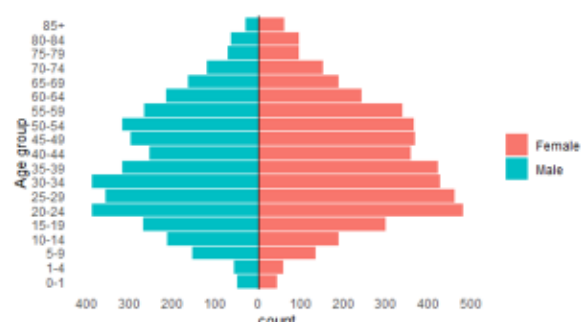
Wales S Gene tested and S gene negative cases – as at 21/12/2020

- There are **8788** cases tested for the S gene SARS-CoV-2 (COVID-19) cases **resident in Wales** between **01/12/2020 - 21/12/2020**
- **1259** cases were identified as being S gene negative (**14.3%**)

S Gene **negative** cases between 01-Dec and 21 Dec 2020



Cases **tested** for S gene between 01-Dec and 21 Dec 2020

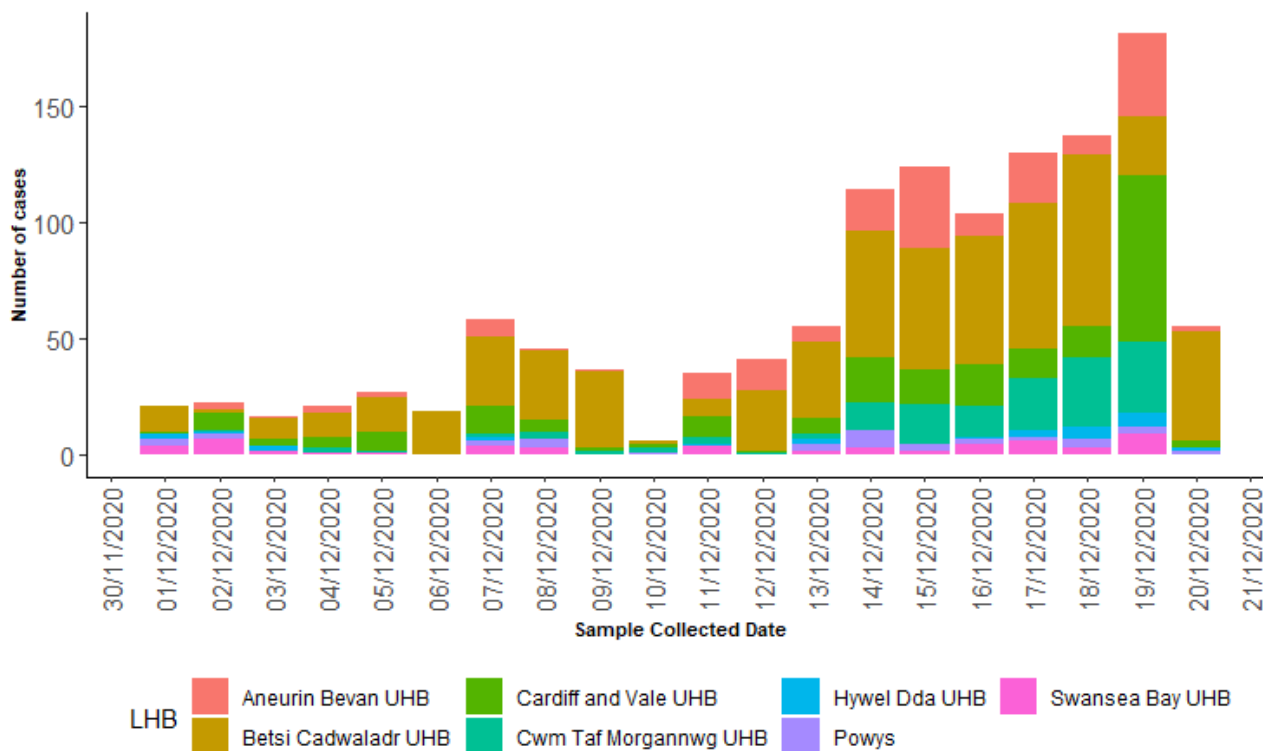


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Trends in S gene negative cases (likely VOC cases) are presented by health board below, to 21 December. **Note that BCUHB and Powys are significantly over-represented in testing due to patterns in allocation of**

samples to Lighthouse Laboratories; CTUHB, HDUHB and SBUHB are under-represented.



ONS COVID-19 Infection Survey

- The Coronavirus (COVID-19) Infection Survey (CIS) is run across the whole of the UK and aims to estimate:
 - How many people have the infection over a given time (positivity).
 - How many new cases occur over a given period (incidence).
 - How many people have antibodies to COVID-19.
- The survey helps track the extent of infection and transmission of COVID-19 among people in private residences, referred to as the community population.
- **The following analysis from the CIS must be treated with caution, as:**
 - Low numbers of positive cases detected in the survey mean the estimates can be volatile.
 - For ease of reference we have labelled the variants as Not S gene dropout and S gene dropout. 'S gene dropout' are the positive case that contain the OR+N gene, which doesn't necessarily mean it's the new variant, but recent evidence suggests it is a substantial driver rises in this category.
 - This data are not as timely as PHW case estimates.
 - Wider analysis by viral experts has indicated that we should only take account of data from the 18 November. The presence of the 'new' variant before this is likely to be due to other variants.

- For the purposes of the graph below, read the yellow line as S-gene drop-out, a proxy for the new variant of COVID-19. It can be seen the variant (S-gene drop-out) has increased in Wales throughout and after the firebreak period. A period when other variants decreased.

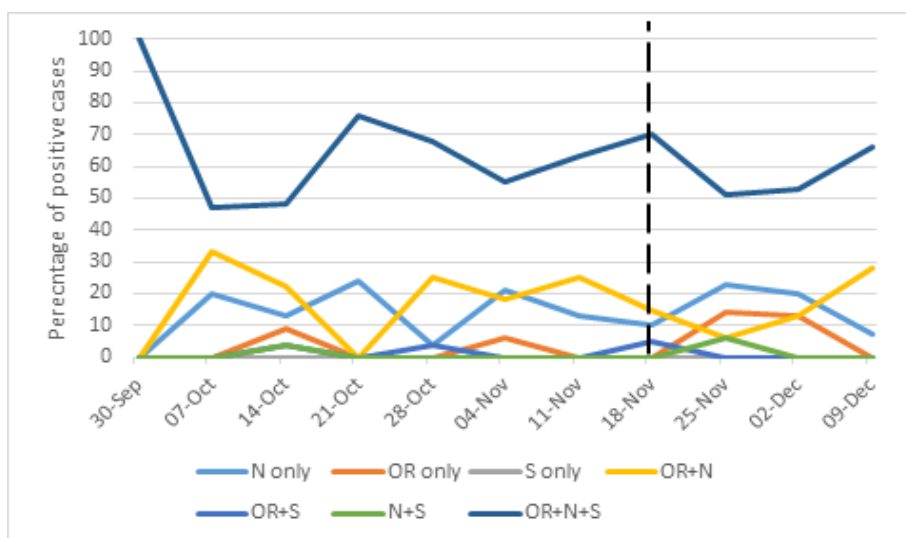
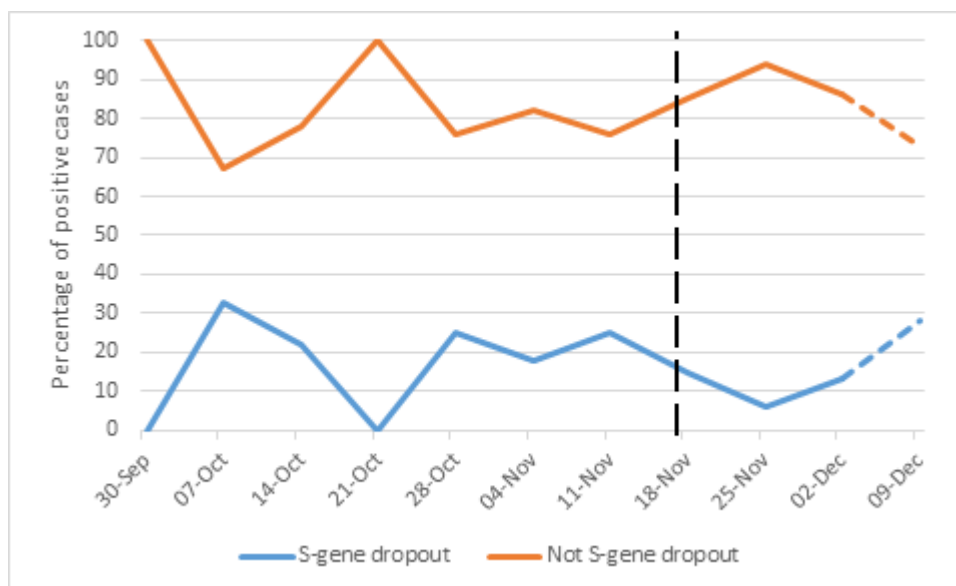


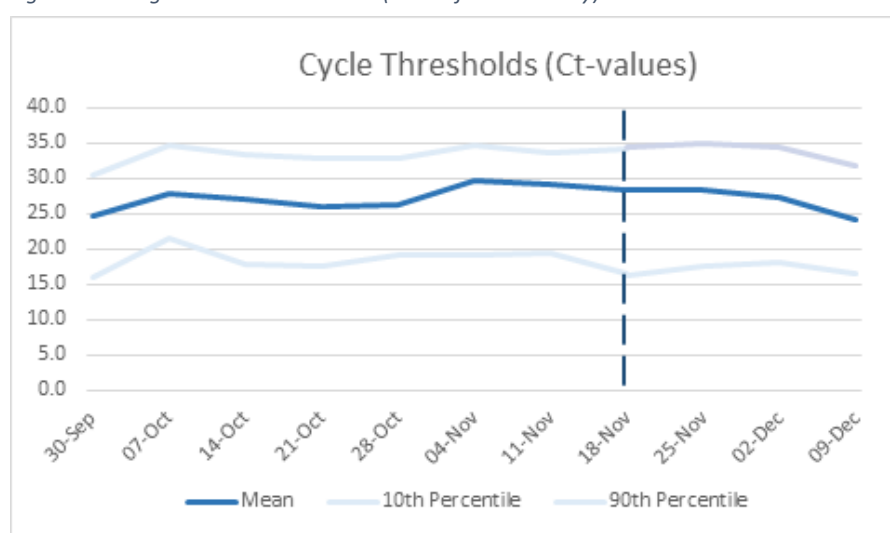
Figure 2. Change in presence of different viral variants in Wales over time (ONS data)

- From LHL data it can be seen that from November onwards the majority of S-gene drop-outs are due to the presence of the new variant (5% on 12 October, 54% on 2 November and 96% on 30 November).
- The proportion of positive cases attributed to S-gene drop-out COVID-19 is increasing. In the latest week (9 December) **28% of the total number of positive cases** detected in the CIS in Wales, were positive for the S-gene drop-out (8 of 29 cases).



- Using the PCR laboratory test for SARS-COV2 infection, extracted viral genetic material is amplified up to 37 times to determine the presence of the virus. The number of times a sample is amplified before returning a positive result is known as the Cycle Threshold (Ct- values). CT values can represent how much virus a person has in their body. Ct-values decrease as viral load increases. The graph below shows a reduction in Ct-Values over the most recent weeks. It is possible that this decrease in Ct-value could be from more people having the new viral variant that could lead to higher viral loads (low confidence).
- Additional analysis is being carried out on the CIS data to look at prevalence of both S-gene drop out COVID-19 and not S Gene drop outs of COVID-19 across the UK, Wales, and other devolved Administrations and regions within the UK. As and when this is completed, it will be considered by TAG.

Figure 4. Change in Ct value over time (ONS Infection Survey).



- Further information on the COVID-19 infection survey in Wales can be found on [the Welsh Government website](#).

Characteristics

- There is evidence the variant spreads faster than the previous virus versions. Sequencing data found that VOC had a higher growth rate compared to other non-VOC variants in the same geographic areas over the same period. Geographically, modelled growth rates are higher in areas with higher proportions of variant virus. Despite being recently detected, the variant is estimated to contribute to more than half of new cases, suggesting that it is out-competing the current virus to become the dominant variant. Finally, there is some evidence that viral loads are higher in cases with the variant, which

was usually associated with increased infectiousness in the case of the D614G variant, which was not present when the virus first emerged but is now ubiquitous and appears to be associated with a moderate effect on SARS-CoV-2 transmissibility.

- The biological mechanisms for the increased transmission rates are under investigation. A possible hypothesis is that the changes in the spike protein mean that virus binds better to cells and enters more easily. By improving host cell infectivity, it increases the probability of the virus getting into cells and initiating an infection.
- There is currently no evidence that the variant is different in severity, or differs by characteristics of sex and ethnicity. The SAGE subgroup NERVTAG stated that there are currently insufficient data to draw any conclusion on the age distribution of cases and the European Centre of Disease Control threat assessment from 20 December says the cases with the VOC 202012/01 variant are predominantly currently identified in people younger than 60 years.
- It is not clear if immunity to SARS-CoV-2 is affected by the variant. Early analysis in England and Wales has not found an increased frequency of repeat infections for this variant cases when compared to reinfections reported for other contemporaneously circulating variants. Immunity is raised to a number of different viral proteins/parts of viral proteins, so a small number of changes is unlikely to have a large impact on immunity.
- The modelling evidence estimates that the variant could have a 70% increase in transmissibility over other viruses circulating at the same time, with an increase in the reproductive number R_t of 0.4 or more. This means that restrictions which reduce transmission (such as social distancing) are reduced in effectiveness, but are still cumulatively effective, by this increased transmissibility.
- There is no evidence that mitigation factors such as social distancing, face-cover wearing or handwashing will be any less effective when performed as intended. The new variant does not change the fundamental truth that limited contact with others limits the opportunities for viral transmission. If one or more of the key mitigation factors are breached or poorly adhered to, this variant is simply better able to establish infection. Presence of the new variant means that greater care and application of existing mitigation measures are followed.
- There is currently no evidence to suggest that the new variant has greater persistence in the environment relative to other SARS-CoV-2 variants circulating in the UK.

Behavioural implications

- From a messaging perspective, it will be important to highlight that as the new variant spreads more efficiently and is more transmissible, then current control measures other than stay at home (e.g. not mixing with other households, social distancing, hand washing, ensuring ventilation in homes, use of face coverings and self-isolation when required), will be more important than ever and are effective in reducing spread of the new variant. If a greater proportion of the population are able to take more protective actions more often (with enabling support in place), this will prevent further harms arising from the new variant as well as the existing form of the virus (and the flu virus).
- While evidence suggests most people continue to undertake the protective behaviours most of the time, and messaging should recognise this, it appears that with current incidence levels minor lapses and non-adherence can have significant impacts on spread⁶. Furthermore, survey data indicate reported confidence in Government has fallen in recent weeks⁷, with evidence suggesting this can have a detrimental impact on adherence⁸. Given this recent reduction in confidence, now would be an opportune time to reinforce public messaging as to why these behaviours and the current restrictions are necessary, particularly in light of the evidence on increasing infectiousness. The population will inevitably be anxious with emerging news of VOC-202012/01. To manage this situation, it remains important that Government is transparent, acknowledges uncertainty and emphasises that COVID-safe behaviours are effective and within our control. This is consistent with previous TAG advice⁹.
- Assessment of population-wide infection trends rely on those with symptoms getting testing. There is potential over a 'holiday' period for testing numbers to subside, as people stay home. To counter this, messaging emphasising the benefits to individuals of getting a test (knowing current status), could help ensure people keep coming forward, and consequently taking steps to minimise spread.

Further steps

- Within Wales the majority of COVID-19 sequencing is undertaken by the PHW Pathogen Genomics Unit (PenGU), who will be continuing to sequence, analyse and share COVID-19 data over the Christmas period. These data are analysed and shared in real time. Additional efforts will need to be undertaken to ensure that PenGU receives positive results from community testing sites in

⁶ <https://gov.wales/technical-advisory-group-policy-modelling-december-2020-and-january-2021>

⁷ See for example <https://gov.wales/survey-public-views-coronavirus-covid-19-4-7-december-2020>

⁸ <https://www.medrxiv.org/content/10.1101/2020.10.19.20215376v1>

⁹ <https://gov.wales/technical-advisory-group-behavioural-insights-support-post-fire-break-wales>

a timely manner. There is a slight lag in the time for sequencing, and issues with the supply of positive samples for sequencing can exacerbate this.

- To provide a more rapid indication of VOC 202012/01 in the community in Wales, a request has been made to test a proportion of Welsh samples, in particular from South Wales, at an alternative LHL that is using a test to detect the SGTF.
- The impact on testing performance is being assessed. A rapid assessment of tests used in Wales has been done. PHW is assessing options for deploying tests to detect VOC without full sequencing using a combination of current lighthouse lab resource and potentially introducing an assay into the Welsh laboratory system.
- The effects on immunity are being assessed by PHE and also by researchers in the Oxford vaccine trial. Surveillance for vaccine failures and effectiveness of the vaccine against the variant will be incorporated into current plans. The effects on reinfections will be assessed in PHE and PHW.
- Samples collected from the waste water programme will be sent for sequencing analysis to better understand the distribution of the new variant in Wales.
- To support planning, we will reconsider our Reasonable Worst Case to include this and further additional evidence as it develops. We will consider a wide range of early 2021 interventions under different assumed increases in transmissibility, and will determine which scenarios are most likely to bring R_t below 1. We will continue to track each scenario twice weekly against the case, hospital and death statistics in Wales, to monitor likely trajectories.