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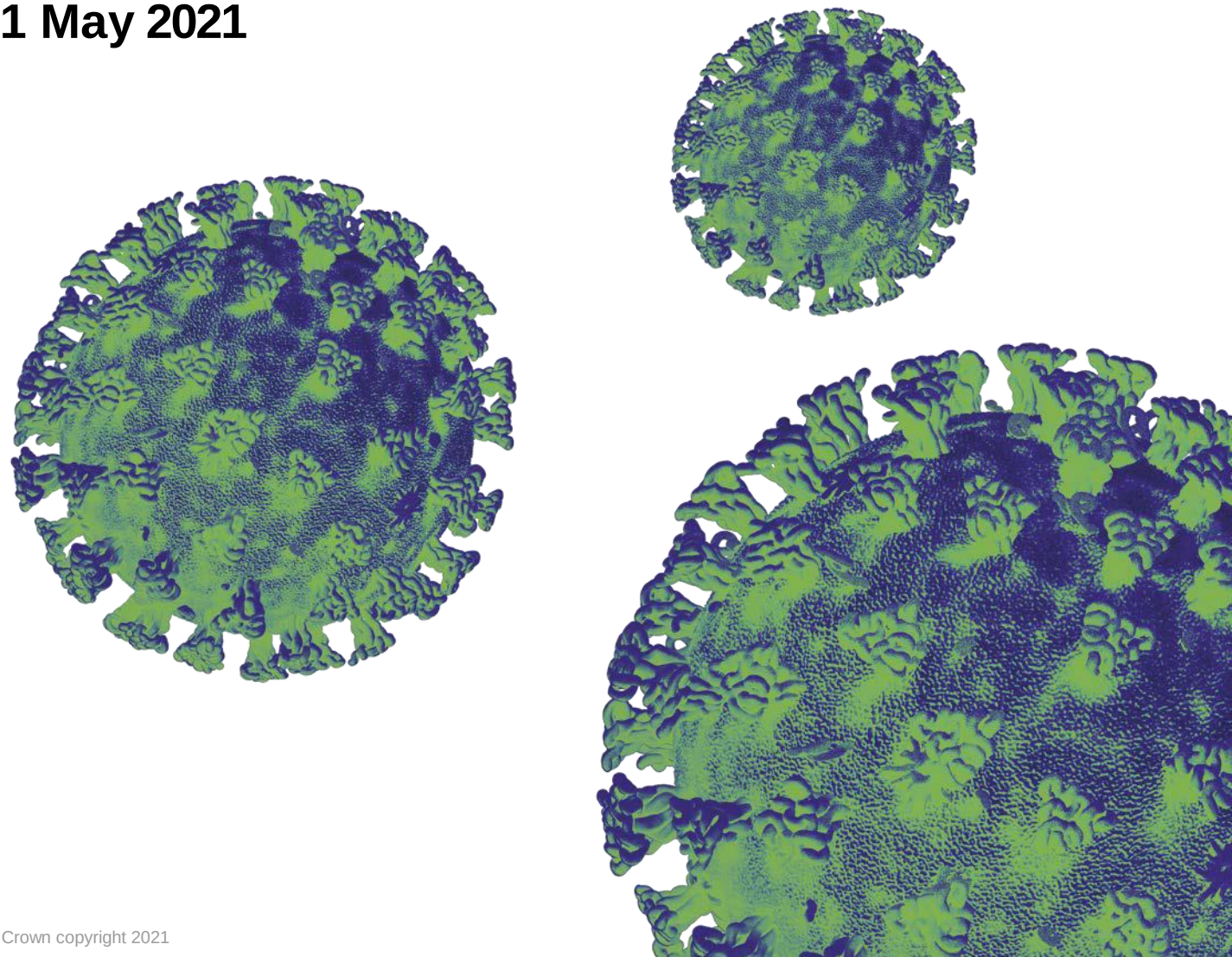
Technical Advisory Group / Covid Intelligence Cell

COVID-19 Briefing on VOC-21APRIL-02 (B.1.617.2)

21 May 2021



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Technical Advisory Group and Covid Intelligence Cell
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24 May 2021

Summary

The COVID-19 Variant of Concern "VOC-21APR-02" is also called B.1.617.2 and was first identified in India, where it is thought to be widespread.

Why is it concerning?

Speed

- There is an increased growth rate compared to the current dominant variant. Current data suggests that there is also a higher secondary attack rate of the B.1.617.2 variant. In vitro analysis suggests that the B.1.617.2 may be more efficient at gaining cell entry than B.1.1.7, providing a growth advantage.
- The rate of growth for B.1.617.2 appears to be greater than the current dominant variant where the two co-occur in the UK; the magnitude in change of transmissibility is uncertain. But the increased transmissibility of B.1.617.2 may lead to a replacement of the dominant variant. If the rate of current observed growth is because B.1.617.2 is more transmissible, this can be expected to result in more cases (and hospitalisations and deaths) than would otherwise have been expected with B.1.1.7 (high confidence).

Severity

- There is no current high quality information on disease severity, however, if the new variant results in more severe disease this would have the potential to result in increased hospitalisations and deaths.

Control

- There is evidence of uncontrolled community transmission in several places in England, at least within the North West, East Midlands and London. As at 19 May 2021, there are 28 cases that we know of in Wales, but this number will increase (high confidence).
- It is highly likely that cases and separate lineages of the B.1.617.2 variant will be imported into Wales from England in the coming days and weeks (high confidence).
- Based on the observed growth to date, a large number of infections likely remain undetected with this variant.

- International travel is opening up right now – but this variant is already present in at least 50 countries, and the red/amber/green list approach is unlikely to prevent large scale seeding[1].

Vaccine effectiveness

- National vaccine effectiveness monitoring shows a reduction in vaccine effectiveness against symptomatic infection after 1 dose of vaccine for B.1.617.2 compared to B.1.1.7 (moderate confidence). Current data suggest this is an absolute reduction of approximately 20% after 1 dose. Vaccine effectiveness is higher and similar between variants after 2 doses with a possible small reduction for B.1.617.2 (low confidence). Although this is observational data subject to some biases, it holds true across several analytic approaches, is consistent with observed outbreaks, and is supported by pseudovirus and live virus neutralisation data[23].
- There are no data on whether prevention of transmission is affected.
- There are insufficient data on vaccine effectiveness against severe disease. Based on neutralisation data, vaccines are expected to remain effective against severe disease. Monitoring continues.

Immunity and reinfection

- A national cohort study of healthcare workers of over four thousand participants UK, 95% of whom have received two doses of vaccine, wide does not currently show any increase in PCR positivity and reinfections are very low[2,4.]
- There is limited evidence of outbreaks in fully vaccinated populations in Delhi and Seychelles and infections of this variant in vaccinated individuals in the UK, although severe disease and hospitalisation in vaccinated cases remains very low.[5]

What don't we know?

- We do not fully know the ratio of cases to harms, including hospitalisations and deaths. Without this we cannot know what number of cases would lead to what number of harms, which means that the government cannot have certainty in choosing its path according to risk appetite.
- We do not yet know the secondary attack rate of the new variant in schools, education establishments or other settings where populations are unvaccinated, this requires further investigation.

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[1] Gisaid.org - Tracking of variants (https://www.gisaid.org/hcov19-variants/)

[2] Investigation of SARS-CoV-2 variants of concern: technical briefings - GOV.UK (www.gov.uk)

[3] COVID-19 vaccine surveillance report - week 19 (publishing.service.gov.uk)

[4] SIREN Study Portal (phe.org.uk)

[5] BBC, Covid: Why has Seychelles seen rising case numbers?

What can we do?

- Act early, harder, wider and deeper than what can be seen in the data on the surface.
- Keep vaccinating. There is no evidence to suggest any diversion from the current priorities of vaccinating the population and isolating infected individuals.
- Manage travel isolation carefully. Importation of new cases from overseas and from England are currently likely to be the main driver of seeding of this variant in Wales.

Further nuances to consider in the approach might include:

- Concentrating available vaccine in areas and populations that are most likely to experience outbreaks of this VOC.
- Accelerating the delivery of second doses of the vaccine to those populations where possible.
- Maintaining and communicating protective behaviours and risk assessments in schools and public places.
- Working closely with community groups and stakeholders on interventions.
- Being highly cautious in relaxing restrictions until more evidence on transmissibility, infection severity and immune escape is available.

Situation

- Variants of Concern (VOCs) and Variants Under Investigation (VUIs) are currently the most significant risk to easing of restrictions in Wales. The main concerns are VOC-20DEC-02 (B.1.351, first identified in South Africa) and the recently emerged VOCs and VUIs of the B.1.617 complex, notably B.1.617.2 which is growing exponentially in parts of the UK. As of 19 May 2021 there are 3,424 (2,169 from the previous week) known B.1.617.2 cases with provisional genotyping or sequencing results in the UK, 28 of which are in Wales.
- We are closely monitoring the situation in England (notably the North West, London and increasingly East Midlands) where S-gene positive cases (S+) have been increasing since the end of March as a proportion of overall case numbers (which are still low) and public health teams have been deployed. S gene negatives were an indicator of the B.1.1.7 variant (first identified in Kent), currently dominant in the UK. Over the winter we have observed the replacement of the previous S-gene positive lineages with B.1.1.7, and genomic data demonstrate that much of the uptick in S-gene positive cases in April and May is due to B.1.617 and its sublineages (Figure 1),

although sporadic introductions of lineages prevalent in other parts of the world are also beginning to be observed.

Figure 1. S-gene positive growth (B.1.617.2 proxy) in PCR tests from England pillar 2 , Source: [PHE VOC Technical Report 12]

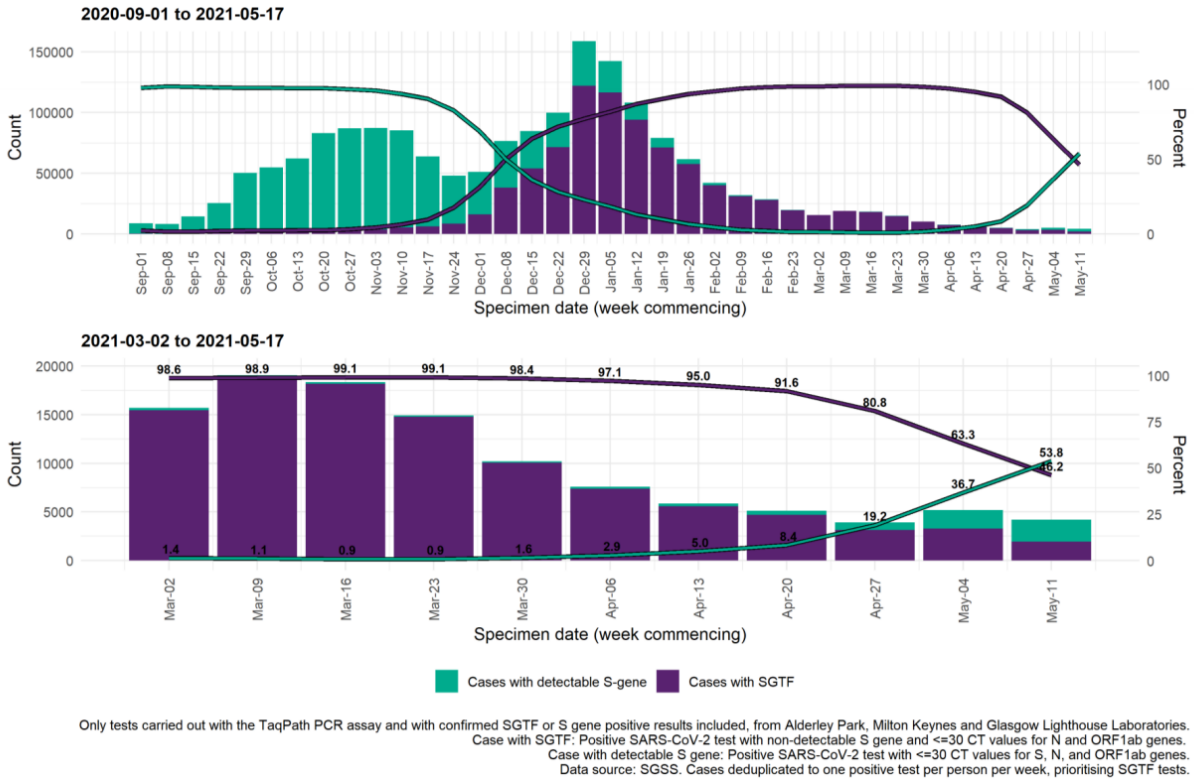
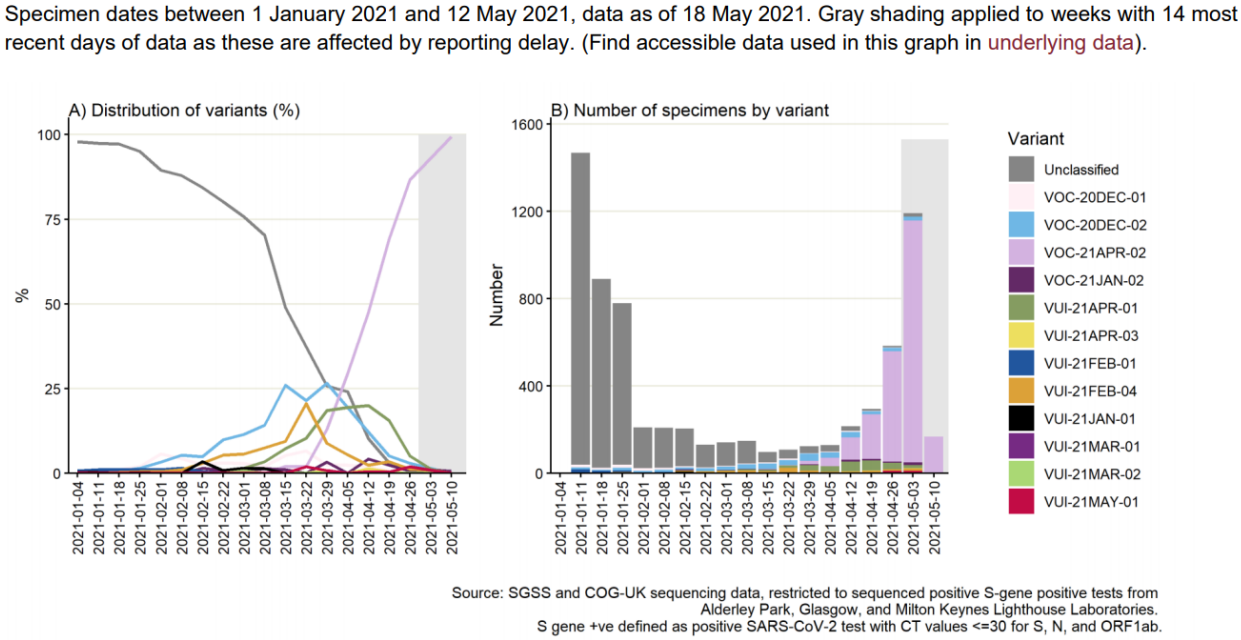


Figure 2: Lineage breakdowns from English Pillar 2 data Distribution of variants among sequenced S gene positive SARS-Cov-2 specimens, Source: [PHE VOC Technical Report 12]



- Recent sequencing suggests that approaching 100% of these S+ cases now fall into a recognised VOC or VUI group, and that these are dominated by VOC-APR21-02 (B.1.617.2, variant first identified in India).
- Although initially skewed by cases in the South Asian population (due to importation from India), there is now evidence of exponential community transmission of this variant in several areas with a high burden of S+ cases across different demographics (NW of Manchester, Bedford, Sefton, Nottingham and to a lesser extent East London).
- Cases in Bolton and neighbouring Blackburn bear the hallmarks of community transmission and a rapid loss of control and exponential growth, with cases doubling approximately every 5-7 days. Given the number of cases that remain in the pipeline for sequencing current, data likely understate the scale of B.1.617.2 spread and it may have already replaced B.1.1.7 to some extent.[6]

Situation report for Wales (data from Public Health Wales)

- As of 19 May 2021, 28 cases of the variant have been identified in Wales. The majority of these cases have been confirmed in those residing in Cardiff and Vale UHB, with 13 cases of VOC-21APR-02 recorded and 8 of VUI-21APR-01. Of the 28 cases, nine are associated with travel from India. Two clusters identified in Cardiff are not linked to travel. Both clusters involve households of multiple occupancy (HMO). The detection of more cases in Wales is certain.
- B.1.617 is a diverse lineage which was first observed in India in October 2020. Since then, it has spread extensively, and has picked up a range of mutations, some of which are of biological relevance. Lineage B.1.617.2 is one of the sublineages of B.1.617 which have arisen since its emergence, and because of the length of time it has been circulating, B.1.617.2 has picked up a considerable amount of genetic diversity.
- The presence of genetic diversity in the source population means it is easier to distinguish putative imports into Wales and community transmission within Wales. Based upon samples sequenced to date by PHW and COG-UK, we can identify at least 11 likely separate cases of introductions into Wales to date.
- The availability of sequencing from other parts of the UK provides a basis for ongoing monitoring of likely imports into Wales. Sequencing of Welsh cases provides a key tool to identify evidence for onward community spread.

Transmissibility is faster than the B.1.1.7 variant most prevalent in the UK (high confidence)

- Emerging evidence suggests that the new variant may be more transmissible than the current dominant strain (B.1.1.7). There are plausible biological explanations why the new variant may be more transmissible, however the transmission conditions (non-protective behaviours) may also factor in the observed growth.

[6] PHE, SARS-CoV-2 variants of concern and variants under investigation, Technical Briefing 10

- One SPI-M modelling group suggests that the R_t number for this variant may be around 1.64, whereas for other variants it is currently below 1; however it may be that this is related to initial clusters in some areas that cannot be generalised to a wider population[7].
- Overall the consensus in SPI-M and SAGE was that the B.1.617.2 variant was more transmissible than B.1.1.7. There was less consensus over the degree of transmissibility, with estimates that it may be over 50% more transmissible than the B.1.1.7 (SPI-M-O consensus statement, 12 May 2021[2]), which was in turn up to 70% more transmissible than wild type variants that were prevalent at the start of the pandemic.
- An increased proportion of B.1.617.2 has been recorded in imported traveller data (of travellers from India) and an increased proportion of B.1.617.2 in Indian genomic data. Aside from the UK, B.1.617.2 has been detected by sequencing 44 countries. The UK sequencing data represent a small sample from what is likely to be a far wider collection of outbreaks and epidemics currently working through the Indian subcontinent.
- Analysis of Secondary attack rates for B.1617.2 compared to the other B.1.617 lineages and B.1.1.7 have been published by Public Health England, suggesting a considerably higher attack rate for B.1617.2 (VOC-21APR-02). These are based on positive tests among contacts recorded in the test and trace system. Secondary attack rates for contacts of those that have travelled were all lower than those that had not travelled, although cases with B.1.617.2 were higher than those for travel cases with B.1.1.7.

Figure 3. Secondary attack rates for the three B.1.617.2 sub-lineages, presented with B.1.1.7 for comparison (29 March 2021 to 28 April 2021, data as at 19 May 2021) Source: PHE VOC Technical Briefing 12

Variant	Cases in those that have travelled (% with contacts)	Cases in those that have not travelled or unknown (% with contacts)	Case proportion that have travelled	Secondary Attack Rate among contacts of those that have travelled (95% CI) [secondary cases/ contacts]	Secondary Attack Rate among contacts of cases that have not travelled or unknown (95% CI) [secondary cases/contacts]
VOC-20DEC-01	1,650 (71.3% with contacts)	23,697 (81.6% with contacts)	6.5%	1.7% (1.6% - 1.9%) [434/25,019]	8.1% (7.9% - 8.3%) [4,950/61,187]
VUI-21APR-01	140 (82.9% with contacts)	107 (81.3% with contacts)	56.7%	2.2% (1.7% - 2.9%) [55/2,490]	11.3% (8.1% - 15.6%) [31/275]
VOC-21APR-02	331 (70.4% with contacts)	698 (81.8% with contacts)	32.2%	3.3% (2.8% - 3.9%) [135/4,058]	12.5% (11.1% - 14.0%) [245/1,959]
VUI-21APR-03	4 (25.0% with contacts)	5 (100.0% with contacts)	44.4%	Unavailable [1/3]	Unavailable [1/12]

Disease severity (insufficient data)

- As of 17 May 2021 there have been 6 deaths in England within 28 days of positive test. There is close monitoring of hospital and healthcare activity in Bolton. In Wales

[7] SPI-M-O: Consensus statement on COVID-19, 12 May 2021

there have not yet been any confirmed deaths in people infected with this variant, but case numbers are rising.

- The majority of cases are very recent and there has been insufficient follow up time to allow an assessment of severity (Insufficient information).

Natural immunity (low confidence)

- A national cohort study of healthcare workers of over four thousand participants UK, 95% of whom have received two doses of vaccine, wide does not currently show any increase in PCR positivity and reinfections are very low[2,8.]
- From a small number of laboratory studies using convalescent serum, a reduction of antibody neutralising activity is observed which is greater than B.1.1.7 but less than B.1.351 (variant first identified in South Africa).
- As of 18 May, a small number of sequenced reinfections for B.1.617.2 have been recorded in England (29) an increase of 16 from the previous week (13). In the previous week there were 487 sequenced reinfections for B.1.1.7, with 513 recorded a week later, an increase of 26.
- Molecular modelling from Swansea University (NB Modelling of this sort can give insight but should not be considered confirmed without lab and real world confirmation): B.1.617.2 is striking and the T478K mutation appears to be a strong immune escape mechanism, particularly in combination with L452R. Both these mutations are in the list of substitutions known to increase ACE2 binding[9], but T478K also serves to severely disrupt the E8 epitope (the "distal loop" disruption). The same epitope is disrupted by the E484K mutation in P1 and B.1.351, and so this very much looks like an immune escape variant by another means.
- Mutational analysis: L452R has been demonstrated to have an impact on the effectiveness of monoclonal antibodies[10] and a 4-6.7 fold decrease in neutralisation titres from convalescent patients and vaccine recipients[11]. PHE studies reported on in the VTG supported the 4 fold decrease in pseudovirus with L452R.

Vaccine Effectiveness (low confidence)

- Discussions at SAGE 89[12] highlighted there is some antigenic distance present between B.1.617.2 and B.1.1.7, although to a lesser extent than B.1.351 (low confidence). This means there may be some reduction in protection given by vaccines or naturally acquired immunity from past infection, although more investigation is required.

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[8] SIREN Study Portal (phe.org.uk)

[9] Science, Prospective mapping of viral mutations that escape antibodies used to treat COVID-19, April 2021

[10] Cell, The Impact of Mutations in SARS-CoV-2 Spike on Viral Infectivity and Antigenicity, September 2020

[11] MedRxiv, Transmission, infectivity, and antibody neutralization of an emerging SARS-CoV-2 variant in California carrying a L452R spike protein mutation, March 2021

[12] SAGE 89 minutes: Coronavirus (COVID-19) response, 13 May 2021

- National vaccine effectiveness monitoring, by PHE, shows a reduction in vaccine effectiveness against symptomatic infection after 1 dose of vaccine for B.1.617.2 compared to B.1.1.7 (moderate confidence). Current data suggest this is an absolute reduction of approximately 20% after 1 dose. Vaccine effectiveness is higher and similar between variants after 2 doses with a possible small reduction for B.1.617.2 (low confidence). Although this is observational data subject to some biases, it holds true across several analytic approaches, is consistent with observed outbreaks, and is supported by pseudovirus and live virus neutralisation data[13][14].

Figure 4. Vaccination status and vaccine effectiveness for B.1.1.7 and B.1.617.2 (PHE VOC Technical Briefing 12, 19 May 2021)

Vaccination status	Vaccine Effectiveness	
	VOC-20DEC-01 (B.1.1.7)	VOC21-APR-02 (B.1.617.2)
Dose 1	51.1% (47.3 to 54.7)	33.5% (20.6 to 44.3)
Dose 2	86.8% (83.1 to 89.6)	80.9% (70.7 to 87.6)

Figure 5. Summary of evidence on vaccine effectiveness against different outcomes (PHE vaccine surveillance report, week 20)

Outcome	Vaccine effectiveness			
	Pfizer-BioNTech		Oxford-AstraZeneca	
	1 dose	2 doses	1 dose	2 doses
Symptomatic disease	55-70%	85-90%	55-70%	85-90%
Hospitalisation	75-85%	90-95%	75-85%	No data
Mortality	75-80%	95-99%	75-80%	No data
Infection	55-70%	70-90%	60-70%	No data
Transmission (secondary cases)*	45-50%	No data	35-50%	No data

High Confidence	Evidence from multiple studies which is consistent and comprehensive
Medium Confidence	Evidence is emerging from a limited number of studies or with a moderately level of uncertainty
Low Confidence	Little evidence is available at present and results are inconclusive

* effectiveness in reducing symptomatic secondary cases in households of a symptomatic index case

[13] Investigation of SARS-CoV-2 variants of concern: technical briefings - GOV.UK (www.gov.uk)

[14] COVID-19 vaccine surveillance report - week 19 (publishing.service.gov.uk)

Potential impacts

- Analysis by the Centre for Mathematical Modelling of Infectious Diseases (CMMID)Covid-19 working group for SPI-M of imported cases of B.1.617.2 into the UK suggests that, based on importations and local cases of B.1.617.2, the R_t of B.1.617.2 was 1.64 (95% CI 1.61-1.67), assuming no change in generation interval. This also assumed that all imported infections from India ceased after the red listing on 23 April (i.e. no leaks from hotel quarantine). This suggests the majority of sequenced cases in the UK could consist of this variant by mid-May 2021, under the assumption that non-B.1.617.2 variants would continue to decline at 3% per day in the UK as they did in late April 2021[15]. This is not necessarily true for Wales yet, but inevitably we will follow England closely.
- SPI-M Roadmap modelling has previously suggested new variants with increased transmissibility are capable of generating a wave of infections larger than previous waves.[16] This was based on modelling the English roadmap but is likely to be transferable to Wales.
- Work is underway to model in detail what a variant with increased transmission would mean for Wales, for instance if it had a 50% higher transmission, but taking into account the likely levels of vaccination and natural immunity we have in the population.

Recommendations

- With the risk associated with the spread of this variant, TAG recommend **early intervention** including:
  - Early consideration of reallocating vaccine resource, targeting first dose vaccination and accelerating delivery of second vaccine in areas that might be more likely to become clusters or areas of higher prevalence (e.g. areas of Cardiff, colleges etc.)
  - Surge testing, including rapid and widespread deployment of lateral flow testing and enhanced contract tracing in areas and settings where B.1.617.2 has been identified.
  - Any rapid testing should ensure that positive cases have samples sent to PHW for sequencing
  - Clear messaging on risk of infections in unvaccinated populations (See Annex I – Behavioural considerations)
  - Bring together IMT chairs to share experience of best practice from areas of highest cases
  - Continued use of risk assessed control measures in school and educational settings

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15 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/988203/S1240_CMMID_COVID-19_Working_Group_Modelling_importations_and_local_transmission_of_B.1.617.2_in_the_UK__13_May_2021.pdf

16 SPI-M-O: Summary of further modelling of easing restrictions – roadmap step 3, 5 May 2021

- Early engagement with relevant stakeholder groups (e.g. Muslim Council for Wales) to foster joint working and co-production

Conclusions

- The overall situation for COVID-19 in Wales is good, with low rates of infections in the community and a significant proportion of the adult population having had at least one dose of vaccine. Where there are outbreaks and clusters, for the most part, the chains of transmission can be described. Contract tracing is working well in identifying exposed individuals. However, the new variant poses a new challenge and could become the dominant variant in Wales. Cases of the new variant will increase in the near future and identifying the sources of infection may become more difficult. Whilst emerging evidence suggests that two doses of vaccine is effective against the new variant, the potential 50% increase in transmission alongside a moderate impact on one dose of vaccine may be sufficient to put pressure on NHS services and increase deaths in Wales. It will be important to carefully monitor the situation in England and prepare for reasonable worst case scenarios is Wales.

Annex I - Behavioural considerations

SAGE has previously published advice on mitigations to reduce the then new Variant of Concern (VoC), B.1.1.7, now commonly referred to as the Kent variant[17]. This advice reinforced the importance of mitigations in place at the time (personal, procedural, engineering and societal) to reduce SARS-CoV-2 transmission, noting they would need be adopted more rigorously and more often, given increased transmissibility. An emphasis was placed on the need to communicate this increased risk of transmission, as well as highlighting that environmental and personal measures, underpinned by effective government support, can reduce transmission, including in the home. While restrictions have been relaxed in recent months in line with the Coronavirus control plan for Wales, many of these mitigations remain in place and remain the most effective actions for breaking chains of transmission.

In framing future activity to promote and support adherence in light of the emergence of the India variant (and other VoCs), it is necessary to consider the current public health position. Rates of infection in the community have fallen, vaccines have been rolled out to the most vulnerable and many restrictions on social contact lifted. The most recent TAC summary of advice[18] shows, not surprisingly, that while adherence to key protective behaviours remains high (e.g. 2m distancing, use of face coverings and hand hygiene), mobility is increasing and there are more social contacts (e.g. fewer people are leaving home for essential purposes only and avoiding public transport, with more returning to workplaces). Recent SPI-B[19] advice notes the likelihood of perceptions of immunity growing in the population, with implications for messaging. With further relaxation of existing restrictions and others anticipated, urging caution and/or re-introducing restrictions may appear counterintuitive, although Ipsos MORI data for Wales[20] do suggest around half of people believe it will be at least a year before things are back to normal.

Given this complexity, a continued focus on communications that present a clear rationale for the need to adhere to personal protective behaviours remains critical. The importance of support for such behaviours should not be underestimated, particularly support for self-isolation (financial, practical and social) and environmental interventions to encourage COVID-safe behaviours across society, including schools, workplaces, retail and hospitality settings. This is consistent with advice from SAGE[21], TAG[22] and others[23], that some protective behaviours are likely to be necessary in the longer-term to minimise future risk of infection when moving towards an endemic state or a 'new normal'.

The universal and consistent adoption of personal protective behaviours, supported by structured, tailored communications and social and environmental support as

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[17] EMG/SPI-B/TWEG: Mitigations to reduce transmission of the new variant SARS-CoV-2 virus, 22 December 2020 - GOV.UK (www.gov.uk)

[18] Technical Advisory Cell: summary of advice 7 May 2021 | GOV.WALES

[19] SPI-B: Behavioural and social considerations when reducing restrictions, 10 February 2021 - GOV.UK (www.gov.uk)

[20] Ipsos MORI: Survey of public views on the coronavirus (COVID-19): 23 to 27 April 2021

[21] SAGE 88 minutes: Coronavirus (COVID-19) response, 5 May 2021

[22] Technical Advisory Group: using behavioural science to inform policy and practice | GOV.WALES

[23] See for example Sustained behavior change is key to preventing and tackling future pandemics | Nature Medicine

set out above, should be framed as 'easy' when compared to the larger-scale restrictions that have been in place for much of the pandemic, particularly when evidence suggests the majority of the population are already capable of maintaining them, while they take little time or resource.

Ongoing messaging should also highlight the risk to the significant minority of the population who remain unprotected from vaccination, including younger people and some in minority ethnic communities. This is important in light of evidence that ethnic minority and socio-economically disadvantaged groups face multiple barriers in applying personal protective behaviours in their workplaces, communities and domestic spaces. Additionally there are statistically significant inequalities in vaccination uptake rates across ethnic (and socio-economic) groups[24]. These factors point to the need for increased behavioural diagnostic activity, and resultant optimisation of interventions (e.g. communication, policy and services) to close these gaps. In the meantime, adherence to personal protective behaviours such as those noted above will provide a layer of protection while vaccine rollout continues.

Emphasis on the continued need to reduce the risk of infection through minimising the number and duration of social contacts, adequate ventilation and assessing context at all times (e.g. levels of community infection, vulnerability of specific individuals, vaccination status and recent social contacts) remains critical. Reinforcing the relatively lower risk of meeting outdoors (compared with indoors) remains essential, as does the fundamental importance of seeking a test when symptomatic, self-isolating as necessary and having the vaccine, including the necessity of the second dose to increase protection. Operationally and behaviourally, challenges remain with the vaccination programme, notably reaching the most vulnerable groups, the younger cohorts who perceive themselves to be less vulnerable and ongoing signals from the relaxation of restrictions.

The broader TAG advice[25] on behavioural considerations to inform the lifting of restrictions remains relevant, including the importance of co-produced[26] and culturally sensitive[27] risk communication, particularly given current evidence on the geography and demographics of new cases of the India variant. Further effort is also required to improve understanding of how context, biases and other influences affect the behaviour of people and drives their decisions, in order to ensure interventions (communication, policy and service provision) reflect real needs and behaviours for greater impact and effectiveness.

[24] Wales COVID-19 vaccination enhanced surveillance - equality report.pdf

[25] Technical Advisory Group: statement on priority considerations relating to personal protective behaviours to inform decisions on easing of restrictions in Spring 2021 | GOV.WALES

[26] SPI-B: Principles for co-production of guidance relating to the control of COVID-19, 8 July 2020 - GOV.UK (www.gov.uk)

[27] SPI-B: Consensus on BAME communication, 22 July 2020 - GOV.UK (www.gov.uk)