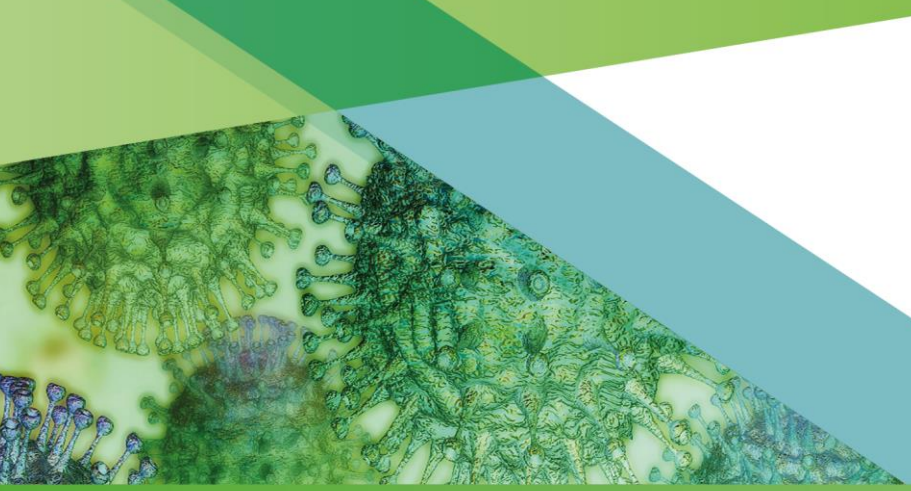

RAPID RISK ASSESSMENT

Risk related to spread of new SARS-CoV-2 variants of concern in the EU/EEA

29 December 2020

Summary

Viruses constantly change through mutation, and so the emergence of new variants is an expected occurrence and not in itself a cause for concern; SARS-CoV-2 is no exception. A diversification of SARS-CoV-2 due to evolution and adaptation processes has been observed globally.

While most emerging mutations will not have a significant impact on the spread of the virus, some mutations or combinations of mutations may provide the virus with a selective advantage, such as increased transmissibility or the ability to evade the host immune response. In such cases, these variants could increase the risk to human health and are considered to be variants of concern.

New variants of current concern

The United Kingdom (UK) has faced a rapid increase in COVID-19 case rates in the South-East, the East and the London area, which is associated with the emergence of a new SARS-CoV-2 variant, VOC 202012/01. As of 26 December 2020, more than 3 000 cases of this new variant, confirmed by genome sequencing, have been reported from the UK. An increasing proportion of cases in the South East, the East and the London area are due to this variant, but cases have also been identified in other parts of the UK. Although it was first reported in early December, the initial cases were retrospectively identified as having emerged in late September. Preliminary analyses indicate that the new variant has increased transmissibility compared to previously circulating variants, but no increase in infection severity has so far been identified. Since 26 December, a few VOC 202012/01 cases have also been reported in other EU/EEA countries (Belgium, Denmark, Finland, France, Germany, Iceland, Ireland, Italy, the Netherlands, Norway, Portugal, Spain and Sweden) and globally (Australia, Canada, Hong Kong SAR, India, Israel, Japan, Jordan, Lebanon, South Korea, Switzerland, Singapore).

In addition to VOC 202012/01, South Africa has reported another SARS-CoV-2 variant, designated as 501.V2, which is also of potential concern. This variant was first observed in samples from October, and since then more than 300 cases with the 501.V2 variant have been confirmed by whole genome sequencing (WGS) in South Africa, where it is now the dominant form of the virus. Preliminary results indicate that this variant may have an increased transmissibility. However, like the VOC 202012/01, at this stage there is no evidence that 501.V2 is associated with higher severity of infection. On 22 December 2020, two geographically separate cases of this new variant 501.V2 were detected in the UK. Both are contacts of symptomatic individuals returning from travel to South Africa. On 28 December 2020, one additional case of this new variant was detected in Finland in a returning traveller from South Africa.

Risks associated with new variants of current concern

ECDC assesses that the probability of SARS-CoV-2 VOC 202012/01 and 501.V2 being introduced and further spread in the EU/EEA is currently **high**. Although there is no information that infections with these strains are

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more severe, due to increased transmissibility the impact of COVID-19 disease in terms of hospitalisations and deaths is assessed as **high**, particularly for those in older age groups or with co-morbidities. The overall risk associated with the introduction and further spread of SARS-CoV-2 VOC 202012/01 and 501.V2 is therefore assessed as **high**.

The probability of increased circulation of any SARS-CoV-2 strains and this placing greater pressure on health systems in the coming weeks is considered to be **high** due to the festive season and, higher still, in countries where the new variants are established. The impact of this increased pressure on health systems is considered to be **high** even if current public health measures are maintained. Therefore, the overall risk of an increased impact on health systems in the coming weeks is assessed as **high**.

Maintaining and strengthening non-pharmaceutical interventions

Member States are recommended to continue to advise their citizens of the need for non-pharmaceutical interventions in accordance with their local epidemiological situation and national policies and, in particular, to consider guidance on the avoidance of non-essential travel and social activities.

Options for delaying the introduction of variants of concern

The options available for delaying the introduction and further spread of a new variant of concern are:

- to perform targeted and representative sequencing of community cases to detect early and monitor the incidence of the variant;
- to increase follow-up and testing of people with an epidemiological link to areas with significantly higher incidence of the variant and to sequence samples from such cases;
- to enhance targeted contact tracing and isolation of suspected and confirmed cases of the variant;
- to alert people coming from areas with significantly higher incidence of the variant to the need to comply with quarantine, as well as getting tested and self-isolating if they develop symptoms;
- to recommend avoiding all non-essential travel, in particular to areas with a significantly higher incidence of the variant.

Although in the short-to-medium term the roll-out of vaccinations will probably contribute to the response, these immediate measures are essential until such time as doses are available in sufficient numbers and have been shown to have a mitigating effect.

Increased detection and characterisation

Member States should continue to monitor for abrupt changes in rates of transmission or disease severity as part of the process of identifying and assessing the impact of variants. Data analysis and assessment of the local, regional and national situation should be performed to identify areas with rapidly changing epidemiology.

National public health authorities should notify cases of the new variant, as well as any other new SARS-CoV-2 variants of potential concern, through the Early Warning and Response System (EWRS) and The European Surveillance System (TESSy) for case-based surveillance and aggregate reporting, which has been adapted for this purpose.

In order to be able to detect introductions of known variants, as well as emergence of new variants of concern, Member States need to perform timely genome sequencing of a significant and representative selection of isolates. The UK has demonstrated that their sequencing programme is able to detect emerging variants. Ideally, Member States should aim for a similar timeliness and fraction of samples sequenced, although this will depend on the availability of resources. If representative sequencing on a similar scale to that carried out by the UK is not feasible, samples could be selected where the involvement of a variant of concern is suspected.

Event background

Viruses constantly change through mutation, making the emergence of new variants an expected occurrence and not in itself a cause for concern; SARS-CoV-2 is no exception. In recent months, a diversification of SARS-CoV-2 due to evolution and adaptation processes has been observed globally.

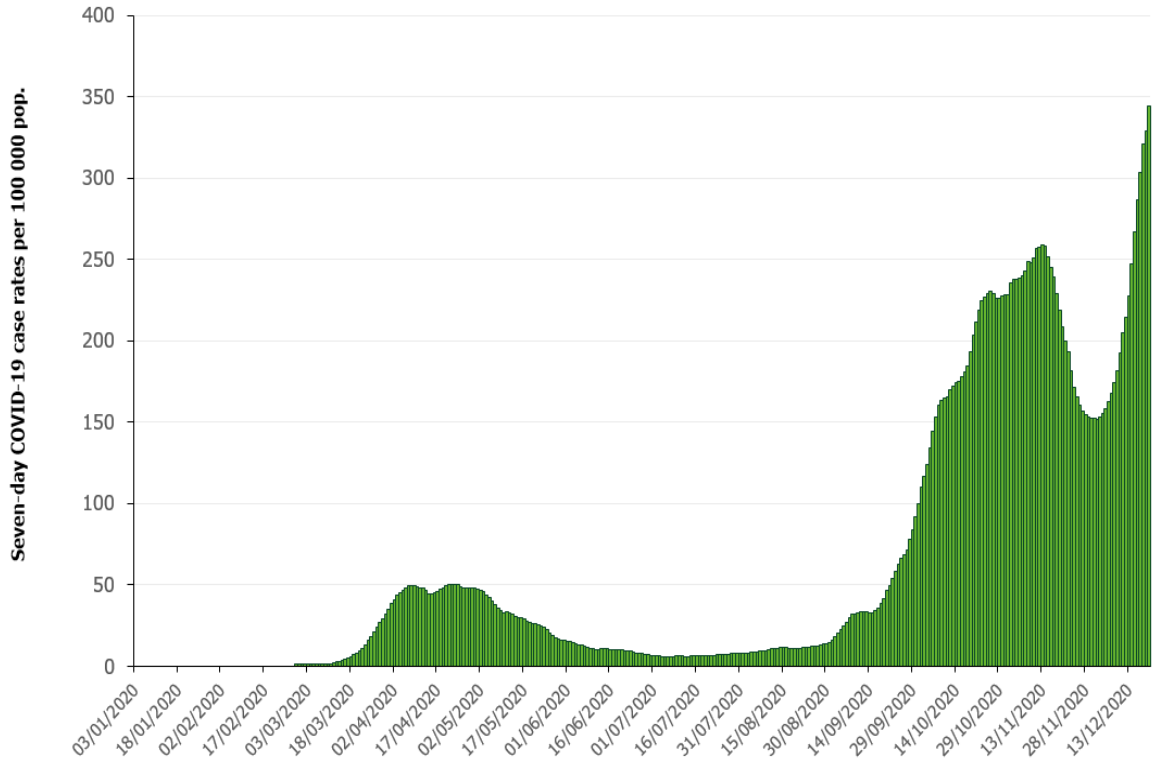
While most emerging mutations will not provide a selective advantage to the virus, some mutations or combinations of mutations may provide the virus with such an advantage. Examples of this could be greater transmissibility due to an increase in receptor binding or the ability to evade the host immune response by altering the surface structures recognised by antibodies. In such cases, these variants are of concern and could be a risk to human health.

This risk assessment presents the latest available information on the recent emergence of two variants of potential concern, VOC 202012/01 discovered in the United Kingdom (UK) and another variant, 501.V2 identified in South Africa. It also assesses the risk of these variants of concern being introduced and spread in the EU/EEA, as well as the increased impact this would have on health systems in the coming weeks.

Variant of Concern (VOC) 202012/01, United Kingdom

Over the last few weeks, the UK has faced a rapid increase in COVID-19 case rates (Figure 1 and 2 and Figure A1 in the Annex). The seven-day case rate has rapidly increased from 162 cases per 100 000 population in week 49, to 227 during week 50/2020 (39% increase) and 344 during week 51/2020 (51% increase).

Figure 1. Seven-day COVID-19 case rates per 100 000 population in the United Kingdom, by specimen date, as of 25 December 2020

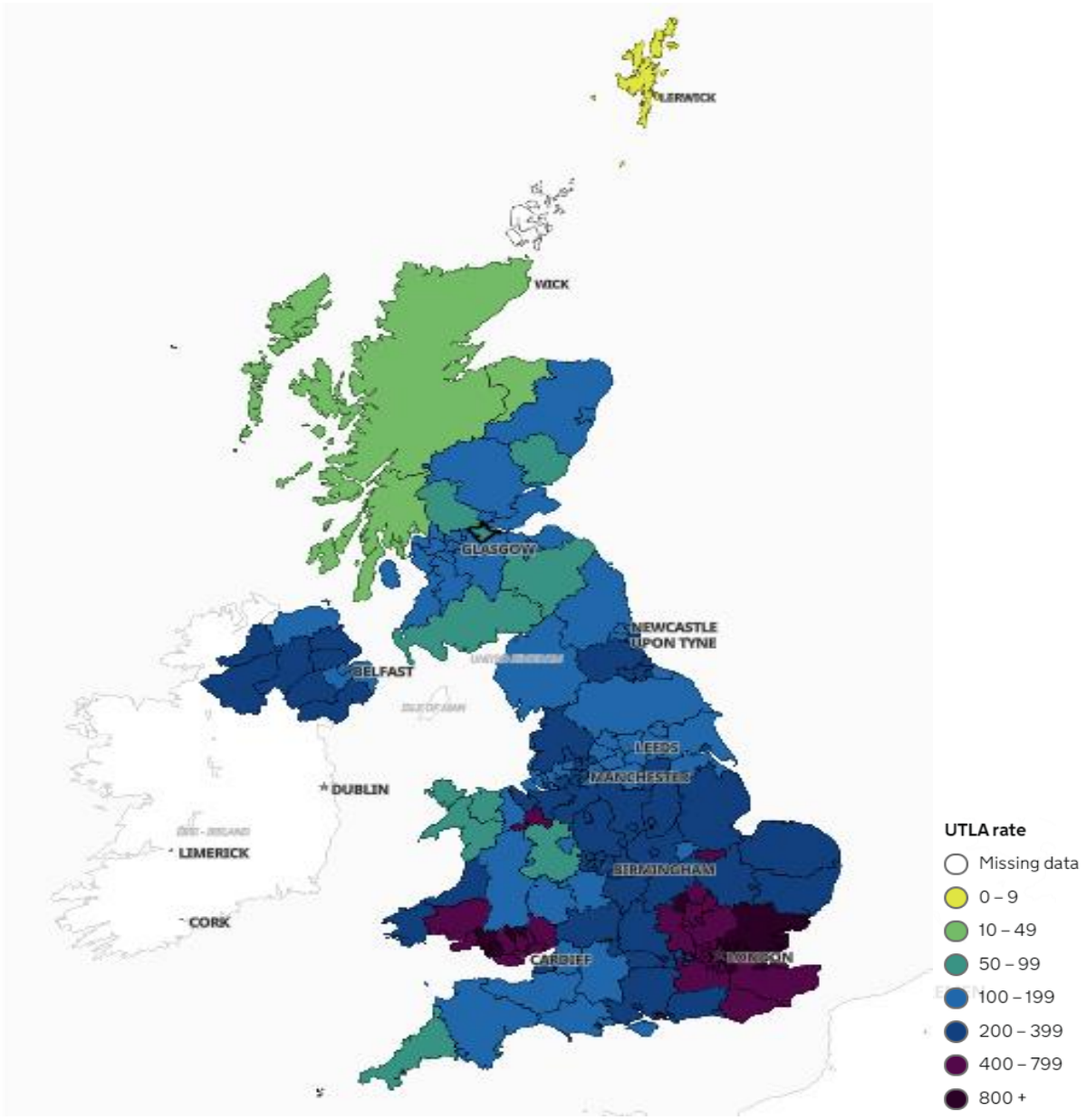


Note: The rate represents individuals with at least one positive COVID-19 test result per 100 000 population in the rolling seven-day period ending on the dates shown. The latest data point available is 25 December 2020.

Source: Data adapted from Public Health England (PHE) data portal [1].

This increase in the weekly rate per 100 000 population is currently more pronounced in three regions: London, the South East and the East of England (see Figure 2 below).

Figure 2. Subnational seven-day rolling rates of new COVID-19 cases per 100 000 population in the UK, as of 21 December 2020

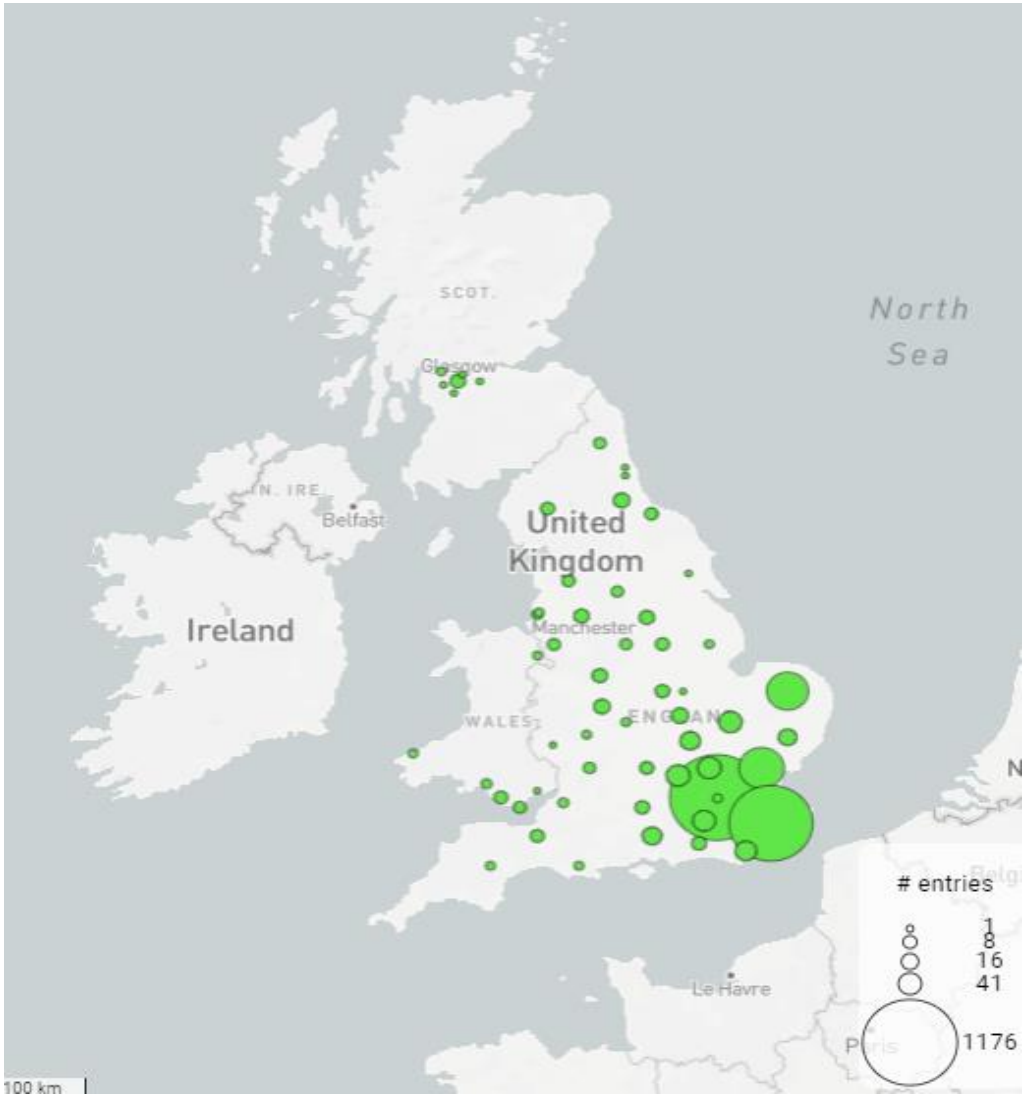


Source: Coronavirus (COVID-19) in the UK [2] accessed on 27 December 2020. UTLA rate is the Upper Tier Local Authorities rate.

Genomic analysis of viral sequence data identified a large proportion of sequenced cases in the South East, the East and the London regions belonging to a new single phylogenetic cluster [3]. The rapid increase in COVID-19 cases overall was temporally associated with the emergence of a new variant in this area in November 2020. This variant is referred to as SARS-CoV-2 VOC 202012/01 (Variant of Concern, year 2020, month 12, variant 01, previously designated VUI, Variant under Investigation). The first instance of VOC 202012/01 was retrospectively identified in a case from 20 September 2020 in the UK [4].

The number of VOC 202012/01 cases confirmed by sequencing has also increased, indicating that it is present in other regions across England, but currently at much lower levels than in the south east of the country, and also that it is present in Wales (Figure 3).

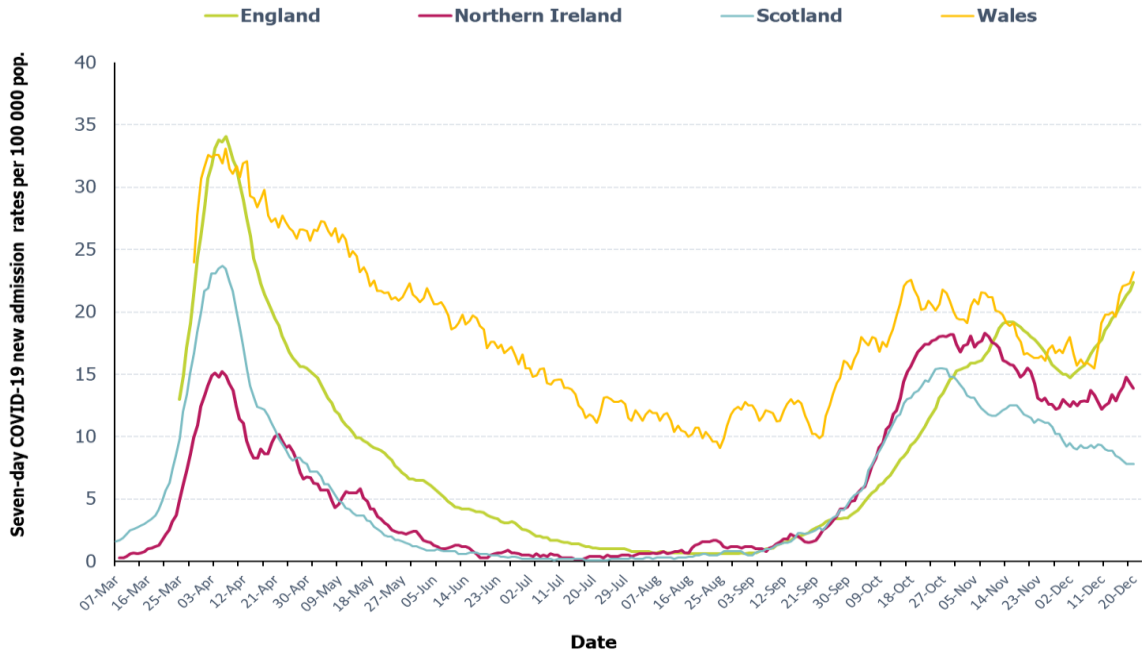
Figure 3. VOC 202012/01 cases confirmed by sequencing, case distribution in the UK, as of 25 December 2020



Source: https://beta.microreact.org/project/vVnFfZG7o3qYUJ6bnDs3Jo-cog-uk-2020-12-20-sars-cov-2-in-the-uk [5]

This increase in case incidence within the community is also visible in the new hospital admissions rolling rate in the UK (England and Wales) (Figure 4).

Figure 4. Seven-day COVID-19 new hospital admissions rates per 100 000 population by nation and specimen date, as of 27 December 2020, United Kingdom

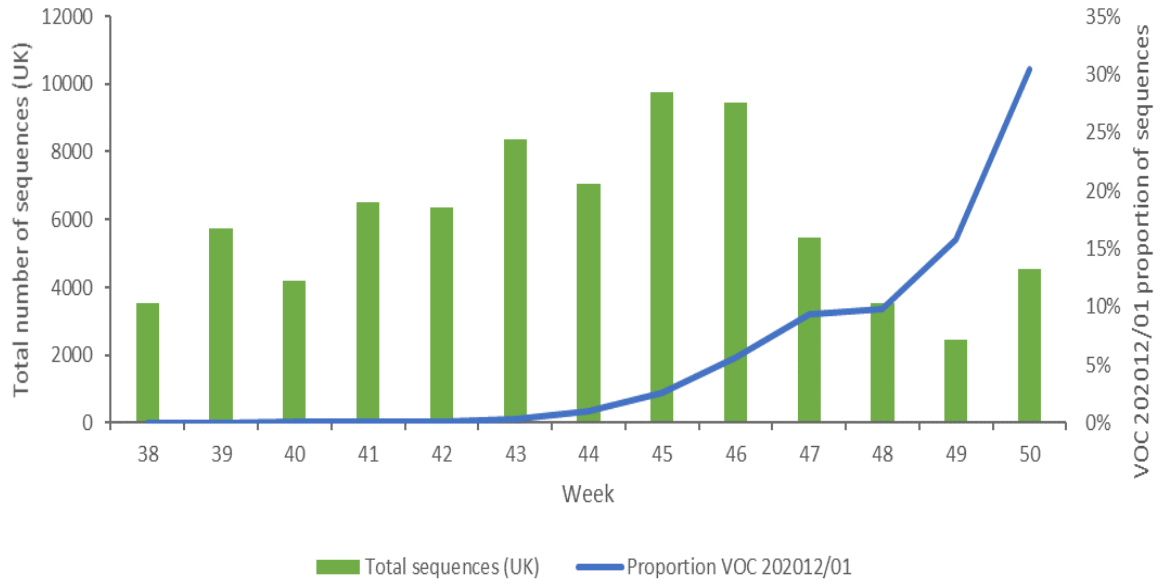


Note: The rate represents COVID-19 patients admitted to hospital per 100 000 population in the rolling seven-day period ending on the dates shown. The latest common data points available are for 20 December 2020. Data adapted from PHE data portal [1].

As of 26 December 2020, the UK reported the daily number of COVID-19 patients admitted to hospital as 2 143 (based on the latest available data, which are for 20 December 2020). This represents an increase of around 200 daily admissions (or 10%) compared to the week before (on 14 December 2020 the number of daily admissions 1 935) [1].

The overall proportion of VOC 202012/01 among all uploaded virus sequences from the UK to the GISAID database has increased substantially, particularly as of week 48/2020 (Figure 5). These sequences are, however, derived from community-based sampling and are not geographically representative or representative of hospitalised cases.

Figure 5. Fraction of UK SARS-CoV-2 sequences classified as VOC 202012/01 per week, and total sequences per week from the UK, published in GISAID EpiCoV up to 27 December 2020



Source: GISAID EpiCov database. Weeks 51 and 52 are omitted due to very few sequences being available for those weeks (252 and 0 respectively).

Case numbers with the variant virus have also been reported from other countries in the EU/EEA and globally (Table 1).

Table 1. Places reporting VOC 202012/01 cases, as of 29 December 2020

Places	Number of cases	Epidemiological information	Sources [Ref.]
England	3 316		Official source [4]
Wales	49	• Median 44 years (11–84), majority southern Wales	Personal communication
Scotland	18		Official source [6]
Northern Ireland	1	• Unknown travel history.	Official source [7]
Denmark	46	• 12 cases are contacts of previous cases; • 20 cases are from Northern Jutland, 20 from the Capital region, two from Zealand and four from southern Denmark; • Only two cases have links to one traveller from the UK; • Two cases may have links to travel from Brazil; • Phylogenetic analysis indicates that all nine cases with a sequence published before 25 December 2020 might originate from a single introduction [8].	Official source [9]
Portugal (Madeira)	21	• Travel history to the UK.	Official source [10] and EWRS
Italy	14	• Eleven cases with travel history to the UK; • Three cases with epidemiological link to the UK.	Official source [4,11-15]
Iceland	13	• Twelve cases with travel history to the UK; • One case with travel history to Denmark.	EWRS
The Netherlands	11	• Ten cases with no travel history to the UK; • One case with travel history to the UK.	Official source [4,16]
Spain	9	• Six cases with travel history to the UK; • Three close contacts of a returning traveller from the UK.	Official source [17,18]
Japan	8	• Seven cases with travel history to the UK; • One close contact of a case; • Four cases were asymptomatic.	Official source [19-21]
Ireland	7		EWRS
India	6	• Travel history to the UK.	Official source [22]
Israel	5	• Four cases with travel history to the UK; • One case with no travel history.	Official source [23,24]
Belgium	4	• Unknown travel history.	Media [25]
Australia	4	• Travel history to the UK; • Two in New South Wales and two in Victoria.	Official source [26]
Canada	4	• Two cases with unknown travel history; • Two cases with no known travel history to the UK.	Official source [27,28]
South Korea	3	• Travel history to the UK.	Official source [29]
Finland	2	• Travel history to the UK.	Official source [30]
Norway	2	• Travel history to the UK.	Official source [31]
Hong Kong SAR	2	• Travel history to the UK.	Official source [32]
Switzerland	2	• Travel history to the UK.	Official source [33]
Jordan	2	• Travel history to the UK.	Official source [34]
Germany	2	• Travel history to the UK; • Three asymptomatic close contacts under investigation.	Official source [35-37]
France	1	• Travel history to the UK.	Official source [38]
Sweden	1	• Travel history to the UK.	Official source [39]
Singapore	1	• Travel history to the UK.	Media [40]
Lebanon	1	• Travel history to the UK.	Official source [41]

EWRS, Early Warning and Response System

On 19 December 2020, in response to the increase in this variant, the nations of the UK announced stricter measures to be applied from 20 December 2020 and over the coming weeks, with affected areas in England going into a 'Tier 4' lockdown: 'Stay-at-home' level with movement restrictions within and between more and less heavily affected areas [42,43]. These measures include recommendations for residents of the most affected areas to restrict movements and travel, including international travel, outside of these areas. The government of Scotland announced stricter measures nationally and a ban on travel between Scotland and rest of UK from 26 December 2020.

On 22 December, the European Commission adopted a 'Recommendation on a coordinated approach to travel and transport in response to the SARS-CoV-2 variant observed in the UK' [44]. The aim of the Commission Recommendation is to have a coordinated approach to travel and transport in response to the SARS-CoV-2 variant observed in the UK to ensure free movement during the pandemic, while discouraging all non-essential travel to limit the further spread of the new variants [45].

Variant 501.V2, South Africa

As of 19 December 2020, a total of 921 922 confirmed COVID-19 cases, including 24 691 deaths, had been reported in South Africa [46]. The country is in its second SARS-CoV-2 epidemic wave (Figure 6) [46,47].

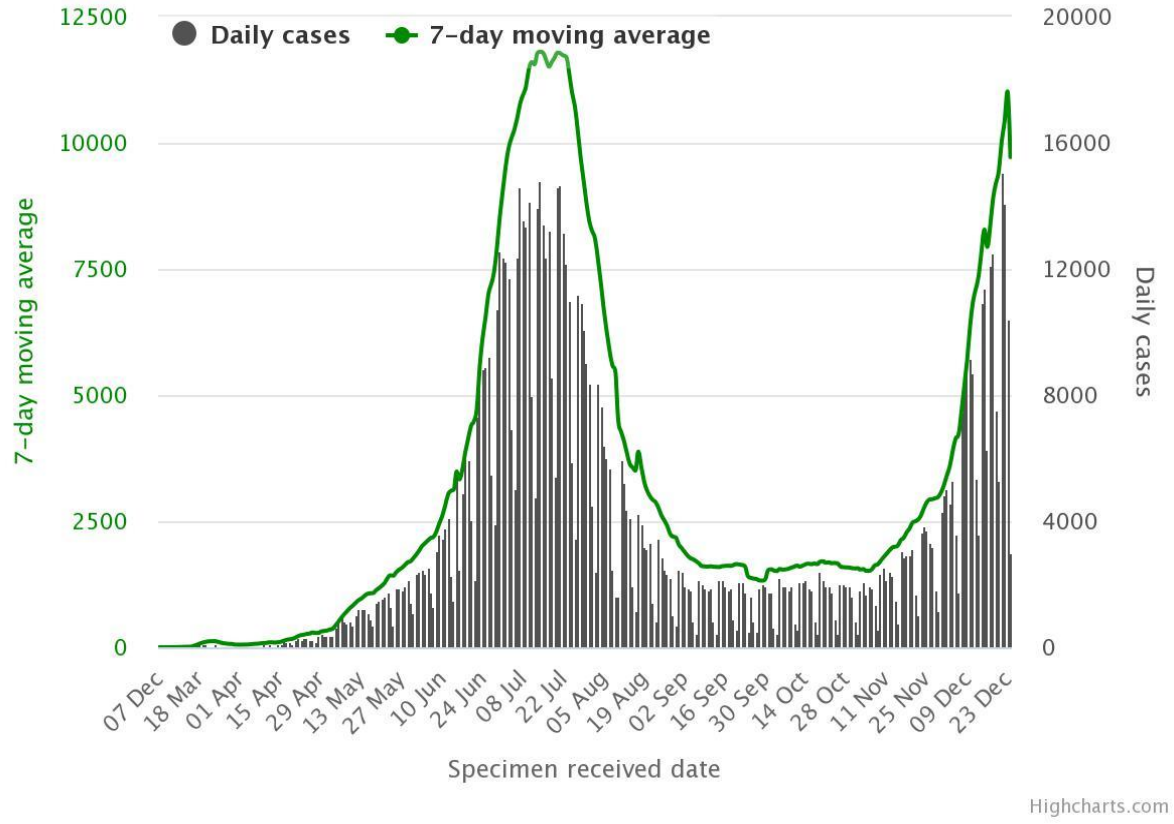
On 18 December 2020, the South African government reported the emergence and rapid increase of a new variant designated 501.V2 [48]. The new variant was detected by the Kwazulu-Natal Research Innovation and Sequencing Platform (KRISP), through routine genomic surveillance of SARS-CoV-2 from samples collected from over 50 different health facilities in Eastern Cape, Western Cape and KwaZulu-Natal. It has multiple changes in the spike protein, including amino-acid modification N501Y which is also present in VOC 202012/01 [49].

Phylogenetic analysis of 2 589 SARS-CoV-2 whole genomes from South Africa collected between 5 March and 25 November 2020 identified 190 sequences of the variant from samples collected between 15 October and 25 November 2020. This analysis indicates that the variant emerged in early August in Nelson Mandela Bay, located on the coast of the Eastern Cape Province. By early November, it was the dominant variant in the Eastern Cape and Western Cape Provinces [50].

Preliminary results indicate that this variant is associated with a higher viral load and faster spread which may be related to higher transmissibility. No evidence is available yet on whether the infection severity is different [51]. The variant emerged in South Africa during the summer season, despite a previously-observed decrease in the circulation of the virus during the summertime in other parts of the world (e.g. Europe).

South Africa has sequenced and published the genomes for 912 samples collected between 1 September and 25 December 2020, with an average delay of 38 days from sampling to publication. So far more than 300 cases with the variant have been confirmed in South Africa [52]. According to analysis performed by KRISP, the variant accounted for almost all cases analysed by genome sequencing in mid-November 2020 [51]. On 22 December 2020, two geographically separate cases of this new variant were detected in the UK [53]. Both are contacts of symptomatic individuals returning from South Africa. On 28 December 2020, one case of this new variant was detected in Finland in a returning traveller from South Africa [30].

Figure 6. Epidemic curve of confirmed COVID-19 cases by day (seven-day moving average), South Africa



Source: National Institute for Communicable Diseases of South Africa - accessed on 25 December 2020.

Epidemiological situation in the EU/EEA and the UK

Detailed epidemiological information on laboratory-confirmed cases reported to The European Surveillance System (TESSy) is published in ECDC's weekly COVID-19 surveillance report and the overview of the epidemiological situation of the COVID-19 pandemic by country is also published in ECDC's weekly COVID-19 country overview.

Overall situation

In ECDC's weekly surveillance report, by the end of week 51 (ending Sunday 20 December 2020), most countries had been seeing a stabilisation or reduction in test positivity and hospital or ICU admissions and/or occupancy due to COVID-19. However, absolute values of these indicators remain high, even where they are stable or decreasing, suggesting that transmission is still widespread (Figure A2, Annex).

Trends in reported cases and testing

For week 51, increases in case notification rates were observed in 14 countries (Cyprus, Czechia, Denmark, Estonia, France, Germany, Ireland, Latvia, Lithuania, the Netherlands, Slovakia, Spain, Sweden and the UK). Case rates among older age groups continued to increase in 12 countries.

Among 24 countries in which weekly test positivity was high (at least 3%), seven countries (Estonia, Ireland, Latvia, Lithuania, the Netherlands, Romania and the UK) observed an increase in test positivity, while it remained stable or had decreased in 17 countries (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czechia, France, Germany, Greece, Hungary, Italy, Luxembourg, Poland, Portugal, Slovakia, Slovenia and Sweden) [54].

Hospitalisation and ICU

For week 51, hospital and/or ICU occupancy and/or new admissions due to COVID-19 were high (at least 25% of the peak level during the pandemic) or had increased compared with the previous week in 30 countries (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the UK [54].

Mortality

Among 29 countries with high 14-day COVID-19 death rates (at least 10 per million), increases were observed in ten (Croatia, Denmark, Estonia, Finland, Germany, Latvia, Lithuania, the Netherlands, Slovakia and United Kingdom). For week 52/2020, all-cause excess mortality data from EU/EEA countries and the UK reported to the EuroMoMo network identified a recent substantial increase in mortality, mainly affecting those aged 45 years and above [55].

Disease background

For additional information on the latest scientific evidence relating to COVID-19, SARS-CoV-2, virus transmission, diagnostic testing, infection, clinical characteristics, risk factors and risk groups, immunity, and vaccines and treatment please visit ECDC's website: https://www.ecdc.europa.eu/en/covid-19/latest-evidence.

Emergence of SARS-CoV-2 variant viruses

Many thousands of variants of SARS-CoV-2 are circulating, and more will emerge over time, most of which will probably have no effect on transmission or disease characteristics. Table 2 summarises selected variants that are, or have been, under investigation (although it is not a comprehensive list of all SARS-CoV-2 variants investigated).

Table 2. Selected SARS-CoV-2 variants

Variant	Definition (amino acid changes)	Potential public health impact of variant	Geographical spread	References
VOC 202012/01	S: **del 69-70**, del 144, **N501Y**, A570D, P681H, T716I, S982A, D1118H	Report of increased transmissibility from the UK.	Prevalent in parts of the UK, cases increasingly detected in other countries.	[56]
501.V2	S: D80A, D215G, E484K, **N501Y** and A701V.	Report of increased transmissibility from South Africa.	Dominant in South Africa, two cases recently detected in the UK.	[50,51,57]
Danish mink variant	S: **del 69-70**, Y453F	Transmission from mink to humans and community spread confirmed, no changes in transmissibility reported.	Prevalent in Denmark. Not detected elsewhere.	[58]
Danish mink cluster 5	S: **del 69-70**, Y453F, I692V, M1229I	Preliminary report of moderate reduction of neutralisation by convalescent sera.	Denmark, not observed since September 2020.	[58]
Various variants with spike amino acid change N439K	S: N439K, often with **del 69-70**	Reports of minor reduction of neutralisation by convalescent sera.	Common in Czechia, Denmark, Ireland, found in lower proportions in many countries.	[59-62]
Nextstrain cluster 20A.EU1	S: A222V	Rapid increase in Spain and then the rest of the EU/EEA at the start of the second wave, probably due to random events and travel patterns.	First observed in Spain, the most common variant in the EU/EEA.	[60]
Nextstrain cluster 20A.EU2	S: S477N N: A376T	Rapid increase in France at the start of the second wave, probably due to founder effects.	First observed in France, prevalent also in Belgium, Czechia, Denmark, Hungary, the Netherlands, Switzerland.	[60]
D614G	S: D614G	Rapid increase during the early stages of the pandemic in the EU/EEA and then worldwide, probably due to a mix of founder effects and increased transmissibility.	Worldwide. All other variants described here are descendant from this one.	[63-66]

Properties of VOC 202012/01

VOC 202012/01 is defined by multiple spike protein changes (deletion 69-70, deletion 144, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H) as well as by mutations in other genomic regions [67]. One of the changes (N501Y) is located within the receptor binding domain (RBD). The variant belongs to Nextstrain clade 20B [68,69], GISAID clade GR [4,70], lineage B.1.1.7 [71,72].

Laboratory findings

Preliminary findings show that there may be an association between infection with the variant and increased viral load. The UK New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) reports that there is a decrease in RT-PCR threshold cycle (Ct) value by around two for this variant compared to other variants, corresponding to an increased viral load by a factor of around four [73]. This evidence is also supported by the number of unique sequencing reads, providing an estimate in increased viral load by around a factor of three [74], though such estimates tend to be less reliable than estimates from RT-PCR. Increased viral load in respiratory samples is likely to be associated with increased shedding of virus and increased transmissibility, but this remains to be confirmed.

There is some evidence indicating that the amino acid change N501Y is associated with increased ACE2 receptor binding strength. A study screened all possible spike protein RBD substitutions using a yeast-surface-display platform, finding an increased binding strength measured as $\log_{10}$ increase in spike-ACE2 complex dissociation constant of 0.24 [75]. This was the third highest increase measured in the study, with only Y453F and N501F providing larger increases. No clear relationship has been established between ACE2 binding and increased transmissibility, but it is plausible that such a relationship exists.

Impact on diagnostic assays

The S-gene deletion at genomic positions 21765-21770, corresponding to residues 69-70 in the spike protein in variant VOC 202012/01 and other variants carrying this mutation, such as mink-related variants from Denmark, may cause some RT-PCR assays targeting the S-gene to produce a negative result (S-gene drop-out). The tri-target (ORF1ab, N, S) COVID-19 TaqPath assay from Thermo Fischer has been reported by the UK to have S-gene dropout for this deletion.

The S-gene drop-out is unlikely to cause an overall false-negative result for SARS-CoV-2 as the S-gene is generally not used by itself for detection of the virus.

The S-gene drop-out can be used to screen for VOC 202012/01 and, in settings with high prevalence of the variant with little or no co-circulation of other variants that cause S-gene drop-out, it can be used as a proxy measure of the incidence of the variant. Sequencing of the S-gene as a minimum is still required to confirm the presence of the variant.

If RT-PCR assays specific to signature mutations for variants of concern become available, these can be used for more rapid and comprehensive screening for specific variants. If such assays are implemented, it is important that the assays are validated for their purpose and that the results are interpreted by staff with molecular biology training. Results should be confirmed by sequencing if possible. If prevention of importation of a variant is a priority, development of such RT-PCR assays is crucial.

Until now, there has not been any report that the new variant viruses would negatively impact rapid antigen detection tests. Since most of the commercially available rapid antigen detection tests are based on the detection of the SARS-CoV-2 nucleoprotein protein, their performance should not be affected by changes in the spike protein. A few rapid antigen detection tests are based on detection of the spike protein and therefore it cannot be ruled out that the identified mutations will not have an effect on them. However, according to the UK, five lateral flow devices, all targeting the nucleocapsid protein which has two amino acid changes for VOC 202012/01 (D3L and S235F), validated by the UK still meet minimum performance criteria for this variant [76].

Evidence for increased transmissibility of VOC 202012/01

Several recent modelling studies based on epidemiological data, including the proportion of VOC 202012/01, indicate that the variant is significantly more transmissible than previously circulating variants, even though there are significant uncertainties regarding the magnitude of the increase. The estimates are given either as an additive increase in the reproductive number (R) or as a multiplicative increase in the transmissibility. It is important to note that any estimated increase in R is specific to the situation where it was measured, in this case the situation in South-East England during the period October–December 2020.

Preliminary findings that there may be an association between infection with the variant and increased viral load indicate the likelihood of increased viral load in respiratory samples, which is probably associated with increased shedding of virus and greater transmissibility.

Modelling studies on the variant VOC 202012/01

NERVTAG reported that based on preliminary analysis of genomic data, an increase could be expected in the case number growth rate for VOC 202012/01 of 71% (95% CI: 67%-75%), which was higher than that for other SARS-CoV-2 variants. In addition, correlation studies estimated an absolute increase in the R-value of between **0.39 and 0.93**.

Using a mixed regression model, the variant frequency was significantly associated with an increase of the time-dependent reproductive number (Rt), estimated by a Bayesian semi-mechanistic transmission model. The increase in Rt was estimated to be **0.74** [95% CI: 0.44-1.29] using a random effect model [56].

Complementary analysis by the Centre for Mathematical Modelling of Infectious Diseases (CMMID) using an age- and regionally structured mathematical model with multiple epidemiological indicators across seven National Health Service (NHS) England regions and genomic surveillance from the COVID-19 Genomics UK Consortium estimated that the variant is **56%** more transmissible (95% CI: 50-74%) than pre-existing circulating variants of SARS-CoV-2. The study does not report that VOC cases were more likely to require hospitalisation or die than cases resulting from pre-existing variants. In addition, four alternative scenarios (increased infectiousness, immune escape, increased susceptibility among children and shorter generation time) have been evaluated against the observed data. The increased infectiousness of the variant was the best able to reproduce the observed relative growth rate of VOC 202012/01 [77] and fit the observed increase in hospitalisations in the NHS regions throughout the East of England, London and the South East in December 2020.

Modelling studies using S-gene drop-out as a proxy for the frequency of VOC 202012/01

Using S-gene drop-out as a proxy for the frequency of VOC 202012/01 during weeks 44–49 2020, the ratio of the weekly growth factors of the S-gene negative cases against S-positive cases was 1.47 (95% CI: 1.34-1.59) [56].

Following additional analysis applying the Bayesian semi-mechanistic transmission model methodology above, the estimated additive effect in a mixed regression model was of the same range, estimated at 0.60 (95% CI: 0.48-0.73) [56].

Possible impact of VOC 202012/01 on vaccine match and effectiveness

There is currently not enough information available to assess whether VOC 202012/01 poses a risk to vaccine match and effectiveness. No phenotypic data are available for the new variant and no data are available on the ability of antibodies

elicited by the vaccines under development to neutralise this variant. As mentioned above, the new virus variant displays several changes in the spike protein, including one in the receptor binding domain (RBD).

Most of the new candidate vaccines are based on the spike protein sequence. It is therefore essential to monitor changes in the spike protein among the circulating SARS-CoV-2 strains and assess possible antigenic changes. Available data from other different mutations in the RBD do not appear to have a significant impact on the ability of sera from subjects vaccinated with the Pfizer/BioNTech mRNA-based vaccine to neutralise such variants [78]. The antigenic characterisation of this new variant is ongoing, and results are expected in the coming weeks. It will be important to carry out surveillance of the field effectiveness of COVID-19 vaccines in use, if possible including variant-virus-specific estimates. Surveillance of primary vaccine failures using variant-virus-specific outcomes may also help in understanding whether there is an impact on vaccine effectiveness.

In addition to antibody-mediated protection, T-cell immunity plays a role in protection against and clearance of COVID-19 virus infections. Although T-cell immunity is being assessed following both SARS-CoV-2 infection and vaccination, it is still unknown to what extent it contributes to protection from infection and disease and whether it can be established as correlate or co-correlate of protection.

Properties of 501.V2 variant

The new SARS-CoV-2 virus variant detected in South Africa is referred to as SARS-CoV-2 variant 501.V2. It is defined by multiple spike protein changes present in all viruses in the cluster (D80A, D215G, E484K, N501Y and A701V), and more recently collected viruses have additional changes [67] (L18F, R246I, K417N, and deletion 242-244) [50]. The deletion may cause issues in some analysis pipelines which may have caused it to be incorrectly excluded in some reported sequences. Three of the changes (K417N, E484K, and N501Y) are located within the RBD. The variant belongs to Nextstrain clade 20C [68,69], GISAID clade GH [4,70], lineage B.1.351.

Possible impact of 501.V2 on vaccine match and effectiveness

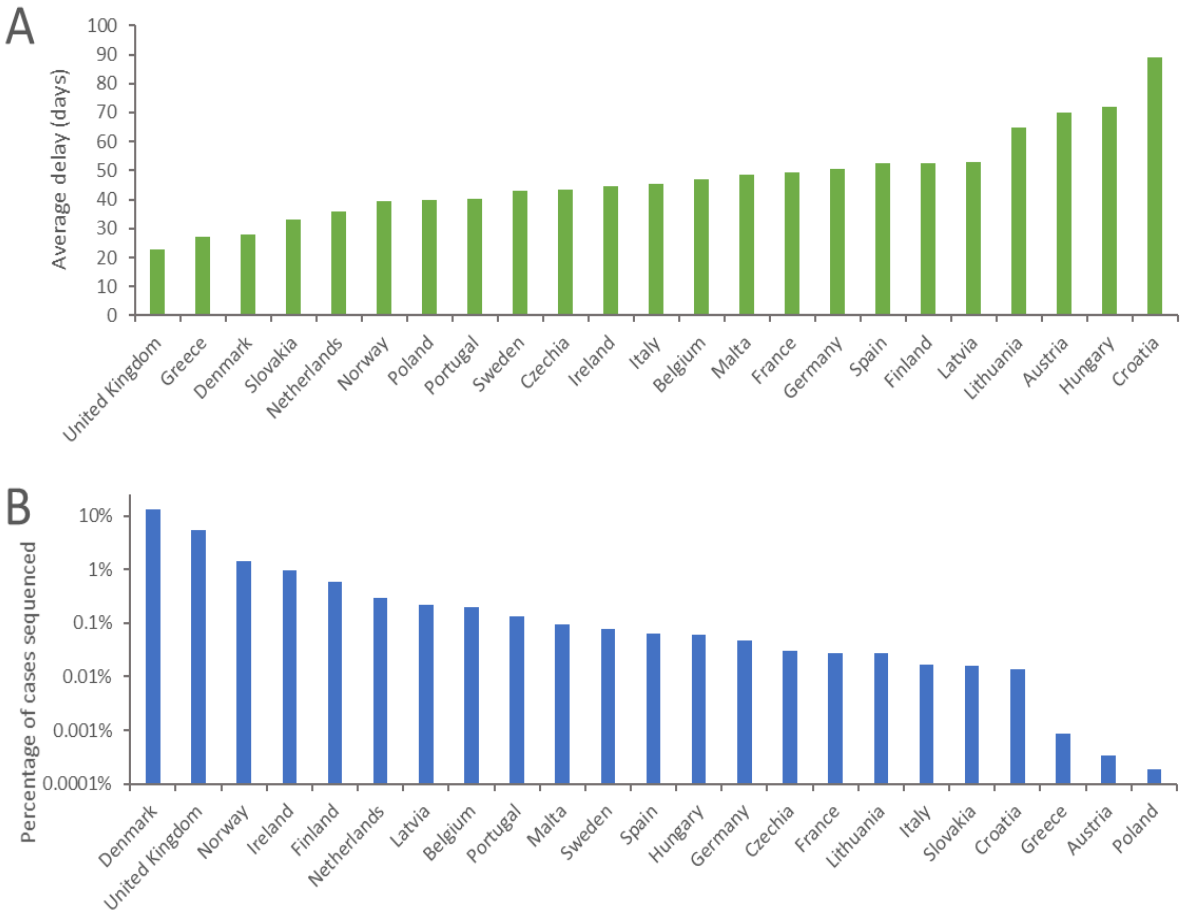
As with VOC 202012/01, there is currently not enough information available to determine whether the 501.V2 poses a possible risk related to vaccine match and effectiveness. The antigenic characterisation of this new variant is ongoing, and results are expected in the coming weeks.

Variant detection requirements and capability in the EU/EEA

To be able to confirm infection with a specific variant, sequencing of the viral genome, or at least the S-gene, is required for samples with a positive test for SARS-CoV-2. Sequencing workflow turnaround times vary. They can be as short as two to three days, but other factors such as transportation of samples to a reference laboratory, sequencing capacity limitations, and data analysis time can heavily influence the actual turnaround time.

The average delay from sample collection to sequence submission, as well as the percentage of cases reported to TESSy that have been sequenced and reported to GISAID EpiCoV since 1 September 2020, is shown in Figure 7. This indicates that the capability of assessing the spread of the variant is very limited in most EU/EEA Member States, with only Denmark demonstrating enough coverage of cases and a sufficiently short delay to be able to detect the introduction of a small number of cases within a month of sampling (13.3% of reported cases sequenced and published with an average delay of 28 days from sample collection.) It also shows that the UK has a high capability for detecting introductions and the emergence of new variants in a timely manner, with 5.3% of cases sequenced and published with an average delay of 23 days. Of all EU/EEA Member States, only Denmark and Norway have sequenced and published more than 1% of cases, and only eight countries have sequenced and published more than 0.1% of cases since 1 September 2020.

Figure 7. Average time from sample collection to sequence publication (A) and percentage of cases reported with sequence (B) in the GISAID EpiCoV database, for samples collected between 1 September 2020 and 27 December 2020, per EU/EEA country having submitted sequenced cases during the period, and the UK



Source: GISAID EpiCoV database (filtered for human SARS-CoV-2 samples only) and TESSy. Cases recorded after 13 December 2020 are not included in the denominator.
Note that all generated sequences are not always uploaded to GISAID EpiCov, which may lead to an underestimation of the ability of some countries to detect the variant through their national genomic surveillance activities. Iceland has reported to ECDC that all cases in the country are sequenced within 48 hours, although these have not been uploaded to GISAID recently.

Risk assessment questions

This assessment is based on information available to ECDC at the time of publication and, unless otherwise stated, refers to the risk that existed at the time of writing. It follows ECDC's rapid risk assessment methodology, with relevant adaptations [79]. The overall risk is determined by a combination of the probability of an event occurring and its consequences (impact) for individuals or the population [79].

This risk assessment addresses the following questions:

- What is the risk associated with the introduction and spread of variants of potential concern in the EU/EEA?
- What is the risk of an increased burden on health systems in the coming weeks?

ECDC risk assessment for the EU/EEA

What is the risk associated with the introduction and spread of variants of potential concern in the EU/EEA?

The risk associated with the introduction and spread of variants of potential concern in the EU/EEA is currently considered to be **high**.

This assessment is based on the following factors:

- The SARS-CoV-2 VOC 202012/01 has been circulating in the UK since at least 20 September 2020. Despite measures being in place throughout the country during part that period, the variant has increased in terms of the number and proportion of all cases in many local areas.
- The variant 501.V2 has been circulating in South Africa since August 2020 and has increased in terms of the number and proportion of cases in local areas and in the country as a whole.
- Cases of SARS-CoV-2 VOC 202012/01 have been reported from Australia, Belgium, Canada, Denmark, Finland, France, Germany, Hong Kong SAR, Japan, Iceland, India, Ireland, Israel, Italy, Jordan, Lebanon, Norway, Portugal, Singapore, South Korea, Spain, Sweden, South Korea, Switzerland and the Netherlands. While most cases reported so far have had epidemiological links to the UK, there are a few cases reported with no travel links to the UK, suggesting local transmission (Table 1). Two cases of 501.V2 have been detected in the United Kingdom in contacts of a person who had travelled to South Africa.
- There is known under-detection of SARS-CoV-2 infection generally, given that many individuals, and particularly those with a milder course of infection or no symptoms, are not tested. Sequencing of SARS-CoV-2 cases that are found to be positive is only performed for a very small minority of cases in most EU/EEA countries, therefore it is highly likely that the number of possible cases of VOC 202012/01 or 501.V2 is under-detected.
- Transmissibility of VOC 202012/01 is estimated to be up to 70% higher than the previously circulating strains of SARS-CoV-2 in the UK. Preliminary results for 501.V2 indicate that the variant is associated with a higher viral load and faster spread, which may be related to higher transmissibility.
- Although some countries have recently enacted temporary travel restrictions, travel between the affected areas of the UK and South Africa and other EU/EEA Member States occurred at moderate levels during the period September-December. Given the substantial circulation of the VOC 202012/01 strain of SARS-CoV-2 in affected areas of the UK with travel links to many other countries within the EU/EEA, and detections of VOC 202012/01 already having occurred in some EU/EEA countries despite low levels of sequencing, the probability of further spread of the SARS-CoV-2 VOC 202012/01 is considered to be **high**. Although 501.V2 has only been detected in the United Kingdom and Finland so far, given its substantial circulation in South Africa over several months and the fact that there have been travel links to countries within the EU/EEA, the probability of further spread is also considered to be **high.**
- Based on data reported by the UK, South Africa and other countries that have detected cases with the SARS-CoV-2 VOC 202012/01 or 501.V2, there is currently no evidence that COVID-19 disease among individuals infected with either of the variant strains is more severe. However, given the evidence that these new variants have an elevated level of transmissibility, it is probable that the impact of the COVID-19 variant strains in terms of increased infections, hospitalisations and deaths would be high, particularly for those in older age groups or with co-morbidities, even if the disease severity is similar. Therefore they will have a **high** impact on populations in which they become established.

In summary, the probability of introduction and further spread of the SARS-CoV-2 VOC 202012/01 and 501.V2 in the EU/EEA is currently assessed as **high**. Although there is no information that infection with these strains is more severe, due to increased transmissibility the impact of COVID-19 disease in terms of hospitalisations and deaths is assessed as **high**, particularly among those in older age groups or with co-morbidities. The overall risk associated with the introduction and further spread of the SARS-CoV-2 VOC 202012/01 and 501.V2 is therefore assessed as **high**.

What is the risk of increased impact on health systems in the coming weeks?

The risk of increased impact on health systems in the coming weeks is currently considered to be **high**.

This assessment is based on the factors below.

- In its risk assessment of 4 December 2020, ECDC anticipated that the increases in travel and social contacts traditionally seen during the end-of-year festive season would be likely to give rise to an increase in cases and hospitalisations, even before the new variants were identified. Modelling indicated that if response measures implemented in October or November were to be lifted on 21 December, a resurgence in COVID-19 hospitalisations could occur as early as the first week of January 2021 [80].
- Since then, the identification of new variants of potential concern with increased transmissibility means that even in the absence of a more severe course of disease in cases infected with the new variants, there would probably be more cases of COVID-19 overall, thereby further increasing the need for hospitalisation (including ICU care) in countries where the new variant becomes established.
- Although not necessarily associated with the variants of concern, as of week 51 hospital and/or ICU occupancy and/or new admissions due to COVID-19 were high or had increased against the previous week in 30 countries, indicating that many health systems are already experiencing high pressure related to COVID-19. Given these factors, if the variants begin to circulate even at low levels in the EU/EEA, the probability of increased impact on health systems would be **high**.
- With strict NPI and other measures in place, the pressure on health systems could be mitigated to an extent, however in the absence of strict NPI measures, the impact on health systems is likely to be **high**.

In summary, the probability of increased demand on health systems in the coming weeks is considered to be **high** due to the festive season and, even higher in countries where the new variants are established. The impact of the increased demand on health systems in considered to be **high** even if current public health measures are maintained. Therefore, the overall risk of increased impact on health systems in the coming weeks is assessed as **high**.

Options for response

There is currently a lack of evidence indicating that the new highly-transmissible variants of the virus mentioned in this rapid risk assessment are widespread in the EU/EEA. However, there is a significant amount of uncertainty, given that sequencing is performed at low levels in many countries and therefore it is probable that there is substantial under-detection.

Irrespective of extent to which the new variants of potential concern are circulating, efficient implementation of non-pharmaceutical measures in response to the epidemiological situation remains essential, until and unless vaccination has been shown to mitigate their impact. As has been seen in the UK, in areas with higher levels of circulation of SARS-CoV-2 VOC 202012/01, stringent measures will probably be required to reduce transmission than in areas with limited or no circulation of the variants.

For countries that have not already confirmed high levels of community transmission of a variant of concern, efforts to delay the spread should mirror those made during the earlier stage of the pandemic:

- perform targeted and representative sequencing of community cases to detect early and monitor the incidence of the variant;
- increase follow-up and testing of people with an epidemiological link to areas with a significantly higher incidence of the variant and sequence samples from such cases;
- enhance targeted contact tracing and isolation of suspected and confirmed cases of the variant;
- alert persons coming from areas with significantly higher incidence of the variant to comply with quarantine measures, as well as testing and self-isolation if they develop symptoms;
- recommend the avoidance of all non-essential travel, in particular to areas with a significantly higher incidence of the variant.

Surveillance, testing and detection

Member States should continue to monitor for abrupt changes in rates of transmission or disease severity as part of the process of identifying and assessing the impact of variants. Data analysis and assessment of the local, regional and national situation should be performed to identify areas with a rapidly changing epidemiology.

Testing and sequencing efforts should be coordinated regionally and nationally. All laboratories should be requested to report their results to the national public health institute that coordinates the collection of information reported to ECDC and the World Health Organization (WHO) in a timely manner.

National public health authorities should notify cases of the new variant as well as any other new SARS-CoV-2 variants of potential concern through the Early Warning and Response System (EWRS) and TESSy for case-based surveillance and aggregate reporting, which has been adapted for this purpose.

The use of rapid antigen detection tests might increase the speed with which cases can be identified for further sampling and sequencing to confirm variant viruses (e.g. cases with travel or other links to areas known to be affected). However, the increased use of rapid antigen detection tests in general might have a negative impact on the number of specimens available for sequencing. Therefore, countries need to identify mechanisms to sample people with a positive antigen test for further analysis of the virus (e.g. by implementing sentinel-like representative surveillance.)

Detection of variant viruses

For the VOC 202012/01 a negative S-gene result for multiplex RT-PCR assays, with positive results for the other targets, has been used as an indicator for the variant being present. For example, for the tri-plex (ORF1ab, N, S) COVID-19 TaqPath assay from Thermo Fischer, the S-gene component is negative for the variant while the other two components are positive. This S-gene drop-out could be used as an indicator to screen for the variant. However, it should be noted that this drop-out is not exclusive to VOC 202012/01, and confirmation using sequencing is always recommended. The S-gene drop-out does not occur for 501.V2.

Sequences should be uploaded to the GISAID EpiCoV database to enable multi-country analysis of the generated sequences. This submission puts further resource requirements on the laboratories but is very important for assessing the prevalence of known variants, as well as for the detection of novel ones.

Member States with sequencing capacity are advised to reinforce their high-throughput sequencing (HTS) to facilitate the detection of this and other variant viruses. For Member States without HTS capacity or unable to implement sequencing of SARS-CoV-2, support to perform HTS can be provided through the WHO Reference Laboratory Network or the ECDC Sequencing Contract. Refer to ECDC guidance on sequencing of SARS-CoV-2 for an overview of technologies and contacts to reference laboratories [81]. A joint ECDC and WHO Regional Office for Europe guidance document on influenza sentinel surveillance during COVID-19 outlines sequencing of representative specimens of influenza and SARS-CoV-2 from established influenza-related sentinel systems [82].

Selection of samples should aim for a good representation of the population (geographical distribution, age groups, etc.) If sequencing capacity is limited to such an extent that a representative sample of a significant proportion of cases cannot be sequenced in a timely fashion, Member States may consider targeting sequencing efforts towards cases where epidemiological, clinical or microbiological information raises suspicion of a variant with increased transmissibility, or other properties of concern. Such information includes:

- travel history to countries where such variants are prevalent (e.g. the UK for VOC 202012/01 or South Africa for 501.V2) or close contacts to cases with travel history to such countries;
- patterns in RT-PCR detection assays that indicate the presence of a mutation in such a variant (e.g. negative result in an S-gene detection assay known to be affected by the spike protein deletions present in VOC 202012/01);
- cases involved in a local increase in COVID-19 without any epidemiological explanation (including but not limited to: cases associated with animal contact, particularly mustelids; recent failure of public health measures that were previously controlling or reducing disease rate; sudden increases in hospitalisation rate).

At present, no specific protocols are available for targeted PCR assays to detect VOC 202012/01 or 501.V2. If RT-PCR assays become available that are specific to signature mutations for variants of concern, these can be used for more rapid and comprehensive screening of specific variants. If prevention of importation of a variant is a priority, development of such RT-PCR assays is crucial.

Monitoring of chronic cases

Chronic and prolonged infections have been reported, some of them in patients with suppressed or compromised immune system [83]. Such infections with persistent low-level virus replication, prolonged infections, and relapses of high virus loads may lead to intra-host virus evolution and the emergence of immune escape variants [84]. It is therefore recommended that cases of chronic infections or virus rebound be followed carefully and sequence isolates detected in such cases over time. SARS-CoV-2 infections in patients with HIV need to be further monitored to identify persistent infections.

Vaccination and reinfection

Vaccination against COVID-19 is starting across the EU/EEA from the end of December 2020. The roll-out of vaccination will probably contribute to the response, although vaccine doses are still only available in limited supply and this will continue to be the case in the short term. COVID-19-vaccinated individuals need to be closely monitored for vaccination failure and breakthrough infections and virus isolates from these cases should be sequenced and reported, irrespective of the strain identified.

Reports of suspected cases of COVID-19 reinfection also need to be investigated and sequence analysis of virus isolates from these cases should be initiated.

Mechanisms for antigenic characterisation to confirm or exclude vaccine escape mutants need to be established to support any need for reassessment of the vaccine composition and strategy.

Environmental sampling

Virus detection and quantification in sewage by RT-PCR with subsequent deep sequencing and minority variant analysis could theoretically be an additional source of information to identify and assess the circulation of new variant viruses in the population. Such systems require validation, including for sensitivity and accuracy for monitoring mixed populations of variants, and should not be implemented until such validation has been undertaken. They are usually not a standard part of regular surveillance activities.

Antigenic characterisation of variant viruses

SARS-CoV-2 genetic evolution has the potential to impact the antigenic properties of the virus, therefore methods for antigenic characterisation should be urgently established if not already in place. Mechanisms need to be developed to identify isolates for these analyses, based on aspects such as genetic divergence.

Measures to contain or reduce transmission

Advice against non-essential travel, quarantine and testing of travellers from affected areas can be considered by countries in which these variants have not been detected and where a containment strategy is considered appropriate and feasible. ECDC will continue to monitor and report on new affected areas in collaboration with the EU/EEA Member States.

In addition to delaying or reducing the importation of cases, measures should focus on the following:

- identifying probable COVID-19 cases with an epidemiological link to cases positive for the new variants or a travel history to areas known to be affected in order to test and isolate them and follow up their contacts;
- continuing to advise the population on the need for NPIs in accordance with the local level of transmission and national policies;
- considering guidance on the avoidance of non-essential travel (regional, national and international) and social activities.

Countries that have detected these variants of concern within their borders may seek to rapidly identify the extent of transmission and assess whether containment of further transmission is possible through rapid and comprehensive testing, contact tracing, and isolation. Advice against non-essential travel, quarantine and targeted testing of travellers from affected areas within a country may still be considered while this assessment is being made.

Countries having ascertained that containment is no longer an option are advised to pursue aggressive mitigation strategies, deploying a combination of enhanced epidemiological surveillance, testing, characterisation and detection, and the stringent implementation of NPIs. Even though in the short-to-medium term the roll-out of vaccination will probably contribute to the response, in the short term the supply of vaccine doses is and will continue to be limited [85]. The selection of NPIs implemented should be determined based upon the overall levels of SARS-CoV-2 transmission, current healthcare capacity usage, and, if feasible, a careful assessment of the transmission dynamics of the new variant. While information is still being gathered on the new variant in the UK, it is advised to err on the side of caution. Where a potentially more transmissible variant is circulating, a more stringent set of NPI measures may be required to reduce the level of transmission.

Considerations for school settings

Age-specific data for areas with and without high VOC 202012/01 circulation are still pending, but it has been observed that overall SARS-CoV-2 test positivity rates were highest among secondary school-age children in England in the week 12–18 December [86], a period during which schools were open, while many other measures were in place. Moreover, the percentage testing positive increased both for primary and secondary school-age children and for young adults during this period when schools were open. Rising case numbers among children, especially secondary school-age children, may relate to infection occurring in community and/or in school settings. For pre-existing strains of SARS-CoV-2, it has been noted that incidence of COVID-19 in school settings appears to be impacted by overall levels of community SARS-CoV-2 transmission [87].

A pre-print modelling study, in which it was estimated that VOC 202012/01 is 56% more transmissible than pre-existing variants of SARS-CoV-2, has suggested that national lockdown measures similar to those in place in November 2020 in England would be insufficient to reduce R_t below 1, unless educational institutions are also closed [77].

School closures would probably be an effective NPI measure if VOC 202012/01 is more transmissible in children, however the modelling study assessed school and university closures broadly together and did not assess the specific effectiveness of closing individual educational institutions (primary school, secondary school, or university). The negative physical, mental health and educational impact caused by proactive school closures on children, notably more vulnerable children, are substantial [87]. Thus, a decision to close schools to control the pandemic should be used as a last resort. Countries should consider using the current period of holiday-related school closures to assess the additional measures might need to be implemented. Further details on the range of in-school NPI measures relevant to EU settings can be found in ECDC's document 'COVID-19 in children and the role of school settings in transmission, first update' [87].

Variant virus evaluation framework

In order to have a full picture and a better understanding of the genomic evolution of SARS-CoV-2, a generic evaluation framework should be developed to be applied for the emergence of such variant viruses.

This framework aims to develop standardised mechanisms, in partnership with global stakeholders, including triggers to investigate and assess newly emerging SARS-CoV-2 variants of potential concern in terms of animal reservoirs, antigenic characteristics, transmissibility, infection severity, cross-protection and the need to adapt vaccine strain recommendations.

Criteria that could be considered for the development of such a framework:

- changing clinical presentation (e.g. infection severity) and epidemiological profile (e.g. increase in morbidity and mortality);
- presence of known genetic markers related to receptor binding, infectivity, severity, etc.;
- changed antigenic characteristics suggested by an increase in re-infections or breakthrough infections following vaccination;
- transmissibility between humans;
- binding properties to human receptor;
- cross-protection, susceptibility and immunity of the population, vaccine coverage, vaccine product use;
- impact on available vaccines;
- impact on available treatment (e.g. antiviral susceptibility of viruses);
- Probable animal reservoir (species) being a risk for adaptive mutations and ongoing source of infection for humans (e.g. mink).

Knowledge gaps

There are currently many uncertainties and knowledge gaps related to the impact of the new VOC 202012/01 or other variants of relevance (i.e. 501V.2), including the introduction and geographical spread across the EU/EEA, affected age-groups, transmissibility and severity, as well as the overall impact of the epidemiology of the disease on a population level, including reinfection and vaccination. Epidemiological and phylodynamic analyses together with antigenic and genetic characterisation analyses are urgently needed.

Limitations

- This assessment is based on data available to ECDC as of 26 December 2020. There are still very limited antigenic and phenotypic data and epidemiological follow-up data on most affected population groups, transmissibility, and potential impact on infection severity is still being gathered.
- Not all people with COVID-19-like symptoms or contacts of confirmed cases are being tested for SARS-CoV2, so the notified cases are an underestimation of the true numbers unless population-wide testing approaches are taken.
- Sequence data are not generated for all confirmed COVID-19 cases and sequence information therefore might not be representative of all circulating SARS-CoV-2 viruses across a country.
- Sequence data generation and analysis both require time to be performed. This, together with the time required to upload to the GISAID database and share publicly means that there may be a substantial lag in the data available to fully assess the occurrence and/or spread of this mutation.
- The epidemiological data used in this assessment are dependent on availability from Member States through surveillance reporting or publicly available websites.
- The data not only reflect the epidemiological situation but are also dependent on local testing strategies and local surveillance systems. It is also important to consider the lag time between infection, symptoms, diagnosis, case notification, death and death notification.
- The effects and impact of lifting or imposing response measures may take weeks to be reflected in the population's disease rates. Assessing the impact of response measures is complex as many countries have lifted or relaxed multiple measures simultaneously at different times since the beginning of the pandemic.
- Changes in individual behaviour, compliance with measures, and cultural, societal, and economic factors all play a role in the dynamics of disease transmission.
- The assessment of the epidemiological situation and the effectiveness of the control measures should therefore be interpreted with caution. Moreover, such assessment requires careful consideration of the national and subnational contexts.

Source and date of request

ECDC internal decision, 22 December 2020.

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Disclaimer

ECDC issues this risk assessment document based on an internal decision and in accordance with Article 10 of Decision No 1082/13/EC and Article 7(1) of Regulation (EC) No 851/2004 establishing a European centre for disease prevention and control (ECDC). In the framework of ECDC's mandate, the specific purpose of an ECDC risk assessment is to present different options on a certain matter. The responsibility on the choice of which option to pursue and which actions to take, including the adoption of mandatory rules or guidelines, lies exclusively with the EU/EEA Member States. In its activities, ECDC strives to ensure its independence, high scientific quality, transparency and efficiency.

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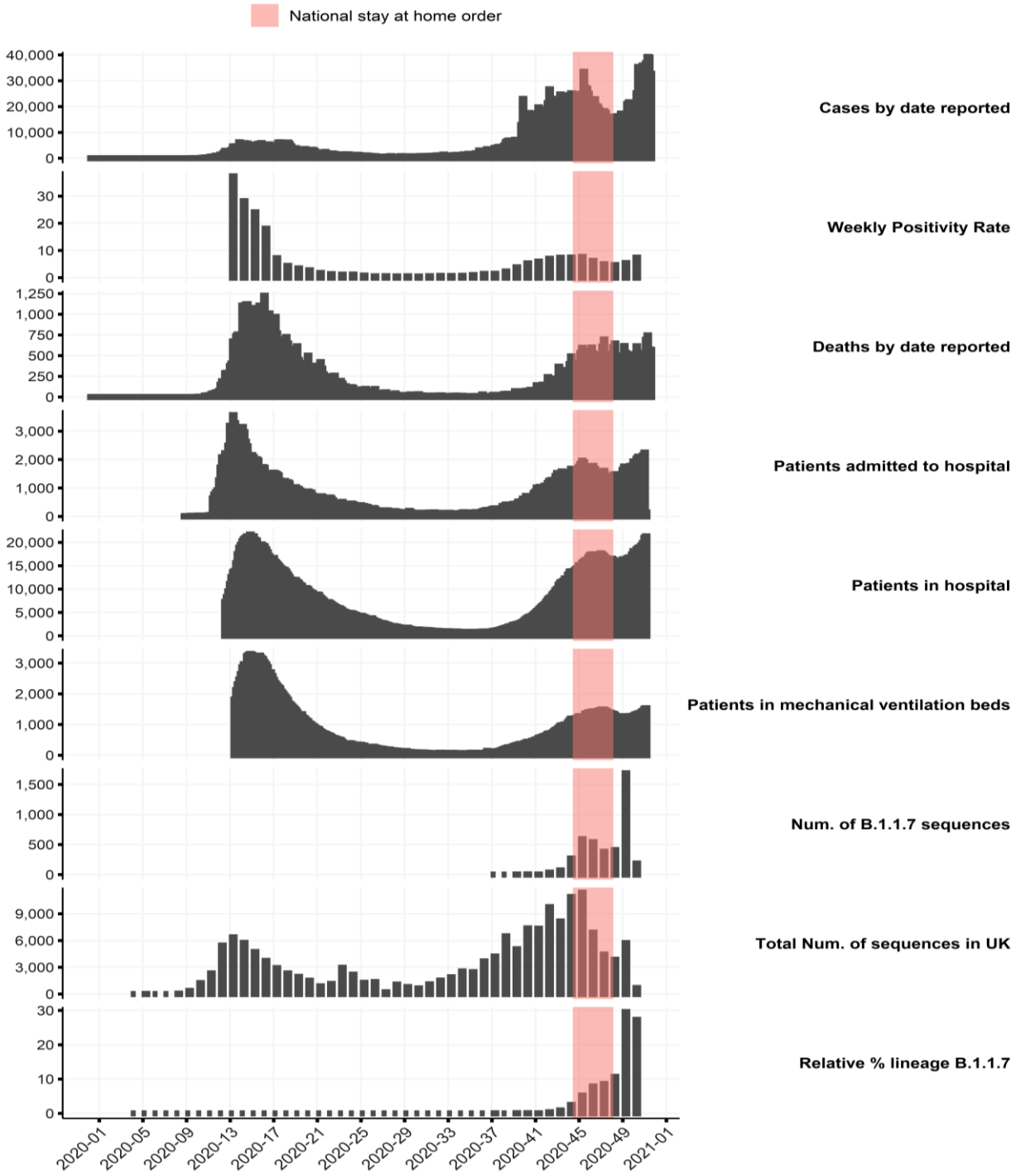
Annex

Figure A1. Multiple daily epidemiological and weekly laboratory and genomic indicators of interest by date in United Kingdom, as of 26 of December 2020, and latest national stay-at-home order in November 2020



***Sources**: The national stay-at-home order in November 2020 was preceded by regional measures not reported in this figure which had been implemented since October 2020. Epidemiological indicators are retrieved as of 26 December 2020 ('Cases by date reported', 'Deaths within 28 days of positive test by date reported', 'Patients admitted to hospital', 'Patients in hospital' and 'Patients in mechanical ventilation beds') [2]. The source of weekly positive rate time series is Data on testing for COVID-19 by week and country as of week 51 [88]. The weekly indicators on genomic data presented in the three bottom panels are computed using metadata file with latest released sequences from the COVID-19 Genomics UK Consortium data hub as of 24 December 2020 [89].*

Figure A2. 14-day COVID-19 case and death notification rates in the EU/EEA and the UK, as of 20 December 2020