

# SARS-CoV-2 – increased circulation of variants of concern and vaccine rollout in the EU/EEA, 14th update

15 February 2021

## Summary

Several EU/EEA countries have observed a decline in the overall incidence of SARS-CoV-2 in recent weeks, most probably due to the impact of tightened non-pharmaceutical interventions (NPIs). Nonetheless, the epidemiological situation is still of serious concern across the EU/EEA, with the majority of countries still experiencing high or increasing notification rates in older age groups and/or high death rates. Although vaccine rollout has started in all EU/EEA countries, targeting priority groups based on their risk of developing severe disease (the elderly and residents in long-term care facilities) as well as healthcare and other front-line workers, it is still too early to detect an impact on COVID-19 mortality or hospitalisations.

While most countries are currently seeing a decline in overall infections as a response to NPIs, the introduction and increased spread of new SARS-CoV-2 variants first identified in the United Kingdom (B.1.1.7), South Africa (B.1.351) and Brazil (P.1) has raised concerns. As suggested by recent anti-lockdown protests and civil disturbances in some European cities, pandemic fatigue could adversely affect the continued acceptance of and compliance with NPIs by the population.

Since 21 January 2021, EU/EEA countries have observed a substantial increase in the number and proportion of SARS-CoV-2 cases of the B.1.1.7 variant, first reported in the United Kingdom. Ireland reports B.1.1.7 to be the dominant circulating SARS-CoV-2 strain and, based on growth trajectories observed, several other countries are expecting a similar situation in the coming weeks. The variant B.1.351 has also been increasingly reported in EU/EEA countries, often, but not only, linked to travel, and it has also been associated with outbreaks. The variant P.1 is so far being reported at lower levels, possibly because it is mainly linked to travel exchange with Brazil, where it appears to be spreading.

The B.1.1.7 variant appears to be more transmissible than the previously predominant circulating strains and may cause more severe infection. Several countries where the variant has become dominant have seen rapid increases in incidence. This has resulted in increased hospitalisations, overstretched health systems and excess mortality. B.1.351 is also associated with increased transmissibility. In addition, there is evidence pointing to the potential for reduced effectiveness for some of the COVID-19 vaccines with this variant.

## Risk assessed in this update

Due to the increased transmissibility, the evidence of increased severity and the potential for the existing licensed COVID-19 vaccines to be partially or significantly less effective against a variant of concern (VOC), combined with the high probability that the proportion of SARS-CoV-2 cases due to B.1.1.7 (and possibly also B.1.351 and P.1) will increase, the risk associated with further spread of the SARS-CoV-2 VOCs in the EU/EEA is currently assessed as **high to very high** for the overall population and **very high** for vulnerable individuals.

Modelling analysis shows that unless NPIs continue, or are strengthened in terms of compliance during the coming months, a significant increase in COVID-19-related cases and deaths in the EU/EEA should be anticipated. Although vaccination will mitigate the effect of replacement with more transmissible variants, and seasonality could potentially reduce transmission during the summer months, easing measures prematurely will lead to a

rapid increase in incidence rates, detection of severe cases and mortality. Delays in vaccine procurement, distribution and administration, should they occur, would also delay the option to ease NPIs. Rapid vaccine deployment among priority groups is needed to reduce hospitalisations, ICU admissions and deaths due to COVID-19.

## Options for response

Based on the current epidemiological situation in the EU/EEA with the increased circulation of more transmissible variants, immediate, strong and decisive public health interventions are essential to control transmission and safeguard healthcare capacity. This will involve all EU/EEA countries ensuring that layered NPIs are strengthened and maintained in the coming months in order to reduce SARS-CoV-2 incidence to the lowest levels possible, thereby also minimising the opportunities for new variants to emerge.

Optimising the implementation of NPIs, including issues related to community use of facemasks and school settings, is essential. Test and trace approaches, including strong surveillance and sequencing, remain the cornerstones of the response. Travel should not be undertaken by people who are ill or who have had recent contact with COVID-19 cases. Furthermore, ECDC recommends that non-essential travel should be avoided as part of general physical distancing measures in the community. In time, targeted and robust vaccination programmes will enable the easing of NPIs.

Variants against which current licensed vaccines might have a reduced efficacy, as observed for some vaccines with the B.1.351 variant first identified in South Africa, will probably continue to emerge in the future. This should be mitigated by designing next-generation vaccines with mutated spike sequences and using alternative viral antigens. Consideration should also be given to their use either as booster doses for those vaccines which have already been developed and are being administered, or, if needed, for the primary series.

Increasing levels of pandemic fatigue need to be properly addressed as a matter of urgency if further waves of infection are to be avoided and population compliance is to be maintained. Public expectations about the likelihood of easing restrictions need to be carefully managed. To facilitate this, authorities should make systematic efforts to ensure that they have a good understanding of community perceptions of the pandemic, the NPIs in place and COVID-19 vaccine acceptance through ongoing behavioural research.

## Event background

The timeline of the major events in the COVID-19 pandemic can be found on ECDC's website:

<https://www.ecdc.europa.eu/en/covid-19/timeline-ecdc-response>. This risk assessment provides an overall update on the COVID-19 situation in the EU/EEA, including latest data on the situation with SARS-CoV-2 VOCs covered by previous targeted risk assessments [1-3].

## Epidemiological situation

The latest available data on the number of cases and deaths globally is published daily on ECDC's website:

<https://www.ecdc.europa.eu/en/covid-19/situation-updates>

As of 11 February 2021, EU/EEA countries have reported 20 478 718 cases and 495 672 deaths (representing 19% of all cases and 21% of all deaths reported worldwide during this period) due to COVID-19.

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 in relation to the COVID-19 pandemic by country is also published in ECDC's weekly COVID-19 country overview.

## Trends in reported cases, testing, hospitalisation, and mortality

By 7 February 2021, the 14-day case notification rate for the EU/EEA was 359 (country range: 8–1 190) per 100 000 population; this rate has been decreasing for three weeks. Between 14 January 2021 and 10 February 2021 (four weeks), the number of countries reporting increased 14-day case notification rates decreased from 13 to eight (Bulgaria, Czechia, Estonia, Greece, Hungary, Latvia, Luxembourg, and Slovakia). The number of countries with increasing test positivity rates decreased from seven to three (Bulgaria, Estonia, and Poland).

The number of countries reporting increasing mortality rates decreased from the previously-reported 10 to two (Slovakia and Spain). However, the pressure on healthcare systems remains high, with two countries reporting

increases in hospitalisation and ICU admission and/or occupancy rates (Belgium and Greece) and all EU/EEA countries<sup>1</sup> except Iceland and Liechtenstein reporting high or increasing rates of hospitalisation and/or occupancy.

For week 2021-05, all-cause excess mortality data reported from participating European countries to the EuroMOMO network identified a substantial excess mortality in some countries (Netherlands, Portugal, and Spain), while in other countries mortality levels were normal. The increased excess all-cause mortality is mainly affecting those aged 45 years and above.

## SARS-CoV-2 variants of concern

The SARS-CoV-2 VOCs which are the focus for this risk assessment include B.1.1.7, as well as the B.1.1.7 variant with an additional E484K mutation; B.1.351 and P.1. Additional information on the characteristics of these variants is provided in the Disease Background section below. Further details on other mutations and variants are provided in previous ECDC risk assessments [2,3].

The VOC **B.1.1.7**, first reported by the UK, continues to predominate in cases reported in the UK, and has been registered in 83 countries globally (Figure A1, Annex). This variant belongs to Nextstrain clade 20B [4,5], GISAID clade GR [6,7] and PANGO lineage B.1.1.7 [8,9]. B.1.1.7 is defined by multiple spike protein changes (deletion 69-70, deletion 144, amino acid change N501Y, A570D, D614G, P681H, T716I, S982A, D1118H) as well as by mutations in other genomic regions [10].

The B.1.1.7 variant has now been detected in all EU/EEA countries that have any significant detection capability (Figure A2, Annex). Since its identification, approximately 57 400 cases have been reported globally, including around 5 700 cases in the EU/EEA. Public Health England has reported 28 genomically confirmed B.1.1.7 cases with an additional mutation (E484K) [11]. This mutation is also carried by the B.1.351 and P.1 variants. Preliminary phylogenetic analysis suggests at least three separate acquisition events.

According to PCR-based screening and whole genome sequencing, the proportion of cases caused by B.1.1.7 has risen in recent weeks [12] and is now very high in some EU/EEA countries, indicating that community transmission is ongoing in many, if not all, EU/EEA countries. European countries indicate the following proportions of B.1.1.7 among all cases sequenced in recent weeks: Denmark 27% [13], France 13.2% (based on ThermoFisher scientific screening, before sequencing confirmation) [14], Germany 5.6% [15], Ireland 75%, Italy 17.8% [16], the Netherlands >30% [17], Poland 9%, Portugal 45%, Spain 0.4–53% (depending on the region) [18], Sweden 11% [19]. These figures vary in terms of sampling strategy used, time-period covered and screening method and, therefore, cannot be directly compared. In countries carrying out sequencing during recent weeks, the proportion of B.1.1.7 cases among all sequenced cases appears to be almost doubling each week, strongly suggesting that the variant is on course to become more dominant than the strains previously circulating in the EU. In the UK, the S-gene dropout proxy for B.1.1.7 cases went from less than 5% of all positive SARS-CoV-2 cases to more than 60% in less than six weeks during November to mid-December 2020, resulting in sharp increases in incidence, hospitalisations and mortality [11]. Environmental surveillance from sewage systems also provides useful insights into the rapidity with which B.1.1.7 can spread. In recent sewage treatment plant samples in Lower Austria, B.1.1.7 accounted for up to 99% of SARS-CoV-2-RNA, while in recent sewage samples from Vienna B.1.1.7 accounted for 30–50% [20].

The **B.1.351** variant, first identified in South Africa, belongs to Nextstrain clade 20C [4,5], GISAID clade GH [6,7], and PANGO lineage B.1.351 [8,9]. B.1.351 is defined by multiple spike protein changes present in all viruses in the cluster (amino acid change D80A, D215G, E484K, N501Y and A701V), and more recently collected viruses have additional changes [10] (amino acid change L18F, R246I, K417N, and deletion 242-244) [21]. Three of the changes (amino acid change K417N, E484K, and N501Y) are located within the receptor-binding domain.

As of 11 February 2021, according to media and official sources, the variant B.1.351 has been identified in 40 countries and approximately 1 400 cases have been reported globally (Figure A3 in Annex). More than 90% of cases sequenced in South Africa since late November have been due to this variant and there is evidence that the variant has been circulating since at least November in Mozambique as well, indicating that it may be widespread in other countries in the region where sequencing is not performed or publicly reported [21,22]. In the EU/EEA, around 350 cases have been identified in 16 countries (Figure A4 in Annex). Although some cases reported in EU/EEA are linked to travel, cases are increasingly reported without an epidemiological link. A large number of cases (295) of this variant have recently been reported in Austria, mostly concentrated in the region of Tyrol; mass testing and tracing is ongoing in response to this increase, and mandatory testing has been implemented for any person leaving Tyrol [23]. Environmental surveillance of a recent sewage sample from a village in Tyrol shows 70% of RNA belonging to lineage B.1.351 [20]. Belgium has reported clusters of cases with this variant in long-term care facilities and one school [24-27]. A rapid upsurge in cases of the variant has also been reported in the French Overseas Territory Mayotte [28]. In countries reporting sequencing results, B.1.351 still comprises <1% of cases sequenced. However, it is unknown if this variant has selective advantage over B.1.1.7, and thereby the potential to compete in settings where the two variants co-circulate.

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<sup>1</sup> Spain's hospital and ICU data are truncated and ECDC has assumed ICU occupancy remains high

Variant **P.1**, first reported by Japan in returning travellers from Brazil, and then later in Brazil, belongs to Nextstrain clade 20B [4,5], GISAID clade GR [6,7] and PANGO lineage P.1. The variant has 11 amino acid changes in the spike protein compared to its ancestral lineage B.1.1.28, three of which are located in the receptor-binding domain. The full set of spike protein changes for the variant are L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, H655Y, T1027I, and V1176F.

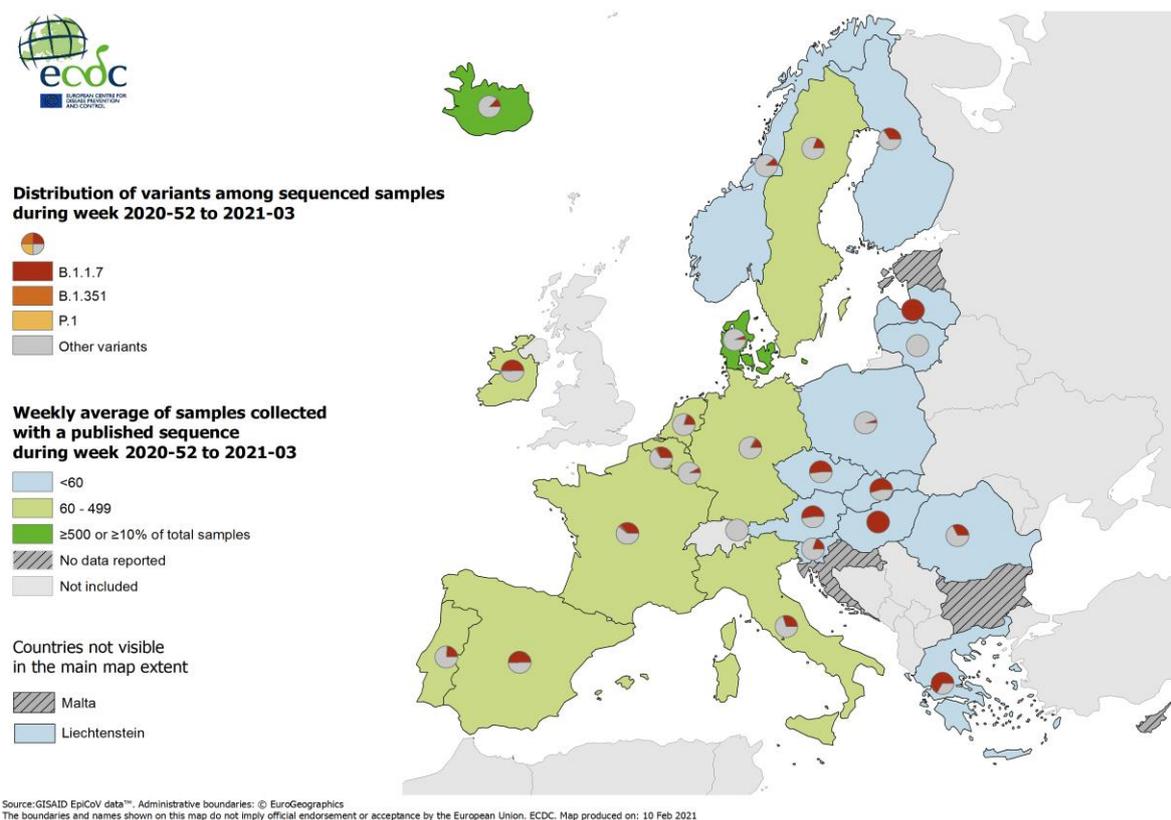
The P.1 variant has since been reported sporadically in travellers elsewhere. As of 11 February 2021, P.1 has been identified in 17 countries and approximately 200 cases have been reported globally. In the EU/EEA, around 30 cases have been identified in five countries and areas (France, including La Reunion, Germany, Italy, the Netherlands and Spain). In countries reporting sequencing results, P.1 still comprises far less than <1% of cases sequenced. There is currently no detected ongoing community transmission of this variant in the EU/EEA but this cannot be excluded, given the current levels of genome sequencing activity.

## Sequencing capacity

Sequencing capacity varies greatly across the EU/EEA; the rate of SARS-CoV-2-positive cases sequenced and reported to GISAID EpiCoV by 11 February for the period of week 52-2020 to week 03-2021 was lower than the recommended level of 10% in all but two EU/EEA countries (Denmark and Iceland) (Figure 1). As efforts continue to perform sequencing and increase capacity, additional VOCs will be detected within the EU/EEA that will require surveillance and evaluation for immune escape. It is important to note that sequencing data are significantly delayed and the proportions displayed in Figure 1 represent the situation two weeks ago for the countries that submitted data to GISAID.

Limited sequencing capacity and/or lack of reporting of variant strains does not mean that they are not circulating in a country. Many EU/EEA countries are still sequencing at very low levels and therefore there is no reason to assume that countries that have not performed screening or reported their results have a lower proportion of this variant circulating.

**Figure 1. Distribution of SARS-CoV-2 variants and average number of samples sequenced in EU/EEA countries, weeks 2020-52 to 2021-03**



*Note: SARS-CoV-2 variant data is collected by the ECDC Epidemic Intelligence team from various sources. Data are subject to retrospective corrections. Users are advised to use all data with caution and be aware of data limitations.*

## Non-pharmaceutical interventions

ECDC collects information on non-pharmaceutical interventions (NPIs) implemented in EU/EEA countries in response to the COVID-19 pandemic. Detailed information on the measures implemented at national level are available in the [Weekly COVID-19 country overview](#). In addition, a repository with all active NPIs from 1 September 2020 for each EU/EEA country is made publicly available by ECDC and the Joint Research Centre (JRC) at <https://covid-statistics.jrc.ec.europa.eu/RMeasures>.

Selected NPIs extracted from the ECDC-JRC Response Measure Database (ECDC-JRC RMD) and related to travel measures for international travellers (testing and quarantining) and the closure of educational institutions are provided in Table 1.

**Table 1. Measures related to international travel and closure of educational institutions currently applied by EU/EEA countries, as of 9 February 2021**

EU/EEA country	International travellers		Closure of educational institutions*			
	Test upon entry or shortly before	Quarantine after arrival	Day-care	Primary schools	Secondary schools	Higher education
<b>Austria</b>	✓	✓			✓	✓
<b>Belgium</b>	✓	✓			Regionally	✓
<b>Bulgaria</b>	✓	✓			Partially*	✓
<b>Croatia</b>	✓	May apply				
<b>Cyprus</b>	✓	✓			Partially*	✓
<b>Czechia</b>	✓	May apply		✓	✓	✓
<b>Denmark</b>	✓	✓			✓	✓
<b>Estonia</b>	✓	Alternative to testing				
<b>Finland</b>	✓	✓			Regionally	Regionally
<b>France</b>	✓					✓
<b>Germany</b>	✓	✓	Partially*	Regionally	Regionally	
<b>Greece</b>	✓	✓		Regionally	Partially*	✓
<b>Hungary</b>	✓	Alternative to testing			✓	✓
<b>Iceland</b>	✓	Alternative to testing				
<b>Ireland</b>	✓	✓	Partially*	✓	✓	✓
<b>Italy</b>	✓	✓	Regionally	Regionally	Partially*, **	
<b>Latvia</b>	✓	✓		Partially*	✓	✓
<b>Liechtenstein</b>		✓				
<b>Lithuania</b>	✓	✓		✓	✓	✓
<b>Luxembourg</b>	✓					
<b>Malta</b>	✓					
<b>Netherlands</b>	✓	✓	Partially*		✓	✓
<b>Norway</b>	✓	✓			Regionally	Partially*, **
<b>Poland</b>	✓	Alternative to testing		Partially*	✓	✓
<b>Portugal</b>	✓	May apply	✓	✓	✓	✓
<b>Romania</b>	May apply	✓			Partially*	✓
<b>Slovakia</b>	✓	✓		Partially*	Partially*	✓
<b>Slovenia</b>	May apply	May apply		Partially*	✓	✓
<b>Spain</b>	✓					Regionally
<b>Sweden</b>	✓				✓	✓

Source: ECDC-JRC Response Measures Database

\* Note that there can be different degrees of closure, ranging from establishing hybrid education (online teaching interchanged with face-to-face teaching, thereby reducing class size), conducting online education only for specific classes or years in an affected school, or conducting online education only for entire schools.

\*\* Secondary and higher educational institutions are partially closed at national level and completely closed in some regions.

## Availability of COVID-19 vaccines in the EU/EEA

Three COVID-19 vaccines have received EU authorisation and are part of the EU Coronavirus Vaccines Strategy Portfolio: Comirnaty (BNT162b2) developed by BioNTech/Pfizer, COVID-19 Vaccine Moderna (mRNA-1273) and COVID-19 Vaccine AstraZeneca (AZD1222). The European Commission has also signed contracts with three further developers of COVID-19 vaccines: Johnson & Johnson, Curevac and Sanofi-GSK and European Medicines Agency (EMA) rolling reviews have been initiated for the vaccine developed by Johnson & Johnson [29] (1 December 2020) and Curevac. Finally, explorative talks have been concluded with Novavax and Valneva and EMA has initiated a rolling review for the vaccine candidate developed by Novavax [30] (3 February 2021).

## Implementation of vaccinations

All EU/EEA countries have developed strategies or plans for the deployment of the available COVID-19 vaccines and the majority of them started their national COVID-19 vaccination campaigns at the end of December, shortly after the first lots of vaccines (Comirnaty developed by BioNTech/Pfizer) were delivered to all EU/EEA countries [31]. At the time of this report, all EU/EEA countries have also started administering the COVID-19 Vaccine Moderna. Moreover, the first lots of COVID-19 Vaccine AstraZeneca are being supplied following its recent conditional marketing authorisation in the EU. Vaccinations are being rolled out in phases and all 30 EU/EEA countries have started vaccinating the priority groups included in their first phase, which were selected based on their higher risk of developing severe disease (the elderly and residents in long-term care facilities), as well as to protect healthcare and other front-line workers. Some countries have already progressed to the groups included in subsequent phases. An overview of the implementation of COVID-19 vaccination strategies and vaccine deployment plans in the EU/EEA was recently published by ECDC [31].

ECDC and the World Health Organization's Regional Office for Europe have jointly implemented a monitoring system to collect information on the vaccine rollout, including information on the number of vaccine doses distributed to countries by the manufacturers and the number of doses administered to individuals by age group and other priority populations. The objective of this data collection process is to provide information on i) the efficiency of the vaccination campaign in terms of administration of doses to the target population at national level ii) the capability of the countries to administer all vaccine doses to individuals and iii) the identification of possible shortcomings in vaccine deployment and campaign rollout. Since 15 January 2021, these data have been collected through The European Surveillance System (TESSy) and may be viewed on a COVID-19 vaccine tracker [32] on ECDC's website.

As of 7 February 2021 [33], a total of 29 EU/EEA countries reported complete or partial data on the vaccine rollout to TESSy. Among the 29 countries reporting that had information available, the estimated vaccine uptake for the first dose among adults (18 years and above) varied between 0.3% and 7.6% (median: 3.5%). Among the 29 countries reporting that had information available, the uptake of two doses among adults (18 years and above) varied between 0.2% and 3% (median: 1.1%). For more information on the vaccine rollout in EU/EEA countries please consult the [weekly report](#) or the [COVID-19 vaccine tracker](#).

Between mid-December 2020 and January 2021, ECDC and the European Commission's Directorate-General for Health and Food Safety jointly organised a stress test of the logistical aspects of COVID-19 vaccination deployment plans. This was conducted in two rounds and with the participation of twelve EU/EEA Member States. The stress test is a focused simulation exercise, whereby participating countries are asked to describe the deployment plans in place for delivering a vaccine with strict cold chain requirements to their target priority groups. All participating Member States were able to describe the process, albeit in varying levels of detail, indicating that they were at different points in their planning [34].

A report on the stress test with EU Member States was recently published [34]. One of the most important aspects of the stress test was to provide an opportunity for those involved in developing their vaccine deployment plan to test it against a realistic scenario, to work through all the elements of deployment and to obtain reassurance that the plan was robust and that any issues identified could be addressed. A similar exercise was recently completed in Albania, Bosnia and Herzegovina, Kosovo, Montenegro, North Macedonia and Serbia.

## 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 treatment please visit ECDC's website: <https://www.ecdc.europa.eu/en/covid-19/latest-evidence>.

## Effectiveness of vaccines against transmission

Data on vaccine efficacy and effectiveness results for different circulating SARS-CoV-2 variants, including the VOCs, presented in Table 2 of this report represent data available as of 10 February 2021.

As the vaccines continue to be rolled out across the world, preliminary evidence on the impact of COVID-19 vaccines against the transmission of SARS-CoV-2 is becoming available.

Real-world data on the effectiveness of vaccines on transmission has been made available from Israel in a preprint article of a study. The study compares individuals aged 60 years or over who had tested positive for COVID-19, where more than 75% of that age group have had a first dose of the BioNTech/Pfizer vaccine, compared to those aged 40–60 years where only 25% have had a first dose. From this the authors inferred that the reduction in viral load of those individuals aged 60+ years over time, compared to the group aged 40–60 years, indicates that vaccination with the BioNTech/Pfizer vaccine may provide individual protection, and may also reduce some viral shedding, thereby possibly lowering transmission [35]. A further preprint article based on an observational study in Israel found that the viral load was reduced four-fold for infections occurring 12–28 days after the first dose of BioNTech/Pfizer vaccine, potentially affecting viral shedding and contagiousness as well as severity of the disease [36].

As time progresses and more of the population are vaccinated, evidence of vaccine impact on transmission will become available. However, at this time there is no evidence available to support the assumption that a person vaccinated against SARS-CoV-2 with any of the currently-available vaccines (including those licensed in the EU) will be completely unable to transmit COVID-19 to a susceptible individual.

## Characteristics of the new variants

### *B.1.1.7 (VOC 202012/01)*

#### **Transmissibility**

Several studies provide evidence of increased transmissibility of B.1.1.7. Davies et al. modelled data from three English regions to estimate that the variant is 56% more transmissible (95% credible interval (CrI): 50–74%) than previously identified SARS-CoV-2 variants [37]. An analysis by Volz et al. estimated that the transmission advantage of B.1.1.7 relative to non-B.1.1.7 lineages increased R by 0.4–0.7, or by 50–75% [38]. Denmark estimates that the effective reproductive number (Rt) for the B.1.1.7 lineage is 1.14 as of 4 February 2021, despite strict lockdown since mid-December, including school closures, compared to an Rt of 0.5–0.7 for the other circulating variants [39]. Finally, based on contact tracing data from the United Kingdom, the attack rates are around 10–55% higher across most age groups when the case is infected with the B.1.1.7 variant [40].

#### **Severity**

Based on preliminary analyses in the United Kingdom, the risk ratio of death was 1.65 (95% CI 1.21–2.25) for cases with B.1.1.7 compared to a matched cohort of non-B.1.1.7 cases [41]. Although there are limitations to the datasets on which this analysis was based, the UK NERVTAG concluded that there is a realistic possibility that B.1.1.7 is associated with increased risk of death, compared to non-B.1.1.7 cases. The UK NERVTAG assessment was strengthened on 11 February 2021 by stating that 'it is likely that infection with VOC B.1.1.7 is associated with an increased risk of hospitalisation and death compared to infection with non-VOC viruses' [42]. Furthermore, increased transmissibility results in a higher absolute number of infections, thereby increasing the number of severe cases when prevention measures are kept constant.

#### **Immunity, reinfection, vaccination**

There is evidence of both memory B cell and T cell immune responses in individuals infected with previous predominant circulating SARS-CoV-2 strains, however a clear correlate for protection has yet to be defined [43-46]. Infection with previous predominant circulating SARS-CoV-2 strains appears to provide immunity against systemic disease for at least five and eight months [47-49]. The presence of neutralising antibodies against SARS-CoV-2 provides the best current indication for protection against reinfection. A reduction in the neutralising capacity of serum polyclonal antibodies - derived from infection with previous predominant circulating SARS-CoV-2 strains - against variant viruses may indicate a reduced capacity to protect against reinfection. Studies on the B.1.1.7 variant indicate that it is modestly more resistant to convalescent plasma, with estimates for the reduction ranging between 3–10-fold [50,51]. Despite this reduction, up to 60% of convalescent serum samples are thought to retain functional activity above neutralising threshold [52].

In the UK, Graham et al. evaluated longitudinal symptom and test reports from 36 920 users of the COVID Symptom Study app testing positive for COVID-19 between 28 September and 27 December 2020. The authors estimated the number of possible reinfections (defined as two positive PCR tests >90 days apart with at least

seven symptom-free days between tests) and the proportion of B.1.1.7 cases over time, estimating a reinfection rate of 0.7% (95% CI 0.6–0.8), with no evidence that this was higher than for the older strains [53].

The effect of spike mutations from the B.1.1.7 lineage on vaccine-elicited sera is that the mRNA vaccines Comirnaty by BioNTech/Pfizer and COVID-19 Vaccine Moderna have no significant impact on neutralisation against pseudo-viruses containing mutations found in B.1.1.7, suggesting that these vaccines can be expected to be effective against B.1.1.7 [54-58]. These studies are not yet peer-reviewed or published.

The clinical efficacy of the adenoviral vector COVID-19 Vaccine AstraZeneca against B.1.1.7 is similar to the efficacy of the vaccine against other circulating lineages in the UK, according to a non-peer reviewed manuscript [59].

The ongoing clinical phase 3 trials of the protein-based vaccine Novavax reported 90% vaccine efficacy against the previous strains of SARS-CoV-2 and more than 85% efficacy against B.1.1.7 [60].

These study results are not yet available for peer-review but have been made available in a press release from the manufacturer.

### **Diagnostic assays**

Negative S-gene RT-PCR results from the Thermo Fischer TaqPath assay have been observed for this variant and can be used to screen for it [61]. Rapid antigen tests validated by the UK are still meeting performance criteria for B.1.1.7 [62].

### ***B.1.1.7+E484K***

There are no estimates of transmissibility or severity available for B.1.1.7 with the E484K mutation. It is likely that this variant has almost identical properties to B.1.1.7 without E484K, but there may be a decrease in neutralisation by monoclonal antibodies and convalescent sera, as observed for other variants with E484K. Studies have been initiated [63].

A preprint paper on the Comirnaty vaccine by BioNTech/Pfizer reported that when B.1.1.7 also carried E484K [54], an almost ten-fold decrease in the titre of neutralising serum antibodies was observed compared to B.1.1.7 alone. Thus the Comirnaty vaccine by BioNTech/Pfizer might be less effective when a variant carries the E484K mutation, although this variant is still rare and has only been identified in a few geographical regions of the UK [60].

### ***B.1.351 (501Y.V2)***

#### **Transmissibility**

Preliminary results, applying a mathematical model previously used to characterise the transmissibility of B.1.1.7 [37] and simplified calibration, estimates that B.1.351 is 50% (95% CrI: 20–113%) more transmissible than previously circulating variants in South Africa [64].

#### **Severity**

There is currently substantial uncertainty as to whether the B.1.351 variant causes a change in disease severity [64].

#### **Immunity, reinfection, vaccination**

In-vitro studies of the neutralising capacity of polyclonal serum antibodies - derived from infection with previously predominant circulating strains of SARS-CoV-2 - against the B.1.351 variant indicate that it is markedly more resistant to convalescent plasma, with estimates for the reduction ranging between 11–33-fold [51], with 10–50% of convalescent serum samples retaining activity above neutralising threshold [51,52]. Loss of neutralisation activity against the B.1.351 variant is largely attributed to the E484K mutation [51,65,66].

In South Africa, 674 of 2 168 (31%) patients in the placebo intention-to-treat arm of a phase 2b vaccine study showed evidence of prior infection at enrolment (seropositive for anti-spike protein IgG). Given the time of enrolment, this probably represented exposure to a non-B.1.351 virus. Analysis at seven days post intervention showed no difference in rates of infection (3.9% (58/1494; 2.961; 4.990) versus reinfection 3.9% (26/674; 2.535; 5.601) with the B.1.351 variant, indicating that seropositivity to previously predominant circulating SARS-CoV-2 strains did not confer additional protection [67].

Sera from those vaccinated with the mRNA vaccines Comirnaty by BioNTech/Pfizer and COVID-19 Vaccine Moderna reported reduced neutralisation (six-fold) against the mutations present in B.1.351 [51]. These results have been reported in non-peer-reviewed manuscripts. Moderna have announced work on an emerging variant booster candidate against the mutations present in B.1.351 and Pfizer have announced they are working on developing a booster shot to protect against variants.

Early data from a non-peer reviewed small phase 2/3 trial reported by a British newspaper [68] suggest that the COVID-19 Vaccine AstraZeneca has shown limited efficacy, as low as 10%, against mild/moderate disease primarily due to B.1.351. It is not yet known if the vaccine protects against severe disease as only young participants, not prone to severe disease, were included in the study. The developer announced that they have started updating the vaccine against B.1.351.

Results from ongoing clinical phase 3 trials of the protein-based vaccine Novavax reported to media show less than 50% vaccine efficacy against B.1.351 [60].

Preliminary efficacy data also reported in a press release following phase 3 trials of the adenoviral vector vaccine by Johnson and Johnson indicate vaccine efficacy against moderate-to-severe COVID-19 infection 28 days post vaccination as 72% in the United States, 66% in Latin America and 57% in South Africa, where nearly all cases of COVID-19 were due to infection with a SARS-CoV-2 variant from the B.1.351 lineage [69].

### Diagnostic assays

There have been no reports of any effect on diagnostic assays.

### P.1

#### Transmissibility

There is currently no microbiological or epidemiological evidence of any change in transmissibility of P.1, but the amino acid change N501Y, also present in B.1.1.7 and B.1.351, suggests that increased transmissibility is plausible.

#### Severity

Nothing is known yet about potential changes in infection severity in those infected with the P.1 variant.

#### Immunity, reinfection, vaccination

In-vitro studies of the neutralising capacity of polyclonal serum antibodies - derived from infection with previously predominant circulating SARS-CoV-2 strains - against the P.1 variant are limited. However, presence of the E484K mutation may indicate a similar profile to B.1.351 [66].

No information on neutralising antibodies is available for the P.1 variant but reported mutations in the spike region may also have a potential impact on vaccine effectiveness, similar to B.1.351.

### Diagnostic assays

There have been no reports of any effect on diagnostic assays.

**Table 2. Efficacy and effectiveness of COVID-19 vaccines authorised for use in the EU or under rolling review with EMA against SARS-CoV-2 and variants of concern**

Vaccine developer	Non-variant and variants of concern			
	Non-variant	B.1.1.7	B.1.351	P.1
<b>BioNTech/Pfizer</b>				
Efficacy	95% (95% CI 90.0%–97.9%) [70] overall efficacy	n.a.	n.a.	n.a.
Effectiveness	51.4% (95% CI - 7.2%–78.0%) after Dose 1, Day 13-24 [71]	n.a.	n.a.	n.a.
<b>Moderna</b>				
Efficacy	94.1% (95% CI, 89.3%–96.8%) [72] overall efficacy	n.a.	n.a.	n.a.
Effectiveness	n.a.	n.a.	n.a.	n.a.
<b>Oxford/ AstraZeneca</b>				
Efficacy	59.5% (95% CI 45.8%–60.7%) [73] overall efficacy	74.6% (95% CI 41.6%–88.9%) (compared to non-B.1.1.7 lineages: 84% (95% CI, 70.7%–97.4%) [59])	n.a.	n.a.
Effectiveness	n.a.	n.a.	n.a. <sup>d</sup>	n.a.
<b>Johnson &amp; Johnson<sup>a,b</sup></b>				
Efficacy	66% [69] overall efficacy <sup>c</sup>	n.a.	57% <sup>c</sup> [69]	n.a.
Effectiveness	n.a.	n.a.	n.a.	n.a.
<b>Novavax<sup>a</sup></b>				
Efficacy	95.6% [60] overall efficacy <sup>c</sup>	89.3% (95% CI 75.2%–95.4%) <sup>c</sup> [74]	49.4% (95% CI 6.1%–72.8%) <sup>c</sup> [74]	n.a.
Effectiveness	n.a.	n.a.	n.a.	n.a.

Note: This table is based on data available to ECDC as of 10 February 2021. n.a. = not available.

<sup>a</sup> Not authorised in EU

<sup>b</sup> One-dose schedule

<sup>c</sup> Press release or interim data release by developer

<sup>d</sup> Results from a newspaper article quote 10% effectiveness against mild to moderate infection [68]

## Co-circulation and emergence of variants of concern

Of the three variants described here, B.1.1.7 is currently much more widespread and abundant in the EU/EEA than the other two. There is currently no evidence that B.1.351 or P.1 are more transmissible than B.1.1.7 in the settings where they were first detected. However, there is evidence that B.1.351 and P.1 might have antigenic properties that may give them a selective advantage over B.1.1.7 in populations with high levels of immunity derived from infection or vaccination. It is also possible that B.1.1.7+E484K could have such antigenic properties. Therefore, there is a possibility that B.1.351, P.1 and B.1.1.7+E484K could begin replacing B.1.1.7 as the immunity levels increase in the population. The implications of such replacements for the effectiveness of the vaccination campaigns currently in progress remains to be clearly defined, although it is still likely that the overall case numbers will drop drastically when the vaccine coverage has reached high levels [75]. Lower overall case numbers reduce the risk of the emergence of new VOCs, while an abundance of partially immune individuals may increase the risk [76].

It is still not fully understood if the current VOCs have emerged as a result of an exceptional event such as prolonged infection in immunocompromised patients, or if they emerged from random mutation driven by a large number of infections overall [10,21,77]. In any case, a higher number of cases is associated with a higher risk of emergence of VOCs. In the current situation, where variants with increased transmissibility and neutralisation escape are already circulating, single mutations in these variants could have serious implications if they have further impact on vaccine effectiveness. It is advised that prolonged situations with a large proportion of the population being partially susceptible should be avoided, zoonotic transmission of SARS-CoV-2 should be monitored, and patients with prolonged infections should be closely monitored and isolated due to the uncertainties associated with how VOCs emerge.

## Paediatric Inflammatory Multisystem Syndrome

Paediatric inflammatory multisystem syndrome (PIMS), also called multisystem inflammatory syndrome in children (MIS-C), is a condition associated with SARS-CoV-2 infection. Following initial reports of paediatric cases admitted to intensive care due to this rare condition, ECDC published a rapid risk assessment in May 2020 [78]. While SARS-CoV-2 generally causes mild disease in children, severe respiratory illness and PIMS sometimes occur, although rarely with a fatal outcome. Children with PIMS present, usually four to six weeks after infection, with a wide clinical spectrum including Kawasaki disease-like symptoms, life-threatening shock and milder forms of illness such as persistent fever, inflammation and gastrointestinal manifestations [79]. Most children with critical illness due to PIMS have a favourable outcome and recover with intensive care support and appropriate treatment. The length of stay in the intensive care is around five days and the mortality is below 3% [79,80]. Early recognition and prompt treatment is essential. Limited evidence for treatment options supports intravenous immunoglobulin (IVIG), corticosteroids, inotropes and other biological immunomodulation agents [81,82]. As children often present with mild symptoms of COVID-19 and are less frequently tested than adults, the true incidence of PIMS remains unknown. Some ethnic backgrounds seem to be disproportionately affected by PIMS, as over 50% of cases are non-white, based on studies from the UK and the US [83].

There is no comprehensive overview of PIMS cases in the EU/EEA. Germany and Switzerland have published data on case series of children with severe COVID-19 infection, leading to PIMS and even death [84-86]. The French national surveillance system registered 111 children with PIMS between April 2020 and January 2021, with a median age of eight years. Among them, 67% were admitted to a paediatric ICU [86]. Between March and August 2020, Sweden also reported 50 children diagnosed with PIMS. In the UK around 600 cases and two deaths have been described to date [87], while in another British study, 78% of those children hospitalised with PIMS did not have any comorbidity [82].

There was some media attention around an increase in cases of PIMS reported in the United Kingdom in early February 2021 [88]. This surge of PIMS cases occurred four to five weeks after the surge of SARS-CoV-2 infections in the second wave and was expected. There is currently no information that the new variants have led to more severe disease in children or that the situation of PIMS is worsening over time [89,90].

## ECDC risk assessment for the EU/EEA

This assessment is based on information available to ECDC at the time of publication and, unless otherwise stated, the assessment of risk refers to the risk that existed at the time of writing. It follows the ECDC rapid risk assessment methodology, with the overall risk determined by a combination of the probability of an event occurring and its consequences (impact) for individuals or the population [91].

### Risk assessment questions

#### **Given the increase in known variants of concern observed in the EU/EEA and the UK, what risk does SARS-COV-2 pose to the general population and vulnerable individuals?**

This assessment is based on the factors outline below.

Although several EU/EEA countries have observed a decline in overall incidence of SARS-CoV-2 in recent weeks, incidence remains moderately high in many countries and very high in several others. Mortality has declined in all but five EU/EEA countries, however, the pressure on the healthcare system remains high, with reported increasing hospitalisation and ICU admission rates in 27 countries.

As of 11 February 2021, 83 countries worldwide are reporting cases of B.1.1.7, 40 countries are reporting B.1.351 and 17 countries are reporting P.1 cases.

Despite measures being in place in most countries, the circulation of variants has progressed in terms of the number and proportion of all cases. There is evidence of community transmission of the variant B.1.1.7 in many EU/EEA countries and a rapid increase in the prevalence of this variant reported in countries performing sequencing. Although overall numbers remain low, several EU/EEA countries have reported community transmission of the variant B.1.351, including outbreaks in several countries. The variant P.1 is reported at low levels in the EU/EEA and is usually linked to travel. In response to the variants, many EU/EEA countries have implemented travel restrictions and/or enhanced testing and quarantine of travellers.

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, including for VOCs, has been increased recently in EU/EEA countries. Nevertheless, it is very probable that the number of possible cases are under-detected, especially as regards the VOCs.

Transmissibility of B.1.1.7 is estimated to be up to 56% higher than the previously circulating strains of SARS-CoV-2 and the reproductive number for this variant remains above 1, despite the implementation of very strict measures in many settings. Preliminary results for B.1.351 indicate that the variant has 50% higher transmissibility. There is no transmissibility estimate for P.1 yet.

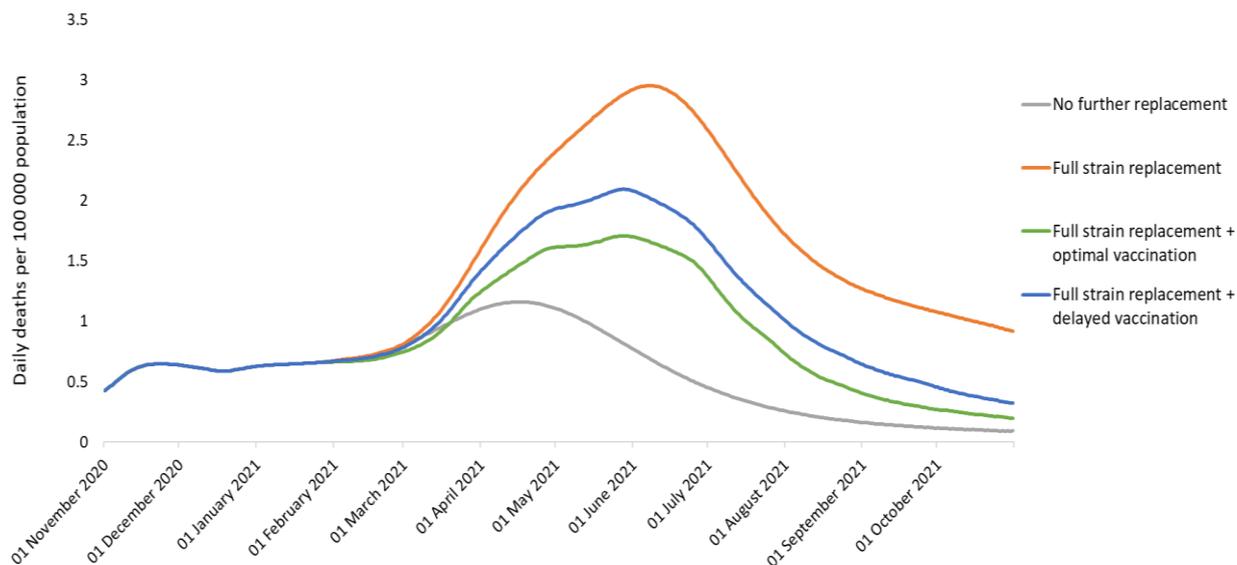
In summary, the probability of further spread of the SARS-CoV-2 VOCs in the EU/EEA is currently assessed as very high.

There is a realistic possibility that B.1.1.7 is associated with increased risk of death compared to non-B.1.1.7 cases. There is substantial uncertainty regarding severity estimates for B.1.351 and P.1. However, increased transmissibility results in a higher absolute number of infections, thereby increasing the number of severe cases when prevention measures are kept constant. An increase in the number of infections will lead to a consequent increase in hospitalisations and deaths, particularly for those in older age groups or with co-morbidities who are not yet vaccinated, even if the disease severity is similar. Furthermore, if the variant B.1.351 or other variants are found to be able to partially or fully evade available vaccines, this would probably prolong or worsen the impact, particularly for those most likely to suffer from severe outcomes. Given the information available on increased severity and transmissibility and the potential for immune escape, the spread of these variants would have a high impact on populations in which they become established, and a very high impact among more vulnerable groups.

In summary, the risk associated with further spread of the SARS-CoV-2 VOCs in the EU/EEA is currently assessed as high to very high for the overall population and very high for vulnerable individuals.

This risk of SARS-COV-2 spread will be affected by the implementation of NPIs as well as by the progress of the rollout of vaccination programmes. ECDC modelling analysis suggests that if a novel strain of SARS-CoV-2 with an increased transmissibility of 70% replaces the previously circulating strains in the EU/EEA by the end of February 2021, the NPIs in place at the end of January 2021 would be insufficient to prevent a substantial increase in COVID-19 mortality, even as vaccines are being rolled out (Figure 2). However, some strengthening of these measures has already taken place. The analysis showed that if Member States achieve the vaccination targets set by the European Commission in its Communication dated 19 January 2021, the peak excess mortality rate due to the new strain will be approximately halved and the majority of excess deaths will be prevented. However, if 25% of doses are delayed by one month and 25% by two months, the impact of the vaccination programme will be substantially reduced. Given that full strain replacement with B.1.1.7 appears likely, mortality rates will probably increase, even with optimal vaccination, if NPIs are not significantly strengthened, with continued high compliance ensured for the coming period.

**Figure 2. Projected daily mortality rate in the EU/EEA, assuming no further replacement by more transmissible strains (grey) and no vaccination, complete replacement with a strain that is 70% more transmissible (orange) and the potential impact of an optimal (green) and delayed (blue) vaccination programme in mitigating the effect in the scenario of complete replacement.**



Note - current non-pharmaceutical interventions are maintained throughout the period [92].

## Options for response

Based on the current epidemiological situation in the EU/EEA, immediate, strong and decisive public health interventions are essential to control transmission and safeguard healthcare capacity. This will involve all EU/EEA countries strengthening the implementation of layered NPIs to reduce SARS-CoV-2 incidence to the lowest levels possible, and rapidly and efficiently rolling out vaccination to the populations most at-risk of high morbidity and mortality from COVID-19. The optimisation of NPIs - particularly issues related to community use of facemasks and considerations for school settings - and the optimal use of vaccination are essential factors. Test and trace approaches, including strong surveillance and sequencing, remain the cornerstones of the response. Finally, considerations for travel-related measures and effective risk communication are provided.

### Strengthened and continued high compliance with non-pharmaceutical interventions

Modelling analysis shows that, unless NPIs continue or are strengthened in terms of compliance over the coming months, a significant increase in COVID-19-related cases and deaths in the EU/EEA is to be anticipated. Although vaccination will mitigate the effect of replacement with more transmissible variants, easing measures prematurely will lead to a rapid increase in incidence rates and mortality. Delays in vaccine procurement, distribution and administration would delay the option to ease NPIs. The rapid deployment of vaccine among priority groups is needed to reduce hospitalisations, ICU admissions and deaths due to COVID-19.

Efficient implementation and strengthening of NPIs in response to the epidemiological situation remains essential for the continuing response to emerging and regularly circulating of SARS-CoV-2 and known variants, until and unless vaccination has been shown to fully mitigate the impact of the pandemic on the population and healthcare services. In areas where new VOCs have emerged or are anticipated to be the dominant variant in circulation, stringent implementation of NPIs is necessary to reduce transmission and safeguard the functioning of healthcare systems. Higher transmissibility implies that the effectiveness of several individual NPIs (e.g. physical distancing or the use of face masks) may be reduced and that more intensive layering of NPIs will be needed to achieve similar results.

NPIs to reduce transmission in the general population are the fundamental elements of the public health approach to controlling COVID-19. Therefore these measures should continue to be implemented and strengthened in accordance with the local epidemiological situation, taking into account that in a situation of increased transmissibility, more measures or stricter compliance will be needed to get the same results as those achieved in the pre-variant situation. Countries should continue or enhance application of NPIs at personal, environmental and society level. Such measures include:

- encouraging physical distancing between individuals as much as possible and limiting the size of public and private gatherings;
- promoting hand hygiene and respiratory etiquette;
- Providing advice on use of face masks where necessary;
- continuing with contact tracing, quarantine of contacts and isolation of cases;
- enhancing compliance with advice to limit transmission in workplaces by encouraging teleworking whenever possible;
- recommending measures to maintain infection prevention and control in all health and social care settings, including long-term care facilities [93];
- providing advice to the population to avoid non-essential travel;
- strengthening in-school mitigation measures and, as a last resort after other measures in society have already been applied, considering partial or complete school closures on a short-term basis.

For an analysis and available evidence on the NPIs used to respond to the COVID-19 pandemic, please refer to ECDC's technical document 'Guidelines for the implementation of NPIs against COVID-19' [94].

### Considerations for the use of face masks

Although there is only low to moderate certainty for the use of medical face masks providing a small to moderate protective effect against COVID-19 [95], face masks should be considered as an appropriate non-pharmaceutical intervention in combination with other measures as part of efforts to control the COVID-19 pandemic.

Taking into account the available evidence, the transmission characteristics of SARS-CoV-2, the feasibility and potential harms associated with the use of various types of face masks, the following options are proposed:

- In areas with community transmission of COVID-19, wearing a medical or non-medical face mask is recommended in confined public spaces and can be considered in crowded outdoor settings.
- For people vulnerable to severe COVID-19, such as the elderly or those with underlying medical conditions, the use of medical face masks is recommended as a means of personal protection in the above-mentioned settings.
- In households, the use of medical face masks is recommended for people with symptoms of COVID-19 or confirmed COVID-19 and for the people who share their household.
- Based on the assessment of the available scientific evidence, no recommendation can be made on the preferred use of medical or non-medical face masks in the community.
- When non-medical face masks are used, it is advisable that masks that comply with available guidelines for filtration efficacy and breathability are preferred.

The very limited scientific evidence regarding the use of respirators in the community does not support their mandatory use in place of other types of face masks in the community. Although respirators would not be expected to be inferior to non-medical or medical face masks, the difficulties to ensure their appropriate fitting and use in community settings as well as potential adverse effects related to lower breathability should be taken into account.

The use of face masks in the community should complement and not replace other preventive measures such as physical distancing, staying home when ill, teleworking if possible, respiratory etiquette, meticulous hand hygiene and avoiding touching the face, nose, eyes and mouth.

The appropriate use of face masks and promoting compliance with their use when recommended as public health measures are key to the effectiveness of the measure and can be improved through education campaigns.

Due to their better filtration efficiency, respirators have been considered for use in the community, in particular since the emergence of more transmissible new variants of SARS-CoV-2. The very limited scientific evidence regarding the use of respirators in the community does not support their mandatory use in place of other types of face masks in the community. Although respirators would not be expected to be inferior to non-medical or medical face masks, the difficulties to ensure their appropriate fitting and use in community settings as well as potential adverse effects related to lower breathability should be taken into account [95].

### Considerations for school settings

Children, in particular younger children, appear to be less susceptible to SARS-CoV-2 infection than older children or adults [102-104], which also seems to be the case for the variant B.1.1.7 [99]. Widespread transmission of SARS-CoV-2 in the community increases the likelihood that COVID-19 cases appear in school settings [96,100]. This in turn creates the possibility of onward transmission in school and subsequently to household settings, particularly in the absence of appropriate in-school mitigation measures. As noted by ECDC and WHO, there are many profound negative impacts of school closures and it is therefore recommended that such closures are a

measure of last resort, implemented as an additional, time-limited layer, where other NPIs have not been able to control local transmission, or are not assessed as being able to do so [96,101].

Increased community circulation of SARS-CoV-2 VOCs may lead to the need for school closures, either in response to school-specific outbreaks or to alleviate current or anticipated pressure on community transmission and the healthcare system [102]. It is generally thought that school closures, if deemed necessary, should initially be arranged for children in the older age groups. An age-structured model from the Netherlands, based on previously predominant SARS-CoV-2 strains in circulation, concluded that the biggest impact on community transmission was achieved by reducing contacts in secondary schools [103]. Modelling from Denmark assumed that children under 10 years of age were 50% less susceptible to SARS-CoV-2 infection than adults. The modelling study indicates that, all other measures being constant, opening only primary schools (Grades 0-4) in February 2021 would not lead to a substantial increase in new cases or hospitalisations, provided that the transmissibility of B.1.1.7 only increases by 40% against the previously circulating SARS-CoV-2 viruses. However, should the relative infection rate be 1.55 or 1.7, then there would be a substantial increase in new daily cases and hospitalisations by April 2021 [104].

Prior to taking decisions to close schools, countries should carefully review the other NPIs in place, while also strengthening in-school measures to reduce the risk of SARS-CoV-2 transmission in school settings [96]. A wide range of mitigation measures should be considered that minimise social mixing between school classes and adult staff. These appear to be effective at reducing the risks of transmission in school settings; documented instances of in-school SARS-CoV-2 transmission are rare where appropriate measures are in place [102,104,111,112].

Decision-making concerning school closures or re-openings should be accompanied by effective risk communication. Schools are important venues for science education and learning about good hygiene practices, such as hand-washing. Students can become effective advocates for disease prevention and control in their homes, the school and the community at large [107].

## Vaccination

Vaccines are a key part of a long-term strategy to bring SARS-CoV-2 under control. The emergence of more transmissible variants may cause increased hospital admissions and deaths in the coming weeks, despite ongoing vaccine deployment. Some emerging variants may also partially escape the immunity induced by the currently available vaccines. For these reasons, it is important to bear in mind the factors set out below.

- Vaccination should be rapidly accelerated to target priority groups.
- Available vaccines should be prioritised for groups at highest risk of severe disease (in particular older adults) in order to efficiently reduce hospitalisations, ICU admissions and deaths, irrespective of any other considerations.
- Consider these options for accelerated vaccine deployment [31,34]:
  - An accurate, real-time inventory management system to assure the availability and maintenance of adequate supplies, minimise potential wastage and accurately forecast demand.
  - Adapting the supply chain to the expected different cold chain requirements of the different vaccines when they become available from the manufacturers.
  - Increasing the availability of doses by extracting more doses from a vial, such as extracting a sixth dose from the five-dose vial of the BioNTech/Pfizer vaccine (if equipment is available).
  - Increasing vaccination mobile teams and mass vaccination centres.
- Consideration can be given to dosing options, such as delaying second doses to provide protection to more individuals in a shorter time period, within the terms of the conditional marketing authorisation.
- Virus mutations that result in a reduction of vaccine effectiveness may occur repeatedly in the future and will need to be mitigated by designing next generation vaccines with mutated spike sequences and using alternative viral antigens, possibly also as booster doses.

## Dosing interval

It is essential to rollout vaccinations rapidly to protect as many people as possible and to lower the opportunities for the virus to further evolve. To achieve rapid vaccination deployment and taking into account the limited doses available, the interval between Dose 1 and 2 has been discussed widely in the EU/EEA and by WHO's Strategic Advisory Group of Experts on Immunization (SAGE). The current EMA product information states that administration of the second dose of the vaccine Comirnaty [70] by BioNTech/Pfizer should be given three weeks after the first dose and recommends an interval of 28 days between the first and second dose for the COVID-19 Vaccine Moderna [72]. On the basis of currently available clinical trial data, WHO's recommendation at present is that the interval between doses may be extended to up to 42 days (six weeks). For the COVID-19 Vaccine AstraZeneca EMA have granted conditional authorisation for the two doses to be given between four and 12 weeks apart. Data from a preprint article on phase 3 efficacy trials of the COVID-19 Vaccine AstraZeneca in the UK and Brazil and phase 1/2 clinical trials in the UK and South Africa (cut-off date for analyses December 2020) on the dosing interval show that higher efficacy is obtained with a longer interval between the first and second dose and that a single dose of vaccine is highly efficacious for the first 90 days [108]. WHO SAGE interim recommendations for use of the COVID-19 Vaccine AstraZeneca suggest preferably administering the second vaccine dose between eight and 12 weeks from the first dose, in the light of the immunogenicity increase with a longer time interval between doses [109].

Evidence is emerging on the effectiveness of the different vaccines following a single dose. A preprint article that has assessed real-world immune responses following vaccination with mRNA-based vaccine Comirnaty by BioNTech/Pfizer in the UK using the recommended two-dose regimen, three months apart on a small sample size (23 participants). The assessment showed that a proportion of individuals above the age of 80 years had a suboptimal neutralising antibody response three weeks after vaccination with vaccine Comirnaty by BioNTech/Pfizer, and that the second dose is associated with robust neutralising responses. The conclusion was that a significant proportion of individuals over 80 years appear to require a second dose of vaccine at three weeks to achieve virus neutralisation [110]. A preprint study from Israel found the effectiveness of the vaccine Comirnaty by BioNTech/Pfizer in an Israeli cohort (participants from 16 years of age, median age 59.7 years) increased gradually day to day from about Day 14, reaching a peak of around 90% effectiveness on Day 21 before any second dose. However, it is unknown how long this immunity will last beyond 21 days without a second dose [111]. The evidence currently available also shows that the COVID-19 Vaccine AstraZeneca provides a good neutralising antibody response already after one dose.

## Number of doses

Further evidence on dosing includes preprint papers looking at the number of doses needed for those individuals who have been infected with SARS-CoV-2 in the past. A study from the US has reported that the antibody response to the first mRNA vaccine dose (for Comirnaty developed by BioNTech/Pfizer, and COVID-19 Vaccine Moderna) in individuals with pre-existing immunity is equal to, or even exceeds the titres found in naïve individuals after the second dose. They also show that the reactogenicity is significantly higher in individuals who have been infected with SARS-CoV-2 in the past [112]. The authors suggest that in naturally infected individuals a single vaccine dose can serve as a boost and may be sufficient to achieve immunity. Similarly, data from another preprint article on mRNA vaccine (BioNTech/Pfizer) found one vaccine dose was sufficient to induce a good antibody response in individuals with a previous history of COVID-19. The authors question whether a second shot in naturally infected individuals is required and suggest postponing this while monitoring antibody response longevity [113]. However, practicalities concerning the verification of previous documented infection while trying to implement rapid vaccination rollout could become challenging and should be carefully considered.

Mathematical modelling can provide estimates of the impact of changing the timing between doses. Modelling should be complemented by real-world data on vaccine effectiveness after each dose, according to age and risk groups, and against health outcomes that could not be assessed in vaccine trials (e.g. transmission, emerging variants, severe COVID-19, duration of protection). Studies of breakthrough infections following Dose 1 have been initiated, but data will only become available in five to six weeks from now.

## Mixing vaccination schedules

As all available COVID-19 vaccines are targeting the SARS-CoV-2 spike protein to induce immunity, the potential to use a mix and match vaccination schedule [114], through the administration of a second dose using a different vaccine product, is currently being studied. A mixed schedule could potentially contribute to improved protection, in addition to adding some flexibility to the vaccine roll-out, although this is yet to be determined. A trial has been launched in the UK (Com-COV) [115] where the COVID-19 Vaccine AstraZeneca will be given followed by the BioNTech/Pfizer vaccine, and vice versa, with four- or 12-week dosing schedules. The trial may include other vaccines when authorised in the future, such as the Johnson and Johnson vaccine and Novavax vaccine. Results will only be available around four to five months from now. AstraZeneca has also announced that there will be a mix-and-match dosing trial with the Sputnik V vaccine, to be conducted in Azerbaijan [116]. At this stage there is no data available on the safety and efficacy of a mix-and-match vaccination schedule.

## Surveillance, testing and detection

### Testing strategies

Testing strategies for SARS-CoV-2 should be flexible and rapidly adaptable to change, depending on the local epidemiology, population dynamics and resources.

Timely testing of people with symptoms, fostered by improving access to testing and encouraging people to seek testing as soon as possible after symptom onset, remain important to enable rapid initiation of contact tracing.

A current priority should be to assess the level of circulation of known VOCs in the community and therefore a representative sample needs to be collected regularly from each country to accurately estimate and monitor prevalence of the VOCs. ECDC's sequencing guidance [117] recommends testing at least 500 random/representative samples per country per week. Fast turnaround time of results is important to be able to inform public health interventions. In parallel, the testing strategy should include coverage of vaccine breakthrough infections, reinfections, prolonged/chronic infections, severe infections, zoonotic infections and outbreaks, especially when the focus will shift to the detection of new variants.

Depending on available resources, testing strategies could include additional objectives, such as outbreak analyses, phylodynamic analyses and other research studies.

### Testing for variants

To be able to confirm infection with a specific variant, sequencing of the whole SARS-CoV-2 genome, or at least the whole or partial S-gene for the current variants, is required. Guidance on sequencing for SARS-CoV-2 has been issued by ECDC [117] and WHO [118]. Countries should build or scale up their high-throughput sequencing capacities.

For early detection and prevalence calculation of VOCs, in addition to alternative methods to sequencing, such as the use of diagnostic screening PCR-based assays that generate results in a few hours, can be valuable. Method selection is key to ensuring the timeliness of results and should depend on the testing strategy objectives set out below.

- Representative samples can be tested to estimate the VOC prevalence either using screening and/or sequencing methods. Sequencing can be used to assess the fraction of S-gene target failure that is VOC (B.1.1.7), to be able to use the pre-screening method as an indicator of the overall situation. Screening methods will enable the timely reporting of results.
- Screening for early detection of circulating VOCs can be used when real-time results are essential. All positive samples, or a selection of them, can be screened for VOCs and a subset then selected for further confirmatory sequencing. Sequencing of viruses from areas with an overall higher increase in cases may be necessary for the initial identification of novel VOCs.
- Whole genome sequencing (WGS) can be used for virus genetic characterisation and monitoring of virus evolution in the long term.

Guidance on sample selection and how to calculate the minimum number of viruses to be sequenced for surveillance purposes can be found in the first update of ECDC's technical guidance on sequencing of SARS-CoV-2 [117]. ECDC continues to monitor detection and transmission of variants throughout the EU/EEA and worldwide on a daily basis using the Early Warning and Response System, official and unofficial reports on publicly available sites, and reporting to TESSy.

### Detection of B.1.1.7, B.1.351 and P.1 without whole genome sequencing

Alternative methods to whole genome sequencing are available for the screening of all three VOCs. By sequencing the part of the genome where characteristic mutations are located it is possible to detect and differentiate between all three variants, and sequencing of the entire S1 subunit is recommended [119]. Using RT-PCR to detect a deletion in ORF1a ( $\Delta$ 3675-3677) [126,127] or the spike protein change N501Y [122] it is possible to identify all three variants, but not to differentiate between them. Detection of the spike deletions  $\Delta$ 69-70 and/or  $\Delta$ 144 can help to differentiate B.1.1.7 from the other VOCs [126,128,129]. To differentiate between B.1.351 and P.1, partial sequencing of the S-gene is currently required.

Community-level screening can be performed by sequencing SARS-CoV-2 from wastewater and the presence of signature mutations can be used to assess the presence of variants, although this technique is still under development [124].

### Laboratory capacity

ECDC has mapped the detection and characterisation capability and capacity for SARS-CoV-2 variants across the EU/EEA in a survey which was sent out to all Member States on 13 January 2021. This is the fifth laboratory capacity survey since the beginning of the COVID-19 pandemic in December 2019.

In this survey, and as of 22 January 2021, three of twenty-nine countries reported that they were not actively investigating the emergence of new SARS-CoV-2 variants. When asked about the current proportion of SARS-CoV-2 positive specimens characterised by sequencing, only three of twenty-nine countries stated that they were sequencing over 10% of SARS-CoV-2 positive specimens. Twenty-four countries did not meet the recommendation set by the European Commission of having a sequencing rate of 5–10%, and two countries did not respond to the question.

In response to the survey, as a first step ECDC is currently extending its sequencing support and offering sequencing services for Member States with limited or low sequencing capacity. Furthermore, ECDC is planning a molecular SARS-CoV-2 external quality assessment (EQA) that will assess VOC detection and identification capacity and capability. ECDC can also offer confirmatory virus neutralisation testing and antigenic characterisation of the virus for those Member States whose public health laboratories do not have the capacity to do so themselves. It can also offer technical support to laboratories that are currently performing neutralisation testing themselves.

### Advice on contact tracing and quarantine

With the increasing circulation of VOCs, identification and follow-up of contacts, adherence to quarantine, timely testing, and early isolation remain the cornerstone of the response and should be reinforced. Contacts need to be informed and followed-up in a timely manner and as completely as possible, in accordance with the recommendations outlined in ECDC's contact tracing guidance [125]. Member States should monitor the performance of their contact tracing programme and assess the effectiveness of local operations in preventing transmission, using indicators such as those in ECDC's monitoring framework for response activities [126]. Countries with very limited circulation of new variants could consider some of the enhanced actions outlined in the rapid risk assessment 'Risk related to the spread of new SARS-CoV-2 variants of concern in the EU/EEA – first update' [1].

## Measures related to travel

Travel measures (defined here as testing and quarantining of travellers) cannot completely prevent the (re)-introduction of SARS-CoV-2 and/or the introduction of new SARS-CoV-2 VOCs. However, a modelling study has shown that slowing down the introduction of the pathogen could prevent the triggering of larger outbreaks in areas where R is close to 1 [127,128]. Travel measures can only complement, and not replace, the implementation of the necessary community measures (such as NPIs, testing, contact tracing, isolation of cases and quarantining of their contacts).

In order to slow down the (re)-introduction and spread of SARS-CoV-2 and/or of new SARS-CoV-2 VOCs, individuals with active infection and those who have had recent contact with COVID-19 cases must not travel. Furthermore, ECDC recommends that non-essential travel should be avoided and that a robust system should be in place for the testing and quarantining of travellers. The expected impact of travel measures needs to be carefully weighed against the public health resources required to implement them and the expected impact they will have on the local epidemiological situation.

Travel measures should be implemented for those coming from areas which continue to have a high level of community transmission, irrespective of the conveyance and the extent of community transmission at the destination. Such measures are particularly important if there is limited evidence – for example, due to insufficient sequencing capacity – of the extent to which new virus variants are circulating in the area from which a traveller is arriving. Any measures implemented on internal or external EU borders need to be non-discriminatory in terms of nationality, place of residence and occupation and will need to take into account the epidemiological situation in the country of departure and arrival.

Escalated measures for travellers that could be considered include:

- quarantining of travellers for 14 days (unless a test is performed during quarantine, see below);
- testing prior to departure/on arrival and on days 5–7 during quarantine, in order to be released from quarantine if testing negative on days 5–7;
- enhanced contact tracing upon identification of a positive case, as described above.

Based on mathematical modelling studies, quarantining of travellers for 14 days appears to be the most effective measure for reducing the risk of transmission, although this creates logistical and socio-economic challenges. Assuming that contact information is collected for travellers to enable follow-up if required, the combination of testing prior to departure/on arrival, quarantine and a single test at around Day 5-7 after arrival appears to offer a reasonable balance of risks and benefits as an alternative to longer quarantine without testing. With every testing and/or quarantine strategy there is some residual risk of COVID-19 importation. It is ultimately the responsibility of the Member State to assess the residual risk linked to a shorter quarantine period – with or without testing – given the local situation and the potential impact on the public health system.

ECDC further recommends the use of Passenger Locator Forms (PLFs), preferably in digitalised format, including during transit through other airports and/or travel hubs on the way to the final destination.

These travel measures apply not only to international cross-border travel, but also to travel within countries/geographical areas where there are high levels of SARS-CoV-2 community transmission at local or regional level. Depending on the epidemiological situation, national authorities should consider implementing similar travel measures at sub-national level, to limit or delay the (re)-introduction and spread of the virus, including the new variants of concern. This will be particularly useful in hard-to-reach geographical areas. Monitoring implementation and compliance with these measures should be part the response in any setting. Any travel-related measure should apply to all travellers, irrespective of the means of transportation and/or their vaccination/immunisation status, at all points of entry.

### Vaccine certificates

ECDC is supportive of a vaccine certificate for COVID-19 to document someone having been given the vaccine, the number of doses, and the type of vaccine administered. ECDC is in discussions with the European Commission and the World Health Organization on a global approach for such a certificate for medical purposes. A structured and robust approach to vaccine documentation (whether through vaccine certificates, a vaccination card, or similar) is of paramount importance, as information on which vaccine product has been administered to whom and when is key to the success of any vaccination programme. The European Council has agreed to work on a standardised and interoperable form of proof of vaccination for medical purposes [129]. Moreover, on 27 January 2021 the E-Health Network adopted and published guidelines to prepare for interoperability between proofs of vaccination for medical purposes [130].

It is important to differentiate between a vaccine certificate, created for the reasons set out above, and a type of 'vaccine passport' used for travel purposes or to obtain other exemptions from mitigation measures in the community. At this point in time, there is no evidence that a fully vaccinated person cannot still be infected and transmit the disease (being asymptomatic) and there is therefore insufficient evidence to exempt travellers with proof of vaccination from quarantine and/or testing. Proof of vaccination should not, at this stage, cause international travellers to be exempt from complying with other travel risk reduction measures [131].

## Risk communication and community engagement for pandemic fatigue

In recent weeks, significant challenges to COVID-19 risk communication activities have developed, caused both by the emergence of the new, more transmissible variants of the virus, and by concerns over the speed of vaccination roll-out across the EU/EEA. Concerns have also been raised about the possible impact of the variants on vaccine effectiveness [132]. As a result, it will be necessary to inform the public that they will need to maintain or strengthen compliance with restrictive measures in order to control the spread of the new virus variants.

The protests and civil disturbances seen in late January in a number of European cities [133,134] indicate that some parts of the public have reached the limits of their tolerance in terms of continuing to comply with measures. Meanwhile, the high expectations at the start of the vaccination programme have been dampened by a set of acknowledged challenges faced during the rollout [135]. Pandemic fatigue – defined by WHO as 'de-motivation to follow recommended protective measures' [136] – appears to be growing in some settings, and this urgently needs to be addressed in order to avoid further waves of infection and minimise the discontent of the population.

In this rapidly evolving situation it is important to carefully manage public expectations concerning the likelihood of restrictions being eased. To do so, the standard principles of risk communication should be employed, including transparency regarding uncertainty, as well as accessibility and clarity of messages [137]. Monitoring levels of trust in public health organisations continues to be an important element of communication efforts, as trust is closely associated with acceptance of and compliance with measures [138]. Specific communication messages for the public should include the information below.

- The paramount importance of strengthening personal protective measures that have been shown to be effective, thereby limiting the risk of exposure, the spread of the new variants, and the opportunity for additional new variants to emerge [139].
- Emphasis of the fact that increasing rates of infection will bring about (i) more hospitalisations and deaths, (ii) more people who may develop long-lasting health problems in the form of 'long COVID', and (iii) more opportunities for the virus to mutate [140].
- Provision of easily understood information about epidemiological developments in the pandemic, including information on the new variants.
- A hopeful message of how continued compliance with the measures will help to control the new variants while also 'buying time' to allow the vaccines to have an impact, thereby facilitating a return to some degree of 'normality' [141].
- The importance of eligible people getting vaccinated as soon as they are able. A rapid roll-out of vaccination is required to protect as many people as possible, while also reducing the opportunities for the virus to mutate.
- Information on the status of national vaccination programmes (including realistic forecasts of who will be vaccinated by when); the prioritisation of population groups for vaccination and the rationale behind the choices; vaccine characteristics in terms of safety and efficacy, and any adaptations made to vaccination strategies. These are vital elements of information in order for the public to maintain trust in the vaccination campaigns.
- Reassurance that researchers, manufacturers and regulatory bodies are exploring ways in which to update vaccines as necessary, and are facilitating their authorisation in order to allow for rapid deployment.

The principles of community engagement should also be used as a means of ensuring that people feel that their concerns are being taken seriously, and that they are being listened to. To this end, it is important that authorities (i) recognise the community as a partner in controlling the pandemic; (ii) ensure that they have a good understanding of community perceptions of the pandemic, and of the measures in place, through ongoing behavioural research (including monitoring of vaccine acceptance as well as social media monitoring to detect and address inaccurate, incorrect and potentially damaging information for the vaccination campaign or concerning other aspects of the pandemic) and (iii) optimise communications with the population sub-groups that are most medically or socially vulnerable - for example through the use of trusted spokespeople [31,34,148,149]. Similarly, it is essential that infected people and their contacts, who are obliged to isolate, are supported – financially and logistically – while they remain at home [142].

## Knowledge gaps

Much of the evidence presented here regarding the SARS-CoV-2 variants is based on unpublished data, which has not been peer-reviewed yet and is currently evolving on a daily basis. Therefore, there are still many knowledge gaps and major uncertainties regarding the interpretation of the data and conclusions.

Major knowledge gaps on virus variants that should be addressed urgently by public health authorities and scientists include the following:

- incidence of variants in EU/EEA populations, where sufficient sequencing is not available;
- clinical presentation (e.g. infection severity) and epidemiological profile (affected population groups);
- competitive advantage of different variants, and consequences of co-circulation;
- unknown genetic markers related to receptor binding, infectivity, severity, etc.;

- antigenic characteristics of variant viruses
- incidence of re-infections or breakthrough infections following vaccination;
- transmissibility between humans;
- binding properties to human receptors, including ACE2 receptors;
- cross-protection, susceptibility and immunity of the population;
- impact on effectiveness and safety of available COVID-19 vaccines and candidates in development;
- impact on possible treatment options (e.g. convalescent sera and antibodies);
- possible animal reservoir (species) being a risk for adaptive mutations and an ongoing source of infection for humans (e.g. mink).

International health authorities need to urgently establish a process for formally assessing the variants, addressing the knowledge gaps and directing changes in public health interventions, such as vaccination strategies and vaccine composition.

## Limitations

This assessment is undertaken on the basis of information known to ECDC at the time of publication and has several key limitations. It is important to consider the time lag between infection, symptoms, diagnosis, case notification, death, and death notification, as well as the time lag for reporting to the EU level. Assessing the impact of response measures is complex due to the implementation of different components of NPIs and the pace of implementation for vaccination programmes. The natural evolution of the virus (including the spread of mutated versions of the virus), compliance with measures, cultural, societal, environmental and economic factors will all continue to play a role in the dynamics of disease transmission.

Much of the evidence currently available on the VOCs is based on preprint manuscripts, which have not yet been appropriately peer-reviewed, or press releases, thereby increasing the uncertainty around these findings.

## Source and date of request

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All experts have submitted declarations of interest, and a review of these declarations did not reveal any conflict of interest.

## 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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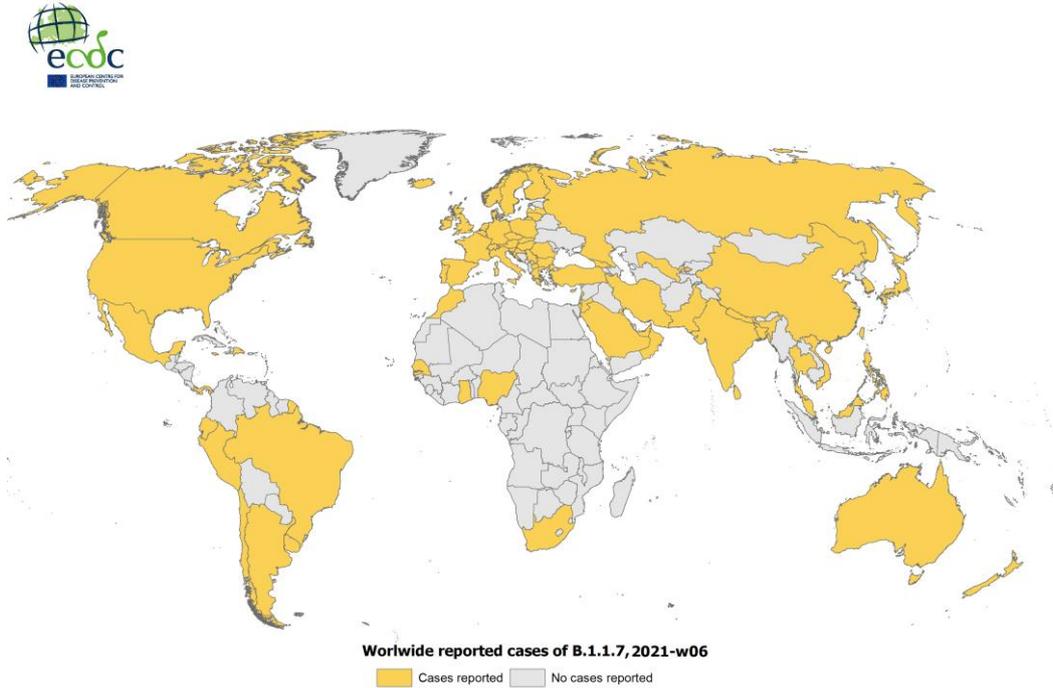
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# Annex

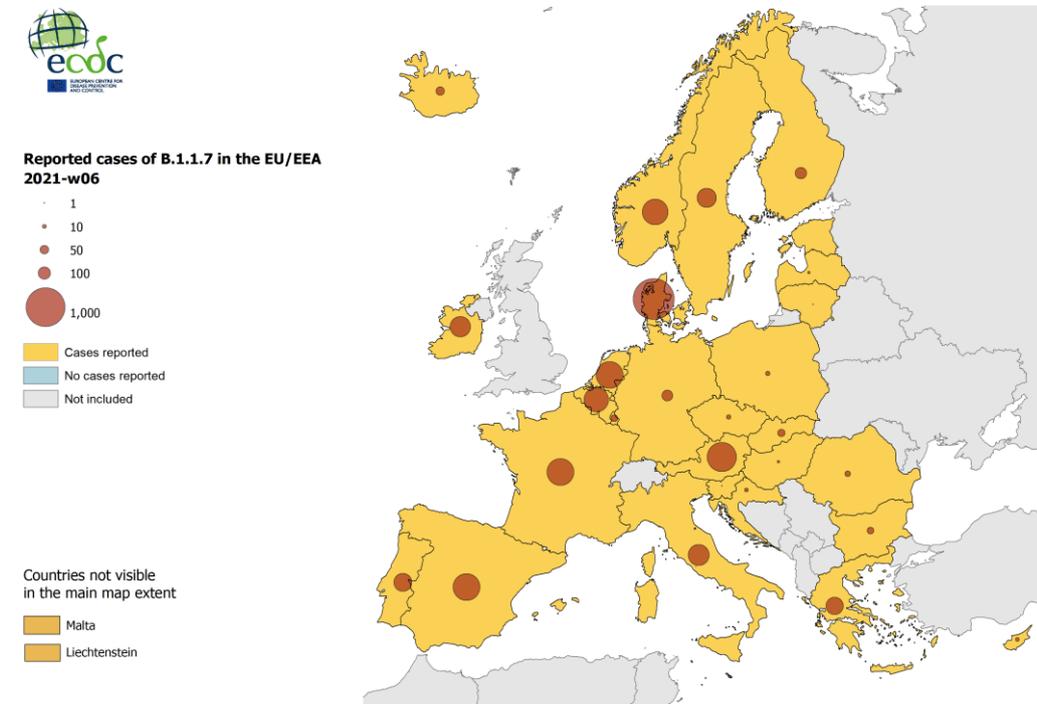
**Figure A1. Number of SARS-CoV-2 lineage B.1.1.7 cases detected worldwide, as of 11 February 2021**



Administrative boundaries: © EuroGeographics © UN-FAO © Turstat. The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on: 11 Feb 2021

*Note: SARS-CoV-2 variant data is collected by ECDC's Epidemic Intelligence team from various sources. Data are subject to retrospective corrections. Users are advised to use all data with caution and be aware of data limitations.*

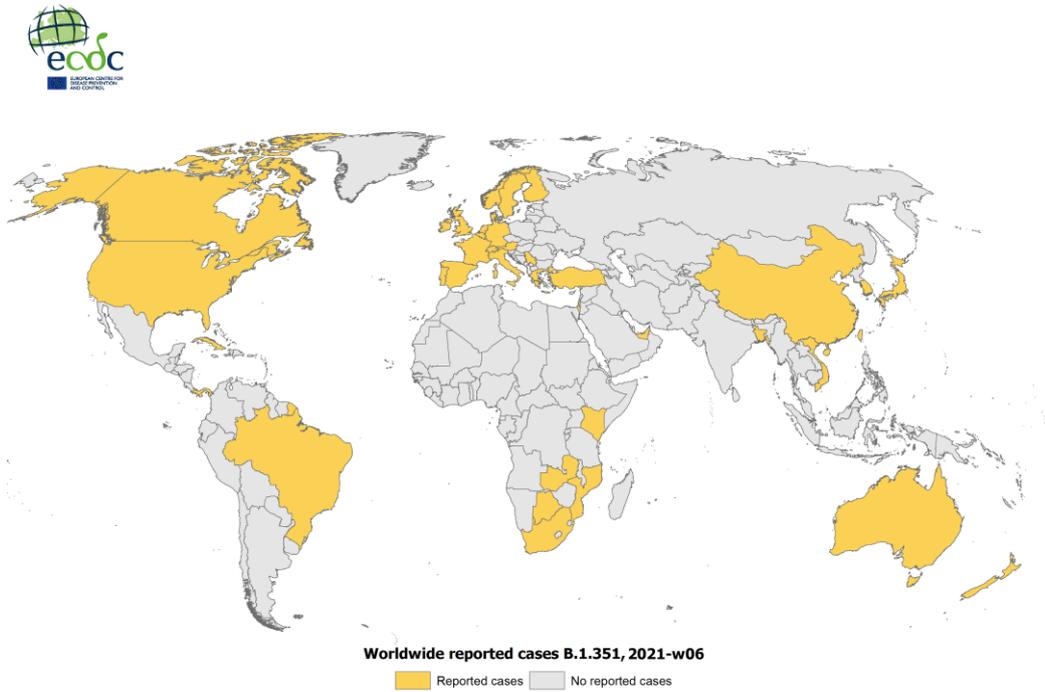
**Figure A2. Number of SARS-CoV-2 lineage B.1.1.7 cases detected in EU/EEA countries, as of 11 February 2021**



Source: GISAID EpiCoV data™. Administrative boundaries: © EuroGeographics. The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on: 11 Feb 2021

*Note: SARS-CoV-2 variant data is collected by ECDC's Epidemic Intelligence team from various sources. Data are subject to retrospective corrections. Users are advised to use all data with caution and be aware of data limitations.*

**Figure A3. Number of SARS-CoV-2 lineage B.1.351 cases detected worldwide, as of 11 February 2021**

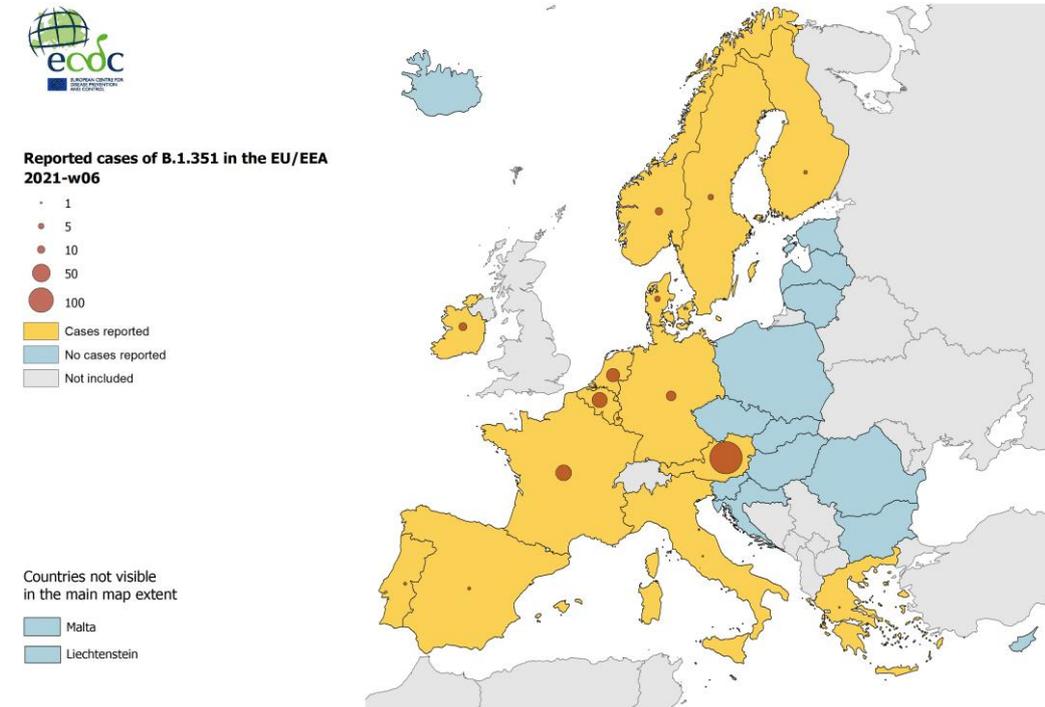


Administrative boundaries: © EuroGeographics © UN-FAO © Turstat.

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*Note: SARS-CoV-2 variant data is collected by ECDC's Epidemic Intelligence team from various sources. Data are subject to retrospective corrections. Users are advised to use all data with caution and be aware of data limitations.*

**Figure A4. Number of SARS-CoV-2 lineage B.1.351 cases detected in EU/EEA countries, as of 11 February 2021**



Source: GISAID EpiCoV data™. Administrative boundaries: © EuroGeographics

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*Note: SARS-CoV-2 variant data is collected by ECDC's Epidemic Intelligence team from various sources. Data are subject to retrospective corrections. Users are advised to use all data with caution and be aware of data limitations.*