RISK ASSESSMENT

Assessing SARS-CoV-2 circulation, variants of concern, non-pharmaceutical interventions and vaccine rollout in the EU/EEA, 15th update

10 June 2021

Summary

Although SARS-CoV-2 transmission remains widespread in large parts of the EU/EEA, most countries report declining trends in 14-day COVID-19 notification rates, hospital and intensive care unit (ICU) occupancy, and mortality. Many countries have initiated partial lifting of different non-pharmaceutical interventions (NPIs) that aim to reduce the degree of citizens physical contact and mobility. Since January 2021, EU/EEA countries have reported an increase in the number and proportion of SARS-CoV-2 cases of variants of concern (VOC) associated with increasing transmissibility and/or severity, with Alpha (B.1.1.7) the current dominant variant across the EU/EEA. Estimates across the region show that a large proportion of the population across Europe still remains susceptible to SARS-CoV-2 and that population immunity is far from being reached. As of 3 June, the median cumulative vaccine uptake in the EU/EEA adult population (aged 18 years and older) had reached 46.2% for at least one vaccine dose and 22.3% for the full vaccination course. The highest level of vaccine uptake was observed among the elderly aged over 80, in which the uptake reached 80.5% for at least one dose and 66.3% for full vaccination coverage. For healthcare workers, the median level of at least one dose uptake was 87% and the median uptake for the full vaccination course was 65.2%. Increased vaccine supply has allowed countries to expand eligibility for vaccination to younger age groups.

Risk assessed in this update

The assessment of the risk posed by the current SARS-CoV-2 pandemic is stratified by four population groups (the vaccinated and unvaccinated general population and the vaccinated and unvaccinated vulnerable population). The assessment is based on the following elements: i) the vaccinated group has a lower probability of infection and ii) a lower impact of such infection than the unvaccinated, while iii) the vulnerable population suffers a higher impact of such infection when compared with the general population. Specific separate assessments were not performed for partially vaccinated and previously infected individuals in this risk assessment, although it is known that some protection is conferred to such persons. Due to differences in the epidemiological situation, vaccination strategies and NPIs implemented, EU/EEA countries are experiencing different levels of risk posed by SARS-CoV-2 to the general population and to vulnerable groups and, thus, require different targeted interventions. ECDC classifies the epidemiological situation in EU/EEA countries into four categories based on the level of concern (low, moderate, high, very high). In most countries, the contribution of the intensity indicators to the overall score has been higher than that of the severity indicators in recent weeks. As such, the overall classification shown below provides a conservative estimate of transmission intensity.

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In countries with an epidemiological situation classified as low concern, widespread transmission is falling with consequent low case notification rates. Due to the large proportion of the vulnerable population vaccinated with at least one dose, very low notification rates are recorded among the elderly. In these countries, the risk posed by the SARS-CoV-2 pandemic is assessed as low for the general population (both vaccinated and unvaccinated) and the vaccinated vulnerable population; for the unvaccinated vulnerable population there is a moderate-to-high risk.

Countries classified as moderate concern continue experiencing widespread SARS-CoV-2 transmission associated with a dominating highly transmissible variant. The highest notification rates are observed in the general population and, although a high proportion of the vulnerable population has been vaccinated with at least one dose, the probability of infection is higher than in the previous group of countries. A large part of the population is still susceptible to the infection. In these countries, the risk posed by the SARS-CoV-2 pandemic ranges from low for the vaccinated general population to high-to-very high for the unvaccinated vulnerable population.

Countries classified as high concern experience widespread SARS-CoV-2 transmission not only in the general population, but also among vulnerable individuals. The NPIs in place appear to be having a limited effect, either because adherence to the measures may not be optimal or the measures in place may not be sufficient to reduce or control exposure. Vaccination uptake in the general population and, particularly, in the vulnerable population appears to be still low. In these countries, the risk posed by the SARS-CoV-2 pandemic ranges from low-to-moderate for the vaccinated general population to very high for the unvaccinated vulnerable population.

The current assessment represents a decrease in the risk levels compared with the 14th update of the ECDC COVID-19 risk assessment published in February 2021 [1]. Still, in any of the country scenarios, should mass gathering events such as the UEFA European Football Championship take place in the absence of sufficient mitigation measures, the risk of local and pan-European transmission risk of COVID-19, including the spread of variants of concern, would increase.

There is a continuous risk of the emergence and spread of variants of concern (VOCs) that are potentially more transmissible or cause serious disease or escape natural or vaccinated immunity. The VOC B.1.617.2 (Delta) associated with increased transmissibility and a slight to moderate reduction in vaccine effectiveness after one vaccine dose is rising in some EU/EEA countries. Modelling suggests that a significant increase in COVID-19-related cases in the EU/EEA remains possible when NPIs are rapidly relaxed or vaccination rollout delayed.

Options for response

One of the main public health goals in the current phase of the pandemic is to reduce severe COVID-19 disease and mortality by ensuring full vaccination for risk groups, including the elderly and those with underlying medical conditions. COVID-19 vaccination campaigns should remain a priority for all countries and vaccine rollout should continue, and possibly be accelerated whilst tailored to ensure access for vulnerable, hard-to-reach and hesitant populations.

Countries with a favourable epidemiological situation and progress toward high vaccine uptake in priority groups may consider adjusting and phasing out their NPIs, following a careful assessment of their local situation. A comprehensive testing strategy to enable the timely detection of cases and a robust system for contact tracing should remain a priority for all public health authorities.

The emergence and spread of VOCs, that are potentially more transmissible or cause more severe disease or escape natural or vaccine-induced immunity, requires strong surveillance measures and enhanced measures to stop, delay or reduce the spread of these VOCs. To be able to confirm infection with a specific variant, timely sequencing of the whole SARS-CoV-2 genome, or at least the whole or partial S-gene for current variants is required.

The risk of introduction of new variants in the EU is closely related to the pandemic evolution, within, as well as outside, of the EU. Efforts to ensure more equitable access to vaccination globally can mitigate the risk of the emergence of new variants.

Introduction of SARS-CoV-2 by travel-related cases, including of new virus variants, can play a role in triggering increased community transmission of COVID-19, particularly when levels of transmission in the receiving locality are low. As such, carefully and rigorously implemented travel measures can have an impact on the introduction and further transmission of new variants of virus, or on re-introduction of any form of virus, if local levels of transmission are low. Travel measures, including the requirement to provide proof of a negative test before travel or on arrival and quarantine for incoming individuals can be tailored according to considerations of vaccination status and VOC circulation and should be coordinated internationally.

Although increasing vaccination coverage will mitigate the effect of replacement with more transmissible variants, decisions to ease measures need to be highly sensitive to the local context and include considerations about the current viral circulation, the prevalence of VOCs and the vaccination status. Modelling analysis shows that a significant increase in COVID-19-related cases in the EU/EEA remains possible if NPIs are relaxed too rapidly.

For events with the potential to give rise to mass gatherings, such as the UEFA Euro 2020, monitoring of the epidemiological situation and implementation of preventive and mitigation measures should be done with a coordinated intersectoral approach.

Risk communication strategies need to highlight the fact that the pandemic is not over yet. People should be well informed about the need to respect NPIs that remain in place and reminded of the importance of full vaccination coverage as an effective measure to protect against infection and severe disease in priority groups and control the future transmission of the virus.

Event background

As of 4 June 2021, more than 171 000 000 COVID-19 cases and 3 500 000 deaths have been reported worldwide. Currently, the countries with the highest case notification rates are the Maldives, Seychelles, Bahrain, Uruguay and Argentina, with the Americas and south-east Asia experiencing the highest case notification rates worldwide [2]. By 3 June, 5.7% of the global population had been fully vaccinated, although vaccination coverage varied by region, with the highest rates of full vaccination coverage in North America (26.4%) and Europe (17.8%), and lower rates in South America (9.4%), Asia (2.3%) and Africa (0.7%) [3].

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.

The latest available data on the number of cases and the number of deaths globally is published daily on ECDC's website: https://www.ecdc.europa.eu/en/covid-19/situation-updates.

EU/EEA countries have reported more than 32 000 000 cases and 725 000 deaths (representing 19% of all cases and 4.9% of all deaths reported worldwide) 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 [4].

Trends in reported cases, testing, hospitalisation, and mortality

By the end of week 21, 2021 (23 May 2021), the 14-day case notification rate for the EU/EEA was 111 per 100 000 population (country range: 10-312). This reflects a decrease of 75% when compared with the case notification rate of 459 at the peak of the last wave of infection in the EU/EEA in week 13, 2021 (ending 4 April 2021). The overall notification rate is at its lowest since Oct 2020 with high testing rates (>4 000 tests per week per 100 000). Decreases in case notification rates have been seen in almost all EU/EEA countries in recent weeks. Testing rates in the EU/EEA increased by 26% between weeks 13 and 20, 2021, from 3 778 to 4 762 per 100 000 population [4].

Rates of hospital and/or ICU admissions and/or occupancy have similarly decreased in 26 out of 27 EU/EEA countries with available data since week 13, 2021, with a median decrease of 73% in hospital admissions. Death notification rates have decreased by 65% from the last peak of 80 per million population during week 15 (ending 18 April 2021) to 28 per million population (country range: 0-71) in week 21, 2021.

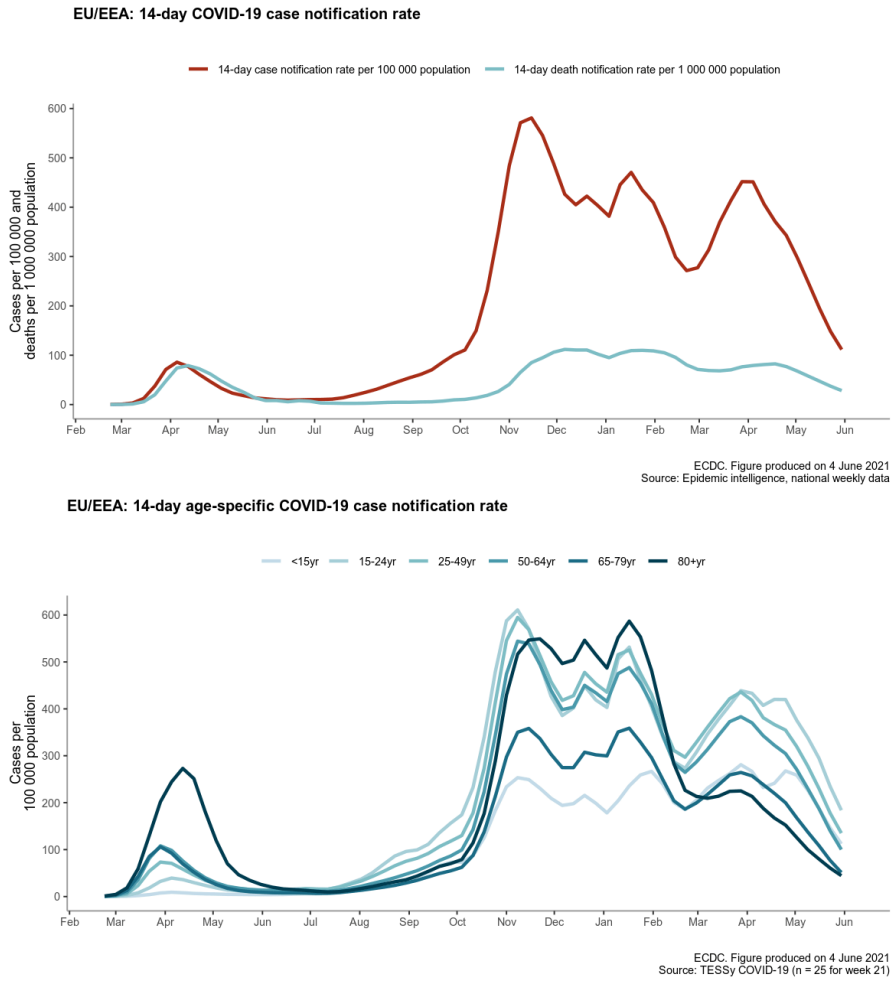
Pooled excess mortality data from EuroMOMO [5] indicate that no excess deaths have been observed among persons aged 85 years and over since week seven to eight, 2021. In contrast, excess deaths were reported during the last wave of infections in Europe (increase starting around week nine and peaking during week 13-14) among 45-64 year olds, 65-74 year olds and to a lesser extent 75-84 year olds.

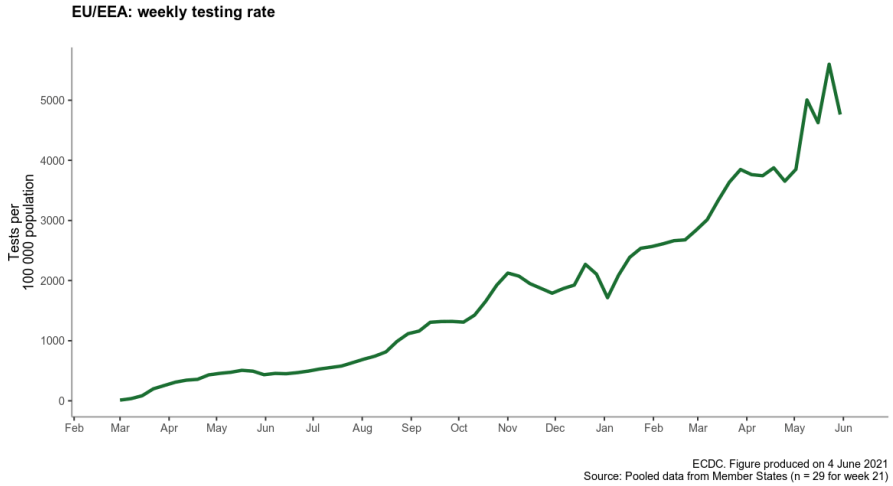
Notification rates among persons aged 80 years and over decreased from 587 per 100 000 during the previous peak in January 2021 (week 2) to 248 in week 13 and 48 per 100 000 in week 21 (total decrease of 92%). Notification rates among persons aged 25-49 years were 593 per 100 000 in week two, 442 in week 13 and 129 per 100 000 in week 20 (total decrease of 78%) [4].

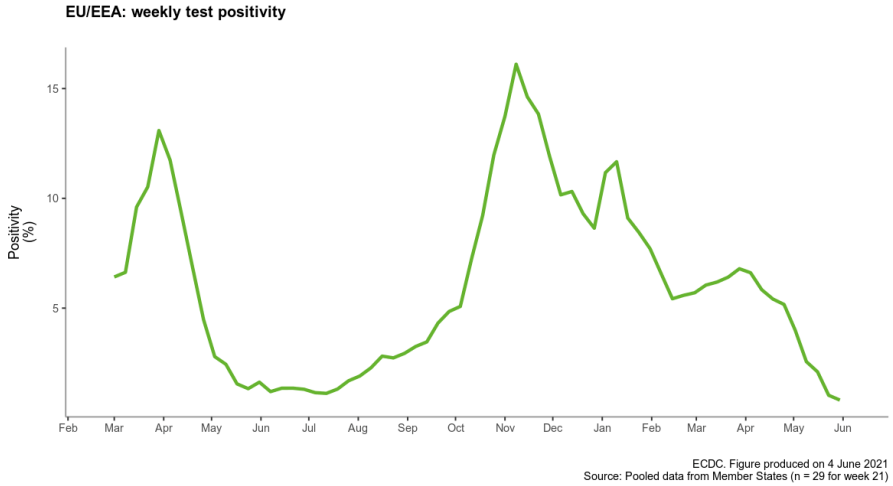
Since week nine, 2021, notification rates among the elderly have been the lowest among all age-groups. It is the first time that this has been observed since the start of the pandemic, and a drastic change from January 2021, when rates were highest among the elderly. The ratio of notification rates among persons aged 80 years to that among 25-49 year-olds decreased from 1.06 in week 3, 2021 to 0.56 in week 13 and 0.48 in week 21.

Despite the decreasing trends, as of week 20, 2021, case notification rates, mortality rates and hospitalisation and ICU admission/occupancy rates remain above the levels detected during the summer of 2020 in almost all EU/EEA countries (Figure 1).

Figure 1. Pooled overall case and death notification rates, age-specific case notification rates, testing rates and test positivity, EU/EEA, March 2020 to May 2021.







SARS-CoV-2 variants of concern

The current list of variants of concern (VOCs) maintained by ECDC currently includes B.1.1.7 (referred to by the new World Health Organization (WHO) labelling for communicating with the public about variants as Alpha), B.1.1.7+E484K, B.1.351 (Beta), P.1 (Gamma), and B.1.617.2 (Delta). Additional information on the characteristics of such VOCs is provided in Annex 1. For the purposes of this document, the variants will be referred to by their Pango lineage name.

The VOC B.1.1.7, first reported by the United Kingdom (UK), has been reported by 138 countries globally in GISAID EpiCoV and it is the predominant variant in the EU/EEA [1]. The UK reported a recent decline in the prevalence of the variant and a corresponding rapid increase of the VOC B.1.617.2 [6], which suggests that replacement of B.1.1.7 by B.1.617.2 could also be observed in the EU/EEA in the coming months.

The VOC B.1.1.7+E484K, first reported in the UK, has a B.1.1.7 genetic background that carries the additional change E484K in the spike protein. This substitution has been associated with reduction in neutralising activity by antibodies and it is also found in VOCs B.1.351 and P.1. The VOC B.1.1.7+E484K has been reported by 32 countries so far in GISAID EpiCoV. Outbreaks involving the B.1.1.7+E484K have been reported in the EU/EEA region, but no significant increase in prevalence has been observed so far.

The VOC B.1.351, first identified in South Africa, has been registered by 91 countries globally in GISAID EpiCoV. Community transmission and outbreaks related to this variant have been reported in the EU/EAA region, but no significant overall increase in prevalence has been observed so far. It 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 (amino acid change L18F, R246I, K417N, and deletion 242-244). Three of the changes (amino acid change K417N, E484K, and N501Y) are located within the receptor-binding domain [1].

The VOC P.1, first reported by Japan in returning travellers from Brazil, and then later in Brazil, has been reported by 54 countries globally in GISAID EpiCoV. Community transmission and outbreaks related to this variant have been reported in the EU/EAA region, but no significant increase in prevalence has been observed so far. The variant is characterised by 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. [1].

The VOC B.1.617.2, first detected in India in December 2020 has been reported by 58 countries globally in GISAID EpiCoV. B.1.617.2 is defined by multiple spike protein changes as well as by mutations in other genomic regions [1]. Recent data reports from the UK public health authorities have shown that this variant is associated with transmissibility at least as high as B.1.1.7, and with a slight to moderate reduction in vaccine effectiveness, especially after only one vaccine dose. Assessment of these data led to an upgrade in the classification of this variant by ECDC on 24 May 2021, from variant of interest (VOI) to VOC [7].

According to data reported as of 23 May 2021, the situation regarding VOIs and VOCs in EU/EEA countries remained stable, with B.1.1.7 being the dominant variant in the EU/EEA. However, only 12 EU/EEA countries were reporting sequences at the recommended level of at least 500 sequences per week or 10% of SARS-CoV-2-positive cases (Belgium, Denmark, Estonia, France, Germany, Hungary, Iceland, Ireland, Luxembourg, Malta, Norway and Poland)[1]. Among the 12 EU/EEA countries with the recommended level of sequence reporting in the period from 10 May to 23 May 2021, 10 had a valid denominator. The median (range) of the VOC reported in all samples sequenced in the period in these 10 countries was 91.6% (70.2–97.1%) for B.1.1.7, 0.5% (0.0–7.2%) for B.1.351, 0.3% (0.0–5.3%) for B.1.617, 0.2% (0.0–10.1%) for P.1 and 0.0% (0.0–1.6%) for B.1.1.7+E484K.

None of the variants of interest (VOIs) were detected with a proportion of greater than 1%: median (range) were 0.0% (0.0–3.1%) for B.1.525, 0.0% (0.0–0.1%) for B.1.620 and 0.0% (0.0–0.0%) for B.1.621. A list of current VOCs and VOIs for the EU/EEA is published on ECDC's website.

Prevalence of SARS-CoV-2 antibodies in Europe

ECDC, in collaboration with WHO EURO, is monitoring the results of the seroprevalence studies performed in the WHO-EURO region. Up to end of 2020, the overall prevalence of SARS-CoV-2 antibodies relating to natural infection in the region still remained at low levels (<15%) [10,11], with large variations between and within countries. Some higher regional estimates (up to 52%) [8,9] of SARS-CoV-2 antibodies were measured in areas with extensive local community transmission. It is likely that a large proportion of the population across Europe still remains susceptible to SARS-CoV-2 infection and that population immunity is far from being reached. Ongoing monitoring of the natural and vaccine-induced immunity in the region remains important, in order to provide a better understanding of the epidemiological situation and help guide the effective implementation of control measures.

Non-pharmaceutical interventions

ECDC collects information on non-pharmaceutical interventions (NPIs) implemented in EU/EEA countries in response to the COVID-19 pandemic. After intensive measures implemented throughout the course of the pandemic and continuing through spring 2021, most EU countries are in the process of relaxing NPI's to a greater or lesser extent.

Detailed up-to-date information on the public health measures implemented at national level are available in the Weekly COVID-19 country overview. In addition, a repository with all current and past NPIs 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.

Vaccination

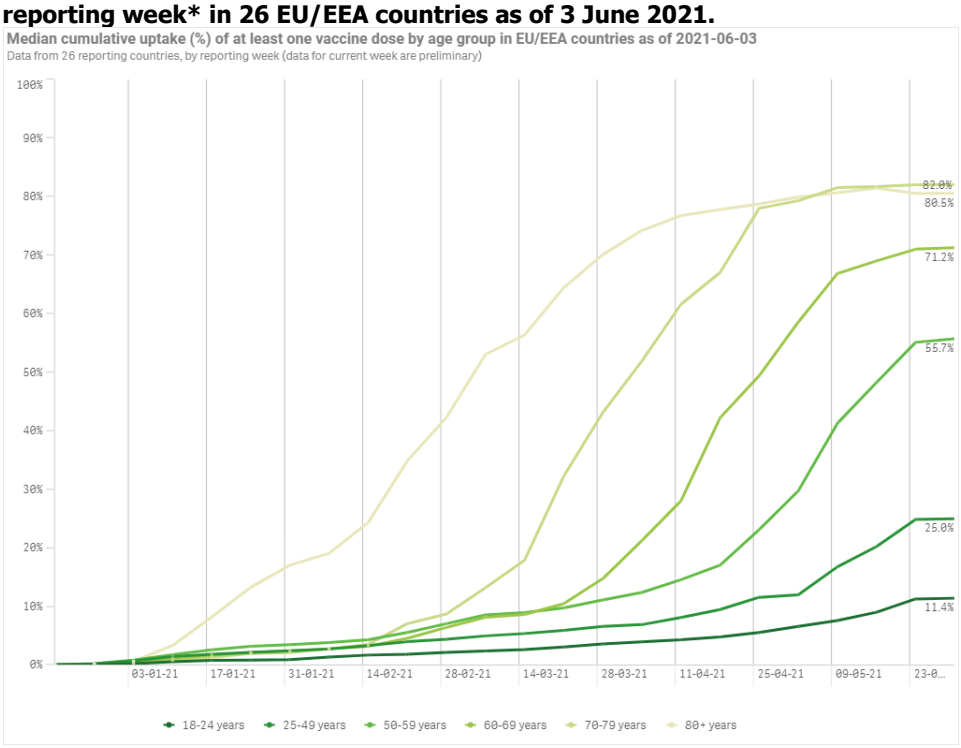
Currently, four COVID-19 vaccines have received conditional marketing authorisation in the EU [12], following evaluation by the European Medicine Agency (EMA), and are part of the EU Coronavirus Vaccines Strategy Portfolio: Comirnaty (BNT162b2) developed by BioNTech/Pfizer, COVID-19 Vaccine Moderna (mRNA-1273), Vaxzevria (AZD1222) previously COVID-19 Vaccine AstraZeneca, and COVID-19 Vaccine Janssen (Ad26.COV 2.5). In addition, vaccines that have not been authorised at the EU level (Sputnik V, Beijing CNBG) are currently being used in one Member State under national licensing arrangements [13]. In most EU/EEA countries, the vaccination rollout started at the end of December 2020, when the first batches of Comirnaty were distributed. Because of limited vaccine supply, prioritisation strategies initially focused on groups with higher risk of exposure to the virus or higher risk of severe disease or death (e.g. healthcare workers and the elderly, including those living in long-term care facilities (LCTFs)). The main objectives for the rollout of vaccination in countries were to reduce the number of deaths, to protect the healthcare workforce, and to reduce the pressure on healthcare systems by reducing the number of individuals being hospitalised and in need of intensive care. The escalation of vaccine supplies has subsequently allowed countries to expand eligibility for vaccination to younger age groups.

[1] Based on data reported to the GISAID EpiCoV database by 25 May 2021, or to TESSy by 23 May 2021 (data referring to the period 3 May to 16 May 2021).

As of 3 June, the median cumulative vaccine uptake in the EU/EEA adult population (aged 18 years and older) reached 46.2% for at least one vaccine dose (range: 14.1-65.8%) and 22.3% for the full vaccination course (range: 10.1-49.7%). The highest level of vaccine uptake was observed among the elderly aged 80+ in which the uptake reached 80.5% for at least one dose (range: 13.8-100%) and 66.3% for full vaccination (range: 9-99.6%) (26 reporting EU/EEA countries). For healthcare workers, the median level of at least one dose uptake was 87% (range: 21.3-100%) and the median uptake for the full vaccination course was 65.2% (range: 19.7-100%) (16 reporting EU/EEA countries).

More information, with country specific data, can be found in ECDC's vaccine tracker [13] and the related weekly vaccine rollout overview [14].

Figure 2. Median cumulative uptake (%) of at least one dose of COVID-19 vaccine, by age group and reporting week* in 26 EU/EEA countries as of 3 June 2021.



Mass gathering: UEFA EURO 2020

The UEFA European Football Championship (UEFA EURO 2020), which was postponed in March 2020 due to the COVID-19 pandemic, will take place between 11 June and 11 July 2021. Eleven countries will host the games, of which seven are EU Member States: Denmark, Germany, Hungary, Italy, the Netherlands, Romania, and Spain. Other countries hosting games are Azerbaijan, Russia and the United Kingdom. Twenty-four teams will be playing the matches during this period, watched by an estimated 460 000 spectators.

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, treatment and vaccines please visit ECDC's website: https://www.ecdc.europa.eu/en/covid-19/latest-evidence.

Effectiveness of vaccination

Evidence from real-world use of COVID-19 vaccines authorised in Europe has confirmed the clinical trial findings and demonstrated high vaccine effectiveness against PCR-confirmed SARS-CoV-2 infection and symptomatic disease [15]. There are also an increasing number of real-world studies, especially coming from Israel, US and the UK, showing high vaccine effectiveness against severe disease, hospitalisation and death. In a large observational study from Israel, vaccine effectiveness was 87% (95% CI 55-100%) against hospitalisation and 92% (95% CI 75-100%) against severe disease after two doses of Comirnaty vaccine [16]. A retrospective cohort study (preprint) in the US found mRNA vaccines (Comirnaty and COVID-19 vaccine Moderna) were 96% (95% CI 95-99) effective at preventing hospitalisation and 98.7% (95%CI 91.0-99.8) effective at preventing deaths when the individuals were fully vaccinated [17].

A test negative case-control study from the UK found that one dose of either Comirnaty or Vaxzevria provided 60-70% protection against symptomatic COVID-19 and about 80% effectiveness at preventing admissions to hospital [18]. In addition, evidence is beginning to emerge on the impact of vaccination on risk of transmission [19]. A large register-based study on prevention of SARS-CoV-2 transmission in households of vaccinated healthcare workers from Scotland suggests that vaccination of a household member reduces the risk of infection in susceptible household members by at least 30% [20]. A recent study examining the impact of vaccination on household transmission in England found that the likelihood of household transmission is 40−50% lower for households where the index cases were vaccinated 21 days or more prior to testing positive (93% of the vaccinated index cases had received only one dose of vaccine), compared to no vaccination[21]. The effects are similar for Comirnaty and Vaxzevria vaccines. There is evidence that vaccination significantly reduces viral load [22] when infection happens in vaccinated individuals and this could translate into reduced transmission, although vaccine effectiveness does vary by vaccine product and target group.

Impact of SARS-CoV-2 variants of concern on COVID-19 vaccine efficacy

In studies that have addressed the VOCs, there is limited preliminary evidence of reduced vaccine efficacy, in particular for B.1.351 and possibly also for P.1 and B.1.617.2 [17-22]. Data are emerging which indicate that vaccine efficacy is maintained for B.1.1.7 [19,23,24]. Infections with VOCs have been reported in fully vaccinated individuals, although the frequency of this and the severity of illness following infection is not yet well understood [19]. Assessment of the emerging variants' potential to escape the immunity induced by the currently available vaccines is ongoing. More information on this will be needed as new variants emerge in the future.

Vaccine effectiveness and number of doses

One dose vs two dose schedule

Effectiveness studies of a single dose of Comirnaty, COVID-19 Vaccine Moderna or Vaxzevria vaccines have shown that a single dose is immunogenic in previously *naïve* vaccine recipients, reduces risk of infection and can reduce risk of severe disease (including hospitalisation) [14,25-28]. However, the follow-up period after one dose is limited in most studies, so the duration of immunity after one dose is not known. The two-dose strategy proposed for many vaccines aims to ensure that potential weak antibody responses generated via a single dose – particularly, but not exclusively in the elderly – are adequately boosted to maximise protection as shown in efficacy clinical trials [29-31].

In addition, the effect that current and emerging VOCs may have on vaccine efficacy and effectiveness and vaccine dosing schedules is emerging. A recent preprint study from the UK on the effectiveness of Comirnaty and Vaxzevria vaccines against symptomatic COVID-19 cases identified as infected with the B.1.617.2 VOC showed that effectiveness was lower after one dose of vaccine with B.1.617.2 cases (33.5%, 95%CI 20.6-44.3) compared to B.1.1.7 cases (51.1%, 95%CI 47.3-54.7) with similar results for both vaccines, however after two doses of either vaccine there were only small non-significant reductions in vaccine effectiveness. These results would support maximising vaccine uptake with two doses among vulnerable groups [28].

In response to the rising cases of the B.1.617.2 VOC, following advice from the UK Joint Committee on Vaccination and Immunisation (JCVI), on 14 May 2021 the UK government reduced the timing for administering the second dose of COVID-19 vaccines from 12 to eight weeks for the priority groups [37] to ensure adequate protection.

One dose following previous SARS-CoV-2 infection (for vaccines given in a two-dose schedule)

In order to achieve rapid vaccination rollout, and taking into account the limited doses available, some EU/EEA countries have put in place policies to vaccinate as many people in the groups at high risk of severe COVID-19 as possible. This includes recommending only one dose of vaccine (in a two-dose schedule) to those individuals who have previously been infected with SARS-CoV-2. There is emerging evidence that for those individuals who have been previously infected with SARS-CoV-2, a single dose of Comirnaty and COVID-19 Vaccine Moderna appears to generate similar antibody, B cell and T cell responses to those found in non-infected individuals who have received two vaccine doses [33-36]. There is also emerging evidence of higher antibody levels after one dose of the Vaxzevria vaccine in previously infected individuals compared to one dose in non-previously infected individuals, and a single dose in previously infected individuals appears to generate similar antibody responses to those found in non-infected individuals who received two doses of vaccine [36-38]. However, follow-up periods for vaccinated individuals completing the full two-dose regimen are not yet sufficiently long enough to be able to draw conclusions on the duration of protection against infection beyond six months. Whilst studies of single-dose regimens for previously infected individuals are promising in the short term, evidence on the duration of protective immunity for such individuals is even sparser.

Based on the available clinical trial data, the current EMA product information for the vaccines authorised in EU/EEA countries is that the Comirnaty, COVID-19 Vaccine Moderna and Vaxzevria vaccines should be provided in a two-dose schedule and the COVID-19 Vaccine Janssen in a one-dose schedule to ensure adequate, long-term protection. The World Health Organization's (WHO) Strategic Advisory Group of Experts on Immunization (SAGE) currently recommends a two-dose schedule for individuals with Comirnaty, COVID-19 Vaccine Moderna and Vaxzevria, and the one-dose schedule for COVID-19 Vaccine Janssen, irrespective of prior infection.

Heterologous COVID-19 vaccine schedule

Heterologous combination of vaccine doses (mix and match), where different COVID-19 vaccines are used for the first and the second dose in a COVID-19 vaccination regime, is already in use in a number EU/EEA countries [44]. After the safety signals from thrombosis with thrombocytopenia syndrome (TTS) following vaccination with Vaxzevria, some countries have started recommending a second dose of an mRNA vaccine (Comirnaty or COVID-19 Vaccine Moderna) to individuals who received a first dose of Vaxzevria [44].

There is some evidence on the immunogenicity, safety and efficacy of heterologous schedules from clinical trials, and also several ongoing studies. A good immune response could be expected from combining different COVID-19 vaccines, as all licensed vaccines induce an immune response against the SARS-CoV-2 spike protein, and it is expected that mixing vaccines could potentially boost immune responses in the process [45].

The Com-Cov study is an ongoing trial in the UK, which started in February 2021. Combinations of Vaxzevria and Comirnaty are tested in four or 12 weeks intervals, and from April, the trial also included the COVID-19 Vaccine Moderna and NVX-CoV2373 by Novavax. A preliminary analysis of reactogenicity indicates an observed slight increase in side effects with a heterologous schedule, such as fever, headache and malaise, albeit mild [46]. Preliminary results reported from the Spanish CombivacS study, show that a combination of Vaxzevria and Comirnaty is well tolerated and induces a sevenfold increase in neutralizing antibodies after a second dose of Comirnaty, which is more than double the effect seen in other studies using a second dose of Vaxzevria, notwithstanding differences in assays. The observed side effects in this study were mild and reported to a similar extent as for homologous vaccination schedules [47].

In addition to the studies and results described above, several EU/EEA countries have either already started or are planning to start various types of studies investigating immunogenicity and safety of different combinations of COVID-19 vaccines. The results from these studies will also be important for potential booster doses in the future, as a mixing of vaccines also increases flexibility in the vaccine rollout.

Reinfection with SARS-CoV-2

Reinfection with SARS-CoV-2 is possible, but appears to be rare [48]. SARS-CoV-2 VOCs have demonstrated increased transmissibility in humans. Seroconversion to previously circulating SARS-CoV-2 strains may generate neutralising antibodies that protect against reinfection by a homologous virus, but the neutralising capacity of these antibodies is reduced against VOCs, particularly those carrying the E484K mutation [48].

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 [49].

Risk assessment question

Based on current vaccination coverage and circulating variants in the EU/EEA, what risk does SARS-CoV-2 pose to the general population and vulnerable individuals?

In recent weeks, a similar picture has been observed in most EU/EEA countries. Rates of notifications, hospitalisations, ICU admissions/occupancy and death have been decreasing [4]. At the same time, the vaccination uptake has been steadily increasing, with over 40% of the EU/EEA population vaccinated with at least one dose of the vaccine and almost 20% fully vaccinated [13]. In most countries, vulnerable populations (individuals with risk factors for severe COVID-19 disease), such as the elderly [50] have been prioritised for vaccination and the median uptake of at least one dose reached 80% in this population group among reporting countries [13]; this has occurred alongside decreasing notification rates in the elderly and an absence of excess mortality in those aged over 85 years since the end of February 2021 [4,5].

Even though vaccine effectiveness varies to a certain degree by vaccine product and target group, a single dose of Comirnaty, COVID-19 Vaccine Moderna or Vaxzevria has been shown to be immunogenic in non-previously infected individuals, reducing the risk of infection, the risk of severe disease (including hospitalisation) and the risk of transmission [14,16,25-28]. The variant of concern B.1.1.7 dominates circulation throughout the EU/EEA. It is associated with increased transmissibility, severity and mortality, but proved not to be associated with immune escape, and effectiveness against infection after two doses of the vaccine remains high [19,23,24]. Finally, large proportions of the EU/EEA population remain susceptible to SARS-CoV-2 [10,11].

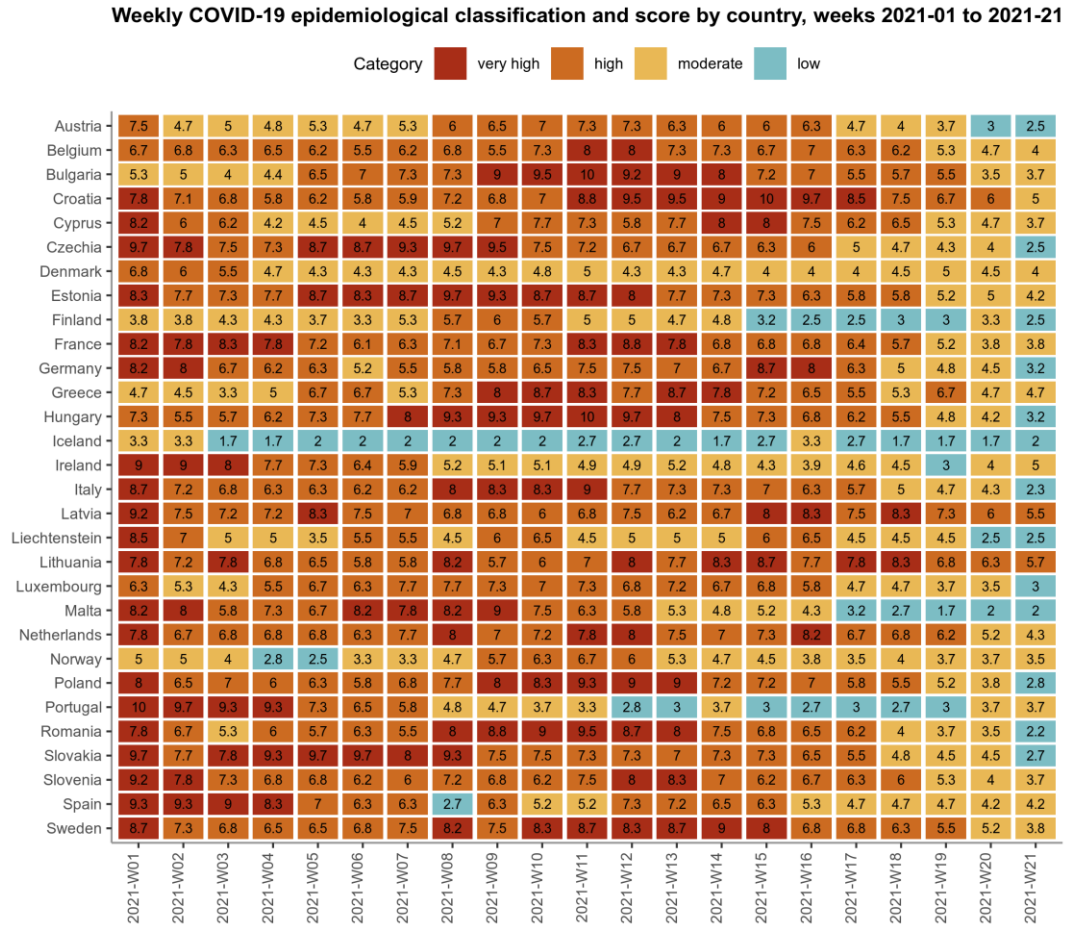
However, due to differences in the epidemiological situation, vaccination strategies and implemented NPIs, EU/EEA countries are experiencing different levels of risk and require different targeted interventions.

ECDC classifies the epidemiological situation in EU/EEA countries into four categories based on the level of concern (low, moderate, high, very high). These are derived from a combination of the absolute value and trend of five weekly COVID-19 indicators (intensity indicators: test positivity and total case notification rates; and severity indicators: hospital or ICU admissions or occupancy, death rates, case rates among people aged 65 years and above; methods outlined in Annex). In most countries, the contribution of the intensity indicators to the overall score has been higher than that of the severity indicators in recent weeks. As such, the overall classification shown below provides a conservative estimate of transmission intensity.

In week 21, 2021, there was no country where the epidemiological situation was classified as very high concern (Figure 3). The distribution across the three remaining categories is as follows:

- Low concern: Austria, Czechia, Finland, Germany, Hungary, Iceland, Italy, Liechtenstein, Luxembourg, Malta, Poland, Romania and Slovakia;
- Moderate concern: Belgium, Bulgaria, Croatia, Cyprus, Denmark, Estonia, France, Greece, Ireland, the Netherlands, Norway, Portugal, Slovenia, Spain and Sweden;
- High concern: Latvia and Lithuania.

Figure 3. Weekly COVID-19 epidemiological classification and score by country in EU/EEA, by week, 2021



The current assessment of the risk posed by the current SARS-CoV-2 pandemic is stratified by four population groups (vaccinated and unvaccinated general population, and vaccinated and unvaccinated vulnerable population), it is based on the different epidemiological situations experienced in the EU/EEA countries, and on the following elements i) the vaccinated group has a lower probability of infection and ii) a lower impact of such infection than the unvaccinated, while iii) the vulnerable population suffers of a higher impact of such infection when compared with the general population.

Countries in which the epidemiological situation is classified as low concern

In these countries, widespread transmission is falling with consequent low case notification rates. Due to the large proportion of the vulnerable population vaccinated with at least one dose, very low notification rates are recorded among the elderly. Based on this, the probability of infection ranges from very low in the vaccinated general population to moderate in the unvaccinated (both general population and vulnerable groups). The impact of the disease ranges from low in the vaccinated general population to very high in the unvaccinated vulnerable population.

General population

- Fully vaccinated: probability of infection VERY LOW + impact of infection LOW ➔ **LOW RISK**
- Unvaccinated: probability of infection MODERATE + impact of infection LOW ➔ **LOW RISK**

Vulnerable populations

- Fully vaccinated: probability of infection LOW + impact of infection MODERATE ➔ **LOW RISK**
- Unvaccinated: probability of infection MODERATE + impact of infection VERY HIGH ➔ **MODERATE-to-HIGH RISK**

Countries classified as moderate concern

These countries continue observing widespread SARS-CoV-2 transmission with the highest notification rates in the general population and, although a high proportion of the vulnerable population has been vaccinated with at least one dose, the probability of infection is higher than in the previous group of countries. These countries still experience widespread transmission associated with a dominating highly transmissible variant and a large part of the population is still susceptible to the infection. Based on this, the probability of infection ranges from low in the vaccinated general population to high in the unvaccinated (both general population and vulnerable groups). As long as NPIs are maintained to avoid worsening of the epidemiological situation, the impact of the disease ranges from low in the general population (both vaccinated and unvaccinated) to very high in the unvaccinated vulnerable population.

General population

- Fully vaccinated: probability of infection LOW + impact of infection LOW ➔ **LOW RISK**
- Unvaccinated: probability of infection HIGH + impact of infection LOW ➔ **LOW-to-MODERATE RISK**

Vulnerable populations

- Fully vaccinated: probability of infection MODERATE + impact of infection MODERATE ➔ **LOW-to-MODERATE RISK**
- Unvaccinated: probability of infection HIGH + impact of infection VERY HIGH ➔ **HIGH-to-VERY HIGH RISK**

Countries classified as high concern

These countries experience widespread SARS-CoV-2 transmission not only in the general population, but also in vulnerable individuals. The NPIs in place appear to be having a limited effect, either because adherence to the measures may not be optimal or the measures in place may not be sufficient to reduce or control exposure. Vaccination uptake in the general population and, particularly, in the vulnerable population appears to be still low. Based on this, the probability of infection ranges from moderate in the vaccinated general population to very high in the unvaccinated (both general population and vulnerable groups). In these settings, due to the pressure to the health system posed by high notification, hospitalisation and death rates, the impact of the disease is higher compared to the previous country groups resulting in moderate impact in the general population (both vaccinated and unvaccinated) and in the vaccinated vulnerable population, and very high in the unvaccinated vulnerable population.

General population

- Fully vaccinated general population: probability of infection MODERATE + impact of infection MODERATE ➔ **LOW-to-MODERATE RISK**
- Unvaccinated general population: probability of infection VERY HIGH + impact of infection MODERATE ➔ **HIGH RISK**

Vulnerable populations

- Fully vaccinated vulnerable population: probability of infection HIGH + impact of infection MODERATE ➔ **MODERATE RISK**

- Unvaccinated vulnerable population: probability of infection VERY HIGH + impact of infection VERY HIGH ➔ **VERY HIGH RISK**

The current assessment represents a decrease in most risk levels compared to the 14th update of the ECDC COVID-19 risk assessment published in February 2021 [1]. This assessment considers the current variant circulation, rollout of vaccination and NPIs in place. Scenarios considering variant replacement and reduced vaccine effectiveness are discussed in the following section based on modelling forecasts. Close monitoring of the evolving epidemiological situation, paying particular attention to the circulation of new variants (e.g. VOC B.1.617.2) associated with reduced vaccine effectiveness and/or increased transmissibility and severity, or to increasing transmission and death rates due to the relaxation of the current NPIs, is key to avoid a rapid increase in the risk level in the coming weeks. In any of the country scenarios, should mass gathering events such as the UEFA Euro 2020 take place in the absence of sufficient mitigation measures, the risk of local and pan-European transmission risk of COVID-19, including the spread of variants of concern, would increase.

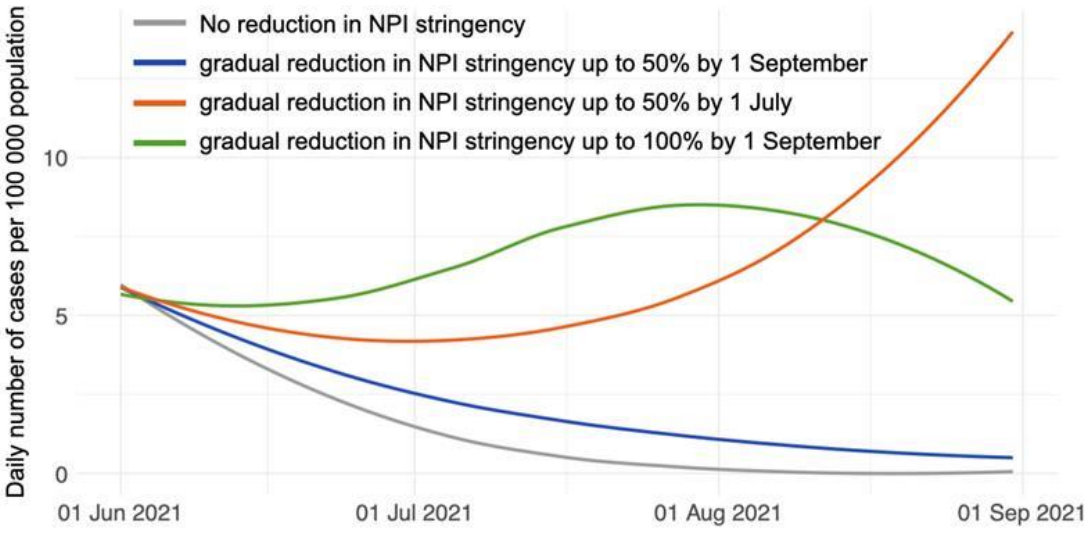
Modelling forecasts

Case notification rates in the EU/EEA have been falling consistently since April 2021 and many countries are now implementing or considering the partial lifting of the NPIs that aim to reduce the degree of physical contact between citizens. If the level of immunity in the population were constant, the lifting of such measures would result in increased levels of viral transmission. However, vaccination rollout continues and case notification rates will depend on the interaction between increasing immunity and the likely increasing contact between people as measures are eased. We simulate the projected number of cases per 100 000 members of the population, assuming that the rollout of the vaccination programme continues at its current rates and allowing for decreasing rates of uptake in older people and increased rates in younger people. We project changes in contact reduction based on the trend in the ECDC-JRC Response Measures Database of the past three months. We project the proportion of a new variant based on the assumed transmission advantage and assuming the same generation interval as the wildtype. The current viral transmission trend is based on reported cases across all EU/EEA Member States, and the forecasted transmission is assumed to be affected by changes in contact reductions, changed transmissibility of the projected mix of variants, and the effects of vaccination. This vaccine effect is reduced proportional to the assumed vaccine escape. Specifically, we forecast vaccination uptake by 10-year age groups, using the data presented in the ECDC Vaccination Tracker and extrapolating continued rollout at the current speed [13]. Figure 4 presents four scenarios:

- Continuation of the NPIs in place today (grey);
- A 50% reduction in the stringency of NPIs by 1 July 2021 (orange);
- A 50% reduction in the stringency of NPIs by 1 September 2021 (blue);
- A 100% lifting of NPIs by 1 September 2021 (green).

Where measures are lifted, the change begins from 1 June 2021 and continues gradually. Where the target date for reduction in NPIs is July, we assume unchanged contact reductions after that date.

Figure 4. Estimation of possible changes in daily COVID-19 incidence in the EU/EEA according to four NPI relaxation scenarios24 May – –31 August 2021.



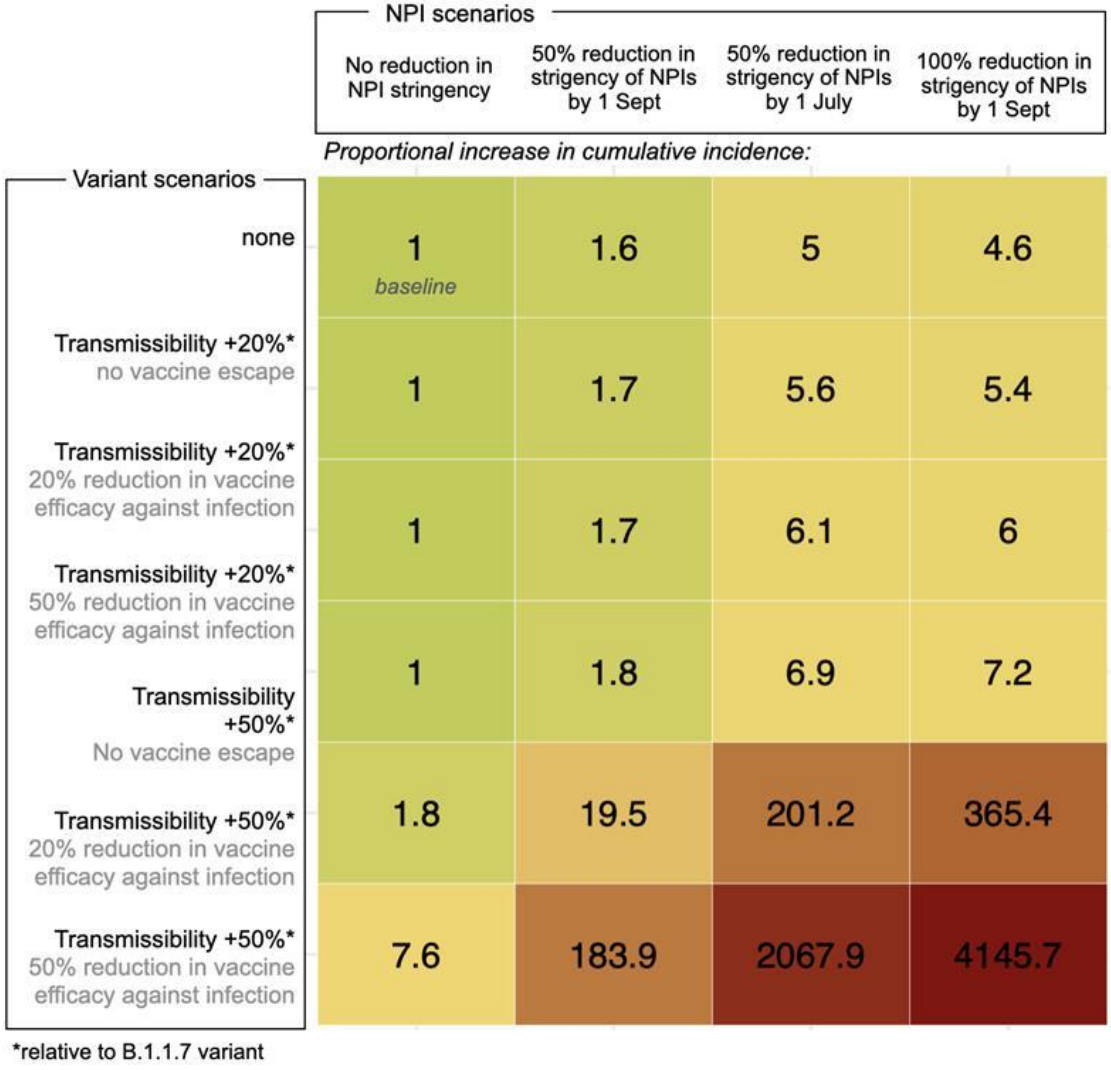
Note: no change in contact reduction (grey) or, alternatively, that current NPIs are gradually reduced up to 50% (green) by 1 July 2021 or 50% (blue) or 100% (orange) by 1 September 2021. We assume that age-prioritised vaccine rollout continues at current rates and that there is no replacement with a new variant. Note that although it appears that case numbers would fall to very low levels if vaccination rates and NPIs are maintained, this does not equate to an elimination scenario.

A slow reduction in the stringency of measures, resulting in a 50% lightening of current measures by 1 September 2021 may result in a continuing fall in case notification rates. However, reaching the same lifting of measures by 1 July 2021 would cause an increase of up to 40% in case notification rates by the end of July when increased vaccination coverage would bring transmission back to manageable levels. Lifting NPIs completely by 1 September 2021 would mean that case notification rates would continue to increase, even as the vaccination rollout proceeds. That is, the increased transmission due to people interacting would be too great a hurdle for the vaccination programmes to overcome.

The dynamics of SARS-CoV-2 transmission may also be affected by the emergence of new variants of concern. We additionally simulate a new variant, which replaces the current circulating strains. If the new variant is 20% more transmissible than the current mix of strains, replacement occurs over a period of 180 days; if it is 50% more transmissible, replacement takes 74 days. To explore the potential impact of a novel variant, we also simulate vaccine escape i.e. the reduced effectiveness of vaccines to prevent infection with SARS-CoV-2.

Figure 5 presents the cumulative number of cases that are predicted per 100 000 members of the EU/EEA population between 1 July 2021 and 31 August 2021 for different assumptions of transmissibility and vaccine escape potential of a new variant.

Figure 5. Proportional increase in the cumulative incidence of COVID-19 in six hypothetical scenarios of strain replacement with variants in EU/EEA between 1 June and 31 August 2021.



Note: The baseline is no variant replacement and no change of NPI stringency (top left).

The impact on case numbers of an emerging variant with 20% increased transmissibility is less than the impact of lifting NPIs by 50%-100% over the summer months. However, clearly, there is an increased risk of lifting NPIs in the presence of a more transmissible variant. If vaccines have a reduced effectiveness at preventing infection against such variants, the population remains susceptible, and numbers could increase rapidly. A variant with an increased transmissibility of 20% and a 50% reduction in vaccine effectiveness gives an estimated increase of 5% in the case numbers between 1 June and 31 August 2021, however this impact would be compounded over time and would lead to rapidly increasing case rates into the autumn.

Options for response

Viral circulation in the EU/EEA has been decreasing in the majority of countries. However, sero-epidemiology studies as mentioned above, are showing overall prevalence of SARS-CoV-2 antibodies relating to natural infection at <15% in the European region at the end of 2020. In addition, the cumulative vaccination uptake, especially for full vaccination in the EU/EEA is still low but increasing in the adult population aged 18 years and older. Vaccine uptake is higher in specific groups of the population targeted in the initial phases of the COVID-19 vaccine rollout, such as people aged 80 years and older, which is anticipated to have an effect on the COVID-19-related hospitalisations and deaths. Although increasing vaccination coverage will also mitigate the effect of replacement with more transmissible variants, decisions to ease measures need to be highly sensitive to the local context and include considerations about the current viral circulation, the prevalence of VOCs, setting, and the vaccination status. Modelling analysis shows that a significant increase in COVID-19-related cases in the EU/EEA remains possible if NPIs are relaxed too rapidly. Optimal use of vaccines remains the cornerstone of the public health response, supplemented by continued early case detection with associated contact tracing (test and trace approaches), strong surveillance and characterisation of circulating viruses by sequencing. Finally, considerations for travel-related measures and effective risk communication are provided.

Vaccination

With increased vaccine availability, the key priority remains to accelerate the vaccine rollout to ensure that all eligible individuals receive a full course vaccination. The main focus should be on further increasing vaccination coverage, with a rapid and effective deployment of vaccines, in order to reduce the number of susceptible individuals, the number of hospitalisations and deaths and the viral circulation in the community. This should be done by pursuing clear vaccination goals following suitable and coherent strategies as established by all EU/EEA countries and indicated in the recent ECDC report on 'Objectives of vaccination strategies against COVID-19' [51].

Achieving high antibody levels via a full vaccination course confers the additional benefit of sustained protection and sufficiently high levels to confer protection even against emerging SARS-CoV-2 variants which have demonstrated increased immune escape potential. In the absence of more definitive data, and in the context of current and emerging VOCs with immune escape potential, any national changes to the recommended schedule should weigh uncertainties in the long-term immunity against the need to rapidly immunise the population, taking into account the national epidemiological situation.

While countries keep working on reaching national goals as well as those set up by the European Commission in January (vaccinating at least 80% of people over the age of 80 years, and 80% of health and social care professionals by March 2021, as well as a minimum of 70% of the adult population by the summer) [52], the ultimate goal is to reopen society entirely and vaccination has a major role to play in reaching this.

As vaccination coverage of adult groups gradually increases and countries start expanding coverage, it will be especially important to monitor vaccine uptake and acceptance across the population and to have strategies in place to reach out to those individuals, groups and/or communities that are hesitant or sceptical. It is also essential to reach those that find it difficult to access vaccination sites, such as vulnerable or hard-to-reach individuals, for example by utilising mobile vaccination sites and teams [53]. Strategies will require constant adaptation to unexpected changes in the epidemiology of the disease as well as any suspected adverse events following immunisation that may affect trust in the vaccination programme. In addition, the acceleration of the vaccination campaign is one important way to protect against emerging more transmissible variants [54]. The risk of introduction of new variants in the EU/EEA is closely related to the pandemic evolution outside the EU/EEA. Efforts to enhance more equitable access to vaccination globally can mitigate the risk of emergence of new variants.

Surveillance and monitoring

Although the effectiveness of COVID-19 vaccines authorised in the EU is generally very high, no vaccine is 100% effective. Infections amongst vaccinated persons (i.e. 'breakthrough infections') are therefore expected and more will be seen as vaccination uptake increases. These may include severe and fatal cases among vaccinated persons, particularly the elderly and those with pre-existing conditions. There is limited preliminary evidence for known circulating variants having immune escape capacity and reduced vaccine susceptibility, particularly the variant B.1.351 [55]. However, the potential remains for the emergence of new variants, which evade the protection conferred by current vaccines. Continued comprehensive surveillance of COVID-19 cases, including severity, vaccination history and ideally linked to sequencing results where available, is therefore essential, in order to rapidly detect the emergence of novel variants, their spread, as well as the public health impact.

Currently, in the EU/EEA, long-term care facilities (LTCFs) are the closed settings with the highest vaccine coverage, and are also home to those with highest risk of severe COVID-19 outcomes. To date, reports of COVID-19 outbreaks of breakthrough infections in LTCFs with high vaccination coverage have mostly had mild or asymptomatic cases [55]. Still, vigilance is required at national level, to ensure early communication of such outbreaks, most especially those with unexpectedly high proportions of severe, hospitalised or fatal cases, including prompt typing of samples.

Identification of new variants which are able to evade a vaccine efficiently would warrant an International Health Regulation (IHR) and EWRS notification, whilst operational discussion of ongoing investigations of any notable LTCF outbreak is well-suited to discussion within the secure ECDC platform 'Epidemic Intelligence Information System' for healthcare-associated infections and antimicrobial resistance (EPIS AMR-HAI), or the recently launched ECDC platform 'EpiPulse'. In support of this, on 6 May 2021, ECDC published the protocol 'Data collection on COVID-19 outbreaks with a completed vaccination programme: LTCFs' and an associated data collection tool [56]. Its main aim is to collect information on the severity of breakthrough COVID-19 infections in outbreaks, by SARS-CoV-2 variant and vaccine product. This activity is not intended to capture all outbreaks, generate comparative statistics, or obtain a (sub-)nationally representative sample.

Testing and sequencing capacity

Testing strategies

Timely testing of people with symptoms, through improving access to testing and encouraging people to seek testing as soon as possible after symptom onset, remains important to enable rapid initiation of contact tracing. Depending on available resources, testing strategies could include additional objectives, such as outbreak analyses, phylodynamic analyses and other research studies. Several EU/EEA countries have introduced the use of rapid antigen detection tests (RADTs) for screening asymptomatic persons at the workplace, school or other settings. The use of RADTs and/or self-RADTs in occupational settings can complement, but not replace, public health measures and existing NPIs aimed at preventing the introduction and spread of SARS-CoV-2. ECDC has published a technical report outlining the considerations on the use of rapid antigen detection (including self-) tests for SARS-CoV-2 in occupational settings [57].

Self-tests using RADTs can offer advantages when used to complement professionally administered RADTs or RT-PCR tests. They can improve the accessibility to testing. They allow individuals to obtain the result quickly, which could support the early detection and subsequent isolation of infectious cases and hence reduce further community transmission [58]. However, shifting the responsibility of reporting test results from health professionals and laboratories to individuals could lead to underreporting, and make response measures such as contract tracing and quarantine of contacts and monitoring of disease trends over time even more challenging.

A current priority is the assessment of the circulation of known VOCs in the community. 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. For Sanger sequencing or next generation sequencing (NGS), amplicon-based sequencing of selected parts of the viral genome are alternative methods for the identification of variants. ECDC has published a document that presents the available methods (screening and sequencing) for detection and identification of circulating SARS-CoV-2 VOCs B.1.1.7, B.1.351 and P.1 [59]. Methods for detection and differentiation of B.1.617 variants are available in the ECDC threat assessment brief published on 11 May 2021 [7].

Diagnostic laboratories should remain vigilant to detect any mismatches of specific RT-PCR assay primers and probes in comparison to circulating virus genomes. It should be noted that the majority of primer/probe binding sites of commercial assays are not publicly known. For in-house or commercial RT-PCR assays for which the primer/probe sequences are available, validation can be done via the ECDC PrimerScan [60] or similar tools that identify mismatches. For commercial assays where the primer/probe sequences are unknown, a validation procedure for the capacity of the molecular assays to detect variants is needed. For laboratories using S-gene target failure to identify variants, it is important to note that S-gene target failure is expected to occur for B.1.1.7among currently circulating VOCs, but as this target failure is not exclusive to B.1.1.7, sequencing is recommended at least for a subset of samples, especially in a low prevalence setting. For laboratories using the ARCTIC protocol for sequencing of SARS-CoV-2 it is important to use the latest version of the primers (https://artic.network/ncov-2019) as mismatches may occur with variant viruses. While RADTs are useful tools for the prompt identification of infectious cases, there are limited data from clinical validation studies in light of the new emerging variants [61]. RADTs detect specific proteins of the virus. Some mutations could alter the structure of these proteins, allowing them to escape detection. Many RADTs however target the nucleocapsid protein (N gene) that is more stable and less likely to mutate than the S gene. Laboratories should always remain vigilant to identify reductions in RADTs sensitivity.

In general, laboratories should have a quality assurance system in place and are encouraged to participate in external quality assessment (EQA) schemes or perform result comparison between laboratories, for a subset of samples. ECDC is planning a molecular EQA for national COVID-19 reference laboratories in June 2021. Please contact PHE.Support.Microbiology@ecdc.europa.eu for more information.

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 [62]. The European Commission has published a Recommendation to support EU/EEA countries in establishing wastewater surveillance systems across the EU [63].

Genomic surveillance and antigenic characterisation of SARS-CoV-2 variants

Early detection, genetic and antigenic characterisation of SARS-CoV-2 variants should be strengthened in all EU/EEA countries.

As part of targeted genomic surveillance, ECDC recommends increased sequencing of travel-related cases according to ECDC's guidance for genomic SARS-CoV-2 monitoring [64]. In order to detect the importation into countries and to slow down the spread of variants of concern in areas or countries where they are not yet present or only circulating at very low levels, ECDC recommends comprehensive sequencing of all SARS-CoV-2 positive cases with travel history to areas/countries where those variants are circulating. This is particularly relevant for, but not limited to, those coming from areas where variants of concern are endemic.

COVID-19-vaccinated individuals need to be closely monitored for breakthrough infections and virus isolates from these cases should be comprehensively sequenced and reported, irrespective of the variant identified [64]. Reports of suspected cases of SARS-CoV-2 reinfection also need to be investigated and sequence analysis of virus isolates from all 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 vaccine composition and strategy.

Furthermore, a representative sample of clusters or outbreaks associated with a specific setting/behaviour/age group with a minimum of five specimens (to be able to assess whether the event is dominated by a certain variant of concern) should be sequenced [64]. Other examples of situations that require sequencing, including to monitor variants of concern, can be cases with an unusual clinical presentation, such as severe infections and deaths in younger age groups with no underlying diseases, prolonged infections, a general change in the clinical presentation and cases where zoonotic transmission has been raised as a possibility and cannot be ruled out. This may indicate a change in pathogen virulence or inter-species transmission which should be monitored.

In addition to targeted genomic surveillance, a current priority should be to assess the level of circulation of known variants of concern in the community. Therefore, representative sequencing should be performed in order to generate data that reflect the overall variant situation in the country [64]. Specimens for genome analysis should be selected as being representative of SARS-CoV-2 cases in the country. Sample collection should be made using methods that ensure the unbiased selection of cases for sequencing. It is important to ensure that sequencing is performed on a sufficient number of cases every week (representative in terms of time), at every level of healthcare systems (representative in terms of clinical spectrum), and in all regions or other administrative areas of a country (representative in terms of geography). This should ensure representativeness in terms of age, gender, and disease severity of cases.

ECDC offers the possibility for antigenic characterisation of SARS-CoV-2 isolates, to support the detection of variant viruses that may escape natural immunity and/or vaccines. This is done through antigenic characterisation of SARS-CoV-2 isolates and by supporting the scaling up of sequencing capacity in EU/EEA countries. Please contact PHE.Support.Microbiology@ecdc.europa.eu for more information.

Non-pharmaceutical interventions

Maintaining and gradual relaxation of non-pharmaceutical interventions

Non-pharmaceutical interventions to reduce transmission in the general population are fundamental elements of the public health approach to controlling COVID-19. Therefore these measures should continue to be implemented and maintained in accordance with the local epidemiological situation, the vaccination coverage in the general population, and the prevalence of VOCs, taking into account that in a situation of increased community transmission, more measures or stricter compliance will be needed.

Due to the low risk of fully vaccinated individuals being infected and suffering from severe COVID-19, some NPIs, such as physical distancing and face mask wearing can be relaxed when fully vaccinated individuals meet other fully vaccinated individuals, as well as when an unvaccinated individual or unvaccinated individuals from the same household or social bubble meet fully vaccinated individuals, if there are no risk factors for severe disease or lower vaccine effectiveness in anyone present (e.g. older age, immunosuppression, other underlying conditions) [19]. However, in the current epidemiological context in the EU/EEA, in public spaces and in large gatherings, including during travel, NPIs should be maintained irrespective of the vaccination status of the individuals.

Where the epidemiological situation allows, countries may consider gradually lifting and adapting their NPIs, e.g. by opening (or keeping open) in-person educational and vocational activities both for children and adults, opening non-essential business, increasing the allowed size of social gatherings and cultural events.

This should be done with adherence to personal measures such as physical distancing, hand hygiene, use of face masks where recommended, and optimal ventilation of closed spaces. If gatherings and events are allowed, the limits on number of participants should still aim to avoid crowding, and gatherings outdoors are preferred when possible. Continuous, intense surveillance, identification of cases, contact tracing and quarantine of contacts remain key for monitoring the epidemiological situation and preventing a further surge of cases while measures are lifted or adapted. Countries' efforts should focus on the vaccination rollout, whilst individuals should continue to apply personal measures such as hand and respiratory hygiene, wearing a face mask when recommended and staying home when ill.

Countries and/or areas where the epidemiological situation remains concerning should maintain their NPIs and introduce additional targeted measures where required. Efforts should focus on the vaccination rollout, enhancing adherence to the current measures, protecting vulnerable populations such as LTCF residents, and ensuring healthcare capacity. Additionally, these countries/areas should consider maintaining physical distancing between individuals as much as possible, maintaining limits on the size of public gatherings, especially those indoors, as well as recommending only limited size 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 as well as limiting transmission in workplaces by encouraging teleworking whenever possible. Individuals in these countries should continue application of recommended NPIs at a personal level. For people vulnerable to severe COVID-19 who are not fully vaccinated, such as the elderly or those with underlying medical conditions, the use of medical face masks is also recommended as a means of personal protection in the above-mentioned settings, and these individuals should follow recommendations on continued physical distancing until fully vaccinated.

For analysis and available evidence on 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' [65]. For analysis and available evidence on the impact of vaccination on NPIs, please refer to ECDC's 'Interim guidance on the benefits of full vaccination against COVID-19 for transmission and implications for non-pharmaceutical interventions' [19].

Contact tracing

Contact tracing remains a key tool to break transmission chains. For countries with high transmission, contact tracing will complement other measures and contribute to reducing transmission. For countries with lower levels of transmission, contact tracing is a key tool in outbreak management and controlling transmission. Contact tracing in the context of cases suspected to be infected with a VOC can help prevent the establishment of the VOC in the country. Countries should follow the latest ECDC contact tracing guidance [66].

Contact tracing can also be used to investigate the source of infection of a newly identified case – so-called backward contact tracing. This can allow for the identification of further cases around that source of infection, and subsequent contact tracing around those additional cases. This is further outlined in the ECDC contact tracing guidance.

For contact tracing to be effective, timeliness is key. This includes testing cases as soon as possible after symptom onset – which requires a high level of public awareness and easy access to testing. Test turnaround time should be minimised, and contacts traced as soon as possible after a positive result. Symptomatic people awaiting the result of their test can be encouraged to encourage their close contacts to adhere to physical distancing until the result is known.

For cases suspected to be infected with a VOC, for example through laboratory pre-screening [59] or an epidemiological link, enhanced contact tracing measures can be considered, as outlined in the ECDC publication 'Risk related to the spread of new SARS-CoV-2 variants of concern in the EU/EEA – first update '[67].

Fully vaccinated contacts who have been exposed to a confirmed COVID-19 case should continue to be managed according to existing ECDC guidance [66]. Health authorities should undertake risk assessment on a case-by-case basis, where possible, and may subsequently classify some fully vaccinated contacts as low-risk contacts. Factors that need to be taken into consideration in such assessments include, for example, the local epidemiological situation in terms of circulating variants, the type of vaccine received, and the age of the fully vaccinated contact (as older people may not mount as effective an immune response). The risk of onward transmission to vulnerable people by the contact should also be considered for individuals who work or reside in an institutionalised setting (e.g. LCTFs) [19].

ECDC and WHO encourage countries to monitor the effectiveness of their contact tracing operations to identify where coverage or timeliness needs to be increased [68]. To learn more about the transmissibility and characteristics of the VOCs, countries are encouraged to collect and analyse data from contact tracing of these cases and to share findings with ECDC, WHO and other EU/EEA countries.

Countries using mobile apps for contact tracing are also encouraged to monitor their effectiveness using the joint WHO-ECDC indicator framework which will shortly be published. On 27 May 2021, the European Commission published the Implementing Decision 2021/858 outlining the function of the digital Passenger Locator Form (dPLF) in the EU/EEA [69].

Travel measures

In general, travel measures are unlikely to have any long-term major impact on the timing or intensity of local epidemics in comparison to rigorous local implementation of NPIs. However, travel measures can be considered when levels of transmission have been reduced to very low levels in the receiving locality or for those coming from areas which continue to have an epidemiological situation of high or serious concern level, irrespective of the conveyance and the extent of community transmission at the destination. Such measures are particularly important if there is clear evidence of circulation of new virus variants, or if the evidence that exists does not allow an accurate assessment (for example, due to insufficient sequencing capacity) of the extent to which new virus variants are circulating in the place of origin. 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 consider the epidemiological situation in the countries of departure and arrival.

Measures that are being considered for incoming travellers include:

- Request of proof of negative pre-departure test or test upon arrival, and quarantine for 5-7 days with a test before release;
- Quarantining of travellers for 14 days without test, in case testing capacity is not sufficient;
- Enhanced contact tracing upon identification of a positive case related to travel, as described above.

Requirements for testing and quarantine of travellers (if implemented) can be waived or modified for fully vaccinated individuals as long as there is no or very low level circulation of immune escape variants in the community in the country of origin [19].

During travel, NPIs should be maintained regardless of the vaccination status of the traveller. Fully vaccinated travellers should also respect any NPIs for fully vaccinated people in the country of destination. Documents informing about the safety measures on various travel conveyances have been developed: air travel [70], cruises [71], and rail [72].

ECDC has published a guidance for COVID-19 quarantine and testing of travellers [73], also highlighting the considerations around the use of RADTs for travelling. RADTs can be useful for detection of infectious cases in the first five days from disease onset, they have, however, reduced sensitivity for detecting asymptomatic cases [57].

It is important to underline that whilst RADTs and regular RT-PCR will detect a SARS-CoV-2 infection, they will not distinguish SARS-CoV-2 variants (including VOCs). Specialised RT-PCR tests or sequencing are able to discriminate the presence of known variants and can be used, if available. RADTs can help to reduce further transmission of SARS-CoV-2 or SARS-CoV-2 VOCs through early detection of highly infectious cases, enabling immediate isolation and the rapid commencement of contact tracing. The UK has evaluated five RADTs (targeting the nucleocapsid protein) and they all detected cases that later on were identified as carrying the variant B.1.1.7, but validation studies for the rest of the VOCs are still lacking [74]. Further validation of RADTs is needed to ensure that they also detect future/emerging variants without reduction in their sensitivity.

An EU digital COVID certificate is planned to be introduced as proof that a person has been vaccinated against COVID-19, has recovered from COVID-19 or has a negative test result with the aim to facilitate safe and free movement during the COVID-19 pandemic. The EU digital COVID certificate can be available in both digital and paper formats and will be in use by 1 July 2021. When travelling, every EU citizen or third-country national legally staying or residing in the EU, who holds an EU digital COVID certificate, should be exempt from free movement restrictions in the same way as citizens of the visited EU country [75,76].

In addition, in the updated recommendation on restrictions to travel from third countries, the Council introduced the 'emergency brake mechanism', where EU/EEA countries can adopt an ad hoc restriction on travel to the EU from countries or regions where the epidemiological situation or the circulation of a VOC is of concern [77].

Mass gathering events

For mass gathering events, such as the UEFA Euro 2020, monitoring of the epidemiological situation and implementation of preventive and mitigation measures should be done with a coordinated intersectoral approach.

EU/EEA travellers to UEFA matches abroad will have to comply with border entry restrictions, including COVID-19 restrictions, and requirements that will be in force at the time of the games in the host country. Access to stadiums could be conditional upon proof of negative COVID-19 test and/or vaccination and/or proof of COVID-19 diagnosis within certain time-periods. Before travelling, travellers should be strongly advised to check the latest COVID-19 restrictions on the official websites of the host country.

For host countries, surveillance, identification of cases, contact tracing and quarantine of contacts remain key cornerstones for monitoring the epidemiological situation and preventing a surge of cases after the event.

Health promotion and risk communication messaging alongside non-pharmaceutical interventions such as physical distancing and measures to avoid crowding as well as environmental, respiratory and hand hygiene should be strictly practiced at all times, both outside and inside sporting venues. Testing strategies for COVID-19 should be established at or near the venues depending on the agreed national policy for access.

If the policy in the hosting country is to allow approximately >50% capacity in the stadiums, then the use of face masks by the attendees should be strongly considered even if the stadium is an open space venue. EU/EEA travellers with significant underlying conditions should be discouraged from attending. In addition, any person with COVID-19 compatible symptoms should not attend match or post-match events, irrespective of their vaccination status.

ECDC enhanced Epidemic Intelligence activities on the Euro 2020 event will take place between 4 June and 16 July 2021 and reports provided in the weekly Communicable Disease Threats Report (CDTR).

Risk communication

With the combination of increasing but still sub-optimal COVID-19 vaccination rates, decreased but still widespread transmission of the virus (including community transmission of several VOCs), and a general, EU-wide relaxation in NPIs, the environment for risk communication activities has become challenging. There is the possibility of an upsurge in the number of infections, and potentially, therefore, for the need to a return to more restrictive NPIs. This would be unpopular both with the general public, who may be struggling with the continuation of NPIs and are anticipating their relaxation, and with the business community, which is looking forward to an irrevocable return to more predictable economic conditions [78].

Within this context, it is important for people to understand that the pandemic is not yet over, and that everything we have collectively achieved in bringing down infection rates must not now be wasted by letting down our guard prematurely. It is important for people to be mindful of the risk posed by certain activities, in particular in relation to the '3 Cs' [79]. Crowded places, close-contact settings, and confined/enclosed spaces. Two key areas may need particular consideration:

- **Public spaces and large gatherings:** The public needs to be informed about, and to accept the safety measures that will be put in place for large sports, music and cultural events that are expected to be held over the summer. Minimising the risk of infection at these events is essential if an upsurge in infections is to be avoided [80].
- **Travel:** In order to minimise the potential spread of infection (and especially of VOCs) across the EU, people may want to consider whether their journey is really necessary – even if it is legally permitted. If they do decide to travel, it is essential that they consider how they can undertake their journey as safely as possible. Further, there is currently a range of different travel restrictions between different EU countries, and citizens will need clear and easy to access to information regarding requirements and measures in place at their destination. In addition, people relying on a negative COVID-19 test result need to understand that this only reflects infection status at the time the test was taken. Subsequent exposure to the virus remains a risk that could render the snapshot test result outdated.

Communication around vaccination needs to strike a balance between the encouraging news on effectiveness of vaccination with caution regarding current unknowns and the related need to remain vigilant. Evidence from real-life usage of COVID-19 vaccines is confirming high effectiveness against symptomatic and severe disease, as well as against PCR-confirmed infection [19], and data also point to correlation between increasing vaccination uptake in all age groups and decreasing mortality in specific age groups [81]. This good news needs to be promoted but balanced with the uncertainties regarding the impact of the vaccines on transmission, duration of protection, and possible protection against emerging SARS-CoV-2 variants [19]. In addition, the vaccine rollout and the epidemiological situation varies across countries. Therefore, people who are fully vaccinated need to be mindful that there is still a potential risk that they could transmit the virus to people who have not yet been or who cannot be vaccinated. Until a high proportion of the population is fully protected, other public health measures will need to remain in place.

As vaccination progresses in the EU/EEA towards the wider population, and as vaccine supply begins to outstrip demand, countries may face challenges in achieving high immunisation rates. This can be related to issues of vaccine acceptance, barriers to access, and perception of low risk from disease in some people. To optimise vaccination uptake, communication and community engagement efforts need to be enhanced, in order to build local vaccine acceptability and confidence, and overcome cultural, socioeconomic, and political barriers that lead to mistrust and hinder uptake [82]. Strategies can include:

- Reminding people of the importance of getting vaccinated to protect themselves and protect others: 'Nobody is safe until everybody is safe' [83];
- Encouraging people to support family and friends who are uncertain about vaccinating, or who face difficulties in accessing services [84];
- Monitoring acceptance and potential barriers through behavioural insights research [85], thereby informing communication strategies;

- Making vaccines available in safe, familiar, and convenient settings in order to facilitate uptake [86];
- Applying strategies to foster demand, including persuasive communication and 'nudge' or default option approaches that seek to encourage behaviour adoption, overcome barriers, and maintenance of behaviour change [87];
- Addressing misinformation circulating that can impact vaccine uptake [88];
- Reminding people of the importance of receiving the full vaccination course (for 2-dose recommendations) to ensure adequate long-term protection.

As vaccine roll out progresses, pharmacovigilance structures will continue to monitor any potential adverse events following immunisation. Early communication about possible side effects, as well as rapid investigation of any safety signals and transparent communication of results will be key to ensure continued community trust in the vaccination programme [89].

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 evolving daily. 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 and elsewhere, 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;
- Duration of protection for a single dose of COVID-19 vaccines (in a two-dose schedule) and the potential for waning immunity;
- 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).

Limitations

This assessment is undertaken based on information known to ECDC at the time of publication and has several key limitations, reason why it should be interpreted with caution taking into account the national and sub-national contexts.

The epidemiological data used in this assessment are dependent on availability from EU/EEA countries 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 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. There is still limited knowledge and uncertainty around VOCs. The assessment of the future trend of disease transmission is limited by the lack of knowledge from previous outbreaks.

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.

This report was written with the coordination and assistance of an Internal Response Team at the European Centre for Disease Prevention and Control. All data published in this risk assessment are correct to the best of our knowledge at the time of publication. Maps and figures published do not represent a statement on the part of ECDC or its partners on the legal or border status of the countries and territories shown.

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Annex 1

Variants of concern

ECDC regularly assesses new evidence on variants detected through epidemic intelligence, rules-based genomic variant screening, or other scientific sources. Currently, five variants designated as VOCs by ECDC are under surveillance in the EU/EEA and around the world: B.1.1.7 (Alpha), B.1.1.7+E484K, B.1.351 (Beta), P.1 (Gamma) and B.1.617.2 (Delta). Another seven SARS-CoV-2 variants are considered variants of interest (VOI) by ECDC and additional variants are being monitoring [90].

B.1.1.7 (Alpha)

Transmissibility

Several studies provide evidence of increased transmissibility of B.1.1.7 [90-93], based on contact tracing data from the UK. Attack rates are around 10-55% higher across most age groups when the case is infected with the B.1.1.7 variant compared to earlier circulating variants in the UK [94].

Severity

Based on studies in the UK and Denmark, B.1.1.7 is associated with increased severity and mortality. The hazard of death associated with B.1.1.7 is 61% (95%CI 42-82%) higher than with pre-existing variants [95] and infection with lineage B.1.1.7 is associated with an increased risk of hospitalisation compared to other lineages (adjusted odd ratio (OR) 1.64 (95%CI 1.32-2.04)) [96].

Immunity, reinfection and vaccination

Sera from subjects immunised using the Vaxzevria vaccine showed reduced neutralisation activity against the B.1.1.7 VOC compared with a non-B.1.1.7 lineage *in vitro*, but the vaccine showed efficacy against the B.1.1.7 VOC. Clinical vaccine efficacy against symptomatic infection was 70.4% (95% CI 43.6–84.5) for B.1.1.7 and 81.5% (95%CI 67.9–89.4) for non-B.1.1.7 lineages [97]. For the Comirnaty vaccine the estimated effectiveness against infection with the B.1.1.7 VOC was 89.5% (95%CI 85.9-92.3) at 14 or more days after the second dose [27] compared to a vaccine effectiveness at seven days or longer after the second dose of 95.3% against any SARS-CoV-2 infection [15].

A study in the UK evaluated longitudinal symptom and test reports spanning a three-month period (28 September-27 December 2020) from 36 920 users of the COVID Symptom Study app which had previously tested positive for COVID-19. Although they observed cases of reinfections (0.7% [95%CI 0.6-0.8]), they did not find evidence for the reinfection rate being higher for the B.1.1.7 variant compared to other pre-existing variants [98].

B.1.1.7+E484K

The data about the transmissibility, severity and immunity of this variant are still very limited.

However, the E484K mutation of the spike protein has been associated with a reduction in neutralisation activity by convalescent and vaccinee sera in multiple studies. For instance, this mutation was shown to reduce the antibody neutralization compared to a wild type variant when introduced in the USA-WA1/2020 background [99]. Another study evaluated the neutralizing activity against SARS-CoV-2 variants of the serum of healthcare workers vaccinated with CoronaVac. They found that the neutralization efficiency was significantly decreased for viruses with the B.1.351, P.1 or B.1.526 genetic backgrounds (which all carry the E484K spike protein change) compared to B.1.1.7 and B.1.429 (which do not carry the change) [100].

B.1.351 (Beta)

Immunity, reinfection, vaccination

A study from Qatar showed that the effectiveness of Comirnaty against any documented infection with the B.1.351 variant was 75.0% (95% CI 70.5-78.9) at 14 or more days after the second dose [101].

Another study investigated the efficacy of Vaxzevria in South Africa with a multi-centre, double-blind, randomised controlled trial [23]. A two-dose regimen of this vaccine did not show protection against mild-to-moderate COVID-19 caused by the B.1.351 variant. In a secondary-outcome analysis, efficacy against B.1.351 was not evident (vaccine efficacy, 10.4%; 95% CI, −76.8 to 54.8). No cases of hospitalisation for severe Covid-19 were observed in the study, hence, the trial findings are inconclusive with respect to whether Vaxzevria protects against severe Covid-19 caused by infection with the B.1.351 variant.

P.1 (Gamma)

Transmissibility

In a recent study the epidemiological characteristics of P.1 and of other lineages endemic in Manaus, Brazil were modelled using a two-category (P.1, non-P.1) Bayesian model. P.1 was estimated to be 1.7 to 2.4-fold more transmissible than other locally circulating variants [102].

Immunity, reinfection, vaccination

A study published in Science on May 2021 estimated, with a modelling approach, the protection against reinfection by P.1 or non-P.1 variants. P.1 can evade 21 to 46% of protective immunity elicited by a previous infection (with a non-P.1 variant) compared to other variants [102].

Another study evaluated the levels of P.1 neutralization following natural infection and vaccination with CoronaVac, an inactivated COVID-19 vaccine developed by the Chinese company Sinovac Biotech. The vaccine has been approved in several countries, amongst them China, Brazil, Turkey, Mexico, Thailand and others, but has not been authorised for use in the EU. Plasma from COVID-19 convalescent donors had 6-fold less neutralizing activity against P.1 compared to the B-lineage. Moreover, five months after booster immunization with CoronaVac, plasma from vaccinated individuals failed to efficiently neutralize the P.1 variant. This suggests that P.1 may escape from neutralizing antibodies derived from previously circulating variants of SARS-CoV-2 [26].

B.1.617.2 (Delta)

Transmissibility

Compared to B.1.1.7, B.1.617.2 is highly likely to be more transmissible based-on epidemiological and in-vitro data. A comparison of secondary attack rates (including in households) of B.1.1.7 and B.1.617.2 showed that B.1.617.2 has higher rates of secondary attack compared to B.1.1.7. However, these data were not yet corrected for vaccination status [6].

Severity

Analyses of data from England and Scotland showed an increased risk of hospitalisation among cases of B.1.617.2. However, the magnitude of the change in risk and link to vaccination are not yet clear and confirmatory analyses are needed [103,104].

Immunity, reinfection, vaccination

In a recent pre-print [28] the effectiveness of Vaxzevria and Comirnaty was compared for the VOCs B.1.1.7 and B.1.617.2. With one dose, vaccine effectiveness dropped from 51.1% for B.1.1.7 (95%CI 47.3-54.7) to 33.5% for B.1.617 (95%CI 20.6-44.3), with the two vaccines showing similar results. With two doses of Vaxzevria, the effectiveness went down from 66.1% (95%CI 54.0-75.0) for B.1.1.7 to 59.8% (95%CI 28.9-77.3) for B.1.617.2. Finally, with two doses of Comirnaty the effectiveness went down from 93.4% (95%CI 90.4-95.5) for B.1.1.7 to 87.9% (95%CI 78.2-93.2) for B.1.617.2. The authors also compared these results with those from another study [27] which investigated effectiveness of the Comirnaty vaccine against the B.1.1.7 and B.1.351 variants. They concluded that the effectiveness against B.1.617.2 of the Comirnaty vaccine after a full course lies between the ones observed for B.1.1.7 and B.1.351. At the moment data are insufficient to assess vaccine effectiveness against severe disease.

Annex 2

Methods for classification of the epidemiological situation in EU/EEA countries

First, the current weekly value is used to assign a score (1-4) to each of five indicators. The thresholds used for indicators 1, 2, 4 and 5 are informed by those published in WHO guidance https://www.who.int/publications/i/item/considerations-in-adjusting-public-health-and-social-measures-in-the-context-of-covid-19-interim-guidance, corresponding to different levels of community transmission. The WHO thresholds have been modified so they work with 14-day rates and further adapted (test positivity thresholds have been lowered) where appropriate to the observed epidemiological situation in the EU/EEA since week 40, 2020. Indicator 3 is a combined hospital/ICU indicator, which utilises available data for each country in following order of priority: hospital admission > ICU admission > hospital occupancy > ICU occupancy. Thresholds for these were determined separately for admissions and current occupancy through internal expert agreement at ECDC.

Indicator		Domain	1	2	3	4	Source
1. 14-day case notification rates per 100k among people aged 65+ years		Severity	<20	20 - <50	50 - <150	≥150	TESSy
2. 14-day COVID-19 death rate per million		Severity	<20	20 - <40	40 - <100	≥100	EI
3. COVID-19 hospital/ICU indicator, current value as a proportion of the peak value in the country to date (%)	Weekly admissions rate per 100k	Severity	<10	10 - <25	25 - <50	≥50	TESSy or public online sources
	Current occupancy (mean weekly occupancy per 100k)		<25	25 - <50	50 - <75	≥75	Public online sources
4. 14-day COVID-19 case notification rate per 100k (all ages)		Intensity	<40	40 - 100	100 - 300	≥300	EI*
5. Test positivity (%) from all national reported tests and cases		Intensity	<2	2 - <4	4 - <10	≥10	TESSy and EI

** TESSy data were used for case rates in France due to a change in the surveillance system which led to negative case values being reported by EI.*

Second, the above scores are **adjusted based on the current trend** of each indicator, with -0.5, 0 or 1 added to each score for decreasing, stable or increasing trends, respectively. As a result, each indicator is can have a possible score of between 0.5 and 5.

The following definitions of trends have been in use for many months in ECDC's weekly country overview report:

- 14-day (two-week) notification rates for cases (all ages and age-specific) per 100 000 and deaths per 1 000 000 population. Trend for week W compares rate on week W with that in week W-1. Countries with low rates (cases: <10, deaths: <2) or which do not meet the criteria below are classified as stable trend. Increasing/decreasing trend: relative rate change (cases: >10%, deaths: >10%) OR absolute rate change (cases: >10, deaths: >5).
- Test positivity (%) = number of confirmed cases/number of tests done per week. Trend for week W compares positivity on week W with that in week W-1. Stable: relative change =<10% or absolute change =<1 percentage points. Increase/decrease: relative positivity change >10% and absolute positivity change >1 percentage points.
- Hospital or ICU admission rate: Trend for week W compares the admission rate per 100 000 population on week W with that in week W-1. Countries with low rates (<10% of the maximum weekly rate during the pandemic) or which do not meet the criteria below are classified as stable trend. Increasing/decreasing trend: relative rate change >10%
- Hospital or ICU occupancy. Trend for day D compares the mean daily occupancy rate per 100 000 population for all days in week W with that in week W-1. Countries with low occupancy (<10% of the maximum 7-day rate during the pandemic) or which do not meet the criteria below are classified as stable trend. Increasing/decreasing trend: relative rate change >10%.

Thirdly, a score for each domain (severity and intensity) is obtained from the mean of the trend-adjusted scores for each contributing indicator. The score for 14-day case notification rates is double-weighted (in both the numerator and denominator) within the intensity domain to make up for the fact that there are only two intensity indicators (compared to three severity indicators) and to give it greater weight than test positivity, which is becoming less reliable due the widespread use of antigen tests.

If data are missing for a given indicator it is not included in the calculation of the mean domain score. This results in a possible mean domain score of between 0.5 and 5.

Finally, the scores for each domain are considered to have equal weighting so are summed to give a final score per country per week of between 1 and 10. This range is divided into quartiles which correspond to the four categories:

1. Low: 1 to <3.25,
2. Moderate: 3.25 to <5.5,
3. High: 5.5 to <7.75
4. Very high: 7.75 to 10.

A **worked example** is shown below

Domain	Indicator	Weekly value	Score (value)	Trend adjustment	Weight	Final score	Domain score	Total score	Category
Severity	Cases 65+yr	70	3	-0.5	1	2.5	1.8	3.8	Moderate
	Hosp/ICU	12	2	-0.5	1	1.5			
	Death rate	30	2	-0.5	1	1.5			
Intensity	Case rate	118	3	-1	2	5	2		
	Positivity	0.3	1	0	1	1			