RAPID RISK ASSESSMENT

Assessment of the further emergence and potential impact of the SARS-CoV-2 Omicron variant of concern in the context of ongoing transmission of the Delta variant of concern in the EU/EEA, 18th update

15 December 2021

Summary

Emergence of the Omicron variant of concern (VOC) raises serious concerns due to preliminary reports of a significant growth advantage and potential immune escape compared to the Delta variant. Although the Omicron VOC cases initially reported in the EU/EEA were linked to travel, an increasing number of cases are now recorded as having been acquired within the EU/EEA, including as parts of clusters and outbreaks. Cases are also being detected through representative sampling in routine surveillance systems. This indicates that community transmission is already ongoing in EU/EEA countries and that further rapid increase in the number of Omicron VOC cases is expected in the next two months.

The overall epidemiological situation in the EU/EEA is still characterised by a high case notification rate and a low, but slowly increasing death rate, driven by the ongoing transmission of the Delta VOC. The Delta VOC remains currently the most prevalent variant. However, based on modelling predictions, and depending on the growth advantage and level of immune escape, the Omicron VOC is likely to become the dominant variant in the EU/EEA within the first two months of 2022. Data are currently too limited to assess the severity of disease caused by the Omicron VOC in the EU/EEA population with sufficient confidence. However, even if the severity of disease caused by the Omicron VOC is equal to or lower than the severity of the Delta VOC, the increased transmissibility and resulting exponential growth of cases will rapidly outweigh any benefits of a potentially reduced severity. It is therefore considered very likely that the Omicron VOC will cause additional hospitalisations and fatalities, in addition to those already expected in previous forecasts that only take into account the Delta VOC.

Effectiveness of vaccines against severe outcomes caused by the Delta VOC remains high. As of 9 December 2021, the cumulative full COVID-19 vaccine uptake in the total population of the EU/EEA is 66.8%. A slow increase in vaccine uptake has been reported in recent weeks and in the adult population the administration of booster doses, as a supplement to the full primary course, has been accelerating. Overall, progress in uptake remains uneven across countries, with four EU/EEA countries still reporting less than 50% full vaccine uptake in their total populations. Early evidence from in vitro neutralisation studies, not yet peer-reviewed, shows a reduced neutralisation capacity of sera from vaccine recipients and convalescent sera against the Omicron VOC compared to other SARS-CoV-2 variants, although large uncertainties persist. In addition, there is still insufficient real-life data on the effectiveness of the vaccines authorised in the EU against the Omicron VOC. According to the evidence currently available, for severe outcomes caused by the Delta VOC and potentially the Omicron VOC, booster doses will increase protection, with the population impact expected to be higher if the booster dose is given to most of the adult population within a short interval. Data currently available support safe and effective administration of a booster dose as early as three months from completion of the primary vaccination. Shortening the administration interval to three months may require adaptation of national vaccine deployment plans.

The mathematical modelling results, presented in detail below, demonstrate that strong and immediate reductions in contact rates are also required to avoid a high spike in cases caused by the Omicron VOC and to keep the COVID-19-related health and mortality burden manageable in the short term, even with an immediate acceleration of vaccine roll-out. In response to high incidence of the Delta VOC, non-pharmaceutical interventions (NPIs) should continue to be

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implemented by all countries and given the impending probable dominance of the Omicron VOC, these need to be further strengthened without delay. The immediate reinforcement of NPIs will slow the spread of the Omicron VOC, to allow countries to gain time for further vaccination roll-out, including booster doses, and to prevent a sudden high impact from the spread of this variant. Without reduction of contact rates through the implementation of NPIs and increased booster vaccination, levels of transmission could rapidly overwhelm EU/EEA healthcare systems.

Risk assessed

The risk to public health posed by the spread of the Omicron VOC in the context of ongoing Delta VOC transmission in the EU/EEA is assessed in this update. The Delta VOC remains the most prevalent variant, but community-associated spread of the Omicron VOC is occurring in the EU/EEA and the Omicron VOC will probably become dominant in early 2022, based on mathematical modelling predictions. We therefore assess the probability of further spread of the Omicron variant in the EU/EEA as **VERY HIGH**.

Although current data on the severity of the infection associated with the Omicron VOC remain limited, evidence to date raises concern that the Omicron VOC may be associated with a significant reduction in vaccine effectiveness against SARS-CoV-2 infection. Even in the case of lower infection/disease severity with the Omicron VOC, a steep, exponential increase in cases caused by the Omicron VOC will result in a growing number of cases with severe disease. As EU/EEA countries are still facing the severe impact of the Delta VOC wave, a further rise in hospitalisations could quickly overwhelm healthcare systems. We therefore assess the impact of the spread of the Omicron VOC as **VERY HIGH.**

Based on the limited evidence currently available, and given the high level of uncertainty, the overall level of risk to public health associated with the further emergence and spread of the SARS-CoV-2 Omicron VOC in the EU/EEA is assessed as **VERY HIGH**.

Options for response

Urgent and strong action is needed to reduce transmission in order to alleviate the already heavy burden on healthcare systems and protect the most vulnerable in the coming months.

Rapid reintroduction and strengthening of NPIs is necessary to reduce the ongoing Delta VOC transmission, slow down the spread of the Omicron VOC and keep the COVID-19-related healthcare and disease burden manageable. These measures include avoiding large public or private gatherings, encouraging the use of face masks, reduced contacts between groups of individuals in social or work settings, teleworking, expanded testing and strong contact tracing. Authorities should consider advising reduced inter-household mixing and exercising additional caution during travel and/or where intergenerational mixing is foreseen during the holiday season. While the proportion of Omicron VOC cases remains low and resource capacity allows, contact tracing should be prioritised for probable or confirmed cases of Omicron VOC infection, irrespective of vaccination status, in a timely manner and as completely as possible.

Vaccination remains a key component of the multi-layered approach needed to reduce the impact of the Omicron VOC, while also addressing the ongoing circulation of the Delta VOC. Efforts should continue to increase full vaccination uptake in individuals who are currently unvaccinated or partially vaccinated. Booster doses will increase protection against severe outcomes from the Delta VOC, and preliminary evaluations also suggest boosters could increase protection against the Omicron VOC. The population impact is expected to be higher if a booster dose is administered to most of the adult population and if this booster dose is given as early as possible, although not before three months after completion of the full vaccination course.

Immediate planning should be considered to increase healthcare capacity to treat the expected higher number of cases. Hospital surge capacities should be re-assessed according to emerging epidemiological data on the severity of the Omicron VOC.

Testing of individuals with symptoms, irrespective of their vaccination status, together with isolation of those testing positive, continues to be important in limiting the spread of SARS-CoV-2. Testing strategies should be flexible and rapidly adaptable to the epidemiological situation and available resources. Genomic surveillance remains of utmost importance for early detection of the presence of the Omicron VOC, to enable the monitoring of epidemiological trends and to guide measures.

Risk communication activities remain vital and these should emphasise the continued importance of being fully vaccinated and seeking an additional or booster vaccine dose. Messaging should continue to stress the importance of continued adherence to NPIs. Countries should consider investing in social listening activities to rapidly identify and address misinformation.

In order to address knowledge gaps in the context of the emerging Omicron VOC, it is critical to report data to ECDC and WHO and to monitor vaccine effectiveness. ECDC has proposed a generic protocol to guide vaccine effectiveness studies and foresees the possibility of voluntary reporting of outbreak data in EpiPulse.

What is new in this assessment?

This Rapid Risk Assessment extends the assessment on the circulation of the Delta VOC and projections for the festive period that was published on 24 November 2021 to include the emergence and spread of the Omicron VOC. The updated forecasts developed for this risk assessment are informed by the latest evidence on Omicron VOC epidemiology, transmissibility, severity, and immune escape.

Event background

Since 31 December 2019 and as of week 2021-48, 266 018 810 cases of COVID-19 have been reported worldwide, including 5 265 092 deaths. As of week 2021-48, EU/EEA (European Union/European Economic Area) countries have reported 47 828 589 cases and 858 432 deaths due to COVID-19, representing 18% of all cases and 16.3% of all deaths reported worldwide. These global and EU/EEA-wide figures are an underestimate of the true number of COVID-19 cases and deaths, due to various degrees of under-ascertainment and under-reporting. More details, including the timeline of major events in the COVID-19 pandemic, the latest available data on the number of cases and deaths globally, laboratory-confirmed cases reported to the European Surveillance System (TESSy), EU/EEA country overviews in relation to the COVID-19 epidemiological situation, vaccine doses administered in the EU/EEA reported to TESSy and data on COVID-19 in long-term care facilities, can be found here:

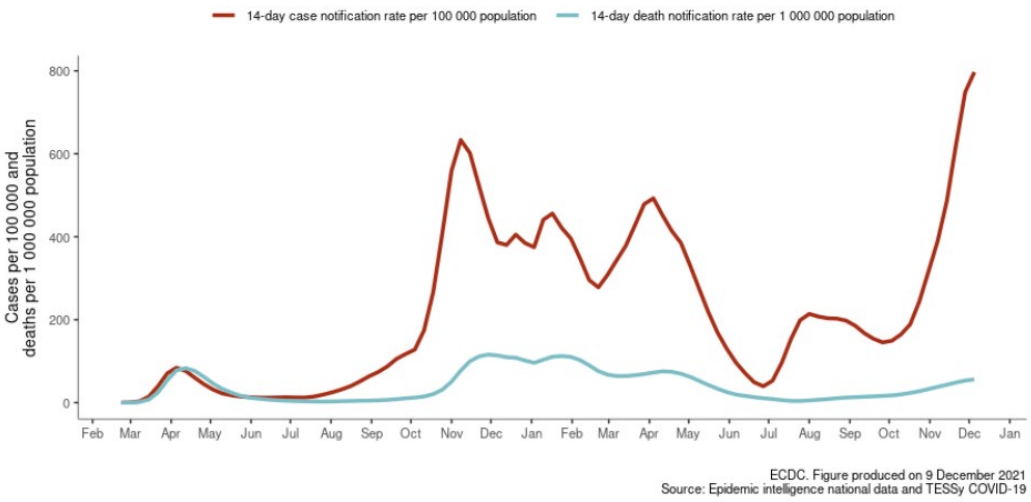
- Timeline of ECDC's response to COVID-19 [1];
- COVID-19 situation updates [2];
- Weekly surveillance report on COVID-19 [3];
- Country Overview Report [4];
- COVID-19 Vaccine Tracker [5].

Trends in epidemiological indicators and vaccine uptake

Epidemiological indicators

At the end of week 48 the overall epidemiological situation in the EU/EEA was characterised by a high and rapidly increasing overall case notification rate and a low, but slowly increasing death rate (Figure 1). At the end of this reporting week, the overall COVID-19 case notification rate for the EU/EEA was 797 per 100 000 population and this has been increasing sharply for nine weeks. Case notification rates were highest among age groups under 15 years old, but notification rates among older age groups have also been rapidly increasing. The 14-day COVID-19 death rate was 55.9 deaths per million population and has continued to increase slowly since early August. Of 30 countries with data on hospital or intensive care unit (ICU) admissions or occupancy up to week 48, 17 countries reported an increasing trend in at least one of these indicators compared to the previous week. There are substantial epidemiological differences between countries with increasing trends, including the intensity of transmission, age distribution of cases, and the levels of hospitalisation and mortality.

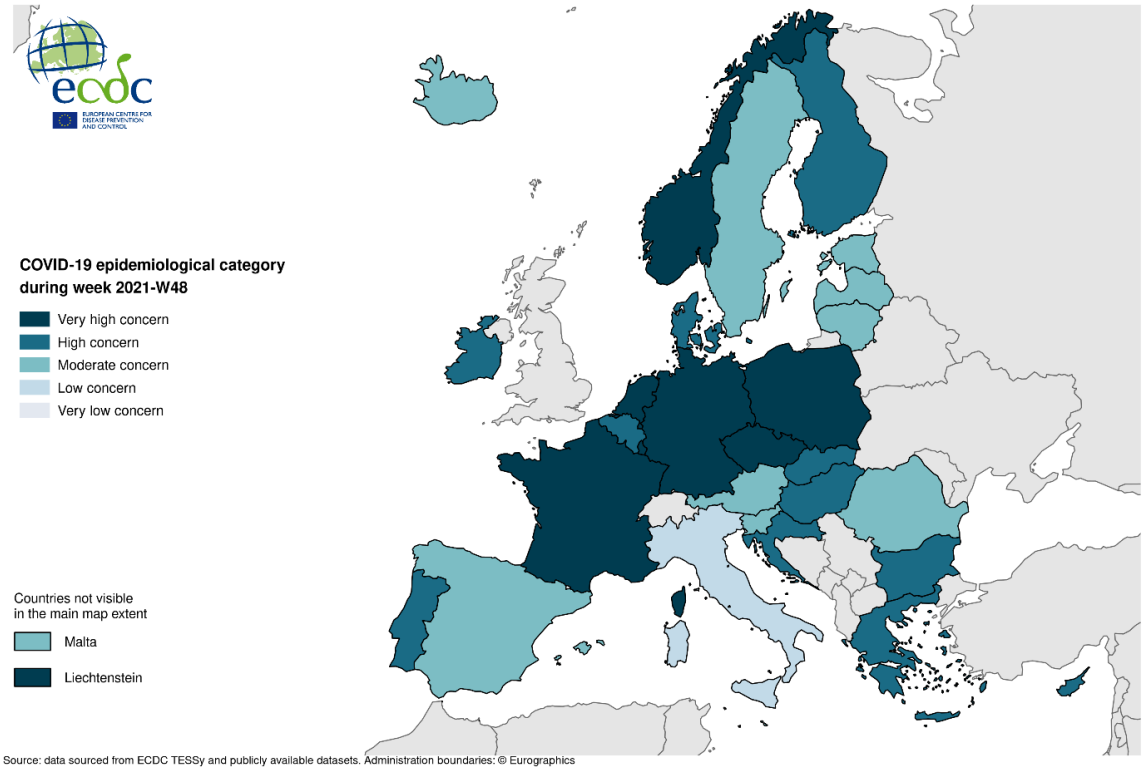
Figure 1. 14-day COVID-19 case and death notification rates in the EU/EEA up to week 48, 2021



Note: Case notification rates need to be interpreted with caution as country testing strategies are heterogenous and vary over time, for example in the use of rapid antigen detection tests (RADTs) or self-testing RADTs in settings such as schools and workplaces.

ECDC assesses each country's epidemiological situation each week using a composite score based on the absolute value and trend of five epidemiological indicators (intensity domain indicators: COVID-19 case notification rates and test positivity; severity domain indicators: case rates among 65+ years, hospital/ICU admission or occupancy and death rates). The scores from each domain are totalled to provide an overall score from 1−10, which is split into quintiles to derive five categories. As of week 48, the overall epidemiological situation in the EU/EEA was categorised as of very high concern, a level of concern which has remained high or very high for the last five weeks. Although the picture in week 48 varied noticeably between countries, the overall epidemiological situation was of high or very high concern in 19 of the 30 EU/EEA countries (Figure 2).

Figure 2. COVID-19 epidemiological categorisation of EU/EEA countries week 48, 2021



Co-circulation of SARS-CoV-2 with influenza and other respiratory viruses in the EU/EEA

Since the start of the influenza season 2021/22 in week 40, influenza has been circulating overall at a baseline-to-low level in the EU/EEA. For week 48/2021, of 24 countries reporting on influenza intensity, 20 (Belgium, Bulgaria, Croatia, Czechia, France, Germany, Greece, Hungary, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovenia) reported baseline intensity and four (Denmark, Estonia, Slovakia and Sweden) reported low intensity. With regard to geographical spread of influenza activity, 14 countries (Bulgaria, Croatia, Czechia, Greece, Hungary, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Malta, Poland, Romania and Slovenia) reported no activity, five (Belgium, Denmark, Germany, Netherlands and Portugal) reported sporadic spread, four (Estonia, France, Norway, Slovakia) reported local activity, and one (Sweden) reported regional spread. Even though influenza activity has remained below the epidemic threshold of 10% influenza positivity in the EU/EEA (based on patients in sentinel primary care settings testing positive for influenza virus infection), rates at or above 10% have been observed in some countries in the eastern part of the WHO European Region.

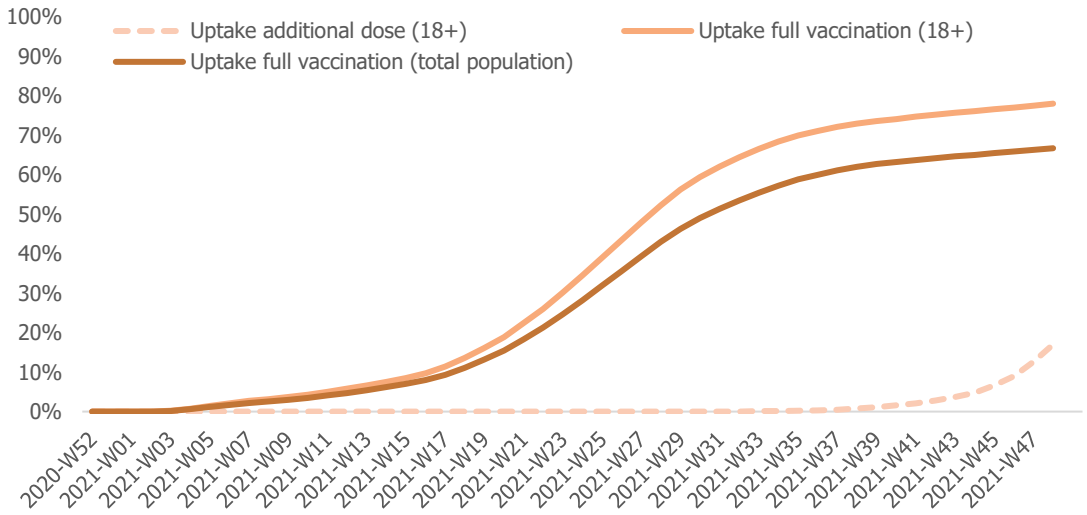
For the current season and up to week 48/2021, 42 out of 7 405 (1.8%) tested sentinel specimens were positive for influenza virus in the EU/EEA. More influenza type A (n=38; 90%) than type B (n=4; 10%) viruses have been detected. Of 29 subtyped A viruses, three (10%) were A(H1)pdm09 and 26 (90%) were A(H3). Of the four influenza type B viruses identified, one (25%) was ascribed to B/Victoria lineage. Regarding non-sentinel specimens, 2 104 out of 327 664 (0.6%) tested positive for influenza, with more type A (n=2009; 95%) than type B (n=95; 5%) viruses detected. Of 688 subtyped A viruses, 87 (13%) were A(H1)pdm09 and 601 (87%) were A(H3). Of the 95 influenza type B viruses identified, six (6%) ascribed to B/Victoria lineage. During this period, 29 laboratory-confirmed influenza-infected patients, reported by France and Sweden, were hospitalised and admitted to ICU, all of whom had influenza type A (17 [59%] A unsubtyped, one [3%] A(H1)pdm09 and 11 [38%] A(H3)). The most frequent age groups were 0 to 4 years (n=9; 31%), 65 years or more (n=7; 24%), and 45 to 54 years (n=4; 14%).

At the end of week 47, data reported to TESSy on respiratory syncytial virus (RSV) detections indicates ongoing RSV activity in the EU/EEA. Since week 41/2021, the reported RSV detection in the EU/EEA has slowly decreased, both in sentinel (15% [87/584] in week 47, 20% [96/421] in week 44, and 24% [92/383] in week 41) and non-sentinel sources (9% [2 384/25 257] in week 47, 13% [2 597/19927] in week 44, and 12% [2 374/19196] in week 41). Nevertheless, at the end of week 47 some countries had reported elevated RSV detection rates (Estonia, Germany, Hungary, the Netherlands, Poland, Slovenia, and Spain) as well as increasing trends (Estonia, Portugal, the Netherlands and Slovenia). Other countries have reported lower levels of circulation or sporadic detections while Denmark and France have observed earlier waves. Data are available in ECDC's Surveillance Atlas [6].

COVID-19 vaccine uptake

As of 9 December 2021 (week 48, 2021), the cumulative full COVID-19 vaccine uptake (completion of primary vaccination course) in the adult population (18+ years) in the EU/EEA reached 78% (range: 31.3–95.8%) with a slow increase in recent weeks. The level of full vaccine uptake in the total population is now 66.8% (range: 26.1–82%) (Figure 3). The increase in full vaccine uptake in the total population has been mostly driven by the roll-out in individuals under 18-years which has now reached 16.4% (range: 1.3–29.3%, 27 reporting countries). In the adult population, the administration of doses as a supplement to a full primary course has been accelerating during the last week. The median level of uptake for an additional dose reached 17% (range:2.4–54.8%, 28 reporting countries) in adults (18+ years), with the highest level of uptake observed in the elderly aged 60 years and over: 44% (range: 4.1–78.8%, 25 reporting countries). Overall, progress in vaccine uptake remains uneven across countries, with four EU/EEA countries still reporting less than 50% of full vaccine uptake in the total population (Bulgaria, Croatia, Romania, and Slovakia).

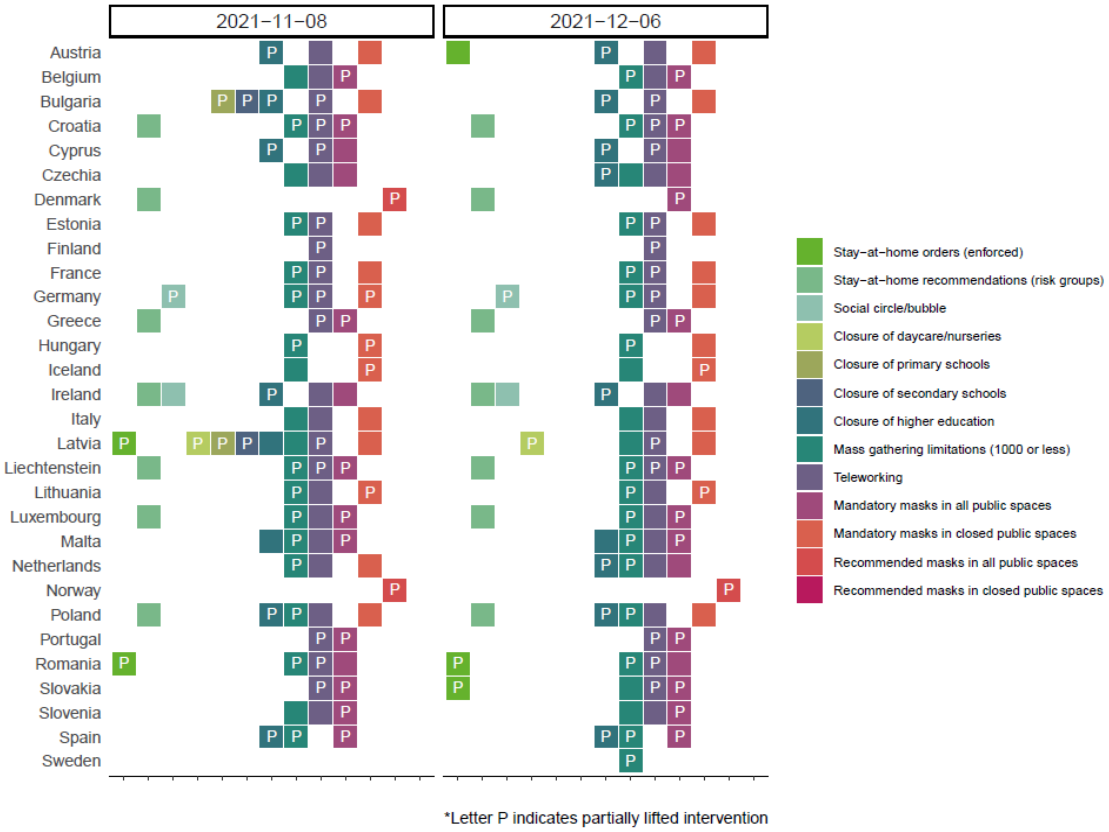
Figure 3. Cumulative uptake of full vaccination in the total population and doses in addition to a full primary course among adults (18+ years) in the EU/EEA as of week 48, 2021



Non-pharmaceutical interventions

Figure 4 shows active non-pharmaceutical interventions (NPIs) recorded in the ECDC-JRC Response Measures Database (RMD) at two points in time: 8 November 2021, as reported in the previous ECDC rapid risk assessment [7], and 6 December 2021. Taking the latest updates of the RMD into account, the same number of measures was recorded during both dates (n= 95). For both timepoints, just over half of all the measures in place were reported as being partially implemented. The number of countries with active measures relating to the mandatory use of face masks in all public spaces has increased, from 14 countries on 8 November 2021 to 16 countries on 6 December 2021. A similar change can be seen for measures restricting access to public events and mass gatherings of 1 000 participants or less, both indoors and outdoors, with 19 countries having such measures in place on 8 November 2021 and 21 countries on 6 December 2021.

Figure 4. Comparison of NPIs for the control of COVID-19 in EU/EEA countries active on 8 November and 6 December 2021



SARS-CoV-2 variants of concern

ECDC is currently monitoring several SARS-CoV-2 variants. Of these, variant B.1.351 (Beta, first detected in South Africa), variant P.1 (Gamma, first detected in Brazil), variant B.1.617.2 (Delta, first detected in India) and variant B.1.1.529 (Omicron, first detected in Botswana and South Africa) are listed as variants of concern (VOC) for the EU/EEA.

As of week 47, the Delta VOC is the most common variant in the EU/EEA countries. Among the 20 countries with an adequate sequencing volume for weeks 46 to 47 (15 November to 28 November 2021), the median (range) of the VOC reported in all samples sequenced was 98.6% (82.3–100.0%) for Delta, 0.0% (0.0–0.0%) for Beta and 0.0% (0.0–0.0%) for Gamma. This distribution was 0.0% (0.0–3.4%) for B.1.1.7 (Alpha), which was downgraded from the list of VOCs on 3 September 2021. Moreover, the median (range) of the variant of interest (VOI) reported in all samples sequenced in these 20 countries was 0.0% (0.0–6.4%) for AY.4.2. ECDC continuously monitors emerging variants. Lists of VOC, VOI and variants being monitored are provided on ECDC's website [8].

As of 26 November 2021, the World Health Organization (WHO) classified the B.1.1.529 variant as a VOC, due to indications of potential immune escape and a potentially increased transmissibility compared to the Delta VOC, assigning it the label Omicron. At the end of week 48, case-level data for 174 cases of the Omicron VOC were reported to TESSy. Data were reported for Omicron sequenced (n = 170), or detected through S-gene target failure (n = 4), with cases from: Austria (31), Finland (4), Ireland (1), Italy (4), Liechtenstein (1), Norway (116), Portugal (9) and Sweden (8). The median age of these 174 cases was 33 (range: 1–81) years and 56% (97) were male. In total, 22 (13%) of the cases were imported or travel-related, while 121 (70%) cases were locally-acquired, including 78 (45%) sampled as part of local outbreak investigations. One hundred and twenty two (70%) cases reported being symptomatic. Only one case was reported to have been hospitalised.

Epidemiological situation for the Omicron VOC

Between 26 November and 12 December 2021 (17:00), 5 435 confirmed Omicron VOC cases were reported worldwide by 69 countries, based on publicly available data (including those reported to GISAID). Of these cases, 23 EU/EEA countries, reported 766 cases based on sequencing results: Austria (17), Belgium (30), Croatia (3), Cyprus (3), Czechia (5), Denmark (195), Estonia (15), Finland (20), France (59), Germany (82), Greece (3), Iceland (20), Ireland (6), Italy (13), Latvia (5), Liechtenstein (1), the Netherlands (62), Norway (109), Portugal (49), Romania (7), Slovakia (3) Spain (36) and Sweden (23) according to information from public sources. In

addition, Denmark and Germany have reported 1 645 and 36 cases respectively, confirmed by a variant-specific PCR. A number of probable cases have been reported in several countries.

While most reported cases were initially linked to travel, an increasing number of cases are now recorded as being acquired within the EU/EEA, including as parts of clusters and outbreaks, with cases also being detected through representative sampling within routine surveillance systems. All cases for which there is information available on severity, were reported as mild or asymptomatic. There have been no Omicron-related deaths reported so far in the EU/EEA. However, these figures should be assessed with caution as the number of confirmed cases is too low and it is too soon to see the development of severe disease in many of the recently detected cases to understand if Omicron's disease clinical spectrum differs from that of previously-detected variants. EU/EEA countries reporting cases without an epidemiological link to travel outside the EU/EEA include Belgium [9], Denmark, France (TESSy), Finland [10], Spain [11], Iceland [12], and Sweden [13]. This indicates that community transmission is already ongoing in EU/EEA Member States. Between 26 November and 12 December 2021, several clusters and/or outbreaks were reported by at least 11 EU/EEA countries, including Belgium [14], Cyprus [15], Croatia [16], Denmark [17], Finland [18], France [19], Iceland [20], Ireland, Italy [21], Norway [22], Portugal [23], Romania [24,25] and Spain [26]. The clusters are related to family gatherings, sports teams, business meetings, conferences and Christmas celebrations. Cluster size varied from two to 123 cases, including confirmed and probable cases. In a large outbreak reported in Norway, most of the participants had received two doses of vaccine [22]. Cases were also reported to have been vaccinated in other clusters (e.g. Romania [24]).

Countries and territories outside of the EU/EEA have reported 4 669 confirmed Omicron cases. The 43 countries and territories reporting confirmed cases are: Argentina, Australia, Bangladesh, Botswana, Brazil, Canada, Chile, Cuba, Hong Kong Special Administrative Region, Fiji, Ghana, India, Israel, Japan, Jordan, Kuwait, Lebanon, Malawi, Malaysia, Maldives, Mexico, Namibia, Nepal, Nigeria, Russia, Saudi Arabia, Senegal, Sierra Leone, Singapore, South Africa, South Korea, Sri Lanka, Switzerland, Taiwan, Thailand, Tunisia, Turkey, Uganda, United Arab Emirates, United Kingdom (including cases reported in Bermuda and Gibraltar), United States of America, Zambia and Zimbabwe. For the WHO European Region, one death with confirmed Omicron VOC was reported in the UK, according to a media report quoting authorities on 13 December 2021 [27]. In addition, the same media report mentioned around 10 hospitalisations with Omicron VOC [27].

Disease background

The section below provides disease background specific to the Omicron VOC. For an overview of earlier variants and SARS-CoV-2 in general please refer to the section with the latest evidence on COVID-19 on ECDC's website [28].

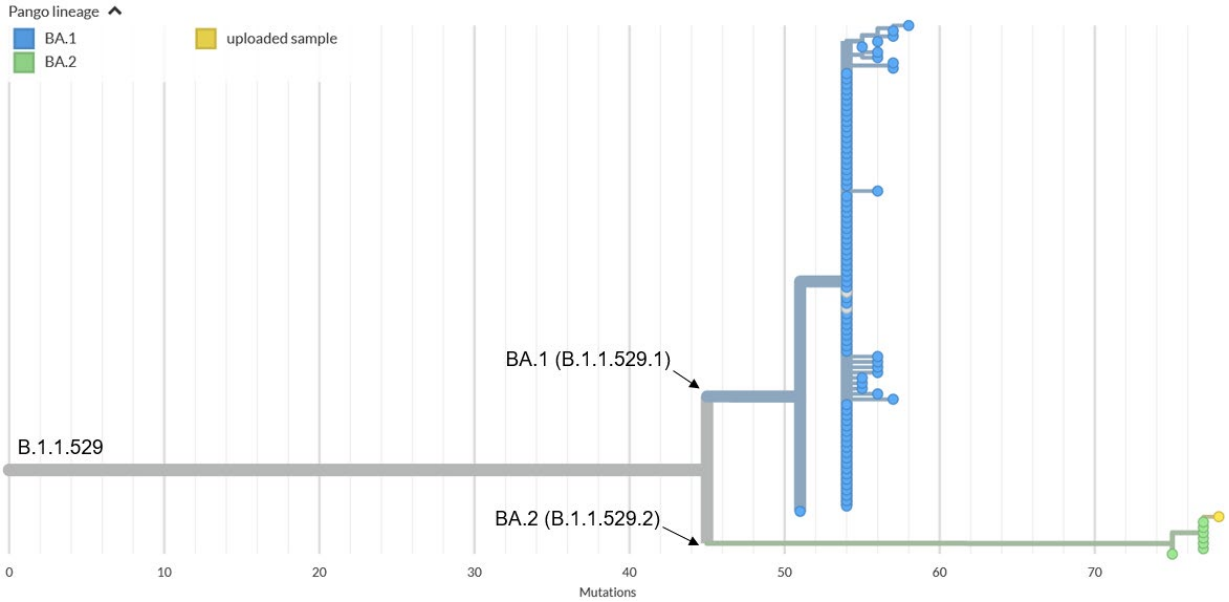
Omicron VOC

Molecular characteristics

The Omicron VOC belongs to the Pango lineage B.1.1.529, which is characterised by 21 amino acid changes in the spike protein compared to the original virus (G142D, G339D, S373P, S375F, K417N, N440K, S477N, T478K, E484A, Q493R, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K). Of these changes, 12 are located in the receptor binding domain (RBD) (residues 319-541).

The lineage B.1.1.529 has recently been partitioned into two sub-lineages BA.1 (B.1.1.529.1) and BA.2 (B.1.1.529.2) [29]. In addition to the characteristic mutation in B.1.1.529, BA.1 is characterised by additional differences in the spike protein (A67V, Δ69-70, T95I, Δ143-145, N211I, Δ212, ins215EPE, S371L, G446S, G496S, T547K, N856K, L981F), and BA.2 is characterised by another set of differences (T19I, L24S, Δ25-27, V213G, S371F, T376A, D405N, R408S). Importantly, BA.2 does not carry the Δ69-70 in the spike protein and therefore is not detectable by S-gene target failure (SGTF) in the Thermo Fischer TaqPath RT-PCR assay [29]. As of 12 December 2021, the BA.1 lineage contains the vast majority of the B.1.1.529 sequences (1545/1452, 99.5%) available from GISAID EpiCoV. All the supporting evidence for the phenotypical properties of Omicron available to date is derived from the BA.1 lineage and is probably not fully applicable to the BA.2 lineage.

Figure 5. Phylogenetic tree describing the Pango lineage B.1.1.529 and its sub-lineages BA.1 (isolates: blue dots) and BA.2 (isolates: green dots)



The tree was generated using the UShER web interface [30]. EPI_ISL_7259716 was used as query sequence and 100 samples were selected by the tool to show the placement of the query with respect to the complete SARS-CoV-2 tree.

Transmissibility

The Omicron VOC displays a significant growth advantage over the Delta VOC and is likely to outcompete the Delta VOC (see section 'Forecasts for Omicron VOC epidemiology'). According to UK data, the Omicron VOC has an increased household transmission risk, increased secondary attack rate and increased growth rate compared to Delta [31]. From these data, the adjusted odds ratio for household transmission from an Omicron VOC index case compared to a Delta VOC index case, based on routine testing data, was estimated to be 3.2 (95% CI 2.0−5.0), and the odds ratio (OR) for a close contact becoming a secondary case was 2.09 (95% CI 1.54−2.79). The household secondary attack rate in the UK was estimated to be 21.6% (95% CI 16.7−27.4%) for the Omicron VOC, compared to 10.7% (95% CI 10.5−10.8%) for the Delta VOC. However, there were a number of limitations in these studies, including lack of adjustment for vaccination and prior infection status of contacts and possible ascertainment bias. Therefore the preliminary results should be interpreted with caution.

Data from South Africa continue to confirm Omicron's growth advantage over other variants. The number of confirmed cases is continuing to rise in affected areas of South Africa, and in the Gauteng province, case rates have been increasing faster than in previous waves [32]. Between mid-August and late October 2021, the effective

reproductive number (Rt) in South Africa was estimated at below 1. It then increased sharply to an estimated 2.2 (95% CI 1.96-2.43) by mid-November, in conjunction with an increase in the number of new diagnoses [33]. As the case numbers increased, a rise in the proportion of samples with S-gene dropout was noted, which is a predictive marker for the presence of the Omicron VOC. This proportion then increased rapidly, from <10% to >95% during November 2021 [32].

In the UK, the proportion of cases with SGTF (now highly predictive of Omicron) continues to grow rapidly [31]. The estimated growth rate of the Omicron VOC based on adjusted SGTF counts was, as of 10 December 2021, 35% per day. Until week 47, the weekly count of cases with SGTF in the UK had routinely been less than 150, making up less than 0.1% of all cases. In specimens from week 48 dated from 30 November 2021 onwards, the number of cases with SGTF in the UK had already increased to 705 [31]. With the currently measured growth rate, the UK has projected that the Omicron VOC case numbers will reach parity with the Delta VOC cases by mid-December in the UK. In other studies and reports, the early doubling time in South Africa was estimated as 1–2 days [34], and the doubling time in Denmark, as of 9 December 2021, was estimated to be 2–3 days [35], which is similar to that estimated for the UK [36].

The above studies all indicate that the Omicron VOC has a growth advantage compared to other variants, including the Delta VOC. However, uncertainties still remain regarding current estimates of transmissibility and further studies are needed to provide reliable estimates of the transmissibility of the variant overall, and in relation to measures in place in different community settings.

Severity

There are insufficient data to currently assess with confidence the severity of disease caused by the Omicron VOC in comparison with other prevalent variants. However, so far severe cases have been rare in the EU/EEA. Among the initial Omicron VOC cases reported by the end of week 48-2021 by EU/EEA countries to TESSy, 70% (122/174) were symptomatic. Of the 117 Omicron VOC cases for which hospitalisation data was provided, only one was reported as hospitalised and no cases were reported as being admitted to the ICU or having died. The majority of EU/EEA cases were detected recently and, when symptomatic, had very recent onset of symptoms. Furthermore, the majority of cases for which age was available were young: 74% (128/174) were between 20 and 49 years of age. Since at least a portion of these cases were travellers or related to outbreaks in social settings, they could also be assumed to be in good health compared to the overall population. Data on vaccination status were not available for the majority of cases.

Data from the Gauteng province, South Africa, indicate an increase in hospital admissions of COVID-19 cases, from 153 cases in week 45 to 2 201 cases in week 48, and in deaths, from 18 deaths in week 45 to 83 deaths in week 49. This increase has been concomitant with the increasing predominance of the Omicron variant among the reported COVID-19 cases [37]. While case rates are increasing more quickly than in previous waves in the Gauteng province, hospitalisation rates are increasing in line with previous waves [37]. This indicates that the increase in hospital admissions is a reflection of the increased case load rather than being due to increased severity. According to an analysis of 211 000 COVID-19-positive cases during the Omicron outbreak, adults are experiencing a 29% lower admission risk, adjusted for vaccination status, relative to South Africa's first wave of infection dominated by D614G in 2020 [38].The high seropositivity in South Africa prior to the Omicron VOC wave could potentially explain the lower disease severity in this population, although case-linked data on previous infection or vaccination are not available [39].

In an outbreak related to a Christmas party in Norway, 80 out of 111 participants were diagnosed with SARS-CoV-2. Of the 80 individuals (mostly between 30 and 50 years of age, fully vaccinated and assessed as probable SARS-CoV-2 Omicron VOC cases), all except one reported symptoms. Over 70% of these 79 cases reported a cough, lethargy, headache, and sore throat, and over half reported fever. Symptom onset was on average three days after the party. No hospital admissions have to date been reported [22]. However, it is important to note that severe outcomes often take several weeks to accumulate and longer to be evident at population level, impacting hospital rates. Current estimates of the Omicron VOC severity are still uncertain and further studies, including longer-term follow up by age group, previous infection, and vaccination status of cases identified, are needed to provide more reliable estimates.

Potential for immune escape

Omicron is the most genetically divergent SARS-CoV-2 variant detected in significant numbers to date during the pandemic. This has raised concerns that it may be associated with a substantial reduction in the effectiveness of vaccines and monoclonal antibody therapies, as well as with an increased risk of SARS-CoV-2 reinfections. Several changes in the sequence coding the spike protein have previously been described and are already associated with an immune escape from neutralising antibodies [40].

Non-peer-reviewed, pre-print data currently available suggest that the neutralisation capacity of vaccinee (primary course) and convalescent sera against Omicron are significantly reduced relative to previous SARS-CoV-2 VOC [41-45]. However, there is evidence that virus neutralisation by sera from individuals who have experienced a combination of infection and full vaccination (primary course), or vaccinated individuals who have received boosters, remain at least partially effective in neutralising Omicron in vitro [41,43-45]. These early neutralisation data provide an indication that there may be reduced vaccine effectiveness, particularly as regards the prevention

of infection. However, results need to be confirmed with larger sample sizes and by additional laboratories for patients with different clinical profiles (brand of vaccine, additional vaccine doses, severity of infection) and sampling intervals following infection and/or vaccination.

It is difficult to directly translate in vitro neutralisation data to clinical outcomes such as protection from infection or severe disease, for which robust vaccine effectiveness and breakthrough infection data are required in clinical settings. As yet, no absolute antibody titre threshold has been established as a correlate of protection for SARS-CoV-2 [46]. Lower neutralising antibody titres in serum sampled three to six months after infection or vaccination may be compensated by the persistence of virus-specific, long-lived B cells that are able to rapidly expand during subsequent infection to generate higher neutralising antibody titres [47-49]. Furthermore, the impact of conserved non-neutralising antibodies or memory T cell responses is not evaluated by in vitro neutralisation studies, although it is likely that they contribute to protection from severe disease [50-52].

Therapeutics

At present only limited evidence is available regarding monoclonal antibody therapies against Omicron. Non peer-reviewed, pre-print data indicates that the combination of casirivimab and imdevimab does not neutralise Omicron in vitro [41,53], whereas the neutralisation capability of sotrovimab is retained against Omicron [54,55]. Initial genetic analysis of the antiviral remdesivir indicates that it is likely to continue to be active against Omicron, however this is yet to be confirmed by laboratory testing [56]. Clinical and laboratory data on the effectiveness of newer oral antivirals against Omicron are not yet available.

Laboratory testing

While RT-PCR tests remain the gold standard in COVID-19 testing because of their high sensitivity and specificity, several EU/EEA countries have introduced the use of RADTs and self-RADTs as a way of further strengthening their overall testing capacity. Despite the emergence of virus variants, no reduction in test sensitivity of RADTs has been reported so far [57]. Preliminary results of the rapid assessment conducted by the Foundation for Innovative New Diagnostics (FIND) suggest that the accuracy of RADTs for confirmation of infection has not been impacted by the emergence of the Omicron variant [58]. Furthermore, initial laboratory validation of lateral flow devices in use by the UK's NHS (National Health Service) Test and Trace has determined similar sensitivity in detecting Omicron to that for Delta [31]. It is important to note that wider performance studies of RADTs for the Omicron variant in settings with high transmission have not yet been conducted. Further studies are ongoing, and laboratories should remain vigilant for reductions in sensitivity of RADTs used to detect different VOCs. Further information on the use of RADTs can be found in the recently updated ECDC technical report [57].

RT-PCR-based S-gene target failure (SGTF) assays that fail to detect the S-gene when it carries the deletion Δ69-70 can be used to screen for the Omicron VOC. However, it should be noted that a newly characterised Omicron sub-lineage BA.2 (B.1.1.529.2) has been described that does not carry the Δ69-70 mutation [29]. Although only a very small number of BA.2 sequences have been identified worldwide so far, caution should be exercised when using the SGTF assays as viruses of this sub-lineage will not be identified by these assays. It should be noted that there are also a low number of sequences of non-Omicron lineage viruses that carry Δ69-70. Therefore, a subset of SGTF-screened cases should be selected for further confirmatory sequencing.

Screening for VOC-specific amino acid substitutions can also be done using specific RT-PCR assays targeting single nucleotide polymorphisms (SNP) [59]. However, it is important to note that existing SNP assays may fail to detect/identify newly emerging variants that do carry the specific SNP, due to amino acid substitutions in neighbouring sites affecting the primer/probe binding. For the Omicron variant specifically, it has been noted that some commercially available SNP assays for the identification of T478K, N501Y and P681H are failing to reliably identify these mutations, despite the fact that this variant carries the mutations in the S-gene [60]. The US FDA currently provides a list of molecular tests that may be affected by mutations in the SARS-CoV-2 Omicron variant [60]. Similarly, the Joint Research Centre (JRC) is monitoring the performance of RT-PCR assays and displays information on the JRC Dashboard [61]. In silico analyses performed by JRC have identified six assays that may fail to detect or have reduced sensitivity to Omicron [62]. Laboratories are urged to verify the efficiency of protocols used on dashboards relating to in silico analysis and clinical validations.

Additional new assays have also been developed for the identification of Omicron (e.g. targeting S371L/S373P, E484A and ins214EPE) [63,64]. A comprehensive list of available assays/protocols for the identification of the Omicron variant and a table with characteristic amino acid substitutions, deletions, or insertions for the screening of different VOCs can be found in Annexes 1 and 2, respectively. WHO 's Regional Office for Europe and ECDC have set up a protocol/information sharing platform, EZCollab, for 'COVID-19 protocol sharing' among national public health laboratories. Registration can be made at: https://ezcollab.who.int/euroflu/flulab/covid19_protocols.

Public perceptions

There is currently little information available on public perceptions of Omicron specifically. This means we do not yet know how the new variant may be influencing people's willingness to follow current NPIs, or their acceptance and uptake of COVID-19 vaccination. Further data collection will be needed to provide an understanding of whether people's perceptions of Omicron will motivate them to engage in more personal protective behaviour, or to get vaccinated. While not specific to Omicron, data collected in Belgium between late November and early

December showed an increase in perception of 'severe risk of infection' among the study population [65]. Researchers posited that this increase was related to awareness of the evolving epidemiological situation, which included the reporting of Omicron cases in Europe. Similarly, the WHO-EARS social listening tool recorded an increase in the topic 'COVID-19 variants' over any other topic during the last 30 days, [66]. Furthermore, based on topics of concern identified through social listening activities, the Robert Koch Institute has updated its COVID-19 FAQs to include the effect Omicron may have on vaccine effectiveness [67]. In summary, although the public's understanding and perception of the risks presented by Omicron still needs to be fully mapped, there are indications of concern about the current COVID-19 epidemiological situation.

Vaccines (effectiveness, waning, evidence for boosters)

The mutations identified in the Omicron VOC, particularly in the receptor binding domain of the spike protein, suggest a significant potential for vaccine escape by this variant compared with the Delta VOC [68]. As described above, preliminary in vitro studies indicate a reduced neutralisation capacity against the Omicron VOC, although large uncertainties still persist [41,42]. However, the protection induced by COVID-19 vaccines does not solely rely on antibody responses against the RBD of the SARS-CoV-2 spike protein. Vaccine-induced cell-mediated immunity directed at epitopes outside the RBD may also play an important role in protection from severe disease following infection by Omicron [28,69].

With regard to vaccine protection against onward transmission, infection and infection with milder disease, the observation that neutralising antibody responses are significantly affected by the Omicron VOC suggests that previous infection and/or vaccination may have a decreased protective effect against these three outcomes, particularly if antibody levels have waned over time. More clinical studies on the effectiveness of boosters against the Omicron VOC are urgently required (to date only one study is available), as well as more studies and real-life data on the impact of the Omicron VOC on waning immunity following vaccination or natural infection. Only then will it be possible to fully understand Omicron's impact on vaccine effectiveness.

Real-life data on the effectiveness of the vaccines authorised in the EU against Omicron VOC are not yet available, with the exception of very preliminary estimates on possible vaccine effectiveness against symptomatic disease due to the Omicron VOC. A moderate-to-high vaccine effectiveness against symptomatic COVID-19 disease is reported in the early period following administration of a booster with Comirnaty (70–75%) [70]. These results strongly support the administration of a booster dose following a full primary course vaccination course as a means of conferring protection against symptomatic disease caused by the Omicron VOC. However, as recognised by the authors, this study, which still has to be peer-reviewed, was carried out at a very early stage after the emergence of Omicron and has a number of limitations. This further underlines the importance and need for more vaccine effectiveness studies on larger populations.

There have also been reports of suspected SARS-CoV-2 reinfections with the Omicron VOC following an infection with another variant [71]. Similarly, there have been reports of clusters of Omicron VOC infections in individuals who had received a full primary vaccination course, followed by a booster dose with mRNA vaccines [72], and in fully vaccinated individuals having had two doses of COVID-19 vaccine (vaccine product unspecified) [22].

Population seroprevalence

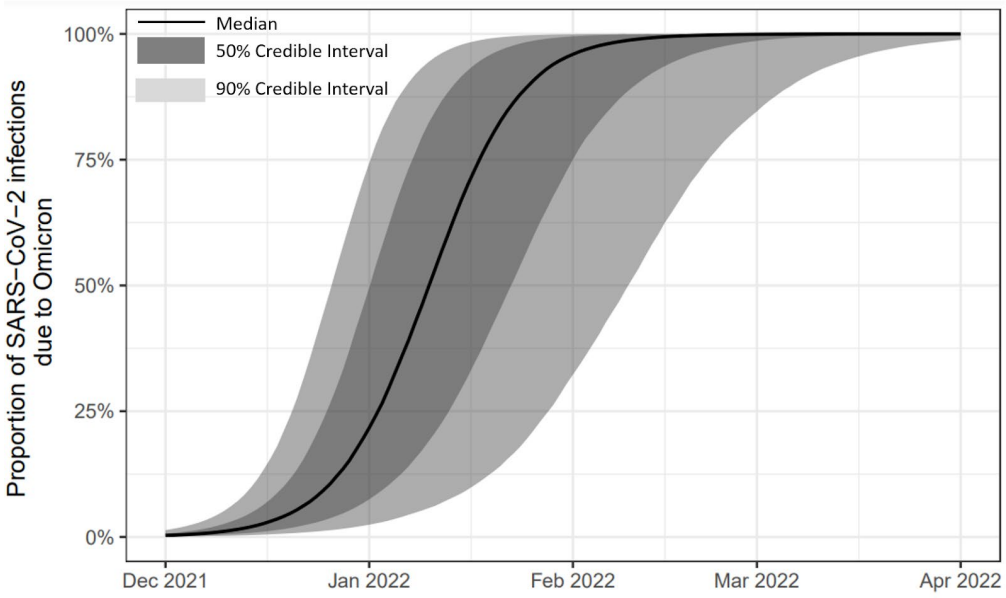
Seroepidemiological studies conducted in the EU/EEA in recent months provide evidence of increasing population seropositivity, with Finland reporting estimates exceeding 90%, and the highest seropositivity results mostly reported in studies conducted among the older cohorts who were the first to be vaccinated [73,74]. Most studies do not discriminate between natural or vaccine-induced immunity. However, the seropositivity data closely follow trends in vaccine coverage across different cohorts and the relatively rapid increase in seropositivity is generally attributed to vaccination. Understanding the true contribution of naturally-acquired immunity in the total population is challenging without specific studies, and estimates based on reported infection incidence are prone to under-ascertainment.

The Omicron VOC, and possible future variants bearing multiple mutations, may significantly erode or evade vaccine- and/or naturally-induced immunity. It is therefore important that there is a good understanding of the proportion of individuals with natural immunity, as well as immunity from vaccines, to help evaluate the potential public health impact of variants including the Omicron VOC. Using different serological assays, it is possible to distinguish between natural and vaccine induced immunity. Among the studies conducted in the European region that have used these assays, a study in Geneva conducted between 1 June and 7 July 2021 reported a total seropositivity of 66.1% (64.1–68.0) and an infection-induced seroprevalence of 29.9% [75]. More recent data from a longitudinal study among blood donors in the UK reported seropositivity estimates of 22.7% (95% CI 22.0% to 23.5%) for infection-induced antibodies and 97.8% for antibodies related to vaccine or natural infection, for the period 4 October to 28 November 2021 [76].

Forecasts for Omicron VOC epidemiology

ECDC has simulated the expected number of fatalities for the Omicron VOC compared to the Delta VOC for different scenarios between 1 December 2021 and 31 March 2022. These scenarios capture the wide range of uncertainty in our current knowledge of the Omicron VOC. The exact time at which the Omicron VOC becomes dominant depends on the growth advantage over the Delta VOC, which will differ across EU/EEA countries. We estimate that if no further measures are taken now, Omicron will probably become a dominant strain in the EU/EEA by February 2022 at the latest, but in some individual EU/EEA countries possibly already towards the end of December 2021 (Figure 6). The predictions in Figure 6 are subject to uncertainty relating to Omicron's transmissibility and immune escape, as well as other factors, and are shown as median estimate (black line), 50% credible interval (dark grey area) and 90% credible interval (light grey area).

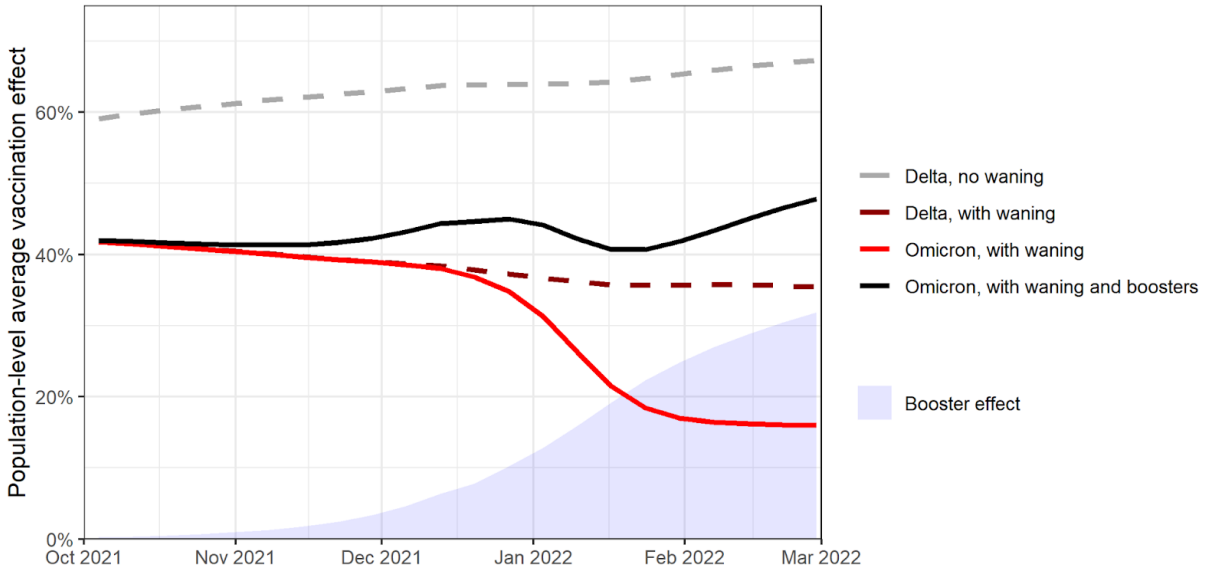
Figure 6. Predicted proportion of SARS-CoV-2 infections caused by the Omicron VOC



Note: results represent 50 000 samples randomly drawn from a set of distributions for the growth advantage of the Omicron VOC over the Delta VOC (with majority of probability mass within the bounds of -0.2; +0.5); the relative reduction in vaccine effectiveness due to immune escape (0.3; 0.6); the relative reduction in natural immunity (0.5; 0.8); and the initial proportion of Omicron VOC infected individuals on 1 December 2021 (0.1%; 1%). We also drew values from a range of the vaccination coverage and natural immunity levels that were representative of the average across the EU/EEA countries, with a vaccination coverage drawn from a distribution of 40–50% and natural immunity of 30–60%. The population-level vaccine protection was estimated from the observed country values and averaged across EU/EEA countries.

Building upon the estimated future trajectory of the Omicron VOC, we can predict an expected decrease in population-wide vaccination protection due to this variant. Figure 7 shows the anticipated impact of both the increasing circulation of Omicron and waning immunity on the population-level average vaccination effect. The substantial reduction in vaccination effect can, to a certain extent, be mitigated by rapid large-scale booster vaccination programmes. The results in Figure 7 are in agreement with previous ECDC rapid risk assessments and threat assessment briefs [7,77], which strongly advocated booster vaccinations. However, the urgency for administration of booster doses has substantially increased, due to the rapid emergence of the Omicron VOC in the EU/EEA.

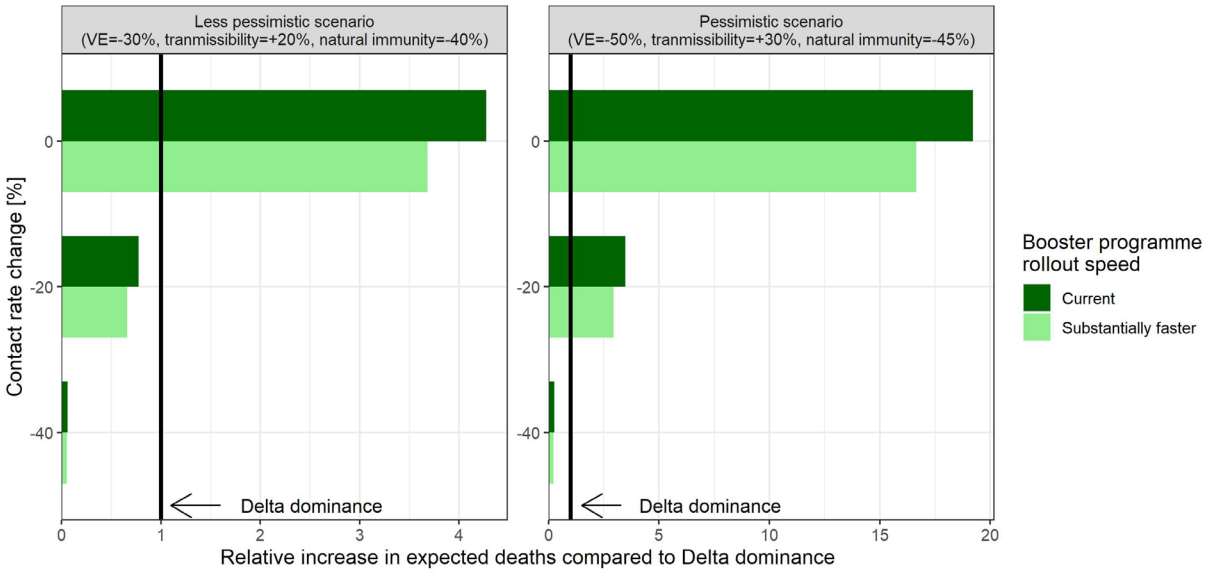
Figure 7. The population-level vaccination effect against infection over time, averaged across the population in the EU/EEA



The estimated population-level vaccination effect against infection is the average protective impact of vaccination on the likelihood of infection across the whole population – a value of 100% would mean complete protection of the whole population. The dashed grey curve shows the vaccination effect (without boosters) for the hypothetical scenario that neglects both the emergence of Omicron and the waning. The dashed red curve shows the vaccination effect (without boosters) for the hypothetical scenario involving the waning of the vaccination effect, but without the emergence of Omicron. The solid red curve shows the expected impact of both Omicron and the waning of the vaccination effect (without vaccine booster doses). The solid black curve shows the same scenario as the expected third scenario, but additionally assumes a booster roll-out for those over 40 years. For the booster roll-out, a speed (boosters per day) of 60% of the roll-out of second doses is shown and the eventual coverage of booster shots is assumed to be 80% of the second dose coverage, while the vaccine effectiveness against infection of the boosters was assumed to be 90%. The shaded area shows the expected impact of boosters, which equals the difference of the expected Omicron scenario with a rapid booster roll-out (black curve) to the expected Omicron scenario without boosters (red curve). We emphasise that the intention of these curves is to show rough order-of-magnitude trajectories, given the significant uncertainties of Omicron VOC's spreading parameters, human behaviour, country-specific parameters, stochasticity and the simplification of modelling assumptions. Furthermore, for the purpose of visualisation, the plot only shows the median values, without the credible interval around each curve.

Lastly, we contrasted the uncertain factors of the Omicron VOC with potential mitigation strategies. We focus on speeding up the current COVID-19 vaccine booster programmes and re-introducing stricter non-pharmaceutical interventions that reduce Rt in the EU/EEA between December 2021 and March 2022. Compared to the current situation of persistent Delta VOC dominance, our results show that if the growth advantage of the Omicron VOC is low, a faster booster roll-out will reduce the number of deaths (as would be expected). However, without reductions in contacts, the relative increase in deaths would be substantially higher compared to a baseline scenario reflecting the current situation of Delta VOC dominance (See Figure 8 - Less pessimistic scenario). A combination of the continued booster programmes and reductions in social contacts that go further than the measures already implemented in November 2021 could stop the increase in death rates. However, at higher levels of assumed Omicron growth advantage, the booster programmes will not be able to induce immunity quickly enough between December 2021 and March 2022 (Figure 8 - Pessimistic scenario).

Figure 8. Change in COVID-19-related fatalities resulting from a dominant Omicron VOC in the EU/EEA between December 2021 and March 2022 when implementing a faster booster vaccine roll-out across different non-pharmaceutical interventions



To capture the reinforcement and reintroduction of NPIs that has already been put in place, we assumed initial Rt to be equal to 1.0. Higher transmissibility, lower vaccine effectiveness (VE) for infection, and lower protection of natural immunity due to Omicron will all substantially increase Rt. The vaccination roll-out reflected the observed rates across the EU/EEA countries, including the booster vaccines. As changes in severity are linear, lower Omicron severity would roughly translate to proportional reduction in the excess severity of Omicron shown in this figure (e.g. a 50% reduction in Omicron severity compared to Delta would result in a 50% reduction in the length of the bars above the value of one, showing the relative increase in expected deaths from Omicron over Delta). Note that the x-axes of the two subfigures are on a different scale. Contact rate reduction could also be achieved through stricter NPIs.

The modelling results described above provide several insights:

- The high levels of SARS-CoV-2 transmission seen in November 2021 will lead to an unavoidable increase in burden due to the Delta VOC in many EU/EEA countries throughout December 2021.
- Omicron VOC is likely to become the dominant variant as early as January 2022, although this is dependent on the growth advantage and immune escape of Omicron VOC.
- The effective vaccine protection to be expected at population-level is decreasing over time due to (a) the waning of vaccine-induced immunity and (b) the reduction in vaccine effectiveness caused by the Omicron VOC (particularly in those individuals not having received the booster).
- The Omicron VOC is likely to cause additional fatalities to those already expected from forecasts which only take the Delta VOC into consideration. However, these fatalities will only be observed with delay after the Omicron VOC has become dominant (given the delay by several weeks in observing COVID-19-related fatalities after SARS-CoV-2 infection, detection and usually hospitalisation).
- The higher the growth advantage of the Omicron VOC and its immune escape, the worse the expected burden will be.
- With the Omicron VOC probably having a higher growth advantage, large and immediate reductions in contact rates are needed to keep the COVID-19-related burden manageable. This is particularly relevant in the light of the upcoming holiday season that usually involves intergenerational mixing across different households, with the risk of super-spreading events.
- The speed of the booster vaccination programmes is the key to reducing the avoidable burden in early 2022.
- The consequence of continuing on the current trajectory and not ramping up (booster) vaccination programmes and contact restrictions to reduce transmission (bring Rt below 1.0) is the likelihood of unprecedented levels of transmission events which could overwhelm healthcare systems. It is also likely that fatalities would not be seen until 2022 after a period of delay.

ECDC risk assessment for the EU/EEA

This assessment is based on evidence available to ECDC at the time of publication and is informed by mathematical modelling of projected disease burden, described above. It follows the ECDC rapid risk assessment methodology, with relevant adaptations, where the overall risk is determined by a combination of the probability and its impact [78].

Risk assessment question

What is the risk to public health posed by the spread of the Omicron VOC in the context of ongoing Delta VOC transmission in the EU/EEA?

The Delta variant is currently the most prevalent variant in EU/EEA, but community-associated spread of the Omicron VOC is already occurring in various EU/EEA countries and the Omicron VOC will very probably become dominant in early 2022, based on modelling predictions. The probability of the Omicron variant spreading is therefore considered to be **VERY HIGH.** Data are currently too limited to assess the severity of disease caused by the Omicron VOC with sufficient confidence. However, even if the severity of disease caused by the Omicron VOC is equal to or lower than the severity of the Delta VOC, the increased transmissibility and resulting exponential growth in cases will rapidly outweigh any benefits in terms of lesser severity. The exponential rise in cases and resulting hospitalisations will probably overwhelm healthcare systems that are already experiencing difficulties coping with the high case load resulting from the ongoing Delta VOC wave. The impact of the Omicron VOC spreading is therefore considered to be **VERY HIGH**.

The risk assessment presented here is based on limited evidence available at the time of publication. At this stage, much of the available data are preliminary and have not undergone validation or peer-review. In addition, evidence is evolving daily, with more Omicron VOC cases being detected and investigated. There are still many knowledge gaps which are outlined in detail in the limitation section below. Based on the currently available limited evidence, and considering the high level of uncertainty, the overall level of risk associated with the further emergence spread of the SARS-CoV-2 Omicron VOC in the EU/EEA is assessed as **VERY HIGH**.

Options for response

Non-pharmaceutical interventions

Maintaining and strengthening of non-pharmaceutical interventions

The modelling results above show that only strong and immediate contact reductions will allow the avoidance of a high spike in cases caused by the Omicron variant. NPIs should continue to be implemented by all countries, based on the high number of Delta VOC cases, and they will need to be strengthened to take into account the upcoming dominance of the Omicron VOC in the community. Countries that are observing a reduction in incidence of the Delta VOC following the introduction of NPIs may expect a strong resurgence of cases if they lift NPIs. Appropriate use of face masks, teleworking, preventing crowding in public spaces, reduction of crowding on public transport, staying home when ill, maintenance of hand and respiratory hygiene measures and ensuring adequate ventilation in closed spaces all remain a priority. More information on specific NPIs can be found in the 17th update of ECDC's rapid risk assessment on SARS-CoV-2 [7].

Efforts to reduce transmission of infection by limiting social and public events will support physical distancing measures, especially during the holiday season, given that the number of indoor interactions among people will be increased. Authorities should consider advising reduced inter-household mixing during the festive season (i.e. creating a social bubble) and exercising additional caution if travel and/or intergenerational mixing is foreseen. Precautionary measures can also include limiting other social contacts and/or use of RADT self-tests before meeting friends and relatives, to minimise the risk of SARS-CoV-2 transmission and associated outbreaks.

Contact tracing

Contacts of probable or confirmed cases of SARS-CoV-2 Omicron VOC infection

Contact tracing can help slow the establishment of the Omicron VOC in the country. While the proportion of Omicron VOC cases remains low and resource capacity allows for the tracing of probable or confirmed cases of SARS-CoV-2 Omicron VOC infection, the enhanced contact tracing measures set out in ECDC's contact tracing guidance [79] should be considered. Contact tracing of such cases should be prioritised and efforts made to trace and follow up both high-risk and low-risk exposure contacts, irrespective of vaccination status, in a timely manner and as completely as possible. In the event of an epidemiological link to an affected area or to a case infected with the Omicron VOC, contact tracing should also be initiated for cases with symptoms indicative of COVID-19

infection, even if they have not yet been tested. Although the most recent ECDC guidance on contact tracing advises differing management approaches for vaccinated and unvaccinated contacts in terms of quarantine and testing, all contacts of probable or confirmed cases of Omicron infection should be managed as if they are unvaccinated, until further evidence on vaccine effectiveness becomes available.

While the proportion of Omicron VOC cases remains low and resource capacity allows, as mentioned above, enhanced contact tracing measures should be considered. This stricter management of contacts includes the investigation of the source of infection of a newly-identified case – known as 'backward contact tracing', tracing back contacts further than two days before symptom onset or positive result, testing of all high and low-risk exposure contacts, starting to trace the contacts of the household members of a case while awaiting their testing results, and releasing high-risk exposure contacts only after a negative RT-PCR test taken on Day 14. Measures also include asking the household members of high-risk contact persons ('secondary contacts') to quarantine until the primary contact has received a negative test result from their initial test and otherwise observing strict physical distancing measures after that. If a contact person has symptoms when they are identified or if they develop symptoms during follow-up, public health authorities should immediately start contact tracing of their contacts before the test result is confirmed.

Each country should adapt their response to the local epidemiological situation and available resources. The rigorous and timely application of contact tracing measures in areas where there are a limited number of cases can play a key role in limiting further spread of the outbreak. If resources allow, contact tracing and management could also reduce the case load in hospitals in geographical locations with more widespread transmission.

Contact tracing related to air travel

With regard to contact tracing of passengers on aircraft, ECDC has developed specific recommendations and these are available in the third update of ECDC's contact tracing guidance [80]. However, this guidance was developed prior to the widespread emergence of variants with high transmissibility. As a more precautionary approach, and if resources allow, contact tracing all passengers and cabin crew members who have travelled on a flight with a confirmed or probable case could be considered. All passengers should be considered as having had high-risk exposure and managed as contacts in accordance with the guidance on contact tracing above. It is recommended that all travel-related cases identified should be prioritised for sequencing or, as a minimum, samples sequenced from all cases with travel history (14 days prior to symptom onset) to areas with confirmed community circulation of the Omicron VOC, or where the epidemiological situation is unclear.

When contact tracing investigations identify contacts or a potential source in another country, public health authorities should collaborate across borders and exchange data securely (for example, using the selective exchange messaging function of the EU's Early Warning and Response System (EWRS) or sharing data using the European Digital Passenger Locator Form) (dPLF) [81]. Supplementary information and links to additional documents can be found on ECDC's contract tracing landing page [82].

Vaccination

Vaccination is a key component of the multi-layered approach needed to reduce the impact of the Omicron VOC in the EU/EEA, while at the same time addressing the ongoing circulation of the Delta VOC. Despite the waning immunity and reduction of effectiveness against infection and mild disease seen with the Delta VOC, the COVID-19 vaccines continue to play a very important role in averting severe disease, hospitalisations and death. Evidence shows how in countries with a high vaccination uptake, hospitalisations and deaths are significantly reduced. Those who are fully vaccinated and have breakthrough infections face a significantly lower risk of developing severe disease than those who are unvaccinated [83-89]. There is now evidence that booster doses lead to a significant increase in protection against both mild and severe disease by counteracting waning [90-94].

Based on the conclusions of the mathematical model above, in addition to the potential reduction of vaccine effectiveness against the Omicron VOC, particularly in non-boosted individuals, waning immunity requires a speed up in the deployment of the booster dose to reduce an avoidable burden in early 2022. While the majority of countries are now considering the administration of a booster dose to all adults aged 18 years and over [7], data currently available support safe and effective administration of a booster dose as early as three months from completion of the primary vaccination. However, shortening the administration interval to three months may require adaptation of national vaccine deployment plans and the capacity to deliver the vaccine to all eligible individuals. Based on recent EMA and ECDC recommendations on heterologous vaccination courses against COVID-19, countries can consider a heterologous booster vaccination strategy as an alternative strategy to homologous boosters [95].

Another priority is the continued effort to increase vaccination uptake across the EU/EEA to limit the spread of SARS-CoV-2, prevent severe outcomes of the disease and ensure effective and equitable coverage across countries and regions in Europe. Priority should be given to the vaccination of people initially targeted by COVID-19 vaccination programmes who remain unvaccinated or who are not yet fully vaccinated, and in particular the elderly, vulnerable, healthcare workers and pregnant women. Key approaches to facilitating vaccine acceptance and uptake include a) understanding the factors that determine low vaccine uptake; b) developing targeted strategies to address these factors; c) addressing inequalities in access and d) monitoring and addressing mis- and disinformation concerning vaccines. Concomitant administration of COVID-19 and seasonal influenza vaccines should be considered, as this is safe and offers efficiencies in terms of administration, logistics and costs.

Increase of healthcare system preparedness and hospital surge capacity

Mitigation efforts and control measures for Delta and Omicron VOCs should be accompanied by reinforcement of healthcare systems and support of healthcare workers in the coming months. Planning for increased capacity should be reviewed in order to treat the expected higher number of cases and re-assessed in accordance with emerging evidence on Omicron's severity. Access to pharmaceuticals for treatment of SARS-CoV-2 infection, oxygen supplies and staffing should also be reviewed. Existing public health tools may be useful [96,97] for this purpose. Several studies have shown increases in healthcare worker fatigue during the pandemic in terms of stress, anxiety and burn out [98]. As the strain on healthcare systems has continued in a number of countries during 2021, it is expected that fatigue among healthcare workers has further increased. This applies not only to the clinicians but also to the public health workforce [99,100]. Interventions to support healthcare workers should consider organisational, social, personal, and psychological aspects, and research should continue to determine their individual effectiveness.

Testing and sequencing

Testing

Testing of people with symptoms, regardless of vaccination status, and isolation of those testing positive continues to be important to limit the spread of SARS-CoV-2 and reduce the burden on the healthcare system. Testing strategies to delay the introduction and spread of the Omicron VOC should be flexible and rapidly adaptable to change, depending on the epidemiological situation and available resources. In general, nucleic acid amplification tests (NAAT) are used as the gold-standard detection method for SARS-CoV-2 and can use one or multiple target genes for amplification.

Depending on available resources, pre-screening of positive samples with PCR-based assays (e.g. SGTF or SNP assays) should be enhanced. A subset of screened cases should be selected for further confirmatory sequencing. Cases with SGTF identified in EU/EEA countries can be reported directly to TESSy, but viruses that are confirmed as the Omicron VOC by sequencing should be reported as such. Details for reporting SGTFs and the Omicron VOC cases can be found in ECDC's reporting protocol [101]. Diagnostic laboratories need to remain vigilant to detect any mismatches of PCR-based assay primers and probes against circulating virus genomes. For all assays, it is vital to keep track of possible incidents of suboptimal performance and to inform the manufacturer of a commercial assay and international SARS-CoV-2 public health networks, ECDC and WHO Regional Office for Europe of any concerns experienced with a specific assay.

In addition to SARS-CoV-2, other circulating respiratory viruses such as influenza and RSV may cause additional challenges for healthcare providers and public health systems during the current pandemic. For more information on testing and the use of multiplex RT-PCR assays for other respiratory viruses please refer to the testing strategy section of the 17th update of the Rapid Risk Assessment [7].

SARS-CoV-2 genetic and antigenic characterisation capacity

Genomic surveillance of currently circulating variants remains of high importance and Whole Genome Sequencing (WGS), or at least complete or partial S-gene sequencing, should be performed to confirm infection with a specific variant. With the emergence of Omicron and the aim of delaying its introduction and spread while Delta continues to circulate widely, ECDC recommends that countries should sequence a number of representative samples to allow detection of a variant at 1% prevalence level. As long as there is no community transmission in the country, ideally, all cases with travel history (14 days prior to the positive test result) to areas with suspected community transmission of Omicron, or where the epidemiological situation is unclear, should be sequenced [77,102].

It should be noted that at times, some amplicons of specific assays may fail to detect certain circulating VOCs, due to primer-template mismatches. This can lead to missed calls at the spike protein residues. For example, in silico analysis has shown that amplicon 76 of the ARTIC v4 protocol could fail for the Omicron VOC due to primer-template mismatches, leading to missed calls at spike protein residues 417, 440 and 446. If this region is not covered, other characteristic mutations can be used to identify the variant. The updated v4.1 version of ARTIC aims to mitigate primer-template mismatch for Omicron [103].

Laboratories are encouraged to further characterise variants antigenically. WHO COVID-19 reference laboratories of the WHO European Region can support countries with antigenic characterisation and the list of reference laboratories can be found here [104]. Further information on antigenic characterisation capacity can be found in Annex 3.

Risk communication

Omicron VOC vs Delta VOC

Although much attention is currently being given to the Omicron VOC, it is important to remind people that the predominant immediate threat is in fact from Delta. While there is substantial scientific uncertainty about many aspects of Omicron, the potentially severe impact of Delta is well understood, and it is therefore essential that messages are disseminated widely to promote both vaccination and appropriate non-pharmaceutical interventions [7]. This is especially important in the build-up to the festive season, when increases in travel and celebratory gatherings create conditions that can be conducive to high levels of infection. In addition, people should be reminded that increases in COVID-19 hospitalisations do not only present serious challenges for health systems, but they also have a significant adverse effect on care and treatment for other conditions.

In the longer term, consideration needs to be given to optimising people's motivation to adhere to protective behaviour in a sustained manner (both vaccination and NPIs). It is likely that some measures will be required at least for a number of months, and it is important that risk communication activities take into account the range of potential social, economic and political effects that these may have on society.

Communication on vaccination

In view of the current limited evidence concerning the Omicron variant and the uncertainties regarding immune escape in relation to available COVID-19 vaccines (and treatments), clear communication of the continued importance of being fully vaccinated and seeking an additional or booster vaccine dose remains vital. There is a need to continuously communicate on the effectiveness and safety of COVID-19 vaccines, and to clearly emphasise the important role that COVID-19 vaccines have been playing in averting severe disease, hospitalisation, and death since the start of the vaccination campaigns. To do this, it is important to communicate the results of studies on the effectiveness and impact of COVID-19 vaccination programmes. As mentioned earlier in the document, this includes the evidence on how hospitalisations and deaths are significantly reduced in countries with high vaccination coverage, and evidence that those who are fully vaccinated and have breakthrough infections face a significantly lower risk of developing severe disease or requiring hospitalisation than those who are unvaccinated [83-89]. Data visualisation is a valuable tool to clearly convey such messages [105,106]. The public should be reassured on the power and effectiveness of the available COVID-19 vaccines, even though adaptations in vaccination strategies are needed (e.g. the administration of a booster or additional COVID-19 vaccine dose), and despite the need to maintain a certain level of NPIs due to the high incidence of COVID-19 cases.

In addition, the public may have questions and concerns around the need for vaccines when faced with an overflow of information concerning the possible impact of the Omicron VOC, especially when there is selective or over-interpretation of results from recent studies. It should be clarified that the scientific process takes time. More studies and real-life evidence will be needed before any firm conclusions can be made. New evidence is continuously emerging, therefore messages on potential updates of vaccines or the need for further boosters need to highlight the current uncertainty in order to avoid confusion in the future.

Identifying and addressing misinformation

As has happened several times during the COVID-19 pandemic, where there has been scientific uncertainty or information voids, the emergence of Omicron creates the potential for the spread of misinformation. In countries where online social listening is not routinely practised (to identify circulating rumours and misperceptions which can then be addressed through risk communication activities), national authorities may wish to consider investing in this important area [107].

Reporting of data to ECDC

While it is extremely important to monitor the vaccine effectiveness of COVID-19 vaccines using prospective study designs, where adjustments can be made for most confounders, it is also possible to assess vaccine effectiveness in outbreak settings. The evidence available from rapid studies can be of particular interest in the context of new questions related to vaccine effectiveness (e.g. studies associated with emerging VOCs). Results from such studies may be rapidly collected and provide preliminary or additional evidence for other estimates. One advantage of outbreak investigations is that in some settings (e.g. schools) vaccination records might be easily obtainable. Investigation can take place simultaneously with implementation of control measures.

With this aim, ECDC has published and advocates the use of a generic protocol that is intended to be adapted to local/national contexts to guide the implementation of vaccine effectiveness studies against SARS-CoV-2 infection (on the occurrence of an outbreak in semi-closed-settings) [108]. Two study designs and their respective methodologies are proposed: cohort and case control study. Semi-closed settings are defined as any setting where the population can be easily identified from enrolment/employment registers (e.g. schools and other educational institutions, or workplaces). ECDC foresees the possibility of voluntary reporting of outbreak-related data in EpiPulse as defined in this document, with the aim of providing a rapid and preliminary analysis of vaccine effectiveness estimates in the context of the emerging SARS-CoV-2 variant Omicron.

Travel measures

There is currently ample evidence that the Omicron VOC has already been introduced into many EU/EEA countries, with some already experiencing community transmission. Travel restrictions during the first days of detection and recognition of the Omicron VOC were designed to buy valuable time in order to better understand its characteristics and cope with the current high circulation of the Delta VOC across EU/EEA countries. Travel measures (e.g. travel restrictions and/or other measures) should always be reviewed in the light of the latest epidemiological situation, and the considerations in the 'Testing' section above.

To prevent SARS-CoV-2 transmission during travel, measures include advice to avoid travelling when experiencing COVID-19 compatible symptoms, maintenance of NPI measures in transportation hubs and during travel (e.g. minimising crowding, observing physical distancing and using face masks during travel, good ventilation, etc.) and the use of recognised EU digital COVID-19 certificates [109].

For countries that are still detecting their first imported Omicron cases and aiming to delay further introductions of the Omicron VOC from areas with a high level of community transmission, in addition to the above-mentioned advice, pre-departure testing (preferably RT-PCR up to 48 hours before or RADT 24 hours before travel) or post-arrival testing and quarantine can be considered for travellers coming from areas with a high level of community transmission of the Omicron VOC [109]. Given the evidence that the Omicron VOC has already been introduced into many EU/EEA countries, with some countries already experiencing community transmission, such measures will probably not be relevant for much longer.

It is important to ensure that public information on the emerging situation and the public health measures is provided to travellers to raise awareness and support compliance. In addition, awareness among healthcare professionals is essential to ensure that all suspected cases of COVID-19 presenting to healthcare facilities have a full travel history taken. For any cases that are identified among travellers from areas with community transmission or where the epidemiological situation is unclear, isolation, and contact tracing should be carefully performed (see section above). Virus isolates from such cases should be prioritised for sequencing to promptly identify cases of the new variant. Cases of the new variant in EU/EEA countries should be reported weekly through The European Surveillance System (TESSy). TESSy allows reporting cases of the Omicron VOC and/or cases with deletion of the S-gene, both through variant-data and case-based data.

Limitations of this risk assessment

This assessment is undertaken based on information known to ECDC at the time of publication and has several key limitations. The epidemiological data used in this assessment are made available 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. In particular, there are many scientific uncertainties and knowledge gaps regarding the Omicron VOC, including those set out below.

- A lack of clear understanding of the epidemiological situation in many countries, given the level of sequencing or lack of screening using S-gene target failure.
- Uncertainties regarding current estimates of transmissibility including secondary attack rates, growth rates, Rt and R0 to provide reliable estimates of the transmissibility.
- Uncertainties regarding estimates of severity (hospitalisation and deaths) including longer-term follow-up by age group, previous infection and vaccination status of cases identified.
- Uncertainties regarding current estimates of immune escape, including from neutralising monoclonal antibody treatments and antivirals.
- Limited information on vaccine effectiveness for different vaccines against the Omicron VOC (direct and indirect effects) for disease, transmission and severe disease by age.
- Lack of information on cross-protection of natural immunity from other SARS-CoV-2 variants, in particular data on reinfection risk and reinfection severity in populations exposed to different SARS-CoV-2 variants during previous pandemic waves.

Source and date of request

ECDC internal decision, 7 December 2021.

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

Disclaimer

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

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Annex 1. List of available assays/protocols for the identification of the Omicron variant

Commercial or in-house assay	Spike gene amino acid substitution	Methodology	References
TIB MolBiol	S371L/S373P	Melting curve	[64,110]
TIB MolBiol	ins214EPE	Melting curve	[64,110]
TIB MolBiol	E484A	Melting curve	[64,110]
Thermo Fisher TaqPath	ΔH69/V70	SGTF	[111]
Seegene			[112]
JRC		Currently being validated	[113]
Israel Ministry of Health Central Virology Laboratory (CVL) and the Israel Institute for Biological Research (IIBR)	nsp6 (Orf1a)	RT-PCR assay – currently being optimised	[114]
University Hospital Geneva	Two partial S gene regions	RT-PCR and Sanger sequencing	[115]
Smorodintsev Research Institute of Influenza (St. Petersburg, Russia)	ORF1 deletion	RT-PCR	[116]
Statens Serums Institut, Denmark	Omicron VOC specific 4-target PCR	RT-PCR	[117]

Annex 2. Characteristic amino acid substitutions, deletions, or insertions for screening of different VOCs*

Spike amino acid variation	Alpha B.1.1.7	Beta B.1.351	Gamma B.1.1.28	Delta B.1.617.2	Omicron B.1.1.529
ΔH69-V70	X				x
ins214EPE					x
S371L/S373P					x
N501Y	X	x	x		x
K417T			x		
K417N		X			x
E484K		X	x		
E484Q	(x)				
E484A					x
P681H	x				x
P681R				x	
T478K				x	

** List not exhaustive.*

IMPORTANT NOTE: Primer/probe mismatches at neighbouring sites in the Omicron VOC (or other) variant may cause failure to detect the amino acid substitution even if the variant carries this substitution. Validation is therefore recommended for detection/characterisation of new variants.

Annex 3. Antigenic characterisation capacity

ECDC has mapped the current capacity of the EU/EEA Member States to perform virus isolation and antigenic characterisation (neutralisation assays) in November 2021 (report under approval). Twenty of the 29 reporting countries indicated having established virus culture for SARS-CoV-2, which is a prerequisite for antigenic characterisation. Fourteen of the twenty countries indicated antigenic characterisation capacity and multiple methods of antigenic characterisation have been implemented.

Antigenic characterisation standardisation

For laboratories to assess how well the antibodies are predicted to protect against the circulating viruses through humoral immunity and from vaccine-induced immunity, it is important to perform neutralisation assays using convalescent plasma/sera from infected and vaccinated individuals and to include international standards (see below) to assess the antigenic characteristics of the circulating variants. Multiple laboratory methods have been developed to determine virus neutralisation capacity. Some examples are plaque reduction neutralisation (PRNT), microneutralisation and pseudovirus neutralisation assays [118-120].

To assess the neutralisation capacity of sera for different patient situations, the serum panels could include sera from different severity levels and different sampling intervals for asymptomatic, symptomatic and vaccinated individuals. Heterologous prime-boost or infection plus any vaccination sera would also be beneficial as comparators.

The laboratories cultivating SARS-CoV-2 viruses should consider that serial propagation of SARS-CoV-2 variants in Vero E6 or other cell types may lead to furin cleavage site mutations that affect how the virus grows and behaves in vitro or in vivo. Propagation of unwanted mutations can be mitigated by growth in cells such as Vero/hSLAM and by frequent sequence confirmation (deep sequence methods preferred) [121].

To compare the neutralisation assay results with other laboratories internationally, WHO International Antibody Standard (WHO IS) or, if WHO IS unavailable, the so-called NIBSC working reagent (21/234) or high-titer reference serum (20/150) should be used for neutralisation assays [122-124]. It should be noted that the WHO IS performs differently for each variant and therefore, any data presented comparing the WHO IS should always identify the variant under test. It is important to include representatives of different variant strains (as a minimum D614G, Alpha, Beta and Delta) in the neutralisation assays. The assays should also ideally be performed in duplicate or triplicate. Assay details without peer review have also been shared by scientists for Omicron VOC neuralisation assays [42,125].

Antigenic characterisation results of new VOCs should immediately be shared with WHO's Regional Office for Europe and ECDC.