THREAT ASSESSMENT BRIEF

Implications of the further emergence and spread of the SARS-CoV-2 B.1.1.529 variant of concern (Omicron) for the EU/EEA – first update

2 December 2021

Summary

The number of countries reporting SARS-CoV-2 Omicron variant of concern (VOC) cases continues to increase globally, with a total of 352 confirmed cases reported by 27 countries as of 16.00 on 1 December 2021, including 70 confirmed cases reported by 13 European Union and European Economic Area (EU/EEA) countries. The majority of confirmed cases have a history of travel to southern African countries, with some having taken connecting flights at other destinations between Africa and Europe. Several European countries have already reported subsequent community or household transmission. All cases for which there is available information on severity were either asymptomatic or mild. To date, there have been no severe cases and no deaths reported among these cases.

Current evidence on transmissibility, severity, and immune escape is highly uncertain for the Omicron VOC. However, preliminary data from South Africa suggest that it may have a substantial growth advantage over the Delta VOC. If this is the case, mathematical modelling indicates that the Omicron VOC is expected to cause over half of all SARS-CoV-2 infections in the EU/EEA within the next few months. The greater Omicron's growth advantage over the Delta VOC and the greater its circulation in the EU/EEA, the shorter the expected time until the Omicron VOC causes the majority of all SARS-CoV-2 infections.

The presence of multiple mutations in the spike protein of the Omicron VOC indicates a high likelihood of reduction of neutralising activity by antibodies induced by infection or vaccination. Preliminary data suggest that the Omicron VOC may be associated with increased risk of reinfection in South Africa. However, the full extent to which the Omicron VOC evades or erodes existing vaccine- or infection-derived immunity remains uncertain in the absence of in vitro neutralisation data, vaccine effectiveness data, and further data on reinfection in populations exposed to different SARS-CoV-2 variants during previous pandemic waves.

Risk assessed

What is the risk associated with the further introduction and spread of the SARS-CoV-2 variant Omicron in the EU/EEA?

The evidence from the initial cases of this new variant that has been collated from around the world is limited, but suggests that the Omicron VOC may be associated with higher transmissibility than the Delta VOC, although robust evidence is still lacking. There remains considerable uncertainty related to vaccine effectiveness, risk for

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reinfections, and other properties of the Omicron VOC. Based on these factors, the probability of further introduction and community spread of the Omicron VOC in EU/EEA countries is currently assessed as **HIGH.**

Current estimates on the severity of the infection associated with the Omicron VOC remain highly uncertain. The currently available evidence raises serious concern that the Omicron VOC may be associated with a significant reduction in vaccine effectiveness and increased risk for reinfections. The degree of protection against severe disease with the Omicron VOC conferred by past COVID-19 infection or by vaccination is not yet known. EU/EEA countries are still facing the severe impact of high numbers of cases of the Delta VOC. The impact of the further introduction and spread of the Omicron VOC could be **VERY HIGH,** but this situation needs to be evaluated as further information emerges.

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

Options for response

To date, the Omicron VOC has already been introduced into many EU/EEA countries. Given the current limited evidence around this new variant and the concerns about its immune escape properties in relation to available COVID-19 vaccines and treatments, a multi-layered approach to delay the spread of this VOC in the EU/EEA is needed.

Due to the ongoing circulation of the Delta VOC, EU/EEA countries are urged to give utmost priority towards the vaccination of people initially targeted by COVID-19 vaccination programmes who remain unvaccinated or who are not yet fully vaccinated. Countries should consider a booster dose for people aged 40 years and older, first targeting the most vulnerable and the elderly, and could then consider a booster dose for all adults aged 18 years and older at least six months after completion of the primary series.

Non-pharmaceutical interventions (NPIs) that have proven to be very effective in reducing transmission of infection should continue to be implemented by countries based on an assessment of their epidemiological situation regarding the Delta VOC, and taking into account the uncertainty of the situation regarding the Omicron VOC. Physical distancing measures, ensuring adequate ventilation in closed spaces, the maintenance of hand and respiratory hygiene measures, the appropriate use of face masks, and staying home when ill all remain relevant.

Enhanced contact tracing measures such as backward contact tracing and stricter management of contacts could help slow the establishment of the Omicron VOC in the country.

Genomic surveillance remains of the utmost importance for early detection of the presence of the variant, to enable the following of epidemiological trends and guide containment measures.

Temporary travel-related measures should be carefully considered in light of the latest epidemiological situation, and should be regularly reviewed as new evidence emerges. Such measures might include the testing and quarantining of travellers who have recently returned from affected countries and sequencing cases identified among travellers. Public information around the emerging situation and the public health measures in place for returning travellers from affected areas are important to raise awareness and support the effective implementation of these measures. However, given the increasing number of cases and clusters in the EU/EEA without a travel history or contact with travel-related cases, it is likely that within the coming weeks the effectiveness of travel-related measures will significantly decrease, and countries should prepare for a rapid and measured de-escalation of such measures.

Event background

On 26 November 2021, ECDC classified a SARS-CoV-2 variant belonging to Pango lineage B.1.1.529 as a variant of concern (VOC) due to concerns regarding immune escape and potentially increased transmissibility compared to the Delta variant. WHO also classified the variant as a VOC and assigned it the label Omicron.

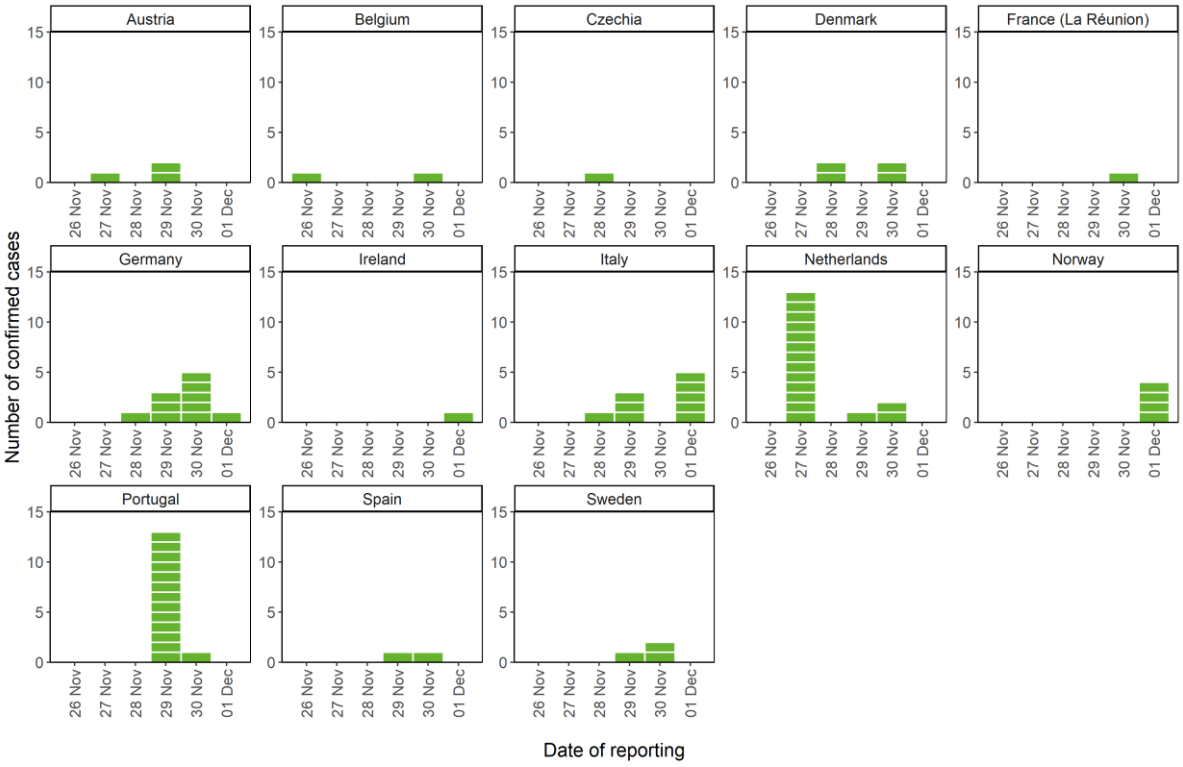
The novel SARS-CoV-2 variant Omicron was first detected in samples collected on 11 November 2021 in Botswana, and subsequently in samples collected from 14 November and onward in South Africa. The number of countries reporting the Omicron VOC cases continues to increase globally, with a total of 352 confirmed cases reported by 27 countries as of 16:00 on 1 December 2021. To date, there have been no severe cases or deaths reported globally.

As of 16:00 on 1 December 2021, 70 confirmed Omicron variant cases have been reported by EU/EEA countries. The cases have been reported by 13 European Union and European Economic Area (EU/EEA) countries: Austria (3) [1], Belgium (2) [2], Czechia (1) [3], Denmark (4) [4], France (1 in Réunion) [5], Germany (10) [6], Ireland (1) [7], Italy (9) [8], the Netherlands (16) [9], Norway (4) [10], Portugal (14) [11], Spain (2) [12], and Sweden (3) [13] according to information from public sources. A number of probable cases have also been reported from

across the region, but these are under investigation. The majority of confirmed cases have a history of travel to southern African countries, with some having taken connecting flights at other destinations between Africa and Europe. Several countries reported community or household transmission (Germany [14], Italy [15], Portugal [16], Israel [17], and the United Kingdom [18,19]). All cases for which there is available information on severity were either asymptomatic or mild. No severe cases and no deaths have been reported among these cases to date.

Outside of the EU/EEA, 282 confirmed cases have been reported in 14 countries and territories outside of the EU/EEA (Australia [20], Botswana [21], Brazil [22], Canada [23,24], Ghana [25], Hong Kong Special Administrative Region [21], Israel [17], Japan [26], Nigeria [27], Saudi Arabia [28], South Africa [21], South Korea [29], Switzerland [30], and the United Kingdom) [31] (as of data available at 16:00 on 1 December 2021).

Figure 1. Confirmed COVID-19 Omicron cases detected in the EU/EEA, by date of reporting, as of 1 December 2021



Source: ECDC Epidemic Intelligence

Sequence reporting from the African region

The reporting of sequencing results in the African region is low overall. Only Botswana, South Africa, Ghana, and the French overseas department Réunion have reported sequences from samples collected within the last 30 days to a level that allows for detection of community transmission of Omicron. This means that ongoing transmission of this variant cannot be excluded for other countries. Since the variant is spread across regions within South Africa and has also been detected in significant numbers in Botswana and Ghana, circulation in other countries is likely.

Table 1. Number of the Omicron VOC sequences reported to GISAID EpiCoV from samples collected since 1 November 2021 from all countries and territories in the African region, as defined by GISAID

Country or territory	Number of Omicron sequences	Total sequences reported
Botswana	19	99
Ghana	33	53
Kenya	0	3
Mayotte	0	15
Nigeria	0	1
Democratic Republic of the Congo	0	8
France (La Réunion)	1	86
Senegal	0	4
South Africa	172	249

Data extracted from GISAID EpiCoV on 1 December 2021 at 15:30 CET.

The Omicron variant of concern properties

The VOC B.1.1.529 (Omicron) belongs to Pango lineage B.1.1.529, Nextstrain clade 21K, and is characterised by 30 amino acid changes, three small deletions and one small insertion in the spike protein compared to the original virus (A67V, Δ69-70, T95I, G142D, Δ143-145, Δ211, L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F). Of these changes, 15 are located in the receptor binding domain (RBD) (residues 319-541). The variant also carries several changes and deletions in other genomic regions (NSP3 – K38R, V1069I, Δ1265, L1266I, A1892T; NSP4 – T492I; NSP5 – P132H; NSP6 – Δ105-107, A189V; NSP12 – P323L; NSP14 – I42V; E – T9I; M – D3G, Q19E, A63T; N – P13L, Δ31-33, R203K, G204R).

Timeline for the detection and initial assessment of Omicron

The first sequence of the variant was uploaded by Hong Kong Special Administrative Region to GISAID EpiCoV [32] on 22 November 2021, with 10 further sequences from Botswana and South Africa uploaded on 23 November 2021 [32]. On 23 November 2021, the variant was first mentioned on the Pango nomenclature GitHub board [33] and on 24 November 2021 it was designated as lineage B.1.1.529. On 24 November 2021, ECDC started assessing the variant. South Africa's Health department broadcast a media brief on the variant on 25 November 2021 [34]. The World Health Organization (WHO) classified the variant as a VOC and assigned the label Omicron on 26 November 2021 [35], with ECDC classifying it as a VOC on the same day [36].

Immunity

The Omicron VOC is the most divergent variant that has been detected in significant numbers during the pandemic to date, which raises serious concerns that it may be associated with significant reduction in vaccine effectiveness and increased risk for reinfections. Several of the changes in the sequence coding the spike protein have been described before and are associated with immune escape from neutralising antibodies, or other properties. A synthetic variant previously described with 20 mutations in the spike protein was associated with almost complete escape from neutralisation by convalescent and vaccinee sera [37]. As the Omicron VOC carries even more mutations in the S-gene compared to the synthetic variant, a very significant effect on neutralisation is expected.

While the presence of multiple RBD mutations in the spike protein of the Omicron VOC indicates a high likelihood of immune escape from neutralising antibodies induced by infection or vaccination, immune escape potential from non-neutralising antibodies and memory T cells directed at non-surface proteins is more difficult to determine. Memory T cell responses may offer a route to durable immunity and protection from severe disease, where virus evolution leads to spike protein mutations that escape pre-existing neutralising antibodies. WHO has reported that there are early signs that the Omicron VOC is associated with increased risk of reinfection in South Africa, but these data are preliminary, and the severity of disease experienced by possible reinfection cases is not yet known [35].

The extent to which the Omicron VOC evades or erodes existing vaccine- or infection-derived immunity remains uncertain in the absence of in vitro neutralisation data, brand- and regimen-specific vaccine effectiveness data, as well as further data on reinfection risk and reinfection severity in populations exposed to different SARS-CoV-2 variants during previous pandemic waves.

Transmissibility

The number of confirmed cases has risen in affected areas of South Africa, and in the Gauteng province case rates are increasing faster than in previous waves [38]. The effective reproductive number R_t was estimated at below 1 from mid-August through late October 2021 and then increased sharply to an estimate of 2.2 (95% CI 1.96-2.43) by mid-November, in conjunction with an increase in the number of new diagnoses [39]. Concurrent to the increases in case numbers, an increase in the proportion of samples with S-gene dropout, a possible marker for the presence of the Omicron VOC, was noted, and this proportion has increased rapidly, from <5% to >50% since early November 2021 [38].

The concurrent rapid increase of cases, the increase of the effective reproductive number R_t and the pace of replacement of the Delta VOC by the Omicron VOC in South Africa all raise concerns that this variant is significantly more transmissible than the Delta VOC. However, the overall COVID-19 case numbers in South Africa are currently low, due to which there could be a disproportional effect of superspreading events involving a specific variant. Nevertheless, these trends that indicate an increased transmissibility of the Omicron VOC, although differing in magnitude, are observed in multiple South African provinces. Increased immune escape compared to the Delta VOC may result in more breakthrough infections among vaccinated individuals, and more reinfections that could contribute to an increase in detected cases. This complicates any assessment of relative transmissibility due to intrinsic biological properties of the Omicron VOC when compared to the Delta VOC. Current estimates of transmissibility remain uncertain, and further studies, including contact tracing data on secondary attack rates, growth rates, R_t and R_0 are needed to provide reliable estimates of the transmissibility of the variant overall and relative to measures in place in different community settings.

Severity

Among the cases reported in the EU/EEA for which there is available information on disease severity, half of the cases were asymptomatic and the other half presented with mild symptoms. No cases with severe disease, hospitalisations, or deaths have been reported among these cases. It is important to note that if the severity is similar to the Delta VOC, hundreds of cases would need to have been identified in order to see patients presenting with complications and that most of these cases were detected recently and, where symptomatic, had very recent onset of symptoms. Severity outcomes often take several weeks to accumulate and longer to be evident at population level, impacting hospital rates. Furthermore, the majority of cases detected in the EU/EEA for which there are available data on age and vaccination status to date have not been of older age and were fully vaccinated. Being travellers, they could also be assumed to be healthier than the general population.

Data from South Africa indicate an increase of hospital admissions of COVID-19 cases in the Gauteng province from 136 on week 45, to 279 in week 46, and to 647 on week 47, concomitantly with the increasing predominance of the Omicron VOC among the reported COVID-19 cases [40]. While case rates are increasing faster than in previous waves in the Gauteng province, hospitalisation rates are in line with previous increases [41]. The age structure of affected cases in South Africa is not known to ECDC, so it is unclear how this may impact on the risk of hospitalisation and/or ICU admission among affected cases.

Previous infection has been shown to be highly protective against severe disease from infection with the Beta VOC, which is the most antigenically divergent variant detected before the Omicron VOC [42]. The high seropositivity in South Africa could therefore potentially lead to less severe disease in this population if the Omicron VOC is associated with increased risk for reinfections, but this is associated with significant uncertainty [43].

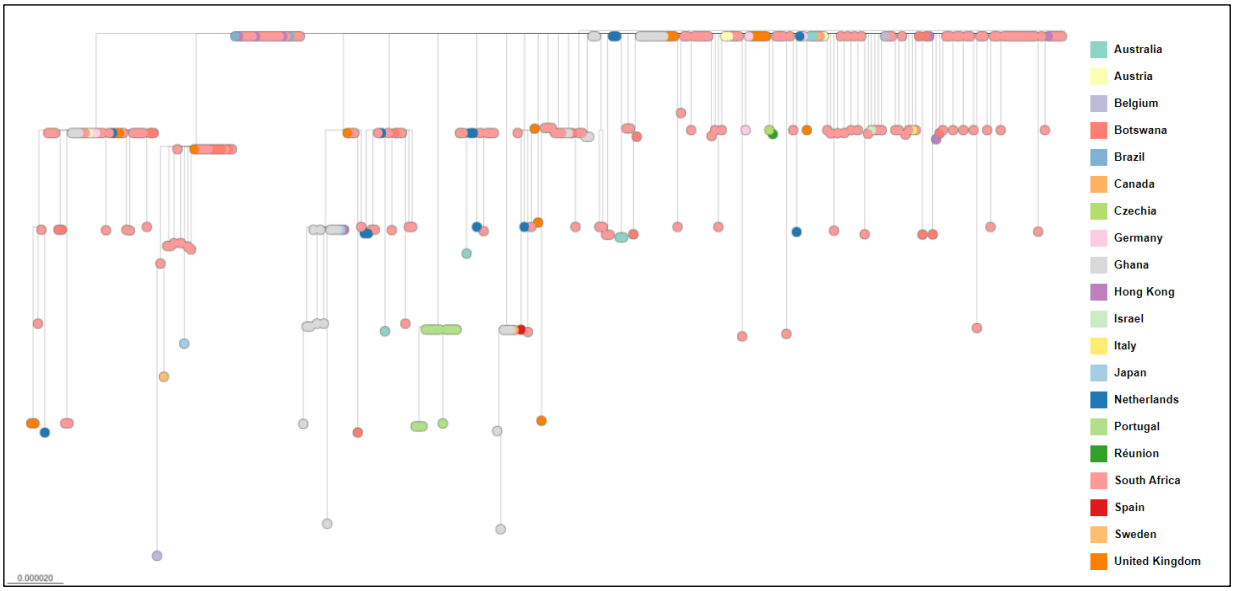
Current estimates on the Omicron VOC severity remain highly uncertain, and further studies, including longer-term follow up by age group, previous infection, and vaccination status of cases identified, are needed to provide more reliable estimates.

Therapeutics

The large number of mutations in the spike protein of the Omicron VOC indicates that the effectiveness of monoclonal antibody antiviral therapeutics targeting this protein of SARS-CoV-2 may be reduced. However, no relevant laboratory or clinical data are available to date.

Genomic diversity

Figure 2. Phylogenetic tree of all Omicron sequences available in GISAID EpiCoV as of 1 Dec 2021



The tree is constructed using a specific pipeline for the Omicron VOC phylogenetic analysis [44], based on the Augur pipeline by the Nextstrain team [45]. The tree is visualised using MicroReact [46]. We gratefully acknowledge both the originating and submitting laboratories for the sequence data in GISAID EpiCoV on which the SARS-CoV-2 variants data are partially based. Data extracted 1 December 2021 at 15:30 CET.

Phylogenetic analysis of all the Omicron VOC sequences available in GISAID EpiCoV indicates that identical ancestral sequences have been detected in several countries (figure 2). Preliminary phylodynamic analysis based on a mutation rate of two substitutions per genome per month indicates that the variant emerged in early October 2021, but this is associated with significant uncertainty, both due to the limited data available and the potential impact of sequencing errors. Phylogenetic analysis of travel-related and community-acquired cases can provide information about outbreaks and community transmission. For example, sequences from Portugal cluster closely in

the tree, indicating that these cases are associated with a single travel-related index case. A similar scenario is likely for several sequences reported by Ghana but the slightly higher diversity within the Ghana cluster could indicate some further onward transmission. Sequences from travellers from South Africa to the Netherlands are dispersed throughout the tree, which indicates that these cases have separately acquired the virus in South Africa. This further supports high levels of community transmission of the Omicron VOC in South Africa.

Modelling insights

To compute the expected time until the proportion of the Omicron VOC would reach 50% of infections, we forecast the proportion of the Omicron VOC and the current Delta VOC over time. We assume growth and decline of infections are exponential with identical generation intervals of both variants. We then forecast the variant proportions over time given different initial proportions of omicron infections and different growth advantages of the Omicron VOC compared to the Delta VOC. For example, a 70% growth advantage of the Omicron VOC in the EU/EEA means that an Omicron VOC infection on average leads to 70% more secondary cases when compared to the Delta VOC. Our forecasts only depend on this relative advantage in growth and are independent of factors that impact the growth of both variants in the same way. Finally, we compute for different forecasting time windows (until 1 January, 1 March, and 1 May 2022) three possible combinations of the hypothetical current proportion of Omicron infections and minimum required growth advantage of the Omicron VOC for it to achieve >50% sequence proportion within the given time (see Table 2).

The model of expected time until the Omicron VOC becomes the majority variant is only a rough estimate that is subject to several simplifying assumptions, including: a well-mixed homogeneous population; the absence of super-spreader events (or other erratic effects on the incidence); a similar effect of non-pharmaceutical interventions on the Omicron variant as on the Delta VOC; the absence of other variants than the Delta VOC or the Omicron VOC; and the same growth rate advantage across the EU/EEA. We emphasise that the growth advantage in the EU/EEA depends on the extent to which the Omicron VOC may escape immunity (vaccine-induced and due to previous infection), the number of individuals that have had COVID-19, and the vaccination coverage in the population.

The time until the Omicron VOC constitutes the majority of infections (>50%) in EU/EEA countries crucially depends on two factors: the current proportion of the Omicron VOC among SARS-CoV-2 infections and the relative growth advantage of the Omicron VOC over the Delta VOC, which we define as percent increase in growth relative to the Delta VOC. Our modelling indicates that the greater the growth advantage over the Delta VOC and the greater the proportion of current infections due to the Omicron VOC, the shorter the expected time until the Omicron VOC causes the majority of all SARS-CoV-2 infections. For example, with a hypothetical proportion of 1% SARS-CoV-2 infections due to the Omicron VOC and a growth advantage of at least 120%, the Omicron VOC would become the majority variant by 1 January 2022; with a hypothetical proportion of 1% SARS-CoV-2 infections due to the Omicron VOC and a growth advantage of at least 30%, the Omicron VOC would become the majority variant by 1 March 2022.

These results depend on many still unknown factors about transmissibility, vaccine immunity escape, natural immunity escape, and others. In addition to the ongoing Delta VOC resurgence in October-November 2021, these unknown factors underline the importance of (more stringent) NPIs, continued high vaccine uptake, and booster doses.

Table 2. Modelling results for the expected time until the Omicron VOC becomes the majority variant

Omicron becomes the majority variant (>50%)	*Hypothetical* current proportion of SARS-CoV-2 infections due to Omicron (on 2 Dec. 2021)	*Hypothetical* growth advantage in the EU/EEA
by 1 January 2022 (1 month)	1%	>120%
	0.1%	>230%
	0.01%	>390%
by 1 March 2022 (3 months)	1%	>30%
	0.1%	>50%
	0.01%	>70%
by 1 May 2022 (5 months)	1%	>15%
	0.1%	>25%
	0.01%	>40%

The expected time until the Omicron VOC becomes the majority variant (i.e., when more than 50% of SARS-CoV-2 infections are due to the Omicron VOC, first column), which follows from the current proportion of SARS-CoV-2 infection due to the Omicron VOC (second column) and its growth advantage in the EU/EEA (third column) which is a combined effect of potential for increased transmissibility, potential for vaccine escape and for natural immunity escape. In each of the nine rows, we consider different hypothetical starting values for the current proportion of Omicron infections and the growth advantage of Omicron in the EU/EEA, since both parameters are unknown at the time of writing.

Risk assessment questions

What is the risk associated with the further emergence spread of the SARS-CoV-2 variant Omicron in the EU/EEA?

ECDC risk assessment for the EU/EEA

The epidemiological situation across the EU/EEA has evolved quickly, and cases of the Omicron VOC have now been reported in 13 countries, mostly among travellers from Africa but with some evidence of limited transmission arising from infected travellers to their contacts. Outside the EU/EEA, the number of countries reporting cases has increased, and the situation in South Africa continues to escalate with a growing number of cases and an increasing number of hospitalisations. However, the true epidemiological situation, both in the EU/EEA and southern African countries, remains unclear as there is likely to be an under-ascertainment of cases of this variant in many countries, partly due to limited sequencing capacity but also related to mild or asymptomatic cases going undiagnosed.

The rapid increase of cases, the increase of the effective reproductive number R_t, and the pace of replacement of the Delta VOC by the Omicron VOC in South Africa all suggest that this variant is more transmissible than the Delta VOC, but robust evidence is still lacking and there remains a high uncertainty. Limited evidence gathered from initial cases reported from EU/EEA countries to date also suggests that Omicron may be associated with high transmissibility as high attack rates have been reported among some household contacts.

Based on these elements, the probability of the further introduction and community spread of the Omicron VOC in EU/EEA countries is currently assessed as **HIGH**, but this needs to be re-evaluated in the light of new evidence becoming available.

Evidence around the severity of the infection associated with the Omicron VOC is currently unclear. While there is some evidence to suggest infections associated with the Omicron VOC may be mild, the data are limited. Emerging data from South Africa suggest many cases have been mild but the population structure of the country is younger than most countries in the EU/EEA and there are many other factors in the populations that differ, such as the underlying levels of natural and vaccine-induced immunity, which may play a part. In addition, the severe consequences of infection with SARS-CoV-2 often take several weeks to develop, so it may take time for the impact, in terms of hospitalisations and deaths, to be evident on a population level. Evidence from cases among returning travellers in the EU/EEA also indicates that cases have been mild, with no reported deaths or hospitalisations to date. However, this population may not be representative as these individuals are likely to be younger but also healthier than non-travellers, i.e. a 'healthy traveller' effect. Current estimates on the Omicron VOC severity remain highly uncertain, and further studies are needed to provide more reliable estimates.

The currently available evidence raises serious concerns that the Omicron VOC may be associated with significant reduction in vaccine effectiveness and increased risk for reinfections. The degree of protection conferred by past infection with COVID-19 or by vaccination against severe disease with the Omicron VOC is not known, and further evidence is urgently needed to assess the effectiveness of current vaccines. Evidence is also needed around the effectiveness of existing treatments for severe cases. In the absence of robust evidence around severity, it may be expected that the same populations with a higher likelihood of severe outcomes from other SARS-CoV-2 variants (the elderly and those with underlying comorbidities) are also likely to have severe outcomes due to Omicron, especially if unvaccinated.

In EU/EEA countries currently facing high numbers of cases of the Delta VOC, the impact of the introduction and spread of Omicron could be **VERY HIGH,** but this situation needs to be further evaluated in the light of emerging information.

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 variant Omicron in the EU/EEA is assessed as **HIGH TO VERY HIGH**.

Options for response

Vaccination

In vitro studies assessing the neutralising capacity of vaccinee and convalescent sera against the Omicron VOC pseudo- or live virus isolates are required to better understand the escape potential against vaccination and infection-acquired immunity. The expected timeline for this data is within two to three weeks from time of publication of this threat assessment. Until these initial studies for the Omicron VOC are available, the focus should be on reinforcing the vaccination efforts to close immunity gaps in order to protect the population and to ensure equitable coverage across countries and regions in Europe.

Vaccination against SARS-CoV-2 continues to successfully avert deaths, reduce hospitalisations and transmission in the EU/EEA, despite the emergence and continued dominance of the Delta VOC. Due to the ongoing active circulation of the Delta VOC, EU/EEA countries are urged to give priority towards vaccination of individuals initially targeted by COVID-19 vaccination programmes that remain unvaccinated or not yet fully vaccinated. It is currently unknown to what extent the Omicron VOC is affecting vaccine effectiveness of the COVID-19 vaccines authorised in the EU/EEA. ECDC is currently finalising a protocol to investigate SARS-CoV-2 outbreaks in semi-closed settings, including those related to the Omicron VOC, to assess vaccine effectiveness. ECDC plans to publish the protocol during the first half of December 2021. EU/EEA colleagues are welcome to contact ECDC if they wish to use or trial an early version of the protocol.

As has been highlighted previously, countries should consider a booster dose for those aged 40 years and above, first targeting the most vulnerable and the elderly and then expanding to all adults aged 18 years and above at least six months after completion of the primary series. Booster doses will increase immunity in the population and sustain transmission control beyond the immediate impact of implementing NPIs, which will be particularly important in light of the emergence of more transmissible variants with potentially reduced vaccine effectiveness.

Non-pharmaceutical interventions

Maintaining and strengthening of non-pharmaceutical interventions

Non-pharmaceutical interventions (NPIs) to help reduce transmission of infection should continue to be implemented by countries based on an assessment of their epidemiological situation regarding the Delta VOC, taking into account the uncertainty of the situation regarding the Omicron VOC. Efforts to support physical distancing, including teleworking and operational modifications that reduce crowding on public transport, along with ensuring adequate ventilation in closed spaces, maintenance of hand and respiratory hygiene measures, the appropriate use of face masks, and staying home when ill remain relevant measures.

Ensuring healthcare capacity and personnel should also be a priority, given the holiday season and the possibility of further or new increases in transmission. Therefore, efforts should continue focusing on strengthening healthcare capacity to manage potentially high numbers of COVID-19 patients.

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. For probable or confirmed cases of SARS-CoV-2 Omicron VOC infection, the enhanced contact tracing measures as set out in the ECDC

contact tracing guidance 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 in a timely manner and as completely as possible. Contact tracing should also be initiated for cases with symptoms indicative of COVID-19 infection, even if they have not yet been tested, in case of an epidemiological link to an affected area or to a case infected with the Omicron VOC.

In the section 'Options for enhanced contact tracing', the ECDC contact tracing guidance [47] sets out these specific enhanced contact tracing measures in detail, such as backward contact tracing and stricter management for contacts. These measures include 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 in the case, the testing of all high and low-risk exposure contacts, starting to trace the contacts of the household members of a case while awaiting the result of the test on tracing of the household members 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 the initial test on tracing and otherwise observe strict physical distance 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 their test result is confirmed.

Contact tracing related to air travel

With regards to contact tracing of passengers on aircrafts, ECDC has developed specific recommendations and these are available in the third update of the ECDC contact tracing guidance [47]. However, this guidance was developed prior to the widespread emergence of variants with high transmissibility. A more precautionary approach in relation to the classification of contacts on planes could therefore be considered in relation to the current situation with the Omicron VOC. This approach should be to consider all passengers and cabin crew members that have travelled on a flight with a confirmed or probable case as having a high-risk exposure and that these fellow passengers are managed as contacts in accordance with the guidance on contact tracing noted above. It is recommended that all travel-related cases identified should be prioritised for sequencing or, as a minimum, sequencing of samples from all cases with travel history (14 days prior to symptom onset) to areas with confirmed wide-spread circulation of the Omicron VOC, or where the epidemiological situation is not clear.

When contact tracing investigations identify contacts or a potential source in another country, public health authorities should collaborate across borders and exchange data in a secure way (through, for example, the selective exchange messaging function of the Early Warning and Response System (EWRS) of the EU or share data using the European Digital Passenger Locator Form) (dPLF) [49].

Additional information and links to additional documents can be found on the ECDC contract tracing landing page [50].

Testing and sequencing

ECDC recommends that with the current emergence of the Omicron VOC, genomic surveillance should be enhanced, and countries are advised to sequence a number of samples that allow quantification of the proportion of a variant at 1% prevalence level, as described in the ECDC guidance for representative and targeted genomic surveillance [51]. Targeted sampling of SARS-CoV-2 positive cases should also ideally aim for comprehensive sequencing of cases with a history of travel to areas with suspected community transmission of the Omicron VOC, cases with unusual/severe clinical presentations (for example all SARI cases) and known reinfections. Retrospective samples from cases with a travel history (14 days prior to positive test result) should be sequenced or genotyped by using PCR-based assays. Samples from a minimum of five cases from outbreaks, clusters and other events with unusual high transmission should also be sequenced. Please see the ECDC guidance for more information about representative and targeted genomic SARS-CoV-2 monitoring [51].

S-gene target failure (SGTF) using the Thermo Fischer TaqPath assay or other similar assays that fail to detect the S-gene when it carries the deletion Δ69-70 can be used to screen for the Omicron VOC. From currently in GISAID deposited sequences in Europe reported during week 44-47 2021 (GISAID data as of 2021-11-30) it can be concluded that no non-Omicron variants with Δ69-70 are circulating and therefore the SGTF can be reliably used as a screening method for the identification of the Omicron VOC. Extremely low number of non-Omicron sequences with Δ69-70 have been submitted to GISAID worldwide. However, it cannot be excluded that other variants with this genetic profile emerge in the future or are already circulating in very low levels. It is therefore recommended that a subset of samples with SGTF should be selected for confirmation by sequencing (at least 10% or according to available resources). 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 instead be reported as such. Details for reporting SGTFs and the Omicron VOC cases can be found in the ECDC reporting protocol [52]. Laboratories should remain vigilant to detect any primer/probe mismatches that would affect the performance of their RT-PCR assays for SARS-CoV-2 detection. Alternative methods for omicron identification are presented in the ECDC technical report 'Methods for the detection and identification of SARS-CoV-2 variants' [53].

Due to the many characteristic mutations of the Omicron VOC, it can be identified from partial S-gene sequences. This should preferably include the receptor-binding-domain (RBD), but any region covering enough characteristic mutations to conclude that the virus is the Omicron can be used. Note that in-silico analysis has shown that amplicon 76 of the ARTIC v4 protocol could fail for the Omicron VOC due to primer-template mismatches, this can lead 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.

ECDC provides support to EU/EEA countries and the western Balkan countries in detection of SARS-CoV-2 variants by whole genome sequencing through a framework contract with Eurofins Genomics. About 3000 samples, from around 10 countries, are sequenced weekly using this contract [54]. Please contact typing@ecdc.europa.eu for more information.

FIND, the global alliance for diagnostics, has conducted a rapid assessment of available evidence in the context of the Access to COVID-19 Tools (ACT) Accelerator Diagnostics Pillar, which they co-lead alongside the Global Fund, with WHO. Preliminary results suggest that the accuracy of Nucleic Acid Amplification Test (NAAT) and Rapid Antigen Detection Test (RADT) has not been impacted [55]. Further studies are ongoing, and laboratories should remain vigilant to detect reductions in sensitivity of the used RADTs.

The Common list of COVID-19 rapid tests prepared by the Health Security Committee technical working group (HSC TWG) on COVID-19 diagnostic tests will be revised accordingly based on emerging information [56].

Countries that have the capacity for antigenic characterisation of SARS-CoV-2 are encouraged to characterise omicron variants and share their results with WHO/ECDC and the COVID-19 network.

For general information on COVID-19 testing, refer to the latest ECDC risk assessment about COVID-19 [57].

The following 'interim' case definition for confirmed and probable SARS-CoV-2 Omicron VOC cases can be used for surveillance and reporting purposes. Omicron VOC cases should be reported weekly to TESSy NCOV and NCOVVARIANT according to the reporting protocol. These definitions can also be considered when reporting Omicron cases to EWRS and to IHR.

Probable case of SARS-CoV-2 Omicron VOC infection

A person with a positive NAAT or RADT for SARS-CoV-2 AND one of the following:

- S-gene target failure or another PCR-based Single Nucleotide polymorphism (SNP) assay indicative of the SARS-CoV-2 Omicron VOC
  OR
- Is a contact of a probable or confirmed case of SARS-CoV-2 Omicron VOC infection

Confirmed case of SARS-CoV-2 Omicron VOC infection

- A person with confirmed sequencing result for the SARS-CoV-2 Omicron VOC

Travel-related measures

Although there is evidence that the new Omicron VOC has already been introduced into many EU/EEA countries, given the current lack of evidence around this new variant and the concerns about its immune escape properties in relation to available COVID-19 vaccines and treatments, a multi-layered approach to delay the spread of this VOC in the EU/EEA should be considered by countries. Any measures that are implemented should be carefully considered in light of the latest epidemiological situation and should be regularly reviewed as new information emerges.

Based on the assumption that cases have already been imported into many EU/EEA countries, internal modelling at ECDC shows that border closures or travel bans are likely to only delay the impact of the novel variant in terms of numbers of cases and hospitalisations in the EU/EEA countries by two weeks, at most. This finding is in line with previous modelling on the Delta VOC but subject to a high degree of uncertainty given the current limited evidence. Restrictions at this point in time may buy countries valuable time to better understand the characteristics of the Omicron VOC and cope with the current resurgence of the Delta VOC across EU/EEA countries. However, given the increasing number of cases and clusters without travel history or contact with travel-related cases, it is likely that within the coming weeks the effectiveness of travel-related measures will decrease and countries should prepare for a rapid and measured de-escalation of such measures.

The following measures should be considered for incoming travellers from areas with known community transmission or where the epidemiological situation is unclear but there have been confirmed cases among returning travellers from these areas:

- requirement of proof of negative RT-PCR or RADT test ideally pre-departure and when possible for a further RT-PCR test upon arrival, and;
- quarantine for a minimum of seven days and ideally for fourteen days since arrival, with a further negative test before release from quarantine. Countries could also consider quarantining the household members of contacts until the primary case has received a negative result of the test performed at tracing.

Proof of vaccination does not exempt from testing and quarantine due to the uncertainty about the effectiveness of the currently available vaccines against this VOC.

Countries should consider contacting and testing (preferably with RT-PCR) any travellers who have recently returned from affected countries that have community transmission (or countries where the epidemiological situation is unclear). Public information around the emerging situation and the public health measures in place for returning travellers from affected areas are important to raise awareness and support the effective implementation of these measures. Awareness among healthcare professionals is also 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 notified through the Early Warning and Response System (EWRS), IHR, and reported weekly through The European Surveillance System (TESSy). TESSy allows reporting cases with B.1.1.529 and/or the cases with deletion of S-gene, both through variant-data and case-based data.

Limitations and knowledge gaps

This risk assessment is undertaken based on the evidence known to ECDC at the time of publication. There remain many scientific uncertainties and knowledge gaps around what is known about this new VOC.

Some of these evidence gaps include:

- There is a lack of clear understanding of the epidemiological situation in many countries that are likely to be affected given the lack of sequencing or screening using S-gene target failure;
- Current estimates of transmissibility remain uncertain and further studies, including contact tracing data on secondary attack rates, growth rates, R_t and R_0 are needed to provide reliable estimates of the transmissibility of the variant overall and relative to measures in place in different community settings;
- Current estimates of severity (hospitalisation and deaths) remain highly 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;
- Current estimates of immune escape are highly uncertain and further studies on virological characterisation, including in-vitro infectivity studies and neutralisation studies evaluating both vaccinee and convalescent sera are needed;
- There is currently no information on vaccine escape and analyses of the vaccine effectiveness for different vaccines against Omicron (direct and indirect effects) for disease, transmission and severe disease by age group are needed;
- Information around 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, 29 November 2021.

Consulted experts

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Disclaimer

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

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