THREAT ASSESSMENT BRIEF

Implications of the emergence and spread of the SARS-CoV-2 B.1.1. 529 variant of concern (Omicron) for the EU/EEA

26 November 2021

Summary

A SARS-CoV-2 variant belonging to Pango lineage B.1.1.529, with a high number of S-gene mutations compared to the original virus was detected at the beginning of November 2021. On 26 November 2021 the variant was designated a variant of concern (VOC) and assigned the label Omicron by the World Health Organization (WHO). The variant is characterised by 30 changes, three small deletions and one small insertion in the spike protein, of these, 15 are in the receptor binding domain. This variant was first detected in samples collected on 11 November 2021 in Botswana and on 14 November 2021 in South Africa. As of 26 November 2021, travel-related cases have also been detected in Belgium, Hong Kong and Israel. The Omicron variant is the most divergent variant that has been detected in significant numbers during the pandemic so far, which raises concerns that it may be associated with increased transmissibility, significant reduction in vaccine effectiveness and increased risk for reinfections. As of 26 November 2021, ECDC has classified this variant as a variant of concern (VOC) due to concerns regarding immune escape and potentially increased transmissibility compared to the Delta variant.

Risk assessed

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

There is considerable uncertainty related to the transmissibility, vaccine effectiveness, risk for reinfections and other properties of the Omicron variant. However, given its immune escape potential and potentially increased transmissibility advantage compared to Delta, we assess the probability of further introduction and community spread in the EU/EEA as **HIGH**. In a situation where the Delta variant is resurgent in the EU/EEA, the impact of the introduction and possible further spread of Omicron could be **VERY HIGH.** In conclusion, the overall level of risk for the EU/EEA associated with the SARS-CoV-2 variant Omicron is assessed as **HIGH to VERY HIGH**.

Options for response

Based on the mutation profile of Omicron, partial immune escape is likely. Due to the uncertainties concerning Omicron immune escape properties, a precautionary approach is important and the timely and urgently reinforced implementation of non-pharmaceutical interventions (NPIs) in the EU/EEA is strongly advised.

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Genomic surveillance remains of utmost importance for early detection of the presence of this variant, to enable the following of epidemiological trends and guide containment measures. At this early stage, avoiding travel to and from the known affected areas, as well as increased testing (with sequencing of confirmed cases), and contact tracing of COVID-19 cases with an epidemiological link to the affected areas is strongly advised. Due to the ongoing active circulation of the Delta variant, EU/EEA countries are urged to give utmost priority towards vaccination of individuals initially targeted by COVID-19 vaccination programmes that remain unvaccinated or not yet fully vaccinated. Countries should consider a booster dose for those 40 years of age and over, first targeting the most vulnerable and the elderly and could then consider a booster dose for all adults 18 years and older at least six months after completion of the primary series.

Event background

As of 26 November 2021, ECDC has 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 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. One case has been detected in Hong Kong with travel history to South Africa, collection date 18 November 2021. As of 26 November 2021, sequences of the variant Omicron have been reported from Botswana [1], South Africa [2], Israel [3],Hong Kong [4] and Belgium [5]. All available sequences are deposited in GISAID EpiCoV [6].

Official sources in Hong Kong state that there is a cluster of two travel-related cases of Omicron [4]. Official sources in Israel report one case in a traveller returning from Malawi, and two suspected cases in other returning travellers are being investigated [3]. The Belgium Minister of Health stated that a case in an unvaccinated traveller has been detected [5]. Botswana confirmed four cases of the Omicron variant in an official press release, stating that they were all fully vaccinated and detected in pre-travel screening [1].

Investigations in South Africa using S-gene target failure (SGTF) of the PCR assays as a proxy for the variant have shown that there is a very sharp increase in incidence across most provinces since mid-November, with the most pronounced increase in the Gauteng province, where SGTF is observed for more than 50% of all tested specimens in the last few days. Sequencing of 77 selected SGTF samples from Gauteng collected between 12 and 20 November 2021 confirmed all of them as Omicron. These findings presented in a press conference held by the South African Ministry of Health on 25 November 2021 suggest that the Omicron variant is already dominant in Gauteng and is present in significant proportions in most parts of South Africa. Overall, COVID-19 case numbers are rapidly increasing in Gauteng, albeit from low levels, and it is likely that this increase is driven by the presence of Omicron.

Several EU/EEA countries [7-10] have implemented travel bans to and from South Africa and surrounding countries (Lesotho, Botswana, Zimbabwe, Mozambique, Namibia, Eswatini).

Variant detection capability in the African region

The reporting of sequencing results in the African region is low overall. Only Botswana and South Africa 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 in South Africa and has also been detected in Botswana, some circulation in other countries is likely.

Table 1. Number of Omicron sequences reported to GISAID EpiCoV from samples collected since 26 October 2021 from all countries and territories in Africa

Country or territory	Number of Omicron sequences	Total sequences reported
Botswana	6	98
Kenya	0	5
Mayotte	0	10
Democratic Republic of the Congo	0	11
Rwanda	0	4
Senegal	0	8
Seychelles	0	10
South Africa	59	100

Omicron properties

The variant B.1.1.529 (Omicron) belongs to Pango lineage B.1.1.529, Nextstrain clade 21K [11], 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, Q493K, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F). Out of these changes, 15 are located in the receptor binding domain (RBD) (residues 319-541). The variant also carries a number of 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).

Immunity

The Omicron variant is the most divergent variant that has been detected in significant numbers during the pandemic so far 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 increased transmissibility, immune escape, or other properties. A synthetic variant previously described with 20 mutations in the spike protein was associated with almost complete escape from convalescent and vaccinee sera [12]. As Omicron carries even more mutations in the S-gene compared to this variant, a very significant effect on neutralisation is expected. However, further virological investigations and vaccine effectiveness studies are needed to assess to which extent the variant will have an impact on vaccine effectiveness and breakthrough infections.

Transmissibility

The rapid pace of replacement of the Delta variant by Omicron in South Africa raises concerns that this variant is significantly more transmissible than Delta, however the overall COVID-19 case numbers in South Africa are currently low which could increase the proportional effect of any superspreading events involving a specific variant. In addition, the high observed growth rate could be due to immune escape. Further data are needed to be able to provide a reliable estimate of the transmissibility of the variant.

Severity

There is currently no information available for assessment of any change in infection severity associated with Omicron. Preliminary information from South Africa is that currently no unusual symptoms have been associated with Omicron, and similar to other variants, some individuals are asymptomatic [13].

Risk assessment questions

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

ECDC risk assessment for the EU/EEA

Considering the fact that travel has been ongoing and is still taking place to and from the countries where cases have been reported, there is a high likelihood of further introduction of the SARS-CoV-2 variant Omicron into the EU/EEA. Outside of the two countries known to be affected in Africa, the variant has also been confirmed in travellers from Africa to Belgium, Hong Kong and Israel, suggesting more widespread transmission is already occurring. It is also likely that there is an under-ascertainment of cases of the variant due to limited sequencing capacities in many countries.

At present, there is no documented evidence of sustained transmission of the variant in EU/EEA countries, although it should be noted that SARS-CoV-2 cases are often under-detected, that there is a lag from detection of a case to obtaining sequencing results and that sequencing volume is still sub-optimal in many EU/EEA countries.

Previous experiences with the Alpha, Beta and Delta variants show that introduction and spread of new variants can happen very rapidly.

Given its immune escape potential and possible transmissibility advantage compared to Delta, Omicron may have the capacity to spread rapidly once introduced to countries in the EU/EEA, making the probability of spread high. However, this assessment is based on substantial uncertainty and will be updated when new information and evidence when available.

If infection with the new variant is acquired, it is likely that at least a part of the population will experience severe disease. There is still no severity information for Omicron, however it is likely that that the same populations with higher likelihood of severe outcomes from other SARS-CoV-2 variants (the elderly, those with underlying comorbidities) are likely to have severe outcomes due to Omicron.

If transmissibility is considerably higher, the current range of prevention and control measures that are available to control the transmission of SARS-CoV-2 may not work as effectively for the new variant. Current vaccines may also not be as effective for the new variant if partial or total immune escape to some of the vaccines currently in use is present. However, NPIs such as the use of face masks, contact tracing and physical distancing will still be effective in controlling transmission.

In terms of treatment, there is currently insufficient information available to assess whether existing treatment such as e.g. monoclonal antibodies, will be effective.

Also, due to the winter respiratory virus season combined with substantial high burden due to COVID-19 cases, the demand for health services within many EU/EEA countries is currently already high.

Based on these elements, the probability of introduction and community spread is currently assessed as **HIGH**, while in a situation where the Delta variant is resurgent in the EU/EEA, the impact of the introduction and possible spread of Omicron could be **VERY HIGH**. In conclusion, the overall level of risk is assessed as **HIGH TO VERY HIGH**.

Options for response

Although there is limited information available on Omicron, the following range of risk control measures should be immediately considered or strengthened in all EU/EEA countries.

Vaccination

Whilst the presence of multiple RBD mutations in the spike protein of Omicron indicate a high likelihood of immune escape from antibody-mediated protection, immune escape potential from memory T cells directed at non-surface proteins following infection or vaccination are more difficult to determine. Memory T cell responses may offer a route to durable immunity where virus evolution leads to spike protein mutations that escape pre-existing neutralising antibodies. This could occur either by offering more efficient support to activated naïve B cells responding to the altered spike protein (CD4 T cells), or through direct lysis of SARS-CoV-2 infected cells (CD8 T cells) [14].

Currently available vaccines may offer some level of protection against hospitalisation and death [13], however in vitro studies evaluating the neutralising capacity of both vaccinee and convalescent sera against Omicron pseudo- or live virus isolates are urgently required to better understand its escape potential against both vaccination and infection-acquired immunity. These data are expected to be available within two to three weeks.

Countries are urged to give utmost priority to individuals initially targeted by COVID-19 vaccination programmes that remain unvaccinated or not yet fully vaccinated. Increasing COVID-19 vaccination coverage in all eligible age groups, but particularly in the elderly, in the vulnerable, and in healthcare workers should remain the priority for public health authorities. There remains an urgent need to close immunity gaps in the adult population and ensure effective and equitable coverage across countries and regions in Europe. National Immunisation Technical Advisory Groups (NITAGs) in EU/EEA countries should consider a booster dose for those 40 years of age and over, targeting the most vulnerable and the elderly first. Countries could also consider a booster dose for all adults 18 years of age and older at least six months after completion of the primary series to increase protection against infection due to waning immunity, which could potentially reduce transmission in the population and prevent additional hospitalisations and death.

Non-pharmaceutical interventions

Even prior to the identification and emergence of Omicron, maintaining or reintroducing NPIs, even in countries with high vaccine uptake, was seen as vital to reduce transmission [15] Timely implementation of NPIs is critical for their success. Appropriate use of face masks, teleworking and operational modifications that reduce crowding on public transport, along with ensuring adequate ventilation in closed spaces and maintenance of hygiene measures can be implemented immediately. Setting limits for the number of participants in social and public events during end-of-year celebrations will support physical distancing efforts. Due to the current epidemiologic context, in combination with the uncertainties involved with the rapidly evolving situation concerning Omicron, timely and urgently reinforced implementation of NPIs in the EU/EEA is strongly advised.

Testing and sequencing

Genomic surveillance is of crucial importance for early detection of the presence and monitoring of epidemiological trends of specific VOCs, VOIs and variants under monitoring, and will provide important information to guide response for this new variant [16]. This includes regular testing of representative samples but also strengthening targeted sampling from persons coming from high-risk areas.

The presence of the deletion Δ69-70 means that S-gene target failure (SGTF) for the Thermo Fischer TaqPath assay can be used as a screening method for Omicron. In a setting with the Delta variant dominating, this can be used as a proxy for Omicron after confirmation of a subset of samples by sequencing. Currently there is no further information available on any effect on sensitivity for other RT-PCR assays or for rapid antigen tests. Countries could consider retrospective SGTF screening of SARS-CoV-2 positive samples from recently returned travellers from Southern African countries to rapidly assess whether cases may have been recently introduced.

Rapid antigen tests should be unaffected based on the analysis of the mutations in the nucleocapsid (N gene) of Omicron viruses, however, verification of this is underway [13].

Sequencing of SARS-CoV-2 from wastewater could be used as a complement to other monitoring methods if such capability is available. In particular, analysis of wastewater from incoming flights could be analysed to detect introductions of the variant.

Measures for travellers

There is currently a lack of evidence that the new SARS-CoV-2 variant is transmitting in EU/EEA countries and its global occurrence, at present, seems to be limited to a few countries. It is important to note that ongoing transmission of the variant cannot be excluded for other countries since sequencing capacity as well as the reporting of sequencing results in the African region is low. However, taking into consideration the concerns about the new variant's immune escape properties, both as regards the available COVID-19 vaccines and the neutralising monoclonal antibody treatments, major efforts to delay the spread of this variant in the EU/EEA should be urgently considered by all countries.

Given assumptions on the likely importation of cases already in EU/EEA countries, internal modelling at ECDC shows that strict travel restrictions are likely to only delay the impact of the novel variant in the EU/EEA countries by two weeks. This finding is in line with previous modelling on the Delta variant but subject to a high degree of uncertainty. Short-term restrictions may give the countries the time to prepare for the novel variant and cope with the current resurgence of the Delta outbreak across EU/EEA countries.

At this early stage, avoiding travel to and from the known affected areas, as well as increased testing (with sequencing of confirmed cases), and contact tracing of COVID-19 cases with an epidemiological link to the affected areas is strongly advised. For such cases, testing, isolation and contact tracing should be carefully performed. The ECDC guidance on contact tracing suggests options for enhanced contact tracing including rigorous measures for cases suspected to be infected with the new variant [17].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), EpiPulse and, when possible, through the European Surveillance System (TESSy).

Measures for incoming travellers from the known affected areas may include:

- increasing awareness about the new variant by providing necessary information to incoming travellers and healthcare workers and prompting early testing and identification of cases with possible epidemiological link with the known affected countries;
- requirement of proof of negative test pre-departure or upon arrival, and quarantine for a minimum of five to seven days with a negative test before release;
- quarantine for 14 days without a test, if testing capacity is not sufficient.

ECDC has published a guidance for COVID-19 quarantine and testing of travellers [18]. NPIs should be maintained throughout travelling regardless of the vaccination status of the traveller. They include, in particular, the use of face masks, avoidance of crowding and maintaining physical distancing, in all forms of transport. Engineering controls for improved ventilation in airplanes, trains and buses should be implemented.

Limitations and knowledge gaps

This assessment is undertaken based on the evidence known to ECDC at the time of publication. There remain many scientific uncertainties and knowledge gaps. At a high level, these include:

- Virological characterisation, including *in-vitro* infectivity studies and neutralisation studies evaluating both vaccinee and convalescent sera
- Epidemiological analyses to estimate growth rates and secondary attack rates
- Assessment of the severity of this strain (impact on hospitalisation and deaths)
- Analyses of the vaccine effectiveness for different vaccines against Omicron (direct and indirect effects)
- Cross-protection of natural immunity from other SARS-CoV-2 variants
- Lack of sequencing and screening using S-gene target failure in many of the likely affected countries means that the true prevalence of this variant is likely underestimated.

Source and date of request

ECDC internal decision, 26 November 2021.

Consulted experts

ECDC experts (in alphabetic order): Leonidas Alexakis, Olivia Alexandra, Xanthi Andrianou, Erik Alm, Agoritsa Baka, Jon Bilbatua, Eeva Broberg, Christiana Carstairs, Orlando Cenciarelli, Orla Condell, Erika Duffell, Catherine Fleming, Luca Freschi, Rok Grah, Luisa Hallmaier-Wacker, Tommi Karki, Katrin Leitmeyer, Aikaterini Mougkou, Rene Niehus, Ajibola Omokanye, Anastasia Pharris, Diamantis Plachouras, Bastian Prasse, Natalia Rachwal, Frank Sandmann, Ettore Severi, Jonathan Suk, Hasan Tareq.

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

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