RAPID RISK ASSESSMENT

Assessment of the further spread and potential impact of the SARS-CoV-2 Omicron variant of concern in the EU/EEA, 19th update

27 January 2022

Summary

The SARS-CoV-2 Omicron variant of concern (VOC) is rapidly replacing SARS-CoV-2 Delta in most European Union/European Economic Area (EU/EEA) countries, and is broadly following a west-to-east progression. As pointed out by earlier in vitro and in vivo studies, Omicron can to a degree evade the protective effects of antibodies elicited by vaccination or natural infection according to factors such as number of vaccinations or time since last vaccination, thus leaving large portions of the EU/EEA population susceptible to infection. This has resulted in sharp increases in the number of COVID-19 cases, reaching an unprecedented intensity of community transmission across the region.

In comparison with earlier circulating variants, Omicron infections appear less likely to lead to a severe clinical outcome that requires hospitalisation or ICU admission. Hence, although the current overall 14-day notification rate in the EU/EEA is 2 621 cases per 100 000 population, which is four times higher than the highest peak observed during the pandemic to date, hospitalisation rates and mortality are below the levels observed in earlier pandemic waves. However, the number of cases among older people has been increasing more recently in several EU/EEA countries, and this could result in a delayed increase of severe cases and deaths. Although the reduction in severity is partially due to inherent characteristics of the virus, results from vaccine effectiveness studies have shown that a significant role in preventing severe clinical outcomes from Omicron infection is played by vaccination, with effectiveness against severe illness increasing significantly among people having received three vaccine doses. Since vaccination uptake is variable across EU/EEA countries (country range: 28.4–82.9%, average 69.4%) and since the uptake of booster doses is still at suboptimal levels in the majority of EU/EEA countries (80% of EU/EEA countries with booster uptake among adults below 60% as of week 2-2022), the expected impact of Omicron will vary, but countries with lower vaccine uptake are expected to experience the highest disease burden. Furthermore, given the very high levels of community transmission observed regardless of overall vaccine uptake, leading to many people being sick at the same time, countries with very high vaccine uptake will also likely undergo a period of substantial pressure on their healthcare systems and on the functioning of the society as a whole (mainly through absence from work and education).

Mathematical modelling results demonstrate that there is a substantial proportion of the population that remains vulnerable to severe outcomes across all EU/EEA countries, especially in those with lower vaccination coverage. Static projections show hospitalisations and mortality are expected to have a proportionally greater impact among people 60 years and older but will also impact people younger than 60 years. In response to the high incidence of Omicron, protection against the risk of high hospitalisation burden can be accomplished by increasing overall vaccination uptake, including rapidly administering booster doses, especially in the older and at-risk population, will protect against the risk of high hospitalisation burden. Furthermore, the vaccines and boosters provide additional longer-term benefits for individuals and society (e.g. preventing absence from work or education and post-acute COVID-19 syndrome).

Suggested citation: European Centre for Disease Prevention and Control. Assessment of the further spread and potential impact of the SARS-CoV-2 Omicron variant of concern in the EU/EEA, 19th update - 27 January 2022. ECDC: Stockholm; 2022.

There are no data so far on the incidence of prolonged symptoms after COVID-19 due to Omicron, nor on whether this differs from the incidence of post-COVID syndrome brought about by previously circulating variants of SARS-CoV-2. It is plausible that the large number of cases of Omicron infection may be followed by a high incidence of post-COVID-19 condition, with a proportionally higher incidence among people who are unvaccinated.

While we expect to be moving towards a more sustainable situation with COVID-19 circulating at manageable levels, we currently remain in a public health emergency pandemic situation, and it is important to note that even in a post-pandemic phase SARS-CoV-2 could still periodically cause high levels of strain on healthcare systems and lead to large outbreaks. Thus, moving forward, multi-layered surveillance, preparedness, and response strategies for addressing COVID-19 will be essential.

Risk assessed

The risk to public health posed by the ongoing spread of Omicron in the EU/EEA is assessed in this update.

Omicron is currently the dominant variant in several EU/EEA countries. In some of these countries, the peak of incidence appears to have been reached recently. Omicron is expected to become dominant in all other EU/EEA countries in the coming weeks. The combination of higher growth rate and immune evasion have contributed to the steady increase in the proportion of cases caused by Omicron, and the replacement of the previously dominant Delta variant. Due to the very high circulation of Omicron in most EU/EEA countries, the **probability of infection** for the EU/EEA population in the coming weeks is considered to be **VERY HIGH**.

Depending on the situation in countries, the exponential rise in cases is expected to have a **HIGH** to **VERY HIGH** impact of in terms of disease burden, pressure on society and strain on healthcare systems through increased hospitalisations and staff absences across different sectors, including among healthcare workers in the immediate coming weeks.

- In counties where COVID-19 vaccination coverage for the complete primary series is higher than 75% in the total population and there is substantial uptake of booster doses among at-risk individuals, ECDC modelling results indicate that while sustained circulation of Omicron continues the high incidence of cases in the community can still result in severe infections among the residual unvaccinated or partially vaccinated population, and there is a residual risk of severe infection among fully vaccinated people belonging to high risk groups, with a **HIGH** impact on healthcare and society. For these countries the impact is expected to be **HIGH**.
- Countries where COVID-19 vaccination coverage for the complete primary series is lower than 75% in the total population and where the uptake of booster doses among at-risk individuals is suboptimal will experience a higher impact. For these countries the impact is expected to be **VERY HIGH**.

Of particular concern are countries where vaccine uptake among risk groups has remained low and where Omicron infection has not yet reached its peak. Based on the factors outlined above and considering the different epidemiological situations in EU/EEA countries, the overall public health and societal risk posed by the ongoing spread of Omicron in the EU/EEA is assessed as **HIGH** to **VERY HIGH**.

Options for response

Vaccination remains a key component of the multi-layered approach needed to reduce the impact of Omicron, while also addressing the ongoing circulation of Delta. All efforts should be made to increase uptake of the primary vaccination course in people who are currently unvaccinated or partially vaccinated. Furthermore, all eligible adults should be offered a booster dose starting from three months after completing the primary vaccination series. A timely administration of booster doses according to national recommendations is expected to have a significant effect in reducing the impact of Omicron infections.

Given the current epidemiological situation within the EU/EEA, the maintenance of key non-pharmaceutical interventions (NPIs) is crucial over the immediate future in order to ensure that the intensity of Omicron circulation remains at manageable levels. These NPIs include physical distancing, consistent and correct mask wearing, avoiding crowded situations, teleworking when possible, staying home when ill, and maintenance of hand and respiratory hygiene, together with good ventilation of indoors settings. The use of face masks should be considered also in crowded outdoor settings. The key to NPI effectiveness is good compliance and prompt implementation in response to the worsening of epidemiological indicators of community transmission. Given the risk of Omicron infection among vaccinated people, measures should be implemented at population level with no exemptions based on vaccination status. Of particular importance is the prevention and control of infections in healthcare settings, where staff shortages due to Omicron infections are being observed and where outbreaks among people with underlying health conditions will be of significant impact.

Countries where vaccine uptake among risk groups has remained very low and where Omicron infection has not yet reached its peak should consider a rapid, proactive implementation of NPIs and business continuity plans to reduce the impact of Omicron.

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, according to the epidemiological and testing capacity situation. This is to ensure the timely identification of any emerging new variants.

When testing capacity is severely limited, priority should be given to hospitalised patients, older people, healthcare workers, and other high-risk groups. If comprehensive testing of all those presenting with symptoms is not feasible, a representative subset of symptomatic cases should be tested, preferably by RT-PCR. Multiplex RT-PCR assays with SARS-CoV-2 and other respiratory viruses (e.g. influenza virus and RSV) can be considered for diagnosis of respiratory infections in healthcare settings. In the current high prevalence situation, priority does not need to be given to confirming positive results from a rapid antigen detection test (RADT) by a second method, as the positive predictive value of RADTs is high.

Given the very high attack rate of Omicron infections in the population, and taking into account the fact that 70% of the EU/EEA population has completed its primary vaccination course, it is expected that at the end of the ongoing Omicron wave the vast majority of the EU/EEA population will have built a degree of cellular immunity against SARS-CoV-2. Although the virus will continue to evolve and new variants will emerge, it is likely that until a major virus genomic shift occurs most of the EU/EEA population will have a degree of protection against severe illness. This may result in a prolonged period of ongoing manageable COVID-19 impact in the population, during which Member States should focus on strengthening their surveillance, healthcare systems, and overall pandemic preparedness. Meanwhile, researchers and vaccine manufacturers should prioritise the development of variant-independent vaccines and of vaccines that are more protective against infection and that confer a longer lasting immunity.

What is new in this assessment?

This Rapid Risk Assessment extends the assessment of the further emergence and potential impact of Omicron in the context of ongoing transmission of the Delta variant that was published on 15 December 2021, to include new epidemiological data on the spread of Omicron, new data on vaccine uptake, updated forecasts, and the latest evidence on Omicron transmissibility, severity, immune escape, vaccine effectiveness, post-COVID-19 condition, and non-pharmaceutical interventions.

Event background

Since 31 December 2019 and as of week 2022-02, 328 558 243 cases of COVID-19 have been reported worldwide, including 5 548 696 deaths. As of week 2022-02, European Union/European Economic Area (EU/EEA) countries have reported 70 036 727 cases and 934 789 deaths due to COVID-19, representing 21.3% of all cases and 16.8% 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

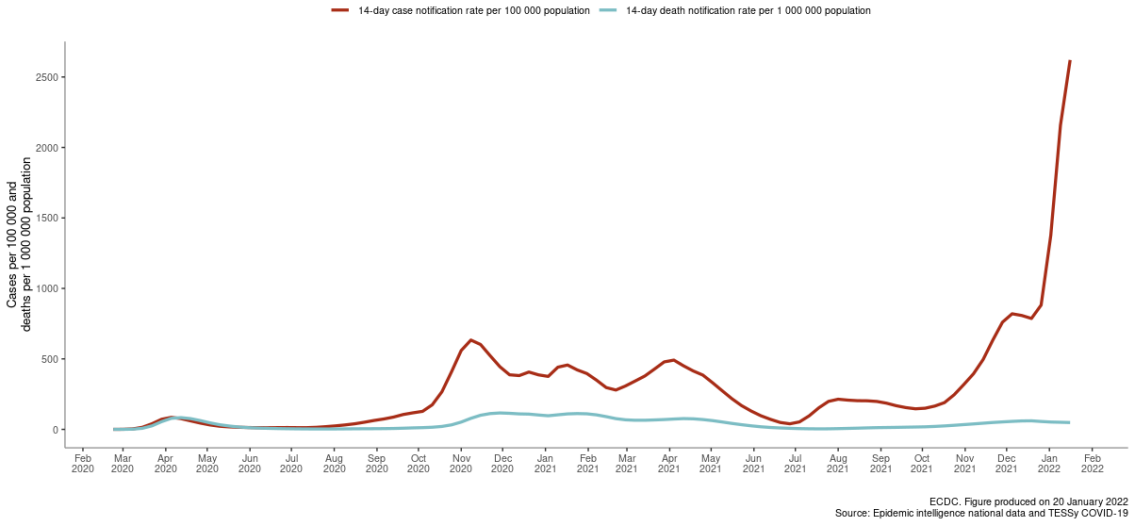
Epidemiological indicators

At the end of week 2-2022 (week ending 16 January 2022), the overall epidemiological situation in the EU/EEA was characterised by a high overall case notification rate that has increased rapidly in the past four weeks, and an elevated but stable death rate (Figure 1). The overall 14-day COVID-19 case notification rate for the EU/EEA has been increasing for four weeks, reaching 2 621 per 100 000 population by the end of week 02-2022. Case notification rates were highest in age groups under 49 years old, although a rapid increase is also being observed in older age groups. The 14-day COVID-19 death rate has been stable for eight weeks, with 48.5 deaths per million population by the end of week 2-2022.

The hospital admission rate for the EU/EEA for week 2-2022 (data reported by 16 countries) was 16.3 per 100 000 population (country range: 2.0 to 36.5) and has been increasing over the last three weeks. Increasing trends of hospital admission rates were observed in four countries during the most recent week of monitoring. Four countries reported a hospital admission rate that was more than 50% of their respective pandemic peak but below this maximum value. One country (Greece) reported a hospital admission rate above their previous pandemic peak.

The ICU admission rate for the EU/EEA for week 2-2022 (data reported by 13 countries) was 1.9 per 100 000 population (country range: 0.3 to 7.1) and has been stable for seven weeks. Increasing trends were observed in three countries since the previous week. Five countries reported an ICU admission rate that was more than 50% of their respective pandemic peak, but none above their previous pandemic peak.

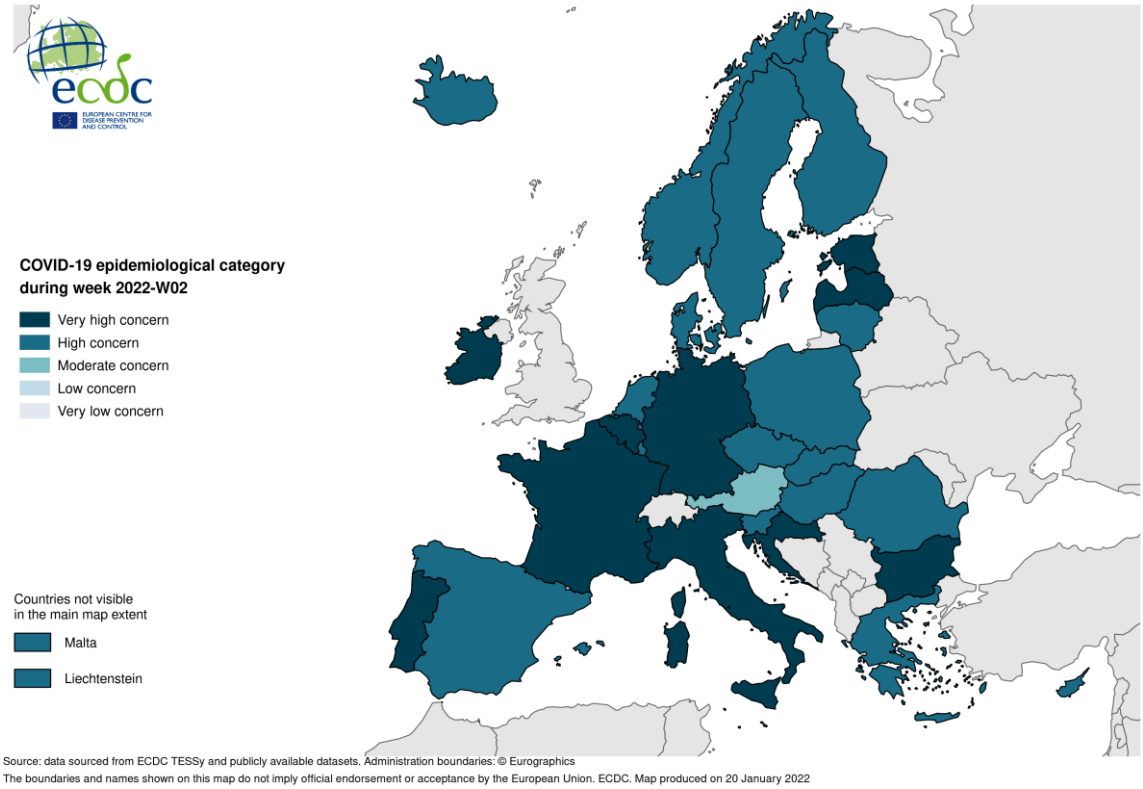
Figure 1. Fourteen-day COVID-19 case and death notification rates in the EU/EEA up to week 2, 2022



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. Although the highest case notification rate so far was observed in week 2-2022, this might still be an underestimation since testing capacities reached their limits in some countries or are relying on RADTs (less sensitive) and self-test RADTs (less sensitive and possibly reported less to the authorities).

As of week 2-2022, the overall epidemiological situation in the EU/EEA was categorised as of very high concern for the third consecutive week, a level of concern that has remained high or very high for the last 14 weeks. The overall epidemiological situation was of high or very high concern in 29 of the 30 EU/EEA countries at the end of week 2-2022 (Figure 2).

Figure 2. COVID-19 epidemiological categorisation of EU/EEA countries week 2, 2022



Note: 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.

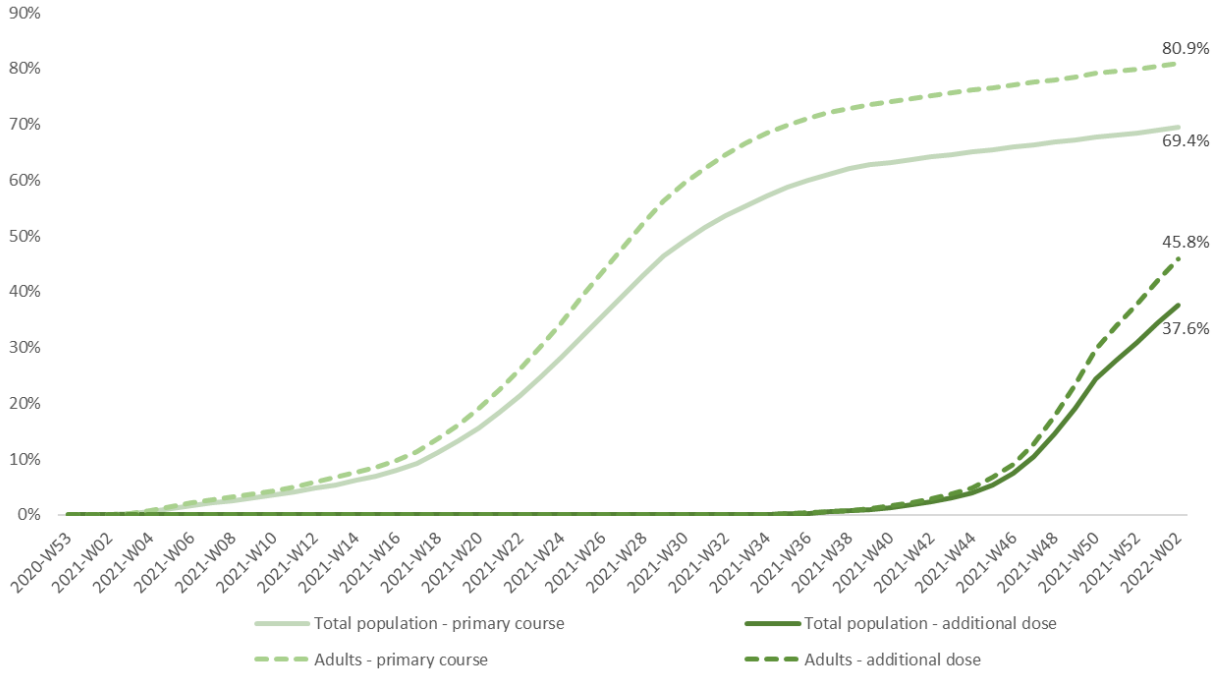
COVID-19 vaccine uptake

As of 16 January 2022 (week 2-2022), over 800 million vaccine doses have been administered in the EU/EEA, 314 million people have received a complete primary vaccination series and over 155 million people in the EU/EEA have already received an extra dose in addition to a complete primary series (30 countries reporting).

Since the start of COVID-19 vaccine deployment in December 2020 and as of 16 January 2022, the cumulative vaccine uptake in the total population in the EU/EEA reached 69.4% (range: 28.4-82.9%) for the complete primary series and 37.6% (range: 7.0-59.7%) for an additional (booster) vaccine dose (pooled data from 30 reporting countries). Among adults (aged 18 years and older) in the EU/EEA, the cumulative vaccine uptake reached 80.9% (range: 33.9-94.3%) for the complete primary series and 45.8% (range: 8.6-75.1%) for an additional vaccine dose (pooled data from 30 reporting countries) (Figure 3). Among those aged 60 years and above the median uptake of an additional dose has already reached 72.5% (range: 11.4-95.5%; 28 countries reporting) [6].

As the cumulative uptake of the primary series of vaccination reaches above 80% in the adult population in the EU/EEA, the increase in vaccine uptake in most countries is driven by the rollout in younger age groups. In addition, there is a rapid increase in the uptake of additional doses. However, progress continues to be unequal across EU/EEA countries. It is notable that a few EU/EEA countries are lagging behind, with three still reporting less than 50% of uptake of the primary series in the total population (Bulgaria, Romania, and Slovakia). More information on the COVID-19 vaccine rollout in EU/EEA countries can be found on the ECDC Vaccine Tracker.

Figure 3. Cumulative uptake of a complete primary series and an additional dose in the total population and among adults (18+ years) in EU/EEA countries as of week 2, 2022

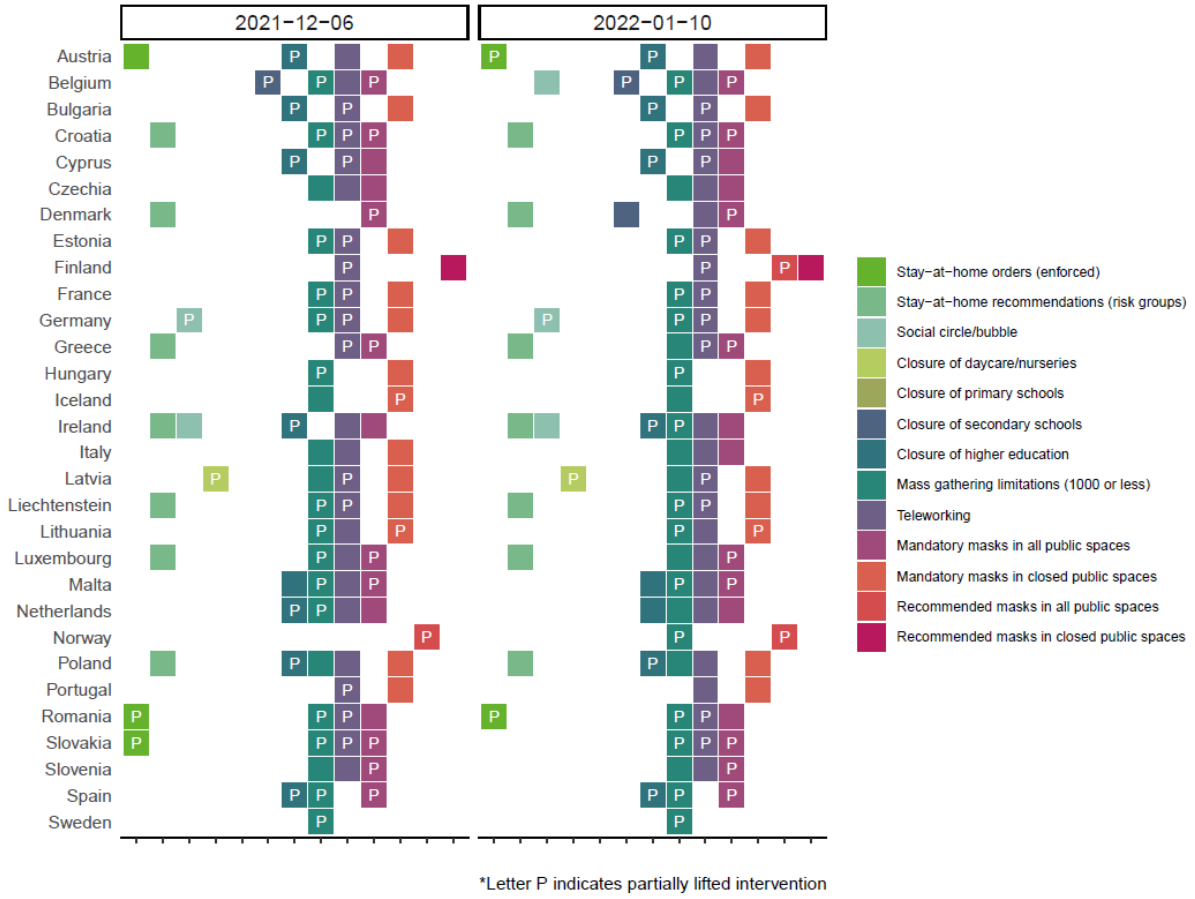


Source: TESSy; data reported by 30 countries as of week 2-2022. The total population includes children and adolescents for whom the vaccine is not yet indicated (i.e. younger than five years) or who may not yet be included in national target groups.

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: 6 December 2021, as reported in the previous ECDC rapid risk assessment [7], and 10 January 2021. In relation to the latest updates of the RMD, a slightly higher number of measures (n= 102) was recorded in comparison to the previous date (n=95). Since that timepoint, more measures in place are reported as fully implemented. The number of countries with active measures relating to the mandatory use of face masks in all public spaces has increased slightly, from 16 countries on 6 December 2021 to 17 countries on 10 January 2022. 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 21 countries having such measures in place on 6 December 2021 and 24 countries on 10 January 2022.

Figure 4. Comparison of NPIs for the control of COVID-19 in EU/EEA countries active on 6 December 2021 and 10 January December 2022



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 [8].

By the end of week 01-2022, Omicron was the most common variant in the EU/EEA countries. While its rapid spread continues, Delta is still co-circulating. Among the 22 countries with an adequate sequencing volume and a valid denominator for weeks 52, 2021 and 1, 2022 (27 December to 9 January 2022), the median (range) of the VOC reported in all samples sequenced in these 22 countries was 69.4% (5.7–99.9%) for B.1.1.529 (Omicron), 23.3% (0.0–93.9%) for B.1.617.2 (Delta), 0.0% (0.0–0.4%) for P.1 (Gamma) and 0.0% (0.0–0.0%) for B.1.351 (Beta). This distribution was 0.0% (0.0–4.9%) for B.1.1.7 (Alpha), which was downgraded from the list of VOCs on 3 September 2021. With regards to other variants of interest (VOI), the median (range) reported in all samples sequenced in these 22 countries was 0.4% (0.0–7.1%) for AY.4.2 and 0.0% (0.0–0.0%) for B.1.621 (Mu). ECDC continuously monitors emerging variants. Lists of VOC, VOI and variants being monitored are provided on ECDC's website [8].

Epidemiological situation for Omicron

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 Delta, assigning it the label Omicron. As of 20 January 2022, Omicron has been identified in all EU/EEA countries.

Between week 46-2021 and week 2-2022 (week ending Sunday January 16th, 2022), COVID-19 case-level data on 155 150 Omicron cases were reported to TESSy by 15 EU/EEA countries, including Austria (number of cases 84 537), Cyprus (343), Estonia (27), Finland (8 149), Ireland (1 404), Italy (3 231), Liechtenstein (35), Luxembourg (974), Malta (296), Norway (50 534), Poland (37), Portugal (570), Romania (92), Slovakia (112), and Sweden (4 809). The median age of these 155 150 Omicron cases was 30 (interquartile range 20–33) years; 7% were aged 60 years and above and 50% were male. Complete data on vaccination status was available for 2 369 (2%) Omicron cases, among which 211 (9%) were reported as having received one dose, 1 646 (69%) were reported as two doses, 255 (11%) were reported as three doses, 18 (1%) were reported as vaccinated with an unknown number of doses, and 239 (10%) were reported as unvaccinated. Among 93 189 Omicron cases with complete data on importation status in weeks 01-2022 and 02-2022 (84.8%), 86 422 (93%) were locally acquired.

From week 52-2021 to week 01-2022 (27 December 2021 to 9 January 2022), 22 EU/EEA countries with adequate sequencing volume reported an estimated prevalence of Omicron of 69.4% (range from 5.7% to 99.9%), increasing from 48.5% in the weeks 51-2021 to 52-2021 (data from TESSy/GISAID EpiCoV™, available in the ECDC weekly Country Overview Report).

As of 20 January 2022, using as reference the most recent data available (collected either from TESSy/GISAID EpiCoV™ or from EU/EEA countries' official national or regional websites), countries where Omicron has become the dominant variant (accounting for more than 50% of sequenced viruses) include Austria (95.4%, 2022-02), Belgium (99.7%, 2022-02), Cyprus (93.9%, 2022-01), Czechia (66.7%, 2022-02), Denmark (98.8%, 2022-02), Finland (99.9%, 2022-02), France (90.8%, 2022-02), Germany (62.5%, 2022-01), Greece (85.6%, 2022-01), Hungary (64.7%, 2022-02), Iceland (90%, 6 January 2022), Ireland (89.2%, 2021-52), Italy (81%, 2022-01), Liechtenstein (88.5%, 2022-01), Lithuania (40.5%, 2021-52), Luxembourg (89.6%, 2022-01), Malta (99.3%, 2022-01), the Netherlands (95.3%, range between labs 93.3% - 98.6%, 10 January 2022), Norway (93.8%, 2022-02), Portugal (86.3%, 2022-01), Slovenia (67% of cases sequenced on 5 January 2022), Spain (87.4%, 2022-01), and Sweden (91.8%, 2022-01). For Cyprus, Ireland, Lithuania, and Malta, sequencing volume was not sufficient to estimate a variant proportion with sufficient precision at a variant prevalence of 5% (more information available here). For Liechtenstein, the proportion represents the seven-day rolling average of the estimated share of the virus variants detected in Switzerland and Liechtenstein.

Countries where Omicron is present but not dominant include Bulgaria (43.5%, 2022-02), Croatia (no national proportion available), Estonia (45.8%, 2022-02), Latvia (5.8%, 2022-02), Poland (26.2%, 2022-02), Romania (37.8%, 2022-02), and Slovakia (29.9%, 2022-02).

Large (20% or higher) increases in the number of cases since last week have been reported in the following countries: Bulgaria, Cyprus, Czechia, Estonia, Germany, Hungary, Italy, Luxembourg, Malta, Spain, and Sweden. For a general overview of the epidemiological COVID-19 situation in the EU/EEA, please see the ECDC weekly Country Overview Report.

Disease background

The section below provides disease background specific to Omicron. 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 [9].

Omicron

Biological characteristics

Although data on cell tropism are preliminary and require further evaluation in population-based studies, there are several studies that show changes of the Omicron replication properties in vitro and/or the animal model. Namely, a changed entry process with an optimised ability for endosomal fusion at the cell surface [10,11], an enhanced binding to its primary receptor ACE2, with an affinity estimated to be twice as high as for the Wuhan-hu-1 strain [12], and attenuated replication in lower respiratory tissues [13,14], meaning that Omicron might prefer to infect cells in the upper respiratory tract. This change in tropism could potentially lead to reduced infection severity and increased transmissibility. A study by Wu et al., based on molecular dynamics simulations and ELISA assays, indicated that the receptor binding domain of Omicron has a weaker affinity to the human ACE receptor than the Delta variant, meaning that Omicron has a high risk of immune evasion [15]. In vitro studies further demonstrated changes in the Omicron entry process towards endosomal, TMPRSS2-independent fusion. This could represent a major shift in the replication properties and could explain a change in tropism for Omicron.

Virus kinetics

As of now, there is no strong evidence that the viral kinetics of Omicron differ from the other variants. Accordingly, there are no implications for isolation and infection control.

Recent data from Japan on Omicron viral shedding using 83 specimens taken from 19 vaccinated people and two unvaccinated people showed that levels of viral RNA were highest at three to six days from diagnosis or symptom onset and gradually decreased over time with no infectious virus (using virus culture) detected in the respiratory samples after 10 days since symptoms onset [16].

Results of a study on the viral dynamics and duration of RT-PCR positivity in people infected with Omicron indicated a lower viral RNA peak (based on Ct values) and a shorter clearance phase than Delta infections on average. However, as in this study the majority of the samples were collected from vaccinated persons, it remains unclear to what extent these differences can be attributable to the overall higher immunity levels or if this is an intrinsic characteristic of Omicron [17]. The rate of clearance was similar (3.13 Ct/day, 95% CI 2.75-3.54 for Omicron; 3.15 Ct/day, 95% CI 2.69-3.64 for Delta). Omicron infections featured a mean duration of PCR positivity of 9.87 days (95% CI 8.83-10.9) compared to 10.9 days (95% CI 9.41-12.4) for Delta infections [17]. Puhach et al. observed modestly lower infectious viral titres in patients infected with Omicron compared to Delta-infected patients. However, this difference was not statistically significant [18].

Preliminary emerging evidence does not seem to suggest higher viral loads in vaccinated people infected with Omicron compared to vaccinated people infected with Delta [18], nor a longer duration of infectious virus shedding [16].

Molecular characteristics

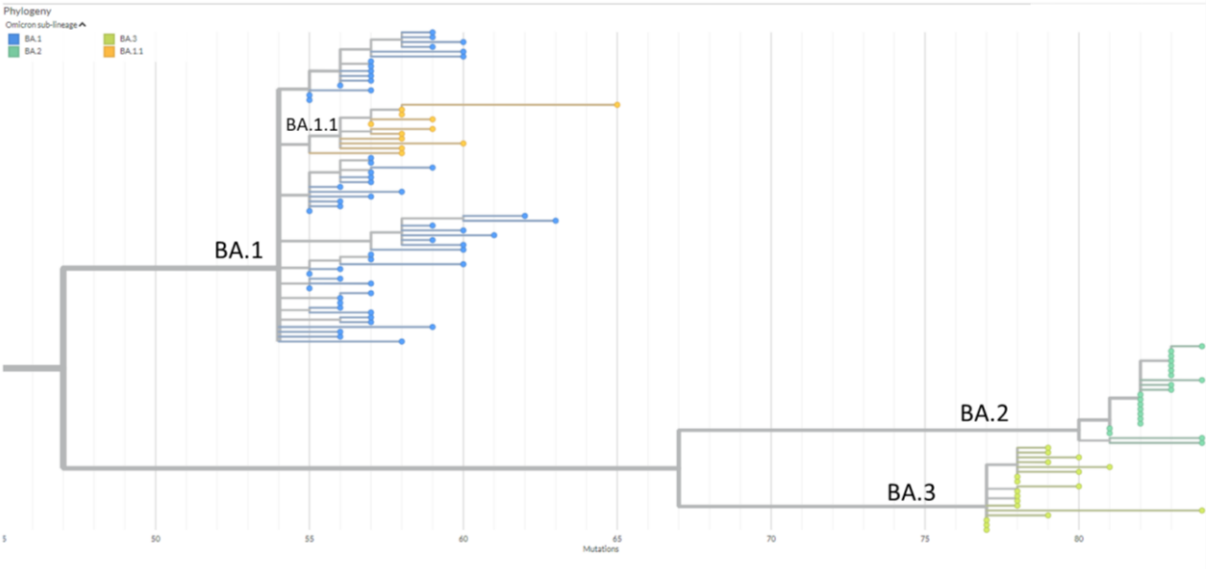
Omicron belongs to the Pango lineage B.1.1.529, which is characterised by 21 amino acid changes in the spike protein compared to the original virus (G142D, G339D, S373P, S375F, K417N, N440K, S477N, T478K, E484A, Q493R, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K). Of these changes, 12 are located in the receptor binding domain (RBD) (residues 319-541). This lineage has recently been partitioned into four sub-lineages BA.1 (B.1.1.529.1) [19], BA.1.1 (B.1.1.529.1.1) [20], BA.2 (B.1.1.529.2) [19] and BA.3 (B.1.1.529.3) [21]. The spike mutational profiles of the sub-lineages are shown in Figure 5. 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 [19]. There have been no recombinants between Omicron and any other variants confirmed as of 18 January 2022.

Figure 5. Spike mutational profile of Omicron sub-lineages

The mutations present in all sub-lineages are coloured in purple and the unique mutations for each sub-lineage are coloured in orange. BA.3 does not carry unique changes in Spike, but it has sub-lineage defining amino acid changes in other proteins - ORF1a:A3657V, ORF3a:T22V and nucleotide substitutions - C832T, C11235T.

As of 25 January 2022, in GISAID EpiCoV, the BA.1 lineage contains most of the B.1.1.529 sequences worldwide (582 648/599 406, 97.2%). BA.2 and BA.3 sub-lineages contain 2.2% and 0.02% of the Omicron sequences, respectively, and 0.6% of Omicron sequences were not assigned to any of the sub-lineages. BA.2 is the dominant sub-lineage in Denmark, while BA.1 is the dominant sub-lineage in all other EU/EEA Member States. All the supporting evidence for the phenotypical properties of Omicron available to date is derived from the BA.1 lineage and may not be fully applicable to the BA.2 lineage. However, the assessment by WHO as of 19 January 2022 is that all sub-lineages of B.1.1.529 are included in the Omicron variant [22].

Figure 6. Phylogenetic tree describing the Pango lineage B.1.1.529 and its sub-lineages



The tree was generated using the UShER web interface [23]. Twenty randomly selected sequences belonging to each of the Omicron sub-lineages from GISAID were used as query sequences.

Transmissibility

The growth advantage of Omicron over Delta is determined by a combination of: i) intrinsic biological properties of the virus that may make it more infectious and transmissible than Delta (e.g. ACE2 receptor binding efficiency or viral replication efficiency); and most importantly ii) immune escape properties resulting in more breakthrough infections among vaccinated people or more reinfections among recovered people when compared to Delta, leading to an increase in detected cases.

Based on the observed epidemiology of Omicron growth rates in South Africa, the United Kingdom (UK), in EU/EEA countries and elsewhere, where Omicron has become the dominant variant in a period of less than four weeks in most settings, it is clear that it has a substantial growth advantage over the previously prominent Delta variant. This rapid replacement has occurred in settings of diverse levels of NPI implementation, vaccination coverage, and previous infection. The extent to which this advantage is intrinsic to the variant's biological properties and what

part of the growth advantage is due to immune escape or waning immunity following vaccination and/or natural infection are less clear.

Given the extensive changes to the receptor binding domain, cell entry and increased ACE2 binding measured in some assays for Omicron and laboratory evidence of increased replication of Omicron in the upper respiratory tract compared to Delta, there may be properties inherent to Omicron that contribute to its increased transmissibility [10,14].

According to a Danish household study, the secondary attack rate was 31% and 21% in households with Omicron and Delta cases, respectively. There was non-significantly increased household transmission among non-vaccinated Omicron cases as compared to Delta (SAR 1.17 times higher; 95% CI 0.99-1.38) while those who have completed the primary series of vaccination had 2.6 times higher SAR (95% CI 2.3-2.9) and booster-vaccinated 3.7 times higher SAR (95% CI 2.6-5.1), indicating that a large proportion of the increased transmissibility of Omicron may be due to immune escape rather than being an intrinsic feature of this variant [24]. Higher secondary attack rates in household and non-household settings for Omicron compared to Delta have also been reported by the UK [25].

While the above parameters refer to sub-lineage BA.1, sub-lineage BA.2 has increased to become dominant in Denmark and is increasing in several other countries, including several EU/EEA Member States. Information on secondary attack rates or biological properties that may be associated with increased transmissibility are not available currently, and the evolution of BA.2 and its characteristics needs close evaluation in the coming weeks.

Aerosol transmission

In most instances, coronaviruses are transmitted primarily from person to person via respiratory droplets, either by being inhaled or deposited on mucosal surfaces, including aerosols produced when coughing and speaking [26]. The concentration of infectious respiratory droplets decreases with increasing distance from the source because the larger ones fall on the ground or surfaces due to gravity while the smaller ones that can remain suspended in the air (aerosols) are diluted. Furthermore, the droplets become less infectious with time [27]. Therefore, transmission is more likely with close proximity to a source. However, there is evidence from several SARS-CoV-2 outbreak investigations that transmission also occurs in closed, poorly ventilated spaces even without close proximity to the source [28-31], supporting the role of aerosols in transmission.

There are no data showing that Omicron has an increased ability to survive or be transmitted through aerosols compared with previously circulating variants. The apparent increased transmissibility of Omicron is due to the immune escape [24] or virological characteristics of the variant (such as higher affinity to the ACE2 receptor and optimised cell entry – see the section above on biological characteristics) rather than a change in the ability to be transmitted through aerosols or increased survival in aerosols.

Pre-symptomatic and asymptomatic transmission

Among more than 110 000 Omicron cases reported to TESSy with known information on symptoms, 76% were reported as symptomatic; fewer than in reported Delta cases (83%) [32]. Data from a household survey in December 2021 in the UK found that 45% (95% CI 44-47%) of those with likely Omicron infections reported symptoms, fewer than those with likely Delta infections (52%; 95% CI 50-55%) [33].

The incubation period is defined as the period from exposure to the appearance of first symptoms. For infection with the ancestral virus, it was estimated to range between one to 14 days in 2020 [34-36] with an estimated mean based on a meta-analysis of 5.68 days (99% CI 4.78-6.59) [37]. However, emerging SARS-CoV-2 variants have shown varying incubation periods [38]. With a reported median incubation period of three days, data from a limited number of outbreaks caused by Omicron indicate a shorter incubation period than for Delta [39-41].

Severity

Among Omicron cases with known outcomes reported into TESSy as of 19 January 2022, 884 (1.14%) were hospitalised, 120 (0.16%) required ICU admission/respiratory support, and 48 (0.06%) died [32]. The pattern of higher rates of hospitalisation, ICU admission, and death with increased age is apparent for Omicron cases, as it was for Delta and previous variants. However, anecdotal information refers to a high percentage of hospitalisations with incidental diagnosis of COVID-19 rather than due to COVID-19. Disentangling admission cause and contributing factors is difficult. ECDC is collaborating with the surveillance network to improve accuracy of reporting.

Evidence from a variety of settings suggest that infections with Omicron have a less severe clinical presentation than ones due to Delta. It is important to highlight that lower age, prior immunity from natural infection, vaccination including booster doses, and improved treatment options will contribute to less severe outcomes from subsequent infection. Therefore, the comparative intrinsic capacity of Omicron to cause severe infection may be underestimated as a consequence of the large numbers of vaccinated or previously infected people that had accumulated prior to its emergence, which was not the case in the beginning of preceding waves. Most studies do not account for waning immunity, or for the likely large amount of under-ascertained reinfections. This could lead to an underestimation of severity.

Similarly, low hospital admission rates (0.3%) and case fatality (<0.1%) for Omicron cases have been observed in Canada [42], and in Texas (US), California (US), and Denmark a shorter median length of hospital stay and/or significantly reduced need for respiratory support were reported for Omicron [43-45]. This observed severity in TESSy data and in the studies was cited as at least partially likely due to the protective effect of vaccination, time since vaccination, co-morbidities, and/or previous infection in some of the people and does not necessarily reflect the inherent severity of Omicron.

Across studies from various settings, the risk of hospitalisation was found to be lower for Omicron than for Delta or other previous variants. While studies used slightly different data, analysis approaches, stratification by vaccinaton status and adjustments for confounding factors, most studies found risk reduction in the range of 50 to 60%.

Preliminary analysis of case-based data submitted by 15 EU/EEA countries to TESSy between week 46 2021 and week 2 2022 was performed to compare the overall adjusted odds ratio (aOR) of hospital admission for infection with Omicron compared to infection with Delta among symptomatic cases. Logistic regression models adjusted for age group, sex, preconditions, reporting country, reporting week and vaccination status showed that Omicron infection was less likely to be reported with admission to hospital compared to infection with Delta (aOR 0.41; 95% CI: 0.37-0.46). In addition, there is ongoing discussion about the need to differentiate patients hospitalised 'with' from those 'due to COVID-19', i.e. patients incidentally discovered positive for SARS-CoV-2 infection, while admitted for another condition. While this issue is difficult to disentangle, ECDC is continuously trying to improve the accuracy of reporting in collaboration with the surveillance network. More in-depth analysis will be performed over the course of the upcoming weeks to better assess the impact of Omicron on severe outcomes reported to TESSy.

A Danish observational cohort study of 188 980 SARS-CoV-2 positive people during November-December 2021, compared the risk ratio of admission for Omicron compared to Delta infection overall and stratified by vaccination status [45] and found that Omicron was associated with an adjusted RR of hospitalisation of 0.64 (95% CI: 0.56-0.75) compared to Delta infection. RR was 0.57 (95%CI 0.44-0.75) among cases with no or one vaccination, 0.71 (95% CI: 0.60-0.86) among two-dose vaccinated, and 0.50 (95% CI: 0.32-0.76) among three-dose vaccinated. Omicron had lower risk than Delta cases regardless of comorbidity or reinfection. The lower hospitalisation risk for Omicron cases among both vaccinated and unvaccinated people suggests a reduced severity of Omicron, but Omicron patients in this study were younger and had fewer comorbidities than those with Delta.

In the UK, after adjusting for sex, age, ethnicity, deprivation, travel, vaccination status and, where ascertained, previous infection, presentation to secondary care with Omicron was approximately half of that for Delta (Hazard Ratio 0.53, 95% CI: 0.50 to 0.57) [46]. They also found a 65% lower hospitalisation risk for people infected with Omicron who had received two doses of a vaccine, and an 81% reduction for those with three doses, compared to unvaccinated people infected with Omicron. This study did not correct for under-ascertainment of previous infection. Another analysis of data from the UK estimated that corrections for undetected previous infections changed the hazard of hospitalisation risk for unvaccinated Omicron cases relative to unvaccinated Delta cases from 0.59 to 0.76 (corrected) [47].

In Scotland, symptomatic people who were S-gene negative (a proxy for Omicron infection, BA.1 sub-lineage) and followed up for at least seven days had a 67% reduced hospitalisation risk compared to S-gene positive cases, while the rate of possible reinfection for Omicron was 10 times that of Delta [48]. People who had received three vaccine doses had a 57% (95% CI 54-60) lower risk of experiencing symptomatic Omicron infection relative to $\geq$25 weeks post second vaccine dose.

In Southern California, the United States, the risk of hospitalisation, ICU admission and mortality were 0.48 (0.36-0.64), 0.26 (0.10-0.73) and 0.09 (0.01-0.75) higher, respectively, among cases with Omicron infection compared to cases with Delta infection [43].

It usually takes several weeks for the accumulation of clinical outcomes before one can draw conclusions on the impact of a specific variant on hospital admissions, intensive care needs, and death rates. It is also essential to account for the relatively young age of most people who have been infected with Omicron to date, and thus far there are little data on the severity among older age groups and people with underlying risk factors. As a result, the clinical profile of Omicron may change as other groups are infected and followed over time.

Significantly, the combination of higher growth rate and immune evasion indicate that any potential advantage Omicron may have in terms of decreased severity might be countered by increased community infection rates that lead to a substantial additional burden for hospitals, while primary care may be overburdened even more than during previous waves. As more evidence builds up, a better assessment of clinical outcomes and long-term consequences, such as post-COVID-19 condition, will be feasible.

All of the above parameters refer to sub-lineage BA.1. In Denmark, where the most BA.2 has been identified to date, no differences in the risk of admissions have been reported between BA.1 and BA.2 [49].

Post-COVID-19 condition

Patients with COVID-19 often report persisting symptoms or develop new symptoms after the acute infection is over [50]. Post-COVID-19 condition, also referred to as 'long COVID', has manifestations from multiple organ systems and its pathophysiology remains unclear and is most likely multifactorial. Increasing age, female sex, and hospitalisation for acute COVID-19 are linked to a higher prevalence of prolonged symptoms [51]. The estimates of prevalence vary widely depending on the time of follow up and the applied definition, and range from 2.3% [51] to 80% [52]. The UK Office of National Statistics estimates that between 7% and 18% of people who have had COVID-19 develop some symptoms of long COVID persisting for at least five weeks [53] leading to an estimated 1.3 million people in the UK (1 in 50) experiencing self-reported post-COVID condition [54]. A study of breakthrough infections suggested that people who have completed the primary vaccination series who developed a breakthrough infection were 49 percent less likely than unvaccinated people to report symptoms persisting at least four weeks after infection [55]. A recent pre-print from Israel also confirmed that people who received two vaccine doses were not more likely to report long-term symptoms than people reporting no SARS-CoV-2 infection and were less likely to report long-term symptoms than unvaccinated people or those who have not completed the primary vaccination series [56]. However, a retrospective cohort study of electronic health records in the US comparing COVID-19 outcomes between vaccinated and unvaccinated people could not identify any effect of vaccination on post-COVID-19 condition [57].

Post-COVID-19 condition has also been reported in children. A large nationwide study in Denmark showed that children with SARS-CoV-2 infection aged 6-17 years reported symptoms more frequently than a control group (percent difference 0.8%). The most common symptoms among school-children with a history of SARS-CoV-2 in this study were loss of smell (relative difference, RD, 12%), loss of taste (RD 10%), fatigue (RD 5%), respiratory problems (RD 3%), dizziness (RD 2%), muscle weakness (RD 2%), and chest pain (RD 1%) [58].

There are currently no data on the incidence of prolonged symptoms after COVID-19 due to Omicron, nor on whether this differs from the incidence due to previously circulating variants of SARS-CoV-2. It is plausible that the large number of cases of Omicron infection will be followed by a high number of people affected by post-COVID-19 condition, with a potentially still higher incidence in people who are unvaccinated.

Potential for immune escape

Omicron is the most genetically divergent SARS-CoV-2 variant detected in significant numbers during the pandemic to date. Several changes in the sequence coding the spike protein have previously been described and are associated with immune escape from neutralising antibodies [59]. Several in vitro studies now confirm that the neutralising capacity of vaccinee (primary series) and convalescent sera against Omicron is significantly reduced relative to previous SARS-CoV-2 variants of concern. However, virus neutralisation by sera from people who have experienced a combination of infection and complete vaccination (primary series), or vaccinated people who have received boosters, remains at least partially effective in neutralising Omicron in vitro [7,60].

While substantial loss of in vitro neutralisation capacity is predictive of reduced vaccine effectiveness against infection, it is difficult to directly translate in vitro neutralisation data to clinical outcomes such as protection from severe disease, for which robust vaccine effectiveness and breakthrough infection data are required in clinical settings (described below) [61]. As yet, no absolute antibody titre threshold has been established as a correlate of protection for SARS-CoV-2 [62]. 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 memory B cells that are able to rapidly expand during subsequent infection to generate higher neutralising antibody titres [63-65]. 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 [66-68].

Early data on memory T cell responses to Omicron indicate that spike-specific CD4 and CD8 T cells induced by prior infection to ancestral SARS-CoV-2 strains or vaccination are highly cross-reactive, providing extensive immune coverage against Omicron [66-72]. Furthermore, the phenotype and functionality of these cross-reactive CD4 and CD8 T cells appear to be similar when responding to ancestral SARS-CoV-2 strains or Omicron [72].

Therapeutics

There is currently only limited evidence regarding monoclonal antibody therapies against Omicron. Non peer-reviewed, pre-print data indicate that several monoclonal antibodies including casirivimab-imdevimab, bamlanivimab/etesevimab, and regdanvimab do not neutralise Omicron in vitro [73], whereas the neutralisation capability of sotrovimab is retained against Omicron [74,75]. Preliminary *in vitro* results show that antivirals such as remdesivir, molnupiravir, and nirmatrelvir also appear to retain their activity, in line with the fact that the viral proteins targeted by them are conserved [76]. Other guidance on therapeutics continues to be valid as with other variants [77].

Vaccine effectiveness

There is emerging but still limited data on the effectiveness of the currently available vaccines against infection and disease caused by Omicron.

In summary, there is growing evidence for significantly lower vaccine effectiveness against Omicron infection and symptomatic disease after primary vaccination compared to the Delta variant, but with the booster dose increasing vaccine effectiveness. The data on hospitalisation is still limited but suggests that protection against severe disease is higher than against infection and mild disease, although lower than the protection against the Delta variant. Studies of vaccine effectiveness against Omicron that have been undertaken for Comirnaty, Spikevax and Vaxzevria have indicated that effectiveness is reduced when compared with vaccine effectiveness against Delta, although there might be differences that need to be further studied.

The estimates of vaccine effectiveness against Omicron from these early studies should be considered as preliminary evidence and may be subjected to possible bias related to differences in immunity and exposure to Omicron in different population groups. In addition, some study results are based on a relatively small number of Omicron cases, and several of the studies are preprints that have not yet been peer-reviewed. Studies and collection of real-life data are ongoing to further assess the level of protection from the vaccines against transmission, infection, and severe disease.

It is important to consider that vaccine effectiveness should be interpreted in the light of the baseline severity and transmissibility of Omicron, compared to previous variants.

Vaccine effectiveness against hospitalisation

A study from South Africa estimated the vaccine effectiveness against hospitalisation caused by Omicron to be 69% (95% CI 48-81%) approximately 25 weeks after primary vaccination with Comirnaty [78]. Another study from South Africa investigated the vaccine effectiveness against hospitalisation caused by Omicron after a homologous booster dose of the COVID-19 Vaccine Janssen, which was estimated to be 85% (95% CI: 54-95%) at one to two months after the booster dose [79]. The vaccine effectiveness against hospitalisation caused by Omicron have also been estimated by the UK HSA to be 64% (95% CI: 54-71%) 2-24 weeks after primary vaccination with any vaccine product, declining to 44% (95% CI: 30-54%) after 25 or more weeks. After a booster dose, the estimated vaccine effectiveness increased to 92% (95% CI: 89-94%), declining to 83% (95% CI: 78-87%) after 10 or more weeks [80].

A separate analysis by UK HSA of people aged 65 years and older found vaccine effectiveness against hospitalisation caused by Omicron of 94% two to nine weeks after the booster dose and of 89% 10+ weeks post booster dose. However, this was based on low numbers [81].

Vaccine effectiveness against infection

An early retrospective cohort study of the Danish population estimated the vaccine effectiveness against documented Omicron SARS-CoV-2 infection (regardless of symptoms) to be 55% (95% CI: 24-74%) and 37% (95% CI: -70-76%) after two doses of Comirnaty and Spikevax, respectively, with rapidly waning effectiveness over time. At three months after the second dose, no protection was detected from the vaccines. A booster dose of Comirnaty restored the vaccine effectiveness to 55% (95% CI: 30-70%) [82].

The vaccine effectiveness against documented infection (regardless of symptoms) was also investigated in a study from the United States, where two doses of Spikevax resulted in a vaccine effectiveness of 30% (95% CI: 5-49%), increasing to 63% (95% CI: 56-68%) after a booster dose. This study also reported considerably lower vaccine effectiveness against Omicron infection among immunocompromised people compared to the general population [83].

The UK Health Security Agency provides regularly updated estimates of vaccine effectiveness against symptomatic infection with Omicron and have reported estimates of 63% (95% CI: 59- 67), 68% (95% CI: 55- 78%), and 25% (95% CI: 1-43%), in the initial period (two to four weeks) after primary vaccination with Comirnaty, Spikevax and Vaxzevria, respectively. From 25 weeks after the second dose, the vaccine effectiveness decreased to low or non-significant levels, but was restored after a booster dose of Comirnaty to 69% (95%CI: 67-70%) for those who had received a primary series of Comirnaty, and to 64% (95%CI: 63-66%) for those who had received Vaxzevria as primary vaccination [25,60]. The UK HSA has also conducted a separate analysis of peopled aged 65 years and older and found that in all periods after vaccination, effectiveness was lower for Omicron compared to Delta. From 20 weeks after the second dose of either Vaxzevria or Comirnaty, minimal or no effect against mild disease was seen for Omicron. Although a booster dose of either Comirnaty or Spikevax temporarily increased the protection, this also waned with time to around 30% vaccine effectiveness against mild disease at 10+ weeks post booster dose [81].

In contrast to the studies from Denmark, UK and US, a study from Canada found no effect in the initial period after two doses of an mRNA vaccine (Comirnaty or Spikevax) against Omicron infection (VE 6%, 95% CI: -25-30%), only after a booster dose some protection was detected (VE 37%, 95% CI: 19-50%) [84]. The authors of the study highlight that the results may be confounded by behaviours that they were unable to account for.

The protection from booster doses was also reported in a study from Scotland, where the booster dose of Cominarty or Spikevax was associated with a vaccine effectiveness of 57% (95% CI: 55-60%), relative to two doses only of Cominarty, Spikevax or Vaxzevria, at 25 weeks or more after the second dose. The level of protection was similar in people aged 16-49 years and people aged over 50 years [48].

Vaccine effectiveness against transmission

In a recent Danish household transmission study, people who have completed the primary series of vaccination experienced secondary attack rates (SAR) of 32% in household with Omicron and 19% in households with Delta. For people who received a booster, Omicron was associated with a SAR of 25%, while the corresponding estimate for Delta was only 11%. There was an increased transmission for unvaccinated people, and a reduced transmission for booster-vaccinated people, compared to fully vaccinated people [24].

Laboratory testing for Omicron

Test performance for omicron

Molecular diagnostic tests

While RT-PCR tests remain the gold standard in SARS-CoV-2testing because of their high sensitivity and specificity, most EU/EEA countries have introduced the use of RADTs and self-RADTs as a way of further strengthening their overall testing capacity. The minimum performance criteria for RT-PCR tests have been set by WHO at desirable sensitivity of ≥90% and desirable specificity of >99% [85]. Most of the RT-PCR tests reach specificity of 100% (95% confidence interval, 96.7-100%) and many a sensitivity of ≥90% [86]. Due to the high number of mutations in Omicron, concerns have been raised about performance of commercial and in-house developed SARS-CoV-2 specific RT-PCR assays. WHO and FIND have stated that the diagnostic accuracy of routinely used RT-PCR assays does not appear to be impacted by Omicron [87,88]. There are, however, certain assays that may be impacted by the mutations that Omicron lineages carry, and the US Food and Drug Administration (FDA) maintains a list of such molecular tests [89]. The Joint Research Centre (JRC) is also monitoring the performance of RT-PCR assays and displays information on the JRC Dashboard [90]. In silico analyses performed by JRC have identified six out of seventeen assays that may fail to detect or have reduced sensitivity to Omicron [90,91]. Laboratories are urged to verify the efficiency of protocols used on dashboards relating to in silico analysis and clinical validations.

Of the 39 frequently used SARS-CoV-2 RT-PCR tests in Switzerland and Liechtenstein (commonly used in other EU/EEA countries) that target many genomic loci, including the ORF1ab region (n=16), the RdRp gene (n=13), the S gene (n=8), the E gene (n=11), the N gene (n=32) and, in one case, the M gene, only two of the S gene targeting PCR assays were affected by Omicron; one with S-gene drop out and one with mismatch and delayed Ct/drop out possible [92].

Screening assays

RT-PCR-based S-gene target failure (SGTF) assays that fail to detect the S-gene when it features the deletion Δ69-70 can be used to screen for the Omicron BA.1 VOC. However, it should be noted that among the four defined Omicron sub-lineages (BA.1, BA.1.1, BA.2 and BA.3), one sub-lineage, namely BA.2 does not feature the Δ69-70 mutation, while the rest of the sub-lineages do [19].

Caution should be exercised when using the SGTF assays, as viruses of this sub-lineage will not be identified by these assays; refer to annex 1 for a detailed list of assays differentiating between the Omicron sub-lineages. Circulation of BA.2 has as of 23 January 2022 been observed above 10% of weekly reported sequences in GISAID EpiCoV in Denmark, Sweden, Botswana, Cambodia, Hong Kong, India, Japan, Singapore, South Africa, and Sri Lanka, and is increasing in several other countries worldwide [19,93]. It should be noted that there are also a low number of sequences of non-Omicron lineage viruses that feature the Δ69-70 deletion. 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) [94]. 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 Omicron 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 [89].

Additional new assays have been developed for the identification of Omicron (i.e. targeting S371L/S373P, E484A and ins214EPE) [95,96]. A comprehensive list of available assays/protocols for the identification of Omicron and a table with characteristic amino acid substitutions, deletions, or insertions for the screening of different VOCs can be found in Annex 1. It should be noted that the S371L/F substitution can be used to differentiate between the BA.1 (S371L) and the BA.2/BA.3 (S371F) sub-lineages. Specific assays targeting S371F/S373P have been developed to distinguish between the different Omicron sub-lineages [97]. Also, BA.2 will not be detected in ins214EPE assays [98].

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.

Rapid antigen detection tests (RADTs)

Overall, is it known that rapid antigen tests (RADTs) are less sensitive and less likely to detect very early infections compared to molecular tests. They do, however reliably identify people with high viral load and results correlate well with infectiousness [99].

Further information on the use of RADTs can be found in the recently updated ECDC technical report [100,101]. For Omicron, the results of the rapid assessment conducted by FIND in 2021 [87] as well as the conclusions described in the latest WHO technical brief suggest that RADTs continue to detect Omicron cases [87,88].

Additionally, the Health Security Committee Technical working group (HSC TWG) on COVID-19 Diagnostic tests, led by the EC, regularly reviews recent studies on the performance of RADTs. The HSC TWG assesses proposals against the criteria established by Council Recommendation EU 2021/C 24/01 as well as additional criteria that were agreed by the experts on 21 September 2021. The common list of RADTs tests is then reviewed by Member States, and, if necessary, can be updated in line with new results from independent validation studies becoming available and new tests entering the market [102].

To complement available data, an increasing number of countries has performed initial validation studies on RADTs. Preliminary evidence from a number of studies suggests that most of them can detect Omicron with similar sensitivity. Namely, studies from the UK, Denmark, and the Netherlands found that a variety of RADTs could detect Omicron as well as they could detect the Delta variant [103,104]. A study from the US directly compared test performances of RT-PCR and RADT on anterior nasal swabs and confirmed that RADTs detect Omicron with a sensitivity similar to that observed for prior variants [105]. A comparative evaluation of the sensitivities of a large number of SARS CoV-2 RADTs of different designs and manufacturers was performed by the German Paul Ehrlich Institute in December 2021 and found a large majority of the tests to meet the minimal sensitivity criteria [106].

Still, some studies suggest that RADTs show a certain reduction in sensitivity when used to identify Omicron-infected individuals [107]. Notably, an American study found the reduction in sensitivity to result in missing to correctly identify infectious people infected with Omicron [108]. According to the American FDA, RADTs are, however, still authorised for the use as directed in the authorized labelling and if used in accordance with the instructions included [89].

Sample type

Overall, optimal specimens for the detection of current infection with SARS-CoV-2 are collected from the upper respiratory tract (i.e. nasopharyngeal swab, oropharyngeal swab, nasopharyngeal aspirate, nasal wash) or if the patient is hospitalised or in intensive care, also from the lower respiratory tract (i.e. bronchoalveolar lavage (BAL), endotracheal aspirate (ETA), expectorated sputum). Saliva can also be considered as a sample type. Available data suggests, however, that only assays detecting SARS-CoV-2 RNA should be used for this sample type as the sensitivity of antigen tests may be further decreased with this sample type [109].

For Omicron, studies on viral loads in different sample types are still scarce. Based on a study from South Africa, it seems as if the pattern of viral shedding might be different for Omicron with higher viral shedding in saliva relative to nasal samples resulting in improved diagnostic performance of saliva swabs. It is to be noted that this study used RT-PCR test result and did not include resting with RADTs [110]. In another small study of only 5 patients comparing saliva versus nasal swabs for PCR testing it was observed that viral load peaked in saliva 1-2 days before nasal samples [108]. Overall, but only based on the limited evidence and observations so far, it can be assumed that the difference in viral shedding of Omicron in the different sample types might be of temporal nature.

With only preliminary data available at this time point diagnostic tests should currently still be used according to manufacturer instructions until more data and validation studies of the individual tests become available.

Sequencing

For general information about sequencing strategies and methods for SARS-CoV-2, refer to the ECDC sequencing guidance [111]. For Omicron, there is an updated v4.1 version of ARTIC that aims to mitigate primer-template mismatch for Omicron. Amplicon dropouts for a specific variant can lead to issues with chimeric consensus sequences if there are any contaminations or simultaneous infections with a second variant, care should be taken to validate any suspected recombinant sequences before they are uploaded to public databases [112].

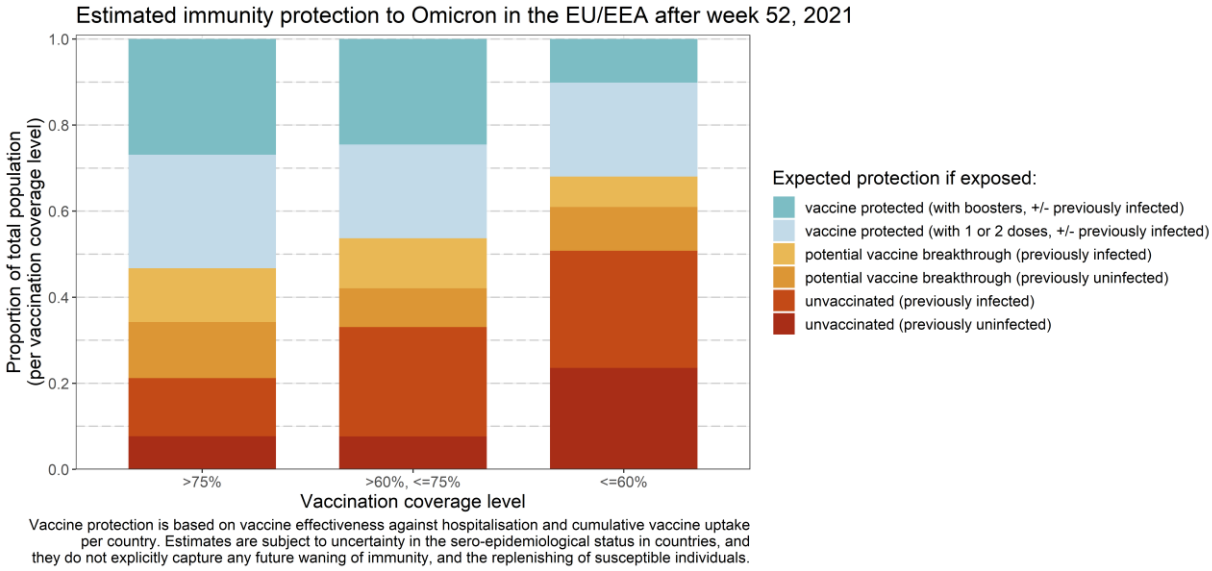
Modelling insights for Omicron epidemiology

The below estimates obtained through mathematical modelling provide insights into the potential hospital and death burden of the currently dominant Omicron variant. It yields new insights into the effects of the booster programme, the changes in vaccine-derived protection, and which parts of the population are vulnerable to Omicron. This approach leads to static estimates, and has been adopted by others previously [113].

We consider several factors that are important for determining the potential Omicron burden: (1) The population that is currently still vulnerable to becoming a symptomatic case and developing severe outcomes of COVID-19 upon exposure to the virus; (2) The number of past infections; and (3) the achieved vaccine-protection as a function of vaccination coverage and waning vaccine-induced and natural immunity. We consider all these factors for individual age groups. Given the tremendous growth rate of Omicron, more than 50% of EU/EEA citizens are assumed to be at risk of exposure to Omicron within the next few months [7,114].

Our model results show that the protection against severe outcomes of COVID-19 is expected to be highest in countries with full vaccination coverage levels above 75% (Figure 7). However, there remains a substantial proportion of unprotected people who are either unvaccinated or at risk of breakthrough infections - see Figure 7. The proportion of people vulnerable to breakthrough infection is increased for Omicron due to the lowered vaccine effectiveness and waning of vaccine-induced immunity (see Section on VEs against Omicron). Due to this substantial number of unprotected and lower vaccine protection against Omicron, the potential disease burden on healthcare systems remains large from those cases at risk of hospitalisation (however, only a proportion of the unprotected people will eventually be hospitalised, following age specific case-hospitalisation rates). The impact can be mitigated through restoring or maintaining higher levels of protection through vaccination and boosters.

Figure 7. Estimated proportions of different degrees of immune protection against hospitalisation ('immunity wall') when exposed to Omicron in the EU/EEA from week 1, 2022

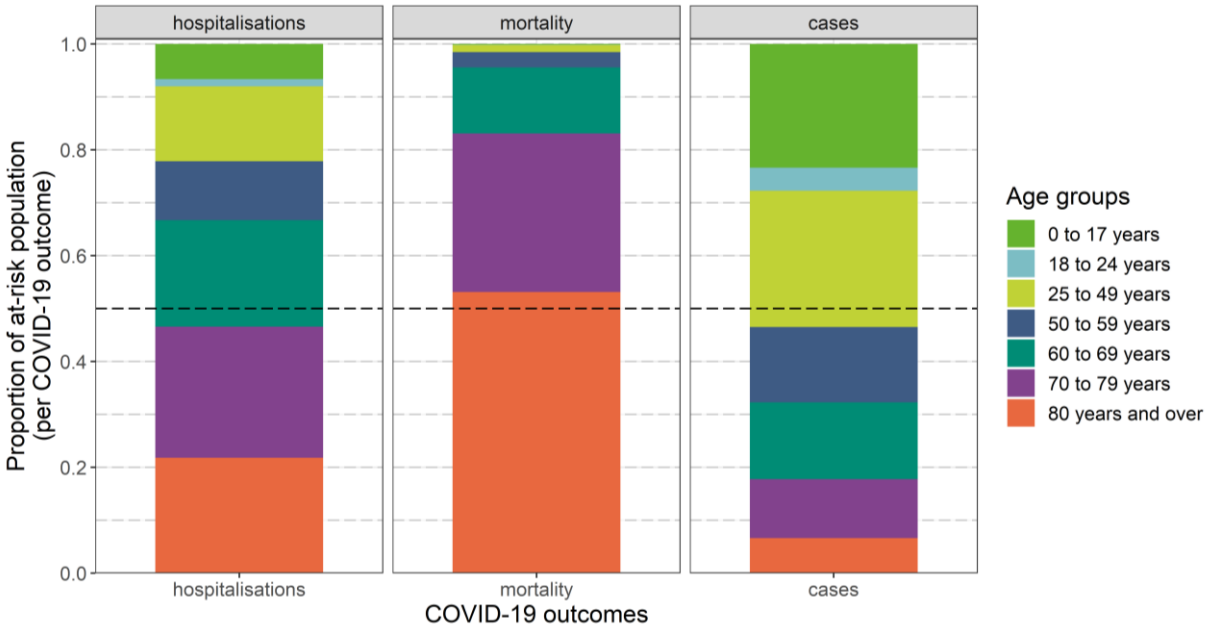


Different levels of proportions of the population with vaccine-derived effective immune-protection (blue shades) or without vaccine-derived immune-protection (orange and red shades).

Note: Of the total population that is vulnerable (unvaccinated, or at risk of potential vaccine breakthrough infection; giving waning of VE and lower VE against Omicron) to severe outcomes when exposed to Omicron: only a small proportion will develop severe disease and be hospitalised, following age specific rates for Omicron. The vaccine effectiveness against severe outcomes in Omicron are assumed to be 30%, 60%, and 84% for first, second, and booster dose, respectively. For previous infected individuals, we assume 1 in 4 was previously reported. The analysis takes into account the protective effect of previous infection by further decreasing the risk of hospitalisation in symptomatic cases by 50%. We assume 30% of infections being asymptomatic.

We estimate the contribution of different age groups to the potential Omicron burden. People older than 60 years are expected to form the majority of hospital admissions, and people older than 80 years may constitute the majority of COVID-19-related mortalities (Figure 8). In contrast, most future symptomatic cases are likely to occur within the group of people younger than 50 years. This emphasises the additional benefits for people and society in terms of preventing losses in productivity as well as days in education. The currently observed hospital admissions are likely to have a different age profile to the ones we have projected in Figure 8, which are based on exposure to the virus being equal across age groups. However, those at highest risk of severe outcomes may not yet have been exposed (due to behavioural and other factors). Our results illustrate the potential for reducing the burden of severe outcomes by targeting older age groups and people at higher personal risk of severe outcomes through vaccination and boosters.

Figure 8. Estimated proportions of the age groups contributing to the total potential burden of hospitalisations, fatalities, and cases caused by the Omicron VOC in the EU/EEA once exposed



The proportions show which age groups are expected to be driving the observed outcomes once a large proportion of the population has been exposed. Hospitalisations: people aged 60 years and older; mortality: people aged 80 years and older.

Finally, if 50% of people in the EU/EEA are assumed to be exposed to Omicron within the next few months [114], the current uptake of boosters achieved by early January may reduce future Omicron hospital admissions by 500 000 to 800 000 across the EU/EEA through restoring higher levels of vaccine protection (with the range given through assuming 20% and 50% lower Omicron severity relative to Delta). Extending the booster programme to all previously vaccinated people could reduce admissions by another 300 000 to 500 000. These results provide a static picture of the burden and they are not a final estimate of the total COVID-19 burden to be expected; they do not take into account the future developments in disease dynamics, the waning of immunity, further immune evasion and the replenishing of susceptible people.

Based on these insights, the following observations can be made:

- The coverage and effectiveness of vaccines and boosters against severe outcomes remains a key determinant of the proportions of protected vs unprotected populations across the EU/EEA.
- Substantial vulnerability to severe outcomes remains in all EU/EEA countries (given the estimates of waning of immunity and immune escape of Omicron).
- Vaccination against COVID-19 and boosters reduce hospital admissions and deaths.
- Hospitalisations and mortality are expected to have a proportionally greater impact on people aged 60 years or older but will impact people younger than 60 years as well.
- Infections may still spread from younger, less vulnerable populations to older, more vulnerable populations once a larger share of the population is exposed to Omicron. This could impact on hospitalisation rates observed up to this point in the Omicron wave.
- Countries can protect the group at highest risk of severe outcomes through increased coverage of vaccination and vaccine boosters.
- Additional potential longer-term benefits of vaccines and boosters for people and society (i.e., preventing absence from work and education, post-COVID-19 syndrome) should be considered.
- These results raise concerns that if there is a high burden of hospital admissions in a short amount of time, hospital capacity and quality of care might be compromised, which may lead to a higher excess mortality.
- New and ongoing studies of high quality on the current sero-epidemiological situation in different EU/EEA countries and the duration of immunity following Omicron infection will be crucial to understand the susceptible population going forward.

The modelling work presented here complements the findings and insights of the ECDC risk assessment and the general conclusions and messages from the previous risk assessment remain valid [7].

Towards an exit strategy, and long-term considerations

Significant uncertainties remain at this stage of the COVID-19 pandemic. Better understanding is required about the waning of natural immunity as well as vaccine-induced immunity, and the extent of protection over time against different variants. In addition, in the context of high global levels of SARS-CoV-2 circulation and the propensity for new variants to emerge, it is generally acknowledged that SARS-CoV-2 is here to stay – the future 'new normal' world will involve COVID-19 [115,116]. Going forward, therefore, it will be essential to continue to monitor for new variants and to identify and address relevant knowledge gaps, through the development of coordinated, multi-layered surveillance, preparedness, and response strategies for addressing COVID-19, and through the funding of appropriate research.

There is growing recognition that while the extensive preventive measures mandated across the EU/EEA over the past two years have contributed to reductions in COVID-19-related mortality and the burden on health services, they have also exacted heavy societal and economic costs [117,118]. Since many EU/EEA countries currently have or are approaching high levels of population immunity (through vaccination and/or through natural infection), now may be the time to consider adapting the broad strategy for addressing the pandemic, from one focused on managing transmission of SARS-CoV-2 to one that aims to manage outcomes of COVID-19. For this, countries will need to balance what, on the one hand, they consider to be an acceptable level of COVID-19 hospitalisation and mortality, against what, on the other hand, is an acceptable level of NPIs, given their societal impact. In order to successfully effect this transition into what may be a post-acute phase of the pandemic, ongoing efforts should ensure that all eligible people are given access to COVID-19 vaccination. Plans are also needed for sustainably protecting vulnerable people for whom vaccination (including booster dose) may not provide strong protection.

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 [119].

Risk assessment question

What is the risk to public health posed by the continued spread of Omicron in the EU/EEA, considering the current high and increasing incidence, the overall severity on a population level, and the particular risks for unprotected populations?

Risk assessed for the EU/EEA as a whole

Omicron is currently the dominant variant in several EU/EEA countries. In some of these countries, the peak of incidence appears to have been reached recently. Omicron is expected to become dominant and to peak in all other EU/EEA countries in the coming weeks, with this dominance progressing, from the west to the east of the continent. The combination of higher growth rate and immune evasion have contributed to the steady increase in the proportion of cases caused by Omicron, and the potential replacement of the previously dominant Delta variant.

The overall 14-day **case notification rate** in the EU/EEA has been rapidly increasing in the past four weeks and reached 2 621 per 100 000 population by the end of week 2-2022 during the current wave, which represents a **four-fold increase** (+314%) when compared with the peak in the overall 14-day case notification rate during the previous wave (Delta VOC) (634 per 100 000 population by the end of week 45-2020).

The 14-day **death rate** has been stable for the last eight weeks and reached 62 per 1 000 000 population by the end of week 2-2022 during the current wave, which represents a **decrease of almost half** (-47%) when compared with the peak in the overall 14-day death rate during the previous wave (117 per 1 000 000 population by the end of week 48-2020).

At the end of week 2-2022, the cumulative **uptake of full COVID-19 vaccination** in the EU/EEA was 69.4% (country range: 28.4–82.9%) in the total population.

Due to the very high circulation of Omicron in most EU/EEA countries, the **probability of infection** for the EU/EEA population in the coming weeks is considered to be **VERY HIGH**.

As outlined in the modelling section, the potential disease burden on healthcare systems remains large, compounded by staff absences in all sectors and shortages of healthcare workers. A lag of several weeks can be expected in the reporting of hospitalisations, intensive care unit (ICU) hospitalisations and deaths by COVID-19, as in all previous waves. These metrics will reflect the Omicron wave in the EU/EEA countries, which started in late December 2021, from the end of January 2022 onwards. In addition, due to the much higher prevalence of COVID-19 in the community, hospitalisations are probably not an appropriate indicator of health system pressure anymore; focus should rather remain on the ICU coverage.

The vaccination coverage represents an important factor when assessing the impact of Omicron. Countries where COVID-19 vaccination coverage for the full primary series is lower than 75% in the total population and where the uptake of booster doses among at-risk individuals is suboptimal, will experience a much **higher impact**. Of **particular concern** are countries where vaccine uptake among risk groups has remained low and where Omicron infection has not yet reached its peak. Depending on the situation in countries, the exponential rise in cases is expected to have a **HIGH** to **VERY HIGH** impact in terms of disease burden, pressure on society and strain on healthcare systems through increased hospitalisations and staff absences across different sectors, including among healthcare workers in the immediate coming weeks.

- In counties where COVID-19 vaccination coverage for the complete primary series is higher than 75% in the total population and there is substantial uptake of booster doses among at-risk individuals, ECDC modelling results indicate that while sustained circulation of Omicron continues the incidence of cases in the community can still result in severe infections among fully vaccinated people belonging to high risk groups, with a **HIGH** impact on healthcare and society. For these countries the impact is assessed as **HIGH**.
- Countries where COVID-19 vaccination coverage for the complete primary series is lower than 75% in the total population and where the uptake of booster doses among at-risk individuals is suboptimal, will experience a higher impact. More disruption is expected in their public health system from the surge of positive cases, overwhelming of the contact tracing and testing capacities, and increased hospitalisations, particularly if risk groups have low vaccine uptake. Absence from work is also expected to affect several sectors besides the health system particularly due to the lower vaccination coverage. For these countries the impact is expected to be **VERY HIGH**.
- Based on the factors outlined above and considering the different epidemiological situations in EU/EEA countries, the overall public health and societal risk posed by the ongoing spread of Omicron in the EU/EEA is assessed as **HIGH to VERY HIGH**.

Taking into consideration the above parameters, the risk to public health for the coming weeks includes potentially the following: pressure on testing capacity, decreased capacity to contact trace even high-risk outbreaks, increasing hospitalisations due to the extremely high number of cases, absence among public health and healthcare staff. However, experience to date of the spread of the Omicron wave points to significant impact and therefore risk to the business continuity within several sectors (e.g. the education system, law enforcement etc.) due to high rates of absence from work.

Options for response

Vaccination

Vaccination is a key component of the multi-layered approach needed to reduce the impact of Omicron in the EU/EEA, while at the same time addressing the ongoing circulation of the Delta variant. Unvaccinated and partially vaccinated people remain at much higher risk of severe outcomes compared to people with a complete primary series [120,121], therefore vaccination of all eligible population remains critical for the control of the impact of the COVID-19 pandemic. While significant waning of immunity against infection and symptomatic disease have become evident some months after full vaccination with two doses of COVID-19 vaccine [122], and this has been further worsened with the emergence of Omicron [46], vaccine effectiveness against severe disease, hospitalisation, ICU admission and death has been more sustained despite the waning [78,82,120]. The administration of a booster dose of COVID-19 vaccine has proven to be able to restore much of the protection acquired from the initial doses of COVID-19 vaccines against outcomes due to Delta [123,124]. However, the emergence of Omicron , with its vaccine escape potential, has partly reduced this added protection from the booster dose against all COVID-19 outcomes, and has reduced its duration against infection and symptomatic disease [25]. However, the protection against severe COVID-19 outcomes from Omicron infection still seems strong several weeks after the booster dose, unlike the protection against milder COVID-19 outcomes (i.e. infection) [120].

Based on these considerations and on the evidence currently available, the priority continues to be the vaccination of all eligible people who are currently unvaccinated and the protection with a booster dose of all vaccinated people who are at risk of severe COVID-19 (i.e. older adults, people with underlying conditions, pregnant women) or who are at high risk of exposure to the virus due to their activities or living conditions (i.e. healthcare workers, people living or working in closed settings, vulnerable groups). Additionally, due to the current Omicron wave, all other eligible vaccinated adults should also consider rapidly getting a booster shot, according to national

recommendations and not earlier than three months from completing the primary vaccination series, to reduce their individual risk of infection and of disease. This will also increase their individual protection against other circulating variants of concern like Delta. Relevant approaches to facilitate and sustain COVID-19 vaccine acceptance and uptake should continue to be implemented as outlined in the previous risk assessment from December 2021 [7].

Non-pharmaceutical interventions

Maintaining of non-pharmaceutical interventions

NPIs should continue to be implemented by all countries, based on the increasing numbers of Omicron cases in the community, and tailored according to the local epidemiological situations and the pressure on healthcare and other essential services [88]. Preventing crowding in public spaces, recommending teleworking, reduction of crowding on public transport, staying home when ill, ensuring adequate physical distancing, and maintenance of hand and respiratory hygiene measures all remain a priority, together with good ventilation. Overall, the key to NPI effectiveness is in community engagement and the prompt implementation of these measures when incidence rises. More information on specific NPIs can be found in the 17th update of ECDC's rapid risk assessment on SARS-CoV-2 [125].

Face masks in the community

In areas with community transmission of COVID-19, wearing a medical face mask, a respirator or a community face covering ('non-medical face mask') complying with available guidelines for filtration efficacy and breathability is recommended in transportation hubs (i.e. ports, airports, train/coach stations), closed public spaces (such as stores, supermarkets and public transport) and in general in any crowded settings, even outdoors.

Selecting the type of face mask should take into account access, availability and tolerability in addition to effectiveness. Based on experimental efficiency data [126-128] and given the lack of high-quality evidence from clinical trials, respirators, are in general expected to be more effective than medical masks while on average non-medical masks are expected to be less effective than both, especially if not constructed in accordance with available EN standards for filtration efficacy and breathability [129].

The appropriate use of properly fitted face masks is important. The face mask should completely cover the face from the bridge of the nose down to the chin. The mask should be correctly adjusted on the bridge of the nose and to the face to minimise open space between the face and the mask.

The choice of suitable respirator for the shape of a user's face (type and size) and performing a pre-use seal check are important requirements to ensure maximum protective effectiveness [130]. The seal check should be repeated every time a user puts on the respirator. In the community, due to difficulties to ensure appropriate use and fitting of respirators, any possible added value of respirators in preventing respiratory infections is expected to be lower than in healthcare settings.

When community face coverings ('non-medical face masks') are used, it is advisable that those that comply with available minimum requirements for filtration efficacy and breathability are used, i.e. CWA 17553 from the European Committee for Standardisation (CEN) [129].

Contact tracing and quarantine of contacts

When resources allow, countries are recommended to follow the ECDC contact tracing guidance [131]. Additional information and publications related to contact tracing can be found on the ECDC contact tracing website [132].

Testing capacity has been reportedly overwhelmed in some areas and the use of self-tests has increased. Public health authorities can consider providing the public with information about how to notify their contacts in case of a positive self-test at home and they should put effort to maintain capacity for contact tracing in high-risk settings (e.g. LTCFs or closed settings).

Isolation

Due to the extremely high number of cases, people with COVID-19 should be instructed to self-isolate upon a positive self-test result, even if confirmation is not possible due to strained testing capacity. Isolation of COVID-19 cases can be discontinued based on the following criteria: a) clinical resolution of symptoms; b) time elapsed since onset of symptoms; c) disease severity; d) immune status; e) occupational status; f) social mixing factors; and/or g) evidence of negative RADT or RT-PCR test(s) from the upper respiratory tract. Ending isolation in a regular situation requires testing performed by a trained professional.

Pragmatic options for adapting quarantine and isolation rules

Countries may consider shortening the duration of quarantine and isolation with or without requiring a negative test to end them, particularly when they face high or extreme pressure on healthcare systems and other functions in society, including essential services. Due to the rapid spread of Omicron, ECDC has published options based on a pragmatic approach, taking into account the need to uphold critical functions in society [133]. Decisions to adapt

the duration of quarantine and isolation require consideration of the residual risk of transmission particularly in certain settings (e.g. healthcare, LTCFs), the local epidemiological situation, the testing and contact tracing capacity and the socio-economic effects of the pandemic in the specific setting. Additional information can be found on the contact tracing webpage [132] and on the guidance on quarantine and isolation webpage [133].

Increase of healthcare system preparedness and hospital surge capacity

Omicron is exerting enormous pressure on healthcare systems around Europe through a combination of increased admissions and high numbers of staff being infected. Recent UK data show a steep increase in infected cases among healthcare workers (HCW) since mid-December 2021 [120]. Healthcare workers on sick leave exacerbate the already significant staff shortages following the pandemic fatigue and burn out. Maintaining an adequate ratio of staff to patients, especially in the ICUs, is critical to maintaining patient safety and quality of care. Currently, several countries face a serious staffing crisis and have deployed medical students, physicians working in the private sector and military personnel to help overstretched hospitals. Many healthcare systems postpone elective operations and non-urgent medical appointments, while the management of other emergencies and chronic conditions may be also negatively impacted.

Due to the high circulation in the community, it is also expected that a number of hospitalised cases will be detected as incidentally positive for COVID-19. Ensuring infection prevention and control measures adherence is essential, particularly in the busy hospital units with high levels of bed occupancy and staff shortages. Mitigation efforts and control measures should be accompanied by reinforcement of healthcare systems, support of HCWs, and strengthening of infection prevention and control measures.

As the strain on healthcare systems is expected to continue in the coming weeks, actions to alleviate the staffing crisis should be taken, which may include appropriate adjustment of isolation periods, ideally with appropriate testing strategies to support early release and continuous vigilance to promptly identify nosocomial clusters. This is essential to provide a safe work environment for HCWs and safe patient care. Emphasis should be given to primary care as a first healthcare provider contact of infected people avoiding the influx to hospital emergency departments.

Testing

Testing strategies should be flexible and rapidly adaptable to the epidemiological situation and available resources.

Diagnostic testing

Diagnostic testing - i.e. testing of people with symptoms compatible with COVID-19, or asymptomatic people with high risk exposure (contact tracing) - remains key to identifying COVID-19 cases, offering appropriate treatment, particularly as new therapeutic options become available, and putting in place preventive measures that will effectively prevent further transmission (i.e. isolation). Diagnostic testing should be done in both vaccinated and unvaccinated people.

For diagnostic purposes, in the current high prevalence situation, the positive predictive value of RADTs is high and therefore there is less need to confirm positive results by a second method. Please refer to the RADT document for defining the PPV/NPV in the different settings and prevalence situations [100].

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. Multiplex RT-PCR assays for respiratory viruses are used in many settings and are indicated for the diagnosis of respiratory infections in hospitalised patients. When available, it would be useful to also include SARS-CoV-2 as well as other respiratory viruses in the diagnostic method for earlier virus detection and limit the spread in the healthcare settings. When testing capacity is severely limited, priority should be given to hospitalised patients, older people, and high-risk groups and HCWs.

Screening testing

Screening testing is done in asymptomatic people when infection may endanger populations that can be highly exposed (i.e. healthcare workers) or when outbreaks could be particularly disruptive for society (i.e. in schools).

The current very high circulation of Omicron in the community will most probably lead to similar concerning increasing trends within the healthcare settings, threatening both hospitalised patients, particularly those who are medically at high risk, and healthcare workers. Nosocomial Omicron spread will result in worse patient outcomes and further reduction in the healthcare work force. Therefore, priority should be given for testing in healthcare settings to enhance protection for healthcare workers and patients. In areas with high community transmission, screening with RADT of all patients admitted to hospital on admission and at regular intervals during the hospital stay is a strategy for the timely detection and isolation of cases to minimise onward transmission, especially to patients with high-risk factors for severe COVID-19 and staff. Regular testing of staff should also be considered for the same reason. When deciding on the intervals for regular screening, availability of tests should be taken into account.

RADTs can also be used for screening and serial testing (every two to three days) of residents and staff working in home care, long-term care facilities, closed settings (i.e. prisons, migrant detention and reception centres) and occupational settings in areas in which there is ongoing community transmission [134]. A modelling study showed that outbreak control depends largely on the frequency of testing, the speed of reporting, and the application of interventions, and that it is only marginally improved by the sensitivity of the test [135]. Additional evidence showed that serial antigen testing every three days, or twice per week, will almost always identify SARS-CoV-2 during early stages of infection, and thus significantly reduce disease transmission [136]. Thus, if resources allow, serial antigen testing is a potentially important public health practice along with other prevention strategies in these settings.

Self-tests, if appropriately performed and if used in serial testing, can rapidly identify infectious cases [137]. They should, however, not be used for any formal certificate. In the current high prevalence situation, associated with high Positive Predictive Value of RADTs, an individual should self-isolate upon a positive self-test result, even if confirmation with a second test is not possible due to limited resources. Negative self-test results of people who are symptomatic and/or high-risk contacts of cases need to be confirmed by another laboratory-based method (RADT or RT-PCR), particularly for those working with vulnerable people, subject to testing capacity.

Testing for surveillance purposes

The rollout of new tests, and especially those that may not be captured by surveillance systems such as self-tests, may distort surveillance indicators [138]. In October 2021, ECDC published COVID-19 surveillance guidance inviting countries to transition from emergency surveillance for COVID-19 to more sustainable, objective-driven, surveillance systems [139]. Among the main messages, ECDC suggested testing and reporting a representative subset of symptomatic cases, preferably by RT-PCR, if comprehensive testing of all those presenting with symptoms is not feasible. Countries should focus on reporting symptomatic cases, i.e. cases that have been tested because of experiencing COVID-19 compatible symptoms, as this will improve comparability [139]. Genomic surveillance remains of importance to enable early detection of VOCs, monitoring of epidemiological trends and to guide measures.

For further information on methods for the detection and characterisation of SARS-CoV-2 variants (including Omicron), please refer to the chapter on laboratory testing above and to the recently updated guidance developed by technical experts from ECDC and the WHO Regional Office for Europe and reviewed by experts at WHO's referral laboratories and members of the SARS-CoV-2 Characterisation Working Group [101].

ECDC has also published the following relevant documents on testing for SARS-CoV-2:

- ECDC's Guidance for representative and targeted genomic SARS-CoV-2 monitoring [111];
- ECDC's COVID-19 surveillance guidance [139];
- Webpage - Diagnostic testing and screening for SARS-CoV-2 [140], September 2021;
- Webpage - Testing strategy for SARS-CoV-2 [141], September 2021.

Schools

Children, notably those under 12 years, remain largely unvaccinated against COVID-19 in the EU/EEA countries. As of week 2, 2022, the uptake of a complete primary series of COVID-19 vaccines among children below 10 years of age in EU/EEA countries is still very low (median:0.1%; range: 0-12.1%; pooled data from 17 countries reporting). The median uptake of the primary series among children and adolescents 10-14 and 15-17 years of age is 34.1% (range: 2.9-60.8%) and 69.4% (range: 17.3-88.1%) respectively (17 countries reporting). All 30 EU/EEA countries currently recommend vaccinating adolescents 12-17 years old, and following EMA authorisation of the paediatric formulation of Comirnaty a number of EU/EEA countries are now also recommending vaccination for all children aged 5-11 years [142]. Modelling data from the Delta period indicated that vaccinating children aged 5-11 years could reduce SARS-CoV-2 transmission in the whole population by approximately 11% (range 8-15% depending on country-specific vaccination uptakes of 30-70%) for a country with a level of vaccine coverage equivalent to the EU/EEA average, although the extent and duration of this protection is currently unknown. The impact of vaccinating children is weaker for countries with a low adult vaccine uptake and stronger for countries with high uptake among adults [143]. However, these modelling data may not apply to Omicron, due to its much higher rate of vaccine escape.

The negative impacts on child health and development mean that schools should only be closed as a last resort measure. However, with continued very high community transmission, the likelihood of transmission in school settings or their broader communities is significantly increased. This in turn increases the likelihood for abnormally high levels of staff and student absence. Thus, mitigation measures in schools remain absolutely essential to ensure that schools can remain safely open for all children and staff over the course of the COVID-19 pandemic. Vaccination and booster dose coverage for school staff should be as close to 100% as possible. Maintaining physical distance, reducing class sizes, staggering activities, improving ventilation, adequate cleaning of school environment, promoting hand hygiene and respiratory etiquette, staying home when symptomatic and getting tested are key measures to prevent SARS-CoV-2 transmission in schools.

Routine COVID-19 testing of school children and staff may be considered as part of a comprehensive in-school prevention strategy, to identify and stop transmission early, thereby reducing the risk of wider staff and student

absence. There is a growing body of evidence describing the added value of systematic in-school testing of students and staff. Where testing capacity is available and can be scaled up this should be considered, particularly in communities with high positivity rates or in response to outbreaks in the school. Meanwhile, 'test-to-stay strategies' allow students with a school exposure to remain in class as an alternative to home quarantine. Testing-to-stay does not appear to increase transmission risk in schools and has the potential to greatly reduce the loss of in-person school days, in particular when implemented alongside other mitigation measures [144-148]. RADTs can contribute to overall SARS-CoV-2 testing capacity, offering the advantage of shorter turnaround times and reduced costs, especially in situations where PCR testing capacity is limited [101]. During periods of high community transmission and testing capacity constraints, RADTs should be strongly considered as an effective option for helping to enable schools and classes to remain open.

Risk communication

Public perceptions and misinformation about Omicron

The rapid shift in dominance within the EU/EEA from Delta to Omicron has been accompanied by renewed uncertainty. Once again, the pandemic has produced a situation in which we are less knowledgeable about the immediate threat than we were just a few months ago, except with regard to Omicron's growth advantage over Delta, which was recognised as very high almost as soon as it emerged.

Findings from several surveys have indicated that the rapid increase in Omicron cases in the EU/EEA has brought about an increase in people's reported motivation to follow preventive measures [149,150]. A recent study in Germany found that people who are aware of the possibility for Omicron to infect vaccinated people, and to overburden health systems, were more likely to accept the recommended preventative measures [151]. However, this acceptance of the measures has been accompanied by a simultaneous decrease in the population's perception that the measures are actually effective against Omicron infection [149-152]. These apparently contradictory responses may point to a degree of fatalism, whereby people want to avoid infection, but they are not sure if they will be able to do so [149,150].

The inevitable information voids that accompany a new VOC facilitate the emergence and spread of misinformation, which can include unfounded assumptions (as per current scientific understanding) that may or may not end up being correct. One of these assumptions is the speculation that Omicron represents essentially the end of the pandemic, after which we will be able to return to 'normal', albeit with COVID-19 as an endemic virus and an accepted risk [153]. With high rates of reported pandemic fatigue and depression in several settings, and accompanying decreases in population wellbeing [149,150], it is not unexpected that people simply want to wish their way out of the current situation.

Given this, it is important for authorities to offer hope to an exhausted population based on facts rather than on speculation. Risk communication activities should also vigorously continue to promote (i) vaccination against COVID-19; and (ii) continued adherence to the preventive measures mandated or recommended by national authorities.

Communication on COVID-19 vaccination

The current situation poses particular challenges for communication on the importance of vaccination. The evolving evidence regarding Omicron's potential for immune escape, the duration of protection and vaccine effectiveness against different outcomes, as well as the related adjustments in vaccine recommendations, may contribute to confusion and questions from the public. Strengthened efforts are needed to clearly communicate that vaccines continue to play a very important role in preventing severe disease, hospitalisation and death, that boosters increase protection [120], and that unvaccinated people remain at much higher risk of severe outcomes compared to vaccinated people [120,154,155].

Debates regarding a possible need for repeated boosting, or expectations on 'variant-adapted' vaccines need to be carefully monitored, so that potential concerns and expectations can be addressed. Such debates may lead some people to prefer to wait for an adapted vaccine [156]. Further, mentions of a possible need for recurrent vaccination within short timeframes could potentially confuse people and affect their willingness to continue to get vaccinated [157]. It is important to remind people that completing the primary vaccination series and getting the booster as per national recommendations is needed now [158]. To address current speculation, the uncertainties at this stage regarding possible future vaccination strategies need to be acknowledged [159].

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. Several of the cited studies in the assessment are only available as preprints that have not yet been peer-reviewed. In particular, there are many scientific uncertainties and knowledge gaps regarding Omicron, including:

- 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.
- Limited availability of epidemiological data from several countries.
- Limited understanding of whether the different Omicron sub-lineages are associated with any significant differences in transmissibility, antigenic properties or infection severity.
- 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 the different vaccines against Omicron (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.
- Uncertainty about the duration of protection against severe disease following a booster shot overall and by risk group.
- Uncertainties regarding impact of Omicron to post-COVID-19 condition and Multisystem Inflammatory Syndrome in Children.
- Uncertainties on the clinical performance of different test formats for Omicron.

Source and date of request

ECDC internal decision, 18 January 2022.

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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

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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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Annex 1. 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	Omicron B.1.1.529
					BA.1	BA.2
ΔH69-V70	x				x	
ins214EPE					x	
S371L/S373P					x	
S371F/S373P						x
N501Y	x	x	x		x	x
K417T			x			
K417N		x			x	x
E484K		x	x			
E484Q	(x)					
E484A					x	x
P681H	x				x	x
P681R				x		
T478K				x	x	x

** List not exhaustive*.

IMPORTANT NOTE: Primer/probe mismatches at neighbouring sites in Omicron (or other) variants 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 2. 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 people 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 [160-162].

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 people. 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) [163].

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-titre reference serum (20/150) should be used for neutralisation assays [164-166]. 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 neuralisation assays [167,168].

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