RAPID RISK ASSESSMENT

Assessment of the current SARS-CoV-2 epidemiological situation in the EU/EEA, projections for the end-of-year festive season and strategies for response, 17th update

24 November 2021

Summary

Increases in case notifications, hospitalisations and intensive care unit (ICU) admissions for SARS-CoV-2 have been observed in October and early November in the majority of EU/EEA countries, after a period of decline in August and September 2021. This has been driven by circulation of the Delta variant (B.1.617.2) in the context of insufficient vaccine uptake and widespread relaxation of non-pharmaceutical interventions (NPIs). Whilst the burden from COVID-19 is particularly high in a number of countries experiencing low vaccine uptake, there is evidence of rising burden even among countries with higher uptake. The current epidemiological situation is to a large part driven by the high transmissibility of the Delta variant that counteracts the reduction in transmission achieved by the current vaccination rollout in the EU/EEA.

To date, 65.4% of the total population and 76.5% of the adult population in the EU/EEA have been fully vaccinated against COVID-19. The overall pace of weekly increase in vaccine uptake in the EU/EEA is slowing down and is mostly driven by the rollout in younger age groups. Four countries are still reporting less than 50% of full vaccine uptake in the total population. Vaccination continues to successfully avert deaths, reduce hospitalisations and transmission in the EU/EEA, despite the emergence and continued dominance of the Delta variant, which is up to 60% more transmissible than the previously dominant variant, Alpha (B.1.1.7).

Available evidence emerging from Israel and the UK shows a significant increase in protection against infection and severe disease following a booster dose in all age groups in the short term. All EU/EEA countries have begun administration of 'additional dose' vaccination (to better protect individuals who mount inadequate immune responses to the primary schedule) and 'booster' vaccinations (to improve protection in individuals for whom immunity may wane over time since completing the primary schedule).

The end-of-year festive season is traditionally associated with activities such as social gatherings, shopping and travelling, which pose significant additional risks for intensified transmission of Delta.

Modelling scenarios that consider vaccine uptake (including 'additional dose' and 'booster' vaccinations), vaccine effectiveness, waning vaccine-induced immunity, vaccination of children, natural immunity and population contact rates, indicate that the potential burden of disease risk in the EU/EEA from the Delta variant is expected to be very high in December and January, unless NPIs are applied now in combination with continued efforts to increase vaccine uptake in the total population.

Modelling forecasts highlight the need for NPIs as an immediate measure to control transmission, in combination with rollout of vaccine booster doses for adults, which should be prioritised for those aged 40 years and over, at least six months after completing a primary vaccine schedule. Booster doses will sustain transmission control beyond the immediate impact of implementing NPIs.

Suggested citation: European Centre for Disease Prevention and Control. Assessment of the current SARS-CoV-2 epidemiological situation in the EU/EEA, projections for the end-of-year festive season and strategies for response, 17th update – 24 November 2021. ECDC: Stockholm; 2021.

Risk assessed in this update

Based on current vaccination coverage and the circulation of the Delta variant in the EU/EEA, what risk does SARS-CoV-2 pose to the general and vulnerable population?

We assess the risk to broad groupings of EU/EEA countries based on their current and projected levels of vaccination coverage for the total population. Through mathematical modelling, we forecast the disease burden (hospitalisations and deaths) between 1 December 2021 and 31 January 2022. The assessment of risk posed by the SARS-CoV-2 pandemic is further stratified for the following groups in the total population: the vaccinated and the unvaccinated general population; the vaccinated and the unvaccinated vulnerable population. The assessment is based on the following elements: i) the vaccinated have a lower probability of infection and ii) a lower impact of such infection than the unvaccinated, while iii) the vulnerable population suffers a higher impact if infection occurs, when compared with the general population. Based on modelling projections, virus circulation and disease burden between 1 December 2021 and 31 January 2022, the following can be anticipated:

- In order to avoid a high COVID-19 burden, countries with a low (<60%) or average (60-80%) vaccine uptake for the total population will require substantial reductions in contacts between people to avoid a high burden from SARS-CoV-2 transmission. For countries that are currently experiencing high COVID-19 burden, high contact reductions can achieve a manageable burden towards the end of the December-January period.
- Countries with higher (>80%) vaccine uptake for the total population could experience a manageable burden at current contact rates. However, this burden could become high if contact rates increase further, as might be expected given the end-of-year festive season.
- Because vaccines offer high protection against severe outcomes of COVID-19 infection, a large number of COVID-19 hospital admissions will be unvaccinated individuals, in particular unvaccinated individuals in risk groups. However, since vaccine effectiveness against severe disease is not 100%, increased notification rates will also lead to an increased number of vaccinated individuals experiencing severe forms of disease requiring hospitalisation. Together with waning immunity over time from vaccination, this explains the proportion of vaccinated individuals among hospitalised COVID-19 patients in some countries with high vaccine uptake.

Options for response

The current average level of vaccine uptake in the EU/EEA will be insufficient to limit the burden of COVID-19 cases and hospitalisations over the winter months.

Countries are urged to give utmost priority to individuals initially targeted by COVID-19 vaccination programmes that remain unvaccinated or not yet fully vaccinated. Increasing COVID-19 vaccination coverage in all eligible age groups, but particularly in the elderly, in the vulnerable, and in healthcare workers should remain the priority for public health authorities. There remains an urgent need to close immunity gaps in the adult population and ensure effective and equitable coverage across countries and regions in Europe.

National Immunisation Technical Advisory Groups (NITAGs) in EU/EEA countries should consider a booster dose for those 40 years and over, targeting the most vulnerable and the elderly. Countries could also consider a booster dose for all adults 18 years and older at least six months after completion of the primary series to increase protection against infection due to waning immunity, which could potentially reduce transmission in the population and prevent additional hospitalisations and death.

Given that pressures to healthcare systems may arise due to co-circulation of other respiratory viruses, NPIs should be implemented or reinforced now, with efforts to communicate the importance of these measures early, to reduce contacts and mixing during the end-of-year festive season.

At this stage, even in countries with high vaccine uptake, maintaining or reintroducing NPIs remains vital to reduce transmission. Timely implementation of NPIs is critical for their success. Appropriate use of face masks, teleworking and operational modifications that reduce crowding on public transport, along with ensuring adequate ventilation in closed spaces and maintenance of hygiene measures that can be implemented immediately. Setting limits for the number of participants in social and public events during end-of-year celebrations will support physical distancing efforts. Once implemented, countries should anticipate that NPIs may need to be retained for a prolonged period of time after the festive/holiday period, at levels that adequately complement vaccination protection, in order to effectively control virus circulation.

Risk communication activities should emphasise the continued importance of hygiene measures and avoidance of unnecessary crowding to the control of virus circulation, particularly as countries work towards increasing vaccine uptake. Messaging should also stress the importance both COVID-19 and influenza vaccines play in protecting people against severe forms of disease.

Given the continued risk of transmission amongst children, high levels of prevention and preparedness are required in the educational system.

Testing, contact tracing, and monitoring and reporting of COVID-19 cases, hospitalisations, deaths and vaccine effectiveness remain vital to guide decisions on public health measures and to understand their impact. In light of the co-circulation of other respiratory viruses (e.g. influenza and respiratory syncytial virus (RSV)), multiplex assays should be considered for testing of several respiratory pathogens simultaneously.

Genomic sequencing of positive samples remains of high importance to characterise currently circulating variants, and to detect the emergence of novel variants with concerning characteristics.

What is new in this assessment?

This Rapid Risk Assessment assesses the risk posed by the circulation of the Delta variant of SARS-CoV-2 between 1 December 2021 to 31 January 2022, based on modelling scenarios and projected levels of vaccination coverage.

Updated forecasts developed for this risk assessment are informed by the latest evidence on SARS-CoV-2 seroprevalence, COVID-19 vaccine effectiveness, and waning vaccine immunity, which are also presented.

Event background

Since 31 December 2019 and as of week 2021-45, 254 053 508 cases of COVID-19 have been reported worldwide, including 5 111 187 deaths. As of week 2021-45, EU/EEA countries have reported 42 872 622 cases and 822 614 deaths due to COVID-19, representing 16.9% of all cases and 16.1% 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. The timeline of the major events in the COVID-19 pandemic can be found on ECDC's website: https://www.ecdc.europa.eu/en/covid-19/timeline-ecdcresponse.

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

Detailed epidemiological information on laboratory-confirmed cases reported to The European Surveillance System (TESSy) is published in ECDC's weekly COVID-19 surveillance report: https://www.ecdc.europa.eu/en/covid-19/surveillance/weekly-surveillance-report.

The overview of the epidemiological situation in relation to the COVID-19 pandemic, by EU/EEA country, is published in ECDC's weekly COVID-19 country overview: http://covid19-country-overviews.ecdc.europa.eu.

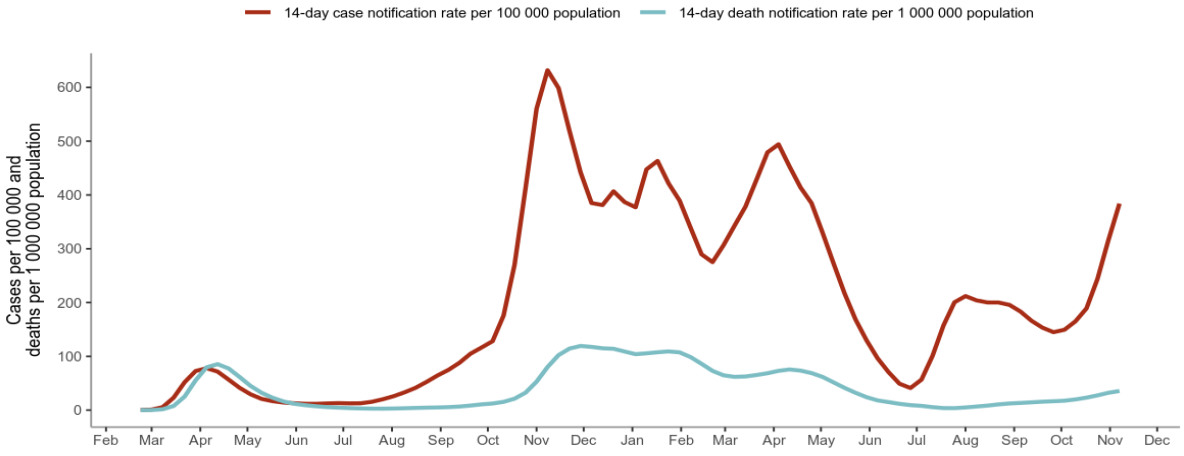
The latest available data on the number of COVID-19 vaccine doses administered in the EU/EEA reported to TESSy are available on ECDC's website: https://vaccinetracker.ecdc.europa.eu/public/extensions/COVID-19/vaccinetracker.html#uptake-tab

The latest available data on COVID-19 in long-term care facilities (LTCFs) are available on the ECDC's website: http://covid19-country-overviews.ecdc.europa.eu/#1_Introduction

Trends in epidemiological indicators and vaccine uptake

At the end of week 44 (week ending Sunday 7 November 2021), the overall epidemiological situation in the EU/EEA was characterised by a high and rapidly increasing overall case notification rate and a slowly increasing death rate (Figure 1). Of 27 countries with data on hospital or ICU admissions or occupancy up to week 44, 24 reported an increasing trend in at least one of these indicators compared to the previous week. Case notification rates were highest among age groups under 50 years old, but rates among older age groups have been rapidly increasing.

Figure 1. 14-day COVID-19 case and death notification rates in the EU/EEA to week 44, 2021

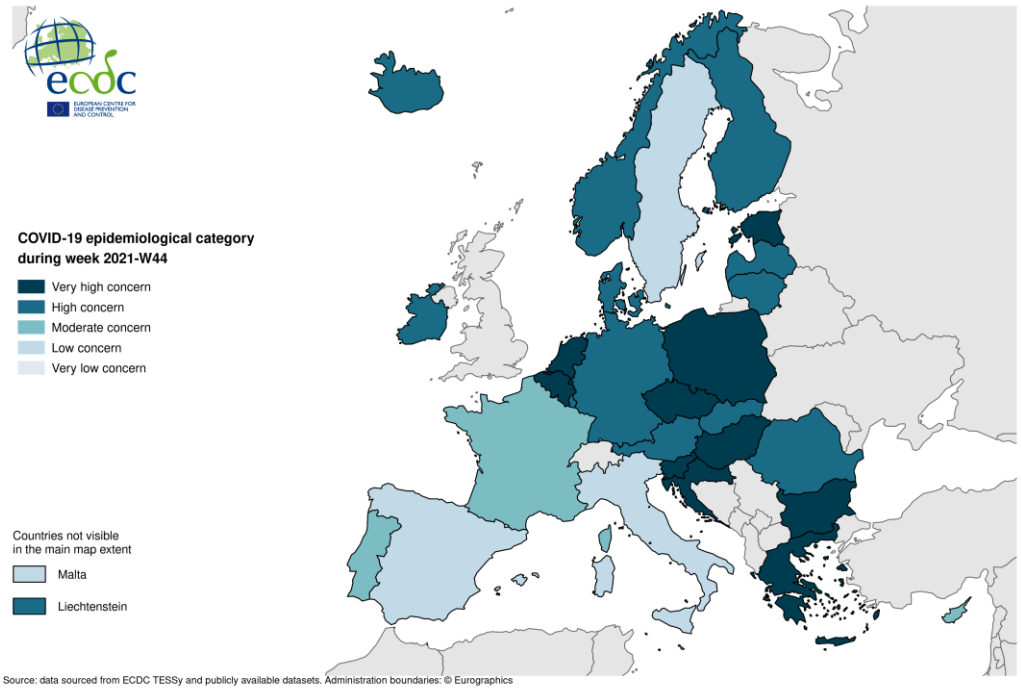


ECDC. Figure produced on 11 November 2021
Source: Epidemic intelligence national data and TESSy COVID-19

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

ECDC assesses each country's epidemiological situation weekly 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 summed up to provide an overall score from 1-10, which is split into quintiles to derive five categories. Although the picture in week 44 varied considerably between countries, the overall epidemiological situation was of high or very high concern in 23 of the 30 EU/EEA countries (Figure 2).

Figure 2. COVID-19 epidemiological categorisation of EU/EEA countries week 44, 2021



Source: data sourced from ECDC TESSy and publicly available datasets. Administration boundaries: © Eurographics
The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on 16 November 2021

The epidemiological situation has deteriorated in most EU/EEA countries in recent weeks. Overall, countries with lower vaccination coverage and with a slower pace of vaccine rollout tend to be those with the highest composite epidemiological scores, corresponding to a more concerning situation. However, uptake of full vaccination in the total population has started to plateau in many countries, and a worsening epidemiological situation is observed even among countries that have some of the highest uptake in the EU/EEA (Figure 3).

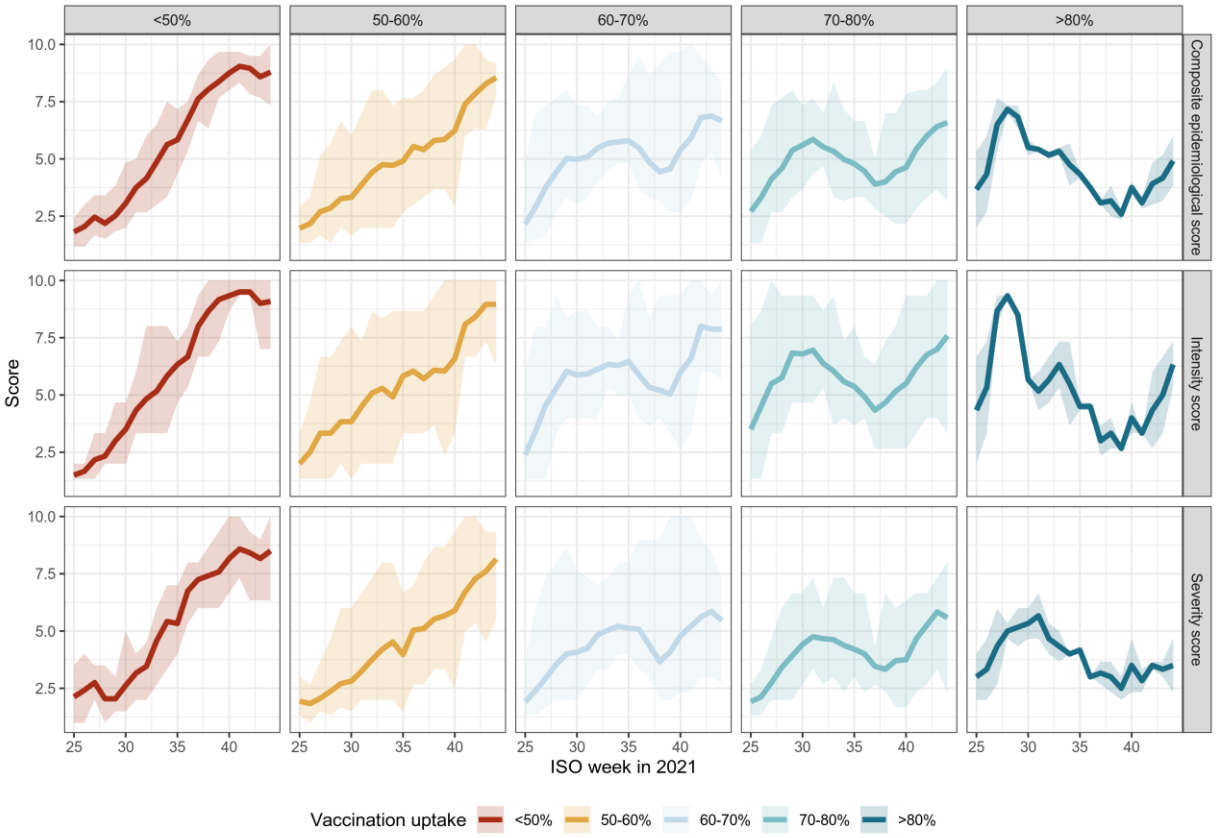
Figure 3. Composite COVID-19 epidemiological score by week, cumulative vaccine uptake for the total population by country, in descending order of vaccine uptake, weeks 25-44, 2021

We assigned countries to five categories based on their current (as of week 44, 2021) cumulative uptake of full vaccination in the total population, then calculated the mean and range of each group's weekly epidemiological score for the period 25 to 44. This was done for the composite score and the scores of the individual intensity and severity domains to see how the trends and levels of each component differed according to vaccine uptake (Figure 4). In general, the mean composite score of the last four weeks was higher with each decreasing category of vaccine uptake below 70%. Countries with uptake below this level have observed a steady increase in the mean composite score since week 28 or earlier, whereas those with uptake above 70% had increases that started much later, in around week 37.

The mean of the current intensity score is slightly lower among countries with uptake above 70%, but its upper range reached the maximum score of 10 in all categories of vaccine uptake below 80%, reflecting the limited effectiveness of the vaccine against infection that allows for widespread circulation, even in highly vaccinated populations.

The clearest gradient is visible for the severity score, whose mean and upper range falls sharply when moving from groups of low to high vaccine uptake. The difference between the current mean intensity and severity scores also increases with vaccine uptake; the severity score is 0.6 points lower than the intensity score for countries with <50% uptake, while this difference was 2.8 points for those with >80% uptake. While this illustrates the protective impact of vaccination against severe outcomes, it is noteworthy that the recent increases in the severity score have occurred in all vaccine uptake categories below 80%. This demonstrates that at current levels of uptake, a substantial burden of severe disease will still occur, particularly where intensity of transmission is high. The lag in the severity indicators means that further increases in this score are likely in the coming weeks, due to the current high case load.

Figure 4. Mean and range of the weekly COVID-19 epidemiological scores (overall composite, intensity and severity domains) from EU/EEA countries grouped according to their current cumulative uptake of full vaccination in the total population, weeks 25-44, 2021



Note: EU/EEA countries have been categorised in groups based on their cumulative uptake of full vaccination in the total population, in ISO week 44 of 2021. 50%: Bulgaria, Romania, Slovakia, Croatia. 50-60%: Poland, Latvia, Slovenia, Estonia, Czechia, Hungary, Lichtenstein, Greece. 60-70%: Lithuania, Austria, the Netherlands, Luxembourg, Cyprus, Germany, Sweden, France. 70-80%: Norway, Finland, Italy, Spain, Belgium, Denmark, Ireland, Iceland. >80%: Portugal, Malta. The line and ribbon represent the mean and range, respectively, of the weekly scores from the countries within each vaccine uptake group. Since the overall composite score (range 1-10) is the sum of intensity and severity domain scores with a range of 0.5-5, the domain scores have been doubled to facilitate plotting using a common scale.

Non-pharmaceutical interventions

Since March 2020, NPIs implemented in EU/EEA countries have proven to be an effective public health tool to decrease the spread of SARS-CoV-2 and reduce not only COVID-19 notification and death rates, but also the incidence of other respiratory diseases like influenza. NPI effectiveness is amplified by swift and decisive implementation, appropriate risk communication and community engagement. The ECDC-Joint Research Centre Response Measures Database (ECDC-JRC RMD) has collated and mapped NPIs implemented by EU/EEA countries in response to the COVID-19 pandemic since January 2020 [1,2].

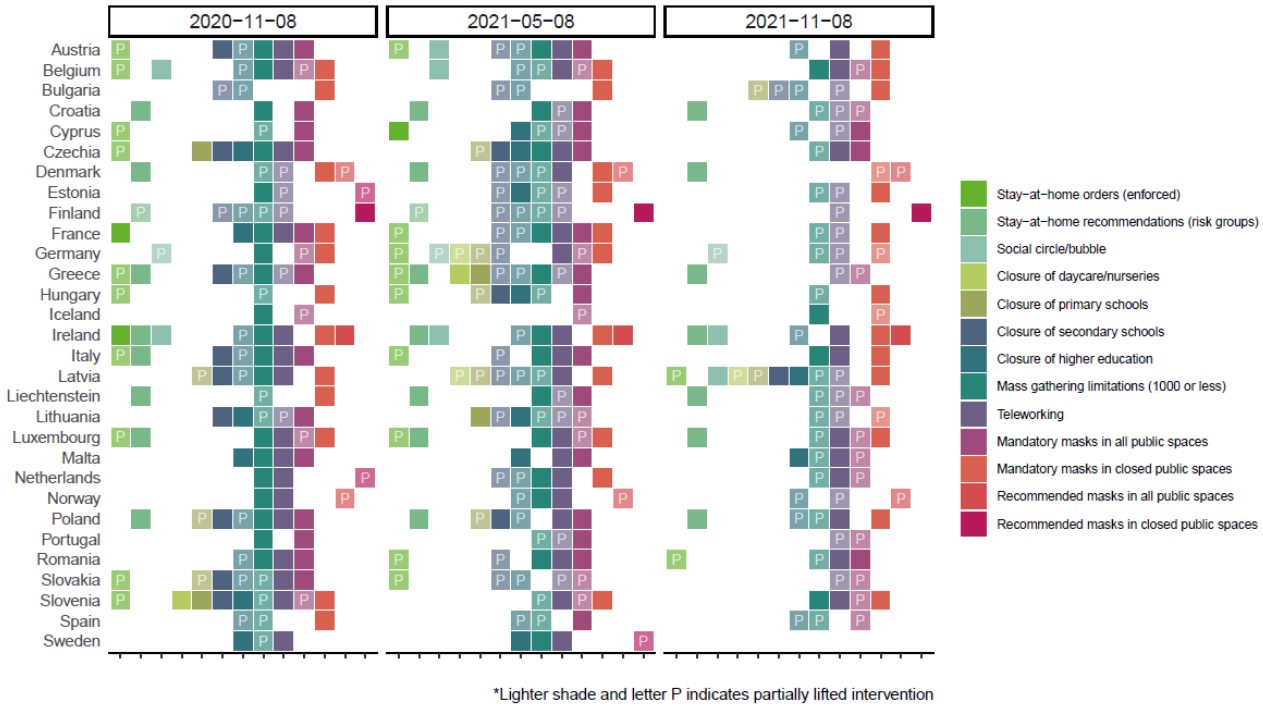
Figure 5 shows different national NPIs in place in EU/EEA countries at three points in time: 8 November 2020, 8 May 2021 and 8 November 2021. On 8 November 2021, there were fewer measures in place overall (n=104) compared with the same day in 2020 (n=145) and six months earlier on 8 May 2021 (n=157). Of all measures in place on 8 November 2021, 58% were recorded as partially lifted compared with the 37% of the measures in place on the same day in 2020 and with 48% of the measures in place on 8 May 2021.

On 8 November 2021, the use of face masks in both indoor and outdoor public spaces was less stringent, with only 14 countries implementing their use, compared to 21 countries in May 2021 and 18 in November 2020. The measures restricting access to public events and mass gatherings, both indoors and outdoors, were also less stringent on 8 November 2021, with 19 countries implementing partial closure of events up to 1 000 participants or less, compared to 24 countries in May 2021 and 29 in November 2020.

Although the number of NPIs registered in the ECDC-JRC RMD for November 2021 is currently lower in most countries when compared to May 2021 and November 2020, after mid-October 2021, the number of NPIs implemented in EU/EEA countries has been increasing, as a response to the increasing notification and death rates.

The current situation is dynamic and so far, the ECDC-JRC RMD has registered increased use of face masks in public spaces and the use of vaccination certificates to access public gatherings and spaces, amongst other NPIs.

Figure 5. Comparison of implementation of NPIs for the control of COVID-19 in EU/EEA countries active on 8 November 2020, 8 May 2021 and 8 November 2021



Note: The visualisation above is a comparison at three points in time, and not a period analysis. Several countries have introduced or lifted various measures between or after the dates selected.

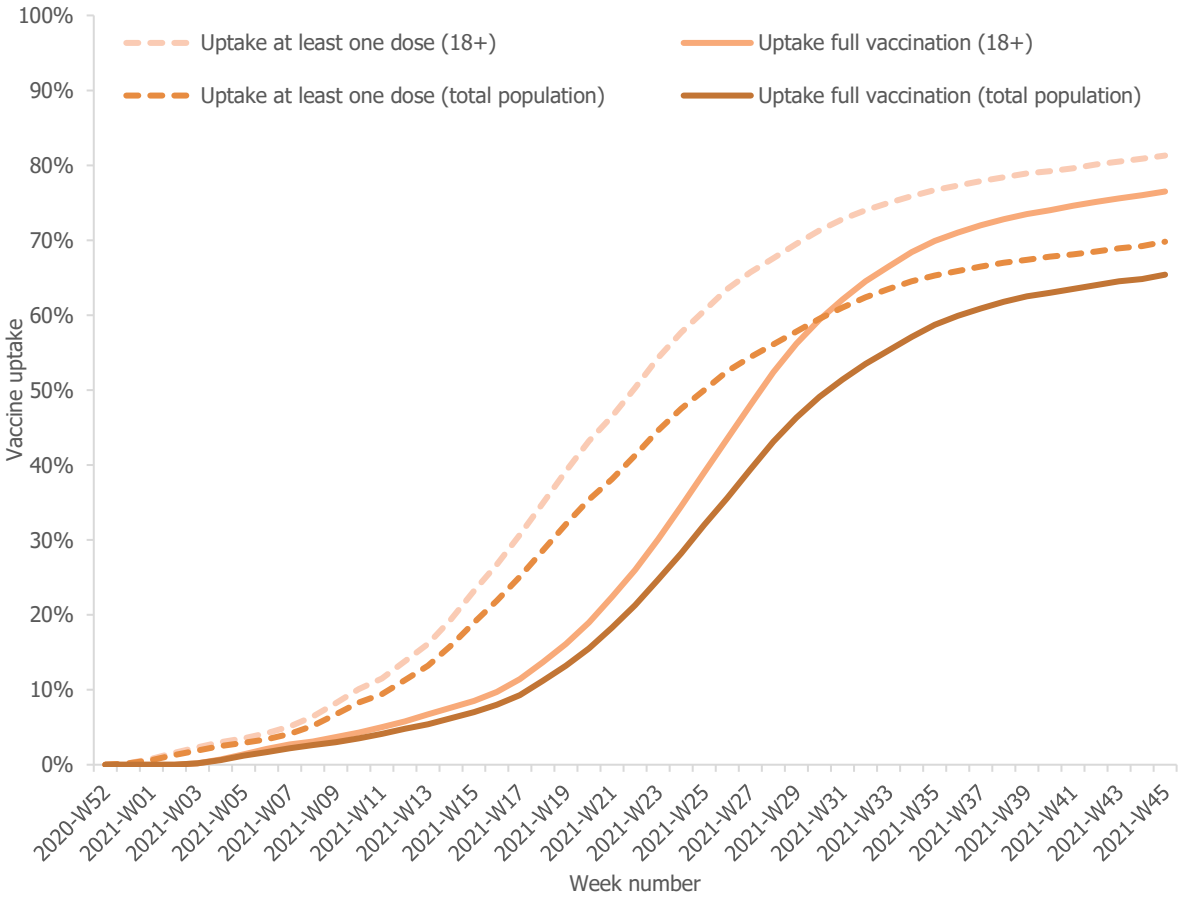
Vaccination

As of 17 November 2021 (week 45, 2021), over 609 million vaccine doses have been administered in the EU/EEA, over 296 million people have received a complete primary vaccination course (30 countries reporting) and over ten million individuals in the EU/EEA have already received an additional dose following the primary vaccination course (22 countries reporting [3]).

The cumulative vaccine uptake in the total population in the EU/EEA reached 69.8% (range: 26-87.9%) for at least one vaccine dose and 65.4% (range: 23.9-81.4%) for the full vaccination course (pooled data from 30 reporting countries). Among adults (aged 18 years and older) in the EU/EEA as a whole, the cumulative vaccine uptake reached 81.3% for at least one vaccine dose (range 31.1-99%) and 76.5% for the full vaccination course (range: 28.4-92.6%) (pooled data from 30 reporting countries) (Figure 6) [4].

As the cumulative vaccine uptake in the adult population in the EU/EEA approaches 75%, the increase in vaccine uptake in the total population is mostly driven by the rollout in younger age groups, including among eligible individuals below 18 years (Figure 7). On the other hand, the overall pace of weekly increase in vaccine uptake in the EU/EEA is slowing down (Figure 6) and the progress is unequal across countries: four EU/EEA countries are still reporting less than 50% of full vaccine uptake in the total population (Bulgaria, Croatia, Romania and Slovakia).

Figure 6. Cumulative uptake of at least one dose of COVID-19 vaccine and full vaccination among adults (18+) and total population in the EU/EEA as of week 45, 2021



Source: TESSy; data reported by 30 countries as of week 45, 2021. The total population includes children and adolescents for whom the vaccine is not yet approved (e.g. below 12 years) or who may not be included in national target groups yet.

Figure 7. Median cumulative uptake of full COVID-19 vaccination by age group in the EU/EEA, as of week 45, 2021

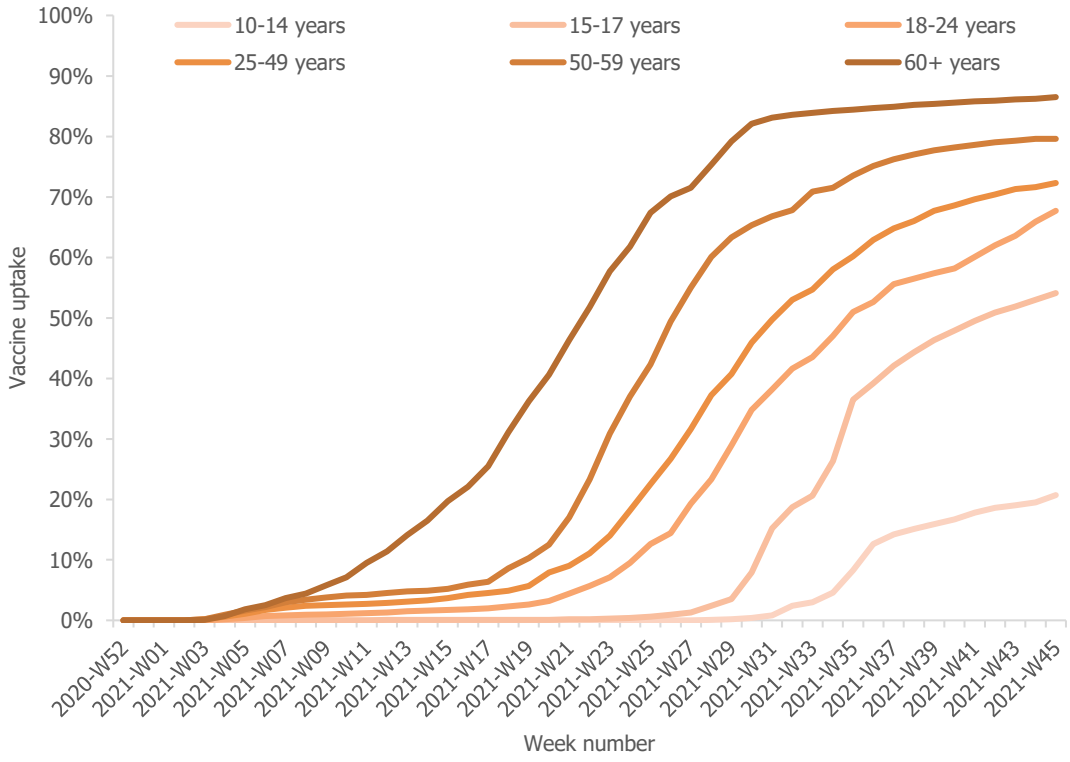


Table 1 shows a summary of the cumulative uptake of full vaccination in the total population, adults (18+), individuals under 18 years and priority groups (e.g., elderly 60+, healthcare workers, residents in long term care facilities).

Table 1. COVID-19 vaccine uptake by target population as of week 45, 2021

Vaccine uptake	Uptake (range)	Reporting countries
Full vaccination in the total population	65.4 (range: 23.9-81.4%)	All 30 EU/EEA countries
Full vaccination among adults (18+)	76.5% (range: 28.6–92.5%)	All 30 EU/EEA countries
Full vaccination among those under 18 years (median)*	15% (range: 1-29%)	27 (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden)
Full vaccination among people aged 60+ years (median)	86.5% (range: 32.1–100%)	27 (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden)
Full vaccination among healthcare workers (median)	87.3% (range: 26.4–100%)	17 (Bulgaria, Croatia, Czechia, Denmark, Estonia, France, Greece, Hungary, Iceland, Ireland, Latvia, Luxembourg, Malta, Romania, Slovenia, Spain, Sweden)
Full vaccination among residents in long-term care facilities (median)	83.5% (range: 38.6–100%)	13 (Bulgaria, Czechia, Denmark, Estonia, Greece, Hungary, Iceland, Ireland, Latvia, Luxembourg, Malta)

*Source: TESSy; data reported as of week 45, 2021; *Vaccines currently authorised and recommended for 12-17-year-olds*

SARS-CoV-2 variants of concern

Delta is currently the dominant variant in the European region, mainly due to an increase in transmissibility compared with other variants [5].

Surveillance of Delta variants with potential immune escape properties is currently of importance as they could increase the number of reinfections and vaccine breakthrough infections. Mutations in the S-gene that have been previously associated with immune escape include both substitutions in receptor binding domain (e.g., E484K) as well as deletions in the N-terminal domain [6]. A recent pre-print which compared Delta with E484K to a Delta virus without such mutation found that E484K is associated with a significant decrease in neutralization by vaccine sera (2.7 fold-change) [7]. Delta variants with spike protein E484X substitutions (E484A, E484K and E484Q) are estimated to be below 5% in all EU/EEA countries and currently there is no signal of an increasing trend (GISAID EpiCov) [7,8].

The UK designated Delta sub-lineage AY.4.2 a variant under investigation on 1 October 2021. ECDC designated AY.4.2 a variant of interest as of 11 November 2021 due to evidence of increased transmissibility compared with other Delta lineages and to facilitate specific reporting of this sub-lineage across EU/EEA countries. This variant is defined by the spike changes Y145H and A222V [9]. AY.4.2 was first detected in the UK in June 2021 and since has been increasing in proportion compared with other circulating Delta sub-lineages in the UK. As of 16 November 2021, the overall proportion of AY.4.2 in the UK is at 15% and it is present in the EU/EEA at low proportions (<5%). Preliminary studies from the UK show that this variant has an estimated growth advantage of 19% compared with other circulating Delta sub-lineages, and this increase in growth rate has been observed across UK regions [9]. AY.4.2 is associated with a small but statistically significant increase in secondary attack rate for household contacts compared with other Delta lineages (12.2% vs. 11.2%). No significant difference in disease severity or vaccine effectiveness has been observed between AY.4.2 and other circulating Delta sub-lineages. A study performed in Denmark showed no difference in neutralization by vaccine sera between AY.4.2 and the Delta parental lineage [7]. The slight increase in transmissibility for AY.4.2 could lead to an increased number of cases and hospitalisations in the EU/EEA if the variant becomes dominant.

ECDC is constantly monitoring emerging variants. We provide lists of variants of concern, variants of interest and variants under monitoring on our website: https://www.ecdc.europa.eu/en/covid-19/variants-concern. These categories define different levels of potential public health impact and available scientific evidence associated with a variant. Such lists are re-assessed and updated, if deemed necessary, on a weekly basis.

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

Since the start of the influenza season 2021/22 in week 40, influenza has been circulating overall on a low level, however, the reported number of detections has been higher than during the 2020/21 season, when there was exceptionally low influenza circulation, and is currently comparable to seasons prior to COVID-19 [10,11]. Up to week 45/2021, a total of 13/4 115 (0.3%) sentinel and 680/200 771 (0.3%) non-sentinel samples have tested positive for influenza virus in the EU/EEA (Appendix 1). The majority of the viruses were type A, and of all 332 subtyped viruses, 29 were reported as A(H1N1)pdm09 and 303 as A(H3). Of the 83 type B viruses, Denmark reported the majority of detections. Although the Netherlands reported non-sentinel detections, they did not report a denominator for the total number of tested specimens. Sweden has reported increasing numbers of detections in non-sentinel specimens, with a low overall test positivity rate of 0.2% (134/56 824), and 0.6% in week 45/2021. A similar situation is observed in Norway and Denmark with a high number of overall tests and sporadic detections in non-sentinel specimens (Norway: 45/58 558; Denmark: 124/ 31 656). Only Croatia observed influenza activity above the seasonal threshold of 10% positivity in week 37/2021 with 37% positive non-sentinel specimens, declining to 10% in week 44/2021 and 1% in week 45/2021. Regular updates of the data are available at: www.FluNewsEurope.org.

Data reported to TESSy on respiratory syncytial virus (RSV) detections indicates ongoing RSV activity in Germany and Sweden with positivity rates up to 60%. Other countries reported lower levels of circulation or sporadic detections whilst the Netherlands, France and Spain have observed earlier waves. Data are available at ECDC's surveillance Atlas: http://atlas.ecdc.europa.eu/public/index.aspx

Disease background

Vaccine effectiveness for the Delta variant: infection, transmission, hospitalisation and averted deaths

The evidence available at the time of publication of the ECDC technical report 'Interim public health considerations for the provision of additional COVID-19 vaccine doses' [12] (published on 1 September 2021) indicated a reduced vaccine effectiveness against infection with the Delta variant, but a maintained high vaccine effectiveness against severe disease and hospitalisation [12]. Additional key evidence after this date is summarised below and largely based on sources from the living systematic review of COVID-19 vaccine effectiveness studies conducted by the International Vaccine Access Center at Johns Hopkins Bloomberg School of Public Health and the WHO [13] and the McMaster University Health Forum COVID-END Evidence Network Living Evidence Synthesis [14].

There are several caveats when looking at real world studies on vaccine effectiveness. Methodological bias is possible in real world vaccine effectiveness observational studies. Studies are performed in different settings (e.g., epidemiological context, presence of variants, dosing interval) on different populations (e.g. risk groups, age groups, previously infected). A comparison of vaccine effectiveness between various studies should be done with caution. Several studies included in this analysis are pre-print and not yet peer reviewed. In addition, it is challenging to disentangle any apparent reduction in vaccine effectiveness over time due to waning immunity from reduction due to immune escape by the Delta variant. Due to the limited availability of COVID-19 vaccines at the start of vaccination campaigns, most countries opted to prioritise vaccination for those individuals most at risk of severe disease (e.g. the elderly and residents in long term care facilities), as well as healthcare workers [15].

Vaccine effectiveness against infection

For all COVID-19 vaccines approved in the EU/EEA, the real-world evidence indicates a somewhat reduced vaccine effectiveness for the Delta variant compared to both results from clinical trials and real-world studies on the previously dominant Alpha variant [12]. For Comirnaty, vaccine effectiveness against infection (any) ranges from around 40% to over 90%, depending on the study and the target group [16-19]. For Spikevax, vaccine effectiveness against infection is between 63-92% [16,18-20], and for Vaxzevria [18,19] and Janssen [16,18], this range is 55-87% and 3-76% respectively. Despite this decrease in protection, the COVID-19 vaccines authorised in the EU are still providing important protection against infection and mild disease, as well as severe disease.

Vaccine effectiveness against transmission

Vaccination may prevent onward transmission by reducing both symptomatic and asymptomatic infections in the population, and in addition, reduce the risk of transmission from those infected after being fully vaccinated. The available evidence indicates that the currently available vaccines reduce transmission less for the Delta variant compared to Alpha; a similar pattern is observed in studies looking at vaccine effectiveness against infection. Vaccine effectiveness studies against transmission can be prone to bias and confounding factors and can measure different outcomes, which affects the estimated vaccine effectiveness. Also, some studies are looking at the vaccine effectiveness in the index case (against onward transmission) and some in the contacts.

A study from the Netherlands (pre-print) [21] estimated vaccine effectiveness against onward transmission by comparing secondary attack rates among household members between vaccinated and unvaccinated index cases, during a period when Delta was the dominating variant. Of the fully vaccinated index cases in this study, the majority received Comirnaty (55%) 24% received COVID-19 Vaccine Janssen, 16% Vaxzevria and 5% Spikevax.

Effectiveness of full vaccination of the index cases against transmission to unvaccinated household contacts was 63% (95% confidence interval (CI) 46-75%). Effectiveness of full vaccination of the index cases against transmission to fully vaccinated household contacts was 40% (95% CI 20-54%). However, fully vaccinated contacts also benefit from their own vaccination with an already reduced risk of getting infected. The lower vaccine effectiveness for onward transmission when contacts are vaccinated could possibly be explained by differences in risk-behaviour. The study results indicate that vaccination protects against onward transmission from a vaccinated index case.

A prospective dynamic cohort [18] study from Spain included over 30 000 close contacts of over 12 000 index cases during the period of April-August 2021. Product specific effectiveness for onward transmission was estimated in close contacts by age group, contact setting, vaccination status of the index case and by SARS-CoV-2 variant. For close contacts of unvaccinated index cases, the adjusted vaccine effectiveness against infection was estimated at 70% (CI, 67-73) for Comirnaty, 85% (CI, 80-88) for Spikevax, 55% (CI, 47-62) for Vaxzevria and 54% (CI, 46-62) for Janssen. For close contacts of fully-vaccinated index cases, the estimates were 59% (CI, 45-69) for Comirnaty, 70% (CI, 52-81) for Spikevax, 41% (CI, 16-58) for Vaxzevria and 23% (CI, -14-48) for Janssen. These estimates are lower amongst people above the age of 60 years across all vaccine products. Results indicate that viral-vector vaccines provide a lower protection against secondary infections in close contacts in comparison to mRNA vaccines.

A recent large-scale study (pre-print) from the UK [22] looking at adult contacts of SARS-CoV-2 infected adult index cases, found that vaccination of the index case reduces transmission of Delta, but less than the Alpha variant for both symptomatic and asymptomatic index cases, and that Comirnaty was more effective in reducing transmission than Vaxzevria. In contacts, PCR positivity was higher in unvaccinated and partially-vaccinated contacts compared to in those fully vaccinated contacts with either Comirnaty or Vaxzevria. The study also found that Delta infections had similar Ct values in vaccinated as unvaccinated cases and that these were lower than for Alpha infections in both symptomatic and asymptomatic infections.

Another cohort study from the UK on household transmission of SARS-CoV-2 found that the secondary attack rates among household contacts of fully vaccinated index cases (25%) was similar to contacts exposed to unvaccinated index cases (23%). There was a similar proportion of vaccinated as unvaccinated cases amongst those index cases leading to secondary transmission. Amongst fully vaccinated household contacts exposed to Delta, the secondary attack rate was 25% compared to 38% in unvaccinated household contacts. The secondary attack rates and vaccine effectiveness was not stratified by vaccine product, however out of the 38 fully vaccinated Delta-infected participants in this study, 14 had received the Comirnaty, 23 Vaxzevria and one the CoronaVac inactivated whole-virion vaccine (Sinovac). In this UK study, vaccination clearly reduced the risk of infection with Delta and accelerated viral clearance [23]. Nonetheless, the authors concluded that if fully vaccinated individuals with breakthrough infections have peak viral load similar to unvaccinated cases, they can efficiently transmit infection in household settings, including to fully vaccinated contacts [23].

Some emerging evidence indicates a higher viral load with Delta infection compared to infection with other variants, and with similar levels in vaccinated individuals as unvaccinated individuals [22,24,25]. However, those vaccinated seem to have a faster decline in viral load than those unvaccinated, indicating a faster clearance of infection [26]. A recent study from Israel found that infected individuals who were recently fully vaccinated with Comirnaty had lower viral loads than unvaccinated individuals. However, this effect started to decline two months post-primary vaccination and disappeared six months after primary vaccination [27].

Vaccine effectiveness against severe outcomes

Real world evidence on the Delta variant are showing that vaccine effectiveness against severe disease, including hospitalisations and deaths, remains very high in the general population, at approximately >80% effectiveness [20,28], albeit with some evidence of a slight decreasing protection in older frail individuals and those with clinical risk factors for more severe disease [29,30]. The main objective of the vaccination strategy with COVID-19 vaccines is to protect those most at risk from severe disease and death. It is undisputed that EU-approved vaccines continue to offer strong protection against severe disease, hospitalisation and death due to COVID-19, and continue to do so despite the emergence of the Delta variant.

Averted deaths

The vaccines are achieving what they were approved to do - protecting people from getting severely sick and dying from COVID-19. According to a recently updated UK report which covers the time period 2 January - 24 September 2021, the age-standardised mortality rate is 32 times higher for unvaccinated people than for those fully vaccinated [31]. A retrospective surveillance study from Israel found that the nationwide vaccination campaign averted almost 25 000 hospitalisations and over 5 500 deaths between December 2020 and April 2021. This estimation indicates that without the national vaccination campaign, the number of hospitalisations and deaths during this time would have been three times as high. This does not include indirect effects and long-term benefits of vaccination [32]. A government study from the US assessed the association between vaccination rates and COVID-19 deaths during the first months of vaccine rollout and found that approximately 140 000 deaths were averted [33].

Evidence of waning immunity following vaccination: booster doses

Evidence on vaccine effectiveness against infection and severe disease outcomes over time has continued to emerge since publication of the ECDC document on 'Interim public health considerations for the provision of additional COVID-19 vaccine doses' in September [12]. This update of the evidence on vaccine effectiveness over time includes studies that measure vaccine effectiveness at fixed intervals following completion of primary vaccination. Studies assessing vaccine effectiveness against infection, hospitalisation and death show that there is a decline in vaccine effectiveness against infection and symptomatic infection for EU-authorised COVID-19 vaccines that correlate with time since completion of primary vaccination, which is similar to what was shown in earlier studies that were analysed in the ECDC September report. Vaccine effectiveness against hospitalisations and deaths continues to remain stable in the majority of studies up to nine months after completion of the primary series, with modest declines observed in older individuals and those with comorbidities.

Vaccine efficacy and vaccine effectiveness over time against infection and symptomatic infection

Updated results from an ongoing randomised controlled trial (RCT) of Comirnaty have found a gradual decline in vaccine efficacy against infection through six months of follow-up in participants 12 years or older. Vaccine efficacy from seven days to less than two months after the second dose was 96.2% (CI, 93.3-98.1) and from four months after the second dose up to 6 months vaccine efficacy was 83.7% (CI, 74.7-89.9) which is an average decline of approximately 6% every 2 months [34].

There is some evidence that vaccine effectiveness against documented infection reduces over time since primary vaccination. The magnitude of reduction varies between different studies from approximately 80-90% 14 days after primary vaccination, decreasing to less than <50% in some studies, with follow-up to seven months in the general population and generally across all EU authorised vaccine products [35-39]. In addition, evidence indicates that protection from viral vector vaccines decreases a little earlier than that provided from mRNA vaccines [38-42]. There is also evidence of reduction of vaccine effectiveness over time up to seven months against moderate disease [39,40], with one study from Sweden observing no effectiveness of Comirnaty against symptomatic disease from seven months through to nine months of follow-up [39]. A heterologous series of either mRNA vaccines or first dose of Vaxzevria followed by a second dose of mRNA vaccine remained higher over time compared to a homologous series according to some evidence [39,41]. In addition, vaccine effectiveness was significantly higher against infection and hospitalisation with a longer interval between doses (3-4 week interval compared to 7-8 weeks) [41]. In some studies, the reduction in protection against infection and moderate disease is more pronounced in older age groups 65+ years and those with comorbidities [39,40]. In terms of vaccine effectiveness and specific cohorts, one recent register-based cohort study from Finland in healthcare workers aged 16-69 years observed waning of vaccine effectiveness of mRNA vaccine series against infection, decreasing from 82% up to three months after the second dose to 53% after 6 months [43]. A cohort study of healthcare workers in the US showed a decrease of vaccine effectiveness of mRNA vaccines against symptomatic infection over five months from 93.9% in March 2021 dropping to 65.5% in July 2021 [44].

Vaccine effectiveness over time against severe disease outcomes

In the general population, the majority of studies have shown that vaccine effectiveness against severe disease, including hospitalisations and deaths continues to remain high for all authorised COVID-19 vaccines, at approximately >80% effectiveness over time since primary vaccination, with a follow-up period of up to approximately six months [35,36,39,40,45]. There is evidence that this can differ across vaccine products, with a recent case control study from the US in hospitalised adults (with a median age of 59 years) observing an overall vaccine effectiveness of 85% for mRNA vaccines but finding a reduction in vaccine effectiveness to prevent hospitalisations from 81% at 14+ days post-second dose to 64% at 120+ days for Comirnaty compared to 89% at 14+ days to 85% at 120+ days for Spikevax [46]. There is also some evidence of a higher decrease of protection against severe disease in older frail individuals and those with clinical risk factors for more severe disease [16,37,39,40]. In the recent Finnish study in healthcare workers described above, vaccine effectiveness remained high (88%) against hospitalisation beyond six months [43].

Vaccine effectiveness against transmission over time

In addition to providing direct protection against COVID-19 disease, available vaccines also substantially reduce transmission, partly by protecting against both symptomatic and asymptomatic infection. However, vaccine effectiveness against infection is decreasing over time since primary vaccination, and there is also evidence emerging that protection against onward transmission is reducing over time. This could contribute to increased transmission of SARS-CoV-2 in the population and could have implications for the epidemiological situation. For example, those vaccinated may have different risk-behaviour than those unvaccinated and thereby could contribute to increased transmission.

Vaccine effectiveness studies against transmission, which are described above, also investigated differences over time of vaccination and protection against onward transmission. In the study from Spain on vaccine effectiveness against secondary infection in close contacts, infection incidence ≥ 90 days after the last dose was compared to infection incidence within 90 days after the last dose of the primary vaccination series. Over the study period, vaccine effectiveness in close contacts (not stratified by vaccination status of the index case) declined 90 days after the second dose of Comirnaty (70% to 63%, p=0.035) and Spikevax (85% to 67%, p=0.003). This was not seen for Vaxzevria (40% to 52%, p=0.746).

The UK study by Eyre found that the impact of vaccination decreased over time since vaccination in index cases; for Delta and Comirnaty, reductions in transmission at two and 12 weeks were 50% (35-61%) and 24% (20-28%), respectively, and 24% (18-30%) and 2% (-2-6%) for Vaxzevria. Protection in contacts also declined in the three months post vaccination.

In the UK cohort study by Singanayagam et al looking at secondary attack rates in vaccinated versus unvaccinated index cases and household contacts, the authors found that risk of infection increased with time in the two to three months since the second dose of vaccine. The median time between the last vaccine dose was 101 days in PCR positive contacts versus 64 days in PCR negative contacts [23].

Vaccine efficacy and vaccine effectiveness of booster doses against infection and severe disease

Clinical trial data available on the vaccine efficacy of booster doses of Comirnaty and observational studies on vaccine effectiveness of booster doses against infection and severe disease that are emerging from Israel and the UK show a significant increase in protection against infection and severe disease following a booster dose of Comirnaty in all age groups in the short term (longest follow-up time in the included studies is approximately 70 days).

The first efficacy results from a phase 3 RCT of a booster of Comirnaty were released by Pfizer and BioNtech. In the trial, the efficacy and safety of a booster dose of the Comirnaty in more than 10 000 individuals 16 years of age and older was evaluated. The median time between second dose and administration of the booster dose or placebo was approximately 11 months. Symptomatic COVID-19 occurrence was measured from at least seven days after booster or placebo, with a median follow-up of two and a half months. They found that the booster dose restored vaccine protection against COVID-19 to the high levels achieved after the second dose, with a relative vaccine efficacy of 95.6% (95% CI: 89.3, 98.6) as the reduction in disease occurrence in the boosted group versus the non-boosted group in those without evidence of prior SARS-CoV-2 infection. Efficacy was consistent irrespective of age, sex, race, ethnicity, or comorbid conditions [47,48].

Observational studies from Israel have investigated the vaccine effectiveness of booster doses against infection and severe disease. Israel started their primary vaccination campaign with Comirnaty in December 2020, starting with the 60+ age group, with the administration of the second dose three weeks after the first dose. At the end of July 2021, a national Comirnaty booster vaccination campaign started in the 60+ age group and expanded to younger age groups on a week-to-week basis, with all those aged 16+ included by August. Israel is recommending a booster dose at least five months after the primary vaccination regimen.

A large population-based study in Israel is using data extracted from the Ministry of Health national database of over a million people on the effectiveness of Comirnaty boosters given to people 60 years or more at least five months after the primary course [49]. The study found that from 12 days after the booster dose, the rate of confirmed infection was lower in the booster group than in the non-booster group by a factor of 11.3 (CI, 10.4-12.3) and the rate of severe illness was lower by a factor of 19.5 (12.9-29.5) following the third dose. The follow-up period was 21 days for documented infection and 16 days for severe disease. Vaccine effectiveness calculated from the rate ratio reported in the manuscript for the incremental vaccine effectiveness against any infection (booster dose vs dose 2) was 92% (CI, 90-93), and for severe disease was 94% (CI, 91-96) [50]. The study investigators pointed out possible biases such as not adjusting for pre-existing clinical conditions related to risk of severe disease and differences in behavioural or health seeking behaviours of those that received a booster compared to those that did not. However, they conclude that the findings give clear indications of the effectiveness of a booster dose even against the Delta variant.

Another population-based study from Israel looked at younger age groups (16+) who received a second dose at least five months after the primary course of vaccination with Comirnaty [49]. The study estimated the rate ratios for confirmed infection, severe disease, and death due to COVID-19 between the booster (who received a booster ≥12 days earlier) and non-booster groups in the different age categories. Confirmed infection rates were ≈10-fold lower in the booster versus non-booster group (ranging 8.8-17.6 across five age groups). Severe illness rates 18.7-fold (CI, 15.7-22.4) lower for ages 60+, and 22.0-fold (CI, 10.3-47.0) lower for ages 40-60. For ages above 60, COVID-19 associated death rates were 14.7-fold (CI, 9.4-23.1) lower compared to the non-booster group (follow up 45 days) [51].

A retrospective study from Israel aimed at evaluating initial short-term effectiveness of a three-dose versus a two-dose regimen of Comirnaty against infection due to the Delta variant of SARS-CoV-2, using two study designs [52]. The main analysis used a test-negative design, and the secondary analysis used a matched case-control design. Across the test-negative and matched case-control analyses, the study estimated a 48-68% reduction in the odds of testing positive for SARS-CoV-2 after 7-13 days, and 70-84% 14-20 days after the booster, compared to two doses with a follow up of 20 days. Data show the waning of vaccine-induced protection against infection counteracted in the short term by the third dose. However, the study did not evaluate the effects on more rare but severe outcomes, such as hospitalisation and death.

Another retrospective cohort study from Israel used a large Israeli health database of nearly one million members over 16 years of age to determine vaccine effectiveness of a third dose of Comirnaty against infection. Comparing infection rates between those who received a third dose with those who did not during August-October 2021 (with a follow-up period of 70 days), the study investigators showed that a booster dose of Comirnaty provided added protection against infection for those vaccinated six months ago with a vaccine effectiveness of 89.1% (95% CI:87.5-90.5%) [53].

Limitations include the short follow-up period and that the 60+ age group were over-represented among those that received the third vaccine dose. Also, the decision to vaccinate and to carry out a PCR test is voluntary which may have introduced bias. Despite this, the study investigators state that these findings indicate that an introduction of the third dose was effective in reducing infection rates in Israel.

A further Israeli retrospective cohort study using Israel's largest healthcare database with over one million individuals aged 16 and over with a median age of 52 years also showed high vaccine effectiveness with the booster dose relative to primary vaccination with a median follow-up time of 13 days. The vaccine effectiveness estimates with Comirnaty booster doses were 88% (CI, 87-90) against infection, 91% (CI, 89-92) against symptomatic disease, 93% (CI, 88-97) against hospitalisations and 81% (CI, 49-97) against deaths as of seven or more days after the booster dose. They found that the booster dose effectiveness against hospital and severe disease was similar between males and females and between those aged 40-69 years and at least 70 years (for those aged 16-39 they found that the rate of severe outcomes was too small for estimation of effectiveness). The effectiveness was also similar among groups defined by the number of comorbidities. They conclude that these finding suggest that a booster dose of Comirnaty is effective in reducing severe outcomes for those that received two doses at least five months before [54].

In a test negative case control study from England on the effectiveness of Comirnaty booster doses against symptomatic infection in those aged over 50 years, comparable estimates to those found in Israeli studies were discovered. The study found a significant increase in protection against symptomatic COVID-19 with a booster dose of Comirnaty. The relative vaccine effectiveness estimate in the 14 days after a booster dose compared to individuals that received a two-dose primary course, was 87.4 in those who received Vaxzevria as a primary course and 84.4 in those who received Comirnaty as a primary course. Using a 2-to-6-day period post-booster dose as the baseline gave similar results. The absolute vaccine effectiveness from 14 days after the booster, using the unvaccinated baseline, was 93.1 in those who had Vaxzevria as their primary course and 94.0 in those who had Comirnaty as their primary course [40].

The follow-up times after administration of the booster dose in the available studies are short, and further monitoring of data is needed to determine the duration of immunity following the booster dose against infection, mild disease and severe disease. As of yet, there are no explicit studies in the preprint or published literature on the effectiveness of boosters on transmission of SARS-CoV-2. However, the emerging data on their effectiveness on restoring a high protection against infection indicate that booster doses are also likely to have an important impact on onward transmission.

Recommendations on an additional dose as an extension of the primary vaccination series

Following an analysis of studies that showed that an additional dose of Comirnaty and Spikevax increased the ability to produce antibodies against the virus that caused COVID-19 in organ transplant patients with weakened immune systems, on 4 October, EMA's Committee for Medicinal Products for Human Use (CHMP) recommended that an additional dose of Comirnaty and Spikevax may be given to people with severely weakened immune systems at least 28 days after their second dose. On 26 October 2021 the WHO Strategic Advisory Group of Experts (SAGE) published their 'Interim guidance recommendations for an extended primary series with an additional vaccination in immunocompromised persons' where they recommend that the primary vaccine series in moderately to severely immunocompromised persons (such as persons with active cancer, transplant recipients, immunodeficiency, HIV and immunosuppressives) should be extended to include an additional dose for all COVID-19 vaccines that have received WHO Emergency Use Listing. The additional dose in an extended primary series is recommended to be given at least one month and within three months after the primary series in order to increase protection for immunocompromised persons [55]. All 30 EU/EEA countries are currently recommending an additional dose as an extension of the primary series to those with weakened immune systems.

Recommendations on booster dose

After evaluating data on Comirnaty that showed a rise in antibody levels when a booster dose is given approximately six months after the second dose, EMA's CHMP concluded that booster doses of Comirnaty may be considered at least six months after the second dose for people aged 18 years and older [56]. Following this recommendation, the CHMP evaluated data on Spikevax that showed that a third dose of Spikevax given six to eight months after the second dose led to a rise in antibody levels in adults whose antibody levels were waning, and on 25 October concluded that a booster dose of the Spikevax may be considered in people aged 18 years and above at least six months after the second dose [57]. On 22 November 2021, EMA started evaluating an application for the use of a booster dose of COVID-19 Vaccine Janssen to be given at least two months after the first dose to people aged 18 years and older. The outcome of this evaluation is expected within weeks, unless supplementary information is needed [58].

All 30 EU/EEA countries are recommending booster doses for waning immunity to different population groups [15]. Countries are recommending a booster dose to those most vulnerable to severe disease and death i.e. residents in LTCFs and the elderly, and a majority are also recommending booster doses to healthcare workers, in particular to those who have direct contact with vulnerable individuals. Some EU countries, such as Germany [59] and France [60] are now also starting to recommend booster doses for younger age groups. Countries are recommending booster doses with mRNA vaccines (Comirnaty or Spikevax) with the majority recommending a booster dose at least six months after primary vaccination. Some countries are also recommending a booster dose with a shorter interval for those who were vaccinated with a primary series of adenovirus vector vaccines, in particular for those who received the COVID-19 Vaccine Janssen, where a second dose of mRNA vaccine at least two months following the first dose is recommended [15].

Following a decision from the U.S. Food and Drug Administration (FDA) on 19 November 2021 to authorise the use of single boosters using either Comirnaty or Spikevax for all individuals 18 years and older, the U.S. CDC expanded their recommendations for booster shots [61]. The recommendations now include all adults aged 18 year and older to receive a booster shot of either Comirnaty or Spikevax at least six months after completing their primary series. The decision is based on the latest vaccine effectiveness data over time and a review of safety data for boosters [62].

Country recommendations for booster doses are rapidly changing as more evidence becomes available on vaccine effectiveness over time against infection, severe disease and the protection offered from booster doses.

Risk factors for breakthrough infections leading to severe disease after vaccination

Unvaccinated individuals are at a much greater risk of being hospitalised or dying from COVID-19 compared to vaccinated individuals [31]. There is evidence that those who are fully vaccinated and have breakthrough infections face a significantly lower risk of developing severe disease or requiring hospitalisation in comparison to those that are unvaccinated [46]. Individuals with underlying conditions and weakened immune systems are associated with an increased risk for breakthrough infections leading to severe disease. There is also some evidence from Israel of an increased risk of breakthrough infections in individuals with longer time since vaccination (waning of vaccine effectiveness) across all age groups [63]. Such waning appears to be more pronounced in the elderly, as shown by several studies where they develop reduced and less durable immune responses to vaccines than younger individuals [63-65]. Thus, it is important to closely monitor increased incidence of breakthrough infections across age groups and to take into account that EU/EEA countries prioritised vaccines to older age groups, hence they will be among the first to experience waning immunity with time after vaccination. This might also affect the increased incidence of severe breakthrough infections in older age groups, and a similar effect might also be seen in younger age groups with an increased time since vaccination.

Older age groups and comorbidities

Several studies have reported older age as a risk factor for breakthrough infection leading to severe disease. An analysis carried out in Italy on breakthrough infections leading to severe disease found that people with breakthrough infections that resulted in deaths had a higher average age (85.5 vs 78.3) than those who were unvaccinated, and they also had a significantly higher number of underlying conditions such as the presence of heart disease (ischemic heart disease, atrial fibrillation and heart failure), dementia and cancer [67].

Similar results were reported in a rapid analysis from Belgium. Hospitalised patients with breakthrough infections were older (median age 82 vs 64) and displayed a higher preponderance of patients with underlying comorbidities (93% vs 75.2%) compared to unvaccinated hospitalised patients [68]. Further, Germany found a higher proportion of severe COVID-19 breakthrough infections in vaccinated individuals aged ≥ 60 increasing with age. The fraction of severe COVID-19 infections was 9% in the 60-69, increased to 16% in the 70–79-year-olds and to 23% in the above 80 years olds [69]. A rapid characterisation of breakthrough infections admitted to the ICU in Ireland showed a median age of 67 (range 30 to 88) and 97% were reported to have an underlying medical condition [70]. A study from the Netherlands on vaccine effectiveness against hospitalisation reported a reduced vaccine effectiveness in older individuals aged 70 years and older. However, the risk of hospitalisation was more than nine times higher among unvaccinated compared to vaccinated individuals in this age group [71].

A recently published review of hospitalisation among vaccine breakthrough COVID-19 infections in the US found that the median age for severe or critical COVID-19 despite being fully vaccinated was 80.5 years. Pre-existing comorbidities in these groups included being overweight, cardiovascular disease and lung disease to a high extent [72]. A study in Qatar that analysed outcomes among patients with breakthrough infections, found that increasing age was associated with a higher risk of severe disease or death, while vaccination is associated with a lower risk [73]. A case control study from the US found that among 1 983 COVID-19 case patients, vaccine breakthrough patients compared with unvaccinated patients tended to be older (median age 67 vs 53 years), were more likely to be white non-Hispanic (64.0% vs 43.0%) and were more likely to be immunocompromised (40.8% vs 11.5%) [46].

Immunocompromised individuals

A retrospective study from the US found that the proportion with breakthrough infections was three times higher in the immunocompromised (IC) cohort compared to the non-IC cohort (N=374 [0.18%] vs. N=604 [0.06%]) in those aged above 16 and vaccinated with two doses of Comirnaty [74]. While individuals in the IC cohort only represented approximately 18% of the fully vaccinated population, they accounted for 38.2% of all breakthrough infections, 59.7% of all hospitalisations, and 100% of inpatient deaths. Although the study period was 10 December 2020 – 8 July 2021, and no variant specific estimates were provided, results indicate immunocompromised individuals to be at higher risk for breakthrough infections and severe outcomes. In a US study of hospitalised patients, authors found that of the 45 hospitalised COVID-19 cases, 44% were IC. mRNA vaccine effectiveness against COVID-19 hospitalisation for those who were IC was estimated at 63% compared to 91% among those who were not [75]. A study conducted in Israel found that IC patients comprised 40% of the fully Comirnaty vaccinated hospitalised patients with COVID-19 illness (N=152) and 47% of those with a poor outcome (i.e., IMV usage or death) [76]. In another study, Comirnaty effectiveness against SARS-CoV-2 infection was reduced substantially in those who were IC compared to the 95% vaccine effectiveness in the general population [77]. In a study conducted in the UK, a vaccine effectiveness of 73% (after two doses of Comirnaty) against acute symptomatic/critical illness among those who were IC compared to 93% vaccine effectiveness in the overall study population [78]. In another study from Israel, Chodick et al. reported a Comirnaty vaccine effectiveness of 71% against preventing SARS-CoV-2 infection in the IC (N=25,459) compared to 90% in the overall study population [79].

Other risk factors

A recent study using daily online survey data found that vaccination with COVID-19 Vaccine Janssen were associated with a higher risk of breakthrough infection compared to vaccination with Comirnaty (COVID-19 Vaccien Janssen vs. Comirnaty: HR (95% CI) = 2.23 (1.40 - 3.56)), while participants vaccinated with Spikevax (Spikevax vs. Comirnaty: HR (95% CI) = 0.69 (0.50 – 0.96) and those residing in urban counties experienced a lower rate of SARS-CoV-2 breakthrough infection compared with those from suburban (HR (95% CI) = 1.39 (1.01 – 1.90) or rural (HR (95% CI) = 1.57 (1.16 – 2.11) counties. There was no significant association between breakthrough infection and participant sex, race, healthcare worker status, prior COVID-19 infection, routine mask use, or overall vaccination rate in the county of residence [80]. Germany reported an increased frequency of breakthrough infections in individuals vaccinated with COVID-19 Vaccine Janssen. The maximum effectiveness of the COVID-19 Vaccine Janssen was estimated to be 36% against symptomatic infection and 59% against hospitalisation [69].

Another study on breakthrough infections in veterans in the US implies that the Delta variant is the primary determinant of infection since the patterns of breakthrough SARS-CoV-2 infection among vaccinated Veterans show a temporal trend overlapping with the emergence of Delta as the dominant variant in July 2021. In this study, the oldest age group (≥65 years) had a similar pattern of breakthrough infections over time compared to the younger age group, despite becoming fully vaccinated three to four months earlier, on average [42]. Similar results are seen in another US study by Rosenberg et al where trends in vaccine effectiveness were highly inversely correlated with increasing Delta variant prevalence [16].

Vaccination in children

Surveillance data from the EU/EEA shows that children have made up an increasing proportion of both notified cases and hospitalisations in EU/EEA countries in recent months, partially due to increased vaccination in older age groups [81]. Given high incidence in this group, risk of transmission between children and from children to other groups, particularly those who are unvaccinated, remains high.

All 30 EU/EEA countries are now recommending COVID-19 vaccination for all adolescents (12-17 years). With this expansion of the vaccine rollout to include adolescents, as of 7 November 2021, the median uptake of full vaccination in those under 18 years reached 14.3% (country range 0.9-28.8% [15]).

The European Medicines Agency is evaluating an application to extend the use of the COVID-19 vaccine Comirnaty, currently approved for use in people aged 12 years and older, to children aged five to 11 years [82]. The evaluation will include the EMA human medicines committee's review of the safety and efficacy data on the vaccine.

Modelling the impact of vaccination of children in the EU/EEA, including those aged five to 11 should this be approved, finds that the impact would be negligible on overall COVID-19 mortality during the short-term, given that time would be needed to scale up vaccination programmes to have enough of an impact on the effective reproductive number and severe outcome. However, as this is considered in longer-term projections, it may indicate a greater impact on transmission, followed by a decrease in mortality and hospitalisations in other age groups.

Natural immunity to SARS-CoV-2

A number of seroepidemiological studies conducted in the EU/EEA provide evidence of increased population seropositivity in recent months. Very few studies are able to discriminate between natural or vaccine-induced immunity, however, the increase is largely attributed to vaccination. Understanding the true contribution of naturally-acquired immunity in the total population is challenging without such studies, and estimates based on reported infection incidence are prone to under-ascertainment. For individuals that develop natural immunity, whilst the absolute rate of reinfection is low in the short term, antibody and T cell responses are highly variable and countries should continue to offer the full vaccination series to recovered individuals.

Prevalence of SARS-CoV-2 antibodies in Europe

Seroepidemiological studies for COVID-19 can estimate the proportion of individuals in a population who have evidence of natural or vaccine-induced immunity. These studies can also help estimate the under ascertainment of reported infections and are of importance for developing modelling forecasts.

Surveys conducted in 2021 have shown a generalised increase in seropositivity from April 2021 onwards across the EU/EEA, with this trend continuing into the autumn. Since September, Sweden, Estonia and Finland have all conducted serosurveys and estimates from these surveys all exceed 75% (range 75.6 – 96.8%) [82-84]. The Finnish Institute for Health and Welfare (THL) have conducted a weekly serosurvey sampling randomly selected members of the general population [85]. Seroprevalence results from THL prior to April were all below 10% but subsequently increased, with antibody levels after August reaching up to 92.9% (81.0 – 97.5%), with most of this increase attributed to vaccination. Other longitudinal studies that have differentiated between natural and vaccine induced immunity different serological assays, such as the study among blood donors in the UK, report similar findings with steadily increasing seropositivity that is mostly attributed to vaccination with seropositivity trends closely trailing cumulative weekly vaccine uptake levels [86].

Some studies in the EU/EEA have reported seroprevalence estimates disaggregated by age groups and seroprevalence mostly found to be lowest in children [82,86,87]. Data from Sweden and Belgium indicated an increase in seropositivity in children after the summer 2021 [83,89]. The Swedish Public Health institute reported a positivity of 42.1 (39.3-44.9) in individuals aged 0-19 in September-October in comparison to 29.7% in May-June, with this increase attributed to the rollout of vaccination among 16–19-year-olds. The survey in Belgium among primary school students in September and October found that 26.6% (21.5 – 32.8%) had antibodies, an increase of 11.2% from May-June 2021, with this increase attributed to natural infection as the group had not been vaccinated.

Several studies have estimated the ratio of seroprevalence to cumulative incidence and one systematic review reported large variation between studies and a median ratio between corrected seroprevalence estimates from national studies and the corresponding cumulative incidence of SARS-CoV-2 infection nine days prior of 18.1 (IQR 5.9–38.7) [90]. Data from THL during 2021 show a decline in the ratio of estimated infections compared to confirmed cases, which is attributed to a more comprehensive testing strategy [85]. Indeed, this observed under-ascertainment will depend on several factors including the course of the pandemic, the availability of tests and local testing strategy, as well as local characteristics such as demographics [91]. Under-ascertainment highlights the limitation of confirmed infections in estimating the true extent of the spread of infection within the population and can help highlight areas where testing levels may be insufficient.

Reinfection with SARS-CoV-2

Following recovery from infection to a previously circulating SARS-CoV-2 strain, risk of reinfection with the Delta variant appears to be low (absolute rate approximately 1%), with protection maintained for at least 180 days [92].

Given that antibody and T cell responses demonstrate highly variable duration in recovered individuals, vaccination is still recommended. For individuals that have recovered from a prior SARS-CoV-2 infection, a number of studies indicate that a single dose of Comirnaty, Spikevax or Vaxzevria generates antibody and cellular immune responses that are comparable – at least in the short term - to naïve individuals who complete a two-dose regimen. However, in light of limited available evidence on clinical endpoints, such as risk of laboratory-confirmed infection and symptomatic disease, for previously-infected individuals receiving just one dose of a vaccine intended as a two-dose regimen, countries should continue to administer two doses, as per EMA authorisation [93].

Modelling forecasts

Introduction

This is an update to the mathematical modelling conducted as part of the previous assessment published on 30 September 2021 [92]. While keeping the presentation of the results similar to the previously published version, the underlying modelling approach has been adapted to include updated parameters and additional aspects of the latest state of known COVID-19 epidemiology.

Since the last rapid risk assessment, the following aspects were added to the model projections:

- Impact of the upcoming holiday season
- Waning of vaccine efficacy on transmission
- Updated estimates of vaccine effectiveness against different endpoints
- Booster doses
- Vaccination of <18-year-olds.

As EU/EEA countries are moving toward the end of 2021, COVID-19 full vaccination coverage appears to have reached a plateau in many countries. Several countries have started rolling out booster programmes and expanded the vaccination programmes to include younger individuals. Since summer 2021, schools have reopened after the summer break, many NPIs have been lifted (see above 'Non-pharmaceutical interventions'), and contact rates have increased steadily across the EU/EEA, as is evident from contact surveys [94] as well as mobility data [95]. In recent weeks, however, several EU/EEA countries have reintroduced NPIs in response to resurgences in the number of infections and an increasing disease burden. Largely due to the safe and effective vaccines, the rise in cases is not translating into similar levels of hospitalisations and deaths as observed in 2020 and in the early months of 2021. Nonetheless, resurgences have also been seen in countries with reasonably high vaccine uptake. The future course of the pandemic will continue to be determined largely by the contact rates between individuals and by immunity conferred through vaccination and/or past infection. Importantly, the Delta variant, estimated to be twice as transmissible as the wild type variant that was circulating in autumn 2020, continues to be dominant across all EU/EEA countries.

Model description and assumptions

Taking into account the high transmissibility of the Delta variant and its AY.4.2 sub-lineage, stagnating vaccination coverage, the waning of vaccine-induced protection, vaccination programmes being extended to children and teenagers, booster programmes starting to be rolled out to older individuals and the re-introduction of NPIs, we estimate the number of cases and deaths in the EU/EEA until the end of January 2022, based on the available epidemiological and vaccination data until the beginning of November 2021. Hospitalisations were not included due to data availability issues for many EU/EEA countries. A crucial challenge for predicting the course of COVID-19 are uncertainties regarding: vaccine effectiveness, the number of recovered individuals with natural immunity, human behaviour and mobility patterns (particularly given the major holiday season in December 2021/January 2022) and the seasonal effects on viral spread. We take these uncertainties into account by considering different prediction scenarios (Table 2, with further scenarios in Appendix 2). By exploring all scenarios, we obtain a predicted landscape of COVID-19 in the period from 1 December 2021 to 31 January 2022. For simplicity, for all scenarios we consider an optimistic set of assumptions: natural immunity protects 100% against reinfection, there is cross-protection across variants, and there is no waning of natural immunity. Thus, our predictions yield an optimistic lower bound on the COVID-19 burden.

Furthermore, we assume that Delta remains the dominant variant, and that this variant is twice as infective as the wildtype SARS-CoV-2 [96], which was dominant in autumn 2020. While we assume that vaccination programmes continue with a sufficient supply of vaccine doses, we do consider the recent stagnation of the vaccination coverage in many Member States. We predict the future vaccine uptake by taking into account the current prioritisation of age groups (boosters), dose spacing, and vaccination in adults [3]. We build upon studies of vaccine efficacy and its waning against the Delta variant (see section on 'Vaccine effectiveness for Delta: infection, transmission, hospitalisation and averted deaths') and weigh estimates for the different vaccine products according to their distribution in each age group and Member State [3].

With the age-specific vaccination coverage, we generate COVID-19 cases by age-group. We further estimate future deaths from the age-based case-fatality rates, which are obtained from data during the dominance of wildtype SARS-CoV-2 in October and November 2020; we adjust those rates according to severity of the Delta variant as well as vaccine protection against severe outcomes by this variant. We simulate forecasts for the seven different scenarios to capture the uncertainty in our key model assumptions.

In our baseline scenario (Scenario 1, Table 2), we assume that contact rates (number of transmission-relevant contacts between individuals per day) stay the same as those observed at the beginning of November 2021, apart from the assumed increase in contact rates during the festive period (for this we assume a linear increase in contacts starting on 1 December 2021 up until 20 December where it stays constant until 5 January 2022.

Thereafter we assume contact rates to fall back to pre-festive value). Additional scenarios consider both high/low initial vaccine effectiveness against infection and its fast/slow waning (Scenarios 2-5, Table 3). To estimate the proportion of recovered population, we use serological survey studies (see references and discussion in 'Natural immunity to SARS-CoV-2' section). We also include a scenario with high and low under-detection of cases (Scenarios 6 and 7, Table 3). To reflect the major festive season in December 2021/January 2022 that is likely to be characterised by intergenerational mixing of individuals across all ages, we assumed the contact rates to increase by 30% in all scenarios [97]. To demonstrate the sensitivity of our results, we provide two additional analyses for all seven scenarios in Table 3 but with different contact rates of +20% and +50% (Appendix 2), respectively.

Table 2. Baseline and alternative forecast scenarios for COVID-19 in the EU/EEA, December 2021 - January 2022

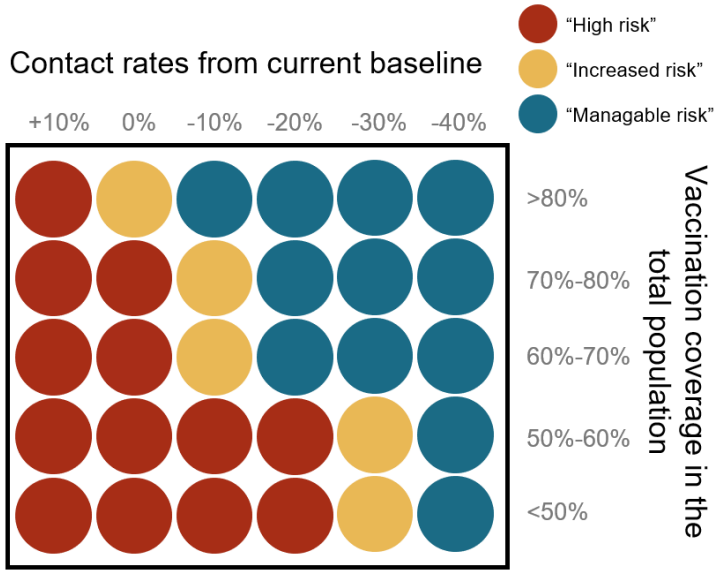
Scenario	1	2	3	4	5	6	7
Scenario name	*Baseline*	*High VE*	*Low VE*	*Fast waning*	*Slow waning*	*High natural immunity*	*Low natural immunity*
Vaccine effectiveness cases	baseline	1.1 x baseline	0.9 x baseline	baseline	baseline	baseline	baseline
Waning of vaccine effectiveness cases	baseline	baseline	baseline	fast waning	slow waning	baseline	baseline
Natural immunity	country estimate	country estimate	country estimate	country estimate	country estimate	1.3 x country estimate	0.76 x country estimate

Note: Summarises the parameters used in the different forecast scenarios with one baseline scenario (scenario 1) and six alternative scenarios. These scenarios reflect uncertain factors which cannot be influenced by EU/EEA countries such as vaccine effectiveness (VE) against the Delta variant and the waning of immunity.

We show the model predictions for different levels of vaccine uptake for the total population. For this we predict the disease burden for individual EU/EEA countries and summarised the predictions that correspond to similar vaccination coverages at the time of the modelling (<50%, 50–60%, 60–70%, 70–80%, >80% vaccination coverage in the total population).

We summarise the predictions across modelling scenarios and EU/EEA countries within the same vaccination level (Figure 8). First, we assign three burden levels to each scenario based on the mortality rate, <33%, >33%, and >100% of the highest peak so far registered in each Member State. Second, we summarise the burden levels across scenarios and countries, assigning 'high risk', 'increased risk', or 'manageable risk', representing the likelihood of high burden levels. Figure 8 shows the summarised predicted burden risk in dependency of different vaccination levels and different contact rates (relative to the current contact rates).

Figure 8. Projected burden of COVID-19 mortality in relation to vaccination coverage and contact rate change between December 2021 and the end of January 2022



Note: The figure shows the risk for mortality burden as circles in blue ('manageable risk'), yellow ('increased risk'), and red ('high risk'), across different vaccination coverages as well as different changes in contact rates from the current situation and assuming 30% increased contacts due to the festive season.

Model results and discussion

Without changes in contact rates from current levels, we estimate that the countries at the highest level of vaccination coverage of more than 80% are at 'increased risk', while those at vaccination coverage levels of less than 80% are at 'high risk' (Figure 8). Therefore, our forecasts show that effective contact reduction is crucial for reducing the risk of an unprecedented high COVID-19 burden in the next months.

EU/EEA countries with a low (<60%) or average (60-80%) vaccine uptake for the total population will require substantial reductions in contacts between people to avoid a high burden. For countries that are currently experiencing high COVID-19 burden, high contact reductions can achieve manageable burden toward the end of the December-January period. EU/EEA countries with higher (>80%) vaccine uptake for total population could experience a manageable burden at current contact rates. However, this burden could become high if contact rates increase further, as might be expected given the end-of-year festive season (Appendix 2). Because vaccines offer high protection against severe outcomes of COVID-19 infection, a large number of COVID-19 hospital admissions will be unvaccinated individuals, in particular unvaccinated individuals in risk groups.

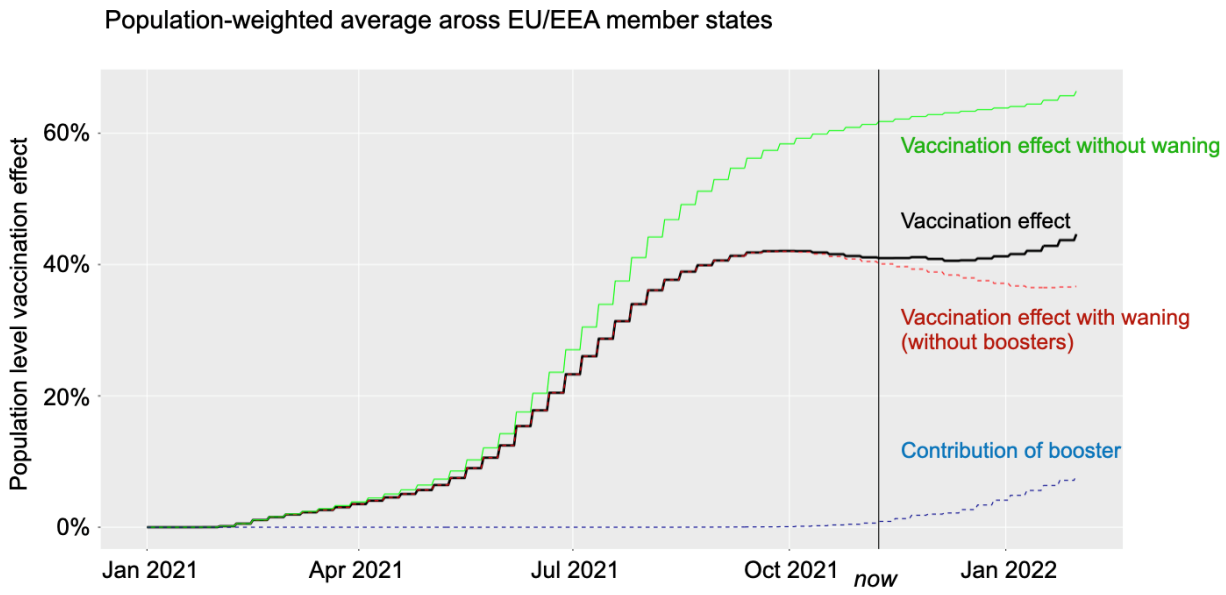
Additionally, we found that an emergence of a new Delta AY.4.2 sub-lineage does not change the risk estimation in Figure 8. The time required for a variant with such growth advantage to become dominant and thus significantly impact the burden is longer than the time period of these projections.

The results above are largely reflective of the high transmissibility of Delta which counteracts the reduction in transmission achieved by the current vaccination rollout in the EU/EEA. The key impact of vaccination is indeed the reduction of the case-fatality rates. Nonetheless, our modelling shows that Delta's transmissibility as well as increasing contact rates (e.g., due to the festive season) could combine to pose a significant risk for exponential growth of cases in the coming months. Such growth can over a short time lead to a burden of cases that outweighs the reduction in case-fatality rates.

The effect of boosters on transmission

Accounting for the vaccine-induced immunity decreasing over time, the population level impact of vaccines can be shown to decrease in a population over time without booster doses (Figure 9), while a booster programme is able to stop and eventually recover the population level impact of vaccines to a level seen before the waning occurred (Figure 9). Nonetheless, given the inevitable delay in boosting vaccine effectiveness and the rollout speed of administering third doses, it will take some time for the population level of immunity conferred by vaccines to return to a higher level again.

Figure 9. Population level effect of vaccination against transmission in the EU/EEA over time including the waning of the vaccine-induced immunity



Population level effect of vaccination (black line, shown as weekly estimates), the impact in the hypothetical situation of the absence of waning on vaccine-induced immunity (green line), the impact with waning immunity but without boosters (red line), and finally the contribution of the boosters alone (blue line). This assumes an illustrative scenario of a booster programme including above 40-year-olds at an intermediate roll-out speed. The expected booster roll-out speed will depend strongly on the individual country context.

Furthermore, the impact of waning immunity on transmission is largest in countries with high vaccination coverage (Appendix 3-Figure 1), which vaccinated a greater share of their population a longer time ago. Although individuals aged older than 70 years may contribute less to reducing transmission than individuals aged 40-70 years (Appendix 3-Figure 2), administering booster doses to older individuals gives more direct benefits in terms of preventing severe outcomes like the number of deaths averted.

Communities of high risk

Finally, any country, including those with high vaccination coverage, is likely to have some communities with low vaccination coverage. Our results suggest that those communities are at a high risk of severe burden. A combination of targeted vaccination campaigns and NPIs could help reduce this risk, ideally tailored to those communities and specific factors that increase hesitancy about vaccines. This may further require increased testing and close monitoring of COVID-19 cases at a local level.

Healthcare fatigue and pressure

We did not account for pressures that health systems face through COVID-19-related hospitalisations and, for example, increased hospitalisations due to a moderate or severe influenza season. As we are just about to enter the winter, the continued strain on health workers who have been under enormous pressure since early 2020 should not be underestimated, and may additionally limit the available healthcare system capacity.

NPI fatigue and the festive season

At the same time, a certain level of fatigue against re-introduced NPIs are to be expected, that could lead to more risky behaviour with potential for infectious events, particularly in private gatherings over the festive season in December 2021/January 2022 (and in light of this being the second festive season of the pandemic, and possible expectations of compensating for the last winter). It seems advisable to encourage people of all ages to be careful over the festive season that is usually characterised by extended periods of intergenerational mixing with close physical contact of members from different households. In older individuals (and those at highest risk of severe outcomes) whose vaccine-induced immunity is waning, while waiting for the boosted protection of the third vaccine dose, there is the risk of (breakthrough) infection that may lead to an increasing burden in January and the months afterwards. Emphasising the importance of the vaccines, while not neglecting the different forms of NPIs in private gatherings, needs to be part of risk communication in EU/EEA countries.

Limitations

There are a number of limitations to this modelling. We use estimates of vaccine efficacy from trials, but those only give an imperfect picture of real-world vaccine effectiveness. Moreover, due to lack of accurate data, we do not use age-stratified vaccine efficacies. More observational studies on the effectiveness of vaccines are needed. We also assumed no substantial role of immune escape variants that would impact vaccine effectiveness given the short time horizon of this assessment until end-January 2022. Behaviour is extremely difficult to measure and to predict. Additionally, there are still many unknowns around natural immunity to SARS-CoV-2, which we are trying to capture through a range of natural immunity scenarios. Furthermore, although the recent news of antiviral drugs are promising, it seems unlikely that they will become widely available in time to make an impact on the COVID-19 burden foreseen up until end-January 2022. Finally, it remains unclear to what extent viral transmission of SARS-CoV-2 is affected by climate and other seasonal factors. Our forecasts should therefore be interpreted in the light of these uncertainties.

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 for scenarios that consider vaccination coverage (including third and booster dose), vaccine effectiveness, waning vaccine immunity, vaccination of children, natural immunity and population contact rates—in the context of the continued circulation of the Delta variant. This assessment of risk covers the period between 1 December 2021 and 31 January 2022 and follows the same ECDC risk assessment methodology applied in previous risk assessments, with the overall risk determined by a combination of the probability of an event occurring (infection with SARS-CoV-2) and its impact for a given population [98].

The current assessment of the risk posed by the SARS-CoV-2 pandemic is stratified by four population groups: the vaccinated and the unvaccinated general population; the vaccinated and the unvaccinated vulnerable population. The assessment is based on the following principles: i) the vaccinated have a lower probability of infection and onward transmission and ii) a lower impact of such infection than the unvaccinated, while iii) whether vaccinated or not, the vulnerable population suffers a higher impact of such infection when compared with the general population. Following the current ECDC forecast (see section on 'Modelling') the risk to EU/EEA countries is assessed based on their current levels of full COVID-19 vaccination coverage in their total population, grouped into three categories (low, average, high). Appendix 4 includes a detailed description of the assessment process per population and vaccination coverage group, where the low and average vaccination coverage countries have been combined for ease of presentation.

Risk assessment question

Based on current vaccination coverage and the circulation of the Delta variant in the EU/EEA, what risk does SARS-CoV-2 pose to the general and vulnerable population?

Countries with low/average vaccination coverage

Countries with a low (<60%) or average (60-80%) vaccine uptake for the total population will require substantial reductions in contacts between people to avoid a high burden. For countries that are currently experiencing high COVID-19 burden, high contact reductions can achieve a manageable burden toward the end of the December-January period.

<u>General population</u>

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

<u>Vulnerable population</u>

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

Countries with high vaccination coverage

Countries with higher (>80%) vaccine uptake for the total population could experience a manageable burden at current contact rates. However, this burden could become high if contact rates increase further, as might be expected given the end-of-year festive season.

General population

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

Vulnerable population

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

** Risk of infection for the unvaccinated population is increased from our previous risk assessment to reflect rising circulation in countries with higher vaccine uptake.*

Additional risk considerations

The assessment of risk, as outlined above, is at the population level and does not correspond to the individual risk of a vaccinated person, where 'full vaccination' refers to completion of a primary series.

In the context of possible circulation of other seasonal respiratory viruses, the projected increase in SARS-CoV-2 cases may place additional strain on healthcare systems and healthcare system capacity. As such, NPIs, coupled with efforts to address low national and sub-national vaccination coverage, will continue to play an important role in limiting disease burden across the EU/EEA between 1 December 2021 and 31 January 2022.

Options for response

Vaccination

The highest priority is the continued and relentless efforts to increase vaccination coverage rates across the EU/EEA to control the spread of COVID-19, particularly in the context of the circulation of the more rapidly transmissible Delta variant. Resources must be prioritised to identify and target the unvaccinated, hesitant and most remote populations in order to provide full vaccination across communities and age groups.

Countries are urged to give utmost priority to individuals initially targeted by COVID-19 vaccination programmes that are unvaccinated or not yet fully vaccinated. Increasing COVID-19 vaccination coverage in all eligible age groups, but particularly in the elderly, in the vulnerable, and in healthcare workers should remain the priority for public health authorities. There remains an urgent need to close immunity gaps in the adult population and ensure effective and equitable coverage across countries and regions in Europe. Concomitant administration of COVID-19 and seasonal influenza vaccines should be considered, as it is safe and provides for efficiencies in administration logistics and costs [98-100].

Increasing vaccination coverage

Continued efforts are needed to further increase vaccination coverage and to ensure that all eligible individuals receive a full course of vaccination. To accomplish this, it is important to understand the factors that determine low vaccine uptake in some population groups, including issues around vaccine acceptance and access, so that targeted, context-specific and effective interventions can be developed. Diagnostic tools are a valuable instrument for this [102,103]. They facilitate assessment of the drivers of sub-optimal vaccine acceptance and uptake in a given population. The 5Cs model can also help to organise and explain factors related to Confidence, Constraints, Complacency, Calculation, and Collective responsibility, thereby guiding the adoption and implementation of appropriate interventions [104].

To increase vaccination coverage, it is also necessary to address inequalities in access to COVID-19 vaccination in different population groups. For example, targeted strategies are needed to address any access and acceptance sissues affecting uptake in socially vulnerable populations [105,106]. Furthermore, the circulation of misinformation around COVID-19 vaccines should be addressed, including monitoring online spaces as a means of gaining insights into the information needs and concerns of the public. These insights can guide proactive and positive communication strategies about vaccination on social media. Evaluation of these strategies should be conducted in order to ensure that lessons are identified and interventions optimised. The development of longer-term initiatives that foster the population's resilience to misinformation should also be considered [107].

There are a number of countries currently using COVID-19 certificates to allow people access to specific places/events, such as restaurants, museums, concerts etc [15]. There is some evidence published on the impact that mandatory COVID-19 certificates can have on vaccine uptake. Mills et al conducted a study to assess the relationship between the introduction of COVID-19 certification on observed vaccine uptake from May to 29 August 2021. The study investigators found that mandatory COVID-19 certification led to a sharp increase in vaccinations 20 days prior to implementation with a lasting effect up to 40 days after. Those countries that had a lower average level of uptake showed more pronounced effects, particularly in some age groups. There was no noticeable effect in countries that had a higher uptake or in times of limited supply or when it was introduced to increase testing [108].

An additional dose as an extension of primary vaccination

In parallel to increasing vaccination coverage with primary vaccination, as specified previously, ongoing efforts to provide an additional dose as an extension of the primary series should now be considered for people who may experience a limited response to the primary series of COVID-19 vaccination, such as some categories of immunocompromised individuals (e.g. solid organ transplant recipients).

Booster doses

There is emerging evidence from a small number of observational studies suggesting that booster doses increase protection against infection and severe disease after waning immunity. This is particularly important both for those most vulnerable to severe disease and to decrease infection, which can potentially reduce the transmission of SARS-CoV-2 in the population. This evidence is supported by ECDC mathematical models presented in this document on the effects of boosters on transmission, which show: i) the waning immunity in adults aged 40-70 year contributes on average almost half of the impact on increased transmission due to waning, while ii) the waning immunity in the other two groups (>70 year and <40 year) each contributes about a quarter of this impact (Appendix 3, Figure 2). This is a result of both the duration since when most individuals in the 40–70-year-old group were vaccinated and the population size of this group. In addition, since a significant proportion of adults aged <40 year were vaccinated less than six months ago (and are not eligible for the booster at this point), it would have a smaller impact giving this group booster doses compared to those >40 year. However, this current situation might change in the coming months when (i) <40 year experience more waning in their vaccine effectiveness of transmission, and (ii) more <40 year become eligible for a booster dose.

The impact of the waning vaccine-induced immunity on Rt is greater in countries with high vaccination coverage, which vaccinated a greater share of their population a longer time ago, and the impact of the waning on transmission is smaller in countries with lower vaccination coverage.

National Immunisation Technical Advisory Groups (NITAGs) in EU/EEA countries should already consider a booster dose for those 40 years and over, targeting those most vulnerable for severe disease such as the elderly (particularly those living in closed settings) and those with comorbidities and healthcare workers to ensure resilience of the healthcare system.

EU/EEA NITAGs could also consider a booster dose for all adults 18 years and older to increase protection against infection due to waning immunity which could potentially reduce transmission in the population and prevent additional hospitalisations and deaths.

Based on EMA recommendations [56,57], countries should consider an mRNA vaccine given as a booster dose at least six months after the primary vaccination series with a homologous booster.

New treatment options for COVID-19

Several medicinal products have been studied to assess their safety and efficacy as potential agents for pharmaceutical prophylaxis or treatment of COVID-19. Systemic corticosteroids and immunomodulatory agents (IL-6 receptor blockers) are recommended for the treatment of moderate and severe COVID-19 [109].

Recently, the combination of neutralising monoclonal antibodies against SARS-CoV-2 casirivimab and imdevimab and the antibody regdanvimab have been granted market authorisation in the EU for the treatment of patients with mild-to-moderate COVID-19 infection at high risk of progressing to severe disease and hospitalisation. In a phase 3 randomised control trial (RCT) with 3 867 patients with mild COVID-19 and at least one risk factor for progression to severe disease, hospitalisation or death from COVID-19 happened to 1% of the treatment arm vs. 3.2% of the placebo (Hazard ratio 0.30) [110]. The combination casirivimab and imdevimab can also be used for prophylaxis against COVID-19 after high-risk exposure in patients at high risk for severe disease [111]. In an RCT with 1 505 healthy adult household contacts of SARS-CoV-2 cases, subcutaneous injection of the antibody combination prevented symptomatic infection significantly more than in the placebo group (adjusted odds ratio 0.17; 95% CI 0.09-0.33) [112]. Monitoring SARS-CoV-2 mutations and their effect on the susceptibility of the virus to monoclonal antibody treatments is important.

In addition, two oral antiviral agents, molnupiravir (a ribonucleoside analogue) and a combination of ritonavir with an investigational SARS-CoV-2 protease inhibitor (PF-07321332), have shown preliminary positive results in Phase 2/3 trials for the prevention of severe COVID-19. The oral administration of these antivirals is an advantage against currently available antiviral treatments against COVID-19. EMA's human medicines committee (CHMP) has started a rolling review of molnupiravir [113] and will support national authorities who may decide on the use of this medicine for COVID-19 treatment prior to its authorisation [114].

Together with high vaccination coverage, these pharmaceuticals could play an important role in the prevention of severe COVID-19 and the longer-term intervention strategies against SARS-CoV-2 in the future. Pricing and availability of both the neutralising antibodies and the oral antivirals against SARS-CoV-2 are going to be a deciding factor for their wider use and in turn, the impact of these pharmaceuticals, in addition to the logistical challenge involved in their need to be administered early in the course of the disease to be effective [115].

Non-pharmaceutical interventions

As described above, even in countries with high vaccine uptake, maintaining or reintroducing NPIs remains vital to reduce transmission. The goal is to implement NPIs in the most timely, effective, coordinated, and targeted manner possible, minimising their undesired social, economic and health impact, including on mental health. Measures to reduce transmission include physical distancing, appropriate use of medical face masks in any place where physical distancing cannot be maintained, hygiene measures and recommendations to stay home when experiencing COVID-19 compatible symptoms. Surveillance, sufficient testing, contact tracing and quarantine of contacts remain an important layer of measures in addition to NPIs to prevent surge of cases [116].

Teleworking is one of the physical distancing measures that can have a significant effect in decreasing transmission in workplaces and in addition, decreases general population movement including preventing congestion on public transportation. Other measures include modifications to the operating arrangements for public transportation to decrease crowding, such as increasing its capacity or staggering opening hours for the various public and retail services.

A recent retrospective case control study in the USA showed that use of face masks when exposed to a known COVID-19 case reduced the odds of contracting the disease by 48%[117], while a modelling study from the UK showed a 3% lower likelihood of testing positive for COVID-19 in persons that need to commute and work in person, when using a face mask [118]. Limiting the size of gatherings (e.g., social and cultural events, entertainment, etc) is one more effective measure with aim to prevent or minimise crowding, with gatherings outdoors preferred over indoors. Engineering controls in mechanically ventilated and naturally ventilated closed spaces, as well as administrative controls to reduce occupancy and use of face masks should be considered for indoor spaces [119]. Organising gatherings in poorly ventilated spaces should be avoided. To decrease the risk of transmission after gatherings, for example the events planned to celebrate the end-of-year festive season, an extension of recommended teleworking could be considered for workers.

Mitigation measures to be considered in educational settings include approaches that prevent crowding (classroom distancing, staggered arriving times, cancellation of certain indoor activities), especially in older age groups, together with hygiene and measures to minimise transmission (handwashing, respiratory etiquette, cleaning, ventilation, face masks in certain circumstances and for certain age groups) [120]. Further guidance on mitigation measures in educational settings, including quarantine and 'test to stay' policies is available in previous ECDC documents [91,115,119].

Research on the effectiveness of NPIs on COVID-19 in Europe indicate that timely introduction of measures leads to higher reduction of cases, while gradual lifting of restrictions results in delay of increasing trends. NPIs, particularly physical distancing measures are more beneficial when they are implemented early and for sufficient duration [121]. Some authors also highlight the significance of combining measures and applying them simultaneously to improve their effectiveness. Emphasis should also be given to appropriate communication to ensure compliance with the measures, especially due to the 'pandemic fatigue' that a large part of the population experience.

Continued mitigation efforts and strengthening of healthcare systems and HCW resilience remain important during winter 2021-2022. Interventions to support HCWs should consider organisational, social, personal, and psychological aspects, and continue to be researched to determine the effectiveness of different interventions [121,122]. For analysis and available evidence on NPIs used to respond to the COVID-19 pandemic, please refer to ECDC's technical document 'Guidelines for the implementation of NPIs against COVID-19' [124].

Testing, contact tracing, surveillance and monitoring

Contact tracing

Contact tracing is an essential public health measure to fight the ongoing COVID-19 pandemic, in conjunction with active case finding and testing, and in synergy with other measures such as physical distancing. Contacts of a case should be promptly identified and provided with information about suitable infection control measures, symptom monitoring, testing and quarantine.

In the latest ECDC guidance [116], the transmissibility of the Delta variant and vaccine effectiveness have been taken into account. Differentiation between the management of vaccinated contacts versus unvaccinated contacts and revised recommendations for contact tracing in the educational setting have been included.

Since 26 October 2021, key indicators for contact tracing are collected weekly through TESSy [125].

Testing

Testing of people with symptoms regardless of vaccination status together with isolation of positive persons, continues to be important to limit the spread of SARS-CoV-2 and to reduce the burden on the healthcare system. Depending on available resources, testing strategies could include additional objectives, such as outbreak analyses, phylodynamic analyses and other research studies. While RT-PCR tests remain the gold standard in COVID-19 testing because of their high sensitivity and specificity, several EU/EEA countries have introduced the use of RADTs and self-RADTs as a way of further strengthening countries' overall testing capacity, particularly in case of limited RT-PCR capacities or where prolonged testing turnaround times result in no clinical and/or public health utility. Further information on options and considerations for the use of RADTs can be found in our recently updated technical report [126].

Diagnostic laboratories should remain vigilant to detect any mismatches of specific RT-PCR assay primers and probes in comparison to circulating virus genomes. For in-house or commercial RT-PCR assays for which the primer/probe sequences are available, validation can be done via the ECDC PrimerScan or similar tools that identify mismatches [127]. For commercial assays where the primer/probe sequences are unknown, a validation procedure for the capacity of the molecular assays to detect variants is needed. Laboratories should also remain vigilant to identify reductions in RADT sensitivity or specificity due to the potential emergence and circulation of new SARS-CoV-2 variants or cross reaction with other co-circulating respiratory viruses.

Laboratories should have quality assurance systems in place and are encouraged to participate in external quality assessment (EQA) schemes.

Besides SARS-CoV-2, other circulating respiratory viruses such as influenza and RSV can induce additional challenges for healthcare providers and public health systems in the current pandemic. Patients presenting influenza-like illness (ILI) or acute respiratory illness (ARI) symptoms in sentinel primary care surveillance sites as well as severe acute respiratory illness (SARI) patients in secondary care should be sampled and tested concurrently for influenza and other circulating respiratory viruses. Diagnostic laboratories could consider the use of multiplex RT-PCR assays [128]. Representative influenza positive specimens should be sent to the influenza reference laboratories (WHO Collaborating Centre) for further genetic and antigenic characterisation.

For more information on testing and testing strategy please refer to the testing strategy section of the 15th update of the Rapid Risk Assessment [129].

SARS-CoV-2 genetic and antigenic characterisation capacity

Genomic surveillance of currently circulating variants remains of high importance for early detection of the presence and epidemiological trends of specific VOCs, VOIs and variants under monitoring, or the emergence of novel variants with concerning characteristics, in particular with the current vaccination efforts.

A representative sample with a sufficient sample size (optimally each week) and targeted samples from specific settings or populations (e.g., all travel-related cases, a representative sample of outbreak cases, cases with unusual clinical presentation) of PCR-positive specimens should be sequenced according to the recommendations of the ECDC guidance for representative and targeted genomic SARS-CoV-2 monitoring [130].

The dominance of the Delta variant does not exclude the emergence of a new variant, as seen previously with Delta substituting the Alpha variant and in case, e.g., a new vaccine escape variant occurs, early detection is key for a fast response. To ensure the detection of such an event with sufficient precision, it is important to sequence the recommended number of samples as outlined in our current genomic surveillance guidance [130].

Depending on available resources, pre-screening PCR tests with specific SNPs for the Delta variant might be used as sensitive first test, followed by representative selection of samples for whole genome sequencing. Furthermore, Member States who need support to reach sequencing targets can use ECDC services for sequencing of SARS-CoV-2 samples by writing an email to typing@ecdc.europa.eu.

Laboratories are encouraged to further characterise variants antigenically. Please contact ECDC at covid.microbiology@ecdc.europa.eu for requesting support for SARS-CoV-2 antigenic characterisation.

Travel measures

Travel restrictions are unlikely to have any long-term major impact on the timing or intensity of local epidemics in comparison to rigorous local implementation of NPIs, particularly in view of the dominance of the Delta variant in all EU/EEA countries. In addition, the newer VOI Delta sub-lineage AY.4.2 is already present in all the EU/EEA countries (albeit in very small percentages), therefore measures to prevent its importation are not useful.

ECDC has published a guidance for COVID-19 quarantine and testing of travellers [131], also highlighting the considerations around the use of RADTs for travelling. Updated options for the use of RADTs, which can be useful for detection of infectious cases in the first five days from disease onset have been published [126].

NPIs should be maintained throughout travelling regardless of the vaccination status of the traveller. In particular, the use of face masks, avoidance of crowding and maintaining physical distancing, in all forms of transport. Engineering controls for improved ventilation in airplanes, trains and buses should be implemented.

EU digital COVID certificate

The EU digital COVID certificate (EU-DCC) has been in use in the EU/EEA since 1 July 2021, and 22 other countries and territories have also since adopted it as proof that a person has been vaccinated against COVID-19, has recovered from COVID-19, or has had a recent negative test result, with the aim of facilitating safe and free movement of people. It is a global standard and the only system currently in use internationally for travellers. According to a recent Member State survey, up to 20 EU Member States currently use the EU Digital COVID Certificate for domestic purposes, such as for access to large events, restaurants, cinemas, museums or care homes and close contact occupations (e.g. fitness centres, hairdressers etc), with an additional national legal basis [132,133], and more are considering its adoption [134]. However, evidence on the role of the EU-DCC or other similar certificates in decreasing SARS-CoV-2 transmission domestically is limited.

Risk communication

The current surge in cases in many EU/EEA countries, along with related decisions to re-introduce or further focus NPIs [135] such as use of COVID-19 passes in several countries for people to access venues and services [136], poses a significant challenge for risk communication. Expectations were high in early 2021 as to the power of vaccines to rapidly bring the pandemic under control, but despite the successful and rapid rollout of national vaccination programmes, large variations in vaccine uptake still prevail across countries and within specific population groups [3]. This, along with the high prevalence of the Delta variant, provides ample opportunity for the virus to spread and cause disease, particularly among the unvaccinated. Furthermore, as the pandemic continues with a succession of 'waves' and cycles of loosening and tightening of restrictions, distrust and less inclination to follow the measures [137] may develop alongside potentially damaging narratives focused on blame [138].

A population that has had a high degree of trust in the authorities' handling of the pandemic [137,139] will likely have greater understanding of, adherence to, and capacity to sustain the more restrictive measures. Being transparent about the level of uncertainty regarding current scientific understanding can help maintain public trust [140]. Further, provision of a clear framework regarding which parameters are being used in order to adjust measures (e.g. vaccine uptake, hospital admissions, etc.) continues to be important for explaining any changes that may be necessary, and thereby for promoting public acceptance of any such changes [92].

Following the key principles of effective risk communication [141], clear, timely and transparent communication needs to: a) recognise the achievements and the impact of national COVID-19 vaccination programmes; b) provide clear information about what vaccines can and cannot do; c) continue to inform about the current epidemiological situation and the rationale for measures being implemented; and d) acknowledge uncertainty where it exists. It may be helpful to include the following considerations when developing messaging:

Emphasising the importance of vaccination

- Reintroduction of NPIs in many countries may increase the risk of some people concluding that COVID-19 vaccines are not effective. It may also further dissuade unvaccinated individuals from being vaccinated, or it may reduce acceptance and uptake by those that were initially willing to vaccinate but are now becoming more complacent [141,142]. To address this, risk communication messages for promoting vaccination should continue to emphasise both the effectiveness and safety of vaccines, and specifically, they should clarify that while vaccinations may not always stop infection, they very substantially reduce hospitalisation rates and deaths. The risk of not vaccinating may be communicated by underlining the comparative risk for severe outcomes (hospitalisation and death) for a non-vaccinated individual versus a vaccinated one.
- Communicating on safety may be demonstrated by showing the proportion of people who experience adverse effects of the vaccine, relative to those who have been seriously affected by the disease [140].
- Risk communication messages involving numbers should be accompanied by visualisations and should be understandable to the general public [140,144].
- In addition to communicating risk, emotional appeals and the use of testimonials can be leveraged to highlight the importance of collective responsibility and address complacency [104,145].

Highlighting the continued need for NPIs

Measures to mitigate further spread are outlined above (see Options for Response - Non-Pharmaceutical Interventions). Motivating people to follow these measures is even more important as we move towards winter and the festive season, when more people will travel and gather indoors.

- Recent data from several countries show decreased adherence to NPIs, including in individuals who have been vaccinated [145-148]. It will be important to communicate the reasons why NPIs are being introduced, how long NPIs will need to stay in place (short, medium and long-term), and what the measures are expected to achieve [150].
- It should be explained that infection is still possible after vaccination, even though the risk is clearly reduced, and that this is why multiple interventions are needed [150]. Hence, this is not an 'either-or scenario' (i.e. vaccination or NPIs), but rather it is an 'and-and scenario', whereby both vaccination and personal protective measures are needed to minimise the spread of the disease [151].
- People may be more motivated to follow recommended NPIs if they understand that modest restrictions now can diminish the need for stronger restrictions later, and that adherence to the measures is in fact a means of maintaining more extensive 'freedoms' for longer [92].

Knowledge gaps

Much of the evidence presented here is based on unpublished data, which is evolving daily. There are still many knowledge gaps and uncertainties regarding interpretation of the data. Knowledge gaps that are being, or still need to be, addressed, include:

SARS-CoV-2 virus and variant characterisation

- Incidence of variants in EU/EEA populations and elsewhere, where sufficient sequencing is not available
  - ECDC is supporting EU/EEA countries to achieve sufficient sequencing of their samples.
- Possible animal reservoir (species) being a risk for adaptive mutations and an ongoing source of infection for humans (e.g., minks).
- Competitive advantage of different variants, and consequences of co-circulation.
- Unknown genetic markers related to receptor binding, infectivity, severity, etc.
- Antigenic characteristics of variant viruses.
- Binding properties to human receptors, including (Angiotensin-converting enzyme 2) ACE2 receptors.
- Seasonality of transmission
  - ECDC is carrying out a systematic literature review on this subject.

Vaccine effectiveness

- Studies evaluating vaccine effectiveness by variant, age group, time since vaccination and different vaccine products and schedules, including with wide geographic representation and from multiple countries.
  - ECDC is supporting studies on vaccine effectiveness.

- The description of the characteristic of cases with breakthrough infections and of the associated virus (i.e., genetic variant) to complement the information on vaccine effectiveness. The monitoring and description of breakthrough infections should be routinely collected and assessed.
    - ECDC is implementing studies on COVID-19 vaccine effectiveness using a multi-country approach and a standardised protocol in a variety of settings (e.g., hospitals, primary care settings, healthcare worker cohort, etc.).

Natural infection

- Robust estimates of sero-prevalence of SARS-CoV-2 differentiated according to natural/vaccine induced immunity.
- Clear extrapolation of seropositivity rates to the total population to determine levels of protection.
- Under-ascertainment of cases.
- Cross-protection.
- Duration of protection following natural infection and the potential for waning immunity.

Clinical

- The severity and incidence of post-COVID condition
    - ECDC is planning a systematic literature review on this subject for adults and children, and collaborating with the European Society of Paediatric Infectious Diseases (ESPID) on post-COVID condition in children.
- Impact of variants on possible treatment options (e.g., neutralising monoclonal antibodies).
- Effectiveness and impact of new antiviral treatments.

Non-pharmaceutical interventions

- Further studies assessing the effectiveness of individual and/or combinations of NPIs are needed; these will be an essential guide to tailoring the use of NPIs to a setting's epidemiological situation. Such studies should take into account different SARS-CoV-2 variants as well as vaccinated versus unvaccinated populations.
- More evidence is needed on the effectiveness of different options for air cleaning in closed spaces.

Behaviour and social sciences

- In-depth understanding of what is driving low vaccine uptake in some populations.
- High quality evaluations of interventions aimed at addressing vaccination misinformation
    - ECDC is currently developing a training on addressing online vaccination misinformation for public health experts and risk communicators, which will include a section on evaluation of interventions.
- High quality evaluations of interventions aimed at facilitating vaccine uptake, including interventions based on incentivisation or mandates.

Limitations

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

The epidemiological data used in this assessment are dependent on availability from EU/EEA countries through surveillance reporting or publicly available websites. The data not only reflect the epidemiological situation but are also dependent on local testing strategies and local surveillance systems.

Limitations regarding the modelling forecast are presented in the relevant section.

It is important to consider the time lag between infection, symptoms, diagnosis, case notification, death, and death notification, as well as the time lag for reporting at the EU level. Assessing the impact of response measures is complex due to the implementation of different components of NPIs and the pace of implementation for vaccination programmes.

The natural evolution of the virus (including the spread of variants of concern), compliance with measures, cultural, societal, environmental, and economic factors will all continue to play a role in the dynamics of disease transmission. There is still limited knowledge and uncertainty around VOCs. The assessment of the future trend of disease transmission is limited by the lack of knowledge from previous outbreaks.

Source and date of request

ECDC internal decision, 9 November 2021

Consulted experts

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

Disclaimer

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

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

Appendix 1

Figure 1. Number of influenza virus detections from sentinel surveillance, by week and reporting country, season 2021/22, EU/EEA

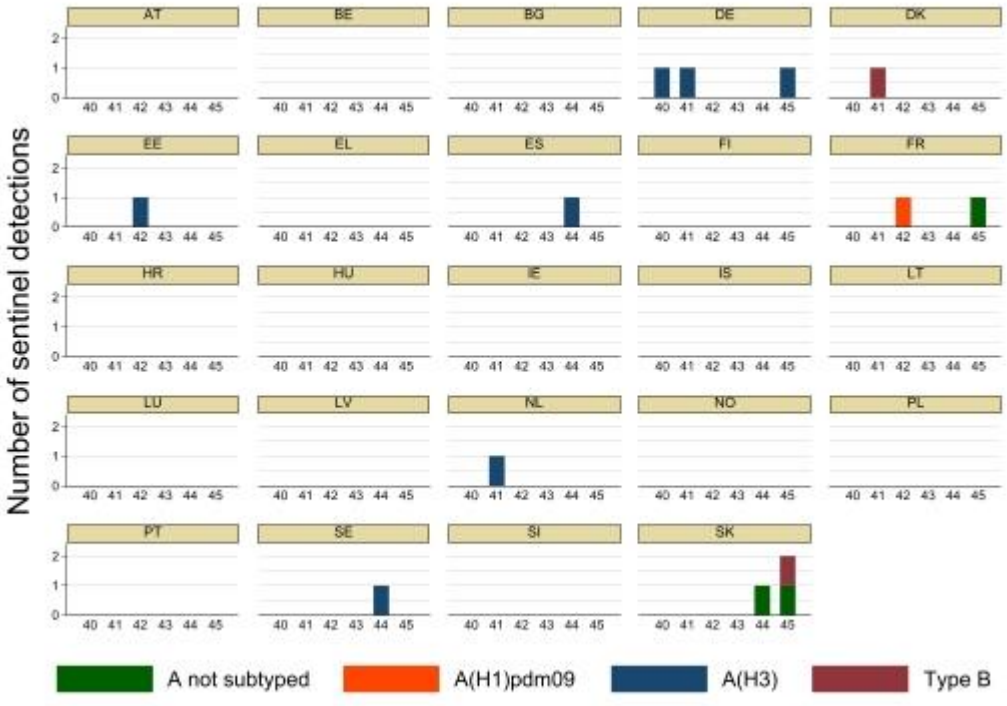


Figure 2. Number of influenza virus detections from sentinel surveillance, by week, season 2021/22, EU/EEA

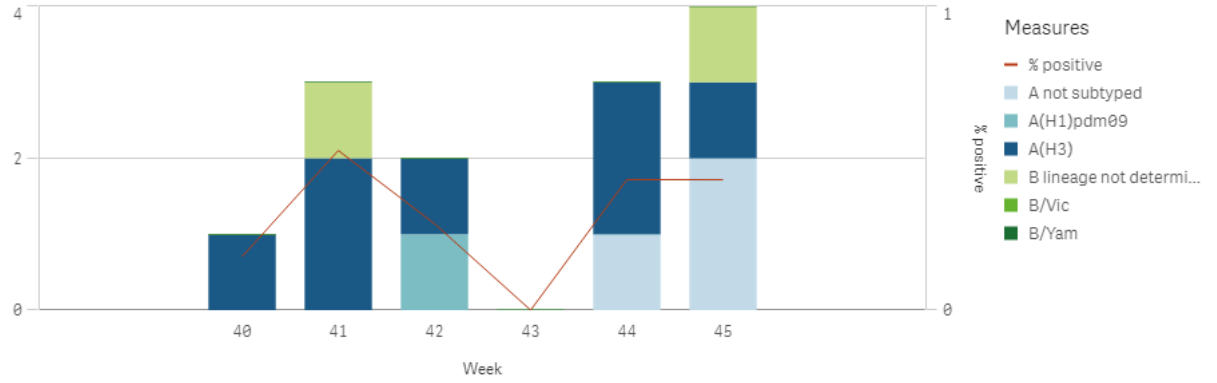


Figure 3. Number of influenza virus detections from non-sentinel surveillance, by week and reporting country, season 2021/22, EU/EEA

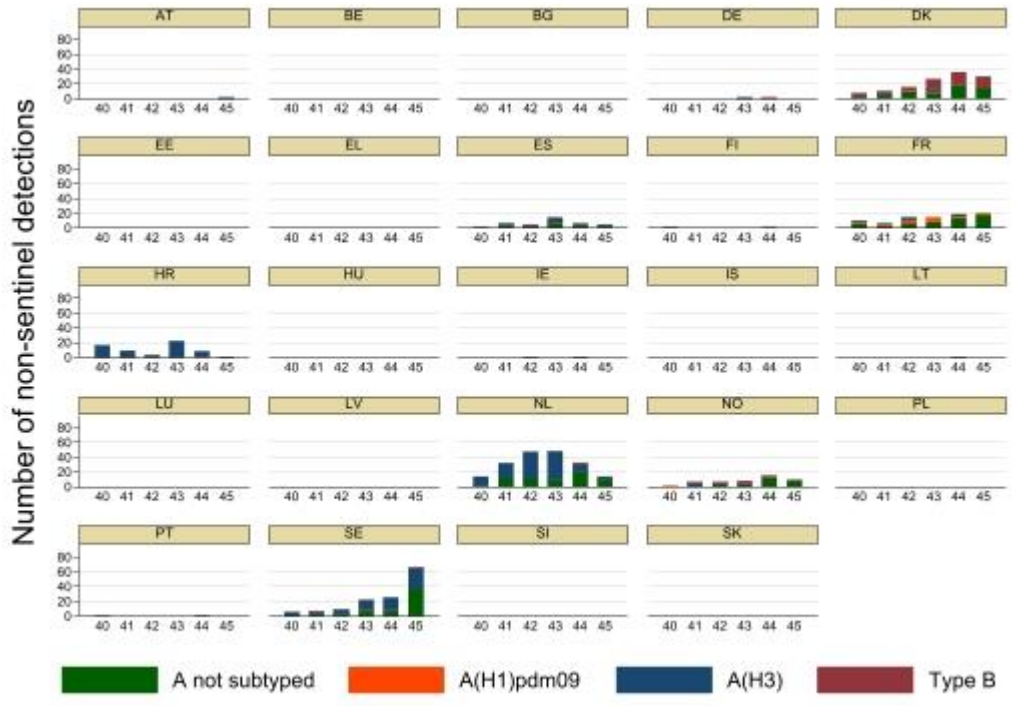
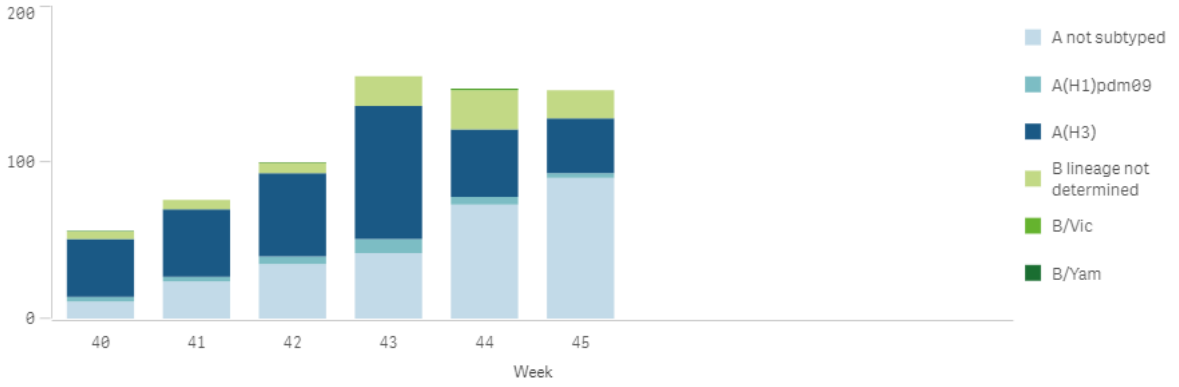
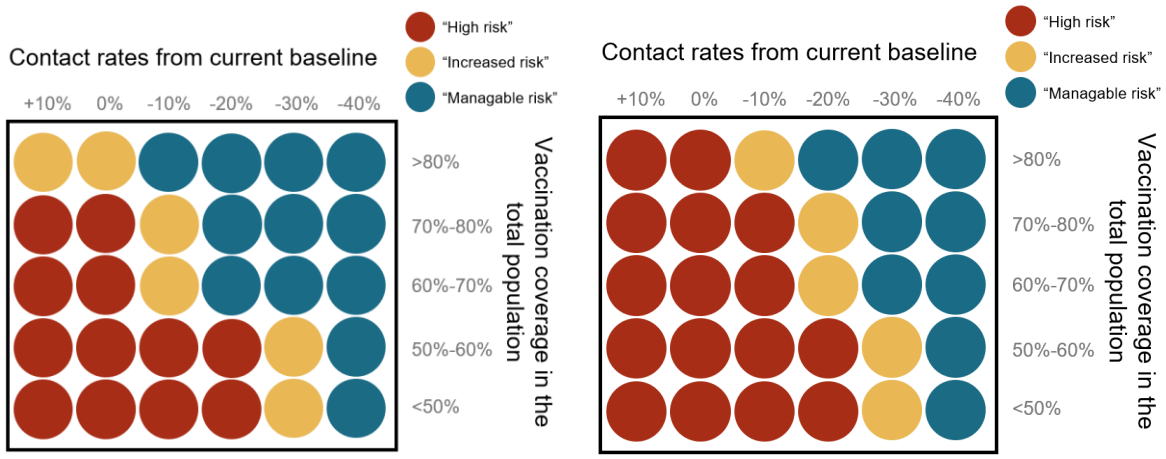


Figure 4. Number of influenza virus detections from non-sentinel surveillance, by week, season 2021/22, EU/EEA



Appendix 2

Figure 1. Projected burden of COVID-19 mortality in relation to vaccination coverage and contact rate change between December 2021 and the end of January 2022 with an additional 20% (left) and 50% (right) increase in contact rates during the holiday season



Appendix 3

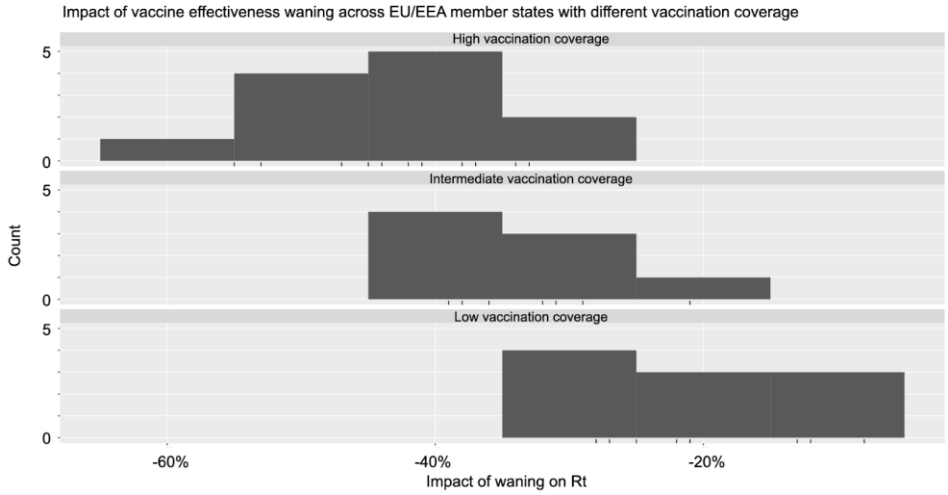
Modelling analysis of waning and booster programmes

The impact of the waning vaccine-induced immunity on Rt is greater in countries with high vaccination coverage (which vaccinated a larger share of their population longer ago; Appendix 3, Figure 1). The impact of the waning on transmission is smaller in countries with lower vaccination coverage.

Proportionally, individuals aged 40-70 years contribute the most to the reduction in transmission if vaccine-induced immunity was not waning, followed by individuals aged older than 70 years (Appendix 3, Figure 2). (Only in one country is the contribution of individuals aged older than 70 years slightly higher than those aged 40-70 years.) However, note that a booster in older individuals may give more direct benefits in terms of preventing severe outcomes than a booster in younger age groups (albeit the older age group contributing less to reducing Rt). Furthermore, the modelling assumed equal eligibility for boosters across age groups, and the contributions of ages 40-70 years partly reflect larger population densities.

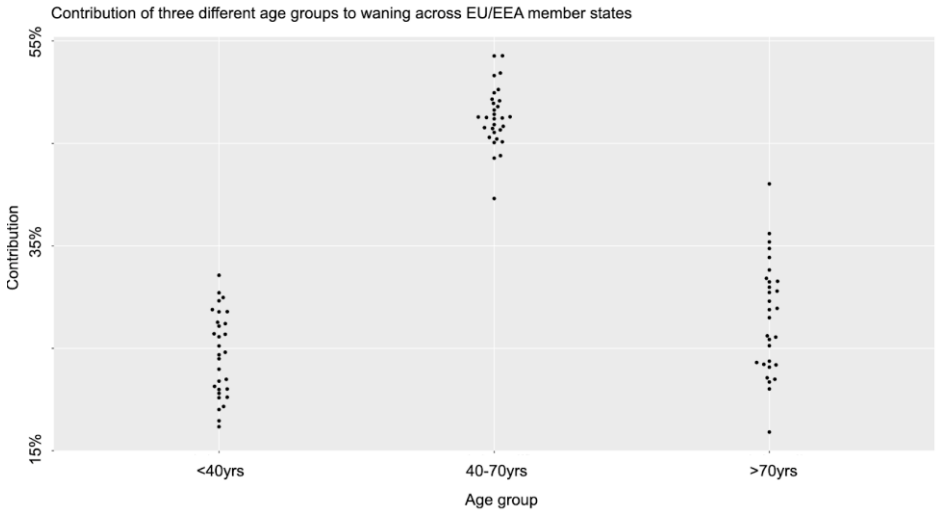
In terms of the number of deaths averted, implementing a booster programme from age 40+ years versus a booster programme from age 80+ years can avert 3-8% of deaths in the EU/EEA area until end of January 2022, depending on the change in contact rates, booster programme rollout speed, and forecast scenarios. Note that given the time window of our forecasts and the rollout speed of administering the booster doses, the visible impact on the number of deaths will mostly be visible toward the end of forecasting window, thus underestimating the true impact of death averted of the coming months.

Figure 1. Frequency of the proportional reduction in Rt if waning of vaccination effect would be undone, shown across EU/EEA Member States, for three groups of countries with high vaccination coverage (>70%), intermediate vaccination coverage (<70% and >60%), and low vaccination coverage (<60%)



Vertical lines underneath the panels indicate the proportional reduction for each EU/EEA country within the three groups.

Figure 2. Proportional contribution of three different age groups (<40 years, 40-70 years, and >70 years) on the waning of the vaccine-induced immunity across the EU/EEA Member States



Each dot represents one country, and the value of the three dots for each country sum to 1

In our modelling we assumed that the value of the vaccine effectiveness against infection is a reasonable proxy for the vaccine effectiveness against Rt, which indicates the expected number of new infections caused by an infectious individual at time t. This may lead to an overestimation of the impact of the initial vaccine rollout on transmission, and thus a more conservative estimate for the impact of subsequent booster programmes.

From studies that assess vaccine effectiveness over time (see 'waning section') we computed the vaccine effectiveness against transmission as a function of time since the primary course of vaccination. We did this computation for each vaccine product and different age groups (where the data allowed). For each country and each calendar week, we then apply this vaccine effectiveness to the vaccination coverage according to the time when doses were administered. This is again done for each vaccine product and age group, and it is then summed according to age group sizes to obtain a population level effect of vaccines against transmission in that population at a given time. To incorporate booster roll-out, we assume that booster doses given in each age group are given to individuals that were fully vaccinated more than six months ago. We assume that a booster dose reinstates a high VE against infection.

Appendix 4

ECDC risk scoring matrix

The current assessment of the risk posed by the SARS-CoV-2 pandemic is stratified by four population groups: the vaccinated and the unvaccinated general population; the vaccinated and the unvaccinated vulnerable population. The assessment is based on the following principles: i) the vaccinated have a lower probability of infection and ii) a lower impact of such infection than the unvaccinated, while iii) whether vaccinated or not, the vulnerable population suffers a higher impact of such infection when compared with the general population. Following the current ECDC forecast, the risk to EU/EEA countries is assessed based on their current levels of full COVID-19 vaccination coverage in their total population, grouped into two categories (low/average and high). The assessment of risk, as outlined below, is at the population level and does not correspond to the individual risk for vaccinated persons.

	Vaccinated vulnerable population		**Unvaccinated** vulnerable population		**Vaccinated** general population		**Unvaccinated** general population	
EU/EEA countries with high (>80%) vaccine uptake for the total population	Probability: MODERATE Impact: HIGH	Risk **MODERATE**	Probability: VERY HIGH* Impact: VERY HIGH	Risk **VERY HIGH**	Probability: MODERATE Impact: LOW	Risk **LOW**	Probability: VERY HIGH* Impact: MODERATE	Risk **HIGH**
EU/EEA countries with a low (<60%) or average (60-80%) vaccine uptake for the total population	Probability: HIGH Impact: VERY HIGH **	Risk **HIGH - VERY HIGH**	Probability: VERY HIGH Impact: VERY HIGH	Risk **VERY HIGH**	Probability: HIGH Impact: LOW	Risk **LOW - MODERATE**	Probability: VERY HIGH Impact: HIGH ***	Risk **HIGH - VERY HIGH**

** Risk of infection for the unvaccinated population is increased from our previous risk assessment to reflect rising circulation in countries with higher vaccine uptake.*
*** In the context of average and low vaccination coverage, we infer from modelling projections that in the absence of measures to effectively reduce population contact rates, then virus circulation and disease burden will be high. Impact is qualitatively assessed to be higher for the vaccinated vulnerable population, given the additional strain on healthcare systems.*
**** In the context of average and low vaccination coverage, we infer from modelling projections that in the absence of measures to effectively reduce population contact rates, then virus circulation and disease burden will be high. Impact is qualitatively assessed to be higher for the unvaccinated general population, given the additional strain on healthcare systems.*

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