RAPID RISK ASSESSMENT

# Assessing SARS-CoV-2 circulation, variants of concern, non-pharmaceutical interventions and vaccine rollout in the EU/EEA, 16th update

30 September 2021


## Summary

Since its emergence in March 2021, the B.1.617.2 (Delta) variant of concern (VOC) has rapidly become predominant across the European Union/European Economic Area (EU/EEA). More than 99% of newly reported cases are attributed to this variant. The Delta variant has demonstrated a significant transmission advantage relative to previously circulating SARS-CoV-2 strains. However, full vaccination remains protective against severe outcomes such as hospitalisation, admission to intensive care and death. Currently available vaccines have played a crucial role in limiting viral circulation and in particular, limiting the impact of infections by the Delta variant.

Despite the fact that over 565 million vaccine doses have been administered in the EU/EEA so far, only 61.1% (range: 18.4–79.4%) of the total population in the EU/EEA have been fully vaccinated to date. The total population includes children and adolescents for whom the vaccine is not available or who may not be included in national target groups yet. There is considerable inter-country and sub-national variation in vaccine uptake, resulting in large proportions of the EU/EEA population remaining susceptible to SARS-CoV-2 infection.

Modelling scenarios that consider vaccination coverage, vaccine effectiveness, natural immunity and population contact rates—in the context of continued Delta circulation—indicate that the potential burden of disease risk in the EU/EEA from the Delta variant is high between now to the end of November, unless vaccination coverage can be increased rapidly in the total population in the next few weeks.


## Risk assessed in this update

The risk assessed in this update is as follows: based on current levels of vaccination coverage and the dominance of the Delta variant in the EU/EEA, what risk does SARS-CoV-2 pose to the general population and the vulnerable population in the coming months?

This update was prompted by the forecast modelling undertaken by ECDC and the planned relaxation of non-pharmaceutical and other measures announced by EU/EEA countries.


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Our previous assessment published on 10 June 2021 (15th update) described the risk at that point in time, and classified EU/EEA countries based on SARS-CoV-2 transmission (expressed as low, moderate, high and very high concern). Here 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 (low <45% total population; average 55-65% total population; high >75% total population). Through mathematical modelling, we forecast the disease burden between now and the end of November 2021. 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 now and end of November 2021, the following can be anticipated:

- Countries with COVID-19 vaccination coverage at or below the current EU average level in the total population and who are planning to relax non-pharmaceutical interventions (NPIs) have a high risk of experiencing a significant surge of cases, hospitalisations and mortality from now until the end of November 2021. In such a scenario, due to very high virus circulation, fully vaccinated vulnerable populations are also at risk of experiencing infection with a severe outcome.
- Countries with COVID-19 vaccination coverage above the current EU average level, and particularly those with the highest current coverage, in the total population have a lower, manageable risk of experiencing a severe surge of cases, hospitalisations and mortality from now until the end of November 2021, unless there is a rapid decline of vaccine effectiveness due to waning immunity.

# Options for response

- Countries should continuously strive to increase their COVID-19 vaccination coverage in all eligible age groups, to limit the burden of infections posed by the Delta variant in the autumn. This requires continuous monitoring of vaccine uptake and associated social determinants to understand where and in which population groups and communities an immunity gap persists.
- According to the current ECDC forecast, depending on the local epidemiological and COVID-19 vaccination coverage situation, non-pharmaceutical interventions will still be needed between now and the end of November to control the circulation and impact of the Delta variant.
- Closing any COVID-19 vaccination gaps in vulnerable populations and healthcare workers before the winter months is also critical to mitigate the risks to healthcare systems, which may be impacted by influenza and other respiratory viruses, in addition to SARS-CoV-2, as the winter season approaches, posing the risk of further increasing the demand for care.
- To increase vaccination coverage, it will be key to address inequalities in access to COVID-19 vaccination in different population groups. It is also 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.
- Risk communication activities should clearly and consistently stress the important role that existing COVID-19 and influenza vaccines play in protecting people against severe disease. Messaging should also highlight the fact that although many countries have relaxed public health measures in recent months, maintaining hygiene measures and avoidance of unnecessary physical crowding remains prudent.
- Given the continuing risk of transmission among unvaccinated children, high levels of prevention and preparedness are required in the educational system.
- In addition to these response options, it remains crucial that COVID-19 surveillance systems are able to effectively monitor and report on COVID-19 cases, hospitalisations and deaths, in order to guide decisions on public health measures and to understand their impact. Vaccine effectiveness should also be monitored to inform vaccination programme strategies.
- Genomic sequencing of 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 from now until the end of November 2021, based on modelling scenarios and projected levels of vaccine coverage
- Updated data on seroprevalence and re-infection by SARS-CoV-2 are included, as well as available evidence on COVID-19 vaccine effectiveness, waning immunity and breakthrough infections.
- Information on vaccine hesitancy and good practice to approach hesitant populations and address misinformation are included, as well as risk communication advice and a list of proposed key messages.

# Event background

Since 31 December 2019 and as of week 2021-37, 229 415 774 cases of COVID-19 have been reported, including 4 699 359 deaths. As of week 2021-37, EU/EEA countries have reported 37 863 314 cases and 764 710 deaths due to COVID-19, representing 16.5% of all cases and 16.3% of all deaths reported worldwide.

These global and EU/EEA figures are likely 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-ecdc-response.

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 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/vaccine-tracker.html#uptake-tab

## Trends in reported cases, testing, hospitalisation and mortality

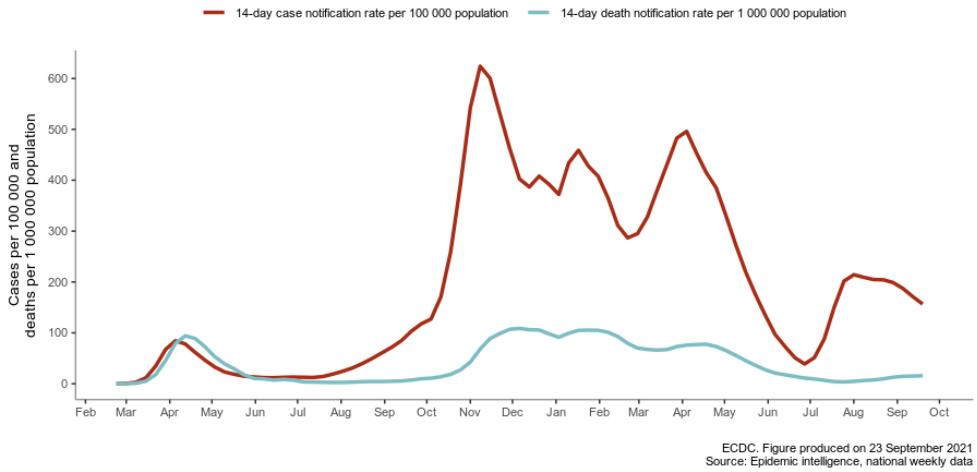
By the end of week 37, 2021 (19 September 2021), the 14-day case notification rate for the EU/EEA was 157 per 100 000 population (country range: 20–652) and the 14-day death rate was 16 deaths per million population (Figure 1a). The overall epidemiological situation in the EU/EEA was characterised by a high and slowly decreasing overall case notification rate and a low, stable death rate (Figure 1a).

Currently, the age groups with the highest reported incidence of infection are those aged 15 to 24 years. The notification rate in this age group has been decreasing across the EU/EEA since week 30, 2021. The increase observed in July and August 2021 amongst children under 15 years of age has begun to level off. Age-specific hospitalisation rates have risen in all ages in line with increases in case rates, but absolute rates of hospital admission remain very low in young age groups (Figure 1b i). Younger age groups account for an increasing proportion of hospital admissions (Figure 1b ii), which is due to comparatively lower hospitalisation rates in older age groups because of vaccination. There is no indication in surveillance data submitted to ECDC by EU/EEA countries of increasing COVID-19 mortality rates among people under 25 years of age.

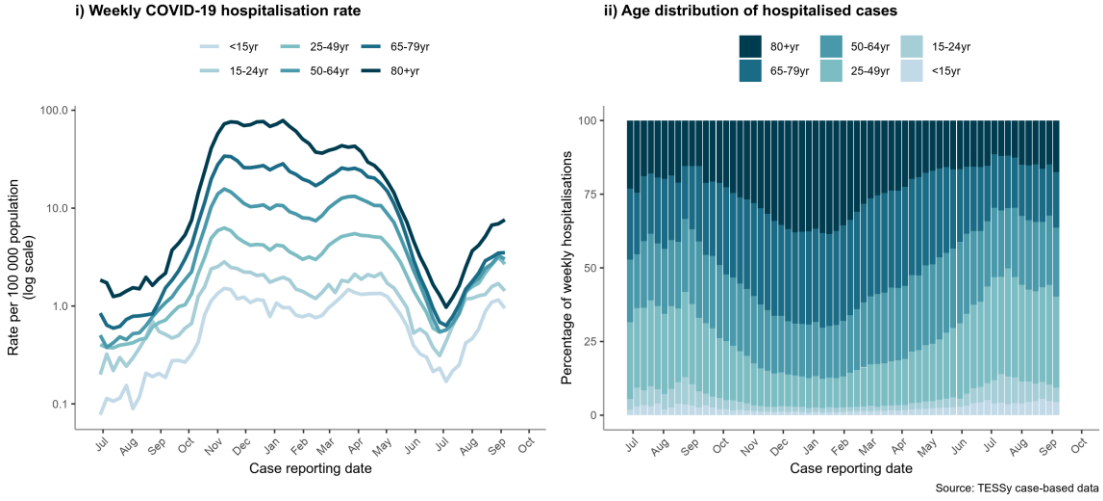
The pooled testing rate for the EU/EEA in week 37, 2021 was high, at 3 573 tests per 100 000 population, but varied markedly by country, from 689 to 42 656 per 100 000 population. Pooled test positivity for the EU/EEA was 2.1% (country range: 0.3–10.2%) and has been stable for nine weeks. Testing rates and test positivity by country need to be interpreted with caution as testing strategies are heterogenous, for example in the use of rapid antigen detection tests (RADTs) or use of self-testing RADTs in settings such as schools and workplaces.

**Figure 1. (a) 14-day overall case and death notification rates in the EU/EEA to week 37, 2021, b) age-specific distribution and rates of hospitalised cases, 12 EU/EEA countries, to week 35, 2021**

**a)**



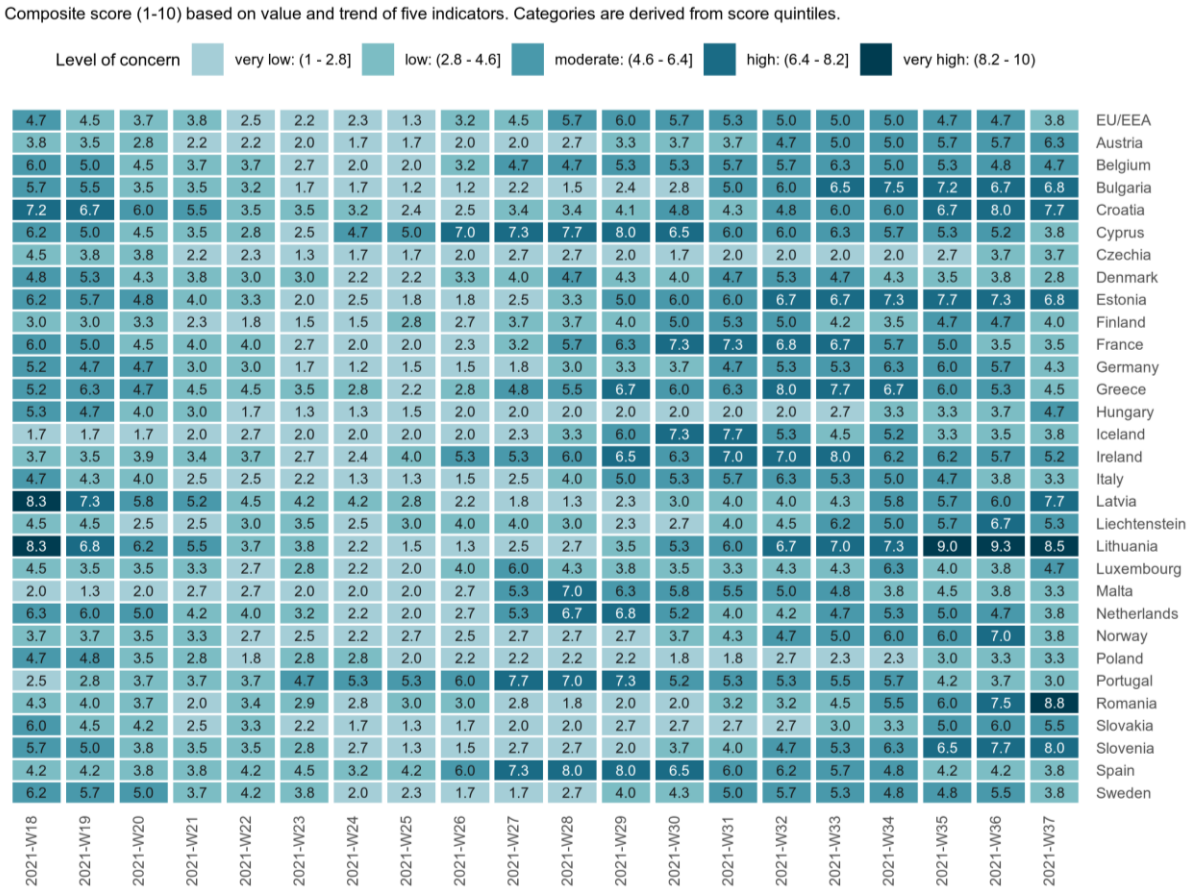

**b)**




*Note: Figure a) is based on pooled data for 30 EU/EEA countries. Figure b) is based on pooled case-based data submitted to TESSy by 12 countries (Austria, Cyprus, Czechia, Finland, Germany, Italy, Luxembourg, Malta, Norway, Portugal, Slovakia and Sweden). Data from weeks 36 and 37 were censored to account for possible delayed reporting of hospitalisation status.*

The trends vary considerably at Member State level, with increasing trends in case notification rates mainly reported in eastern parts of the EU/EEA. Several countries also report increases in severity indicators including cases in older age groups, hospitalisation and mortality. Figure 2 shows a composite score for each country based on the absolute value and trend of five COVID-19 epidemiological indicators (intensity indicators: test positivity and total case notification rates; and severity indicators: hospital or ICU admissions or occupancy, death rates, case rates amongst people aged 65 years and above) [1]. In week 37, the epidemiological situation in the EU/EEA overall was categorised as of low concern. In the same week, two countries were categorised as of very high concern (Lithuania and Romania), five countries as of high concern (Bulgaria, Croatia, Estonia, Latvia and Slovenia), seven countries as of moderate concern (Austria, Belgium, Hungary, Ireland, Liechtenstein, Luxembourg, and Slovakia) and 16 countries as of low concern (Cyprus, Czechia, Denmark, Finland, France, Germany, Greece, Iceland, Italy, Malta, Netherlands, Norway, Poland, Portugal, Spain and Sweden) (Figure 2). No country was categorised as of very low concern.

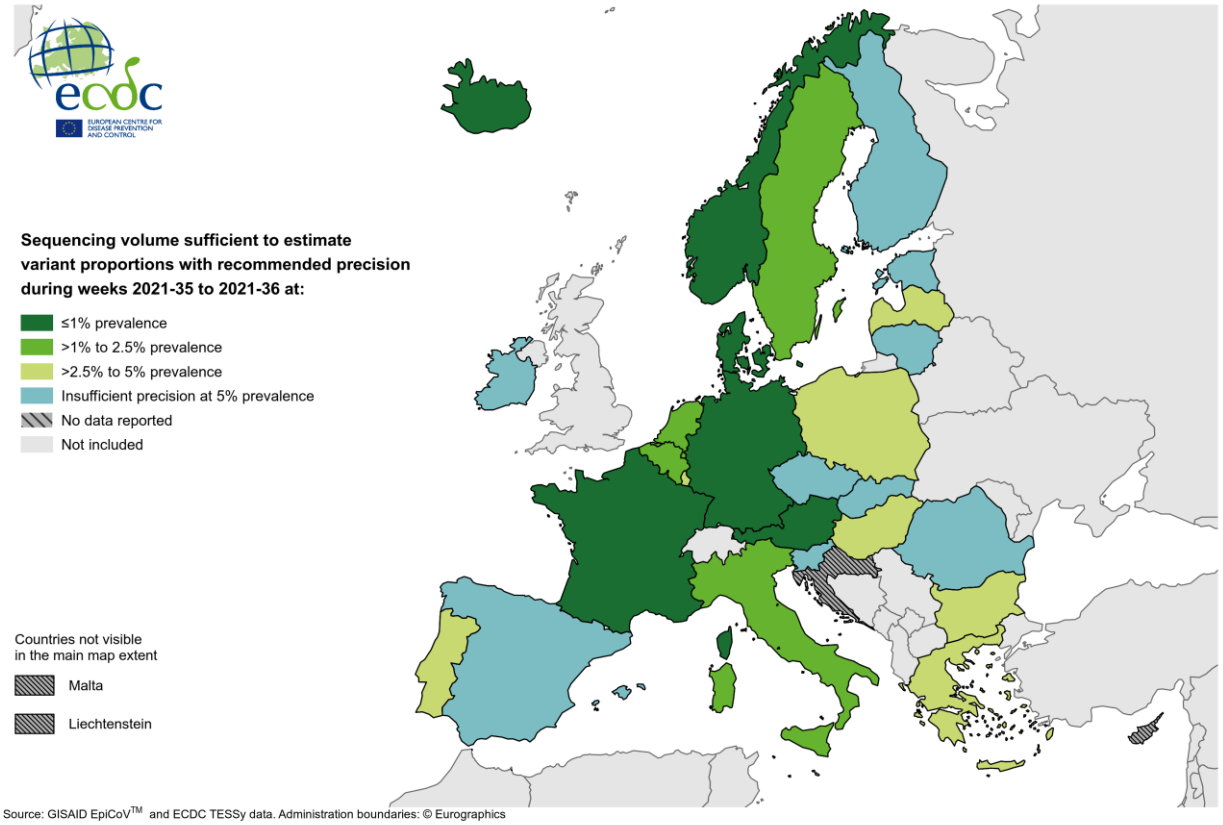
**Figure 2. Weekly COVID-19 epidemiological classification and score by country in the EU/EEA, weeks 18 to 37, 2021**




# SARS-CoV-2 variants of concern

Sequencing capacity varies greatly across the EU/EEA. ECDC uses data reported to the GISAID EpiCoV database or to TESSy, to estimate the distribution of variants in countries reporting an adequate average weekly volume of sequenced SARS-CoV-2-positive cases [2]. In weeks 35-36, 2021, 17 countries reported an adequate average weekly sequencing volume (six with sufficient precision at a variant prevalence of 1% or lower, four with sufficient precision at a variant prevalence of >1-2.5%, and seven with sufficient precision at a variant prevalence of >2.5-5%), nine countries reported an inadequate sequencing volume (with insufficient precision at a variant prevalence of 5%), and four did not report any data (Figure 3) [3].

**Figure 3. Distribution of SARS-CoV-2 sequencing volume of sufficient precision by EU/EEA country, weeks 35-36, 2021**




Source: GISAID EpiCoV™ and ECDC TESSy data. 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 22 September 2021

Among the variants of concern (VOC), Delta (B.1.617.2) dominates in all EU/EEA countries, accounting for a median of 99.6% (range 72.0–100.0%) of sequenced samples in the 17 countries with sufficient sequencing volume and a valid denominator in week 35-36, 2021. In the same weeks, Alpha, Beta and Gamma accounted for <1% of the cases. The current dominance of Delta across the EU/EEA is a marked change from the variant prevalence reported in our previous Risk Assessment, for the period 10 to 23 May 2021, when Alpha was the dominant VOC, accounting for 91.6% (70.2–97.1%) of the sequenced samples, while Delta accounted for 0.2% (0.0–10.1) [1].

Estimates for the basic reproductive number ($R_0$) for Delta range from 3.2 to 8, with a mean of 5.08 [4]. Delta is estimated to have a relative increase in the pooled basic reproductive number compared with the Alpha (+29%, 95% CI 24-33%) and wild type variants (+97%, 95% CI 76-117%) [5]. This increased transmissibility, which is nearly double that of the wild type SARS-CoV-2 virus that circulated during autumn 2020, is a key factor in Delta's rapid dominance.

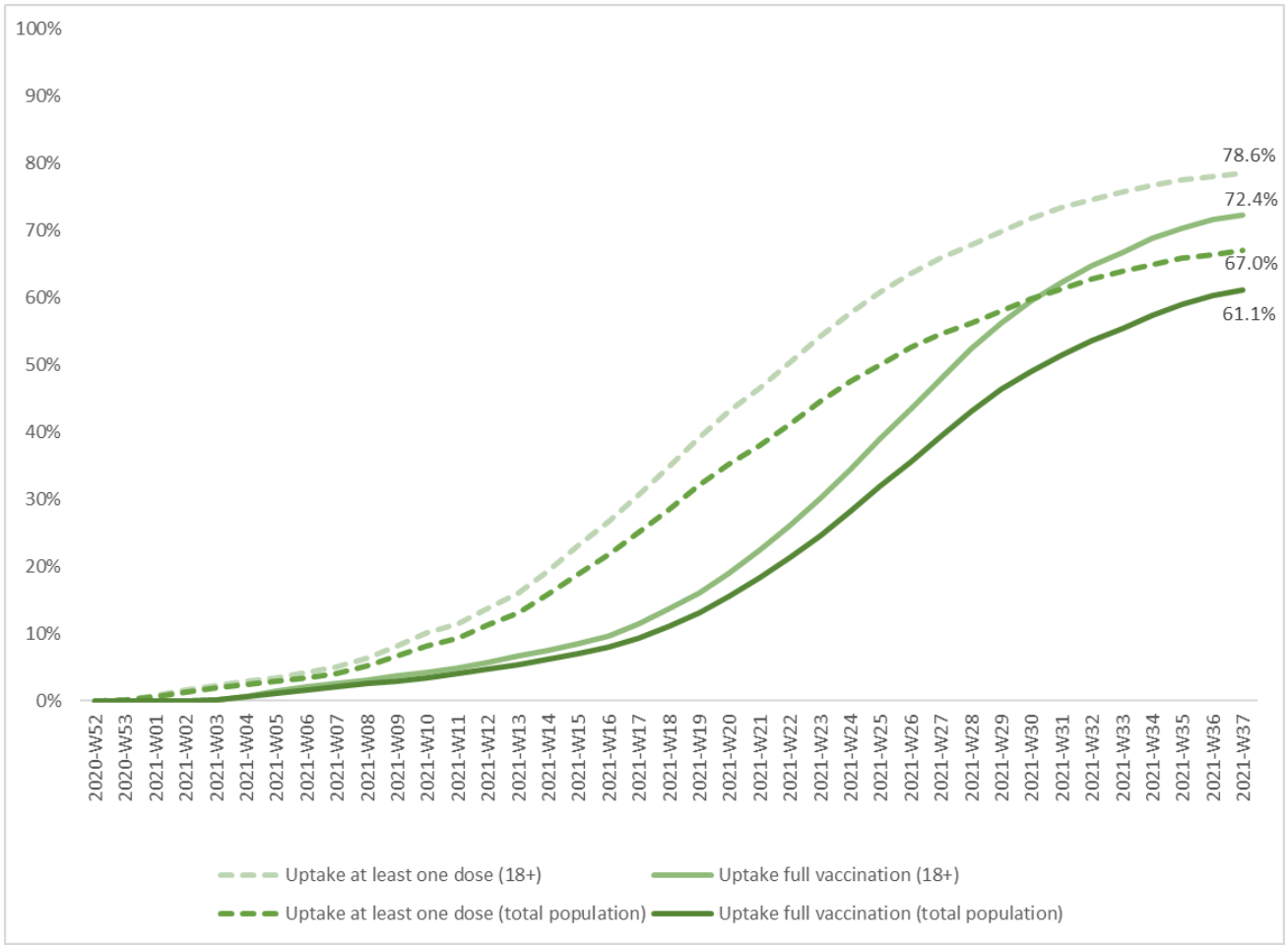
In studies in Scotland and England, the Delta variant has been associated with a two-fold increase in the risk of hospitalisation and emergency care compared with the Alpha variant [6,7], although a similar study from Norway found no difference in the risk for hospitalisation for cases with the Delta variant [8]. Analysis of the impact of the Delta variant on the risk of death due to COVID-19 is affected by the rollout of vaccination programmes at the same time as the variant emerged [6].

If a new variant (including a current VOC with additional mutations) with a significant transmissibility advantage over Delta starts circulating in the EU/EEA, it is likely that it will take at least two to three months from the initial detection of an increasing trend to it becoming dominant based on previous introductions of VOCs and modelling over a range of levels of transmission advantages. There is also a possibility that new variants with a lower $R_0$ than Delta but associated with significantly reduced vaccine effectiveness and/or increased risk for reinfections could be introduced and start to co-circulate with Delta as levels of immunity increase in the population. However, there are currently no concerning signals for other variants in the EU/EEA, so no major impact on the epidemiological situation in the EU/EEA before the end of 2021 is expected from emerging VOCs.

# Vaccination

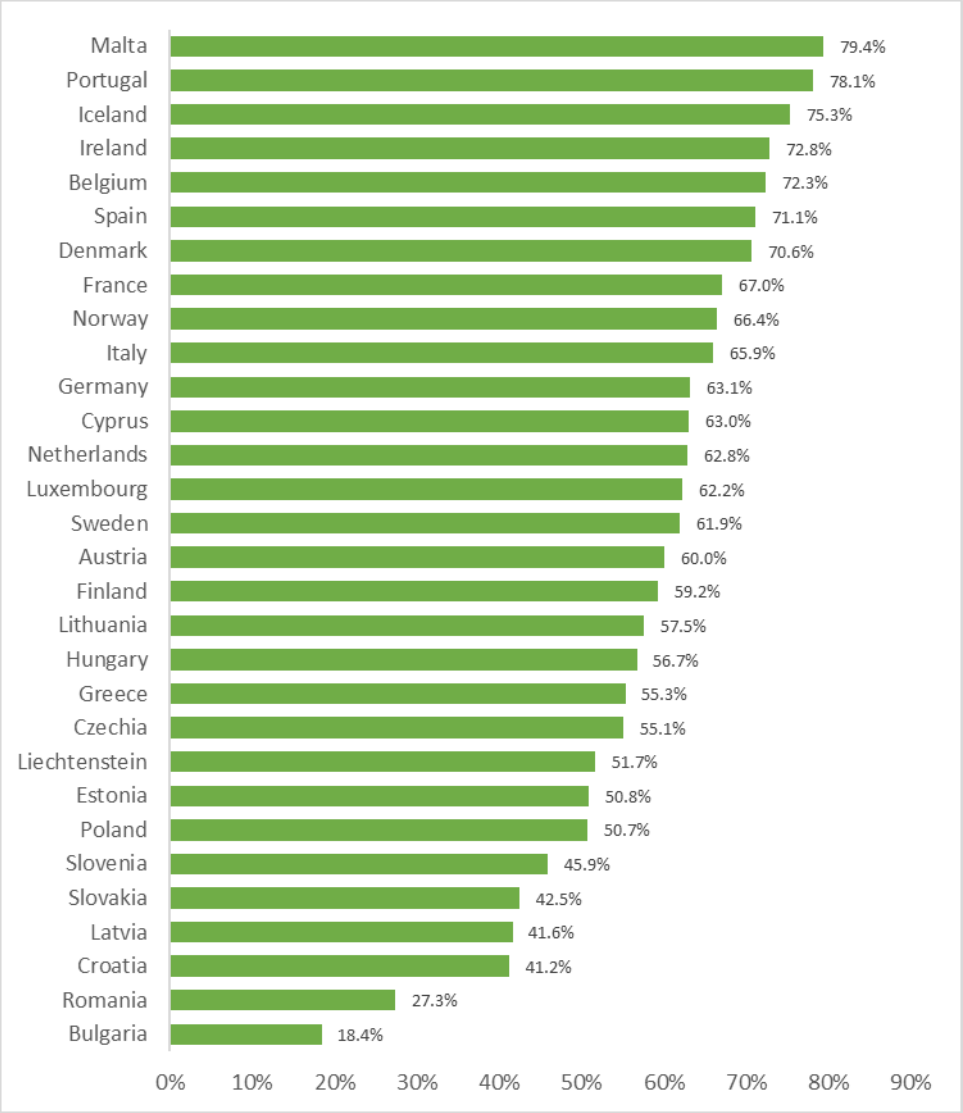
As of 19 September 2021, 43.1% of the world population are reported to have received at least one dose of a COVID-19 vaccine, including only 1.9% of people in low-income countries [9]. As of 19 September 2021 (week 37, 2021), over 565 million vaccine doses have been administered in the EU/EEA. Since the start of the COVID-19 vaccine deployment in December 2020, the cumulative vaccine uptake in the adult population (aged 18 years and older) in the EU/EEA has reached 78.6% for at least one vaccine dose (range 23.5-97.3%) and 72.4% for the full vaccination course (range: 22-90.7%) (30 reporting countries). When estimated over the total population, including children and adolescents for whom the vaccine is not available or who may not be included in national target groups yet, the cumulative vaccine uptake in the EU/EEA is 67% (range 19.8-86.5%) for at least one vaccine dose and 61.1% (range: 18.4-79.4%) for the full vaccination course (30 reporting countries). Approximately 26 million people in the EU/EEA have received their first dose but have not yet completed their primary vaccination course. As the overall cumulative uptake in the adult population reaches above 70%, the pace of weekly increase in uptake is decreasing (Figure 4). Furthermore, progress with vaccination rollout is unequal across EU/EEA countries (Figure 5) and is plateauing at low levels in some of them (Appendix 1) [10].

**Figure 4. Cumulative uptake (%) of at least one COVID-19 vaccine dose and full vaccination course amongst adults (18+) and total population in EU/EEA countries as of week 37, 2021**




*Source: TESSy; data reported by 30 countries as of week 37, 2021.*

**Figure 5. Cumulative uptake of full COVID-19 vaccination course in the total population by EU/EEA country as of week 37, 2021**

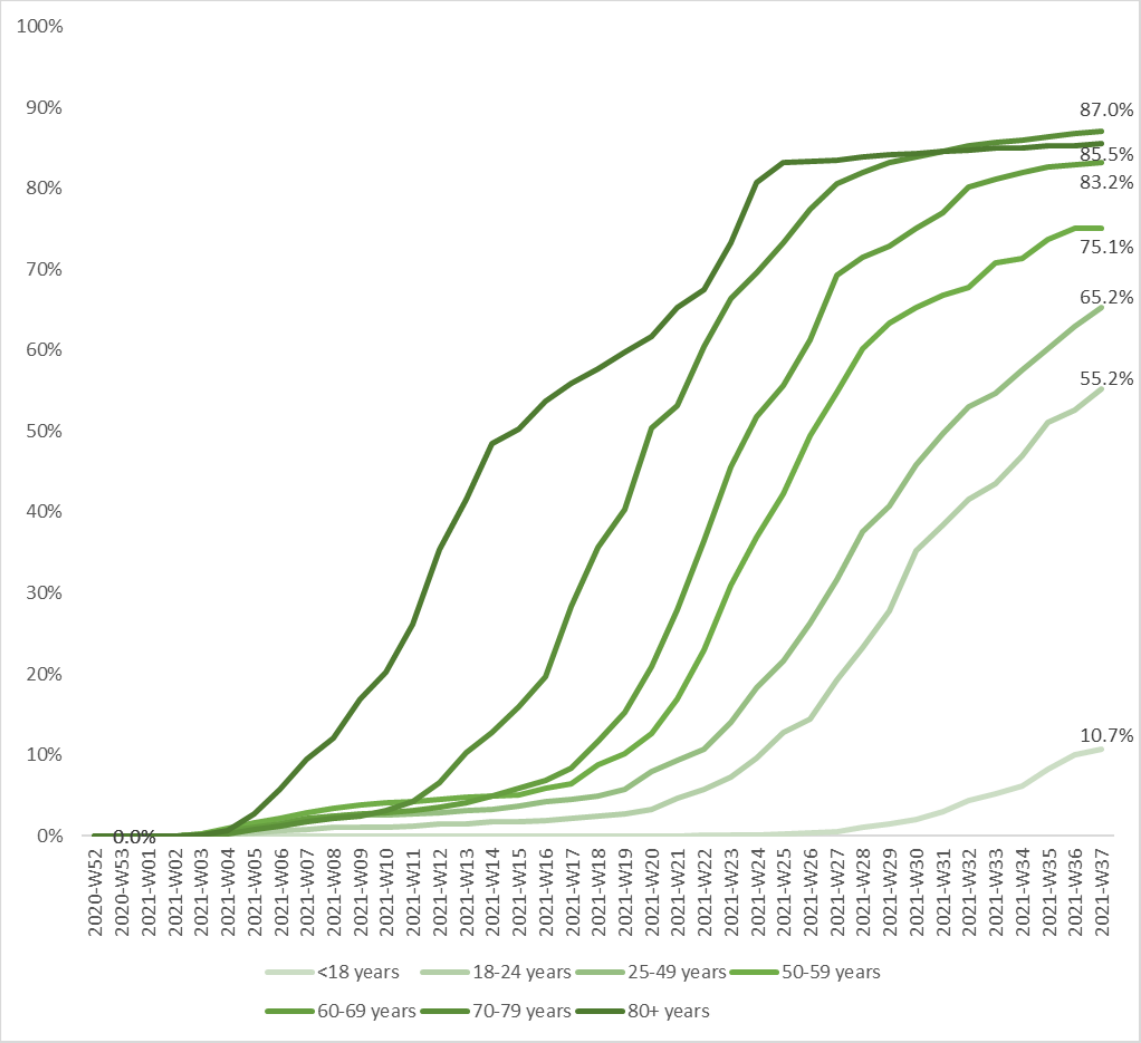



*Source: TESSy; data reported by 30 countries as of week 37, 2021. See the Notes on data in the ECDC Vaccine Tracker for country specific disclaimers.*

Cumulative vaccine uptake is higher in target groups that have been prioritised since the beginning of vaccine rollout, such as the elderly and healthcare workers (HCWs). In people aged 80 years and above, the median vaccine uptake amongst EU/EEA countries is 87.1% (range 20.1–100%) for at least one dose, and 85.3% (range 19.4–100%) for the full vaccination course (27 countries reporting). For people 60 years and above, the median vaccine uptake is 88.6% (range: 29.8–100%) for at least one dose and 85% (range: 28-100%) for the full vaccination course (27 countries reporting). Sixteen countries have already administered the full vaccination course to more than 80% of the population aged 60 years and above. [11].

As vaccine uptake increased in priority groups (the elderly, residents in long-term care facilities, HCWs, etc.), countries have progressively expanded rollout to include younger age groups, in some cases to the entire population including children aged 12 years and above. Figure 6 presents the median cumulative uptake of full vaccination by age group amongst EU/EEA countries.

**Figure 6. Median cumulative uptake of full COVID-19 vaccination course by age group, EU/EEA, week 52, 2020 - week 37, 2021**




*Source: TESSy; data reported by 27 countries as of week 37, 2021 (missing Germany, Liechtenstein and the Netherlands; for the age group <18 also missing Denmark and Poland).*

Of note, in many countries the rollout of COVID-19 vaccines has been unequal at subnational level and significant differences in vaccine uptake at population level may be observed across regions. For example, in Italy, against a national full vaccination coverage of approximately 77.7% in the population over 12 years of age, vaccine uptake in Sicily has reached 69.6% (accessed on 27 September 2021) [12]. In Germany, vaccine uptake in the total population also greatly varies across federal states from 57.5% in Saxony to 78.5% in Bremen (63.9% at national level) (accessed on 27 September 2021) [13]. Similarly in Austria, vaccine coverage in the total population ranges from 55.5% in Upper Austria to 67.9% in Burgenland (60.4% at national level) (accessed on 28 September 2021) [14]. In Belgium, vaccine coverage in the adult population has exceeded 90% in Flanders but is lagging behind in Brussels (64%) (accessed on 27 September 2021) [15].

Most EU/EEA countries report that vaccine supply is no longer an issue, with challenges now mainly related to communication, vaccination acceptance and low vaccine uptake in certain population groups, communities and geographical areas due to hesitancy and access issues [16].

More country-specific data on vaccine uptake, can be found in ECDC's vaccine tracker [10] and the related weekly vaccine rollout overview [11].

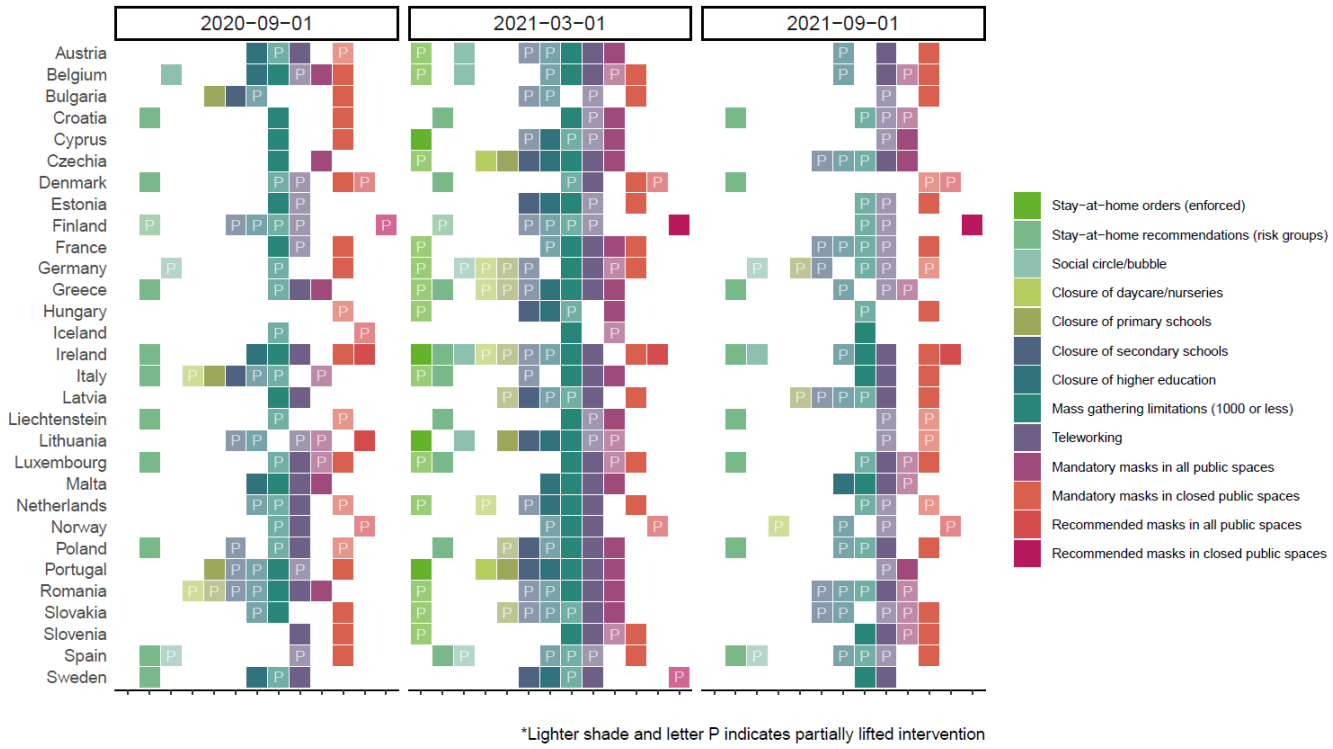
# Non-pharmaceutical interventions

Non-pharmaceutical interventions (NPIs) such as the use of face masks, improved ventilation in closed spaces and physical distancing measures are fundamental elements of the public health response to controlling COVID-19. Non-pharmaceutical interventions have proven valuable tools for the public health response if implemented swiftly and decisively with the appropriate risk communication and community engagement. In addition, these measures are similarly effective against other respiratory viruses including influenza.

The ECDC Response Measure Database collects the different NPIs implemented by country in the EU/EEA since January 2020 to prevent the spread of the SARS-CoV-2 virus. Figure 7 shows the different NPIs in place at three points in time: 1 September 2020, 1 March 2021 and 1 September 2021.

Several NPIs have been relaxed or fully lifted in a number of EU/EEA countries, with less measures in place overall (n=113) in September 2021 compared with March 2021 (n=183). In addition, 58% of the NPI measures which remained in place in September 2021 were recorded as partially lifted compared with 40% of measures partially lifted in March 2021.

**Figure 7. Comparison of implementation of NPIs for the control of COVID-19 in EU/EEA countries in September 2020, March 2021 and September 2021**




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

**Stay-at-home orders and recommendations:** Stay-at-home orders are the clearest example of the differences between time points, with 17 countries implementing such partial or full orders in March 2021 and no countries doing so in September 2021. Regarding stay-at-home recommendations for risk groups, 10 countries had these in place in March 2021 and eight countries still had these recommendations in September 2021.

**Mass gatherings:** During the spring of 2021, nearly all EU/EEA countries introduced limitations on the number of people allowed to gather at public events, both indoors and outdoors. In September 2021, these measures have been either eased (allowing a larger number of people to gather in public spaces or introducing other partial measures) or lifted in most countries, with six Member States still reporting full closure and 13 partial closure of events up to 1 000 participants or less.

**Teleworking:** Recommendations have largely remained in place between 1 March and 1 September 2021, however, in September the recommendation is reported as partial in more countries.

**Use of facemasks in community settings:** The mandatory use of facemasks has also decreased from 17 countries having full or partial mask mandates in all public spaces in March 2021 to 11 countries in September 2021. Furthermore, there is variation in the degree to which the mandates are implemented.

**Exemptions to NPIs:** In Spring 2021, 23 countries introduced varied exemptions to implemented NPIs for the total population when fully vaccinated, ranging from requiring digital covid certificates to attend public gatherings for example, to lifting quarantine requirements or allowing different sized gatherings or social encounters for those that are vaccinated.

**Schools:** By September 2021, only one country had partial closure of daycare facilities, in contrast to six countries having had partial or wider closures in March 2021. Similarly, in primary and secondary schools, fewer countries had partial or full closures in September 2021 compared with March 2021. For higher education, fewer countries had remaining partial or full closures, although 12 countries still reported partial closures and one country full closure in September 2021.

**Regional implementation:** Since the end of 2020, a rising number of measures have been implemented at a lower geographical level. This reflects regional differences in incidence within countries and detection of local outbreaks and is not fully captured by the ECDC Response Measure Database.

**Use of self-tests in specific settings**: In a survey performed by ECDC in July 2021, 12 out of 22 countries responded that they were using RADT self-tests in different settings. In seven countries, self-tests were either mandatory (4) or recommended (3) in schools and six countries had mandatory (2) or recommended (4) use in workplaces. Other settings mentioned were LTCF, kindergartens, restaurants, hotels, airports etc. As the information was gathered through a survey, no more recent update is available.

# Potential co-circulation of SARS-CoV-2 with influenza and other respiratory viruses

Since the implementation of strict public health and physical distancing measures in February 2020, seasonal influenza virus circulation has been significantly reduced in the EU/EEA as well as globally. This situation of very low influenza circulation continued during the 2020/21 season and the summer months 2021 [17-19]. However, in recent weeks, an increasing number of cases due to influenza A(H3N2) virus have been reported from several countries across the European Region [18]. These cases were reported from sentinel and non-sentinel surveillance system including hospital settings. Influenza A(H3N2) viruses have been shown in the past to primarily affect the elderly and the very young (i.e. children below five years of age), cause severe and large outbreaks in long-term care facilities [20-22], lead to high excess mortality in the elderly population [23-25] and increase pressure on healthcare systems. Vaccine effectiveness (VE) data from previous regular influenza seasons for A(H3N2) viruses have been overall low to moderate and low to very low, particularly in the elderly who are most at risk of severe disease [26-31]. The limited circulation during this and last year might also contribute to a higher susceptibility in the population with less people being exposed to influenza viruses.

Due to lack of influenza circulation in the past year, the timing of an eventual influenza epidemic in Europe is difficult to predict. An earlier onset of the seasonal influenza epidemic (usually peaking around weeks 49-06) than in pre-COVID-19 seasons is possible, potentially adding pressure and burden on healthcare settings.

Influenza and SARS-CoV-2 co-infections have been only documented rarely, which is likely due to the limited circulation of influenza viruses during this pandemic. One study in the United Kingdom showed higher severity in these co-infected cases early in the pandemic when influenza was still circulating [32]. The risk groups for severe influenza disease largely overlap with groups most at risk of severe COVID-19 disease and death. Therefore, there could be several benefits to the co-administration of COVID-19 vaccines with seasonal influenza vaccination campaigns. The infrastructure for seasonal influenza vaccination is already in place and can be modified according to the epidemiological context of COVID-19. Previous evidence from co-administration of other vaccines has not shown any safety or effectiveness concerns, although evidence from the co-administration of mRNA vaccines with other vaccines is still scarce. The US American Committee on Immunisation Practices (ACIP) stated in their recommendations that COVID-19 vaccines and other vaccines may be administered at the same time [33]. Results from the phase three randomised trial (preprint) of the safety and efficacy of NVX-CoV2373 (Novavax; currently not authorised for use in the EU) shows that the safety, immunogenicity, and efficacy profile of the COVID-19 vaccine is maintained while co-administered with the seasonal influenza vaccine, with only a slight decrease in vaccine efficacy from 89.8% (95% CI: 79.7–95.5) to 87.5% (95% CI: -0.2–98.4) [34]. In the UK, preliminary (unpublished) evidence from the ComFluCOV trial [35] indicates that co-administration of the influenza and COVID-19 vaccines is generally well tolerated with no reduction in immunogenicity, the two vaccines may be co-administered where operationally practical [36,37].

Similar to seasonal influenza, respiratory syncytial virus (RSV) detection levels were significantly lower during the 2020/21 season in many countries around the world including in EU/EEA countries. Non-pharmaceutical interventions implemented to control SARS-CoV-2 transmission are believed to prevent the transmission of RSV; with measures in daycare centres and schools possibly playing a bigger role in this [38]. However, a number of countries reported out-of-season RSV epidemics in 2021 [39,40].

## Societal and healthcare worker fatigue

Several studies have shown increases in HCW fatigue during the pandemic in terms of stress, anxiety and burn out as well as other metrics [41,42]. As the strain on healthcare systems has continued in several countries in 2021, it is expected that fatigue amongst HCWs has only further increased. Whilst some studies have shown opposite effects, possibly because of an increased sense of motivation and recognition by society, the future workload and fatigue within healthcare is likely to remain high due to the COVID-19 pandemic but also possibly in terms of other communicable diseases such as influenza or respiratory syncytial virus (RSV), as already seen in some areas [39,43-45]. Further increases in the healthcare burden will happen due to backlog of diagnosis and treatment for non-communicable diseases such as cancer, during the pandemic in 2020-2021 [46].

Pandemic fatigue was identified almost a year ago by WHO as a significant factor of 'de-motivation to follow recommended protective measures' and continues to be a significant challenge for countries [47]. Pandemic fatigue brings with it the risk of increased infection rates, increased strains on healthcare capacity, increased impact on the economy and society, and the likelihood that even stricter measures may be needed in the near future to control the further spread of the virus [48].

# Disease background

For additional information on the latest scientific evidence relating to COVID-19, SARS-CoV-2, virus transmission, diagnostic testing, infection, clinical characteristics, risk factors and risk groups, immunity, treatment and vaccines please visit ECDC's website: https://www.ecdc.europa.eu/en/covid-19/latest-evidence.

## Impact of Delta on COVID-19 vaccine effectiveness

An update of the evidence of vaccine effectiveness against SARS-CoV-2 infection by severity (mild/moderate disease, severe disease, hospitalisation, death) and variants of concern was included in the recently published ECDC technical report 'Interim public health considerations for the provision of additional COVID-19 vaccine doses' [49].

Multiple studies indicate a decrease in vaccine effectiveness against SARS-CoV-2 infection with the Delta variant compared with wild-type and Alpha. The impact of the Delta variant on vaccine effectiveness against severe disease, hospitalisation and death was less pronounced with high effectiveness maintained overall. However, this needs to be carefully monitored over time, particularly amongst older adults where some signs of decreased protection against hospitalisations have now been reported by some countries. Below we present a few relevant updates on vaccine effectiveness in the context of the current dominance of the Delta variant.

The Danish Public Health Institute published an official communication of an analysis of data from 2 000 breakthrough infections between 1 March and 3 August 2021, including the periods when Alpha and then Delta variants were dominant in Denmark. They found a high vaccine effectiveness against hospitalisations due to the Delta variant following two doses of Comirnaty (94.4%; 95% CI: 91.1–96.5) or Vaxzevria (96.6%; 95% CI: 75.3–99.5) (not possible to estimate for Spikevax as there were no cases during the study period) with slightly lower effectiveness for the Alpha VOC after two doses of Comirnaty (85.6%; 95% CI: 80.4–89.5) (not possible to estimate for Vaxzevria as there were no cases during the study period). These findings may be partly due to people who were vaccinated during the Delta variant study period being considerably younger than those who were vaccinated during the Alpha variant study period. However, the estimates of vaccine effectiveness against infection were slightly lower for the Delta variant (Comirnaty: 78.8%, 95% CI: 77.2–80.4; Spikevax: 88.1%, 95% CI: 83.6–91.4; Vaxzevria: 73.7%, 95% CI: 70–77) compared with the Alpha variant (Comirnaty: 81%, 95% CI: 79.4–82.4; Spikevax: 95.9%, 95% CI: 91.4–98.1; Vaxzevria: 93.2%, 95% CI: 89.5–95.5) [50].

A recent study conducted in Portugal estimated vaccine effectiveness against hospitalisation and deaths in adults 65 years and older, receiving either Comirnaty or Spikevax, between February and August 2021 and found slightly lower vaccine effectiveness estimates in the ≥80 years olds compared with younger age groups 14 days after the administration of the second dose, but overall sustained protection against hospitalisations and deaths up to 98 days (three months) from the administration of the second dose in all age groups [51].

Studies from Israel [52,53] and the US [54,55] on waning immunity showed evidence of reductions in effectiveness of Comirnaty against infections ≥5 months after being fully vaccinated, but still high vaccine effectiveness against hospitalisation and severe disease overall.

In older age groups and in residents of long-term care facilities there is some emerging evidence of possibly decreased effectiveness of COVID-19 vaccines against not only infections, but also against hospitalisation. A study from the US amongst nursing home residents found that protection from Comirnaty or Spikevax against SARS CoV-2 infection for the fully vaccinated in the pre-Delta period was 75%, declining to 53% in the Delta period [56]. In addition, two recent studies from the US have shown that vaccine effectiveness against hospitalisation is lower in older adults (Bajema et al: VE ≥65 years: 79.8% vs 18–64 years: 95.1%; Grannis et al: VE ≥75 years: 76% vs 18–74 years: 89%) with Comirnaty or Spikevax [57,58].

On 9 September 2021, Public Health England released new data on the duration of immunity after full vaccination with Comirnaty or Vaxzevria, which are similar to those from Israel and the US. For both vaccines, waning of vaccine effectiveness against symptomatic disease is seen from around 10 weeks after the second dose and is mostly observed in older adults. Vaccine effectiveness against symptomatic disease due to Delta variant peaked in the early weeks after the second dose and then fell to 47.3% (95% CI: 45–49.6) and 69.7% (95% CI: 68.7–70.5) beyond 20 weeks after completion of the primary series with Vaxzevria and Comirnaty, respectively. Waning of vaccine effectiveness against symptomatic disease was greater for individuals aged 65 and above compared with 40-64-year-olds. Nevertheless, after completion of the primary series, protection against hospitalisations remained high throughout the follow-up period, at 77.0% (95% CI: 70.3–82.3) and 92.7% (95% CI: 90.3–94.6) with Vaxzevria and Comirnaty, respectively. Greater waning of vaccine effectiveness against hospitalisation was observed amongst individuals aged 65 and above, in vulnerable and frail individuals and 40-64-year-olds with underlying medical conditions compared with healthy adults [59].

It is difficult to ascertain if reductions in effectiveness against SARS-CoV-2 infections over time are due to waning immunity or Delta partially escaping vaccine protection. The Delta variant is characterised by higher transmissibility, higher viral loads in the respiratory tract, as well as partial escape from cellular and humoral responses which could contribute to lower VE, particularly in the elderly.

# Natural immunity to SARS-CoV-2

## Prevalence of SARS-CoV-2 antibodies in Europe

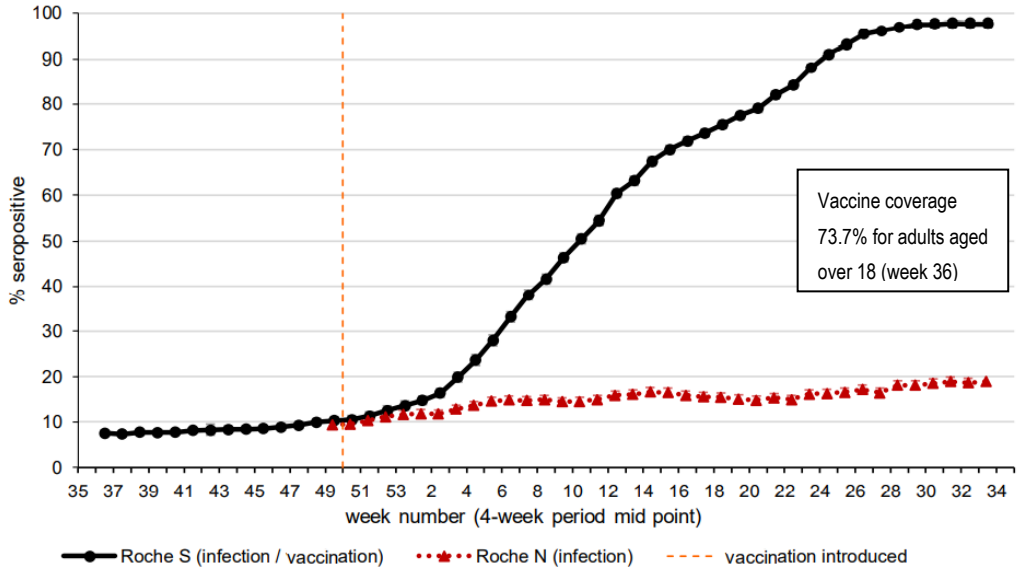
Seroprevalence studies, in which infection- or vaccination-derived serum antibody levels are determined for representative subsets of a population can provide useful estimates of existing population exposure to, and protection against, infection with SARS-CoV-2 [60].

Data from studies conducted during 2020 showed evidence of low national seroprevalence (<10%) across the WHO European region, except for a few sub-national populations that had experienced intense community transmission, with estimates ranging up to 52% [61]. Although seroprevalence varied markedly between and within countries, the overall results indicate that during 2020, only a low proportion of the European population had evidence of immunity to SARS-CoV-2. During 2020, estimates of seroprevalence varied by age across studies with no obvious overall trends.

Data from SARS-CoV-2 serosurveys conducted around the world are systematically collected by Serotracker [62]. Many of these studies have been classified as having a medium or high risk of bias, with weak methodological approaches including the use of convenience sampling, low sample sizes and suboptimal laboratory assays. Nevertheless, the results from studies within the EU/EEA all show a steady increase in the seroprevalence from April 2021 onwards (estimates between 32.8% in Sweden [63] up to 68% in Estonia [64] during June). The sharp increases in seropositivity observed correspond closely to the rollout of COVID-19 vaccination programs across the region, with the highest seroprevalence currently observed amongst older age groups who were vaccinated first. Findings from a study among blood donors in Sweden in March 2021, just prior to the widespread rollout of vaccination in the population, found a seroprevalence of around 22% which probably reflects the baseline level of natural immunity amongst adults at that time [65]. Later results from the same study showed a seroprevalence of 51.9% amongst the Swedish blood donors for the period of June 24 to 4 August 2021.

Most of the published seroprevalence studies in the EU/EEA region do not yet differentiate the level of natural versus vaccine-induced immunity, even though this is potentially possible using different serological assays for research purposes. The UK have conducted longitudinal testing of blood donor samples using nucleoprotein (nucleocapsid antigen) (N) and spike (S) assays to differentiate natural and vaccine-induced immunity, with the N assays detecting antibodies from natural infection and S assays detecting both post-infection and vaccine-induced antibodies [66]. This testing has shown a dramatic rise in antibodies since the introduction of vaccination with the latest data (see Figure 8) indicating that 97.7% of donors aged 17 and over have antibodies from either infection or vaccination. The data suggest that these antibodies are mostly related to vaccination, with a seroprevalence of around 20% due to natural infection.

**Figure 8. Four-weekly rolling SARS-CoV-2 antibody seroprevalence (% seropositive) in blood donors in England, 2020 -2021 [66]**




Estimates of seroprevalence have been compared with the corresponding global cumulative incidence of confirmed COVID-19 infections. These comparisons have shown large variations with seroprevalence estimates generally considerably higher than the reported cumulative incidence, with one study estimating the median ratio of seroprevalence to cumulative incidence of SARS-CoV-2 infection to be almost 18 [67]. Other systematic reviews have shown a broad range of ratios with all findings suggesting a high level of case under-ascertainment due to insufficient testing in some locations and the fact that many cases that are pauci- or asymptomatic go undetected [68,69].

Taken together, estimates of existing population exposure to, and protection against, infection with SARS-CoV-2 via seroprevalence studies are challenging because of wide variability in seroprevalence estimates, largely driven by biases in population sampling. Furthermore, use of case notification rates to determine true population exposure to SARS-CoV-2 can be misleading because of under-ascertainment, given that not all SARS-CoV-2 infected individuals undergo testing or seroconvert. The extent of under-ascertainment is driven by context-specific factors that change over time, such as testing strategy and capacity. Additional research is needed to better understand the consequence of waning antibody responses for serosurveys and for accurate extrapolation of results from seroprevalence studies to the level of protection in the population.

## Reinfection with SARS-CoV-2

Evidence on duration of immunity for recovered individuals is ideally drawn from longitudinal cohorts comparing infection risk amongst naïve and recovered individuals at three or six monthly intervals. Unfortunately, such studies are sparse. A systematic review of 11 key studies conducted by Health Information and Quality Authority in Ireland suggests that the reinfection risk amongst recovered individuals is low (absolute rate 0%–1.1%), with protection maintained for up to 10 months post initial infection [70]. More recently, Vitale et al. observed protection from reinfection for recovered individuals for a period of at least 12 months [71]. However, a critical limitation of these studies is that their observation periods predate the emergence and subsequent dominance of the Delta variant across the EU/EEA.

Preliminary analysis of national surveillance data from the UK indicates that recovered individuals have an increased risk of reinfection with Delta compared with the previously dominant Alpha strain, with the overall odds approximately 46% higher [72]. The Public Health England analysis included 83 197 individuals ≥15 years of age, who became SARS-CoV-2 PCR positive during an 11-week observation period (12 April and 27 June 2021), of whom 980 (1.2%) were possible reinfections. The adjusted odds ratio of reinfection with the Delta variant was 1.46 (95% CI 1.03 to 2.05) compared with the previously dominant Alpha variant. The risk of reinfection was not elevated for Delta if the primary infection occurred <180 days earlier (adjusted odds ratio = 0.79, 95% CI 0.49–1.28) but was higher for those with a prior infection ≥180 days earlier (adjusted odds ratio = 2.37, 95%CI 1.43–3.93). This finding has not yet been replicated in other settings, and additional age-stratified data on reinfection risk over time, specifically in the context of the Delta variant, is needed.

In the absence of a universal immune correlate which can be measured in recovered individuals to infer protection, the virus-neutralising capability of serum antibodies provide the best current indication of protection from reinfection. Whilst most SARS-CoV-2 infected individuals will develop serum antibodies, recovered individuals demonstrate highly variable antibody dynamics over time [73], with waning of neutralising antibodies widely documented [74]. In a key study by Planas *et al.*, sera collected from 56 convalescent individuals six months post-symptom onset were shown to be four-fold less potent against the Delta variant relative to the Alpha variant. The authors also observed a similar four-fold reduction in a separate cohort of 26 convalescent individuals evaluated 12 months post-symptom onset, stressing that neutralisation activity was globally low by month 12 [75].

Waning of serum antibodies may be entirely mitigated by the presence of SARS-CoV-2-specific memory B cells, which can rapidly expand when supported by SARS-CoV-2-specific memory T cells. Memory T cells may also contribute to protection and recovery from infection by directly lysing SARS-CoV-2 infected cells. However, specific T cell correlates remain elusive [76-78].

Taken together, the risk of reinfection with the Delta variant remains low, albeit with evidence of increased risk relative to the previously circulating Alpha variant.

# Modelling forecasts

As EU/EEA countries are entering the autumn months of 2021, COVID-19 vaccination coverage appears to be reaching a plateau, with the rate of weekly increase slowing in most age groups, following a large-scale vaccination programme. Since last spring, many NPIs have been lifted (see above 'Non-pharmaceutical interventions') and contact rates have increased steadily across the EU/EEA, as can be seen in contact surveys [79] as well as mobility data [80]. The future course of the pandemic will be determined largely by the contact rates between people 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 last autumn, is dominant across all EU/EEA Member States.

In view of the high transmissibility of the Delta variant, stagnating vaccination coverage and relaxation of NPIs, we estimate the number of cases, deaths, and hospitalisations in the EU/EEA until the end of November 2021, taking into account available epidemiological and vaccination data up to 8 September 2021. A crucial challenge for trying to predict the course of COVID-19 are the uncertainties regarding: vaccine effectiveness, the number of recovered individuals with natural immunity, human mobility patterns and the seasonal effects of the viral spread. We take these uncertainties into account by considering different prediction scenarios (Table 1). By exploring all scenarios, we obtain a predicted landscape of COVID-19 in Autumn 2021. 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 within one year. Thus, our predictions, which are based on this optimistic setting, yield a 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 [5], which was dominant last autumn. We further assume that vaccination programmes continue with a good supply of vaccine doses, but vaccination coverage starts to stagnate. These vaccination projections take into account the current prioritisation of age groups and dose spacing [10]. We use studies of vaccine efficacy against the Delta variant and weigh estimates for the different vaccine products according to their distribution in the EU/EEA [10]. We use a bootstrap method to obtain effectiveness mean and range estimates, and repeat this for effectiveness against cases, hospitalisation, and death. We use mean values in our baseline forecast scenario and the range estimates in additional scenarios.

We then generate COVID-19 cases by age-group, considering shifted age case distribution due to vaccination. We further estimate projected hospitalisations from the age-based case-hospitalisation 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, including for partially and fully vaccinated individuals. We simulate forecasts for the 11 different scenarios to capture the uncertainty in our key model assumptions (see Table 1).

In our baseline scenario (scenario 1, Table 1), we assume that contact rates (rates of transmission-relevant contacts between people) stay the same as those observed at the beginning of September 2021. We use Google mobility data [80] to inform changes in viral transmission in the forecast period compared with last year. Additional scenarios consider high and low VE against infection and against severe disease (scenarios 2-5, Table 1). To reflect current case detection rates, we use serological survey studies conducted in 2021 (see references and discussion in 'Natural immunity to SARS-CoV-2' section) and cumulative detected cases to estimate that for each detected case in the EU/EEA, 2.2 additional undetected individuals developed natural immunity. To reflect variability and uncertainty of this under-detection factor, we use a bootstrap method and obtain a value range that we include as additional scenarios (scenarios 6-9, Table 1). In one additional scenario we assume a seasonal forcing of transmission that we estimated in an analysis that adjusts for NPI and other effects. In another scenario we apply half of that seasonal forcing (scenarios 10 and 11, Table 1).

**Table 1. Baseline and alternative forecast scenarios for COVID-19 in the EU/EEA, Autumn 2021**

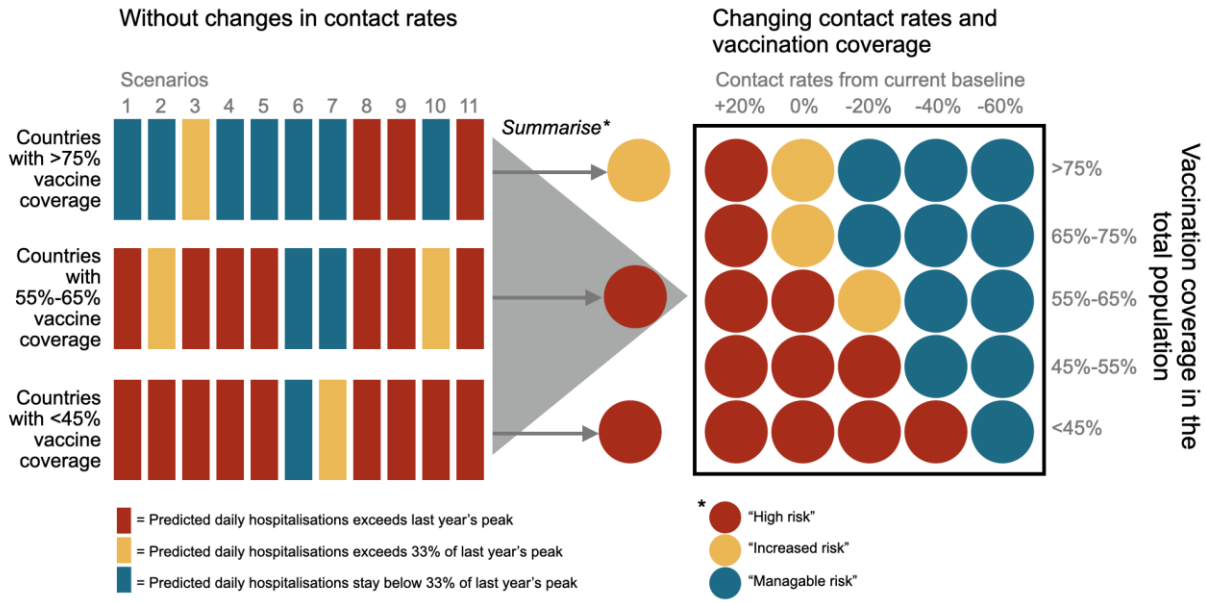
| Scenario | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Scenario name | *Baseline* | *High VE cases* | *Low VE cases* | *High VE severe* | *Low VE severe* | *Very high natural immunity* | *High natural immunity* | *Low natural immunity* | *Very low natural immunity* | *Half seasonal forcing* | *Seasonal forcing* |
| Contact rates between people | Current mobility | Current mobility | Current mobility | Current mobility | Current mobility | Current mobility | Current mobility | Current mobility | Current mobility | 0.5xSeasonality | 1xSeasonality |
| Natural immunity | 3.2 x cases | 3.2 x cases | 3.2 x cases | 3.2 x cases | 3.2 x cases | 10.7 x cases | 6 x cases | 1.7 x cases | 1 x cases | 3.2 x cases | 3.2 x cases |
| VE cases | 71% | 76% | 66% | 71% | 71% | 71% | 71% | 71% | 71% | 71% | 71% |
| VE severe (hospitalisation/death) | 82%/82% | 82%/82% | 82%/82% | 90%/90% | 74%/74% | 82%/82% | 82%/82% | 82%/82% | 82%/82% | 82%/82% | 82%/82% |

*Note to Table 1: Gives the parameters used in the different forecast scenarios with one baseline scenario (scenario 1) and ten alternative scenarios. These scenarios reflect uncertain factors which cannot be modified by Member States such as vaccine efficacy against the Delta variant. Scenario 10 applies seasonal forcing estimated elsewhere, and scenario 11 applies half of this seasonal forcing. VE: vaccine efficacy.*

We show the model predictions based on full course vaccine coverage in the total population. For easier readability, the left side of Figure 9 shows the main three vaccination coverage levels while all five levels are considered on the right-hand side. Note that we do not model future vaccination in <18-year-old populations as that varies greatly between Member States. Moreover, projections are based on a mean vaccination coverage for each country group, such that for countries with a coverage below this mean, prediction would be worse. The thresholds of the qualitative classification by vaccination coverage are based on the distribution of vaccine coverage levels assessed at the time of the modelling. Overall, countries with <45% vaccination coverage in total population fall into the low coverage group, those with 45–55% into low-intermediate coverage, countries with 55–65% into intermediate coverage, those with 65–75% into intermediate-high coverage, and countries with >75% vaccination coverage in the total population are seen in a high vaccination group.

For every predicted scenario, we visualise our forecasts with a rectangle whose colour indicates the hospitalisation burden (assuming unchanged contact rates from those currently observed): blue indicates low daily hospitalisations (below 33% of the past EU/EEA peak during the COVID-19 pandemic), yellow indicates substantial hospitalisation burden (over 33%, but not exceeding the past EU/EEA peak), and red indicates very high hospitalisation burden (exceeding the past EU/EEA peak). The left-hand side of Figure 9 shows the predicted burden of the 11 scenarios and the three main vaccination levels. We then summarise the predictions across modelling scenarios (Figure 9, arrows to circles): Without changes in contact rates from current levels, the countries at the highest level of vaccination coverage are at 'increased risk', while those at average or low vaccination coverage are at 'high risk' (Figure 9). From this we show predicted risk of healthcare burden based on different vaccination coverage and contact pattern levels (Figure 9, right-hand side).

**Figure 9. Projected burden of COVID-19 hospitalisations in relation to vaccination coverage between now and the end of November 2021.**




*Note: The left subfigure shows model projections (assuming unchanged current contact rates) as rectangles in blue (predicted burden that stays below 33% of the COVID-19 pandemic's peak hospitalisation rate), yellow (burden above 33% but below peak rate), and red (burden exceeds the peak rate). These projections are shown for three levels of vaccination coverage (rows, full vaccination course in the total population), and across 11 different scenarios (columns) that vary parameters (see Table 1). While the vaccination levels can be increased by Member States, the parameters are a biological reality and cannot be influenced. The different scenario outcomes are then summarised into single categories (depicted as circles).*
*The right-hand side shows the risk for hospital 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 baseline. The vaccination coverage range represent current coverage, but as the projected values change only by few %, the range also represents the future vaccination coverage.*

Our forecasts show that a combination of high vaccination coverage and effective contact reduction (see section 'Options for response - Non-pharmaceutical interventions') is crucial for reducing the risk of high COVID-19 burden on healthcare systems in Autumn 2021 (see Figure 9). EU/EEA countries with low vaccination coverage will likely require substantial reductions in contacts between people or otherwise risk a high burden on their healthcare system. Similarly, countries with intermediate vaccination coverage will also likely require contact reductions to avoid a high burden. Lastly, EU/EEA countries with high vaccination coverage could experience a manageable burden at current contact rates, but this burden would increase if contact rates increase further. Moreover, even in countries with high vaccination coverage, a high burden is possible due to potential waning of vaccine effectiveness (see Appendix 2) or low levels of natural immunity. Because vaccines offer high protection against severe outcomes of COVID-19 infection, a large proportion of COVID-19 hospital admissions will be unvaccinated individuals, in particular unvaccinated individuals in risk groups. This will especially be true in countries with low vaccination coverage, where a high burden of severe illness is projected. A high burden of severe illness, however, is also a risk for intermediate and high vaccination locations. This is because the high transmissibility of Delta roughly outweighs the reduction in transmission achieved by the current vaccination rollout. The key impact of vaccination is indeed the reduction of the case-hospitalisation and case-fatality rates, thus decoupling case burden and burden of severe disease. Nonetheless, our modelling shows that Delta's transmissibility as well as increasing contact rates could combine to pose a significant risk for exponential growth of cases this autumn. Such growth may lead to a burden of cases that outweighs the reduction in case-hospitalisation rates, thereby leading to a comparable or higher burden than last winter.

This risk for exponential growth will be further exacerbated by the potential for waning of vaccine effectiveness against transmission. We estimate that if substantial waning of vaccine immunity occurs, the risk of high healthcare burden strongly increases for all vaccination scenarios, thus requiring even further contact reduction (see Appendix 2). Furthermore, hospitalisation rates for COVID-19 infection modelled here do not account for further pressures that health systems may face through, for example, increased hospitalisations due to a moderate or severe influenza season. Finally, any country, including those with high vaccination coverage, is likely to have communities with low vaccination coverage. Our results suggest that those communities are at a high risk for a substantial burden of severe illness. A combination of targeted vaccination campaigns and NPIs could help reduce this risk. This may further require close monitoring of COVID-19 cases on a local scale.

### *Limitations*

There are a number 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. Behaviour is extremely difficult to measure and to predict and here google mobility data is used as a proxy for contact rates. Additionally, there are still many unknowns around natural immunity to SARS-CoV-2, which we are trying to capture through a wide range of natural immunity scenarios. 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, vaccine effectiveness, natural immunity, and population contact rates—in the context of the continued circulation of the Delta variant. Unlike the previous Risk Assessments, which provided a risk estimate for a single point in time, this assessment of risk covers the period between now and the end of November 2021. Nonetheless, assessment follows the same ECDC risk assessment methodology as in the 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 [81].

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 (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 3 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 to facilitate presentation.

# Risk assessment question

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

### Countries with low vaccination coverage

Current ECDC modelling indicates that without substantial changes in population contact rates, countries or regions with vaccination coverage in the total population that is below the current EU average level are projected to experience a high burden of hospitalisations and deaths between now and end of November 2021.

<u>General population</u>

- Fully vaccinated: probability of infection HIGH + impact of infection LOW ➔ **LOW-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 average vaccination coverage

Without moderate changes in contact rates, countries or regions with vaccination coverage in the total population that is at the EU average level are projected to experience a high burden of hospitalisations and deaths unless their population has high natural immunity from previous SARS-CoV-2 infections.

General population

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

Vulnerable population

- 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 or regions with levels of vaccination coverage in the total population that is above the current EU average level, and particularly those with the highest levels of coverage, may have a manageable burden of hospitalisations and deaths unless there is strong waning of immunity post-vaccination and/or their population has low natural immunity.

General population

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

Vulnerable population

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

### 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.

In case of substantial waning of vaccine efficacy against infection and/or seasonal transmission, the likelihood of high disease burden and need for reduced contact rates increases for all countries at all levels of vaccination coverage.

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, non-pharmaceutical measures, 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 in the autumn.

## Options for response

In view of the dominant circulation of the Delta variant, the unequal COVID-19 vaccine uptake across and within EU/EEA countries and the forecast of increased burden of SARS-Cov-2 cases in the next two months, improving national vaccination coverage should be the absolute priority for all public health authorities in Autumn 2021. A possible early start of the influenza season and the potential co-circulation of the two viruses may further stress healthcare systems. Furthermore, if A(H3N2) viruses are the dominant virus subtype as detected until now, the elderly would also be disproportionately affected. Non-pharmaceutical interventions (NPIs) such as use of face masks, improved ventilation in closed spaces and physical distancing measures should remain in the response toolbox to be tailored to the needs of the community. Testing for SARS-CoV-2 should continue to be available using accredited testing methods. Surveillance systems should continue to monitor primary, secondary and tertiary care, and disease incidence by severity, in order to guide decisions on public health measures and to understand their impact. Finally, risk communication should try to keep a balance between optimism while maintaining awareness that 'the pandemic in not over, yet'.

# Vaccination

Considering the overall progress in national COVID-19 vaccination programmes in the EU/EEA and the increased availability of vaccine supplies, the current priority for EU/EEA countries remains to increase vaccination coverage, close the immunity gaps and ensure that all eligible individuals receive a full course of vaccination, especially those individuals at higher risk of severe COVID-19 disease who have not yet been reached. While increasing overall population coverage to the maximum level possible is critically important, as shown by the modelling forecast scenarios in this assessment, priority needs to continue to be given to ensuring that all those most vulnerable to COVID-19 infection and its consequences are fully vaccinated.

Despite overall progress in vaccination coverage, the progress in vaccine uptake in the adult population and specific priority groups (i.e., elderly and residents in LTCFs, HCW) has been unequal across EU/EEA countries and at subnational level, where pockets of geographic areas or population groups with low uptake persist, including in countries that have reached high levels of vaccination coverage overall. In order to expand the vaccine rollout, it will be especially important to continuously monitor vaccine uptake and associated social determinants to understand where and in which population groups and communities the immunity gap persists. The extent and characteristics of unvaccinated individuals will play a major role in the future dynamic of the pandemic and it should be monitored to inform vaccination strategies.

As recently published in a ECDC technical report [49], strategies should include the administration of additional vaccine doses as part of a primary vaccination series for people with severely weakened immune systems (e.g., solid organ transplant recipients), as they may not achieve an adequate level of protection from the standard primary vaccination. Full vaccination against COVID-19 of all eligible family contacts and close contacts, including professionals providing care, of immunocompromised and vulnerable individuals should also be considered. Consideration could also be given to providing an additional dose as a precautionary measure to older frail individuals, in particular those living in closed settings (e.g. residents of long-term care facilities). In light of emerging evidence of waning immunity after vaccination and of reduced vaccine effectiveness against the currently dominant Delta variant, monitoring of vaccine effectiveness data and description of breakthrough infections, particularly amongst vulnerable groups at risk of severe COVID-19 and amongst those living in closed settings, is ongoing in EU/EEA countries and at ECDC to continue to inform policy decisions on the use of additional doses. Other groups for consideration for the use of additional doses could be healthcare workers and other staff who work in close contact with individuals at risk of severe COVID-19.

Finally, the co-circulation and a potential rise in influenza infections during the ongoing COVID-19 pandemic in the autumn and winter months could have severe consequences for vulnerable populations and place an additional burden on health systems already strained by COVID-19. Seasonal influenza vaccination campaigns are well established in EU/EEA countries and are usually organised during the autumn to provide adequate protection in time for the start of the influenza season. Given the possibility of co-circulation of SARS-CoV-2 and influenza viruses in the autumn, capacity building for influenza diagnostic testing should be planned and Member States should ensure that optimal influenza vaccine coverage is achieved before the start of the winter influenza season. EU Member states have agreed to have policies and programmes in place to target healthcare workers, older adults, and individuals with chronic health conditions for influenza vaccination. Many Member States also include children and pregnant women in their programmes. In addition to influenza vaccines, two antiviral medicines are authorised in the EU to prevent severe influenza disease [82].

## Increasing vaccination uptake

Efforts should be made to ensure that as many eligible citizens as possible are protected by full COVID-19 vaccination. A key principle to consider when seeking to facilitate vaccination uptake is that populations are diverse, and interventions need to be targeted and context-specific: a one-size-fits-all strategy is unlikely to be optimally effective. It is therefore necessary to diagnose the reasons for under-vaccination in a given sub-population in order to plan the most appropriate intervention. The '3Cs' model, as suggested by the WHO's SAGE Working Group on Vaccine Hesitancy, offers a potentially useful framework for diagnosis and then action (Appendix 4) [83]. This model identifies Convenience, Complacency and Confidence as key factors associated with vaccine uptake. The relative importance of the 3Cs can change over time in a certain sub-population, so it is important for the authorities to conduct regular diagnoses of the reasons for under-vaccination, thereby providing a basis for adapting the interventions as necessary.

Healthcare workers are widely trusted within the EU/EEA for information on vaccination, and they therefore play a particularly critical role in promoting COVID-19 vaccination and in addressing people's questions or concerns about the vaccines. They should also be a key target for tailored communication and community engagement efforts to address any acceptance issues that they may face themselves, both to avoid putting themselves, their families, their colleagues and patients at risk of SARS-CoV-2 infection, but also as any concerns that they have may be amplified if they communicate these to their patients. Some EU/EEA countries have issued COVID-19 vaccination mandates for healthcare workers and personnel working in long-term care facilities. However, it is important to note the potential negative effects of such mandates, whether ethical, political, or legal.

This issue is discussed further in Appendix 4, which also presents strategies implemented in EU/EEA countries to address hesitant populations as well as key strategies to address misinformation. It is hoped that other Member States may learn from and apply these in their own context to increase COVID-19 vaccine uptake.

# Non-pharmaceutical interventions

Non-pharmaceutical interventions such as the use of face masks, improved ventilation in closed spaces and physical distancing measures as well as contact tracing should continue to be implemented in accordance with the local epidemiological situation, the vaccination coverage in the total population and taking into account the increased transmissibility of the Delta variant. The forecasts presented in this assessment indicate that until and unless sufficiently high vaccination coverage has been achieved, it will be necessary to maintain, or strengthen NPIs through the coming autumn months, according to assessments of vulnerability considering the vaccination coverage, the epidemiological situation, public health and healthcare system capacity in a country or region.

Fully vaccinated individuals with underlying diseases and risk factors may be increasingly vulnerable in the coming months, given the increased likelihood of exposure to the Delta variant combined with the potential for waning immunity. Therefore, vulnerable groups, independent of their vaccination status, should be advised to continue adhering to NPIs such as use of face masks when in crowded situations as a means of personal protection, physical distancing and personal hygiene measures like appropriate handwashing.

Continued mitigation efforts and strengthening of healthcare systems and HCW resilience remain important during autumn and 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 [41,84] .

According to the ECDC forecast (See 'Modelling' and Figure 9), some measures to limit physical contacts will be needed in the next months to avoid an increased burden of COVID-19 hospitalisations and potentially deaths. However, in countries where the epidemiological situation and the vaccination coverage of the total population allows (regions with high vaccination coverage), authorities may consider a gradual relaxation of NPIs. Measures that can be considered in order to avoid increases in cases, if the epidemiological situation and vaccine coverage levels are at a level likely to be associated with the further rises indicated in the ECDC forecast, include physical distancing measures such as permitting teleworking and distance education, particularly for those vulnerable to severe COVID-19 outcomes, or those living with vulnerable people. Other measures include modifications to public transportation to decrease crowding, such as increasing its availability. If gatherings are allowed (e.g., social and cultural events, entertainment, etc) their preparations should aim to prevent or minimise crowding, with gatherings outdoors preferred. Recommendations to stay home from school and work when ill with COVID-19 compatible symptoms should also continue.

Surveillance, identification of cases, contact tracing and quarantine of contacts remain key for monitoring the epidemiological situation and preventing a further surge of cases while measures are lifted or adapted [85].

In countries or regions where the epidemiological situation remains concerning and vaccination uptake remains at the current average level or below, NPIs should be maintained. Efforts should focus on enhancing adherence to the current measures, protecting vulnerable populations (e.g., LTCF residents and unvaccinated vulnerable groups) and ensuring healthcare capacity. In particular, these countries/regions should consider maintaining physical distancing measures between individuals as much as possible, maintaining limits on the size of public gatherings, especially those indoors, as well as recommending only limited size private gatherings, providing advice on the appropriate use of face masks where necessary, continuing with contact tracing, quarantine of contacts and isolation of cases, as well as limiting transmission in workplaces by encouraging teleworking whenever possible and promoting hand hygiene and respiratory etiquette for all. Additional targeted voluntary measures could also be considered.

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' [86]. For analysis and available evidence on the impact of vaccination on NPIs, please refer to ECDC's 'Interim guidance on the benefits of full vaccination against COVID-19 for transmission and implications for non-pharmaceutical interventions' [87].

# Schools

As ECDC outlined in July 2021, in regions where an increasing percentage of adults are fully vaccinated against COVID-19 but where children are not vaccinated or vaccinated at low levels, it may be anticipated that in the coming months increasingly greater proportions of reported SARS-CoV-2 cases will be amongst children [88]. Given this continued risk of transmission amongst unvaccinated children, a high level of preparedness is required in the educational system for the 2021/2022 school year [88].

The high transmissibility of the Delta variant means that the risk of transmission in school settings is higher than with previously circulating SARS-CoV-2 strains, given comparable control measures in place [89,90]. While severe COVID-19 outcomes in children remain relatively rare compared with other age groups [91], increases in case numbers amongst children could lead to higher absolute numbers of severe outcomes, notably hospitalisations, in this age group. In the US, the number of children and adolescents hospitalised due to COVID-19 increased nearly five-fold during late-June to mid-August 2021 due to the circulation of the Delta variant, but the proportion of children and adolescents having severe disease due to COVID-19 infection was noted to be similar to periods prior to the dominance of Delta [92].

School closures have been shown to have significant negative physical, mental and educational impacts on children, as well as the economic impact on society more broadly, and therefore alternative mitigation and response strategies should be given priority, as outlined below.

Combinations of NPIs in the form of physical distancing to prevent crowding, as well as hygiene, improved ventilation, masks and other measures remain important tools for the prevention of transmission in school settings. Measures should be adapted to levels of community SARS-CoV-2 transmission and healthcare system utilisation, as well as to the educational setting and age group, and their implementation should consider the need to provide an optimal learning and social environment while reducing transmission risks [88]. Measures to reduce SARS-CoV-2 transmission in school settings may also help to mitigate the transmission of other respiratory viruses commonly circulating in the autumn and winter months amongst the paediatric population. 'Test-to-stay' strategies could additionally be considered in an attempt to minimise disruption and school absenteeism in school settings while also limiting opportunities for further transmission [88,93,94]. Daily testing has been used successfully to keep children in schools, despite positive cases in a class. In a UK open-label cluster-randomised trial, daily contact testing of school-based contacts was found to be a non-inferior safe alternative to self-isolation [93].

# Testing, surveillance and monitoring

## Testing strategies

Testing of people with symptoms, through improving access to testing and encouraging people to seek testing as soon as possible after symptom onset remains important to enable rapid identification of cases and initiation of contact tracing to limit the spread of SARS-CoV-2. Depending on available resources, testing strategies could include additional objectives, such as outbreak analyses, asymptomatic case detection, phylodynamic analyses and other 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 utility [95].

In January 2021, Member States agreed to maintain a common and updated list of COVID-19 RADTs that are considered appropriate for use and are in line with countries' testing strategies. This common list of RADTs is regularly being reviewed by Member States through the Health Security Committee (HSC), and, if necessary, being updated in line with new results from independent validation studies becoming available and new tests entering the market.

Diagnostic laboratories should remain vigilant to detect any mismatches of specific RT-PCR assay primers and probes in comparison to circulating virus genomes. It should be noted that the majority of primer/probe binding sites of commercial assays are not publicly known. For in-house or commercial RT-PCR assays for which the primer/probe sequences are available, validation can be done via the ECDC PrimerScan [96] or similar tools that identify mismatches. 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. For laboratories using the ARCTIC protocol for sequencing of SARS-CoV-2 it is important to use the latest version of the primers as mismatches may occur with variant viruses [97].

During the ongoing COVID-19 pandemic period, and as influenza is already being detected in some countries ahead of the normal start of the influenza season, when the number of cases presenting to sentinel surveillance sites are low, all patients with 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 SARS-CoV-2 viruses; a multiplex RT-PCR assay can be considered [98]. Representative influenza positive specimens should be sent to the influenza reference laboratories for further genetic and antigenic characterisation as well as antiviral resistance monitoring.

In general, laboratories should have a quality assurance system in place and are encouraged to participate in external quality assessment (EQA) schemes or perform result comparisons between laboratories for a subset of samples. The ECDC funded External Quality Assessment (EQA) on molecular detection of SARS-CoV-2 with the focus on variants for national COVID-19 laboratory panels was distributed in the week of 13 September 2021.

Community-level screening can be performed by sequencing SARS-CoV-2 from wastewater and the presence of signature mutations can be used to assess the presence of variants, although this technique is still under development [99]. The European Commission has published a Recommendation to support EU/EEA countries in establishing wastewater surveillance systems across the EU [100]. For more information on RADTs, self-test RADTs, assessment of the circulation of VOCs in the community and community level screening from wastewater, please refer to the testing strategy section of the 15th update of the Rapid Risk Assessment [1].

## Sequencing capacity

Genomic surveillance of currently circulating variants (including regular representative samples and targeted samples from special settings and populations) is 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.

General considerations regarding testing strategies, diagnostic assays, sequencing and antigenic characterisation with relevance for circulating SARS-CoV-2 variants are provided in the latest ECDC rapid risk assessment [1] and in the ECDC guidance for representative and targeted genomic SARS-CoV-2 monitoring [2].

A representative sample with a sufficient sample size (optimally each week) and targeted samples from special 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 [2]. This allows for early identification and monitoring of emerging variants or of known variants with novel mutations that may have a potential impact on phenotypic characteristics of the virus. All or a representative subset of viruses detected in samples from sentinel sources should be sequenced.

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.

## Surveillance and monitoring

Considering a potential increase in the incidence of SARS-CoV-2 over the autumn and winter, COVID-19 surveillance systems need to be able to effectively monitor disease incidence by severity, to guide decisions on public health measures and to understand their impact. Vaccine effectiveness needs to be monitored to determine the need for additional doses and inform optimal vaccination programmes and strategies.

In order to achieve these objectives, comprehensive surveillance or sentinel surveillance systems with high population coverage covering primary (such as expanded sentinel influenza surveillance), secondary and tertiary care (for example SARI surveillance) should be in place. Particular focus should be placed on collecting complete data on key variables, such as severity of infection and vaccination history, ideally linked to sequencing results where available [101]. Sentinel influenza surveillance systems and SARI surveillance systems also need to be strengthened in anticipation of potential co-occurring outbreaks and circulation of other respiratory viruses such as influenza or respiratory syncytial virus (RSV). Surveillance of all-cause mortality (such as carried out by the EuroMOMO network [102]) should continue in order to rapidly detect and quantify excess mortality from COVID-19.

In the event a new SARS-CoV-2 variant emerges, monitoring their spread and rapid assessment of their characteristics remains important in order to issue potential containment measures.

Monitoring of COVID-19 outbreaks in long-term care facilities (LTCFs) is also important. While these settings have in general the highest vaccine coverage, they are also home to those with the highest risk for severe COVID-19 outcomes. Numerous outbreaks in LTCFs have been reported in the EU/EEA during the summer and early autumn, with breakthrough infections being reported in fully vaccinated residents and sometimes with fatalities [103]. ECDC issued a specific protocol on data collection of COVID-19 outbreaks in LTCFs on 6 May 2021, and an update on 3 September 2021. Its main aim is to collect information on the severity of breakthrough COVID-19 infections in outbreaks at LTCFs and to obtain a timely estimate of vaccine effectiveness in these settings, by SARS-CoV-2 variant and vaccine product. This activity is not intended to capture all outbreaks, generate comparative statistics, or obtain a (sub-)nationally representative sample [104].

Historically, outbreaks of influenza in LTCFs with high morbidity and mortality have been observed when influenza A(H3N2) circulated. Outbreaks of A(H3N2) virus in LTCFs are early signals of a severe influenza season and healthcare providers should consider influenza testing as well as vaccination and possibly pre-and postexposure prophylaxis with antivirals (neuraminidase or cap-dependent endonuclease inhibitors) [105,106].

# Travel measures

Travel measures 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. Travel measures would be important if implemented very early, consistently and completely, if there was evidence of circulation of a new SARS-CoV-2 variant, particularly an immune escaping one, to delay its introduction.

ECDC has published a guidance for COVID-19 quarantine and testing of travellers [107], also highlighting the considerations around the use of RADTs for travelling. RADTs can be useful for detection of infectious cases in the first five days from disease onset, they have, however, reduced sensitivity for detecting asymptomatic cases [108].

During travel, NPIs should be maintained regardless of the vaccination status of the traveller. In particular, the use of face masks, avoidance of crowding and maintaining physical distancing as well as improved ventilation in stations and transportation modes (airplanes, trains, buses etc) should be maintained. Fully- vaccinated travellers should also respect any NPIs for fully- vaccinated people in the country of destination. Documents informing about which give more information on the safety measures on various travel conveyances have been developed in collaboration with other EU agencies: air travel [109], cruises [110] and railways [111].

The EU digital COVID certificate (EU-DCC) has been in use in the EU/EEA countries and a number of third countries since 1 July 2021, 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 to facilitate safe and free movement. When travelling, every EU citizen or third-country national legally staying or residing in the EU, who holds an EU digital COVID certificate, should be exempt from free movement restrictions in the same way as citizens of the visited EU country [112].

# Risk communication

With the dominance of the Delta variant across the EU/EEA, continued community transmission, and pockets of low vaccination coverage across most countries, it is important to maintain the overarching message to the population that 'the pandemic is not yet over'. This is a challenging message to disseminate, given widespread expectations that increasing overall vaccination rates would, in broad terms, allow people to return to a relatively 'normal' life again.

However, the epidemiological situation needs to be balanced against these expectations. Authorities may want to consider the potentially substantial risks in over-promising what may be possible in terms of re-opening society. The Canadian province of Alberta provides a recent example of what can happen if COVID-19 restrictions are loosened too soon, with the healthcare system struggling to manage the highest rate of hospitalisations yet seen in the pandemic. 61% of eligible Albertans are fully vaccinated (as of September 19), but approximately 91% of those in Intensive Care Units over the past 120 days have been unvaccinated [113]. The province's political leadership has found it necessary to issue a public apology for opening up too much too soon, and has reimposed COVID-19 restrictions in a reversal of previous policy [114].

Consistency in messaging, within the confines of what is known scientifically, has been stressed throughout the pandemic as a key principle for facilitating trust in the authorities, and thereby for adherence to the recommended measures [115]. As such, efforts should be made to avoid circumstances that may require back-tracking over promises made regarding the re-opening of society. Populations that are weary of living under pandemic restrictions may not respond well if the restrictions are first removed and then re-imposed [116].

There is also a communication challenge to be addressed in situations where some restrictions remain in place even though there is good overall vaccination coverage. People may question the vaccine's effectiveness under such circumstances, especially when the original message was that vaccination would lead to a return to normality. In these circumstances, it is important to clarify that the Delta variant is now dominant throughout most of the EU/EEA [117], which it was not earlier in the year, and that the vaccines are now working well to mitigate against this more challenging epidemiological situation.

## Proposed key messages

### *Key messages for citizens*

- Public health authorities need to continuously remind all eligible citizens of the importance of being fully vaccinated. Vaccines are the key tool to controlling this pandemic. Those who remain unvaccinated are putting themselves and people close to them at risk. Safe and effective vaccines are available and are highly protective against COVID-19 related severe disease, hospitalisation and death.
- Those partially vaccinated need to be reminded of the importance of completing their vaccination course, as evidence shows that taking the second dose in two-dose vaccine regimens provides optimum protection.
- Those fully vaccinated need to be aware that, even if they are well protected against infection and severe disease, there is still the possibility of breakthrough infections. This is to be expected, as no vaccine is 100% effective, though breakthrough infections do tend to produce milder illness. People with multiple comorbidities and/or low immunity are at highest risk of breakthrough infection and they may face more severe illness, and therefore they need to take additional precautions to further protect themselves.
- All citizens should also be reminded to continue to follow national recommendations regarding protective measures that are effective in reducing the spread of infection. These include respiratory and hand hygiene, as well as staying at home when having any symptoms of respiratory disease. Other measures can be considered, such as the use of face masks, improved ventilation indoors and physical distancing, as per national recommendations.

### *Key message for authorities*

- Public health authorities need to stress the importance of vaccines as a powerful tool in helping to control the pandemic.
- The Delta variant is creating a rapidly evolving situation which requires additional measures to control community spread, even in well-vaccinated populations. Without these measures, there will be an inevitable increase in cases, which will also lead to an increase in hospitalisations and deaths. This may undermine, in the public eye, the perceived effectiveness of the vaccine, which in turn could adversely affect uptake.
- Uncertainty needs to be acknowledged. To maintain public trust, it is important to be transparent about the evolving evidence in relation to vaccine effectiveness, the impact of the dominant variant circulating and uncertainty regarding duration of protection from vaccines.
- In this context, people need to understand that vaccine recommendations as well as public health measures may need to be adapted to further control the pandemic. Providing a clear framework regarding which parameters are being used in order to adjust measures (e.g. vaccine coverage, hospital admissions, etc.) can be helpful to explain any changes that may be necessary.

# Knowledge gaps

Much of the evidence presented here is based on unpublished data, which is evolving daily. Therefore, there are still many knowledge gaps and major uncertainties regarding the 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 Member States 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. mink).
- 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 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.
- 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
- Impact of variants on possible treatment options (e.g., monoclonal antibodies).

### *Behaviour and social sciences*

- In-depth understanding of what is driving low vaccination 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 vaccination 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, 15 September 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.

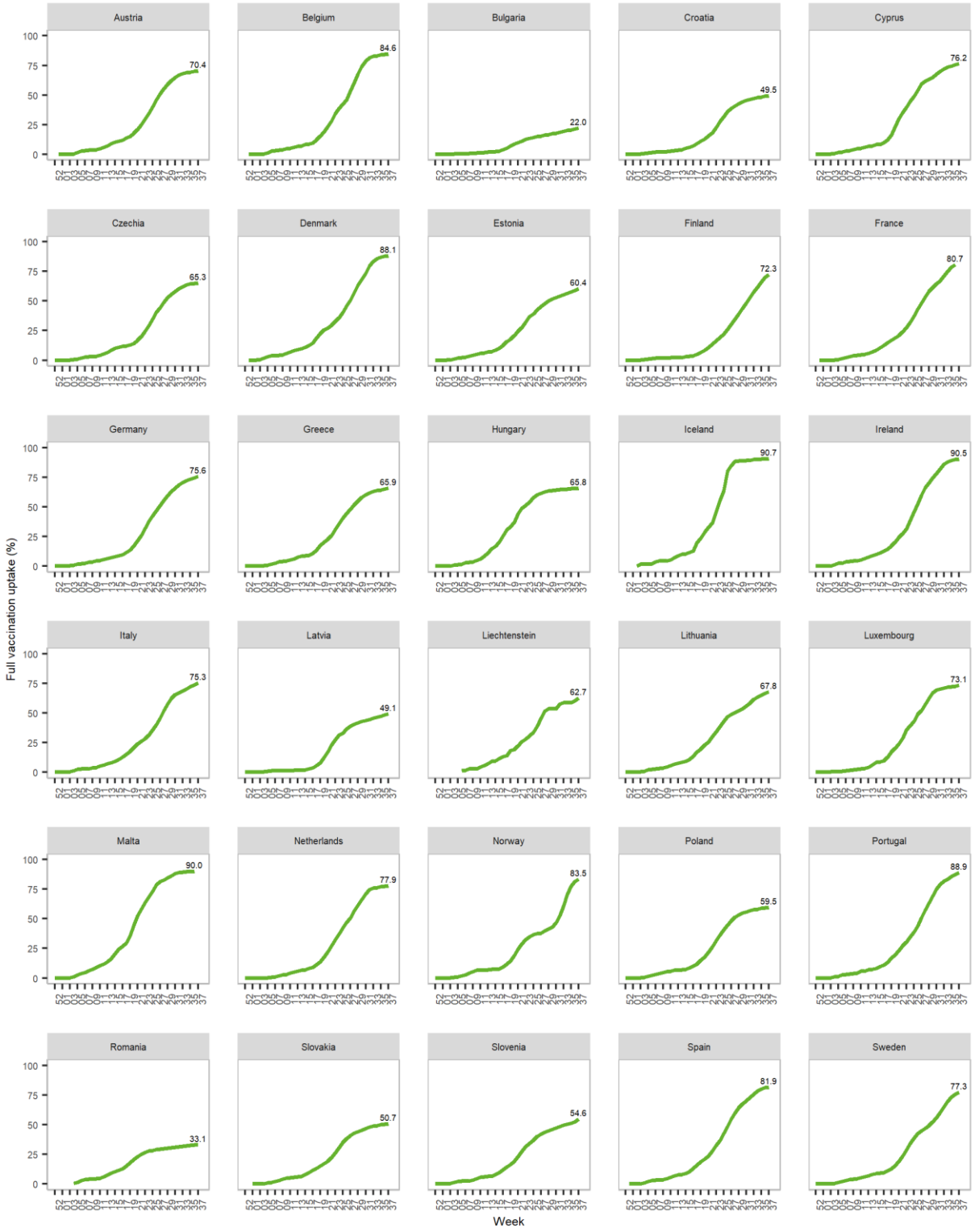
# Disclaimer

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 Member States. 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

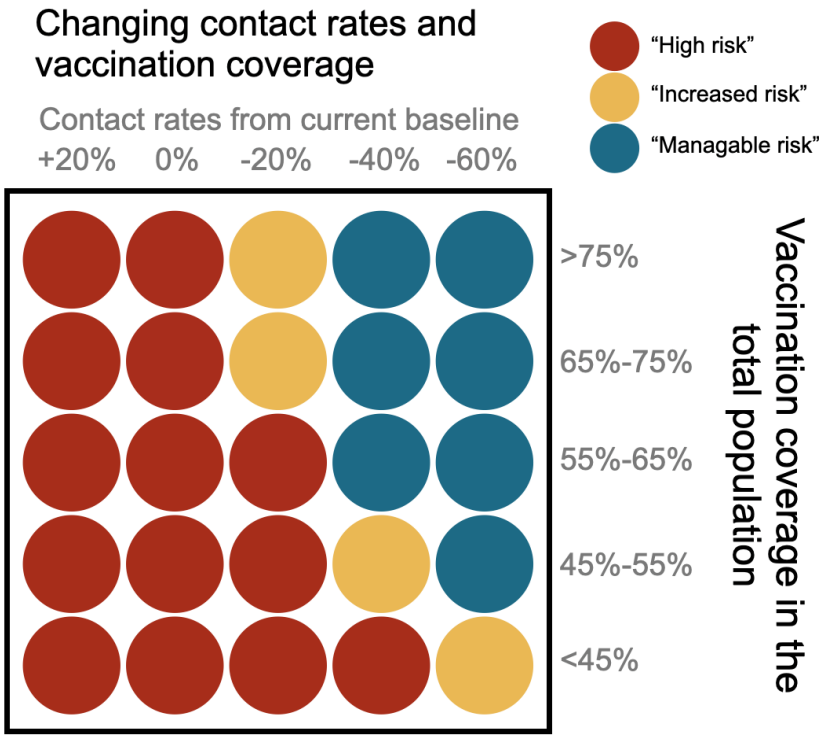
**Cumulative uptake of full COVID-19 vaccination amongst adults in EU/EEA countries as a percentage (%) of the adult population as of week 37, 2021**




*Source: TESSy; data reported by 30 countries as of week 37, 2021. See the Notes on data in the ECDC Vaccine Tracker for country-specific disclaimers.*

# Appendix 2

**Projected scenario outcomes across different COVID-19 vaccine coverages of the total population and contact rates relative to current baseline assuming waning of vaccine effectiveness against cases (mean of 57%, range 53%-61%)**




*All other parameters are as in Table 1.*

# Appendix 3

### 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 the highest levels of vaccination coverage in the total population** | Probability: MODERATE<br>Impact: HIGH | Risk **MODERATE** | Probability: HIGH<br>Impact: VERY HIGH | Risk **HIGH - VERY HIGH** | Probability: MODERATE<br>Impact: LOW | Risk **LOW** | Probability: HIGH<br>Impact: MODERATE | Risk **MODERATE** |
| **EU/EEA countries with vaccination coverage in the total population at or below the EU/EEA average** | Probability: HIGH<br>Impact: VERY HIGH * | Risk **HIGH - VERY HIGH** | Probability: VERY HIGH<br>Impact: VERY HIGH | Risk **VERY HIGH** | Probability: HIGH<br>Impact: LOW | Risk **LOW - MODERATE** | Probability: VERY HIGH<br>Impact: HIGH ** | Risk **HIGH - VERY HIGH** |

** 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.*

# Appendix 4

## Interventions to address vaccine-hesitant populations

Diversity across EU/EEA countries – regarding the stage of vaccine campaigns as well as the wider social and political context – means that there can be no one-size-fits-all strategy to tackling vaccine hesitancy across the region. Adapted and context-specific strategies are needed. However, before such strategies are designed and deployed, it is necessary that countries diagnose the specific drivers of hesitancy in different populations [118]. Various scales and indexes have been developed for this purpose, including the Global Vaccine Confidence Index, which has been used regularly in the EU/EEA region [119,120], the Vaccine Confidence Scale [121], and the Vaccine Hesitancy Scale [122]. The WHO SAGE Working Group on Vaccine Hesitancy has also drafted a series of survey questions that can be used to support immunisation programs [123,124].

The interventions to address vaccine hesitancy detailed below are categorised using the '3Cs' model, as suggested by the WHO's SAGE Working Group on Vaccine Hesitancy. This model identifies Convenience, Complacency and Confidence as key components of vaccine hesitancy [83]. The strategies below may be selected, combined, and prioritised given a country's particular context and stage of vaccination.

Hesitancy due to *Convenience* may occur when people face barriers caused by geographical accessibility, cost, perceived poor quality of the vaccination services, and the suitability of time and place of the vaccination [83]. Belgium has sought to address access barriers facing socially-vulnerable populations by sending out mobile teams to key sites - such as homeless shelters, aid centres for migrants, transit homes, and shelters for victims of domestic abuse - and offering one-shot vaccines directly without requiring registration [125]. Key community locations, such as churches and mosques, have also been used by mobile teams in the Netherlands to reach under-vaccinated populations). Other countries have been addressing access issues by offering vaccination without appointments (Austria, Czechia, Liechtenstein) or at transportation hubs (Czechia, Estonia) and shopping centres (Czechia, Latvia), while others have been covering people's transport costs to the vaccination venue.

Hesitancy may be driven by *Complacency* when the risk presented by COVID-19 is perceived as low in an individual and/or group, and as such the perceived benefits of vaccination are perceived as marginal or irrelevant [83]. Addressing complacency requires clear, consistent, and transparent communication of the risks of COVID-19 for the specific groups in question, in easily understood language, along with explanations of the relative benefits of vaccination [115]. While messaging on risk shows variable outcomes dependent on the individual receiving the message [126,127], a 2021 study in the UK demonstrated that those who were strongly hesitant were most persuaded to vaccinate when messaging directly addressed personal benefit alongside a person's risk from the virus, rather than focusing on wider community benefits of vaccination [128]. Research from France and Spain suggests that chatbots can be used effectively to communicate with individuals on the risks and benefits of vaccination [129,130]. This interaction and dialogue is reportedly more likely to positively influence willingness to vaccinate than one-way messaging on risks vs. benefits.

Vaccine hesitancy can also be caused by a lack of *Confidence* in the vaccine, the health system, or those who make decisions about vaccination recommendations. Strategies to tackle issues of confidence should focus on building trust and community engagement. In Ireland, the Department of Health has created a network of young science communicators from across the country [131], who actively post content on social media to engage with, share experiences and answer the questions that young people across the country have concerning COVID-19 vaccination. Through this they aim to create a dialogue that will foster trust and thereby increase vaccine uptake in this group [132,133]. In Belgium, an innovative pilot programme involving community health workers runs to increase people's knowledge of the healthcare system and their trust in it, particularly in vulnerable populations [134]. Members of the communities themselves are informing individuals about the COVID-19 vaccine, linking them up with and accompanying them to their first vaccination, as well as doing follow-up activities [135].

## Addressing misinformation

The term 'misinformation' refers to information that is false or incorrect according to current scientific knowledge. Misinformation includes disinformation, which is false or incorrect information that is knowingly and wilfully disseminated for economic or political purposes, as opposed to false and incorrect information that people disseminate, believing it to be correct.

Misinformation has the potential to undermine people's intentions to be vaccinated [136]. Within the context of the 3Cs model described above [83], misinformation could potentially have a strong influence on Confidence or on Complacency. Work conducted by ECDC has identified four core areas on which effective strategies for countering online vaccine misinformation should be built [136]:

- ***Monitoring misinformation on social media***. Social media sites are major outlets and amplifiers of vaccine misinformation, and they provide the venue for a large proportion of ongoing anti-vaccine debates. For health authorities, understanding this discourse is crucial if they are to design effective communication messages and strategies to stop misinformation from spreading. Monitoring of disinformation that targets the EU, its Member States, core institutions, and core values is conducted by the EU Disinfo Lab, using both traditional and social media platforms [137].
- ***Pre-emptive interventions***. These can include (i) pre-bunking or 'inoculation', which provides people knowledge in advance of how misinformation is spread, thereby giving them the ability to 'resist' such information should they be exposed to it; and (ii) interventions that promote digital, health and/or science literacy.
- ***Debunking misinformation***. Debunking refers to a technique of correcting erroneous claims by providing counter-arguments to messages containing misinformation. Efforts to debunk misinformation can be made even in settings without a substantial infrastructure for this sort of work, but care is needed as there is evidence that debunking exercises can backfire [138].
- ***Evaluation of the effectiveness of interventions***. This should include collection and analysis of both quantitative and qualitative evaluation data, as well as the perspectives and experiences of both the providers and recipients of services. Where possible, both process and impact should be included in any evaluation.

# Interventions targeting healthcare workers

Results of a Flash Eurobarometer survey published in June 2021 confirm that EU citizens continue to see health professionals, doctors, nurses and pharmacists as their most trusted sources of information on COVID-19 vaccines [139]. Healthcare workers therefore play a key role in promoting COVID-19 vaccination and in addressing people's questions or concerns about the vaccines. They are also a key target group for tailored communication efforts to address any acceptance issues that they themselves face, both to avoid putting themselves, their families, their colleagues and patients at risk of SARS-CoV-2 infection, but also as any concerns they have may be amplified if they communicate these to their patients.

WHO identifies five key strategies to empower health workers to help ensure a successful public response to COVID-19 vaccination [140]: a) Understand health worker barriers and drivers of vaccination; b) Engage health workers as active partners in shaping vaccination efforts; c) Motivate, support and acknowledge health workers; d) Build health workers' knowledge, skills and confidence on COVID-19 vaccination and its communication; e) Value health workers as a target group and partners for information on any vaccine safety events; they are a key source of information both on any adverse reaction they witness and on public perceptions and concerns around the issue, and they also need to receive timely information regarding any safety events and how to respond to patients' concerns.

# Considerations around incentives and mandates

Some EU/EEA countries have implemented incentives as part of their strategies to increase COVID-19 vaccine uptake [16]. For example, people who are vaccinated may participate in lotteries, receive vouchers or coupons to visit restaurants, or they may be granted access to recreational public venues and events. Literature on behavioural aspects of vaccination highlights some considerations and caveats in relation to past experiences with such programmes [141]. For example, whilst incentives may affirm the importance of vaccination, they can also signal that some people are not choosing to get vaccinated, which in turn gives a message that vaccination is not a normative behaviour. In addition, researchers have cautioned that even if financial incentives to 'get vaccinated' may seem appealing when focused on groups with persistently low vaccination rates, and they may produce a short-term increase in vaccination, they are not a panacea: broader, complementary strategies will still be needed [142].

A few EU/EEA countries have issued COVID-19 vaccination mandates, in particular for healthcare workers and personnel working in long-term care facilities. Other countries are also contemplating this strategy when, despite communication efforts, further increases in uptake have become difficult to achieve [16]. Even though mandatory requirements can be highly effective, researchers caution that depending on the reasons for under-vaccination, other strategies may be sufficient or more advisable [141]. Potential negative effects need to be carefully considered by policymakers. These include rejection of such measures by those who are ambivalent or unfavourable, anger from those who feel their freedom to act is being curtailed (making them even more susceptible to anti-vaccination messages), and motivation for people to seek ways to legally opt out of vaccination. Further, such decisions may have substantial practical, ethical and legal implications. Any such decision should be preceded by a thorough ethical analysis, conducted by experts in medical ethics, as highlighted by WHO [143].

# References


1. European Centre for Disease Prevention and Control (ECDC). Assessing SARS-CoV-2 circulation, variants of concern, non-pharmaceutical interventions and vaccine rollout in the EU/EEA, 15th update – 10 June 2021. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/rapid-risk-assessment-sars-cov-2-circulation-variants-concern
2. European Centre for Disease Prevention and Control (ECDC). Guidance for representative and targeted genomic SARS-CoV-2 monitoring. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/guidance-representative-and-targeted-genomic-sars-cov-2-monitoring
3. European Centre for Disease Prevention and Control (ECDC). COVID-19 country overviews. Stockholm: ECDC; 2021. Available at: http://covid19-country-overviews.ecdc.europa.eu/
4. Liu Y, Rocklöv J. The reproductive number of the Delta variant of SARS-CoV-2 is far higher compared to the ancestral SARS-CoV-2 virus. J Travel Med [Preprint]. 2021. DOI: 10.1093/jtm/taab124. Available at: https://academic.oup.com/jtm/advance-article/doi/10.1093/jtm/taab124/6346388
5. Campbell F, Archer B, Laurenson-Schafer H, Jinnai Y, Konings F, Batra N, et al. Increased transmissibility and global spread of SARS-CoV-2 variants of concern as at June 2021. Euro Surveill. 2021;26(24) Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.24.2100509
6. Twohig KA, Nyberg T, Zaidi A, Thelwall S, Sinnathamby MA, Aliabadi S, et al. Hospital admission and emergency care attendance risk for SARS-CoV-2 delta (B.1.617.2) compared with alpha (B.1.1.7) variants of concern: a cohort study. Lancet Infect Dis [Preprint]. 2021. DOI: 10.1016/S1473-3099(21)00475-8. Available at: https://www.sciencedirect.com/science/article/pii/S1473309921004758
7. Sheikh A, McMenamin J, Taylor B, Robertson C. SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. Lancet. 2021 Jun 26;397(10293):2461-2. Available at: https://www.sciencedirect.com/science/article/pii/S0140673621013581
8. Veneti L, Valcarcel Salamanca B, Seppälä E, Starrfelt J, Storm ML, Bragstad K, et al. No difference in risk of hospitalisation between reported cases of the SARS-CoV-2 Delta variant and Alpha variant in Norway. medRxiv [Preprint]. 2021. DOI: 10.1101/2021.09.02.21263014. Available at: https://www.medrxiv.org/content/10.1101/2021.09.02.21263014v1
9. Our World in Data. Coronavirus (COVID-19) Vaccinations. Oxford: Global Change Data Lab; 2021. Available at: https://ourworldindata.org/covid-vaccinations
10. European Centre for Disease Prevention and Control (ECDC). The COVID-19 Vaccine Tracker. Stockholm: ECDC; 2021. Available at: https://vaccinetracker.ecdc.europa.eu/public/extensions/COVID-19/vaccine-tracker.html#uptake-tab
11. European Centre for Disease Prevention and Control (ECDC). COVID-19 Vaccine rollout overview, week 36, 2021. Stockholm: ECDC; 2021. Available at: https://covid19-vaccine-report.ecdc.europa.eu/
12. Presidenza del Consiglio dei Ministri. Commissario Straordinario Covid-19. Ministero della Salute. Report Vaccini Anti COVID-19. Rome: Governo Italiano; 2021. Available at: https://www.governo.it/it/cscovid19/report-vaccini/
13. Bundesministerium für Gesundheit. Aktueller Impfstatus. Berlin: Bundesministerium für Gesundheit; 2021. Available at: https://impfdashboard.de/en/
14. Bundesministerium für Soziales Gesundheit Pflege und Konsumentenschutz. Corona-Schutzimpfung in Österreich. Vienna: Bundesministerium für Soziales, Gesundheit, Pflege und Konsumentenschutz; 2021. Available at: https://info.gesundheitsministerium.at/impressum
15. Sciensano. Belgium COVID-19 Epidemiological Situation. Brussels: Sciensano; 2021. Available at: https://datastudio.google.com/embed/reporting/c14a5cfc-cab7-4812-848c-0369173148ab/page/hOMwB
16. European Centre for Disease Prevention and Control. Overview of the implementation of COVID-19 vaccination strategies and vaccine deployment plans in the EU/EEA – 23 September 2021. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/overview-implementation-covid-19-vaccination-strategies-and-deployment-plans
17. Adlhoch C, Mook P, Lamb F, Ferland L, Melidou A, Amato-Gauci AJ, et al. Very little influenza in the WHO European Region during the 2020/21 season, weeks 40 2020 to 8 2021. Euro Surveill. 2021 Mar;26(11) Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.11.2100221
18. European Centre for Disease Prevention and Control (ECDC) and World Health Organization (WHO). Flu News Europe. Stockholm and Copenhagen: ECDC and WHO; 2021. Available at: https://flunewseurope.org/
19. Melidou A, Pereyaslov D, Hungnes O, Prosenc K, Alm E, Adlhoch C, et al. Virological surveillance of influenza viruses in the WHO European Region in 2019/20 - impact of the COVID-19 pandemic. Euro Surveill. 2020;25(46) Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.46.2001822
20. Melidou A, Hungnes O, Pereyaslov D, Adlhoch C, Segaloff H, Robesyn E, et al. Predominance of influenza virus A(H3N2) 3C.2a1b and A(H1N1)pdm09 6B.1A5A genetic subclades in the WHO European Region, 2018-2019. Vaccine. 2020;38(35):5707-17. Available at: https://www.sciencedirect.com/science/article/pii/S0264410X20308045

21. Segaloff H, Melidou A, Adlhoch C, Pereyaslov D, Robesyn E, Penttinen P, et al. Co-circulation of influenza A(H1N1)pdm09 and influenza A(H3N2) viruses, World Health Organization (WHO) European Region, October 2018 to February 2019. Euro Surveill. 2019;24(9) Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2019.24.9.1900125
22. Adlhoch C, Snacken R, Melidou A, Ionescu S, Penttinen P. Dominant influenza A(H3N2) and B/Yamagata virus circulation in EU/EEA, 2016/17 and 2017/18 seasons, respectively. Euro Surveill. 2018;23(13) Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2018.23.13.18-00146
23. Nielsen J, Vestergaard LS, Richter L, Schmid D, Bustos N, Asikainen T, et al. European all-cause excess and influenza-attributable mortality in the 2017/18 season: should the burden of influenza B be reconsidered? Clin Microbiol Infect. 2019;25(10):1266-76. Available at: https://www.sciencedirect.com/science/article/pii/S1198743X19300588
24. Vestergaard LS, Nielsen J, Krause TG, Espenhain L, Tersago K, Bustos Sierra N, et al. Excess all-cause and influenza-attributable mortality in Europe, December 2016 to February 2017. Euro Surveill. 2017;22(14) Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2017.22.14.30506
25. Statens Serums Institut (SSI). EUROMOMO. Graphs and maps. Copenhagen: SSI; 2021. Available at: https://www.euromomo.eu/graphs-and-maps
26. Flannery B, Kondor RJG, Chung JR, Gaglani M, Reis M, Zimmerman RK, et al. Spread of Antigenically Drifted Influenza A(H3N2) Viruses and Vaccine Effectiveness in the United States During the 2018-2019 Season. J Infect Dis. 2020;221(1):8-15. Available at: https://academic.oup.com/jid/article/221/1/8/5609441
27. Belongia EA, Simpson MD, King JP, Sundaram ME, Kelley NS, Osterholm MT, et al. Variable influenza vaccine effectiveness by subtype: a systematic review and meta-analysis of test-negative design studies. Lancet Infect Dis. 2016;16(8):942-51. Available at: https://www.sciencedirect.com/science/article/pii/S1473309916001298
28. Valenciano M, Kissling E, Reuss A, Jiménez-Jorge S, Horváth JK, Donnell JM, et al. The European I-MOVE Multicentre 2013-2014 Case-Control Study. Homogeneous moderate influenza vaccine effectiveness against A(H1N1)pdm09 and heterogenous results by country against A(H3N2). Vaccine. 2015;33(24):2813-22. Available at: https://www.sciencedirect.com/science/article/pii/S0264410X1500465X
29. Kuliese M, Mickiene A, Jancoriene L, Zablockiene B, Gefenaite G, Study G. Age-Specific Seasonal Influenza Vaccine Effectiveness against Different Influenza Subtypes in the Hospitalized Population in Lithuania during the 2015-2019 Influenza Seasons. Vaccines (Basel). 2021;9(5) Available at: https://www.mdpi.com/2076-393X/9/5/455
30. Stuurman AL, Bollaerts K, Alexandridou M, Biccler J, Díez Domingo J, Nohynek H, et al. Vaccine effectiveness against laboratory-confirmed influenza in Europe - Results from the DRIVE network during season 2018/19. Vaccine. 2020;38(41):6455-63. Available at: https://www.sciencedirect.com/science/article/pii/S0264410X20310057
31. Rose AMC, Kissling E, Gherasim A, Casado I, Bella A, Launay O, et al. Vaccine effectiveness against influenza A(H3N2) and B among laboratory-confirmed, hospitalised older adults, Europe, 2017-18: A season of B lineage mismatched to the trivalent vaccine. Influenza Other Respir Viruses. 2020;14(3):302-10. Available at: https://onlinelibrary.wiley.com/doi/10.1111/irv.12714
32. Stowe J, Tessier E, Zhao H, Guy R, Muller-Pebody B, Zambon M, et al. Interactions between SARS-CoV-2 and influenza, and the impact of coinfection on disease severity: a test-negative design. Int J Epidemiol. 2021;50(4):1124-33. Available at: https://academic.oup.com/ije/article/50/4/1124/6263422
33. Centers for Disease Control and Prevention (CDC). Coadministration of COVID-19 vaccines with other vaccines. Atlanta: CDC; 2021. Available at: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#Coadministration
34. Toback S, Galiza E, Cosgrove C, Galloway J, Goodman AL, Swift PA, et al. Safety, Immunogenicity, and Efficacy of a COVID-19 Vaccine (NVX-CoV2373) Co-administered With Seasonal Influenza Vaccines. medRxiv [Preprint]. 2021. DOI: 10.1101/2021.06.09.21258556. Available at: https://www.medrxiv.org/content/10.1101/2021.06.09.21258556v1
35. National Health Service (NHS) University hospitals Bristol and Weston. Preliminary results from Bristol study among evidence considered for interim advice from JCVI to administer COVID-19 and flu vaccines at the same time, if booster programme required: NHS; 2021. Available at: https://cpb-eu-w2.wpmucdn.com/blogs.bristol.ac.uk/dist/b/750/files/2021/07/July-participant-update-JCVI-interim-advice.pdf
36. Public Health England (PHE). JCVI issues updated advice on COVID-19 booster vaccination. London: PHE; 2021. Available at: https://www.gov.uk/government/news/jcvi-issues-updated-advice-on-covid-19-booster-vaccination
37. Department of Health & Social Care. JCVI statement regarding a COVID-19 booster vaccine programme for winter 2021 to 2022. London: UK Government; 2021. Available at: https://www.gov.uk/government/publications/jcvi-statement-september-2021-covid-19-booster-vaccine-programme-for-winter-2021-to-2022/jcvi-statement-regarding-a-covid-19-booster-vaccine-programme-for-winter-2021-to-2022

38. van Summeren J, Meijer A, Aspelund G, Casalegno JS, Erna G, Hoang U, et al. Low levels of respiratory syncytial virus activity in Europe during the 2020/21 season: what can we expect in the coming summer and autumn/winter? Euro Surveill. 2021;26(29) Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.29.2100639
39. Ujiie M, Tsuzuki S, Nakamoto T, Iwamoto N. Resurgence of Respiratory Syncytial Virus Infections during COVID-19 Pandemic, Tokyo, Japan. Emerg Infect Dis. 2021;27(11) Available at: https://wwwnc.cdc.gov/eid/article/27/11/21-1565_article
40. PathWest. Paediatric respiratory pathogen report. Week 24, 14th June 2021–20th June 2021. Perth: Government of Western Australia; 2021. Available at: https://ww2.health.wa.gov.au/~/media/Corp/Documents/Health-for/Infectious-disease/Paediatric-Respiratory-Pathogen-Weekly-Report/2021/Paediatric-Respiratory-Pathogen-Report-Week-24-2021.pdf
41. Pollock A, Campbell P, Cheyne J, Cowie J, Davis B, McCallum J, et al. Interventions to support the resilience and mental health of frontline health and social care professionals during and after a disease outbreak, epidemic or pandemic: a mixed methods systematic review. Cochrane Database Syst Rev. 2020;11(11):Cd013779. Available at: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013779/full
42. Batra K, Singh TP, Sharma M, Batra R, Schvaneveldt N. Investigating the Psychological Impact of COVID-19 among Healthcare Workers: A Meta-Analysis. Int J Environ Res Public Health. 2020;17(23) Available at: https://www.mdpi.com/1660-4601/17/23/9096
43. Ruiz-Fernández MD, Ramos-Pichardo JD, Ibáñez-Masero O, Cabrera-Troya J, Carmona-Rega MI, Ortega-Galán Á M. Compassion fatigue, burnout, compassion satisfaction and perceived stress in healthcare professionals during the COVID-19 health crisis in Spain. J Clin Nurs. 2020;29(21-22):4321-30. Available at: https://onlinelibrary.wiley.com/doi/10.1111/jocn.15469
44. Baker RE, Park SW, Yang W, Vecchi GA, Metcalf CJE, Grenfell BT. The impact of COVID-19 nonpharmaceutical interventions on the future dynamics of endemic infections. Proc Natl Acad Sci U S A. 2020;117(48):30547-53. Available at: https://www.pnas.org/content/117/48/30547.long
45. Foley DA, Phuong LK, Peplinski J, Lim SM, Lee WH, Farhat A, et al. Examining the interseasonal resurgence of respiratory syncytial virus in Western Australia. Arch Dis Child [Preprint]. 2021. DOI: 10.1136/archdischild-2021-322507. Available at: https://adc.bmj.com/content/early/2021/08/24/archdischild-2021-322507.long
46. Maringe C, Spicer J, Morris M, Purushotham A, Nolte E, Sullivan R, et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. Lancet Oncol. 2020;21(8):1023-34. Available at: https://www.sciencedirect.com/science/article/pii/S1470204520303880?via%3Dihub
47. World Health Organization Regional Office for Europe (WHO-Euro). Pandemic fatigue - reinvigorating the public to prevent COVID-19: policy framework for supporting pandemic prevention and management: revised version November 2020. Copenhagen: WHO-Euro; 2020. Available at: https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/publications-and-technical-guidance/2020/pandemic-fatigue-reinvigorating-the-public-to-prevent-covid-19,-september-2020-produced-by-whoeurope
48. European Centre for Disease Prevention and Control (ECDC). Rapid Risk Assessment: Risk of COVID-19 transmission related to the end-of-year festive season. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/risk-assessment-covid-19-festive-season
49. European Centre for Disease Prevention and Control (ECDC). Interim public health considerations for the provision of additional COVID-19 vaccine doses. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/covid-19-public-health-considerations-additional-vaccine-doses
50. Statens Serum Institut (SSI). Der er fortsat høj vaccineeffektivitet for covid-19-vaccinerne. Copenhagen: SSI; 2021. Available at: https://www.ssi.dk/aktuelt/nyheder/2021/der-er-fortsat-hoj-vaccineeffektivitet-for-covid-19-vaccinerne
51. Nunes B, Rodrigues AP, Kislaya I, Cruz C, Peralta-Santos A, Lima J, et al. mRNA vaccine effectiveness against COVID-19-related hospitalisations and deaths in older adults: a cohort study based on data linkage of national health registries in Portugal, February to August 2021. Euro Surveill. 2021;26(38) Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.38.2100833
52. Mizrahi B, Lotan R, Kalkstein N, Peretz A, Perez G, Ben-Tov A, et al. Correlation of SARS-CoV-2 Breakthrough Infections to Time-from-vaccine; Preliminary Study. medRxiv [Preprint]. DOI: 10.1101/2021.07.29.21261317. Available at: https://www.medrxiv.org/content/10.1101/2021.07.29.21261317v1
53. Goldberg Y, Mandel M, Bar-On YM, Bodenheimer O, Freedman L, Haas EJ, et al. Waning immunity of the BNT162b2 vaccine: A nationwide study from Israel. medRxiv [Preprint]. DOI: 10.1101/2021.08.24.21262423. Available at: https://www.medrxiv.org/content/10.1101/2021.08.24.21262423v1
54. Tartof SY, Slezak JM, Fischer H, Hong V, Ackerson BK, Ranasinghe ON, et al. Six-Month Effectiveness of BNT162B2 mRNA COVID-19 Vaccine in a Large US Integrated Health System: A Retrospective Cohort Study. Preprints with The Lancet [Preprint]. 2021. DOI: 10.2139/ssrn.3909743. Available at: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3909743

55. Scobie HM, Johnson AG, Suthar AB, Severson R, Alden NB, Balter S, et al. Monitoring Incidence of COVID-19 Cases, Hospitalizations, and Deaths, by Vaccination Status - 13 U.S. Jurisdictions, April 4-July 17, 2021. Morb Mortal Wkly Rep. 2021;70(37):1284-90. Available at: https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e1.htm
56. Nanduri S, Pilishvili T, Derado G, Soe MM, Dollard P, Wu H, et al. Effectiveness of Pfizer-BioNTech and Moderna Vaccines in Preventing SARS-CoV-2 Infection Among Nursing Home Residents Before and During Widespread Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant - National Healthcare Safety Network, March 1-August 1, 2021. Morb Mortal Wkly Rep. 2021;70(34):1163-6. Available at: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e3.htm
57. Bajema KL, Dahl RM, Prill MM, Meites E, Rodriguez-Barradas MC, Marconi VC, et al. Effectiveness of COVID-19 mRNA Vaccines Against COVID-19-Associated Hospitalization - Five Veterans Affairs Medical Centers, United States, February 1-August 6, 2021. Morb Mortal Wkly Rep. 2021;70(37):1294-9. Available at: https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e3.htm
58. Grannis SJ, Rowley EA, Ong TC, Stenehjem E, Klein NP, DeSilva MB, et al. Interim Estimates of COVID-19 Vaccine Effectiveness Against COVID-19-Associated Emergency Department or Urgent Care Clinic Encounters and Hospitalizations Among Adults During SARS-CoV-2 B.1.617.2 (Delta) Variant Predominance - Nine States, June-August 2021. Morb Mortal Wkly Rep. 2021;70(37):1291-3. Available at: https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e2.htm
59. Public Health England (PHE). Duration of protection of COVID-19 vaccines against clinical disease. London: PHE; 2021. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1017309/S1362_PHE_duration_of_protection_of_COVID-19_vaccines_against_clinical_disease.pdf
60. Sughayer MA, Mansour A, Al Nuirat A, Souan L, Ghanem M, Siag M. Dramatic rise in seroprevalence rates of SARS-CoV-2 antibodies among healthy blood donors: The evolution of a pandemic. Int J Infect Dis. 2021;107:116-20. Available at: https://www.sciencedirect.com/science/article/pii/S1201971221003714
61. Vaughan A. et al. Seroprevalence of SARS-CoV-2 across the WHO European Region, January - December 2020. Manuscript in development.
62. SeroTracker dashboard. Calgary: University of Calgary - Centre for Health Informatics; 2021. Available at: https://serotracker.com/en/Explore
63. Folkhälsomyndigheten. Förekomsten av antikroppar mot SARS-CoV-2 i Sverige, 26 april - 9 maj 2021. Stockholm: Folkhälsomyndigheten; 2021. Available at: https://www.folkhalsomyndigheten.se/contentassets/45eafde72689438a8a21efa93a5591a4/forekomsten-antikroppar-mot-sars-cov-2.pdf
64. Tartu Ülikool. Koroonaviiruse levimuse uuring "Covid-19 aktiivne seire". Tartu: Tartu Ülikool; 2021. Available at: https://www.ut.ee/et/teadus/koroonaviiruse-levimuse-uuring-covid-19-aktiivne-seire
65. Folkhälsomyndigheten. Påvisning av antikroppar mot SARS-CoV-2 hos blodgivare. Stockholm: Folkhälsomyndigheten; 2021. Available at: https://www.folkhalsomyndigheten.se/contentassets/376f9021a4c84da08de18ac597284f0c/pavisning-antikroppar-mot-sars-cov-2-blodgivare.pdf
66. Public Health England (PHE). Weekly national Influenza and COVID-19 surveillance report - week 37 report (up to week 36 data). London: PHE; 2021. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1018187/Weekly_Flu_and_COVID-19_report_w37.pdf
67. Bobrovitz N, Arora RK, Cao C, Boucher E, Liu M, Donnici C, et al. Global seroprevalence of SARS-CoV-2 antibodies: A systematic review and meta-analysis. PLoS One. 2021;16(6):e0252617. Available at: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0252617
68. Byambasuren O, Cardona M, Bell K, Clark J, McLaws M-L, Glasziou P. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis. Official Journal of the Association of Medical Microbiology and Infectious Disease Canada. 2020;5(4):223-34. Available at: https://jammi.utpjournals.press/doi/10.3138/jammi-2020-0030
69. Byambasuren O, Dobler CC, Bell K, Rojas DP, Clark J, McLaws ML, et al. Comparison of seroprevalence of SARS-CoV-2 infections with cumulative and imputed COVID-19 cases: Systematic review. PLoS One. 2021;16(4):e0248946. Available at: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0248946
70. O Murchu E, Byrne P, Carty PG, De Gascun C, Keogan M, O'Neill M, et al. Quantifying the risk of SARS-CoV-2 reinfection over time. Rev Med Virol. 2021:e2260. Available at: https://onlinelibrary.wiley.com/doi/10.1002/rmv.2260
71. Vitale J, Mumoli N, Clerici P, De Paschale M, Evangelista I, Cei M, et al. Assessment of SARS-CoV-2 Reinfection 1 Year After Primary Infection in a Population in Lombardy, Italy. JAMA Intern Med. 2021. Available at: https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2780557
72. Public Health England (PHE). SARS-CoV-2 variants of concern and variants under investigation in England. London: PHE; 2021. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1005517/Technical_Briefing_19.pdf

73. Chia WN, Zhu F, Ong SWX, Young BE, Fong SW, Le Bert N, et al. Dynamics of SARS-CoV-2 neutralising antibody responses and duration of immunity: a longitudinal study. Lancet Microbe. 2021;2(6):e240-e9. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7987301/
74. Cromer D, Juno JA, Khoury D, Reynaldi A, Wheatley AK, Kent SJ, et al. Prospects for durable immune control of SARS-CoV-2 and prevention of reinfection. Nat Rev Immunol. 2021;21(6):395-404. Available at: https://www.nature.com/articles/s41577-021-00550-x
75. Planas D, Veyer D, Baidaliuk A, Staropoli I, Guivel-Benhassine F, Rajah MM, et al. Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization. Nature. 2021;596(7871):276-80. Available at: https://www.nature.com/articles/s41586-021-03777-9
76. Shrotri M, van Schalkwyk MCI, Post N, Eddy D, Huntley C, Leeman D, et al. T cell response to SARS-CoV-2 infection in humans: A systematic review. PLoS One. 2021;16(1):e0245532. Available at: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0245532
77. Hellerstein M. What are the roles of antibodies versus a durable, high quality T-cell response in protective immunity against SARS-CoV-2? Vaccine X. 2020;6:100076. Available at: https://www.sciencedirect.com/science/article/pii/S2590136220300231
78. Bertoletti A, Tan AT, Le Bert N. The T-cell response to SARS-CoV-2: kinetic and quantitative aspects and the case for their protective role. Oxford Open Immunology. 2021;2(1) Available at: https://doi.org/10.1093/oxfimm/iqab006
79. SIMID consortium. SOCRATES CoMix. Antwerp: SIMID consortium; 2021. Available at: http://www.socialcontactdata.org/socrates-comix/
80. Google. See how your community is moving around differently due to COVID-19. Google; 2021. Available at: https://www.google.com/covid19/mobility/
81. European Centre for Disease Prevention and Control (ECDC). Operational tool on rapid risk assessment methodology. Stockholm: ECDC; 2019. Available at: https://www.ecdc.europa.eu/en/publications-data/operational-tool-rapid-risk-assessment-methodology-ecdc-2019
82. European Centre for Disease Prevention and Control (ECDC). Expert opinion on neuraminidase inhibitors for the prevention and treatment of influenza - review of recent systematic reviews and meta-analyses. Stockholm: ECDC; 2017. Available at: https://www.ecdc.europa.eu/en/seasonal-influenza/prevention-and-control/antivirals
83. MacDonald NE, SAGE Working Group on Vaccine Hesitancy. Vaccine hesitancy: Definition, scope and determinants. Vaccine. 2015;33(34):4161-4. Available at: https://www.sciencedirect.com/science/article/pii/S0264410X15005009
84. Veenema TG, Closser S, Thrul J, Kalb LG, McDonald KM, Himmelfarb CD, et al. Mental Health and Social Support for Healthcare and Hospital Workers During the COVID-19 Pandemic. Baltimore: Johns Hopkins Center for Health Security. Available at: https://www.centerforhealthsecurity.org/our-work/publications/mental-health-and-social-support-for-healthcare-and-hospital-workers-during-the-covid-19-pandemic
85. European Centre for Disease Prevention and Control (ECDC). Contact tracing for COVID-19. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/covid-19/prevention-and-control/contact-tracing-covid-19
86. European Centre for Disease Prevention and Control (ECDC). Guidelines for the implementation of non-pharmaceutical interventions against COVID-19. Stockholm: ECDC; 2020. Available at: https://www.ecdc.europa.eu/en/publications-data/covid-19-guidelines-non-pharmaceutical-interventions
87. European Centre for Disease Prevention and Control (ECDC). Interim guidance on the benefits of full vaccination against COVID-19 for transmission and implications for non-pharmaceutical interventions. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/interim-guidance-benefits-full-vaccination-against-covid-19-transmission
88. European Centre for Disease Prevention and Control. COVID-19 in children and the role of school settings in transmission - second update. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/children-and-school-settings-covid-19-transmission
89. Head JR, Andrejko KL, Remais JV. Model-based assessment of SARS-CoV-2 Delta variant transmission dynamics within partially vaccinated K-12 school populations. medRxiv [Preprint]. 2021. DOI: 10.1101/2021.08.20.21262389. Available at: https://www.medrxiv.org/content/10.1101/2021.08.20.21262389v1
90. National Centre for Immunisation Research and Surveillance. COVID-19 in schools and early childhood education and care services – the experience in NSW: 16 June to 31 July 2021. Sydney: NSW Health; 2021. Available at: https://www.ncirs.org.au/sites/default/files/2021-09/NCIRS%20NSW%20Schools%20COVID_Summary_8%20September%2021_Final.pdf
91. European Centre for Disease Prevention and Control (ECDC). COVID-19 surveillance report. Stockholm: ECDC; 2021. Available at: https://covid19-surveillance-report.ecdc.europa.eu/
92. Delahoy MJ, Ujamaa D, Whitaker M, O'Halloran A, Anglin O, Burns E, et al. Hospitalizations Associated with COVID-19 Among Children and Adolescents - COVID-NET, 14 States, March 1, 2020-August 14, 2021. Morb Mortal Wkly Rep. 2021;70(36):1255-60. Available at: https://www.cdc.gov/mmwr/volumes/70/wr/mm7036e2.htm

93. Young BC, Eyre DW, Kendrick S, White C, Smith S, Beveridge G, et al. Daily testing for contacts of individuals with SARS-CoV-2 infection and attendance and SARS-CoV-2 transmission in English secondary schools and colleges: an open-label, cluster-randomised trial. Lancet [Preprint]. 2021. DOI: 10.1016/S0140-6736(21)01908-5. Available at: https://www.sciencedirect.com/science/article/pii/S0140673621019085
94. Lanier WA, Babitz KD, Collingwood A, Graul MF, Dickson S, Cunningham L, et al. COVID-19 Testing to Sustain In-Person Instruction and Extracurricular Activities in High Schools - Utah, November 2020-March 2021. Morb Mortal Wkly Rep. 2021;70(21):785-91. Available at: https://www.cdc.gov/mmwr/volumes/70/wr/mm7021e2.htm
95. European Centre for Disease Prevention and Control (ECDC). Considerations on the use of self-tests for COVID-19 in the EU/EEA. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/considerations-use-self-tests-covid-19-eueea
96. European Centre for Disease Prevention and Control (ECDC). ECDC PrimerScan. Stockholm: ECDC; 2021. Available at: https://primerscan.ecdc.europa.eu/?assay=Overview
97. Artic Network. SARS-CoV-2. Artic Network; 2020. Available at: https://artic.network/ncov-2019
98. European Centre for Disease Prevention and Control (ECDC) and World Health Organization Regional Office for Europe (WHO-Euro). Operational considerations for influenza surveillance in the WHO European Region during COVID-19: interim guidance. Stockholm and Copenhagen: ECDC and WHO-Euro; 2020. Available at: https://www.ecdc.europa.eu/en/publications-data/operational-considerations-influenza-surveillance-european-region-during-covid-19
99. Jahn K, Dreifuss D, Topolsky I, Kull A, Ganesanandamoorthy P, Fernandez-Cassi X, et al. Detection of SARS-CoV-2 variants in Switzerland by genomic analysis of wastewater samples. medRxiv [Preprint]. 2021. DOI: 10.1101/2021.01.08.21249379. Available at: https://www.medrxiv.org/content/10.1101/2021.01.08.21249379v2
100. European Commission (EC). Commission recommendation of 17.3.2021 on a common approach to establish a systematic surveillance of SARS-CoV-2 and its variants in wastewaters in the EU. Brussels: EC; 2021. Available at: https://ec.europa.eu/environment/pdf/water/recommendation_covid19_monitoring_wastewaters.pdf
101. European Centre for Disease Prevention and Control (ECDC). Coronavirus disease 2019 (COVID-19) data reporting protocol version 5.1, 26 July 2021. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/COVID-19-Reporting-Protocol-v5.1.pdf
102. Statens Serum Institut (SSI). EuroMOMO Bulletin, Week 36, 2021. Copenhagen: SSI; 2021. Available at: https://www.euromomo.eu/
103. European Centre for Disease Prevention and Control (ECDC). COVID-19 outbreaks in long-term care facilities in the EU/EEA in the context of current vaccination coverage, 26 July 2021. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/rapid-risk-assessment-covid-19-outbreaks-long-term-care-facilities-eueea
104. European Centre for Disease Prevention and Control (ECD)C. Data collection on COVID-19 outbreaks in closed settings with a completed vaccination programme: long-term care facilities, version 2.0. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/data-collection-covid-19-outbreaks-closed-settings-completed-vaccination
105. European Medicines Agency (EMA). Xofluza. Amsterdam: EMA; 2021. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/xofluza
106. European Medicines Agency (EMA). Antiviral medicines for pandemic influenza. Amsterdam: EMA. Available at: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/pandemic-influenza/antiviral-medicines-pandemic-influenza
107. European Centre for Disease Prevention and Control (ECDC). Guidance for COVID-19 quarantine and testing of travellers. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/guidance-covid-19-quarantine-and-testing-travellers
108. European Centre for Disease Prevention and Control (ECD)C. Options for the use of rapid antigen tests for COVID-19 in the EU/EEA and the UK. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/options-use-rapid-antigen-tests-covid-19-eueea-and-uk
109. European Union Aviation Safety Agency (EASA) and European Centre for Disease Prevention and Control (ECDC). COVID-19 Aviation Health Safety Protocol: Operational guidelines for the management of air passengers and aviation personnel in relation to the COVID-19 pandemic. Cologne and Stockholm: EASA and ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/covid-19-aviation-health-safety-protocol
110. European Maritime Safety Agency (EMSA) and European Centre for Disease Prevention and Control (ECDC). Guidance on the gradual and safe resumption of operations of cruise ships in the European Union in relation to the COVID-19 pandemic. Lisbon and Stockholm: EMSA and ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/COVID-19-cruise-ship-guidance
111. European Union Agency for Railways (ERA) and European Centre for Disease Prevention and Control (ECDC). COVID-19 Rail Protocol. Valenciennes and Stockholm: ERA and ECDC; 2020. Available at: https://www.era.europa.eu/content/covid-19-rail-protocol_en

112. European Commission (EC). EU Digital COVID Certificate. Brussels: EC; 2021. Available at: https://ec.europa.eu/info/live-work-travel-eu/coronavirus-response/safe-covid-19-vaccines-europeans/eu-digital-covid-certificate_en
113. Government of Alberta. COVID-19 Alberta statistics. Alberta: Government of Alberta; 2021. Available at: https://www.alberta.ca/stats/covid-19-alberta-statistics.htm#vaccine-outcomes
114. CBC news. Alberta to launch proof-of-vaccination program, declares health emergency amid surge in COVID-19 cases. Toronto: CBC news; 2021. Available at: https://www.cbc.ca/news/canada/edmonton/kenney-shandro-hinshaw-update-covid-19-1.6177210
115. World Health Organization (WHO). Communicating risk in public health emergencies. Geneva: WHO; 2017. Available at: https://apps.who.int/iris/bitstream/handle/10665/259807/9789241550208-eng.pdf?sequence=2
116. Kihara L., Leussink D. Pandemic fatigue complicates Japan's COVID fight, risks recovery delay. Reuters; 2021. Available at: https://www.reuters.com/world/asia-pacific/pandemic-fatigue-complicates-japans-covid-fight-risks-recovery-delay-2021-08-18/
117. European Centre for Disease Prevention and Control (ECDC). SARS-CoV-2 variants dashboard. Stockholm: ECDC. Available at: https://www.ecdc.europa.eu/en/covid-19/situation-updates/variants-dashboard
118. Oduwole EO, Pienaar ED, Mahomed H, Wiysonge CS. Current tools available for investigating vaccine hesitancy: a scoping review protocol. BMJ Open. 2019;9(12):e033245. Available at: https://bmjopen.bmj.com/content/9/12/e033245.long
119. Larson HJ, de Figueiredo A, Xiahong Z, Schulz WS, Verger P, Johnston IG, et al. The State of Vaccine Confidence 2016: Global Insights Through a 67-Country Survey. EBioMedicine. 2016;12:295-301. Available at: https://www.sciencedirect.com/science/article/pii/S235239641630398X
120. Larson H, de Figueiredo A, Karafllakis E, Rawal M. State of Vaccine Confidence in the EU 2018. Brussels: European Commission; 2018. Available at: https://ec.europa.eu/health/sites/default/files/vaccination/docs/2018_vaccine_confidence_en.pdf
121. Gilkey MB, Reiter PL, Magnus BE, McRee AL, Dempsey AF, Brewer NT. Validation of the Vaccination Confidence Scale: A Brief Measure to Identify Parents at Risk for Refusing Adolescent Vaccines. Acad Pediatr. 2016;16(1):42-9. Available at: https://www.sciencedirect.com/science/article/abs/pii/S1876285915002156
122. Shapiro GK, Tatar O, Dube E, Amsel R, Knauper B, Naz A, et al. The vaccine hesitancy scale: Psychometric properties and validation. Vaccine. 2018;36(5):660-7. Available at: https://www.sciencedirect.com/science/article/pii/S0264410X17317966
123. World Health Organization (WHO) Strategic Advisory Group of Experts on Immunization (SAGE) Working Group on Vaccine Hesitancy. Vaccine Hesitancy Survey Questions Related to SAGE Vaccine Hesitancy Matrix. Geneva: WHO; 2016. Available at: https://www.who.int/immunization/programmes_systems/Survey_Questions_Hesitancy.pdf
124. World Health Organization (WHO) Strategic Advisory Group of Experts on Immunization (SAGE) Working Group on Vaccine Hesitancy. Report of the SAGE Working group on vaccine hesitancy. Geneva: WHO; 2014. Available at: https://www.who.int/immunization/sage/meetings/2014/october/1_Report_WORKING_GROUP_vaccine_hesitancy_final.pdf
125. Pronczuk M. Vaccine effort in Europe confronts anger, disinformation and suspicion. New York: New York Times; 2021. Available at: https://www.nytimes.com/2021/07/29/world/europe/brussels-vaccination-undocumented.html
126. Schwarzinger M, Watson V, Arwidson P, Alla F, Luchini S. COVID-19 vaccine hesitancy in a representative working-age population in France: a survey experiment based on vaccine characteristics. Lancet Public Health. 2021;6(4):e210-e21. Available at: https://www.sciencedirect.com/science/article/pii/S2468266721000128
127. Sprengholz P, Eitze S, Felgendreff L, Korn L, Betsch C. Money is not everything: experimental evidence that payments do not increase willingness to be vaccinated against COVID-19. J Med Ethics. 2021;47(8):547-8. Available at: https://jme.bmj.com/content/47/8/547.long
128. Freeman D, Loe BS, Yu LM, Freeman J, Chadwick A, Vaccari C, et al. Effects of different types of written vaccination information on COVID-19 vaccine hesitancy in the UK (OCEANS-III): a single-blind, parallel-group, randomised controlled trial. Lancet Public Health. 2021;6(6):e416-e27. Available at: https://www.sciencedirect.com/science/article/pii/S2468266721000967
129. Altay S, Hacquin A, Chevallier C, Mercier H. Information Delivered by a Chatbot Has a Positive Impact on COVID-19 Vaccines Attitudes and Intentions. PsyArXiv [Preprint]. 2021. DOI: 10.31234/osf.io/eb2gt.. 2021. Available at: https://doi.org/10.31234/osf.io/eb2gt
130. Fundación Espñaola para la Ciencia y la Tecnología (FECYT). Evolución de la percepción social de aspectos científicos de la COVID-19. Madrid: FECYT; 2021. Available at: https://www.fecyt.es/es/publicacion/evolucion-de-la-percepcion-social-de-aspectos-cientificos-de-la-covid-19
131. Department of Health. SciComm Collective. Dublin: Government of Ireland; 2021. Available at: https://www.gov.ie/en/campaigns/32187-scicomm-collective/
132. SciComm Collective Ireland. How Long Do COVID 19 Vaccines Last. Instagram. 18 September 2021. Available at: https://www.instagram.com/p/CT9GW9iFoq5/

133. SciComm Collective Ireland. COVID-19 vaccines and your period. Facebook 20 August 2021. Available at: https://www.facebook.com/scicommcollectiveire/videos/204016551775671/
134. Les Mutualités Libres. Un accompagnement personnalisé par les mutualités des publics fragilisés. Brussels: Les Mutualités Libres; 2021. Available at: https://www.mloz.be/fr/communiques/un-accompagnement-personnalise-par-les-mutualites-des-publics-fragilises
135. Develtere L. Community health workers begrijpen waarom de weg naar de juiste zorg zo moeilijk is. Borgerhout: Sociaal.Net; 2021. Available at: https://sociaal.net/achtergrond/community-health-workers-begrijpen-waarom-de-weg-naar-de-juiste-zorg-zo-moeilijk-is/
136. European Centre for Disease Prevention and Control. Countering online vaccine misinformation in the EU/EEA. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/Countering-online-vaccine-misinformation-in-the-EU-EEA.pdf
137. EU DISINFOLAB. A vibrant home for disinformation activists and experts. Brussels: EU DISINFOLAB; 2021. Available at: https://www.disinfo.eu/
138. Pluviano S, Watt C, Della Sala S. Misinformation lingers in memory: Failure of three pro-vaccination strategies. PLoS One. 2017;12(7):e0181640. Available at: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0181640
139. European Commission (EC). Attitudes on vaccination against Covid-19. Brussels: EC; 2021. Available at: https://europa.eu/eurobarometer/surveys/detail/2512
140. World Health Organization Regional Office for Europe (WHO-Euro). Health workers in focus: policies and practices for successful public response to COVID-19 vaccination. Copenhagen: WHO-Euro; 2021. Available at: https://apps.who.int/iris/bitstream/handle/10665/339854/WHO-EURO-2021-1944-41695-57054-eng.pdf
141. Brewer NT, Chapman GB, Rothman AJ, Leask J, Kempe A. Increasing Vaccination: Putting Psychological Science Into Action. Psychol Sci Public Interest. 2017;18(3):149-207. Available at: https://journals.sagepub.com/doi/10.1177/1529100618760521
142. Volpp KG, Cannuscio CC. Incentives for Immunity - Strategies for Increasing Covid-19 Vaccine Uptake. N Engl J Med. 2021;385(1):e1. Available at: https://www.nejm.org/doi/10.1056/NEJMp2107719
143. World Health Organization (WHO). COVID-19 and mandatory vaccination: ethical considerations and caveats. Geneva: WHO; 2021. Available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-Policy-brief-Mandatory-vaccination-2021.1