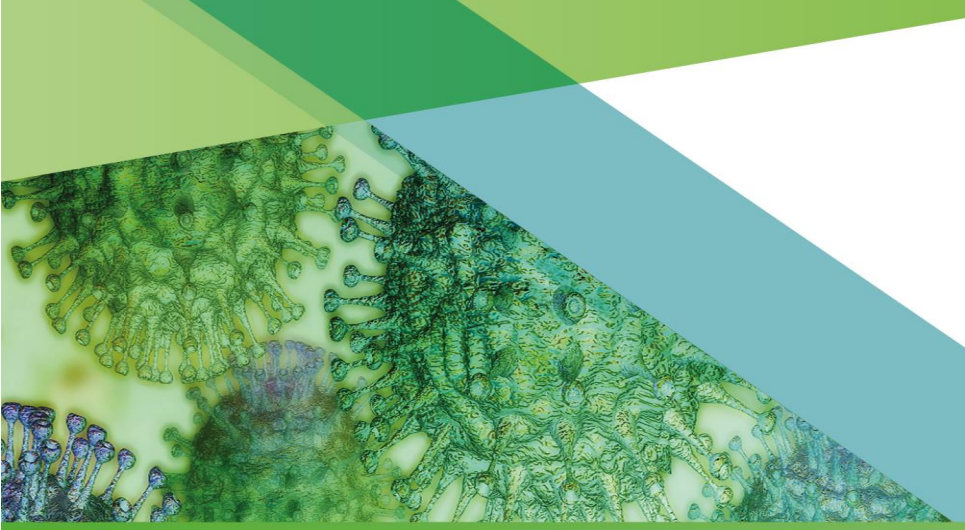


TECHNICAL REPORT

Interim public health considerations for COVID-19 vaccination of children aged 5-11 years

1 December 2021

Key messages

- Surveillance data show that children aged 5-11 years have made up an increasing proportion of both notified cases and hospitalisations in EU/EEA countries in recent months. Although hospitalisations have increased in line with case rates in all age groups in the EU/EEA, disease severity of COVID-19 in children is generally mild with a favourable clinical outcome. Severe COVID-19 remains rare among children (of 65 800 notified symptomatic COVID-19 cases in children aged 5-11 years, reported from 10 EU/EEA countries during the period of B.1.617.2 (Delta) variant of concern (VOC) dominance, 0.61% were hospitalised and 0.06% needed intensive care unit (ICU)/respiratory support).
- The relative contribution of children to overall SARS-CoV-2 circulation may have increased due to factors including the emergence of the highly transmissible Delta VOC and increased vaccination coverage in older age groups.
- The presence of an underlying condition among children aged 5-11 years is associated with about 12 times higher odds of hospitalisation and 19 times higher odds or of ICU admission. However, the majority (78%) of hospitalised children of this age had no reported underlying medical condition.
- Paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2/multi-inflammatory syndrome in children (PIMS-TS/MIS-C) and post COVID-19 condition have been reported in children aged 5-11 years, although it is difficult to quantify the prevalence and burden of these conditions. In a United States (US) Centers for Disease Control and Prevention (CDC) report, myocarditis was reported up to 37 times more often in unvaccinated children less than 16 years old with a COVID-19 diagnosis compared to other patients from the same age group.
- Beyond the direct health impacts of COVID-19 disease, the COVID-19 pandemic has affected the physical and mental health and well-being of children aged 5-11 years. Numerous factors, such as disruptions to important everyday social and educational activities, have caused anxiety and distress in this age group.
- Modelling data indicate that vaccinating children aged 5-11 years could reduce SARS-CoV-2 transmission in the whole population, although the extent and duration of this protection is currently unknown. It is estimated that the impact on the effective reproduction number (R_t) in the population as a whole would be a decrease of 11% (range: 8-15%, depending on vaccine uptake parameters of 30-70%) for an average country in the EU/EEA. This is comparable to the effect of some non-pharmaceutical interventions. The impact of vaccinating children is weaker for countries with a low adult vaccine uptake and stronger for countries with high uptake among adults.
- On 25 November 2021, the European Medicines Agency (EMA) granted a positive opinion for use of the Comirnaty COVID-19 vaccine in children aged 5-11 years based on a placebo-controlled randomised clinical trial in which more than 3 000 children in this age group received this vaccine.

Suggested citation: European Centre for Disease Prevention and Control. Interim public health considerations for COVID-19 vaccination of children aged 5-11 years, 1 December 2021. ECDC: Stockholm; 2021.

- Children aged 5-11 years who are at risk of severe COVID-19 should be considered a priority group for vaccination against COVID-19, as in other age groups. However, since hospitalisation, PIMS-TS/MIS-C and post COVID-19 condition can also occur among children with no known risk factors, consideration could be given to the vaccination of all children aged 5-11 years.
- COVID-19 vaccine safety data in children aged 5-11 years are currently limited, and the level of natural immunity in the unvaccinated and its duration are currently unknown and likely heterogeneous across the population.
- The main priority of COVID-19 vaccination campaigns seeking to reduce COVID-19-related morbidity and mortality remains to increase vaccine uptake in the eligible adult population. Before taking policy decisions on COVID-19 vaccination in children, potential harms and benefits – including the direct and indirect effects on health and well-being – should be considered alongside the vaccine uptake and epidemiological situation in a particular country. Aspects around implementation and health equity should also be taken into consideration.

Scope of this document

This technical report provides information on the following aspects:

- Overview of current plans for COVID-19 vaccination of children aged 5-11 years in the EU/EEA
- Assessment of the burden of COVID-19 in children aged 5-11 years
- Role of children in SARS-CoV-2 transmission
- Available data on COVID-19 vaccines in children
- Estimated impact of vaccinating children on the R_t
- Objectives of vaccination of children, considering individual benefits and population benefits

This technical report provides a set of interim public health considerations to support EU/EEA public health authorities taking decisions on the administration of COVID-19 vaccines to children aged 5-11 years. As new evidence is continuously being generated and safety is being monitored on an ongoing basis, it is essential to consider the latest available information and recommendations issued by regulatory and public health authorities at the national level.

Target audience

Target audiences for this document are the European Commission, the Health Security Committee (HSC), the EU/EEA National Immunisation Technical Advisory Groups (NITAGs), the national public health institutes and ministries of health in the EU/EEA, as well as public health experts and decision makers at national and subnational levels.

Background

As of 30 November 2021, four COVID-19 vaccines have received conditional marketing authorisation in the EU/EEA following evaluation by the European Medicines Agency (EMA). These vaccines are: COVID-19 vaccine Comirnaty, COVID-19 vaccine Spikevax, COVID-19 vaccine Vaxzevria, and COVID-19 vaccine Janssen. Comirnaty and Spikevax are authorised for use in people aged 12 years and older [1,2], while the other two vaccine products are currently only authorised for use in people aged 18 years and older [3,4].

In EU/EEA countries, the roll-out of COVID-19 vaccine campaigns started at the end of December 2020, when the first vaccine doses were delivered. On 19 January 2021, the European Commission set out actions to step up the response against the pandemic and accelerate the roll-out of vaccination campaigns, with the targets of vaccinating at least 80% of people over the age of 80 years and 80% of health and social care professionals in every Member State by March. In addition, a minimum of 70% of the adult (18 years and older) population were to be vaccinated by the summer [5]. EU/EEA countries initially prioritised vaccination of older adults, residents and personnel in long-term care facilities, healthcare and social care workers, and people with certain comorbidities, and have gradually progressed to vaccinating younger age groups in the general population [6]. As of 17 November (week 45), the cumulative vaccine uptake in the total population in the EU/EEA reached 69.8% (country range: 26-87.9%) for at least one vaccine dose and 65.4% (range: 23.9-81.4%) for the full vaccination course (pooled data from 30 reporting countries). Among adults in the EU/EEA as a whole, the cumulative vaccine uptake reached 81.3% for at least one vaccine dose (range: 31.1-99%) and 76.5% for the full vaccination course (range: 28.4-92.6%) (pooled data from 30 reporting countries) [7].

On 10 May 2021, the US Food and Drug Administration (FDA) issued an Emergency Use Authorization for the use of Comirnaty in 12-15-year-olds [8], and on 28 May it was approved by EMA after evaluation of data on efficacy and safety for the indicated age group [9]. On 23 July, Spikevax was also approved by EMA for this age group [10]. As of 30 November, all EU/EEA countries have initiated vaccination in children aged 12-15 years [6].

As of 19 November, the median cumulative uptake of at least one dose of COVID-19 vaccine and full COVID-19 vaccination in individuals under 18 years old was 18.3% (range: 1.3–32.8%) and 15.0% (range: 1.0–29.0%), respectively (based on 27 reporting countries) [11].

On 25 November 2021, EMA recommended granting an extension of indication for Comirnaty to include use in children aged 5-11 years [12]. The same application was evaluated by the US FDA and, on 29 October, Comirnaty was authorised by the FDA for emergency use in children aged 5-11 years [13]. While many EU/EEA countries continue to experience considerable case notification rates and varying rates of vaccination coverage in different age groups, the question of whether or not the vaccination strategy should be broadened to include children under the age of 12 years is gaining increased attention.

Current status concerning vaccination of children in the EU/EEA

Planned vaccination of children under 12 years old

According to information collected through the Integrated Situational Awareness and Analysis (ISAA) report in October 2021, 3 of 20 responding countries were planning to expand vaccination to children under the age of 12 years if the EMA authorised a COVID-19 vaccine for that age group. Several countries reported that this was under discussion [6].

Table 1. Planned recommendation for COVID-19 vaccination of children under 12 years old (n = 20 countries)

Planned recommendation	Countries
Vaccination of all children	Czechia, Lithuania, Hungary
Under discussion	Belgium, Croatia, Latvia, Luxembourg, Malta, Netherlands, Poland, Portugal, Spain
Other	Austria*, Germany*, Iceland**, Ireland***, Romania*, Norway***, Slovenia*, Sweden*

** Will be discussed after European Medicines Agency (EMA) recommendation.*
*** Likely to recommend vaccination, but currently undecided.*
**** To be determined.*

COVID-19 in children aged 5-11 years

What is the susceptibility of children aged 5-11 years to SARS-CoV-2 infection?

It is important to note that throughout the pandemic there has been a high variability for reported SARS-CoV-2 prevalence among children across time and across geographical regions, as this depends on many factors, including testing policies, children's social mixing patterns (affected by whether schools have been open or closed), and mitigation measures implemented in specific settings such as schools and households. This has complicated the comparison of studies that assess the susceptibility of children to SARS-CoV-2 infection, as well as their contribution to onward transmission.

Children of all ages appear to be equally susceptible to SARS-CoV-2 infection compared to adults, even if severe disease is comparatively much less common in children [14]. However, the literature is quite heterogeneous on this topic. For example, a multicentre serologic study of SARS-CoV-2 transmission in households conducted in Germany in 2020, but published in 2021, concluded that children were less susceptible to SARS-CoV-2: the secondary attack rate in household members under 18 years of age was 8-13% lower than in adults [15]. While multiple additional studies have also suggested that unvaccinated children may be less susceptible to SARS-CoV-2 infection than unvaccinated adults [14,16], potential reporting biases due to lower case ascertainment in children may have contributed to this interpretation, particularly for studies conducted in 2020, when SARS-CoV-2 testing capacities were often limited and testing was prioritised for symptomatic patients [14].

More recent incidence and seroprevalence studies have tended to conclude that there are no significant differences in susceptibility to SARS-CoV-2 infection across age groups [17,18]. This is notably the case for study designs that have conducted repeated testing among study participants, irrespective of symptoms. A prospective cohort study from Austria repeatedly tested over 10 000 staff and students for SARS-CoV-2 infection using a gargling solution and RT-qPCR [19]. The authors concluded that SARS-CoV-2 prevalence did not differ across age groups, pupils or teachers, or primary or secondary schools, but did observe an association between prevalence and regional community incidence and social deprivation [19]. A prospective study of students, parents and teachers linked to a single school in Belgium, conducted between 21 September and 31 December 2020, involved weekly testing of all study participants [20] and found no significant difference in the infection rates between children and adults (odds ratio (OR): 0.58; 95% confidence interval (CI): 0.22-1.41). In the US, a large prospective cohort study of households in Utah and New York took place from September 2020 through April 2021 and involved weekly RT-PCR of all 1 236 included study participants, regardless of symptoms [21]. It was reported that the

incidence rate ratio (IRR) for children aged 5-11 years compared to adults was 0.9 (CI: 0.5-1.4; p=.55) [21]. The study also reported that 50% of positive cases among children aged 5-11 years were asymptomatic, as compared to 12% for adults [21]. Moving forward, the relative incidence of SARS-CoV-2 infection among children is likely to increase, depending upon the different levels of vaccine uptake across age groups.

It is important to note that most currently published scientific studies were conducted prior to the emergence (or the dominant circulation) of the Delta VOC, which is now predominant across the EU/EEA. As the Delta VOC has a significant transmission advantage over previously circulating SARS-CoV-2 strains, there is significantly increased susceptibility to SARS-CoV-2 infection among all age groups [22]. As far as children are concerned, for example, a COVID-19 outbreak caused by the Delta VOC at an elementary school demonstrated the high susceptibility of unvaccinated elementary school-aged children when exposed to an index patient (in this instance, an unvaccinated teacher), with an attack rate of 50% and the risk of infection among students correlated to the seating proximity to the teacher [23]. In England in September 2021, as the autumn semester started, the age groups with the highest weighted prevalence of SARS-CoV-2 (predominantly Delta VOC) were among school-aged children aged 5-12 years (2.32%) and 13-17 years (2.55%) [24]. In a follow-up round of the same study, school-aged children continued to have the highest weighted prevalence, which rose to 4.95% in children aged 5-12 years and 5.21% in children aged 13-17 years for the time period mid-October to mid-November 2021 [25].

What is the likelihood of secondary SARS-CoV-2 transmission by children aged 5-11 years?

Throughout much of the COVID-19 pandemic, research that has sought to ascertain the relative contribution of children to overall levels of SARS-CoV-2 transmission has been limited by factors such as school closures and lockdowns, which often altered children's social mixing patterns differently than they did for adults; varying implementation of infection prevention and control measures in household and school settings; and case ascertainment in children, given that children are more likely than adults to have asymptomatic SARS-CoV-2 infection.

Despite such limitations, the scientific literature clearly demonstrates the possibility of onward transmission of SARS-CoV-2 by children of all ages [14]. Most of the scientific literature reports on SARS-CoV-2 transmission from strains that preceded the Delta VOC. Currently, the likelihood of secondary transmission from all age groups, including children aged 5-11 years, has likely increased due to the higher transmissibility and dominance of the Delta VOC over other SARS-CoV-2 strains [22].

Transmission by children likely depends on multiple factors, including symptom type and severity, viral load and shedding duration, host factors (such as baseline susceptibility and immune responses), as well as the viral variant [26]. The balance of evidence suggests that peak respiratory tract viral load in children infected with SARS-CoV-2 does not differ from adults, but that the duration of respiratory tract viral shedding is shorter in children when compared to the adult population [14,27]. In a recently published analysis of RT-PCR cycle threshold values, it was concluded that both symptomatic and asymptomatic children may have high SARS-CoV-2 viral loads, irrespective of a child's age or of disease severity [28]. However, a separate study concluded that there was a higher viral load in the nasopharynx of symptomatic children, as compared to asymptomatic children [29].

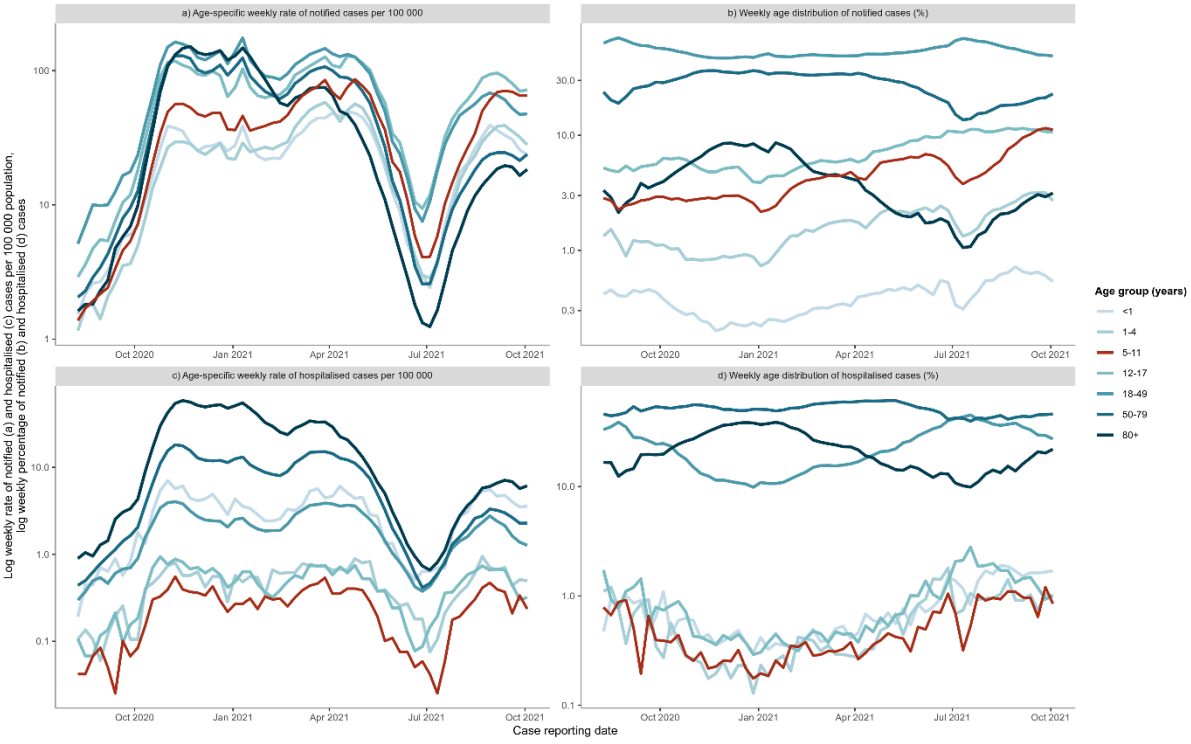
There are mixed results in the literature (the vast majority of which does not report on the Delta VOC) about whether children are more or less likely to transmit SARS-CoV-2 than adolescents or adults, given equivalent vaccination status, as previously reported [14]. A recently published multicentre serologic SARS-CoV-2 household transmission study from Germany, conducted during 2020, concluded that the secondary attack rates increased with the age of the index patients: the lowest secondary attack rates were from children under 12 years old (12%), rising to around 31% for adolescents and adults less than 60 years old, and higher yet for adults over 60 years old [15]. Of note, is that less severe disease in children may lead to less seroconversion [30]. On the other hand, a study published in August 2021 examined 6 280 households with paediatric index cases in Ontario, Canada, between 1 June and 31 December 2020. The study concluded that, compared to 14-17-year-olds, 0-3-year-olds had higher odds of transmitting SARS-CoV-2 to household contacts. There were no significant differences in the odds of transmission by 4-8-year-olds or 9-13-year-olds in comparison with 14-17-year-olds [31]. A study published in September 2021 reported on a convenience sample of 202 COVID-19-positive patients in the US and found that contacts of index cases aged less than 18 years (and especially under 5 years old) were more likely to be symptomatic than contacts of index cases aged 18-44 years, although the results were not statistically significant [32]. A large, ongoing community survey of SARS-CoV-2 transmission in England reported that during the study period (mid-October to mid-November 2021) those living in larger households and those with children in the household had a higher prevalence of SARS-CoV-2 swab positivity than single-person households and those without children, although the odds ratios for specific age ranges of children in households was not reported [25]. Alongside households, educational settings offer a crucial source of evidence for understanding transmission of SARS-CoV-2 by children. Irrespective of the relative differences in secondary attack rates between children and adults, research from Sweden [33] and the US [34] has shown an elevated risk of SARS-CoV-2 infection for adults living in households with children attending schools in-person. While the Swedish study did not address children in the age group 5-11 years [33], the US study concluded that the risk to adults rose as school grade increased and was highest with children in grades 9 to 12 [34]. Notably, however,

the study also concluded that such risks can be mitigated through the introduction of appropriate control measures in educational settings. A separate study from Italy concluded that there was a lower probability of infection in children that had a school contact as compared to a household contact, speculating that in-school mitigation measures – for example, infrastructural adjustments, social distancing and symptomatic testing of pupils and staff – may have contributed to this finding [35]. A preprint systematic literature review concluded that transmission in educational settings during 2020 was minimal when appropriate measures were in place [36], although this review was completed prior to the dominance of the Delta VOC, which has increased the likelihood of transmission in school settings [14]. Conversely, a study of children, parents and teachers linked to a single school in Belgium concluded that among study participants testing positive for COVID-19, most transmission events occurred within the school setting and most household transmission events were from a child or teacher that had acquired the infection at school; however, this finding may have been affected by the study design [20]. While there are few official reports tallying SARS-CoV-2 outbreaks in school settings, data from Germany indicate that following the reopening of schools after the summer 2021 break, the number of reported outbreaks in school settings increased more rapidly, as compared to this period in 2020. This could be explained by such factors as the greater transmissibility of the Delta VOC or the expansion of testing in school settings [37].

What is the incidence of SARS-CoV-2 infection and COVID-19 symptomatic disease in children aged 5-11 years in the EU/EEA?

Analysis of pooled data reported by 10 EU/EEA countries (Austria, Cyprus, Finland, Germany, Ireland, Italy, Luxembourg, Malta, Slovakia, Sweden) to The European Surveillance System (TESSy) showed that weekly notification rates of symptomatic COVID-19 cases increased sharply in all age groups from July 2021 (Figure 1a). Among children aged 5-11 years, case rates increased between 5 July and 3 October 2021, from 5.9 to 65.0 per 100 000 population, an 11-fold increase and the second highest rate after the 12-17 years age group (71.9 per 100 000). In the same period, the 5-11 years age group, which makes up 6.6% of the combined population of these countries, went from accounting for 3.8% to 11.2% of weekly cases, a 3-fold increase (Figure 1b).

Figure 1. Pooled age-specific weekly rate of notified and hospitalised symptomatic cases per 100 000 population and age distribution of notified and hospitalised cases reported to TESSy, 3 August 2020 to 3 October 2021



What are the frequency and proportion of hospitalisations and deaths from COVID-19 in children aged 5-11 years in the EU/EEA?

Hospitalisation of children diagnosed with COVID-19 has also increased, broadly in line with the rise in cases in this age group, but remains at much lower levels in children than in adults. For symptomatic cases reported in the same period (5 July to 3 October 2021), the weekly rate of hospitalised cases in children aged 5-11 years rose from 0.025 to 0.24 per 100 000 population, a nine-fold increase (Figure 1c). At the same time, this group went from contributing 0.3% to 0.8% of weekly hospitalised cases, a 2.7-fold increase (Figure 1d).

Crude risks for severe outcomes were estimated using pooled data from the 10 EU/EEA countries with complete data on hospitalisation, severe hospitalisation (ICU admission and/or requiring ventilation or extracorporeal membrane oxygenation) and death, for the period in which the Delta VOC became and remained dominant (weeks 28 to 39 2021). Among the 65 800 symptomatic cases aged 5-11 years that were notified during this period, 399 were hospitalised (risk: 0.61%; 95% CI: 0.55-0.67%) and 42 were severely hospitalised (risk among all cases: 0.06% (95% CI: 0.05-0.09%); risk among hospitalised cases: 10.5% (95% CI: 7.7-14.0%)). Deaths were extremely rare, with only two reported. There were no differences in the distribution by sex of these outcomes (chi-squared p>0.22).

What are the factors associated with COVID-19 hospitalisation and severe disease in children aged 5-11 years?

From the analysis of pooled data reported by 10 EU/EEA countries (Austria, Cyprus, Finland, Germany, Ireland, Italy, Luxembourg, Malta, Slovakia, Sweden) to TESSy for the period 3 August 2020 to 3 October 2021, the presence of an underlying condition among cases aged 5-11 years was associated with 12.0 (range: 9.0-16.0) times higher odds of hospital admission and 19.0 (range: 10.1-34.1) times higher odds of severe hospitalisation. Despite the higher odds in children with one or more underlying condition, the majority (78%) of hospitalised children of this age had not reported an underlying medical condition. Diabetes, cancer and cardiac disease were most commonly reported among hospitalised cases with a comorbidity. However, this may depend on context, as different access to care, hospitalisation criteria and prevalence of underlying conditions could affect the associations observed in surveillance data and the literature.

According to the literature, underlying conditions increase the risk of hospitalisation or severe outcomes [38,39]. The most common comorbidities reported in hospitalised children are diabetes and gastrointestinal, neurological, cardiac and pulmonary diseases, specifically asthma [40,41]. A significant proportion of hospitalised children with SARS-CoV-2 infection are also obese [42,43]. Data based on 2 293 hospitalised children with confirmed COVID-19 in the US demonstrated that obesity (adjusted risk ratio (aRR): 1.4; 95% CI: 1.2–1.6) was associated with increased risk of severe COVID-19 in children aged 5–11 years [44]. A recently published systematic review and meta-analysis identified underlying conditions, such as neurological diseases and obesity, to be associated with increased odds of death [39]. They also found seven studies showing that age less than 10 years increased the odds of death by 1.76 times, and only two studies with low-quality evidence concluding that age less than 6 months was associated with severe disease. Authors addressed that findings from these studies should be interpreted with caution, as the various sample sizes or differences in definitions could lead to contradictory conclusions on risk factors associated with severe disease or death. It is also important to note that pre-existing underlying diseases in children would likely lower the threshold for hospital admission and potentially inflate the observed associations.

Another systematic review and data analysis mainly covering wildtype and Alpha VOC circulation showed that sex was not associated with critical care or death [45]. Compared with children aged 1-4 years, infants (less than 1 year old) had increased odds of admission to critical care (OR: 1.63; 95% CI: 1.40-1.90) and death (OR: 2.08; 95% CI: 1.57-2.86). Odds of death were increased among children older than 10 years (10-14 years age group OR: 2.15 (95% CI: 1.54-2.98); >14 years age group OR: 2.15 (95% CI: 1.61-2.88)). A higher number of comorbid conditions was associated with higher odds of admission to critical care and death for COVID-19. For critical care admission, odds ratios were: one comorbidity OR: 1.49 (95% CI: 1.45-1.53); two comorbidities OR: 2.58 (95% CI: 2.41-2.75); three or more comorbidities OR: 2.97 (95% CI: 2.04-4.32). The odds ratios for death were: one comorbidity OR: 2.15 (95% CI: 1.98-2.34); two comorbidities OR: 4.63 (95% CI: 4.54-4.74); three or more co-morbidities OR: 4.98 (95% CI: 3.78-6.65). The odds of admission to critical care were increased for all comorbidities except for asthma (OR: 0.92; 95% CI: 0.91-0.94) and malignancy (OR: 0.85; 95% CI: 0.17-4.21), with increased odds of death in all co-morbidities considered, except for asthma. Neurological and cardiac comorbidities were associated with the greatest increase in odds of severe disease or death. Obesity increased the odds of severe disease and death independently of other comorbidities. Among hospitalised children and adolescents, severe disease or death from SARS-CoV-2 infection was more often observed among infants, teenagers, those with cardiac or neurological conditions, those with two or more comorbid conditions, and those who were obese. While odds ratios were high, the absolute increase in risk for most comorbidities was small compared to children without underlying conditions.

According to the scientific literature, what is the burden of COVID-19 in children aged 5-11 years?

Notified cases in children are dependent on the testing frequency in this age group, which has varied over time and between countries. In-school testing approaches are likely to have been expanded over time with the broader implementation of rapid antigen detection tests (RADTs) and in an effort to keep schools open. Furthermore, children are more likely to have mild disease and evidence suggests that overall asymptomatic rates of COVID-19 in children range from 13-50% [14,21,46,47].

The level of immunity from natural infection in children can be estimated from seroprevalence studies but may vary considerably between geographic areas and populations. Several studies show that seroprevalence has increased over time since the beginning of the pandemic and is increasing among children [18,48]. Some studies on European populations (with data collected between May and July 2021) have reported seroprevalence rates ranging from 15-31% in children under 12 years old [48-51]. According to a national seroprevalence study in the US, the seroprevalence in the 5-11 years age group increased from 13% in Nov to Dec 2020 to 42% in May to June 2021 [52]. Reporting delays limit the ability to provide an up-to-date estimate of the current seroprevalence in the EU/EEA. It should be noted that not all children seroconvert after an infection with SARS-CoV-2 [30] and the proportion that seroconvert may be lower than the proportion in adults [53].

Based on data from the United Kingdom (UK) that was prospectively collected from a cohort of children aged 5-17 years, presentation to the emergency department or admission to hospital was reported for 14 of 276 (2.2%) children aged 5-11 years with Alpha VOC infection and 8 of 227 (3.5%) children in this age group with Delta VOC infection [54]. According to surveillance data from Israel, 291 628 children have been registered in the national COVID-19 registry. Of these, 568 (0.35%) were admitted to the hospital, 8% had moderate/severe disease, and none died [55].

Data from the German paediatric COVID-19 registry (for the period March 2020 to August 2021) showed that among 1 680 children hospitalised due to COVID-19, 85 children (5%) were admitted to ICU and 13 died (0.8%), but COVID-19 was confirmed as the main cause of death for only 6 of the 13 children who died [56].

According to an analysis from the US CDC, the rate of new COVID-19 cases and COVID-19-related emergency department visits increased for the age groups 0–4 years, 5–11 years, and 12–17 years after the Delta VOC became the predominant circulating variant (August 2020 to June 2021, compared to July to August 2021) [57]. Hospital admissions of patients with confirmed COVID-19 also increased in the 0–17 years age group during this period. It could not be concluded from the analysis whether the increase in emergency department visits and hospitalisations were related to an increased severity of disease caused by the Delta VOC compared to earlier circulating variants, or to other factors such as increased transmission during that time.

A national study from England provides further estimates of mortality among children [58]. A total of 3 105 children and young people died from all causes during the first year of the COVID-19 pandemic in England. Of these deaths, 61 occurred in individuals who tested positive for SARS-CoV-2. Of these, 25 individuals died of SARS-CoV-2 infection, 22 from acute infection and 3 from PIMS-TS/MIS-C. A proportion of 99.995% of children and young people with a positive SARS-CoV-2 test survived. The 25 individuals who died of SARS-CoV-2 equates to a mortality rate of two per million for the 12 023 568 children and young people living in England. In the age group 5-9 years, the corresponding mortality rate was 1 per million.

Mortality estimates from national statistical data reported by Germany, Italy, Spain and France up to February 2021 ranged from one to two per million in the age group 0-9 years [59].

What are the possible clinical manifestations of COVID-19 in children aged 5-11 years?

The clinical manifestations of COVID-19 in children aged 5-11 years are well documented. Most children with COVID-19 have mild symptoms or asymptomatic disease and a very low risk of death [14,59]. In a prospective cohort study from the UK, children in this age group reported three symptoms as a median and experienced shorter hospital stays (five days; interquartile range (IQR): 2-9 days) than adolescents [60]. The most common symptoms for the age group 5-11 years were fever, headache, fatigue, and sore throat.

Most published literature on disease severity in children report data from the time before the Delta VOC became predominant. Some studies that covered both adults and children have suggested that individuals infected with the Delta VOC are at higher risk of hospitalisation compared to previous dominant variants [61,62]. According to a UK prospective cohort study including 109 626 children aged 5-17 years, COVID-19 caused by the Delta VOC in children aged 5-11 years resembles COVID-19 caused by the Alpha VOC [54]. The median illness duration in this age group was approximately five days (IQR: 2–9.75) for both variants (Delta VOC: 5 days (IQR: 2-9); Alpha VOC: 5 days (IQR: 2–9.75)), while the number of symptoms appeared slightly greater with Delta VOC compared to Alpha VOC infection. In this age group, the most common symptoms were the same for both variants: rhinorrhoea (i.e. runny nose) (n = 130 (47.1%) of 276), headache (n = 110 (39.9%) of 276), and fatigue (n = 107 (38.8%) of 276) with Alpha

VOC infection and headache (n = 138 (60.8%) of 227), rhinorrhoea (n = 122 (53.7%) of 227), and fatigue (n = 111 (48.9%) of 227) with Delta VOC infection. The odds of several symptoms were higher with Delta VOC than Alpha VOC infection, including headache and fever. Few children presented to the emergency department or were admitted to hospital: 14 of 276 children aged 5-11 years (2.2%) with Alpha VOC infection and 8 (3.5%) of 227 children in this age group with Delta VOC infection [54]. In the US, the proportion of hospitalised children and adolescents admitted to an ICU due to COVID-19 during the pre-Delta period did not differ during the Delta-predominant period (26.5% and 23.2%, respectively) [63]. However, the median length of hospital stay reduced from three days during the pre-Delta period to two days during the Delta-predominant period.

A US CDC report about patients with at least one inpatient or hospital-based outpatient encounter, with discharge between March 2020 and January 2021, found that patients younger than 16 years with COVID-19 had 36.8 (95% CI: 25.0-48.6) times higher risk of myocarditis compared to patients in the same age group without COVID-19 diagnosis [64]. The incidence of cardiac involvement due to SARS-CoV-2 infection in Danish adolescents aged 12–17 years was 355 and 187 per million for males and females, respectively (1 in 2 800 males and 1 in 5 300 females) during the first 12 months of the COVID-19 pandemic [65]. According to the Danish National Patient Register, the monthly incidence of myocarditis was 3 and 0.5 per million Danish males and females aged 12–17 years, respectively, during the period 2014 to 2018.

What is the occurrence of multisystem inflammatory syndrome (PIMS-TS/MIS-C) and of post COVID-19 condition in children aged 5-11 years who are infected with SARS-CoV-2?

Following the initial wave of COVID-19 hospitalisations, a novel syndrome with hyperinflammatory response in children emerged, initially identified by physicians in the UK in April 2020. The Royal College of Paediatrics and Child Health defined it as paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS), while the World Health Organization (WHO) and the US CDC refer to it as multisystem inflammatory syndrome in children (MIS-C) [66,67]. Unfortunately, there is currently no specific test available to diagnose this syndrome. [66]. Hence, the diagnosis of PIMS-TS/MIS-C is based on clinical signs and symptoms, as well as evidence of a previous SARS-CoV-2 infection or exposure. Children who develop the syndrome are generally previously healthy, and the primary infection with SARS-CoV-2 is usually mild or asymptomatic [68].

PIMS-TS/MIS-C is rare and shares common clinical features with other paediatric inflammatory syndromes such as Kawasaki disease, toxic shock syndrome, and macrophage activation syndrome. Children with PIMS-TS/MIS-C often present four to six weeks after infection, with a wide clinical spectrum including Kawasaki disease-like symptoms, life-threatening shock, and milder forms of illness such as persistent fever, inflammation, and gastrointestinal manifestations [68]. The median age of children diagnosed with the syndrome is eight years [69].

Most children with critical illness due to PIMS-TS/MIS-C have a favourable outcome and recover with intensive care support and appropriate treatment. According to studies, 60% of children with PIMS-TS/MIS-C need to be admitted to an intensive care unit (ICU), with an average length of ICU stay of around 5 days and an average total hospital stay of around 10 days [42,68]. In a cohort of 286 children and adolescents from 55 centres across 17 European countries, a high incidence (93%) of myocardial involvement was evident [70]. A multi-institutional study on PIMS-TS/MIS-C in 76 children found that myocarditis, heart failure and coronary artery involvement were the most common cardiovascular manifestations [71]. Critical illness is associated with increasing age of children in some studies [72,73]. A population-based study of PIMS-TS/MIS-C found that 36% of children had persistent symptoms eight weeks after diagnosis [74].The mortality associated with PIMS-TS/MIS-C was approximately 1% in an observational cohort study of young people admitted to the hospital with COVID-19 in the UK [41].

A systematic review covering 68 studies of various study designs reported data from a total of 953 PIMS-TS/MIS-C cases [75]. The clinical pattern was heterogenous among the studies and the most commonly reported symptoms were fever (99.4%), gastrointestinal symptoms (85.6%) and cardiocirculatory manifestations (79.3%). The median time of hospitalisation was 8 days (IQR: 7–12) in single cases and 4-12 days in cohorts, and 18 of the reported cases were fatal. The most common risk factor for the condition was being overweight, which was present in 25% of the cases. Data analysis from the Norwegian national COVID-19 registry showed an increased risk of PIMS-TS/MIS-C in children with chronic comorbidities [76].

Early recognition and prompt treatment of PIMS-TS/MIS-C cases is essential. Limited evidence for treatment options supports the use of intravenous immunoglobulin (IVIG), corticosteroids, inotropes and other biological immunomodulation agents [77,78].

As children often present with mild symptoms of COVID-19 and are less frequently tested than adults, the true proportion of cases that develop PIMS-TS/MIS-C remains unknown. The incidence of PIMS-TS/MIS-C across seven US regions was estimated to be approximately 3 per 10 000 individuals younger than 21 years of age infected with SARS-CoV-2 [79]. There is no comprehensive overview of PIMS-TS/MIS-C cases in the EU/EEA. Germany and Switzerland published data from a case series study of children with severe COVID-19 infection leading to PIMS-TS/MIS-C and even death [80,81]. The German Society for Paediatric Infectious Diseases has

identified 389 children who developed PIMS-TS/MIS-C as of August 2021, with an estimated incidence of 2-5 cases per 10 000 SARS-CoV-2-infected children and no deaths [56]. The French national surveillance system registered 648 children with PIMS-TS/MIS-C between March 2020 and September 2021, with a median age of seven years (25% of cases were 4 years old or younger and 75% were 11 years old or younger). Among them, 40% were girls, 41% had a history of admission to a paediatric ICU and one nine-year-old died. In France, the cumulative incidence of the syndrome is estimated at 44.6 cases per million children [82,83]. In Spain, a paediatric COVID-19 registry indicated that among children hospitalised due to PIMS-TS/MIS-C, 61% developed cardiac complications [84]. Sweden has reported 260 children diagnosed with PIMS-TS/MIS-C, most of them without any underlying disease and, while around 25% of them were admitted to ICU, no deaths have been recorded as of September 2021 [85]. During the same period, Norway identified 22 children with PIMS-TS/MIS-C, resulting in an incidence of 1.0 per 1 000 SARS-CoV-2-infected children [76]. A nationwide cohort study in Denmark estimated the occurrence of PIMS-TS/MIS-C cases among SARS-CoV-2-infected children as 1 in 4 100 in children younger than 12 years and 1 in 3 700 in children older than 12 years [86]. Monitoring for potential long-term health consequences of PIMS-TS/MIS-C should be performed as information is currently limited.

In addition to PIMS-TS/MIS-C, the presence of post COVID-19 condition has been reported in cohorts of children from a number of countries [87]. Post COVID-19 condition is characterised by persistent symptoms such as headache, fatigue, dyspnoea, chest pain, cognitive impairment, and sleeping disturbances that last up to several months after SARS-CoV-2 infection. A review covering 14 studies from 12 countries reporting on persistent symptoms following COVID-19 in children and adolescents found a considerable variation in estimated prevalence between the studies, from 4-66% of cases [87]. There were also considerable variations regarding the age group of the study population, the definition of the condition and symptoms, and the follow-up time. Six studies reported a positive correlation between the prevalence of persisting symptoms and increasing age. Some studies also reported correlations between prevalence and female sex, allergic diseases and worse pre-infection physical and mental health. In the majority of studies, symptoms did not persist longer than 12 weeks in most children. Of five studies that included a control group consisting of children and adolescents without SARS-CoV-2 infection, two did not find persistent symptoms to be more prevalent in children and adolescents with evidence of SARS-CoV-2 infection [87].

Data from the UK's National Statistics Office has also shown a significant number of children reporting symptoms several weeks after their initial SARS-CoV-2 infection, estimating the prevalence for the 2-11 years age group to be 0.2% [88]. A large cohort study (the CLoCk study) surveyed 3 065 children and young people aged 11-17 years who tested PCR positive for SARS-CoV-2 and 3 739 who tested PCR negative [89]. Three months after the test result, 30.3% and 16.2%, respectively, experienced more than three symptoms. In a similar but smaller study in Latvia, among 236 children who tested positive for SARS-CoV-2, 53% had two or more persistent symptoms [90]. A national survey in the Netherlands showed that among the 89 children suspected of post COVID-19 condition, 18% were admitted to hospital due to long-term symptoms [91]. A large German study based on data from 11 950 children and adolescents with confirmed COVID-19 recently published findings on morbidity outcomes three months after the date of COVID-19 diagnosis [92]. The paediatric cohort had significantly higher incidence rates of symptoms across both physical (IRR overall: 1.31 (95% CI:1.24-1.38); IRR confirmed COVID-19: 254.58; IRR control group: 194.45) and mental (IRR overall: 1.39 (95% CI:1.28-1.52); IRR confirmed COVID-19: 102.17; IRR control group: 73.24) health outcome domains. The outcomes with the highest IRR were malaise/fatigue/exhaustion, cough, and throat/chest pain. Similar IRRs were found in the age groups 0-11 years and 12-17 years. In conclusion, there is evidence that children can suffer from long-term sequelae after SARS-CoV-2 infection, but the exact burden is still to be determined and is a priority for further research.

What is the indirect impact of the COVID-19 pandemic on the health and well-being of children aged 5-11 years?

The COVID-19 pandemic has indirectly impacted the health and well-being of children aged 5-11 years in multiple ways. Restrictions such as physical distancing, school closures, and cancelled sport and recreation activities drastically decreased peer interaction, as well as contact with older family and community members. It will take years before we can truly assess the overall impact of COVID-19 on children's health and development. In terms of loss of family members, it has been estimated that by 30 April 2021, over 1.1 million children globally experienced the death of a primary caregiver during the COVID-19 pandemic [93]. Such children are expected to be at an elevated risk of experiencing mental health problems, violence, and family poverty [93].

School disruptions have affected millions of children globally and in the EU/EEA since the onset of the pandemic and this, in turn, has affected not only their education [94,95] but also their health [14]. There has also been a disproportionate impact on the most vulnerable children and their families [14,96,97]. While the pandemic has not uniformly led to the deterioration of children's physical or mental health [98], as some children may have experienced benefits (e.g. increased family time) [99], the overall evidence points to increased risks to children's health during the pandemic. A systematic review based on 72 studies from 20 countries demonstrated that school closures had considerable impact on children and adolescents' mental health, as between 18-60% of young people were found to be at risk of psychological distress, particularly anxiety and depressive symptoms. Screen time and social media use increased, physical activity was reduced, and sedentary behaviour and unhealthy dietary habits increased [100]. A rapid systematic review on the impact of school closures on child and

adolescent health reported negative impacts on child sleep quality and behaviour (including a worsening capacity for inhibitory self-control), as well as predictions for increased levels of childhood obesity and greater learning challenges for children from disadvantaged families (due to lack of parental abilities to support, lack of internet access, and digital disparities) [101]. In the UK, one preprint study reporting on a time that included a period of lockdown reported worsening mental health and an increase in behavioural problems among 4-11-year-olds [102]. A study documenting the impact of the COVID-19 pandemic on health inequalities in England reported an increased risk of child poverty and developing mental health issues for children from disadvantaged backgrounds [103]. The report also highlighted increases in domestic abuse [103], and it has elsewhere been highlighted that children are at increased risk of domestic violence when schools are closed [104]. A study from Germany reported that, during the pandemic, increases in children witnessing domestic violence and verbal/emotional abuse were associated with families with higher parental stress, job losses, and younger parent and child ages [99]. In the first year of the pandemic in the US, a rise was observed in young patients with eating disorders, depression and suicidal thoughts [105,106]; these concerns, and the other factors described herein, led the American Academy of Paediatrics, the American Academy of Child and Adolescent Psychiatry, and the Children's Hospital Association to declare a national state of emergency in children's mental health in 2021 [107].

Isolation and quarantine measures are often linked to reports of COVID-19 in educational settings and continue to cause substantial disruptions to children's lives, particularly to their learning. Remote learning quality and effectiveness is significantly lower than in-school learning and varies greatly by context, learners' background, family digital literacy, as well as access to internet and technology [108]. School closures may have disproportionately affected students that were low-achieving prior to the pandemic [109]. In addition to direct loss of learning, negative impacts on children's education include reduced educational performance, increased risk of disengagement and school dropout, and a reduction in motivation and feelings of connection with the school community [14,94,100,110-112].

Education and development of skills is a strong health determinant, as well as predictor for future labour opportunities and earnings. This relationship is expected to disadvantage children affected by the COVID-19 pandemic in multiple ways. In terms of economic consequences, the loss of learning and skills are estimated to cause a reduction in future earnings and income possibilities [113]. For each month of skill loss, about a 1% drop in lifetime earnings for affected children has been projected, which constitutes an estimated decrease in national income by 0.5% per year [114]. These impacts are greater on vulnerable populations, and disruptions in schooling and recreational activities have interacted with other COVID-19-related hardships to disproportionately affect students with lower socio-economic backgrounds [115,116].

Efficacy, safety and anticipated impact of COVID-19 vaccination of children aged 5-11 years

What are the preliminary data on efficacy and safety of COVID-19 vaccines in children aged 5-11 years?

As of 30 November 2021, clinical trials in children are ongoing for the vaccines Comirnaty and Spikevax (Table 2). A published study from the clinical trial of Comirnaty in children aged 5-11 years has reported neutralising antibody responses generally consistent with those in adolescents and adults, and vaccine efficacy against COVID-19 infection of 90.7% (95% CI: 67.7 to 98.3) [117]. Previous clinical trials on adolescents (12-17 years old) have shown high efficacy for both vaccines in this age group [118,119] and a cohort study on adolescents from Israel during the period when the Delta VOC was dominant demonstrated high vaccine effectiveness for Comirnaty against SARS-CoV-2 infection in adolescents [120].

Table 2. Ongoing clinical trials for COVID-19 vaccination of children under 12 years old

Title	Population studied	Endpoints	Main findings	Comments
Pfizer/BioNTech (Comirnaty): A Phase 1/2/3 Study to Evaluate the Safety, Tolerability, and Immunogenicity of an RNA Vaccine Candidate Against COVID-19 in Healthy Children and Young Adults, NCT04816643 [121]	11 422 participants, 6 months to 30 years old.	Safety/efficacy/ immunogenicity	According to a study published on 20 September 2021, reporting data from 2 268 children aged 5-11 years, participants who received two 10 µg doses had antibody titres and a side effect pattern comparable to those in the age group 16-25 years who received two 30 µg doses [117].	Results from the age group six months to five years are expected in the fourth quarter of 2021.
ModernaTX, Inc (Spikevax): A Study to Evaluate Safety and Effectiveness of mRNA-1273 COVID-19 Vaccine in Healthy Children Between 6 Months of Age and Less Than 12 Years of Age, NCT04796896 [122]	13 275 participants, 6 months to 11 years old.	Safety/efficacy/ immunogenicity	According to a press release from the company on 25 October 2021, reporting data from 4 753 children aged 6-11 years, participants who received two doses of 50 ug had a robust neutralising antibody response and a safety and tolerability profile generally consistent with those in adolescents and adults [123].	Estimated primary completion date: 12 June 2023.

Only vaccines currently authorised in the EU/EEA are listed in the table.

Regarding safety aspects, assessment of COVID-19 vaccines in the adult and adolescent populations have shown a number of side effects, of which most are mild to moderate, while some safety signals have been reported and are being continuously investigated [124]. In the clinical trial of Comirnaty in children aged 5-11 years, the safety data showed some mild to moderate side effects that improved within a few days and no severe event was detected [117]. The safety profile was reported to be similar to that of adolescents [119], with the most common side effects being fever, injection-site pain, severe fatigue, headache, chills, and muscle pain. However, it should be noted that this trial did not have the power to detect rare events because of the sample size (n = 1 517 children received the vaccine). Data from additional participants was added to the safety assessment in the application to EMA and the FDA (n = 3 100 children received the vaccine) [13]. Besides the available data from the clinical trial, there is uncertainty regarding potential rare adverse events in this specific age group that could only be detected with increasing vaccination numbers and longer follow-up time.

From the post-authorisation safety monitoring in adults and adolescents, there have been reports of an association between vaccination against COVID-19 and myocarditis and pericarditis, particularly for mRNA vaccines [125-128]. The cases have primarily been detected among male adolescents aged 16 years or older after the second dose of the vaccine, and most cases have recovered relatively quickly. Myocarditis and pericarditis have been added to the list of side effects in the product information of Comirnaty and Spikevax [129,130], but further monitoring and evaluation are ongoing in order to assess the magnitude and importance of this complication in adolescents and adults.

In this context, it should be noted that SARS-CoV-2 infection is also associated with an increased risk of myocarditis that is exacerbated in young males [64,131,132].

What is the estimated impact of vaccinating children aged 5-11 years on the effective reproduction number (R_t)?

Although the direct physical health burden of COVID-19 in children is generally considered to be low, there could be a significant indirect contribution of children to the overall COVID-19 burden in the whole population, due to SARS-CoV-2 infections that are transmitted from children to adults. In order to estimate the impact of vaccinating children aged 5-11 years on the R_t in the whole population, ECDC's internal mathematical modelling approach has been used. Other related work has also estimated the impact of vaccinating children on the spread in the whole population [133-135].

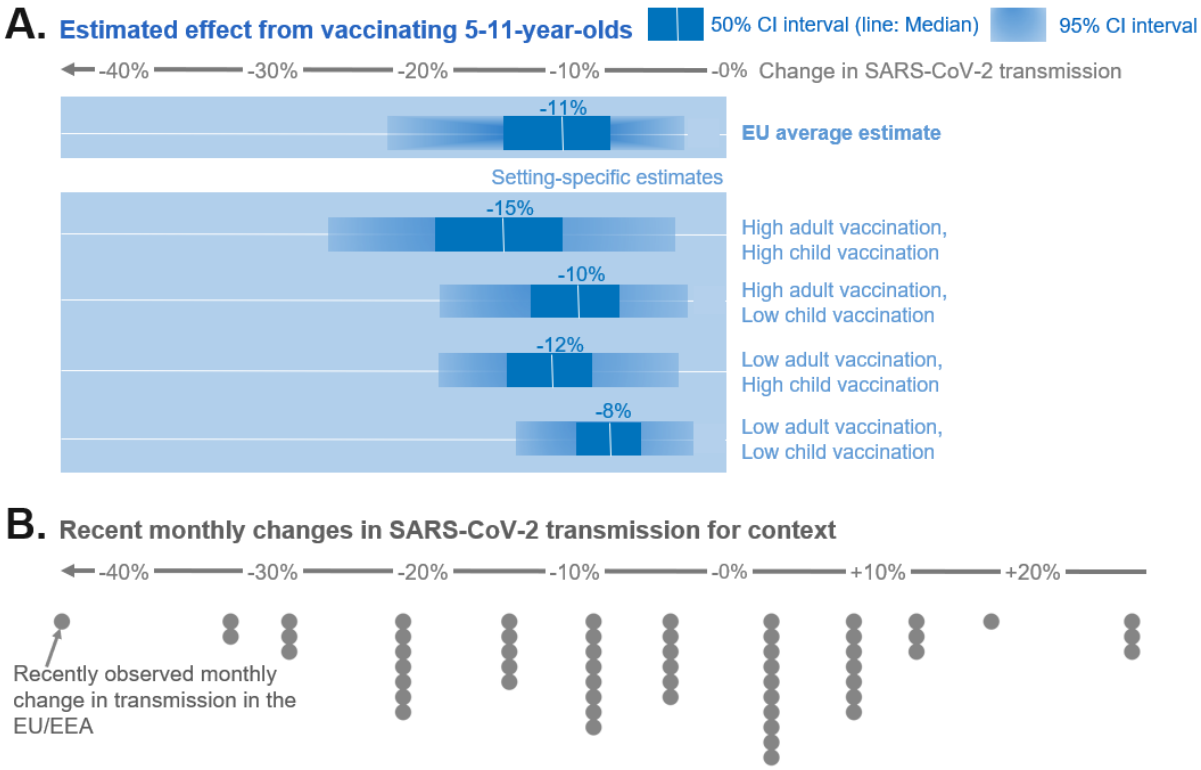
The impact of vaccinating children on viral transmission in the community depends on various parameters, including the contact rates (the number of daily contacts that people have) between different age groups; the vaccination coverage, dosage and schedules, as well as type of vaccines administered, in the adult (18 years and older) and adolescent (12-17 years) populations; the vaccine effectiveness against transmission and its duration; the age distribution of the population; and the age-specific susceptibility and infectivity of individuals. Many of these parameters are known with substantial uncertainty and some parameters are country specific. In order to take these uncertainties into account, the model considers that every parameter lies within a given range; for instance, the fraction of individuals that have had a SARS-CoV-2 infection is likely between 10-50% [22,136]. By repeating the calculation for all parameter ranges and their combinations, the model can predict a range of estimates for the possible decrease of the R_t in the whole population attributable to the vaccination of children.

In the model, the population is divided into four age groups: 0-5 years, 5-11 years, 12-17 years, and 18 years or older [137]. The motivation for considering separate age groups was two-fold. First, it allows for specification of the vaccination coverage, vaccine efficacy and prevalence of natural immunity independently for each age group. Second, it allows for the capture of heterogeneous contact rates within and between age groups; for instance, the number of contacts between children and adults (e.g. at kindergarten or school) or the number of contacts among adults, due to leisure (e.g. at the gym) or work. The contact rates were directly linked to viral transmission from one age group to another. Contact rates between age groups were obtained from the contact mixing study CoMix [138]. The CoMix study provides longitudinal contact data from more than 20 European countries during different phases of the COVID-19 pandemic. For this model, contact rates between age groups were averaged over countries [138].

The reduction of the R_t depends strongly on country-specific parameters, particularly on the vaccination coverage in the adult population. Thus, the impact of vaccinating children aged 5-11 years is estimated for four different settings. First, parameters that reflect the EU average of 75% adult vaccination coverage were considered. For the EU average parameters, the impact of a child vaccination coverage of 30-70% was evaluated. Second, four different hypothetical scenarios were considered as country settings with: a high vaccine uptake in both adults (85%) and children (50-70%), a high vaccine uptake in adults (85%) but a low vaccine uptake in children (30-50%), a low vaccine uptake in adults (55%) but a high vaccine uptake in children (50-70%), and a low vaccine uptake in both adults (55%) and children (30-50%).

The results show that the decrease of the R_t occurs once the child vaccine uptake has reached the low or high plateau of 30-50% or 50-70%, respectively. The reduction of the R_t and a decrease of hospitalisations and deaths due to child vaccinations will only be seen progressively, in the medium to long term, depending on the speed of the child vaccination roll-out.

Figure 2. The estimated impact of vaccinating children on the spread of SARS-CoV-2



A: The blue bars show the estimated range of the relative decrease of the effective reproduction number (R_t) due to vaccinating children aged 5-11 years for five parameter settings: the EU average and four hypothetical countries with different vaccination coverages for adults and children (aged 5-11 years). The width of these bars represents the 95% confidence interval (CI), which is due to uncertainties in parameters such as vaccine effectiveness and waning of immunity.
B: To contextualise the relative changes in SARS-CoV-2 transmission, R_t was computed for all EU/EEA countries over time, from 1 August 2021 (the start of the dominance of the Delta variant of concern) to 31 October 2021. The relative changes of R_t from one month to the next were then computed and rounded, and are shown as dot plots in grey (one dot represents a change in transmission in one country, either from August to September or from September to October). The majority of these changes (80%) lie between -30% and +15% and are likely caused by a variety of factors, including continued vaccine roll-out, changes in human contact rates, and seasonal transmission patterns.

Figure 2 shows the estimated relative reduction of the R_t in the population as a whole for the EU average and four hypothetical country settings with different vaccine uptakes in adults and children. For the EU average, it is estimated that vaccinating children aged 5-11 years decreases the R_t in the population as a whole by 10.9% (95% CI: 2.8-22.4%). For a country with high vaccine uptake in adults and high vaccine uptake in children, a reduction of the R_t by 14.7% (95% CI: 3.4-26.3%) is estimated. For a country with high adult vaccination coverage but low child vaccination coverage, an effect of 9.9% (95% CI: 2.4-18.9%) is estimated. For a country with low adult vaccination coverage but high child vaccination coverage, an effect of 11.7% (95% CI: 3.0-19.0%) is estimated. Finally, for a country with low adult vaccination coverage and low child vaccination coverage, a reduction of 7.88% (95% CI: 2.1-13.9%) is estimated. Although results indicate similar impact on the R_t for high adult and low child vaccination coverage as for low adult and high child vaccination coverage, this does not imply that vaccinating children can be a substitute for high vaccination coverage of adults, not least because of the different frequencies of severe disease between age groups. These comparisons are designed only to illustrate how vaccination of children, at a fixed adult coverage levels, may impact transmission.

These modelling estimates indicate that vaccinating children reduces the R_t at most by about 15% (within a likely range of 3-26%), with the greatest proportional impact if a high adult vaccination coverage has already been accomplished. For countries with low adult vaccination coverage, the incremental effect of vaccinating children is weaker. When seen in the context of recent changes in viral transmission intensity, these estimates fall well within the observed range of fluctuations in the R_t (Figure 2B). This indicates that the estimated effect of vaccinating children on SARS-CoV-2 transmission is comparable to the magnitude of the effect of factors that are driving recent changes in transmission, such as changes in response measures and human behaviour, seasonal changes in transmission, and vaccination roll-out.

Potential objectives for vaccinating children aged 5-11 years

Protecting children from the direct health risks of COVID-19

The primary objective of vaccinating children is the protection of their individual health against COVID-19. It is clear from the data presented that not all children in this age group have the same risk of developing severe COVID-19 or experiencing its sequelae (e.g. post COVID-19 condition) [139]. Children at high medical risk of severe COVID-19 (i.e. those with underlying conditions that increase the risk of severe COVID-19) would particularly benefit from vaccination and should be prioritised once the vaccine is authorised in their age group. Other children, such as those belonging to socially vulnerable groups, could also be more frequently exposed to SARS-CoV-2 and to the risk of more severe health outcomes [140-142].

For the majority of children, the risk of developing severe COVID-19 appears to be low (lower than 0.01%); however, some may experience the rare but severe PIMS-TS/MIS-C or disease sequelae like post COVID-19 condition, which may affect their quality of life for an unclear amount of time.

Protecting children from the indirect impacts of the COVID-19 pandemic

The formative years of early childhood are crucial to future health and well-being, during which children experience rapid cognitive, social, emotional, and physical development. The COVID-19 pandemic restrictions have had a strong negative impact on children and their families. Significant negative effects on the physical and mental health, as well as the overall well-being, of children have been documented [14,93,99-101,143,144]. Vaccinating children could offer them increased opportunities to more safely spend time with friends and extended family, resume social and extracurricular activities, and socialise safely.

The negative impact of school disruption has been substantial during the COVID-19 pandemic, including direct loss of learning, reduced educational performance, and increased risk of disengagement and school dropout [14,110-112]. For vulnerable or at-risk children, including those with medical vulnerabilities or special education needs, vaccination could help to ensure their safe access to education. With continued community transmission, vaccination of children more generally could significantly prevent repetitive learning disruptions due to isolation and quarantine practices after exposure to a confirmed case.

Furthermore, vaccination could allow for the relaxation of in-school protection measures and non-pharmaceutical interventions, such as the use of masks and physical distancing, which may in some contexts be disruptive to normal school life.

Reducing the overall burden of COVID-19 among children

As the Delta VOC is highly transmissible, a large number of infections could rapidly occur among unvaccinated populations with frequent social interactions. Despite the low individual risk of developing severe COVID-19 faced by healthy children aged 5-11 years, a very high number of infections in this age group could nonetheless lead to a large absolute number of severe cases over a limited time period.

Non-pharmaceutical measures, such as physical distancing or the wearing of face masks, are helpful in reducing SARS-CoV-2 transmission. However, it may be challenging to implement these measures in this age group, perhaps particularly outside of controlled settings (e.g. school) and over a long period of time.

Vaccination against COVID-19 could therefore be helpful in reducing the overall burden of COVID-19 among children aged 5-11 years, given a favourable individual benefit-risk profile and sufficient and lasting protection against SARS-CoV-2 transmission, which could reduce the need for strict non-pharmaceutical measures.

Reducing SARS-CoV-2 circulation in the overall population

The overall circulation of SARS-CoV-2 may remain moderate-to-high if some age groups with a lot of contacts (e.g. children) are largely unvaccinated. In countries where transmission rates remain high, this could also have important public health consequences with regard to the frequency of severe disease and the pressure on healthcare.

According to the modelling analysis in this report, which is in line with results from other studies [134], vaccinating children – particularly in contexts where vaccine uptake in adults has already reached a high coverage level – could significantly contribute to reducing the overall viral circulation in the population and potential increases in the number of severe cases and hospitalisations. This will strongly depend on how much the vaccination of children reduces SARS-CoV-2 transmission and on the duration of such protection [139].

Considerations around implementation

Programmatic considerations

To date, there are not yet programmes in place for wide-scale vaccination of children aged 5-11 years in the EU/EEA, but should such programmes be developed they could either be offered:

- as a stand-alone vaccination apart from routine vaccination in this age group or
- concomitantly to other vaccines, as per national vaccination policies.

There are several examples of locations and settings that can be used to deliver COVID-19 vaccination to children. According to information collected from EU/EEA countries in October 2021, COVID-19 vaccination in adolescents has primarily been offered at vaccination centres, general practitioner (GP) clinics or family doctors, and schools [6]. Several countries also offered COVID-19 vaccination at hospitals, paediatrician clinics, mobile vaccination sites or pharmacies.

Regardless of the chosen approach, the following questions can be considered:

- What setting will allow for the highest uptake in this age group?
- Will there be a positive or negative impact on existing vaccination programmes?
- How will data on concomitant vaccination be collected?
- Can access to the vaccine be facilitated for all family members (i.e. children and unvaccinated family members may become vaccinated in the same setting) to increase uptake based on convenience?

Facilitating vaccination acceptance and uptake

An extension of the use of COVID-19 vaccines for children under 12 years of age will pose a series of communications challenges. The 5Cs model (confidence, constraints, complacency, calculation, and collective responsibility) provides a framework for understanding and is a tool that Member States can use to understand factors influencing vaccine acceptance among parents and caregivers, as well as for designing strategies to promote uptake [145].

A review of studies investigating COVID-19 vaccination acceptance in parents found that while levels of parental vaccine acceptance vary between countries, there has been an overall trend towards more acceptance of the COVID-19 vaccine over time [146-149]. This may be because initial concerns about safety and the speed of the vaccine's development (confidence, as in the 5Cs model) have been allayed in many parents' minds. In several studies conducted in the EU/EEA, and based on data collected in June 2021 or later, more than 70% of parents reported that they would like to have their children vaccinated against COVID-19 [147,149-151]. Nonetheless, parents of younger children have been found to be more hesitant than parents of older children [151,152], while a small but consistent minority of parents in all of the studies where this particular issue was investigated report that they will refuse COVID-19 vaccination for their children [147,153,154].

As it has been stressed in communications on COVID-19, most children who get the disease have mild symptoms and are at very low risk of severe disease or death. This has informed parental risk perception and may have led to the 5C of complacency, thereby decreasing vaccine acceptance. Surveys done in Germany, for example, show that only around one third of parents perceive the risk of infection and severity of infection to be high in children under 12 years of age if they would remain unvaccinated [155]. This leads to questions about why children should be vaccinated at all [156,157]. To address this issue, communication initiatives will need to clearly state the rationale behind recommendations to vaccinate children (including specific risk groups). The benefits in relation to direct protection versus societal benefits – such as limiting community spread, controlling spread in schools, normalising the lives of children and families, and restoring children's well-being – should be addressed.

Parental concerns around the safety of COVID-19 vaccines for children would also need to be addressed. In some national and regional contexts, concerns could have emerged from previous safety anxieties related to other vaccination programmes for children and adolescents, and these may affect trust in the safety of the vaccine [158]. Fear of unknown long-term consequences, side effects, and insufficient information about COVID-19 vaccines have been cited by parents in a study in the Netherlands as the primary reasons for not wanting their children to be vaccinated [151]. Such concerns may be exacerbated by reports (either false, misconstrued, or amplified) of children who have been enrolled in vaccine trials and who subsequently experienced vaccine injury [159] or by unsubstantiated concerns that COVID-19 vaccines can cause infertility [156]. Consequently, to increase confidence in the safety of vaccines there should be clearly communicated, up-to-date and transparent information from trusted sources on vaccine efficacy and safety, including information about the rigorous clinical trials conducted and the processes in place to continuously monitor safety of the vaccines for children [160,161].

Risk communication strategies for COVID-19 vaccination in children should leverage trusted sources such as teachers, family paediatricians and GPs [162]. A previous study conducted across 18 EU/EEA countries has shown that parents who consult GPs regarding vaccination of children are more likely to be confident in vaccination than those who do not. In addition, those who discuss vaccination with their paediatricians as a trusted source are more likely than those speaking to GPs to be confident in vaccinating their children [163]. Efforts should therefore be made to prepare GPs and paediatricians to discuss COVID-19 vaccination with parents and children, and to ensure that parents do not feel judged for raising their concerns [164].

Similarly, schools may also play a key role in increasing health literacy of children and their parents, promoting critical thinking and decision-making skills around vaccination [165,166], while also providing a familiar environment for such learning and decision-making to take place [14,167]. Resources could be created to guide teachers in promoting health literacy and awareness of vaccination, in addition to information (e.g. posters, leaflets, presentations) created by schools for both parents and children, as is being done for families and children aged 12-18 years in France and Poland [165,166]. Schools may also be used as vaccination venues, thereby increasing access to vaccination for children and adolescents, as is already being done for young people aged 12-18 years in many EU/EEA countries [6]. Children should also be included in risk communication and engagement strategies. Where appropriate, children should be encouraged to learn about vaccination and decision-making on vaccination [168]. By providing children with the opportunity to ask questions and have their concerns addressed, young people can contribute actively and in an age-appropriate way to their own vaccination decision-making process [151].

Ethical considerations

Before any decision on vaccination strategies, a careful analysis of potential harms and benefits must be undertaken, in which ethical aspects from a broad perspective should be included. This is particularly important when the target group consists of young children, who are in need of special safeguards and care because of their physical and mental immaturity [169]. Moreover, children aged 5-11 years are dependent on their guardians to decide whether or not they will take the vaccine (or national authorities in the case of mandatory vaccinations), meaning that they are unable to take autonomous consensual decisions. In the balancing of harms and benefits, the issues discussed earlier in this report regarding indirect health risks and societal aspects must be added to the direct medical concerns, as well as aspects regarding acceptability of the vaccine and health equity. This assessment is complicated by the limited evidence about the effect of vaccinating children on the overall burden of disease in this age group and in the general population.

Decisions on vaccination raise questions regarding individual versus societal benefits. One general principle is that vaccines should be beneficial for the individual or at least for the specific age group that is concerned. However, the fact that vaccination of children has the potential to reduce transmission of the disease and thereby protect the general population cannot be neglected and may have an impact on national or regional decisions regarding vaccination of children. A discussion that can follow, is whether it is justified to vaccinate children if it is interpreted as a substitute for non-pharmaceutical interventions or to make up for a failure to reach adequate vaccination coverage in other age groups, as well as how impactful such an intervention would be over time with the currently available vaccines. In this context, it should be acknowledged that any harm caused either by the vaccine itself or related to the implementation of the vaccination strategy can have a negative impact on the general trust in vaccines [170]. For any decision on the vaccination of children, it is therefore important to provide transparent and adequate information regarding the facts and principles that guided the decision [171,172].

Another aspect that should be considered is how COVID-19 vaccination may impact health equity among children. It is known that the pandemic has affected socio-economically vulnerable children and adolescents disproportionately [115,116,173]. It has therefore been argued that vaccination of children could reduce health inequalities, and that vaccination campaigns should be designed to reach vulnerable groups of children [173]. Although it is known from other vaccination programmes that vaccination coverage rates in general are lower in socio-economically vulnerable groups [174], it could also be argued that unvaccinated children could benefit from the expected reduced viral circulation following vaccination in this age group.

With regards to global health equity, ethical consideration should also be given to the current shortage of COVID-19 vaccines in many countries – a disparity that could be worsened by the administration of additional COVID-19 vaccine doses in EU/EEA countries. Earlier this year, WHO called for a moratorium on additional doses in order to improve the availability of vaccines for low- and middle-income countries [175], and a similar argument has been made regarding expanding vaccination to new age groups [176].

Conclusions

- Surveillance data show that children aged 5-11 years have made up an increasing proportion of both notified cases and hospitalisations in EU/EEA countries in recent months. Although hospitalisations have increased in line with case rates in all age groups in the EU/EEA, disease severity of COVID-19 in children is generally mild with a favourable clinical outcome. Severe COVID-19 remains rare among children (of 65 800 notified symptomatic COVID-19 cases in children aged 5-11 years, reported from 10 EU/EEA countries during the period of B.1.617.2 (Delta) variant of concern (VOC) dominance, 0.61% were hospitalised and 0.06% needed intensive care unit (ICU)/respiratory support).
- The relative contribution of children to overall SARS-CoV-2 circulation may have increased due to factors including the emergence of the highly transmissible Delta VOC and increased vaccination coverage in older age groups.

- The presence of an underlying condition among children aged 5-11 years is associated with about 12 times higher adjusted odds of hospitalisation and 19 times higher odds of ICU admission. However, the majority (78%) of hospitalised children of this age had no reported underlying medical condition.
- Paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2/multi-inflammatory syndrome in children (PIMS-TS/MIS-C) and post COVID-19 condition have been reported in children aged 5-11 years, although it is difficult to quantify the prevalence and burden of these conditions. In a United States (US) Centers for Disease Control and Prevention (CDC) report, myocarditis was reported up to 37 times more often in unvaccinated children less than 16 years old with a COVID-19 diagnosis compared to other patients from the same age group.
- Beyond the direct health impacts of COVID-19 disease, the COVID-19 pandemic has affected the physical and mental health and well-being of children aged 5-11 years. Numerous factors, such as disruptions to important everyday social and educational activities, have caused anxiety and distress in this age group.
- Modelling data indicate that vaccinating children aged 5-11 years could reduce SARS-CoV-2 transmission in the whole population, although the extent and duration of this protection is currently unknown. It is estimated that the impact on the effective reproduction number (R_t) in the population as a whole would be a decrease of 11% (range: 8-15%, depending on vaccine uptake parameters of 30-70%) for an average country in the EU/EEA. This is comparable to the effect of some non-pharmaceutical interventions. The impact of vaccinating children is weaker for countries with a low adult vaccine uptake and stronger for countries with high uptake among adults.
- On 25 November 2021, the European Medicines Agency (EMA) granted a positive opinion for use of the Comirnaty COVID-19 vaccine in children aged 5-11 years based on a placebo-controlled randomised clinical trial in which more than 3 000 children in this age group received this vaccine.
- Children aged 5-11 years who are at risk of severe COVID-19 should be considered a priority group for vaccination against COVID-19, as in other age groups. However, since hospitalisation, PIMS-TS/MIS-C and post COVID-19 condition can also occur among children with no known risk factors, consideration could be given to the vaccination of all children aged 5-11 years.
- COVID-19 vaccine safety data in children aged 5-11 years are currently limited, and the level of natural immunity in the unvaccinated and its duration are currently unknown and likely heterogeneous across the population.
- The main priority of COVID-19 vaccination campaigns seeking to reduce COVID-19-related morbidity and mortality remains to increase vaccine uptake in the eligible adult population. Before taking policy decisions on COVID-19 vaccination in children, potential harms and benefits – including the direct and indirect effects on health and well-being – should be considered alongside the vaccine uptake and epidemiological situation in a particular country. Aspects around implementation and health equity should also be taken into consideration.

Limitations and knowledge gaps

- COVID-19 vaccine efficacy and safety data in children aged 5-11 years are currently scarce and are being monitored.
- Incidence and overall burden of post COVID-19 condition in children aged 5-11 years cannot be accurately quantified.
- In the modelling analysis of the impact of vaccination of children on viral transmission, variations in social behaviour according to spatial/geographical heterogeneities, fluctuations of contacts over time, heterogeneities within age groups, age-specific transmissibility and risk of infection could not be quantified and accounted for.
- Potential changes in social behaviour and mixing patterns in the coming months are difficult to predict and assess.
- The impact of vaccinating children aged 5-11 years on the total burden of COVID-19 (including hospitalisation and deaths) in various age groups is uncertain.
- Data on vaccine effectiveness against transmission of the Delta VOC are currently limited and missing for children aged 5-11 years.
- Data on waning vaccine effectiveness are difficult to disentangle from reduced vaccine effectiveness due to the Delta VOC and could vary by disease outcome and age group.
- Accurate data on natural immunity in the unvaccinated population (and by age) is missing and its duration is currently unknown and likely heterogeneous across the population.
- The likelihood of getting infected with the Delta VOC for different age groups is difficult to quantify.
- The emergence of new variants of concern will introduce new uncertainties, thereby necessitating reassessment of the potential impact of vaccinating children.

Contributing ECDC experts

In alphabetical order: Kim Brolin, Nick Bundle, Edoardo Colzani, Nishi Dave, Charlotte Deogan, Tarik Derrough, Rok Grah, John Kinsman, Aikaterini Mougkou, Nathalie Nicolay, Ajibola Omokanye, Lucia Pastore Celentano, Anastasia Pharris, Bastian Prasse, Gabrielle Schittecatte, Jonathan Suk, Karin Wilbe Ramsay, Andrea Würz

External reviewers

Marco Cavaleri, European Medicines Agency (EMA)

Disclaimer

All data published in this report is correct to the best of our knowledge at the time of publication.

References

1. European Medicines Agency (EMA). COVID-19 Vaccine Moderna - COVID-19 mRNA Vaccine (nucleoside modified). Amsterdam: EMA; 2021. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/covid-19-vaccine-moderna
2. European Medicines Agency (EMA). Comirnaty - COVID-19 mRNA vaccine (nucleoside-modified). Amsterdam: EMA; 2021. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/comirnaty
3. European Medicines Agency (EMA). COVID-19 Vaccine Janssen - COVID-19 vaccine (Ad26.COV2-S [recombinant]). Amsterdam: EMA; 2021. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/covid-19-vaccine-janssen
4. European Medicines Agency (EMA). Vaxzevria (previously COVID-19 Vaccine AstraZeneca) - COVID-19 Vaccine (ChAdOx1-S [recombinant]). Amsterdam: EMA; 2021. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/vaxzevria-previously-covid-19-vaccine-astrazeneca
5. European Commission. Communication from the Commission to the European Parliament and the Council. A united front to beat COVID-19. Brussels: EC; 2021. Available at: https://ec.europa.eu/info/sites/info/files/communication-united-frontbeat-covid-19_en.pdf
6. European Centre for Disease Prevention and Control (ECDC). Overview of the implementation of COVID-19 vaccination strategies and deployment plans in the EU/EEA, 11 November 2021. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/overview-implementation-covid-19-vaccination-strategies-and-deployment-plans
7. European Centre for Disease Prevention and Control (ECDC). Weekly COVID-19 country overview. Week 45, 2021. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/covid-19/country-overviews
8. US Food and Drug Administration (FDA). Pfizer-BioNTech COVID-19 vaccine. Silver Spring: FDA; 2021. Available at: https://www.fda.gov/media/144412/download
9. European Medicines Agency (EMA). First COVID-19 vaccine approved for children aged 12 to 15 in EU. Amsterdam: EMA; 2021. Available at: https://www.ema.europa.eu/en/news/first-covid-19-vaccine-approved-children-aged-12-15-eu
10. European Medicines Agency (EMA). COVID-19 vaccine Spikevax approved for children aged 12 to 17 in EU. Amsterdam: EMA; 2021. Available at: https://www.ema.europa.eu/en/news/covid-19-vaccine-spikevax-approved-children-aged-12-17-eu
11. European Centre for Disease Prevention and Control (ECDC). COVID-19 Vaccine Tracker. Stockholm: ECDC; 2021. Available at: https://vaccinetracker.ecdc.europa.eu/
12. European Medicines Agency (EMA). Comirnaty COVID-19 vaccine: EMA recommends approval for children aged 5 to 11. Amsterdam: EMA; 2021. Available at: https://www.ema.europa.eu/en/news/comirnaty-covid-19-vaccine-ema-recommends-approval-children-aged-5-11
13. US Food and Drug Administration (FDA). Press release: FDA Authorizes Pfizer-BioNTech COVID-19 Vaccine for Emergency Use in Children 5 through 11 Years of Age. Silver Spring: FDA; 2021. Available at: https://www.fda.gov/news-events/press-announcements/fda-authorizes-pfizer-biontech-covid-19-vaccine-emergency-use-children-5-through-11-years-age
14. European Centre for Disease Prevention and Control (ECDC). 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
15. Stich M, Elling R, Renk H, Janda A, Garbade SF, Müller B, et al. Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 in Households with Children, Southwest Germany, May-August 2020. Emerg Infect Dis. 2021 Oct 25;27(12) Available at: https://pubmed.ncbi.nlm.nih.gov/34695369/
16. Viner RM, Mytton OT, Bonell C, Melendez-Torres GJ, Ward J, Hudson L, et al. Susceptibility to SARS-CoV-2 Infection Among Children and Adolescents Compared With Adults: A Systematic Review and Meta-analysis. JAMA Pediatrics. 2021;175(2):143-56. Available at: https://doi.org/10.1001/jamapediatrics.2020.4573
17. Misra P, Kant S, Guleria R, Rai SK, WHO Unity Seroprevalence study team of AIIMS. Serological prevalence of SARS-CoV-2 antibody among children and young age (between age 2-17 years) group in India: An interim result from a large multi-centric population-based seroepidemiological study. medRxiv. 2021:2021.06.15.21258880. Available at: http://medrxiv.org/content/early/2021/06/16/2021.06.15.21258880.abstract
18. Ulyte A, Radtke T, Abela IA, Haile SR, Berger C, Huber M, et al. Clustering and longitudinal change in SARS-CoV-2 seroprevalence in school children in the canton of Zurich, Switzerland: prospective cohort study of 55 schools. BMJ. 2021;372:n616. Available at: http://www.bmj.com/content/372/bmj.n616.abstract

19. Willeit P, Krause R, Lamprecht B, Berghold A, Hanson B, Stelzl E, et al. Prevalence of RT-qPCR-detected SARS-CoV-2 infection at schools: First results from the Austrian School-SARS-CoV-2 prospective cohort study. The Lancet Regional Health – Europe. 2021;5. Available at: https://doi.org/10.1016/j.lanepe.2021.100086
20. Meuris C, Kremer C, Geerinck A, Locquet M, Bruyère O, Defêche J, et al. Transmission of SARS-CoV-2 After COVID-19 Screening and Mitigation Measures for Primary School Children Attending School in Liège, Belgium. JAMA Netw Open. 2021;4(10):e2128757-e. Available at: https://doi.org/10.1001/jamanetworkopen.2021.28757
21. Dawood FS, Porucznik CA, Veguilla V, Stanford JB, Duque J, Rolfes MA, et al. Incidence Rates, Household Infection Risk, and Clinical Characteristics of SARS-CoV-2 Infection Among Children and Adults in Utah and New York City, New York. JAMA Pediatrics. 2021;e214217. Available at: https://doi.org/10.1001/jamapediatrics.2021.4217
22. European Centre for Disease Prevention and Control (ECDC). 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. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/rapid-risk-assessment-assessing-sars-cov-2-circulation-variants-concern
23. Lam-Hine T, McCurdy SA, Santora L, Duncan L, Corbett-Detig R, Kapusinszky B, et al. Outbreak Associated with SARS-CoV-2 B.1.617.2 (Delta) Variant in an Elementary School - Marin County, California, May-June 2021. MMWR Morbidity and mortality weekly report. 2021 Sep 3;70(35):1214-9. Available at: https://doi.org/10.15585/mmwr.mm7035e2
24. Chadeau-Hyam M, Wang H, Eales O, Haw D, Bodinier B, Whitaker M, et al. REACT-1 study round 14: High and increasing prevalence of SARS-CoV-2 infection among school-aged children during September 2021 and vaccine effectiveness against infection in England. medRxiv. 2021:2021.10.14.21264965. Available at: http://medrxiv.org/content/early/2021/10/22/2021.10.14.21264965.abstract
25. Chadeau-Hyam M, Eales, O, Bodinier, B, Wang, H, Haw, D, Whitaker, M, et al. REACT-1 round 15 final report: Increased breakthrough SARS-CoV-2 infections among adults who had received two doses of vaccine, but booster doses and first doses in children are providing important protection. London: Imperial College London; 2021. Available at: http://hdl.handle.net/10044/1/92501
26. Rostad CA, Kamidani S, Anderson EJ. Implications of SARS-CoV-2 Viral Load in Children: Getting Back to School and Normal. JAMA Pediatr. 2021 Oct 1;175(10):e212022. Available at: https://doi.org/10.1001/jamapediatrics.2021.2022
27. Polese-Bonatto M, Sartor ITS, Varela FH, Giannini GLT, Azevedo TR, Kern LB, et al. Children Have Similar Reverse Transcription Polymerase Chain Reaction Cycle Threshold for Severe Acute Respiratory Syndrome Coronavirus 2 in Comparison With Adults. Pediatr Infect Dis J. 2021 Nov 1;40(11):e413-e7. Available at: https://journals.lww.com/pidj/Fulltext/2021/11000/Children_Have_Similar_Reverse_Transcription.11.aspx
28. Yonker LM, Boucau J, Regan J, Choudhary MC, Burns MD, Young N, et al. Virologic features of SARS-CoV-2 infection in children. medRxiv. 2021 Aug 17. Available at: https://www.medrxiv.org/content/10.1101/2021.05.30.21258086v2
29. Strutner J, Ramchandar N, Dubey S, Gamboa M, Vanderpool MK, Mueller T, et al. Comparison of RT-PCR Cycle Threshold Values from Respiratory Specimens in Symptomatic and Asymptomatic Children with SARS-CoV-2 Infection. Clinical Infectious Diseases. 2021;ciab403. Available at: https://doi.org/10.1093/cid/ciab403
30. Tagarro A, Sanz-Santaeufemia FJ, Grasa C, Cobos E, Yebra J, Alonso-Cadenas JA, et al. Dynamics of RT-PCR and Serologic Test Results in Children with SARS-CoV-2 Infection. The Journal of pediatrics. 2021:S0022-3476(21)00905-7. Available at: https://pubmed.ncbi.nlm.nih.gov/34571020
31. Paul LA, Daneman N, Schwartz KL, Science M, Brown KA, Whelan M, et al. Association of Age and Pediatric Household Transmission of SARS-CoV-2 Infection. JAMA Pediatrics. 2021;175(11):1151-8. Available at: https://doi.org/10.1001/jamapediatrics.2021.2770
32. Burke RM, Calderwood L, Killerby ME, Ashworth CE, Berns AL, Brennan S, et al. Patterns of Virus Exposure and Presumed Household Transmission among Persons with Coronavirus Disease, United States, January-April 2020. Emerg Infect Dis. 2021 Sep;27(9):2323-32. Available at: https://doi.org/10.3201/eid2709.204577
33. Vlachos J, Hertegård E, H BS. The effects of school closures on SARS-CoV-2 among parents and teachers. Proc Natl Acad Sci USA. 2021 Mar 2;118(9). Available at: https://doi.org/10.1073/pnas.2020834118
34. Lessler J, Grabowski MK, Grantz KH, Badillo-Goicoechea E, Metcalf CJE, Lupton-Smith C, et al. Household COVID-19 risk and in-person schooling. Science. 2021 Jun 4;372(6546):1092-7. Available at: https://dx.doi.org/10.1126%2Fscience.abh2939
35. Calvani M, Cantiello G, Cavani M, Lacorte E, Mariani B, Panetta V, et al. Reasons for SARS-CoV-2 infection in children and their role in the transmission of infection according to age: a case-control study. Italian Journal of Pediatrics. 2021;47(1):193. Available at: https://doi.org/10.1186/s13052-021-01141-1

36. Vardavas C, Nikitara K, Mathioudakis A, Hilton-Boon M, Phalkey R, Leonardi-Bee J, et al. The role of educational settings in the transmission chain of SARS-CoV-2 in 2020: a systematic review. medRxiv. 2021:2021.10.13.21264932. Available at: http://medrxiv.org/content/early/2021/10/16/2021.10.13.21264932.abstract

37. Robert Koch Institut. Wöchentlicher Lageberich des RKI zur Coronavirus-Krankheit-2019 (COVID-19) 14.10.21. Berlin: RKI; 2021. Available at: https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Situationsberichte/Wochenbericht/Wochenbericht_2021-10-14.pdf

38. Preston LE, Chevinsky JR, Kompaniyets L, Lavery AM, Kimball A, Boehmer TK, et al. Characteristics and Disease Severity of US Children and Adolescents Diagnosed With COVID-19. JAMA Netw Open. 2021 Apr 1;4(4):e215298. Available at: https://doi.org/10.1001/jamanetworkopen.2021.5298

39. Shi Q, Wang Z, Liu J, Wang X, Zhou Q, Li Q, et al. Risk factors for poor prognosis in children and adolescents with COVID-19: A systematic review and meta-analysis. EClinicalMedicine. 2021 Nov;41:101155. Available at: https://doi.org/10.1016/j.eclinm.2021.101155

40. Graff K, Smith C, Silveira L, Jung S, Curran-Hays S, Jarjour J, et al. Risk Factors for Severe COVID-19 in Children. Pediatr Infect Dis J. 2021 Apr 1;40(4):e137-e45. Available at: https://doi.org/10.1097/inf.0000000000003043

41. Swann OV, Holden KA, Turtle L, Pollock L, Fairfield CJ, Drake TM, et al. Clinical characteristics of children and young people admitted to hospital with covid-19 in United Kingdom: prospective multicentre observational cohort study. BMJ. 2020;370:m3249. Available at: http://www.bmj.com/content/370/bmj.m3249.abstract

42. Abrams JY, Oster ME, Godfred-Cato SE, Bryant B, Datta SD, Campbell AP, et al. Factors linked to severe outcomes in multisystem inflammatory syndrome in children (MIS-C) in the USA: a retrospective surveillance study. Lancet Child Adolesc Health. 2021 May;5(5):323-31. Available at: https://doi.org/10.1016/s2352-4642(21)00050-x

43. Antoon JW, Grijalva CG, Thurm C, Richardson T, Spaulding AB, Teufel RJ, 2nd, et al. Factors Associated With COVID-19 Disease Severity in US Children and Adolescents. J Hosp Med. 2021 Oct;16(10):603-10. Available at: https://doi.org/10.12788/jhm.368910

44. Woodruff RC, Campbell AP, Taylor CA, Chai SJ, Kawasaki B, Meek J, et al. Risk Factors for Severe COVID-19 in Children. Pediatrics. 2021 Oct 22 Available at: https://doi.org/10.1542/peds.2021-053418

45. Harwood R, Yan H, Da Camara NT, Smith C, Ward J, Tudur-Smith C, et al. Which children and young people are at higher risk of severe disease and death after SARS-CoV-2 infection: a systematic review and individual patient meta-analysis. medRxiv. 2021:2021.06.30.21259763. Available at: http://medrxiv.org/content/early/2021/07/08/2021.06.30.21259763.abstract

46. Badal S, Thapa Bajgain K, Badal S, Thapa R, Bajgain BB, Santana MJ. Prevalence, clinical characteristics, and outcomes of pediatric COVID-19: A systematic review and meta-analysis. Journal of Clinical Virology. 2021;135:104715. Available at: https://www.sciencedirect.com/science/article/pii/S1386653220304571

47. Qi K, Zeng W, Ye M, Zheng L, Song C, Hu S, et al. Clinical, laboratory, and imaging features of pediatric COVID-19: A systematic review and meta-analysis. Medicine (Baltimore). 2021;100(15):e25230-e. Available at: https://pubmed.ncbi.nlm.nih.gov/33847620

48. Stringhini S, Zaballa M-E, Pullen N, Perez-Saez J, de Mestral C, Loizeau AJ, et al. Seroprevalence of anti-SARS-CoV-2 antibodies 6 months into the vaccination campaign in Geneva, Switzerland, 1 June to 7 July 2021. Euro Surveill. 2021;26(43):2100830. Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.43.2100830

49. Public Health Agency of Sweden. Påvisning av antikroppar mot SARS-CoV-2 i blodprov från öppenvården. Solna: Public Health Agency of Sweden; 2021. Available at: https://www.folkhalsomyndigheten.se/nyheter-och-press/nyhetsarkiv/2021/juli/antikroppar-mot-covid-19-okar-i-alla-grupper/

50. Public Health Scotland. Population-based seroprevalence surveillance 13 October 2021. Edinburgh: Public Health Scotland; 2021. Available at: https://publichealthscotland.scot/publications/enhanced-surveillance-of-covid-19-in-scotland/enhanced-surveillance-of-covid-19-in-scotland-population-based-seroprevalence-surveillance-13-october-2021/

51. Sciensano. Prevalence and incidence of antibodies against SARS-CoV-2 in children and school staff measured between December 2020 and June 2021: Findings of the third testing period – brief summary. Elsene: Sciensano; 2021. Available at: https://www.sciensano.be/en/biblio/prevalence-and-incidence-antibodies-against-sars-cov-2-children-and-school-staff-measured-between-2

52. US Food and Drug Administration (FDA). Event Materials for Vaccines and Related Biological Products Advisory Committee Meeting October 26, 2021. Meeting Presentation- Epidemiology of COVID19 in Children Aged 5 – 11 years. Silver Spring: FDA; 2021. Available at: https://www.fda.gov/media/153508/download

53. Toh ZQ, Anderson J, Mazarakis N, Neeland M, Higgins RA, Rautenbacher K, et al. Reduced seroconversion in children compared to adults with mild COVID-19. medRxiv. 2021:2021.10.17.21265121. Available at: http://medrxiv.org/content/early/2021/10/18/2021.10.17.21265121.abstract

54. Molteni E, Sudre CH, Canas LS, Bhopal SS, Hughes RC, Chen L, et al. Illness characteristics of COVID-19 in children infected with the SARS-CoV-2 Delta variant. medRxiv. 2021:2021.10.06.21264467. Available at: http://medrxiv.org/content/early/2021/10/07/2021.10.06.21264467.abstract

55. Ben-Shimol S, Livni G, Megged O, Greenberg D, Danino D, Youngster I, et al. COVID-19 in a Subset of Hospitalized Children in Israel. Journal of the Pediatric Infectious Diseases Society. 2021;10(7):757-65. Available at: https://doi.org/10.1093/jpids/piab035

56. Deutschen Gesellschaft für Pädiatrische Infektiologie. Infektions- und Übertragungsrisiken von SARS-CoV-2 und die Morbidität und Mortalität bei Kindern und Jugendlichen. Einfluss von saisonalem Verlauf, Virusvarianten und Impfeffekten. Stellungnahme der Deutschen Gesellschaft für Krankenhaushygiene (DGKH) und der Deutschen Gesellschaft für Pädiatrische Infektiologie (DGPI). Berlin: DGPI; 2021. Available at: https://dgpi.de/sars-cov-2-risiken-kinder-einfluss-saisonalem-verlauf-virusvarianten-impfeffekt/

57. Siegel DA, Reses HE, Cool AJ, Shapiro CN, Hsu J, Boehmer TK, et al. Trends in COVID-19 Cases, Emergency Department Visits, and Hospital Admissions Among Children and Adolescents Aged 0-17 Years - United States, August 2020-August 2021. MMWR Morbidity and mortality weekly report. 2021;70(36):1249-54. Available at: https://pubmed.ncbi.nlm.nih.gov/34499628

58. Smith C, Odd D, Harwood R, Ward J, Linney M, Clark M, et al. Deaths in children and young people in England after SARS-CoV-2 infection during the first pandemic year. Nature Medicine. 2021;10.1038/s41591-021-01578. Available at: https://doi.org/10.1038/s41591-021-01578-1

59. Bhopal SS, Bagaria J, Olabi B, Bhopal R. Children and young people remain at low risk of COVID-19 mortality. Lancet Child Adolesc Health. 2021;5(5):e12-e3. Available at: https://pubmed.ncbi.nlm.nih.gov/33713603

60. Molteni E, Sudre CH, Canas LS, Bhopal SS, Hughes RC, Antonelli M, et al. Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2. Lancet Child Adolesc Health. 2021;5(10):708-18. Available at: https://pubmed.ncbi.nlm.nih.gov/34358472

61. Sheikh A, McMenamin J, Taylor B, Robertson C, Public Health S, the EIIC. SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. Lancet. 2021;397(10293):2461-2. Available at: https://pubmed.ncbi.nlm.nih.gov/34139198

62. 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. The Lancet Infectious Diseases. 2021;S1473-3099(21):00475-8. Available at: https://doi.org/10.1016/S1473-3099(21)00475-8

63. 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. MMWR Morbidity and mortality weekly report. 2021;70(36):1255-60. Available at: https://pubmed.ncbi.nlm.nih.gov/34499627

64. Boehmer TK, Kompaniyets L, Lavery AM, Hsu J, Ko JY, Yusuf H, et al. Association Between COVID-19 and Myocarditis Using Hospital-Based Administrative Data - United States, March 2020-January 2021. MMWR Morbidity and mortality weekly report. 2021;70(35):1228-32. Available at: https://pubmed.ncbi.nlm.nih.gov/34473684

65. Nygaard U, Holm M, Bohnstedt C, Chai Q, Schmidt LS, Hartling UB, et al. Population-based incidence of myopericarditis after COVID-19 vaccination in Danish adolescents. The Pediatric Infectious Disease Journal. 2021. Available at: https://journals.lww.com/pidj/Fulltext/9000/POPULATION_BASED_INCIDENCE_OF_MYOPERICARDITIS.95639.aspx

66. World Health Organization (WHO). Multisystem inflammatory syndrome in children and adolescents with COVID-19. Scientific Brief. Geneva: WHO; 2021. Available at: https://www.who.int/publications/i/item/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19

67. Royal College of Paediatrics and Child Health (RCPCH). Paediatric multisystem inflammatory syndrome temporally associated with COVID-19 (PIMS) - guidance for clinicians. London: RCPCH; 2021. Available at: https://www.rcpch.ac.uk/resources/paediatric-multisystem-inflammatory-syndrome-temporally-associated-covid-19-pims-guidance

68. Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, et al. Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2. Jama. 2020 Jul 21;324(3):259-69. Available at: https://jamanetwork.com/journals/jama/fullarticle/2767209

69. Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. N Engl J Med. 2020;383(4):334-46. Available at: https://pubmed.ncbi.nlm.nih.gov/32598831

70. Valverde I, Singh Y, Sanchez-de-Toledo J, Theocharis P, Chikermane A, Di Filippo S, et al. Acute Cardiovascular Manifestations in 286 Children With Multisystem Inflammatory Syndrome Associated With COVID-19 Infection in Europe. Circulation. 2021 Jan 5;143(1):21-32. Available at: https://doi.org/10.1161/circulationaha.120.050065

71. Sacco K, Castagnoli R, Vakkilainen S, Liu C, Delmonte OM, Oguz C, et al. Multi-omics approach identifies novel age-, time- and treatment-related immunopathological signatures in MIS-C and pediatric COVID-19. medRxiv. 2021:2021.09.24.21263853. Available at: http://medrxiv.org/content/early/2021/09/27/2021.09.24.21263853.abstract

72. Tripathi S, Gist KM, Bjornstad EC, Kashyap R, Boman K, Chiotos K, et al. Coronavirus Disease 2019-Associated PICU Admissions: A Report From the Society of Critical Care Medicine Discovery Network Viral Infection and Respiratory Illness Universal Study Registry. Pediatric critical care medicine: a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies. 2021 Jul 1;22(7):603-15. Available at: https://doi.org/10.1097/pcc.0000000000002760

73. Ouldali N, Yang DD, Madhi F, Levy M, Gaschignard J, Craiu I, et al. Factors Associated With Severe SARS-CoV-2 Infection. Pediatrics. 2021;147(3):e2020023432. Available at: http://pediatrics.aappublications.org/content/147/3/e2020023432.abstract

74. Kahn R, Berg S, Berntson L, Berthold E, Brodin P, Bäckström F, et al. Population-based study of multisystem inflammatory syndrome associated with COVID-19 found that 36% of children had persistent symptoms. Acta Paediatr. 2021 Nov 22. Available at: https://doi.org/10.1111/apa.16191

75. Hoste L, Van Paemel R, Haerynck F. Multisystem inflammatory syndrome in children related to COVID-19: a systematic review. Eur J Pediatr. 2021;180(7):2019-34. Available at: https://pubmed.ncbi.nlm.nih.gov/33599835

76. Størdal K, Ruiz PL-D, Greve-Isdahl M, Surén P, Knudsen PK, Løvdal Gulseth H, et al. Risk factors for SARS-CoV-2 infection and hospitalisation in children and adolescents in Norway: A nationwide population-based study. medRxiv. 2021:2021.07.01.21259887. Available at: http://medrxiv.org/content/early/2021/07/05/2021.07.01.21259887.abstract

77. Harwood R, Allin B, Jones CE, Whittaker E, Ramnarayan P, Ramanan AV, et al. A national consensus management pathway for paediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS): results of a national Delphi process. The Lancet Child & Adolescent Health. 2021;5(2):133-41. Available at: https://doi.org/10.1016/S2352-4642(20)30304-7

78. Schlapbach LJ, Andre MC, Grazioli S, Schöbi N, Ritz N, Aebi C, et al. Best Practice Recommendations for the Diagnosis and Management of Children With Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2 (PIMS-TS; Multisystem Inflammatory Syndrome in Children, MIS-C) in Switzerland. Front Pediatr. 2021;9(396). Available at: https://www.frontiersin.org/article/10.3389/fped.2021.667507

79. Payne AB, Gilani Z, Godfred-Cato S, Belay ED, Feldstein LR, Patel MM, et al. Incidence of Multisystem Inflammatory Syndrome in Children Among US Persons Infected With SARS-CoV-2. JAMA Netw Open. 2021;4(6):e2116420-e. Available at: https://doi.org/10.1001/jamanetworkopen.2021.16420

80. Fouriki A, Fougère Y, De Camaret C, Blanchard Rohner G, Grazioli S, Wagner N, et al. Case Report: Case Series of Children With Multisystem Inflammatory Syndrome Following SARS-CoV-2 Infection in Switzerland. Front Pediatr. 2021;8(863). Available at: https://www.frontiersin.org/article/10.3389/fped.2020.594127

81. Remppis J, Ganzenmueller T, Kohns Vasconcelos M, Heinzel O, Handgretinger R, Renk H. A case series of children and young people admitted to a tertiary care hospital in Germany with COVID-19. BMC Infectious Diseases. 2021;21(1):133. Available at: https://doi.org/10.1186/s12879-021-05791-8

82. Santé Publique France. Surveillance des cas de syndrome inflammatoire multi-systémique pédiatrique (PIMS ou MIS-C). Bilan au 28 septembre 2021. Saint-Maurice: Santé Publique France; 2021. Available at: https://www.santepubliquefrance.fr/etudes-et-enquetes/surveillance-nationale-des-cas-de-syndrome-inflammatoire-multi-systemique-pediatrique-pims/documents/bulletin-national/surveillance-des-cas-de-syndrome-inflammatoire-multi-systemique-pediatrique-pims-ou-mis-c-.-bilan-au-28-septembre-2021

83. Toubiana J, Poirault C, Corsia A, Bajolle F, Fourgeaud J, Angoulvant F, et al. Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study. BMJ. 2020;369:m2094. Available at: http://www.bmj.com/content/369/bmj.m2094.abstract

84. Moraleda C, Serna-Pascual M, Soriano-Arandes A, Simó S, Epalza C, Santos M, et al. Multi-inflammatory Syndrome in Children Related to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Spain. Clinical Infectious Diseases. 2021;72(9):e397-e401. Available at: https://doi.org/10.1093/cid/ciaa1042

85. Svensk Barnreumatologisk Förening (SBRF). Uppdaterat utlåtande från Svensk Barnreumatologisk Förening angående MIS-C, (Multisystem Inflammatory Syndrome), oktober 2021. SBRF; 2021. Available at: https://reuma.barnlakarforeningen.se/2021/10/12/uppdaterat-utlatande-fran-svensk-barnreumatologisk-forening-angaende-mis-c-multisystem-inflammatory-syndrome-augusti-2021/

86. Holm M, Hartling UB, Schmidt LS, Glenthøj JP, Kruse A, Rytter MH, et al. Multisystem inflammatory syndrome in children occurred in one of four thousand children with severe acute respiratory syndrome coronavirus 2. Acta Paediatrica. 2021;110(9):2581-3. Available at: https://doi.org/10.1111/apa.15985

87. Zimmermann P, Pittet LF, Curtis N. How Common Is Long COVID in Children and Adolescents? The Pediatric Infectious Disease Journal. 2021;40(12): e482-e487. Available at: https://journals.lww.com/pidj/Fulltext/9000/How_Common_Is_Long_COVID_in_Children_and.95677.aspx

88. Office for National Statistics (ONS). Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK: 7 October 2021. Estimates of the prevalence of self-reported "long COVID" and associated activity limitation, using UK Coronavirus (COVID-19) Infection Survey data. Newport: ONS; 2021. Available at: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/7october2021

89. Stephenson T, Shafran R, De Stavola B, Rojas N, Aiano F, Amin-Chowdhury Z, et al. Long COVID and the mental and physical health of children and young people: national matched cohort study protocol (the CLoCk study). BMJ Open. 2021;11(8):e052838-e. Available at: https://pubmed.ncbi.nlm.nih.gov/34446502

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8392739/

90. Roge I, Smane L, Kivite-Urtane A, Pucuka Z, Racko I, Klavina L, et al. Comparison of Persistent Symptoms After COVID-19 and Other Non-SARS-CoV-2 Infections in Children. Front Pediatr. 2021;9:752385. Available at: https://pubmed.ncbi.nlm.nih.gov/34778143

91. Brackel CLH, Lap CR, Buddingh EP, van Houten MA, van der Sande L, Langereis EJ, et al. Pediatric long-COVID: An overlooked phenomenon? Pediatric pulmonology. 2021 Aug;56(8):2495-502.

92. Roessler M, Tesch F, Batram M, Jacob J, Loser F, Weidinger O, et al. Post COVID-19 in children, adolescents, and adults: results of a matched cohort study including more than 150,000 individuals with COVID-19. medRxiv. 2021:2021.10.21.21265133. Available at: http://medrxiv.org/content/early/2021/10/22/2021.10.21.21265133.abstract

93. Hillis SD, Unwin HJT, Chen Y, Cluver L, Sherr L, Goldman PS, et al. Global minimum estimates of children affected by COVID-19-associated orphanhood and deaths of caregivers: a modelling study. Lancet. 2021;398(10298):391-402. Available at: https://pubmed.ncbi.nlm.nih.gov/34298000

94. McCoy DC, Cuartas J, Behrman J, Cappa C, Heymann J, López Bóo F, et al. Global estimates of the implications of COVID-19-related preprimary school closures for children's instructional access, development, learning, and economic wellbeing. Child Development. 2021;92(5):e883-e99. Available at: https://doi.org/10.1111/cdev.13658

95. United Nations Children's Fund (UNICEF) and European Training Foundation (ETF). Preventing a 'lockdown generation' in Europe and Central Asia. Building resilient societies with young people in the era of COVID-19. New York: UNICEF; 2020. Available at: https://www.unicef.org/eca/media/14671/file/UNICEF_ETF_report.pdf

96. Melchior M. Social inequalities in children's mental health: isn't it time for action? European Child & Adolescent Psychiatry. 2021;30(9):1317-8. Available at: https://doi.org/10.1007/s00787-021-01855-x

97. Hefferon C, Taylor C, Bennett D, Falconer C, Campbell M, Williams JG, et al. Priorities for the child public health response to the COVID-19 pandemic recovery in England. Archives of Disease in Childhood. 2021;106(6):533. Available at: http://adc.bmj.com/content/106/6/533.abstract

98. Ford T, John A, Gunnell D. Mental health of children and young people during pandemic. BMJ. 2021;372:n614. Available at: http://www.bmj.com/content/372/bmj.n614.abstract

99. Calvano C, Engelke L, Di Bella J, Kindermann J, Renneberg B, Winter SM. Families in the COVID-19 pandemic: parental stress, parent mental health and the occurrence of adverse childhood experiences—results of a representative survey in Germany. European Child & Adolescent Psychiatry. 2021;Mar 1:1-13. Available at: https://doi.org/10.1007/s00787-021-01739-0

100. Viner R, Russell S, Saulle R, Croker H, Stansfeld C, Packer J, et al. Impacts of school closures on physical and mental health of children and young people: a systematic review. medRxiv. 2021:2021.02.10.21251526. Available at: http://medrxiv.org/content/early/2021/02/12/2021.02.10.21251526.abstract

101. Chaabane S, Doraiswamy S, Chaabna K, Mamtani R, Cheema S. The Impact of COVID-19 School Closure on Child and Adolescent Health: A Rapid Systematic Review. Children. 2021;8(5). Available at: https://doi.org/10.3390/children8050415

102. Waite P, Pearcey S, Shum A, Raw JAL, Patalay P, Creswell C. How did the mental health symptoms of children and adolescents change over early lockdown during the COVID-19 pandemic in the UK? JCPP advances. 2021 Apr;1(1):e12009. Available at: https://acamh.onlinelibrary.wiley.com/doi/10.1111/jcv2.12009

103. Michael Marmot JA, Peter Goldblatt, Eleanor Herd, Joana Morrison. Build Back Fairer: The COVID-19 Marmot Review. The Pandemic, Socioeconomic and Health Inequalities in England. London: Institute of Health Equity; 2021. Available at: https://www.health.org.uk/publications/build-back-fairer-the-covid-19-marmot-review

104. Baron EJ, Goldstein EG, Wallace CT. Suffering in silence: How COVID-19 school closures inhibit the reporting of child maltreatment. Journal of Public Economics. 2020;190:104258. Available at: https://www.sciencedirect.com/science/article/pii/S0047272720301225

105. Otto AK, Jary JM, Sturza J, Miller CA, Prohaska N, Bravender T, et al. Medical Admissions Among Adolescents With Eating Disorders During the COVID-19 Pandemic. Pediatrics. 2021;148(4):e2021052201. Available at: http://pediatrics.aappublications.org/content/148/4/e2021052201.abstract

106. Mayne SL, Hannan C, Davis M, Young JF, Kelly MK, Powell M, et al. COVID-19 and Adolescent Depression and Suicide Risk Screening Outcomes. Pediatrics. 2021;148(3). Available at: https://doi.org/10.1542/peds.2021-051507

107. American Academy of Pediatrics (AAP). AAP-AACAP-CHA Declaration of a National Emergency in Child and Adolescent Mental Health. Itasca: AAP; 2021. Available at: https://www.aap.org/en/advocacy/child-and-adolescent-healthy-mental-development/aap-aacap-cha-declaration-of-a-national-emergency-in-child-and-adolescent-mental-health

108. Human Rights Watch. "Years Don't Wait for Them". Increased Inequality in Children's Right to Education Due to the Covid-19 Pandemic. New York: Human Rights Watch; 2021. Available at: https://www.hrw.org/report/2021/05/17/years-dont-wait-them/increased-inequalities-childrens-right-education-due-covid

109. Grewenig E, Lergetporer P, Werner K, Woessmann L, Zierow L. COVID-19 and educational inequality: How school closures affect low- and high-achieving students. European Economic Review. 2021;140:103920. Available at: https://www.sciencedirect.com/science/article/pii/S0014292121002245

110. Dove N WJ, Gustafson R, Corneil T. Impact of School Closures on Learning, Child and Family Well-Being During the COVID-19 Pandemic. Vancouver: BC Centre for Disease Control & BC Children's Hospital; 2020. Available at: http://www.bccdc.ca/Health-Info-Site/Documents/Public_health_COVID-19_reports/Impact_School_Closures_COVID-19.pdf

111. Engzell P, Frey A, Verhagen MD. Learning loss due to school closures during the COVID-19 pandemic. Proceedings of the National Academy of Sciences. 2021;118(17):e2022376118. Available at: http://www.pnas.org/content/118/17/e2022376118.abstract

112. United Nations Educational SaCOU. Adverse consequences of school closures. Paris: UNESCO; 2021. Available at: https://en.unesco.org/covid19/educationresponse/consequences

113. Azevedo JP HA, Goldemberg D, Iqbal SA, Geven K. Simulating the potential impacts of COVID-19 school closures on schooling and learning outcomes: A set of global estimates. New York: The World Bank; 2020. Available at: https://thedocs.worldbank.org/en/doc/798061592482682799-0090022020/original/covidandeducationJune17r6.pdf

114. Psacharopoulos G, Collis V, Patrinos HA, Vegas E. The COVID-19 Cost of School Closures in Earnings and Income across the World. Comparative Education Review. 2021;65(2):271-87. Available at: https://doi.org/10.1086/713540

115. Gallagher-Mackay K, Srivastava P, Underwood K, Dhuey E, McCready L, Born KB, et al. COVID-19 and education disruption in Ontario: emerging evidence on impacts. Science Briefs of the Ontario COVID-19 Science Advisory Table. 2021;2(34). Available at: https://doi.org/10.47326/ocsat.2021.02.34.1.0

116. United Nations Children's Fund (UNICEF) and European Training Foundation (ETF). The State of the World's Children 2021. On My Mind: Promoting, protecting and caring for children's mental health. New York: UNICEF; 2021. Available at: https://www.unicef.org/reports/state-worlds-children-2021

117. Walter EB, Talaat KR, Sabharwal C, Gurtman A, Lockhart S, Paulsen GC, et al. Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age. New England Journal of Medicine. 2021. Available at: https://doi.org/10.1056/NEJMoa2116298

118. Ali K, Berman G, Zhou H, Deng W, Faughnan V, Coronado-Voges M, et al. Evaluation of mRNA-1273 SARS-CoV-2 Vaccine in Adolescents. New England Journal of Medicine. 2021. Available at: https://doi.org/10.1056/NEJMoa2109522

119. Frenck RW, Klein NP, Kitchin N, Gurtman A, Absalon J, Lockhart S, et al. Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents. New England Journal of Medicine. 2021;385(3):239-50. Available at: https://doi.org/10.1056/NEJMoa2107456

120. Glatman-Freedman A, Hershkovitz Y, Kaufman Z, Dichtiar R, Keinan-Boker L, Bromberg M. Effectiveness of BNT162b2 Vaccine in Adolescents during Outbreak of SARS-CoV-2 Delta Variant Infection, Israel, 2021. Emerg Infect Dis. 2021 Nov;27(11):2919-22. Available at: https://wwwnc.cdc.gov/eid/article/27/11/21-1886_article

121. BioNTech SE. A Phase 1/2/3 Study to Evaluate the Safety, Tolerability, and Immunogenicity of an RNA Vaccine Candidate Against COVID-19 in Healthy Children and Young Adults. NCT04816643. Bethesda: US National Library of Medicine; 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT04816643

122. ModernaTX I. A Study to Evaluate Safety and Effectiveness of mRNA-1273 COVID-19 Vaccine in Healthy Children Between 6 Months of Age and Less Than 12 Years of Age. NCT04796896. Bethesda: US National Library of Medicine; 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT04796896
123. Moderna Inc. Press release: Moderna Announces Positive Top Line Data from Phase 2/3 Study of COVID-19 Vaccine in Children 6 to 11 Years of Age. Cambridge: Moderna, Inc.; 2021. Available at: https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-positive-top-line-data-phase-23-study-covid-19
124. European Medicines Agency (EMA). Safety of COVID-19 vaccines. Amsterdam: EMA; 2021. Available at: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/safety-covid-19-vaccines
125. US Centers for Disease Control and Prevention (CDC). Myocarditis and Pericarditis Following mRNA COVID-19 Vaccination. Atlanta: CDC; 2021. Available at: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis
126. European Medicines Agency (EMA). Comirnaty and Spikevax: possible link to very rare cases of myocarditis and pericarditis. Amsterdam: EMA; 2021. Available at: https://www.ema.europa.eu/en/news/comirnaty-spikevax-possible-link-very-rare-cases-myocarditis-pericarditis
127. EPI-PHARE. Myocardite et péricardite après la vaccination Covid-19. Saint-Denis: EPI-PHARE; 2021. Available at: https://www.epi-phare.fr/rapports-detudes-et-publications/myocardite-pericardite-vaccination-covid19/
128. Public Health Ontario. Myocarditis and Pericarditis Following Vaccination with COVID-19 mRNA Vaccines in Ontario: December 13, 2020 to September 4, 2021. Toronto: Public Health Ontario; 2021. Available at: https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-myocarditis-pericarditis-vaccines-epi.pdf?sc_lang=en
129. European Medicines Agency (EMA). Comirnaty Product Information Safety Updates. Amsterdam: EMA; 2021. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/comirnaty#safety-updates-section
130. European Medicines Agency (EMA). Spikevax Product Information Satefy Updates. Amsterdam: EMA; 2021. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/spikevax
131. Barda N, Dagan N, Ben-Shlomo Y, Kepten E, Waxman J, Ohana R, et al. Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting. New England Journal of Medicine. 2021;385(12):1078-90. Available at: https://doi.org/10.1056/NEJMoa2110475
132. Rathore SS, Rojas GA, Sondhi M, Pothuru S, Pydi R, Kancherla N, et al. Myocarditis associated with Covid-19 disease: A systematic review of published case reports and case series. International journal of clinical practice. 2021 Nov;75(11):e14470. Available at: https://onlinelibrary.wiley.com/doi/10.1111/ijcp.14470
133. Ainslie KEC, Backer J, de Boer P, van Hoek AJ, Klinkenberg D, Altes HK, et al. The impact of vaccinating adolescents and children on COVID-19 disease outcomes. medRxiv. 2021:2021.10.21.21265318. Available at: http://medrxiv.org/content/early/2021/10/25/2021.10.21.21265318.abstract
134. Milne GJ, Carrivick J, Whyatt D. Non-pharmaceutical interventions and vaccinating school children required to contain SARS-CoV-2 Delta variant outbreaks in Australia: a modelling analysis. medRxiv. 2021:2021.10.03.21264492. Available at: http://medrxiv.org/content/early/2021/10/04/2021.10.03.21264492.abstract
135. Tran Kiem C, Massonnaud CR, Levy-Bruhl D, Poletto C, Colizza V, Bosetti P, et al. A modelling study investigating short and medium-term challenges for COVID-19 vaccination: From prioritisation to the relaxation of measures. EClinicalMedicine. 2021 Aug;38:101001. Available at: https://doi.org/10.1016/j.eclinm.2021.101001
136. Vaughan A, et al. Seroprevalence of SARS-CoV-2 across the WHO European Region, January - December 2020. Manuscript in development. 2021.
137. Britton T, Ball F, Trapman P. A mathematical model reveals the influence of population heterogeneity on herd immunity to SARS-CoV-2. Science. 2020;369(6505):846-9. Available at: https://pubmed.ncbi.nlm.nih.gov/32576668
138. Verelst F, Hermans L, Vercruysse S, Gimma A, Coletti P, Backer JA, et al. SOCRATES-CoMix: a platform for timely and open-source contact mixing data during and in between COVID-19 surges and interventions in over 20 European countries. BMC Medicine. 2021;19(1):254. Available at: https://doi.org/10.1186/s12916-021-02133-y
139. Wong BLH, Ramsay ME, Ladhani SN. Should children be vaccinated against COVID-19 now? Archives of Disease in Childhood. 2021:archdischild-2020-321225. Available at: http://adc.bmj.com/content/early/2021/09/22/archdischild-2020-321225.abstract
140. Mujica OJ, Victora CG. Social vulnerability as a risk factor for death due to severe paediatric COVID-19. Lancet Child Adolesc Health. 2021 Aug;5(8):533-5. Available at: https://pubmed.ncbi.nlm.nih.gov/34119026/

141. Stevens AJ, Ray AM, Thirunavukarasu A, Johnson E, Jones L, Miller A, et al. The experiences of socially vulnerable groups in England during the COVID-19 pandemic: A rapid health needs assessment. Public health in practice. 2021 Nov;2:100192. Available at: https://doi.org/10.1016/j.puhip.2021.100192

142. Martins-Filho PR, Quintans-Júnior LJ, de Souza Araújo AA, Sposato KB, Souza Tavares CS, Gurgel RQ, et al. Socio-economic inequalities and COVID-19 incidence and mortality in Brazilian children: a nationwide register-based study. Public Health. 2021;190:4-6. Available at: https://pubmed.ncbi.nlm.nih.gov/33316478

143. Loades ME, Chatburn E, Higson-Sweeney N, Reynolds S, Shafran R, Brigden A, et al. Rapid Systematic Review: The Impact of Social Isolation and Loneliness on the Mental Health of Children and Adolescents in the Context of COVID-19. Journal of the American Academy of Child & Adolescent Psychiatry. 2020;59(11):1218-39.e3. Available at: https://www.sciencedirect.com/science/article/pii/S0890856720303373

144. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. The Lancet. 2020;395(10227):912-20. Available at: https://www.sciencedirect.com/science/article/pii/S0140673620304608

145. European Centre for Disease Prevention and Control (ECDC). Facilitating COVID-19 vaccination acceptance and uptake in the EU/EEA. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/facilitating-covid-19-vaccination-acceptance-and-uptake

146. Fedele F, Aria M, Esposito V, Micillo M, Cecere G, Spano M, et al. COVID-19 vaccine hesitancy: a survey in a population highly compliant to common vaccinations. Human vaccines & immunotherapeutics. 2021 Oct 3;17(10):3348-54. Available at: https://www.tandfonline.com/doi/full/10.1080/21645515.2021.1928460

147. Irish Department of Health. Amárach public opinion survey: Vaccines - 23 August 2021. Dublin: Irish Department of Health; 2021. Available at: https://www.gov.ie/en/collection/6b4401-view-the-amarach-public-opinion-survey/#may-august-2021

148. Ruggiero KM, Wong J, Sweeney CF, Avola A, Auger A, Macaluso M, et al. Parents' Intentions to Vaccinate Their Children Against COVID-19. J Pediatr Health Care. 2021 Sep-Oct;35(5):509-17. Available at: https://pubmed.ncbi.nlm.nih.gov/34217553

149. Santé Publique France. Comment évolue l'adhésion à la vaccination et aux gestes barrières contre la Covid-19 ? Résultats de la vague 26 de l'enquête CoviPrev. Marseille: Santé Publique France; 2021. Available at: https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-et-infections-respiratoires/infection-a-coronavirus/documents/enquetes-etudes/comment-evolue-l-adhesion-a-la-vaccination-et-aux-gestes-barrieres-contre-la-covid-19-resultats-de-la-vague-26-de-l-enquete-coviprev

150. Finnish Institute for Health and Welfare (THL). THL issues instructions that men under 30 years of age should only be offered the Comirnaty coronavirus vaccine. Helsinki: THL; 2021. Available at: https://thl.fi/en/web/thlfi-en/-/thl-issues-instructions-that-men-under-30-years-of-age-should-only-be-offered-the-comirnaty-coronavirus-vaccine

151. National Institute for Public Health and the Environment MoHWaSR. Young people's willingness to vaccinate. Bilthoven: RIVM - Corona Gedragsunit; 2021. Available at: https://www.rivm.nl/documenten/vaccinatiebereidheid-bij-jongeren

152. CS Mott Children's Hospital. More parent-provider communication about COVID vaccine needed. Mott Poll Report. Ann Arbor: CS Mott Children's Hospital, University of Michigan; 2021. Available at: https://mottpoll.org/reports/more-parent-provider-communication-covid-vaccine-needed

153. Ebrahimi OV, Johnson MS, Ebling S, Amundsen OM, Halsøy Ø, Hoffart A, et al. Risk, Trust, and Flawed Assumptions: Vaccine Hesitancy During the COVID-19 Pandemic. Frontiers in Public Health. 2021;9(849). Available at: https://www.frontiersin.org/article/10.3389/fpubh.2021.700213

154. Kaiser Family Foundation (KFF) Polling. KFF COVID-19 Vaccine Monitor: April 2021. San Fransisco: KFF Polling; 2021. Available at: https://www.kff.org/coronavirus-covid-19/poll-finding/kff-covid-19-vaccine-monitor-april-2021/

155. COSMO COVID-19 Snapshot Monitoring. Risikowahrnehmung. COSMO COVID Snapshot Monitoring. Erfurt: Erfurt University; 2021. Available at: https://projekte.uni-erfurt.de/cosmo2020/web/topic/risiko-emotionen-sorgen/10-risikowahrnehmung/#risiko-f%C3%BCr-kinder

156. McGuire K. Parental COVID-19 vaccine hesitancy may be next challenge for vaccination campaigns: The Conversation. London: The Conversation; 2021. Available at: https://theconversation.com/parental-covid-19-vaccine-hesitancy-may-be-next-challenge-for-vaccination-campaigns-162742

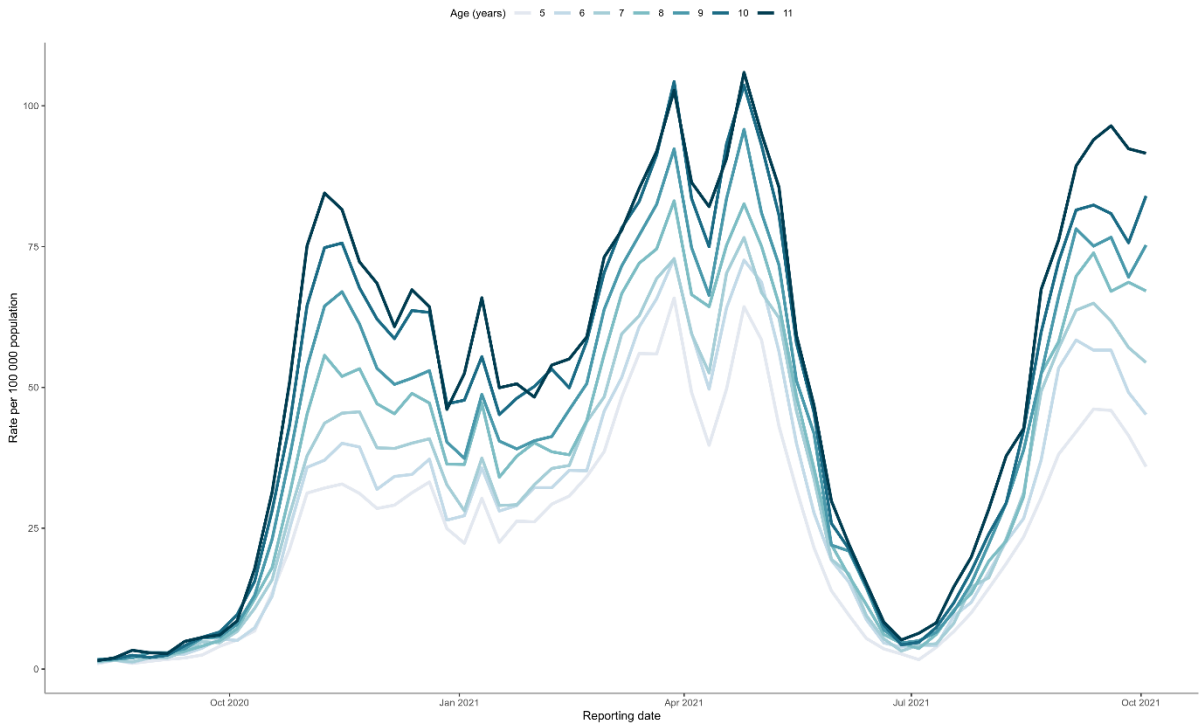
157. André L. Quel rôle pour les enfants dans l'immunité collective? Podcast 18/08/2021. Le Temps du Debat. France Culture; 2021. Available at: https://www.franceculture.fr/emissions/le-temps-du-debat-dete/le-temps-du-debat-emission-du-mercredi-18-aout-2021

158. World Health Organization (WHO). COVID-19 vaccines: safety surveillance manual. Geneva: WHO; 2020. Available at: https://apps.who.int/iris/handle/10665/338400

159. Zadrozny B. Covid vaccines for children are coming. So is misinformation. NBC News; 2021. Available at: https://www.nbcnews.com/tech/tech-news/vaccine-misinformation-poised-spike-covid-shots-kids-roll-rcna4360
160. 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. The Lancet Public health. 2021 Jun;6(6):e416-e27. Available at: https://www.sciencedirect.com/science/article/pii/S2468266721000967
161. National Academies of Sciences, Engineering and Medicine. Strategies for Building Confidence in the COVID-19 Vaccines. Washington: The National Academies Press; 2021. Available at: https://www.nap.edu/catalog/26068/strategies-for-building-confidence-in-the-covid-19-vaccines
162. World Health Organization (WHO). Communicating risk in public health emergencies. A WHO guideline for emergency risk communication (ERC) policy and practice. Geneva: WHO; 2018. Available at: https://www.who.int/publications/i/item/9789241550208
163. Hadjipanayis A, van Esso D, Del Torso S, Dornbusch HJ, Michailidou K, Minicuci N, et al. Vaccine confidence among parents: Large scale study in eighteen European countries. Vaccine. 2020 Feb 5;38(6):1505-12. Available at: https://doi.org/10.1016/j.vaccine.2019.11.068
164. El-Showk S. Don't demonize parents who are hesitant to vaccinate - discuss their worries instead. Nature. 2019 Nov;575(7784):S57. Available at: https://doi.org/10.1038/d41586-019-03641-x
165. Ministère de l'Éducation nationale, de la Jeunesse et des Sports (EDUSCOL). Sensibiliser les jeunes de 12 à 18 ans à la vaccination. EDUSCOL; 2021. Available at: https://eduscol.education.fr/2792/vaccination-des-jeunes-de-12-18-ans
166. Health Security Committee. Country responses to questionnaire in the Health Security Committee. Brussels: EU comission; 2021. Available at: https://ec.europa.eu/health/sites/default/files/preparedness_response/docs/ev_20210915_sr_en.pdf
167. European Centre for Disease Prevention and Control (ECDC). Countering online vaccine misinformation in the EU/EEA. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/countering-online-vaccine-misinformation-eu-eea
168. World Health Organization (WHO). Schooling during COVID-19: recommendations from the European Technical Advisory Group for schooling during COVID-19. Geneva: WHO; 2021. Available at: https://apps.who.int/iris/handle/10665/340872
169. United Nations Children's Fund (UNICEF). Convention on the Rights of the Child. Treaty no. 27531, United Nations Treaty Series. New York: UNICEF; 1989. Available at: https://www.unicef.org/child-rights-convention/convention-text
170. Yvonne Bordon. Public trust in vaccines. Nature Milestones. New York: Springer Nature; 2020. Available at: https://www.nature.com/articles/d42859-020-00024-5
171. Organisation for Economic Co-operation and Development (OECD). Enhancing public trust in COVID-19 vaccination: The role of governments. Paris: OECD; 2021. Available at: https://www.oecd.org/coronavirus/policy-responses/enhancing-public-trust-in-covid-19-vaccination-the-role-of-governments-eae0ec5a/
172. World Health Organization (WHO). Vaccination and trust. Geneva: WHO; 2017. Available at: https://www.euro.who.int/en/health-topics/disease-prevention/vaccines-and-immunization/publications/2017/vaccination-and-trust-2017
173. Brusa M, Barilan YM. Voluntary COVID-19 vaccination of children: a social responsibility. Journal of Medical Ethics. 2021;47(8):543. Available at: http://jme.bmj.com/content/47/8/543.abstract
174. Arat A, Burström B, Östberg V, Hjern A. Social inequities in vaccination coverage among infants and pre-school children in Europe and Australia – a systematic review. BMC Public Health. 2019;19(1):290. Available at: https://doi.org/10.1186/s12889-019-6597-4
175. World Health Organization (WHO). WHO Director-General's opening remarks at the media briefing on COVID-19 - 4 August 2021. Geneva: WHO; 2021. Available at: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-4-august-2021
176. Gur-Arie R, Kraaijeveld S, Jamrozik E. An ethical analysis of vaccinating children against COVID-19: benefits, risks, and issues of global health equity. Wellcome Open Res. 2021;6(252). Available at: https://doi.org/10.12688/wellcomeopenres.17234.1

Appendix 1

Figure A1. Pooled weekly COVID-19 age-specific case notification rates, week 32 2020–week 39 2021



Pooled data from Austria, Cyprus, Finland, Germany, Ireland, Italy, Luxembourg, Malta, Slovakia and Sweden.

Appendix 2

Figure A2. The estimated impact of vaccinating children on the spread of SARS-CoV-2 for different values of adult vaccine uptake