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Importance of Coronavirus Disease 2019 Vaccination in Children: Viewpoint and Recommendations of the Union of European National Societies of Pediatrics

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oronavirus disease 2019 (COVID-19) vaccines, approved by the US Food and Drug Administration¹ (FDA) and the European Medicine Agency² (EMA), have been shown to be safe and effective^{3,4} in the adult population at preventing severe disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) worldwide.^{5,6} The use of COVID-19 vaccination in children aged 12-17 years has been the subject of extensive debate, as the assessment of risks and benefits was considered more complex than in adults.^{7,8} Different circumstances were taken into account, including common reactions, infrequent serious side effects, possible impact on routine immunization programs, as well as vaccine supply and cost of vaccination.⁹ However, COVID-19 vaccines for individuals of this age group were authorized initially for emergency use and later approved by the stringent regulatory authorities FDA and EMA and have since been adopted with widespread use in several countries worldwide.¹⁰ In addition, both the FDA and EMA in October/November 2021 authorized the use of COVID-19 vaccines in children 5-11 years of age. Their approval followed a thorough evaluation process demonstrating the same high standards of quality, safety, immunogenicity, and efficacy observed in the older populations.^{11,12} COVID data tracking indicates that in the US, 20.1% of the 5- to 11-year-old population have received at least 1 dose of COVID-19 vaccine by December 16. The percentage of fully vaccinated subjects in the 5- to 11-year-old group is 11.3%; 62.3% of adolescents in the 12- to 17-year-old age group have received at least 1 dose of COVID-19 vaccine.⁴

In Europe, the debate over the extension of the use of COVID-19 vaccine in children <17 years old is ongoing. The 27 member states of the European Union (EU) showed different views and adopted divergent policies. It is unclear whether a unitary position will eventually be taken by the EU and non-EU countries on the use of COVID-19 vaccination in individuals <17 years of age. In the meantime, the European Centre for Disease Prevention

COVID-19	Coronavirus disease 2019
EMA	European Medicine Agency
EPA-UN-	The European Paediatric Association/Union of National
EPSA	European Paediatric Societies and Associations
EU	European Union
FDA	Food and Drug Administration
MIS-C	Multisystem inflammatory syndrome in children
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2

and Control reported that in the first week of December 2021, only 20.8% of the European population aged 12-17 years received at least 1 dose of vaccine, whereas no vaccinations were reported in children 5-11 years old.¹³

This commentary authored by the European Paediatric Association/Union of National European Paediatric Societies and Associations (EPA-UNEPSA), discusses the importance of implementing SARS-CoV-2 vaccination in children. The aim of this article is to advocate and raise awareness among pediatricians, lawmakers, public health officers, and school educators on the importance of COVID-19 vaccination in these 2 population groups. Vaccination of children and adolescents will protect them from the risks of SARS-CoV-2 infection and its short- and long-term complications.^{14,15}

Importance of COVID-19 Vaccination in Children 12-17 Years Old

COVID-19 vaccination in children 12-17 years old is recommended by the US and European regulatory authorities.^{1,2} Available studies on SARS-CoV-2 seroprevalence and viral shedding are unable to establish conclusively whether adolescents are infected at the same rate as adults.¹⁶ Data on transmission from children to others are limited; some studies suggest similar infection rates, whereas others indicate lower infection rates among children. Early in the pandemic, some studies estimated that adults might have greater susceptibility to infection compared with individuals <20 years of age.¹⁷ However, recent data in the US indicate that children have a greater seroprevalence than adults, and the infection to case ratio is greater in

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children. Children and adolescents are known to spread the virus to other age groups, and secondary transmission from children has been documented in both household and school settings.^{18,19} In early studies, children and adolescents represented a smaller proportion of symptomatic subjects and showed a reduced number of cases of severe disease and deaths due to SARS-CoV-2 infection compared with older age groups.^{20,21} However, the combination of mild and asymptomatic infection and reduced care-seeking in younger age groups are likely contributors to undertesting and underreporting of cases.²² Deficient monitoring of SARS-CoV-2 in this age population²¹ suggests that adolescents may remain largely undetected and therefore have a role in SARS-CoV-2 transmission. Intense social relations characterizing adolescence may be an additional factor contributing to the viral spread. Data from India reported the seropositivity rate for the Delta variant in children 6-18 years was comparable with that in older age groups.¹⁶

In the US, the proportion of cases in children has significantly increased from the 2.6% observed in the beginning of the pandemic to about 24% of all cases.²³ Recent data indicate a 38%-40% seroprevalence rate in children aged 5-17 years, which was greater compared with adults and older adults.^{11,24} Similar data are reported in EU countries.²⁵ In addition, the median number of infections per reported case for children <17 years old was 6.2, compared with the general population, with a median of 2.4 infections per reported case. Data reported by the World Health Organization also suggest that SARS-CoV-2 infection rates in children, adolescents, and adults are similar,¹⁶ and European Centre for Disease Prevention and Control reports that test positivity among the 10- to 19-yearold age group mirror those of most other age groups.²⁵ Collectively, these data indicate that children and adolescents are at least as likely as adults to be infected with SARS-CoV-2 but are less likely to be reported.

The risk of complications due to SARS-CoV-2 infection in the pediatric population supports COVID-19 vaccination in children and adolescents.²⁶ Multisystem inflammatory syndrome in children (MIS-C), long-COVID-19, and indirect effects on mental health and education are among the serious conditions that can be caused by even mild COVID-19, particularly in subjects with underlying medical conditions.^{27,28} In the US, approximately one-third of those <17 years old who are hospitalized with COVID-19 require admission to the intensive care unit, and severity of illness for hospitalized cases is comparable with influenza. Although MIS-C is relatively infrequent in subjects affected by COVID-19, studies from Europe and North America have reported groups of adolescents requiring admission to intensive care units due to multisystem inflammatory conditions and toxic shock syndrome.²⁸ COVID-19 is currently among the top 10 causes of death for children in the US and Europe.^{28,29}

Value of COVID-19 Vaccination in Children 5-11 Years Old

In the US, after the Centers for Disease Control and Prevention recommended COVID-19 vaccination for children aged 5-11 years in November 2021,³⁰ distribution of pediatric doses of the vaccine to pediatric offices, pharmacies, and health centers was scaled up rapidly toward full capacity. The COVID-19 vaccine in children in this age group also was approved by Health Canada, and in the first week of December 2021, 17.5% of individuals in this age range received at least 1 dose.³¹ The European Medicines Agency approved the use of COVID-19 vaccine for children aged 5-11 years in November 2021, and the rollout in this age group started in Italy and France in December 2021.^{32,33} It is important to ensure that all school-aged children <12 years are protected from COVID-19 infection.^{34,35}

Approvals by regulatory authorities in the US and Europe were based on evidence that the efficacy and immunogenicity of these vaccines are as high as those in older individuals and show rare serious adverse effects.³⁰ Myocarditis associated with mRNA COVID-19 vaccines is a sporadic adverse event predominantly seen in male adolescents and young adults following the second vaccine dose, which has raised concern about this risk in younger children. However, based on available data from the years preceding COVID-19, the risk of vaccine-associated myocarditis in 5- to 11-year-old children is expected to be extremely low compared with adolescents and young adults, in whom such risk is already low.³⁶ We still do not have long-term outcome data on myocarditis following vaccination. However, preliminary survey data at three months following diagnosis showed that 52% reported no symptoms within the previous 2 weeks and 90% of cardiologists or health care providers felt their patient was fully or probably recovered.^{37,38} The advantages of vaccination are considered to largely outweigh this risk, as the occasional cases of myocarditis associated with COVID-19 vaccination are predominantly mild and the risk of myocarditis following COVID-19 is greater than the risk of myocarditis after COVID-19 vaccination.³⁷⁻⁴⁰

The rare cases of MIS-C reported in adults following COVID-19 vaccination advised the importance of monitoring for this possible adverse event in children 5-11 years old. However, data from vaccine trials in children <12 years old have not identified any potential signal triggering this event.³⁹ It is also important to take into account that the number of children 5-11 years old who have died due to COVID-19 during the pandemic is greater than the mortality rates of the infections for which children were routinely vaccinated before COVID-19 vaccines were made available, including meningo-coccal disease, measles, varicella, and rotavirus.³⁶ The risk of severe disease in children with underlying medical conditions, and the importance of protecting children from any severe outcome related to COVID-19 infection, are all compelling reasons for vaccination of children 5-11 years old.^{36,41}

Conclusions

Although children and adolescents with COVID-19 show generally less frequent and severe symptoms, they acquire and spread the coronavirus and present with clinical complications including hospitalization and death.⁴²⁻⁴⁴ The \blacktriangleleft

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EPA-UNEPSA joins the American Academy of Pediatrics in welcoming the decision of the US and European regulatory authorities to authorize COVID-19 vaccination in children and adolescents who do not have contraindications using a COVID-19 vaccine authorized for use for their age.⁴⁵ The EPA-UNEPSA recommends the implementation of COVID-19 vaccination programs in these age groups⁸ to protect children and adolescents' health and allow them to fully engage in all of the activities that are essential for their full development and wellbeing.46,47 The recent authorization of COVID-19 vaccination for children from 5 to 11 years old in the US and Europe is anticipated to have an important impact in reducing the burden of COVID-19, through prevention of severe COVID-19 disease in the fully vaccinated in this age group, as well as through mitigation of transmission among close contacts. Vaccinated children and adolescents would not be exposed to the adverse mental and behavioral consequences associated with isolation, quarantine, and missing of school.48

In the EU, data from December 2021 show a 96% weekly increase of children hospitalized with laboratory-confirmed COVID-19, of whom 69% were <4 years old, strongly suggesting the importance of COVID-19 vaccination in younger children.⁴⁹ Vaccine trials in children aged 6 months to 5 years are underway in the US under careful supervision by the FDA, and key data are expected to be released in the coming months. ■

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