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Viewpoint of the European Pediatric Societies over Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vaccination in Children Younger Than Age 12 Years Amid Return to School and the Surging Virus Variants

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Since its first appearance in the Wuhan region of China in December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a worldwide public health and socioeconomic crisis.¹ According to the World Health Organization Coronavirus (COVID-19) dashboard, as of September 2021, there have been more than 217 million confirmed cases and 4.5 million deaths reported.² Mass vaccination campaigns against SARS-CoV-2 are ongoing worldwide. Currently, 5.38 billion doses have been administered globally, 39.9% of the world population has received at least 1 dose of a COVID-19 vaccine, and approximately 40 million are administered each day. However, only 1.8% of people in low-income countries have received at least 1 dose,³ and there will likely be increasing high demand for the limited supplies of vaccine against SARS-CoV-2 in many areas, raising important ethical issues and socioeconomic debates on how vaccine distribution should be prioritized.

Children are returning to class after long pandemic closures. As a new school year begins, local governments in low- and high-income countries are struggling over teacher vaccinations and mask mandates amid the surge of virus variants.⁴ With the fast spread of the more contagious delta variant and SARS-CoV-2 vaccines not available for much of the global school-aged population, children's health risks have become a pressing public health issue. A global debate is underway on whether SARS-CoV-2 vaccination should be made available in children younger than age 12 years and be made mandatory for those attending schools.

This commentary, authored by the working group on social pediatrics of the European Paediatric Association/Union of National European Paediatric Societies and Associations (EPA-UNEPSA), presents the viewpoint of EPA-UNEPSA and its partner society European Confederation of Primary

Care Paediatricians (ECPCP), on SARS-CoV-2 vaccination in children younger than age 12 years. The aim is to raise awareness of pediatricians, lawmakers, public health officers, and school educators on the importance of extending vaccination after a careful risk assessment is made. We emphasize that proper and safe vaccination procedures should be initiated after satisfactory clinical trials are completed and following formal approval by public authorities.⁵

Increased Cases of COVID-19 in Children following the Emergence of Virus Variants

These changes may affect the virus's properties, including ability of spreading, severity of associated diseases, and resistance to preventive and therapeutic measures.⁶ The emergence of SARS-CoV-2 variants rapidly spreading worldwide pose an increased risk to global public health. In Europe, the delta variant initially arose in the United Kingdom in April 2021⁶ and later became the dominant strain in the majority of the European countries. Currently, the classification developed by the World Health Organization to identify specific variants of interest and variants of concern helps to prioritize an effective global monitoring and research, to elaborate the development of public health guidance to prevent the spread of COVID-19, and ultimately to inform the ongoing response to the COVID-19 pandemic⁶ (Table; available at www.jpeds.com).

After the delta variant became the most dominant circulating strain, the number of children contracting COVID-19 has increased.⁷ After the infection initially declined among children in early Summer 2021, the US and European

AAP	American Academy of Pediatrics
COVID-19	Coronavirus disease 2019
ECPCP	European Confederation of Primary Care Paediatricians
EPA-UNEPSA	European Paediatric Association/Union of National European Paediatric Societies and Associations
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2

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countries showed an impressive 5-fold increase of cases in this population. As reported by the American Academy of Pediatrics (AAP), during a 4-week period between July and August 2021, COVID-19 cases in children increased from 38 000 to nearly 204 000 and numerous states reported an increase, although moderate, in child hospitalizations amid the ongoing delta surge.⁷ Similarly, a significant increase in COVID-19 cases is reported in Europe. In the United Kingdom, there has been a 5-fold greater rate of COVID-19 test positivity among children 5-12 years of age (0.35% prevalence) and adults ages 18-24 years (0.36% prevalence) than in those 65 years of age or older.⁸ Furthermore, of great concern is the increase of pediatric multisystem inflammatory syndrome in children associated with COVID-19, which showed an incidence of about 100 affected children per week.⁹ In Italy, the local National Institute of Health reports that after the emergence of the delta variant, the increase of COVID-19 cases involved the population 0-9 years old, whereas the older age groups showed a decline in cases.¹⁰ In Israel, emerging data indicate a sharp rise in SARS-CoV-2 infections during the first months of 2021 in the population 0-9 and 10-19 years, with more than 50 000 children and teens testing positive.¹¹

The Importance of Using COVID-19 Vaccine in Children Younger Than 12 Years after Rigorous Risk Assessment and Approval Procedures

The debate over the importance of COVID-19 vaccination in children younger than 12 years rapidly arose after the emergence of aggressive virus variants. In this population, the number of infections sharply grew in parallel with the number of severe cases, which led to the hospitalization of young children.⁹ In particular, the delta variant showed to be more contagious to children and from children than the older variants. SARS-CoV-2 may spread in schools, homes, and gatherings where kids typically can get infected most and although the virus has been less aggressive in children than adults, not all children have been immune to some severe health risks associated to the infection, including multi-system inflammatory syndrome in children.⁹

Two main approaches may be considered in vaccine prioritization: directly vaccinate people at greatest risk for severe outcomes and indirectly protect the weakest part of the population by vaccinating those who do the most transmitting.¹² The experience provided by the influenza vaccination programs, which suggest that children are vaccinated due to their critical role in transmission,^{13,14} shows that direct protection is superior when reproduction numbers are high, but indirect protection is greater when transmission is low.¹⁵

The rationale behind vaccinating children younger than 12 years would be not only to help the communities reach

herd immunity, minimize viral transmission, and reduce the risk of development of virus variants but also to protect this age group from the SARS-CoV-2 infection and disease. Vaccines undergo rigorous regulatory approval procedures to ensure their safety, efficacy, and quality.¹⁶ Clinical trials are currently underway for the COVID-19 vaccine in children younger than 12 years old and is strictly monitored in the US by the Food and Drug Administration and in Europe by the European Medicines Agency.^{17,18} Currently, trials of the COVID-19 mRNA vaccines in younger children are under way.¹⁹ The studies aim to assess safety and immune responses after 2 vaccinations with 3 different dose sizes.¹⁹ A trial of AstraZeneca's COVID-19 vaccine in children aged 6-17 years started in March 2021 in the United Kingdom. However, this trial was paused as a precautionary measure following reports of blood clots in adults who received this vaccine.¹⁹ A study compared rates of 25 adverse events between vaccinated and unvaccinated adult individuals.²⁰ Few adverse events were associated with the vaccine, including swelling of the lymph nodes, appendicitis, and herpes zoster. Myocarditis was associated with an excess of 2.7 cases per 100 000 vaccinated persons.²⁰

Several pediatric organizations urge for an early emergency approval of the vaccine in children younger than age 12 years and a possible administration of the vaccine off-label in this age group, who currently have no available vaccine. However, the EPA-UNEPSA, ECPCP, and their member pediatric societies join AAP in strongly discouraging such practice.

Conclusions

SARS-CoV-2 vaccines proved their effectiveness to prevent severe illness and hospitalization in adults and adolescents. EPA-UNEPSA, ECPCP, and their member European pediatric societies urge national authorities to work intently toward the authorization of safe SARS-CoV-2 vaccine programs. The vaccination in children younger than age 12 years will allow a large number of children to attend school, spend time with friends, travel with their families, and enjoy their communities safely.²¹⁻²³ European pediatric societies join AAP recommendations against giving the vaccine to children younger than 12 years before rigorous clinical trials are completed, adverse events carefully assessed, and not until vaccines are authorized and adequate dosage established by the respective national agencies. This ensures that vaccines are safe and effective for this age group. ■

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Table. SARS-CoV-2 VOC and VOI (September 2021)

WHO labels	Pango lineage*	GISAIID clade†	Nextstrain clade‡	Additional amino acid changes shown	Earliest documented samples	Date of designation
Currently designated VOC						
Alpha	B.1.1.7	GRY	20I (V1)	+S:484K//+S:452R	United Kingdom, 09/2020	18/12/2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, 05/2020	12/18/2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, 11/2020	11/01/2021
Delta	B.1.617.2	G/478K.V1	21A	+S:417N	India, 10/2020	VOI: 04/04/2021 VOC: 11/05/2021
Currently designated VOI						
Eta	B.1.525	G/484K.V3	21D	–	Multiple countries, 12/2020	3/17/2021
Iota	B.1.526	GH/253G.V1	21F	–	US, 11/2020	3/24/2021
Kappa	B.1.526	G/452R.V3	21B	–	India, 10/2020	4/4/2021
Lambda	B.1.526	GR/452Q.V1	21G	–	Peru, 12/2020	6/14/2021
Lambda	B.1.526	GH	21H	–	Colombia, 01/2021	8/30/2021

VOC, variants of concern; VOI, variants of interest; WHO, World Health Organization.

*Pango lineage: The Phylogenetic Assignment of Named Global Outbreak Lineages (PANGOLIN) is a software tool developed by members of the laboratory of Andrew Rambaut, with an associated web application developed by the Centre for Genomic Pathogen Surveillance in South.

†GISAIID clade: Global initiative on sharing avian influenza data (GISAIID) (<https://www.gisaid.org/about-us/mission/>).

‡Nextstrain clade: Nextstrain is an open-source project to harness the scientific and public health potential of pathogen genome data (<https://nextstrain.org/>).