European Technical Advisory Group of Experts on Immunization (ETAGE) interim recommendations, June 2021

Inclusion of adolescents aged 12–15 years in national COVID-19 vaccination programmes
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Copenhagen: WHO Regional Office for Europe; 2021.
Background

*SAGE recommendations on the use of Pfizer BioNTech COVID-19 vaccine, BNT162b2*

On 27 May 2021, SAGE reviewed data from Pfizer-BioNTech Phase 2/3 randomized controlled trial in adolescents 12–15 years of age and concluded that the known and potential benefits of BNT162b2 outweigh the known and potential risks in this age group. SAGE indicated the intended use of BNT162b2 for persons 12 years of age and older. SAGE recommended that countries should consider using BNT162b2 in adolescents age 12–15 only when high coverage with a complete vaccination series has been achieved in the high priority groups as identified in the WHO Prioritization Roadmap. Adolescents 12–15 years of age with comorbidities that put them at significantly higher risk of serious COVID-19 disease, alongside other high-risk groups, may be offered vaccination.1

SAGE stated that as a matter of global equity, as long as many parts of the world are facing extreme vaccine shortages, WHO recommends that countries that have achieved high vaccine coverage in the high-risk populations prioritize global sharing of COVID-19 vaccines through the COVAX facility before proceeding to vaccination of children and adolescents who are at low risk for severe disease.

**ETAGE notes**

*Burden of COVID-19 in adolescents*

In the WHO European Region, children and adolescents age 5-14 years accounted for around 6–9% of total COVID-19 cases reported weekly in the period from October 2020 – April 2021. Since the week of 22 March 2021, the age-specific case notification rates showed a decreasing trend in all age groups. However, starting from the week of 26 April 2021, children and adolescents age 5-14 years represent a growing proportion of recent COVID-19 cases. This trend may reflect decreasing morbidity in older population due to increasing cumulative vaccination rates, as well as changes in testing strategies in schools.

Most adolescents infected with SARS-CoV-2 experience a mild, moderate or asymptomatic course of the disease with main symptoms being cough and fever.3,4 Hospitalizations due to

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COVID-19 in adolescents are rare: cumulative rates of COVID-19 associated hospitalization in children and adolescents age 10-19 years was 0.8% in European Union (EU)/European Economic Area (EEA) countries in the period from 1 August 2021 through 6 June 2021\(^5\). During the period of October 2020–April 2021, 87 deaths due to COVID-19 were reported in children and adolescents 5-14 years of age in the WHO European Region (18 reporting countries).

Current evidence suggests that adolescents with chronic medical conditions may be at increased risk of severe illness from SARS-CoV-2 infection that may require hospitalization. A study conducted in the United States found that asthma, gastrointestinal conditions, diabetes, immunosuppression and obesity were associated with higher risk of hospitalization in adolescents\(^6\). The risk factors may vary across countries and may be influenced by the health systems and management of chronic diseases.

Adolescents infected with SARS-CoV-2, including those with a mild or asymptomatic course, are at risk of developing Multisystem Inflammatory Syndrome in Children (MIS-C), a severe, potentially fatal, rare\(^7,8,9\) multiorgan inflammatory condition with persistent fever\(^10\). The half of MIS-C occurred in children and adolescents between the ages of 4 and 13 years; the median age was 8-9 years\(^8,11,12\). The evidence on MIS-C is limited and risk-factors are not yet known.

In addition, SARS-CoV-2 infection can result in prolonged illness, known as ‘post COVID condition’ or ‘long COVID’ despite an asymptomatic or mild course of COVID-19 disease\(^13\).

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\(^12\) Health Department-Reported Cases of Multisystem Inflammatory Syndrome in Children (MIS-C) in the United States (as of 2 June 2021). (https://www.cdc.gov/mis-c/cases/index.html) (Accessed on 17 June 2021)
This condition, not yet clearly defined, has also been described in adolescents, though less often than in adults\textsuperscript{14,15}.

**Impact on SARS-CoV-2 transmission**
Adolescents infected with SARS-CoV-2 can transmit SARS-CoV-2, but evidence suggests that their role in transmission of infection is less prominent compared to adults\textsuperscript{16,17,18}. Some studies showed that adolescents may contribute to transmission in households and communities, including to immunocompromised individuals\textsuperscript{19}. The occurrence of SARS-CoV-2 variants of concerns, associated with higher rate of transmissibility, may change the importance of adolescents’ role in transmission.

**Efficacy of Pfizer BioNTech COVID-19 vaccine, BNT162b2**
Pfizer BioNTech randomized, double-blind, placebo-controlled Phase 2/3 clinical trial that was expanded to enroll approximately 2200 participants age 12–15 years, showed a vaccine efficacy against symptomatic SARS-CoV-2 infection of 100% (95% CI: 75.3%, 100%) from at least 7 days after dose 2. Vaccine efficacy was also supported by immunobridging data from vaccine recipients age 12–15 years compared with those from recipients aged 16–25 years. The immune response to 2 doses of BNT162b2 in adolescents age 12–15 years was at least as high as the response observed in persons age 16–25 years\textsuperscript{20}.

**Safety of Pfizer BioNTech COVID-19 vaccine, BNT162b2**
Limited safety data are available for adolescents age 12–15 years given the small sample size of the trial (N=2260, of whom half received vaccine). BNT162b2 was well tolerated in this age group and showed a similar reactogenicity pattern to that seen in those age 16–25 years. The frequency of serious adverse events was low among participants; five serious adverse events (0.4%) were reported among vaccine recipients and two (0.2%) among placebo recipients. None

\textsuperscript{17} Zhu et al. A Meta-analysis on the Role of Children in Severe Acute Respiratory Syndrome Coronavirus 2 in Household Transmission Clusters. Clinical Infectious Diseases; 72 (12):e1146-e1153 Doi: 10.1093/cid/ciaa1825
of the serious adverse events were assessed by the investigator as related to the study intervention\textsuperscript{18}.

**Post-marketing safety data**
The COVID-19 Subcommittee of the WHO Global Advisory Committee on Vaccine Safety is reviewing reports of a small number of cases of myocarditis reported in individuals vaccinated with the COVID-19 mRNA vaccines. These cases seem to occur predominantly in adolescents and young adults (<30 years old). Recent data reported to Advisory Committee on Immunization Practices (ACIP) in the United States show a marked male predominance. In most of the reported cases, the individuals had a mild course and have recovered. More rigorous studies using alternative data sources and more robust study designs including comparison of vaccinated and unvaccinated populations are needed to assess a potential causal association between the event and the vaccine. Some countries, such as Israel, the United Kingdom and the United States have embarked upon such studies.

**Potential impact on adolescents psychological and social well-being**
Some studies have shown that the mental health of adolescents worsened during the pandemic more than expected based on the observed trends over the past decade\textsuperscript{21}. Reaching high COVID-19 vaccination coverage in adolescents might facilitate reduction of non-pharmaceutical public health measures, which might, in turn, positively affect the psychosocial well-being of adolescents and normalize their social life.

**Decisions of countries in the WHO European Region and globally**
Following European Medical Agency recommendations on the use of BNT162b2 vaccine in adolescents age 12–15 years, the health authorities in Austria, France, Italy, Israel, Lithuania, Poland, Romania, Spain, San Marino, Switzerland, Canada and US included individuals 12–15 years of age into their national COVID-19 vaccination campaigns. Germany and the Netherlands recommended selective vaccination of adolescents with pre-existing underlined conditions, which put them at increased risk of severe COVID-19 disease, as well as adolescents who are in close contact with vulnerable unvaccinated or immunocompromised individuals.

**Uptake of COVID-19 vaccines**
By 10 June 2021, approximately 30% of the population of the WHO European Region received at least one dose of COVID-19 vaccine and 17% were fully vaccinated. The highest coverage rates are achieved in priority target groups: medical workers (71% with at least one dose; 53%...
fully vaccinated) and older adults age ≥60 years (67% with at least one dose; 44% fully vaccinated)22.

There are significant differences between the proportions of vaccinated populations in different countries: the national coverage with at least one dose ranges from 0.5% in Turkmenistan to more than 63% in San Marino and Israel. In general, the coverage is significantly lower in low- and middle-income countries (LMICs), which have had limited access to COVID-19 vaccines. Currently, the global production capacity of COVID-19 vaccines is insufficient, and limited vaccine supply to LMICs is likely to continue.

**ETAGE conclusions**

ETAGE concurs with the SAGE advice that in the current situation of limited vaccine supply, countries should prioritize vaccination of populations at high risk of severe and fatal COVID-19 outcomes, including adolescents age 12–15 years, as well as those of 16–17 years of age, with underlying conditions and those who are in contact with vulnerable individuals. With increasing vaccine supply, more post-marketing vaccine safety data and high coverage in high-risk groups, countries may wish to consider vaccinating all adolescents age 12-15 years.

**ETAGE recommendations**

*Decision making on vaccination of adolescents*

ETAGE recommends that countries should consider the following criteria while making decisions on vaccination of adolescents age 12–15 years:

- Proportion of priority target groups vaccinated against COVID-19, including health care workers, older adults, individuals of any age with co-morbidities, and socio-economic groups who are at the highest risk of severe disease and death.
- Proportion of vaccinated teachers and school workers.
- Availability of sufficient quantities of COVID-19 vaccines (available or confirmed vaccine supply). More than 43 728 000 adolescents age 12–15 years living in the WHO European Region constitute around 5.5% of the total population eligible for vaccination. Countries should secure adequate vaccine supply to ensure that vaccination of healthy adolescents will not interrupt or delay vaccination of priority target groups.

*Communication of decision on adolescent vaccination*

In order to promote public trust and acceptance, the decisions on vaccination of adolescents should be made through transparent processes that are based on shared values, appropriate

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representation and input by affected parties. These decisions may change based on new evidence, including new safety data. Countries should develop and implement effective communication strategies to improve the public’s perception and understanding of the vaccine prioritization processes.

**Prevention and management of immunization stress-related responses**
Experience with vaccinating adolescents showed that individual or clusters of immunization stress-related responses (ISRR) may occur during mass immunization campaigns (meningococcal, measles/rubella, human papillomavirus (HPV) vaccines). ETAGE urges countries to undertake comprehensive measures to avoid and prevent, expeditiously detect and effectively manage and respond to such adverse events.

All health care professionals involved in immunization should be informed about and trained in the characteristics of ISRR, including measures to prevent or minimize their occurrence and recognition of the symptoms and signs and differentiating these from other conditions in order to address them when they occur in one or more vaccine recipients. Environmental factors such as overheated, crowded waiting areas, lack of privacy during immunization and exposure to negative social media and communications during school and mass immunization campaigns should also be addressed to decrease the risks of ISRR\(^2\). The national immunization programme should ensure that the crisis communication plan is in place to provide rapid and effective response to ISRR or any other potential event that may erode trust in vaccination.

**AEFI reporting**
In the context of COVID-19 vaccination of adolescents, surveillance systems need to be adapted to identify and respond to adverse events following immunization (AEFI) and adverse events of special interest in this age group.

**Continuing prevention of SARS-CoV-2 transmission**
ETAGE reminds authorities that vaccination is an extremely powerful tool in strengthening the response to COVID-19. However, while all licensed COVID-19 vaccines are highly efficacious, no one vaccine is 100% effective. Appropriate precautionary measures should be continued, since COVID-19 vaccination will not provide guaranteed protection against getting infection and transmitting it to others.

**Global equity**
Currently, the global production capacity of COVID-19 vaccines is insufficient, and many countries face vaccine shortages. Some LMICs in the WHO European Region have vaccinated

less than 3% of their populations and have not been able to vaccinate vulnerable groups. Inclusion of adolescents in COVID-19 vaccination programmes would increase the number of people eligible for vaccination and lead to further increases in national, regional and global vaccine supply constraints. When considering COVID-19 vaccination of adolescents, countries should take into account the impact of their decisions on equity of access to COVID-19 vaccines between countries and for those at highest risk.

*ETAGE recommendations on including adolescents in national COVID-19 vaccination programmes are interim and will be updated as new evidence become available.*
The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

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