Coronavirus disease 2019 vaccine for children in China: when to start? Mandatory or voluntary?

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To the Editor: As the coronavirus disease 2019 (COVID-19) pandemic continues to expand in many countries, and the more transmissible variants emerged, the second wave could be more severe and result in a greater peak of infection and mortality. There is an urgent need to develop effective vaccines, which remains a critical tool to control the pandemic. Vaccination is equally important in areas where outbreaks persist and in well-controlled countries.

Many vaccines are in development and phase III clinical trial testing, which are being administered to adult populations only. As of April 4, 2021, a total of 604,032,357 vaccine doses have been administered, reported by World Health Organization.[1] While in China, there are five vaccines in phase III clinical trials, in which CoronaVac (Sinovac Life Sciences, Beijing, China), an inactivated vaccine and the recombinant tandem-repeat dimeric receptor binding domain-based protein subunit vaccine (ZF2001; Anhui Zhifei Longcom Biopharmaceutical Co., Ltd., Hefei, China), has demonstrated to be well tolerated and immunogenic. Vaccination of healthcare personnel (HCP) and common adults has been promoted widely in China. Then comes the question: When will the children be vaccinated?

If we want to formulate our national severe acute respiratory syndrome coronavirus 2 immunization strategy, children should not be forgotten because herd immunity could be reached once if about 60% of the population is immunized. Vaccinating children could have beneficial knock-on effects in the wider community through blocking transmission of COVID-19. Moreover, children and adolescents might soon be contributing more to the spread due to the emergence of faster-spreading variants, along with rising adult vaccination rates in many areas. Though no direct evidence was found regarding the transmission from children to adults, the risk of family cluster transmission from children harboring virus and hygiene practices in these young children are difficult to achieve which should be taken into consideration in policy making for epidemic control.

But early adult trials showed that people who received the vaccine could develop "enhanced disease" if they later became infected, and thromboembolic events potentially linked to the Oxford-AstraZeneca and Johnson & Johnson vaccines have aroused concern. When there will be a vaccine approved for children remains uncertain. There are five different vaccine production platforms for COVID-19, live attenuated vaccine/the whole virus, inactivated virus vaccine, sub-unit vaccine, viral vector-based vaccine, and RNA/DNA vaccine. Pfizer-BioNTech and Moderna have now enrolled teens in clinical trials of their vaccines (ClinicalTrials.gov; Nos. NCT04368728, NCT04649151, and NCT04796896). A randomized, double-blinded, single-center, placebo-controlled phase 1 and 2 clinical trial in children and adolescents aged 3 to 17 years (ClinicalTrials.gov; No. NCT04551547) in China has an estimated primary completion date of September 2021. Among vaccines in ongoing clinical trials in children, Pfizer and Moderna's vaccines use mRNA technology, which have high immunogenicity, capacity for rapid development, and potential for low-cost manufacture, but these vaccines require ultra-cold storage, which makes the vaccine tricky to ship to remote regions. While Sinovac vaccine works differently, it is an inactivated virus vaccine. It has the pre-existing technology and has already been tested for SARS-CoV and other diseases, which makes it safe and stable, but otherwise the inactivated vaccine requires the booster shots to maintain the immunity. Safety and effectiveness are the two most important issues of vaccines. Considering the timing of disclosure of the results of these trials [Table 1], vaccination of children in China has already started.

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Table 1: The present coronavirus disease 2019 vaccines for children.

Identifier/status	Sponsor	Country	Biological	Eligible age	Estimated completion date
NCT04368728 (Recruiting)	BioNTech/ Pfizer	United States	RNA vaccine BNT162b1/b2	≥12 years	October 29, 2021 (primary) April 6, 2023 (final)
NCT04649151 (Active, not recruiting)	Moderna	United States	mRNA-1273	12 to <18 years	June 30, 2022
NCT04796896 (Recruiting)	Moderna	United States	mRNA-1273	6 months to <12 years	June 10, 2023
NCT04551547 (Recruiting)	Sinovac	China	Inactivated vaccine	3–17 years	February, 2021 (primary) September, 2021 (final)

Another problem concerned is vaccine hesitancy, which is a long-standing issue reported in >90% of countries in the world. Countries where acceptance >80% tended to be Asian nations with strong trust to central governments (China, Korea, and Singapore). Leng *et al*[2] found that vaccine effectiveness, side-effects, and proportion of acquaintances vaccinated were the most important factors that influence the public's preferences for COVID-19 vaccination in China. Similar study revealed that high effectiveness of the vaccine and the long protective duration were the first two factors affecting the individual preference for the uptake of the COVID-19 vaccine in China.[3] While another study showed that information about vaccination safety from authoritative sources, doctor's recommendations, and vaccination convenience play an important role in vaccine hesitancy in China.[4]

To be mandatory or not is a big question facing public health decision makers. In the USA, state regulations mandate that children cannot attend school if they are not vaccinated. School immunization mandates are also a traditional, well-established rule in China. There are different voices about whether to mandate COVID-19 vaccination of children or not.[5,6] Supporters mainly focus on the role of children contributing to spread, the chance of developing severe forms of COVID-19 like multi-system inflammatory syndrome in children, and the protection of vaccine. While the opponents list the concern of the safety and effectiveness of the vaccines, different immune responses of children, and ethical considerations. We can also draw lessons from the policy and guidelines of other vaccines, like influenza, to optimize the COVID-19 vaccine administration.

Vaccination of children for COVID-19 will eventually come, while making pediatric vaccination mandatory is not only about medicine and ethics but also a concern of socio-economic distress. Considering the severe burden of morbidity, mortality, and socio-economic distress caused by COVID-19, though there are some concerns, we believe that vaccinating children is our best hope to control COVID-19. When a safe and effective vaccine for children is developed, countries and regions with different epidemic situations can formulate different vaccination strategies for children. Like in China, where the epidemic is well controlled, voluntary vaccination may be a good choice. While in areas with severe epidemic, compulsory policies would be more reasonable. Furthermore, some issues that impact vaccination decisions in certain subgroups of children also need to be concerned, especially those with autoimmune diseases receiving immunosuppressive regimens. Even if people are widely vaccinated, behaviors like mask wearing and social distancing should not be abandoned. Collaborative efforts of governments, health policy makers, and HCP will always be needed.

Conflicts of interest

None.

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