Mandatory Coronavirus Disease 2019 Vaccine for Children?

To the Editor—Opel et al1 proposed 9 criteria to consider when evaluating when a coronavirus disease 2019 (COVID-19) vaccine should be mandatory in school immunization programs. Two of these criteria deserve further reflection.

First, these authors believed that the most important criterion is to have evidence that the vaccine is safe for children, through data obtained in prelicensing trials and postlicensure studies that should show “an acceptable level of risk.”1 All of the 11 phase 3, placebo-controlled randomized trials included in the World Health Organization database2 will be conducted in adults (Table). It would be prudent to start phase 3 trials in children once there is enough 1-year safety data in adults. So, prelicensing data on 1-yearsafety (and efficacy) in children is conducted aiming to obtain long-term (≥1 year) safety results; any candidate vaccine fulfilling the US Food and Drug Administration considerations that COVID-19 candidate vaccines providing 50% efficacy, but ensuring a minimum efficacy of greater than 30% could be licensed.4 Until phase 3 trials results in adults are published, the worst scenario would be that COVID-19 licensed vaccines have an efficacy of 50%. However, this could not be an issue if it is confirmed that transmission of SARS-CoV-2 by children is less important than by adults.5

If clinical development of COVID-19 candidate vaccines in children is conducted aiming to obtain long-term (≥1 year) safety results, any candidate vaccine fulfilling the US Food and Drug Administration requirements for efficacy4 and the other 7 criteria1 might be considered for inclusion in mandatory school immunization programs if deemed appropriate by health authorities, but this will be unlikely before 2024.

Table. Phase 3 Randomized Placebo-Controlled Trials Included on the World Health Organization Database as of September 17, 20202

<table>
<thead>
<tr>
<th>Sponsor/manufacturer</th>
<th>Countrya</th>
<th>ID</th>
<th>Age of participants, y</th>
<th>No. of participants</th>
<th>Follow-up period, y</th>
<th>Location of trial</th>
<th>Recruitment status</th>
<th>Last update postedb</th>
</tr>
</thead>
<tbody>
<tr>
<td>AstraZeneca</td>
<td>United Kingdom</td>
<td>ISRCTN89951424</td>
<td>18-55</td>
<td>2000</td>
<td>1</td>
<td>Brazil</td>
<td>Unknownc</td>
<td>Aug 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NCT04516746</td>
<td>≥18</td>
<td>30000</td>
<td>2</td>
<td>United States</td>
<td>Not yet recruiting</td>
<td>Aug 18</td>
</tr>
<tr>
<td>BioNTech-Pfizer</td>
<td>Germany-United States</td>
<td>NCT04368728c</td>
<td>18-85</td>
<td>29481</td>
<td>2</td>
<td>Argentina, Brazil, Turkey, United States</td>
<td>Recruiting</td>
<td>Sep 4</td>
</tr>
<tr>
<td>CanSino</td>
<td>China</td>
<td>NCT04526990</td>
<td>≥18</td>
<td>40000</td>
<td>1</td>
<td>Pakistan</td>
<td>Recruiting</td>
<td>Sep 16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NCT04540419</td>
<td>18-85</td>
<td>500</td>
<td>0.5</td>
<td>Russia</td>
<td>Not yet recruiting</td>
<td>Sep 7</td>
</tr>
<tr>
<td>Gamaleya</td>
<td>Russia</td>
<td>NCT04530396</td>
<td>18-111</td>
<td>40000</td>
<td>0.5</td>
<td>Russia</td>
<td>Recruiting</td>
<td>Sep 11</td>
</tr>
<tr>
<td>Janssen</td>
<td>United States</td>
<td>NCT04505722</td>
<td>≥18</td>
<td>60000</td>
<td>2</td>
<td>Brazil, Chile, Colombia, Mexico, Peru, Philippines, South Africa, Ukraine, United States</td>
<td>Not yet recruiting</td>
<td>Aug 10</td>
</tr>
<tr>
<td>ModernaTX</td>
<td>United States</td>
<td>NCT04470427</td>
<td>≥18</td>
<td>30000</td>
<td>2</td>
<td>United States</td>
<td>Recruiting</td>
<td>Sep 9</td>
</tr>
<tr>
<td>Sinovac</td>
<td>China</td>
<td>NCT04456595</td>
<td>18-59</td>
<td>8870</td>
<td>1</td>
<td>Brazil</td>
<td>Recruiting</td>
<td>Aug 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>INA-WXFM0YX</td>
<td>18-59</td>
<td>1620</td>
<td>Not provided</td>
<td>Indonesia</td>
<td>Not provided</td>
<td>Aug 10</td>
</tr>
<tr>
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<td>≥18</td>
<td>15000</td>
<td>1</td>
<td>United Arab Emirates</td>
<td>Unknown</td>
<td>Jul 19</td>
</tr>
</tbody>
</table>

a Of the sponsor/manufacturer. Because the follow-up period of trials sponsored by western companies will last 1 to 2 years, the first long-term (1-year) safety and efficacy results will not be available before the last quarter of 2021. With regards to recruitment status, it should be noted that some trials could have started after the last update was posted on the registry.

b Clinical trials registries were checked on September 17, 2020.

The registry only reports that the trial is “ongoing.”

This is a phase 1/2/3 trial.

Recruitment (phase I) started on April 29, 2020; the registry does not report whether phase 3 recruitment has already started.


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Conflict of Interest Disclosures: None reported.


In Reply

We appreciate the comments made by Dal-Ré in response to our Viewpoint.1 Foremost, we appreciate Dal-Ré’s attempt to further clarify how the safety and efficacy criteria should guide whether to mandate a coronavirus disease 2019 (COVID-19) vaccine for children. We have a few additional thoughts.

First, although Dal-Ré expresses frustration that the safety and efficacy data for a COVID-19 vaccine needed to justify mandatory school immunization programs may not be available until 2024, we believe that such a timeline may be perfectly justifiable. It is essential that we have a high degree of certainty regarding the safety of a COVID-19 vaccine before compelling its administration to children. Prelicensure and postlicensure safety data are needed to achieve this high degree of certainty. Accumulating these data, as Dal-Ré reiterates, takes time.

It could be argued that less comprehensive safety data be required in the context of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic when considering whether to mandate a COVID-19 vaccine for children. These arguments would hinge on the claim that the benefits (protection from serious illness and faster reduction in the spread of SARS-CoV-2) outweigh the risks that accompany a lower degree of certainty of the vaccine’s safety profile. We think such claims are perilous. Although it may be justifiable to shorten some safety benchmarks to expedite the availability of a COVID-19 vaccine to some high-risk populations, we argue that safety should not be compromised for speed when considering mandating a COVID-19 vaccine for children, especially because children are at low likelihood of serious illness.2

Second, it is helpful here to emphasize the distinction between mandating a vaccine, such as compelling administration before school entry, and recommending a vaccine, as might be done by the Advisory Committee on Immunization Practices. The criteria to consider for each, and the weight attached to such criteria, are not the same. Vaccine efficacy is illustrative here. Most vaccines mandated for school entry are more than 80% effective at preventing disease, with several having greater than 90% effectiveness. We contend that a COVID-19 vaccine should have a comparable effectiveness if we intend to make it mandatory for children to attend school. This does not mean that the efficacy of a COVID-19 vaccine needs to be 80% to 90% to justify recommending it for children. Although high vaccine efficacy is desirable, it is not always achievable (eg, influenza vaccine) and need not be as heavily weighted in determinations to recommend (vs mandate) a vaccine.

Lastly, even recommendations for a COVID-19 vaccine for children are moot until we have data from children included in COVID-19 vaccine trials. We agree with the growing consensus to begin such studies now.3-5 The announcement by Pfizer that they received approval from the US Food and Drug Administration to include children 12 years and older in its COVID-19 vaccine trial is progress. We hope that this is followed by enhanced transparency about federal plans and timelines for including even younger children in COVID-19 vaccine trials.

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Early High-Dose Gluten Intake to Prevent Celiac Disease: Data Do Not Allow Conclusions

To the Editor A secondary analysis of the Enquiring About Tolerance (EAT) trial concludes that high gluten intake from age 4 months reduces later celiac disease (CD).1 Of 1303 enrolled participants, 77% were tested for transglutaminase type 2 (TG2)