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# Vaccinating children against SARS-CoV-2

## Hard to justify right now for most children in most countries

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Following widespread vaccination against SARS-CoV-2 of older adults and other highly vulnerable groups, some high income countries are now considering vaccinating children; just days ago, the US Food and Drug Administration authorized the use of the Pfizer/BioNTech vaccine in children 12-15 years of age. Young people have been largely spared from severe covid-19 so far,<sup>1,2</sup> and the value of childhood vaccination against respiratory viruses in general remains an open question for three reasons: the limited benefits of protection in age groups that experience only mild disease<sup>3</sup>; the limited effects on transmission because of the range of antigenic types and waning vaccine induced immunity<sup>4</sup>; and the possibility of unintended consequences related to differences in vaccine induced and infection induced immunity.<sup>5</sup> We discuss each in turn.

### Protection

The cost-benefit balance of any vaccination campaign depends on disease burden in the target population and available resources.<sup>6</sup> Covid-19 severity in children under the age of 12 is similar to that of influenza,<sup>7</sup> and as health resources are stretched thin even in high income countries vaccinating children is unlikely to be a priority. Preliminary data suggest that disease caused by variants of concern remains mild in young children,<sup>8-10</sup> although close monitoring of newly emerging variants remains essential. Were one to emerge that caused severe disease in children (like Middle East respiratory syndrome), vaccinating children would become a priority.

Additionally, vaccination may be particularly valuable for some subgroups. Certain chronic conditions, including obesity, predispose children to more severe covid-19,<sup>11</sup> and those with markers of inflammation and cardiac distress, such as high levels of C reactive protein, interleukin-6, and brain natriuretic peptide, are more likely to develop serious sequelae such as multisystem inflammatory syndrome.<sup>12</sup> Studies to identify whether laboratory markers before infection can predict risk of multisystem inflammatory syndrome should be a research priority, to help target vaccination to vulnerable children.

### Transmission

Recent studies provide evidence that mass vaccination reduces population transmission of SARS-CoV-2.<sup>13</sup> School age children and teenagers generally have higher rates of social contact than older adults,<sup>14</sup> so vaccinating children might reduce circulation of pathogen and protect older and more vulnerable adults from exposure.<sup>15</sup> However, children seem to be less susceptible than adults to both infection and transmission of SARS-CoV-2,<sup>16,17</sup> and

countries such as Norway maintained low transmission rates despite keeping primary schools open. Both suggest a limited role for young children in sustaining chains of transmission<sup>18</sup> and that vaccinating children is likely to be of marginal benefit in reducing the risk to others.

New variants are emerging as the virus adapts to its human host and to the immunity generated by previous SARS-CoV-2 infections and vaccination. It is therefore essential to continue monitoring disease severity across all age groups so vaccination strategies can be adapted rapidly if required. For example, adults seem to retain substantial immunity for at least eight months after vaccination or natural infection,<sup>19-21</sup> but if ageing immune systems and waning immunity against new variants lead to shorter protection from severe disease, updated vaccines for adults and vaccinating children to reduce transmission may become more desirable. Additionally, emergence of variants with increased severity in children, or in adults with previous immunity, would signal a more urgent need to control both transmission and disease through vaccinating children.

### Unintended consequences

Unfortunately, as virus circulation decreases, the age of primary infection increases, and since age is directly associated with pathogenicity, vaccinating children would likely lead to lower infection rates but higher case fatality rates.<sup>22</sup> Additionally, depending on the relative durations of immunity induced by vaccines and infection, and the rate of viral antigenic change, vaccinating children might increase the frequency of large seasonal epidemics, leading to overall increases in virus induced morbidity and mortality.<sup>5</sup>

Finally, mRNA vaccines against SARS-CoV-2 induce greater antibody responses than natural infection but may elicit CD8 T cell responses that are less broadly protective against future variants.<sup>23,24</sup> Further studies on the differences between vaccine and infection induced immunity should be done to explore and quantify these trade-offs.

### Balanced decision

Should childhood infection (and re-exposures in adults) continue to be typically mild, childhood vaccination will not be necessary to halt the pandemic. The marginal benefits should therefore be considered in the context of local healthcare resources, equitable distribution of vaccines globally, and a more nuanced understanding of the differences between vaccine and infection induced immunity.

Once most adults are vaccinated, circulation of SARS-CoV-2 may in fact be desirable, as it is likely to lead to primary infection early in life when disease is mild, followed by booster re-exposures throughout adulthood as transmission blocking immunity wanes but disease blocking immunity remains high.<sup>22 25</sup> This would keep reinfections mild and immunity up to date.

Monitoring disease severity remains critical, however, in both immunologically naive children and vaccinated or previously infected adults, so we can adapt our control strategies as the virus adapts to us.

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