

## Vaccinating Children against COVID-19: A race against time in the middle of death and devastation

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### Abstract:

The coronavirus disease 2019 (COVID-19) is a contagious viral infection of the respiratory system caused by SARS-coronavirus-2 (SARS-CoV-2). The outbreak of the disease was first reported in Wuhan, China in December 2019. The spread of COVID-19 is continuous and was declared a pandemic disease by the World Health Organization (WHO) on 11 March, 2020. As of 20 May 2020, more than 4.7 million people have contracted the disease and 318,789 people have died.

Vaccines save millions of lives each year. The development of safe and effective COVID-19 vaccines is a huge step forward in our global effort to end the pandemic and to get back to doing more of the things we enjoy with the people we love.

**Keywords:** Covid-19, Covid Vaccine, Covid Pandemic

In China, only 0.9% of 72,314 infected people were children with a 0% mortality also pointed out that children are less affected by the disease, but they might be a carrier, transmitting the disease to other people.[1]

The Korean Centres for Disease Control & Prevention (KCDC) released the data of a total of 8,413 COVID-19 cases on 18 March. Similar to China, only 1.03% of the total of infected people were children aged below 10 years of age. Moreover, in Italy, 0.49% of the 24,879 people infected with COVID-19 were children younger than 10 years old. The same pattern was seen in the data released about 2,449 known-age Covid-19 patients in the USA. There was not a single child recorded to be admitted to an intensive care unit (ICU) in the USA. Despite the low incidence of COVID-19 among children, it appears that the virus mostly affects adults and the elderly, particularly those who have other health problems. The reasons why children are less susceptible to COVID-19 remain unclear. Here, we hypothesized that the MMR vaccination might be a reason why children have protection against the

disease.

In terms of epidemiology, children and the elderly are two groups of people who are at high risk of contracting infectious illnesses. However, data released from COVID-19 patients show that children are less susceptible to contracting the disease, compared to adults and the elderly. Understanding the immunological base of children's protection against COVID-19 can prevent and control further spreading the disease.[2]

COVID-19 has affected millions of people since SARS-CoV-2 was identified in December 2019. Children account for 1%–3% of diagnosed COVID-19 cases and have less severe disease and better prognosis than adults, with deaths being extremely rare and mainly affecting adolescents and those with significant underlying comorbidities.[3] Early epidemiological studies suggest that children do not contribute much to the spread of SARS-CoV-2 and that younger children may be less likely to get infected or transmit the virus compared with older children or adults.[4]

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Most children with SARS-CoV-2 infection are either asymptomatic or develop mild and non-specific respiratory symptoms. Some children have, however, developed paediatric inflammatory multisystem syndrome (PIMS-TS; also known as multisystem inflammatory syndrome in children), which shares features with Kawasaki disease and toxic shock syndrome and typically occurs 2 to 4 weeks after SARS-CoV-2 infection.[5]

The low rates of severe disease and death associated with SARS-CoV-2 infection in children and young people would suggest that they should not be prioritised for vaccination during early vaccine deployment. SARS-CoV-2 vaccine trials have so far rightly focused on adults, and safety data are currently restricted to adults in vaccine trials, with limited data in children. Additionally, large-scale postimplementation surveillance following mass immunisation will be needed to assess the risk of rare events, including immune mediated conditions such as antibody dependent enhancement and PIMS-TS in vaccinated individuals. **HIGH-RISK CHILDREN** Specific paediatric risk groups may benefit from immunisation during the early vaccine deployment stage.

Given the limited data on safety and effectiveness of SARS-CoV-2 vaccines in children at present, however, it may be prudent to initially recommend any vaccination for older children (eg,  $\geq 12$  years old) who appear to be more at risk of severe and fatal disease than younger children<sup>1</sup> and then extend recommendation to children of all ages as more data become available. Since severe COVID-19 is rare in children, however, there are limited data on relative risks of hospitalisation, paediatric intensive care unit (PICU) admission or death in children with specific comorbidities unlike adults.[1] Additionally, children with the highest risk of COVID-19 may have shielded and thus reduced their risk of exposure to the virus. For non-COVID-19 infections, younger age, underlying pulmonary pathology and immunocompromising conditions were associated with more severe outcomes in children.[2] During the first wave of the pandemic in England, there were eight deaths in SARS-CoV-2 positive children, including four that were attributed to COVID-19, of

which three were in children aged 10–15 years with severe underlying neuro-disabilities.[3] A large prospective UK study reported neurological conditions (11%; 65/614) as the most prevalent underlying condition in children hospitalised with COVID-19.5 In a small cross-sectional study of 46 North American PICUs, 24 of 48 (50%) children aged  $\leq 21$  years had at least one comorbidity, including 19 (40%) with complex medical problems, defined as children with long-term dependence on technological support (including tracheostomy) associated with developmental delay and/or genetic anomalies.[6] Adults with cerebral palsy also had a higher risk of hospitalisation and death due to COVID-19, while the risk was only slightly higher in adults with learning disabilities other than Down syndrome. While such data are currently limited in children, it is biologically plausible that Down syndrome and cerebral palsy may also be associated with an increased risk of severe COVID-19.

Considering all the data so far, children with varying degrees and severities of neuro-disabilities appear to be overrepresented among the small number of cases reported with severe or fatal COVID-19. Given the well-described high risk of large outbreaks in closed institutional settings, one potential group that might benefit from early immunisation could be children with severe neuro-disabilities, including cerebral palsy, residing in or in regular attendance at special educational needs or disabilities schools and colleges, paediatric rehabilitation centres, residential schools and care homes for such children. This might give direct protection against COVID-19 in settings where many of the most vulnerable of children might be together. This is also a well-defined group that could easily be identified for targeted immunisation in the early vaccine deployment stage. This same cohort of children with severe and profound learning disability form part of the group with chronic neurological diseases that is recommended for annual influenza vaccination in the UK. Another potential group for vaccination early in vaccine deployment would be adolescents aged 16–17 years working in health and care settings (especially care homes) who are likely to have similar occupational risks of SARS-CoV-2 exposure as their adult counter parts.[7]

Although data are limited in children, there are other potential groups that may also be at increased risk of severe and/ or fatal COVID-19 such as the immunocompromised, including (stem cell) transplant recipients and haemoglobinopathies such as sickle cell disease as has been reported in adults.[1] Children with immunocompromising conditions including malignancies represented 8% (48/615) of COVID-19 hospitalisations in the UK and 23% (11/48 children) of PICU admissions for severe COVID-19 in North America.[6, 8] Vaccine efficacy may be lower in immunocompromised children, so this group may require additional vaccine doses and/or different scheduling compared with immune-competent children. Further vaccine immunogenicity, effectiveness and safety data are needed before recommending vaccination of this highly vulnerable group. Additionally, the current investigational SARS-CoV-2 vaccines have different mechanisms of action, and it is likely some vaccines may be more immunogenic and efficacious for immunocompromised individuals than others.[9]

As more safety and effectiveness data emerge and vaccine availability increases, wider recommendations for vaccination can be considered, particularly for other high-risk children. It is likely that the major risk groups for influenza vaccination may also be applicable to SARS-CoV-2 and therefore, over time, these same risk groups—especially those with chronic respiratory conditions including ex-premature infants with chronic lung disease and those with chronic heart disease— could also be recommended SARS-CoV-2 vaccination.[8,10] Whether all children will eventually be vaccinated will depend on a number of factors. These include the role of children in transmission as well as the safety, effectiveness and duration of protection afforded by available vaccines. Most importantly, it will depend on whether such vaccines interrupt transmission, thereby inducing indirect (herd) protection for the population, as has been demonstrated with the UK childhood influenza immunisation programme. Up-to-date recommendations for SARS-CoV-2 vaccination in the UK will be maintained in the 'Green Book' (Immunisation against Infectious Disease).[10]

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