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## What do we know about covid-19 vaccines in under 5s?

It took a year for covid-19 vaccines to be tested and approved for use in children. As countries now reach out to the youngest age group, **David Cox** reports on the evidence for their effectiveness and deployment

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On 18 June 2022, regulators in the US voted to authorise the rollout of Pfizer and Moderna's covid-19 vaccines to children under the age of 5, meaning that the jabs will now be available to an estimated 20 million babies and toddlers.<sup>1</sup> The decision sees the US join Argentina, Bahrain, Chile, China, Cuba, Hong Kong, the United Arab Emirates, and Venezuela in offering covid-19 vaccines to the youngest age category.<sup>2</sup> Regulators in Europe are predicted to follow in the coming weeks.

Commissioners at the US Food and Drug Administration (FDA) said that vaccinating under 5s will provide vital protection against hospital admissions and death, with Peter Marks, director of the FDA's Centre for Biologics Evaluation and Research, describing it as "a milestone."

But not all scientists are convinced that vaccinating under 5s will make a meaningful difference in tackling the pandemic.

"The risk of severe covid-19 in children is very, very low in terms of hospital admissions, fatalities, and long term problems," says Shamez Ladhani, a paediatric infectious diseases specialist at St George's Hospital, London. "You end up having to vaccinate a lot of children to have a little bit of improvement in terms of outcomes at a population level." According to Office for National Statistics data for the week ending 3 July, hospital admission rates for children under 5 in the UK were just eight per 100 000, compared with 59.33 per 100,000 for 75 to 84 year olds.<sup>3</sup>

Moreover, in the wake of omicron and its subsequent subvariants, most under 5s are thought to have now been exposed to the SARS-CoV-2 virus, perhaps limiting the need for vaccines which have a reduced ability to prevent infection. "Most of these kids already have some immunity from exposure to the virus," says Ladhani. "The benefits of vaccinating on top of a previous infection, using a strain from two and a half years ago, are not known."

### Clinical trial data

One of the criticisms of both Pfizer and Moderna's vaccines is that the interim data from clinical trials show they are relatively ineffective in preventing symptomatic infection in young children.

Moderna's two dose regimen is between 37% and 51% effective at preventing children under 6 from becoming infected.<sup>4</sup> Pfizer claim their vaccine, administered in three doses, to be 80% effective at preventing infection in children between 6 months

and 4 years old—this figure was, however, based on a sample of 10 children.<sup>4</sup>

"The top line efficacy results from interim analysis are not impressive," says Hamid Merchant, a researcher in the department of pharmacy at the University of Huddersfield. "Although the vaccines are likely to be approved by the Medicines and Healthcare Products Regulatory Agency, they'll probably be deemed non-essential for healthy children under 5."

And it's not just Pfizer and Moderna. There are limited efficacy data available for the three other covid-19 vaccines currently approved for under 5s in various countries—those produced by Chinese companies Sinopharm and Sinovac, and the Soberana vaccine from Cuba. Earlier this year, a study of Sinovac's vaccine in 49 694 3-5 year olds in Chile, found that it was just 38% effective at protecting against symptomatic infection.<sup>5</sup>

Of course, how researchers and public health officials perceive the risk-benefit ratio of rolling out vaccines to under 5s varies around the world and depends on the impact covid-19 has had on that country. Sweden has had just a handful of fatalities in those aged under 18,<sup>6</sup> and vaccines are still not available to children aged 5-11 years. But in Brazil the virus has killed an average of two children under the age of 5 each day<sup>7</sup>—a rate which equates to around one in every five deaths among under 5s worldwide. Understandably, doctors are keen to boost protection levels, fearful of the impact that future variants might have.

"The main concern is protecting these children and avoiding interrupting scholarly activities," says Pilar Veras, a researcher at the Instituto de Ciências Biomédicas II in São Paulo. "We can't know for sure if a new variant will have a more significant impact on children than the previous ones."

In Australia, paediatricians are seeing an increase in hospital admissions of children with multiple respiratory virus co-infections, such as respiratory syncytial virus, influenza, and covid-19. Public health officials feel, therefore, that there is still something to gain from vaccinating younger age groups.

"Although children under 5 don't appear to get as unwell, there is still a risk for hospital admission," says Nick Wood, associate director of clinical services and vaccine safety at the National Centre for Immunisation Research and Surveillance in Sydney. "One of the benefits of vaccination would be to reduce the impact of covid-19 in the severity of multiple infections."

## Sceptical parents

Even if vaccines are made available to children, it remains to be seen whether parents will accept them. The Kaiser Family Foundation has already noted that vaccination rates among under 5s in the US have peaked and are now decreasing, just weeks after they became available.<sup>8</sup>

Data looking at the proportion of 5-11 year olds in the US and UK who have received covid-19 vaccines since they became available to this age group have already provided indications that many parents are not convinced they are necessary.

So far just 36% of 5-11 year olds in the US have had at least one dose of a covid-19 vaccine since they were approved in November 2021.<sup>9</sup> Rates are lower in England where only 10% of 5-11 year olds have received a single dose.<sup>10</sup> In one survey conducted in March, 41% of parents of UK primary school children said that they would not have their children vaccinated if offered the jab.<sup>10</sup>

This may represent part of a concerning trend. A new analysis from Unicef and the World Health Organization reported a noticeable global decline in routine childhood immunisations against measles, polio, diphtheria, tetanus, and pertussis since 2019.<sup>11</sup>

Others, however, feel it is likely because the UK's Joint Committee on Vaccination and Immunisation (JCVI) has downplayed the benefits of vaccination in young children. "The advice from JCVI was that vaccines for this age group are non-essential," says Merchant, "The low uptake is not surprising."

Vaccine uptake in Australia is much higher with more than half of 5-11 year olds having received one jab, and 40% being double vaccinated.<sup>12</sup> This followed a sustained grassroots engagement approach with initiatives such as the Vaccine Champions Program and Building Confidence in Covid-19 Vaccines sessions emphasising the importance of childhood immunisation to communities across the country.

"There are benefits to vaccinating children under 5—both direct and indirect," says Margie Danchin, a consultant paediatrician at the Royal Children's Hospital in Melbourne, who has been involved in both initiatives. "We know children are at low risk of severe disease, but it does occur, and while vaccines have a reduced impact on transmission, there is still some value."

Ladhani feels that the major public health risks which come with making vaccines available to under 5s is not so much safety—all studies so far have reported minimal side effects—but what he calls "opportunity costs."

With nearly four million children in this age group, he predicts that vaccinating all of them against covid-19 would drive down inoculation rates for other diseases, through healthcare resources becoming over-stretched.

"To give one opportunity, you have to take it away from somewhere else," Ladhani says. "That's unfortunately how our healthcare works. Routine childhood immunisation may then be delayed because there aren't enough immunisers. A lot of our disease control is based on herd immunity protection. If we don't vaccinate enough kids, we may not be able to maintain that population control of diseases that we don't see anymore."

## Nasal vaccines: game changer?

Ladhani feels it might be easier to see the benefits of vaccinating this age group if the available jabs were able to prevent infection more robustly, limiting community transmission in the process. In

future a new generation of covid-19 vaccines, ones that are administered intranasally, might be able to help with this.

Intranasal flu vaccines have proved far more effective in preventing cases of influenza in children because they produce mucosal antibodies that provide protection at the point of entry for the virus. Data has shown that they have boosted vaccine efficacy to more than 87% in children, compared with rates of 30-60% with injectable vaccines.<sup>13</sup>

There are currently a range of nasal covid-19 vaccines in clinical development, including candidates from AstraZeneca, Bharat Biotech, CanSinoBIO, Lancaster University, National Taiwan University Hospital, Sputnik V, and the Université de Tours.

"Since the introduction of nasal flu jabs for school children in the UK, we were able to achieve the desired outcome from mass flu immunisation in the UK," says Merchant. "Our experience with nasal flu vaccines suggests that a multivalent covid nasal vaccine is a likely solution for preventing infections in children and blocking community transmission."

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