Intended for healthcare professionals

Rapid response to:

Head To Head Covid-19

Should we delay covid-19 vaccination in children?

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Rapid Response:

Should COVID-19 be a vaccine disease or a childhood disease?

Dear Editor

In the discussion regarding COVID-19 vaccination of children, several aspects seem to be missing.

First, vaccination of children is based on a small Pfizer-sponsored phase 3 trial of 2260 adolescents randomized to BNT162b2 COVID-19 vaccine or saline. The resulting paper concludes that the vaccine ”had a favorable safety profile”(1). However, based on data presented in supplementary table 2, in the age group 12-15 years, 7/1131 vaccinated vs. 2/1129 unvaccinated had a severe adverse event (1), i.e. a 3-fold increased risk. In the 16-25 years age group presented in the same paper, 9/536 vaccinated vs. 3/561 unvaccinated had a severe adverse event (1), i.e. likewise a 3-fold increased risk. The combined results indicate a 3.28 (95% confidence interval 1.21 to 8.94)-fold increased risk in severe adverse events in the vaccinated adolescents/young adults (2). In absolute numbers, 1 of 100 vaccinated experienced a severe event, vs. 3 of 1000 unvaccinated. Data was not presented by sex.

A protective vaccine can have negative non-specific and sex-differential effects on overall health (3). For instance, a protective measles vaccine had to be withdrawn after being associated with 2-fold higher all-cause mortality for females (4). A partially protective malaria vaccine was recently likewise associated with 2-fold higher female mortality (5). These epidemiological observations indicate that while the vaccines protected against the target disease, they increased the susceptibility to other diseases. In other words, the specific protection came at the price of increased susceptibility to other diseases. This epidemiological phenomenon of negative non-specific effects has been linked to innate immune tolerance (3, 6). Though the number of participants was small, the only study so far of BNT162b2 COVID-19 vaccine indicates that this vaccine induces innate immune tolerance towards bacterial and viral ligands (7). Thus, protection against COVID-19 could come at the price of increased risk of other infections.

andemic vaccines have later been found out to have caused rare but severe side effects, like Guillain-yndrome in recipients of flu vaccines in 1976, and narcolepsy linked to one brand of swine flu influenza

vaccine in 2009(8). None of the phase 3 trials of COVID-19 vaccines were designed to study either non-specific sex-differential effects, or rare but severe long-term side effects (8).

Given the low risk of severe COVID-19 in previously healthy children - none in the Pfizer-sponsored phase 3 trial (1) - it is not clear that vaccine benefits outweigh harm in healthy children.

Second, arguments for vaccinating children include that infection in children could lead to more dangerous variants. Variants of concern have typically been the result of persistent infections in immunocompromised people that can cause the virus to mutate more frequently because the person's immune system cannot clear the virus as quickly as the immune system of a healthy person (9). Presumably healthy children, who typically have very mild/short-lasting infections, are unlikely to give rise to variants of concern. Noteworthy, individuals, who have had COVID-19 infection, will likely have broad resistance towards SARS-CoV2 variants(10), and thus contribute importantly to herd immunity.

This leads us to the third point: Should COVID-19 be a vaccine disease or a childhood disease? There has been surprisingly little discussion about the future of COVID-19. Many people seem to assume that COVID-19 will become a disease for which we vaccinate the whole population perhaps annually or biannually. This will be expensive - and potentially harmful, if the (repeated) vaccinations have negative effects. We do not think vaccination of the whole population is necessary either; in fact, it may be counter-productive for society.

The known endemic human Corona-viruses (HCoV) infect most people before age 15; thereafter people may become re-infected again, but as evidenced by the lack of IgM responses, the response is a recall response (11). These HCoV rarely cause severe disease until the age of immunosenescence and we would never contemplate vaccinating against HCoVs at the population level, even if vaccines existed.

Given that we are so lucky that SARS-CoV2 very rarely cause severe disease in children, the safest and cheapest way forward seems to be to tame SARS-CoV2 to a common childhood disease like other HCoV. This would happen by allowing SARS-CoV2 to infect children, who thereby likely become protected against severe disease well into late adulthood. Importantly, this transition of SARS-CoV2 into a childhood disease would be delayed if there is too little SARS-CoV2 circulating. As noted by others: “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 … This would keep reinfections mild and immunity up to date”(12).

In conclusion, there are good arguments why not vaccinating children may in fact serve several purposes at the individual as well as at the societal level:
• Not vaccinating children protects children against the potential unknown harms of COVID-19 vaccinations.
• Not vaccinating children gives them the opportunity to develop a broad natural immunity, contributing to herd immunity, and speeding up the transition of SARS-CoV2 into a childhood disease.
The avoided costs of making COVID-19 a vaccine disease, for which we vaccinate the whole population maybe annually or biannually, could be well spend on other health related issues such as smoking, cancer, obesity, and mental health.

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