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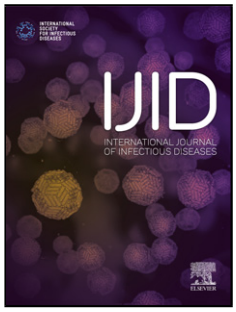

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Herd Immunity and Vaccination of children for COVID19

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Recognized individual risk factors for a more severe clinical outcome of COVID-19 are age above 65 years and underlying comorbidities, such as obesity, chronic obstructive lung disease and diabetes (1;2). Whilst, the frequency of severe cases and mortality among children are reported to be extremely low when compared with adults (3), transmission from

children could be an important contributor to the spread of SARS-CoV-2, as with other respiratory viruses. However, the relative importance of children in SARS-CoV-2 transmission is still unclear, in particular whether asymptomatic children, those with low viral loads and perhaps with prolonged viral shedding play an important role. Few studies describe children as index cases in familial clusters (4;5) and clearly children more often have asymptomatic infections when compared with adults (3;5;6). It is of urgent importance in modelling the pandemic to undertake careful surveillance, including asymptomatic children and rates of infection based on serology, to better characterize infection in children and their role in transmission networks.

Even if different control measures slow down and eventually and locally stop the spread of COVID-19 disease, the successful suppression of this disease still leaves the population at risk of resurgence due to insufficient acquisition of immunity. If herd immunity can be induced, it would act as a barrier to stop the spread of infection (7). In addition to vaccines, variable susceptibility and exposure largely determine herd immunity. Vaccination of children to induce herd immunity has proven successful in preventing the spread of many infectious diseases, where children have a significant role in transmission. A high level of immunity in one age group, who play a role in transmission, can create herd immunity for others (8), and it is evident that immunization of children is more effective than vaccination of elderly people, in certain situations, as demonstrated in immunization against influenza (8;9), pneumococcal disease (10), rotavirus (11) and many others. It is noteworthy that the relative role of different age groups in transmission must be taken into account – for example vaccination of adoelscents and young adults prevents spread of meningococcal disease, but infants and toddlers must be targeted to induce herd immunity for pneumococcal, and Hib disease, and school-age children for influenza transmission. Children may need protection also, as some become ill, although almost never severely. The indirect benefits of COVID-19 vaccination in children may provide or create some protection for older, unvaccinated populations. When

children are vaccinated, it will be easier to achieve enough immunity needed for overall protection in a given population.

COVID-19 mortality is strongly age-dependent, and Africa has a comparably younger population than other continents (12). Thus, children might be an important target for interventions aimed at reducing transmission in countries with young populations, especially since access through school immunisation may be more straightforward than accessing adults. Although, the priority for COVID-19 vaccination would logically be for those at highest risk of infection, such as healthcare workers, and those at highest risk of severe disease, such as older adults, vaccination of children may be another important group for their own protection and to support herd immunity.

A multisystem inflammatory syndrome, similar to Kawasaki disease, has recently been recognized, and may be associated with SARS-CoV-2 infection, perhaps as a post-infectious inflammatory syndrome. One quarter of these cases may develop coronary vascular damage and other cardiac complications. As there is growing evidence of a link between a SARS CoV-2 infection and this inflammatory syndrome (13), the condition should be included as a potential adverse event of special interest in vaccine studies. Although it is thought that some of the described cases do not have any evidence of an immune response to SARS-CoV-2, it is still unclear whether the phenomenon could be mediated by immune responses to novel vaccines.

Since children remain relatively unaffected by COVID19 disease, it is important to accrue substantial safety data among adults before initiating paediatrics studies, and to further understand the biology of the Kawasaki syndrome to inform the risk-benefit relationship for vaccination of children. In addition, efficacy trials in adults with disease endpoints would be important to provide certainty that new vaccines do not induce enhanced disease, when vaccinees are exposed virus in the community, as has been described in some animal models with previous coronavirus vaccines.

COVID-19 vaccine studies are essential to protect older adults from the disease, but to affect transmission at a large scale and achieve herd immunity it may be necessary to obtain high population coverage with vaccines, including the paediatric population. COVID-19 vaccine trials in children will allow development of evidence-based vaccination policy and combined with more robust data on the role of children in transmission, could greatly assist decision-making.

It is important that vaccine developers focus on investigation of new COVID19 vaccines among adults as the primary target population, but we should not ignore children and an important group in the population who may benefit from direct protection and play a key role in the overall immunity in the population.

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Conflict of interest: The authors TPV and PGK disclose no conflict of interest. AJP is Chair of UK Dept. Health and Social Care's (DHSC) Joint Committee on Vaccination & Immunisation (JCVI) and is a member of the WHO's SAGE. AJP is an NIHR Senior Investigator. The views expressed in this article do not necessarily represent the views of DHSC, JCVI, NIHR or WHO. AJP is the chief investigator on trials of a coronavirus vaccine, Chadox1 nCov19.

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