

# Vaccinating adolescents wisely against COVID-19

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Every vaccine that is marketed for mass use, in large populations or worldwide, is characterised by high efficacy and rare adverse reactions. The latter are not identified in the regulatory trials, but in phase IV evaluation during use in the real world, the ones regulated by vaccination calendars or vaccination campaigns. The assessment of the benefit to risk ratio is only possible over time with appropriate monitoring of the risks attributable to the vaccine, but also to other causes. When the benefit is determined by the need to deal with a worldwide infection with dramatic outcomes and to rapidly counteract, or at least contain, a virus, as is the case with COVID-19, the benefit to risk ratio estimate is invalidated by numerous factors and the relationship may be completely altered. In this case, the criteria for using the vaccine become critical instead: the identification of the target population, priorities, vaccination strategies, characteristics and availability of the vaccine. The use of these criteria must also be monitored to achieve an optimal, safe and effective performance. This is the most critical aspect, particularly during a pandemic, as the first 6 months of vaccination against COVID-19 have shown. The definition, monitoring and evaluation of the observed and expected positive, symptomatic and deceased cases, the adverse reactions, and the antibody titres and their duration are the essential elements for estimating the benefit to risk ratio. Such a timely and effective approach was planned only in some countries. The priority, target populations for vaccination were identified everywhere, from the start, as being the elderly and healthcare personnel.

For the other populations, the criteria were varied and dissimilar between and within nations in terms of yield of the vaccine interventions. Unfortunately, this is true only for a part of the world population, since the majority are still waiting for vaccines.<sup>1</sup> The gap between available vaccines and vaccinated people raises concern around production and

distribution of vaccines, and global health equity.<sup>2</sup> Moreover, race/ethnic disparities in testing, infection rates and hospitalisation across the COVID-19 pandemic did not spare children.<sup>3</sup> Additionally, social determinants affect child health in the COVID-19 era.<sup>4</sup>

In this scenario, the use of the Pfizer vaccine in the population of children aged 12–17 years old was recently approved by the Food and Drug Administration (FDA), the European Medicines Agency (EMA) and a few national drug agencies following the results of a phase III trial conducted with 2260 adolescents (1131 vaccinated as adults).<sup>5</sup> Trials on the same population age range using the Moderna vaccine were also concluded and the use approved by the FDA and the EMA, while phase III trials starting from 6 months of age are also underway with other vaccines.

Adolescents and children rarely get sick with COVID-19. The symptoms are mild in the majority of cases,<sup>6</sup> and remote outcomes, as for adults, need to be monitored over time. In a few rare cases, a systemic inflammatory disease similar to Kawasaki syndrome, multi-organ inflammatory syndrome COVID-19, has been observed. Although characterised by potentially serious symptoms, the effectiveness of immunomodulatory medications has been reported.<sup>7 8</sup> Regarding the transmissibility of the infection between peers, cohabitants and contacts, the limits of tracing and the various preventive strategies still need to be defined in many countries, both nationally and locally. The numerator in the benefit to risk ratio in children aged 12–17 years old is therefore lower, overall, than that in other age groups. Direct, individual benefits of COVID-19 vaccination in adolescents are limited compared with older age groups. The overall direct benefits of adolescent vaccination will depend primarily on the incidence of SARS-CoV-2 infection and the prevalence of underlying conditions that increase the risk of severe COVID-19 in this age group. The overall benefit to the general population of



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vaccinated adolescents will be proportional to the transmission of SARS-CoV-2 within this age group and among other groups. Given the reduced individual benefit to risk ratio expected from vaccination against COVID-19 in adolescents compared with older age groups, the epidemiological situation, the coverage of at-risk groups and their possible trend should be carefully assessed before planning the mass vaccination of children and adolescents.

With respect to the risks, in Israel 257 cases of myocarditis were reported in 5 million vaccinated children aged 12–17 years old.<sup>9</sup> These 50 cases per million are many compared with the cases of thrombocytopenia reported in adults after vaccination with a viral vector (1 per million), but represent a rate that is close to the expected rate in the general paediatric population, and concern an infection that is, in any case, curable and with a good outcome.<sup>10</sup> COVID-19 vaccination therefore so far only seems to be measurable in terms of benefits, although these are of different magnitude between age groups. The vaccination is effective in reducing severe symptoms and sequelae and, depending on the vaccine, is effective against some of the variants identified so far. There is still a need for evidence regarding the effectiveness in contagiousness and the duration of coverage over time. In agreement with the European Centre for Disease Prevention and Control,<sup>10</sup> it can therefore be stated that, as for other age groups, adolescents at high risk of COVID-19 should be vaccinated. Vaccination of adolescents should be considered in the broader context of the prevention strategy for the entire population, the epidemiological situation of the infection and its variants, the status (rate) of population coverage, and priorities. Extending COVID-19 vaccination to population groups with a lower individual risk of serious disease implies that the availability and access of vaccines is such as to ensure fairness in their use.

More generally, the opportunity to vaccinate adolescents, and soon also children, raises some considerations on the communication methods in recent months and on the chronic inattention paid to this particular population. School-aged children and adolescents represent one of the categories most affected by psychological disorders from the pandemic.<sup>11</sup> Schools were closed and were among the last to reopen. School activities and education were not considered essential activities in many countries. Justifying the vaccination of young people today to ensure a safe reopening of the next school year should foresee a greater involvement of those same students, also with brief lessons on prevention.

Adolescents have experienced isolation at a crucial time in their development. This has resulted in an increase in mental health problems. There needs to be recognition of this problem alongside interventions to

help rectify the experiences. Young people are the most socially active segment of the population. A social welfare plan for young people alongside vaccination is needed. One needs to recognise the importance of school as a place for social interaction as well as education. Both are essential for the well-being of young people. The rights of young people have been most severely affected by the lockdown measures introduced by governments in response to COVID-19.

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