Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Considerations of hybrid immunity and the future of adolescent COVID-19 vaccination

Pre-licensure clinical trials for the BNT162b2 COVID-19 vaccine showed high efficacy among adolescents. Similarly, post-licensure studies in this population found high mRNA vaccine effectiveness against both SARS-CoV-2 infection and hospitalisation during the pre-omicron period. However, emergence of the omicron variant in November, 2021, as well as later omicron subvariants, resulted in decreased COVID-19 vaccine effectiveness and more rapid waning of protection, particularly against infection. Incidence of infection and subsequent seroprevalence across age groups, including adolescents, dramatically increased in the early omicron-dominant period; as of February, 2022, infection-induced seroprevalence estimates among adolescents aged 12–17 years in the USA were approximately 75%, and greater than 86% among those aged 12–15 years in England.

There is a growing body of research examining the protection afforded by hybrid immunity, which refers to immune protection in individuals who have had at least one dose of a COVID-19 vaccine and at least one previous SARS-CoV-2 infection before or after vaccination. Studies among adults in Canada and Qatar found that hybrid immunity provided more robust protection against omicron infection than either previous infection or vaccination alone. In The Lancet Infectious Diseases, Annabel Powell and colleagues provide the first estimates of protection against SARS-CoV-2 infection from hybrid immunity among adolescents aged 12–17 years.

Using a population-based, observational, test-negative, case-control design, Powell and colleagues estimated protection against symptomatic SARS-CoV-2 infection among adolescents in England by combinations of previous infection with specific individual SARS-CoV-2 variants and at least one dose of mRNA vaccine. The authors used national, community-based PCR testing data during periods of delta (B.1.617.2) and omicron (B.1.1.529; BA.1 and BA.2) predominance (Aug 9, 2021–March 31, 2022). The study population consisted of more than 1·1 million symptomatic adolescents with linked vaccination records, including nearly 115,000 adolescents with previously documented SARS-CoV-2 infection. Among unvaccinated adolescents, the authors found substantially lower protection from previous infection (wildtype, alpha [B.1.1.7], or delta) against subsequent omicron infection compared with against subsequent delta infection, and only 59% protection from a previous omicron infection against omicron reinfection. Hybrid immunity showed more robust protection against omicron infection, irrespective of the primary infection variant. Among the infection and vaccination combinations studied, the greatest protection against omicron (96%) was seen in adolescents with a previously documented omicron infection and two mRNA vaccine doses; this protection was maintained through 24 weeks, the maximum follow-up time available for this combination.

The study by Powell and colleagues is an important addition to the COVID-19 vaccine literature and the first to report on hybrid immunity in the adolescent population, who might have higher rates of previous infection than some adult age groups. The authors also analysed the potential effect of timing of vaccination relative to infection; although limited by low case numbers, the findings suggest robust protection from hybrid immunity regardless of the order of infection and vaccination. The study was not without limitations. The end of the community-based PCR testing programme in England resulted in the omission of later omicron subvariants from this analysis; only omicron BA.1 and BA.2 were examined, and those data were combined. Additionally, the study was unable to examine the protection afforded by the combination of previous omicron infection and three mRNA vaccine doses, and the authors did not assess protection against severe COVID-19 outcomes. Despite this, the authors’ examination of the protection of infection alone, mRNA vaccination alone, and infection and vaccination combinations in the adolescent population provides a wealth of information for researchers and policy makers. However, new omicron subvariants and novel, bivalent vaccine products produce new questions. These unknowns, in addition to increasingly complex, heterogeneous immune protection within populations, create challenges for decision making regarding vaccination.
Increased infection-induced seroprevalence,\textsuperscript{4,5} the waning of COVID-19 vaccine effectiveness,\textsuperscript{8,9} and the relatively low rates of severe COVID-19 outcomes in adolescents have called into question the need for additional COVID-19 vaccine doses in this population. However, the durable protection of SARS-CoV-2 infection alone previously seen against delta infections\textsuperscript{10} was not evident against omicron infections in the present study by Powell and colleagues.\textsuperscript{9} Hybrid immunity has shown more robust and longer-lasting protection than previous infection or vaccination alone, which we feel provides argument for continued primary series and booster vaccination in populations with previous infection, including adolescents. Similarly, WHO states that prevention of mild disease, indirect impact on transmission, and reduction of post-COVID-19 conditions provides a strong rationale for vaccinating even low-priority groups, irrespective of previous SARS-CoV-2 exposure.\textsuperscript{8} The absolute burden of severe disease due to high COVID-19 transmission is an additional consideration for continued vaccination.

In the future, improved understanding of hybrid immunity might allow for the integration of infection and vaccine-induced immunity considerations into COVID-19 vaccination strategies. However, given the current unknown long-term impacts of COVID-19 and repeat SARS-CoV-2 infection, and the increased immune evasion of recent variants and subvariants, remaining up-to-date with COVID-19 vaccination provides the best protection against future SARS-CoV-2 infection and related complications, including for adolescents. Ongoing monitoring of the breadth and duration of protection from infection and vaccination combinations in all age groups should be prioritised as SARS-CoV-2 continues to evolve.

We declare no competing interests.

"Stephanie A Irving, Sarah A Buchan stephanie.a.irving@kphpcr.org
Kaiser Permanente Center for Health Research, Portland, OR 97227, USA (SAI); Public Health Ontario, Toronto, ON, Canada (SAB); Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada (SAB); ICES, Toronto, ON, Canada (SAB)

1 Frenck RW Jr, Klein NP, Kitchin N, et al. Safety, immunogenicity, and efficacy of the BNT162b2 COVID-19 vaccine in adolescents. N Engl J Med 2021; 385: 239–50.
2 Ionescu IG, Skowronski DM, Sauvageau C, et al. BNT162b2 effectiveness against delta & omicron variants in teens by dosing interval and duration. medRxiv 2022; published online July 13. https://doi.org/10.1101/2022.06.27.22276790 (preprint).
3 Chemaitelly H, AlMukdad S, Ayoub HH, et al. COVID-19 vaccine protection among children and adolescents in Qatar. N Engl J Med 2022; published online Nov 2. https://doi.org/10.1056/NEJMoa2220058.
4 Clarke KEN, Jones JM, Deng Y, et al. Seroprevalence of infection-induced SARS-CoV-2 antibodies—United States, September 2021–February 2022. MMWR Morb Mortal Wkly Rep 2022; 71: 606–08.
5 Office for National Statistics. Coronavirus (COVID-19) latest insights: antibodies. 2022. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19latestinsights/antibodies#antibodies-in-children (accessed Nov 4, 2022).
6 WHO. Interim statement on hybrid immunity and increasing population seroprevalence rates. June 1, 2022. https://www.who.int/news/item/01-06-2022-interim-statement-on-hybrid-immunity-and-increasing-population-seroprevalence-rates (accessed Nov 4, 2022).
7 Altarawneh HN, Chemaitelly H, Ayoub HH, et al. Effects of previous infection and vaccination on symptomatic omicron infections. N Engl J Med 2022; 387: 21-34.
8 Caraz S, Skowronski DM, Brisson M, et al. Estimated protection of prior SARS-CoV-2 infection against reinfection with the omicron variant among messenger RNA-vaccinated and nonvaccinated individuals in Quebec, Canada. JAMA Netw Open 2022; 5: e2236670.
9 Powell AA, Kinsemb F, Stowe J, et al. Protection against symptomatic infection with delta (B.1.617.2) and omicron (B.1.1.529) BA.1 and BA.2 SARS-CoV-2 variants after previous infection and vaccination in adolescents in England, August, 2021–March, 2022: a national, observational, test-negative, case-control study. Lancet Infect Dis 2022; published online Nov 24. https://doi.org/10.1016/S1473-3099(22)00729-0.
10 Palaton T, Saciuk A, Hadad HO, et al. Naturally-acquired immunity dynamics against SARS-CoV-2 in children and adolescents. medRxiv 2022; published online June 21. https://doi.org/10.1101/2022.06.20.22221650 (preprint).

An opportunity seized: rapid clinical research provides insights into monkeypox virus dynamics and durations of infectiousness

Monkeypox is not a new disease; it was first detected in humans in the Democratic Republic of the Congo in 1970. Clinicians and scientists in countries in west and central Africa have previously reported the course of disease and virological findings from a number of clade I and clade II monkeypox virus outbreaks.\textsuperscript{1-3} However, the unprecedented international outbreaks in 2022, caused by clade IIb monkeypox virus, and driven by human-to-human transmission, have provided additional opportunities to describe clinical manifestations and investigate viral dynamics in individuals with monkeypox.