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.

Omicron-adapted vaccines might require longer follow-up to reveal true benefits

Endless SARS-CoV-2 omicron subvariants with drifting antigens highlight the importance of the neutralisation breadth of antibodies that confer protection to current and future SARS-CoV-2 variants.[1] Due to the metabolic cost, natural expansion of neutralisation breadth is time-limited and might be saturated by repeated antigen exposures.[2,3] Current vaccination strategies thus rely on artificial expansion of neutralisation breadth using variant antigens (eg, the upcoming bivalent Wuhan-Hu-1-omicron BA.5 vaccine).

Intriguingly, data on the bivalent Wuhan-Hu-1-omicron BA.1 vaccine mRNA-1273.214 showed a less than two-times increase in neutralising antibody titres against omicron BA.1, BA.4, and BA.5 subvariants compared with the Wuhan-Hu-1-only mRNA-1273 vaccine, both administered as a second booster dose.[4] Such a marginal advantage over existing vaccines is disappointing when omicron-adapted vaccines are hoped to effectively block transmission. However, we reason that the short follow-up time of 29 days might overlook later benefits of omicron-adapted vaccines.

Durability of antibody responses after vaccination or infection is limited by the lifespan of antibody-secreting cells. Meanwhile, the affinity maturation process selects B cells with a higher and broader affinity to the exposed antigen, which partly compensates the loss of antibody-secreting cells in convalescing or vaccinated individuals.[3,5] When these individuals are exposed to omicron BA.1 antigens, as in the mRNA-1273.214 study, neutralising antibodies would initially be secreted by cells derived from existing Wuhan-Hu-1-trained B cells with suboptimal affinity to BA.1 antigens.[6] The affinity maturation process would more efficiently select clones with optimal affinity to BA.1 and other subvariants from these BA.1-neutralising cells rather than from the pre-boosted Wuhan-Hu-1-trained pool (appendix p2).[7] This prolonged process was evident in breakthrough infections and a bivalent beta vaccine study in primates, with both showing increased neutralisation breadth 60 days after exposure.[8,9] By contrast, omicron neutralisation after Wuhan-Hu-1 booster vaccination would rely on less efficient affinity maturation of the Wuhan-Hu-1-trained pool.[5] Therefore, longer follow-up might reveal a larger difference in omicron neutralisation titres between omicron-adapted and Wuhan-Hu-1 booster recipients.

Omicron-adapted booster vaccination might extend the duration of immune protection by compensating immune decay. A previous study showed that, although antibody levels gradually declined after infection, neutralisation titres against Wuhan-Hu-1 and variants remained stable up to 1-year after infection thanks to the compensatory increase in neutralisation potency and breadth.[10] A longer affinity maturation process since first exposure in Wuhan-Hu-1 booster recipients might also contribute to more durable neutralisation activity against omicron subvariants than in primary vaccination recipients.[11] We expect more long-term than immediate benefits after omicron-adapted booster vaccination, which, given sufficient time, might better protect against current and emerging omicron subvariants than Wuhan-Hu-1 boosters.

We declare no competing interests.

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See **Online** for appendix