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Vaccine effectiveness against delta and omicron variants of SARS-CoV-2

mRNA vaccines give good protection against the most serious outcomes

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Never before had humanity seen such a swift, concerted response to the emergence of a lethal infectious disease as happened during the SARS-CoV-2 pandemic. Scientists, clinicians, publishers, the pharmaceutical industry, governments, and authorities allied to develop, approve, and roll-out targeted therapies and new vaccines within barely a year. As of 24 April 2023, more than 13.3 billion vaccine doses had been administered worldwide according to the World Health Organization.[1]

The scientific community responded to the pandemic in an unprecedented way, but the continuously changing attributes of SARS-CoV-2 seemed to outpace their prevention and therapeutic strategies. Thousands of mutations occurred, some of which conferred a degree of immune escape, making early research findings about transmission dynamics and vaccine effectiveness more or less obsolete. The linked retrospective cohort study by Bohnert and colleagues (doi:10.1136/bmj-2022-074521),[2] therefore, provides valuable new data about vaccine effectiveness in the periods when the delta (B.1.617.2) and omicron (B.1.1.529) were predominant variants.

Such real world studies of effectiveness are only possible where data for vaccinations, infections, admissions to hospitals, and deaths can be combined. For reasons of data protection and other obstacles, the countries that can provide access to such data are mainly the Scandinavian countries,[3] Israel,[4] and the UK[5 6], along with the US, where database linkage was made possible early in the pandemic.[7 8]

Bohnert and colleagues built their cohort from adults (≥18 years) who tested positive for SARS-CoV-2 between July and November 2021 (delta period) or between January and June 2022 (omicron period) and were registered in the covid-19 Shared Data Resource of the US Department of Veterans Affairs. Overall, 279 989 adults were followed up for 30 days after infection. Using data linkage within the Veterans Health Administration and Centers for Medicare and Medicaid Services, the authors collected data for admission to hospital, intensive care unit admission, ventilation use, and death. Effects of vaccination on these outcomes were assessed in analyses adjusted for a large number of potential sociodemographic, geographical, and clinical confounders.

Their findings provide evidence that three doses of an mRNA vaccine gave substantial protection against death in both delta (80%) and omicron (78%) periods, along with 61% protection against admission to hospital. All forms of vaccination were associated with lower odds for all endpoints studied. However, three vaccine doses were associated with better outcomes than two doses, underlining the importance of completing the primary vaccination course. While these effects are impressive, the duration of protection appeared to wane after three months in the omicron period. Compared with the first 90 days, the odds of death increased by 30% during the period 91-150 days after three vaccine doses (adjusted odds ratio 1.31 (95% confidence interval 1.09-1.58)), and the odds of hospital admission increased by 16% (1.16 (1.07 to 1.25)).

Since all vaccines available in the US during and before the study period were based on the original Wuhan-Hu-1 virus type, whether these vaccines would protect against severe disease caused by later variants is not clear. Early serological studies[9 10] that evaluated whether sera from individuals who were vaccinated could neutralise delta or omicron variants (and therefore prevent infection) did not look promising, so real world data for effectiveness against severe disease, not just infection, is essential to inform vaccine recommendations.

Bohnert and colleagues' study follows previous real world studies with different methods that indicated somewhat weaker, but still significant, protection against the new variants with respect to severe disease and death, particularly among those who completed their primary immunisation schedule.[4 8 11]

Although the new study has some advantages, especially in accounting for a large number of potential confounders, the authors acknowledge several limitations. Their study population of Veterans had a large proportion of men and individuals with multimorbidity and is not representative of the general US population, so the findings might not be completely generalisable. However, because the main interest is the relation between vaccination and outcome and not incidences, serious bias from the composition of their study population is unlikely. Direct comparison between delta and omicron periods was not possible mainly because of large differences in vaccination coverage between these periods. Separate analyses for older individuals (eg, 60 years and older) would have added value to their findings since immune senescence progresses at this age.

Bohnert and colleagues' study helps to answer some of the pressing questions around vaccination recommendations, but others need further investigation. Their study covers mainly the period when omicron BA.1 and BA.2 variants were dominating. Since then, new and possibly more immune evasive variants have emerged.[12] Bivalent

vaccines (original Wuhan virus plus the omicron BA.1/2 or the BA.4/5 variants) have been approved by the US Food and Drug Administration, the European Medicines Agency, and the UK Medicines and Healthcare products Regulatory Agency but data comparing their performance with monovalent vaccines are scarce. Finally, the new study shows that vaccine effectiveness falls after three months. Researchers should now explore whether this downward trend continues or levels off.

Competing interests: The BMJ has judged that there are no disqualifying financial ties to commercial companies. The authors declare the following other interests: MK has an investigator initiated research grant about TBE from Pfizer, he gave advice to Valneva in the context of Chikungunya vaccination, and to Bluesky Vaccines for oncological vaccines.

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