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.

We declare no competing interests.

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SARS-CoV-2 delta variant: a persistent threat to the effectiveness of vaccines

Vaccine effectiveness studies are important tools to assess the usefulness of vaccines during the post-approval period in the real-world context. Global experience in evaluating many previous vaccines has enabled formulation of best practices and guidelines for conducting such observational epidemiological studies in a short time frame,[1] to guide immunisation policies. These studies are of particular importance during the COVID-19 pandemic, where the roll-out of vaccines has been much faster than usual.

In *The Lancet Infectious Diseases*, Devashish Desai and colleagues[2] report the findings from their test-negative, case-control, vaccine effectiveness study of a whole-virion inactivated SARS-CoV-2 vaccine, BBV152, during the peak of the second wave of the COVID-19 pandemic in New Delhi, India, which was presumably driven by the delta (B.1.617.2) variant. The adjusted vaccine effectiveness against symptomatic COVID-19 after two doses of BBV152, with the second dose administered at least 14 days before RT-PCR testing, was 50% (95% CI 33–62). This is, to our knowledge, a first independent report on the vaccine effectiveness of BBV152, which is being administered to millions of people in India and other low-income and middle-income countries.[3] The key message of the study is the reduced effectiveness of BBV152, even with two doses of vaccine, against SARS-CoV-2 infections attributed to the delta variant compared with the effectiveness against the wild type (77·8% [95% CI 65·2–86·4]) that was reported in the phase 3 trial.[4] It is important to note that the vaccine effectiveness estimated was not against delta variant infections only, but against infections that occurred during the surge in SARS-CoV-2 cases dominated by the delta variant.[5]

A strength of the study by Desai and colleagues is the test-negative, case-control design in an organised study population—employees of a tertiary-level health-care institution—who were offered unbiased vaccination and testing services. The study has some methodological limitations, such as absence of comorbidity data and no objective assessment of previous infection, as discussed by the authors. The decline in vaccine effectiveness against SARS-CoV-2 infection during a delta-driven surge in cases is neither surprising nor exclusive to inactivated SARS-CoV-2 vaccines including BBV152. The delta variant has high transmissibility, infectivity, and virulence, which causes severe disease.[5,6] These attributes might have contributed to a reduced vaccine effectiveness against symptomatic infections, which has been reported to be as low as 56% for other vaccines in multiple studies worldwide.[7,8] Furthermore, this study was conducted in a high-risk population with a high exposure to SARS-CoV-2 in a tertiary care hospital caring for patients with COVID-19, in the context of a massive surge in infections, with high test-positivity rates of up to 34%, which could have been


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the key factor for the observed reduction in vaccine effectiveness.

Although BBV152 might not be as effective against symptomatic infection by the delta variant as it was against the wild type, a more useful outcome of vaccination is the protection against moderate and severe COVID-19. Moderate-to-severe disease warrants hospitalisation and intensive medical care, and therefore puts strain on health-care systems. Vaccination has been shown to protect against hospitalisation and death, even during the delta surge.[7] This study does not provide evidence in this regard. But, if one were to consider vaccine effectiveness studies for other inactivated vaccines which indicated a better protection against moderate-to-severe disease than infection, it could be presumed that BBV152 might also have a similar performance.[9,10] Future studies should be designed with the emphasis to evaluate protection against moderate-to-severe COVID-19 and to analyse immune correlates of protection, such as neutralising antibodies and antigen-specific T-cell response, against the wild type and the delta variant in BBV152-vaccinated individuals. This emphasis might provide evidence on the need for a booster dose, especially in populations with comorbid conditions. Nevertheless, faced with the challenge of protecting as much of the population as possible, the ongoing vaccination drive should be continued as a public health intervention against SARS-CoV-2, along with strict adherence to other non-pharmacological interventions, particularly in the context of variant-driven surges.

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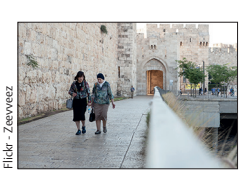
Rapid COVID-19 vaccine rollout: immense success but challenges ahead



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In *The Lancet Infectious Diseases*, Eric Haas and colleagues[1] estimated the benefits of the rapid mass roll-out of the Pfizer–BioNTech vaccine in Israel between Dec 20, 2020, and April 10, 2021. They found substantial benefits of the vaccine in terms of preventing thousands of deaths, hospitalisations, and new SARS-CoV-2 infections in individuals aged 16 years and older.[1] Thanks to the successful vaccination programme, non-pharmaceutical restrictions were gradually lifted in Israel in February–March, 2021,[1,2] and the national economy is reported to have recovered in April–June 2021, with an estimated economic growth of more than 5·5% forecasted for 2021.[3]

The mass COVID-19 vaccination roll-out in Israel has been followed with great interest internationally because it was the fastest roll-out globally, and achieved high levels of vaccine uptake within a few months.[1] The vaccination programme was introduced at the beginning of a new outbreak wave in Israel in December, 2020, when the alpha (B.1.1.7) variant was predominant.[1,2] The authors report that nearly 74% of individuals aged 16 years or older in Israel had received two vaccine doses by April 10, 2021,[1] increasing to 81% by June 1, 2021.[2] Despite a new outbreak wave caused by the delta (B.1.617.2) variant in Israel, with case