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.

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.

We declare no competing interests.

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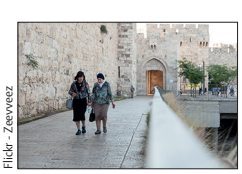
Rapid COVID-19 vaccine rollout: immense success but challenges ahead



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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

numbers in August, 2021, being at similar levels to those in October, 2020, and January, 2021,[4] the number of new cases are not translating into similar numbers of deaths.[4] This situation underlines the continued importance of individuals being fully vaccinated despite emerging variants, which is also supported by the experience of other countries with high uptake of COVID-19 vaccines, like the UK.[4]

Haas and colleagues found that, when they looked at the direct benefits of vaccination, COVID-19 vaccines were far more effective at preventing deaths than mild infections.[1] Other countries have also seen substantial decreases in mortality after the introduction of COVID-19 vaccination programmes, which have shifted the disease burden from mortality to morbidity.[5] Combined with the growing concern about COVID-19 cases with persistent symptoms (often called long COVID), this shift in the disease burden highlights the need to better understand non-fatal COVID-19 and its effects on health-related quality of life. Notably, Israel started vaccinating individuals aged 12–15 years in June, 2021,[2] who are at lower risk of COVID-19-related mortality than older individuals.

The study excluded individuals with previous laboratory-confirmed SARS-CoV-2 infection.[1] By Jan 1, 2021, more than 400 000 individuals were reported to have recovered from COVID-19 in Israel.[2] Hence, the direct benefits of the vaccination programme are a conservative estimate because previous infection does not guarantee perfect protection, and one dose of the Pfizer–BioNTech vaccine after a previous SARS-CoV-2 infection leads to similar antibody levels as two vaccine doses.[6]

Additionally, the effect of COVID-19 vaccination extends beyond the direct benefits of the vaccination programme, with reductions in COVID-19 cases being reported in all age groups and among unvaccinated individuals in Israel.[2] Haas and colleagues acknowledge that the indirect effects and the long-term benefits of vaccination were outside the scope of the analysis.[1] Additional indirect benefits that have been reported elsewhere include the alleviated effect of COVID-19 on the mental health of health-care workers and the general public,[7,8] the recovery of the national economy,[3] and freeing up vital resources like hospital beds and staff for other patients without COVID-19.

Challenges remain and new challenges will undoubtedly continue to arise. For instance, more variants are likely to emerge that increase the potential for breakthrough infections in vaccinated individuals, which will force manufacturers to adapt the vaccines. Similarly, in light of newly emerging variants, the duration of vaccine-induced protection against both symptomatic disease and asymptomatic infection is unclear, raising questions of the need for (and appropriateness of) regular booster doses (which started to be offered in Israel in August, 2021).[9] Many countries also use different COVID-19 vaccine dosing intervals from the officially licensed interval used in Israel, and combine different vaccine products in the national vaccination programmes, including in heterologous vaccination schedules. From a global perspective, other issues outside the scope of this Article[1] are vaccine equity, access, and affordability.[10] Despite the challenges ahead, Haas and colleagues' research documents the immense success that rapid COVID-19 vaccine roll-out had in terms of reducing COVID-19-related morbidity and mortality at the population level.

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Primaquine and the power of adherence in radical cure


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Primaquine has long held pride of place in malaria treatment as the only 8-aminoquinoline with the main indication of providing a radical cure—ie, destruction of the liver hypnozoites unique to *Plasmodium vivax* and *Plasmodium ovale* malaria.[1]

Recurrent *P vivax* parasitaemia results in a cumulative risk of anaemia. The risk and frequency of relapses vary by geographical location. This radical cure is hampered by poor user adherence due to the relatively long treatment duration of 14 days and the hard-to-explain hypnozoite concept. The further complexity of the situation has been highlighted by systematic analyses confirming a high risk of *P vivax* parasitaemia after treatment for falciparum malaria in co-endemic areas.[2,3] This high risk of *P vivax* recurrence is considered to be due to the activation of hypnozoites, in people who have probably previously been exposed to both species, presumably triggered by the acute febrile *Plasmodium falciparum* infection.

In *The Lancet Infectious Diseases*, Jeanne Poespoprodjo and colleagues[4] evaluated both of these highly relevant facets of malaria treatment in Papua, Indonesia, an area with approximately 50% of malaria attributable to *P falciparum* and 45% to *P vivax*. Their results showed a significant benefit of providing 14 days of primaquine radical cure (0·5 mg/kg per day), after dihydroartemisinin–piperaquine primary treatment, to patients presenting with either falciparum or vivax malaria. The 14-day radical cure with primaquine in 21 matched clusters was either supervised (on alternate days) or unsupervised, and there was a significantly reduced incidence risk (hazard ratio 0·23 [95% CI 0·07–0·76]; p=0·016) and rate (incidence rate ratio 0·63 [95% CI 0·42–0·94]; p=0·025) of *P vivax* recurrence in the supervised group than in the unsupervised group in 6 months of follow-up.

The long-standing issue of adherence is still a key challenge in malaria treatment. A systematic review found that adherence to primaquine regimens for *P vivax* treatment ranged from 25% to 85%.[5] Adherence is improved when patients are directly observed, are tested, have a definite diagnosis, and when monitoring of intake can be ensured. Self-reporting of intake is highly unreliable, as shown in studies that used medication containers measuring time of opening.[5] Supervision of dosing has been shown to improve adherence, as in the study by Poespoprodjo and colleagues, where monitoring of treatment intake was done on every second day in the supervised group. Such supervision is, however, extremely time-consuming, labour-intensive, and difficult—if not impossible—to implement outside of a study context.

Could adherence to the radical cure be improved by applying shorter primaquine regimens,[6] or with the more slowly eliminated 8-aminoquinoline tafenoquine as a single 300 mg dose? If we consider that compliance is inversely proportional to the complexity of the regimen, then this would appear to be an excellent option. Tafenoquine for single-dose radical cure of *P vivax* has been coupled with chloroquine previously.[7] Now, in the quest for adding a radical cure to *P falciparum* treatment in Asia, a region with chloroquine resistance, one must ask whether an artemisinin-based combination therapy plus tafenoquine will also be suitable? The haemolytic potential of tafenoquine is not lower than that of primaquine, and both require glucose-6-phosphate dehydrogenase (G6PD) testing before use.[8] In many Asian countries, the first-line treatment for *P falciparum* is an artemisinin-based combination therapy. In the study by Poespoprodjo and colleagues,[4] the first-line treatment used was dihydroartemisinin–piperaquine. The promise of tafenoquine as a partner drug for radical cure with drugs other than chloroquine has, however, been diminished by the results of another study in Indonesia which showed a poor efficacy (21%) of dihydroartemisinin–piperaquine coupled with tafenoquine to prevent relapsing infection compared with dihydroartemisinin–piperaquine coupled with primaquine (52% efficacy).[10] Co-administration of