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 case detection system. In this trial, a combination of passive and active case detection was used, which renders comparison with the RTS,S phase 3 trial difficult. An element of active case detection is often used in phase 2b trials such as this one, but it is recommended that purely passive case detection is used in pivotal phase 3 trials, as this method has greater relevance for extrapolation to public health.

The analysis method for the primary endpoint estimates efficacy in terms of time to first episode of clinical malaria. Although common practice, this method only presents information on the first episodes of clinical malaria, despite the fact that second and subsequent episodes are common in the same individuals in moderate to high transmission settings. Therefore, the more relevant measure for public health is reduction in all episodes of clinical malaria. To the authors' credit, this policy-relevant measure is provided as an additional analysis, and efficacy does not appear to be substantially different to the primary endpoint.

While the reported efficacy in this trial is higher than many of the published RTS,S trials, there is no direct comparison between vaccinations timed to occur with the beginning of each malaria season, and case detection methods differ. The question of superiority therefore remains unanswered. However, the great progress with R21/MM is beneficial for malaria vaccination research. Advantages might include the lower antigen dose and the lack of requirement for AS01. In due course large-scale, well collected safety data will be essential to build the risk–benefit assessment; the experience with SARS-CoV-2 has provided another reminder that important adverse events might only be detected once millions of immunisations have been recorded. Ongoing efforts to strengthen pharmacovigilance in Africa might soon have another priority use case to monitor. RTS,S/AS01 benefits from 7 years of efficacy follow-up; long-term follow-up of R21-vaccinated children in phase 2b and 3 trials will be needed for policy determinations in the years ahead.

It is good news to see another potential malaria vaccine showing great promise, and a critical next step is generation of high-quality phase 3 data from representative epidemiological settings with target populations, vaccination schedule, booster dose timing, study design, and relevant outcome measures agreed with African regulators, policy makers, and WHO.

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COVID-19 vaccine impact in Israel and a way out of the pandemic

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In December, 2020, Israel initiated a national campaign to vaccinate its population with Pfizer–BioNTech's mRNA COVID-19 vaccine BNT162b2 (tozinameran). Israel's Ministry of Health recommended a two-dose schedule with a 21-day interval between doses. Israel delivered more than 10 million doses within 4 months; by April 19, 2021, 54% of the entire population of 9·1 million people, and 88% of people aged 50 years or older, had received two doses.[1] Factors contributing to Israel's rapid roll-out include its small geographical and population sizes; advanced information technology that allowed prioritisation, allocation, and documentation of vaccines for eligible individuals; effective cooperation between government and community-based health funds, which were charged with providing vaccines to those they insured; and experience in rapid large-scale emergency responses.[2]

Amir Levy/Stringer/Getty Images

Vaccines were rolled out around the time of Israel's third and largest wave of SARS-CoV-2 infections, with a peak 7-day moving average of 8328 new infections per day, which resulted in a 2-month national lockdown. Thus, Israel's setting provided a robust platform on which to examine vaccine effectiveness and the impact of high vaccine coverage in real-life conditions at a national level. From March, 2021, onwards, Israel reported a rapid decline in COVID-19 cases across all age groups, despite the easing of lockdown restrictions and reopening of education and commerce. By April 19, 2021, the 7-day moving average of new cases dropped to 149 per day, indicating effective control of the pandemic within the country's borders.[1,3] The marked reduction in new cases prompted the Israeli Government to ease nationwide restrictions, including the discontinuation of face covering use in open spaces.

In *The Lancet*, Eric Haas and colleagues report on a nationwide observational study of the impact and vaccine effectiveness of BNT162b2 in Israel.[3] Israel's Ministry of Health used aggregated data from the national SARS-CoV-2 surveillance and vaccination programme dataset to compare infection and disease incidence between vaccinated and unvaccinated people. Overall, of 232 268 SARS-CoV-2 infections during the study period (Jan 24 to April 3, 2021), 154 648 (66·6%) occurred in people aged 16 years or older and were included in the analyses (of which 20·4% were in the Arab sector, 15·7% in the ultra-Orthodox sector, and 63·9% in the general Jewish [non-ultra-Orthodox] sector). Adjusted estimates of vaccine effectiveness at 7 days or longer after the second dose were 95·3% (95% CI 94·9–95·7) against SARS-CoV-2 infection, 91·5% (90·7–92·2) against asymptomatic SARS-CoV-2 infection, 97·0% (96·7–97·2) against symptomatic SARS-CoV-2 infection, 97·2% (96·8–97·5) against COVID-19-related hospitalisation, 97·5% (97·1–97·8) against severe or critical COVID-19-related hospitalisation, and 96·7% (96·0–97·3) against COVID-19-related death. Vaccine effectiveness against symptomatic SARS-CoV-2 infection, COVID-19-related hospitalisation, and COVID-19-related death exceeded 96% across all age groups, including older adults (aged ≥75 years and ≥85 years). These results closely mirror the efficacy estimates of the BNT162b2 vaccine reported in the phase 3 trial.[4]

The strengths of the study include its nationwide design, mandatory routine reporting of new infections and of vaccination status to the national dataset, large sample size, exclusive use of BNT162b2, and occurrence of a highly efficient vaccine roll-out during peak transmission of SARS-CoV-2, which resulted in high vaccination coverage of most of the adult population. However, several limitations should be considered when interpreting the results. First, social desirability bias affecting symptom questionnaire respondents and presymptomatic infections at the time of questioning could have contributed to an overestimation of vaccine effectiveness against asymptomatic infection. Additionally, patients with COVID-19 who reported symptoms were defined as asymptomatic if they did not report fever or respiratory symptoms. This unorthodox case definition might have resulted in a substantial overestimation of vaccine effectiveness against asymptomatic SARS-CoV-2 infection.[5] Second, during early 2021, the B.1.1.7 variant of SARS-CoV-2 was estimated to account for 95% of cases in Israel, and the results thus indicate that the vaccine was effective against this variant of concern. However, the study did not report on effectiveness against other variants of concern, such as B.1.351 and P.1. Concerns regarding breakthrough infections were recently raised as a case-cohort study from Israel reported a disproportionally high infection rate with the B.1.351 variant in fully vaccinated compared with unvaccinated individuals.[6] Nevertheless, the incidence of B.1.351 infection in Israel to date remains low. Rapid mass vaccination coupled with non-pharmaceutical interventions[7] might have successfully controlled its spread.

Haas and colleagues' findings from Israel suggest that high vaccine coverage rates could offer a way out of the

pandemic.[5,8] Regrettably, rapid population level coverage cannot be easily replicated in many other countries. The global use of the BNT162b2 vaccine is limited by supply issues, high costs, and ultra-cold chain storage requirements. Global COVID-19 vaccine roll-out has been sluggish, and vaccine distribution is inequitable despite the achievements of COVAX, mainly due to the lack of adequate manufacturing scalability.[9,10] Rapid expansion of deployment of other effective vaccines with more achievable cold chain storage requirements remains an urgent global priority.[9]

Facing such challenges, alternative approaches must be considered to allow rapid protection of at-risk populations against severe COVID-19. One such approach is deferring the second dose to accelerate and maximise coverage of the first dose in the population. Indeed, the situation in Scotland looks promising: the first dose of BNT162b2 was associated with a vaccine effectiveness of 91% (85–94) for COVID-19-related hospitalisation at 28–34 days post-vaccination.[11] Israel's robust dataset could allow further assessment and corroboration of first-dose short-term effectiveness and lead other countries to considering deferring the second vaccine dose.[3] Post-introduction vaccine effectiveness studies such as those from Israel[3] and the UK[5,11] will gain increasing importance in augmenting the current evidence, which has so far been based only on data from phase 3 efficacy trials. WHO has published a best practice guidance document on how to conduct vaccine effectiveness assessments using observational study designs.[12]

Israel's experience provides impetus for countries to proactively pursue high vaccine coverage to protect the population;[8] however, rollout would need to follow the WHO prioritisation roadmap to maximise the public health impact, in light of vaccine supply constraints. More post-introduction vaccine effectiveness studies will be required. Timely reporting of vaccine effectiveness against variants of concern, the duration of protection across age groups and geographical settings, and the effectiveness of alternative dosing regimens is crucial to provide data-driven immunisation policies.[12]

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Gain in survival after metabolic–bariatric surgery

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The incidence of obesity is increasing at a dramatically fast pace. By 2030, one in every two adults is projected to have obesity in the USA.[1] The situation is not better in Europe. A WHO projection predicts that obesity is affecting 35% of adults in the UK[2] and is increasing in many EU countries at a similar rate.

A population-based cohort study[3] of 3·6 million adults in the UK estimated an obesity-related reduction in life expectancy of 5·9 years and 9·1 years for a never-smoker man with class I or class II obesity, respectively; and 4·2 years and 7·7 years for a never-smoker woman with class I or class II obesity, respectively. The presence