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Signals of hope: gauging the impact of a rapid national vaccination campaign

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A rapid coronavirus disease 2019 (COVID-19) vaccination rollout has led Israel to become the country with the highest rate of vaccinated individuals per capita worldwide. Here, we summarize the first signs for the real-world effectiveness and impact of the vaccination campaign.

Israel launched its coronavirus disease 2019 (COVID-19) vaccination campaign on 20 December 2020, 9 days after the Food and Drug Administration issued an Emergency Use Authorization for the use of the BNT162b2 (BioNTech/Pfizer) vaccine. Initially, vaccines were prioritized for individuals at high risk for severe COVID-19, including individuals aged 60 years or older, residents of assisted living facilities, health-care employees and individuals with severe baseline comorbidities. The vaccination campaign was then gradually expanded to include individuals aged 55 and 40 years or older on 12 January and 19 January 2021, respectively. On 21 January 2021, adolescents aged 16–18 years were also prioritized for vaccination to enable their return to school and orderly holding of exams. On 28 January 2021, the vaccination campaign expanded to those aged 35 years or older. On 4 February 2021, all individuals aged 16 years or older became eligible to receive the vaccine.

This vaccination campaign quickly placed Israel as the country with the highest rate of vaccinated individuals per capita in the world throughout this period. Several synergistic factors contributed to this success. These include Israel's small geographical area and population size, the availability of a relatively large number of vaccine doses, outreach efforts, experience in timely responses to large-scale national emergencies and a public health system provided by only four health maintenance organizations, with availability of community-based nurses[1]. However, the campaign also had several drawbacks. Although Israel has a public health-care system and vaccinations were widely available for the entire population, vaccination rates strongly correlated with socioeconomic status[2]. In addition, the daily vaccination rate decreased following the vaccination of high-risk populations as younger individuals were more reluctant to be vaccinated. Results from a phase III randomized placebo-controlled trial of BNT162b2 demonstrated that a two-dose regimen with a 21-day interval conferred 95% protection against COVID-19 infection in individuals 16 years or older[3]. However, once a new vaccine is introduced, additional post-licensure studies are needed to measure both its real-life effectiveness and its impact on the population at large. These two forms of evaluation are complementary: the first measures the direct effects of the vaccine on the individual and the second measures the impact on the entire population. Both measures may diverge from results obtained in clinical trials. Real-life effectiveness may be impacted by a heterogeneous and population-dependent effect of the vaccine, suboptimal vaccine handling and low adherence to vaccination schedules. The impact on the population as a whole depends not only on vaccine effectiveness but also on factors such as vaccine coverage, vaccine allocation among different groups, and the effects of social mixing between the different groups on disease transmission[4].

Assessing the effectiveness and the impact of the vaccination campaign in Israel was challenging, as the government imposed a third lockdown during the early weeks of the campaign. In addition, more virulent variants of the virus, such as SARS-CoV-2 B117, emerged in Israel. Despite these challenges, roughly 2 months into the campaign, real-life evidence for the effectiveness and impact of the vaccine are starting to accumulate. The first report estimated an effectiveness (relative risk reduction) of 51% on days 13–24 after the first dose of BNT162b2. This was based on a comparison of the cumulative incidence of SARS-CoV-2 infection during days 13–24, compared with days 1–12, after the first dose[5]. A second study matched newly vaccinated individuals to unvaccinated controls. The estimated vaccine effectiveness was 46% and 92% for documented SARS-CoV-2 infection 14–20 days after the first dose and 7 or more days after the second dose, respectively[6]. These findings are encouraging, showing consistency between real-life effectiveness and the results reported in the randomized control trial[3].

Evidence regarding the impact of the vaccine on the population level is also accumulating. We showed changes in the dynamics of the pandemic, which included a larger and earlier decrease in cases and hospitalizations among older individuals who were prioritized to receive the vaccines. This effect was more pronounced in cities that started vaccinating earlier than those that started later, and was not observed during the previous

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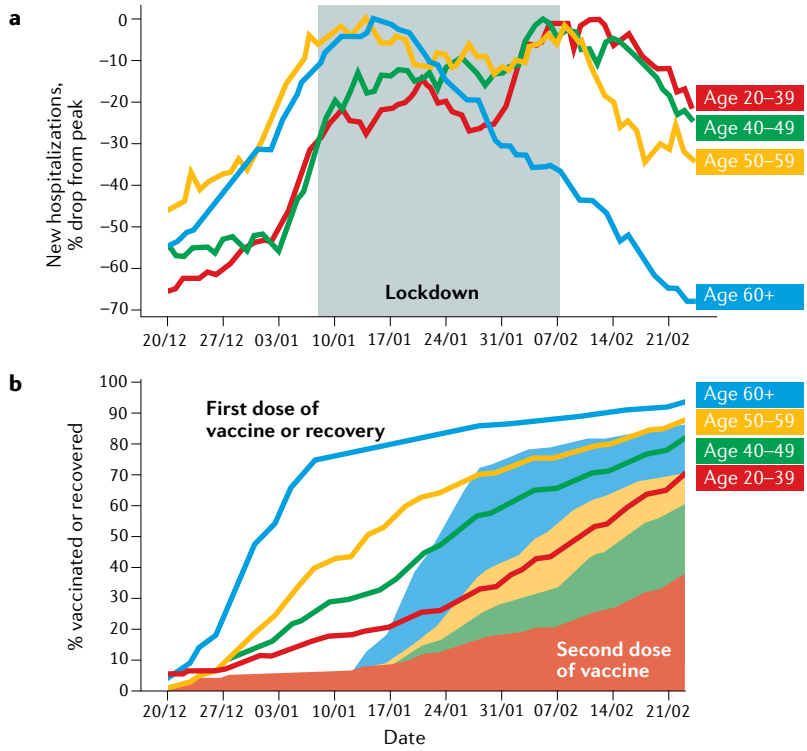

Fig. 1 | **The real-life impact of vaccination in Israel.** Comparison of different age groups over time. **a** | Shown is the percentage of the drop in new hospitalizations compared with the maximum number of individuals who had been hospitalized within the respective age group. **b** | Cumulative percentage of individuals who either recovered from COVID-19 or were vaccinated with the first dose (solid line) and percentage of individuals who received the second dose of the vaccine (shaded area). See also Rossman et al.[7].

lockdown in Israel[7]. In addition, our analysis clearly demonstrated a notable shift in the age distribution of hospitalized patients (FIG. 1). Furthermore, adolescents (aged 16–18 years) were also prioritized during the vaccination campaign and COVID-19 cases and the positivity rates of diagnostic tests dropped much more rapidly in this age group than in 13–15 year olds who had not been vaccinated. De-Leon et al.[8] also presented a model-based analysis that showed a decline in new moderate and severe cases, in particular of patients aged over 60 years, which occurred approximately 1 week earlier than expected on the basis of lockdown alone. Two additional studies provided evidence for a reduced viral load in vaccinated individuals[9,10] and may indicate lower infectiousness post vaccination, which may impact on viral spread and disease transmission. Notably, although clinical trial and real-life evidence indicated an effectiveness of the vaccine as early as 2 weeks following the first dose, the impact on the population level as a whole, as observed by the improvement in the number of new cases and hospitalized patients, only started approximately 3–4 weeks after the initiation of the vaccination campaign.

As mentioned above, the impact of a vaccine depends not only on its effectiveness but also on factors such as vaccine coverage and allocation to different groups. These factors should be carefully considered in determining vaccination rollout strategies. For example, vaccinating individuals at the highest risk for severe morbidity is indisputably of high importance. However, prioritizing individuals who are not considered as being at a high risk but are more prone to transmit the disease (such as individuals working in health-care settings or in confined spaces with close proximity to others) should also be considered. Strategies to increase vaccination rates, especially in younger and healthier individuals who are more reluctant to be vaccinated, are also advised. The Israel ministry of health tried to tackle this in various creative ways, including the opening of vaccination centres at night, removing the need for pre-registration, setting up 'vaccine carts' in nature reserves on weekends and offering incentives such as free meals. Finally, it should be emphasized and communicated to the public that vaccination does not confer full protection, especially following the first dose, and that continued adherence to public health prevention guidance is still important for those vaccinated. Informing the public of the initial results of real-life impact and effectiveness in real time is also important, as these positive signals may increase public trust and initiate a positive-feedback loop towards higher vaccination rates.

In conclusion, patience was needed before the real-life effect of the mass vaccination campaign in Israel became apparent, despite the lockdown imposed during the early days of the campaign and despite a very high vaccination rate. This pattern may also hold true in countries dealing with more virulent strains and with a high prevalence of SARS-CoV-2 infection at baseline.

We hope that these first insights will help to inform vaccination campaigns elsewhere. Although more longitudinal studies are needed, we believe that these preliminary studies, showing both a real-life effectiveness of the vaccine and an early impact on the dynamic of the COVID-19 pandemic on the population level, are very encouraging.

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Competing interests
The authors declare no competing interests.