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.

level of response seen through natural infection and also after the second dose of vaccine in individuals who are naive in terms of previous exposure to SARS-CoV-2 virus.[4,5]

Third, the reported 47% reduction in infection rates on days 1–14 does not mirror findings reported in any of the phase 3 randomised clinical trials including populations that were mostly virus-naive individuals[6–8] or in preliminary analyses[9,10] of much larger population-based cohorts than that described by Amit and colleagues.[1]

The immunologically straightforward explanation of these results is that the first dose of BNT162b2 was given to a population of HCWs, a substantial proportion of whom had been exposed to the SARS-CoV-2 infection and therefore the first dose of vaccine was, in essence, equivalent to a booster dose generating a secondary immune response. How else could the infection rate reduction between days 1–14 be explained?

Of note, the difference on days 1–14 (47% vaccine efficacy) and days 15–28 (85%) is 38%, which lies within other estimates of vaccine efficacy for the much larger population cohorts from Israel (33–59% rate of reduction).[10]

Additionally, the reporting days for infections in this study (days 15–28) are not only unusual, given that the second dose is scheduled for day 22, but also hide the fact that if only a single dose was given, the neutralising antibodies would be falling by days 22–28 (with decreasing immunity) rather than rising quickly as they do with a second dose of mRNA vaccine.[11]

On this basis, we feel the authors should withdraw their Correspondence until they can provide a more substantive report with all the appropriate serology of these HCWs before the first vaccine dose.

The UK Government and Public Heath England, along with the general media, have seized these results to support and justify the UK policy of delaying the second dose of BNT162b2 to 12 weeks, but our concerns need to be addressed to ensure scientific rigour. As we have noted previously,[12] we have reason to believe delaying the second dose of BNT162b2 carries considerable personal and population risks.

JFRR holds shares and was a Director and Chief Scientific Officer, 2003–13, at Oncimmune, which was spun out from the University of Nottingham, UK, as a company for early diagnosis of cancer using detection of autoantibodies to cancer antigens. In 2020, Oncimmune used the technology platform for measuring antibodies to SARS-COV-2 antigens; JFRR had not been involved in this development. HFS declares no competing interests.

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Authors' reply


Jack Guez/Getty Images

We thank John Robertson and Herb Sewell for their interest in our Correspondence.[1] We reported early rate reductions in SARS-CoV-2 infections and COVID-19 disease in health-care workers (HCWs) working at the Sheba Medical Center, Israel, receiving the BNT162b2 mRNA vaccine.[1]

In Israel, individuals previously infected with SARS-CoV-2 were ineligible for vaccination at the time of our evaluation. Indeed, 538 (6%) of 9647 HCWs at the Sheba Medical Center were infected before vaccine roll-out and excluded from the analysis.[1] Moreover, serology screening before receiving the first dose was offered to HCWs in our hospital. Overall, 5835 HCWs, none of whom were known to have been infected previously, were tested. 59 (1%) tested positive for antibody and consequently did not receive the vaccine. Therefore, we considered the HCW cohort included in this analysis mostly antibody-negative. Theoretically, a small proportion of HCWs could have been antibody-positive due to unrecognised past infection and were not tested before receiving the first dose; however, extrapolating from the large proportion of tested HCWs, these numbers should be negligible. Moreover, a proportion of antibody-positive people will be included in most vaccine efficacy evaluations and therefore reflect real-life settings.[2,3]

We report adjusted rate reductions of 30% (95% CI 2–50) in all SARS-CoV-2 infections and of 47% (17–66) in symptomatic COVID-19 during days 1–14 after first dose of BNT162b2. Two biases should be considered in interpreting this estimate of vaccine efficacy after first dose period (days 1–4): referral bias, where symptoms developing after the first dose were attributed to

vaccine adverse events and testing was postponed,[4] and deferral bias where those who are symptomatic, recently recovered, or recently exposed might defer their vaccination and thus be under-represented in the vaccinated group.[2] Additionally, strong evidence exists for increasing vaccine efficacy during days 7–14 after the first dose.[2,5] This interval is included in our rate reductions estimate for the 1–14 days after first dose period.

Finally, we report adjusted rate reductions of 75% (72–84) in all SARS-CoV-2 infections and 85% (71–92) in symptomatic COVID-19 during days 15–28 after the first dose of BNT162b2. Our findings are indeed from a relatively small cohort compared with more recent vaccine efficacy assessments; nonetheless, our estimates of vaccine efficacy during days 15–28 are in keeping with those found in larger cohorts: among HCW participants of the HEROES-RECOVER trial in the USA,[3] vaccine efficacy in preventing SARS-CoV-2 infection 14 days or more after receiving the first dose of an mRNA vaccine was 80% (59–90). Among HCW participants of the SIREN study in England, vaccine efficacy against SARS-CoV-2 infection 21 days or more after receipt of the first dose was 70% (55–85).[2] In a national assessment done in Scotland, vaccine efficacy against COVID-19 hospitalisation was 53% (45–59), 69% (62–75), and 78% (71–83) 7–13 days, 14–20 days, and 21–27 days after receipt of a first dose of BNT162b2.[5] These data showing adequate early vaccine efficacy after a single dose of BNT162b2 should be considered when setting priority groups and optimising dosing schedules in countries facing vaccine shortages.

EL reports personal fees from Sanofi Pasteur, unrelated to this Correspondence. All other authors declare no competing interests.

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Vaccines can save children with non-preventable diseases

Xiang Li and colleagues[1] modelled the health impact of vaccination programmes in low-income and middle-income countries and predicted that approximately 120 million deaths will be averted in children born between 2000 and 2030. They took into consideration both the direct effect of vaccination on vaccinated cohorts and the indirect effects in the population through herd immunity. Although these data are immensely helpful for policy makers, we believe that the indirect impacts of vaccination go even further than suggested.

At the largest paediatric hospital in Bangladesh, a large proportion of the more than 20 000 admissions per year are due to vaccine-preventable diseases such as rotavirus and typhoid, against which vaccines are yet to be introduced.[2–4] One in four children requiring hospitalisation (ie, approximately 6000 children each year) are refused admission because of unavailability of beds. Refused admissions include patients with severe perinatal asphyxia, preterm birth complications, neonatal sepsis, or meningitis who are at high risk of death or disability.[2]

According to hospital bed data from the World Bank, Bangladesh, like most low-income and middle-income countries, has a small number of beds for the population (ie, only 0·8 beds per 1000 people), suggesting a similar admission scenario in other resource-constrained settings. In southern Asia, more than 25% of about 1·9 million deaths of children younger than 5 years every year are caused by meningitis, sepsis, and pneumonia.[5] Preterm birth complications account for another 25% of deaths.[5] Thus, any vaccine-preventable disease that has a large effect on admissions to hospital will exacerbate treatments and outcomes of other diseases in the context of reduced hospital capacity. Hence, in estimating vaccine impact, we should also consider the impact on mortality of the number of people who are refused admission because of vaccine-preventable hospital admissions.

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For more on **hospital bed data from the World Bank** see https://data.worldbank.org/indicator/SH.MED.BEDS.ZS