vaccine was associated with neutralization titers against the omicron variant that were 20.0 times higher than those assessed after the second dose of vaccine, and these titers may substantially reduce the risk of breakthrough infection. The decline in neutralization of the omicron variant 6 months after the booster injection was similar to the decline in neutralization titers against the D614G variant 7 months after the second dose.

The limitations of our study include small sample sets that may not reflect neutralization in diverse populations, differences in the length of time before boosting among the groups, and a lack of post-boost efficacy data. These limitations may be addressed in further studies.

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This trial is ongoing; access to patient-level data and supporting clinical documents may be available to qualified external researchers on request and subject to review once the trial is complete.

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Waning mRNA-1273 Vaccine Effectiveness against SARS-CoV-2 Infection in Qatar

TO THE EDITOR: In early 2021, Qatar launched a mass immunization campaign with the mRNA-1273 (Moderna)[1] vaccine against coronavirus disease 2019 (Covid-19).[2] We assessed the persistence of real-world vaccine effectiveness against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and against Covid-19–related hospitalization and death.

We used a test-negative, case–control study design to estimate vaccine effectiveness, applying the same methods used recently to assess waning effectiveness of the BNT162b2 (Pfizer–BioNTech) vaccine in the same population.[3] Case participants (persons with a positive polymerase-chain-reaction [PCR] test for SARS-CoV-2) and controls (PCR-negative persons) were matched

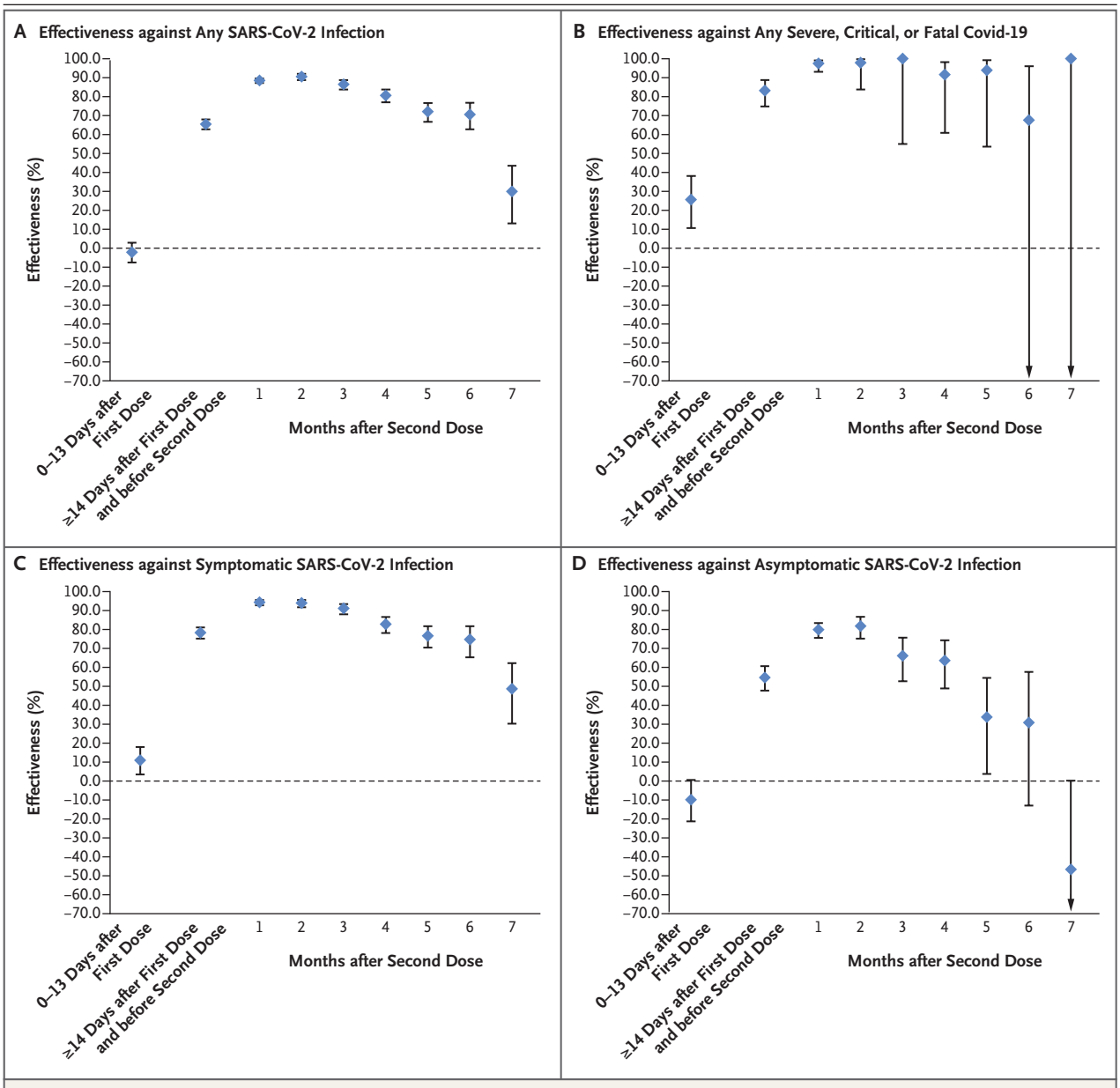

Figure 1. Effectiveness of the mRNA-1273 Vaccine.

Data are presented as point estimates of vaccine effectiveness, and the I bars indicate the corresponding 95% confidence intervals. Arrows indicate that the lower boundary of the 95% confidence interval exceeds the scale of the y axis.

one to one according to sex, 10-year age group, nationality, reason for PCR testing, and calendar week of PCR test. Effectiveness was estimated against documented infection (a PCR-positive swab, regardless of the presence of symptoms) and against any severe Covid-19 cases (acute-care hospitalizations), critical Covid-19 cases (intensive care unit hospitalizations), or fatal Covid-19 cases (Covid-19–related deaths).

Between January 1 and December 5, 2021, a total of 893,779 persons received at least one dose of mRNA-1273, and 887,726 completed the

two-dose regimen. The median date of the first dose was May 27, 2021, and the median date of the second dose was June 27, 2021. The median time between the first and second doses was 28 days (interquartile range, 28 to 30). By December 5, 2021, a total of 2962 breakthrough infections had been recorded among those who received two doses. Of these infections, 19 progressed to severe disease, 4 to critical disease, and 0 to fatal disease.

The process that was used to select the study population is shown in Figure S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org. Tables S2, S3, and S4 show the characteristics of the participants included in the analyses. Only approximately 35% of the cases were diagnosed because of symptoms. The remaining cases were diagnosed because of PCR testing for contact tracing, surveys or random testing campaigns, individual requests, and routine health care testing.

The effectiveness of the mRNA-1273 vaccine against infection was negligible for the first 2 weeks after the first dose, increased to 65.5% (95% confidence interval, 62.7 to 68.0) at 14 or more days after the first dose, and reached its peak at approximately 90% in the first 3 months after the second dose (Fig. 1A and Table S5). Effectiveness declined gradually starting from the fourth month after the second dose and was less than 50% by the seventh month after the second dose. Effectiveness against severe, critical, or fatal Covid-19 reached its peak at essentially 100% right after the second dose, and there was no evidence for declining effectiveness over time (Fig. 1B). A sensitivity analysis that was adjusted for previous infection and health care worker status showed similar results (Table S6).

Effectiveness among participants younger than 50 years of age and among those 50 years of age or older was similar in absolute value and showed the same pattern of waning (Table S7). Effectiveness against symptomatic as compared with asymptomatic infection showed the same pattern of waning, but effectiveness against symptomatic infection was consistently higher than that against asymptomatic infection and waned more slowly (Fig. 1C and 1D and Table S8). The above measures largely reflected effectiveness against the B.1.351 (or beta) and B.1.617.2 (or delta) variants that dominated the incidence of infection during the study.[3-5] Limitations of these estimates are described in Section S1.

The mRNA-1273–induced protection against infection appeared to wane month by month after the second dose. Meanwhile, protection against hospitalization and death appeared to be robust, with no evidence of waning for several months after the second dose.

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