have been driven by disease in younger participants, which indicates the presence of potential confounding behavioral factors in these participants that may have led to a higher exposure to the virus.

Limitations of this analysis include a difference in the number of participants in each group who did not continue to the open-label phase and a lack of randomization. Although a potential bias can be attributed to differences in the risks among the participants remaining in the trial, we observed consistent findings in a proportional-hazards analysis that was adjusted according to the original risk stratification factors in the trial. In addition, the current analysis evaluated Covid-19 cases during a 2-month period. With longer follow-up, the results and the differences between the two groups may change.

Analysis of the open-label phase of the ongoing COVE trial continues. Longer-term data may provide a better understanding of the efficacy of the mRNA-1273 vaccine over time.

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

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Severity of SARS-CoV-2 Reinfections as Compared with Primary Infections

TO THE EDITOR: Qatar had a first wave of infections with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from March through June 2020, after which approximately 40% of the population had detectable antibodies against SARS-CoV-2. The country subsequently had two back-to-back waves from January through May 2021, triggered by the introduction of the B.1.1.7 (or alpha) and B.1.351 (or beta) variants.[1] This created an epidemiologic opportunity to assess reinfections.

Using national, federated databases that have captured all SARS-CoV-2–related data since the onset of the pandemic (Section S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org), we investigated the risk of severe disease (leading to acute care hospitalization), critical disease (leading to hospitalization in an intensive care unit [ICU]), and fatal disease caused by reinfections as compared with primary infections in the national cohort of 353,326 persons with polymerase-chain-reaction (PCR)–confirmed infection between February 28, 2020, and April 28, 2021, after exclusion of 87,547

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Table 1. Severity of SARS-CoV-2 Reinfections as Compared with Primary Infections in the Population of Qatar.

Disease Outcome*	Reinfection†	Primary Infection†	Odds Ratio (95% CI)
	no. of persons with outcome/no. of persons with infection that was not severe, critical, or fatal		
Severe disease	4/1300	158/6095	0.12 (0.03–0.31)
Critical disease	0/1300	28/6095	0.00 (0.00–0.64)
Fatal disease	0/1300	7/6095	0.00 (0.00–2.57)
Severe, critical, or fatal disease	4/1300	193/6095	0.10 (0.03–0.25)

* Severe disease, critical disease, and fatal disease were defined on the basis of the World Health Organization criteria for classifying severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection severity and coronavirus disease 2019 (Covid-19)–related death.

† Reinfections were matched with up to five primary infections according to sex, 5-year age group, nationality, and calendar week of polymerase-chain-reaction testing. The final sample therefore includes persons with reinfection who were matched to five or fewer persons with primary infection.

persons with a vaccination record. Primary infection was defined as the first PCR-positive swab. Reinfection was defined as the first PCR-positive swab obtained at least 90 days after the primary infection. Persons with reinfection were matched to those with primary infection in a 1:5 ratio according to sex, 5-year age group, nationality, and calendar week of the PCR test date (Fig. S1 and Table S1 in the Supplementary Appendix). Classification of severe, critical, and fatal Covid-19 followed World Health Organization guidelines, and assessments were made by trained medical personnel through individual chart reviews.

Of 1304 identified reinfections, 413 (31.7%) were caused by the B.1.351 variant, 57 (4.4%) by the B.1.1.7 variant, 213 (16.3%) by "wild-type" virus, and 621 (47.6%) were of unknown status (Section S1 in the Supplementary Appendix). For reinfected persons, the median time between first infection and reinfection was 277 days (interquartile range, 179 to 315). The odds of severe disease at reinfection were 0.12 times (95% confidence interval [CI], 0.03 to 0.31) that at primary infection (Table 1). There were no cases of critical disease at reinfection and 28 cases at primary infection (Table S3), for an odds ratio of 0.00 (95% CI, 0.00 to 0.64). There were no cases of death from Covid-19 at reinfection and 7 cases at primary infection, resulting in an odds ratio of 0.00 (95% CI, 0.00 to 2.57). The odds of the composite outcome of severe, critical, or fatal disease at reinfection were 0.10 times (95% CI, 0.03 to 0.25) that at primary infection. Sensitivity analyses were consistent with these results (Table S2).

Reinfections had 90% lower odds of resulting in hospitalization or death than primary infections. Four reinfections were severe enough to lead to acute care hospitalization. None led to hospitalization in an ICU, and none ended in death. Reinfections were rare and were generally mild, perhaps because of the primed immune system after primary infection.

In earlier studies, we assessed the efficacy of previous natural infection as protection against reinfection with SARS-CoV-2[2,3] as being 85% or greater. Accordingly, for a person who has already had a primary infection, the risk of having a severe reinfection is only approximately 1% of the risk of a previously uninfected person having a severe primary infection. It needs to be determined whether such protection against severe disease at reinfection lasts for a longer period, analogous to the immunity that develops against other seasonal "common-cold" coronaviruses,[4] which elicit short-term immunity against mild reinfection but longer-term immunity against more severe illness with reinfection. If this were the case with SARS-CoV-2, the virus (or at least the variants studied to date) could adopt a more benign pattern of infection when it becomes endemic.[4]

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Viral Dynamics of SARS-CoV-2 Variants in Vaccinated and Unvaccinated Persons

TO THE EDITOR: Two opposing forces that are shaping the coronavirus disease 2019 (Covid-19) pandemic are the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern and the uptake of vaccines. Measurement of SARS-CoV-2 viral load over the course of acute infection can inform hypotheses about the mechanisms that underlie variation in transmissibility according to variant and vaccination status.[1]

Recent evidence suggests that infections with the delta variant feature higher peak viral loads than those in other lineages[2] and that vaccine recipients who are infected with SARS-CoV-2 may clear the infection more quickly than unvaccinated persons.[3] However, descriptions of SARS-CoV-2 viral dynamics have been principally based on cross-sectional studies in which testing was triggered by the onset of symptoms. Such study designs overlook viral dynamics during the early stages of infection and introduce bias in viral load measurements from different periods of the pandemic.[4] To overcome these limitations, we collected and analyzed a prospective, longitudinal set of 19,941 SARS-CoV-2 viral samples obtained from 173 participants as part of the occupational health program of the National Basketball Association between November 28, 2020, and August 11, 2021. (Details regarding the characteristics of the population are provided in Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org.)

Using a Bayesian hierarchical statistical model,[5] we compared SARS-CoV-2 viral dynamics among 36 participants who were infected with the B.1.1.7 (alpha) variant, 36 participants with the B.1.617.2 (delta) variant, and 41 participants with a variant that was not of current interest or concern, along with 37 vaccinated and 136 unvaccinated participants. We found no meaningful difference in the mean peak viral load (with a lower peak cycle threshold [Ct] indicating a higher viral load), proliferation duration, clearance duration, or duration of acute infection of either the alpha or the delta variant as compared with variants not of interest or concern, as evidenced by overlapping 95% credible intervals (Fig. 1A, 1B, and 1C, Table S2, and Fig. S1). We also found no meaningful difference in the mean peak viral load or proliferation duration between vaccinated and unvaccinated participants (Fig. 1D and 1E, Table S2, and Fig. S2).

A lower peak Ct was slightly more frequent in infections with the delta variant than in those with the alpha variant or variants not of interest or concern: 13.0% of the posterior delta trajectories had a Ct count of less than 15 (9.6 $\log_{10}$ RNA copies per milliliter), as compared with 6.9% for the alpha variant and 10.2% for variants not of interest or concern (Fig. 1F and Fig. S1G). It is unclear whether this finding reflects a biologic characteristic of the delta variant, the limited number of cases, the higher proportion of delta infections among vaccine recipients, or other fac-

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