CORRESPONDENCE

# Efficacy of Natural Immunity against SARS-CoV-2 Reinfection with the Beta Variant

**TO THE EDITOR:** The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) beta (B.1.351) variant of concern harbors mutations that can mediate immune evasion, and it appears to be less sensitive than the alpha (B.1.1.7) variant or wild-type virus to antibodies in serum samples obtained from immunized persons.[1] This situation poses a question as to whether natural infection elicits an inferior immune response against SARS-CoV-2 reinfection with the beta variant, as compared with the alpha variant or wild-type virus.

Qatar experienced two waves of SARS-CoV-2 infection from January 2021 through April 2021, which were dominated by the beta and alpha variants (Section S1 of the Supplementary Appendix, available with the full text of this letter at NEJM.org).[2] Leveraging national databases in Qatar, we used a retrospective, matched-cohort study design to investigate the incidence of SARS-CoV-2 reinfection with the beta or alpha variant.

We estimated the efficacy of immunity induced by natural infection against reinfection by comparing the incidence of SARS-CoV-2 reinfection in the national cohort of persons who had had a previous polymerase-chain-reaction (PCR)–confirmed infection before January 1, 2021, with the incidence of SARS-CoV-2 infection in the national cohort of antibody-negative persons who had no evidence of previous infection before study onset. To control for differences in exposure risk, we matched persons in a 1:1 ratio on the basis of age, sex, and nationality, after excluding those who had a record of vaccination. Follow-up was from March 8 to April 21, 2021.

Figure S1 shows the process that was used to identify reinfections and infections in these cohorts, and Table S2 presents the demographic characteristics of the persons in the cohorts. The median date of previous PCR-confirmed infection was June 21, 2020 (interquartile range, May 24 to August 20, 2020). Kaplan–Meier curves show the cumulative incidence of reinfection among persons with previous PCR-confirmed infection (previous-infection cohort) as compared with that of infection among antibody-negative persons (antibody-negative cohort) (Fig. 1). At 42 days of follow-up, the cumulative incidence was 0.27% (95% confidence interval [CI], 0.22 to 0.32) in the previous-infection cohort and 3.44% (95% CI, 3.27 to 3.61) in the antibody-negative cohort for the beta variant and 0.03% (95% CI, 0.02 to 0.06) and 1.35% (95% CI, 1.25 to 1.46), respectively, for the alpha variant.

Incidence rates of infection with the beta variant were estimated at 4.34 cases per 10,000 person-weeks (95% CI, 3.64 to 5.19) in the previous-infection cohort and at 56.25 cases per 10,000 person-weeks (95% CI, 53.50 to 59.14) in the antibody-negative cohort. With regard to the alpha variant, the corresponding incidence rates were 0.53 cases per 10,000 person-weeks (95% CI, 0.32 to 0.89) and 22.44 cases per 10,000 person-weeks (95% CI, 20.73 to 24.30). The efficacy of natural infection against reinfection, which was derived by comparing the incidence rate in both cohorts, was estimated at 92.3% (95% CI, 90.3 to 93.8) for the beta variant and at 97.6% (95% CI, 95.7 to 98.7) for the alpha variant. Details are provided in Table S3.

Additional analyses comparing the incidence of reinfection among antibody-positive persons with the incidence of infection among antibody-negative persons or adjusting for differences in testing frequency across the cohorts, for the varying phase of the pandemic, or for competing risks of variant infections and death were all consistent with the main study results. However, the efficacies were slightly lower overall (Section S2).

Protection by previous SARS-CoV-2 infection against reinfection with the beta variant was observed, even 1 year after the primary infection, but protection was slightly lower than that against

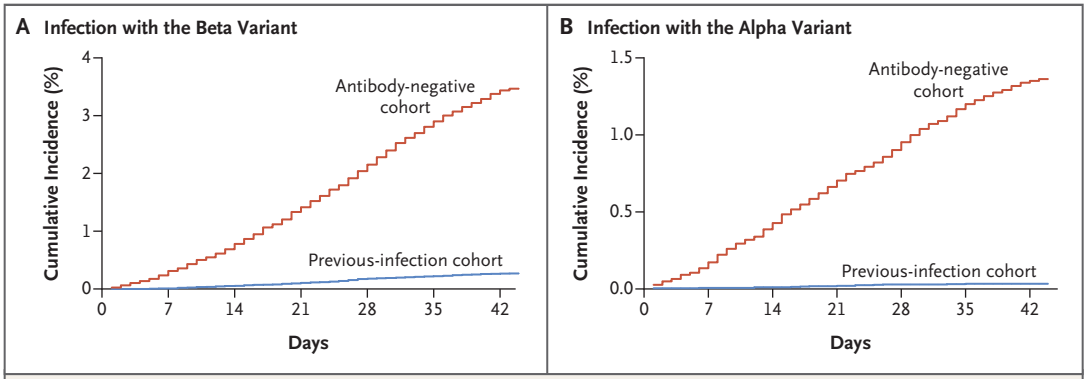


**Figure 1. Cumulative Incidence of Documented SARS-CoV-2 Reinfection with the Beta or Alpha Variant.**

Kaplan–Meier curves show the cumulative incidence of documented reinfection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) beta (B.1.351) or alpha (B.1.1.7) variant in the cohort of persons with previous SARS-CoV-2 infection as confirmed on polymerase-chain-reaction assay (previous-infection cohort), as compared with the incidence of documented SARS-CoV-2 infection in the matched cohort of antibody-negative persons (antibody-negative cohort). Persons in the cohorts were matched in a 1:1 ratio on the basis of age, sex, and nationality. Follow-up was from March 8 to April 21, 2021.

the alpha variant and wild-type virus circulating in Qatar.[3-5] These findings give some insights into the hypothesis that natural immunity may provide protection against known variants of concern.

Hiam Chemaitelly, Ph.D.

Weill Cornell Medicine–Qatar
Doha, Qatar

Roberto Bertollini, M.D., M.P.H.

Ministry of Public Health
Doha, Qatar

Laith J. Abu-Raddad, Ph.D.

Weill Cornell Medicine–Qatar
Doha, Qatar
lja2002@qatar-med.cornell.edu

for the National Study Group for COVID-19 Epidemiology*

*The members of the National Study Group for COVID-19 Epidemiology are listed in the Supplementary Appendix, available with the full text of this letter at NEJM.org.

Supported by the Biomedical Research Program; the Biostatistics, Epidemiology, and Biomathematics Research Core and the Genomics Core at Weill Cornell Medicine–Qatar; the Qatar Ministry of Public Health; Hamad Medical Corporation; and Sidra Medicine. The Qatar Genome Program supported the viral genome sequencing.

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

This letter was published on December 15, 2021, at NEJM.org.

**1.** Planas D, Bruel T, Grzelak L, et al. Sensitivity of infectious SARS-CoV-2 B.1.1.7 and B.1.351 variants to neutralizing antibodies. Nat Med 2021;27:917-24.
**2.** Abu-Raddad LJ, Chemaitelly H, Butt AA. Effectiveness of the BNT162b2 Covid-19 vaccine against the B.1.1.7 and B.1.351 variants. N Engl J Med 2021;385:187-9.
**3.** Abu-Raddad LJ, Chemaitelly H, Malek JA, et al. Assessment of the risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reinfection in an intense reexposure setting. Clin Infect Dis 2021;73(7):e1830-e1840.
**4.** Abu-Raddad LJ, Chemaitelly H, Coyle P, et al. SARS-CoV-2 antibody-positivity protects against reinfection for at least seven months with 95% efficacy. EClinicalMedicine 2021;35:100861.
**5.** Abu-Raddad LJ, Chemaitelly H, Ayoub HH, et al. Introduction and expansion of the SARS-CoV-2 B.1.1.7 variant and its reinfections in Qatar: a nationally-representative cohort study. PLoS Med. in press.

DOI: 10.1056/NEJMc2110300