CORRESPONDENCE

Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.1.1.7 and B.1.351 Variants

TO THE EDITOR: The messenger RNA vaccine BNT162b2 (Pfizer–BioNTech) has 95% efficacy against coronavirus disease 2019 (Covid-19).[1] Qatar launched a mass immunization campaign with this vaccine on December 21, 2020. As of March 31, 2021, a total of 385,853 persons had received at least one vaccine dose and 265,410 had completed the two doses. Vaccination scale-up occurred as Qatar was undergoing its second and third waves of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, which were triggered by expansion of the B.1.1.7 variant (starting in mid-January 2021) and the B.1.351 variant (starting in mid-February 2021). The B.1.1.7 wave peaked during the first week of March, and the rapid expansion of B.1.351 started in mid-March and continues to the present day. Viral genome sequencing conducted from February 23 through March 18 indicated that 50.0% of cases of Covid-19 in Qatar were caused by B.1.351 and 44.5% were caused by B.1.1.7. Nearly all cases in which virus was sequenced after March 7 were caused by either B.1.351 or B.1.1.7.

Data on vaccinations, polymerase-chain-reaction testing, and clinical characteristics were extracted from the national, federated Covid-19 databases that have captured all SARS-CoV-2–related data since the start of the epidemic (Section S1 of the Supplementary Appendix, available with the full text of this letter at NEJM.org). Vaccine effectiveness was estimated with a test-negative case–control study design, a preferred design for assessing vaccine effectiveness against influenza (see the Supplementary Appendix).[2] A key strength of this design is the ability to control for bias that may result from differences in health care–seeking behavior between vaccinated and unvaccinated persons.[2]

The estimated effectiveness of the vaccine against any documented infection with the B.1.1.7 variant was 89.5% (95% confidence interval [CI], 85.9 to 92.3) at 14 or more days after the second dose (Table 1 and Table S2). The effectiveness against any documented infection with the B.1.351 variant was 75.0% (95% CI, 70.5 to 78.9). Vaccine effectiveness against severe, critical, or fatal disease due to infection with any SARS-CoV-2 (with the B.1.1.7 and B.1.351 variants being predominant within Qatar) was very high, at 97.4% (95% CI, 92.2 to 99.5). Sensitivity analyses confirmed these results (Table S3).

Vaccine effectiveness was also assessed with the use of a cohort study design by comparing the incidence of infection among vaccinated persons with the incidence in the national cohort of persons who were antibody-negative (Section S2). Effectiveness was estimated to be 87.0% (95% CI, 81.8 to 90.7) against the B.1.1.7 variant and 72.1% (95% CI, 66.4 to 76.8) against the B.1.351 variant, findings that confirm the results reported above.

The BNT162b2 vaccine was effective against infection and disease in the population of Qatar, despite the B.1.1.7 and B.1.351 variants being predominant within the country; however, vaccine effectiveness against the B.1.351 variant was approximately 20 percentage points lower than the effectiveness (>90%) reported in the clinical trial[1] and in real-world conditions in Israel[4] and the United States.[5] In Qatar, as of March 31, breakthrough infections have been recorded in 6689 persons who had received one dose of the vaccine and in 1616 persons who had received two doses. Seven deaths from Covid-19 have been also recorded among vaccinated persons: five after the first dose and two after the second dose. Nevertheless, the reduced protection against infection with the B.1.351 variant did not seem to translate into poor protection against

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Table 1. Vaccine Effectiveness against Infection and against Disease in Qatar.

Type of Infection or Disease	PCR-Positive Persons		PCR-Negative Persons		Effectiveness (95% CI)*
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	
	number of persons				*percent*
Infection					
PCR-confirmed infection with the B.1.1.7 variant†					
After one dose	892	18,075	1241	17,726	29.5 (22.9–35.5)
≥14 days after second dose	50	16,354	465	15,939	89.5 (85.9–92.3)
PCR-confirmed infection with the B.1.351 variant‡					
After one dose	1329	20,177	1580	19,926	16.9 (10.4–23.0)
≥14 days after second dose	179	19,396	698	18,877	75.0 (70.5–78.9)
Disease§					
Severe, critical, or fatal disease caused by the B.1.1.7 variant					
After one dose	30	468	61	437	54.1 (26.1–71.9)
≥14 days after second dose	0	401	20	381	100.0 (81.7–100.0)
Severe, critical, or fatal disease caused by the B.1.351 variant					
After one dose	45	348	35	358	0.0 (0.0–19.0)
≥14 days after second dose	0	300	14	286	100.0 (73.7–100.0)
Severe, critical, or fatal disease caused by any SARS-CoV-2					
After one dose	139	1,966	220	1,885	39.4 (24.0–51.8)
≥14 days after second dose	3	1,692	109	1,586	97.4 (92.2–99.5)

* Vaccine effectiveness was estimated with the use of a test-negative case–control study design,[2] with persons found positive by polymerase-chain-reaction (PCR) testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) serving as cases in the analysis and those found negative by PCR serving as controls. PCR-positive and PCR-negative persons were matched one to one according to age, sex, nationality, and reason for PCR testing. Vaccine effectiveness was calculated as described by Jackson and Nelson[2] (see the Supplementary Appendix).

† A B.1.1.7 infection was identified as an S gene "target failure" in an analysis conducted with the TaqPath COVID-19 Combo Kit platform (Thermo Fisher Scientific), with the criteria of a PCR cycle threshold value no higher than 30 for the genes encoding both the nucleocapsid protein (N) and ORF1ab but a negative outcome for the gene encoding the spike protein (S) applied. The median date of vaccination was March 1 for PCR-positive persons and February 28 for the matched PCR-negative persons.

‡ Because only B.1.351 and B.1.1.7 viruses were identified in viral genome sequencing in Qatar after March 7, 2021, the criteria used to identify a B.1.351 infection involved the complement of the criterion for S that was used to identify a B.1.1.7 infection — that is, any infection with a cycle threshold value no higher than 30 for the genes encoding N, ORF1ab, and S between March 8 and March 31 was regarded as a B.1.351 infection. The median date of vaccination was March 7 for the PCR-positive persons and March 1 for the matched PCR-negative persons.

§ Effectiveness against severe, critical, or fatal disease caused by PCR-confirmed SARS-CoV-2 infection was analyzed. The B.1.1.7 and B.1.351 variants were dominant in Qatar during the study period. Severe, critical, and fatal coronavirus disease 2019 (Covid-19) were defined on the basis of the World Health Organization criteria[3] for classifying SARS-CoV-2 infection severity and Covid-19–related death.

the most severe forms of infection (i.e., those resulting in hospitalization or death), which was robust, at greater than 90%.

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