Effectiveness and Durability of the BNT162b2 Vaccine against Omicron Sublineages in South Africa

TO THE EDITOR: Data are limited regarding the effectiveness of the BNT162b2 vaccine (Pfizer–BioNTech) against the BA.4 and BA.5 sublineages of the B.1.1.529 (omicron) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that drove the recent fifth wave of infection in South Africa.[1] We previously reported a vaccine effectiveness of 70% after two doses of the BNT162b2 vaccine against severe disease during the fourth wave of omicron infection driven by the BA.1 sublineage in South Africa.[1,2]

In this analysis, we separately assessed the effectiveness and durability of the BNT162b2 vaccine against BA.1 or BA.2 and against BA.4 or BA.5 among members of Discovery Health, a medical care organization that provides health insurance to 3.7 million persons in South Africa. During the period from November 15, 2021, to June 24, 2022, a total of 32,883 patients who had been hospitalized for medical treatment underwent polymerase-chain-reaction testing for SARS-CoV-2, a period that spanned the BA.1–BA.2 and BA.4–BA.5 omicron waves. Of these patients, 5909 (18.0%) were found to be positive for SARS-CoV-2 (Table S4 in the Supplementary Appendix, available with the full text of this letter at NEJM.org).

In this population, we assessed the effectiveness of two doses and three doses (i.e., the original two-dose series plus a booster) of the BNT162b2 vaccine against hospital admission for the treatment of possible sequelae of coronavirus disease 2019 (Covid-19) according to whether the BA.1 and BA.2 sublineages were dominant (November 15, 2021, to February 28, 2022) or whether the BA.4 and BA.5 sublineages were dominant (April 15 to June 24, 2022).[1]

We applied a test-negative design and data-exclusion rules to obtain estimates of vaccine effectiveness. In this analysis, we used a logistic-regression model after adjustment for covariates to estimate vaccine effectiveness as 1 minus the odds of vaccination among positive cases. Vaccination status was analyzed according to the time that had elapsed since the administration of the most recent dose of vaccine (not vacci-

Table 1. BNT162b2 Vaccine Effectiveness against Hospitalization for Covid-19 in South Africa, According to the Dominant Omicron Sublineage.*

Time since Most Recent Vaccine Dose	VE of Dose 2		VE of Dose 3	
	BA.1–BA.2 Omicron Wave	BA.4–BA.5 Omicron Wave	BA.1–BA.2 Omicron Wave	BA.4–BA.5 Omicron Wave
	percent (95% CI)			
0–13 days	66.7 (38.3–82.0)	—	—	—
14–27 days	80.3 (62.8–89.5)	—	81.6 (68.1–89.4)	—
1–2 mo	61.3 (54.7–66.9)	—	66.4 (53.7–75.6)	68.8 (59.5–76.0)
3–4 mo	56.3 (51.6–60.5)	47.4 (19.9–65.5)	50.0 (4.4–73.9)	46.8 (35.3–56.2)
5–6 mo	45.6 (39.3–51.3)	26.3 (7.1–41.6)	—	—
7–8 mo	38.4 (16.9–54.4)	23.6 (11.1–34.3)	—	—
≥9 mo	—	19.3 (6.3–30.5)	—	—

* In South Africa, the BA.1 and BA.2 sublineages of the omicron variant were dominant from November 15, 2021, to February 28, 2022; the BA.4 and BA.5 sublineages were dominant from April 15 to June 24, 2022. Estimates of vaccine effectiveness (VE) are provided only if the P value was less than 0.05 for the between-group difference in the calculation of the odds ratio from the test-negative case–control design, if the number of polymerase-chain-reaction assays on admission was available, and if more than 10 admissions were observed for the estimate. Estimates of vaccine effectiveness have not been adjusted for multiplicity. CI denotes confidence interval.

nated, 0 to 13 days, 14 to 27 days, 1 to 2 months, 3 to 4 months, 5 to 6 months, 7 to 8 months, or ≥9 months).

Among the patients who had received two doses of vaccine, waning of effectiveness against hospitalization was evident as early as 3 to 4 months after vaccination during both periods when the omicron sublineages were dominant. The vaccine effectiveness was 56.3% (95% confidence interval [CI], 51.6 to 60.5) during the BA.1–BA.2 wave and 47.4% (95% CI, 19.9 to 65.5) during the BA.4–BA.5 wave (Table 1). Although boosting with a third dose maintained vaccine effectiveness against severe disease caused by all four sublineages at 1 to 2 months, the vaccine effectiveness had decreased by 3 to 4 months to an effectiveness of 50.0% (95% CI, 4.4 to 73.9) during the BA.1–BA.2 wave and 46.8% (95% CI, 35.3 to 56.2) during the BA.4–BA.5 wave.

Thus, after either two doses or three doses of the BNT162b2 vaccine, we found rapid waning of vaccine effectiveness against the current sublineages of the omicron variant with respect to protection against hospitalization. Our data indicate that boosting maintains vaccine effectiveness against severe disease caused by the current omicron sublineages, although the evidence of rapid waning of durability indicates the need for regular boosting as early as 4 months after the last dose or the need for vaccines to incorporate variants of concern to maintain protection.

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Anti-Spike Mucosal IgA Protection against SARS-CoV-2 Omicron Infection

TO THE EDITOR: Mucosal IgA can provide immunity against respiratory viruses.[1] Vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) boosts mucosal IgA responses,[2] and neutralizing IgA, including neutralizing IgA against the B.1.1.529 (omicron) variant of SARS-CoV-2, has been detected after infection with wild-type SARS-CoV-2.[3] However, the potential role of mucosal IgA in protection against SARS-CoV-2 infection is still largely unknown.

We evaluated SARS-CoV-2–specific mucosal antibody responses in 338 triple-vaccinated health care workers (Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org) at the time of their enrollment in a 4-week quantitative polymerase-chain-reaction screening study in January and February 2022.[4] Mucosal antibody responses were then evaluated over time in 57 participants who became infected with the omicron variant during the screening period (Fig. 1A). Mucosal IgA and IgG responses were analyzed in relation to previously obtained serologic and viral data.[4]

Wild-type SARS-CoV-2 spike-specific mucosal IgA and IgG were detected in 210 participants (62%) and 337 participants (>99%), respectively (Fig. S1A and S1B). Levels of spike-specific mu-