CORRESPONDENCE

Effectiveness of Ad26.COV2.S and BNT162b2 Vaccines against Omicron Variant in South Africa

TO THE EDITOR: The B.1.1.529 (omicron) strain of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly become dominant among the variants of concern in the coronavirus disease 2019 (Covid-19) pandemic in all regions of the world. The omicron variant now accounts for 95.4% of genetic sequences of SARS-CoV-2 in Africa, 96.0% in North America, and 87.6% in South America. This variant has been shown to escape antibody neutralization by both the BNT162b2 messenger RNA vaccine (Pfizer–BioNTech) and the Ad26.COV2.S vaccine (Johnson & Johnson–Janssen),[1,2] which are the only two Covid-19 vaccines that have been administered in South Africa. We established the early effectiveness of the two-dose BNT162b2 vaccine regimen during the omicron-driven fourth wave in South Africa.[2] The national vaccine program in South Africa has distributed 26,262,060 doses of the BNT162b2 vaccine and 8,477,267 doses of the Ad26.COV2.S vaccine. As of May 1, 44.8% of adults in South Africa had been fully vaccinated with two doses of the BNT162b2 vaccine or a single dose of the Ad26.COV2.S vaccine. Assessing vaccine effectiveness is critical for national vaccine programs.

Starting in October 2021, health care workers who were participating in phase 3b of the Sisonke study of the early vaccine access program[3] were eligible to receive a second dose of the Ad26.COV2.S vaccine (Fig. S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). Using data from Discovery Health, a South African managed care organization, we estimated the vaccine effectiveness of the original two-dose series of the BNT162b2 vaccine and a second (booster) dose of the Ad26.COV2.S vaccine against severe Covid-19 caused by the omicron variant. Severe Covid-19 was defined as hospitalization or admission to an intensive care unit (ICU) or to high care. (The latter refers to the practice of locating patients' beds close to the nursing station so that they can be observed 24 hours a day.) We analyzed data sets that included the results of polymerase-chain-reaction (PCR) assays to detect SARS-CoV-2, preauthorization admission data, a full history of members' claims records, chronic disease registrations, and data regarding body-mass index to assess individual risk factors. Vaccination status was determined from claims data in the private sector. We compared vaccine effectiveness against severe Covid-19 during the period from November 15, 2021, to January 14, 2022, when the omicron-driven fourth wave was occurring in South Africa (Tables S1 and S4 in the Supplementary Appendix).

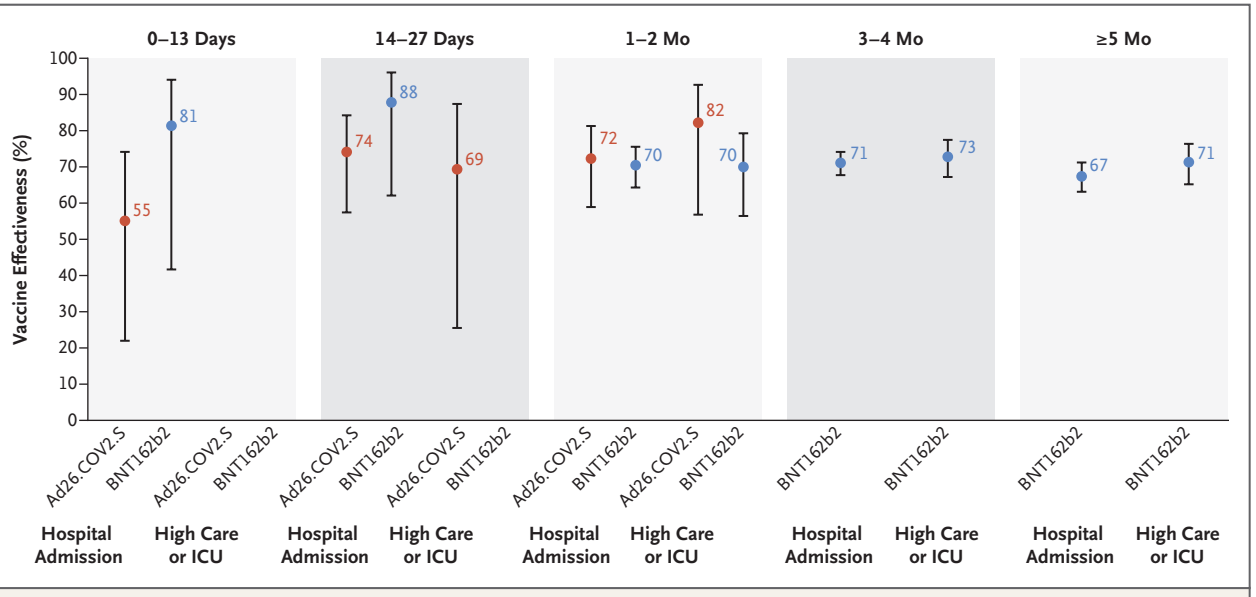

Figure 1. Vaccine Effectiveness against Severe Covid-19 during a Surge of the Omicron Variant in South Africa (November 15, 2021, to January 14, 2022).

Shown is the estimated effectiveness of the BNT162b2 messenger RNA vaccine (Pfizer–BioNTech) and the Ad26.COV2.S vaccine (Johnson & Johnson–Janssen) against severe Covid-19, which was defined as disease resulting in hospitalization or admission to an intensive care unit (ICU) or to high care (the practice of locating patients' beds close to the nursing station for 24-hour observation). Effectiveness data are shown according to the time period after the administration of the second dose of vaccine. If no value is provided for a specific time period in either vaccine group, data were not collected for that vaccine during that time period. I bars indicate 95% confidence intervals.

We applied a test-negative design and data exclusion rules to obtain estimates of vaccine effectiveness[4] (Table S3). In this analysis, we used covariate-adjusted logistic regression to estimate vaccine efficacy. We also performed a sensitivity analysis using only PCR results within the Gauteng province (which includes Johannesburg and several other heavily populated cities), given the geographic concentration of the omicron variant during the study period. Vaccine effectiveness was compared between the two vaccine groups according to the number of days since the second vaccine dose had been administered (0 to 13 days, 14 to 27 days, 28 to 87 days [1 to 2 months], 88 to 147 days [3 to 4 months], and 148 days [5 months] or longer) (Tables S3 and S4). Follow-up was shorter in the Ad26.COV2.S vaccine group because vaccination in the BNT162b2 group had been initiated earlier in the study.

During the omicron surge, we analyzed the results of 162,637 PCR tests, of which 93,854 (57.7%) had been obtained from participants who had received two doses of the BNT162b2 vaccine given at least 42 days apart or two doses of the Ad26.COV2.S vaccine given 4 to 6 months apart. Among these participants, the test positivity rate was 34%; of those with a positive PCR test, 1.6% had been admitted to a hospital and 0.5% to an ICU or to high care.

Among the participants in the Ad26.COV2.S vaccine group, the vaccine effectiveness against hospitalization for Covid-19 was 55% (95% confidence interval [CI], 22 to 74) within 13 days after the second dose, 74% (95% CI, 57 to 84) at 14 to 27 days, and 72% (95% CI, 59 to 81) at 1 to 2 months. Among the participants in the BNT162b2 vaccine group, the vaccine effectiveness was 81% (95% CI, 41 to 94) within 13 days after the second dose, 88% (95% CI, 62 to 96) at 14 to 27 days, 70% (95% CI, 64 to 76) at 1 to 2 months, 71% (95% CI, 68 to 74) at 3 to 4 months, and 67% (95% CI, 63 to 71) at 5 months or longer. Among the Ad26.COV2.S vaccine recipients, the vaccine effectiveness against ICU admission or high care was 69% (95% CI, 26 to 87) at 14 to 27 days and 82% (95% CI, 57 to 93)

at 1 to 2 months after the second dose; among the BNT162b2 vaccine recipients, the vaccine effectiveness against ICU admission or high care was 70% (95% CI, 56 to 79) at 1 to 2 months, 73% (95% CI, 67 to 77) at 3 to 4 months, and 71% (95% CI, 65 to 76) at 5 months or longer (Fig. 1).

After two doses, both vaccines were equally effective against severe disease caused by the omicron variant. These estimates of vaccine effectiveness were calculated in a South African population with a high background prevalence of SARS-CoV-2 exposure during the Covid-19 pandemic.[5] These data provide reassurance about the continued value of the national Covid-19 vaccine program during a surge in the omicron variant.

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1. Cele S, Jackson L, Khoury DS, et al. SARS-CoV-2 Omicron has extensive but incomplete escape of Pfizer BNT162b2 elicited neutralization and requires ACE2 for infection. December 17, 2021 (https://www.medrxiv.org/content/10.1101/2021.12.08.21267417v3). preprint.
2. Collie S, Champion J, Moultrie H, Bekker L-G, Gray G. Effectiveness of BNT162b2 vaccine against Omicron variant in South Africa. N Engl J Med 2022;386:494-6.
3. Bekker L-G, Garrett N, Goga A, et al. Effectiveness of the Ad26.COV2.S vaccine in health-care workers in South Africa (the Sisonke study): results from a single-arm, open-label, phase 3B, implementation study. Lancet 2022;399:1141-53.
4. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of Covid-19 vaccines against the B.1.617.2 (Delta) variant. N Engl J Med 2021;385:585-94.
5. Madhi S, Kwatra G, Myers J, et al. South African population immunity and severe Covid-19 with Omicron variant. December 21, 2021 (https://www.medrxiv.org/content/10.1101/2021.12.20.21268096v1). preprint.

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Detection of Prions in a Cadaver for Anatomical Practice

TO THE EDITOR: The global incidence of prion diseases is approximately 1 to 2 cases per million population per year, and the incidence in Japan is 1.4 cases per million per year; however, among persons 70 years of age or older in Japan, the incidence is 6 cases per million per year. The incidence of undiagnosed cases is, by definition, not known,[1] but it has been suggested that it may be as high as 1 case per 30,000.[2] The potential for exposure to prions through accidental contact with prion-infected tissues, as reported in a case published in the *Journal*,[3] is of concern, since prions are not inactivated by formalin fixation. Because experiments in animals have shown that abnormal prion protein (PrP^{Sc}) accumulates in the central nervous system long before the onset of disease, the risk of iatrogenic transmission from "prion carriers" to other persons is possible.

We have started using real-time quaking-induced conversion to screen for prion disease in the cadavers received by our institution for