Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Patients receiving maintenance dialysis experience substantial COVID-19–associated morbidity and mortality.1,3 Vaccines are an effective tool for combating COVID-19, with early studies showing that 2 doses of a SARS-CoV-2 messenger RNA (mRNA) vaccine elicit a seroresponse in >90% of maintenance dialysis patients, albeit at lower levels than in the general population.3,5–8

In late June 2021, the Delta variant became the dominant SARS-CoV-2 strain in the United States.6 At this time, the rate of breakthrough infection among fully vaccinated patients was higher than expected, possibly as a result of waning antibody concentrations. Tartof et al reported a decrease in protection offered by the BNT162b2 (Pfizer) vaccine from 93% at baseline to 53% after at least 4 months.7 Among patients receiving maintenance dialysis, a notable proportion (10%-15%) did not show a response to 2 doses of an mRNA vaccine; additionally, among initial responders to vaccines, more than half experienced waning immunity by 4-6 months, particularly those whose initial response was lesser.5,8

The impact of lesser initial vaccine response and subsequent waning antibody levels on clinical outcomes among maintenance dialysis patients is not known. Additionally, the impact of the Delta variant on vaccine effectiveness in this population is unknown. Accordingly, we describe the incidence of COVID-19 diagnoses and COVID-19–related hospitalization or death among unvaccinated, partially vaccinated, and fully vaccinated adult dialysis patients during the pre-Delta and Delta-dominant periods. Additionally, among the subset of vaccinated patients with available titers for immunoglobulin G (IgG) antibody against SARS-CoV-2 spike protein, we explore the association between antibody levels and clinical outcomes.

Methods

Study Population

Dialysis Clinic Inc (DCI) is the largest not-for-profit dialysis provider in the United States, operating 260 outpatient dialysis clinics in 29 states. All adult (age ≥18 years) nontransient (ie, not visiting from a non-DCI clinic) maintenance dialysis patients treated between February 1 and December 18, 2021, in DCI clinics contributed time at risk, excluding patients (1) with a known COVID-19 diagnosis before February 1, 2021, or before care at DCI; (2) enrolled in a SARS-CoV-2 vaccine trial; and/or
PLAIN-LANGUAGE SUMMARY

SARS-CoV-2 vaccine effectiveness and the association between antibody levels and severe COVID-19 clinical outcomes (ie, hospitalization or death) among maintenance dialysis patients are poorly defined. From February 1 through June 18, 2021 (pre–Delta variant period) and June 19 through December 18, 2021 (Delta variant–dominant period), vaccine effectiveness rates against severe COVID-19 events were 84% and 70%, respectively. A longer interval since achievement of full vaccination status was associated with higher risk for severe COVID events. Having antibodies to SARS-CoV-2 spike protein above a key threshold level was associated with lower risks of COVID-19 diagnosis and COVID-related hospitalization or death. Barring changes associated with new SARS-CoV-2 variants, our findings demonstrate high effectiveness of SARS-CoV-2 vaccines and suggest that monitoring SARS-CoV-2 antibody levels and administering additional vaccine doses to maintain adequate immunity may be beneficial.

Outcomes

All new COVID-19 diagnoses that occurred during the study period were each assigned to the appropriate vaccination status at the time of diagnosis. CDC definitions for “unvaccinated” (to include the period extending ≤13 days after the first vaccine dose), “partially vaccinated” (applicable to mRNA vaccines only; defined as the period starting 14 days after the first mRNA vaccine dose to ≤13 days after the second mRNA vaccine dose) and “fully vaccinated” (≥14 days after 2 mRNA-1273 [Moderna] or BNT162b2 [Pfizer] vaccines or 1 Ad26.COV2.S [Janssen] vaccine). For all breakthrough cases, defined as a COVID-19 diagnosis in a patient deemed fully vaccinated, the clinic was contacted to verify the reason for SARS-CoV-2 testing; for exposure to a person with known COVID-19 or for positive symptom screening or as required by a non–dialysis clinic/hospital protocol before providing a COVID-19–unrelated service/procedure or as part of protocolized screening (eg, nursing home). COVID-19–related hospitalizations or deaths were defined by documented primary diagnosis for the episode of care as COVID-19 (International Classification of Diseases, Tenth Revision code U01.7).

COVID-19 cases, hospitalizations, and deaths were identified throughout the study period and further subdivided into pre–COVID-19 Delta variant (February 1 to June 25, 2021) and COVID-19 Delta variant–dominant (June 26 to December 18, 2021) periods. Those diagnosed with COVID-19 were followed for hospitalization or death through January 17, 2022.

Data Extraction

All baseline patient demographic and clinical variables used in this analyses were retrospectively obtained from
the DCI electronic health record. These variables include SARS-CoV-2 vaccine name and dates administered, age, sex, race, ethnicity, US state and county of residence, congregate living status (eg, nursing home, long-term care facility), modality, date of initiation of maintenance dialysis, body mass index, dialysis dose delivered (Kt/V), serum albumin concentration, hepatitis B surface antibody test results, immunosuppression (immune-modulating medications, prior transplant, immunodeficiency disorder), substance use disorder (tobacco, alcohol, or drug), and other comorbid conditions. Any SARS-CoV-2 infection occurring more than 14 days after completing SARS-CoV-2 vaccination was deemed a breakthrough COVID-19 case even if asymptomatic. Data integrity checks for COVID-19 documentation were performed weekly. These include comparing consistency of all available concurrent documentation, including de novo International Classification of Diseases, Tenth Revision COVID-19 diagnoses within the problem list, patient under investigation status during symptom screening every visit, and new COVID-19 diagnosis screening indicator during every visit, as well as any laboratory report indicating a positive test for SARS-CoV-2. Inconsistencies detected are referred to corporate nurses who directly communicate with individual clinic staff members for resolution.

Statistical Analyses

Each eligible patient who received dialysis treatment for at least 1 day during the study period contributed days at risk. Patients could move from the unvaccinated group to the partially vaccinated and fully vaccinated groups. Patients could contribute days at risk for each applicable category unless they experienced a SARS-CoV-2 infection or censoring event (eg, end of study, non–COVID-related death, transplant, loss to follow-up, and receipt of another SARS-CoV-2 vaccination). Thus, a patient might contribute 1-3 “subperiods at risk.” For example, consider a patient who was fully vaccinated during the period from February 1 to December 18, 2021. Before reaching this status, the patient would have experienced 2 subperiods at risk, namely the “unvaccinated subperiod” and the “partially vaccinated subperiod.” We noticed that the follow-up time (ie, exposure time) was quite different between patients and among vaccination categories. Thus, the logarithmic transformation of the follow-up time was used as the offset variable in the logistic regression models.

Case rates and odds ratios and 95% CIs from logistic regression models for SARS-CoV-2 infection and the composite outcome of COVID-19–related hospitalization or death within 30 days of COVID-19 diagnosis were compared, first by vaccine status with unvaccinated patients as the reference group and second by vaccine type among those who were fully vaccinated. In the logistic regression, the dependent variable is the logit transformation of the probability of event in the subperiod at risk. Unadjusted and adjusted odds ratios (AORs) were derived. The AOR was derived from the multivariable logistic model adjusted for age, sex, race, diabetes, dialysis modality, congregate living status, dialysis adequacy, albumin, hepatitis B virus (HBV) seroimmunity, disability, comorbidity, number of and specific comorbidities (diabetes, chronic obstructive pulmonary disease, chronic heart failure, hypertension, peripheral vascular disease, cancer, alcohol or drug abuse), immunocompromised status, and the 75th percentile of county SARS-CoV-2 infection rate (to account for geotemporal variability in the intensity of the epidemic) during each study period.

Vaccine effectiveness was calculated using as $(1 – \text{AOR}) \times 100$. Vaccine effectiveness for Ad26.COV2.S could not be determined as a result of small sample size and uneven geographic distribution.

To assess association of anti-spike IgG titer values with COVID-19 cases or hospitalization/death among patients with breakthrough COVID-19 diagnoses, we evaluated the subset with available anti-spike IgG titer results. Patient anti-spike IgG titer values were included if obtained 7-45 days before COVID-19 diagnosis or if the last known postvaccination anti-spike IgG value was less than 1, a level considered undetectable. Results subsequently were de-identified and aggregated, and the association between the most proximate anti-spike IgG titer result to the identified case and clinical outcomes was evaluated descriptively. In addition, case rates and AORs for SARS-CoV-2 infection and composite for COVID-related hospitalization or death within 30 days of COVID-19 diagnosis were calculated for anti-spike IgG values grouped as follows: less than 1, 1 to less than 2, 2 to less than 7, 7 to less than 10, and 10 or greater. We selected the various cutoff points to compare outcomes in those with undetectable levels of less than 1 (reported by assay manufacturer; 45 BAU/mL) or less than 2 (internal DCI laboratory validation; 78 BAU/mL), those at an assay threshold above which COVID-19–related hospitalization or death were not observed (≥7; 212 BAU/mL), and those at an assay level recently reported as associated with higher odds of breakthrough infection (<10; 282 BAU/mL).

This study was reviewed and approved for exemption by the WCG institutional review board (work order 1-1456342-1). Statistical analyses were performed using SAS software, version 9.4.

Results

Among 18,028 maintenance dialysis patients at DCI facilities during the study period, 15,942 (88%) were included (Fig S1). Among eligible patients, 12,403 (78%) were fully vaccinated by December 18, 2021, 6,853 (55%) with mRNA-1273, 5,132 (41%) with BNT162b2, 368 (3%) with Ad26.COV2.S, and 50 (0.4%) with some combination of vaccines. An additional 480 (3%) patients were partially vaccinated (276 with mRNA-1273 and 204 with
BNT162b2), and 3,059 (19%) were unvaccinated. Patients’ mean age and dialysis vintage were 63 ± 15 years and 43 ± 56 months, respectively. The majority (87%) of patients were receiving in-center hemodialysis, 57% had diabetes, and 26% were considered immunocompromised per CDC criteria (Table 1).

**Table 1. Patient Baseline Characteristics at Study Entry**

| Demographic Characteristic | All Patients (N = 15,942) | Fully Vaccinated (n = 12,403) | Partially Vaccinated (n = 480) | Unvaccinated (n = 3,059) | P |
|----------------------------|---------------------------|-------------------------------|--------------------------------|--------------------------|---|
| Age, y                     | 63 ± 15                   | 64 ± 14                       | 61 ± 15                        | 59 ± 16                  | <0.001 |
| Age ≥65 y                  | 7,785 (49%)               | 6,379 (51%)                   | 207 (43%)                      | 1,199 (39%)              | <0.001 |
| Age category               |                           |                               |                                |                          | <0.001 |
| <55 y                      | 4,293 (27%)               | 2,952 (24%)                   | 156 (32%)                      | 1,185 (39%)              | <0.001 |
| 55-64 y                    | 3,864 (24%)               | 3,072 (25%)                   | 117 (24%)                      | 675 (22%)                | <0.001 |
| 65-74 y                    | 4,443 (28%)               | 3,613 (29%)                   | 119 (25%)                      | 701 (23%)                | <0.001 |
| ≥75 y                      | 3,352 (21%)               | 2,766 (22%)                   | 88 (18%)                       | 498 (16%)                | <0.001 |
| Female sex                 | 6,708 (42%)               | 5,114 (41%)                   | 224 (47%)                      | 1,370 (45%)              | <0.001 |
| Race and ethnicity         |                           |                               |                                |                          | <0.001 |
| Non-Hispanic Black         | 5,586 (35%)               | 4,294 (35%)                   | 183 (38%)                      | 1,109 (36%)              | <0.001 |
| Hispanic                   | 968 (6%)                  | 801 (6%)                      | 20 (4%)                        | 147 (5%)                 | <0.001 |
| Other                      | 1,083 (7%)                | 925 (7%)                      | 21 (4%)                        | 137 (4%)                 | <0.001 |
| Unknown                    | 1,400 (9%)                | 1,027 (8%)                    | 51 (11%)                       | 322 (11%)                | <0.001 |
| Non-Hispanic White         | 6,905 (43%)               | 5,356 (43%)                   | 205 (43%)                      | 1,344 (44%)              | <0.001 |
| Dialysis vintage, mo       | 43 ± 56                   | 44 ± 56                       | 38 ± 51                        | 42 ± 56                  | 0.01 |
| BMI, kg/m²                 | 29 ± 8                    | 29 ± 8                        | 30 ± 8                         | 29 ± 8                   | 0.06 |
| Congregate livinga         | 638 (4%)                  | 510 (4%)                      | 19 (4%)                        | 109 (4%)                 | 0.4 |
| Home dialysis              | 1,953 (13%)               | 1,571 (13%)                   | 40 (9%)                        | 342 (12%)                | 0.02 |
| Peritoneal dialysis        | 1,821 (12%)               | 1,465 (12%)                   | 38 (8%)                        | 318 (11%)                | 0.6 |
| Home hemodialysis          | 132 (1%)                  | 106 (1%)                      | 2 (1%)                         | 24 (1%)                  | 0.5 |
| Adequate dialysis doseb    | 13,729 (90%)              | 10,962 (91%)                  | 388 (85%)                      | 2,379 (87%)              | <0.001 |
| Serum albumin, g/dL        | 3.8 ± 0.5                 | 3.8 ± 0.4                     | 3.7 ± 0.5                      | 3.7 ± 0.5                | <0.001 |
| HBV seroimmunityc          | 8,921 (58%)               | 7,196 (59%)                   | 242 (52%)                      | 1,483 (53%)              | <0.001 |
| Potential immunosuppression| 4,066 (26%)               | 3,190 (26%)                   | 120 (26%)                      | 756 (27%)                | 0.8 |
| Immune-modulating medications| 2,166 (14%)               | 1,689 (14%)                   | 64 (14%)                       | 413 (15%)                | 0.6 |
| Prior transplant           | 1,096 (7%)                | 879 (7%)                      | 24 (5%)                        | 193 (7%)                 | 0.2 |
| Immunodeficiency disorder  | 2,880 (19%)               | 2,273 (19%)                   | 81 (18%)                       | 526 (19%)                | 0.8 |
| Disability                 | 599 (4%)                  | 461 (4%)                      | 27 (6%)                        | 111 (4%)                 | 0.08 |
| Tobacco use                | 1,602 (10%)               | 1,195 (10%)                   | 66 (14%)                       | 341 (12%)                | <0.001 |
| Alcohol abuse disorder     | 491 (3%)                  | 375 (3%)                      | 27 (6%)                        | 89 (3%)                  | 0.044 |
| Drug abuse disorder        | 382 (3%)                  | 257 (2%)                      | 19 (4%)                        | 106 (4%)                 | <0.001 |
| No. of comorbidities       | 2.9 ± 1.8                 | 2.9 ± 1.8                     | 3.1 ± 1.9                      | 2.8 ± 1.8                | 0.003 |
| Diabetes mellitus          | 8,860 (57%)               | 7,101 (58%)                   | 288 (62%)                      | 1,471 (52%)              | <0.001 |
| Hypertension               | 12,266 (80%)              | 9,689 (60%)                   | 357 (77%)                      | 2,220 (79%)              | 0.2 |
| CHF                        | 3,138 (20%)               | 2,394 (20%)                   | 117 (25%)                      | 627 (22%)                | <0.001 |
| COPD                       | 2,138 (14%)               | 1,668 (14%)                   | 67 (15%)                       | 403 (14%)                | 0.7 |
| Stroke/cerebrovascular disorder| 1,270 (8%)               | 992 (8%)                      | 45 (10%)                       | 233 (8%)                 | 0.5 |
| PVD                        | 1,767 (11%)               | 1,400 (12%)                   | 60 (13%)                       | 307 (11%)                | 0.4 |
| Thyroid disorder           | 2,107 (13%)               | 1,690 (14%)                   | 52 (11%)                       | 365 (12%)                | 0.01 |
| History of cancer          | 1,483 (10%)               | 1,193 (10%)                   | 48 (9%)                        | 242 (9%)                 | 0.1 |

Results presented as count (%) or mean ± SD. Patients are grouped based on their vaccination status at the end of follow-up. *Unvaccinated* includes patients who never received a vaccine or recipients of a single dose of a vaccine ≤14 days earlier; “fully vaccinated” includes patients who had received the first mRNA vaccine dose ≥14 days earlier but the second dose <14 days earlier; “fully vaccinated” includes all patients whose last vaccine dose was ≥14 days earlier. For the table, categories are mutually exclusive. Abbreviations: BMI, body mass index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; HBV, hepatitis B virus; PVD, peripheral vascular disease.

*Residing in nursing home or long-term care facility.

Adequate dialysis defined by hemodialysis single-pool Kt/V ≥1.2 or peritoneal dialysis weekly Kt/V ≥1.7.

HBV seroimmunity defined as hepatitis B surface antibody ≥10 mIU/mL.

**Vaccination Status and Vaccine Effectiveness Against COVID-19**

There were 1,173 documented COVID-19 cases, with 826 (70%) occurring during the Delta variant–dominant period. COVID-19 rates per 10,000 patient-days and vaccine effectiveness for each time period are shown in Table 2.
There were 535 (46%) cases that occurred among those considered fully vaccinated, with most of these breakthrough cases (511 [96%]) occurring during the Delta-dominant period; 137 (26%) of patients with breakthrough cases met CDC criteria for being immunosuppressed. The median follow-up time for all participants was 57 (IQR, 28–198) days. This included time to infection or censoring point for nonevent cases. However, among those diagnosed with COVID-19, the median time from being considered fully vaccinated was 153 (IQR, 119–198) days.

Median days to breakthrough infection among vaccines were 174 (IQR, 138–222), 159 (IQR, 126–204), and 156 (IQR, 133–180) days for mRNA-1273, BNT162b2, and Ad26.COV2.S, respectively (P = 0.02).

Over the entire study period, the COVID-19 case rate was significantly lower among fully vaccinated patients than among unvaccinated patients: 2.21 vs 3.65 per 10,000 patient-days (AOR, 0.55 [95% CI, 0.48–0.63]; Table 2). Vaccine effectiveness was 45% overall, with mRNA-1273 having the highest vaccine effectiveness at 50%, followed by BNT162b2 at 37%.

During the Delta variant–dominant period, across all vaccination status groups, COVID-19 case rates increased. Fully vaccinated patients had lower COVID-19 case rates (3.25 vs 6.49 per 10,000 patient-days; AOR, 0.46 [95% CI, 0.39–0.54]), with 54% vaccine effectiveness compared with unvaccinated patients; mRNA-1273 had the highest vaccine effectiveness rate at 60%.

**Vaccine Effectiveness Against COVID-19–Related Hospitalization or Death**

There were 424 COVID-19–related hospitalizations/deaths during the study period, including 112 COVID-19–related deaths, with 60 deaths among unvaccinated, 5 among partially vaccinated, and 47 among fully vaccinated patients (mRNA-1273, n = 22; BNT162b2, n = 22; A26.COV2.S, n = 3). Of the 112 COVID-related deaths, 33 (30%) COVID-19–related deaths occurred in immunocompromised patients. During the overall study period, the incidences of COVID-19–related hospitalization/death were 1.45 per 10,000 patient-days among unvaccinated patients and 0.78 per 10,000 patient-days among vaccinated patients (AOR, 0.47 [95% CI, 0.38–0.58]). For fully vaccinated patients, the vaccine effectiveness against hospitalization or death was 53% overall (63% with mRNA-1273 and 39% with BNT162b2; Table 3).

Among all vaccination status groups, COVID-19 case rates and vaccine effectiveness against COVID-19–related hospitalization/death worsened during the Delta variant–dominant period. In the model comparing patients by vaccination status, fully vaccinated patients had the lowest case rate per 10,000 patient-days and the lowest AOR for SARS-CoV-2 infection and related hospitalization/death in the pre-Delta and Delta-dominant periods. In the model comparing vaccination status and vaccine types, patients fully vaccinated with mRNA-1273 experienced the lowest case rate per 10,000 patient-days and the highest vaccine effectiveness against COVID-19–related hospitalization/death in the pre-Delta and Delta-dominant periods.

**Anti-Spike IgG Level and Breakthrough COVID-19**

Anti-spike IgG levels were available in 3,152 (20%) patients during the study period. Compared with anti-spike IgG levels of 10 or higher (282 BAU/mL), each lower anti-spike IgG threshold evaluated was associated with higher case rates and AORs for infection (Table 4). Anti-spike IgG levels <1 were significantly associated with COVID-19-related hospitalization or death in unadjusted analyses, but this finding was no longer statistically significant after adjustment (OR, 1.43 [95% CI, 0.67–3.05]; Table 5).

Among the population with antibody assessment, there were 137 breakthrough cases (BNT162b2, n = 53; mRNA-1273, n = 52; Ad26.COV2.S, n = 32), with the antibody level most proximate to diagnosis measured a median of 25 (IQR, 12–55) days before COVID-19 diagnosis. The frequency of COVID-19 cases requiring hospitalization across anti-spike IgG levels and BAUs per milliliter is shown in Fig 1A and B, respectively. Nearly half of breakthrough cases (67 of 137 [49%]) and the majority of COVID-19–related hospitalizations (27 of 52 [52%]) occurred when the anti-spike IgG level was undetectable. The majority of COVID-19 cases (109 of 137 [80%]) and COVID-related hospitalizations (45 of 52 [87%]) occurred at an anti-spike IgG level lower than 10 (282 BAU/mL). Among 20 COVID-19–related deaths, anti-spike IgG levels were undetectable in 12 patients (60%), 1–10 (45–282 BAU/mL) in 5 (25%), and at least 10 (≥282 BAU/mL) in 3 (15%). The majority of COVID-related hospitalizations (50 of 52 [96%]) and COVID–19–related deaths (18 of 20 [90%]) occurred at <400 BAU/mL.

**Discussion**

SARS-CoV-2 vaccines are highly effective in patients receiving maintenance dialysis, with lower risk for COVID-19 cases and COVID-19–related hospitalization or death among those who are fully vaccinated. Breakthrough COVID-19 cases and COVID-19–related hospitalizations or death among dialysis patients increased when the Delta variant became dominant, even among those considered fully vaccinated. Overall, even though vaccines remained protective, vaccine effectiveness during the Delta-dominant period was approximately 39% lower than that observed in the pre-Delta period for breakthrough SARS-CoV-2 infection. The lower vaccine effectiveness may reflect weaker antibody production or T-cell response among maintenance dialysis patients.8 Although anti-spike IgG antibodies decrease over time in vaccinated patients,8 vaccine effectiveness in preventing COVID-19 infection and hospitalization/death remains high compared with unvaccinated patients. For COVID-19–related hospitalization, vaccine effectiveness was similar between pre-Delta and Delta-
| Days at Risk | COVID-19 Diagnoses | OR (95% CI) | Vaccine Effectiveness |
|--------------|--------------------|-------------|----------------------|
|              | Total | Median [IQR] | No. | Rate per 10,000 d | Unadjusted | Adjusted |               |
| **February 1 to December 18, 2021** | | | | | |
| Unvaccinated | 14,806 | 1,467,403 | 57 [31-116] | 535 | 3.65 | 1.00 (reference) | 1.00 (reference) |
| Partially vaccinated | 12,433 | 398,222 | 28 [21-28] | 103 | 2.59 | 0.67 (0.54-0.83) | 0.67 (0.54-0.84) |
| BNT162b2 | 5,132 | 964,666 | 199 [148-234] | 237 | 2.46 | 0.66 (0.56-0.77) | 0.63 (0.54-0.75) |
| mRNA-1273 | 6,853 | 1,377,141 | 215 [166-246] | 267 | 1.94 | 0.52 (0.44-0.60) | 0.50 (0.42-0.58) |
| Ad26.COV2.S | 368 | 71,477 | 240 [143-250] | 29 | 4.06 | 1.13 (0.77-1.68) | – |
| **February 1 to June 19, 2021 (pre-Delta variant period)** | | | | | |
| Unvaccinated | 12,055 | 740,332 | 52 [26-80] | 191 | 2.58 | 1.00 (reference) | 1.00 (reference) |
| Partially vaccinated | 10,101 | 272,431 | 28 [21-28] | 56 | 2.06 | 0.78 (0.58-1.66) | 0.77 (0.56-1.66) |
| BNT162b2 | 3,987 | 286,575 | 69 [51-94] | 9 | 0.31 | 0.12 (0.07-0.21) | 0.11 (0.07-0.23) |
| mRNA-1273 | 5,750 | 411,262 | 72 [54-88] | 13 | 0.32 | 0.12 (0.06-0.23) | 0.13 (0.06-0.23) |
| Ad26.COV2.S | 278 | 17,478 | 62 [59-76] | 1 | 0.57 | 0.22 (0.03-1.56) | – |
| **June 20 to December 18, 2021 (Delta variant period)** | | | | | |
| Unvaccinated | 3,265 | 422,187 | 182 [72-182] | 274 | 6.49 | 1.00 (reference) | 1.00 (reference) |
| Partially vaccinated | 1,440 | 70,021 | 28 [21-54] | 41 | 5.86 | 0.86 (0.61-1.20) | 0.90 (0.63-1.28) |
| BNT162b2 | 4,814 | 619,530 | 125 [99-182] | 227 | 3.66 | 0.59 (0.50-0.70) | 0.54 (0.44-0.66) |
| mRNA-1273 | 6,458 | 897,918 | 152 [103-182] | 254 | 2.83 | 0.45 (0.38-0.54) | 0.40 (0.33-0.49) |
| Ad26.COV2.S | 335 | 50,056 | 182 [123-182] | 28 | 5.59 | 0.85 (0.57-1.28) | – |

Although patients can contribute time to any vaccination status, the N in the first column (no. of individuals contributing to time at risk) refers to patients’ status at the end of follow-up. “Unvaccinated” includes patients who never received a vaccine; those who received a single dose ≤14 days earlier; “partially vaccinated” includes patients who received the first mRNA vaccine dose ≥14 days earlier after but the second dose <14 days earlier; “fully vaccinated” includes all patients who received the last vaccine dose ≥14 days earlier. Median days at risk included time to event (i.e., infection) or time to censoring point for nonevent cases (e.g., end of study, non–COVID-19–related death, transplant, loss to follow-up, receipt of another SARS-CoV-2 vaccination). The median time was calculated for all patients. Multivariable logistic model was used to derive OR, adjusted for age, sex, race, diabetes, dialysis modality, congregate living status, dialysis adequacy, albumin, hepatitis B virus seroimmunity, disability, comorbidity, number of and specific comorbidities (diabetes, chronic obstructive pulmonary disease, chronic heart failure, hypertension, peripheral vascular disease, cancer, alcohol or drug abuse), immunocompromised status, and 75th percentile of county SARS-CoV-2 infection rate to account for geotemporal variability in the intensity of the epidemic. Abbreviations: mRNA, messenger RNA; OR, odds ratio.
Table 3. COVID-19–Related Hospitalization/Death Rates per 10,000 Patient-Days and Vaccine Effectiveness From February 1 Through December 18, 2021

| N       | Days at Risk | Events ≤30 d From COVID-19 Diagnoses | OR (95% CI) | Vaccine Effectiveness |
|---------|--------------|--------------------------------------|-------------|-----------------------|
|         | Total        | Median [IQR]                         | No.         | Rate per 10,000 d     | Unadjusted | Adjusted   |               |
|---------|--------------|--------------------------------------|-------------|-----------------------|------------|------------|---------------|
| February 1 to December 18, 2021 |              |                                      |             |                       |            |            |               |
| Unvaccinated | 14,806       | 1,404,729 [54 [30-98]]              | 200         | 1.45                  | 1.00       | 1.00       | –             |
| Partially vaccinated | 12,433       | 396,399 [28 [21-28]]               | 41          | 1.03                  | 0.70       | 0.67       | 33%           |
| Fully vaccinated | 12,403       | 2,346,397 [207 [153-242]]          | 183         | 0.78                  | 0.51       | 0.47       | 53%           |
| BNT162b2 | 5,132        | 933,674 [198 [142-234]]            | 91          | 0.97                  | 0.67       | 0.61       | 39%           |
| mRNA-1273 | 6,853        | 1,339,710 [214 [161-245]]          | 79          | 0.59                  | 0.40       | 0.37       | 63%           |
| Ad26.COV2.S | 368          | 67,853 [240 [123-250]]             | 13          | 1.92                  | 1.35       | 1.30       | –             |
| February 1 to June 19, 2021 (pre-Delta variant period) |              |                                      |             |                       |            |            |               |
| Unvaccinated | 12,055       | 737,051 [52 [27-79]]              | 62          | 0.84                  | 1.00       | 1.00       | –             |
| Partially vaccinated | 10,101       | 272,714 [28 [21-28]]               | 20          | 0.73                  | 0.87       | 0.89       | NA            |
| Fully vaccinated | 10,031       | 715,583 [69 [51-94]]              | 11          | 0.15                  | 0.17       | 0.16       | 84%           |
| BNT162b2 | 3,987        | 286,045 [69 [40-101]]             | 6           | 0.21                  | 0.25       | 0.22       | 78%           |
| mRNA-1273 | 5,750        | 411,078 [72 [54-88]]              | 4           | 0.10                  | 0.11       | 0.13       | 87%           |
| Ad26.COV2.S | 278          | 17,478 [62 [59-76]]              | 1           | 0.57                  | 0.68       | 0.68       | –             |
| June 20 to December 18, 2021 (Delta variant period) |              |                                      |             |                       |            |            |               |
| Unvaccinated | 3,265        | 402,236 [182 [57-182]]            | 123         | 3.06                  | 1.00       | 1.00       | –             |
| Partially vaccinated | 1,440        | 68,762 [28 [21-50]]               | 18          | 2.62                  | 0.84       | 0.80       | NA            |
| Fully vaccinated | 11,647       | 1,534,287 [143 [99-182]]          | 171         | 1.11                  | 0.34       | 0.30       | 70%           |
| BNT162b2 | 4,814        | 604,472 [124 [96-182]]            | 84          | 1.39                  | 0.44       | 0.39       | 61%           |
| mRNA-1273 | 6,458        | 878,136 [151 [101-182]]          | 75          | 0.85                  | 0.27       | 0.23       | 77%           |
| Ad26.COV2.S | 335          | 48,205 [182 [114-182]]            | 12          | 2.49                  | 0.81       | 0.81       | –             |

Although patients can contribute time to any vaccination status, the N in the first column (no. of individuals contributing to time at risk) refers to patients’ status at the end of follow-up. “Unvaccinated” includes patients who never received a vaccine and those who received a single dose of a vaccine ≤14 days earlier; “partially vaccinated” includes patients who received the first mRNA vaccine dose ≥14 days earlier but the second dose <14 days earlier; “fully vaccinated” includes all patients who received the last vaccine dose ≥14 days earlier. Median days at risk included time to event (ie, infection) or time to censoring point for non-event cases (eg, end of study, non-COVID-19–related death, transplantation, loss-of-follow-up, received another SARS-CoV-2 vaccination). The median time was calculated for all patients. Multivariable logistic model was used to derive odds ratio, adjusted for age, sex, race, diabetes, dialysis modality, congregate living status, dialysis adequacy, albumin, hepatitis B virus seroimmunity, disability, comorbidity, number of and specific comorbidities (diabetes, chronic obstructive pulmonary disease, chronic heart failure, hypertension, peripheral vascular disease, cancer, alcohol or drug abuse), immunocompromised status, and 75th percentile of county SARS-CoV-2 infection rate to account for geotemporal variability in the intensity of the epidemic. Abbreviations: mRNA, messenger RNA; NA, not applicable; OR, odds ratio.

*Patient hospitalized for COVID-19 before receipt of second mRNA vaccine.
Table 4. Association of Peri-Infection Anti-Spike IgG Values With Risk for COVID-19 Diagnosis

| Anti-Spike IgG Threshold | N   | Person-Days at Risk | COVID-19 Diagnoses | Rate per 10,000 d | OR (95% CI) |
|-------------------------|-----|---------------------|--------------------|------------------|-------------|
|                         |     |                     |                    |                  | Unadjusted | Adjusted   |
| <1                      | 2,515 | 164,908             | 55                 | 3.34             | 2.60 (1.72-3.94) | 2.41 (1.46-3.98) |
| 1-2                     | 854  | 38,964              | 15                 | 3.85             | 2.97 (1.62-5.42) | 2.60 (1.22-5.56) |
| 2-7                     | 1,844 | 67,836              | 23                 | 3.39             | 2.58 (1.54-4.35) | 2.49 (1.37-4.53) |
| ≥7-10                   | 528  | 21,302              | 5                  | 2.35             | 1.78 (0.70-4.56) | 1.28 (0.39-4.24) |
| ≥10                     | 7,042 | 293,817             | 39                 | 1.33             | 1.00 (reference) | 1.00 (reference) |
| Total                   | 12,783 | 586,827             | 137                | 2.33             | –          | –          |

N indicates number of individuals contributing to time at risk. Each anti-spike IgG group OR was adjusted using a multivariable logistic model that included age, sex, race, diabetes, dialysis modality, congregate living status, dialysis adequacy, albumin, hepatitis B virus seroimmunity, disability, comorbidity, number of and specific comorbidities (diabetes, chronic obstructive pulmonary disease, chronic heart failure, hypertension, peripheral vascular disease, cancer, alcohol or drug abuse), immunocompromised status, and 75th percentile of county SARS-CoV-2 infection rate to account for geotemporal variability in the intensity of the epidemic. Abbreviations: IgG, immunoglobulin G; OR, odds ratio.

dominant periods and remained high compared with unvaccinated patients.

There may be differences in outcomes by vaccine type. Overall and during each time period evaluated, vaccine effectiveness against COVID-related hospitalization or death was greater with mRNA-1273 than with BNT162b2 compared with those who were unvaccinated. In our study population, Ad26.COV2.S vaccine was not only associated with lower antibody response, but likely was associated with higher breakthrough and COVID-19–related hospitalization rates than the mRNA vaccines, particularly when compared with mRNA-1273.

Although the CDC did not specifically designate dialysis patients as immunocompromised persons who should receive routine administration of a third COVID-19 mRNA vaccine dose, it did cite dialysis patients as a possible immunocompromised group for whom clinical judgment is important.17 The CDC recommends that moderately to severely immunocompromised patients receive a third dose of mRNA vaccine 4 weeks after the second mRNA vaccine dose or 4 weeks after the first dose of Ad26.COV2.S vaccine; an additional first booster dose should be administered 3 months after the third dose of vaccine. Alternatively, if dialysis patients are not considered immunocompromised, a booster dose of vaccine should be administered 4-5 months after the second mRNA vaccine dose or 2 months after the initial adenovirus vector vaccine.17

Recognizing that not all maintenance dialysis patients produce anti-spike IgG antibodies to the same degree and that antibodies decrease over time, the administration of additional vaccine doses should not be arbitrarily based on time. Because anti-spike IgG antibody titers correlate with SARS-CoV-2–neutralizing titers and clinical efficacy, many clinicians associate the detectable presence of antibodies with clinical protection. Presently, the CDC and Food and Drug Administration do not recommend using COVID-19 antibody testing to guide clinical decision-making.21,22 Adopting a “test-and-treat” approach with routine measurement of anti-spike IgG levels followed by additional doses of vaccine as needed to maintain adequate antibody levels may be warranted, but this requires confirmation. Recently, Anand et al similarly reported that anti-spike IgG values lower than 10 were associated with higher odds for breakthrough infection. In our results (Tables 4 and 5), a vast majority of COVID-19 cases (109 of 137 [80%]) and COVID-19–related hospitalizations (45 of 52 [87%]) occurred at an anti-spike IgG level lower than 10 (<282 BAU/mL). This approach, whereby vaccine administration is predicated on maintaining antibody levels, has been well demonstrated with HBV vaccination among dialysis patients.23

Study strengths include the national population of a midsized dialysis provider in the United States with real-world clinical outcomes. However, there are limitations associated with this study. Because of its observational design, residual biases (eg, misclassification of vaccine exposure in patients vaccinated outside the clinic, inability to identify all asymptomatic infections or those identified

Table 5. Association of Peri-Infection Anti-Spike IgG Values With Risk for COVID-19–Related Hospitalization or Death

| Anti-Spike IgG Threshold | N   | Person-Days at Risk | Events ≤30 d From COVID-19 Diagnosis | Rate per 10,000 Days | OR (95% CI) |
|-------------------------|-----|---------------------|-------------------------------------|---------------------|-------------|
|                         |     |                     |                                     |                     | Unadjusted | Adjusted   |
| <1                      | 2,515 | 165,750             | 21                                  | 1.27                | 1.98 (1.06-3.70) | 1.43 (0.67-3.05) |
| 1-2                     | 854  | 39,037              | 6                                   | 1.54                | 2.39 (0.95-6.03) | 2.50 (0.90-6.92) |
| 2-7                     | 1,844 | 68,312              | 4                                   | 0.59                | 0.90 (0.31-2.66) | 0.50 (0.12-2.19) |
| ≥7-10                   | 528  | 21,344              | 2                                   | 0.94                | 1.45 (0.34-6.27) | 0.77 (0.10-5.82) |
| ≥10                     | 7,042 | 293,652             | 19                                  | 0.65                | 1.00 (reference) | 1.00 (reference) |
| Total                   | 12,783 | 588,095             | 52                                  | 0.88                | –          | –          |

N indicates no. of individuals contributing to time at risk. Each anti-spike IgG group OR was adjusted using a multivariable logistic model that included age, sex, race, and 75th percentile of county SARS-CoV-2 infection rate to account for geotemporal variability in the intensity of the epidemic. Abbreviations: IgG, immunoglobulin G; OR, odds ratio.
outside the facility, reasons for unvaccinated status) and confounding may exist. The electronic health records do not contain standardized documentation of COVID-19 symptoms, and therefore we could not estimate vaccine effectiveness with regard to mitigating or tempering symptom severity. Individual patient adherence to mask and social distancing recommendations is not known, and there was a relatively low number of patients with antibody titer measurements and infection or hospitalization. We did not know the specific SARS-CoV-2 variant for each infection and attributed all infections to the Delta variant after June 19, 2021. Finally, our study did not include the Omicron variant surge.

In conclusion, SARS-CoV-2 vaccines were effective in maintenance dialysis patients, reducing the risks of COVID-19 cases and COVID-19–related hospitalization or death during the pre-Delta and Delta variant–dominant periods. COVID-19 cases surged during the Delta-dominant period, and current immunosuppression criteria are limited in identifying dialysis patients at the highest breakthrough risk. Further research is needed to evaluate SARS-CoV-2 vaccine effectiveness and the utility of antibody titer monitoring to determine which patients are at the highest risk for COVID-19 and to guide the timing of additional vaccine administration.

Supplementary Material

Supplementary File (PDF)

Figure S1: Flow diagram of study cohort.

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