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.

is supported by grants R35HL139424, R01DK095072, and R01AG027002 from the National Heart Lung Blood Institute, NIDDK, and NIA. ARZ is supported by NIA grants R01AG045441, RF1AG061221, R01AG065722, and R21AG061632. Funders played no role in study design; collection, analysis, and interpretation of data; writing the report; or the decision to submit the report for publication.

Financial Disclosure: SMP is a consultant for Janssen and Mission Therapeutics; member of scientific advisory boards for Cytokinetics and Aerpio; and recipient of royalties from UpToDate and honoraria from the American Society of Nephrology. ARZ is supported by grant funding paid directly to Brown University by Sanofi Pasteur for collaborative research on infections and vaccinations in nursing home residents as well as respiratory syncytial virus in infants. VM serves as Chair of the Scientific Advisory Committee at NaviHealth, Inc, was former Chair of the Independent Quality Committee at HCR ManorCare, and is the former Director of PointRight Inc, where he holds less than 1% equity; and received personal fees from NaviHealth outside the submitted work. The remaining authors declare that they have no relevant financial interests.

Acknowledgements: We thank Jeff Hiris, Yoojin Lee, and Cyrus Kosar from Brown University and the Genesis HealthCare IT leadership team for their ongoing technical support and guidance on this project.

Disclaimer: The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the US Government.

Peer Review: Received June 8, 2021. Evaluated by 2 external peer reviewers, with direct editorial input from a Statistics/Methods Editor, an Associate Editor, and the Editor-in-Chief. Accepted in revised form September 12, 2021.

 Published online November 7, 2021 with doi 10.1053/j.ajkd.2021.09.009

References

1. Grabowski DC, Mor V. Nursing home care in crisis in the wake of COVID-19. *JAMA*. 2020;324(1):23.
2. Panagiotou OA, Kosar CM, White EM, et al. Risk factors associated with all-cause 30-day mortality in nursing home residents with COVID-19. *JAMA Intern Med*. 2021;181(4):439-448.
3. Mehta HB, Li S, Goodwin JS. Risk factors associated with SARS-CoV-2 infections, hospitalization, and mortality among US nursing home residents. *JAMA Netw Open*. 2021;4(3):e216315.
4. Tarazi WW, Finegold K, Sheingold SH, Wong Samson L, Zuckerman R, Bosworth A. COVID-19-related deaths and excess deaths among Medicare fee-for-service beneficiaries. *Health Affairs*. 2021;40(6):879-885.
5. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature*. 2020;584(7821):430-436.
6. Akchurin O, Meza K, Biswas S, et al. COVID-19 in patients with CKD in New York City. *Kidney360*. 2021;2(1):63-70.
7. Pakhchanian H, Raiker R, Mukherjee A, Khan A, Singh S, Chatterjee A. Outcomes of COVID-19 in CKD patients: a multicenter electronic medical record cohort study. *CJASN*. 2021;16(5):785-786.
8. Oetjens MT, Luo JZ, Chang A, et al. Electronic health record analysis identifies kidney disease as the leading risk factor for hospitalization in confirmed COVID-19 patients. *PLoS One*. 2020;15(11):e0242182.
9. Flythe JE, Assimon MM, Tugman MJ, et al. Characteristics and outcomes of individuals with pre-existing kidney disease and COVID-19 admitted to intensive care units in the United States. *Am J Kidney Dis*. 2021;77(2):190-203.e1.
10. Levin A, Stevens PE. Summary of KDIGO 2012 CKD Guideline: behind the scenes, need for guidance, and a framework for moving forward. *Kidney Int*. 2014;85(1):49-61.

RESEARCH LETTER

Seroresponse to SARS-CoV-2 Vaccines Among Maintenance Dialysis Patients

To the Editor:

As of October 2021, 3 SARS-CoV-2 vaccines are available in the United States, and all appear highly effective in the general population. Studies suggest high seroresponse to messenger RNA vaccines among maintenance dialysis patients, albeit lower than that in the general population.[1-6] Data regarding adenoviral vector vaccines and predictors of vaccine nonresponse are limited by small sample sizes.[7] Accordingly, we retrospectively analyzed seroresponse to SARS-CoV-2 vaccines among maintenance dialysis patients, updating an earlier report.[8]

DCI is a national not-for-profit provider caring for more than 15,000 patients at 260 outpatient dialysis clinics across 29 states. As of January 2021, DCI physicians had the option of activating a SARS-CoV-2 vaccine protocol, in which anti–spike immunoglobulin G antibodies (SAb-IgG) were measured monthly with routine lab work (details in Item S1). We obtained demographic and clinical data, vaccination dates, and SAb-IgG titers from the DCI electronic health record. We excluded patients with previously diagnosed COVID-19 or positive SAb-IgG titer before or within 10 days after first vaccine dose.

In primary analyses, seroresponse was defined by at least one ≥1 SAb-IgG titer ≥1 U/L at 14-74 days after completion of a vaccine series. Because samples for antibody titers were drawn alongside monthly labs, most patients have 2 assessments in this 60-day period. Associations of demographic and clinical factors with vaccine seroresponse were analyzed using multivariable log Poisson regression with robust variances. Secondary analyses used alternate definitions of vaccine seroresponse: (1) ≥1 SAb-IgG titer ≥2 U/L at 14-74 days after vaccine series completion, and (2) SAb-IgG titer ≥1 U/L on the first assessment at least 14 days after vaccine series completion. This study was reviewed and approved by the WCG IRB (Work Order 1-1456342-1) with exemption for informed consent. Statistical analyses were performed using SAS v9.4.

Between January 1 and June 30, 2021, 1,528 patients (437 BNT162b2/Pfizer, 766 mRNA-1273/Moderna, and 325 Ad26.COV2.S/Janssen recipients) across 130 dialysis facilities had SAb-IgG titers measured after SARS-CoV-2 vaccination (Fig S1). Baseline characteristics were similar to those of the broader DCI vaccinated patient population. Between 14 and 74 days after vaccine series completion,

Table 1. Patient Characteristics by SARS-CoV-2 Vaccine Administered

Demographics	All Vaccinated DCI Patients[a] (N = 9,599)	Study Patients				
		Overall (N = 1,528)	BNT162b2/ Pfizer (n = 437 [29%])	mRNA-1273/ Moderna (n = 766 [50%])	Ad26.COV2.S/ Janssen (n = 325 [21%])	*P*[e]
Age, y	64.9 ± 13.5	64.2 ± 13.5	66.8 ± 12.9	64.0 ± 13.9	61.3 ± 12.6	<0.001
Female sex	3,901 (40.6%)	646 (42.3%)	191 (43.7%)	308 (40.2%)	147 (45.2%)	0.2
Race						<0.001
White	4,639 (48.3%)	768 (50.3%)	198 (45.3%)	447 (58.4%)	123 (37.8%)	
Black	3,287 (34.2%)	356 (23.3%)	80 (18.3%)	116 (15.1%)	160 (49.2%)	
Native American	262 (2.7%)	126 (8.3%)	61 (14.0%)	60 (7.8%)	5 (1.5%)	
Asian/Pacific Islander	347 (3.6%)	93 (6.1%)	49 (11.2%)	37 (4.8%)	7 (2.2%)	
Other/unknown	1,064 (11.1%)	185 (12.1%)	49 (11.2%)	106 (13.8%)	30 (9.2%)	
Hispanic ethnicity	590 (6.2%)	205 (13.4%)	63 (14.4%)	134 (17.5%)	8 (2.5%)	<0.001
Dialysis vintage, mo	48.9 ± 56.1	53.0 ± 58.1	50.9 ± 57.6	52.4 ± 57.0	57.4 ± 61.2	0.3
Body mass index, kg/m^2	28.8 ± 7.3	28.4 ± 7.1	28.4 ± 7.4	28.1 ± 6.4	29.2 ± 8.0	0.06
Long-term care facility	1,046 (10.9%)	139 (9.1%)	41 (9.4%)	69 (9.0%)	29 (8.9%)	0.9
Home dialysis	1,335 (13.9%)	224 (14.7%)	59 (13.5%)	130 (17.0%)	35 (10.8%)	0.02
Peritoneal dialysis	1,225 (12.8%)	198 (13.0%)	50 (11.4%)	113 (14.8%)	35 (10.8%)	
Home hemodialysis	110 (1.2%)	26 (1.7%)	9 (2.1%)	17 (2.2%)	0 (0.0%)	
Adequate dialysis dose[b]	7,155 (74.5%)	1,205 (78.9%)	350 (80.1%)	597 (77.9%)	258 (79.4%)	0.7
Serum albumin, g/dL	3.8 ± 0.4	3.9 ± 0.4	3.9 ± 0.4	3.9 ± 0.4	3.8 ± 0.4	0.05
Other vaccines within 14 days	881 (9.2%)	129 (8.4%)	40 (9.2%)	62 (8.1%)	27 (8.3%)	0.8
Pneumococcal	186 (1.9%)	32 (2.1%)	5 (1.1%)	21 (2.7%)	6 (1.9%)	0.2
HBV	717 (7.5%)	101 (6.6%)	35 (8.0%)	44 (5.7%)	22 (6.8%)	0.3
Influenza	38 (0.4%)	6 (0.4%)	2 (0.5%)	4 (0.5%)	0 (0.0%)	0.9
HBV seroimmunity[c]	6,231 (64.9%)	1,099 (71.9%)	317 (72.5%)	557 (72.7%)	225 (69.2%)	0.3
Potential immunosuppression	1,738 (18.1%)	276 (18.1%)	94 (21.5%)	126 (16.5%)	56 (17.2%)	0.08
Immune-modulating medications[d]	1,260 (13.1%)	197 (12.9%)	69 (15.8%)	91 (11.9%)	37 (11.4%)	0.1
Prior transplant	670 (7.0%)	102 (6.7%)	32 (7.3%)	53 (6.9%)	17 (5.2%)	0.5
Immunodeficiency disorder	342 (3.6%)	71 (4.7%)	23 (5.3%)	31 (4.1%)	17 (5.2%)	0.5
Hospitalization within 14 days	1,195 (12.5%)	194 (12.7%)	58 (13.3%)	103 (13.5%)	33 (10.2%)	0.3
Disability	430 (4.5%)	62 (4.1%)	16 (3.7%)	30 (3.9%)	16 (4.9%)	0.7
Tobacco use	1,530 (15.9%)	205 (13.4%)	48 (11.0%)	101 (13.2%)	56 (17.2%)	0.04
Alcohol abuse disorder	1,023 (10.7%)	143 (9.4%)	38 (8.7%)	71 (9.3%)	34 (10.5%)	0.7
Drug abuse disorder	441 (4.6%)	51 (3.3%)	14 (3.2%)	27 (3.5%)	10 (3.1%)	0.9
No. of comorbidities	3.0 ± 1.8	2.9 ± 1.7	2.9 ± 1.6	2.9 ± 1.6	3.1 ± 1.8	0.1
Diabetes mellitus	5,765 (60.1%)	909 (59.5%)	269 (61.6%)	437 (57.1%)	203 (62.5%)	0.2
Hypertension	8,023 (83.6%)	1,310 (85.7%)	371 (84.9%)	657 (85.8%)	282 (86.8%)	0.8
Congestive heart failure	2,090 (21.8%)	298 (19.5%)	72 (16.5%)	150 (19.6%)	76 (23.4%)	0.06
COPD	1,500 (15.6%)	230 (15.1%)	65 (14.9%)	100 (13.1%)	65 (20.0%)	0.01
Stroke/cerebrovascular disorder	909 (9.5%)	114 (7.5%)	33 (7.6%)	51 (6.7%)	30 (9.2%)	0.3
Peripheral vascular disease	1,297 (13.5%)	178 (11.7%)	43 (9.8%)	78 (10.2%)	57 (17.5%)	0.001
Thyroid disorder	1,558 (16.2%)	248 (16.2%)	64 (14.7%)	136 (17.8%)	48 (14.8%)	0.3
History of cancer	1,018 (10.6%)	136 (8.9%)	41 (9.4%)	74 (9.7%)	21 (6.5%)	0.2

Continuous variables given as mean ± standard deviation. Abbreviations: COPD, chronic obstructive pulmonary disease; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; DCI, Dialysis Clinic, Inc.

[a]Patients fully vaccinated with an emergency-use approved vaccine series of one type without additional doses as of June 30, 2021, excluding those with prior COVID-19.

[b]Hemodialysis single-pool Kt/V≥1.2 or peritoneal dialysis weekly Kt/V≥1.7.

[c]Hepatitis B virus (HBV) seroimmunity defined as antibody to HBV surface antigen ≥10 mIU/mL.

[d]Medications include anti-inflammatory medications, antineoplastic agents, corticosteroids, and certain anti-infective medications.

[e]*P* value for comparisons across the 3 vaccine types among study patients.

437 (29%), 946 (62%), and 145 (9%) had 1, 2, and more than 2 titers checked, respectively. BNT162b2/Pfizer recipients tended to be older (Table 1).

Vaccine seroresponse occurred in 87% of BNT162b2/Pfizer, 96% of mRNA-1273/Moderna, and 37% of Ad26.COV2.S/Janssen recipients (Table S1). Patients without seroresponse were assumed to maintain the absence of seroresponse between the last titer assessment and the 74th day after vaccine series completion. Among those without seroresponse, the median duration of this period was 19.5 [IQR, 12-29], 24.5 [IQR, 12-34], and 16 [IQR, 9-20] days for BNT162b2/Pfizer, mRNA-1273/Moderna, and Ad26.COV2.S/Janssen recipients, respectively (Fig S2).

At titer ≥2 U/L, seroresponse was slightly lower for all vaccine types, most notably Ad26.COV2.S/Janssen. When limiting to the first SAb-IgG titer ≥14 days after vaccine series completion, seroresponse rate was significantly lower only among Ad26.COV2.S/Janssen recipients (Table S1). Vaccine type, older age, non-Black and non–Native American race, immune-modulating medications, history of transplantation, and lower serum albumin were associated with lower likelihood of seroresponse (Fig 1).

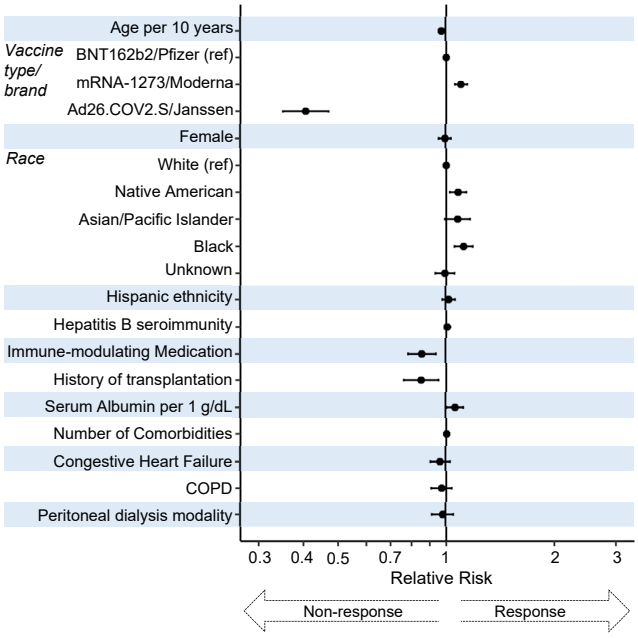

Figure 1. Multivariable regression of clinical characteristics associated with SARS-CoV-2 vaccine response. Response defined as SAb-IgG titer ≥1 U/L measured 14-74 days after vaccine series completion. The association for number of comorbidities is expressed per additional comorbidity. Peritoneal dialysis is compared to hemodialysis (either in-center or home). Analysis was performed with multivariable log Poisson regression with robust variances. See Table 1 notes for abbreviations and definitions.

Among maintenance dialysis patients, mRNA vaccines against SARS-CoV-2 elicited seroresponse in the vast majority, consistent with prior reports.[1-6] In contrast, seroresponse to Ad26.COV2.S/Janssen was low, consistent with an earlier small study,[7] suggesting that maintenance dialysis patients should receive mRNA-based SARS-CoV-2 vaccines, particularly given their high morbidity and mortality from COVID-19.[9]

The low seroresponse rate to Ad26.COV2.S/Janssen is concerning because postvaccination SAb-IgG titers correlate with protection from COVID-19, possibly via direct neutralization of the spike protein.[10] Of note, as a single-dose regimen, response to Ad26.COV2.S/Janssen was assessed 3-4 weeks earlier relative to the initial vaccine dose than response to mRNA vaccines. However, longer-term data elsewhere do not indicate increased response over time.[11] Thus, even allowing for possible later increase in seroresponse, the Ad26.COV2.S/Janssen vaccine appears less effective than mRNA vaccines among maintenance dialysis patients.

The difference between BNT162b2/Pfizer and mRNA-1273/Moderna may reflect differences in dosage (100 vs 30 μg of mRNA content, respectively), or, given the earlier availability of BNT162b2/Pfizer, unaccounted-for confounding factors. Admittedly, the SAb-IgG titer needed for protection from COVID-19 and the role of vaccine-induced cellular immunity remain uncertain, issues that are complicated by emerging variants. Other than vaccine type, predictors of vaccine nonresponse were largely factors related to potential immunocompromise.[2,3]

Our study limitations include potential selection bias and unaccounted-for confounders. We did not examine breakthrough infections, which are a growing concern. Also, although assessing SAb-IgG titer ≥14 days after completion of vaccine series meets the current definition of "fully vaccinated," there remains a difference in timing relative to the initial dose between 1- and 2-dose regimens.

In conclusion, among maintenance dialysis patients, mRNA vaccines are associated with greater seroresponse and therefore should be preferred. Further study is needed on the durability of this seroresponse; its correlation with breakthrough infection, morbidity, and mortality; and the role of additional vaccine doses, particularly among Ad26.COV2.S/Janssen vaccine recipients.

Caroline M. Hsu, MD, Daniel E. Weiner, MD, MS, Gideon N. Aweh, MS, Harold J. Manley, PharmD, Vladimir Ladik, MS, Jill Frament, PharmD, Dana Miskulin, MD, MS, Christos Argyropoulos, MD, Kenneth Abreo, MD, Andrew Chin, MD, Reginald Gladish, MD, Loay Salman, MD, Doug Johnson, MD, and Eduardo K. Lacson, MD, MPH

Supplementary Material

Supplementary File (PDF)

Figures S1-S2; Item S1; Table S1.

Article Information

Authors' Affiliations: Tufts Medical Center, Boston, Massachusetts (CMH, DEW, DM, EKL); Dialysis Clinic Inc (DCI), Nashville, Tennessee (GNA, HJM, VL, JF, DJ, EKL); University of New Mexico, Albuquerque, New Mexico (CA); Louisiana State University Health Sciences Center, Shreveport, Louisiana (KA); University of California, Davis, Sacramento, California (AC); Nephrology of North Alabama, Decatur, Alabama (RG); and Albany Medical College, Albany, New York (LS).

Address for Correspondence: Caroline M. Hsu, MD, 800 Washington St, Box #391, Boston, MA 02111. Email: chsu1@tuftsmedicalcenter.org

Authors' Contributions: Research area and study design: CMH, DEW, GNA, HJM, DM, EKL; data acquisition: GNA, VL, JF, CA, KA, AC, RG, LS; data analysis and interpretation: CMH, DEW, GNA, HJM, VL, JF, DM, EKL; statistical analysis: GNA; supervision or mentorship: DEW, DJ, EKL. Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual's own contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated and resolved, including with documentation in the literature if appropriate.

Support: This report was supported by DCI. CMH receives support from ASN KidneyCure's Ben J. Lipps Research Fellowship, which had no role in study design, data collection, reporting, or the decision to submit.

Financial Disclosure: GNA, HJM, VL, JF, DJ, and EKL are all employees of DCI, where DJ is Vice Chair of the Board. DEW, DM, CA, KA, AC, RG, and LS receive salary support to their institution from DCI. CMH declares that she has no relevant financial interests.

Prior Presentation: A preprint version of this Research Letter was posted August 22, 2021 at medRxiv with doi 10.1101/2021.08.19.2126229.

Peer Review: Received June 14, 2021 as a submission to the expedited consideration track with 3 external peer reviews. Direct editorial input from a Statistics/Methods Editor, an Associate Editor, and the Editor-in-Chief. Accepted in revised form October 25, 2021. Further information on expedited consideration (AJKD Express) is available in the Information for Authors & Journal Policies.

Publication Information: © 2021 by the National Kidney Foundation, Inc. Published online November 7, 2021 with doi 10.1053/j.ajkd.2021.10.002

References

1. Broseta JJ, Rodríguez-Espinosa D, Rodríguez N, et al. Humoral and cellular responses to mRNA-1273 and BNT162b2 SARS-CoV-2 vaccines administered to hemodialysis patients. *Am J Kidney Dis*. 2021;78(4):571-581.
2. Agur T, Ben-Dor N, Goldman S, et al. Antibody response to mRNA SARS-CoV-2 vaccine among dialysis patients - a prospective cohort study. *Nephrol Dial Transplant*. 2021;36(7):1347-1349.
3. Longlune N, Nogier MB, Miedougé M, et al. High immunogenicity of a messenger RNA-based vaccine against SARS-CoV-2 in chronic dialysis patients. *Nephrol Dial Transplant*. 2021;36(9):1704-1709.
4. Bensouna I, Caudwell V, Kubab S, et al. SARS-CoV-2 antibody response after a third dose of the BNT162b2 vaccine in patients receiving maintenance hemodialysis or peritoneal dialysis. *Am J Kidney Dis*. 2022;79(2):185-192.
5. Chan L, Fuca N, Zeldis E, Campbell KN, Shaikh A. Antibody response to mRNA-1273 SARS-CoV-2 Vaccine in hemodialysis patients with and without prior COVID-19. *CJASN*. 2021;16(8):1258-1260.
6. Labriola L, Scohy A, Van Regemorter E, et al. Immunogenicity of BNT162b2 SARS-CoV-2 vaccine in a multicenter cohort of nursing home residents receiving maintenance hemodialysis. *Am J Kidney Dis*. 2021;78(5):766-768.
7. Mulhern J, Fadia A, Patel R, et al. Humoral response to mRNA versus an adenovirus vector-based SARS-COV2 (Ad26.COV2.S) vaccine in dialysis patients. *CJASN*. 2021;16(11):1720-1722.
8. Lacson E, Argyropoulos C, Manley H, et al. Immunogenicity of SARS-CoV-2 vaccine in dialysis. *JASN*. 2021;32(11):2735-2742.
9. Hsu CM, Weiner DE, Aweh G, Salenger P, Johnson DS, Lacson E. Epidemiology and outcomes of COVID-19 in home dialysis patients compared with in-center dialysis patients. *J Am Soc Nephrol*. 2021;32(7):1569-1573.
10. Earle KA, Ambrosino DM, Fiore-Gartland A, et al. Evidence for antibody as a protective correlate for COVID-19 vaccines. *Vaccine*. 2021;39(32):4423-4428.
11. Barouch DH, Stephenson KE, Sadoff J, et al. Durable Humoral and Cellular Immune Responses 8 Months after Ad26.COV2.S Vaccination. *N Engl J Med*. 2021;385(10):951-953. doi:10.1056/NEJMc2108829