Current Transplantation Reports (2022) 9:174–184
https://doi.org/10.1007/s40472-022-00366-1

KIDNEY TRANSPLANTATION (ML HENRY AND R PELLETIER, SECTION EDITOR)

COVID-19 Vaccine Efficacy and Immunogenicity in End-Stage Renal Disease Patients and Kidney Transplant Recipients

Nicolas F. Moreno[1] · Robert McAdams[1] · John A. Goss[2] · N. Thao. N. Galvan[2]

Accepted: 1 March 2022 / Published online: 29 April 2022

Abstract

Purpose of Review To summarize the current literature with respect to COVID-19 vaccine efficacy patients with end-stage renal disease on dialysis and kidney transplant recipients.

Recent Findings Immunosuppressed patients are at greater risk of morbidity and mortality from COVID-19 infection. Patients with ESRD and KTR are immunosuppressed and mount a weaker antibody response to COVID-19 mRNA vaccination, and factors including immunosuppressant medications have been implicated for this weakened response. Third and fourth doses of vaccine doses have been shown to increase seropositivity and antibody production in kidney transplant recipients and patients on dialysis. Retrospective studies have demonstrated decreased mortality in vaccinated, immunosuppressed patients.

Summary ESRD and KTR patients have decreased antibody response to COVID-19 vaccines, but third and fourth doses have been shown to increase antibody production. Though a correlate of protection between antibody production and efficacy has yet to be fully established in this subset of the population, all US professional bodies who treat ESRD and KTR patients advocate for full vaccination against SARS-CoV-2 based on the data available. Studies demonstrating decreased mortality in vaccinated patients are promising on efficacy. Importantly, because KTR patients mount a weaker antibody response than ESRD patients, vaccination prior to kidney transplantation is critical.

Keywords COVID-19 · Vaccination · Transplantation · Dialysis · ESRD · Kidney · Renal · Efficacy

Nicolas F. Moreno and Robert McAdams contributed equally to the production of this manuscript.

This article is part of the Topical Collection on *Kidney Transplantation*

Clinical pearls:
- ESRD and KTR have a greater risk of mortality with COVID-19 infection relative to the general population. KTR have a greater risk of mortality relative to ESRD patients
- mRNA vaccines BNT162b2 and mRNA-1273 produce a weaker antibody response in ESRD patients on dialysis and kidney transplant recipients when compared to the general population but vaccination confers greater protection than not
- A third and fourth dose confers greater antibody response and increased seropositivity
- Anti-metabolite immunosuppressants, B cell modulators, belatacept, calcineurin inhibitors reduce the antibody response to vaccination
- Vaccinated household contacts and caregivers would likely bestow some protection against infection
- Vaccination of ESRD patients *prior* to kidney transplantation is critical

✉ N. Thao. N. Galvan
thao.galvan@bcm.edu

Extended author information available on the last page of the article

Abbreviations

BAU	Binding antibody units
CNI	Calcineurin inhibitor
COVID-19	Coronavirus disease 2019
CoP	Correlate of protection
ESRD	End-stage renal disease
KTR	Kidney transplant recipients
MMF	Mycophenolate mofetil
MFA	Mycophenolic acid
RCT	Randomized controlled trial
SOTR	Solid organ transplant recipient
UK	United Kingdom
VNA	virus nalieutrzing antibodies

Introduction

During the COVID-19 pandemic, patients with end-stage renal disease (ESRD) and kidney transplant recipients (KTR) were identified as high-risk groups susceptible to infection and its sequelae. They have an increased risk of contracting SARS-CoV-2 infection and experiencing severe disease

due to their greater exposure to the health care system, their immunosuppression secondary to renal dysfunction, immunosuppressive medications, and comorbidities. These two immunocompromised sub-populations have been associated with increased risk of severe disease, hospitalization, and mortality attributed to COVID-19 infection compared to the general population [1, 2]. A large comparative prospective study utilizing a database of over 17 million adults looked at risk factors associated with greater mortality early in the pandemic and found that worsening renal function was associated with greater mortality with a hazard ratio of 3.69 [3•]. Furthermore, a large-scale review of the European Renal Association COVID-19 Database performed by Goffin et al. in 2020 assessed the mortality between ESRD and KTR patients, finding that KTR had a 78% greater risk of mortality with COVID-19 infection when compared to the ESRD cohort, a disparity that was even more severe within the first year post-transplant [4]. Jering et al. found in a large-scale comparison that solid organ transplant recipients (SOTR) who were hospitalized for COVID-19 infection had higher odds of requiring intensive care and mechanical ventilation than those hospitalized for other reasons. When compared to SOTR with non-COVID pneumonia, those recipients with COVID infections were more likely to die [5]. Udomkarnjunanun et al. found in a large-scale review that risk factors among KTR that increased risk of mortality included older age, those with deceased donor allografts and those who presented with dyspnea, acute kidney injury, and pneumonia [6]. Comorbidities that worsened risk included diabetes, cardiovascular disease, and an active cancer diagnosis. Upon the introduction and approval of vaccines against COVID-19 by the FDA, ESRD patients and KTR were within the highest priority group to receive these vaccines, understanding their vulnerability within the context of an airborne pandemic. The use of these vaccines has been demonstrated to lower risk of infection, hospitalization, and mortality in the general population through ongoing clinical trials [7, 8]. Even today, the FDA recommends additional consideration for vaccination of immunocompromised patients, including an additional dose during the primary vaccination series [9]. However, published data demonstrating decreased immunogenicity of COVID-19 vaccines in KTR and ESRD patients have elicited concerns to investigate modified vaccine strategies within this immunocompromised subset of the population [10]. Thus, we sought to update the consensus of data on COVID-19 vaccine efficacy and immunogenicity in these two populations through a review of the most recent peer-reviewed literature available up to January 2022.

Society Guidelines and Recommendations for Vaccination in ESRD and KTR

On October 15, 2021, the American Society of Nephrology disseminated a statement on vaccine imperatives for patients on dialysis written by Blake et al. [11•]. It emphasized the importance of vaccination among patients with ESRD to mitigate their heightened risk of complications and mortality secondary to COVID-19 infection. The authors acknowledged the limitation of using serological response as a measure of efficacy. Many studies used assays with incomparable measures of positivity, as well as inconsistent inclusion of control subjects. Despite these qualifications, the authors came to the conclusion that a two-dose mRNA regimen was superior to a one-dose regimen in hemodialysis patients. The authors also raised the possibility that a one-shot regimen may provide an adequate immune response in hemodialysis patients with previous COVID-19 infection, though no recommendation was issued based on this hypothesis. The most urgent call to action was for vaccination of hemodialysis patients with at least two-shot vaccination regimens, and their exemption from "extended intervals" that have been used as a strategy for vaccine rationing in some countries.

On January 5, 2022, the American Society of Transplantation and the American Society of Transplant Surgeons disseminated an updated joint statement on COVID-19 vaccination in Organ Transplant Candidates and Recipients [12•]. This communication noted several key tenets that should shape our understanding of, and approach to, vaccinating those high-risk populations. Among these, the societies emphasized that (1) transplant patients have a weaker response to the two-dose vaccine series compared to the general population, (2) a third (or fourth [13•]) dose of mRNA vaccines has been shown to increase antibody titers and seropositivity in these patients, (3) higher levels of neutralizing antibodies have been correlated with reduced disease incidence in the general population, and levels of antibodies that are not sufficient to prevent infection may still reduce the severity of infection if it does occur. To this point, there have been no randomized controlled trials (RCT) that assess the effectiveness of three-shot COVID-19 vaccination regimens in this population of patients. Though the limitations of available data are clear, immunogenicity may be the best surrogate for vaccine efficacy at this crucial point in time.

Seroconversion as a Surrogate for COVID Vaccine Efficacy

Establishing the highest level of evidence provided by RCTs has poor feasibility in ESRD and KTR patients. The most compelling reason is that randomizing the

distribution of life-saving vaccines in a high-risk population would almost certainly lead to adverse outcomes based on the data currently available. So it becomes critical to establish a surrogate measure for efficacy that can be used to evaluate vaccines in sub-populations, as well as in subsequent periods where new pathogenic variants emerge. Thus, researchers have attempted to establish antibody status as a correlate of protection (CoP) against COVID-19 infection. A study by Lumley et al. followed 12,541 healthcare workers in the United Kingdom (UK) for a period of 31 weeks and correlated their antibody status with the likelihood of testing positive for COVID-19. They found that seropositive healthcare workers had a 0.13 positive tests per 10,000 days at risk, while seronegative healthcare workers had 1.09 positive PCT tests per 10,000 days at risk [14]. A subsequent study by Earle et al. analyzed the correlation between antibody response and efficacy for 7 COVID-19 vaccines based on data published in their respective phase 1 and 2 clinical trials. When the group calibrated virus neutralizing antibody (VNA) levels between the 7 studies to human convalescent serum, they found a high correlation between the calibrated ratio and vaccine efficacy. Among the 7 vaccines, VNAs accounted for 77.5% of the variation in efficacy between studies, and the IgG binding antibody accounted for 94.2% of that variation [15]. Thus, the titers appear to provide a reliable CoP for efficacy in the study populations. Furthermore, Feng et al. analyzed data from the randomized efficacy trial of the ChAdOx1 nCoV-19 vaccine, finding that 264 binding antibody units (BAU)/mL of anti-spike and 506 BAU/mL of anti-receptor binding domain (RBD) antibodies were correlated with an 80% vaccine efficacy against symptomatic infection [16]. In a similar fashion, Khuory et al. aggregated data from COVID-19 vaccine clinical trials and built a model demonstrating an association between neutralizing antibodies and protection from COVID-19 infection [17•]. However, these data are not sufficient to demonstrate a CoP in the ESRD or KTR populations, as those patients were largely excluded from efficacy studies in COVID-19 vaccine clinical trials [18•].

With respect to the ESRD population, a study by Anand et al. followed 2,563 dialysis patients who had received 2 doses of mRNA1273, BNT182b2, or Ad26.COV2.S vaccines. The study found that among 56 breakthrough cases, all patients had pre-breakthrough antibody levels equivalent to <785 BAU/mL. Among the vaccinated cohort, 20% lost detectable RBD IgG response within 6 months following vaccination, and peak and pre-breakthrough RBD values of <506 BAU/mL were associated with higher odds of breakthrough infection [19•]. Unfortunately, a convincing CoP has yet to be established in the KTR population.

COVID-19 Vaccine Seropositivity in ESRD Patients on Hemodialysis

Studies on seroconversion in ESRD patients on hemodialysis differ by type of vaccine given, number of doses, and time from dose to humoral response measurement (Table 1). Humoral response to COVID-19 vaccination in ESRD patients on hemodialysis is generally low compared with healthy controls. Seroconversion rates vary from 17.4 [22] to 96% [21]. In a cohort of 1136 dialysis patients, Stumpf et al. recorded a response rate of 95.3% 4 to 5 weeks following the second dose of either BNT182b2 or mRNA1273 vaccine. While the seroconversion for ESRD patients at the final endpoint was roughly that of healthy controls, more time was needed for ESRD patients to reach this peak. At 3–4 weeks, 61.9% of dialysis patients had detectable IgG or IgA antibodies to Spike S1 protein, compared with 96.4% of healthy controls sampled at the same time [20•]. This

Table 1 Seroconversion rates of COVID-19 vaccination in ESRD patients on dialysis

First author	*n*	Vaccine	Doses	Seroconversion	Interval*
Stumpf [20•]	1136	Pfizer, Moderna	2	95.3%	4–5 weeks
Grupper [21]	56	Pfizer	2	96%	30 days
Lesny [22]	23	Pfizer, Oxford	1	17.4%	14 days
Danthu [23•]	78	Pfizer	2	85.5%	8 days
Bertrand [24]	9	Pfizer	2	88.9%	30 days
Rincon-Arevalo [25]	41	Pfizer	2	70.5%	7 +/− 2 days
Yi [26]	31	Pfizer, Moderna	1	87%	28 days
Sattler [27]	26	Pfizer	2	84.6%	8 days
Espi [28]	83	Pfizer	2	89.2%	10–14 days

n = Number of patients on hemodialysis used in each study for determining seroconversion rates

Seroconversion rates are reported as percentage of patients for whom anti-spike protein antibodies were measured above a predetermined positive threshold by each individual study

*Interval between last dose given and measurement of seroconversion rate

delayed response is in line with previous reports [21, 22, 23•, 25]. In contrast to reports of high seroconversion rates in dialysis patients, Lesny et al. reported a rate of 17.4% in a cohort of 23 patients one week after the initial dose. The seroconversion rate reported in this study is largely an outlier when compared to other studies of efficacy in ESRD patients [22]. This may be attributed to the use of a single dose, shorter time interval to measurement, and a relatively small sample size compared with other similar studies. In a study of 106 maintenance hemodialysis patients, including 23 with a history of kidney transplantation, Espi reported a seroconversion rate of 82% by 10 to 14 days after receiving the second dose of the BNT162b2 vaccine [28]. They further divided those with a positive humoral response into high-response and low-response groups. Hemodialysis and immunosuppressive regimens were identified as independent variables associated with nonresponse to the vaccine, while prior history of COVID-19 infection was positively correlated with humoral response.

Lower Magnitude of Humoral Response in ESRD Patients on Hemodialysis

The magnitude of antibody response to COVID-19 vaccination is lower in ESRD patients on dialysis when compared with healthy controls. In a study by Danthu et al., 85.5% of patients undergoing hemodialysis produced a detectable humoral response by day 36 following the first dose of BNT162b2. These patients, however, displayed a much lower antibody titer than their healthy control counterparts. Median antibody titers in the hemodialysis group were 6.6 AU/ml at 36 days and 276 AU/ml at day 58, compared with 1,086 AU/ml at day 36 and 925 AU/ml at day 58 in the control group [23•]. This finding is consistent with other studies [21, 22, 28]. In 2002, Kovacic demonstrated a positive correlation between hemodialysis efficiency, measured in Kt/V, and hepatitis B virus surface antibody following hepatitis B vaccination [29]. Espi and Danthu have reported a positive correlation between Kt/V and antibody response to BNT162b2 vaccination as well [23•, 28]. In this light, the uremic environment is likely a factor in the weaker humoral response seen in CKD patients [23•, 28, 30]. This is supported by the correlation between anti-HBs and SARS-CoV-2 antibody titers in patients undergoing hemodialysis [23•].

COVID-19 Vaccine Seropositivity in Kidney Transplant Recipients

In KTR vaccinated against COVID-19, seropositivity has been reported at significantly decreased rates compared to the general population (Table 2). In an early study, Boyarsky et al. reported seroconversion of 14.2% among KTR who received one dose of mRNA vaccine (mRNA-1273 or BNT162b2) [10]. A subsequent study by Boyarsky et al. which included 322 KTR reported seroconversion of 48% in those patients. Interestingly, 37% of patients failed to seroconvert after 1 dose of mRNA vaccine but developed antibodies following a second dose [37•]. Rozen-Zvi et al. found a seroconversion rate of 36.4% in 308 KTR following 2 doses of the BNT162b2 vaccine [34]. Marion et al. also contributed a study that demonstrated 33% seroconversion among 271 KTR who received 2 doses of mRNA vaccine [38]. Some studies have reported even lower seroconversion rates, including 4% among 74 KTR [23•], 2.5% among 40 KTR [25], and 2 and 5.7% measured on days 28 and 60 respectively, among 35 KTR [47]. However, comparison of these studies is challenging due to variability in study populations, timing of response measurement, and assay characteristics that may have influenced seropositivity. Bentomane et al. published a study that reported 11.7% seropositivity following 1 dose, and 47.8% seropositivity 28 days after a second dose of vaccine [35•]. Subsequently, in a study of 159 KTR with failed (n=95) or weak response (n = 64) to 2 doses of mRNa vaccine, Bentomane et al. reported antibody titers above 50 BAU/mL in 81.3% of patients who previously had a weak response to vaccine, but only 27.4% of previous nonresponders (median 586 BAU/mL) [51]. Kamar et al. conducted a study including 101 SOTR (78 KTR) which demonstrated 4% seropositivity prior to administration of a second dose of vaccine, 40% before a third dose, and 68% 4 weeks after the third dose was given [43]. Subsequently, Kamar et al. published a case series of 37 solid organ transplant recipients (25 KTR) who did not respond to the first 3 doses of BNT162b2 or else had a weakened response (5/37). They found that those who had a weakened response prior to the third dose had a nearly 100-fold increase in measured antibodies after the fourth dose. Among the 31 patients who had no response prior to the fourth dose, 41.9% of those patients (54% among KTR) became seropositive (mean antibody concentration, 9.5 BAU/ml) [13•]. Recently, Benning et al. characterized the humoral response against the alpha, beta, and delta COVID-19 variants in 173 KTR who received 2 doses of COVID-19 vaccine (including combinations of BNT182b2, mRNA1273, and ChAdOx1 nCoV-19) when compared to healthy controls. Though the neutralizing antibody response was diminished in KTR compared to healthy controls, all seropositive KTR demonstrated neutralizing activity against Alpha variant, 64% against Beta variant, and 67% against Delta variant [52•].

Results from the above-mentioned studies must be analyzed with caution, as the studies took place in a variety of settings that include different geographic locations, prevalence of different variants of interest, inclusion of patient populations that are not easily comparable, and in some

Table 2 Seroconversion rates of COVID-19 vaccination in kidney transplant recipients

Reference	*n*	Vaccine	Doses:	Seroconversion	Interval*
Espi [28]	15	Pfizer	2	73.3%	10–14 days
Danthu [23•]	74	Pfizer	2	4.1%	8 days
Bertrand [24]	45	Pfizer	2	17.8%	30 days
Rincon-Arevalo [25]	40	Pfizer	2	2.5%	7 +/− 2 days
Yi [26]	145	Pfizer, Moderna	1	6.2%	28 days
Sattler [27]	39	Pfizer	2	2.6%	8 days
Massa [31]	61	Pfizer	2	44.3%	28 days
			3	62.3%	28 days
Korth [32]	23	Pfizer	2	22%	15.8 days
Stumpf [33]	71	Pfizer	1	6%	3 weeks
		Pfizer	2	32%	8 weeks after 1st
Rozen-Zvi [34]	308	Pfizer	2	38.4%	28 days
Bentomane [35•]	205	Moderna	2	48%	28 days
Boyarsky [36]	7	Janssen	1	14%	1 month
Boyarsky [37•]	322	Pfizer, Moderna	1	11%	21 days
			2	48%	29 days
Grupper [21]	136	Pfizer	2	37.5%	16 days
Marion [38]	271	Pfizer	2	33%	28 days
Cucchiari [39]	117	Moderna	2	29.9%	2 weeks
Husain [40]	28	Pfizer, Moderna	2	25%	2–6 weeks
Marinaki [41]	10	Pfizer	2	20%	10 days
Midtvedt [42]	141	Pfizer	2	18%	25–89 days
Kamar [13•, 43]	78	Pfizer	3	46.6%	14 days
	25		4	54.2%	4 weeks
Dębska-Ślizień [44]	142	Pfizer, Moderna	2	51.41%	14–21 days
Marlet [45]	97	Pfizer, Moderna	2	43%	95 days
	160		3	47%	52 days
Kantauskaite [46]	225	Pfizer, Moderna	2	24.9%	14 days
Chavarot [47, 48]	35	Pfizer	2	5.7%	28 days
	62		3	6.4%	28 days
Bruminhent [49]	37	Sinovac	2	9%	14 days
Stumpf [20•]	368	Pfizer, Moderna	1	7.6%	3–4 weeks
			2	42%	4–5 weeks
Ou [50•]	592	Pfizer, Moderna	1	13.0%	21 days
	400		2	47.8%	29 days

n = Number of kidney transplant recipients used in each study for determining seroconversion rates

Seroconversion rates are reported as percentage of patients for whom anti-spike protein antibodies were measured above a predetermined positive threshold by each individual study

*Interval between last dose given and measurement of seroconversion rate

cases different definitions of seropositivity. However, they largely demonstrate that (1) KTR have decreased antibody response following COVID-19 vaccination compared to the general population, (2) additional doses increase antibody production in some weak responders and non-responders, and (3) there is a need to investigate characteristics that affect a patient's likelihood to produce antibodies.

COVID-19 Vaccination is More Effective Prior to Kidney Transplantation

A study by Grupper et al. addressed the timing of COVID-19 vaccination and kidney transplantation by comparing 19 patients vaccinated prior to transplantation with 109 patients vaccinated after. A markedly higher proportion of patients vaccinated before transplantation (90%) produced anti-spike antibodies compared to those vaccinated after (45%). Of note, maintenance immunosuppression regimens were similar

between the two groups. The exception to this was 100% (19/19) of patients vaccinated before the transplant received mycophenolate compared with 75% (82/109) in the post-transplant group. Multivariate analysis related vaccination after transplantation to the risk of seronegativity with an odds ratio of 22.4 when compared to pre-transplant vaccination. Age, lower lymphocyte count, and time on dialysis were also correlated with seronegativity, although to a lesser extent than post-transplantation vaccination [53•].

Studies Examining the Effect of Immunosuppressive Drugs

Many studies have demonstrated associations between immunosuppressive drug therapy and nonresponse to COVID-19 vaccines. Triple immunosuppressive therapy, including calcineurin inhibitors (tacrolimus or cyclosporine), antimetabolites (MMF/MFA/azathioprine), and corticosteroids have been associated with non-response and weakened response to COVID-19 vaccines [10, 20•, 34, 35•, 44, 54]. A study by Boyarsky et al., including 219 COVID-naive kidney transplant recipients, found that antimetabolite maintenance immunosuppression decreased the likelihood of antibody response following 1- and 2-dose vaccination [10]. A later study by Boyarsky et al. supported these findings with 57% (268/473) of SOTR treated with antimetabolites failing to produce a detectable antibody response following 2 doses, compared with 18% (33/185) SOTR not treated with antimetabolites [37•]. These findings have been echoed by others, who found that Mycophenolate mofetil (MMF) and mycophenolic acid (MFA) treatments regimens have been strongly associated with humoral non-response following COVID-19 vaccination in KTR [20•, 34, 35•, 44, 46, 51, 54, 55]. Ou et al. performed a prospective cohort study of 609 COVID-naive kidney transplant recipients and found a 16.7-fold decreased odds of positive titers following 2-doses of vaccine in patients treated with belatacept [50•]. These findings are reinforced by other studies [20•, 35•], including Chavarot et al., who also observed breakthrough infection in 6.6% (12/181) of belatacept-treated KTRs 8-30 days after their last vaccine dose, including 9 (5.0%) at least 2 weeks after their last vaccine dose, which were defined as breakthrough infections. Additionally, a third dose of either vaccine failed to improve humoral response in KTRs treated with belatacept [47].

These studies must be reviewed with the consideration that KTR are typically treated with multiple immune-suppressing drug regimens such as triple immunosuppressive therapy. Thus, there is a high potential for confounders if studies do not control for co-variation among drugs. As previously stated, factors including patient characteristics and the prevalence of variants of interest during different time periods may also be at play. The most significant takeaway from these studies is that immunosuppressive therapies, especially those including antimetabolites, belatacept, or rituximab [56, 57] appear to be associated with decreased immune response to COVID-19 vaccination. At this time, the evidence is insufficient to recommend any modification of immunosuppressive therapy for KTR prior to or following COVID-19 vaccination. However, these findings do lend support to the conclusion that patients should be vaccinated before the initiation of immunosuppressant treatments whenever feasible and that more data is needed regarding immunosuppressant medications and its influence on vaccine response.

Studies Examining the Differences Between Vaccines

Stumpf et al. found significantly increased seroconversion with mRNA-1273 (49%) compared to BNT162b2 (26%) in kidney transplant recipients. Seroconversion rates were higher for mRNA-1273 (97%) than BNT162b2 (88%) in hemodialysis patients as well, although to a lesser degree [20•]. This finding was supported by a higher frequency of RBD-specific IgG production induced by mRNA-1273 (95%) than BNT162b2 (85%). The study by Boyarsky et al. found that 22% of solid organ transplant recipients produced a humoral response after the first dose of mRNA-1273, compared with 8% with BNT162b2. These rates improved to 60% and 49% for mRNA-1273 and BNT162b2, respectively, after second dose administration, but a significant difference between the vaccines persisted [37•]. These findings are consistent with studies by Dębska-Ślizień and Marlet [44, 45]. The seroconversion efficacy of the ChAdOx1 (AstraZeneca) vaccine is not as well-studied in ESRD and kidney transplant recipients as the mRNA-1273 and BNT162b2 vaccines. In a cohort of 25 kidney transplant recipients who did not produce a humoral response to the two-dose BNT162b2 regimen, Schrezenmeier et al. found that 6 out of 11 patients given the ChAdOx1 vaccine produced detectable antibodies, compared to just 3 out of the 14 patients that received a third dose of the BNT162b2 vaccination [55]. Lesny et al. compared humoral response 2 weeks after a single dose of either BNT162b2 (N=11) or ChAdOx1 (N=14) in patients on hemodialysis and found no significant difference in antibody production between the two groups [22]. Boyarsky et al. studied the effect of the Ad26.COV2.S Janssen COVID-19 vaccine in 12 solid organ transplant recipients [36]. This study included 7 KTR, only one of which produced a positive humoral response 1 month after the single dose was given. Of note, all 7 KTR were on immunosuppressive regimens that included antimetabolites.

Boyarsky et al. also described a decreased likelihood for older patients to develop an immune response, and an increased response in patients who received the mRNA-1273 vaccine compared to BNT162b2 [10, 37•].

Additional factors associated with increased likelihood of seropositivity among the studies reviewed include previous COVID-19 infection, vaccination prior to transplant, younger age, and vaccination with an mRNA vaccine [39, 53•, 58].

Incidence of COVID-19 Infection and Mortality in Vaccinated SOTR

In a retrospective analysis of data concerning 2151 SOTR (including 967 KTR) obtained from a single-center electronic medical record (EMR) system, Aslam et al. investigated the incidence of symptomatic COVID-19 infection in fully vaccinated patients (predominantly with mRNA1273) and controls who received 1 or no COVID-19 vaccines. The investigators discovered an incidence rate of 0.065 per 1000 person-days in vaccinated transplant recipients and 0.34 per 1000 person-days in the control group [59]. These data correlate to an incidence risk for symptomatic COVID-19 infection of 0.19 in vaccinated transplant recipients compared to their unvaccinated counterparts. In a subsequent study, Aslam et al. addressed concerns of potential confounding factors related to variable prevalences of COVID-19 in the community during their prior study period. They assessed EMR data concerning 1904 SOTR (including 820 KTR) sourced from one hospital system and affiliated hospitals over a longer study period. The study model, which accounted for population-level changes in COVID-19 prevalence, demonstrated a significantly lower hazard for COVID-19 in vaccinated patients (predominantly with mRNA1273) compared to unvaccinated counterparts [60•]. A study by Ravanan et al. performed retrospective analysis on data obtained from four linked UK registries that included 39,727 SOTR who received 2 doses of vaccine, (predominantly BNT162b2 or ChAdOx1) 1738 who received 1 dose of vaccine, and 6748 who were unvaccinated. Among this cohort, the mortality rate after testing positive for COVID-19 was 7.7% among fully vaccinated SOTR and 12% among unvaccinated SOTR and those who received 1 dose [61•].

These retrospective studies provide reassurance that despite low seroconversion rates noted in many studies of SOTR and KTR, vaccination appears to provide protection against symptomatic infection and death secondary to COVID-19 in these populations. However, the treatment and control groups in these studies are not randomly assigned or blinded, and thus are subject to the effects of confounders including factors correlated with patient vaccination status. Additionally, the prevalence of COVID-19 infection in the relevant communities including the spread of variants of interest, and even hospital-level shortages in resources at different timepoints prevent the data from being interpreted as representative of efficacy or even a robust CoP. Nonetheless, the large sample sizes do increase confidence in the conclusion that vaccination appears to provide protection for KTR.

Immunocompromised Patients are Protected by Vaccinated Household Members

It would be remiss to discuss COVID vaccination in immunocompromised patients without discussing the vaccination of their caregivers and household members. While it is sobering to understand that the humoral response to mRNA COVID vaccination is less in ESRD and KTR patients when compared to the general population, there is value in recognizing that the immunocompetent people who surround that patient can mount an excellent immune response. While not studied specifically in ESRD and KTR patients, Hayek et al. report indirect protection of (unvaccinated) children from SARS-CoV-2 infection through parental vaccination with BNT162b2 [62]. When both parents were vaccinated with two doses of BNT162b2, the risk of COVID infection decreased by 71.7% during the Alpha variant time period and 58.1% during Delta variant time period. This is also known as "cocooning," the creation of a protective layer for the immunocompromised patient of household contacts and caregivers by vaccination and is, in fact, how we currently protect infants from pertussis [63]. It has been argued that COVID vaccination ought to be prioritized for caregivers of patients with cancer, and cocooning patients immunocompromised from ESRD and KTR would follow the same logic. In essence, another effective way of protecting a patient with ESRD and KTR is to ensure their caregivers and household contacts are fully vaccinated against SARS-CoV-2 to overcome the fact that immunosuppressed patients do not mount as robust a response to the vaccines [64].

Conclusion

This review summarizes the most-recent literature available on COVID-19 vaccine efficacy in ESRD patients on hemodialysis and KTR. Vaccination with either Pfizer BNT162b2 or Moderna mRNA-1273 produces a weaker antibody response in ESRD patients on dialysis and kidney transplant recipients when compared to the general population. Humoral immune responses are typically even weaker in KTR patients than in hemodialysis patients, which is strongly related to immunosuppressive therapy. BNT162b2 has been correlated with lower rates of seropositivity in

both populations when compared with mRNA-1273. However, the third and fourth doses improved weak responses and increased seropositivity rates significantly. Vaccination before kidney transplantation has been shown to significantly improve humoral response compared with vaccination after transplantation, and thus more likely to confer protection. Vaccination of ESRD patients prior to kidney transplantation is critical. Given the high mortality associated with COVID-19 infection and high prevalence of comorbidities in both populations, vaccination protocols that include at least a third dose are highly recommended. Vaccination against COVID-19 is recommended by the National Kidney Association, American Society of Nephrology, the American Society of Transplantation, and the American Society of Transplant Surgeons, professional societies who understand the vulnerabilities of the population they care for, and the protections necessary to reduce morbidity and mortality. Because the protective response to vaccination against SARS-CoV-2 is lessened in the immunocompromised patient, family members, household contacts and caregivers ought to be fully vaccinated, which would likely confer a significant amount of protection against infection. ESRD and KTR patients must also continue the life-saving preventive measures that combat this aerosolized pathogen which include respirator/fitted-mask wearing, social distancing, and improved ventilation and filtration.

Funding No funding was received to produce this study.

Data Availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of Interest The authors of this manuscript have no conflicts of interest to disclose as described by *Current Transplantation Reports.*

References

Papers of particular interest, published recently, have been highlighted as:
• Of importance

1. Chen CY, Shao SC, Chen YT, et al. Incidence and Clinical Impacts of COVID-19 Infection in Patients with Hemodialysis: Systematic Review and Meta-Analysis of 396,062 Hemodialysis Patients. Healthcare (Basel). 2021;9(1):47. https://doi.org/10.3390/healthcare9010047.
2. Thaunat O, Legeai C, Anglicheau D, et al. IMPact of the COVID-19 epidemic on the moRTAlity of kidney transplant recipients and candidates in a French Nationwide registry sTudy (IMPORTANT). Kidney Int. 2020;98(6):1568–77. https://doi.org/10.1016/j.kint.2020.10.008.
3.• Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature. 2020;584(7821):430–6. https://doi.org/10.1038/s41586-020-2521-4. **This study found greater mortality from COVID-19 to be associated with worsening renal function with a hazard ratio of 3.69.**
4. Goffin E, Candellier A, Vart P, et al. COVID-19-related mortality in kidney transplant and haemodialysis patients: a comparative, prospective registry-based study. Nephrol Dial Transplant. 2021;36(11):2094–105. https://doi.org/10.1093/ndt/gfab200.
5. Jering KS, McGrath MM, McCausland FR, Claggett B, Cunningham JW, Solomon SD. Excess mortality in solid organ transplant recipients hospitalized with COVID-19: A large-scale comparison of SOT recipients hospitalized with or without COVID-19. Clin Transpl. 2022;36(1):e14492. https://doi.org/10.1111/ctr.14492.
6. Udomkarnjananun S, Kerr SJ, Townamchai N, et al. Mortality risk factors of COVID-19 infection in kidney transplantation recipients: a systematic review and meta-analysis of cohorts and clinical registries. Sci Rep. 2021;11(1):20073. https://doi.org/10.1038/s41598-021-99713-y.
7. Baden LR, El Sahly HM, Essink B, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2021;384(5):403–16. https://doi.org/10.1056/NEJMoa2035389.
8. Polack FP, Thomas SJ, Kitchin N, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020;383(27):2603–15. https://doi.org/10.1056/NEJMoa2034577.
9. Interim Clinical Considerations for Use of COVID-19 Vaccines | CDC. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html. Accessed 25 Jan 2022.
10. Boyarsky BJ, Werbel WA, Avery RK, et al. Immunogenicity of a Single Dose of SARS-CoV-2 Messenger RNA Vaccine in Solid Organ Transplant Recipients. JAMA. 2021;325(17):1784–6. https://doi.org/10.1001/jama.2021.4385.
11.• Blake PG, Hladunewich MA, Oliver MJ. COVID-19 Vaccination Imperatives in People on Maintenance Dialysis: An International Perspective. CJASN. 2021;16(11):1746–8. https://doi.org/10.2215/CJN.07260521. **Blake et al (American Society of Nephrology) issued a statement encouraging vaccination in ESRD patients due to increased risk of complications and mortality from COVID-19 infection.**
12.• Joint Statement about COVID-19 Vaccination in Organ Transplant Candidates and Recipients. Published online January 5, 2022. https://www.myast.org/sites/default/files/ISHLT-AST-ASTSjointsocietyguidancevaccine_FINALDec30_0.pdf. **The American Society of Transplantation and American Society of Transplant Surgeons issued a joint statement detailing the weaker immune response to vaccination seen in SOTR and candidates and emphasized the importance of third and fourth booster doses of mRNA COVID-19 vaccines.** Accessed 25 Jan 2022.
13.• Kamar N, Abravanel F, Marion O, et al. Assessment of 4 Doses of SARS-CoV-2 Messenger RNA–Based Vaccine in Recipients of a Solid Organ Transplant. JAMA Netw Open. 2021;4(11):e2136030. https://doi.org/10.1001/jamanetworkopen.2021.36030. **Kamar et al published a case series detailing significantly increased immune response following a fourth dose of Pfizer BNT162b2 vaccine in SOTR.**
14. Lumley SF, O'Donnell D, Stoesser NE, et al. Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers. N Engl J Med. 2021;384(6):533–40. https://doi.org/10.1056/NEJMoa2034545.

15. Earle KA, Ambrosino DM, Fiore-Gartland A, et al. Evidence for antibody as a protective correlate for COVID-19 vaccines. Vaccine. 2021;39(32):4423–8. https://doi.org/10.1016/j.vaccine.2021.05.063.
16. Feng S, Phillips DJ, White T, et al. Correlates of protection against symptomatic and asymptomatic SARS-CoV-2 infection. Nat Med. 2021;27(11):2032–40. https://doi.org/10.1038/s41591-021-01540-1.
17.• Khoury DS, Cromer D, Reynaldi A, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. Nat Med. 2021;27(7):1205–11. https://doi.org/10.1038/s41591-021-01377-8. **Khoury et al associated neutralizing antibodies with protection from COVID-19 infection using data from COVID-19 vaccine clinical trials.**
18.• Glenn DA, Hegde A, Kotzen E, et al. Systematic Review of Safety and Efficacy of COVID-19 Vaccines in Patients With Kidney Disease. Kidney Int Rep. 2021;6(5):1407–10. https://doi.org/10.1016/j.ekir.2021.02.011. **Glenn et al reviewed clinical trials for COVID-19 vaccines, finding that patients with "serious renal disease" and kidney transplant recipients were largely excluded from efficacy studies.**
19.• Anand S, Montez-Rath ME, Han J, et al. SARS-CoV-2 Vaccine Antibody Response and Breakthrough Infection in Patients Receiving Dialysis. Ann Intern Med. Published online December 14, 2021:M21–4176. https://doi.org/10.7326/M21-4176. **Anand et al associated antibody levels <785 BAU/mL following 2 doses of COVID-19 vaccination with breakthrough infections in a large cohort of dialysis patients.**
20.• Stumpf J, Siepmann T, Lindner T, et al. Humoral and cellular immunity to SARS-CoV-2 vaccination in renal transplant versus dialysis patients: A prospective, multicenter observational study using mRNA-1273 or BNT162b2 mRNA vaccine. Lancet Reg Health Eur. 2021;9:100178. https://doi.org/10.1016/j.lanepe.2021.100178. **Stumpf et al found a seroconversion rate of 95.3% in a cohort of 1,136 patients on hemodialysis following the second dose of either BNT162b2 or mRNA-1273.**
21. Grupper A, Sharon N, Finn T, et al. Humoral Response to the Pfizer BNT162b2 Vaccine in Patients Undergoing Maintenance Hemodialysis. CJASN. 2021;16(7):1037–42. https://doi.org/10.2215/CJN.03500321.
22. Lesny P, Anderson M, Cloherty G, et al. Immunogenicity of a first dose of mRNA- or vector-based SARS-CoV-2 vaccination in dialysis patients: a multicenter prospective observational pilot study. J Nephrol. 2021;34(4):975–83. https://doi.org/10.1007/s40620-021-01076-0.
23.• Danthu C, Hantz S, Dahlem A, et al. Humoral Response after SARS-CoV-2 mRNA Vaccination in a Cohort of Hemodialysis Patients and Kidney Transplant Recipients. JASN. 2021;32(9):2153–8. https://doi.org/10.1681/ASN.2021040490. **Danthu et al found a lower magnitude of antibody response in hemodialysis patients compared with healthy controls.**
24. Bertrand D, Hamzaoui M, Lemee V, et al. Antibody and T Cell Response to SARS-CoV-2 Messenger RNA BNT162b2 Vaccine in Kidney Transplant Recipients and Hemodialysis Patients | American Society of Nephrology.
25. Rincon-Arevalo H, Choi M, Stefanski AL, et al. Impaired humoral immunity to SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients and dialysis patients. Sci Immunol. 2021;6(60):eabj1031. https://doi.org/10.1126/sciimmunol.abj1031.
26. Yi SG, Knight RJ, Graviss EA, et al. Kidney Transplant Recipients Rarely Show an Early Antibody Response Following the First COVID-19 Vaccine Administration. Transplantation. 2021;105(7):e72–3. https://doi.org/10.1097/TP.0000000000003764.
27. Sattler et al. Impaired humoral and cellular immunity after SARS-CoV-2 BNT162b2 (tozinameran) prime-boost vaccination in kidney transplant recipients. JCI. https://doi.org/10.1172/JCI150175.
28. Espi M, Charmetant X, Barba T, et al. The ROMANOV study found impaired humoral and cellular immune responses to SARS-CoV-2 mRNA vaccine in virus-unexposed patients receiving maintenance hemodialysis. Kidney Int. 2021;100(4):928–36. https://doi.org/10.1016/j.kint.2021.07.005.
29. Kovacic V, Sain M, Vukman V. Efficient haemodialysis improves the response to hepatitis B virus vaccination. Intervirology. 2002;45(3):172–6. https://doi.org/10.1159/000065873.
30. Espi M, Koppe L, Fouque D, Thaunat O. Chronic Kidney Disease-Associated Immune Dysfunctions: Impact of Protein-Bound Uremic Retention Solutes on Immune Cells. Toxins. 2020;12(5):300. https://doi.org/10.3390/toxins12050300.
31. Massa F, Cremoni M, Gérard A, et al. Safety and cross-variant immunogenicity of a three-dose COVID-19 mRNA vaccine regimen in kidney transplant recipients. eBioMedicine. 2021;73. https://doi.org/10.1016/j.ebiom.2021.103679.
32. Korth J, Jahn M, Dorsch O, Anastasiou OE, Sorge-Hädicke B, Eisenberger U, Gäckler A, Dittmer U, Witzke O, Wilde B, et al. Impaired Humoral Response in Renal Transplant Recipients to SARS-CoV-2 Vaccination with BNT162b2 (Pfizer-BioNTech). Viruses. 2021;13:756. https://doi.org/10.3390/v13050756.
33. Stumpf J, Tonnus W, Paliege A, et al. Cellular and Humoral Immune Responses After 3 Doses of BNT162b2 mRNA SARS-CoV-2 Vaccine in Kidney Transplant. Transplantation. 2021;105(11):e267. https://doi.org/10.1097/TP.0000000000003903.
34. Rozen-Zvi B, Yahav D, Agur T, et al. Antibody response to SARS-CoV-2 mRNA vaccine among kidney transplant recipients: a prospective cohort study. Clin Microbiol Infect. 2021;27(8):1173.e1–4. https://doi.org/10.1016/j.cmi.2021.04.028.
35.• Benotmane I, Gautier-Vargas G, Cognard N, et al. Low immunization rates among kidney transplant recipients who received 2 doses of the mRNA-1273 SARS-CoV-2 vaccine. Kidney Int. 2021;99(6):1498–500. https://doi.org/10.1016/j.kint.2021.04.005. **Bentomane et al published a study showing poor antibody response after first and second doses of mRNA vaccine in KTR.**
36. Boyarsky BJ, Chiang TPY, Ou MT, et al. Antibody Response to the Janssen COVID-19 Vaccine in Solid Organ Transplant Recipients. Transplantation. 2021;105(8):e82–3. https://doi.org/10.1097/TP.0000000000003850.
37.• Boyarsky BJ, Werbel WA, Avery RK, et al. Antibody Response to 2-Dose SARS-CoV-2 mRNA Vaccine Series in Solid Organ Transplant Recipients. JAMA. 2021;325(21):2204–6. https://doi.org/10.1001/jama.2021.7489. **Boyarsky et al found decreased humoral immune response to COVID-19 vaccination in KTR and ESRD patients after first and second doses.**
38. Marion O, Del Bello A, Abravanel F, et al. Safety and Immunogenicity of Anti-SARS-CoV-2 Messenger RNA Vaccines in Recipients of Solid Organ Transplants. Ann Intern Med. 2021;174(9):1336–8. https://doi.org/10.7326/M21-1341.
39. Cucchiari, et al. Cellular and humoral response after mRNA-1273 SARS-CoV-2 vaccine in kidney transplant recipients. Am J Transplant. https://doi.org/10.1111/ajt.16701.
40. Husain SA, Tsapepas D, Paget KF, et al. Postvaccine Anti–SARS-CoV-2 Spike Protein Antibody Development in Kidney Transplant Recipients. Kidney Int Rep. 2021;6(6):1699–700. https://doi.org/10.1016/j.ekir.2021.04.017.
41. Marinaki S, Adamopoulos S, Degiannis D, et al. Immunogenicity of SARS-CoV-2 BNT162b2 vaccine in solid organ transplant

recipients. Am J Transplant. 2021;21(8):2913–5. https://doi.org/10.1111/ajt.16607.
42. Midtvedt K, Tran T, Parker K, et al. Low Immunization Rate in Kidney Transplant Recipients Also After Dose 2 of the BNT162b2 Vaccine: Continue to Keep Your Guard up! Transplantation. 2021;105(8):e80–1. https://doi.org/10.1097/TP.0000000000003856.
43. Kamar N, Abravanel F, Marion O, Couat C, Izopet J, Del Bello A. Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients. N Engl J Med. 2021;385(7):661–2. https://doi.org/10.1056/NEJMc2108861.
44. Dębska-Ślizień A, Ślizień Z, Muchlado M, et al. Predictors of Humoral Response to mRNA COVID19 Vaccines in Kidney Transplant Recipients: A Longitudinal Study—The COViNEPH Project. Vaccines. 2021;9(10):1165. https://doi.org/10.3390/vaccines9101165.
45. Marlet J, Gatault P, Maakaroun Z, et al. Antibody Responses after a Third Dose of COVID-19 Vaccine in Kidney Transplant Recipients and Patients Treated for Chronic Lymphocytic Leukemia. Vaccines. 2021;9(10):1055. https://doi.org/10.3390/vaccines9101055.
46. Kantauskaite M, Müller L, Kolb T, et al. Intensity of mycophenolate mofetil treatment is associated with an impaired immune response to SARS-CoV-2 vaccination in kidney transplant recipients. Am J Transplant. 2021;00:1–6. https://doi.org/10.1111/ajt.16851.
47. Chavarot N, Morel A, Leruez-Ville M, et al. Weak antibody response to three doses of mRNA vaccine in kidney transplant recipients treated with belatacept. Am J Transplant. 2021;21:4043–51. https://doi.org/10.1111/ajt.16814.
48. Chavarot N, Ouedrani A, Marion O, et al. Poor Anti-SARS-CoV-2 Humoral and T-cell Responses After 2 Injections of mRNA Vaccine in Kidney Transplant Recipients Treated With Belatacept. Transplantation. 2021;105(9):e94. https://doi.org/10.1097/TP.0000000000003784.
49. Bruminhent J, Setthaudom C, Chaumdee P, et al. SARS-CoV-2-specific humoral and cell-mediated immune responses after immunization with inactivated COVID-19 vaccine in kidney transplant recipients (CVIM 1 study). Am J Transplant. Published online October 17, 2021. https://doi.org/10.1111/ajt.16867.
50.• Ou MT, Boyarsky BJ, Chiang TPY, et al. Immunogenicity and Reactogenicity After SARS-CoV-2 mRNA Vaccination in Kidney Transplant Recipients Taking Belatacept. Transplantation. 2021;105(9):2119–23. https://doi.org/10.1097/TP.0000000000003824. **Ou et al found a 16.7-fold decreased odds of seroconversion among KTR treated with belatacept.**
51. Benotmane I, Gautier G, Perrin P, et al. Antibody Response After a Third Dose of the mRNA-1273 SARS-CoV-2 Vaccine in Kidney Transplant Recipients With Minimal Serologic Response to 2 Doses. JAMA. Published online July 23, 2021. https://doi.org/10.1001/jama.2021.12339.
52.• Benning L, Morath C, Bartenschlager M, et al. Neutralization of SARS-CoV-2 Variants of Concern in Kidney Transplant Recipients after Standard COVID-19 Vaccination. CJASN. 2022;17(1):98–106. https://doi.org/10.2215/CJN.11820921. **Benning et al demonstrated the neutralizing capacity of serum from 173 seropositive KTR against alpha, beta, and delta COVID-19 variants.**
53.• Grupper A, Katchman E, Ben-Yehoyada M, et al. Kidney transplant recipients vaccinated before transplantation maintain superior humoral response to SARS-CoV-2 vaccine. Clin Transpl. 2021:e14478. https://doi.org/10.1111/ctr.14478. **Grupper et al found a significantly higher antibody response rate among KTR vaccinated before transplantation compared to those vaccinated after transplantation.**
54. Grupper A, Rabinowich L, Schwartz D, et al. Reduced humoral response to mRNA SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients without prior exposure to the virus. Am J Transplant. Published online May 7, 2021:10.1111/ajt.16615. https://doi.org/10.1111/ajt.16615.
55. Schrezenmeier E, Rincon-Arevalo H, Stefanski AL, et al. B and T Cell Responses after a Third Dose of SARS-CoV-2 Vaccine in Kidney Transplant Recipients. J Am Soc Nephrol. Published online October 19, 2021:ASN.2021070966. https://doi.org/10.1681/ASN.2021070966.
56. Simpson-Yap S, De Brouwer E, Kalincik T, Rijke N, Hillert JA, Walton C, Edan G, Moreau Y, Spelman T, Geys L, Parciak T, Gautrais C, Lazovski N, Pirmani A, Ardeshirdavanai A, Forsberg L, Glaser A, McBurney R, Schmidt H, et al. Associations of Disease-Modifying Therapies With COVID-19 Severity in Multiple Sclerosis. Neurology. 2021;97(19):e1870–85. https://doi.org/10.1212/WNL.0000000000012753.
57. Andersen KM, Bates BA, Rashidi ES, Olex AL, Mannon RB, Patel RC, Singh J, Sun J, Auwaerter PG, Ng DK, Segal JB, Garibaldi BT, Mehta HB, Alexander GC. National COVID Cohort Collaborative Consortium. Long-term use of immunosuppressive medicines and in-hospital COVID-19 outcomes: a retrospective cohort study using data from the National COVID Cohort Collaborative. Lancet. Rheumatol. 2022;4(1):e33–41. https://doi.org/10.1016/S2665-9913(21)00325-8.
58. Haskin O, Ashkenazi-Hoffnung L, Ziv N, et al. Serological Response to the BNT162b2 COVID-19 mRNA Vaccine in Adolescent and Young Adult Kidney Transplant Recipients. Transplantation. 2021;105(11):e226–33. https://doi.org/10.1097/TP.0000000000003922.
59. Aslam S, Adler E, Mekeel K, Little SJ. Clinical effectiveness of COVID-19 vaccination in solid organ transplant recipients. Transpl Infect Dis. Published online August 3, 2021:e13705. https://doi.org/10.1111/tid.13705.
60.• Aslam S, Liu J, Sigler R, et al. COVID-19 vaccination is protective of clinical disease in solid organ transplant recipients. Transpl Infect Dis. n/a(n/a). https://doi.org/10.1111/tid.13788. **Aslam et al performed a retrospective study of 1904 SOTR including 820 KTR, which demonstrated a lower hazard risk for symptomatic COVID-19 infection in vaccinated compared to unvaccinated patients.**
61.• Ravanan R, Mumford L, Ushiro-Lumb I, et al. Two Doses of SARS-CoV-2 Vaccines Reduce Risk of Death Due to COVID-19 in Solid Organ Transplant Recipients: Preliminary Outcomes From a UK Registry Linkage Analysis. Transplantation. 2021;105(11):e263–4. https://doi.org/10.1097/TP.0000000000003908. **Ravana et al performed a retrospective study of 39,727 SOTR, finding decreased mortality in patients that received 2 doses of COVID-19 vaccine compared to those who received 1 dose or unvaccinated patients.**
62. Hayek S, Shaham G, Ben-Shlomo Y, et al. Indirect protection of children from SARS-CoV-2 infection through parental vaccination. Science. Published online January 27, 2022:eabm3087. https://doi.org/10.1126/science.abm3087.
63. Rowe SL, Tay EL, Franklin LJ, et al. Effectiveness of parental cocooning as a vaccination strategy to prevent pertussis infection in infants: A case-control study. Vaccine. 2018;36(15):2012–9. https://doi.org/10.1016/j.vaccine.2018.02.094.
64. Woodfield MC, Pergam SA, Shah PD. Cocooning against COVID-19: The argument for vaccinating caregivers of patients with cancer. Cancer. 2021;127(16):2861–3. https://doi.org/10.1002/cncr.33598.

Authors and Affiliations

Nicolas F. Moreno[1] · Robert McAdams[1] · John A. Goss[2] · N. Thao. N. Galvan[2]

[1] McGovern Medical School, University of Texas Health Science Center, Houston, TX, USA

[2] Michael E. DeBakey Department of Surgery, Division of Abdominal Transplantation, Baylor College of Medicine, Houston, TX, USA