OPEN

Transplantation Amid a Pandemic: The Fall and Rise of Kidney Transplantation in the United States

Shivani S. Bisen, BA,[1] Laura B. Zeiser, ScM,[1] Brian Boyarsky, MD, PhD,[2] William Werbel, MD,[3] Jon Snyder, PhD,[4] Jacqueline Garonzik-Wang, MD, PhD,[5] Macey L. Levan, JD, PhD,[1] Dorry L. Segev, MD, PhD,[1,4] and Allan B. Massie, PhD, MHS[1]

Background. Following the outbreak of coronavirus disease 2019 (COVID-19) in the United States, the number of kidney waitlist additions and living-donor and deceased-donor kidney transplants (LDKT/DDKT) decreased substantially but began recovering within a few months. Since then, there have been several additional waves of infection, most notably, the Delta and Omicron surges beginning in August and December 2021, respectively. **Methods.** Using SRTR data, we compared observed waitlist registrations, waitlist mortality, waitlist removal due to deteriorating condition, LDKT, and DDKT over 5 distinct pandemic periods to expected events based on calculations from preepidemic data while accounting for seasonality and secular trends. **Results.** Although the number of daily waitlist additions has been increasing since May 2020, the size of the active waitlist has consistently declined, reaching a minimum of 52 556 on February 27, 2022. The recent Omicron surge knocked LDKT from 25% below baseline (incidence rate ratio [IRR] = $_{0.69}0.75_{0.81}$) during the Delta wave to 38% below baseline (IRR = $_{0.58}0.62_{0.67}$). DDKT, however, was less affected by the Omicron wave (IRR = $_{0.85}0.89_{0.93}$ and $_{0.88}0.92_{0.96}$ during the Delta and Omicron waves, respectively). Waitlist death decreased from 56% above baseline (IRR = $_{1.43}1.56_{1.70}$) during Delta to 41% above baseline during Omicron, whereas waitlist removal due to deteriorating condition remained at baseline/expected levels during the Delta wave (IRR = $_{0.93}1.02_{1.12}$) and the Omicron wave (IRR = $_{0.99}1.07_{1.16}$). **Conclusions.** Despite exceptionally high COVID-19 incidence during the Omicron wave, the transplant system responded similarly to prior waves that imposed a lesser disease burden, demonstrating the transplant system's growing adaptations and resilience to this now endemic disease.

(*Transplantation Direct* 2023;9: e1423; doi: 10.1097/TXD.0000000000001423).

INTRODUCTION

The onset of the coronavirus disease 2019 (COVID-19) pandemic in March 2020 had profound effects on the American transplant system. At first, the United States responded with strict social distancing measures, and many healthcare systems suspended organ transplantation.[1] A survey conducted during the first wave of infection reported that 84.0% of American transplant centers placed restrictions on deceased donor kidney transplantation (DDKT) and that 71.8% completely suspended

Received 5 October 2022.

Accepted 26 October 2022.

[1] Department of Surgery, Quantitative Core, Center for Surgical and Transplant Applied Research (C-STAR), Grossman School of Medicine, New York University, New York, NY.

[2] Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD.

[3] Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD.

[4] Scientific Registry of Transplant Recipients, Minneapolis, MN.

[5] University of Wisconsin School of Medicine and Public Health, Madison, WI.

The authors declare no conflicts of interest.

This work was supported by grant number K24AI144954 from the National Institute of Allergy and Infectious Diseases (NIAID) and K01DK101677 from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The analyses described here are the responsibility of the authors alone and do not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products or organizations imply endorsement by the US Government.

All authors participated in research design/planning. S.S.B., L.B.Z., and A.B.M. participated in data collection/entry. L.B.Z. and A.B.M. participated in data management. S.S.B., L.B.Z., and A.B.M. participated in data analysis. S.S.B., L.B.Z., and A.B.M. participated in data interpretation. All authors participated in preparation of the article. M.L.L., D.L.S., and A.B.M. supervised the research.

Correspondence: Allan Massie, PhD, Department of Surgery, Quantitative Core, Center for Surgical and Transplant Applied Research (C-STAR), New York University Grossman School of Medicine, 1 Park Avenue, New York, NY 10016. (allan.massie@nyulangone.org).

ISSN: 2373-8731

DOI: 10.1097/TXD.0000000000001423

living donor kidney transplantation (LDKT), with more stringent restrictions being placed in regions with higher COVID-19 incidence.[2] Accordingly, an earlier study from our group reported that, during the first wave of the COVID-19 epidemic in March/April 2020, the number of new listings, DDKT, and LDKT dropped 18%, 24%, and 87%, respectively, below expected values.[1] Likewise, pediatric DDKT and LDKT declined by 47% and 82%, respectively, whereas waitlist inactivation and removals due to death or deteriorating condition increased by 152% and 189%, respectively, compared with expected levels, but these effects were not sustained past the early parts of the pandemic.[3] Following these early increases in waitlist death and declines in transplant volume and waitlist additions,[1,4,5] the United States experienced an early, but incomplete, recovery in transplant rates beginning in early May 2020, even as COVID-19 incidence increased in the United States.[4,6]

Since these reports were published, the United States has been hit with its largest wave of infection yet, caused by the rapidly transmissible Omicron variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[7] The Omicron variant started becoming an appreciable proportion of COVID-19 cases mid-December 2021 and became 97.8% of circulating variants by mid-January 2022.[8] By January 12, 2022, the Omicron surge peaked at 802 699 confirmed new cases, compared with a pre-Omicron peak of 251 772 confirmed new cases on January 8, 2021.[6] Considering the immense disease burden, this ongoing fourth wave may have been sufficient to disrupt transplant centers' strategies for resuming and continuing procedures in the context of COVID-19. Furthermore, as of February 3, 2022, only 64% of the US population and 74.2% of the US adult population were fully vaccinated.[9] With this unprecedented wave of infection and ongoing rollback on nonpharmaceutical interventions (mask enforcement, restaurant capacity restrictions, etc), it is clear that COVID-19 is an ongoing problem and will continue to be so for years. It is crucial to understand the dynamics of prior waves so that transplant centers and public health officials can communicate regarding the next steps for bringing kidney transplantation back to prepandemic rates, and we can protect our patients if, and when, COVID-19 remerges in the United States.[10]

In order to develop an updated understanding regarding the impact of the COVID-19 pandemic on kidney transplantation, a retrospective database analysis was conducted with data from the Scientific Registry of Transplant Recipients (SRTR) to quantify such changes. We examined the daily changes in kidney transplant (KT) waitlist registration, waitlist death, waitlist removal due to deteriorating health condition, DDKT, and LDKT during each of 5 pandemic periods and compared them to expected levels based on calculations from preepidemic data.

MATERIALS AND METHODS

Data Source

This study used data from the SRTR. The SRTR data system includes data on all donors, waitlisted candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network (OPTN), and has been described elsewhere.[11] The Health Resources and Services Administration, US Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors.

Study Population

The study population consisted of kidney-only candidates registered on the US kidney waitlist between January 1, 2016, and February 28, 2022.

US COVID-19 Cases

To illustrate the 4 major waves of COVID-19 infection in the United States, we plotted a running-mean smooth of the daily number of COVID-19 cases in the United States for each day between January 21, 2020, and March 1, 2022, using publicly available data from The New York Times GitHub.[12]

Daily Counts of Waitlist Events

For each day between November 1, 2019, and February 28, 2022, we plotted the daily number of active and inactive waitlisted KT candidates. We also plotted daily counts of new waitlist registrations, waitlist deaths, waitlist removals due to deteriorating health, DDKTs, and LDKTs over the same time period, overlaid with a running-mean mean smooth. Because >99% of waitlist registrations, LDKTs, and waitlist removals due to deteriorating health occurred on weekdays, weekends were excluded for these events.

Infection Eras

To study the effects of the COVID-19 pandemic on US kidney waitlist events, 4 distinct waves or time periods of high COVID-19 incidence were identified. These waves were defined as March 15 to May 31, 2020 (Initial wave); December 1, 2020, to January 31, 2021 (Winter 2020–2021 wave); August 1 to September 30, 2021 (Delta wave); and December 1, 2021, to February 28, 2022 (Omicron wave). A fifth time period included within-pandemic nonwave periods (Nonwave period) June 1, 2020, to November 30, 2020; February 1, 2021, to July 31, 2021; and October 1, 2021, to November 30, 2021. Finally, a sixth period, serving as a prepandemic baseline period, included January 1, 2016, to March 14, 2020.

Changes in Waitlist Events Over the Pandemic Waves

Poisson regression was used to calculate relative changes in the average number of daily waitlist registrations, DDKTs, and LDKTs, comparing each pandemic period to the baseline period. Because the number of waitlist deaths and removals due to deteriorating health are influenced by the number of candidates on the waitlist at a given time, we used Poisson regression to estimate changes in the rate of death/dropout over each pandemic period relative to baseline by modeling the event count per day and including the log of the waitlist size each day as an offset.

The total number of excess waitlist deaths was estimated for each pandemic wave or period by comparing observed to expected deaths for that time period. Using data on observed deaths during the baseline period, we used Poisson regression to model the expected number of deaths for each day during the pandemic. The differences between the observed and expected number of deaths were calculated to identify the number of excess deaths each day, and Poisson regression was used to estimate the average number of excess deaths per day in each pandemic period.

To account for possible seasonal patterns in waitlist events not attributable to the pandemic, as well as consistent long-term trends, all models were adjusted for seasonality (using indicator variables for seasons defined as March 15–May 31, August 1–September 30, and December 1–February 28) and secular trends.

Statistical Analysis

Confidence intervals and *P* values are 2-sided with an alpha of 0.05. Confidence intervals are reported according to the methods of Louis and Zeger.[13] All analyses were performed using Stata 17.0/MP for Linux (College Station, TX).

RESULTS

US COVID-19 Cases

The first case of COVID-19 in the United States was reported on January 21, 2020, and the daily number of cases exceeded 100 beginning March 7, 2020 (Figure 1). There was an average of 23 015 cases per day in the Initial wave, 203 369 during the Winter 2020–2021 wave, 137 672 during the Delta wave, and 337 276 during the Omicron wave.

Daily Counts of Waitlist Events

Between November 1, 2019, and March 14, 2020, there was an average of 65 397 individuals active on the KT waitlist, and this number dropped to an average of 62 277 active members during the Initial wave (Figure 2). A rapid decline in active waitlist members was observed on April 23, 2020, when one transplant center changed its entire waitlist to inactive, but this decline was followed by a large increase in the active KT waitlist on April 30 when the same center reactivated its waitlist. Following the Initial wave, the number of active candidates has decreased steadily (Figure 2). The average daily waitlist count was 59 406 during the Winter 2020–2021 wave, 56 899 during the Delta wave, 55 375 during the Omicron wave, and 59 167 during the Nonwave period.

During the baseline period, new waitlist registrations averaged 149 per day, but during the Initial wave of infection, waitlist registrations decreased to an average of 119 per day. Waitlist registrations then increased to 141 during the Winter 2020–2021 wave and 156 during the Delta and Omicron waves (Figure 3). During the Nonwave period, new waitlist registrations averaged 153 per day.

The counts of DDKT were fairly consistent between COVID waves, with the average number of DDKT ranging from 40 transplants per day during the Initial wave to 48 and 49 per day during the Delta and Omicron waves, respectively (Figure 4A). However, DDKT was lower in all waves than the Nonwave period, when DDKT averaged 52 transplants per day.

LDKT reached a low of 8 transplants per day during the Initial wave but then increased during the Winter 2020–2021 (19 transplants per day on average) and Delta waves (21 transplants per day on average). The average number of daily transplants decreased to 19 per day during the Omicron wave (Figure 4B). Within the pandemic, LDKT was highest during the Nonwave period at an average of 23 transplants per day.

Average daily waitlist deaths increased over the first 2 pandemic waves (16 deaths per day and 21 deaths per day during the Initial and Winter 2020–2021 waves, respectively) and then decreased to an average of 14 per day during the Delta wave (Figure 5A). An average of 15 waitlist deaths occurred each day during the Omicron wave. During the Nonwave period, an average of 13 waitlist candidates died on the waitlist each day.

Waitlist removals for deteriorating health condition averaged 13 per day during the Initial and Winter 2020–2021

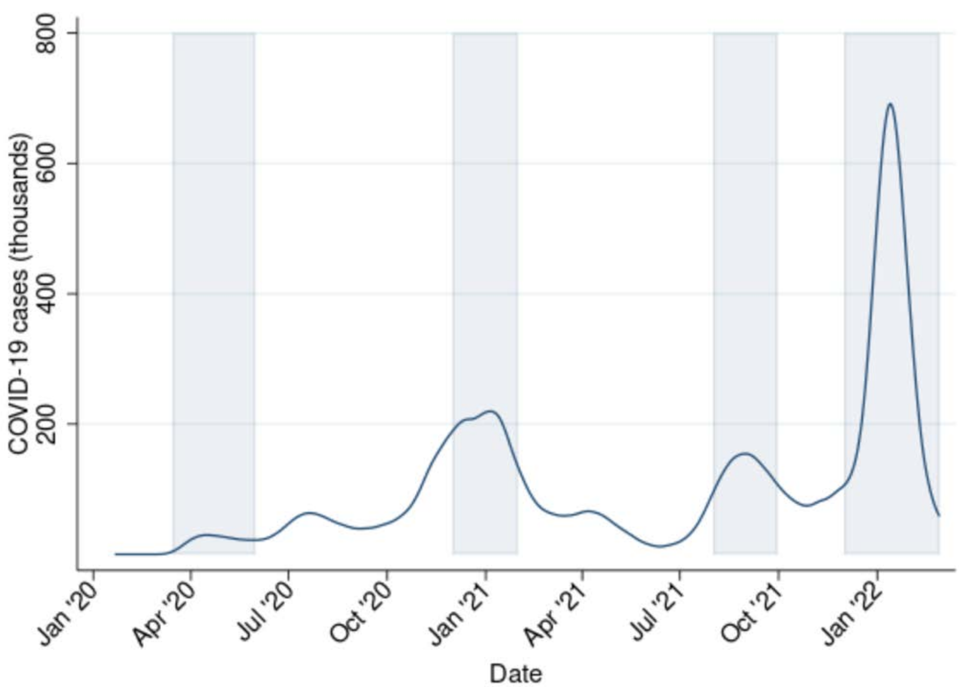

FIGURE 1. Reported COVID-19 cases in the United States, January 21, 2022, to March 8, 2022. Running-mean smooth applied. Shaded areas depict the 4 COVID-19 waves. COVID-19, coronavirus disease 2019.

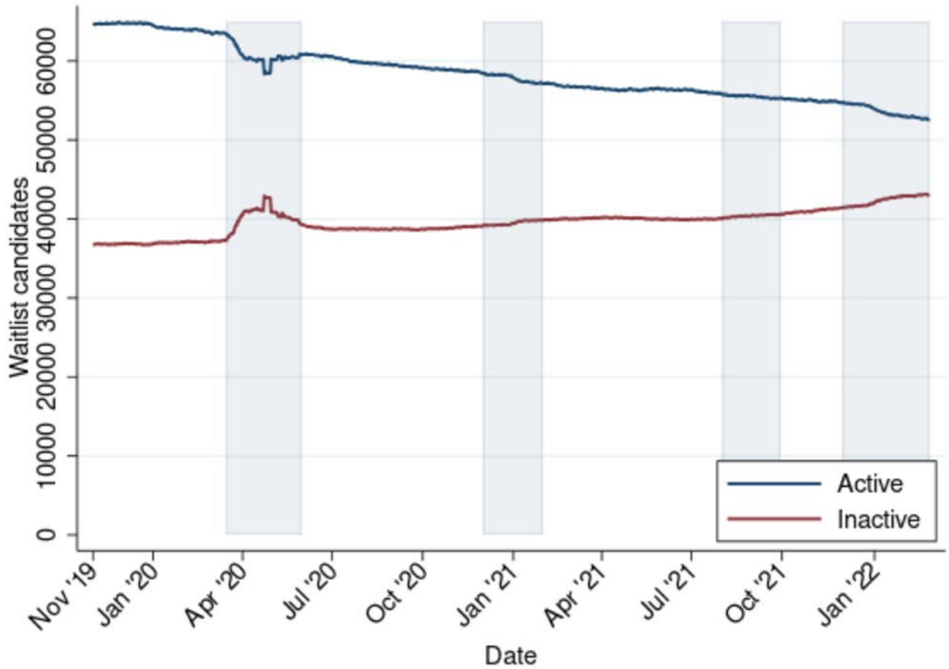

FIGURE 2. Kidney transplant waitlist and active status, November 2019 to February 2022. Counts of those listed as active and inactive on the transplant waitlist per day. Shaded areas depict the 4 COVID-19 waves. COVID-19, coronavirus disease 2019.

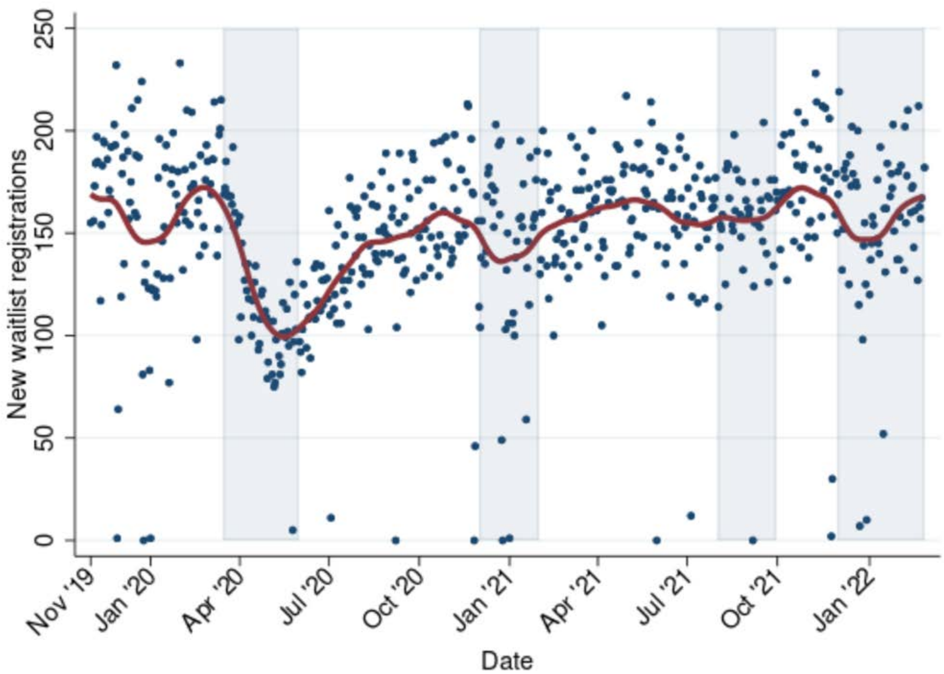

FIGURE 3. Kidney waitlist registrations, November 2019 to February 2022. Counts of new waitlist registrations per weekday, with running-mean smooth applied. Shaded areas depict the 4 COVID-19 waves. COVID-19, coronavirus disease 2019.

waves and 16 per day during the Delta and Omicron waves, respectively (Figure 5B). An average of 15 candidates were removed because of deteriorating health during the Nonwave period.

Changes in Waitlist Events Over the Pandemic Waves

Waitlist registration has consistently remained below expected levels throughout the pandemic at 32%, 18%, 16%, 14%, and 15% lower than baseline during the Initial, Winter 2020–2021, Delta, Omicron, and Nonwave periods of infection (Table 1). DDKT did the same at 18%, 8%, 11%, and 8% below baseline during the Initial, Winter 2020–2021, Delta, and Omicron waves but was 3% higher than expected during the Nonwave period. LDKT substantially declined to 71% below baseline during the Initial wave of high COVID-19 incidence (incidence rate ratio [IRR] = ${}_{0.27}0.29_{0.32}$) and was found to be 31% below baseline

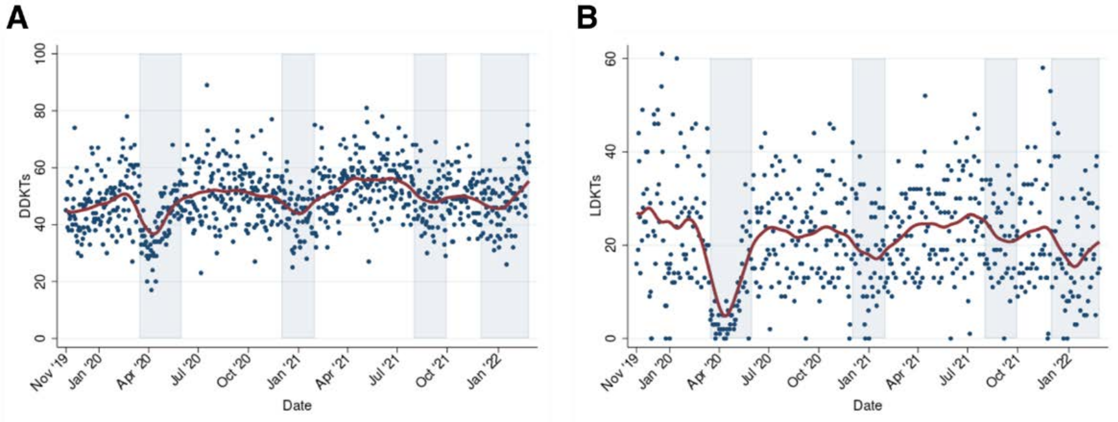

FIGURE 4. Kidney transplant occurrences. Counts of (A) DDKTs per day and (B) LDKTs per weekday, respectively, with running-mean smooth applied, November 2019 to February 2022. Shaded areas depict the 4 COVID-19 waves. COVID-19, coronavirus disease 2019; DDKT, deceased donor kidney transplant; LDKT, living donor kidney transplant.

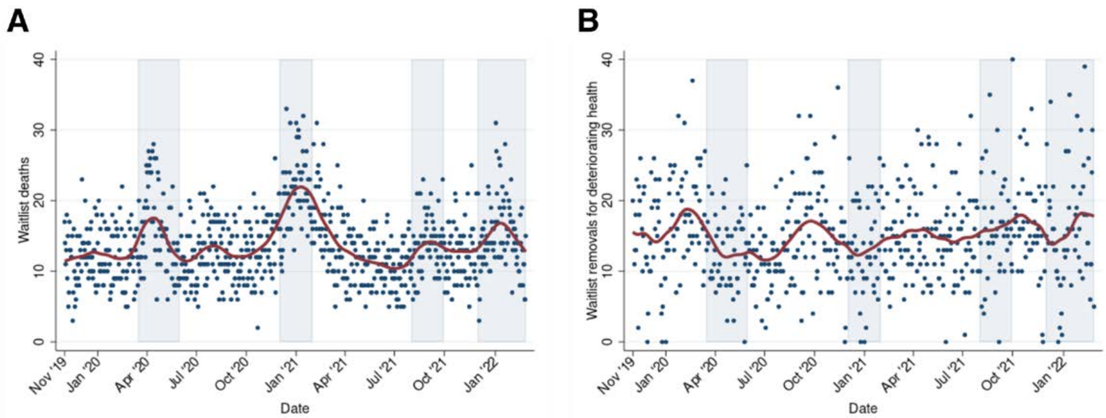

FIGURE 5. Kidney waitlist outcomes. Counts of (A) deaths while on the kidney waitlist per day and (B) removals from the kidney waitlist due to deteriorating health condition per weekday, respectively, with running-mean smooth applied, November 2019 to February 2022. Shaded areas depict the 4 COVID-19 waves. COVID-19, coronavirus disease 2019.

during the Winter 2020–2021 wave (IRR = $_{0.64}0.69_{0.75}$), 25% below baseline during the Delta surge (IRR = $_{0.69}0.75_{0.81}$), and 20% below baseline during the Nonwave period (IRR = $_{0.76}0.80_{0.83}$); these are all potential improvements from the Initial wave. The recent Omicron surge, however, sent LDKT back down to 38% below baseline (IRR = $_{0.58}0.62_{0.67}$). Waitlist death was consistently above expected levels during all 4 waves of high COVID-19 incidence and the Nonwave period at 51%, 86%, 56%, and 41% above baseline during the Initial, Winter 2020–2021, Delta, and Omicron waves and 34% above baseline during the Nonwave period. Waitlist removal due to deteriorating condition was lower than baseline during the Initial (IRR = $_{0.71}0.77_{0.84}$) and Winter 2020–2021 (IRR = $_{0.75}0.83_{0.91}$) waves but returned to expected levels during the Delta surge (IRR = $_{0.93}1.02_{1.12}$), Omicron wave (IRR = $_{0.99}1.07_{1.16}$), and the Nonwave period (IRR = $_{0.93}0.97_{1.02}$).

TABLE 1.

Changes in the rates of waitlist registration and waitlist outcomes during 4 waves of the COVID-19 epidemic in the United States

COVID-19 wave	Waitlist registration	DDKT	LDKT	Waitlist death	Deteriorating condition
Initial	$_{0.66}$**0.68**$_{0.70}$	$_{0.79}$**0.82**$_{0.86}$	$_{0.27}$**0.29**$_{0.32}$	$_{1.40}$**1.51**$_{1.61}$	$_{0.71}$**0.77**$_{0.84}$
Winter 2020–2021	$_{0.80}$**0.82**$_{0.85}$	$_{0.88}$**0.92**$_{0.96}$	$_{0.64}$**0.69**$_{0.75}$	$_{1.74}$**1.86**$_{1.99}$	$_{0.75}$**0.83**$_{0.91}$
Delta	$_{0.81}$**0.84**$_{0.86}$	$_{0.85}$**0.89**$_{0.93}$	$_{0.69}$**0.75**$_{0.81}$	$_{1.43}$**1.56**$_{1.70}$	$_{0.93}1.02_{1.12}$
Omicron	$_{0.84}$**0.86**$_{0.88}$	$_{0.88}$**0.92**$_{0.96}$	$_{0.58}$**0.62**$_{0.67}$	$_{1.31}$**1.41**$_{1.52}$	$_{0.99}1.07_{1.16}$
Nonwave	$_{0.84}$**0.85**$_{0.87}$	$_{1.002}$**1.03**$_{1.05}$	$_{0.76}$**0.80**$_{0.83}$	$_{1.28}$**1.34**$_{1.40}$	$_{0.93}0.97_{1.02}$

Bold denotes statistical significance.
COVID-19, coronavirus disease 2019; DDKT, deceased donor kidney transplantation; LDKT, living donor kidney transplantation.

Excess Deaths Over the Pandemic Waves

A total of 8940 waitlist deaths were observed from March 15, 2020, to February 28, 2022, among which 1033 (11.6%) were attributed to COVID-19 in the SRTR. There was an average of 7, 10, 7, 5, 5, and excess deaths per day over the Initial, Winter 2020–2021, Delta, Omicron, and Nonwave periods of the pandemic, totaling 405, 613, 303, 409, and 1345 excess deaths in the Initial, Winter 2020–2021, Delta, Omicron, and Nonwave periods, respectively.

DISCUSSION

In this national registry study of the outcomes of kidney waitlist registrants during the COVID-19 pandemic, we found that the initial COVID-19 wave of March to May 2020 delivered a substantial impact on outcomes: a 71%

decline in LDKT, an 18% decline in DDKT, a 32% decline in waitlist registration, and a 51% increase in waitlist mortality. The subsequent Winter 2020–2021 and Delta waves had only modest effects on waitlist registration (a 18% and 16% decline, respectively) and DDKT (an 8% and 11% decline, respectively) but a larger effect on LDKT (a 31% and 25% decline, respectively). With a 86% increase in Winter 2020–2021, waitlist mortality was less impacted by the Initial and Delta waves (51% and 56%, respectively). Following the most recent Omicron wave, which resulted in over thirty million recorded cases in the United States, there was only a 14% decrease in waitlist registrations, an 8% decline in DDKT, and a 28% decline in LDKT. There was an estimated 41% increase in waitlist mortality during the Omicron wave; although concerning, this is substantially lower than the 86% increase above baseline observed during the Winter 2020–2021 wave, even though there were far more recorded cases nationwide during the Omicron wave. The Nonwave period was comparable to the pre-COVID baseline in terms of waitlist removal due to deteriorating condition, but the former showed a decreased volume of waitlist registration and LDKT and an increased volume of DDKT and waitlist death compared with the prepandemic baseline. Although we report substantial excess mortality during COVID-19 waves, we observed fewer excess deaths per day during the Omicron wave than during the prior Delta wave, even though burden of COVID-19 infection in the United States was substantially higher during Omicron. Throughout the course of the epidemic, there has been a steady decline in the active KT waitlist, from 64 757 at the start of November 2019 to 52 614 by the end of February 2022. Taken as a whole, our findings demonstrate that the national transplant system in the United States has been able to adapt to COVID-19 becoming an endemic disease in the United States, with relatively minor disruptions in care even in the context of extremely high COVID-19 incidence.

Our findings describing the first wave are generally consistent with our prior work, although the numbers are slightly different in some cases because of different methods being used, different time windows used to define the Initial wave, and potential delays in mortality ascertainment.[1] The OPTN also reported considerable reductions in the number of KTs and waitlist additions during the Initial wave of the pandemic, coupled with an increase in waitlist deaths.[5] This experience was not unique to KT, though; numerous reports have been made on the declines observed in the United States in heart, lung, and liver transplantation as well.[14,15] Similar declines were observed globally with an estimated 16% reduction in transplant events in 2020, with kidney transplantation showing the greatest decline (19%) and heart transplantation showing the least (5%).[14]

The decision to reduce and resume transplant activity was made by individual transplant centers and health systems,[16] but speculations can be made regarding our observed trends. Because of limitations in the cause-of-death data, the true etiology of the consistently high waitlist mortality cannot be described; increased risk of death from COVID-19 among dialysis patients may be a contributing factor.[17] During the first few months of the pandemic, 10.2% of the United Kingdom's waitlisted patients who acquired a COVID-19 infection died,[18] and the virus also accounted for 42% of deaths in French candidates.[19] Declines in donor referrals were observed internationally,[20–22] but organ procurement organizations in the United States actually reported a 12.4% increase in referrals during the initial pandemic period.[23] Donors often spend an additional 36 to 48 hours in intensive care before donation; with beds, ventilators, and staff being shunted toward COVID-19 patients, it is possible that the donor and their evaluation process could not be accommodated.[15,20] Furthermore, discussions for consent for organ donation were often held virtually because of visiting restrictions during the pandemic. However, telephone approaches have been found to be less effective than in-person approaches.[20,24] Lastly, the weekly discard rate for consented kidneys varied throughout the pandemic in accordance with the different waves of COVID-19 and geographic burden of COVID-19 at that point in the pandemic, helping to account for even more lost transplant opportunities.[25]

Potential explanations for the consistently low LDKT levels are center-specific practices of cancellation of elective surgeries dependent on local disease burden and individual instances of delayed procedures when patients tested positive before the surgery. During the Initial, Winter 2020–2021, and Omicron waves, LDKT recipient volume was more significantly impacted/lower from baseline than DDKT. Our dataset does not contain information on center-level decision-making, but we suspect that this may be because it is relatively easy for centers to delay LDKT in the context of elevated risk or in response to temporary disruptions to healthcare delivery. In contrast, a center that declines a DDKT offer on behalf of a patient has no guarantee that another offer will arrive in the near future. In fact, in March 2020, one team proposed a phased approach to decreasing transplant activity depending on risk tolerance, hospital capacity, and local disease burden; a 25% reduction in transplant activity would entail no LDKT, with DDKT still allowed, whereas a 100% reduction in transplant activity was suggested if the health system was completely overwhelmed by COVID-19.[26] Their proposal aligns with our observed increased decline in LDKT versus DDKT. Additionally, perhaps DDKT was less affected than LDKT throughout the pandemic because a declined deceased donor kidney can still be offered to another individual on the waiting list, whereas the LDKT must be delayed entirely. A survey conducted in spring 2021 found that 70% of centers declined organs and delayed transplantation until the patient tested negative, whereas 27% delayed the surgery for 30 days without retesting.[27] Despite publicized reports of unvaccinated patients being moved to a lower position on the waitlist, or even being removed, emerging in 2021,[28–31] the aforementioned survey reported that <7% of programs inactivated patients who were unvaccinated or partially vaccinated.[27] It appears that, instead of shutting down completely in the face of the pandemic, as time has gone on, transplant centers have developed a protocol to reject organs when absolutely necessary because of COVID-19 concerns but deliver this life-changing surgery as soon as it is deemed safe by the center, even though the safety of these practices has not been established in the literature.[27]

Several factors may account for the increased resilience of the transplant system since the Initial wave, including increased COVID-19 testing capacity,[3,32] prioritized COVID-19 testing for donors and recipients,[33] normalization of COVID-19 prevention protocols in hospitals and the community,[34–36] improvements in the treatment of COVID-19,[37–39] and the advent of effective vaccines.[40–42] A study on liver transplantation throughout the pandemic noted that deferring living donor transplantation was commonplace and considered ethical to protect healthy donors' health and that COVID minimal-exposure pathways have been created to resume living donor transplantation as local disease burden has declined.[15] We suspect similar practices were used for resuming KT amid the pandemic. Additionally, each new wave of COVID-19 increases the proportion of the population that has previously had the disease, thus reducing disease severity and transmissibility.

The risk of performing KT during a pandemic must also be balanced with the risk and outcomes of COVID-19 in transplant recipients and those with end-stage renal disease and those waiting for a KT.[32] In this study, we report substantial excess mortality among KT waitlist registrants. However, substantial excess mortality presumably attributable to COVID-19 has also been reported among KT recipients in the United States.[43] Transplant recipients infected with COVID-19 bear substantially higher morbidity and mortality risk than the general population.[44–54] However, a French study reported that excess mortality due to COVID-19 was 73% higher among KT waitlist candidates than among KT recipients.[19] KT recipients also have dramatically lower antibody response to COVID-19 vaccines than the general population.[55–62] Nevertheless, delaying transplant and spending more time on dialysis have been associated with increased graft failure following KT.[63] Hence, the advent of COVID-19 need not represent a reason to delay KT, but transplant recipients should be counseled about their increased susceptibility to the virus; postvaccination measurement of antibody titers may be appropriate to further inform patients about their risk.

Our study must be understood in the context of its limitations. The data analyzed by our study came from a national transplant registry that derives its data from individual centers. Each center may have different standards for data collection, reporting, and quality control. Furthermore, because we analyzed national registry data, we are unable to determine why individual centers experienced the observed changes in KT, why individual patients were inactivated from the waitlist, or what the particular circumstances were surrounding an individual patient's death. The only causes of waitlist removal we modeled were DDKT, LDKT, mortality, and deteriorating condition; it is possible that a few removals for "other" reasons may be COVID-related. Regardless of these limitations, using national registry data allowed for us to make reasonably sound, broadly generalizable assessments to address our research question. An additional limitation is a potential delay in the reporting of waitlist mortality; there may have been deaths from the Omicron wave that were not reported in the most recent data available to us. However, we corrected for estimated delays in reporting based on observed delays in prior years.

In conclusion, despite profound effects on the transplant system during the Initial wave of COVID-19, we report relatively minor disruptions to care or increases in waitlist mortality risk during subsequent waves, with the exception of substantially increased waitlist mortality during the winter of 2020–2021. Our findings give hope that the transplant system will be able to withstand future waves of COVID-19 as well. Given that it is unlikely that the United States will experience another period of high COVID-19 incidence quite like Omicron, the findings of this study should serve as a message of success for the nephrology and transplant communities in helping a vulnerable patient population survive an unprecedented national epidemic.

ACKNOWLEDGMENTS

This research was made possible with generous support of the Ben-Dov family. The data reported here have been supplied by the Minneapolis Medical Research Foundation (MMRF) as the contractor for the SRTR. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the SRTR or the US Government.

REFERENCES

1. Boyarsky BJ, Werbel WA, Durand CM, et al. Early national and center-level changes to kidney transplantation in the United States during the COVID-19 epidemic. *Am J Transplant.* 2020;20:3131–3139.
2. Boyarsky BJ, Chiang TP-Y, Werbel WA, et al. Early impact of COVID-19 on transplant center practices and policies in the United States. *Am J Transplant.* 2020;20:1809–1818.
3. Charnaya O, Chiang TP-Y, Wang R, et al. Effects of COVID-19 pandemic on pediatric kidney transplant in the United States. *Pediatr Nephrol.* 2021;36:143–151.
4. Goff RR, Wilk AR, Toll AE, et al. Navigating the COVID-19 pandemic: Initial impacts and responses of the Organ Procurement and Transplantation Network in the United States. *Am J Transplant.* 2021;21:2100–2112.
5. Cholankeril G, Podboy A, Alshuwaykh OS, et al. Early impact of COVID-19 on solid organ transplantation in the United States. *Transplantation.* 2020;104:2221–2224.
6. Johns Hopkins University and Medicine. *COVID-19* map. *Johns Hopkins Coronavirus Resource Center*. Available at https://coronavirus.jhu.edu/map.html. Accessed December 28, 2020.
7. Koley T, Kumar M, Goswami A, et al. Structural modeling of Omicron spike protein and its complex with human ACE-2 receptor: Molecular basis for high transmissibility of the virus. *Biochem Biophys Res Commun.* 2022;592:51–53.
8. Centers for Disease Control and Prevention. *COVID data tracker - variant proportions. 2022*. [cited February 4, 2022] Available at https://covid.cdc.gov/covid-data-tracker/#variant-proportions. Accessed on February 4, 2022.
9. Centers for Disease Control and Prevention. *COVID data tracker. 2022*. [cited January 15, 2022] Available at https://covid.cdc.gov/covid-data-tracker. Accessed January 15, 2022.
10. McElroy LM, Sanoff SL, Collins BH. Kidney transplant in the COVID era: Cautious optimism and continued vigilance. *Am J Transplsant*. 2020;20:2971–2972.
11. Massie AB, Kucirka LM, Kuricka LM, et al. Big data in organ transplantation: registries and administrative claims. *Am J Transplant.* 2014;14:1723–1730.
12. The New York Times. Coronavirus (Covid-19) data in the United States. 2022. [cited March 18, 2022] Available at https://github.com/nytimes/covid-19-data. Accessed March 18, 2022.
13. Louis TA, Zeger SL. Effective communication of standard errors and confidence intervals. *Biostatistics.* 2009;10:1–2.
14. Aubert O, Yoo D, Zielinski D, et al. COVID-19 pandemic and worldwide organ transplantation: a population-based study. *Lancet Public Health.* 2021;6:e709–e719.
15. Merola J, Schilsky ML, Mulligan DC. The impact of COVID-19 on organ donation, procurement, and liver transplantation in the United States. *Hepatol Commun.* 2021;5:5–11.
16. Sussman JS. COVID-19: effect on organ donation and transplantation. Congressional Research Service. 2020. Available at https://crsreports.congress.gov/product/pdf/IN/IN11345. Accessed July 17, 2022.
17. Hsu CM, Weiner DE, Aweh G, et al. COVID-19 among US dialysis patients: risk factors and outcomes from a national dialysis provider. *Am J Transplant.* 2021;77:748–756.
18. Ravanan R, Callaghan CJ, Mumford L, et al. SARS-CoV-2 infection and early mortality of waitlisted and solid organ transplant recipients in England: a national cohort study. *Am J Transplant.* 2020;20:3008–3018.
19. Thaunat O, Legeai C, Anglicheau D, et al; French nationwide Registry of Solid Organ Transplant Recipients with COVID-19. 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;98:1568–1577.
20. Nimmo A, Gardiner D, Ushiro-Lumb I, et al. The global impact of COVID-19 on solid organ transplantation: two years into a pandemic. *Transplantation.* 2022;106:1312–1329.
21. Manara AR, Mumford L, Callaghan CJ, et al. Donation and transplantation activity in the UK during the COVID-19 lockdown. *Lancet.* 2020;396:465–466.
22. Legeai C, Savoye E, Cantrelle C, et al. Impact of COVID-19 on 2020 transplant activity and waiting lists in France. *J Liver Transplant*. 2022;5:100051.
23. Ahmed O, Brockmeier D, Lee K, et al. Organ donation during the COVID-19 pandemic. *Am J Transplant.* 2020;20:3081–3088.
24. Singh JM, Ball IM, Hartwick M, et al. Factors associated with consent for organ donation: a retrospective population-based study. *CMAJ* 2021;193:E1725.
25. Li MT, King KL, Husain SA, et al. Deceased donor kidneys utilization and discard rates during COVID-19 pandemic in the United States. *Kidney Int Rep.* 2021;6:2463–2467.
26. Kumar D, Manuel O, Natori Y, et al. COVID-19: a global transplant perspective on successfully navigating a pandemic. *Am J Transplant.* 2020;20:1773–1779.
27. Axelrod DA, Ince D, Harhay MN, et al. Operational challenges in the COVID-19 era: asymptomatic infections and vaccination timing. *Clin Transplant.* 2021;35:e14437.
28. Jabour T. Organ transplant patient says she was denied procedure because of vaccine mandate. WCIV. 2021. Available at https://abcnews4.com/news/local/organ-transplant-patient-gets-denied-procedure-because-of-vaccine-mandate. Accessed April 13, 2022.
29. Barnsley W. Unvaccinated Queenslanders face being denied lifesaving operations. 7NEWS. 2021. Available at https://7news.com.au/lifestyle/health-wellbeing/queensland-health-confirms-organ-transplant-recipients-need-to-be-vaccinated-for-covid-c-4830704. Accessed April 13, 2022.
30. Schreiber M. Some US patients waiting for organ transplants must get Covid vaccine or be removed from list. Guardian. 2021. Available at https://www.theguardian.com/society/2021/oct/08/patients-waiting-organ-transplants-vaccinated-covid. Accessed April 13, 2022.
31. News JA, Kaiser Health. More organ transplant centers require patients to get Covid-19 vaccine, or get bumped down waitlist. CNN. 2021. Available at https://www.cnn.com/2021/10/08/health/organ-transplant-vaccine-khn-partner/index.html. Accessed July 12, 2022.
32. Azzi Y, Bartash R, Scalea J, et al. COVID-19 and solid organ transplantation: a review article. *Transplantation.* 2021;105:37–55.
33. Lieberman JA, Mays JA, Wells C, et al. Expedited SARS-CoV-2 screening of donors and recipients supports continued solid organ transplantation. *Am J Transplant.* 2020;20:3106–3112.
34. Ahlers MJ, Aralis HJ, Tang WL, et al. Non-pharmaceutical interventions and COVID-19 burden in the United States. *medRxiv*. 2021.
35. Rader B, White LF, Burns MR, et al. Mask-wearing and control of SARS-CoV-2 transmission in the USA: a cross-sectional study. *Lancet Digit Health*. 2021;3:e148–e157.
36. Islam H, Islam A, Brook A, et al. Evaluating the effectiveness of county-wide mask mandates at reducing SARS-CoV-2 infection in the United States. *J Osteopath Med.* 2022;122:211–215.
37. The RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med.* 2021;384:693–704.
38. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19 — final report. *N Engl J Med.* 2020;383:1813–1836.
39. Bebenek I, Bannister R, Dubinion J, et al. COVID-19 therapeutics and vaccines: a race to save lives. *Toxicol Sci.* 2022;185:119–127.
40. Korang SK, von Rohden E, Veroniki AA, et al. Vaccines to prevent COVID-19: a living systematic review with trial sequential analysis and network meta-analysis of randomized clinical trials. *PLoS One.* 2022;17:e0260733.
41. Fiolet T, Kherabi Y, MacDonald C-J, et al. Comparing COVID-19 vaccines for their characteristics, efficacy and effectiveness against SARS-CoV-2 and variants of concern: a narrative review. *Clin Microbiol Infect.* 2022;28:202–221.
42. Gupta S, Cantor J, Simon KI, et al. Vaccinations against COVID-19 may have averted up to 140,000 deaths in the United States. *Health Aff (Millwood).* 2021;40:1465–1472.
43. Massie AB, Werbel WA, Avery RK, et al. Quantifying excess deaths among solid organ transplant recipients in the COVID-19 era. *Am J Transplant.* 2022;22:2077–2082. doi:10.1111/ajt.17036
44. Marinaki S, Tsiakas S, Korogiannou M, et al. A systematic review of COVID-19 infection in kidney transplant recipients: a universal effort to preserve patients' lives and allografts. *J Clin Med.* 2020;9:2986.
45. Mahalingasivam V, Craik A, Tomlinson LA, et al. A systematic review of COVID-19 and kidney transplantation. *Kidney Int Rep*. 2020;6:24–45.
46. Crespo M, Pérez-Sáez MJ, Redondo-Pachón D, et al. COVID-19 in elderly kidney transplant recipients. *Am J Transplant.* 2020;20: 2883–2889.
47. Alberici F, Delbarba E, Manenti C, et al. A single center observational study of the clinical characteristics and short-term outcome of 20 kidney transplant patients admitted for SARS-CoV2 pneumonia. *Kidney Int.* 2020;97:1083–1088.
48. Banerjee D, Popoola J, Shah S, et al. COVID-19 infection in kidney transplant recipients. *Kidney Int.* 2020;97:1076–1082.
49. Pereira MR, Mohan S, Cohen DJ, et al. COVID-19 in solid organ transplant recipients: Initial report from the US epicenter. *Am J Transplant.* 2020;20:1800–1808.
50. Elias M, Pievani D, Randoux C, et al. COVID-19 infection in kidney transplant recipients: disease incidence and clinical outcomes. *J Am Soc Nephrol.* 2020;31:2413–2423.
51. Nair V, Jandovitz N, Hirsch JS, et al. COVID-19 in kidney transplant recipients. *Am J Transplant.* 2020;20:1819–1825.
52. Chavarot N, Gueguen J, Bonnet G, et al; Critical COVID-19 France Investigators. COVID-19 severity in kidney transplant recipients is similar to nontransplant patients with similar comorbidities. *Am J Transplant.* 2021;21:1285–1294.
53. Akalin E, Azzi Y, Bartash R, et al. Covid-19 and kidney transplantation. *N Engl J Med*. 2020;382:2475–2477.
54. Merhi B, Gohh R. Kidney transplantation and COVID-19. *Rhode Island Medical J.* 2020;103:34–37.
55. 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:e72–e73.
56. Yahav D, Rahamimov R, Mashraki T, et al. Immune response to third dose BNT162b2 COVID-19 vaccine among kidney transplant recipients—a prospective study. *Transpl Int.* 2022;35:10204.
57. Benotmane I, Gautier-Vargas G, Cognard N, et al. Weak anti-SARS-CoV-2 antibody response after the first injection of an mRNA COVID-19 vaccine in kidney transplant recipients. *Kidney Int.* 2021;99:1487–1489.
58. Reischig T, Kacer M, Vlas T, et al. Insufficient response to mRNA SARS-CoV-2 vaccine and high incidence of severe COVID-19 in kidney transplant recipients during pandemic. *Am J Transplant.* 2022;22:801–812.
59. 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;325:1784–1786.
60. Werbel WA, Boyarsky BJ, Ou MT, et al. Safety and immunogenicity of a third dose of SARS-CoV-2 vaccine in solid organ transplant recipients: a case series. *Ann Intern Med.* 2021;174:1330–1332.
61. 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;325:2204–2206.
62. 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.* 2021;21:2719–2726.
63. Prezelin-Reydit M, Combe C, Harambat J, et al. Prolonged dialysis duration is associated with graft failure and mortality after kidney transplantation: results from the French transplant database. *Nephrol Dial Transplant.* 2018;34:538–545.