Original Clinical Science—General

OPEN

Insights From Refusal Patterns for Deceased Donor Kidney Offers

Grace Guan, MS,[1] Sanjit Neelam, MS,[2] Joachim Studnia, MS,[2] Xingxing S. Cheng, MD, MS,[3] Marc L. Melcher, MD, PhD,[4] Michael A. Rees, MD, PhD,[5,6] Alvin E. Roth, PhD,[7] Paulo Somaini, PhD,[8] and Itai Ashlagi, PhD[1]

Background. The likelihood that a deceased donor kidney will be used evolves during the allocation process. Transplant centers can either decline an organ offer for a single patient or for multiple patients at the same time. We hypothesize that refusals for a single patient indicate issues with individual patients, whereas simultaneous refusals for multiple patients indicate issues with organ quality. **Methods.** We investigate offer refusal patterns between January 1, 2022, and December 31, 2023, using Organ Procurement and Transplantation Network data. We aggregate refusals at the same timestamp by a center and define a multiple patient refusal as >1 or >5 patients simultaneously refused. We report the refusal codes associated with single and multiple patient refusals and the nonutilization rate after receiving single and multiple patient refusals by cross-clamp. **Results.** Patient-related refusal reasons are more commonly single patient refusals, whereas organ-related refusal reasons are more commonly multiple patient refusals. Multiple patient refusals before cross-clamp are associated with nonutilization, but single patient refusals are positively correlated with utilization. The nonutilization rate was 28% for organs without pre-clamp refusals, 35% with a single center sending a multiple patient refusal, but only 12% with a single center sending a single patient refusal. **Conclusions.** The risk of nonutilization can be assessed early in the offering process based on the number of single and multiple patient refusals received by a specific time (e.g., cross-clamp). Understanding refusal patterns can guide the development of transparent protocols for accelerated placement.

(*Transplantation* 2025;00: 00–00).

INTRODUCTION

In 2023, 3765 U.S. patients died while waiting for a deceased donor kidney transplant. Meanwhile, 7888 kidneys recovered from deceased donors (27.3%) were not used.[1] However, many kidneys are accepted quickly by patients at the top of the waiting list, many others, including kidneys with a Kidney Donor Profile Index (KDPI) < 85%, are offered to—and turned down by—transplant programs

Received 24 January 2025. Revision received 3 March 2025.

Accepted 22 March 2025.

[1] Department of Management Science and Engineering, Stanford University, Stanford, CA.

[2] Institute for Computational and Mathematical Engineering, Stanford University, Stanford, CA.

[3] Department of Medicine, Division of Nephrology, Stanford University, Stanford, CA.

[4] Department of Surgery, Stanford University, Stanford, CA.

[5] Department of Urology, University of Toledo Medical Center, Toledo, OH.

[6] Alliance for Paired Donation, Perrysburg, OH.

[7] Department of Economics, Stanford University, Stanford, CA.

[8] Graduate School of Business, Stanford University, Stanford, CA.

G.G. is supported in part by the National Science Foundation Graduate Research Fellowship under grant 1656518 and the Stanford Data Science Scholars Program. P.S. acknowledges support from the Business, Government, and Society research fund. I.A. acknowledges the support from the National Science Foundation (Award 2312156). I.A. and P.S. acknowledge support from the Kidney Transplant Collaborative. G.G. and I.A. acknowledge Jamie Kang and Jiacheng Zou for their research assistance.

The authors declare no conflicts of interest.

G.G., X.S.C., M.L.M., M.A.R., A.E.R., P.S., and I.A. designed the study. G.G., S.N., and J.S. participated in data analysis. All authors participated in the writing of the article.

The data reported here have been supplied by the United Network for Organ Sharing as the contractor for the Organ Procurement and Transplantation Network. Code was in Python 3.10.12 with the following package versions: NumPy 1.26.1, Pandas 2.1.3.

Any opinion, findings, and conclusions or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of the National Science Foundation. 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 Organ Procurement and Transplantation Network or the U.S. Government.

Visual abstract is available online at doi.org/10.1097/TP.0000000000005434.

Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantjournal.com).

Correspondence: Grace Guan, MS, Department of Management Science and Engineering, Stanford University, 475 Via Ortega, Stanford, CA 94305. (gzguan@stanford.edu).

ISSN: 0041-1337/20/0000-00

DOI: 10.1097/TP.0000000000005434

on behalf of thousands of patients.[2-5] Serial offers and turndowns result in increasingly long cold ischemia times (CITs), as the kidney remains in storage while waiting. The quality of an organ degrades with long CIT,[3,6,7] resulting in a higher likelihood of nonuse. Consequently, to reduce nonuse, a possible strategy is to allocate organs at risk of serial turndowns and nonuse preferentially to transplant programs and patients who are more likely to accept. This approach is known as accelerated placement. When initiated by organ procurement organizations (OPOs) at their own discretion, outside the allocation system, such protocols are called out-of-sequence allocation. Out-of-sequence allocation is becoming more prevalent: >14% of donors had at least 1 organ placed out-of-sequence in 2023, highlighting the need for the Kidney Allocation System to create a principled and accessible accelerated placement program.[8]

Assessing an organ's quality and predicting whether it might be subject to serial turndowns and nonuse, before significant CIT has accrued, could help identify organs that would benefit from accelerated placement, but presents many challenges. In 2019–2020, the Kidney Accelerated Placement project attempted to create such a pathway for organs that were difficult to place.[9] However, it did not result in better kidney utilization. The investigators concluded that the at-risk organs were identified too late.[9] The Organ Procurement and Transplantation Network (OPTN), the governing body of solid organ transplantation in the United States, is currently poised to implement another accelerated placement program, again identifying at-risk organs based on the KDPI.[10] However, prior research has shown that the KDPI is insufficient to predict which organs will not be placed[11,12]: Of organs with KDPI between 21% and 85%, 22% are not used.[13] The OPTN's first Kidney Accelerated Placement project used a KDPI cutoff of 85% and was not successful.[9]

Dynamic information arriving during the organ placement process may predict nonutilization of organs. Prior studies have demonstrated that post-clamp information such as biopsy and pump values predict nonutilization,[12] but they may arrive too late in the offer process to direct accelerated placement. We hypothesize that additional information received during the offering process, but before the cross-clamp, also provides additional value beyond the KDPI in assessing the risk of nonutilization. Specifically, transplant centers may decline offers based on organ quality or recipient factors. Uncovering which refusals are based on organ quality early can help identify organs at high risk of nonuse and determine candidacy for accelerated placement.

We begin by interpreting the data generated by offers and refusals during the allocation process. A novel feature of our analysis is taking advantage of the timestamps of the refusals to bundle simultaneous refusals by a center as a single refusal event. We distinguish between a center refusing an organ for a single patient or simultaneously refusing it for multiple patients, based on the hypothesis that the former is likely because of a mismatch between that patient and that organ, and the latter is correlated with an issue with the organ. We aim to determine how informative early refusals are in identifying organs at high risk of nonutilization. These refusal patterns can help in making decisions about when and which organs should be considered for accelerated placement.[9]

MATERIALS AND METHODS

Data

We used 2 datasets from the OPTN. The Standard Transplant Analysis and Research dataset included de-identified information on transplant recipients and/or waitlist candidates, and deceased donors. The Potential Transplant Recipient dataset included de-identified match-run information for each donor. Our analysis focused on kidneys recovered between January 1, 2022, and December 31, 2023, as new and more refined refusal codes went into effect on December 2, 2021.[14]

We excluded from the analysis donors with >1 match run, a null value for the OPO (match or recovery) or hospital location, with different match and recovery OPOs, with 0 kidneys recovered, whose match run only included bypass offers or abnormal response values (**Supplemental Digital Content**, **SDC**, https://links.lww.com/TP/D275), and who had null clamp time. We also removed any bypass offers. The final number of donors analyzed was n = 27 709. We stratified several of our analyses by donors who had all recovered kidneys transplanted and donors who had at least 1 recovered kidney not used.

Data Collection on Offers and Refusals

An OPO begins the allocation of an organ by making initial (provisional) offers to centers for specific patients. These offers are often made to multiple patients simultaneously. Among offers that have been initially accepted, the OPO follows up by making primary offers, sequentially in priority order. The dataset includes timestamps for initial offers, initial responses, and final responses, as well as refusal codes, which are entered by centers or OPO staff for declined offers. If the offer was initially declined, the initial and final response times are the same. Timestamps at which primary offers are made are not recorded in the data. Although provisional offers may sometimes be made simultaneously, the responses by transplant centers to these provisional offers are not necessarily given at the same time. To be clear, we analyze the timestamps of the refusals, rather than the timestamp when the offers were made.

When a center declines an offer to a specific patient, it often declines the offer for >1 of its patients simultaneously. We bundle refusals for an organ from the same center that occurred at the same timestamp into a multiple patient refusal. If there were no other refusals for the organ by the center at the same timestamp, we termed this a single patient refusal. We refer to each such refusal aggregation (i.e., both single and multiple patient refusals) as a center refusal, and examples of each are given in **Table S1** (**SDC**, https://links.lww.com/TP/D275). We analyzed the number of patients in multiple patient refusals and the number of different refusal codes within each multiple patient refusal.

We analyze the frequency of refusal codes for center refusals at different times of the offering process, ranging from 8 h before to 30 h after the cross-clamp. We assign a refusal code to a center refusal by taking the most frequent code, breaking ties by the first code that appears out of the most frequent codes. Next, we measured the average number of unique centers contacted as well as the average number of center refusal received over the same period.

To investigate centers' decision-making following single patient and multiple patient refusals, we computed the probability that the organ would be accepted following a reoffer at the 100 centers with the highest offer volumes.

Our construction of single patient and multiple patient refusals does not distinguish between whether the refusals followed provisional or primary offers, as all refusals can be informative. We conduct robustness checks of some results by analyzing refusals for primary offers only.

Informativeness of Center Refusals Before Clamp

We computed the probability of nonutilization stratified by the number of unique centers that have sent a single patient or multiple patient refusal by clamp time. To address the potential confounding between KDPI and the number of multiple patient refusals, we investigated how multiple patient refusals before clamp affect the probability of nonutilization, stratified by KDPI in increments of 10%. We also conducted a more detailed analysis by conditioning on KDPI as a continuous variable (**Supplemental Digital Content, SDC**, https://links.lww.com/TP/D275). Additionally, we looked at the fraction of donors that had been accepted in each hour from clamp time to 30 h after clamp, stratified both by KDPI and by whether at least 3 distinct centers had sent multiple patient refusals before clamp. We conducted a robustness check by changing the definition of multiple patient refusal to include >5 simultaneous patients refused.

Approval for this study was obtained from the Stanford University Institutional Review Board (Protocol 68925).

RESULTS

Data Collection on Offers and Refusals

There were 880 647 center refusals (single or multiple patient), containing a total of 37 797 232 offer refusals, for donors with match runs between January 1, 2022, and December 31, 2023, of which 69.1% (608 279) were multiple patient refusals and 30.9% (272 368) were single patient refusals. Of the multiple patient refusals, 98% had the same refusal code reported for all patients refused simultaneously.

The median number of patients in a multiple patient refusal was 25 (Q1: 6, Q3: 70; distribution shown in **Figure S1, SDC**, https://links.lww.com/TP/D275). Table 1 displays all refusal codes, and how frequently each appeared for single and multiple patient refusals. Reasons related to some form of incompatibility to a specific patient were more frequently seen in single patient refusals (last rows of Table 1, highlighted in orange), whereas reasons related to organ quality and hesitation by the center to accept the organ for any patient were more frequently seen for multiple patient refusals (first rows of Table 1, highlighted in blue). For example, just 12% of center refusals with the code 724—"Candidate requires multiple organ transplant" were multiple patient refusals, whereas 83% of center refusals with the code 711—"Organ anatomical damage or defect" were multiple patient refusals.

More than 80% of center refusals associated with the following codes were multiple patient refusals: 715—"Biopsy results unacceptable," 712—"Actual or projected cold ischemic time too long," 710—"Organ preservation: Unacceptable method or findings," 743—"Malignancy or suspected malignancy," 713—"Warm ischemic time too long," 711—"Organ anatomical damage or defect," and 744—"Epidemic/Pandemic—Donor" (Table 1). More than 90% of center refusals associated with the following codes were single patient refusals: 723—"Candidate requires different laterality," 721—"Candidate transplanted or pending transplant," 727—"Candidate unavailable," 726—"Candidate temporarily ineligible because of insurance or financial issue," 732—"Positive physical crossmatch," 733—"Positive virtual crossmatch/unacceptable antigens," 728—"Candidate refused," and 722—"Candidate's condition improved, transplant not needed" (Table 1). Of all of the multiple patient refusals, 86.1% occurred with an organ-related refusal code, and of all of the single patient refusals, 50.6% occurred with a patient-related refusal code (Table 1).

Almost all refusals with a reason associated with biopsy (code 715) arrived at least 2 h after clamp time (Figure 1). A greater ratio of multiple patient refusals to single patient refusals occurred after cross-clamp (**Figure S2, SDC**, https://links.lww.com/TP/D275). A notable increase in refusal related to CIT too long (code 712) started at 4 h after clamp (Figure 1). At this time, donors whose kidneys were transplanted had been offered to an average of 7 transplant centers and had received an average of 11 center refusals (Figure 2A), and donors with at least 1 kidney not used had been offered to an average of 11 transplant centers and had received an average of 17 center refusals (Figure 2B).

We then examined the organ disposition based on refusals at the 100 centers with the highest offer volumes. If a center entered a multiple patient refusal, of the organs that were reoffered to the same center, 8% were accepted at the same center, 21% were accepted at a different center, and 71% were not accepted by any center. In contrast, if the center entered a single patient refusal, of the organs that were reoffered to the same center, 19% were accepted at the same center, 38% were accepted at a different center, and 43% were not accepted by any center.

Informativeness of Center Refusals Before Clamp

While 4 847 731 of the 37 797 232 refusals (12.8%) occurred before cross-clamp, 230 380 of the 880 647 center refusals (26.2%) occurred before cross-clamp (**Figure S2 [SDC**, https://links.lww.com/TP/D275] displays the time distribution of center refusal occurrences]). The rate of nonutilization for organs that had not been refused before clamp was 28% (Figure 3A, bottom left square). Using this as a baseline, the likelihood of nonutilization increased as the number of centers sending multiple patient refusals increased. If just 1 center had entered a multiple patient refusal (moving up 1 cell in Figure 3A), the nonutilization rate increased to 35%. However, if 5 or more centers enter multiple patient refusals, the likelihood of nonutilization increased to 88% (Figure 3A, top left square). Conversely, the likelihood of nonutilization decreased as the number of single patient refusals increased. Compared with the baseline nonutilization rate of 28% for organs with no refusals before clamp time, a single patient refusal from 1 center (moving right 1 cell in Figure 3A) was associated with a reduction in the nonutilization rate to 12%. Furthermore,

TABLE 1.

Frequency of center refusal reasons appearing between January 1, 2022, and December 31, 2023

Refusal code	Refusal reason	Percentage of center refusals with this reason that are single patient	Percentage of center refusals with this reason that are multiple patient	No. (percentage) of center refusals that are single patient	No. (percentage) of center refusals that are multiple patient
715	Biopsy results unacceptable	9.5%	90.5%	9374 (3.4%)	88 921 (14.6%)
712	Actual or projected cold ischemic time too long	9.9%	90.1%	19 690 (7.2%)	178 775 (29.4%)
710	Organ preservation: Unacceptable method or findings	13.4%	86.6%	3945 (1.5%)	25 546 (4.2%)
743	Malignancy or suspected malignancy	15.4%	84.6%	407 (0.2%)	2243 (0.4%)
713	Warm ischemic time too long	15.8%	84.2%	2023 (0.7%)	10 771 (1.8%)
711	Organ anatomical damage or defect	17.0%	83.0%	7996 (2.9%)	39 099 (6.4%)
744	Epidemic/pandemic—donor	17.9%	82.1%	2369 (0.9%)	10 873 (1.8%)
717	Unacceptable organ-specific test results, specify	20.9%	79.1%	17 733 (6.5%)	67 143 (11.0%)
742	Donor infection or positive culture	23.2%	76.8%	568 (0.2%)	1885 (0.3%)
716	Organ-specific test results not available, specify	24.1%	75.9%	554 (0.2%)	1743 (0.3%)
714	Biopsy not available	27.0%	73.0%	798 (0.3%)	2160 (0.4%)
790	Disaster emergency management consideration	27.4%	72.6%	23 (0.0%)	61 (0.0%)
750	Donor medical history, specify	28.1%	71.9%	19 440 (7.1%)	49 743 (8.2%)
700	Donor age	29.2%	70.8%	18 334 (6.7%)	44 392 (7.3%)
798	Other, specify	29.6%	70.4%	18 040 (6.6%)	42 838 (7.0%)
751	Donor instability/high vasopressor usage	32.0%	68.0%	132 (0.1%)	280 (0.1%)
760	Resource time constraint (OPO, TXC, donor hospital, etc.)	33.2%	66.8%	98 (0.0%)	197 (0.0%)
762	Recovery team availability	37.5%	62.5%	9 (0.0%)	15 (0.0%)
763	Transplant team or transplant facility availability	39.7%	60.3%	171 (0.1%)	260 (0.0%)
753	DCD donor neurological function/not expected to arrest	41.7%	58.3%	1749 (0.6%)	2444 (0.4%)
741	Positive infectious disease screening test: CMV, HBV, HCV, etc.	43.6%	56.4%	1278 (0.5%)	1656 (0.3%)
752	Prolonged downtime/CPR	43.9%	56.1%	268 (0.1%)	343 (0.1%)
764	Transportation availability	45.2%	54.8%	47 (0.0%)	57 (0.0%)
701	Organ size, specify	50.1%	49.9%	7191 (2.6%)	7154 (1.2%)
761	Donor family time constraint	57.1%	42.9%	4 (0.0%)	3 (0.0%)
740	PHS risk criteria or social history	60.0%	40.0%	1659 (0.6%)	1104 (0.2%)
730	No candidate serum for crossmatching	66.6%	33.4%	3793 (1.4%)	1899 (0.3%)
720	Candidate temporarily medically unsuitable	74.0%	26.0%	49 773 (18.3%)	17 460 (2.9%)
765	Exceeded policy defined response time	77.8%	22.2%	713 (0.3%)	203 (0.0%)
731	No donor cells/specimen for crossmatching, or no time for crossmatch	80.3%	19.7%	497 (0.2%)	122 (0.0%)
725	Epidemic/pandemic—candidate	86.6%	13.4%	1546 (0.6%)	240 (0.0%)
734	No. of HLA mismatches unacceptable	87.8%	12.2%	1399 (0.5%)	195 (0.0%)
724	Candidate requires multiple organ transplant	88.1%	11.9%	39 113 (14.4%)	5272 (0.9%)
723	Candidate requires different laterality	90.6%	9.4%	358 (0.1%)	37 (0.0%)
721	Candidate transplanted or pending transplant	90.7%	9.3%	13 443 (4.9%)	1384 (0.2%)
727	Candidate unavailable	90.8%	9.2%	4138 (1.5%)	419 (0.1%)
726	Candidate temporarily ineligible because of insurance or financial issue	92.5%	7.5%	2285 (0.8%)	185 (0.0%)
732	Positive physical crossmatch	94.6%	5.4%	3341 (1.2%)	191 (0.0%)
733	Positive virtual crossmatch/unacceptable antigens	94.9%	5.1%	10 466 (3.8%)	567 (0.1%)
728	Candidate refused	95.0%	5.0%	7470 (2.7%)	395 (0.1%)
722	Candidate's condition improved, transplant not needed	97.1%	2.9%	133 (0.1%)	4 (0.0%)

The third and fourth columns give what proportion of center refusals with that reason are single or multiple patient. The fifth through eighth columns provide the total number of center refusals that are single patient and multiple patient for each reason, along with the percentage of all single patient and multiple patient center refusals that correspond to each refusal reason. This format allows for a comparison of refusal patterns between single patient and multiple patient contexts. The table is sorted in decreasing order by the percentage of refusals that are multiple patient (fourth column). Organ-related refusal reasons are highlighted in blue. Patient-related refusal reasons are highlighted in orange. Ambiguous refusal reasons are highlighted in gray.

CMV, cytomegalovirus; CPR, cardiopulmonary resuscitation; DCD, donation after circulatory death; HBV, hepatitis B virus; HCV, hepatitis C virus; HLA, human leukocyte antigen; OPO, organ procurement organization; PHS, public health service; TXC, transplant center.

if 5 or more centers enter single patient refusals, the nonutilization rate dropped even further to just 9% (Figure 3A, bottom right square). These trends continue across all of Figure 3. Changing the threshold for defining a multiple patient refusal did not alter the associations (Figure 3B). Similar patterns were observed when looking at 3 h after

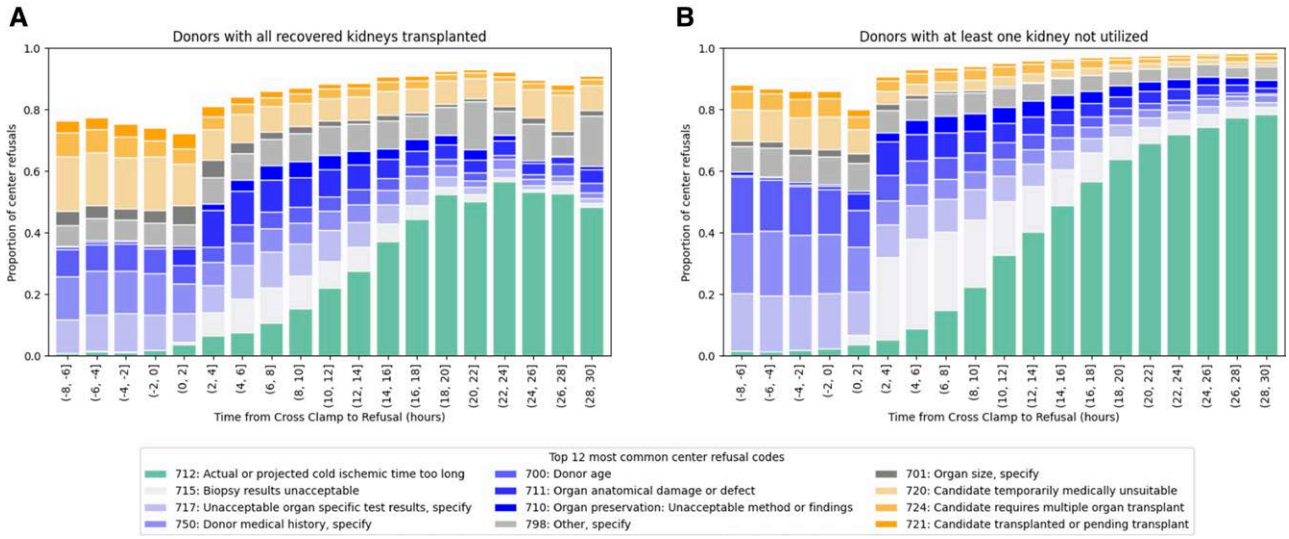

FIGURE 1. Distribution of the top 12 most common center refusal codes across time intervals, where simultaneous refusals are treated as a single center refusal. The x-axis describes the time interval, in hours, since clamp time, while the y-axis shows the frequency distribution of each the refusal codes. A, Results for donors with all recovered kidneys transplanted. B, Results for donors with at least 1 kidney not used. Organ-related refusal reasons are colored in blue. Patient-related refusal reasons are colored in orange. Ambiguous refusal reasons are colored in gray.

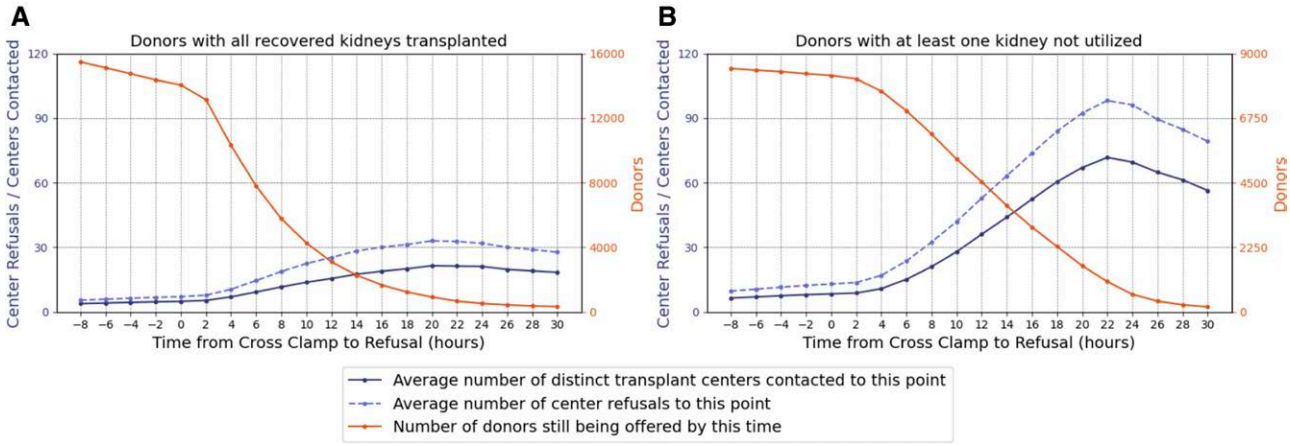

FIGURE 2. Center communications during the allocation process over time. The x-axis shows the time since clamp, while the purple y-axis shows the average number of communications by that time: the solid line represents the number of transplant centers contacted, and the dashed line represents the number of center refusals received. The orange y-axis displays the number of donors that had at least 1 offer after that corresponding hour. A, Results for donors with all recovered kidneys transplanted. B, Results for donors with at least 1 kidney not used.

clamp (**Figure S3, SDC**, https://links.lww.com/TP/D275), when restricting the analysis only to refusals generated from primary offers (ignoring provisional offers) (**Figure S4, SDC**, https://links.lww.com/TP/D275), and when stratifying donors by KDPI groups (**Figures S5** and **S6, SDC**, https://links.lww.com/TP/D275).

Additional multiple patient refusals increased the probability of nonutilization across all KDPI bins (Figure 4). For example, when considering a multiple patient refusal as 1 where >1 patients were simultaneously refused (Figure 4A), a donor with KDPI between 41% and 50% had a baseline likelihood of nonutilization of 12.8% (green point). However, if at least 5 distinct centers had sent a multiple patient refusal before clamp (purple point), the probability of nonutilization increased to 43.7%, a statistically significant increase ($P < 10^{-6}$). A greater number of multiple patient refusals increased the risk of nonutilization even when conditioning on KDPI as a continuous variable (**Table S2, SDC**, https://links.lww.com/TP/D275).

Accounting for multiple patient refusals, and stratifying by KDPI buckets, the time required to place an organ increased (Figure 5). For example, considering a multiple patient refusal as 1 where >1 patients were simultaneously refused (Figure 5A), organs from donors with KDPI <20% with at least 3 centers sending a multiple patient refusal by clamp (dark green dashed line) had a similar placement pattern to organs from donors with KDPI between 61% and 85% (orange solid line).

DISCUSSION

Marginal organs are often offered to thousands of patients. However, timestamp data reveals that transplant centers often decline an organ offer for multiple patients at

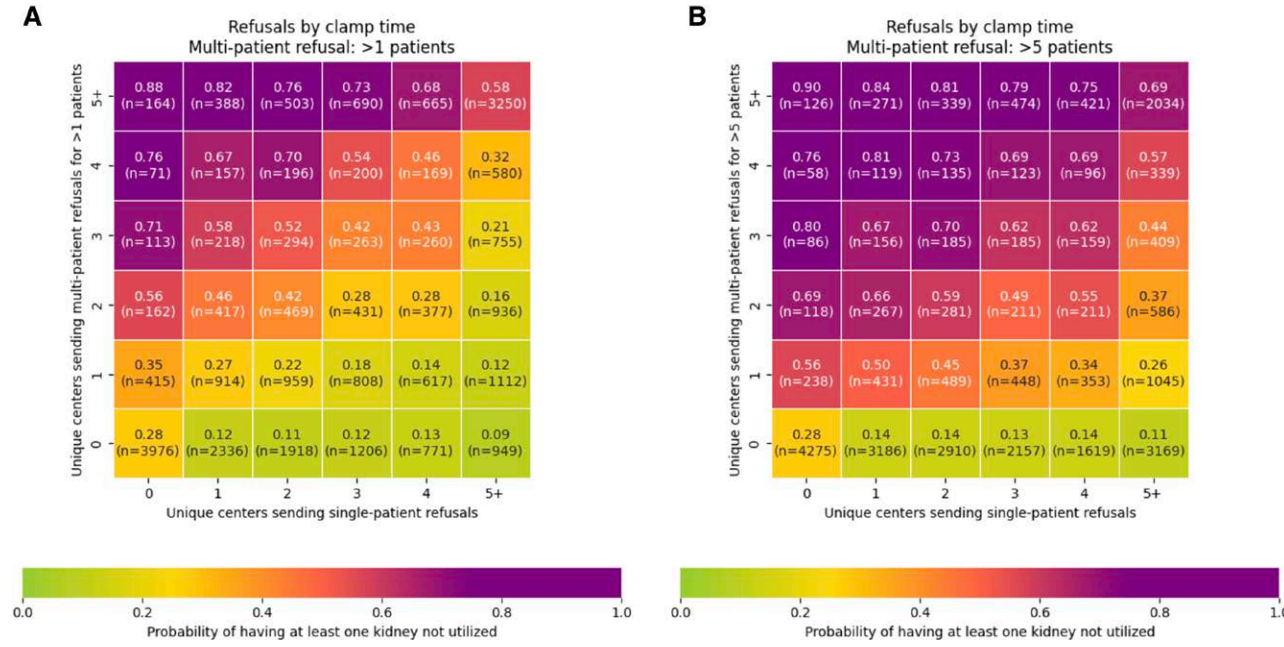

FIGURE 3. Significance of the number of transplant centers who have sent multiple patient simultaneous refusals and single patient refusals by clamp on nonutilization. The x-axis and y-axis correspond to the number of distinct centers entering single patient and multiple patient (defined as simultaneous refusals for >1 patients [A] and >5 patients [B]) refusals by clamp time, respectively. The numbers in each cell are the probability of having at least 1 kidney not used and the number of donors with these numbers of center refusals (in parentheses).

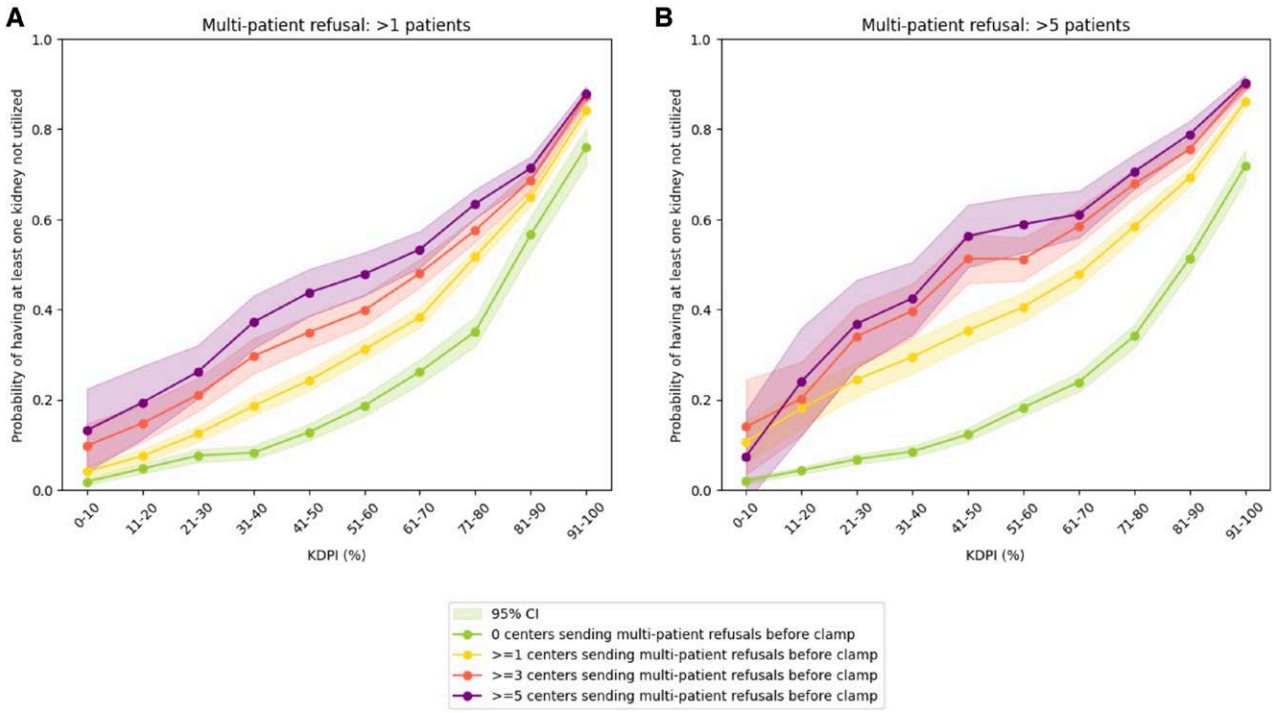

FIGURE 4. Probability of having at least 1 kidney not used by KDPI and multiple patient refusals by clamp time. The x-axis represents the KDPI bin. The y-axis represents the probability that at least 1 kidney of the donor will not be used. The green line is the baseline (no multiple patient refusals by clamp). The other lines visualize the increase in likelihood of nonutilization after multiple patient refusals (simultaneous refusals for >1 patients [A] and >5 patients [B]). Shaded intervals reflect the 95% CI. CI, confidence interval; KDPI, Kidney Donor Profile Index.

the same time. In this article, we aggregated refusals at the same timestamp by a transplant center, hypothesizing that refusals for a single patient indicate issues with individual patients, whereas multiple patient simultaneous refusals indicate an issue with organ quality. In 98% of these multiple patient simultaneous refusals by centers, there is exactly 1 refusal code for all simultaneously refused offers, supporting our choice to bundle the decisions of centers that occur at the same time. Of 37797232 offer refusals, after aggregating simultaneous refusals at the same

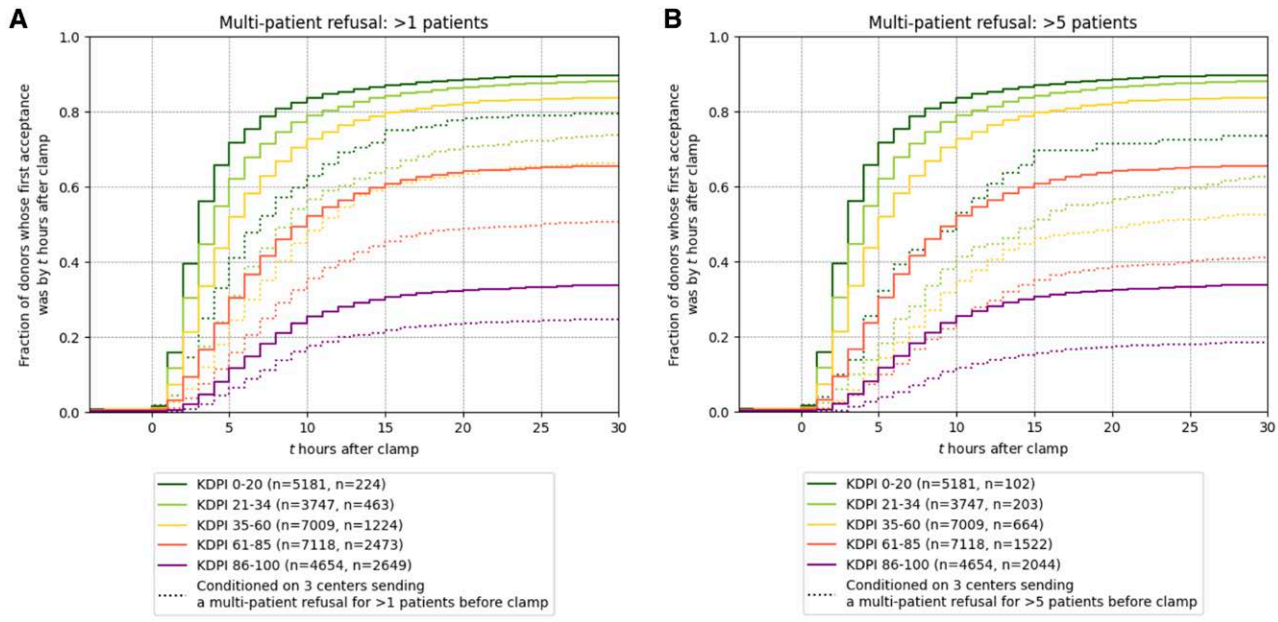

FIGURE 5. The time it takes to place a donor's kidneys conditional on multiple patient refusals. The solid line shows the proportion of donors whose first organ was accepted by *t* hours after clamp, whereas the dotted line shows the same for donors for whom at least 3 different centers have sent multiple patient refusals for >1 patients (A) and >5 patients before clamp (B). KDPI, Kidney Donor Profile Index.

timestamp, there were 880 647 center (single or multiple patient) refusals.

Refusal codes related to the organ are more frequently used by centers in multiple patient refusals (e.g., 90% of center refusals with the code "715—Biopsy results unacceptable" were simultaneous refusals for multiple patients), and reasons related to the patient are more frequently seen in single patient refusals (e.g., 97% of refusals with the code "722—Candidate's condition improved, transplant not needed" were single patient refusals) (Table 1). An alternative approach would be to use refusal codes entered by centers. However, the codes themselves can be unclear, and because they are often entered quickly, they are potentially not precise. For example, 50% of center refusals with the code "701—Organ size, specify" were single patient refusals, and 50% were multiple patient refusals, as this refusal reason does not specify whether the incompatibility was because of factors related to the patient or to the organ (Table 1). Therefore, the text of the refusal reasons should be clarified to elicit preferences from centers more effectively. Moreover, upon declining an offer, a center can be asked "are you declining this organ offer because of the organ quality or because of a factor related to the patient to whom it is being offered?," and whether the center is still interested in the organ, and for which patients. These 2 approaches would help to learn about centers' preferences, and or prime the centers to update their filters for organ offers.[15,16]

Center refusals occur before clamp time for 26% of refusals; as such, this early indicator can provide valuable insights into the likelihood of organ nonutilization. Even relatively few multiple patient refusals before clamp are associated with increased likelihood of nonutilization (moving along the vertical axes of Figure 3). Single patient refusals are positively correlated with utilization (moving along the horizontal axes of Figure 3). These results hold true even when conditioning on KDPI (Figure 4). Multiple patient refusals also increase the time it takes for an organ to be placed (Figure 5). Overall, there could be many valid clinical concerns regarding a donor that are not represented in the KDPI or any other risk index based on registry data. These include the concerns for infection or malignancy, anatomical or surgical aberrations, procurement issues, and other medical factors.[17] We show that multiple patient refusals, even those before cross-clamp, can identify these organs reliably regardless of the specific reason and without need for additional data collection, making it a highly promising tool for developing accelerated pathways of kidney allocation.

Currently, the OPTN is working toward "enhanc[ing] system efficiencies through the improvement of offer acceptance practices and processes."[18] We find that CIT becomes the most common center-level refusal reason 10 h after clamp (Figure 1), suggesting that following the prescribed allocation process may be too slow to avoid long CIT. This observation contrasts with earlier findings by Mohan et al[11] who reported that CIT is the least common reason for organ nonutilization. The difference arises since Mohan et al[11] uses a single nonutilization reason reported by the OPO, whereas we analyze the refusal reasons reported by centers. Furthermore, we analyze timestamps to determine the point at which CIT becomes the predominant center refusal reason. Figure 1 shows that while center refusals for CIT start to become a sizable portion of the refusals around 4 h after clamp time, it does not emerge as the most common center refusal reason until 10 h have passed after clamp time.

In the United Kingdom, a fast-track system is used to expedite offers following a few offer refusals.[19] One criterion for a kidney to be offered through the fast-track scheme is if 5 transplant centers have already refused the kidney for either donor- or organ-quality reasons.[19]

Using refusal data and distinguishing between single and multiple patient refusals can add power to this approach to determine which organs are at risk of nonutilization. Figure 6 shows an example of such an allocation pathway, using single and multiple patient refusals to guide when to begin accelerated placement. If at clamp time, based on the centers that have already sent single and multiple patient refusals, the probability of nonutilization is above a certain threshold, an accelerated placement pathway may commence. For example, if 3 centers have sent a multiple patient refusal, and no centers have sent a single patient refusal before clamp, the historical probability of nonutilization of these organs is 71%, suggesting that accelerated placement could help place the organ (Figure 3A). However, if 3 centers have sent a single patient refusal, and no centers have sent a multiple patient refusal before clamp, the historical probability of nonutilization of these organs is 12%, so the organ can continue to be offered in-sequence (Figure 3A). The threshold for these policies can be adjusted based on both OPO- and organ-specific factors, as well as CIT. These numbers can be recalculated every hour, as these concepts can be extended to any timeframe early in the allocation process. As time passes, other information becomes available, such as biopsy information and pump values, which are extremely informative. These numbers can be a valuable complement to this medical information.[3] This approach could be further complemented by machine learning algorithms.[12,20,21]

Our findings identify a simple framework to identify marginal organs early during the allocation process by counting single and multiple patient refusals. However, our analysis does not suggest to whom the out-of-sequence allocation protocol should offer the organ. Conditional upon reoffering, at the largest centers, after a multiple patient simultaneous refusal, 8% of organs were accepted at the same center (compared with 19% after a single patient refusal). Despite this, multiple patient simultaneous refusals do not imply that the center is not interested in the organ for any of its patients. Some patients may be better off receiving a marginal organ over waiting several years for a better organ. However, such patients are naturally lower on the waiting list, and these refusals may arrive when the CIT is already too long. A center may accept an out-of-sequence offer for such patients despite earlier refusals for other patients.

One limitation of our analysis is that we interpret the number of patients simultaneously refused as indicative of the underlying reason for refusal. However, the assumption that single patient refusals reflect issues with individual patients, while multiple patient simultaneous refusals reflect concerns about organ quality, may be more nuanced. For example, a transplant center might record simultaneous refusals for multiple patients under a single vague refusal reason, such as 750—"Donor medical history, specify," even though these could represent multiple single patient refusals for various distinct reasons. Alternatively, transplant surgeons might enter a refusal for a single patient to wait for the responses from other surgeons, even if they already view the organ as marginal. Nevertheless, when aggregated, we find that multiple patient refusals are strongly associated with organ-related refusal reasons and nonutilization.

The current allocation process is based on a static priority order that does not adapt to measurable changes in the risk of nonutilization. As the OPTN works toward increasing both utilization of organs and the efficiency of the organ placement process,[22] the data generated by single and multiple patient refusals before clamp time could serve to inform the design of an adaptive and transparent allocation offering process (Figure 6). Such a change requires the dynamic transition from an early focus on equity to an increasing focus on utility as CIT increases during the allocation process, as the data shows that OPOs are not reaching centers quickly enough to avoid long CIT. The straightforward approach of counting single and multiple patient refusals can help assess an organ's quality in real-time and can help identify organs that may be appropriate for accelerated placement.

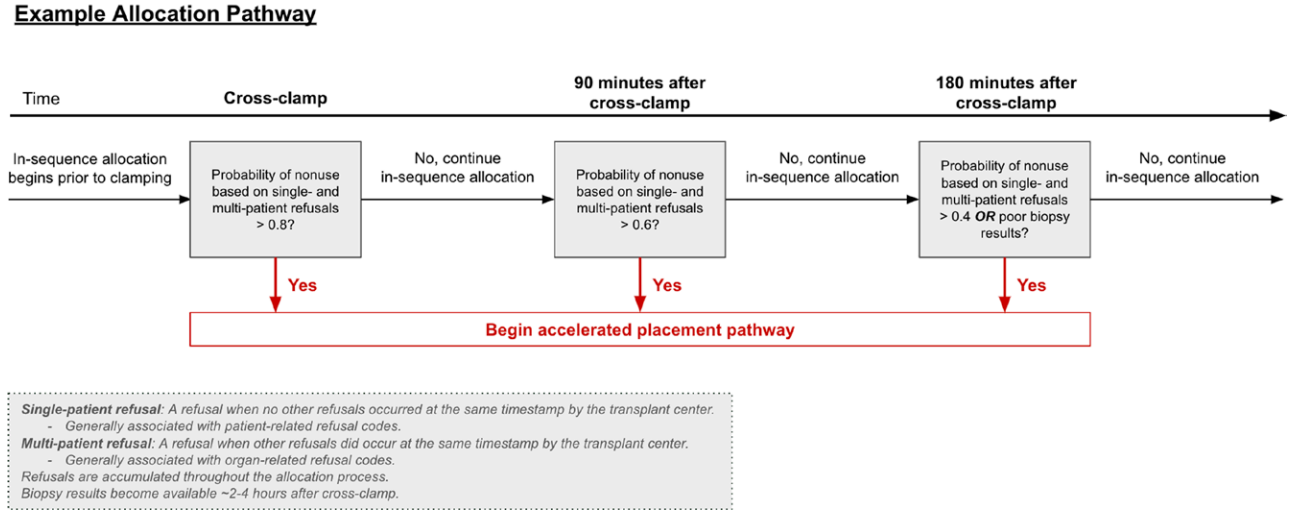

FIGURE 6. Example allocation pathway based on single and multiple patient refusals. The historical probability of nonutilization based on single and multiple patient refusals can be taken from Figure 3 or Figure 4 and can be used to determine when to begin an accelerated placement pathway. The threshold for these policies can be adjusted based on organ procurement organization (OPO)- and organ-specific factors, as well as cold ischemia time (CIT). The time of decision-making is flexible and can be performed at any point during the allocation process.

ACKNOWLEDGMENTS

The authors thank the anonymous editors and referees for their insightful comments.

REFERENCES

1. Organ Procurement and Transplantation Network. National data. Available at https://optn.transplant.hrsa.gov/data/. Accessed January 10, 2025.
2. Wolfe RA, LaPorte FB, Rodgers A, et al. Developing organ offer and acceptance measures: when 'good'organs are turned down. *Am J Transplant*. 2007;7:1404–1411.
3. Barah M, Kilambi V, Friedewald JJ, et al. Implications of accumulated cold time for US kidney transplantation offer acceptance. *Clin J Am Soc Nephrol*. 2022;17:1353–1362.
4. Agarwal N, Ashlagi I, Somaini P, et al. Dynamic incentives in wait list mechanisms. In: American Economic Association, Vol 108. Nashville, TN; 2018:341–347.
5. Cron DC, Husain SA, King KL, et al. Increased volume of organ offers and decreased efficiency of kidney placement under circle-based kidney allocation. *Am J Transplant*. 2023;23:1209–1220.
6. Debout A, Foucher Y, Trébern-Launay K, et al. Each additional hour of cold ischemia time significantly increases the risk of graft failure and mortality following renal transplantation. *Kidney Int*. 2015;87:343–349.
7. Peters-Sengers H, Houtzager JHE, Idu MM, et al. Impact of cold ischemia time on outcomes of deceased donor kidney transplantation: an analysis of a national registry. *Transplant Direct*. 2019;5:e448.
8. Liyanage LN, Akizhanov D, Patel SS, et al. Contemporary prevalence and practice patterns of out-of-sequence kidney allocation. *Am J Transplant*. 2025;25:343–354.
9. Noreen SM, Klassen D, Brown R, et al. Kidney accelerated placement project: outcomes and lessons learned. *Am J Transplant*. 2022;22:210–221.
10. Organ Procurement and Transplantation Network. Accelerated placement of hard-to-place kidneys. Available at https://optn.transplant.hrsa.gov/professionals/improvement/improving-organ-usage-and-placement-efficiency/protocols-for-expedited-placement-variance/accelerated-placement-of-hard-to-place-kidneys/. Accessed January 22, 2025.
11. Mohan S, Chiles MC, Patzer RE, et al. Factors leading to the discard of deceased donor kidneys in the United States. *Kidney Int*. 2018;94:187–198.
12. Barah M, Mehrotra S. Predicting kidney discard using machine learning. *Transplantation*. 2021;105:2054–2071.
13. Mohan S, Yu M, King KL, et al. Increasing discards as an unintended consequence of recent changes in United States Kidney Allocation Policy. *Kidney Int Rep*. 2023;8:1109–1111.
14. United Network for Organ Sharing. Updated list of organ refusal reasons are now in effect. Available at https://unos.org/news/updated-list-of-organ-refusal-reasons-are-now-in-effect/. Accessed January 24, 2025.
15. Yu M, King KL, Husain SA, et al. Use of offer bypass filters under the updated kidney allocation system. *Kidney360*. 2024;5:756–758.
16. King KL, Husain SA, Cohen DJ, et al. The role of bypass filters in deceased donor kidney allocation in the United States. *Am J Transplant*. 2022;22:1593–1602.
17. Narvaez JRF, Nie J, Noyes K, et al. Hard-to-place kidney offers: donor- and system-level predictors of discard. *Am J Transplant*. 2018;18:2708–2718.
18. United Network for Organ Sharing. National collaborative focusing on organ offer acceptance to launch at the end of January 2023. Available at https://unos.org/news/national-collaborative-organ-offer-acceptance-launches-jan-2023/. Accessed March 27, 2024.
19. Callaghan CJ, Mumford L, Pankhurst L, et al. Early outcomes of the new UK deceased donor kidney fast-track offering scheme. *Transplantation*. 2017;101:2888–2897.
20. Massie AB, Desai NM, Montgomery RA, et al. Improving distribution efficiency of hard-to-place deceased donor kidneys: predicting probability of discard or delay. *Am J Transplant*. 2010;10:1613–1620.
21. Zhou S, Massie AB, Holscher CM, et al. Prospective validation of prediction model for kidney discard. *Transplantation*. 2019;103:764–771.
22. Organ Procurement and Transplantation Network. Improving organ usage and placement efficiency. Available at https://optn.transplant.hrsa.gov/professionals/improvement/improving-organ-usage-and-placement-efficiency/. Accessed January 10, 2025.