

## ORIGINAL ARTICLE

# The first 9 years of kidney paired donation through the National Kidney Registry: Characteristics of donors and recipients compared with National Live Donor Transplant Registries

Stuart M. Flechner<sup>1</sup> | Alvin G. Thomas<sup>2</sup> | Matthew Ronin<sup>3</sup> | Jeffrey L. Veale<sup>4</sup> | David B. Leiser<sup>5</sup> | Sandip Kapur<sup>6</sup> | John D. Peipert<sup>7</sup> | Dorry L. Segev<sup>2</sup> | Macey L. Henderson<sup>2</sup> | Ashton A. Shaffer<sup>2</sup> | Matthew Cooper<sup>8</sup> | Gareth Hil<sup>3</sup> | Amy D. Waterman<sup>4</sup>

<sup>1</sup>Cleveland Clinic, Cleveland, OH, USA

<sup>2</sup>Johns Hopkins University, Baltimore, MD, USA

<sup>3</sup>National Kidney Registry, Babylon, NY, USA

<sup>4</sup>University of California, Los Angeles, Los Angeles, CA, USA

<sup>5</sup>East Carolina University, Greenville, NC, USA

<sup>6</sup>Cornell University, New York, NY, USA

<sup>7</sup>Department of Medical Social Sciences, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

<sup>8</sup>Georgetown University, Washington, DC, USA

## Correspondence

Stuart M. Flechner  
Email: flechns@ccf.org

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The practice of kidney paired donation (KPD) is expanding annually, offering the opportunity for live donor kidney transplant to more patients. We sought to identify if voluntary KPD networks such as the National Kidney Registry (NKR) were selecting or attracting a narrower group of donors or recipients compared with national registries. For this purpose, we merged data from the NKR database with the Scientific Registry of Transplant Recipients (SRTR) database, from February 14, 2008, to February 14, 2017, encompassing the first 9 years of the NKR. Compared with all United Network for Organ Sharing (UNOS) live donor transplant patients (49 610), all UNOS living unrelated transplant patients (23 319), and all other KPD transplant patients (4236), the demographic and clinical characteristics of NKR transplant patients (2037) appear similar to contemporary national trends. In particular, among the NKR patients, there were a significantly ( $P < .001$ ) greater number of retransplants (25.6% vs 11.5%), hyperimmunized recipients (22.7% vs 4.3% were cPRA >80%), female recipients (45.9% vs 37.6%), black recipients (18.2% vs 13%), and those on public insurance (49.7% vs 41.8%) compared with controls. These results support the need for greater sharing and larger pool sizes, perhaps enhanced by the entry of compatible pairs and even chains initiated by deceased donors, to unlock more opportunities for those harder-to-match pairs.

## KEYWORDS

clinical research/practice, donors and donation: living, donors and donation: paired exchange, kidney transplantation/nephrology

**Abbreviations:** ABOi, ABO incompatibility; BMI, body mass index; CIT, cold ischemia time; cPRA, calculated PRA; DSA, donor-specific antibody; eGFR, estimated glomerular filtration rate; KPD, kidney paired donation; NKR, National Kidney Registry; OPTN, Organ Procurement and Transplantation Network; SRTR, Scientific Registry of Transplant Recipients; UNOS, United Network for Organ Sharing.

## 1 | INTRODUCTION

The concepts and practical considerations for kidney paired donation (KPD) were suggested more than 3 decades ago when living kidney transplant was almost exclusively performed between biological relatives.<sup>1</sup> During the past 3 decades, the practice of live donor kidney transplant between spouses and unrelated individuals has matured and become standard practice in virtually all transplant centers.<sup>2</sup> A number of additional advances have made the clinical practice of exchanging kidneys between patients in different transplant centers commonplace. The major pieces that needed to be tested and validated were the successful outcomes obtained when unrelated donors and recipients exchange kidneys and the ability to safely preserve and ship living donor kidneys over distances sufficient to permit exchanges between multiple geographic regions.<sup>3-7</sup> The National Kidney Registry (NKR) is a voluntary network currently with 83 transplant centers in 32 US states that is focused on the timely transplant of live donor kidneys through the use of novel computational algorithms that facilitate exchanges of kidneys between member centers. At the current time, this consortium has performed the largest number of KPD transplants in the United States.<sup>8</sup>

Important questions to ask as kidney paired exchange continues to grow are, precisely who is entered into these networks, and who are the donors and recipients actually being transplanted? The primary indications for KPD are ABO incompatibility (ABOi) and/or lymphocytotoxic crossmatch reactivity.<sup>3-7</sup> In addition, a smaller but growing number of patients are compatible pairs who are seeking anatomic, physiologic, or immunologic advantage from a paired exchange.<sup>9</sup> Another question to explore at this time is whether KPD transplants are favoring one demographic group over another. On a national level, the transplant of a kidney between a donor and a recipient is governed by a set of rules that is intended to emphasize medical criteria, safety, equity, and ethical constructs.<sup>10-12</sup> We focus on these questions in an effort to identify whether unintended consequences have emerged in patient selection during kidney paired exchange.

## 2 | METHODS AND MATERIALS

### 2.1 | The NKR

In this study, the authors used data from the NKR, which is a non-profit, 501c organization composed of 76 transplant centers within the United States that were participating during the study period. The NKR policies are available online.<sup>8</sup> Protocols for evaluating patients, performing the transplant procedures, and postoperative care are outlined by the NKR but were ultimately carried out at the participating transplant centers abiding by, and in concordance with, the individual center protocols. To date, the NKR has facilitated > 2000 KPD exchanges, > 80% of which involve shipping the living donor organ across the United States. The NKR repository is updated at quarterly intervals from each of the participating transplant

centers performing KPD transplants within the network. For the purpose of this report, the study population consisted of all NKR donors and recipients transplanted between February 14, 2008, and February 14, 2017; this represented 2037 consecutive KPD transplants, 9 years inclusive.

### 2.2 | Scientific Registry of Transplant Recipients

This study also included data from the Scientific Registry of Transplant Recipients (SRTR) external release made available in September 2017. The SRTR data system includes data on all donors, waitlist candidates, and transplant recipients in the United States, submitted by members of the Organ Procurement and Transplantation Network (OPTN), and has been previously described.<sup>13</sup> The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight to the activities of the OPTN and SRTR contractors. Using SRTR, we identified 101 718 adult (age ≥18 years) recipients (all donor sources) who underwent kidney transplant between February 14, 2008, and February 14, 2017.

### 2.3 | Data linkage

Data from KPD transplants facilitated through the NKR reported in the registry were linked to the SRTR data and cross-validated by using encrypted unique identifiers, transplant center, transplant date, donor ABO, donor sex, recipient ABO, and recipient sex.

### 2.4 | Statistical analysis

These study patients were compared with 3 distinct control populations from which the NKR transplants were subtracted.

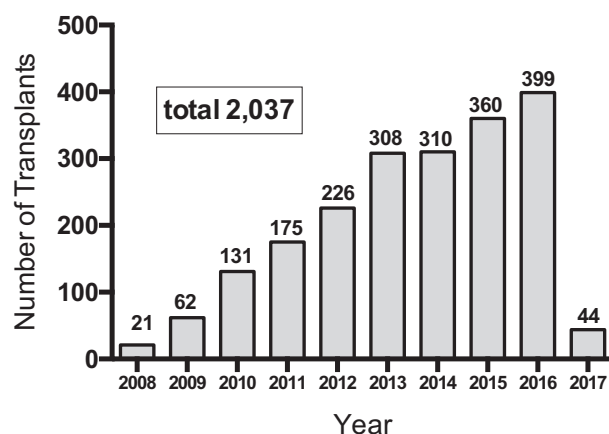
Control Population 1 consisted of all live donor kidney-only transplants reported to the SRTR registry between February 14, 2008, and February 14, 2017, and included 49 610 transplants.

Control Population 2 consisted of all living unrelated kidney-only transplants reported to the SRTR registry between February 14, 2008, and February 14, 2017. Any recipient-donor pairs who were biologically related were excluded. This group included 23 319 transplants.

Control Population 3 consisted of all living unrelated kidney-only transplants from the SRTR registry between February 14, 2008, and February 14, 2017, that were designated as part of the UNOS or any other KPD network, excluding the NKR. Any KPD recipient-donor pair who were biologically related were excluded. This group included 4236 transplants.

The demographic, immunologic, and clinical data for the transplanted donors and recipients were collected and tabulated. These data included recipient date of transplant and center, age, sex, race/ethnicity (white, black, Hispanic, Asian, other), year on dialysis, body mass index (BMI [kg/m<sup>2</sup>]), hepatitis C virus serology, diabetes, hypertension, prior transplants, preemptive transplants, education level, employment status, public/private insurance, and HLA sensitization at transplant according to calculated panel reactive antibody (cPRA 0%, 1%-79%,

## Annual Growth of NKR Transplants



**FIGURE 1** Annual growth of National Kidney Registry transplants, February 14, 2008, to February 14, 2017

80%-97%, and 98%-100%). Donor characteristics included age, sex, race/ethnicity (white, black, Hispanic, Asian, other), BMI ( $\text{kg}/\text{m}^2$ ), and estimated glomerular filtration rate (eGFR) (abbreviated Modification of Diet in Renal Disease) at donation. Additional transplant characteristics included ABO-compatible and ABOi pairs, the number of HLA O mismatches (HLA-A, -B, -DR), and the recorded total cold ischemia times (CITs) at revascularization. The study was reviewed and approved by the Cleveland Clinic Institutional Review Board (No. 16-784).

Differences in recipient, donor, and transplant characteristics between NKR and control transplants were assessed by using the  $\chi^2$  (categorical variables) and Mann-Whitney rank-sum (continuous variables) tests. We used a 2-sided  $\alpha$  of .05 to indicate a statistically significant difference. All analyses were performed by using Stata 15/MP for Linux (College Station, TX).

## 3 | RESULTS

The annual growth in NKR transplants has continued through the initial 9 years of the program, with 2037 transplants performed to the study end date of February 14, 2017 (Figure 1). These exchanges have been facilitated through 416 nondirected donor-initiated chains

ranging from 2 to 35 pairs in length (mean [SD] = 4.42 [3.78]) and 86 loops (mean [SD] = 2.34 [0.67]) per chain. Kidneys were shipped between 22 states, including 14.7% within centers, 4.4% within the same city and < 25 miles, and 80.9% > 25 miles. Transport included surface transportation and both commercial and charter flights. The median CIT (hours) for the NKR transplants was 8.7 (IQR 5.2-12.0, range 2-25), and the mean number of HLA-A, -B, -DR mismatches was 3.85 (median 4, range 0-6). The time waiting from entry into KPD to actual transplant ranged from 0 to 42 months and varied according to recipient ABO blood type and cPRA. Recipients with blood types AB, A, and B had shorter mean wait times (1.89, 2.69, and 3.73 months, respectively) compared with recipients with type O (6.48) (all  $P < .0001$ ) (Table 1). The mean wait time for cPRA of 0% was 3.48 months; 1%-19%, 3.67 months; 20%-79%, 3.78 months; 80%-97%, 5.41 months; and 98%-100%, 9.44 months ( $P < .0001$ ).

Actuarial 1-, 3-, and 5-year graft survival rates for the NKR transplants and the 3 control groups are provided in Figure 2. The differences among the groups were not significant at 1 and 3 years. However, the differences did reach significance ( $P < .01$ ) at 5 years. For the NKR transplants, the frequency of primary nonfunction (recipient was never off dialysis) was 0.34% ( $n = 7$ ) and the frequency of delayed graft function (first week dialysis) was 4.9% ( $n = 101$ ).

### 3.1 | Recipient characteristics

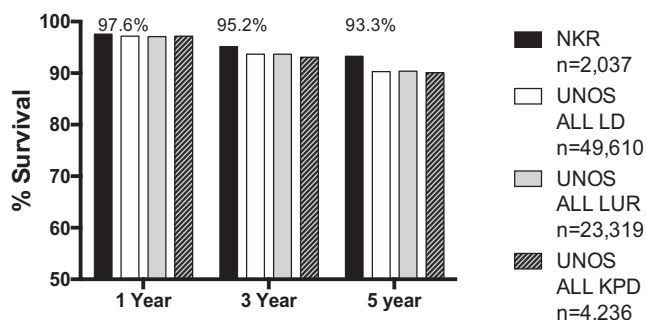
Recipient and donor demographics are provided in Table 2 compared with the 3 control populations (all UNOS live donors, all UNOS living unrelated donors, other KPD transplants). The NKR recipient median age of 50 years (IQR 39-60) is comparable to that of the controls, while the proportion of women (45.9%) is significantly higher ( $P < .001$ ) than in the 3 control populations. The NKR transplants had fewer white recipients (60.8%) than did the controls ( $P < .001$ ). In particular, the proportion of black KPD recipients (18.2%) was significantly larger ( $P < .001$ ) than that of the control proportions (13%, 11.7%, and 13.4%, respectively). The proportion of NKR Hispanic recipients (11.5%) was somewhat less than the total UNOS living donor transplant recipients (14.7%) but similar to the other controls. The NKR recipients represented a significantly ( $P < .001$ ) increased proportion of retransplants 25.6% compared with the controls (11.5%, 12.3%, and 17.1%, respectively) but a similar proportion of preemptive

**TABLE 1** Wait times, ABO blood types, and HLA sensitization for National Kidney Registry transplant recipients

Recipients	Wait time registration to transplant		cPRA				
	Mean months	Range months	0%	1%-19%	20%-79%	80%-97%	98%-100%
A: 731	2.69	0-29	295	49	194	130	63
B: 372	3.73	0-27	185	24	90	51	22
O: 786	6.48 <sup>a</sup>	0-37	351	60	209	116	50 (2.5%)
AB: 148	1.89	0-42	79	10	33	20	6
Total			910	143	526	317	141
2037 (100%)			44.6%	7%	25.8%	15.6%	7%

<sup>a</sup>O vs all groups  $P < .0001$ .

### Graft Survivals NKR vs. UNOS Controls 2008-2017



**FIGURE 2** Actuarial all-cause kidney transplant 1-, 3-, and 5 year graft survivals for National Kidney Registry vs United Network for Organ Sharing (UNOS) all live donors, UNOS living unrelated donors, and UNOS kidney paired donors

transplants (35.8%). Compared with controls, the NKR recipients had a greater number of years on dialysis (median 1.3 vs 0.5, 0.6, and 0.9, respectively,  $P < .001$ ) before transplant. The BMI was within 1 kg/m<sup>2</sup> for the entire population. A lower proportion (44.3%,  $P < .001$ ) of the NKR recipients were employed at the time of transplant compared with the controls (48.6%, 52.3%, and 46.4%, respectively). In addition, a greater proportion (49.7%,  $P < .001$ ) of the NKR recipients were on public health insurance plans at the time of transplant compared with the controls (41.8%, 39.2%, and 45.3%, respectively).

### 3.2 | Donor characteristics

Donor demographics are also provided in Table 2 compared with the same 3 control populations. The median NKR donor age of 45 years (IQR 35-53) was similar to the median age of the UNOS living unrelated and other KPD donors but 3 years older than all UNOS living donors ( $P < .001$ ). The NKR had a similar proportion of female donors (62.3%) compared with the control populations (62.1%, 64.4%, and 61.8%, respectively). The proportion of NKR donors who were black (10.5%) was similar to the proportion of all UNOS living donors (11.1%,  $P = 0.4$ ) but significantly greater than the proportion of all UNOS living unrelated donors (7.7%,  $P < .001$ ) and all UNOS KPD donors (7.5%,  $P < .001$ ). The proportion of NKR Hispanic donors (10.1%) was similar to all UNOS living unrelated (10.5%) and all UNOS KPD (10.1%) donors but significantly less than all UNOS living donors (14.4%,  $P < .001$ ). Only 2.2% of the NKR transplants were ABOi, which is similar to the 3 control groups (1.6%, 1.8%, and 2.2%, respectively). Of these 46 NKR ABOi donors, 32 were A to O (29 A2 to O), 2 were A to B, 1 was B to A, 4 were B to O, 2 were AB to A, and 5 were AB to B.

At the present time, about 53% of all live donor kidney transplants in the United States are performed using biologically related donors. Controls 2 and 3 were selected for only living unrelated donor recipient transplants. The NKR cohort included 5.5% who were biologically related pairs, which most often represented local loops or chain ends.

The BMI of the NKR donors (26.2 kg/m<sup>2</sup>) was essentially the same as the BMI of the 3 control groups (26.7, 26.6, and 26.3 kg/m<sup>2</sup>, respectively). In addition, the median eGFR of the NKR donors (102.2 mL/min per 1.73 m<sup>2</sup>) was similar to that of all UNOS living unrelated donors (103.4 mL/min per 1.73 m<sup>2</sup>) and all UNOS KPD donors (101.9 mL/min per 1.73 m<sup>2</sup>) but slightly lower than that of all UNOS donors (104 mL/min per 1.73 m<sup>2</sup>) ( $P < .01$ ). For NKR donors, the 24-hour urine protein excretion ranged between undetectable and 252 mg/d. The left kidney was donated in 89.4% of transplants, and the right, in 10.5%. The 2- and 3-renal artery kidneys donated accounted for 21% and 2%, respectively.

### 3.3 | NKR transplants

The NKR transplants were performed on a significantly greater proportion of HLA hyperimmunized patients (Figure 3 and Table 1). Only 45.8% of the NKR recipients had a pretransplant cPRA of 0%, while the control populations represented 71.3%, 71%, and 60% unsensitized recipients ( $P < .001$ ). The NKR transplants representing the hard-to-match cPRA ranges of 80% to 97% were accomplished for 15.3% of the recipients, while the 3 controls represented only 3%, 3.1%, and 6.9% ( $P < .001$ ). Only 0.8% of the NKR transplants were between 0 HLA mismatched pairs, which was significantly fewer than all UNOS living donor transplants (7.3%,  $P < .001$ ). The NKR transplants representing the extremely hard-to-match cPRA >98% were accomplished for 7.4% of the recipients, while the 3 controls represented only 1.3%, 1.1%, and 2.9% ( $P < .001$ ). In summary, 22.7% of the NKR transplants were performed in hard- and/or extremely hard-to-match recipients, recalling that these patients had not received a 0 mismatched deceased donor kidney from the UNOS national sharing program as well.

Among the 2037 NKR transplants, 11.7% were reported to have undergone desensitization at the transplant centers—222 for donor-specific crossmatch activity and 17 for ABOi. The treatments used for desensitization are represented in Table 3. While intravenous immunoglobulins and plasmapheresis were the most common interventions, the doses and timing of the various agents used were not recorded in the NKR database. In addition, the stringency of the incompatibilities or the specific posttransplant management protocols used by the centers were not available.

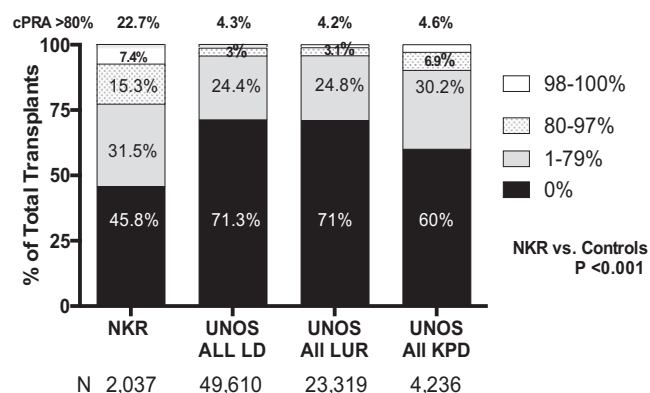
Between the starting and ending dates of this study, there were 59 donor-recipient pairs enrolled and transplanted as compatible pairs. The reasons given for entering paired exchange were to receive a younger kidney (27%), receive a larger kidney (21%), overcome low-level donor-specific antibodies (DSAs) (13%), receive a better HLA match (22%), avoid complex donor kidney anatomy (5%), and help more patients (altruism) (12%). Among the enrolled compatible pairs, 37% were biologically related, 32% were spouses, and 31% were unrelated. More important, of these compatible pairs, 82% of the donors were blood group O, enrolling an additional 48 into the matching pool. For the compatible pairs, the mean age for donors was 49.2 years; for recipients, 38.9 years; and for actual kidney donors, 40.1 years. For those seeking a younger donor as the reason

TABLE 2 Recipient and donor characteristics

Recipient characteristics		NKR	All UNOS non-NKR living donor transplants	P value	All UNOS non-NKR living unrelated donor transplants	P value	All UNOS non-NKR KPD living donor transplants	P value
N		2037	49 610		23 319		4236	
Median (IQR) age, y		50.0 (39.0-60.0)	49.0 (36.0-59.0)	<.001	50.0 (40.0-59.0)	.5	50.0 (39.0-59.0)	.2
Female, %		45.9	37.6	<.001	34.7	<.001	42.7	<.02
White, %		60.8	66.3	<.001	70.8	<.001	67.6	<.001
African American, %		18.2	13	<.001	11.7	<.001	13.4	<.001
Hispanic, %		11.5	14.7	<.001	11.5	1.0	12.4	.3
Asian, %		8.4	4.7	<.001	4.7	<.001	4.7	<.001
Other, %		1.1	1.3	.4	1.3	.4	1.6	.1
Previous transplant, %		25.6	11.5	<.001	12.3	<.001	17.1	<.001
Preemptive transplant, %		35.8	35.1	<.001	35.3	<.001	27.8	<.01
Median (IQR) years on dialysis		1.3 (0.0-2.9)	0.5 (0.0-1.6)	<.001	0.6 (0.0-1.7)	<.001	0.9 (0.0-2.3)	<.001
Median (IQR) BMI, kg/m <sup>2</sup>		26.6 (23.3-31.0)	27.1 (23.5-31.4)	.01	27.5 (23.9-31.7)	<.001	27.4 (23.7-31.7)	<.001
College educated, %		64.3	59.6	<.001	65.2	.4	63.1	.4
Employed, %		44.3	48.6	<.001	52.3	<.001	46.4	.1
Public insurance, %		49.7	41.8	<.001	39.2	<.001	45.3	<.01
Diabetes, %		19	20.4	.1	21.1	.03	20.3	.2
Hypertension, %		15.8	16.1	.7	15.3	.6	15.9	.9
Hepatitis C virus infection, %		2.3	2.2	.8	2.2	.7	2.2	.8
Donor characteristics								
Median (IQR) age, y		45.0 (35.0-53.0)	42.0 (33.0-51.0)	<.001	45.0 (35.0-53.0)	.5	44.0 (34.0-52.0)	<.01
Female, %		62.3	62.1	.9	65.4	<.01	61.8	.7
African American, %		10.5	11.1	.4	7.7	<.001	7.5	<.001
Hispanic, %		10.1	14.4	<.001	10.5	.6	10.1	1.0
ABO incompatible, %		2.2	1.6	.04	1.8	.3	2.2	.9
0 HLA mismatch, %		0.8	7.3	<.001	0.4	.02	0.8	1
Median (IQR) cold ischemia, h		8.7 (5.2-12.0)	1.0 (0.7-2.0)	<.001	1.0 (0.7-2.0)	<.001	1.4 (0.8-3.0)	<.001
Median (IQR) BMI, kg/m <sup>2</sup>		26.2 (23.3-28.9)	26.7 (23.8-29.7)	<.001	26.6 (23.8-29.6)	<.001	26.3 (23.6-29.3)	.03
Median (IQR) eGFR, mL/min/1.73 m <sup>2</sup>		102.2 (85.8-115.1)	104.0 (87.8-117.2)	<.01	103.4 (87.4-116.1)	.02	102 (85.8-115.0)	.9
Biologically related, %		5.5	53	<.001	0	<.001	0	<.001

NKR, National Kidney Registry; UNOS, United Network for Organ Sharing; KPD, kidney paired donation.

## cPRA Ranges: NKR vs. UNOS Controls 2008-2017



**FIGURE 3** The distribution of cPRA at transplant for National Kidney Registry kidney recipients vs recipients of United Network for Organ Sharing (UNOS) all live donors, UNOS living unrelated donors, and UNOS kidney paired donors

**TABLE 3** Methods of desensitization used by National Kidney Registry transplant centers for ABO- and/or HLA-incompatible recipients (N = 2037 recipients over 9 years)

Treatment	Patients receiving therapy, n
Intravenous Ig/cytomegalovirus Ig	207
Plasmapheresis	86
Thymoglobulin	51
Bortezomib	6
Rituximab	39
Ecilizumab	4
Splenectomy	1

to enter as a compatible pair, the mean age difference between the paired and actual donors was 23.1 (range 11-42) years. The remaining pairs seeking an anatomic or HLA advantage, or the absence of DSAs, were successfully matched. By entering these compatible pairs, 146 additional transplants were facilitated, and of these, 43 recipients were transplanted with a cPRA >80%.

### 3.4 | Untransplanted patients

When reporting actual KPD results, it is important to identify who was not transplanted once entered into paired exchange. At the end of February 2017, there were 280 unmatched recipients active for transplant. Not surprisingly, the majority were blood group O and were hyperimmunized. The actual distribution was ABO: O (74%), A (14%), B (11%), and AB (1%). Those unmatched by cPRA were for cPRA of 0% (23%), 1% to 79% (22%), 80% to 95% (8%), 95% to 99% (18%), and 100% (29%). A better metric for tracking the accumulation of those recipients difficult to match for transplant may be the number of untransplanted recipients as a percent of those actually

transplanted at the end of each calendar year. As provided in Figure 4, since inception NKR has experienced a peak in unmatched recipients in year 2 (79%) that has fallen but leveled off at 35% to 40% during the past 3 years. In addition, the number of broken chains diminished each year to about 3% annually (Table 4). These often occur after the logistics for a swap have been made, but intervening conditions such as a change in donor or recipient medical status emerges. Some of these can be repaired by bridging a donor or with advanced donation.<sup>14</sup> More worrisome, but infrequent, are the number of real-time swap failures occurring after swaps have commenced on the day of exchanges. Since inception of the NKR program, there have been 8 (0.4%). These real-time swap failures were repaired within the network by end-of-chain paybacks according to established policy.<sup>8,15</sup>

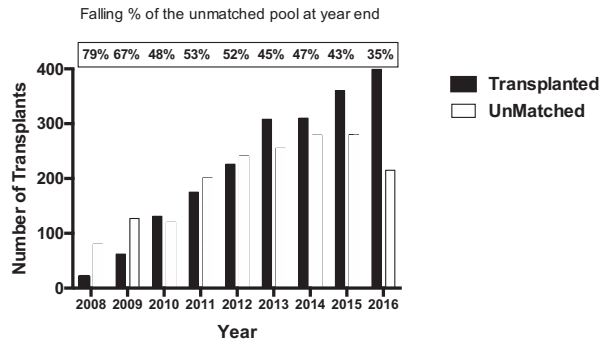
## 4 | DISCUSSION

During the past 15 years, there has been a substantial effort to increase live donor kidney transplant through KPD, beginning as single-center internal swaps to organized networks such as the NKR.<sup>3-7,16,17</sup> These swaps have primarily been composed of 2, 3, or more simultaneous exchanges (loops) and nonsimultaneous chains driven by nondirected donors. As reported to UNOS, national KPD numbers have increased from <10 in 2002 to 450 in 2010, to 587 in 2015, and to 642 in 2016.<sup>18</sup> The underlying motivation for this effort is to transplant more recipients with compatible live donor kidneys, which has been demonstrated to result in less delayed graft function, better measured kidney function, and longer graft survival and to diminish deceased donor candidate rolls.<sup>18,19</sup> The NKR is a voluntary program available to transplant centers governed by a medical board that establishes rules for sharing kidneys that are compliant with current national regulations and policies for living kidney donation and transplantation. These regulations and sharing paradigms are transparent and publically available at [https://kidneyregistry.org/transplant\\_center.php#policies](https://kidneyregistry.org/transplant_center.php#policies).

The evolution of the NKR has been a continual process of introducing innovations and solutions to problems as they arise to ensure an efficient workflow. These advances are first suggested, then modeled in small test series, then validated in real-time practice, and finally approved by the NKR Medical Board. Once implemented, new policies are posted on the NKR website and educational programs are provided for the member centers. The following are 5 examples of major policy changes that have streamlined the practice of KPD and removed logistical barriers that delayed or cancelled actual transplants. First, a donor pre-select function on the website is used to accept or decline all potential donors in the pool for a newly enrolled recipient. By excluding donors with anatomic, physiologic, or immunologic incompatibilities, centers avoid undesirable matches that could disrupt chains. Second, the implementation of a cryopreserved bank of donor cells for each enrolled kidney donor permits repetitive crossmatching and exploratory crossmatching of highly sensitized recipients without depending on the acquisition additional blood



Annual NKR Transplants vs. Unmatched Recipients



**FIGURE 4** End of year number of actual National Kidney Registry transplants vs those unmatched candidates remaining in the pool

from donors. Third, the introduction of large server capacity to store all donor computed tomography scanning on the website, available when kidney donors are first enrolled, permits rapid decision-making by recipient centers as to donor anatomy and acceptability when the matches are first made. Duplicate imaging, separate consent for imaging, time for shipping images, and so on are, thus, eliminated. Discussions between donor and recipient surgeons are also facilitated. Fourth, the introduction of the advanced donation and voucher programs has permitted the repair of many short-term chain disruptions and helped support donors in completing their individual decisions to proceed with kidney donation.<sup>14,20</sup> Fifth, applying strict deadlines for logistic calls and kick off calls between the centers and the NKR facilitators can detect and repair any disruptions as the swaps unfold.

An important feature of NKR is the participation of small, medium-sized, and large kidney transplant programs in all regions of the United States. The participating centers also represent densely urban, suburban, and rural populations and both academic and community-based programs that include a broad spectrum of donors, recipients and clinical practices. Therefore, is the population of patients transplanted through the NKR in some way different or

narrowly selected compared with other live donor transplants at the current time? Are changes needed to detect and manage discrepancies or the lack of opportunities for potential recipients and donors?

The answer to these questions appears to be “no” (Table 2). The demographics of the NKR recipients and donors demonstrate similar diversity to the overall numbers in the United States for all live donor transplants, for all living unrelated transplants, and for other KPD exchanges. In particular, the proportion of patients who are older, female, or a racial minority or those on public insurance are similar or overrepresented in the NKR compared with the other control populations used in this study. This is perhaps not surprising considering the inclusion of transplant centers from all geographic regions and population density previously mentioned. It would appear that the same clinical selection criteria and financial screening practices that govern in-center live donor kidney transplantation apply to KPD on a national level.<sup>10</sup> It is important to emphasize that selection criteria and eligibility characteristics for donors and recipients are made by each transplant center, not by a centralized body. No group of patients with end-stage renal disease appears to be restricted from the opportunity for paired exchange.

The characteristics for the actual NKR kidney donors also do not appear to be substantially different from those of the national controls (Table 2). The median age, BMI, eGFR, and percentage of donors who were female or a minority were all within similar clinical ranges, although a few statistical differences emerged between black donors (NKR 10.5% vs all living unrelated donors 7.7%,  $P < .001$ ) and fewer female donors (NKR 62.3% vs all living unrelated donors 65.4%,  $P < .01$ ).

The results reported here suggest that the NKR is actually transplanting a somewhat more difficult-to-match population of recipients. The NKR recipients represented a significantly ( $P < .001$ ) increased number of retransplants (25.6%) compared with the controls (11.5%, 12.3%, and 16.1%), even though the number of preemptive (dialysis-free) transplants (35%) is about the same. While comparing the risk for medical morbidity is limited in such a registry analysis, surrogate markers such as the proportion of persons with diabetes, with hypertension, and with hepatitis C virus infection and age were

Year	Bridge donors, n	Broken chains, n	Broken per year, %	Real-time swap failures, n
2008	9	3	33	0
2009	29	2	7	1
2010	61	2	3	0
2011	75	0	0	0
2012	54	4	7	0
2013	37	3	8	3
2014	49	4	8	2
2015	53	1	2	1
2016	68	2	3	1
2017	64	1	3	0
Total	499	22		8 (0.4%)

**TABLE 4** Broken chains each year

about the same for all groups. The reported outcomes for the NKR transplants equaled or exceeded the control groups for all-cause graft survival (Figure 2). This may be explained by the fact that the majority of NKR transplants were both ABO compatible and HLA crossmatch negative. When KPD exchanges produce compatible transplants, excellent results have been reported in both the United States and other parts of the world.<sup>7,21-24</sup> In addition, as recently reported in depth, the shipping of kidneys during paired exchange has not been associated with inferior transplant outcomes.<sup>25</sup> Although the number with primary nonfunction (0.34%) was low, the number with first week dialysis (4.9%) is higher than in-center exchanges. Some have suggested that live donor kidneys older than 55 years may be more susceptible to extra CITs.<sup>26</sup>

As reported in Figure 3, the NKR recipients were significantly ( $P < .001$ ) more sensitized to HLA, perhaps related to the greater numbers of retransplants, than were the controls. Notably, 22.7% of NKR recipients had a cPRA >80%, 7.4% had a cPRA >98%, and 2.5% were both blood group O and had a cPRA >98%. Many of these recipients were unable to find a suitable deceased donor kidney as well. While HLA sensitization leading to donor-specific crossmatch reactivity is a primary indication to enter paired exchange, it is also a leading indicator of waiting time once enrolled. The NKR has not intentionally limited or discouraged entering highly sensitized recipients into the network. While the number of KPD transplants that were ABOi (2.2%, excluding A2 into O) or were intentionally desensitized (11.7%) were not common, this may be an area for future growth.<sup>27,28</sup>

Some have speculated that the accumulation of hyperimmunized O recipients with non-O donors will overwhelm paired exchange networks,<sup>29</sup> but these concerns appear to be unwarranted (Figure 4). The unmatched pool of candidates at year's end has in fact declined to about 35% to 40% of those transplanted, although the predominant characteristics of those unmatched candidates were 74% ABO blood type O and 29% cPRA = 100%. While the difficulty to find donors for these hard-to-match recipients has thus far depended on the entry of blood type O nondirected donors for chain initiation, future expansion of KPD via increasing network pool sizes, compatible pair enrollments,<sup>9</sup> the possibility of deceased donor chain initiation,<sup>30</sup> and global sharing<sup>31</sup> may further expand these opportunities.

The limitations of this study are similar to those present in any registry-based analysis. While some data were not collected or lacked granularity, by merging both the national and local (NKR) data sets, we were able to capture a wide array of relevant covariates. Although such a merge may be redundant for some variables (ie, race, sex, insurance), it reduced missing data to <2% for each category. On a center level, it is not known how many potential KPD patients were evaluated and ultimately excluded based on local medical or psychosocial criteria. There were certainly center-level decisions made for donor acceptance criteria such as the degree of allosensitization or anatomic or physiologic risk:benefit determinations for a particular swap.

In conclusion, the practice of KPD in general and the NKR network in particular is expanding annually, offering the opportunity for compatible live donor kidney transplant to more patients. The demographic

and clinical characteristics of those actually transplanted appear similar to contemporary national trends. However, an analysis such as this do not fully capture the enormous number of logistic considerations that need to be accommodated between patients, families, and transplant centers. These results encourage broader sharing and larger pool sizes to unlock more opportunities for harder-to-match pairs.

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## DISCLOSURE

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