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Expanding Kidney Paired Donation Through Participation by Compatible Pairs

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In kidney paired donation (KPD), incompatible pairs exchange kidneys so that each recipient receives a compatible organ. This modality is underutilized partly because of the difficulty of finding a suitable match among incompatible pairs. Alternatively, recipients with compatible donors might enter KPD arrangements in order to be matched with a donor predicted to give greater allograft durability or for other altruistic reasons. Using simulated donors and recipients, we investigated the impact of allowing recipients and their compatible donors to participate in KPD. For KPD programs of any size, the participation of compatible donor/recipient pairs nearly doubled the match rate for incompatible pairs (28.2% to 64.5% for single-center program, 37.4% to 75.4% for national program). Legal, logistical, and governmental controversies have hampered the expansion of KPD in the United States by delaying the creation of a national program. The inclusion of compatible pairs into small single-center pools could achieve match rates that would surpass that which could be realized by a national list made up of only incompatible pairs. This new paradigm of KPD can immediately be instituted at the single-center level, while the greatest gains will be achieved by incorporating compatible pairs into a national program.

Key words: Altruistically unbalanced exchange, blood type incompatibility, donor exchange, incompatible donors, live donor kidney transplantation, paired kidney exchange

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Introduction

Kidney paired donation (KPD) is emerging as a viable modality for transplanting patients with incompatible living donors by matching them to pairs with reciprocal incompatibilities (1–3). Through KPD, the pool of kidney donors can be expanded to include live donors who might otherwise not have been afforded the opportunity to donate to a loved one. Although estimates indicate that several thousand patients each year cannot receive a kidney from a healthy, willing donor because of blood type or HLA incompatibilies, only 145 patients have been transplanted through KPD in the United States, suggesting that significant barriers to utilization exist (4).

Efforts to expand KPD have included: a proposal for a nationwide KPD registry and match run (5,6), using optimization algorithms to match pairs (6,7), including three-way matches (1,8–10), combining KPD with desensitization by relaxing the requirement for a negative crossmatch for highly sensitized patients (1,11), and involving nondirected donors in KPD (12,13).

Even in an optimized, national KPD program, fewer than 50% of incompatible pairs are predicted to find a match. The chances of matching are considerably lower in single-center or regional programs (6). This is primarily due to the blood group imbalance in the pool of incompatible pairs (14,15). Because most blood group-O donors can give directly to their intended recipients, O donors will rarely need to enter a KPD pool, with the exception being those who have a positive crossmatch with their recipient. Therefore, O recipients in the KPD pool who must rely on scarce O donors will have difficulty finding a match. Some have suggested that enrolling compatible pairs with O donors in KPD could increase the match rate for the incompatible pairs (16,17). Compatible paired donation (CPD) is pictured in Figure 1.

KPD between compatible and incompatible donor/recipient pairs has previously been referred to as 'altruistically unbalanced' (18). This critical terminology suggests that only compatible pairs with altruistic intentions would be interested in participating in such a program, and that such pairs may feel coerced to do so. Although the potential benefit to compatible pairs for participating in KPD has never been rigorously studied, there may be some cases in which these pairs do stand to benefit directly from participation,

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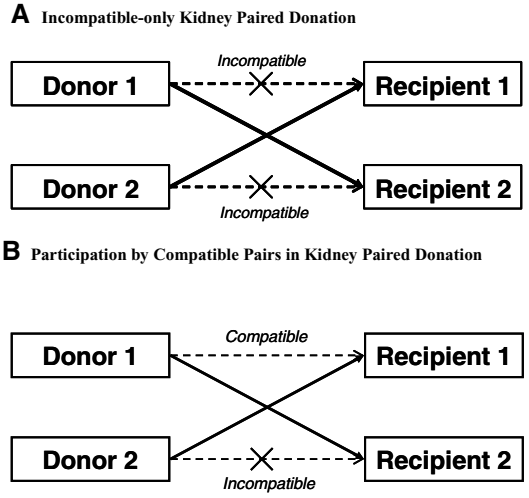

Figure 1: Strategies for expanding the pool of live donor kidneys. (A) The current paired donation system. Only donors who are ABO-incompatible or crossmatch-incompatible with their intended recipients are included in the pool. (B) The proposal to allow participation in kidney-paired donation by compatible donor/recipient pairs. Compatible pairs might benefit by finding a better donor for their recipient, such as one who is younger or more immunologically favorable.

thus eliminating the purported unbalance. Even if it were true that no such benefits could be realized such that only altruistically motivated pairs would be interested in participating, this does not in any way suggest that there is anything *prima facie* wrong with such altruistic motivations. Kranenburg et al. have suggested that concerns about the potential coercion of donors under an altruistically unbalanced donation arrangement can be addressed prospectively by the transplant team and that the time has come to consider such altruistic acts as valid and valuable rather than with suspicion (19). Regardless, in some cases these paired donations might benefit both the compatible and incompatible pairs by matching recipients to donors predicted to produce a longer graft half-life or a lower risk of rejection.

There are at least two ways in which a recipient with a compatible donor might directly benefit from participating in paired donation: (1) by finding a younger donor, or (2) by avoiding a high immunologic risk donor/recipient combination (child-to-mother or husband-to-wife). Donor age has been identified as the most significant factor influencing long-term outcomes of living donor kidney transplants (20). Of 1300 direct donations per year from blood group-O donors to non-O recipients, over 20% involve donors over age 50, and 3–5% involve donors over age 60 (4). For a female recipient, even with a negative crossmatch to her donor, antibody-mediated rejection may occur in a mother who receives a kidney from her offspring or the father of her child due to exposure in utero to paternal HLA antigens (21). Of direct donations to non-O recipients from blood group-O donors, nearly 20% were to a female recipient from her spouse or offspring (4). Although the significance of these benefits may remain 'unbalanced' for the different pairs, such unbalances are a common and accepted part of the current practice of KPD.

Alternatively, a compatible pair might enroll in KPD for purely altruistic reasons, in the hopes of facilitating a live donor transplant for one or more recipients with incompatible donors. To date, over 9000 healthy people have donated kidneys to recipients who were unrelated to them, with unrelated nonspousal donors representing over 20% of live donor transplants since 2003. Furthermore, over 400 people have come forward to be live donors with no particular recipient in mind, and this number is increasing every year (4). It would be reasonable to predict that some donors with compatible recipients would enter into KPD with similar altruistic motivations, particularly because they have committed to live donation and have direct experience with the impact of renal failure on a loved one.

Using simulated donors and recipients, we project the impact of compatible pair participation on KPD, both in single-center KPD programs and in the proposed national system. We characterize the blood group imbalance in the pool of incompatible donor/recipient pairs, and find that correcting it by the inclusion of recipients with compatible donors would have a profound effect on incompatible pair match rates. Further, we show that many compatible donor/recipient pairs could obtain a meaningful predicted graft survival benefit in recompense for the additional complexity of paired donation. We also demonstrate that this approach is consistent with accepted ethical tenets and could be implemented immediately by individual transplant programs while the operational and logistical challenges posed by a national KPD program are being overcome.

Methods

Simulated patients

Data about patients' incompatible live kidney donors are not currently collected. Using a decision tree model we have previously described, we simulated pools of donor/recipient pairs (6,15). Our decision tree adapts methodology originally developed by Zenios et al. (14). Recipients and their social networks of potential donors are created with blood types, ethnicity, HLA profiles drawn from UNOS data, population averages and inheritance for related individuals. Donors then undergo a virtual workup, which eliminates unwilling or medically unsuitable donors. If no donor can be found for a particular recipient, then that recipient is censored from our simulation. If any compatible donor is available, then that recipient and donor comprise a compatible pair. Otherwise, the recipient and one of his incompatible donors comprise an incompatible pair.

Demographics

Input demographics of the donor/recipient pairs are shown in Table 1 (15). The blood group breakdown for simulated pairs found to be compatible is shown in Figure 2. As shown in Table 2, donor age was assigned in 12 intervals of width 5 years except at the extremes, by the donor's relationship to the recipient, based on UNOS data (4).

Table 1: Demographic assumptions for all simulated donor/recipient pairs

Race of recipients	%
Caucasian	52.55
African-Am	30.45
Hispanic	17.00
PRA Range of recipients	
0–9	71.31
9–80	18.66
80–100	10.02
HLA-A,-B,-DR of donors and recipients	by race
Positive crossmatch rate by PRA	
PRA 0–9	5
PRA 10–80	45
PRA 80–100	90
Donor relationship to recipient	
Sibling	38.07
Friend	18.64
Parent	17.60
Child	15.92
Spouse	9.78

Number of pairs in pool

Two pool sizes were considered: first, a national registry with a monthly match run as proposed by UNOS (5) and second, a single-center program. The larger pools contained 250 incompatible pairs, representing the estimated monthly participation in a national KPD match (5,15), plus 539 compatible pairs, which was the number of live kidney donations per month in 2003. The single-center pools contained 25 incompatible pairs and 54 compatible pairs, based on similar derivations. To estimate the overall number of incompatible pairs transplanted within single-center programs only, we simulated a 3-month accumulation of incompatible and compatible pairs in the same proportion, scaled to each center's historical kidney transplant volume.

Optimized matches

In each match run, a graph-theoretic optimization algorithm determined which pairs should be matched so that the largest number of transplants would occur. A graph, as the term is used here, is a collection of nodes, each of which represents a single recipient and all of his available donors, and links (edges), which connect each pair of nodes if and only if a paired donation would be feasible between the two recipients and their donors. We simulated our patient databases using custom C++ code, compiled using g++ on a Linux 64-bit computer. The patients and their donors constituted the nodes of each graph, and the links of the graph were created by sequentially testing the reciprocal compatibility of each pair of nodes.

A typical paired donation graph will contain some nodes with many links, representing different options for paired donations involving those recipients. At most one link for each node can be realized as a paired donation. A matching is a subset of links on a graph that represents a feasible combination of paired donations. The optimization procedure that selects the best matching is known as the Edmonds algorithm after its originator (22), though more efficient implementations are used in practice (23,24). The third-party callable library LEDA version 5.2 (25), available from Algorithmic Solutions Software GmbH, provided graph construction tools and the optimization routines. Weights, which are positive integers describing the value of each link, were either 200 for matches between two incompatible pairs, or 100 for matches between a compatible and an incompatible pair. The optimal matching is the one with the largest cumulative weight, and an optimal matching was found using LEDA's MAX_WEIGHT_MATCHING function.

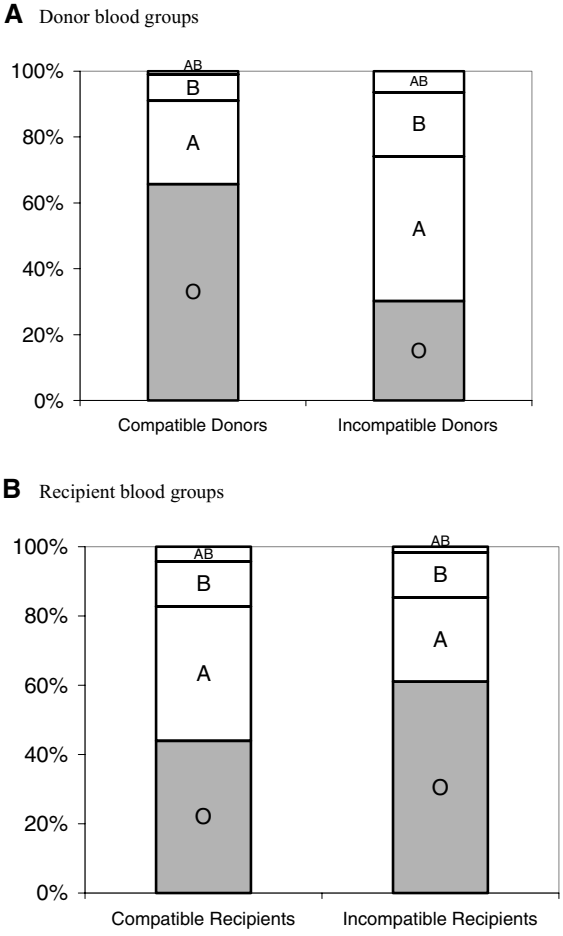

Figure 2: Blood groups of simulated compatible and incompatible donor/recipient pairs. (A) Donor blood groups. (B) Recipient blood groups.

The optimization algorithm maximized the number of incompatible pairs that matched, and only matched compatible pairs with incompatible pairs if such a match was necessary to enable a transplant for an incompatible pair. In some simulations, compatible/incompatible pair matches were limited to those which provided a benefit to the compatible pair, while other simulations allowed altruistic participation by compatible pairs, limited only to matches that did not cause a disadvantage to the compatible recipient. Because of the logistical difficulties of three-way donations, only two-way paired donations were considered. Figure 3 compares optimized matching, including compatible pairs, with the current system of excluding compatible pairs.

Definition of benefit to compatible pairs and altruistic participation

We considered compatible pairs to potentially benefit from a KPD match if: (1) the compatible pair had a donor whose age was at least two intervals (about 10 years) older than the matched donor and (2) the compatible pair had a female recipient with either a spouse or child donor and the spouse or child was in the same age range or older than the matched donor. Since there is equipoise in the literature about the effect of HLA matching on outcome, we chose not to consider improved HLA matching in our algorithm. Altruistic CPD was defined as a compatible pair enabling a novel match for

Table 2: Simulated donor age intervals, by relationship of donor to recipient

Age	Sibling (%)	Friend (%)	Parent (%)	Child (%)	Spouse (%)
0–20	3.23	2.47	0.46	5.75	0.21
21–25	9.51	9.17	2.39	18.67	2.10
26–30	13.45	11.67	5.29	22.40	6.60
31–35	16.43	14.43	9.55	22.23	10.87
36–40	17.81	16.38	14.37	17.70	14.16
41–45	16.40	15.80	18.19	9.25	17.62
46–50	11.69	14.34	18.21	3.34	17.88
51–55	7.00	9.05	14.96	0.56	15.03
56–60	3.21	4.57	10.14	0.08	9.25
61–65	1.03	1.53	4.46	0.02	4.56
66–70	0.21	0.47	1.57	0.01	1.30
71-max	0.05	0.12	0.41	0.00	0.41

an incompatible pair in which the donor of the compatible pair was no more than one age interval older or younger than the donor of the incompatible pair.

Statistical analysis

For each experiment, we performed 100 Monte Carlo simulations, creating two sizes of pools of compatible and incompatible donor/recipient pairs, as specified above. For each pool, three different match runs were conducted: one including only incompatible donor/recipient pairs, one adding all compatible donor/recipient pairs and one adding only the subset of compatible donor/recipient pairs who would benefit from KPD. We calculated the match rate for incompatible pairs per blood group combination in the three scenarios. For compatible pairs, we projected the number who would be involved in KPD matches for each scenario.

We separately determined the likelihood that recipients with compatible donors would benefit from KPD as the likelihood that a single compatible pair would find a match to a preferred donor from a pool of 25 incompatible donor/recipient pairs. All reported comparisons were statistically significant using a *t*-test (alpha < 0.01). Furthermore, we performed a sensitivity analysis to determine how varying levels of participation by compatible donors would affect the match rates for incompatible pairs. In these experiments, we assumed that only 10%, 20%, etc. of compatible pairs would be willing to participate in KPD, and that the remaining compatible pairs would proceed with direct donation.

Results

Blood types of compatible pairs

Blood group frequencies of donor/recipient pairs shown in Figure 2 were determined by simulation. CPD corrects the blood group imbalance seen in pools of incompatible pairs: while only 30% of incompatible pairs have O donors, 61% of incompatible pairs have O recipients. On the other hand, 67% of compatible pairs have O donors, and one-third of these donate to non-O recipients.

Match rates and impact of CPD

Participation by compatible pairs brings into KPD many donors of the blood types that would be in short supply among incompatible pairs, with the result that compatible pairs would greatly increase the match rate for incompatible pairs. Table 3 shows the percentage of incompatible pairs that could receive a transplant in each of the three scenarios, for both single-center and nationwide pools.

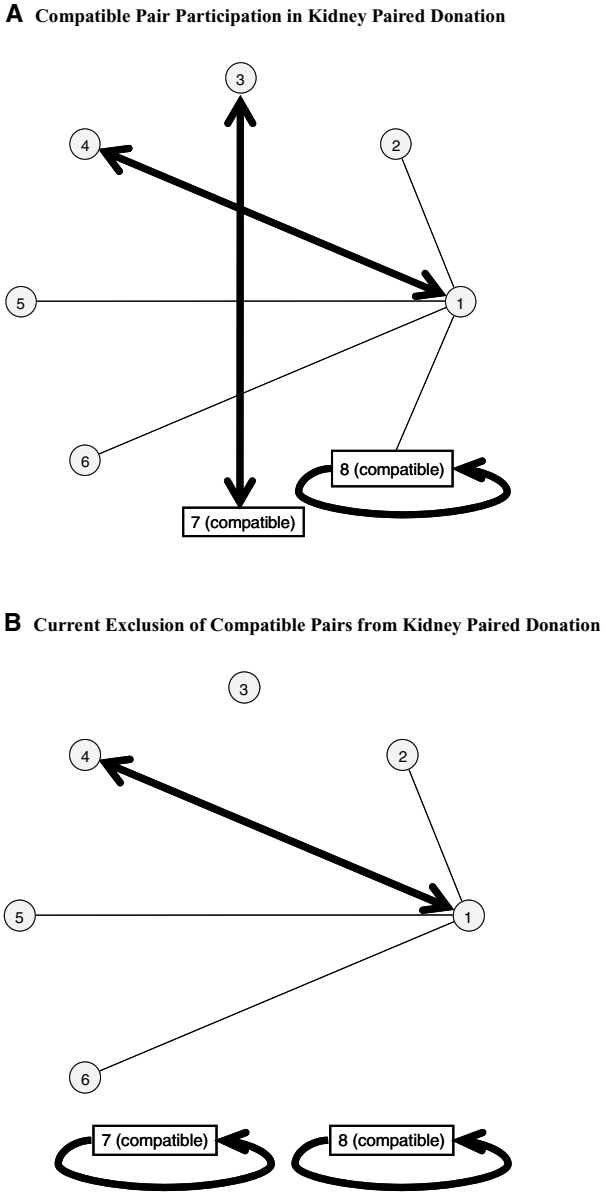

Figure 3: Incorporating compatible pairs into kidney-paired donation pools. (A) An optimized set of matches achieves 5 transplants in a pool of 6 incompatible pairs and 2 compatible pairs. Although compatible pair 8 has some possible matches, more transplants result if compatible pair 8 proceeds with direct donation, because incompatible pair 1 can match to other incompatible pairs. (B) The current practice of excluding compatible pairs from kidney-paired donation pools would result in only 4 transplants. The incompatible pair 3 is unable to find a match without the participation of compatible pairs, and so the donor of pair 3 does not donate and the recipient of pair 3 cannot receive a kidney.

Table 3: Average number and percentage of simulated donor/recipient pairs who find kidney paired donation matches, based on total number of pairs registered in the kidney-paired donation program

	Incompatible pairs (n = 25)		Compatible pairs (n = 54)	
Single-center program Participation in KPD	Number matched	% matched	Number matched	% matched
Incompatible pairs only	7.06	28.2	0	0
Including all compatible pairs who could benefit	13.42	53.7	6.36	11.7
Including all altruistic and benefiting compatible pairs	16.13	64.5	9.07	16.8
	Incompatible pairs (n = 250)		Compatible pairs (n = 539)	
National KPD registry, matched monthly Participation in KPD	Number matched	% matched	Number matched	% matched
Incompatible pairs only	93.62	37.4	0	0
Including all compatible pairs who could benefit	172.59	69.0	78.97	14.7
Including all altruistic and benefiting compatible pairs	188.61	75.4	94.99	17.6

Single-center KPD transplant programs could nearly double the proportion of incompatible pairs matched, from 28.2% to 53.7% by participation of compatible pairs that would gain a donor age benefit, and to 64.5% if additional compatible pairs motivated by altruism were included. For a national registry, incompatible pair match rates are 37.4% with only incompatible pairs, 69% with compatible pairs who benefit and 75.4% with all incompatible pairs included. Thus, nearly all of the advantage of matching incompatible pairs to compatible ones could be achieved by using only matches that benefit the compatible pairs.

The impact of CPD is substantiated by the finding that the number of transplants (1316 transplants) that could be garnered from the cumulative effect of single-center programs enrolling compatible pairs exceeds the number predicted to result from a national pool made up of only of incompatible pairs (1123 transplants). However, if every compatible donor/recipient who could benefit joined a national KPD registry, then an estimated 948 additional matches for incompatible pairs could be realized, bringing the total to 2071 annually.

Enabling KPD for all blood groups

Compatible participation in KPD would approximately double match rates for incompatible pairs. For instance, of incompatible pairs with blood group-O recipients, only 27% could match in an incompatible-only pool, while 71% could match if compatible pairs who benefit participated. Projected match rates for every blood group combination among incompatible pairs are shown in Table 4. The largest shifts that occur when compatible pairs participate in CPD are shown in the top row of the tables (O recipients) and the last column of the tables (AB donors), where match rates are dramatically increased.

In traditional KPD, we predict that 35% of incompatible pairs will fail to match because they cannot find a donor of the right blood group, and 27% will fail to match because they are broadly sensitized. With compatible participation, only 6% of incompatible pairs will fail to find a donor of the correct blood group, while 25% will still fail to match because of sensitization.

Compatible pair participation and benefits

A single compatible pair would have a 34% chance of finding a benefit through KPD in a center-based KPD program, and a 48% chance in a national registry (Figure 4). If, instead of just a few compatible pairs participating, all compatible pairs were willing to participate in KPD, then 11.7% of compatible pairs in single-center programs and 14.7% of

Table 4: Percentage of simulated incompatible pairs who can find matches in a national kidney-paired donation registry, by blood group of the donor and blood group of the recipient of the incompatible pair

Recipient \ Donor	O (%)	A (%)	B (%)	AB (%)
A. Match rates for incompatible pairs when compatible pairs do not participate				
O	54.2	13.7	15.0	1.0
A	59.9	49.7	74.8	12.9
B	57.6	74.1	45.9	10.6
AB	60.4	55.4	56.4	14.3
B. Match rates for incompatible pairs when compatible pairs who benefit participate				
O	59.1	78.5	78.1	42.5
A	63.0	56.1	85.3	67.4
B	61.0	85.3	54.0	63.7
AB	62.5	59.2	56.4	38.1
C. Match rates for incompatible pairs when compatible pairs all participate				
O	61.5	89.3	87.9	67.9
A	65.0	58.3	86.7	82.5
B	63.3	87.5	54.5	82.1
AB	65.6	59.9	56.4	42.9

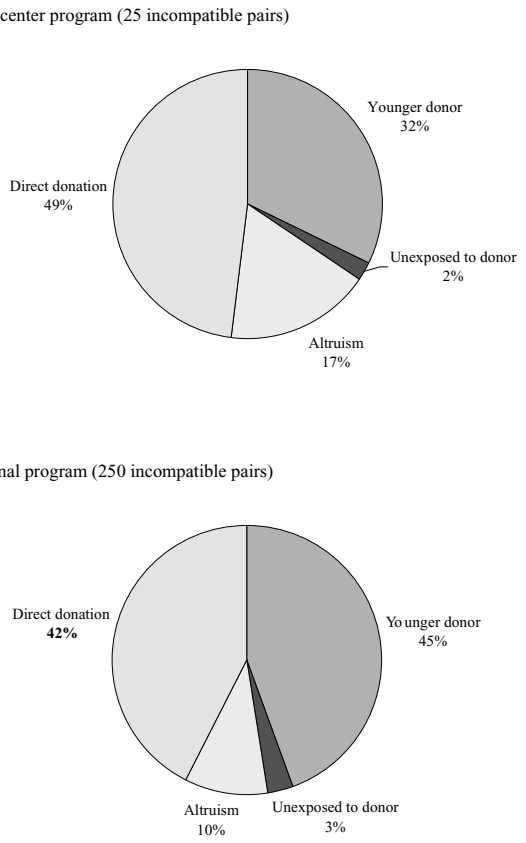

Figure 4: Likelihood that any one compatible pair will match in KPD, if no other compatible pairs participate. A compatible pair may benefit if they match with a younger donor. A female recipient may benefit if she matches to a nonspousal, nonoffspring donor, because she finds a donor of a similar age and to whose antigens she has not been exposed. A compatible pair may participate altruistically if the recipient can be matched to a medically similar donor. Some compatible pairs cannot benefit themselves or others by matching in the kidney-paired donation pool, and would then proceed with direct donation. (A) Single-center program (25 incompatible pairs). (B) National program (250 incompatible pairs).

compatible pairs in a national system would be projected to find a more favorable donor through KPD (Table 3). Note that if a large number of compatible pairs are interested in seeking a better match through KPD (Table 3), the chances for a compatible pair to find a match are lower than if only one compatible pair enters a KPD program in search of a better donor (Figure 4). This is true because all of the participating compatible pairs hope to match to a fixed number of incompatible pairs with young donors.

Donor age in compatible pair KPD matches

Donor age of simulated pairs was assigned in intervals that are generally 5 years wide. Figure 5 shows the distribution of donor age differences in KPD matches involving compatible pairs in a single-center program. The mode of the distribution is a two age interval difference between the donors of the compatible pair and the incompatible pair; in other words, the most frequent scenario gives the recipient of the compatible pair a donor who is roughly 10 years younger than the original intended donor. If compatible pairs participate altruistically, about 45% of the matches involve very small age differences of about 5 years in either direction. If compatible pairs only participate when it benefits them, then 70% of the matches involve either a 10 or a 15 year age difference, 19% of the matches involve an age difference larger than 15 years and 11% of the matches involve lower immunologic risk.

Impact of compatible pair participation rate

Although we have shown that a significant proportion of compatible pairs would directly benefit from participation, we cannot say what proportion of compatible pairs would be willing to participate in KPD. Still, any level of participation by compatible pairs would have a significant effect on the match rate for incompatible pairs, as shown in Figure 6. For a small pool of 25 incompatible pairs, even 10% participation by compatible pairs would result in a 26% increase in the number of incompatible pairs matched. If only half of compatible pairs registered for a national KPD match, about 70% of the potential increase in the incompatible pair match rate could be achieved. Compatible pair participation in even very small incompatible pools could enable incompatible pairs to match at rates that rival a national paired donation registry without compatible participation (Table 5). In a program with 15 incompatible pairs registered and 40% of compatible pairs willing to consider paired donation, 39.6% of incompatible pairs are predicted to match. In a national paired donation program that excludes compatible pairs, only 37.4% of incompatible pairs are predicted to match.

Characteristics of matched incompatible pairs with and without compatible pairs

While overall incompatible match rates in small programs with compatible pairs may be comparable to incompatible match rates in a national program excluding compatible pairs, the populations who match will be different (Table 6). Highly sensitized recipients will be more likely to match in a national program excluding compatible pairs (3.9%) than in a single-center program with 15 incompatible pairs and 40% compatible participation (0.3%). However, O recipients with A donors are less likely to match in a national program excluding compatible pairs (13.9%) than in the aforementioned single-center program (24.6%).

Conclusions

As the crisis in organ supply deepens, it is incumbent upon the transplant community to maximize donations wherever possible and morally justifiable. Traditional KPD will be limited by the blood group imbalance in the population of recipients with incompatible donors. If recipients with

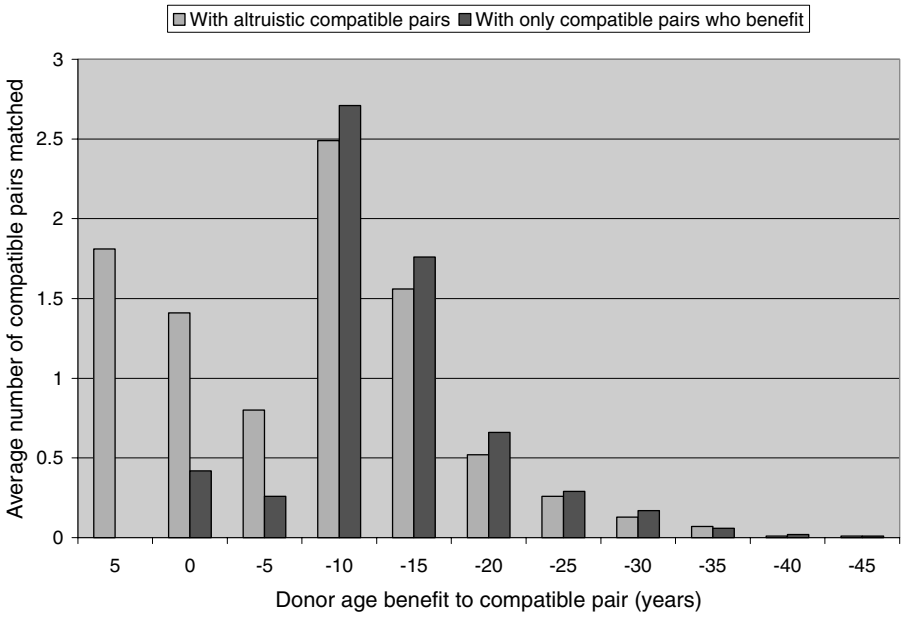

Figure 5: Average number of compatible pairs, in single-center programs with 25 incompatible donors, who match to a younger or similar age donor in kidney paired donation. Ages of simulated donors are assigned in intervals of 5 years, and the age difference between donors separated by one interval boundary is roughly 5 years. A donor age difference of 5 years means that a compatible pair has matched to a donor who is about 5 years older than the compatible pair's donor. At or beyond a 10 year donor age difference, the compatible pair is considered to have received an age benefit by matching to a younger donor through kidney paired donation. Some compatible pairs benefit because a female recipient avoids receiving her husband's or child's kidney, but do not receive an age benefit because their matched donor is about the same age or only 5 years younger than their intended donor. In both scenarios pictured, it is assumed that 100% of compatible pairs are willing to participate in kidney paired donation.

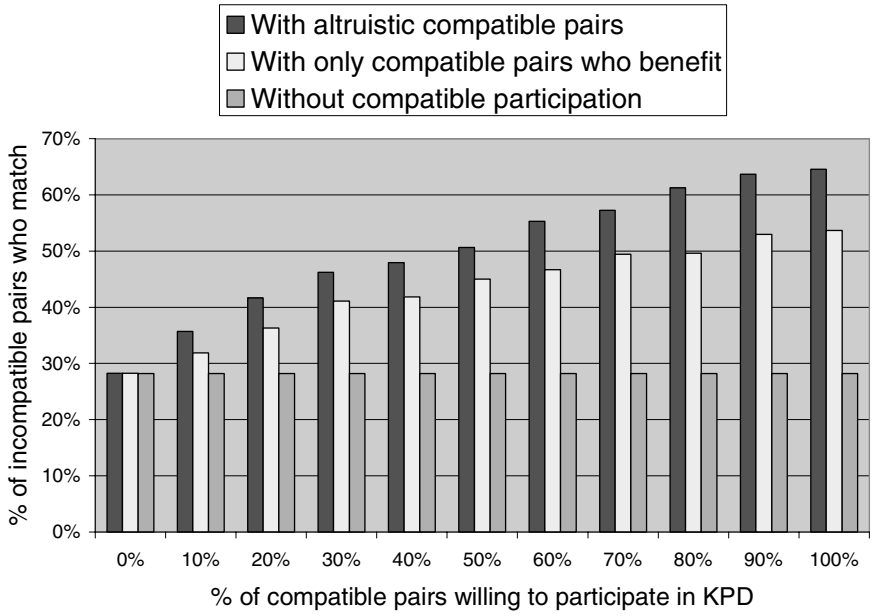

Figure 6: Percent of incompatible pairs in single-center programs who can be matched for kidney paired donation. On the horizontal axis are varying assumptions about the proportion of all recipients with compatible donors who would participate in a kidney paired donation registry. Compatible pairs who benefit include those who match with a younger donor, or whose female recipient matches to a nonspousal, nonoffspring donor. Altruistic compatible pairs are those whose recipient can be matched to a medically similar donor. Some compatible pairs would proceed with direct donation even though they are included in a paired donation registry.

Table 5: Percentage of incompatible pairs who could be matched for kidney paired donation, in programs with varying numbers of incompatible pairs and a varying rate of participation by compatible pairs who could benefit from a paired donation match[1]

Percentage of the compatible pairs who could benefit who are also willing to participate	Number of incompatible pairs in pool				
	15	25	50	100	250
0%	22.4	28.2	32.8	35.0	*37.4*
10%	27.8	32.0	**37.8**	**40.9**	**42.0**
20%	34.0	33.8	**40.4**	**44.4**	**46.6**
30%	33.8	**40.2**	**43.8**	**47.1**	**51.3**
40%	**39.6**	**39.9**	**46.8**	**50.7**	**53.8**
50%	**41.1**	**45.4**	**49.3**	**53.1**	**58.4**
60%	**40.3**	**47.0**	**52.7**	**56.9**	**61.1**
70%	**44.2**	**48.0**	**53.6**	**59.2**	**63.5**
80%	**45.9**	**52.6**	**56.7**	**61.0**	**66.1**
90%	**48.2**	**54.1**	**58.2**	**64.4**	**67.3**
100%	**50.1**	**53.6**	**58.8**	**64.5**	**69.0**

[1]Altruistically motivated CPD is not considered.
The boldface numbers highlight programs for which the incompatible pair match rate with compatible participation is greater than the incompatible pair match rate in a national program without compatible participation (in italics).

compatible donors participated in KPD, they would create match opportunities for many incompatible pairs. Nationally, including compatible pairs in KPD would enable almost a thousand kidney transplants each year that would not occur through traditional KPD.

In many cases, KPD can offer predicted allograft survival benefit to a recipient with a compatible donor. Moreover, the benefits of compatible pair participation can be obtained even in small single-center paired donation programs in which the logistical challenges of pairing with other centers are not present. In single-center simulations, we found that 34% of compatible pairs could benefit from paired donation. The incompatible pair gains an opportunity to receive a live donor kidney, and at least 80% of the matches would involve a donor no more than 15 years older than their intended donor. It is likely that recipients with incompatible live donors would prefer a compatible but somewhat older live donor to waiting (likely for years) for an unknown deceased donor.

We believe it is imperative that the transplant community finds ways to offer this opportunity to compatible pairs. The most compelling ethical objections that have been raised against expanding KPD to include compatible pairs are that it has the potential to be coercive and that it involves an altruistically unbalanced exchange arrangement. But these arguments are not sufficiently compelling to justify not moving forward with the implementation of this program. Moreover, given the potential benefits that would likely come from this program, it would seem paternalistic to bar compatible pairs from entering such a program. Worries about coercion can prospectively be addressed by transplant teams (18) in ways that are consistent with those in place for evaluating all persons who come forward to be evaluated for living donation. There is no reason to think that these donors should be evaluated with any more or less rigor than others coming forward to be evaluated for donation. Also, the idea that offering participation in KPD to compatible pairs would result in new and more pernicious forms of donor coercion seems dubious. If anything, these compatible pairs would seem to be *less* vulnerable to coercive influences than others who are not part of a willing and compatible pair; in this case, saying no costs them nothing. The other argument—that saying yes costs them too much and is 'unbalanced'—seems to miss what

Table 6: Comparison of characteristics of recipients with incompatible donors who find matches for kidney paired donation, under varying assumptions about the size of the incompatible pool and the participation rate of compatible pairs who could benefit from paired donation

Number of incompatible pairs	15	25	50	100	*250*
% of incompatible pairs matched	39.6	40.2	40.4	40.9	*37.4*
% of compatible pairs participating	40.0	30.0	20.0	10.0	*0.0*
% of O recipients with A donors matched	24.6	32.0	36.8	42.1	*13.7*
% of O recipients matched	30.0	35.9	39.5	43.7	*27.2*
% of highly sensitized recipients matched	0.3	0.7	1.3	2.0	*3.9*

The basis for comparison (shown in italics) is a national kidney paired donation program without the participation of any compatible pairs. These particular program sizes and incompatible participation levels are shown because each has a similar overall match rate for incompatible pairs.

may be the most morally relevant feature of altruism. As one of the authors (MS) has argued elsewhere, the altruism expressed by donation is an important part of what makes it morally praiseworthy; it displays unselfish regard to others, sometimes at risk to oneself (26). Rather than continuing to view such altruistic motivations as suspect and their outcomes as 'unbalanced', we suggest the transplant community consider abandoning attempts to assign gradations to the quality of one's altruism based on just how much one gives up. Altruistic donation by definition involves unselfish giving to benefit others, often at some cost to the donor. It will remain the job of the transplant community to ensure that the risks and costs these altruistic donors take on are both medically reasonable and medically justifiable.

We acknowledge the following limitations of our study. All donor and recipient data are simulated, because actual data about the characteristics of incompatible pairs do not currently exist. There will likely be differences among single-center programs in the case mix between compatible and incompatible pairs, which could mean that our projections are either too conservative or too optimistic. If there are very few incompatible pairs listed, then it will be less likely that a compatible pair can find a beneficial match. Regardless, the conclusion that compatible pairs will improve matching opportunities for incompatible pairs and also have a reasonable chance of finding a predicted organ survival benefit from participating in KPD, can likely be generalized to any case mix that will arise. This is supported by the sensitivity analysis in Figure 6, where even a modest 10% compatible pair participation demonstrated a tangible advantage. Similarly, although we have limited our analysis to two-way matches in consideration of the logistical complexity of a three or more-way match, we feel that our conclusions can be generalized to larger KPDs because the latter are still limited by the paucity of O donors in the pool.

These data provide at least two valuable insights. First, they show that the match rate for small KPD pools can be greatly enhanced by inclusion of compatible pairs. This would make it possible for single centers to create their own viable KPD programs without joining consortia, regional or national schemes. Matching at the single-center level would eliminate donor travel, donor separation from family members and familiar health care providers, increased cold ischemia time associated with shipping kidneys, the need for cooperation between transplant centers, standardization of protocols between centers and privacy and legal concerns. The data show that there would be more total transplants accomplished from single-center KPD pools that included compatible pairs than from a national program that included only incompatible registrants. We still strongly support a national program and the data clearly show that by including compatible pairs in a national pool most would not have to travel and the number of matches would be maximized. However, there are significant barriers to a national program and while those barriers are being addressed and overcome, CPD would allow the creation of productive single-center KPD programs.

Secondly, in a single-center program, a recipient with a compatible donor has a 34% chance of matching to a donor 10 or more years younger than their intended donor or avoiding a child-to-mother or spousal combination, and an additional 17% chance of matching to a similar donor, but one which altruistically facilitates a transplant opportunity for an incompatible pair. Thus, the majority of compatible pairs could achieve benefit from joining a KPD program.

In conclusion, the strategy of allowing compatible pairs to participate in KPD can be implemented immediately at the single-center level, allowing transplant programs to maintain control over their list and patients. Once the logistical barriers are overcome, a larger number of matches for all pairs would be achieved in a national program that allows compatible participation.

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