Nonsimultaneous Chains and Dominos in Kidney-Paired Donation—Revisited

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Since 2008, kidney exchange in America has grown in part from the incorporation of nondirected donors in transplant chains rather than simple exchanges. It is controversial whether these chains should be performed simultaneously 'domino-paired donation', (DPD) or nonsimultaneously 'nonsimultaneous extended altruistic donor, chains (NEAD). NEAD chains create 'bridge donors' whose incompatible recipients receive kidneys before the bridge donor donates, and so risk reneging by bridge donors, but offer the opportunity to create more transplants by overcoming logistical barriers inherent in simultaneous chains. Gentry et al. simulated whether DPD or NEAD chains would produce more transplants when chain segment length was limited to three transplants, and reported that DPD performed at least as well as NEAD chains. As this finding contrasts with the experience of several groups involved in kidney-paired donation, we performed simulations that allowed for longer chain segments and used actual patient data from the Alliance for Paired Donation. When chain segments of 4–6 transplants are allowed in the simulations, NEAD chains produce more transplants than DPD. Our simulations showed not only more transplants as chain length increased, but also that NEAD chains produced more transplants for highly sensitized and blood type O recipients.

Introduction

Kidney exchange (also called kidney-paired donation, [KPD]) allows patients with incompatible living donors to obtain transplants from other living donors, such as nondirected donors (NDDs) or donors belonging to other incompatible pairs (1–8). NDDs can either be matched to a recipient on the waiting list or to an incompatible pair, but in the latter case, the donor of the incompatible pair can be further matched to another incompatible pair and so forth (2,6). Thus, through appropriate matching, a single NDD can facilitate more than one transplant (2,6,9). A sequence of matches initiated by a NDD is called a *chain*.

Until recently, all the surgeries in a chain were done simultaneously (2,6,10,11). However when a chain begins with a NDD, the cost of a break in the chain is less than when an exchange is conducted entirely among patient–donor pairs, since no patient–donor pair needs to give a kidney before they receive one (6,9). Following the first report of a nonsimultaneous chain, a substantial number of nonsimultaneous NDD chains have been reported (10,11). Nonsimultaneous chains can be longer than simultaneous chains, since the larger number of operating rooms and surgical teams required by a long chain do not need to be assembled simultaneously. The desire to extend chains beyond the logistical capacity for simultaneous surgeries seems to be one of the motivations for some of the recently reported nonsimultaneous chains, along with the additional motivation of further extending the chain to as yet unidentified patients by recruiting the last donor in the chain to be a 'bridge donor' who can extend the chain at a later time.

Gentry et al. evaluated whether the risk of reneging in nonsimultaneous chains was justified by increased numbers of transplants compared with simultaneous chains by simulating these different methods for matching NDDs (12).
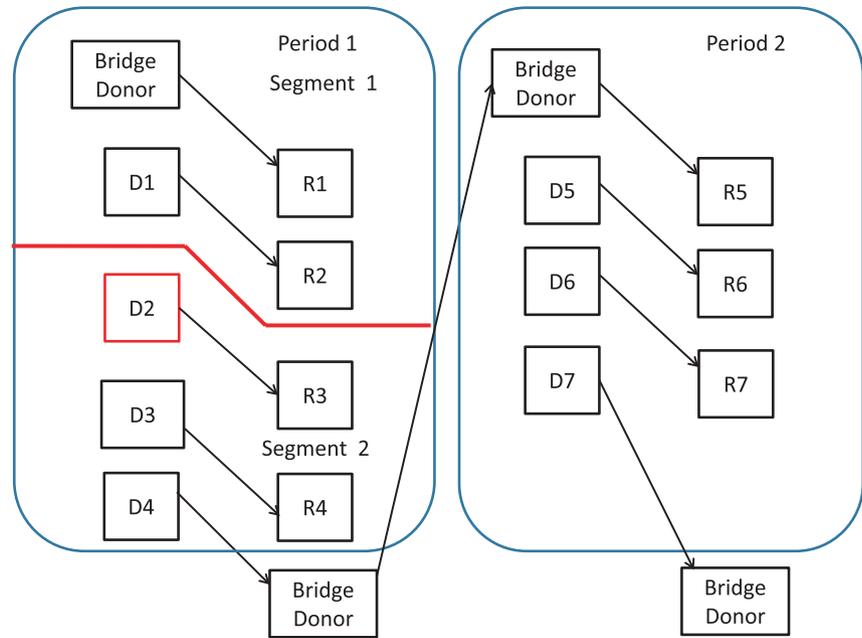
Figure 1: In the first period, a chain of length 4 is found and is divided into two segments. D2 becomes a short-term bridge donor and D4 becomes a (regular) bridge donor. In period 2, a chain of length 3 beginning with D4 is found and D7 becomes a bridge donor.

In the first method, called domino-paired donation (DPD), the NDD starts a simultaneous chain among incompatible pairs, with the donor in the last pair donating to a candidate on the waiting list without a willing, but incompatible donor (2,6). In the second method, the NDD initiates a non-simultaneous extended altruistic donor (NEAD) chain consisting of several segments (9). Each segment is a short simultaneous chain, where the last donor of each segment becomes a *bridge donor*. Thus, instead of giving to a candidate on the waiting list without a willing, incompatible donor, the bridge donor waits to be matched to another incompatible pair and initiate another segment.

Gentry et al. compared DPDs that involve at most two incompatible pairs and end with a simultaneous donation to a candidate on the deceased donor waiting list (for a total of three transplants) with NEAD chains in which each simultaneous segment contains at most three incompatible pairs and ends with a bridge donor that could continue the chain (also for a total of three transplants) (12). Their simulations suggested that DPDs would provide as many if not more transplants than NEAD chains and raised important questions about whether the risk of reneging in NEAD chains is warranted. In this paper, we utilize the actual clinical database of all pairs enrolled in the Alliance for Paired Donation (APD) to build a simulation model to test whether simultaneous DPD chains or NEAD chains would result in more transplants.

Our simulation is built on the output of the matching software of the APD using the entire dataset of all the incompatible pairs and NDDs that have been enrolled in the APD system since its inception in 2006. This APD matching software identifies potential matches as compatible based on

(1) the blood type of the donor and recipient; (2) a virtual crossmatch utilizing donor antigens (HLA A, B, Bw, Cw, DR, DRw and DQ) and recipient anti-HLA antibodies; and (3) the preferences of the incompatible pair and their transplant center such as the distance that they are willing to travel. A compatibility matrix was created of all the donors and recipients in the system and this matrix informed the simulations rather than artificially generated patients and assumptions.

To begin our simulations, we used the same assumptions as Gentry et al. and then we tested new assumptions—such as allowing longer chains—consistent with the actual clinical experience of the APD. We reproduce the results of Gentry et al. when we use the parameters they used. However, when we employ optimization that allows longer chains to be identified, the situation is reversed and nonsimultaneous chains facilitate more transplants. Given that many of the recently reported chains were significantly longer than three transplants, this modification may be critical in evaluating the potential impact of these two approaches.

Throughout our simulations, we retain the restriction of Gentry et al. that a simultaneous segment contains at most three incompatible pairs (i.e. we keep the logistical restriction of no more than six simultaneous surgeries). However, our simulations allow longer chains of length 4–6 to be identified, with the caveat that these chains would have short-term bridge donors that allowed shorter clusters of transplants within the chain to be performed simultaneously. For example, if we allow chains of at most length 4 within each period, then every chain of length 4 is divided into two segments each of length 2 (Figure 1). Thus, the

Table 1: Distributions (as a percentage of the entire pool) of blood types and PRA in the Alliance for Paired Donation Registry, the United Network for Organ Sharing Registry and in the general population according to the American Red Cross (17,18)

Source		Blood type				PRA level		
		A	B	AB	O	0–9	10–79	80–100
APD	Candidates	24.3	13.8	2.4	59.3	36.6	27.2	36.2
	Potential donors	42.5	14.9	6.6	35.8			
UNOS	Wait list candidates	27.6	16.6	2.6	53.1	59.5	21.7	16.2
	Living donor recipients	38.1	12.8	3.8	45.3	83.8	9.5	1.7
	Living donors	26.3	7.7	0.9	65.1			
General population	Caucasian	40	11	4	45			
	African American	26	19	4	51			
	Hispanic	31	10	2	57			
	Asian	28	25	7	40			

transplants in each segment can be done on consecutive days. Our main finding is that NEAD chains provide more transplants than DPDs when optimization including longer segments is enabled.

Methods

Data

In each of our simulations we use empirical data from the registry of the APD. Previous studies have generated data from simulated distributions (12–14). The empirical data includes 651 candidate/donor pairs and 73 nondirected and bridge donors in the registry of the APD. Each individual has a blood type, and each candidate also has a PRA. The APD uses the PRA values reported by the participating transplant centers. Virtual crossmatch is based on center-reported unacceptable antigen specificities identified by the participating center using their sensitivity cut-off criteria. Most centers identify their unacceptable specificities using flow cytometry- or Luminex-based testing and report a calculated PRA using the UNOS cPRA calculator (15). We do not have information of false positive virtual crossmatches as we do not perform actual crossmatches on patients with a positive virtual crossmatch. Seventy-two candidates were registered with more than one donor. The blood type and PRA distribution of candidates and donors in the registry is given in Table 1, which also gives the comparable figures for patients in the UNOS database and for the general America population by race according to the American Red Cross (16,17).

The dataset of the Alliance for Pair Donation used in these simulations consisted of a compatibility matrix that specified each donor's (including NDDs) computer-identified compatible recipients. These compatibilities were determined through blood compatibility, a virtual crossmatch and preferences such as whether the transplant center would accept a shipped kidney. In addition, a weight matrix was used for the optimization that assigned a weight to computer-identified compatible recipient/donor pairs based on waiting time, HLA match, PRA, prior crossmatch history and pediatric status. The simulations were completed by randomly selecting subsets of this dataset and assessing the outcome with the assumptions tested.

Base case

Each simulation consists of eight periods, each representing a month. Each period the population is generated from the empirical data using sampling with replacement. In our base case simulation, every period 30 incompatible pairs (a pair is a candidate and his/her incompatible donor(s)) and one NDD join the pool. (We also consider the case in which two NDDs join the pool every period, as in Gentry et al. (12)). In each period we run an optimal

matching algorithm that finds the maximum number of transplants that can take place using two-way and three-way exchanges (these do not involve NDDs), and DPDs or NEAD chains that begin with NDDs. Gentry et al. used simulated data and simulations over 24 periods (12). (The reason for running 8 periods rather than 24 as in Gentry et al. is computational complexity—the number of variables grows exponentially with the maximum chain length. To show consistency with the results of Gentry et al., we perform sensitivity analysis over 24 periods.)

Since computer matching uses a virtual crossmatch to identify compatibility, different types of failures can occur that will prevent a donor from donating to his/her allocated recipient (i.e. positive flow crossmatch or withdrawal of an incompatible donor). We incorporate a *failure rate* which is a probability that a computer-identified compatible recipient/donor (CIC R/D) pair cannot participate in the exchange. In case of any such failure between a given CIC R/D, we mark them as incompatible for the rest of the simulation. If a failure occurs in a chain, all the recipients before the link in which the failure occurs are transplanted. However, if a failure occurs in a simultaneous exchange (a cycle), then the entire cycle does not take place. The base crossmatch failure rates we use depend on the PRA level to reflect the increased likelihood of a positive crossmatch as a cause of the failure to proceed to transplantation (see Table 2). An additional exogenous failure we simulate can take place for various reasons such as sickness before the transplant. In all of our simulations, a CIC R/D remains compatible so long as no failure occurs between them and neither has left the pool.

The last donor in each segment of a NEAD chain becomes a *bridge donor*, i.e. a donor whose intended recipient has received a kidney and becomes a NDD for the next segment. To distinguish between bridge donors who initiate a new segment in the following period and those who initiate a segment within the current period, we refer to the latter as *short-term bridge* donors. A *short-term bridge* donor will likely donate within days to weeks, whereas a regular *bridge donor* may take months to continue their

Table 2: Distribution of crossmatch failure rates by recipient PRA. By the term *crossmatch failure rates*, we mean the likelihood that a computer-identified compatible match (by virtual crossmatch) will subsequently fail to result in a transplant because of a positive 'real-world' crossmatch involving donor cells and recipient serum

PRA level	Crossmatch failure rate
75–100	0.5
50–74	0.35
25–49	0.2
0–24	0.05

Table 3: Glossary of terms describing the policies simulated

1. DPD: each NDD initiates a chain of length at most 2, in which the last donor gives directly to a recipient on the waiting list. Thus DPDs produce up to three transplants including the recipient on the waiting list

2. NDPD-k (nonsimultaneous long DPDs): each NDD initiates a chain of length at most k, in which the last donor gives directly to a recipient on the waiting list. We will consider NDPDs of length k = 4 and k = 5. Thus a NDPD-4 produces up to five transplants including the recipient on the waiting list and similarly a NDPD-5 produces up to six transplants. If a chain of length 3 has been found (excluding the patient on the waiting list) it is divided into two segments in which the first segment is of length 2. If a chain of length 4 or 5 is found it is divided into two segments in which the first segment is of length 3. Chains of length 1 or 2 are considered as single segments

3. NEADk (nonsimultaneous long NEAD chains): each NDD initiates a NEAD chain where in each period a chain of length at most k is found. We will consider NEAD chains of length k = 3, 4, 5 and k = 6. If a chain of length 4 is found within a single period it is divided into two segments of length 2 each. If a chain of length 5 or 6 is found it is divided into two segments in which the first segment is of length 3

chain. Both types of bridge donors may *renege* or may not be able to donate in the next segment. In our base case we simulate this with probabilities of 0.5% for *short-term bridge* donors (*inter-renege rate*) and 1% (*renege rate*) for bridge donors, and vary these probabilities for sensitivity analysis. The difference between probabilities for each type of bridge donor reflects that for *short-term bridge* donors, the segment including the short-term bridge donor and the following bridge donor can be done in two consecutive days since these have been found simultaneously, whereas the segment following the bridge donor will not be found until the next period. After each period, incompatible pairs might also leave the pool. Thus at the end of each period, pairs that did not get a transplant leave the pool with an *attrition rate* we have estimated at 2%.

Optimization

In every period, we run an optimization algorithm on the current pool of incompatible pairs and NDDs to find the maximum number of transplants using two-way and three-way exchanges (cycles), and DPD or NEAD chains beginning with NDDs. Once the maximum number of transplants is determined, the software finds in this subset of solutions one with the maximum weight (i.e. optimizing waiting times, HLA matches, transplants for highly sensitized patients and children). Our simulations consider chains up to length six in each period, depending on the test we perform.

Policies and analysis

We considered the effects on kidney exchanges of the three policies presented in Table 3.

In the NEAD policies, the last donor in the chain of a period becomes a bridge donor. In the NEAD-4, NEAD-5 and NEAD-6 policies, a donor between segments within a period becomes a short-term bridge donor. In the NEAD chains, we do not allow bridge donors to have AB blood type (consistent with clinical experience and APD policy).

For each scenario we ran 200 Monte Carlo simulations. A 'Monte Carlo' simulation is one in which probability distributions are specified for various events (such as the probability of a patient having a certain blood type, a donor of a certain blood type, a positive crossmatch with another donor, etc.), and then many simulations are run in which each event is sampled from the appropriate probability distribution (18). The name derives from the concept that tracking the result of spinning the same roulette wheel at a casino in Monte Carlo many times would provide the likelihood of the wheel stopping at the different positions on the wheel.

We are mainly interested in (i) the ratio of the number of transplants between policies, (ii) the percentage of instances in which one policy produces more transplants than the other and (iii) the number of high PRA and blood type O patients who receive a transplant.

Results

In the first two scenarios, the failure rates are set to zero. We first simulate only DPD, NDPD-4, NEAD-3 and NEAD-4 over 24 periods (Figure 2) and then we run a similar simulation for all policies over eight periods (Figure 3). As mentioned above, scenarios with 'long' chain policies are run over eight periods due to computational (memory) complexity.

In both scenarios the DPD policy provides more transplants than NEAD-3 for renege rates higher than 0.05. This is similar to the results by Gentry et al. (see Figure 7 in Gentry et al.). However, when longer chains are allowed—either by introducing short-term bridge donors to DPD chains or by allowing longer NEAD chains—nonsimultaneous chains achieve more transplants than simultaneous chains. NDPD-4 consistently outperforms DPD and provides more transplants than both NEAD-3 and NEAD-4 except for small renege rates, and NEAD-6 and NEAD-5 provide more transplants than any type of DPD for renege rates smaller than 0.05 (see Figure 3). NEAD-6 provides 6–7% more transplants compared to DPDs with no short-term bridge donors.

Incorporating crossmatch failure rates

Having demonstrated that NEAD-5 and NEAD-6 policies performed better than other NEAD policies and/or DPD policies for renege rates of 5% or less, we continue our analysis by incorporating aspects not previously considered such as failure rates and short-term bridge donor renege rates as discussed in our base case parameters above.

In all simulations described below, crossmatch failure rates are incorporated (as in Table 2) that account for the crossmatch results that have been observed in clinically active KPD programs (the APD has experienced a positive flow crossmatch rate of 50% in patients with a PRA>80% and a negative virtual crossmatch, largely due to unspecified DP and DQ-alpha specificities).
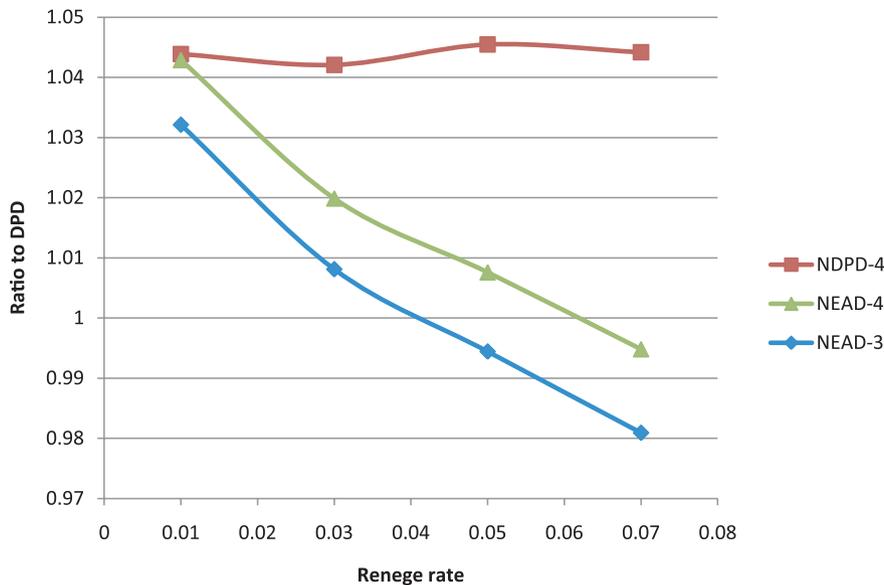
Figure 2: Reproduction of Gentry et al.'s simulation. The failure rate is set to 0 and the number of periods is 24. The y-axis is the ratio between the number of transplants in a given policy to the number of transplants in DPD. Observations above 1.00 reflect more transplants than from DPD.

Renege rate

We performed sensitivity analysis on the bridge donor renege rate, since the available clinical evidence—with no reneges observed in the APD and very few reported elsewhere—gives little basis for a reliable point estimate. The results are depicted in Figure 4. Notably, every NEAD policy produces more transplants than any DPD policy. For any renege rate, NEAD-6 provides 10% more transplants than DPD. As longer chains are allowed, the number of transplants increases: failures cause the compatibility matrix to be sparser, so fewer matches can be made and chains become more useful.

We also analyzed, for different pairs of policies, the percentage of instances in which one policy outperforms the

other. The results are graphed in Figure 5. In approximately 80% of the instances, NEAD-6 provides more transplants than DPD, and in approximately 60–65% of the instances NEAD-6 produces more transplants than NEAD-5. Of particular note, when incorporating a positive crossmatch failure rate consistent with actual clinical data, the result that DPD outperforms NEAD-3 as observed by Gentry et al. is reversed in 70% of instances, and overall NEAD-3 allowed 3–5% more transplants depending on the renege rate.

Highly sensitized and blood type O recipients

We also checked in the base case the percentages of high PRA (>80%) patients and blood type O patients who receive transplants as a surrogate marker for the quality
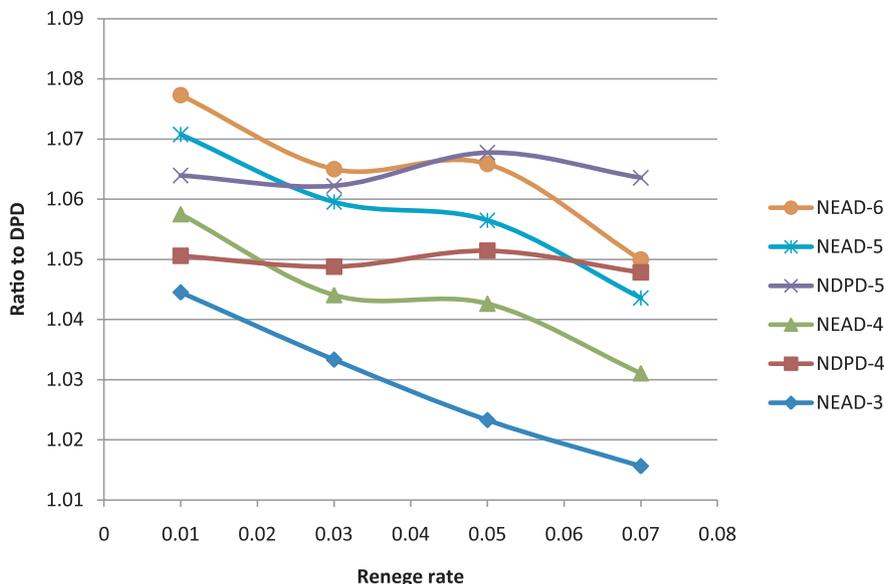

Figure 3: Comparing NEAD-k and NDPD-k policies to DPD. The failure rate is set to zero and the number of periods is 8. The sensitivity analysis is on renege rates of 0.01–0.07. The y-axis is the ratio between the number of transplants in a given policy to the number of transplants in DPD.
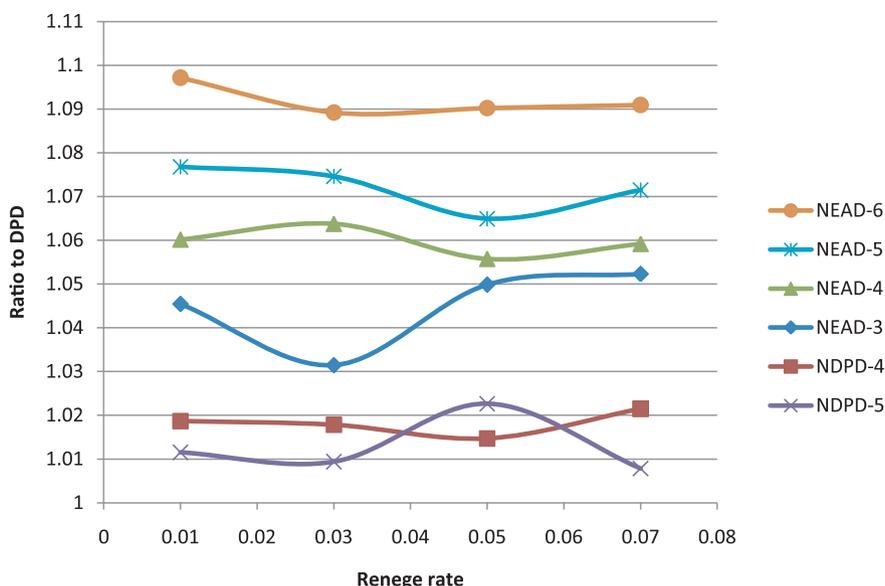
Figure 4: Comparing NEAD-k and NDPD-k policies to DPD, with sensitivity analysis on the renege rate from 0.01 to 0.07. Failure rate is set as in Table 2.

of transplants achieved by the different approaches. The number of highly sensitized and blood type O recipients transplanted increase when NEAD chains are used (see Table 4) as compared with DPD. The number of transplants in this hard to transplant group increases as k, the maximum length chain that can be scheduled, grows.

Exogenous failure rate

Figures 6–8 present sensitivity analyses on the exogenous failure rate (e.g. proposed donor rejected by recipient center for medical reasons), an additional failure rate that does not depend on a patient's PRA, as the one in Table 2 does. Figure 6 shows that the ratio between the number of transplants that NEAD policies produce to the number of transplants DPD policies produce increases as the exogenous

failure rate increases. When there is 16% exogenous failure rate, NEAD-6 produces 15% more transplants than DPD. This is a critical finding given that Hanto et al. found that less than 20% of the computer-identified compatible recipient/donors proceeded to transplantation (19). Note that long DPDs produce hardly any more transplants than DPD as the exogenous failure rate gets high.

Next we evaluate the average chain length of NEAD-k and NDPD-k chains given an exogenous failure rate varying from 0–16% (Figure 7). As longer chains are considered in the optimization, average chain length grows. This confirms the advantage of allowing longer chains. As both failures and reneging can occur, this result shows that policies that allow for longer chains produce more transplants
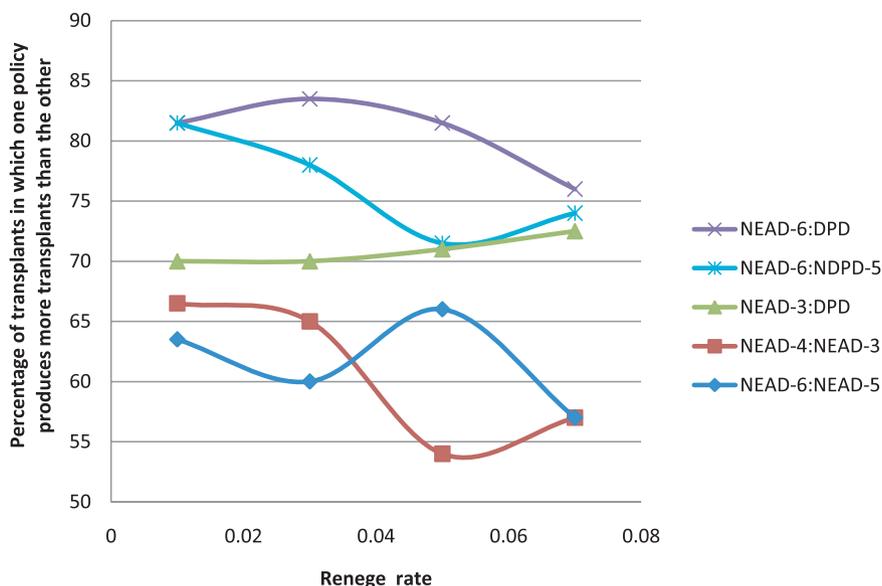

Figure 5: Significance of the results comparing NEAD-k and NDPD-k policies to DPD — percentage of instances in which one policy is producing more transplants than the other.

Table 4: The first row shows for each policy the ratio between the number of high PRA (PRA > 80%) recipients to the total number of high PRA patients that entered the pool. The second row shows the ratio between the number of high PRA recipients that were part of a chain to the total number of high PRA recipients (that were part of either a cycle or a chain). The third row shows the ratio between the number of recipients that have high PRA to the total number of recipients. The 4th–6th rows are similar ratios for blood type O patients

|	DPD	NEAD-3	NDPD-4	NEAD-4	NDPD-5	NEAD-5	NEAD-6
Percentage of high PRA patients receiving transplants	6.4/87.1 (7.3%)	8.4/87.1 (9.7%)	7.5/87.1 (8.7%)	9.7/87.1 (11.2%)	7.6/87.1 (8.8%)	10.2/87.1 (11.7%)	10.6/87.1 (12.2%)
Percentage of high PRA recipients receiving transplants in chains	1/6.4(15.7%)	3.4/8.4 (39.7%)	2.3/7.5 (31.3%)	4.9/9.7 (50.2%)	2.8/7.6 (36.3%)	5.8/10.2 (57.1%)	6.6/10.6 (62.6%)
Percentage of recipients that are high PRA	6.6/58.3 (11%)	8.4/65.7 (12.9%)	7.5/62.3 (12.1%)	9.7/67.2 (14.5%)	7.6/61.3 (12.5%)	10.2/68.1 (15%)	10.6/68.2 (15.6%)
Ratio of blood type O patients that receive transplants	18.5/138.5 (13.4%)	21.2/138.5 (15.4%)	21.1/138.5 (15.3%)	23/138.5 (16.7%)	21.2/138.5 (15.3%)	23.7/138.5 (17.1%)	23.8/138.5 (17.3%)
Percentage of blood type O recipients receiving transplants in chains	2.7/18.5 (14.5%)	6/21.2 (28.4%)	5.7/21.1 (27.3%)	8.4/23 (36.5%)	6.5/21.2 (31.1%)	10.1/23.6 (42.7%)	11.8/23.9 (49.7%)
Percentage of recipients that are blood type O	18.5/58.3 (31.8%)	21.2/65.7 (32.4%)	21.1/62.3 (33.9%)	23/67.2 (34.3%)	21.2/61.3 (34.6%)	23.6/68.1 (34.7%)	23.9/68.2 (35%)
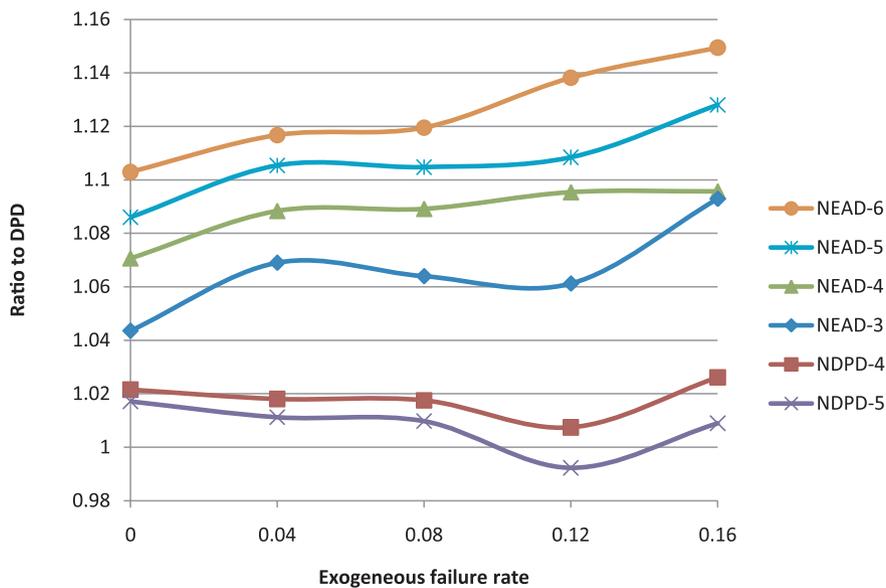
Figure 6: Comparing the ratio of total number of transplants between each policy to the DPD policy, with sensitivity analysis on the exogenous failure rate from 0 to 0.12.
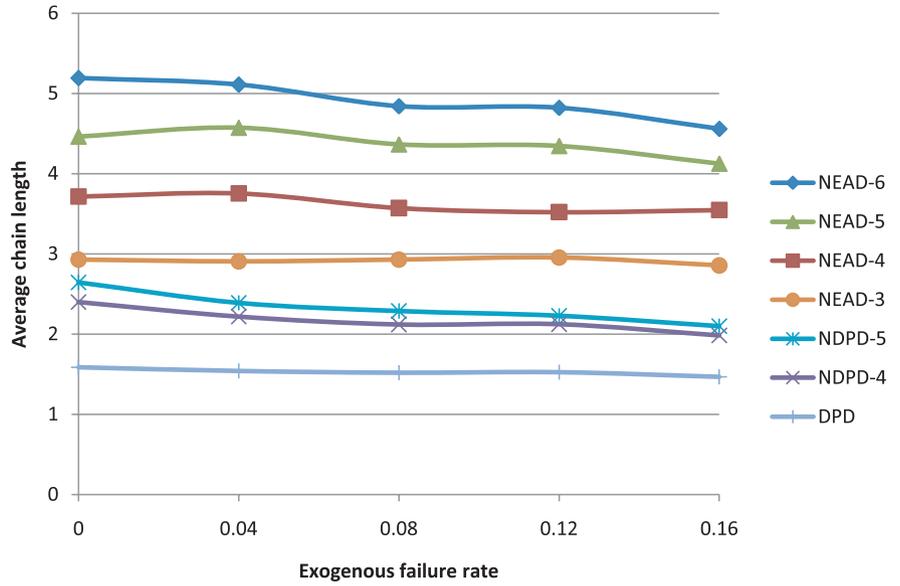
Figure 7: Average chain lengths under the NEAD-k and NDPD-k policies, with sensitivity analysis on the exogenous failure rate from 0 to 0.12.

precisely because of the longer chains. Exogenous failure rates might have resulted in a reduction of the average chain (and DPD) length, but even when the failure rate is 16%, both policies maintain longer chain lengths as longer chains are allowed. Figure 8 shows that in over 80% of instances, NEAD-6 produced strictly more transplants than DPD.

Population size

We examined how the size of the pool changes the effectiveness of the policies. The results in Figure 9 show that NEAD chains produce more transplants than DPD policies. We were unable to simulate the NEAD-6 policy for 40 pairs added/month due to computational complex-

ity. That the benefit decreases with population size is to be expected since the relative increase in the number of transplants due to chains started by a single NDD joining the exchange every period decreases with the larger exchange pool. However, both NEAD chains provide more transplants than DPD policies.

Short-term bridge donor renege rate

Figure 10 plots the effects of short-term bridge donor renege rates. NEAD policies produce more transplants than DPDs. We set the renege rate to 2% in this simulation to allow for a greater range of short-term bridge donor renege rate values.
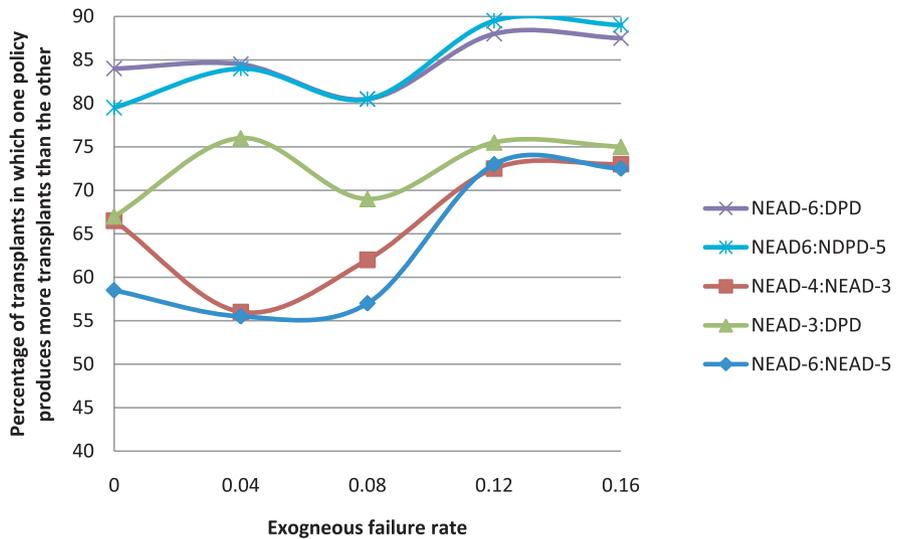

Figure 8: Significance of the results comparing NEAD-k and DPD-k policies to DPD, with sensitivity analysis on the exogenous failure—percentage of instances in which one policy is producing more transplants than the other.
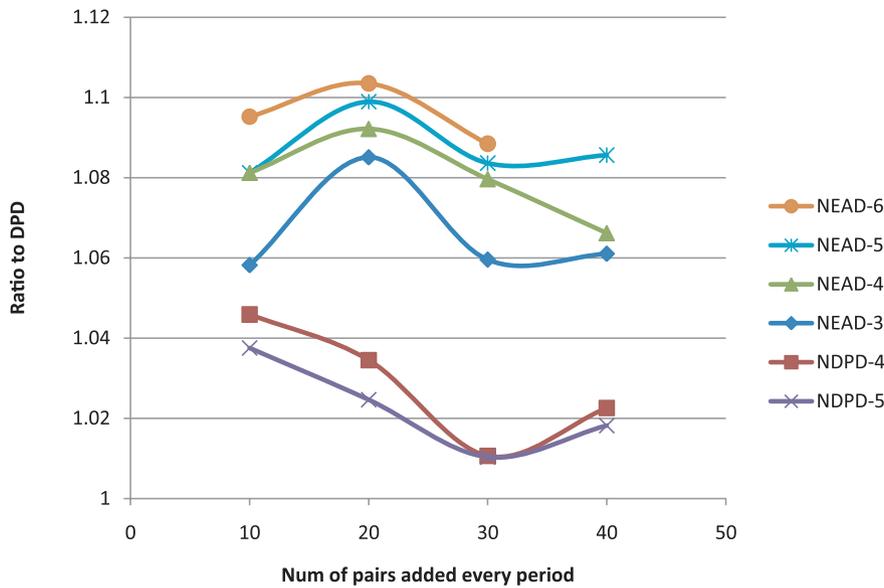
Figure 9: Comparing the ratio of total number of transplants between each policy to the DPD policy, with sensitivity analysis on the number of pairs joining the pool every period.

Discussion

Since the introduction of nonsimultaneous NDD chains (9) the use of nonsimultaneous chains has become increasingly common (20). One reason for this is to allow longer chains than can be accomplished simultaneously. The present paper considers simulations that take this emerging clinical practice into account. Many other aspects of paired donation programs will also impact the success of such practices (quality of HLA typing, status of donor evaluation, willingness to desensitize), but these factors were not considered, and so our conclusions await further validation from additional clinical experience. Given our assumptions, we find that as nonsimultaneous chains are allowed to be long, the benefit of keeping the last donor

in the chain as a bridge donor grows. This raises both the total number of transplants achieved and the number of transplants for high PRA and blood type O patients. Even so, it will be prudent in clinical practice to limit the length of time that bridge donors are allowed to wait before choosing to end chains by donating the bridge donor's kidney to a candidate on the deceased donor waiting list who lacks a willing donor.

These findings contrast with the recent work of Gentry et al. whose simulations suggested that simultaneous DPD transplant chains would result in as many or more transplants as nonsimultaneous NEAD chains. The difference in the conclusions of Gentry et al. and our data results from different assumptions: Gentry et al. limited chain
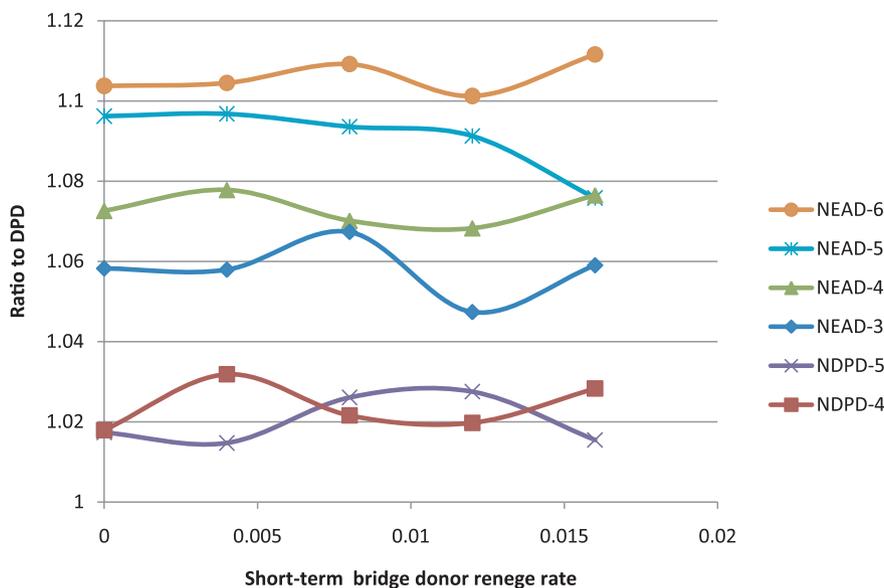

Figure 10: Sensitivity analysis on the short-term bridge donor renege rate. The bridge donor renege rate is fixed to 0.02. The y-axis is the ratio between the number of transplants in a given policy to the number of transplants in DPD.

length to a maximum of three transplants per chain segment and we allowed for longer chain segments. When we used similar assumptions, we obtained similar results. Thus, limiting the length of chain segments turns out to be a critically important assumption, particularly as longer chain segments are more consistent with the types of chains that are being arranged in current clinical practice.

A second important aspect of our simulations was the use of actual patient data to build the database and the incorporation of clinically relevant failure rates for computer-identified compatible recipient–donor pairs related to both positive crossmatches adjusted for the PRA of the recipient and an exogenous failure rate for the myriad other reasons that computer-identified matches fail to culminate in a transplant. Given the clinical experience of the APD and others that over 80% of the computer-identified matches fail to move forward to successful transplantation, sensitivity analysis of failure rates is a critical component of simulating paired donation (19). Our results suggest that a second advantage of nonsimultaneous KPD chains compared with simultaneous KPD chains is that the advantage of NEAD chains over DPD chains increases as the failure rate increases.

A final important observation in this study is the demonstration that nonsimultaneous KPD chains not only produce more transplants than simultaneous KPD chains, they also allow for higher quality transplants to be achieved. Quality of transplant is more difficult to define than quantity, but nonetheless deserves mention. Generally the transplant community thinks of quality of transplant in terms of HLA match, age of the donor/recipient, waiting time or transplanting hard to transplant patients. For the present analyses, we consider quality to be obtaining transplants for highly sensitized patients or patients with blood type O. We found that a third advantage of NEAD chains over DPD chains is that NEAD chains allow for more pairs with high PRAs or blood type O recipients to be transplanted.

Initially, the proposal to combine kidney exchange with long chains that could be kept open or end promptly with a donation to the list (21) was met with resistance from the medical community, and organized kidney exchange initially focused on exchanges between only two pairs, and on very short list exchange chains (8,22,23). The possibility of doing NDD chains nonsimultaneously has removed some of those barriers. It still remains to learn how best to utilize all the forms of simultaneous and nonsimultaneous cycles and chains that are now available. The results of the present simulations, based on the clinical experience and patient–donor population of the APD, suggest that pursuing the possibility of nonsimultaneous, long chains may serve to increase both the number and quality of kidney transplants achieved through KPD.

Disclosure

The authors of this manuscript have conflicts of interest to disclose as described by the *American Journal of Transplantation*. Dr. Rees reports receiving grant support for the Alliance for Paired Donation from Novartis, Genzyme, Astelles, Roche, Wyeth and Pfizer Pharmaceuticals.

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