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NEAD Chains in Transplantation

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To the Editor:

Gentry and Segev speculate above that the results reported in Ashlagi et al. [1], that non-simultaneous extended altruistic donor (NEAD) chains produce more transplants than domino paired donation (DPD), would be reversed if the computation were conducted for more periods. Here we carry out the computation and show that, contrary to their conjecture, nonsimultaneous chains continue to allow more transplants than simultaneous chains, even over a longer time horizon. Furthermore, more highly sensitized patients are transplanted by allowing chains to continue with bridge donors rather than automatically ending with donations to patients on the deceased donor waiting list.

Gentry et al. [2] used simulations to show that NEAD chains consisting of a maximum of three transplants in each period, produce fewer transplants than simultaneous DPD chains over 24 periods. They restricted non-simultaneous chains to have segments just as short as DPDs. This doesn't correspond to clinical practice: non-simultaneous chains relieve the logistical constraints that arise when all surgeries must be performed simultaneously. Long NEAD chains have been successfully implemented in practice (e.g. Rees et al.[3]).) The only multiregional paired donation program that does not utilize NEAD chains is the UNOS kidney paired donation pilot program (UNOS-KPDPP). We respond to this letter providing data we hope will help change what we believe is a flawed UNOS policy.

In [1] we found that allowing for longer chains reverses Gentry et al.'s result. Simulations in [1] involved only eight periods. Gentry and Segev assert in their letter that extending the simulation for more periods would reverse our results to agree with theirs. However they do not carry out this computation, they only speculate about it.

Figure 1 shows that this conjecture is not supported by actual simulations. We perform the simulations for unrestricted length chains for 24 or more periods and we refer to policies where NEAD chains and DPDs can be of any length in each period as NEAD-L and DPD-L chains. The vertical-axis is the ratio of the number of transplants conducted under a given policy compared to the number of transplants conducted under the restriction of a maximum of three transplants as imposed by Gentry et al. The horizontal-axis is the number of periods simulated. Figure 1a shows that NEAD chains not only produce more transplants than DPD chains, but also produce up to 25% more transplants for patients with PRA greater than 80%.

Gentry and Segev did not address exogenous failure rates in their manuscript, nor in their letter. This omission is critical given the experience of real KPD programs. As of August 2011, the UNOS-KPDPP has transplanted only two people since starting in October of 2010: more than 90% of the offers made by the UNOS-KPDPP have failed to culminate in transplants. Using an exogenous failure rate of only 15%, Figure 1b shows that NEAD-L chains produce 17% more transplants and nearly 30% more transplants for highly sensitized patients than DPDs restricted to three transplants. Importantly, the higher the exogenous failure rate, the better NEAD chains perform compared with DPD chains (compare Figure 1a with 1b).

Gentry et al [2] compared short simultaneous chains (DPDs) with short-segment nonsimultaneous chains that always continue with bridge donors. Here and in [1] we begin to also compare nonsimultaneous chains of different lengths ending either in a donation to the list or continuing with a bridge donor. More work needs to be done to determine when to end a nonsimultaneous chain with a list donation, or continue it with a bridge donor.

Mathematics can be enormously powerful alongside correct modeling, and has contributed matching algorithms used in KPD (see [4] and [5]). Here it is used to show that NEAD chains outperform DPDs despite the risk of reneging bridge donors. We believe the UNOS-KPDPP should be based on real data—to date, clinical experience and simulations support the use of NEAD chains.

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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Figure 1: The ratio of different policies (as defined above and in Aslagi et al. [1] with the following additions: PRA- means that the ratio is calculated considering only recipients with a PRA>80%; and –L means that chains of unrestricted length were used) to DPD-3. The renege rate is set to 0.02 and the false negative crossmatch "failure rate" is as in Table 2 of our paper. Figure 1a assumes no exogenous failure rate, while Figure 1b assumes a 15% exogenous failure rate.

Figure 1a: No exogenous failure rate.

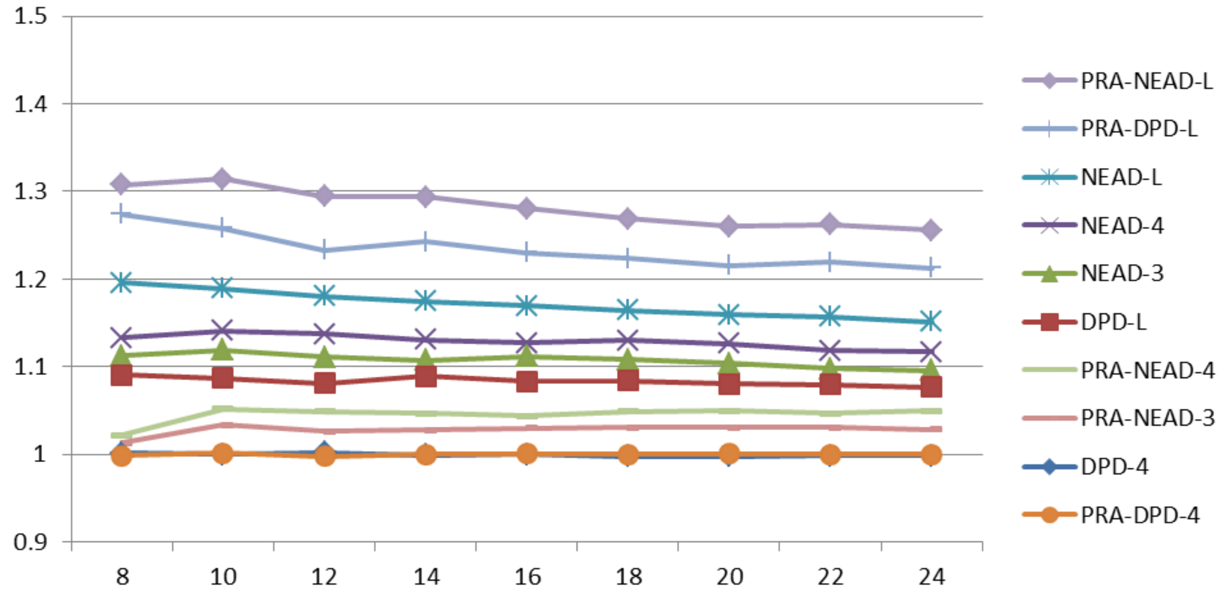

Figure 1b: Exogenous failure rate set to 0.15.