

Allowing Deceased Donor-Initiated Kidney Paired Donation (KPD) Chains

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Executive Summary.....	2
Is the sponsoring Committee requesting specific feedback or input about the proposal?	2
What problem will this project solve?	3
Background	3
What is a deceased donor-initiated chain?	5
How might a deceased donor-initiated chain work?.....	6
How does this concept support the OPTN Strategic Plan?	9

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Concept Paper

Sponsoring Committee: OPTN Kidney Transplantation Committee

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Executive Summary

Demand for kidneys far exceeds supply. As of July 2017, approximately 97,000 candidates are registered on the OPTN Wait List for a deceased donor kidney. Kidney paired exchange chains have potential for greatly increasing the number of transplants in the nation. A study published in 2013 found that a non-directed donor triggers 4.8 transplants on average and 6 if the non-directed donor is a blood type O¹. Although KPD chains may ultimately end in donation to the waitlist, deceased donor kidneys are currently not used to begin chains. Using deceased donor kidneys to initiate KPD chains could greatly expand the number of transplants overall as each deceased donor kidney could unlock multiple transplant opportunities. Deceased donor-initiated chains may also better utilize kidneys to maximize the potential of KPD donors and deceased donors to increase the overall number of transplants.

Is the sponsoring Committee requesting specific feedback or input about the concept paper?

1. Does the community generally support the OPTN/UNOS creating policy to incorporate deceased donor-initiated chains into KPD? If so, which model, described below, does the community prefer?
2. Are there other methods for using deceased donor kidneys to initiate KPD chains that the workgroup should consider?
3. How can policy be developed so as to protect vulnerable or disadvantaged populations (e.g. blood type O, pediatrics, minority populations, etc.)?
4. Should policy apply to all KPD programs nationwide, or be more limited in scope?
5. Should policy solutions be tested in the form of a variance or pilot?
6. General feedback as desired

¹ Melcher ML, Veale JL, Javaid B, et al. Kidney transplant chains amplify benefit of nondirected donors. JAMA 2013 Feb;Surg/Vol 148 (NO.2):165-169.

What problem will this project solve?

Currently over 97,000 people in the United States are registered on the deceased donor waiting list for a kidney transplant. In 2016, only 19,060 individuals received were transplanted. Of those, 13,431 received a deceased donor transplant and 5,629 a living donor transplant. Despite a surge in kidney paired donation transplant in recent years (an increase to 642 transplants in 2016 from 72 in 2006), the discrepancy between the demand for kidney transplants and the supply of donated organs persists. Deceased donor kidney transplantation has remained static since 2006, at the same time living donor transplants have steadily declined (peak occurred in 2004 with 6,648 transplants). Without the rise in kidney paired donation (KPD), the drop in living donor transplants would be far worse. While the number of kidneys available for transplant remains in short supply, the number of individuals added to the kidney transplant waitlist increases each year (36,938 added in 2016).² Of those candidates who have identified a willing and medically suitable living donor, approximately one third of these donors are unable to donate to them directly due to either ABO or histological incompatibility.³ Although kidney paired donation programs have made progress in reducing this barrier to incompatibility, several issues (e.g. multiple regional and national KPD programs, the increase in internal exchanges at single centers, low enrollment of blood type O non-directed donors and the high percentage of sensitized candidates registered) have hindered the full potential of kidney paired donation. Using deceased donor kidneys to initiate KPD chains could greatly expand the number of transplants overall as each deceased donor kidney could unlock multiple transplant opportunities. Other models, such as a list exchange between KPD and the deceased donor waitlist, when combined with KPD chains may also maximize the potential of KPD donors and deceased donors to increase kidney transplantation.

Literature has shown that including NDD chains in KPD increase the number of kidney transplants^{1,4,5}. This is possible because the non-directed donor enters the system without a paired candidate. Since deceased donor kidneys would also enter the KPD system without a paired candidate, it is reasonable to presume that deceased-donor initiated chains will also increase the number of KPD transplants. Since many KPD candidates are also registered on the deceased donor waitlist, an increase in the number of KPD transplants will also decrease the number of candidates waiting for a deceased donor.

Background

KPD transplants have grown rapidly since the first two transplants were performed in 2000. Transplant hospitals reported 642 KPD transplants in 2016, comprising over 11% of all living donor kidney transplants in the United States, based on OPTN data.⁶ KPD began with only closed loop matches, which are limited by reciprocal matching. The first paired donor is matched to a recipient and this recipient's paired donor must then reciprocally match back to the first donor's paired candidate. The first closed loop match occurred in 2000 with 2 pairs and 2 transplants. In 2004 nondirected donor chains were integrated into KPD, eliminating the constraint of reciprocal matching because each donor only needs to match with the next recipient in the chain.⁷ Chains initially ended immediately in closed loops with a donation to the waitlist and all donations occurring simultaneously. Chain expanded to nonsimultaneous, extended,

² OPTN Data. <https://optn.transplant.hrsa.gov/data/>. Accessed 21 July 2017.

³ Montgomery, RA and AA Zachary. "Transplanting patients with a positive donor-specific crossmatch: A single center's perspective." *Pediatric Transplantation*. 2004; 8: 535-542.

⁴ Michael A. Rees et al., A nonsimultaneous, extended, altruistic-donor chain, 360 *New Eng J Med*. 1096, 1096 (2009).

⁵ Roth AE, Sonmez T, Unver MU, et al. Utilizing list exchange and nondirected donation through 'chain' paired kidney donations. *Am J Transplant*. 2006;6:2694-2705.

⁶ OPTN, United Network for Organ Sharing. <https://optn.transplant.hrsa.gov/data/>. Accessed 21 July 2017.

⁷ Montgomery RA, Gentry SE, Marks WH, Warren DS, Hiller J, Houpp J, Zachary AA, Melancon JK, Maley WR, Rabb H, Simpkins C, Segev DL. Domino paired kidney donation: a strategy to make best use of live non-directed donation. *Lancet*. 2006 Jul; 368(9533):419-21.

altruistic-donor (NEAD) chains in just a few years⁴. NEAD chains increase the possibility of non-directed donor chains with the addition of bridge donors and donor nephrectomies taking place over days, weeks, or months.

Although data is limited on the overall number of transplants that have resulted from non-directed donor-initiated chains, reports of their success is growing. Through the New England Paired Kidney Exchange (NEPKE), Hanto reported 23 transplants from 8 non-directed donor chains plus one list exchange chain between 2003 and 2008.⁸ In 2009, Rees reported that the Alliance for Paired Donation (APD) saw 22 transplants from 6 non-directed donor initiated chains with more bridge donors in the queue to donate.^{9,10} Melcher reported 272 transplants facilitated by 54 chains, with the mean number of transplants per chain 5 (range 1 to 21).¹¹ In the OPTN UNOS KPDPP, non-directed donor initiated chains accounted for 30% of all KPD transplants (n=65) through April 30, 2017.¹² In addition to increasing the total number of transplants, Melcher et al found that NDD chains increase transplants for difficult to match pairs and ethnic minorities and simulation studies by Ashlagi et al report that NEAD chains produce more transplants in general and specifically for highly sensitized and blood type O recipients than closed chains.^{13,14} Patients on the deceased donor waitlist also benefit when chains end by the last living donor kidney being transplanted into a candidate who does not have a living donor.^{13,15} Wall et al (2017) offer additional perspective on the ethical and logistical complexities of utilizing deceased donor kidneys to trigger KPD chains.¹⁶

In 2013, the OPTN/UNOS received a request to consider developing policy allowing deceased donor initiated chains. The Kidney Committee's standing KPD workgroup met to consider the project and developed three potential models for initiating deceased donor KPD chains, as well as consider the ethical, logistical and operational implications for such a policy. The project was put on hold in 2014 due to competing priorities before being reinstated in October 2016. This new workgroup began its work by reviewing existing literature and project materials on this topic and discussing potential concerns and challenges that will need to be addressed when constructing policy. The Kidney Committee also sent a letter in August 2016 requesting early input on this project from the OPTN/UNOS Ethics Committee. The Ethics Committee responded and requested that the workgroup specifically evaluates challenges identified from perspective of equity, and that any solutions produced should also address how they can be monitored and enforced. The Committee specifically requested review of the following concerns:

1. Potential negative effects on equity in access to kidney transplantation
 - a. Potential depletion of O-type deceased donor kidneys available for the waitlist
 - b. Unequal distribution across ethnic minority groups
2. A deceased donor kidney may be better quality than organ ultimately donated back to waitlist
3. Potential negative impact to trust in deceased donor allocation if living donors break KPD chains and undermine return of kidneys to the waitlist

To date, the workgroup has reviewed the three principal deceased donor chain models identified and is beginning early evaluation of each option. The group opted to release a Concept Paper to solicit early stakeholder feedback on this project.

⁸ Hanto RL, Reitsma W, Delmonico FL. "The development of a successful multiregional kidney paired donation program." *Transplantation*. 2008 Dec 27;86(12):1744-8.

⁹ Rees MA, Bargnesi D, Samy K, et al. Altruistic donation through the Alliance for Paired Donation. *Clin Transpl*. 2009:235-46.

¹⁰ Veale J, Hil G. The National Kidney Registry: transplant chains—beyond paired kidney donation. *Clin Transpl*. 2009:253-64.

¹¹ Michael A. Rees et al., A nonsimultaneous, extended, altruistic-donor chain, *360 New Eng J Med*. 1096, 1096 (2009).

¹² OPTN, United Network for Organ Sharing. <https://optn.transplant.hrsa.gov/data/>. Accessed 21 July 2017.

¹³ Melcher ML, Veale JL, Javadi B, et al. Kidney transplant chains amplify benefit of nondirected donors. *JAMA Surg* 2013; 148:165–169.

¹⁴ Ashlagi I, Gilchrist DS, Roth AE, Rees M. Nonsimultaneous chains and dominos in kidney paired donation revisited. *American Journal of Transplantation* 11, no 5(2011): 984-994.

¹⁵ Cole EH, Nickerson P, Campbell P, et al. The Canadian kidney paired donation program: A national program to increase living donor transplantation. *Transplantation* 2015; 99: 985–990.

¹⁶ Wall, Anji E., Jeffrey L. Veale, and Marc L. Melcher. "Advanced Donation Programs and Deceased Donor Initiated Chains-2 Innovations in Kidney Paired Donation." *Transplantation* (2017).

Inquiries to Date

The success of non-directed donor chains with increasing the overall number of kidney transplants led to an increased interest in this topic among members of the transplant community as indicated through new publications and inquiries submitted to the OPTN. In 2016, the OPTN received three separate inquiries from programs requesting policy clarifications surrounding the use of deceased donor organs as chain-initiating kidneys.

An OPO inquired as to whether designating a KPD program candidate as “medically urgent,” thus affording the candidate increased wait list priority for a DD kidney, is an acceptable method for initiating a chain. The exchange-ending living donor would then donate back to the wait list. Two other OPOs inquired in the same year whether a deceased donor family could “name” a KPD candidate to initiate a chain as a directed donation. The OPO would provide the name of the intended KPD recipient to the family, and the exchange-ending living donor would then donate back to the waitlist.

In addition to these inquiries, Walter Reed National Military Medical Center announced at the 2016 White House Summit on Organ Donation their intention to use deceased donor kidneys to initiate a living donor chain through use of their military share program.¹⁷

What is a deceased donor-initiated chain?

A deceased donor-initiated chain is a KPD chain in which a candidate receives a deceased donor transplant in exchange for their paired living donor’s donation. Using deceased donor kidneys in KPD chains raises concerns regarding equity and utility of allocating deceased donor kidney to KPD candidates, such as a candidate receiving a deceased donor kidney in exchange for a living donor kidney and allocation of chain-ending kidneys so as not to disadvantage any one blood type.

The Deceased Donor Chains Work Group reviewed three models for establishing these chains:

1. a candidate-driven system
2. list exchange chains
3. a donor-driven system

This paper will discuss some of these possibilities and describe the potential challenges identified by the work group for each. The Workgroup could like the community to consider the following questions when reviewing these models:

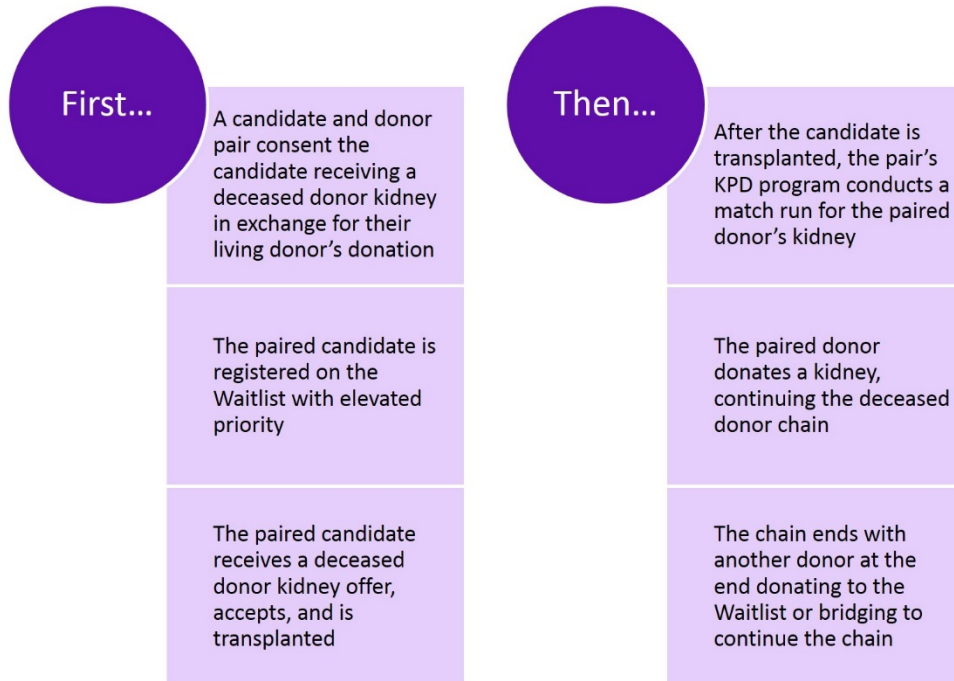
1. Which of the models described below, if any, do you support?
2. What concerns do you have about any given model?
3. Are there other methods for utilizing deceased donors as chain-initiating kidneys that the Workgroup should consider?

¹⁷ Pondrom, Sue. "White House Holds Summit on Organ Transplantation." *American Journal of Transplantation* 16, no. 8 (2016): 2241-2242.

How might a deceased donor-initiated chain work?

Candidate-Driven KPD Model

Figure 1: A Candidate-Driven KPD Chain (illustration)

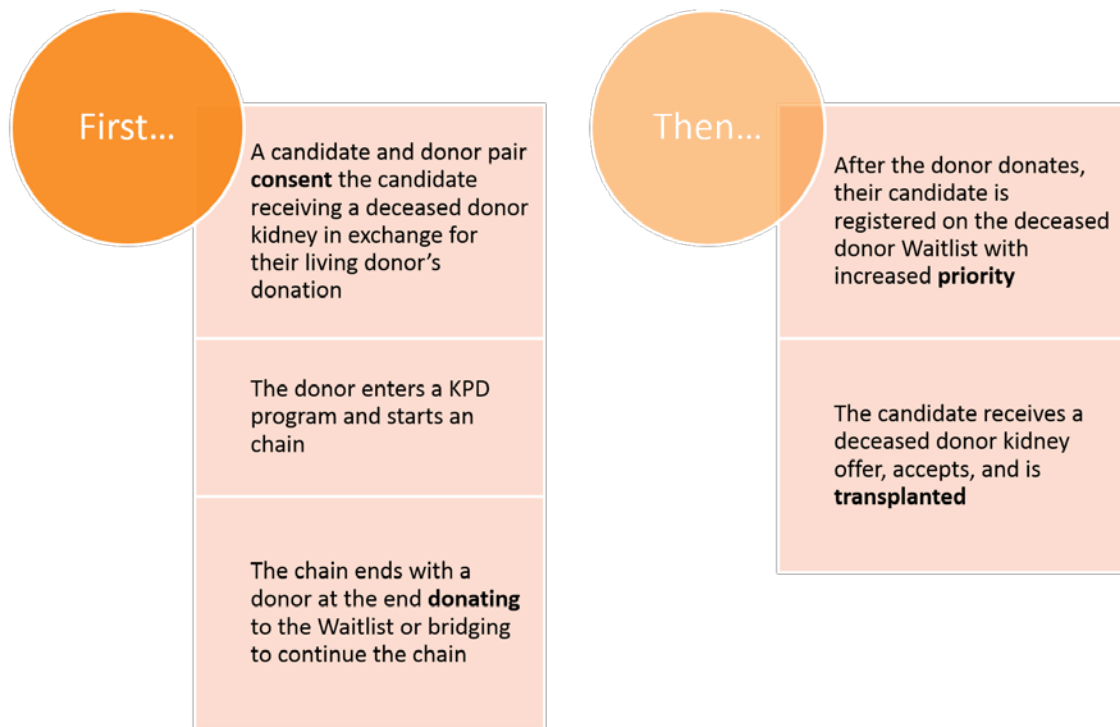


In a *candidate-driven system*, a candidate enrolled in KPD is given predetermined priority on the deceased donor waitlist in exchange for their paired donor donating. These types of exchanges have a few defining features: one, the candidate and the paired donor first consent to a deceased donor transplant in exchange for the living donor's donation. Once consent is granted, the candidate receives elevated priority on the deceased donor waitlist for a kidney transplant. Once the paired candidate receives their deceased donor kidney transplant, their paired donor initiates a KPD exchange. This agreement is not binding and the donor can decline to donate at any time. The chain continues with a bridge donor or donates to waitlist. Melcher et al discuss the benefits and challenges to employing this model in their 2016 paper, *Utilization of Deceased Donor Kidneys to Initiate Living Donor Chains*.¹⁸

¹⁸ Melcher, M. L., Roberts, J. P., Leichtman, A. B., Roth, A. E., & Rees, M. A. (2016). Utilization of deceased donor kidneys to initiate living donor chains. *American Journal of Transplantation*.

List Exchange Chains

Figure 2: A List Exchange KPD Chain (illustration)



In a *list exchange system*, a donor/candidate pair enters the KPD program together. The paired living donor is matched to a paired candidate to begin a chain, similar to a non-directed donor chain. The chain continues with a bridge donor or donates to the waitlist. After the living donor donates, their paired candidate receives elevated priority on the deceased donor waitlist.

A list exchange variance was in effect in OPTN/UNOS Regions 1, 2, 5, 9 and 11 from 2001-2014, ending when the new Kidney Allocation System (KAS) was implemented in December 2014. Region 1 had the highest volume of list exchanges during this time. In 2004, the New England Organ Bank established the New England Program for Kidney Exchange (NEPKE) and expanded the standard list exchange variance to include list exchange chains in KPD. Three candidates received a deceased donor transplant from NEPKE list exchange chains^{19,20} Delmonico discusses Region 1's list exchange program in detail in his 2004 paper, *Donor Kidney Exchanges*.²¹

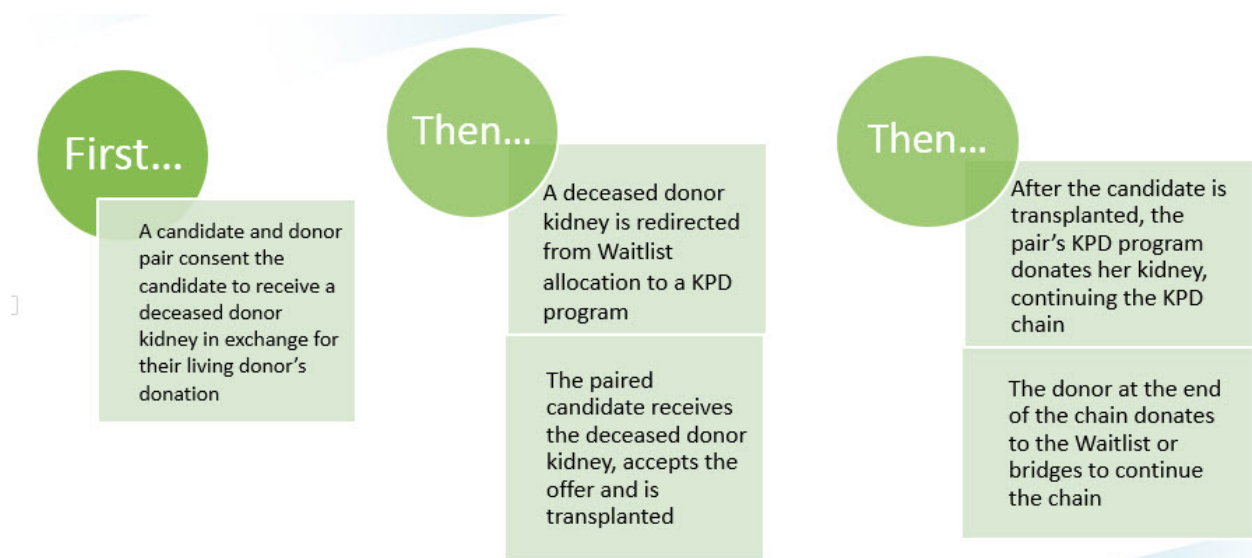
¹⁹ New England Program for Kidney Exchange. "NEPKE Data Report 2004-2011." 30 April 2011.

²⁰ Roth AE, Sonmez T, Unver MU, et al. Utilizing list exchange and nondirected donation through 'chain' paired kidney donations. *Am J Transplant*. 2006;6:2694-2705.

²¹ Delmonico, F. L., Morrissey, P. E., Lipkowitz, G. S., Stoff, J. S., Himmelfarb, J., Harmon, W., ... & Milford, E. (2004). Donor kidney exchanges. *American Journal of Transplantation*, 4(10), 1628-1634.

Donor-Driven KPD Model

Figure 3: A Donor-Driven KPD Chain (illustration)



In a *donor-driven system*, a deceased donor kidney is redirected from the waitlist allocation for placement with a KPD program. Criteria would be set for which deceased donors could be redirected in this manner. The deceased donor's information would be entered (transferred) to a KPD system. A match would immediately be run with the donor's information and a chain identified. A paired candidate receives the deceased donor transplant in a similar time frame from standard deceased donor allocation. The paired donor and rest of the chain moves forward with standard KPD timing and logistics. The chain continues with a bridge donor or donates to waitlist.

Summary of Three Models

	Candidate Driven	List Exchange Chains	Donor Driven
Distinguishing feature	<ul style="list-style-type: none"> FIRST: Candidate receives increased priority on Waitlist THEN: Candidate is transplanted THEN: Paired living donor donates 	<ul style="list-style-type: none"> FIRST: Paired living donor donates THEN: Paired candidate receives priority on Waitlist 	<ul style="list-style-type: none"> FIRST: Deceased donor organ redirected from the Waitlist allocation to a specific KPD program and their matching priorities THEN: KPD Candidate matched and transplanted THEN: Paired living donor donates

How does this concept support the OPTN Strategic Plan?

1. *Increase the number of transplants:* The focus of this project will increase the number of transplants by maximizing the potential of deceased donation and KPD. Permitting a deceased kidney donor to initiate a chain in the KPD system would potentially increase the number of kidney transplants overall, without decreasing the number of donors available for the deceased donor waiting list. An article in the American Journal of Transplantation notes that although each deceased donor kidney conventionally results in the transplantation of a single patient from the deceased donor waitlist, a chain initiated with a deceased kidney would result in a minimum of two transplants. Since all OPTN KPD candidates are also on the deceased donor waitlist, deceased donor chains are expected to help reduce demand for kidneys, as each deceased donor chain may unlock multiple transplant opportunities.
2. *Improve equity in access to transplants:* There is no impact on this goal.
3. *Improve waitlisted patient, living donor, and transplant recipient outcomes:* There is no impact on this goal.
4. *Promote living donor and transplant recipient safety:* There is no impact on this goal.
5. *Promote the efficient management of the OPTN:* There is no impact on this goal.