



# Innovations in kidney paired donation transplantation

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## Purpose of review

To analyze the innovations that have increased the reliability, convenience, and outcomes of kidney paired donation (KPD) that has led to thousands of living donor kidney transplants across the United States.

## Recent findings

Over the past 10 years, KPD has grown over 200% on an annual basis. Though concerns had existed over cold ischemia time, research has shown that there is no correlation between travel time of a shipped kidney and the transplant outcome. The voucher program has started to continue to expand how to overcome obstacles to donation by solving the issue of a pair chronological incompatibility.

## Summary

KPD is a relatively new field and the innovations it has spawned should continue to improve availability of high-quality living donor organs. The introduction of the family voucher should continue this trend.

## Keywords

kidney transplantation, paired exchange, transplant

## INTRODUCTION

By expanding the donor pool and providing incompatible pairs, an opportunity to receive a living donor kidney transplant, or enabling compatible pairs an opportunity to receive a better match, kidney paired donation (KPD) is a remarkable innovation in and of itself. As KPD becomes an increasingly common approach to kidney transplantation, advancements and innovations within KPD have furthered that growth by more than 200% from 10 years ago (Fig. 1) [1].

## SHIPPING LIVING DONOR KIDNEYS

Perhaps the most significant of any advancement in KPD occurred on 30 July 2008, when a living donor kidney was shipped across the United States unaccompanied on a commercial airline [2]. Before this sentinel event, donors typically travelled to their KPD matched recipient's city for major surgery at an unfamiliar hospital, recovering apart from family and friends. The shipping of living donor kidneys eliminated this significant barrier to KPD participation, and resulted in a much larger pool of donor/recipient pairs. This innovation drastically increased the likelihood of recipients finding a match, and donors no longer were required to leave their preferred surroundings to participate in a kidney exchange.

With research demonstrating no correlation between cold ischemic time (CIT) and graft failure [3<sup>\*\*\*</sup>], the shipping of living donor kidneys has become the standard in the United States with nearly 3000 living donor kidneys traversing the country to date [4].

The increase in transporting living donor kidneys via commercial airlines introduced a potential risk of losing visibility to the whereabouts of these organs. To mitigate this risk, in 2010 the National Kidney Registry (NKR) began providing all donor centers with global positioning system (GPS) devices to ship with the kidneys. On numerous occasions, the GPS has helped to identify instances in which the kidney was not placed on the scheduled flight. In cases like these, the kidney can be quickly recovered and the shipment expedited on a different flight to the recipient center.

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**Curr Opin Organ Transplant** 2019, 24:429–433

DOI:10.1097/MOT.0000000000000669

## KEY POINTS

- KPD provides the ability for patients to be matched against a larger donor pool, increasing the opportunity for kidney transplantation.
- Laboratory innovations such as cryopreservation have increased the convenience for donors whereas improving the speed of the paired exchange process.
- Better outcomes of NKR paired exchange transplants, when compared to other types of living kidney donation, is attributed to superior antibody avoidance.
- Vouchers take KPD one step further by resolving the problem when donor recipient pairs are incompatible by time.

Consistent with a larger pool of incompatible donor/recipient pairs, better human leukocyte antigen (HLA) matches are achieved with the avoidance of desensitization. As paired exchange volume has increased, the use of desensitization has decreased (Fig. 2) [5]. Patients with a calculated panel reactive antibodies (cPRA) lower than 99% can generally find a clean match through the NKR in less than 6 months. Patients with a cPRA greater than 99%, who are unable to find a clean match after 6 months, often combine desensitization with KPD to reduce donor-specific antibodies conflicts and achieve better outcomes. In a recent report that reviewed the first 9 years of KPD transplants facilitated through

the NKR, there was a 27% lower 5-year graft failure rate when compared to traditional directed living donor transplants (Fig. 3) [6,7<sup>\*\*\*</sup>]. NKR researchers attribute the better KPD transplant outcomes to superior antibody avoidance [6].

## LABORATORY

Lab innovations have expanded outside of HLA matching and into process improvement initiatives for paired exchange, benefiting the transplant centers and donors alike. Among the process innovations is the use of exploratory cross matching to test for HLA compatibility in advance of initiating a swap [8]. Although the use of exploratory cross matching helped a few highly sensitized patients get transplanted and reduced the rate of swap failures because of unacceptable cross match results, it was still difficult to obtain a fresh blood sample from a donor for what was not yet an actual match. It was not until 2015 when the NKR implemented multi-center donor blood cryopreservation that exploratory cross matching became fully utilized and yielded substantial results all whereas not inconveniencing the donor. This cryopreservation innovation enabled transplant centers to dramatically reduce the time to complete a cross match from 1–2 weeks to 1–2 days, facilitating more transplants for highly sensitized patients and reducing swap failures caused by unacceptable cross matches. Donor blood cryopreservation also reduces the number of times a donor needs to have blood drawn

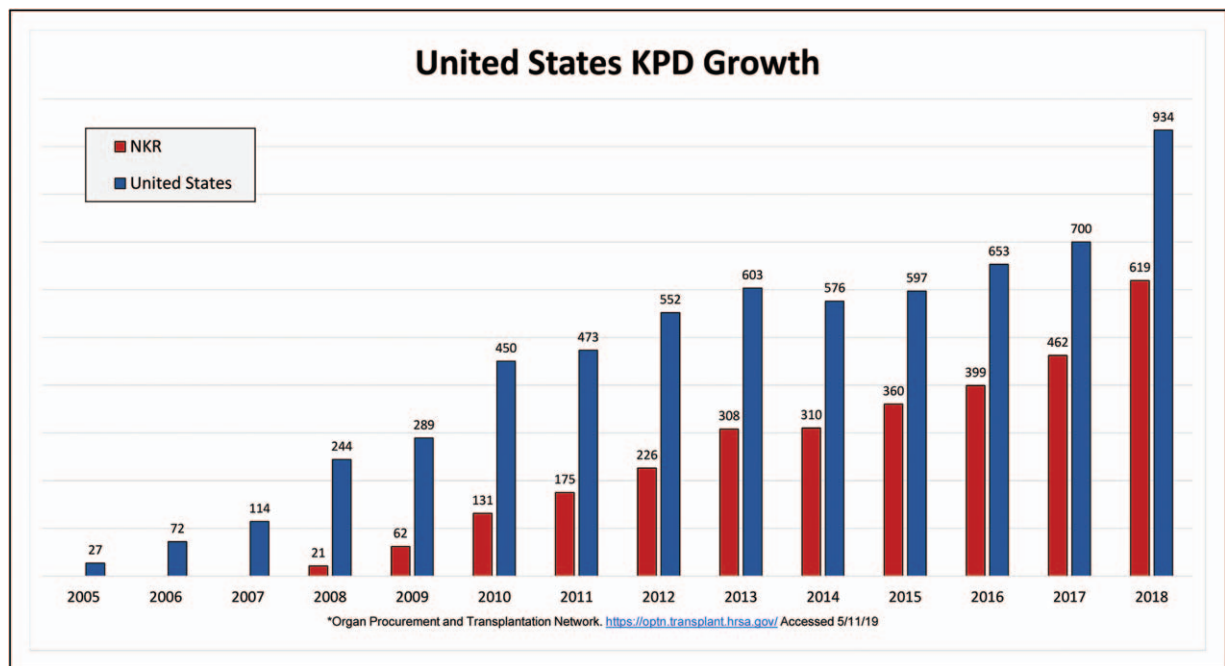
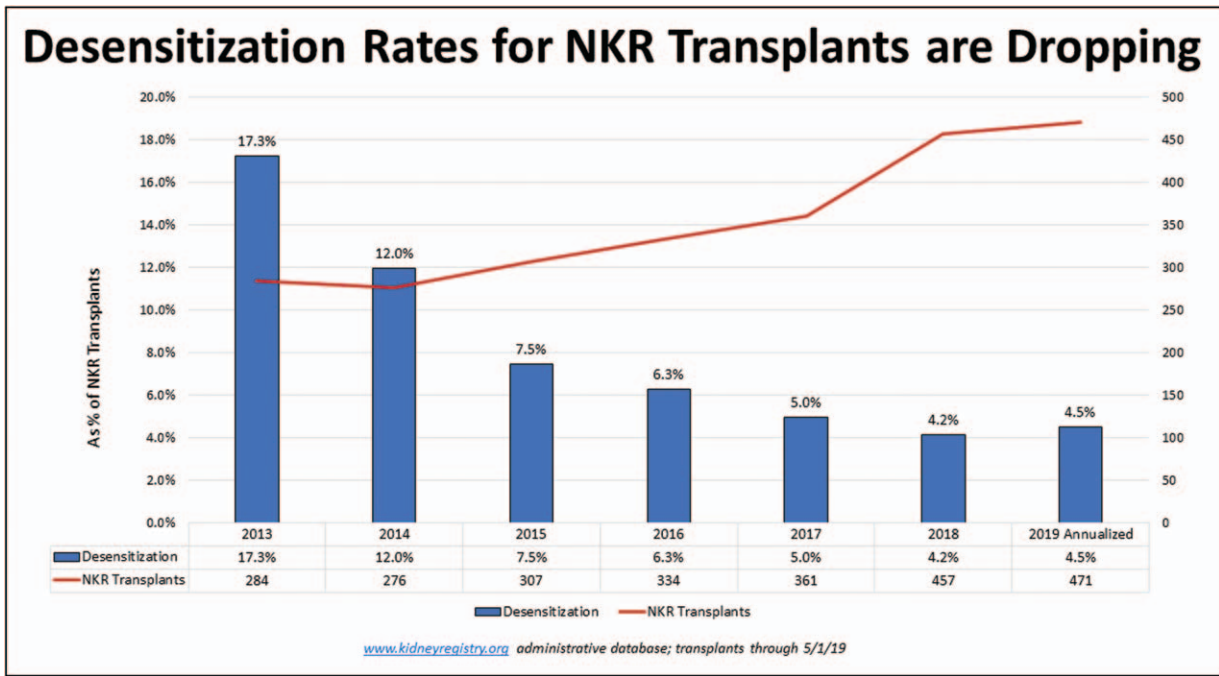


FIGURE 1. US paired exchange growth.



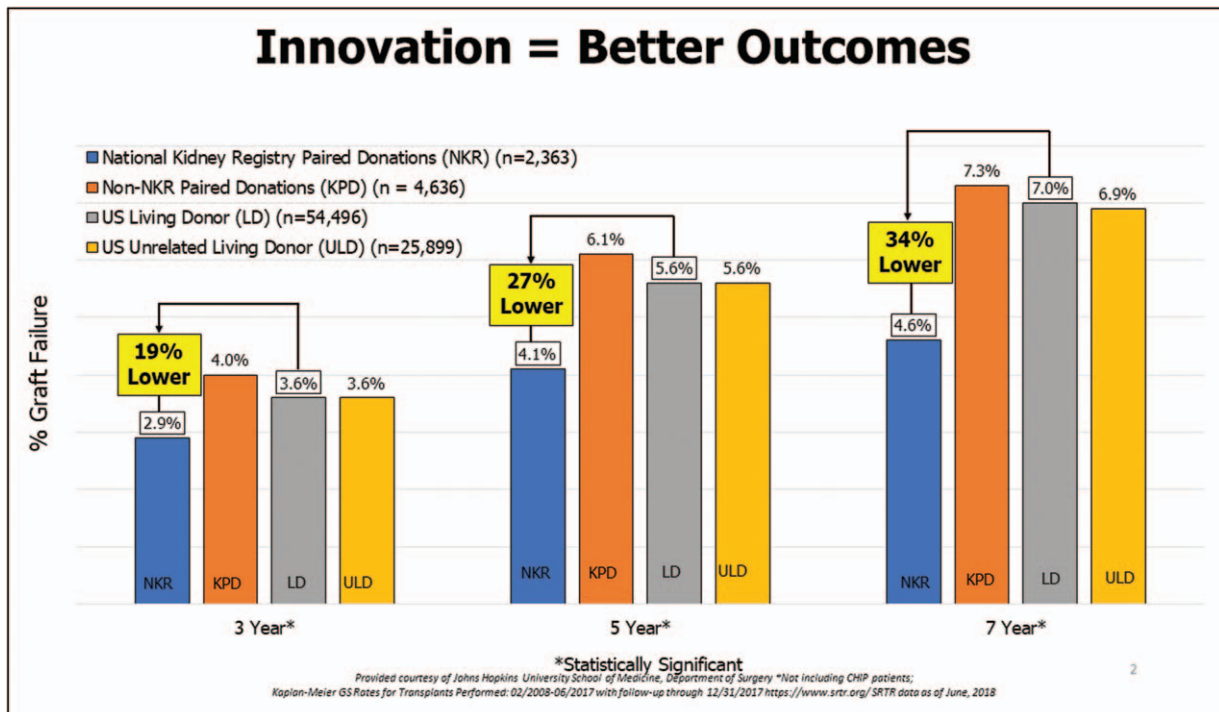
**FIGURE 2.** Desensitization in National Kidney Registry (NKR) transplants.

for cross matching, making paired exchange more convenient for donors [9].

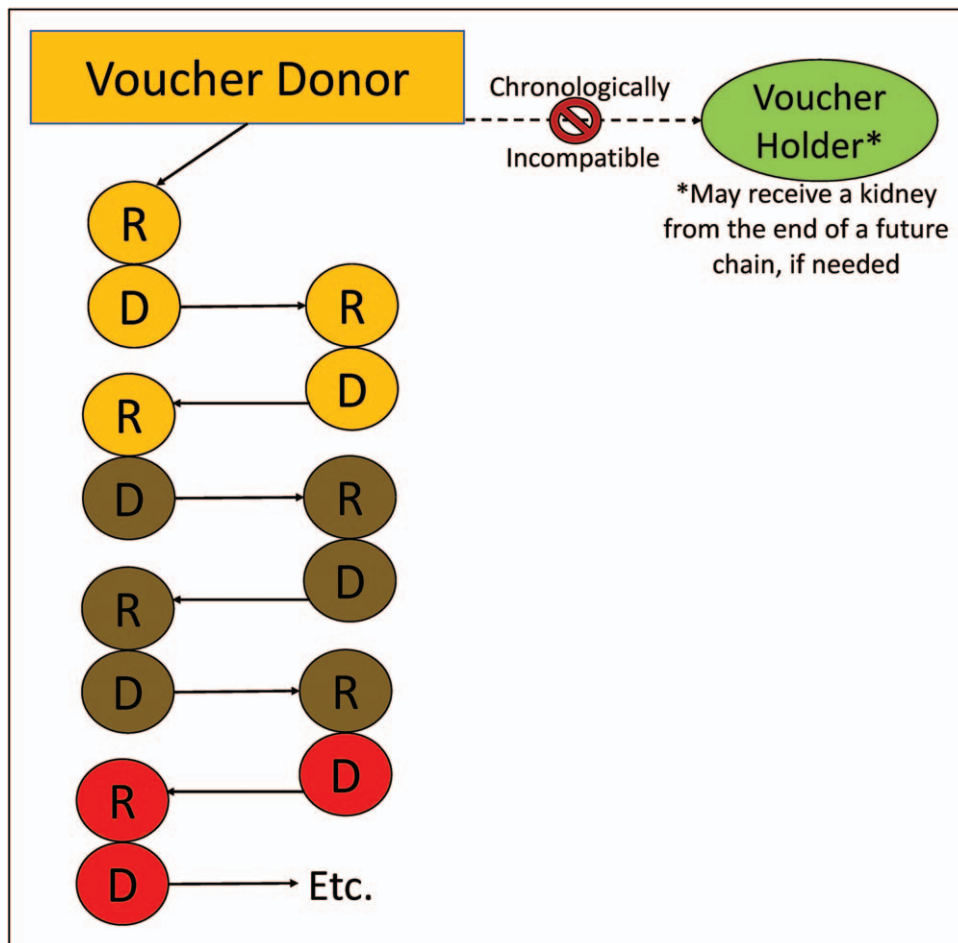
### MATHEMATICAL AND LOGISTICAL OPTIMIZATION

The success of KPD goes beyond the surgical procedure or immunosuppressive medications and hinges

on matching algorithms, computer software, and logistical optimization. In 2012, Dr. Lloyd Shapley (UCLA) and Dr. Alvin Roth (Harvard) won the Nobel Prize in part for applying the ‘Gale-Shapley matching algorithm’ to kidney exchanges. As KPD has continued to grow, more complex mathematical algorithms have been developed and real-time



**FIGURE 3.** Transplant outcomes.



**FIGURE 4.** Voucher donation.

feedback can be provided to the transplant center based on their donor's matching potential, preference settings, and composition of the pool. A KPD pool of 100 incompatible donor/recipient pairs has the potential to be shuffled into trillions of possible chain combinations [10]. This requires the implementation of powerful software systems to perform this computation. One example of logistical optimization is the development of anatomical image sharing among member centers of the NKR. Previously, transplant coordinators were burdened by sharing the computerized tomography (CT) images of the donors' kidney anatomy with outside centers. Delays occurred as computer disks of the images were mailed across the country, and surgeons often had difficulty viewing the CT images as their computers required special viewing programs to be installed. Now images of the kidney anatomy from the donor hospital can be viewed by the recipient surgeon anywhere at any time with the click of the mouse through the NKR website.

### THE VOUCHER

KPD was first completed in South Korea in the form of two-paired exchange, also referred to as a swap, [11] and later with the addition of nondirected donors evolved into chains [12]. The next big evolution of KPD could be the 'voucher' in which donors donate their kidney when convenient and their intended recipient receives a transplant when/if needed [13<sup>\*\*\*</sup>]. KPD dogma initially dictated that the donor operations should occur simultaneously, or that the paired original donor should only donate after their intended recipient (often family member) had received a kidney. However, by performing the donor procedure 'out-of-sequence' or 'in-advance' of the intended original recipient's transplantation enables operating rooms/surgeons the much-needed flexibility, and at the same time more convenience for donors who often have donation time constraints [13<sup>\*\*\*</sup>,14]. Vouchers take advanced donation one-step further, as the intended recipients (voucher holders) are not yet in need of a kidney transplant and may never need a kidney transplant.

Additionally, voucher donors often function similar to nondirected donors and can trigger chains of transplants, as they do not have a paired recipient in the current chain (See Fig. 4).

Up to this point, donor/recipient pairs have only been considered incompatible by blood type or cross-match, however donor/recipient pairs can also be incompatible by 'time' and the voucher concept helps resolve this 'chronological incompatibility' [13<sup>13</sup>]. The natural next step in the voucher program is the 'family-voucher.' As some potential altruistic donors may be reluctant to donate a kidney in case a healthy family member (child/spouse) would need it in the future. The family-voucher, launched by the NKR in 2019, enables an altruistic donor to voucher up to five healthy family members and one voucher can be redeemed in the low likelihood one of the family members requires a kidney transplant in the future [15].

## CONCLUSION

KPD is a relatively new field and the innovations it has spawned should continue to improve availability of high-quality living donor organs, outcomes for recipients, convenience for donors, and better process management for KPD and traditional living kidney donation alike.

## Acknowledgements

None.

## Financial support and sponsorship

None.

## Conflicts of interest

T.D. is the Chief Financial Officer of the NKR. J.V. is a member of the NKR Medical Board.

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