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A Systematic Review of Kidney Paired Donation: Applying Lessons From Historic and Contemporary Case Studies to Improve the US Model

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Keywords
kidney paired donation, kidney, transplantation, incompatible kidney transplantation, kidney swap, paired kidney exchange, living donor transplantation

Disciplines
Business

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May 13, 2014

Abstract

Because kidney paired donation (KPD) is a young practice, there exists no detailed inventory of the history of paired exchanges, the activities of operating KPD organizations, or recommendations for improvement. This paper attempts to address each of these considerations by providing a comprehensive analysis of KPD. The first section gives a brief background on KPD, including a review of kidney compatibility and the forms of KPD. The second details the history and distinctive features of KPD programs, internationally and within the United States. Next, the third section presents case studies of national pairing organizations and individual transplant centers, highlighting differences and similarities that may explain variations in performance. Finally, the fourth section identifies the three major challenges facing the growth of KPD in the US – the balkanization of patient pools, lack of coordination among transplant centers, and positive cross match disruptions – and offers recommendations based on institutional best practices to mitigate each. Information on the history of KPD and recommendations were compiled through an extensive literature review. Many of the details included in the case studies were garnered from interviews with representatives from transplant centers and pairing organizations.

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Disciplines: Health Care Management and Public Policy

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Introduction

Background

From 1992 to 2014, the number of patients on the waiting list for kidney transplantation ballooned from 22,063 to over 100,000.[1] An increasing number of patients in need of a kidney transplant accompanied by stagnant organ donation rates has resulted in a substantial kidney shortage in the United States. As transplantation constitutes the primary treatment for end-stage renal disease (ESRD), this shortage poses a significant threat to the health of patients. Indeed, from 2008 to 2011 over 20,000 waitlisted patients died or became too ill for surgery.[2]

Recently, kidney paired donation (KPD) has arisen as a possible solution to the intensifying shortage of kidneys in the US and abroad. In a KPD exchange, two or more patient-donor couples agree that donors incompatible with their respective patients will donate a kidney to another patient with the expectation that their donation will be reciprocated on behalf of their patient. KPD provides numerous benefits, including better matches, kidneys from living donors (which last longer than kidneys from deceased donors), and less waiting and dialysis time.

When first executed, hospitals arranged these exchanges independently amongst their own patients, but soon databases and registries emerged to organize exchanges on a greater scale. Accordingly, the annual number of KPD transplants performed nationwide has increased from 2 in 2000 to 429 in 2011.[3] The last several years have seen the emergence of larger pairing organizations, such as the Alliance for Paired Donation (APD), the National Kidney Registry, and more recently the creation of a pilot paired exchange program by the United Network for Organ Sharing (UNOS). Proliferation of these matching systems promises to enhance the efficiency of living kidney donation, allowing for more transplants to take place.

Kidney Compatibility

There are two major matching considerations when donating a kidney: ABO blood type and HLA type. A patient can have blood type A, B, AB, or O. Type O kidneys can be donated to any patient, but type O patients can only receive type O kidneys. Type A and type B kidneys can donate to patients of their own blood type or type AB patients. Type AB kidneys can only be donated to type AB patients. The latter consideration, HLA type, refers to tissue type and consists of a combination of six proteins. The more of a mismatch between the patient and donor's HLA types, the less likely a transplant will be successful. Furthermore, it is possible that a patient's body contains antibodies targeted to the donor's HLA type. This "positive cross match" precludes transplantation.

[1] U.S. Department of Health and Human Services. (2014, May 12). *Data*. Retrieved May 12, 2014, from Organ Procurement and Transplantation Network: http://optn.transplant.hrsa.gov/data/

[2] The Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients. (2011). *Annual Data Report: Kidney*.

[3] Ibid.

Forms of Kidney Paired Exchange

Since Rapaport's initial proposal of the concept in 1986, KPD has evolved and is now visible in many forms.[4] The simplest procedure is a two-way exchange (Figure 1), whereby two incompatible pairs with reciprocal incompatibilities swap, the donor from the first pair donating to the recipient of the second pair, and the donor from the second pair donating to the recipient of the first pair. Three-way exchanges add another incompatible pair (Figure 2), which simultaneously increases the number of donations while making it easier for hard-to-match pairs by not requiring reciprocal incompatibilities. This advantage can be scaled to include more incompatible pairs, though such exchanges face considerable logistical challenges.

Newer strategies have become more complicated. A list exchange involves an incompatible donor donating to a candidate on the deceased kidney waitlist in return for a future deceased donor kidney (Figure 3). Critics warn that list exchanges systematically disadvantage blood type O waitlist candidates, because the most common exchange would include non-blood type O donor kidneys for blood type O deceased donor kidneys. Some now advocate the use of compatible pairs in KPD match runs desiring a better match (Figure 4), which would benefit O recipients and pairs with AB donors by making rare O donors and AB recipients more accessible.

Finally, initiation of an exchange by an altruistic or non-directed donor allows two more KPD exchange options: domino-paired donation chains (DPD) chains and non-simultaneous extended altruistic donor (NEAD) chains. In a DPD chain, the non-directed donor donates to the recipient of an incompatible pair, the donor of which either continues the chain by donating to another incompatible recipient, or ends the chain by donating to the waitlist (Figure 5). A NEAD chain alters the DPD chain structure in that the transplants are not executed simultaneously, which is standard KPA practice in order to eliminate risks of reneging by the donor. In a NEAD chain, the chain progresses as in a DPD chain, but the last donor becomes a "bridge donor." The bridge donor waits to perform another series of exchanges when they are matched, extending the chain to another segment of patient-donor couples (Figure 6).[5]

[4] Rapaport, F. T. (1986, June). The Case for a Living Emotionally Related International Kidney Donor Exchange Registry. *Transplantation Proceedings, 18*(3), 5-9.

[5] Wallis, C. B., Samy, K. P., Roth, A. E., & Rees, M. A. (2011). Kidney Paired Donation. *Nephrology Dialysis Transplantation, 26*(7), 2091-2099.

Figure 1: A Two-way Exchange

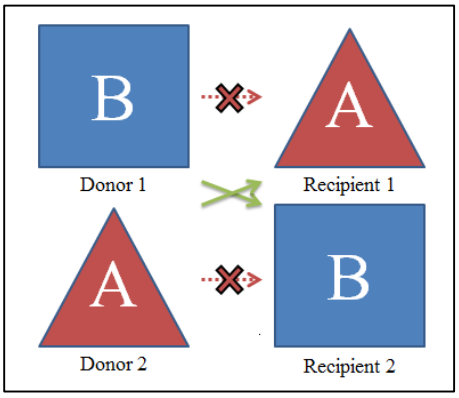


Figure 2: A Three-way Exchange

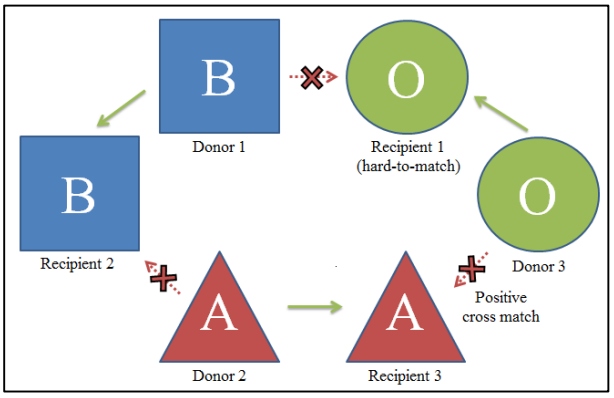


Figure 3: A List Exchange

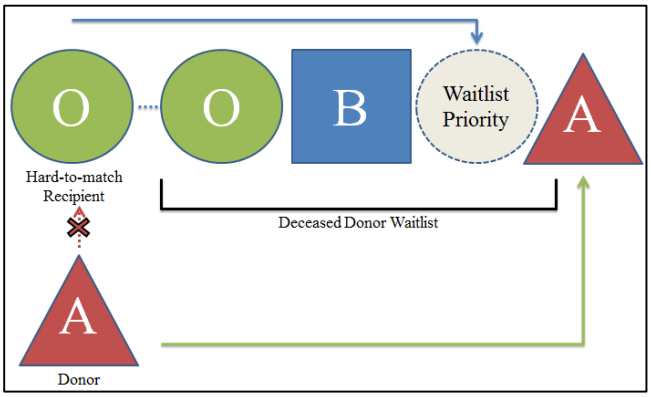


Figure 4: Use of a Compatible Pair

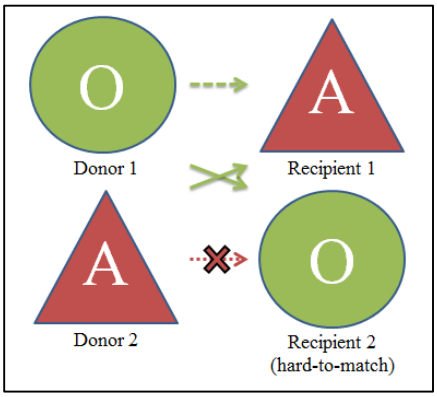


Figure 5: A Domino-paired Donation Chain

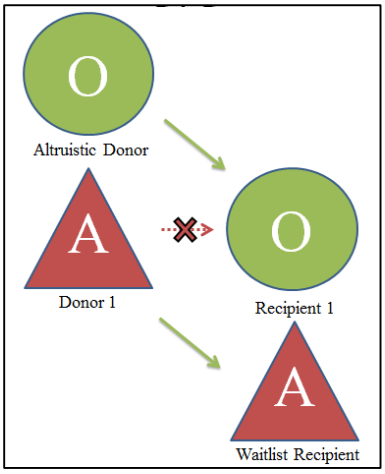
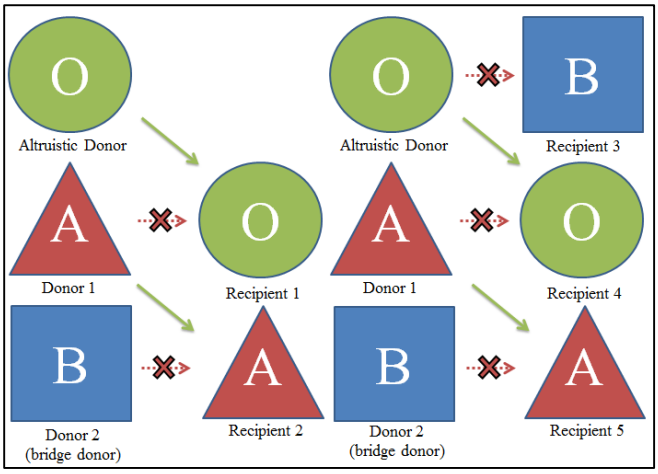


Figure 6: A NEAD Chain



History of Kidney Paired Donation

International Development

Many countries outside the US have identified kidney paired exchange as an answer to shortages in deceased kidneys. Significant KPD programs have emerged in countries such as South Korea, the Netherlands, and Australia in addition to isolated reports of KPD exchanges performed in places such as India and Israel. This section recounts the history of prominent KPD programs around the world, emphasizing distinctive features.

South Korea

In 1991, South Korean doctors under Park were the first in the world to perform a paired kidney exchange between two ESRD patients, each paired with a willing but incompatible donor due to positive cross match.[6] Korea has long faced shortages of donors, largely due to social and cultural views on transplantation. Specifically, most Koreans feel that deceased donors would be humiliated by organ harvesting, a sentiment stemming from the Confucianism idea holding that one's body should by fully intact upon burial. Consequently, Korea's unique cultural norms have limited the supply of kidneys to living donation.[7] In this environment, Korean medical professionals had a strong incentive to pursue KPD, which promised to provide for more transplants without the violation of Korean customs.

By 1995, the world's first KPD program was organized at Yonsei University College of Medicine in Seoul.[8] Since then, KPD has become a common method of kidney transplantation in Korea. In one transplant center, for instance, 22 percent of living kidney donations were performed through KPD exchanges from 1991 to 2010.[9] In 2001, the National Korean KPD program was formed to coordinate paired exchanges among the country's transplant centers. A nonprofit organization, the Korean Organ and Tissue Donor program, facilitates allocations. As of 2013, the program had arranged 179 transplants among 16 transplant centers, including two- to six-way exchanges.[10]

The South Korean population is particularly conducive to KPD, because it has fewer people with blood type O and more with blood type B compared to European and North American populations. Furthermore, there exist fewer highly sensitized recipients and more compatible pairs hoping for a better match. Finally, the South Korean program has benefited from many non-directed donors.

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[6] Park, K., Moon, J. I., Kim, S. I., & Kim, Y. S. (1999). Exchange Donor Program in Kidney Transplantation. *Transplantation, 67*(2), 336-338.

[7] Kim, J. R., Elliott, D., & Hyde, C. (2004, March). Korean health professionals' attitudes and knowledge toward organ donation and transplantation. *International Journal of Nursing Studies, 41*(3), 299-307.

[8] Huh, K. H., Kim, M. S., Chang, H. K., Ahn, H. J., Lee, S. H., Lee, J. H., et al. (2008, August). Exchange living-donor kidney transplantation: merits and limitations. *Transplantation, 86*(3), 430-435.

[9] Kim, J. R., Elliott, D., & Hyde, C. (2004, March). Korean health professionals' attitudes and knowledge toward organ donation and transplantation. *International Journal of Nursing Studies, 41*(3), 299-307.

[10] Mierzejewska, B., Durlik, M., Lisik, W., Baum, C., Schroder, P., Kopke, J., et al. (2013, March). Current approaches in national kidney paired donation programs. *Annals of Transplantation*, 112-124.

Europe

Adoption of KPD in Europe has varied across countries. Switzerland performed the first European paired exchange in 1999, involving two married couples.[11] Romania followed soon after, performing the country's first exchange in 2001 and subsequently developing two substantial single-center programs that successfully executed 56 transplants within five years.[12]

In 2004, the Netherlands created the first national KPD program in Europe. Under the Dutch system, the Dutch Transplant Foundation coordinates pairing efforts between the country's seven transplant centers, which all participate. Every KPD candidate is placed on a shared registry.[13] From 2004 to 2011, 187 of the 472 pairs enrolled (40 percent) received a transplant, one of the highest in the world.[14] In addition, the Dutch program boasts the highest percentage of matches that result in a transplant of any other program at 78 percent.[15] Observers credit the success of the Dutch system to its simple allocation algorithm, which places few restrictions on matches, and its central HLA reference laboratory that organizes all cross match testing.[16]

Following the Netherlands' example, the United Kingdom launched a national KPD program in 2006 and made its first pairing in 2007. The UK's National Living Donor Kidney Sharing Schemes (NLDKSS) is administered by the government's National Health Service Blood and Transplant (NHSBT). From January 2007 through June 2012, the NLDKSS enrolled 692 patients and transplanted 166 of them (24 percent).[17] Two explanations for this somewhat low figure include the program's previous ban on altruistic donors and its current restriction on chain length. NLDKSS allowed altruistic donors in 2012 and saw a jump in transplants arranged, but the program continues to permit only two- and three-way exchanges. While logistics for longer chains are more difficult to manage, barring them decreases the amount of transplants possible among small patient pools.[18]

The most recent addition to the European KPD landscape is the Spanish Crossover Donation Plan (Plan Nacional de Donación Cruzada), which began operation in 2009. Spain's KPD program centers on the government's National Transplant Organization (ONT), which coordinates pairings among 21 hospitals across the country from a single shared registry. As of

[11] Thiel, G., Vogelbach, P., Gürke, L., Gasser, T., Lehmann, K., Voegele, T., et al. (2001, February-March). Crossover renal transplantation: hurdles to be cleared! *Transplantation Proceedings, 33*(1-2), 811-816.

[12] Lucan, M. (2007, June). Five Years of Single-Center Experience With Paired Kidney Exchange Transplantation. *Transplantation Proceedings, 39*(5), 1371-1375.

[13] Mierzejewska, B., Durlik, M., Lisik, W., Baum, C., Schroder, P., Kopke, J., et al. (2013).

[14] Hilbrands, L. (n.d.). *How to manage domino transplantation: The Dutch living donation program.* Retrieved May 6, 2014, from Stiftung Lebendspende: http://www.stiftung-lebendspende.de/files/hilbrands_living_donation_munchen.pdf

[15] Ferrari, P., & Klerk, M. D. (2009). Paired kidney donations to expand the living donor pool. *Journal of Nephrology, 22*(6), 699-707.

[16] Ibid.

[17] Burnapp, L. (2013). *National Living Donor Kidney Sharing Schemes.* National Health Service, Blood and Transplant.

[18] Manlove, D. F., & O'Malley, G. (2012). *Paired and Altruistic Kidney Donation in the UK: Algorithms and Experimentation.* Technical Report, University of Glasgow, School of Computing Science.

2013, the ONT had arranged 51 paired exchanges since inception. Today, the program is small and developing – in September 2013, the program contained only 89 patient-donor couples.[19] It should be noted that Spain enjoys the highest deceased donation rates in the world. Such favorable views of organ donation bode well for KPD.[20]

European adoption of KPD has been irregular largely due to legal barriers to adoption. Many European countries, such as Germany and France, permit organ donation only to family relations or good friends on ethical grounds. In fact, a similar UK law was changed immediately prior to the creation of the NLDKSS in 2006. For continued proliferation of KPD programs, European transplant laws will need to be modified to permit unrelated donors.[21]

Australia

KPD in Australia began with a single-center program in Perth, Western Australia in October 2007. Over the course of a year, the WA program successfully arranged and executed three two-way exchanges and one three-way exchange for the benefit of nine patients.[22] Following WA's success, the Australian Paired Kidney Exchange (AKX) program was established in 2010. Organized under the Australian Government's Organ and Tissue Authority, the AKX program has enjoyed considerable success in its limited history. As of December 31, 2013, the AKX program had facilitated 80 paired exchanges among 21 transplant centers, primarily through two- and three-way exchanges. Ultimately, an impressive 41 percent of registered couples have received a transplant.[23]

One unique feature of the AKX program that contributes to this success is its National Organ Matching System (NOMS). Rather than utilizing a traditional low-resolution identification of HLA antigens, NOMS incorporates a high-resolution HLA identification at the allelic level. The result is a matching system that allocates according to the Dutch algorithm, but modified to run a "virtual cross match" during allocations, maximizing the number of matches with predicted negative cross match. This reduces the possibility of disrupting the entire chain in case of a positive cross match.[24]

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[19] Prats, J. (2013, October 8). *El trasplante de riñón cruzado despega en España*. Retrieved May 4, 2014, from El País: http://sociedad.elpais.com/sociedad/2013/10/08/actualidad/1381220931_646565.html

[20] Matesanz, R., Domínguez-Gil, B., Coll, E., de la Rosa, G., & Marazuela, R. (2011, April). Spanish experience as a leading country: what kind of measures were taken? *Transplant International, 24*(4), 333-343.

[21] Klerk, M. D., Keizer, K. M., Claas, F. H., Witvliet, M., Haase-Kromwijk, B. J., & Weimar, W. (2005, September). The Dutch National Living Donor Kidney Exchange Program. *American Journal of Transplantation, 5*(9), 2302-2305.

[22] Ferrari, P., Woodroffe, C., & Christiansen, F. T. (2009). Paired kidney donations to expand the living donor pool: the Western Australian experience. *The Medical Journal of Australia, 190*(12), 700-703.

[23] Australian Government: Organ and Tissue Authority. (2013). *Australian Paired Kidney Exchange (AKX) Program.* Biannual Report.

[24] Ferrari, P., Fidler, S., Wright, J., Woodroffe, C., Slater, P., Van Althuis-Jones, A., et al. (2011, February). Virtual Crossmatch Approach to Maximize Matching in Paired Kidney Donation. *American Journal of Transplantation, 11*(2), 272-278.

Canada

Canada launched its Living Donor Paired Exchange (LDRE) program as a three-province pilot in 2009 before expanding it nationwide in 2010. The LDRE is a KPD registry managed by the nonprofit Canadian Blood Services in cooperation with transplant centers across the country. Previously, KPD exchanges were performed by provinces, territories, and programs with separate registries.[25] As of September 2013, LDRE had enrolled 468 patient-donor couples and had performed 218 transplants.[26] Notably, LDRE limits its matches to amount to no more than a five-way exchange.[27] Important aspects of the Canadian system are standardized patient work-up procedures and HLA laboratory practices across all transplant centers. The LDRE also has a dedicated staff that coordinates transplants as well as an advisory committee of transplant professionals to address logistical and medical issues that arise.[28]

Domestic Development

Compared to international programs, development of KPD in the US has occurred in a balkanized fashion. Rather than the adoption of distinct regional programs or a single national program, several multicenter programs and numerous single-center programs with overlapping footprints exist in the US. This section provides an overview of the legal developments that enabled KPD's proliferation in the US as well as a history of several important regional programs that pioneered KPD. National programs will be discussed in the next section.

Legal Development

In 1984, Congress passed the National Organ Transplant Act (NOTA), which established the Organ Procurement and Transplantation Network (OPTN) to operate the nation's organ donation programs. The United Network for Organ Sharing (UNOS) was granted the first contract to administer this program and it has held the contract since. Responding to a commercial endeavor to create an organ market, Congress outlawed the buying and selling human organs. Section 301 of NOTA stated:

> "It shall be unlawful for any person to knowingly acquire, receive, or otherwise transfer any human organ for valuable consideration for use in human transplantation…"[29]

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[25] Canadian Blood Services. (2010, November 30). *Kidney Exchange Registry Goes National*. Retrieved May 5, 2014, from Canadian Blood Services: http://www.blood.ca/CentreApps/Internet/UW_V502_MainEngine.nsf/9749ca80b75a038585256aa20060d703/a9da5ee7a67d8b57852577eb00486ce4?OpenDocument

[26] Malik, S., & Cole, E. (2014, March). State of the Art Practices and Policies in Kidney Paired Donation. *Current Transplantation Reports, 1*(1), 10-17.

[27] Tucker, E. (2012, February 14). *Q & A: How does the Canadian kidney exchange work?* Retrieved May 3, 2014, from Global News: http://globalnews.ca/news/211538/q-a-how-does-the-canadian-kidney-exchange-work/

[28] Malik, S., & Cole, E. (2014).

[29] 98th United States Congress. (1984, October 12). National Organ Transplant Act.

At the outset of KPD, it was unclear if paired exchanges constituted "valuable consideration" and were consequently illegal under NOTA. While some organizations performed KPD exchanges, many hospitals refused to participate, wary of legal repercussions. Meanwhile, medical professionals held numerous consensus conferences to discuss the ethical, legal, and medical implications of KPD. In these forums, a clear accord emerged in favor of KPD. Medical professionals quickly grasped the potential KPD had to address the severe national kidney shortage.[30] [31] By 2005, conferences were being held to deliberate the possibility of regional or national exchange programs.[32]

In response to the medical community's support of KPD as well as the increasing number of paired exchanges, Congress amended NOTA in 2007 with the Charlie W. Norwood Living Organ Donation Act. This amendment clarified section 301 by adding the sentence, "The preceding sentence does not apply with respect to human organ paired donation."[33] Congress agreed with the UNOS Associate General Counsel's argument that paired donation constituted a gift, rather than consideration.[34]

Following the amendment's passage, KPD became widely accepted. New KPD organizations were formed and existing ones grew in size. Of particular importance, the NOTA amendment allowed UNOS to create a national exchange. Though the organization had originally presented a KPD concept in 2004 and had detailed a specific proposal in 2006, the board of directors was unwilling to proceed due to uncertainty regarding the law. With that hurdle cleared, the OPTN/UNOS kidney transplantation committee issued requests for information to operating pairing organizations and lunched its pilot program in 2010.[35]

Regional Pairing Organizations

New England Program for Kidney Exchange

The first KPD exchange in the United States was performed by surgeons Anthony P. Monaco and Paul E. Morrissey at Rhode Island Hospital (RIH) in 2000.[36] In the following year, 14 New England transplant centers including RIH established a KPD program for UNOS Region

[30] Adams, P. L., Cohen, D. J., Danovitch, G. M., Edington, R. M., Gaston, R. S., Jacobs, C. L., et al. (2002, August 27). The nondirected live-kidney donor: ethical considerations and practice guidelines: A National Conference Report. *Transplantation, 74*(4), 582-589.

[31] Spital, A. (2005, November). Increasing the Pool of Transplantable Kidneys Through Unrelated Living Donors and Living Donor Paired Exchanges. *Seminars in Dialysis, 18*(6), 469-473.

[32] Gentry, S. E., Shapiro, R., & Segev, D. L. (2014). Chapter 2: Kidney Paired Donation Programs for Incompatible Living Donors and Recipients. In J. Steel, *Living Donor Advocacy: An Evolving Role Within Transplantation* (pp. 17-26).

[33] 110th United States Congress. (2007, December 7). Charlie W. Norwood Living Organ Donation Act.

[34] Williams, E. D., Reyes-Akinbileje, B., & Swendiman, K. S. (2009). *Living Organ Donation and Valuable Consideration.* United States Congressional Research Service.

[35] Sokohl, K. (2010, March-April). Getting It Right: Kidney committee easing into KPD with two-step pilot project. *UNOS Update*.

[36] Roth, A. (2010). *Kidney Exchange.* Class Lecture, Harvard University.

1. At this stage, matches were manually arranged between centers in the region when internal options were exhausted. As a result, only 12 KPD transplants were performed in the Region 1 program between 2000 and 2005.[37]

In 2004, Roth et al. proposed a "kidney exchange clearinghouse in New England" that would apply game theory algorithms to kidney matching among the region's 14 participating transplant centers. In September, the Renal Transplant Oversight Committee of New England approved the proposal, creating the New England Program for Kidney Exchange (NEPKE) to support the effort.[38] From the incorporation of the proposed computerized matching system in June 2005 to June 2010, the number of KPD transplants arranged by NEPKE leaped to 58.[39]

Initially, NEPKE only arranged two- and three-way exchanges via an Excel spreadsheet entry system. In 2007, a secure web-based data entry system was integrated into the matching software. The program's first four-way offer was extended in 2008, followed by its first DPD chain in 2010. Likewise in 2010, the program increased match run frequency from every 45 days to every two weeks, resulting in an increased number of matches. NEPKE's success corresponded to a decrease in the need for deceased kidney donation.[40]

With the foundation of the UNOS KPD pilot program, NEPKE was chosen as a regional "coordinating center" to act as an intermediary between transplant centers and UNOS. NEPKE ultimately shut down in favor of the pilot program on December 31, 2011.[41]

Johns Hopkins Incompatible Kidney Transplant Program

The Johns Hopkins Incompatible Kidney Transplant Program (InKTP) has performed KPD exchanges since 2001. Surgeons at Johns Hopkins are credited with numerous KPD achievements, including the first three-, five-, six-, and eight-way exchanges in 2003, 2005, 2007, and 2009, respectively.[42] InKTP is a small multicenter KPD program consisting of six transplant centers based in The Johns Hopkins Hospital. In addition to pairing many patients internally, InKTP works with both the UNOS KPD pilot program and the NKR, to be discussed further in detail later. Similar to NEPKE, Johns Hopkins served as a coordinating center during the foundation of the UNOS program.[43]

Since beginning to arrange KPD exchanges, Johns Hopkins' patient pool has become saturated with highly sensitized patients (likely to experience positive cross match), who have

[37] Hanto, R. L., Saidman, S., Roth, A. E., & Delmonico, F. (2010, July). The Evolution of a Successful Kidney Paired Donation Program. *Transplantation, 90*(25), 940.

[38] Roth, A. E., Sönmez, T., & Ünver, M. U. (2005, May). A Kidney Exchange Clearinghouse in New England. *The American Economic Review: Papers and Proceedings, 95*(2), 376-380.

[39] Hanto, R. L., Saidman, S., Roth, A. E., & Delmonico, F. (2010).

[40] Ibid.

[41] Roth, A. (2010).

[42] Johns Hopkins Medicine. (2014). *Transplantation*. Retrieved May 1, 2014, from Johns Hopkins Medicine: http://www.hopkinsmedicine.org/usa/excellence/transplantation.html

[43] U.S. Department of Health and Human Services. (2010, October 5). *Kidney Paired Donation Pilot Program to Begin Matching in October; Participating Programs Named*. Retrieved March 11, 2014, from Organ Procurement and Transplantation Network: http://optn.transplant.hrsa.gov/news/newsDetail.asp?id=1404

historically been very difficult to pair. To address this challenge, Montgomery, director of the Johns Hopkins Comprehensive Transplant Center, developed desensitization procedures that can mitigate to some degree the issues associated with sensitized patients. Currently, the majority of Johns Hopkins' pairings combine KPD with desensitization. By permitting "unacceptable" antigens which can be removed through minimal sensitization, Johns Hopkins enlarged the body of potential matches in their patient pool and, consequently, enjoyed significant increases in transplant rates.[44] Desensitization is becoming more common elsewhere, but Johns Hopkins' frequent use of the technique in conjunction with KPD is a relatively unique practice.

Other Organizations

In addition to the major regional programs discussed and the national programs to be described below, several smaller organizations have existed within the field.

- North Central Donor Exchange Cooperative (NCDEC): a KPD program consisting of 12 transplant centers in North Dakota, South Dakota, Minnesota, Iowa, and Wisconsin.[45] Of note, NCDEC performs virtual cross matches during the matching process to reduce chances of positive cross match and cooperates with other pairing organizations.[46]
- Washington Regional Transplant Community (WRTC): an organ procurement organization (OPO) that, like many other OPOs, managed a KPD program among the five transplant centers within its service area. In fact, WRTC pioneered OPO-led KPD. With the advent of the UNOS KPD Pilot Program as well as other national organizations, OPO-led KPD programs like the WRTC were discontinued.[47]
- North American Paired Donation Network (PDN): in 2006 the largest KPD program in existence, the PDN was a consortium of regional KPD programs from across the country that formed the first national KPD organization.[48] By 2013, the PDN had become defunct.[49] Former PDN member transplant centers now belong to the national organizations discussed below.

[44] Montgomery, R. A., Lonze, B. E., & Jackson, A. M. (2011, August). Using donor exchange paradigms with desensitization to enhance transplant rates among highly sensitized patients. *Current Opinion in Organ Transplantation, 16*(4), 439-443.

[45] North Central Donor Exchange Cooperative. (2014). *Home*. Retrieved May 11, 2014, from North Central Donor Exchange Cooperative: http://www.ncdec.org/default.asp

[46] Akkina, S. K., Muster, H., Steffens, E., Kim, S. J., Kasiske, B. L., & Israni, A. K. (2011, January). Donor Exchange Programs in Kidney Transplantation: Rationale and Operational Details From the North Central Donor Exchange Cooperative. *American Journal of Kidney Diseases, 57*(1), 152-158.

[47] Washington Regional Transplant Community. (2014). *Living Kidney Donor program*. Retrieved May 11, 2014, from Washington Regional Transplant Community: http://www.beadonor.org/donation-facts/living-donation/living-kidney-donor-program

[48] Woodle, E. S., Goldfarb, D., Aeder, M., Lal, T., Rike, A., Weimart, N., et al. (2005). Establishment of a nationalized, multiregional Paired Donation Network. *Clinical Tranplantation*, 247-58.

[49] GuideStar. (2014). *GuideStar Premium Report for Paired Donation Network.*

Single-Center Exchange Programs

Despite the increasing prominence and proliferation of pairing organizations, some transplant centers choose to arrange exchanges themselves from among their patient pool. Methodist Specialty and Transplant Hospital in San Antonio constitutes the largest single-center exchange program in the world, performing 134 KPD transplants during a three-year period beginning in 2008.[50]

The main rationale for transplant centers carrying out their own KPD program is that it makes the logistics much easier. Instead of coordinating with other transplant centers and pairing organizations, a single transplant center can manage the logistics internally. This includes standardized work ups and patient control, and it avoids the complexities associated with shipping kidneys. When a match is arranged, transplant centers acting independently can usually complete the transplant much more quickly than a pairing organization, which reduces patient uncertainty and the risk of reneging.

On the other hand, the large downside for single-center programs is that they will be less able than pairing organizations to arrange matches because of a smaller participant pool. A larger pool of KPD participants increases the chances of a successful match, as well as the quality of each match, due to greater heterogeneity among kidneys. Thus, only large transplant centers can sustain a stand-alone KPD program. Single-center exchange programs trade longer wait times and potentially lesser quality matches for increased efficiency when matches are made.

[50] Bingaman, A. W., Wright, F. H., Kapturczak, M., Shen, L., Vick, S., & Murphey, C. L. (2012, August). Single-Center Kidney Paired Donation: The Methodist San Antonio Experience. *American Journal of Transplantation, 12*(8), 2125-2132.

Case Studies in Kidney Paired Donation

In order to gain a detailed understanding of KPD in the US today, this section examines several case studies of KPD practices. First, the three major national pairing organizations – the National Kidney Registry, the Alliance for Paired Donation, and the UNOS KPD Pilot Program – are discussed. Then, three individual transplant centers are examined to convey their perspectives regarding KPD. Information contained in these case studies was obtained both through literature review and interviews with personnel.

National Pairing Organizations

National Kidney Registry

The National Kidney Registry (NKR) is regarded as the leading pairing organization in the US, largely by virtue of the fact that it was the first major player to effectively arrange exchanges nationwide. NKR works with network of 68 partner transplants centers that are generally components of major medical centers.[51]. Since its founding in 2007, the number of NKR's transplants facilitated annually has grown from 21 in 2008 to 308 in 2013, and it recently celebrated its 1,000th arranged transplant in March 2014.[52] This number dwarfs the comparable figure by the Alliance for Paired Donation and the UNOS KPD Pilot Program.

Aside from pairing based on compatibility (HLA type and cross match), NKR allows recipients to express preferences regarding their donated kidney that will be incorporated as restraints in the matching process. Specifically, recipients can specify maximum donor age, minimum donor weight, willingness to receive a shipped kidney, and minimum HLA points (degree of HLA match). Donors can also express their willingness to travel.[53] Patients are not charged for enrollment in NKR's system, though hospitals must pay a fee to cover operational costs that amounts to roughly $5,000 per transplant.[54]

Each transplant center inputs patient information and preferences into NKR's Toolbox and Swap Expert software. On a daily basis, NKR runs its software to create matches among patients active in the system. Generally, match runs attempt to maximize the number of transplants that can be arranged, except when hard-to-match pairs can be paired or time is limited. When time is limited (e.g. an NDD with a limited timeframe for donation), NKR matches to maximize the probability of making it to transplant within the timeframe, based on factors such as whether donors have been accepted by pre-select (see below), cross match has already been completed and found to be negative, and the center has the capability to transplant within three days of receiving the offer. In normal cases where multiple possible match combinations exist, NKR gives preference to patients

[51] National Kidney Registry. (2014). *Kidney Transplant Centers*. Retrieved March 3, 2014, from National Kidney Registry : http://www.kidneytransplantcenters.org/?for=next-steps

[52] Sinacore, J. (2014, March 12). *National Kidney Registry Facilitates 1000th Transplant*. Retrieved 1 March, 2014, from National Kidney Registry: http://www.kidneyregistry.org/pages/p292/PR_1000th_Transplant.php

[53] National Kidney Registry. (n.d.). *Swap Expert for EASYMATCH.* Retrieved March 1, 2014, from National Kidney Registry: http://www.kidneyregistry.org/docs/swap_expert_pdf1.pdf

[54] Mierzejewska, B., Durlik, M., Lisik, W., Baum, C., Schroder, P., Kopke, J., et al. (2013).

with the longest wait times in the NKR system and children. Matches are communicated to the partner transplant centers, which usually have three days to accept or reject the match and ten days to perform the cross match.[55]

Transplant coordinators report that the greatest challenges to transplant are positive cross matches and patient health. To combat the frequency of positive cross matches, NKR created a function whereby physicians can pre-select possible matches for highly sensitized patients in the NKR database to increase the odds of a successful match. In response, the rate of positive cross matches has declined significantly, though it remains a barrier to transplant.[56] Patient health failures continue to disrupt matched chains.

NKR's approach begins with an altruistic donor to begin a NEAD chain and ends when a bridge donor is not matched with another chain segment and instead donates to the deceased waitlist (see above). Note that NKR arranges matches exclusively through chains, averaging five transplants each. Indeed, NKR has pioneered an innovative approach of executing a chain out of order, something it calls a "modified-sequence asynchronous transplant chain" or MATCH chain.[57]

Once NKR has outlined a chain, it prepares a logistical plan for carrying out the transplants. Transplant coordinators describe the process as being NKR-led, with numerous conference calls among the participant centers moderated by NKR, which has standardized checklists to ensure all factors are considered. NKR dictates the timetable and sets forth strict guidelines as to the transportation of kidneys between centers. Transplant coordinators view NKR's efficiency and initiative in organizing logistics to be a great strength for the organization.[58]

Alliance for Paired Donation

The Alliance for Paired Donation (APD) was founded initially in 2001 when Ohio's nine transplant centers joined together to engage in KPD as the Ohio Solid Organ Transplantation Consortium (OSOTC). Under the OSOTC, the program had little success, resulting in 12 transplants for the 75 patient-donor couples registered (16 percent). In May 2006, the group reorganized as the APD, and by March 2007 the program had completed its first KPD exchanges.[59]

Since then, the APD has program has performed over 160 KPD transplants ranging from traditional two- or three-way exchanges to the first non-simultaneous extended altruistic donor (NEAD) chain. Meanwhile, the number of transplant centers cooperating with the APD has grown

[55] National Kidney Registry. (n.d.). *Medical Board Policies*. Retrieved March 1, 2014, from National Kidney Registry: http://www.kidneyregistry.org/transplant_center.php

[56] Charlton, M. (2014, January 16). Kidney Paired Exchange at NewYork-Presbyterian/Weill Cornell Medical Center. (B. J. Ellison, Interviewer)

[57] Mierzejewska, B., Durlik, M., Lisik, W., Baum, C., Schroder, P., Kopke, J., et al. (2013).

[58] Barnett, K. (2014, January 31). Kidney Paired Donation at PinnacleHealth. (B. J. Ellison, Interviewer)

[59] Rees, M. A. (2007). *Kidney Paired Donation.* Alliance for Paired Donation.

to over 70, operating in 30 states throughout the country.[60] Like NEPKE and Johns Hopkins, the APD was selected to be a coordinating center for the UNOS pilot program in 2010.[61]

A distinguishing feature of the APD model is its sophisticated matching software, which scores recipients based on eight criteria:

1. Age difference between the recipient and the donor
2. Recipient age (more points awarded to children below 18 years of age)
3. Degree of HLA matching between donor and recipient
4. cPRA level (a measure of sensitization)
5. Travel distance
6. Previous status as kidney donor
7. CMV and EBV virus infection status
8. Time spent on waiting list

Under this system, the software first matches ABO type before performing a virtual cross match, which depends on the centers' specified unacceptable antigens, subject to modification by the APD's central laboratory. Then, points are applied depending on the factors listed above. Notably, the APD performs match runs daily. This system permits the APD to allocate kidneys on the basis of many different criteria, which allowed the organization to develop NEAD chains.[62] Note that the APD does not charge fees for its services, instead relying on philanthropic donations.

UNOS Kidney Paired Donation Pilot Program

Though a Kidney Paired Donation Pilot Program (KPDPP) was initially proposed by UNOS as early as 2004, UNOS performed its first match in 2010. Because UNOS administers the nation's organ transplant system, it enjoys widespread access to transplant centers across the country. As a result, despite being less developed and newer than NKR and the APD, UNOS partners with 131 centers (as of October 2013), which constitutes over half of living donor programs in the US.[63] Nevertheless, UNOS has arranged fewer exchanges than both organizations: 60 transplants from October 2010 to August 2013.[64]

Similar to NKR, the KPDPP allows candidates to specify preferences regarding the kidney they receive. Recipients can stipulate age range, BMI, willingness to travel, and the status of certain diseases (i.e. donor Hepatitis B or Epstein-Barr virus status). Unlike NKR, UNOS does not charge patients or hospitals beyond the flat fee required to register for the UNOS kidney transplant waiting list. In its match runs, UNOS utilizes a point weighting system like the APD's based on the following six criteria to choose among possible matches:

[60] Mierzejewska, B., Durlik, M., Lisik, W., Baum, C., Schroder, P., Kopke, J., et al. (2013).
[61] U.S. Department of Health and Human Services. (2010).
[62] Mierzejewska, B., Durlik, M., Lisik, W., Baum, C., Schroder, P., Kopke, J., et al. (2013).
[63] Andreoni, K. (2013). *OPTN/UNOS Kidney Paired Donation Pilot Program.* United Network for Organ Sharing.
[64] Leishman, R. (2013). *OPTN Kidney Paired Donation Pilot Program.* United Network for Organ Sharing.

1. Zero antigen mismatch between donor and candidate
2. Highly sensitized candidate (over 80% probability of positive cross match)
3. Prior living donor status of candidate
4. Pediatric candidate (less than 18 years of age)
5. Waiting time accumulated within the KPDPP
6. Geographic proximity[65]

Transplant centers enter candidates' basic information into UNOS's UNet matching software, which draws medical information from the kidney transplant wait list upon registration. Since beginning with monthly matching runs in 2010, UNOS has increased its matching frequency to a weekly basis, occurring every Monday. UNOS arranges two- and three-way exchanges as well as chains that are capped at four patient-donor pairs.[66]

Since its initial match run with 43 candidates and 45 donors, the size of the UNOS system has consistently grown in number. During Match Run #79 on September 3, 2013, for example, the UNOS UNet included 221 candidates and 231 donors and arranged one three-way exchange and one four-chain exchange for a total of seven candidates aided. Accordingly, the number of matches per month has increased steadily from seven in October 2010 to 42 in April 2013. On average, this results in a match for approximately 6 percent of candidates each run. When matches are made, the success rate in terms of the proportion of matches resulting in transplants is very low: 10.9 percent from November 2012 to January 2013.[67] Those matches that fail to reach transplant are largely due to positive cross match, unacceptable antigens, patient or donor health, or candidate or donor preferences.[68] UNOS has also implemented a pre-select tool to reduce frequency of positive cross match. When matches reach the planning phase, transplant coordinators perceive UNOS as more hands-off than NKR. Individual transplant centers work closely together to plan logistics such as operating times and travel.[69]

In 2013, UNOS/OPTN conducted a survey of 231 living donor programs in the U.S. to gauge barriers to participation in the KPDPP. On the positive side, respondents indicated that the KPDPP's UNet system was easy to use, UNOS provided sufficient program support and communicated well, and the KPDPP was efficient and transparent. Respondents also indicated several major areas for improvement. First, transplant centers want to reduce the time from offer to transplant (on average, about 90 days, though it depends on the type of match arranged[70]). Second, respondents reported inter-center communication to be lacking. Third, while UNet is easy

[65] Kidney Transplantation Committee. (2008). *Proposal for a National Kidney Paired Donation (KPD) Pilot Program.* Briefing Paper, United Network for Organ Sharing.
[66] Ibid.
[67] Andreoni, K. (2013).
[68] Leishman, R. (2013).
[69] Barnett, K. (2014).
[70] Leishman, R. (2013, December 4). The UNOS Kidney Paired Donation Pilot Program. (B. J. Ellison, Interviewer)

to use, transplant centers view the data entry as time-consuming. Fourth, participants want to increase the KPDPP's success in terms of match offers and transplants. Finally, UNOS's requirement that patients receive two years of follow-up care, unreimbursed, is a burden that falls squarely on participating transplant centers.[71]

Discussion: Comparing NKR and the UNOS KPDPP

While NKR, the APD, and the UNOS KPDPP have many similarities, several differences between the three major national pairing organizations may help to explain disparities in terms of scope and success rates.

First, it seems that NKR allows for the placement of the least amount of restrictions on the universe of possible matches. For example, NKR only permits patients to express basic preferences such as age or weight, while UNOS patients can specify acceptable donor blood pressure or minimum donor creatinine clearance. Furthermore, NKR's matching algorithm appears simple compared to the point weighting systems of the APD and UNOS. By adding constraints, the APD and UNOS lessen the number of potential matches, though it is possible these restrictions increase the quality of matches once they are made. Nevertheless, pairing organizations and transplant centers often recommend a relaxing of preferences for recipients who have waited in the system for a long time in order to increase their chances for a match.

Second, UNOS enjoys several advantages over NKR and ADP by virtue of being the government-contracted organ transplant organization in the US. UNOS does not require additional fees beyond the flat fee necessary to register for the kidney transplant wait list, but NKR charges hospitals for operational costs. Nonetheless, while transplant centers recognize this advantage, they will still pay NKR's fee if it results from a transplant. UNOS also has greater access to transplant centers, because all living donor centers already have a relationship with UNOS. It appears, however, that this advantage remains basically untapped as only 41 percent of respondents to the OPTN KDP Pilot Program Participation Survey reported that their center had entered at least one pair into the KPDPP.[72] A final advantage for the KPDPP is its enhanced ability to integrate its system with the wait list, because it operates both.

Third, NKR's advantages over the ADP and the KPDPP stem mainly from its "first mover advantage." While the ADP was formed at the same time as NKR, ADP began as a regional organization. As the first major nationwide pairing organization, NKR has built a strong reputation that its partners trust with their patients. This is evidenced by NKR's larger participant pool (of over 500 pairs)[73] and its greater number of arranged matches, despite having fewer partners than UNOS or the ADP. Transplant coordinators explain that NKR's matching process is faster, and once matches have been made NKR has a streamlined logistics process that is easier for transplant

[71] Andreoni, K. (2013).

[72] Ibid.

[73] Toulis, P., & Parkes, D. C. (2014). A Random Graph Model of Multi-Hospital Kidney Exchanges. *Games and Economic Behavior (Submitted)*.

centers to follow. They also explain, however, that the KPDPP is catching up and that more experience will likely reduce the gap between NKR and UNOS.[74]

Fourth, the KPDPP's requirement that transplant centers provide follow-up care for donors unreimbursed constitutes an additional cost imposed by UNOS, but not by NKR or the APD. Transplant coordinators have indicated that, while transplant centers are willing to provide this care, the cost does not go unnoticed.

A final significant difference between NKR, the ADP, and the KPDPP is the types of exchanges allowed by each. NKR only matches through NEAD chains, the ADP uses exchanges and chains, and the KPDPP performs two- and three-way matches and caps chains at four transplants. It is possible that the KPDPP's restrictions on exchanges and chains limit potential matches that could result in more transplants. In addition, capping chains at four transplants directly limits the number of matches enabled by altruistic donors, which are rare. By contrast, the NKR does not restrict its chains, and was responsible for the longest chain in history involving 30 transplants and 60 participants.[75]

Transplant Centers

NewYork-Presbyterian Hospital / Weill Cornell Medical Center

Located in New York City, NewYork-Presbyterian Hospital is the largest hospital in the U.S. with approximately 2,600 beds.[76] The hospital is associated with two medical schools: Columbia University College of Physicians and Surgeons and Weill Cornell Medical Center. NewYork-Presbyterian Hospital/Weill Cornell Medical Center (NYP/WCMC) began performing internal two-way exchanges in 2007, but quickly recognized the restriction associated with a limited number of patients. Accordingly, NYP/WCMC became one of the founding member transplant centers of the NKR in 2008. This relationship has facilitated over 100 transplants, and between 2011 and 2012 KPD accounted for nearly 20 percent of the medical center's kidney transplant volume.[77]

During a patient's evaluation for kidney transplant, physicians at NYP/WCMC emphasize the benefits of KPD. NYP/WCMC's pre-transplant orientation video includes KPD, and physicians take particular care in explaining KPD if the patient has an incompatible donor. If a patient opts into KPD, NYP/WCMC enrolls them immediately in NKR, rather than attempting to arrange an internal match. Chief Transplant Coordinator Marian Charlton explains that NKR arranges better matches in a shorter amount of time, but also notes NYP/WCMC's attitude regarding KPD. While internal matches might make the transplant process easier to organize,

[74] Barnett, K. (2014).

[75] Sack, K. (2012, February 18). 60 Lives, 30 Kidneys, All Linked. *The New York Times*, p. A1.

[76] Gamble, M. (2013, June 20). *50 Largest Hospitals in America*. Retrieved March 17, 2014, from Becker's Hospital Review: http://www.beckershospitalreview.com/lists/50-largest-hospitals-in-america-2013.html

[77] Gaber, A. O. (2013). *Current Topics in Transplantation.*

NYP/WCMC strongly believes in the benefits of KPD and understands the broader benefits of creating a single, large patient pool. This practice distinguishes NYP/WCMC.[78]

NYP/WCMC works exclusively with NKR. Ms. Charlton describes NYP/WCMC's decision as stemming from NKR's efficient and easy-to-use computer system, the organization's forward-looking approach to problem solving, and the effort it exerts to arrange transplants. For a time, NYP/WCMC enrolled some patients in the UNOS KPDPP, but found the UNOS system to be too slow – NKR matched the patients before UNOS. Transplant coordinators find it difficult to manage patients in multiple registries, and thus many transplant centers to choose one pairing organization with which to work.[79]

An average match takes approximately six months to arrange, but the time from enrollment to match varies significantly – a straightforward exchange can be found within a month or two while a highly sensitized patient can wait two or three years before finding a match. Nevertheless, Ms. Charlton reports that all patients healthy enough for transplant eventually receive a kidney. Moreover, all of the transplants that have been executed through NKR have been successful.[80]

California Pacific Medical Center

California Pacific Medical Center (CPMC) is a 785-bed hospital in San Francisco.[81] CPMC performed its first KPD transplant in 2003, and has subsequently performed more complex exchanges, including a 5-way exchange in 2011, for a total of approximately 15-20 KPD transplants each year. CPMC arranges the majority of its KPD transplants internally, though it does partner with NKR and the UNOS KPDPP. In fact, CPMC collaborated with the UCLA Medical Center to be a coordinating center in the first stage of the KPDPP.[82]

When a patient first opts into KPD, CPMC first attempts to arrange matches internally because it can exercise a greater degree of control over the surgical procedures and transplant logistics than it can while arranging a match through a pairing organization. Consequently, CPMC usually executes a transplant within three weeks of a match. CPMC Department of Transplantation Administrative Director Dr. Christine Moyle points out that reimbursement for surgical services is an added complexity associated with pairing organizations. The recipient transplant center pays the cost for donor surgeries, but because health care costs can vary considerably across the country, it is often much less costly to perform matches internally. Finally, pairing organizations require patients to have completed a full clinical work up and be ready for transplant when they enroll. CPMC can input patient-donor pairs into their system before they are fully ready for transplant, facilitating shorter patient waiting times.[83]

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[78] Charlton, M. (2014).

[79] Ibid.

[80] Ibid.

[81] U.S. News and World Report. (2014). *California Pacific Medical Center*. Retrieved March 3, 2014, from U.S. News and World Report: http://health.usnews.com/best-hospitals/area/ca/california-pacific-medical-center-6930032

[82] Moyle, C. (2014, January 17). Kidney Paired Donation at California Pacific Medical Center. (B. J. Ellison, Interviewer)

[83] Ibid.

CPMC must pay a swap fee for the use of its Matchmaker software when it performs internal matches, though it does avoid costs associated with coordinating transplants across different medical centers. CPMC runs Matchmaker at least once each week, but sometimes more frequently depending on demand and whether patients are willing to relax specified conditions in order to find a match. In addition to providing typical clinical information, these conditions include desired BMI, age, and travel distance. Urgency and the donor's length of wait in the system are not considered.[84]

While the majority of CPMC's matches result from its internal matching program, NKR performs roughly two of every five matches. Because CPMC views NKR as more developed than the KPDPP, it registers more patients with NKR than UNOS. In addition, Dr. Moyle cites UNOS's requirement that donors receive two years of follow-up care as a deterrent to the use of the KPDPP. Currently, transplant centers bear this cost unreimbursed, though it is difficult to retain donors for follow-up care as it is. Nevertheless, a small number of patients are paired through the UNOS KPDPP. Many patients are registered in both programs to give them as many matching opportunities as possible.[85]

PinnacleHealth System

Headquartered in Harrisburg, PA, PinnacleHealth is a nonprofit hospital system with 577 beds serving central Pennsylvania.[86] In March 2000, PinnacleHealth began offering kidney transplant services, and in October 2009 it began to work with NKR for KPD exchanges. Today, the health care system works with both NKR and the UNOS KPDPP. Since beginning to perform KPD, PinnacleHealth has been involved in 26 paired donations.[87]

PinnacleHealth educates both donors and patients about KPD as soon as it becomes clear that a transplant is needed. Transplant Services Director Kim Barnett has observed that patient-donor pairs are generally more receptive to KPD if they are informed upfront, rather than after they have been told they are incompatible. As a note, PinnacleHealth's policy is to input all altruistic donors into the KPD databases.

Once a patient or donor has opted into KPD, PinnacleHealth enrolls them in both NKR and the KPDPP. Ms. Barnett explains that, "being a mid-size program, [PinnacleHealth] do[es] not have the internal support to arrange [exchanges] among [their] own patients." In order to get the best and quickest matches for patients, PinnacleHealth wants access to the largest network of possible donor-patient pairs available. All patients that have enrolled in KPD have successfully received a kidney. While three patients have waited over two years for a match, the wait time

[84] Ibid.

[85] Ibid.

[86] PinnacleHealth. (2013, November 27). *PinnacleHealth System and Penn State Hershey to Explore Enhanced Relationship*. Retrieved March 4, 2014, from PinnacleHealth: http://www.pinnaclehealth.org/General/About-Us/News/PinnacleHealth-News-Releases/PinnacleHealth-System-and-Penn-State-Hershey-to-Ex.aspx

[87] Barnett, K. (2014).

experienced by KPD patients is consistently less than those patients on the deceased kidney wait list.[88]

Discussion: Observations on Transplant Centers' Engagement in KPD

Size Affects Engagement in KPD

A transplant center's size seems to greatly affect the manner in which it approaches KPD. Specifically, large hospitals are more prone to arrange transplants internally. In some cases, such as Methodist Hospital in San Antonio, the transplant center will be completely self-sustaining, matching only among its patients. In most cases, however, a large transplant center will give priority to internal matches, enrolling patients in a pairing organization only when they are unlikely to find a match within the transplant center. CPMC is an example of this. As has been explained, transplant centers are strongly incentivized to arrange internal matches because they are easier to arrange, take less time, and are less costly than dealing with a pairing organization.

Conversely, small centers are more likely to utilize pairing organizations simply because they do not have the patient pool to support internal matches. As a result, the best solution to an incompatible patient-donor pair is exposure to the larger patient pools offered by pairing organizations. PinnacleHealth illustrates this observation well.

Philosophy Affects Engagement in KPD

Organizational views on KPD seem to affect whether a transplant center attempts to arrange internal matches or utilizes a pairing organization. While internal matches are easier and more efficient for an individual transplant center, a larger patient pool provides better matches for more people overall. The extent to which a transplant center recognizes the societal value of a larger – ideally, singular – patient pool can determine their willingness to engage with pairing organizations. For example, NYP/WCMC, one of NKR's founding transplant centers, directly enrolls all KPD patients in NKR's database. NYP/WCMC incurs the additional costs associated with pairing organizations despite being able to arrange many matches internally as the largest hospital in the country, because it views KPD as a viable solution to the kidney shortage in the U.S. if widely adopted.

[88] Ibid.

Challenges and Recommendations

After examining the historical context as well as international and domestic programs, it is possible to apply some best practices to the most significant challenges facing KPD in the US today. Namely, the three largest challenges evidenced throughout this paper are: the balkanization of patient pools, lack of coordination among pairing organizations, and disruptions caused by positive cross matches. This section describes the nature of each challenge and offers solutions to answer, mitigate, or avoid them.

Balkanization of Patient Pools

The greatest challenge to KPD's success is the balkanization of patient pools: transplant centers and pairing organizations operate independently of one another, preventing matches that could potentially exist between patient pools. Between single-center programs, regional pairing programs, and nationwide pairing organizations, dozens of patient pools exist across the U.S. Because many transplant centers prefer to arrange matches internally and find it difficult to manage patients in multiple pools, there is generally little overlap between pools.

A larger pool creates more heterogeneity among kidneys, which in turn allows for a greater number and improved quality of matches. Medical professionals recognize this, and KPD appears to be moving increasingly toward larger pairing organizations. Transplant center membership in NKR, the ADP, and the UNOS KPDPP has been increasing. As of now, transplant coordinators trust NKR's experience and track record the most, but see UNOS – the government-contracted organ transplantation organization – as aiming to create a single KPD patient pool across the country.

The following recommendations seek to enlarge, consolidate, and optimize pairing organizations' patient pools to more effectively arrange a greater number of matches.

Consolidate Pairing Organization

The most straightforward answer to balkanized patient pools in the US is to consolidate regional and national pairing organizations. Segev et al. estimate a single national program would result in more transplants, better HLA concordance, higher five-year graft survival rates, a reduction in the number of pairs required to travel, and strong benefits to highly sensitized patients. Altogether, these improvements could save the health care system as much as $750 million, yet there has been little movement toward merging.[89] Existing regional and national pairing organizations argue that the presence of multiple players has led to innovation and competition. Nevertheless, a recent consensus conference of relevant stakeholders concluded that a single national registry should be an overarching goal of KPD going forward.[90] To accomplish this

[89] Segev, D. L., Gentry, S. E., Warren, D. S., Reeb, B., & Montgomery, R. A. (2005, April). Kidney Paired Donation and Optimizing the Use of Live Donor Organs. *The Journal of the American Medical Association, 293*(15), 1883-1890.

[90] Melcher, M. L., Blosser, C. D., Baxter-Lowe, L. A., Delmonico, F. L., Gentry, S. E., Leishman, R., et al. (2013, April). Dynamic Challenges Inhibiting Optimal Adoption of Kidney Paired Donation: Findings of a Consensus Conference. *American Journal of Transplantation, 13*(4), 851-860.

outcome, a government mandate is all but necessary. A compromise could include the consolidation of most pairing organizations into two or three national ones, increasing the size of patient pools while retaining some competition.

Incorporate Internally Matchable Pairs into Matching Algorithms

As has been discussed, individual transplant centers have significant incentives to retain their easily matched pairs internally, resorting to external sources solely with the most hard-to-match pairs. It is individually rational for a transplant center to supply its pairs to a pairing organization only if the resulting allocation would give the center at least as many matched pairs as the center would arrange on its own. Without a guarantee that this would be the case, a transplant center will not submit easy to match patients to a pairing organization.

Currently, most kidney exchange programs do not offer such a guarantee, instead working to maximize the number of total transplants (subject to some weighting), ignoring transplant centers' incentives to match internally. Ashlagi and Roth argue that incorporating this guarantee would increase the number of matches by more than 10 percent by inducing transplant centers to submit more patient-donor couples to the pairing organization. After all, they would have nothing to lose. Notably, Ashlagi and Roth find the costs of integrating individual rationality in the matching algorithm to be quite small.[91]

Extend Eligibility to Compatible Pairs

KPD programs require the patient and donor demonstrate incompatibility before enrolling, but this excludes compatible pairs that could also benefit from an exchange. Namely, some compatible patient-donor couples might want a better match. For instance, a compatible pair might benefit from a match with a younger donor or a female recipient might benefit from matching with an unrelated donor to whose antigens she has not been exposed. Gentry et al. find that enlarging a patient pool by including compatible pairs nearly doubles the pool's match rate, whether it is a single-center program or a national program.[92] While many express ethical concerns regarding an otherwise suitable couple exchanging kidneys with strangers, compatible pairs can willingly choose to participate in anticipation of a better match or due to altruism, which underpins the ethical logic for non-directed donors.

Collaboration with Canadian KPD Program

Another way to expand KPD patient pools is to broaden KPD programs beyond the US border. Garonzik-Wang et al. reported a 10-way exchange initiated by a non-directed donor that included one Canadian patient-donor couple in 2009. Doctors at McGill University performed the international donor and recipient surgeries, and both organs were transported on chartered international flights with cold ischemia times amounting to less than six hours. Notably, Garonzik-

[91] Ashlagi, I., & Roth, A. E. (2012). New Challenges in Multihospital Kidney Exchange. *American Economic Review: Papers & Proceedings, 102*(3), 354-359.

[92] Gentry, S. E., Segev, D. L., Simmerling, M., & Montgomery, R. A. (2007, July). Expanding Kidney Paired Donation Through Participation by Compatible Pairs. *American Journal of Transplantation*, 2361-2370.

Wang point out that the flights between Baltimore and Montreal are shorter than many other flights within the US.[93] Partnering with Canadian transplant centers, in particular the national LDRE program, would grant UNOS or other US pairing organizations a significantly larger patient pool that would improve matches and outcomes for patients in both countries.

One obstacle to international KPD cooperation lies in UNOS Policy 3.3.7, which was implemented in November 2008, immediately prior to the abovementioned exchange. Under Policy 3.3.7, transplant centers can only accept living donor organs recovered at OPTN member transplant centers.[94] OPTN/UNOS approved the policy with the intent of limiting a black market for organs, but this also restricts pairing organizations' ability to cooperate with international transplant centers. Though the organizers of the above exchange obtained a waiver, broader collaboration between American and Canadian pairing organizations would require the altering of Policy 3.3.7.

Allow Longer Chains

Several of the KPD programs discussed limit the length of exchanges performed, usually citing the logistical complexities associated with long chains. Roth et al. (2007) demonstrated that the addition of chains longer than three-way exchanges provided little benefit and that "*all* [emphasis in the original] efficient exchanges can be accomplished in exchanges involving no more than four incompatible pairs."[95] These findings, however, were based on assumptions of large patient pools that grow without limit. The existing programs described above have many highly sensitize patients and relatively small, balkanized patient pools. In these circumstances, Roth et al. (2012) find that the inclusion of longer chains (particularly NEAD chains) significantly increase match rates, especially among highly sensitized patients.[96]

Lack of Coordination among Transplant Centers

As a new field, KPD is implemented very differently across organizations. Transplant centers, states, and insurance companies have their own procedures, documentation, payment structures, and policies governing KPD. These discrepancies can cause delays in transplantation and add costs as professionals spend time adapting materials for use between organizations. A notable example is the practice of pairing organizations charging recipient centers the cost of the donor surgery. Health care costs vary significantly across the US, causing uncertainty regarding the amount cooperating with a pairing organization will cost a transplant center. As seen in the case of CPMC, this uncertainty can discourage centers from working with pairing organizations.

[93] Garonzik-Wang, J. M., Sullivan, B., Hiller, J. M., Cass, V., Ychervenkow, J., Feldman, L., et al. (2013, October). International kidney paired donation. *Transplantation, 96*(7), 55-56.
[94] Ibid.
[95] Roth, A. E., Sönmez, T., & Ünver, M. U. (2007). Efficient Kidney Exchange: Coincidence of Wants in Markets with Compatibility-Based Preferences. *American Economic Review, 97*(3), 828-851.
[96] Ashlagi, I., Gamarnik, D., Rees, M. A., & Roth, A. E. (2012, July). The Need for (long) Chains in Kidney Exchange. *NBER Working Paper Series*.

The reform below promises to address this issue, facilitating its expansion and continued growth.

Standardization of Procedures and Costs

Irwin et al. propose a national pairing system patterned off of the current practices for deceased kidney donations. Under this system, organ procurement centers (OPOs) are charged with coordinating the donation process, including the packaging and transportation of organs. Utilizing the existing structure of 58 OPOs nationwide allows for the standardization of both procurement procedures and costs. OPOs would manage financial transactions, billing the recipient transplant center a standard acquisition charge (SAC) that includes donor evaluation, procurement, transportation, and overhead expenses. Of course, to successfully standardize expenses, uniform donor evaluation processes would also have to be implemented as the numerous procedural discrepancies between transplant centers incur different costs.[97]

Positive Cross Match Complications

The most common disruption to a KPD exchange or chain remains positive cross matches.[98] Historically, a positive cross match has precluded a particular donation within an exchange to take place, ruining the entire match. Furthermore, highly sensitized patients have a very difficult time finding a match and often face lengthy wait times. With advances in technology and structural changes to national KPD programs, preclusive cross matches can be, for the most part, prevented or avoided. The following recommendations will reduce unanticipated positive cross match results, benefit highly sensitized patients, and enable a greater number of matches to be carried through to transplant.

Desensitization Procedures

Johns Hopkins' use of innovative desensitization techniques demonstrates that it is possible to reduce patients' sensitivity and thus the chance of positive cross match. Montgomery found that desensitization resulted in increased rates of transplantation and improved health outcomes. By implication, pairing organizations can relax HLA requirements and accept previously unacceptable antigens that will be eliminated through sensitization. This helps highly sensitized patients, who currently face meager transplantation rates of 6.5% annually, as well as pairing organizations, which will reap the benefits of easier to match patient pools.[99] Widespread implementation of desensitization protocols promises to reduce the number of sensitized patients, and thus the instances of disruptive positive cross matches.

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[97] Irwin, F. D., Bonagura, A. F., Crawford, S. W., & Foote, M. (2012). Kidney Paired Donation: A Payer Perspective. *American Journal of Transplantation*, 1388-1391.

[98] Hogan, M. (2012, July). In National Paired Donation Pilot, Most Match Offers Declined. *Nephrology Times, 5*(7), pp. 8-9.

[99] Montgomery, R. A., Lonze, B. E., King, K. E., Kraus, E. S., Kucirka, L. M., Locke, J. E., et al. (2011, July). Desensitization in HLA-Incompatible Kidney Recipients and Survival. *The New England Journal of Medicine*, 318-326.

Incorporate High Definition Virtual Cross Matches into Matching Algorithm

Australia's AKX program is innovative in its performance of high definition virtual cross matching as part of the pairing process. Incorporating this advanced technology into its matching algorithm has resulted in considerably high match rates, even among small patient pools.[100] Extensive use of high definition matching technology and subsequent virtual cross matching as part of the allocation process would provide considerable benefits to any KPD program, national, regional, or single-center.

Uniform Histocompatibility Standards

A final lesson learned from international case studies is the usefulness of a central histocompatibility laboratory. In the Netherlands, the single reference library performs cross matches to ensure it can proceed once a match is made. In cases of positive cross match, the program attempts to find a substitute. The major benefit of a central histocompatibility laboratory is the application of uniform standards regarding unacceptable antigens. Systems based on dozens of transplant centers with widely conflicting standards can be plagued by positive cross matches.[101] If a single reference laboratory or a system or regional laboratories are deemed to be unfeasible, the coordination of histocompatibility standards can yield fruitful results. Such coordination reduced NKR's unexpected positive cross match rate from 57 percent to 9 percent.[102]

Conclusion

In review, this paper has attempted to provide a comprehensive snapshot of kidney paired donation today and apply institutional best practices to address obstacles to growth. From the historical context to case studies of KPD in practice and finally the identification of challenges and recommendations, this paper has consolidated previously disparate information for use by researchers, students, and medical professionals. While KPD is currently underutilized in the US, KPD has benefitted and promises to further benefit the lives of thousands of patients. Furthermore, KPD has profoundly changed the medical landscape. As one transplant coordinator put it: "KPD has brought the transplant community together. I've been working in transplant for 25 years. We used to all operate as silos, but now there is communication. We may never meet these people, but we collaborate every day."[103]

[100] Ferrari, P., Fidler, S., Wright, J., Woodroffe, C., Slater, P., Althuis-Jones, A. V., et al. (2010, February). Virtual Crossmatch Approach to Maximize Matching in Paired Kidney Donation. *American Journal of Transplantation, 11*(2), pp. 272-278.

[101] Gentry, S. E., Shapiro, R., & Segev, D. L. (2014).

[102] Veale, J., & Hil, G. (2010). National Kidney Registry: 213 Transplants in Three Years. *Clinical Transplants*, 333-344.

[103] Charlton, M. (2014).

Bibliography

110th United States Congress. (2007, December 7). Charlie W. Norwood Living Organ Donation Act.

98th United States Congress. (1984, October 12). National Organ Transplant Act.

Adams, P. L., Cohen, D. J., Danovitch, G. M., Edington, R. M., Gaston, R. S., Jacobs, C. L., et al. (2002, August 27). The nondirected live-kidney donor: ethical considerations and practice guidelines: A National Conference Report. *Transplantation, 74*(4), 582-589.

Akkina, S. K., Muster, H., Steffens, E., Kim, S. J., Kasiske, B. L., & Israni, A. K. (2011, January). Donor Exchange Programs in Kidney Transplantation: Rationale and Operational Details From the North Central Donor Exchange Cooperative. *American Journal of Kidney Diseases, 57*(1), 152-158.

Andreoni, K. (2013). *OPTN/UNOS Kidney Paired Donation Pilot Program.* United Network for Organ Sharing.

Ashlagi, I., & Roth, A. E. (2012). New Challenges in Multihospital Kidney Exchange. *American Economic Review: Papers & Proceedings, 102*(3), 354-359.

Ashlagi, I., Gamarnik, D., Rees, M. A., & Roth, A. E. (2012, July). The Need for (long) Chains in Kidney Exchange. *NBER Working Paper Series*.

Australian Government: Organ and Tissue Authority. (2013). *Australian Paired Kidney Exchange (AKX) Program.* Biannual Report.

Barnett, K. (2014, January 31). Kidney Paired Donation at PinnacleHealth. (B. J. Ellison, Interviewer)

Bingaman, A. W., Wright, F. H., Kapturczak, M., Shen, L., Vick, S., & Murphey, C. L. (2012, August). Single-Center Kidney Paired Donation: The Methodist San Antonio Experience. *American Journal of Transplantation, 12*(8), 2125-2132.

Burnapp, L. (2013). *National Living Donor Kidney Sharing Schemes.* National Health Service, Blood and Transplant.

Canadian Blood Services. (2010, November 30). *Kidney Exchange Registry Goes National*. Retrieved May 5, 2014, from Canadian Blood Services: http://www.blood.ca/CentreApps/Internet/UW_V502_MainEngine.nsf/9749ca80b75a038585256aa20060d703/a9da5ee7a67d8b57852577eb00486ce4?OpenDocument

Charlton, M. (2014, January 16). Kidney Paired Exchange at NewYork-Presbyterian/Weill Cornell Medical Center. (B. J. Ellison, Interviewer)

Ferrari, P., & Klerk, M. D. (2009). Paired kidney donations to expand the living donor pool. *Journal of Nephrology, 22*(6), 699-707.

Ferrari, P., Fidler, S., Wright, J., Woodroffe, C., Slater, P., Althuis-Jones, A. V., et al. (2010, February). Virtual Crossmatch Approach to Maximize Matching in Paired Kidney Donation. *American Journal of Transplantation, 11*(2), pp. 272-278.

Ferrari, P., Fidler, S., Wright, J., Woodroffe, C., Slater, P., Van Althuis-Jones, A., et al. (2011, February). Virtual Crossmatch Approach to Maximize Matching in Paired Kidney Donation. *American Journal of Transplantation, 11*(2), 272-278.

Ferrari, P., Woodroffe, C., & Christiansen, F. T. (2009). Paired kidney donations to expand the living donor pool: the Western Australian experience. *The Medical Journal of Australia, 190*(12), 700-703.

Gaber, A. O. (2013). *Current Topics in Transplantation.*

Gamble, M. (2013, June 20). *50 Largest Hospitals in America*. Retrieved March 17, 2014, from Becker's Hospital Review: http://www.beckershospitalreview.com/lists/50-largest-hospitals-in-america-2013.html

Garonzik-Wang, J. M., Sullivan, B., Hiller, J. M., Cass, V., Ychervenkow, J., Feldman, L., et al. (2013, October). International kidney paired donation. *Transplantation, 96*(7), 55-56.

Gentry, S. E., Segev, D. L., Simmerling, M., & Montgomery, R. A. (2007, July). Expanding Kidney Paired Donation Through Participation by Compatible Pairs. *American Journal of Transplantation*, 2361-2370.

Gentry, S. E., Shapiro, R., & Segev, D. L. (2014). Chapter 2: Kidney Paired Donation Programs for Incompatible Living Donors and Recipients. In J. Steel, *Living Donor Advocacy: An Evolving Role Within Transplantation* (pp. 17-26).

GuideStar. (2014). *GuideStar Premium Report for Paired Donation Network.*

Hanto, R. L., Saidman, S., Roth, A. E., & Delmonico, F. (2010, July). The Evolution of a Successful Kidney Paired Donation Program. *Transplantation, 90*(25), 940.

Hilbrands, L. (n.d.). *How to manage domino transplantation: The Dutch living donation program.* Retrieved May 6, 2014, from Stiftung Lebendspende: http://www.stiftung-lebendspende.de/files/hilbrands_living_donation_munchen.pdf

Hogan, M. (2012, July). In National Paired Donation Pilot, Most Match Offers Declined. *Nephrology Times, 5*(7), pp. 8-9.

Huh, K. H., Kim, M. S., Chang, H. K., Ahn, H. J., Lee, S. H., Lee, J. H., et al. (2008, August). Exchange living-donor kidney transplantation: merits and limitations. *Transplantation, 86*(3), 430-435.

Irwin, F. D., Bonagura, A. F., Crawford, S. W., & Foote, M. (2012). Kidney Paired Donation: A Payer Perspective. *American Journal of Transplantation*, 1388-1391.

Johns Hopkins Medicine. (2014). *Transplantation*. Retrieved May 1, 2014, from Johns Hopkins Medicine: http://www.hopkinsmedicine.org/usa/excellence/transplantation.html

Kidney Transplantation Committee. (2008). *Proposal for a National Kidney Paired Donation (KPD) Pilot Program.* Briefing Paper, United Network for Organ Sharing.

Kim, H. S., Kwon, O. J., & Kang, C. M. (2012, January-February). The Utilization and Advantages of an Exchange Donor Program in Living Donor Renal Transplantation: A Single-Center Experience. *Transplantation Proceedings, 44*(1), 14-16.

Kim, J. R., Elliott, D., & Hyde, C. (2004, March). Korean health professionals' attitudes and knowledge toward organ donation and transplantation. *International Journal of Nursing Studies, 41*(3), 299-307.

Klerk, M. D., Keizer, K. M., Claas, F. H., Witvliet, M., Haase-Kromwijk, B. J., & Weimar, W. (2005, September). The Dutch National Living Donor Kidney Exchange Program. *American Journal of Transplantation, 5*(9), 2302-2305.

Leishman, R. (2013). *OPTN Kidney Paired Donation Pilot Program.* United Network for Organ Sharing.

Leishman, R. (2013, December 4). The UNOS Kidney Paired Donation Pilot Program. (B. J. Ellison, Interviewer)

Lucan, M. (2007, June). Five Years of Single-Center Experience With Paired Kidney Exchange Transplantation. *Transplantation Proceedings, 39*(5), 1371-1375.

Malik, S., & Cole, E. (2014, March). State of the Art Practices and Policies in Kidney Paired Donation. *Current Transplantation Reports, 1*(1), 10-17.

Manlove, D. F., & O'Malley, G. (2012). *Paired and Altruistic Kidney Donation in the UK: Algorithms and Experimentation.* Technical Report, University of Glasgow, School of Computing Science.

Matesanz, R., Domínguez-Gil, B., Coll, E., de la Rosa, G., & Marazuela, R. (2011, April). Spanish experience as a leading country: what kind of measures were taken? *Transplant International, 24*(4), 333-343.

Melcher, M. L., Blosser, C. D., Baxter-Lowe, L. A., Delmonico, F. L., Gentry, S. E., Leishman, R., et al. (2013, April). Dynamic Challenges Inhibiting Optimal Adoption of Kidney Paired Donation: Findings of a Consensus Conference. *American Journal of Transplantation, 13*(4), 851-860.

Mierzejewska, B., Durlik, M., Lisik, W., Baum, C., Schroder, P., Kopke, J., et al. (2013, March 19). Current approaches in national kidney paired donation programs. *Annals of Transplantation*, 112-124.

Montgomery, R. A., Lonze, B. E., & Jackson, A. M. (2011, August). Using donor exchange paradigms with desensitization to enhance transplant rates among highly sensitized patients. *Current Opinion in Organ Transplantation, 16*(4), 439-443.

Montgomery, R. A., Lonze, B. E., King, K. E., Kraus, E. S., Kucirka, L. M., Locke, J. E., et al. (2011, July). Desensitization in HLA-Incompatible Kidney Recipients and Survival. *The New England Journal of Medicine*, 318-326.

Moyle, C. (2014, January 17). Kidney Paired Donation at California Pacific Medical Center. (B. J. Ellison, Interviewer)

National Kidney Registry. (2014). *Kidney Transplant Centers*. Retrieved March 3, 2014, from National Kidney Registry : http://www.kidneytransplantcenters.org/?for=next-steps

National Kidney Registry. (n.d.). *Medical Board Policies*. Retrieved March 1, 2014, from National Kidney Registry: http://www.kidneyregistry.org/transplant_center.php

National Kidney Registry. (n.d.). *Swap Expert for EASYMATCH.* Retrieved March 1, 2014, from National Kidney Registry: http://www.kidneyregistry.org/docs/swap_expert_pdf1.pdf

North Central Donor Exchange Cooperative. (2014). *Home*. Retrieved May 11, 2014, from North Central Donor Exchange Cooperative: http://www.ncdec.org/default.asp

Park, K., Moon, J. I., Kim, S. I., & Kim, Y. S. (1999). Exchange Donor Program in Kidney Transplantation. *Transplantation, 67*(2), 336-338.

PinnacleHealth. (2013, November 27). *PinnacleHealth System and Penn State Hershey to Explore Enhanced Relationship*. Retrieved March 4, 2014, from PinnacleHealth: http://www.pinnaclehealth.org/General/About-Us/News/PinnacleHealth-News-Releases/PinnacleHealth-System-and-Penn-State-Hershey-to-Ex.aspx

Prats, J. (2013, October 8). *El trasplante de riñón cruzado despega en España*. Retrieved May 4, 2014, from El País: http://sociedad.elpais.com/sociedad/2013/10/08/actualidad/1381220931_646565.html

Rapaport, F. T. (1986, June). The Case for a Living Emotionally Related International Kidney Donor Exchange Registry. *Transplantation Proceedings, 18*(3), 5-9.

Rees, M. A. (2007). *Kidney Paired Donation.* Alliance for Paired Donation.

Roth, A. (2010). *Kidney Exchange.* Class Lecture, Harvard University.

Roth, A. E., Sönmez, T., & Ünver, M. U. (2005, May). A Kidney Exchange Clearinghouse in New England. *The American Economic Review: Papers and Proceedings, 95*(2), 376-380.

Roth, A. E., Sönmez, T., & Ünver, M. U. (2007). Efficient Kidney Exchange: Coincidence of Wants in Markets with Compatibility-Based Preferences. *American Economic Review, 97*(3), 828-851.

Sack, K. (2012, February 18). 60 Lives, 30 Kidneys, All Linked. *The New York Times*, p. A1.

Segev, D. L., Gentry, S. E., Warren, D. S., Reeb, B., & Montgomery, R. A. (2005, April). Kidney Paired Donation and Optimizing the Use of Live Donor Organs. *The Journal of the American Medical Association, 293*(15), 1883-1890.

Sinacore, J. (2014, March 12). *National Kidney Registry Facilitates 1000th Transplant*. Retrieved 1 March, 2014, from National Kidney Registry: http://www.kidneyregistry.org/pages/p292/PR_1000th_Transplant.php

Sokohl, K. (2010, March-April). Getting It Right: Kidney committee easing into KPD with two-step pilot project. *UNOS Update*.

Spital, A. (2005, November). Increasing the Pool of Transplantable Kidneys Through Unrelated Living Donors and Living Donor Paired Exchanges. *Seminars in Dialysis, 18*(6), 469-473.

The Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients. (2011). *Annual Data Report: Kidney.*

Thiel, G., Vogelbach, P., Gürke, L., Gasser, T., Lehmann, K., Voegele, T., et al. (2001, February-March). Crossover renal transplantation: hurdles to be cleared! *Transplantation Proceedings, 33*(1-2), 811-816.

Toulis, P., & Parkes, D. C. (2014). A Random Graph Model of Multi-Hospital Kidney Exchanges. *Games and Economic Behavior (Submitted)*.

Tucker, E. (2012, February 14). *Q & A: How does the Canadian kidney exchange work?* Retrieved May 3, 2014, from Global News: http://globalnews.ca/news/211538/q-a-how-does-the-canadian-kidney-exchange-work/

U.S. Department of Health and Human Services. (2010, October 5). *Kidney Paired Donation Pilot Program to Begin Matching in October; Participating Programs Named*. Retrieved March 11, 2014, from Organ Procurement and Transplantation Network: http://optn.transplant.hrsa.gov/news/newsDetail.asp?id=1404

U.S. Department of Health and Human Services. (2012). *United States Organ Transplantation.*

U.S. Department of Health and Human Services. (2014, May 12). *Data*. Retrieved May 12, 2014, from Organ Procurement and Transplantation Network: http://optn.transplant.hrsa.gov/data/

U.S. News and World Report. (2014). *California Pacific Medical Center*. Retrieved March 3, 2014, from U.S. News and World Report: http://health.usnews.com/best-hospitals/area/ca/california-pacific-medical-center-6930032

Veale, J., & Hil, G. (2010). National Kidney Registry: 213 Transplants in Three Years. *Clinical Transplants*, 333-344.

Wallis, C. B., Samy, K. P., Roth, A. E., & Rees, M. A. (2011). Kidney Paired Donation. *Nephrology Dialysis Transplantation, 26*(7), 2091-2099.

Washington Regional Transplant Community. (2014). *Living Kidney Donor program*. Retrieved May 11, 2014, from Washington Regional Transplant Community: http://www.beadonor.org/donation-facts/living-donation/living-kidney-donor-program

Williams, E. D., Reyes-Akinbileje, B., & Swendiman, K. S. (2009). *Living Organ Donation and Valuable Consideration.* United States Congressional Research Service.

Woodle, E. S., Goldfarb, D., Aeder, M., Lal, T., Rike, A., Weimart, N., et al. (2005). Establishment of a nationalized, multiregional Paired Donation Network. *Clinical Tranplantation*, 247-58.