

## CHAPTER 23

# The National Kidney Registry: 175 Transplants in One Year

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Kidney paired donation and particularly the increasing utilization of chains of transplants initiated by a non-directed donor (NDD, 1-4) have increased the number of living donor transplants performed each year. Since facilitating its first transplants in 2008, the National Kidney Registry (NKR) has organized more transplants than any other exchange program in the world. By the end of 2011, NKR had facilitated 389 transplants, including 175 in 2011 (Fig.1). The 2011 transplants had an average wait time of 4.9 months from enrollment to transplant and included 49 patients (28%) with cPRA scores >80% (Fig. 2). By working with the majority of the top U.S. transplant centers (by volume) and leveraging cutting edge computer technology, the National Kidney Registry has broken through many of the barriers that have stalled other paired exchange efforts.

## THE NKR APPROACH

The NKR was started and is personally managed by a dad who wanted to donate a kidney to his daughter, but could not because he was crossmatch incompatible. The frustrating search for a compatible donor for his daughter, including his attempted participation in every U.S. paired exchange program existing in 2007, led him to recognize that there had to be a better way to organize paired exchange transplants.

### Rapid innovation

NKR's performance has benefited from the start-up team's deep industry experience in

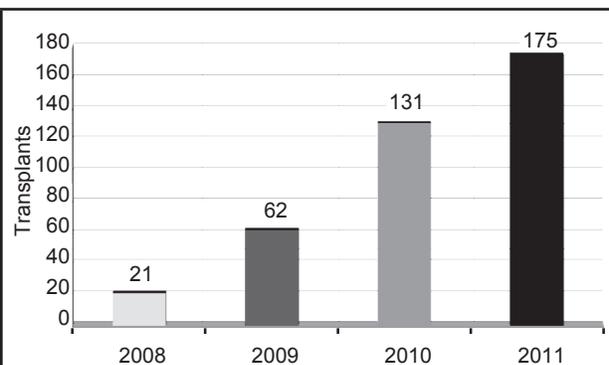


Figure 1. NKR Transplants Facilitated by Year.

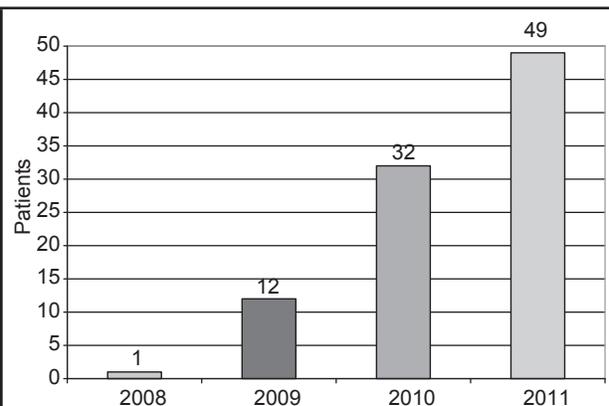


Figure 2. Number of patients with cPRA >80% transplanted.

logistics, technology, capital market systems and operations management. This experience proved critical in allowing for rapid evolution in these underdeveloped areas of paired exchange. The team also relied on the active support and oversight from an experienced Medical Board made up of transplant professionals. As a result, many bold and technically difficult innovations have been implemented, including:

- Implementation of Swap Expert, an artificial intelligence application for patient advice
- Creation of the Toolbox to determine preference and avoid listing impact in real-time
- Implementation of the donor pre-select function to accept donors in advance of matches
- Enhancement of real-time matching software allowing for 20+ deep match offers
- Use of Simultaneous Mutually Exclusive Loops and Chain matching (SMELAC)
- Introduction of a standardized financial model for centers to pay each other
- Creation of a streamlined process to support CMS regulatory requirements
- Utilization of a web portal for easy pair enrollment and fast center startup
- Elimination of all personal health information avoiding HIPAA issues
- Use of donor and recipient preferences to control the match process
- Standardized identification and listing of all relevant HLA antigens and antibodies
- Inclusion of non-A1 donors to match O and B patients with acceptable titers
- Real-time matching systems supporting immediate match identification and chain repair
- Straight Through Processing for match offer tracking and process control
- Utilization of existing infrastructure to ship kidneys eliminating need for donor travel
- Implementation of real-time geotracking technology for shipped kidneys
- Creation of children & high PRA program for ending chains to patients without donors

### **Cutting edge computer technology**

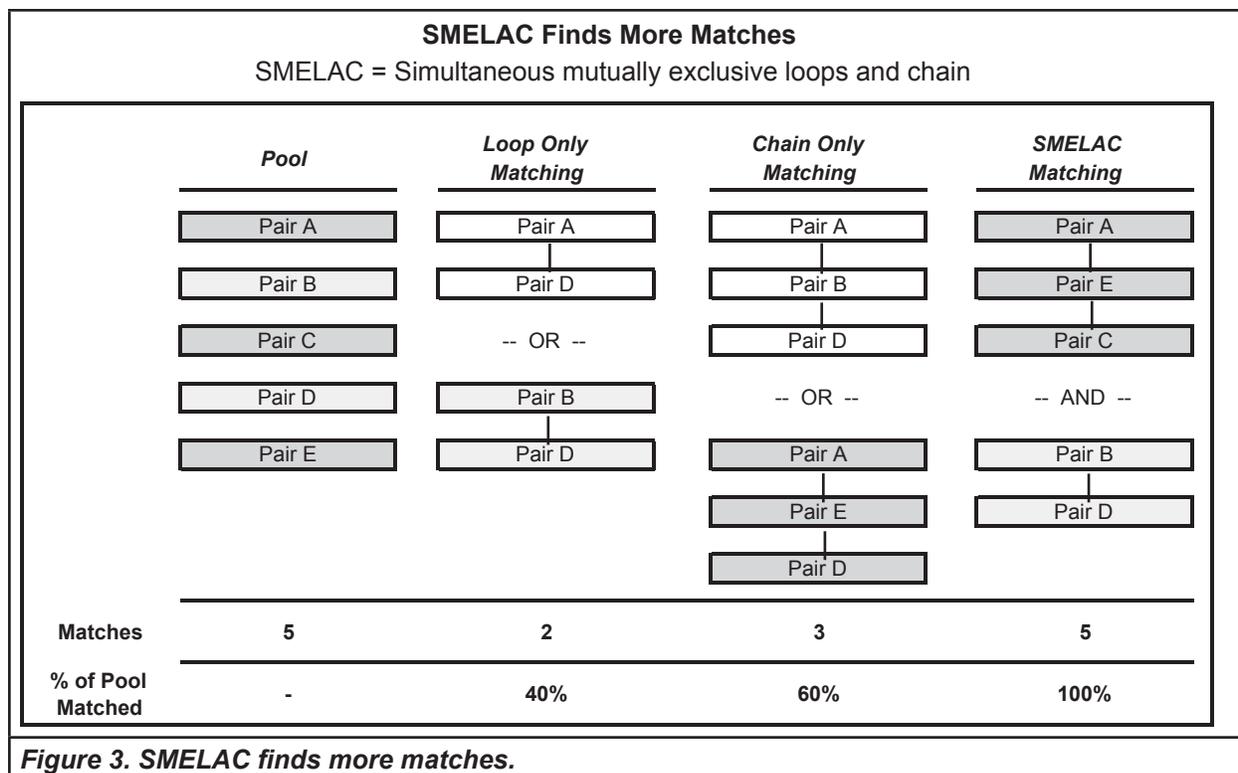
As the length of the matched clusters that make up the segments of each transplant chain is extended, the number of transplants that can be facilitated increases dramatically. For example, a pool of 100 incompatible donor/recipient pairs running a 3-deep cluster will generate approximately 10 billion combinations. If the length of the cluster increases by just one, to 4-deep, the number of possible combinations increases to 100 trillion. Utilizing software that can find a cluster

length of 20 deep, a staggering 10 to the 78th power of combinations are possible. Optimizing for ABO and HLA compatibility, age considerations, travel restrictions, additions of NDDs, additions of new pairs and other donor/recipient preferences requires extremely sophisticated software for finding and evaluating possible matches.

Over the past decade, different registries have developed a variety of computerized systems to support multi-center loop and chain matching. Most of the early systems were based on integer programming algorithms which were the best tools to solve the complex mathematical problem presented by the traditional paired exchange reciprocity requirement. With the advent of chains, these original integer programming solutions had to be modified to accommodate the radically different mathematical challenge presented by chains. The NKR system was initially created based solely on the chain matching model utilizing technology components employed by modern capital market exchange systems (e.g. New York Stock Exchange) departing from integer programming algorithms historically used for paired exchange. In 2011 the SMELAC algorithm was implemented, further increasing the match capture rates by combining loops and chains into a single search. Figure 3 illustrates how the SMELAC algorithm finds more matches.

### **Advanced matching strategies**

Clinical experience in paired exchange demonstrates that the transplant center managing the donor/recipient pair has a significant impact on the probability of the pair finding a match in an exchange. Centers that have implemented the advanced matching strategies (Table 1) supported by the Toolbox and Swap Expert decision support systems are able to transplant significantly more patients through paired exchange, indicating that there is a material center effect at work in paired exchange. We are seeing paired exchange centers of excellence emerge as patients become more aware of, and seek out those centers that demonstrate superior performance in paired exchange.



**Table 1. Advanced Matching Strategies, transplanting hard-to-match recipients.**

- Utilize non A1 donors for O and B recipients with acceptable titers
- Include compatible pairs in swaps (e.g. O donors with non A recipients)
- Utilize NKR ToolBox and Swap Expert decision support systems
- Relax preference restrictions (e.g. accept shipped kidney, etc.) based on pair match power sensitivities
- Raise MFI thresholds - combine with desensitization protocols for highly sensitized recipients
- Utilize multiple paired donors – O donors are 10X more powerful in a swap
- Start chains and take advantage of the NKR CHIP program to get patients without donors transplanted
- Increase pool size by enrolling more pairs at your center and encouraging other centers to join.
- Reach out using center hosted seminars on paired exchange, call all patients on wait list and educate pairs upon initial intake.

### Online decision support tools

#### The Toolbox

The Toolbox module (Fig. 4) was implemented in 2011 to provide information that allows participating centers to leverage advanced matching strategies and to provide real-time feedback to transplant centers regarding a pair's match power and the impact different preference settings and avoid listings can have on the pair match power using

the live pool information. The Toolbox automates the metrics for calculating the pair match power based on all of the donors and recipients active in the pool at any given time. To determine the pair match power, the recipient is evaluated to determine how many donors in the pool match them, and the paired donor is evaluated to determine how many recipients in the pool they match. The recipient score and donor score are then multiplied against each other to determine the pair's match power. This score defines how easy or hard it will be to find a match in the NKR program and is the basis of determining which advanced matching strategies should be employed to get the patient transplanted.

The Toolbox also facilitates the automated upload of high resolution antibody information (MFI values) supporting sensitivity analysis for unacceptable HLA antigen listing strategies. The automated upload also eliminates the data entry errors which are prevalent when entering avoids

for highly sensitized patients and therefore reduces cross match failures.

### Donor pre-select

The donor pre-select module (Fig. 5) was also introduced in 2011 and allows for the review, acceptance or rejection of all donors that match a given recipient in the NKR system. This feature has dramatically reduced the number of failed match offers and gives the transplant centers specific information on donors in advance of a match offer so that informed medical decisions can be made regarding the suitability of donors for any given recipient.

### Swap expert

The Swap Expert (Fig. 6) is an artificial intelligence application that helps transplant centers and patients decide on preference settings and matching strategies that maximize compatibility while minimizing wait time. The Swap Expert leverages the matching knowledge accumulated by the NKR staff and delivers it in a usable form to patients and transplant centers. In addition to the Swap Expert's

**Paired Recipients** | **CHIP Recipients** | **Transplanted Recipients** | **All Paired Donors** | **Add Recipient**

**Edit Recipient [FK1939]** | **Paired Donors** | **Toolbox** | **Potential Donors**

Modify Recipient preferences to see how they impact their matching power.

Max Donor Age:  Min HLA Points:  Min Donor Weight (kg):  Accept Shipped Kidney?  Yes  No Willing to Travel?  Yes  No

**Pair Match Pow** **JK1973**

■ Pre-Pref ■ P<sub>i</sub> ■ Pair Power

	Recipient	Donor 1	Donor 2	Donor 3	Donor 4	Donor 5	Donor 6
Alias:	FK1939	JK1973	--	--	--	--	--
Antibodies:	0	--	--	--	--	--	--
Blood Type:	O	A	--	--	--	--	--
Age:	73	39	--	--	--	--	--
Sex:	M	F	--	--	--	--	--
Height (cm):	188	173	--	--	--	--	--
Weight (kg):	120	82	--	--	--	--	--
Days in NKR:	0	262	--	--	--	--	--
Pre-Pref Matches:	87	16	--	--	--	--	--
Post-Pref Matches:	85	15	--	--	--	--	--
Pre-Pref Match Power:	32.7%	4%	--	--	--	--	--
Post-Pref Match Power:	32%	3.8%	--	--	--	--	--
Adjusted NKR cPRA:	0%	--	--	--	--	--	--
Travel?	--	No	--	--	--	--	--

**Antibodies**

Cutoff Level to Use:  Low  Medium  High

MFI Methodology:  Min MFI  Avg MFI  Max MFI

Select/Upload Profiles

- To manually select avoids, simply expand the list below and manually select.
- To automatically export your HLA Fusion data for upload, you need to install NKR.exe (an HLA Fusion add-on application).
  - Download NKR.exe
  - Download Instructions

Figure 4. The Toolbox.

automated output, NKR staff reviews this output with Member Centers to train medical staff on the nuances of paired exchange matching strategies.

**Donor Pre-Select - Summary**

Pre-Screening

Matches Accepted	Matches Declined	Matches Pending	Total One-Ways	% Reviewed
16	5	13	34	61%

Recipients	Compatible Donors	Preferences
Alias ABO Age Weight Avoids	ABO Age Weight Points HLA Med Notes Creatinine Clearance	Donor Donor HLA Age Weight Match Travel
JS1966 O 46 86 2	O 49 42 50 <input type="button" value="Read"/> 117	<input type="button" value="Accept"/> <input type="button" value="Decline"/> <input type="button" value="View"/>
	O 61 79 40 <input type="button" value="Read"/> 141	<input type="button" value="Accept"/> <input type="button" value="Decline"/> <input type="button" value="View"/>
	O 26 61 0 <input type="button" value="Read"/> 121	<input type="button" value="Accept"/> <input type="button" value="Decline"/> <input type="button" value="View"/>
	O 56 60 0 <input type="button" value="Read"/> 183	<input type="button" value="Accept"/> <input type="button" value="Decline"/> <input type="button" value="View"/>
	O 42 63 0 <input type="button" value="Read"/> 100	<input type="button" value="Accept"/> <input type="button" value="Decline"/> <input type="button" value="View"/>
LP1962 O 50 179 14	O 29 80 50 <input type="button" value="Read"/> 112	<input type="button" value="Accept"/> <input type="button" value="Decline"/> <input type="button" value="View"/>
	O 40 69 45 <input type="button" value="Read"/> 110	<input type="button" value="Accept"/> <input type="button" value="Decline"/> <input type="button" value="View"/>
	O 46 63 40 <input type="button" value="Read"/> 94	<input type="button" value="Accept"/> <input type="button" value="Decline"/> <input type="button" value="View"/>
	O 48 100 35 <input type="button" value="Read"/> 100	<input type="button" value="Accept"/> <input type="button" value="Decline"/> <input type="button" value="View"/>
	O 46 102 35 <input type="button" value="Read"/> 221	<input type="button" value="Accept"/> <input type="button" value="Decline"/> <input type="button" value="View"/>
	O 38 62 25 <input type="button" value="Read"/> 149	<input type="button" value="Accept"/> <input type="button" value="Decline"/> <input type="button" value="View"/>
	O 66 84 25 <input type="button" value="Read"/> 125	<input type="button" value="Accept"/> <input type="button" value="Decline"/> <input type="button" value="View"/>
	O 26 61 0 <input type="button" value="Read"/> 121	<input type="button" value="Accept"/> <input type="button" value="Decline"/> <input type="button" value="View"/>

**Donor Pre-Select - Detail**

Pre-Screening | **Edit Recipient** | Paired Donors | Recipient Toolbox | Potential Donors | Evaluate

Donor Recipient: 5616\_201966

Medical & Demographic Info

ABO:  O  A  B  AB (Max: 6)

Age:   (Max: 65)

Weight (kg):   (Max: 0)

Height (cm):

Gender:  F  M

Which Kidney?:  Left  Right

Creatinine Clearance:

Number of Arteries:

Number of Veins:

Number of Ureters:

Kidney CT/AS Length (cm):

Kidney CT/AS Width (cm):

Kidney 3D-CT Volume (cc):

Recipient Preferences

Min donor weight (in kg)

Max donor age

Min HLA match pts.

Recipient will accept shipped kidney

Recipient willing to travel

Donor willing to travel

Recipient Insurance: Health Alliance

**Reason for recipient kidney failure:** Polycystic Kidney Disease

**Out of the ordinary donor medical issues:** right kidney with 9mm upper pole cyst

HLA	Donor Antigens	Recipient Antigens	HLA Points	Recipient Avoids
A	1 26	1 1	10	
B	8 51	8 57	15	
DR	17 9	17 17	25	

Figure 5. Donor pre-select software. A. summary screen, B. donor pre-select - detail.

**NKR Swap Expert  
Patient Advisory for BROD**

**Enter Missing Information:** (There is no missing information.)

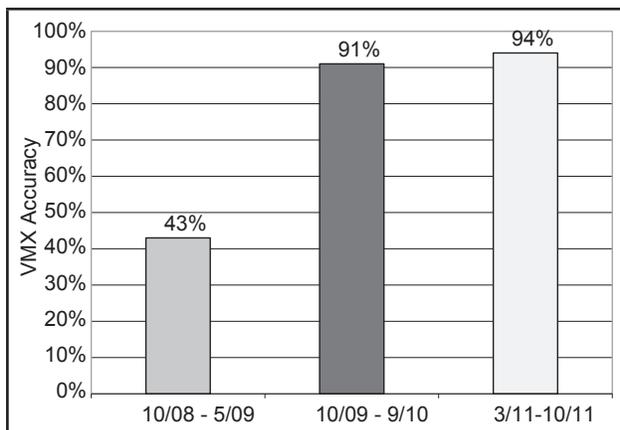
- Manage Antibody Avoids:** You have a significant number (35) of antibody "avoids" recorded in the system. These avoids combined with blood type incompatibility are blocking matches with 98.4% of the 251 donors in the system at the time this patient advisory was created. This is the most important variable impacting your chance of finding a match in the system. There are three strategies related to antibodies avoids you can employ to find a match in the system.
  - You can continue to wait for new donors to enter the system that are compatible to you. This approach is generally used when patients are doing well on dialysis or are not yet on dialysis and do not have a problem waiting for a match.
  - You can work with your transplant center to determine if any of the avoids listed in the system have dropped in intensity and can be removed from your profile. Antibodies change over time so they should be measured and updated every three months.
  - If your center has the expertise to provide desensitization services, you should speak with them to see if you are a candidate for combining desensitization with paired exchange.
- Relax Preference Restrictions:** Because you have a significant number of antibody avoids (35) listed in the system, you may need to be less restrictive in setting your preferences in order to increase your chance of finding a match. At the time this patient advisory was created, your recipient preferences were blocking 0% of the 4 biologically compatible donors in the system. The table below shows your current preferences as well as the least restrictive preferences that will maximize your odds of finding a match.

Preference	Current Setting	Less Restrictive Preferences
Maximum Donor Age	70	70
Minimum Donor Weight	0	0
Minimum HLA Match Points	0	0
Accept Shared Kidney	Yes	Yes

**Figure 6. Swap Expert.**

### Standardized listing of all relevant HLA antigens and antibodies

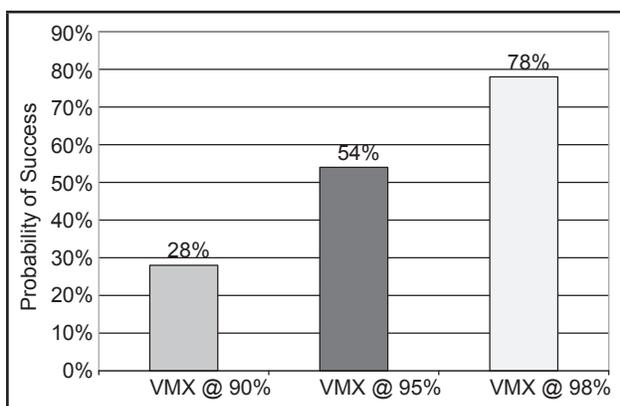
When the NKR program was in the start-up phase, unexpected cross match failures were disrupting more than half of the match offers being made. In May 2009, the virtual cross match accuracy rate was 43%. At that time, a national lab director group was formed by the leading NKR centers to improve virtual cross match accuracy. By the end of 2011, the virtual cross match accuracy rate had increased to 94% increasing the number of matches that actually made it to successful transplantation. This dramatic improvement (Fig. 7) has greatly accelerated the rate



**Figure 7. Improved Virtual Cross Match Accuracy.**

of paired exchange transplantation and is the direct result of the collaboration of many experienced and skilled lab directors from leading NKR centers. Key innovations that have improved the process include:

- Standardization of all antigen and antibody codes
- Review of all cross match failures by participating laboratory directors
- Corrective action plans for centers failing cross matches
- Required entry of HLA-DP antibodies and HLA-DP donor antigens



**Figure 8. Increasing probability of success by VMX accuracy.**

As the virtual cross match accuracy increased, driven by the innovations adopted by the national lab director team, it became feasible to make larger match offers. As a result, in 2010 NKR's matching system was upgraded to find clusters up to 12 deep so that large match offers could be made. Table 2 and Figure 8 demonstrate the importance that virtual cross match accuracy has on the probability of a 12-deep match offer actually working. Since the implementation of 12-deep matching capabilities, several 12-deep chains have actually gone from offer to completion. As a result of the success with 12 deep chains, the NKR matching system was

**Table 2. Probability of Success with 12-deep.**

Position	VMX at 90%	Cumm VMX	VMX at 95%	Cumm VMX	VMX at 98%	Cumm VMX
1	90%	90%	95%	95%	98%	98%
2	90%	81%	95%	90%	98%	96%
3	90%	73%	95%	86%	98%	94%
4	90%	66%	95%	81%	98%	92%
5	90%	59%	95%	77%	98%	90%
6	90%	53%	95%	74%	98%	89%
7	90%	48%	95%	70%	98%	87%
8	90%	43%	95%	66%	98%	85%
9	90%	39%	95%	63%	98%	83%
10	90%	35%	95%	60%	98%	82%
11	90%	31%	95%	57%	98%	80%
12	90%	28%	95%	54%	98%	78%

enhanced to go 20-deep at the end of 2010 and further enhanced in 2011 with no depth limitations.

**Shipping living donor kidneys**

Shipping living donor kidneys was an unsettling prospect to many transplant clinicians. The perceived association between prolonged cold ischemic time and poorer graft function, which has incorrectly been considered the defining difference between living and deceased donor kidneys (5), caused some physicians to move cautiously. Lacking a strong bias and with the flexibility in the start times of chain transplants, shipping living donor kidneys was the model that the donors and recipients preferred and expressed via the NKR preferences. The willingness to ship living donor kidneys expanded the options for pairs as it broadened the geographic area from which compatible donors and recipients could participate. In 2011 NKR centers shipped more than 100 living donor kidneys, sometimes from coast to coast. Many had cold ischemia times of more than 14 hours (6). A recent compilation of the outcomes for 56 shipped living donor kidneys from 30 centers, including many shipped by NKR centers, showed good early function despite longer cold ischemia, and attests to the safety and feasibility of the practice (7).

**Creation of the children and high PRA program (CHIP)**

Several members of the NKR Medical Board pointed out in 2010 that the NKR matching system could be utilized to get patients transplanted who do not have donors and who also have a low probability to receive a deceased donor transplant because they are very highly sensitized. By sharing bridge donors and non-directed donors across the NKR network, the process has improved the odds of finding a match for these hard-to-match patients without donors. Later in the testing of the program, the NKR Medical Board voted to include pediatric candidates in the program.

The program was subsequently named the CHIP (Children and High PRA) program. Table 3 outlines the CHIP program parameters. In 2011, the CHIP program facilitated transplants for 43 patients including 4 children.

**Standard financial model between centers**

One of the underappreciated barriers to paired exchange transplantation was the payment process between transplant centers. An efficient payment process is necessary so that the donor centers can recover their costs for providing donor surgical services. This barrier became a crisis in late 2009 when an NKR-facilitated triple exchange was cancelled a day prior to surgery because the transplant centers involved could not agree on how much to pay each other. Not only were 3 patients left on dialysis, but this last minute cancellation was the catalyst for a broken chain as the bridge donor

**Table 3. Children & High PRA (CHIP) Program. The CHIP program helps patients without donors who are either children or are disadvantaged because they are sensitized.**

- NKR member centers with net chains started >0 may enroll up to 30 candidates in the CHIP program.
- Net chains started is the total number of chains that a center starts less the total number of chains a center ends.
- CHIP candidates must be children (18 or younger) or sensitized adults.
- The most likely blood types to find a CHIP match are “AB”, “A” and “B” blood types.
- The CHIP program is used as a last resort. The probability of a match dramatically improves when a paired donor(s) is available.

for this cluster eventually withdrew. In the wake of this devastating situation, the leading NKR member centers came together and developed a standard financial model that has eliminated nearly all of the problems related to payments between centers in NKR facilitated exchanges.

### Streamlined regulatory compliance

In 2011 CMS issued new guidelines for living donor services which required centers participating in swaps to have written agreements between hospitals for living donor services. Since the NKR centers were already using a standard financial model, all that was needed was an additional compliance section. The revised executed CMS compliant agreements are posted to the NKR web site with other required compliance information (already resident in the NKR database) providing the basis for the automated process for regulatory compliance (Fig. 9).

### RESULTS

The innovations pioneered by the National kidney Registry and its Medical Board have surpassed all prior paired exchange efforts as measured by performance metrics covering areas including patient wait time, program matching efficiency, and the ability to get highly sensitized patients matched and transplanted.

#### Patient wait time

Nothing is more important to a patient undergoing dialysis than the expected wait time for a transplant. This is the most important performance measure for paired exchange programs. There are 2 fundamental methods for calculating paired exchange wait time: 1) transplanted patient wait time and 2) enrolled patient wait time (Figs. 10,11). Transplanted patient wait time is the actual wait time for those patients who have been transplanted. Enrolled patient wait time is not an exact measure because it is unknown when an enrolled patient will be transplanted. However this metric can be estimated using a calculation borrowed from modern inventory control theory by dividing the

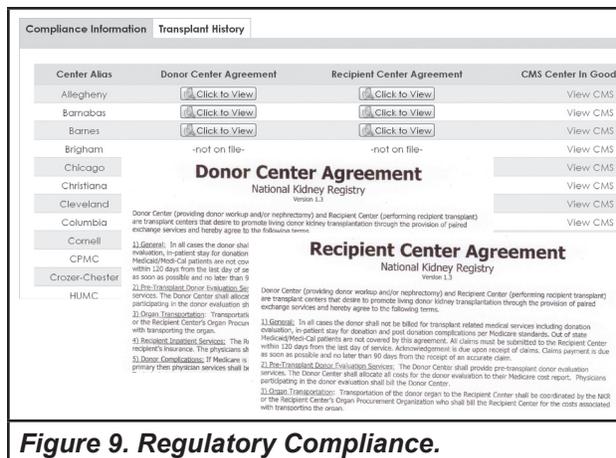


Figure 9. Regulatory Compliance.

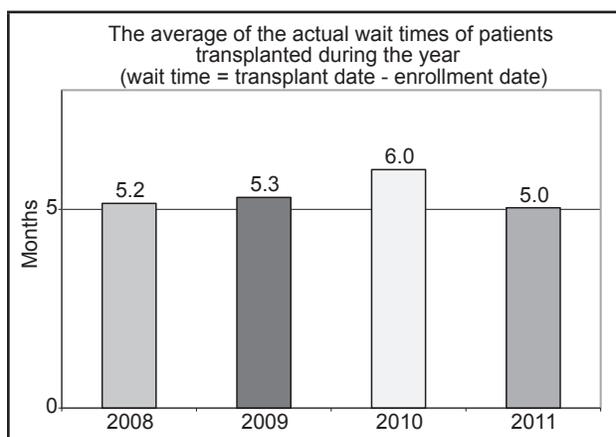


Figure 10. Transplanted patient average wait time.

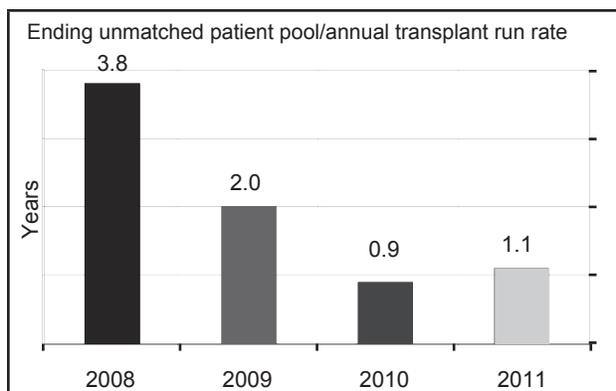


Figure 11. Enrolled patient projected wait time.

pool size (inventory) by the annual exchange transplant run rate (usage). For example, if the pool size is 200 and the transplant run rate is 100 then an enrolled patient will wait an average of 2 years to get transplanted.

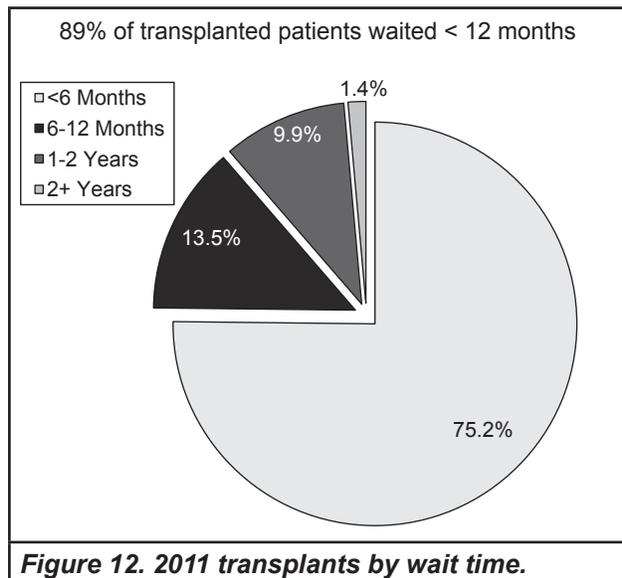
Obviously pairs have very different actual wait times for getting matched and transplanted as

**Table 4. NKR Expected Months Wait Time.**

Patient Blood Type	Donor Blood Type	cPRA 0%	cPRA 1-50%	cPRA 51-80%	cPRA 81-95%	cPRA >95%
AB (Easiest)	O	No Data	No Data	No Data	2	15
	B	No Data	No Data	No Data	No Data	No Data
	A	1	No Data	5	No Data	No Data
	AB	No Data	No Data	No Data	3	18
A	O	2	3	3	3	23
	B	4	2	8	2	10
	A	No Data	4	14	3	17
	AB	2	No Data	No Data	No Data	54
B	O	4	No Data	7	72	16
	B	No Data	1	No Data	6	No Data
	A	5	3	5	15	No Data
	AB	4	No Data	No Data	No Data	No Data
O (Hardest)	O	3	4	5	7	84
	B	7	30	No Data	No Data	No Data
	A	12	12	12	40	350
	AB	70	No Data	No Data	8	No Data

depicted in Table 4, which shows the forecasted wait time for each blood type combination and cPRA category, but enrolled patients wait time is very helpful in evaluating the overall efficiency of the pool.

Additional informative wait time metrics include the percent of transplants completed in less than six months (Fig. 12) and the forecasted wait time for various pair blood type combinations and patient cPRAs (Fig. 13).

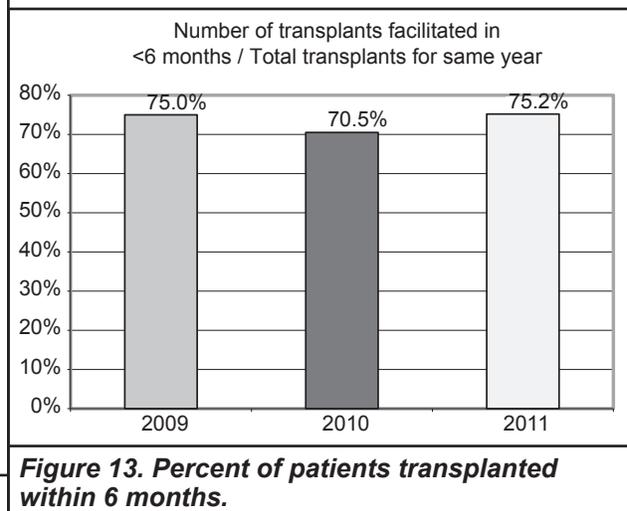


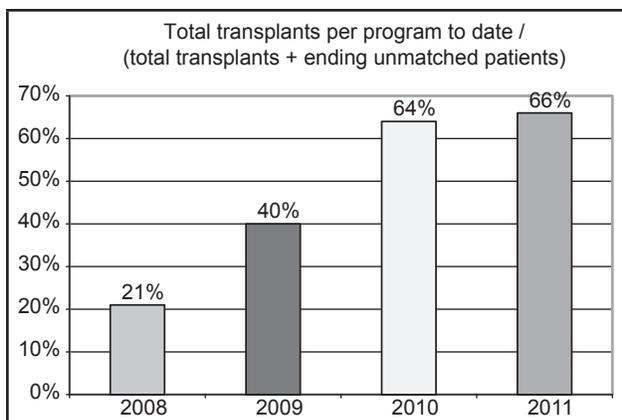
**Program matching efficiency**

Measures of exchange program matching efficiency include the percent of the pool that has been transplanted - the higher this percentage, the better. Figures 14 and 15 show the percent of pool measures by year with a breakdown of the cumulative NKR pool at the end of 2011.

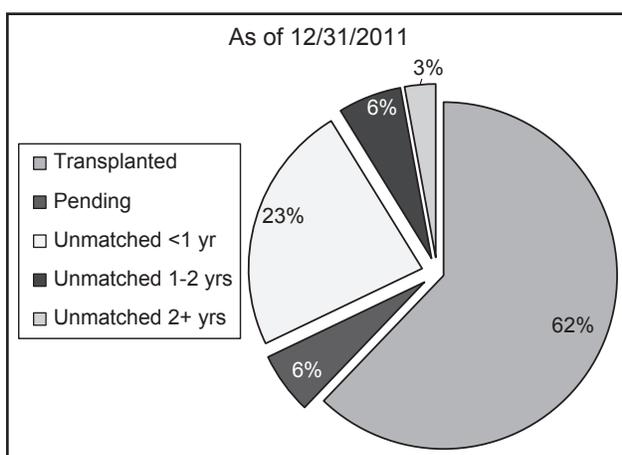
**Matching highly sensitized patients**

One of the key measures of paired exchange performance is the ability to match and transplant highly sensitized patients. It is these highly





**Figure 14. Cumulative pool transplanted by year.**



**Figure 15. Cumulative pool distribution by status.**

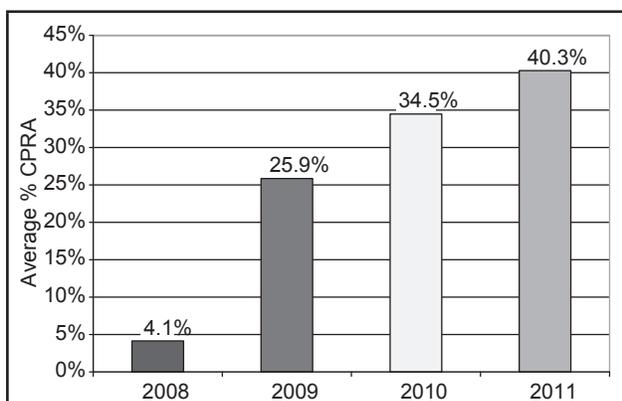
sensitized patients that accumulate in paired exchange systems because they are the hardest to match. Two metrics that show the matching performance of the NKR system for these hard to match patients are shown in Figures 16 and 17. The cPRA calculation used in these metrics is based on

the actual number of matches using the NKR donor pool and the actual avoids entered in the recipient records. This cPRA calculation co-varies with the standard UNOS cPRA but is sometimes higher since the UNOS cPRA calculation does not reflect the additional antibodies (HLA-Cw, -DP) tracked in the NKR system.

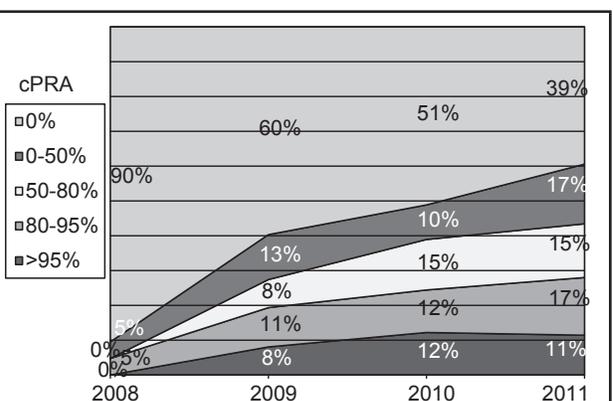
During 2011, the NKR witnessed an unprecedented increase in the number of highly sensitized patients that were successfully matched and transplanted accompanied with an increase in the percent of highly sensitized patients in the pool (Figs. 18, 19). Going forward, this dynamic is expected to continue as the pool size increases, driven by hard-to-match patients, which will increase the size of the donor pool, facilitating more transplants for the highly sensitized patients.

**Bridge Donor withdrawal**

There has been much debate about whether bridge donors can be trusted to pass on the generosity and donate to the next recipient in the chain after their intended recipient has already received a kidney transplant. A number of strategies have been adopted to streamline transplantation of bridge donors and to avoid prolonged waits before donation (Table 5). Based on NKR observations of nearly 400 exchange transplants, bridge donor withdrawals have declined as a percentage of bridge donors each year (Table 6). The reasons for bridge donor withdrawals were not given for 2 of the 3 that occurred in 2008 and the third withdrew



**Figure 16. Average cPRA of transplanted patients by year.**



**Figure 17. Transplanted patients by year by cPRA.**

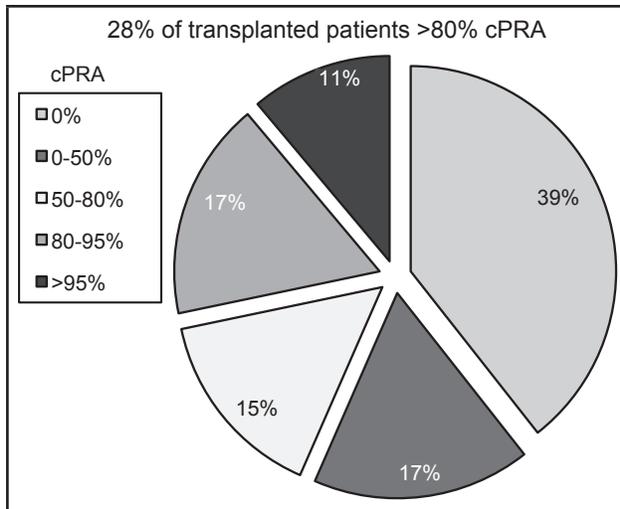


Figure 18. 2011 transplants by cPRA.

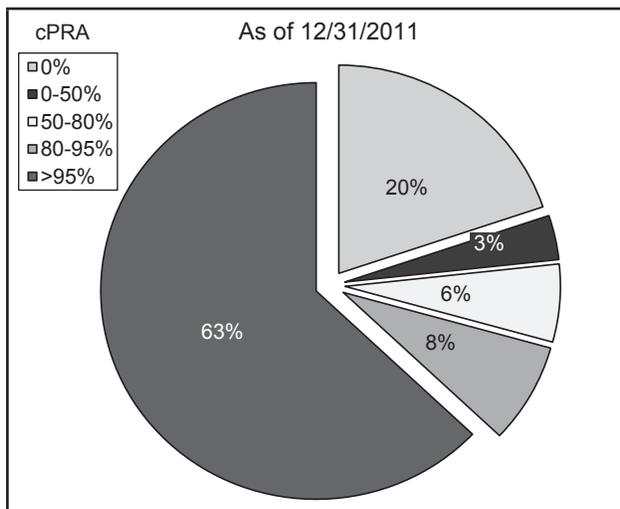


Figure 19. 2011 pool composition by cPRA.

because of a long wait, multiple crossmatch failures and job issues, In 2009 two donors withdrew, one because of a prolonged wait to donate and the second for medical reasons. Both withdrawals in 2010 were due to medical concerns. By 2011 the bridge donor withdrawal rate had dropped to zero. Figure 20 shows how 6 of these 7 bridge donor withdrawals affected transplant chains greater than 1 deep.

### ETHICAL CONSIDERATIONS

With the growth of living donor transplants and particularly chains where donors are allocated to patients they do not know, there is a need for the transplant community to establish some

Table 5. Strategies to Eliminate Broken Chains.

- Utilize larger clusters/ longer chains
- Transplant clusters simultaneously
- Pre-approve bridge donor candidates
- Only hold O donors as bridge donors
- End A, B and AB donors to the list
- Don't allow bridge donors to wait too long
- Avoid excessive bridge donor blood draws
- Complete full bridge donor medical evaluations
- Avoid canceling swaps at the last minute

Table 6. Bridge Donor Withdrawals.

Year	# Bridge Donors	# Withdrawn	% Withdrawn
2008	9	3	33%
2009	29	2	7%
2010	61	2	3%
2011	75	0	0%
Total Bridge Donors	174	7	

guidelines. At a minimum, centers starting chains must fully disclose to non-directed donors all of the potential donation options. Additionally, there must be transparency in all aspects of paired exchange including governance, results reporting, the unnecessary utilization of desensitization and center “hold backs” that are hurting patients.

### Governance

In 2011 the NKR enhanced its bylaws to formalize the role of the Medical Board to control all medical policies through majority vote of the Board. Six committees were formed to oversee the key areas of expertise critical to paired exchange success. These key areas also benefit from consensus decisions among Member Centers. Medical Board meetings are held periodically with formal voting on all significant medical policy changes or additions (e.g. match offer selection policy). Figure 21 shows a snapshot of the NKR Medical Board at the end of 2011.

### Transparency

Transparency for paired exchange programs has been a challenge because accurate performance reporting requires a comprehensive database and complex data presentation tools.

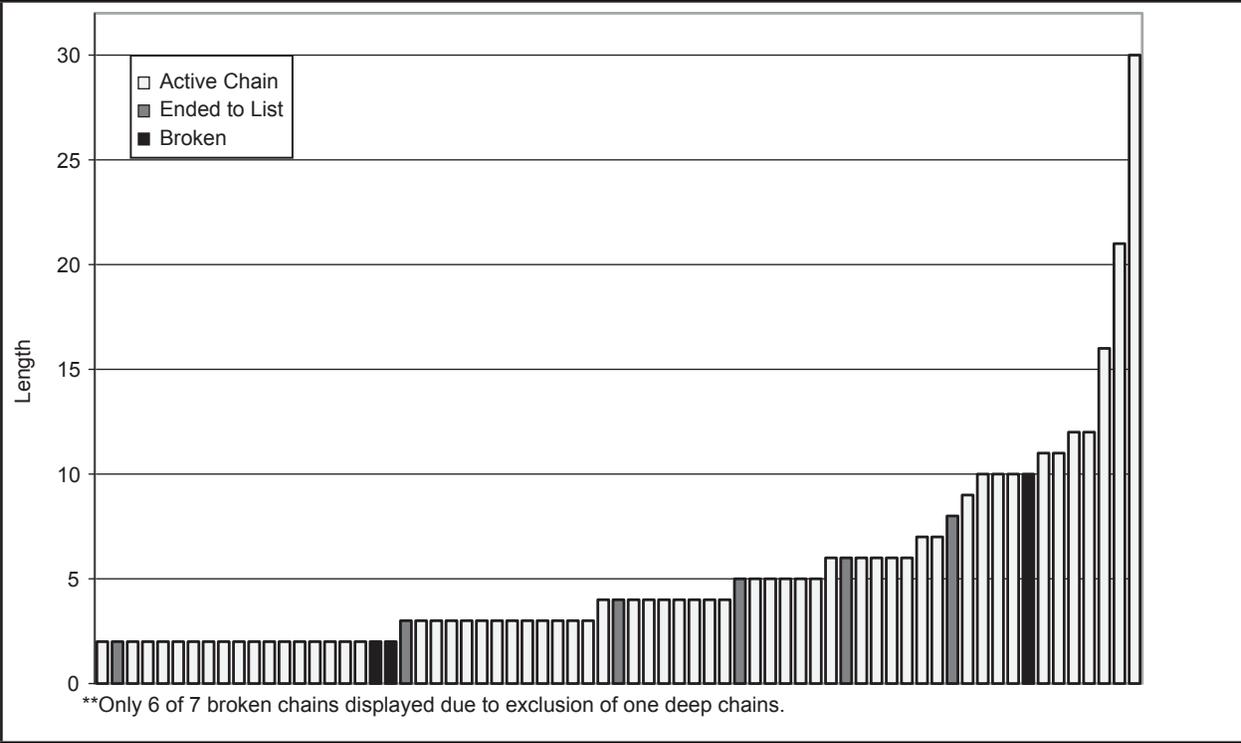


Figure 20. Effect of bridge donor withdrawal on chain lengths.

National Kidney Registry Medical Board					
Revised 12/13/2011					
Yolanda Becker, MD	Howard Gebel, PhD	Suzanne McGuire, RN	David Serur, MD		
Michael Cecka, PhD	Pam Heckathorn Hale	Marc Melcher, MD, PhD	Helen Spicer, RN		
Marian Charlton, RN	Valerie Johnson, MD, PhD	John Milner, MD	Angela Stimpson		
Gabriel Danovitch, MD	Sandip Kapur, MD	Marie Morgieovich, ANP	Barry Straube, MD		
Michael Dattoli, MD	Steven Katznelson, MD	John Roberts, MD	Jeffrey Veale, MD		
Connie Davis, MD	Debbie Mast	Sally Satel, MD			
<b>Surgery</b> Chair & Surgical Director Jeffrey Veale, MD	<b>Nephrology</b> Chair & Medical Director David Serur, MD	<b>Histo</b> Chair & Lab Director Michael Cecka, PhD	<b>Research</b> Chair & Research Director Marc Melcher, MD	<b>Operations</b> Chair & Paired Exchange Director Marian Charlton, RN	<b>Finance &amp; Admin</b> Co-chairs Debbie Mast & Gigi Spicer, RN
Barry Browne, MD Luis Fernandez, MD Sandi Kapur, MD John Milner, MD John Roberts, MD Chris Troppmann, MD Henrie Tan, MD	Tony Bonagura, MD Shlomo Cohney, MD Gabe Danovitch, MD Connie Davis, MD Fuad Shihab, MD Christine Wu, MD	LeeAnn Baxter-Lowe, PhD Darshana Dadhania, MD Nick DiPaolo, PhD Malek Kamoun, MD, PhD John Lunz, PhD Paul Warner, PhD	LeeAnn Baxter-Lowe, PhD Connie Davis, MD Malek Kamoun, MD David Leeser, MD John Milner, MD Jeffrey Veale, MD	Janine Sabetto-Castillo, RN Diane James, RN Paula Mark, RN Suzanne McGuire, RN Marie Morgieovich, RN Dianne la Pointe-Rudow, NP Tammy Wright, RN	Angie Korsun Andrea Tietjen Kari Jones Ursula Lebron-Banks Bill Vaughan

Figure 21. National Kidney Registry Medical Board.

NKR is setting the standard for transparency by communicating results on a quarterly basis to the transplant community. Many of the results that are reported by NKR quarterly are also presented in the Results section of this chapter.

Additional transparency is needed to manage the unnecessary “promotion” of desensitization when paired exchange can be employed to find a clean match, which leads to better patient outcomes. In some cases, paired exchange programs inappropriately combine desensitization with paired exchange because their donor pool is too small. This is not in the best interest of the patient when a good match that does not require desensitization can be found in a larger pool such as the NKR.

Single center “hold backs” are also delaying transplants and forcing poor matches when transplant centers attempt to keep exchanges “in-house”. This practice is evident at a handful of centers in the U.S. and puts the patient’s interests in conflict with the transplant center’s interest. Single center swaps rarely move faster or find better matches than those organized by national programs such as the NKR because of the limited size of the single center donor pool and the lack of sophisticated software utilized in single center swaps. Organizing single center swaps does have some advantages as they are logistically simpler and slightly more profitable because they eliminate costs related to shipping and matching.

### **NDD allocation and coercion**

Social concerns for NDDs include their motivation, possible hidden compensation and psychiatric history to name a few. Our experience indicates that only 1% of inquiring NDD candidates make it all the way through the evaluation process to actual donation. In addition to appropriate medical and psychological screening, other ethical issues exist. Should the kidney be allocated to the center’s deceased donor list, 6-antigen match national list, a child, or to start a chain? These questions can only be answered by the donor, so it is important that donors know all the options before they decide when and where to donate.

### **Utility vs Justice**

Candidates on the deceased donor waiting list collectively benefit when non-directed living donor organs are allocated to initiate chains. Living donors are liberated throughout a chain, removing patients from the wait list. Without chains these living donors would never have been utilized due to incompatibility. This net gain of living donors reduces the competition for deceased donors for those candidates on the waiting list allowing other patients to move up the wait list and take the place of the recipients on the wait list that received a kidney from a living donor in a chain. The resulting multiplier effect is powerful. For example, if one donor starts a chain that is closed after 6 transplants, 5 recipients are removed from the wait list when they receive a living donor transplant and one recipient on the wait list receives a kidney directly from the last living donor in the chain.

### **FUTURE DIRECTIONS**

The future of paired exchange is one of rapid growth. This will be driven by transplant center outreach efforts that are educating the 80,000+ patients on the wait list, including thousands that have incompatible donors. An increasing number of patients with compatible donors are also entering swaps to improve their match while helping other patients with incompatible donors get transplanted. By the end of the decade, the current practice of living donors giving their kidney to a friend or family member may be a relic of the past (except for well-matched siblings/relatives) with most donors giving their kidney to a stranger in a chain so that all recipients get better matched donors, allowing the transplanted kidneys to last longer. The increased volume in paired exchange will set the stage to match many more patients and greatly expand the donor pool. This will facilitate transplants for thousands of additional patients, saving the US health care system billions in dialysis-related costs.

### **Compatible pairs**

Many medical professionals and their patients are beginning to realize that compatible pairs

can improve their donor recipient match and improve the patient's outcome by participating in an exchange (10,11). These benefits are most pronounced for compatible pairs comprising an O donor and unsensitized non-O patient, since there are shortages of O donors in all exchange programs. Improved matches are usually evaluated on 3 dimensions; donor age, HLA match and donor size. Although the improvements in patient outcomes are well documented related to donor age and HLA match, there is limited research to demonstrate donor size improves graft survival or half-life (12). In addition to finding a better matched donor and potentially achieving a better outcome, the compatible pair will typically facilitate many more transplantations by filling a missing gap in the chain and increasing the liquidity of the pool.

### **Economic benefits of paired exchange transplantation**

The economic benefits of paired exchange to the US health care system over the next decade may be in excess of \$100 billion dollars. When ESRD patients are removed from dialysis through paired exchange transplantation, an enormous economic savings accrues. There are 3 primary financial beneficiaries of a paired exchange transplant 1) transplant centers 2) insurance companies and their self-insured customers and 3) Medicare and the US government. When a paired exchange transplant takes place, the transplant center/hospital realizes approximately \$90,000 - \$200,000 in incremental revenue. If the patient is covered by private insurance, the insurance company saves about \$300,000 (Table 7) based on figures provided by the largest health insurance companies in the United States. Finally Medicare and the US government save approximately \$1,100,000 per patient transplanted, mostly by avoiding ongoing dialysis costs (Table 8). To date, neither the insurance industry nor Medicare has provided any material financial support to paired exchange efforts with most of the funding coming from charitable contributions and transplant centers. When Medicare and the insurance industry begin providing financial contributions to support

**Table 7. Insurance Company Savings for each exchange transplant.**

Annual Dialysis Costs *	\$150,000
Years on Dialysis	X 3
Dialysis Savings	\$450,000
Cost of Transplant	(\$100,000)
Post-Transplant Costs	(\$50,000)
Net Savings	\$300,000
* Pittsburg Inquirer 9/28/09 – does not include other dialysis related costs	

**Table 8. Medicare Savings for each exchange transplant.**

Dialysis Less Transplant Maintenance (GAO study)	\$42,388
Disability & Lost Tax Revenue (NKR White Paper)	\$18,500
Total Annual Savings	\$60,888
Average Kidney Life Years *	X 20
	\$1,217,760
Approximate Cost of Transplant	(\$100,000)
Present Value of Savings (assumes inflation is roughly equal to the U.S. government cost of capital)	\$1,117,760
* Does not include additional kidney life years from compatible pairs who achieve better compatibility through paired exchange.	

paired exchange commensurate with their financial gain, many more of their customers/members will receive transplants.

### **Combining desensitization with chains**

Transplant teams specializing in desensitization often see the rapid growth of chain transplantations as a threat to their clinical workload. Likewise, proponents of exchanges often point out the added expense (\$28,979 / transplant) and immune-mediated injury associated with desensitization (13). However, these 2 approaches are not mutually exclusive and are actuality quite complementary. With access to desensitization and chain matching, a center can essentially stack the deck in favor of the patient. For example, a potential recipient who has multiple HLA antibodies, some of which are stronger and others that are weaker. When this pair is placed into a registry, the weaker antibodies that are removed through desensitization can be ignored in the matching process. In this case, the

center would not list these weak antibodies for this patient and the patient could receive a transplant through a chain in combination with desensitization. The combination of paired exchange and desensitization is often the best modality of highly sensitized patients. The NKR has added a “toolbox” to the website that allows centers to see the effects

of removing one or more unacceptable antigens on the matchability (i.e. pair match power) of their registered pairs. This allows Member Centers to understand in advance the potential impact that combining desensitization with paired exchange will have on the probability of finding a match and the expected wait time for an exchange transplant.

<b>NKR Program Statistics.</b>					
		<b>2008</b>	<b>2009</b>	<b>2010</b>	<b>2011</b>
1	Transplants Facilitated	21	62	131	175
2	Ending Unmatched Patient Pool	80	127	120	201
3	Cumulative Transplants	21	83	214	389
4	Cumulative Patient Pool	101	210	334	590
5	Percent of Pool Transplanted	21%	40%	64%	66%
6	Enrolled Patient Average Wait Time	3.8	2.0	0.9	1.1
7	Transplanted Patient Average Wait Time	5.1	5.3	6.0	5.0
8	Average cPRA of Transplanted Patients	4.1%	25.9%	34.5%	40.3%
9	Number of Transplants Completed by cPRA				
10	>95%	0	5	16	20
11	80-95%	1	7	16	29
12	50-80%	0	5	19	27
13	0-50%	1	8	13	30
13	0%	19	37	67	69
14	Sub-total	21	62	131	175
15	Percent of Transplants Completed by cPRA				
16	>95%	0%	8%	12%	11%
17	80-95%	5%	11%	12%	17%
18	50-80%	0%	8%	15%	15%
19	0-50%	5%	13%	10%	17%
20	0%	90%	60%	51%	39%
21	Sub-total	100%	100%	100%	100%
22	Number of Transplanted Patients with cPRA >80%	1	12	32	49
23	Percent of Transplanted Patients with cPRA >80%	5%	19%	24%	28%
24	Number of Unmatched Patients by cPRA at year-end				
25	>95%				152
26	80-95%				15
27	50-80%				14
28	0-50%				14
29	0%				50
30	Sub-total				245
31	Percent of Unmatched Patients by cPRA at year-end				
32	>95%				62%
33	80-95%				6%
34	50-80%				6%
35	0-50%				6%
36	0%				20%

<b>NKR Program Statistics, cont'd.</b>					
		<b>2008</b>	<b>2009</b>	<b>2010</b>	<b>2011</b>
37	Sub-total				100%
38	Number of Transplants Completed by Wait Time				
39	< 6 months	21	42	74	106
40	6-12 months	0	10	14	19
41	1-2 years	0	4	15	14
42	2+ years	0	0	2	2
43	Sub-total	21	56	105	141
44	Percent of Transplants Completed by Wait Time				
45	< 6 months	100.0%	75.0%	70.5%	75.2%
46	6-12 months	0.0%	17.9%	13.3%	13.5%
47	1-2 years	0.0%	7.1%	14.3%	9.9%
48	2+ years	0.0%	0.0%	1.9%	1.4%
49	Sub-total	100%	100%	100%	100%
50	Total Chains Started	3	8	28	38
51	Total Loops Completed	0	3	2	3
53	Number of broken chains	3	2	2	0
54	Bridge donors held	9	29	61	75
55	Percent of broken chains	33%	7%	3%	0%

## **THE NEW YORK TIMES ARTICLE "60 LIVES, 30 KIDNEYS, ALL LINKED"**

The following *New York Times* article describes one of the longest living donor chains to date. The editors of *Clinical Transplants* thank Joe Sinacore at National Kidney Registry for acquiring the copyrights from The New York Times and making it possible for us to include this extraordinary article in this book.

Originally printed in *The New York Times*, February 18, 2012.

By Kevin Sack

RIVERSIDE, Calif. — Rick Ruzzamenti admits to being a tad impulsive. He traded his Catholicism for Buddhism in a revelatory flash. He married a Vietnamese woman he had only just met. And then a year ago, he decided in an instant to donate his left kidney to a stranger.

In February 2011, the desk clerk at Mr. Ruzzamenti's yoga studio told him she had recently donated a kidney to an ailing friend she had bumped into at Target. Mr. Ruzzamenti, 44, had never even

donated blood, but the story so captivated him that two days later he called Riverside Community Hospital to ask how he might do the same thing.

Halfway across the country, in Joliet, Ill., Donald C. Terry Jr. needed a kidney in the worst way. Since receiving a diagnosis of diabetes-related renal disease in his mid-40s, he had endured the burning and bloating and dismal tedium of dialysis for nearly a year. With nobody in his family willing or able to give him a kidney, his doctors warned that it might take five years to crawl up the waiting list for an organ from a deceased donor.

"It was like being sentenced to prison," Mr. Terry recalled, "like I had done something wrong in my life and this was the outcome."

As a dawn chill broke over Chicago on Dec. 20, Mr. Terry received a plump pink kidney in a transplant at Loyola University Medical Center. He did not get it from Mr. Ruzzamenti, at least not directly, but the two men will forever share a connection: they were the first and last patients in the longest chain of kidney transplants ever constructed, linking 30 people who were willing to give up an organ with 30 who might have died without one.

What made the domino chain of 60 operations possible was the willingness of a Good Samaritan, Mr. Ruzzamenti, to give the initial kidney, expecting nothing in return. Its momentum was then fueled by a mix of selflessness and self-interest among donors who gave a kidney to a stranger after learning they could not donate to a loved one because of incompatible blood types or antibodies. Their loved ones, in turn, were offered compatible kidneys as part of the exchange.

Chain 124, as it was labeled by the nonprofit National Kidney Registry, required lockstep coordination over four months among 17 hospitals in 11 states. It was born of innovations in computer matching, surgical technique and organ shipping, as well as the determination of a Long Island businessman named Garet Hil, who was inspired by his own daughter's illness to supercharge the notion of "paying it forward."

Dr. Robert A. Montgomery, a pioneering transplant surgeon at Johns Hopkins Hospital, which was not involved in the chain, called it a "momentous feat" that demonstrated the potential for kidney exchanges to transform the field. "We are realizing the dream of extending the miracle of transplantation to thousands of additional patients each year," he said.

The chain began with an algorithm and an altruist. Over the months it fractured time and again, suspending the fates of those down the line until Mr. Hil could repair the breach. Eventually, he succeeded in finding needle-in-a-haystack matches for patients whose antibodies would have caused them to reject organs from most donors.

Until now, few of the donors and recipients have known one another's names. But 59 of the 60 participants consented to be identified by The New York Times and to tell the stories, each with distinct shadings, that ultimately connected them.

Despite an intensely bitter breakup, a Michigan man agreed to donate a kidney for his former girlfriend for the sake of their 2-year-old daughter. A woman from Toronto donated for her fifth cousin from Bensonhurst, Brooklyn, after meeting him by chance in Italy and then staying in touch mostly by text messages.

Children donated for parents, husbands for wives, sisters for brothers. A 26-year-old student from Texas gave a kidney for a 44-year-old uncle in California whom he rarely saw. In San Francisco, a 62-year-old survivor of Stage 4 Hodgkin's lymphoma donated for her son-in-law.

On Aug. 15, Mr. Ruzzamenti's kidney flew east on a Continental red-eye from Los Angeles to Newark and was rushed to Saint Barnabas Medical Center in Livingston, N.J. There it was stitched into the abdomen of a 66-year-old man.

The man's niece, a 34-year-old nurse, had wanted to give him her kidney, but her Type A blood clashed with his Type O. So in exchange for Mr. Ruzzamenti's gift, she agreed to have her kidney shipped to the University of Wisconsin Hospital in Madison for Brooke R. Kitzman's transplant. It was Ms. Kitzman's former boyfriend, David Madosh, who agreed to donate a kidney on her behalf despite their acrimonious split.

Mr. Madosh's kidney flew to Pittsburgh for Janna Daniels, a clerical supervisor, who got her transplant at Allegheny General Hospital. And her husband, Shaun, a mechanic, sent his kidney to Mustafa Parks, a young father of two at Sharp Memorial Hospital in San Diego.

On and on the chain extended, with kidneys flying from coast to coast, iced down in cardboard boxes equipped with GPS devices and stowed on commercial aircraft.

In a system built on trust, one leap of faith followed another. The burdens of scheduling operations all across the country — so donors would not have to travel — meant that operations were not always simultaneous, or even sequential. The most worrisome risk was that donors would renege once their loved ones received kidneys.

After John A. Clark of Sarasota, Fla., got a transplant on Sept. 28 at Tampa General Hospital, his wife, Rebecca, faced a 68-day wait before it was her turn to keep the chain going. Ms. Clark said that it crossed her mind to back out, but that she swatted away the temptation. "I believe in karma," Ms. Clark said, "and that would have been some really bad karma. There was somebody out there who needed my kidney."

## An Organ to Spare

It is considered a quirk of evolution that humans have two kidneys when they need only one to filter waste and remove excess fluid from the body. Yet when kidneys fail, whether from diabetes or high blood pressure or genetic disorders, they tend to fail in tandem.

Death can arrive in a matter of weeks for many renal patients if they do not have their blood cleansed through dialysis. The process takes almost four hours, three times a week, and leaves many too drained to work. Only half of dialysis patients survive more than three years.

Many of the 400,000 Americans who are tethered to dialysis dream of a transplant as their pathway back to normal. But with the demand for kidneys rising faster than the number of donors, the waits have grown longer. While about 90,000 people are lined up for kidneys, fewer than 17,000 receive one each year, and about 4,500 die waiting, according to the United Network for Organ Sharing, which maintains the wait list for the government.

Only a third of transplanted kidneys come from living donors, but they are coveted because they typically last longer than cadaver kidneys. For kidneys transplanted in 1999, 60 percent of organs from live donors were still functioning after 10 years, compared with 43 percent of organs from deceased donors.

Although other living tissue can be transplanted — slices of pancreas, liver and intestine, bone marrow and lobes of lung — kidneys are uniquely suited because donors have a spare and the operations are almost always successful.

A reason there are not more live kidney donations, however, is that about a third of transplant candidates with a willing donor find that they are immunologically incompatible. Some, because of previous transplants, blood transfusions or pregnancies, may have developed antibodies that make them highly likely to reject a new kidney.

Using a blood-filtering technique known as plasmapheresis, doctors can now lower the odds that a recipient will reject an incompatible kidney. But the procedures are taxing and expensive.

Domino chains, which were first attempted in 2005 at Johns Hopkins, seek to increase the number of people who can be helped by living donors. In 2010, chains and other forms of paired exchanges resulted in 429 transplants. Computer models suggest that an additional 2,000 to 4,000 transplants could be achieved each year if Americans knew more about such programs and if there were a nationwide pool of all eligible donors and recipients.

Such transplants ultimately save money as well as lives. The federal Medicare program, which pays most treatment costs for chronic kidney disease, saves an estimated \$500,000 to \$1 million each time a patient is removed from dialysis through a live donor transplant (the operations typically cost \$100,000 to \$200,000). Coverage for kidney disease costs the government more than \$30 billion a year, about 6 percent of the Medicare budget.

Dialysis, which in the United States is almost always administered in outpatient clinics, saps the productivity of caregivers as well as of patients. Nearly two years ago, Kent Bowen, 47, of Austin, Tex., gave up his job hanging gutters, and much of his freedom, so he could provide dialysis at home to his mother, Mary Jane Wilson.

Before donating a kidney for her as part of the chain on Dec. 7 at Methodist Hospital in Houston, Mr. Bowen said he looked forward not only to helping his mother, but also to a long-deferred fishing trip.

"In all actuality," he said, "giving a kidney is a small price to pay for getting my life back."

## Understanding the Pain

Garet Hil and his wife, Jan, may never fully recover from the snowy night in February 2007 when they took their 10-year-old daughter in with flu symptoms and emerged with a shocking diagnosis of nephronophthisis, a genetic kidney-wasting disease. They could not imagine sacrificing her youth to dialysis.

Because Mr. Hil and his daughter shared the same blood type, he assumed he would be able to give her one of his kidneys. But two days before surgery, doctors canceled the operations



**THE FOUNDER:** *Garet Hil formed the National Kidney Registry after his daughter became ill.*

after discovering that his daughter had developed antibodies that would most likely cause rejection.

Jan Hil and six other family members volunteered but were also ruled out. Mr. Hil and his daughter joined several of the registries that had started to arrange kidney exchanges, but the pools were small and they never found a match. Fortunately, one of Mr. Hil's nephews then was tested and was able to donate.

After the successful transplant, Mr. Hil, a veteran business executive, could not shake his frustration that a more effective registry for paired kidney donation did not exist. "The exchange systems out there weren't industrial strength," he said.

By the end of 2007, the Hils had formed the National Kidney Registry and rented office space in an old clapboard house in Babylon, N.Y. The couple invested about \$300,000 to start it, and Mr. Hil, who is now 49, ran the registry without a salary.

"The goal was very simple: get everybody transplanted in under six months if you had a living donor," he said. "One of the things that drove us was the enormity of the problem. The other thing that drove us was that we understood the pain of being in that situation."

Mr. Hil turned out to be the right person to infuse the budding science of kidney exchange with an entrepreneurial spark. A former Marine

reconnaissance ranger with an M.B.A. from the Wharton School, he had managed a series of data and logistics companies in Boston and New York and understood the worlds of both computing and finance.

He had made his money and could step off the career track to give the registry his time and the resources of his software-consulting firm. He had a background in quantitative math and enough drive to plow through medical texts about organ compatibility. Over time, he led a team in designing sophisticated software that evolved to build ever-longer chains.

Disney-hero handsome, with a cleft chin and thick wavy hair, Mr. Hil marketed his registry to hospitals with PowerPoints and passion. The transplant world initially regarded him as an interloper. But he has now persuaded 58 of the country's 236 kidney transplant centers, including many of the largest, to feed his database with information about pairs of transplant candidates and their incompatible donors.

Starting at 5 a.m. each workday, Mr. Hil manipulates several hundred pairs into transplant chains with a few clicks of a mouse. Last year, he arranged 175 transplants this way, including the 30 in Chain 124, more than any other registry. On average, patients received transplants about a year after being listed.

The same year that Mr. Hil's daughter got sick, Congress amended the National Organ Transplant Act to clarify that paired exchanges do not violate federal laws against selling organs. The blessing from Washington broke down resistance in many hospitals just as the National Kidney Registry was opening for business.

### **The Evolving Chain**

Although the first live kidney was transplanted in 1954 in Boston, three decades passed before a Stony Brook University surgeon named Felix T. Rapaport first theorized about kidney swaps in a 1986 journal article. Korean surgeons completed the first exchanges in 1991, but they were not successfully attempted in the United States for nearly another decade.

Simple swaps among two pairs, with the operations performed at the same hospital on the same day, quickly evolved into complex exchanges among three pairs and then four and then six.

Then in 2007, a transplant surgeon at the University of Toledo Medical Center, Dr. Michael A. Rees, had a forehead-slapping insight. If an exchange began with a Good Samaritan who donated to a stranger, and if the operations did not have to be simultaneous, a chain could theoretically keep growing, limited only by the pool of available donors and recipients. Dr. Rees reported in 2009 that he had strung together a chain of 10 transplants.

Mr. Hil seized on the idea and set out to build an algorithm that would enable even more transplants. Nowadays, his pool typically consists of 200 to 350 donor-recipient pairs. That is enough to generate roughly a googol — 10 to the 100th power — of possible chains of up to 20 transplants if all of the pairs are compatible, said Rich Marta, the registry's senior software designer.

The program quickly eliminates matches that will not work because of incompatible blood types or antibodies, or because a transplant candidate insists that a donor be under a certain age or a close immunological match. It then assembles up to a million viable combinations at a rate of 8,000 per second.

The algorithm ranks the possible combinations by the number of transplants they would enable, with weight given to chains that find kidneys for hard-to-match patients and those who have waited a long time.

There are several registries like Mr. Hil's, each with a distinct approach. Largely unregulated by government, they invite sensitive questions about oversight and ethics, including how kidneys are allocated. A number of medical societies are convening in March to seek consensus on that and other issues related to paired exchanges.

Mr. Hil knows the patients in his pool only by code names and leaves all personal interactions to the hospitals. He keeps several chains running at a time, and says tending to them is like playing three-dimensional chess.

Chain 124 even included one pair that was immunologically compatible. Josephine Bonventre, a 40-year-old real estate agent from Toronto with Type O blood, could have donated a kidney directly to her fifth cousin, Cesare Bonventre, a 27-year-old tile worker from Brooklyn with Type B.

But a second level of matching requires the synching of six antigens, a series of proteins that determine compatibility. By joining the chain and donating down the line, on Dec. 6 at NewYork-Presbyterian Hospital, Josephine enabled Cesare to get a stronger match — three antigens instead of one. Her donation as a valued Type O then set off the final 11 transplants.

The registry did not charge transplant centers for its services until 2010, when Mr. Hil imposed fees to help cover costs. Hospitals now pay membership dues and a charge of \$3,000 per transplant that is reimbursed by many private



**LINKS IN THE CHAIN:** Josephine Bonventre and Cesare Bonventre.



**A COUSIN'S GIFT:** Josephine Bonventre's donation allowed her cousin to get a stronger match, and also set off the final 11 transplants.

insurers but not by Medicare. The transplant recipients must be insured.

Each year, the registry's chains have grown longer, with Chain 124 topping the previous record by seven transplants. "We've just scratched the surface," said Mr. Hil, who wears gold kidney-shaped cufflinks.

Long transplant chains save more lives than short chains. But they come with trade-offs because the longer they grow, the higher the risk that a donor will renege or that a link will break for other reasons.

The record-breaking chain survived its share of logistical setbacks. On Aug. 29, after the first five transplants, Mr. Hil lost a link because a donor could not take the necessary two to four weeks away from work. Later that day, he lost another when a transplant coordinator informed him that a potential recipient was an illegal immigrant and therefore could not be covered by Medicare.

In late October, an entire segment fell apart when a donor at California Pacific Medical Center in San Francisco backed out for unexplained "personal reasons." It was as if one domino had fallen short of the next, leaving those still standing frozen in place.

"This makes us all sick," Dr. Steven Katznelson e-mailed Mr. Hil. "We did not see this coming."

"Wow," Mr. Hil wrote back. The donor "just put 23 patients at risk."

The dependency of each link on the others kept patients on edge. "Things can happen," Candice Ryan fretted a few days before her Dec. 5 transplant at Massachusetts General Hospital. "You just pray that everything goes well. I can't relax until I'm asleep and on the table."

Depending on the makeup of his registry at any moment, Mr. Hil likes to stretch his chains as long as reasonable and then end them if a donor is difficult to match or if one chain is draining others of potential transplants.

He does so by arranging for the final kidney to go to a fortunate transplant candidate like Mr. Terry who does not have a willing donor.

## **The Initial Link**

Until recently, hospitals regularly turned away Good Samaritan donors on the working assumption that they were unstable. That has changed somewhat with experience. But when Rick Ruzzamenti showed up at Riverside Community Hospital asking to give a kidney to anyone in need, he still underwent rounds of psychological screening as well as medical tests.

The doctors and social workers did not know what to make of Mr. Ruzzamenti at first. He had a flat affect and an arid wit, and did not open up right away. As the hospital's transplant coordinator, Shannon White, pressed him about his motivations and expectations, he explained that his decision seemed rather obvious.

"People think it's so odd that I'm donating a kidney," Mr. Ruzzamenti told her. "I think it's so odd that they think it's so odd."

The hospital wanted to make sure that he was not expecting glory, or even gratitude. Mr. Ruzzamenti stressed that no one should mistake him for a saint.

He had, after all, been a heavy drinker in his youth and had caroused his way through the Navy. He could be an unsmiling presence at work, where he helped manage a family electrical contracting business. He admitted that he did not visit his parents or grandmother enough.

Despite his occasional surliness, Mr. Ruzzamenti said he felt driven to help others when possible.

And as he considered the relative risks and benefits of organ donation, particularly to relieve a whole chain of suffering, it just made so much sense. "It causes a shift in the world," he said.

Perhaps, he said, there was some influence from a Tibetan meditation he had practiced when he was first drawn to Buddhism six years ago. It is known as Tonglen. "You think of the pain someone's in, and imagine you take it from them and give them back good," he said.

Mr. Ruzzamenti said he was in a position to donate only because the economy had dried up so much of his work. He was essentially unemployed

and could take time off to recuperate. The 30 kidney recipients, he observed dryly, could “all thank the recession.”

When Mr. Ruzzamenti told his wife, My Nhanh, about his plans, she made it abundantly clear, despite her rudimentary English, that she would leave him and return to Vietnam if he followed through. She had immigrated only eight months before, after a marriage largely arranged by the Buddhist temple where Mr. Ruzzamenti volunteered as a groundskeeper. If he died on the table, she demanded, how would she get by in a country where she felt so out of place?

“I wanted to scare him,” Ms. Ruzzamenti, who is known as Lucy, said as she combed her husband’s close-cropped hair with her fingers. “And to tell him that it scares me.”

Mr. Ruzzamenti was impressed by his petite wife’s ferocity — “She’s a bully,” he said — but he disregarded her threat. He knew research showed that the risk of death from kidney retrieval surgery was 3 in 10,000 and that people with one kidney live as long as those with two. To him, there was little doubt that any good he created would far outweigh any temporary discomfort to him or his wife.

As it happened, Mr. Ruzzamenti experienced an unusual level of pain during his recuperation at Riverside. It sometimes left him balled up in agony, and the Demerol only made him hallucinate.

He did not really want company. But when the pain stirred him awake at night, he could see Lucy sleeping in the hospital bed beside his.

### **Acts of Devotion**

There were other love stories along the way. Gregory Person and Zenovia Duke, both now 38, had been junior high prom dates in 1987 in Astoria, Queens. They lost touch and then reconnected on Facebook after each had divorced. They saw each other occasionally, but he lived in Queens and she near Albany, so the relationship never got serious.

Not long after they reconnected, Mr. Person’s half-sister died of kidney failure and he pledged to help someone else beat the disease if ever given the chance. Then Ms. Duke learned she needed a transplant.

On Aug. 31, Ms. Duke received a kidney from a woman in California and Mr. Person sent his to Ohio. As they recuperated at NewYork-Presbyterian, Mr. Person found himself regularly hobbling down to her room. Once they were both back on their feet, they started dating more regularly.

“I’ve never had any person in my life actually do what they say they’re going to do,” Ms. Duke said, “especially men. It spoke volumes that he was a man of his word.”

It was a different kind of devotion that led David Madosh, 47, to donate a kidney for Brooke

Kitzman, 30. Their four-year relationship, which had produced a 2-year-old daughter, soured just as he was getting tested as a potential donor. The breakup, caused partly by the strains of her illness, was ugly enough that when Ms. Kitzman later matched to become part of the chain, she put the odds at no better than 50-50 that Mr. Madosh would still donate.

But Mr. Madosh, who lost his mother when he was 5, did not want his daughter, Elsie, to lose hers.

The youngest of 12 children, he said he had been passed from one foster home to the next, eight in all, some that he described as little more than labor camps. “I don’t want my daughter to have to experience that,” said Mr. Madosh, a tree cutter by trade. “No matter what it takes, a daughter needs her mother.”

Ms. Kitzman said she was grateful for Mr. Madosh’s kidney, and had told him so when they visited in a hospital corridor. But both made it clear that his act of charity had barely eased the tension between them.

Mr. Madosh said he took satisfaction enough from seeing Elsie at play with her re-energized mother. “When her mama comes to get her, and she gives her hugs and kisses, that’s it right there,” he said.

### **A Wish Come True**

On Dec. 19, Chain 124 hurtled toward its conclusion with a final flurry of procedures at Ronald Reagan U.C.L.A. Medical Center in Los Angeles. Between dawn and dusk, three kidneys were removed and three were transplanted in

neighboring operating rooms. One flew in from San Francisco. The last took off for O'Hare.

At the end of the cluster were Keith Zimmerman, 53, a bearish, good-humored man with a billygoat's beard, and his older sister, Sherry Gluchowski, 59. She had recently moved from California to Texas but returned to donate her kidney.

The siblings had always been close, although family members marveled at their ability to bicker for 15 minutes over the proper way to construct a peanut butter sandwich. Their mother, Elsa Rickards, remembered teaching them as children "that they might not have their mommy and daddy all the time, but they will always have each other."

Mr. Zimmerman, who runs a repossession firm with his wife in Santa Clarita, had been given a diagnosis of kidney disease 25 years ago. With the help of a nutritionist, he had managed to avoid dialysis until the very last day before his transplant, when his doctor said the procedure was needed to clear his body of excess fluid.

In his hospital room before surgery, with seven family members shoehorned into every nook, Mr. Zimmerman calmed his nerves by listening to Aaron Neville on his iPod. He said he considered himself "the lottery winner" in the chain because his kidney would be coming from a healthy 28-year-old, Conor Bidelspach of Bend, Ore.

The surgery to remove a kidney, known as a nephrectomy, is remarkably bloodless these days.

With Mr. Bidelspach on the table, Dr. Peter G. Schulam cut four dime-sized incisions on the left side of the abdomen. Through tubes inserted in the openings, the surgeon and his team maneuvered their cauterizing scalpels and a laparoscopic camera, which relayed images of Mr. Bidelspach's insides to monitors overhead.

The scalpel's super-heated pincers clamped down like crab claws, searing the kidney from surrounding tissue. There was no need to cut any muscle.



**FROM START TO FINISH:** A donation by a Good Samaritan, Rick Ruzzamenti, upper left, set in motion a 60-person chain of transplants that ended with a kidney for Donald C. Terry Jr., bottom right.

Once the kidney was free of connective tissue, Dr. Schulam clamped and snipped the renal artery and vein and ureter. He captured the kidney in a plastic bag, cinched it shut, and withdrew it quickly through a finger-length incision along the pelvic line.

The doctor poured the kidney into a bowl of ice and drained it of remaining blood. The slush in the blue bowl turned fruit-punch pink.

As others stitched up Mr. Bidelspach, Dr. Schulam wheeled the kidney on a cart into an adjoining operating room, where Mr. Zimmerman was already anesthetized. After stretching a hole in Mr. Zimmerman's midsection with a metal retractor, Dr. Jeffrey L. Veale lowered the kidney into place and sewed in the renal artery and vein. As soon as he unclamped them, the kidney pinked up with blood flow. Before attaching the ureter to the bladder, he gently massaged the tip of the narrow tube between two fingers and watched it spurt a few drops of urine.

"No more dialysis for Mr. Zimmerman," Dr. Veale declared. "This total stranger's kidney is making him pee." He left Mr. Zimmerman's own kidneys to shrivel harmlessly in place (removing them would add to surgical risk).

Meanwhile, Dr. Schulam was in yet another operating room removing Ms. Gluchowski's kidney.

He placed it in a plastic bag filled with a preservative solution and knotted it shut, like a goldfish brought home from the pet store. It was packed in a plastic tub, topped with ice, and loaded into a cardboard box marked "Left Kidney — Donated Human Organ/Tissue for Transplant — Keep Upright."

A courier in one of Quick International's big red vans drove Sherry Gluchowski's kidney through stop-and-go traffic on Interstate 405 to the Los Angeles airport. Cynthia Goff, an operations supervisor for the courier company who had volunteered to accompany the kidney to Chicago, rolled the box into the terminal strapped atop her carry-on with a bungee cord. A pit bull, waiting to be placed in its travel kennel, strolled by and sniffed.

After security agents checked the box with a desktop scanner, Ms. Goff rolled the kidney down the concourse, past a currency exchange and a



***IN TRANSIT: A courier, Cynthia Goff, saw that the kidney donated by Sherry Gluchowski in Los Angeles got to its recipient in Chicago.***

store selling Elmo dolls for Christmas. Escorted onto United 564, an overnight flight that would land in Chicago at 5 a.m., she stowed the box in the business-class closet, next to a flight attendant's overcoat.

Airplanes carrying donor organs are granted special status, allowing them to move to the front of takeoff lines and ahead of air traffic. Mr. Hil, who tries to avoid routing kidneys on connecting flights and always schedules backups, said none of his registry's transplants had been held up by transportation problems.

By the time Ms. Gluchowski's kidney made it to Loyola and was transplanted into Mr. Terry, it had been cold for almost 12 hours. Early studies have found no evidence that shipping live kidneys such distances affects their immediate function.

Chain 124 ended at Loyola because Mr. Hil had arranged for the final kidney to go to a hospital that had produced a Good Samaritan donor to start a chain in the past, thus closing a loop. Dr. John Milner, a transplant surgeon at Loyola, said he then selected Mr. Terry to receive the kidney because he was the best immunological match on the hospital's wait list.

When Dr. Milner called with the news in early December, Mr. Terry was floored at his remarkable good fortune. Having felt unfairly condemned when he was first placed on dialysis, he now wondered what he had done to deserve a gift that 90,000 others needed just as much.

As it sank in that this would be the last of 30 interconnected transplants, Mr. Terry began to feel guilty that he would be ending the chain. "Is it going

to continue?" he asked Dr. Milner. "I don't want to be the reason to stop anything."

"No, no, no," the doctor reassured him. "This chain ends, but another one begins."

**SUMMARY**

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 Since organizing its first swap in 2008, the National Kidney Registry had facilitated 389 kidney transplants by the end of 2011 across 45 U.S. transplant centers. Rapid innovations, advanced computer technologies, and an evolving understanding of the processes at participating transplant centers and histocompatibility laboratories are among the factors driving the success of the NKR. Virtual

cross match accuracy has improved from 43% to 94% as a result of improvements in the HLA typing process for donor antigens and enhanced mechanisms to list unacceptable HLA antigens for sensitized patients. By the end of 2011, the NKR had transplanted 66% of the patients enrolled since 2008. The 2011 wait time (from enrollment to transplant) for the 175 patients transplanted that year averaged 5 months.

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