Kidney Paired Donation: An Overview of the U.S. Experience/Mayo Experience

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Outline

- Background of Kidney Paired Donation (KPD)
- Kidney Compatibility in KPD
- Forms of Kidney Paired Exchange
- History of Kidney Paired Donation
- KPD in the US
- Highlights of the major National US Pairing Organizations
- Mayo Internal KPD program

Background

- Substantial kidney shortage in the United States
- Kidney paired donation (KPD): arose as possible solution to the intensifying shortage of kidneys in the US and abroad
- KPD exchange: **2 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 recipient

Benefits of KPD

- Better matches
- Kidneys from living donors (Better allograft survival than kidneys from deceased donors)
- Less waiting time
- Increases chances to have a preemptive transplant
- Less dialysis time so less mortality and morbidity

Kidney Compatibility in KPD

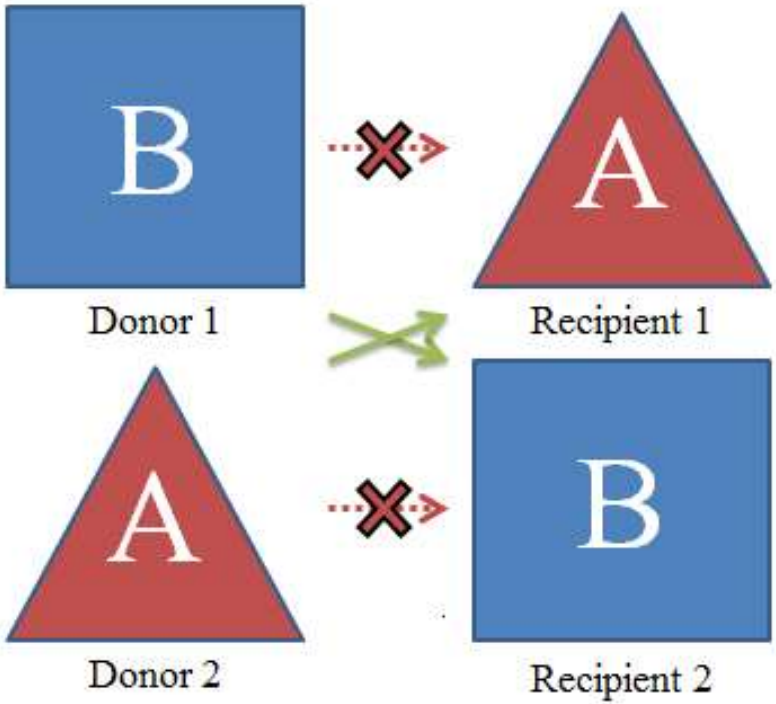
Two major matching considerations when donating a kidney:

- ABO blood type/possibility to combine ABOi with KPD
- HLA matching
  - Can choose kidneys without any directed DSA / Avoid “positive crossmatch”
  - Allow highly allo-sensitized patients to get access to transplantation (combine + low flow crossmatch)

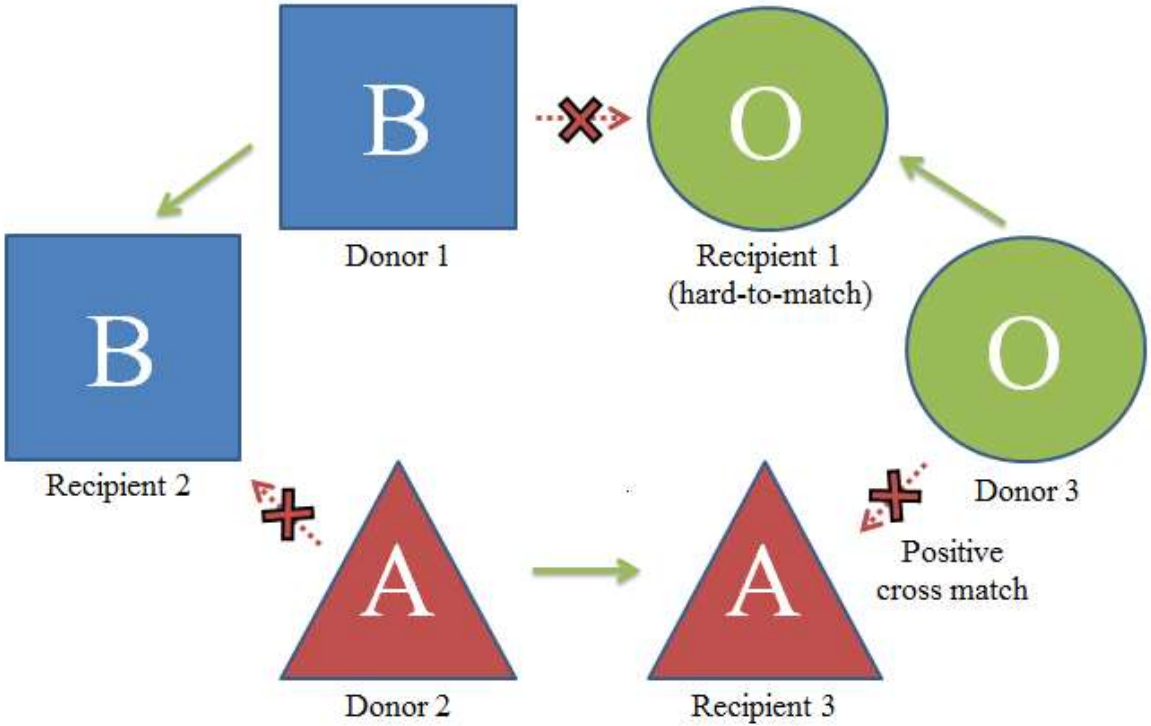
Other Benefits:

- Avoid age & body size discrepancy: e.g. match younger recipients with younger donors…
- Avoid CMV and EBV mismatches

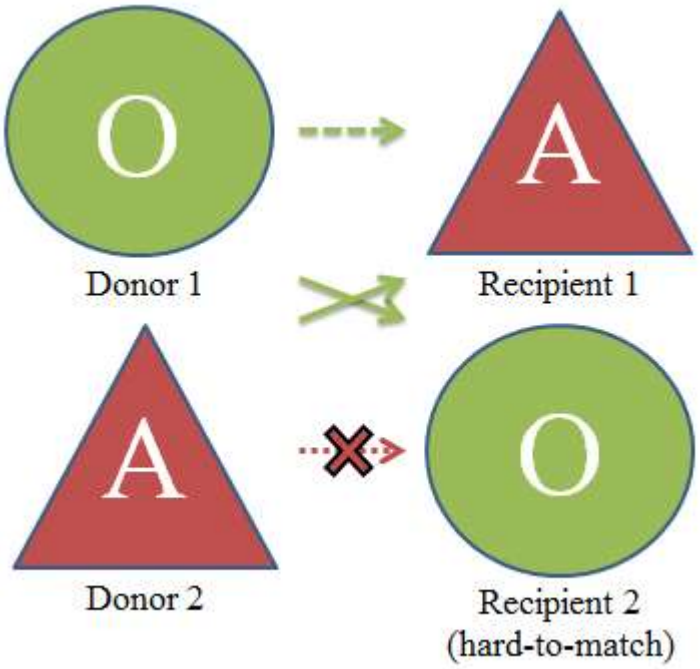
Forms of Kidney Paired Exchange: Two-way Exchange



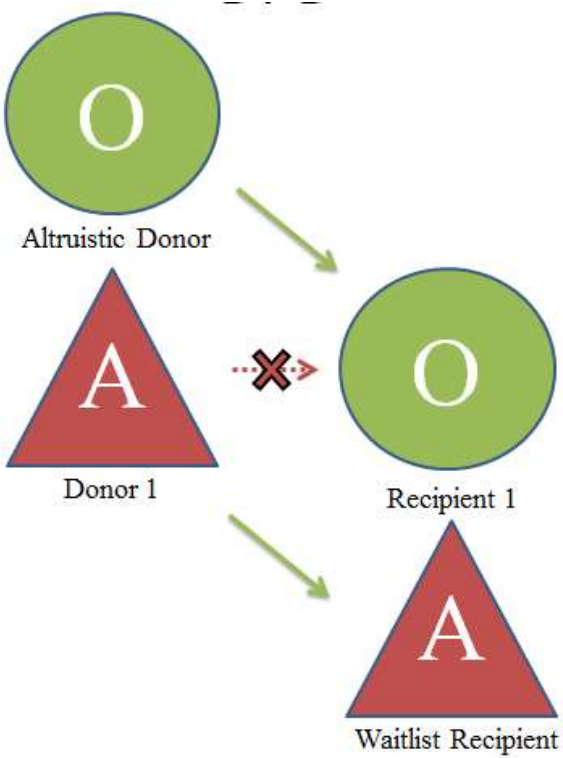
Forms of Kidney Paired Exchange: Three-way Exchange



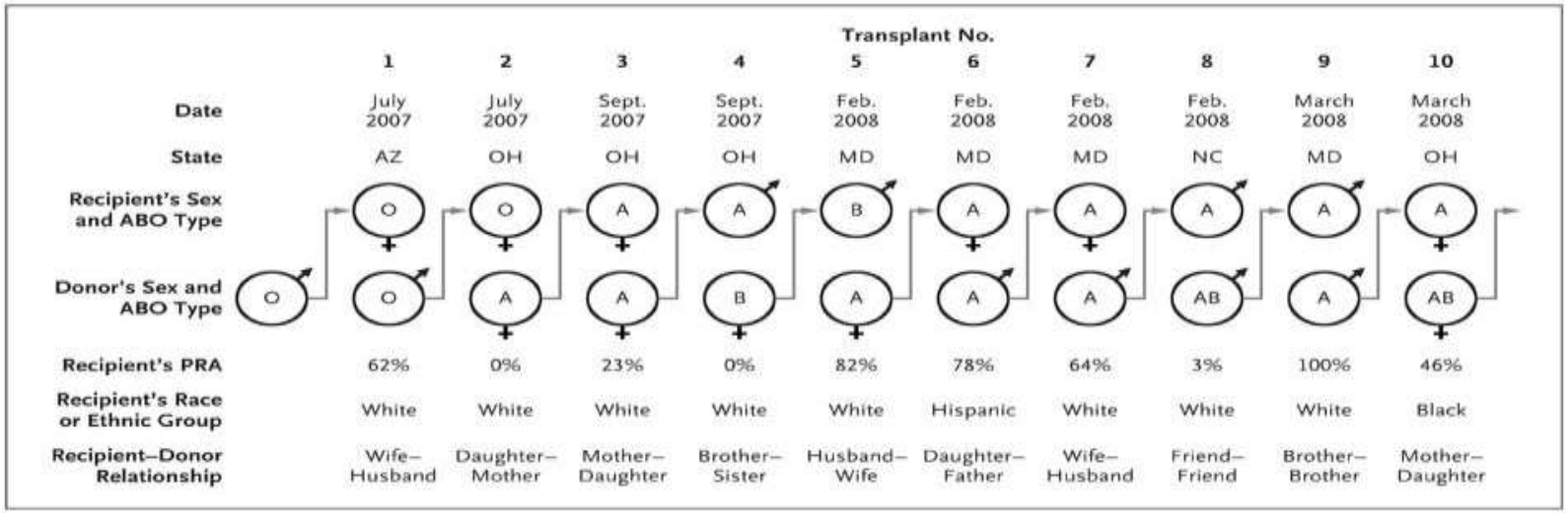
Forms of Kidney Paired Exchange: Use of a Compatible Pair



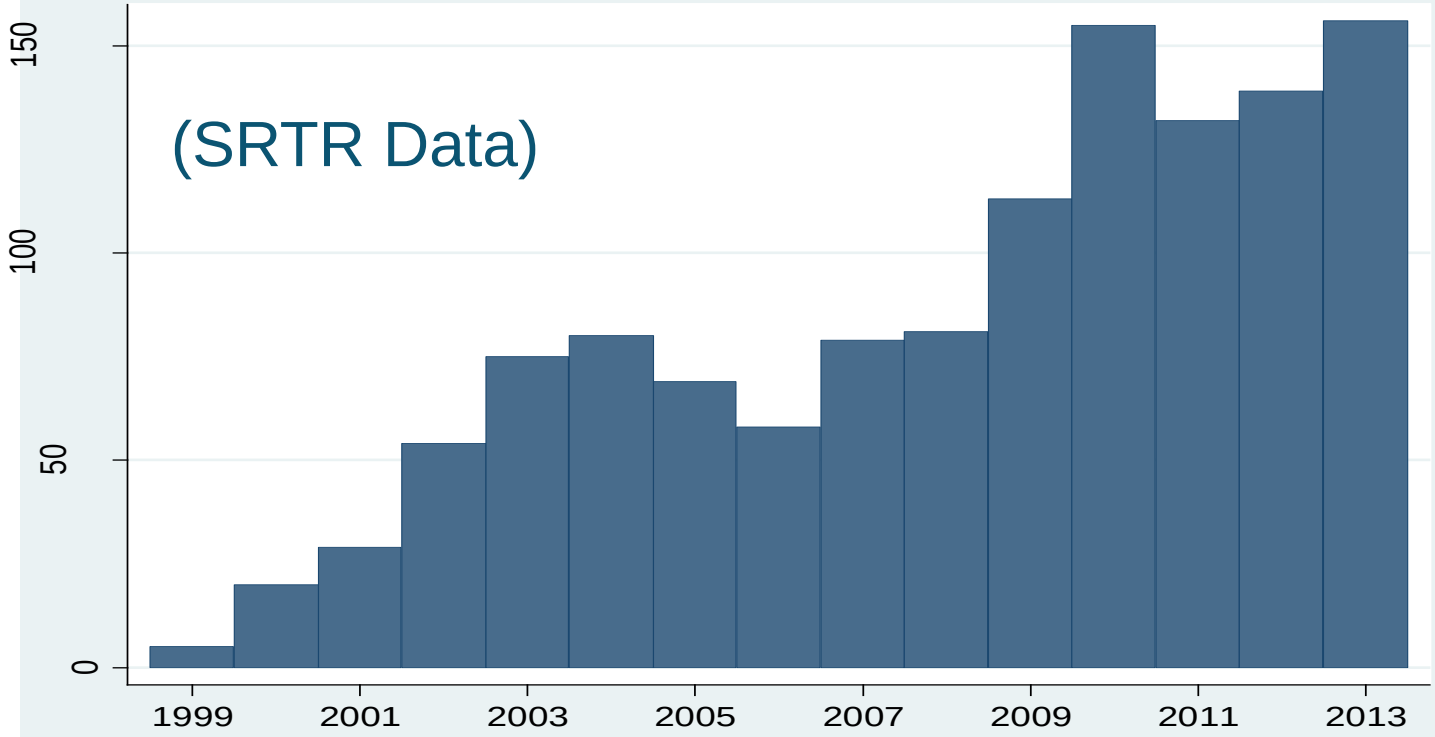
Forms of Kidney Paired Exchange: *Domino-paired Donation Chain triggered by a Non-Directed Donor (NDD)*



Forms of Kidney Paired Exchange: Use of a non-simultaneous extended altruistic donor (NDD)



Non-Directed Donors (NDD) in the US: >1300



Advantages

- The use of compatible pairs (desiring a better match) in KPD match runs:

➢ Benefit O recipients and pairs with A, B or AB donors by making rare O donors more accessible

- Non-simultaneous extended altruistic donor chains

➢ The transplant surgeries are not executed simultaneously

➢Last donor becomes a **“bridge donor”**

➢The bridge donor waits to perform another series of exchanges/extend the chain

Disadvantages

- **Considerable logistical challenges:**
  - Aligning Operating Rooms's times; technical surgical difficulties in one center influence the chain
  - Commercial flights between distant transplant centers: cancellations, weather conditions etc…
  - Unexpected positive final crossmatches
  - Unexpected donor or recipient illnesses
- **Risks of reneging by the donor: *(le donneur renonce)***
  - Bridge donor

History of Kidney Paired Donation

- **South Korea:**

➢ 1991: First in the world to perform a PKE between 2 ESRD patients with incompatible donors due to + cross match

➢ Cultural norms limited the supply of kidneys to living donation (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)

➢ National Korean KPD program: 22 % of living kidney donations performed through KPD exchanges

- **Europe:**

➢ **Switzerland:** performed the first European paired exchange in 1999, involving 2 married couples

➢ **Romania:** first exchange in 2001

➢ **Netherlands:** created the first national KPD program in Europe in 2004

➢ **UK:** launched a national KPD program in 2006 and made its first pairing in 2007

➢ **Spanish** Crossover Donation Plan (Plan Nacional de Donación Cruzada) began in 2009

History of Kidney Paired Donation

- **Europe: <u>Legal barriers</u>**

➢ Some European transplant laws do not permit unrelated donors

➢ Germany & France: permit organ donation **only to family members** or **good friends on ethical grounds, *recently changed***

- **Australia:**

➢ Started in 1 center in Perth, Western Australia in October 2007

➢ Australian Paired Kidney Exchange (AKX) program was established in 2010

- **Canada:**

➢ Living Donor Paired Exchange (LDRE) program as a 3-province pilot in 2009 before expanding it nationwide in 2010

➢ LDRE limits its matches to amount to no more than a <u>five-way</u> exchange

History of Kidney Paired Donation: USA

- **USA:**

➢ 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

➢ Responding to a commercial endeavor to create an organ market, Congress **outlawed** the buying and selling human organs:

Section 301 of National Organ Transplant Act of 1984 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…."

History of Kidney Paired Donation: USA

- **USA: <u>Ethical Considerations</u>**

➢ It was unclear if paired exchanges constituted **“<u>valuable consideration</u>”** and were consequently illegal under NOTA

➢ Many hospitals refused to participate, wary of legal repercussions

➢ Medical professional and Transplant Societies held numerous consensus conferences to discuss the ethical, legal, and medical implications of KPD in early 2000’s

➢ Argument: KPD can address the severe national kidney shortage

➢ By 2005, conferences were being held to deliberate the possibility of regional or national exchange programs

➢ **Congress amended National Organ Transplant Act of 1984 *<u>in 2007</u>* with the Charlie W. Norwood Living Organ Donation Act**:

clarified section 301 by adding the sentence, **“The preceding sentence does not apply with respect to human organ paired donation.”**

➢ Congress agreed with the UNOS Associate General Counsel’s argument that **paired donation constituted a <u>gift</u>, rather than consideration**

History of Kidney Paired Donation: USA

- **USA: <u>Ethical Considerations</u>**

➢ NOTA amendment allowed UNOS to create a national exchange

➢ With that hurdle cleared, the OPTN/UNOS kidney transplantation committee issued requests for information to operating pairing organizations and launched its **<u>pilot program</u>** in **2010**

➢ KPD became widely accepted

➢ New KPD organizations were formed

KPD in the US

- New England Program for Kidney Exchange

  - Rhode Island Hospital in 2000
  - in 2010, the program increased match run frequency from every 45 days to every 2 weeks, resulting in an increased number of matches

- Johns Hopkins Incompatible Kidney Transplant Program

  - Performed KPD exchanges since 2001
  - Combines Desensitization with KPD

- North Central Donor Exchange Cooperative (NCDEC):

12 transplant centers in North Dakota, South Dakota, Minnesota, Iowa, and Wisconsin

- Single-Center Exchange Programs

  - Methodist Specialty and Transplant Hospital in San Antonio constitutes the **largest single-center** exchange program in the world, performing 134 KPD transplants during a 3-year period beginning in 2008

National Pairing Organizations

- **National Kidney Registry (NKR)**
- Alliance for Paired Donation
- UNOS Kidney Paired Donation Pilot Program

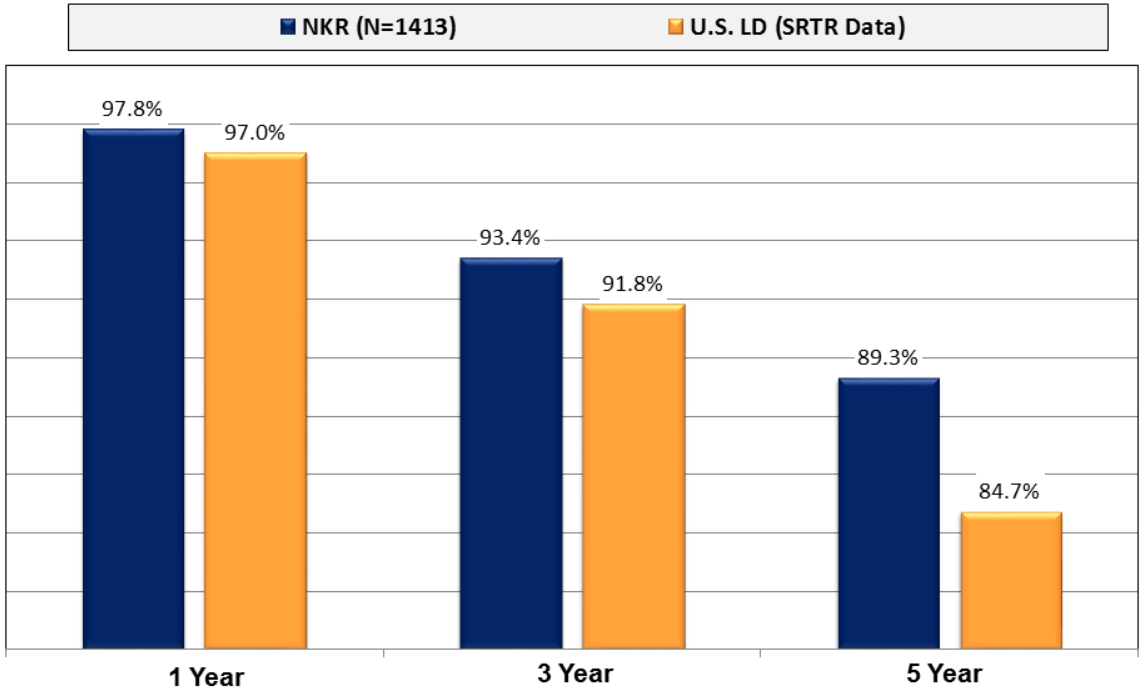
National Kidney Registry (NKR)

- Leading pairing organization in the US: Most academic and large transplant centers across the US
- Founded in 2007
- Celebrated its 1,000 arranged transplants in March 2014
- NKR allows recipients to express preferences: maximum donor age, minimum donor weight, willingness to receive a shipped kidney, minimum HLA points (degree of HLA matching), Avoidance of EBV /CMV mismatches…
- Donors can also express their willingness to travel
- 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**
- Once NKR has outlined a chain, it prepares a logistical plan for carrying out the transplants: 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
- Points system: Priority to centers that place NDD/O donors in the pool
- **Highlights:** Efficiency and initiative in organizing logistics

NKR Graft Survival Advantage

NKR Transplants vs. U.S. Living Donor Transplants

As of 6/30/2015

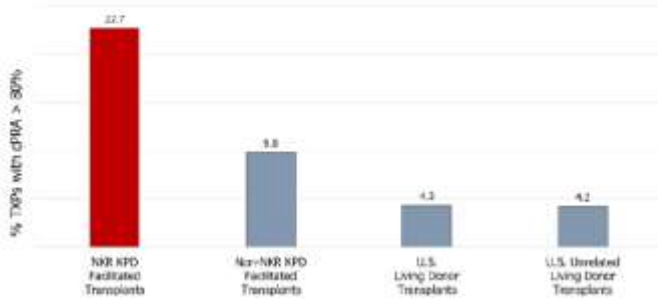


*NKR Kaplan-Meier GS calculations provided courtesy of UCLA Departments of Nephrology and Urology

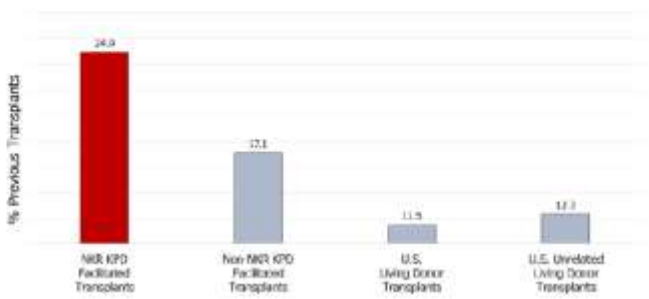
**U.S LD - Scientific Registry of Transplant Recipients. www.srtr.org/annual_reports/2011/509d_ki.aspx Accessed 7/9/15

Better Outcomes Despite Harder Cases

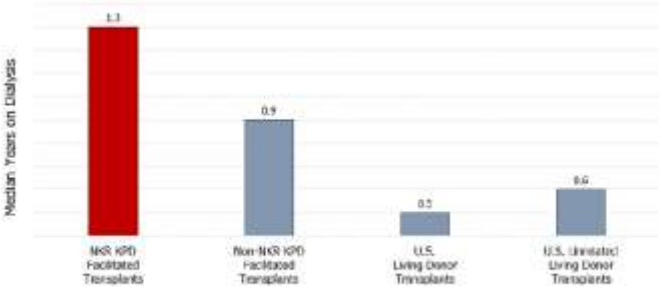
More Highly Sensitized Patients



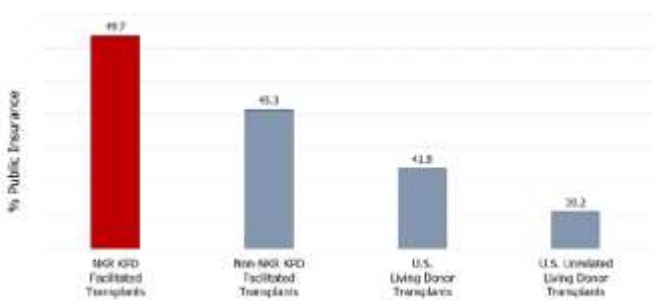
More Re-Transplants



More Time on Dialysis



More Patients with Public Insurance



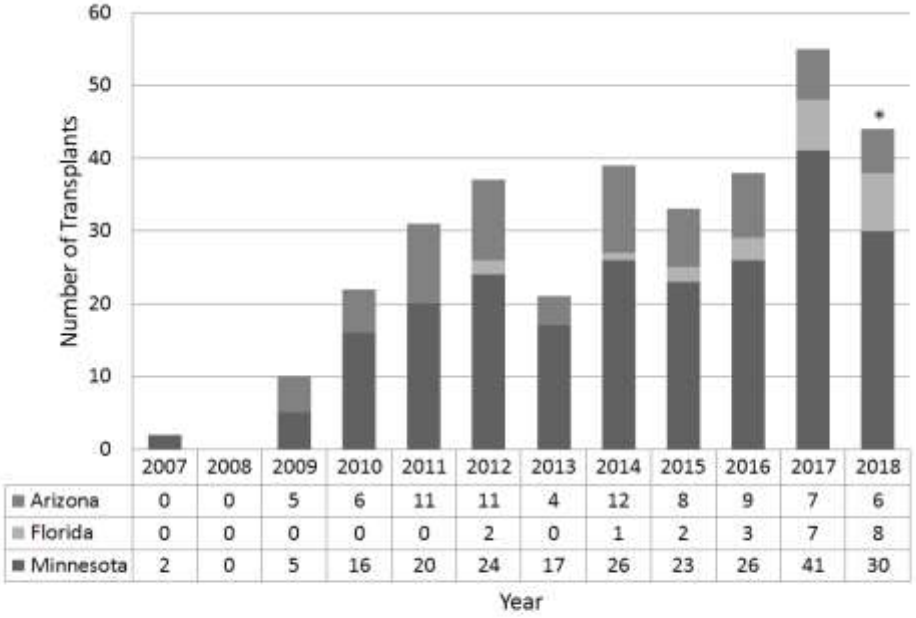
Source: *Flechner, et all. (2018-04-30). "The first 9 years of kidney paired donation through the National Kidney Registry: Characteristics of donors and recipients compared with National Live Donor Transplant Registries". American Journal of Transplantation. 18 (11): 2730–2738.*

MAYO CLINIC

Mayo Clinic *Locations*

Mayo Clinic Internal KPD Program Highlights

KPD started in 2007 in Minnesota location with 2 pairs only and soon after Arizona and Florida joined KPD



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Arizona	0	0	5	6	11	11	4	12	8	9	7	6
Florida	0	0	0	0	0	2	0	1	2	3	7	8
Minnesota	2	0	5	16	20	24	17	26	23	26	41	30

Figure 1. An increased number of kidney transplants were facilitated by kidney paired donation at the 3-Mayo sites. The location refers to the recipient's transplant center.

- 2018: was our busiest year: 76 Transplants
- Second busiest Internal KPD program in the USA
- We combine + low flow especially against Class I DSA/rarely ABOi
- Dedicated team of 1 coordinator in each site, 2 tx nephrologists, 1 tx surgeon, HLA-lab personnel in every site

Incorporation of HLA/ABO Compatible Pairs in KPD

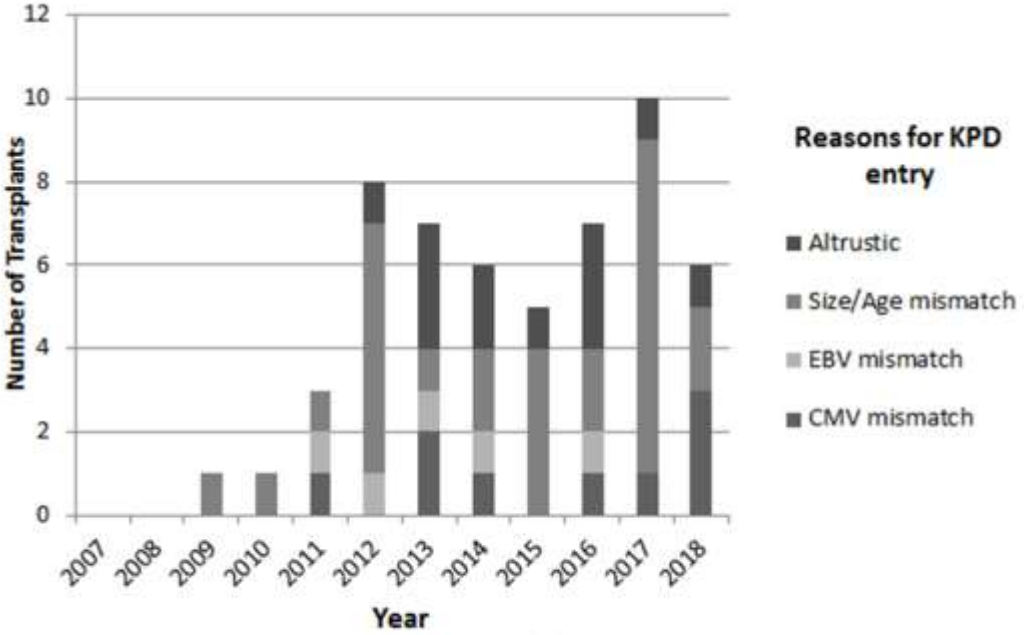


Figure 2. Increasing number of recipients of HLA/ABO compatible pairs transplanted at 3-Mayo sites. The last transplant studied from 2018 was performed on 6/1/2018.

Table 2: Chains and Swaps that included Mayo donors and Recipients only (n=298 recipients)

	Chain N=37	Swap N=46	p-value
Total Transplanted n(%)	184 (61.7%)	114 (38.3%)	
Transplanted per chain/swap(IQR)	4(3-7)	2(2-3)	P<0.0001
Compatible pairs n(%)	17(46.0%)	22(47.8%)	P=0.86
International pairs n(%)	2(5.4%)	2(4.4)	P=0.82
Include recipient with cPRA ≥80%	23(62.2%)	15(32.6%)	P<0.01
Include recipient with cPRA ≥ 90	16(43.2%)	11(23.9%)	P=0.06
Include recipient with cPRA ≥ 98	5(13.5%)	7(15.2%)	P=0.83
Include recipient with cPRA ≥ 99	2(5.4%)	7(15.2%)	P=0.14
Include recipient with cPRA ≥100	1(2.7%)	4(8.7)	P=0.95
Include ABO incompatibles	34(91.9%)	33(71.7)	P=0.02
Time to completion days median (IQR)	11 (0-83)	0(0-0)	P<0.0001

Chains started with a non-directed donor and ended with a living donor transplant going to the deceased donor list. Swaps consisted of donor and recipient pairs only.

Mayo Clinic Internal KPD Program Highlights:
Use of Compatible Pairs to Facilitate More Transplants

Table 3 Advantages of KPD to recipients of HLA/ABO compatible pairs

	CMV mismatch N=10(18.5%)	EBV Mismatch N=5 (9.3%)	Age/Size mismatch N=28(51.9%)	Altruistic N=11 (20.3%)
CMV (-) recipients who gained CMV (-)donor n(%)	9(90)	4(80)	4/13(30.7)	NA
EBV (-) recipients who gained EBV (-)donor n(%)	**	5(100)	1/4(25)	NA
Age difference Median (IQR) years younger of actual donor	6.5 (-1.5,14.25)	24(3,29.5)	18(13,25)	13(-6,27)
p-value (age)	.10	0.12	<0.0001	.11
LKDPI difference Median LDKPI (IQR) score less than original donor	3.5(-6.75,17.75)	2(-8,41)	31.5(12.3,47)	26(-1,46)
p-value (LKDPI)	.39	.31	<.0001	.01
HLA Class II mismatch difference Median (IQR)	-0.5(-1.3,2)	1(-2,1.5)	0(-1,0.75)	0(0-1)
p-value (Class II mismatch)	.86	1.0	.91	.78
Time from original donor approval to transplant Median (IQR) Days	53.5(43.8,78.3)	61(23.5,149.5)	54(34,76.3)	89(62,174)
Preemptive transplantation n(%)	5(50)	2(40)	11(39.3)	6(54.6)
Actual donor kidney shipped from different Mayo Location n(%)	4(40)	3(60)	10(35.7)	1(9.1)

* The difference in age, BMI, and HLA class II match was calculated by taking original donor value minus actual donor value. ** No EBV negative recipients were in the CMV mismatch compatible pair group. Time in KPD p=.36. Preemptive transplantation p=.82. Shipped kidneys p=.19

Challenges/Improvements/Conclusions

- Transplant centers and pairing organizations operate independently of one another
- The need for Procedures and Costs standardization (USA)
- Uniform Histocompatibility Standards
- **Financial (USA)**
  - Usually donor bills recipient insurance: More complex when at different centers!
  - Who covers donor complications?
  - Who pays for multiple donor/NDD evaluations?
- Consolidate **regional & national** pairing organizations in **1 single US program**
- **All potential living donors *should be informed* about KPD early in the educational process, prior to compatibility testing**
- **Extend Eligibility to Compatible Pairs**

