

# Can I “borrow” your kidney?

## National Kidney Exchange, Altruistic Donors and Voucher Systems

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1

## Outline

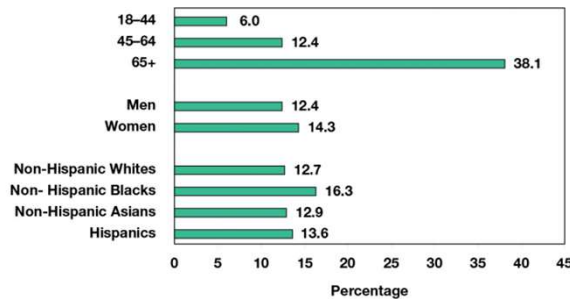
- Live donor kidney transplant as a treatment option for ESRD
- Kidney paired exchange programs- what is KPD and how does it facilitate live donor transplant of incompatible donor-recipient pairs?
- Innovations in KPD including inclusion of compatible pairs, non directed donor chains, and advance donation
- Impact of the National Kidney Registry, a KPD program, on live donor transplants in the US

2

## Chronic kidney disease (CKD) is common



- Rising prevalence of chronic kidney disease in the US
- More common in people >65 years old, black people and Hispanic people



Source: CDC.gov

3

## Growing population of end stage renal disease (ESRD)

Between 2000–2019

- Number of new ESRD cases increased by 42%
- Total number of people with ESRD doubled
- Diabetes (47%) and hypertension (29%) remained the leading causes of ESRD in 2019
- ESRD is expensive accounting for \$37.3 billion of Medicare expenditures in 2019



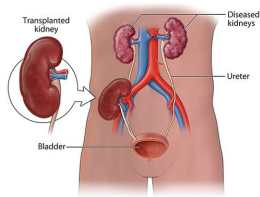
Source: CDC.gov; gminsights.com

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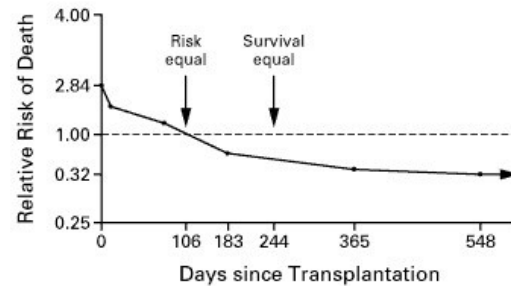
## Treatment options for ESRD



Dialysis



Kidney Transplant



Adjusted relative risk of death among 23275 deceased donor renal transplant recipients

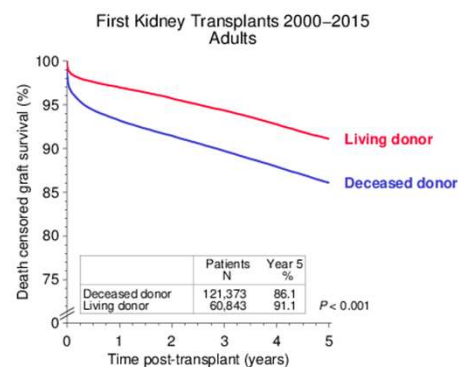
Kidney transplant confers a survival benefit compared to staying on dialysis

Wolfe RA, *et al.* NEJM 1999

5

## Benefits of live donor kidney transplant

- Avoid extended waiting times for deceased donor
- Better organ quality (healthy donor, short ischemic time)
- Graft usually functions immediately
- Improved patient and graft survival with kidney transplant from a living donor vs. deceased donor



Susal C. Collaborative Transplant Study 2012

6

## Basic eligibility criteria to be a live donor

- Healthy (good kidney function, no major risk factors for kidney disease)
  - Significant age/ size mismatch can result in suboptimal graft function
- Willing to donate
- ABO-compatible (recipient with no anti-A/ anti-B antibodies against the donor)
- HLA-compatible (recipient with no HLA antibodies against the donor)

There is a higher risk of **acute rejection and shortened graft survival** with **ABO- and HLA-incompatible transplants**

- Desensitization to ABO and HLA antigens is difficult and expensive

7

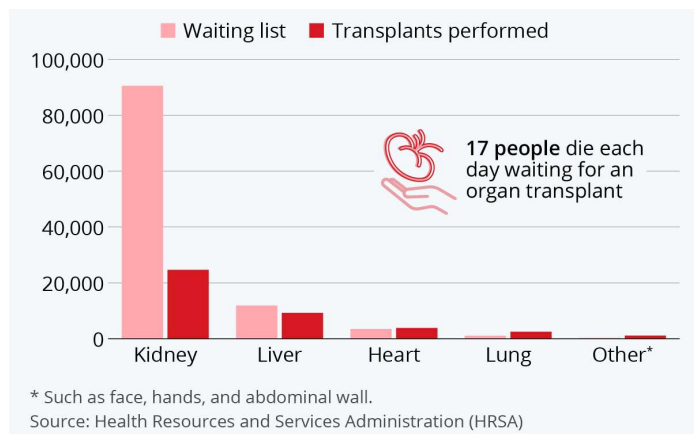
## Crisis of kidney shortage in the US

### US (2022)

- 90311 waiting for a kidney
- 5819 transplants so far

### California (2022)

- 17726 waiting for a kidney
- 662 transplants so far
- 134 (20%) from a live donor



Data extracted from HRSA 10/25/22

8

Can incompatible pairs get a live donor transplant without desensitization?

9

## The theory and practice of market design



### A Kidney Exchange Clearinghouse in New England

Alvin E. Roth  
Tayfun Sönmez  
M. Utku Özgür

AMERICAN ECONOMIC REVIEW  
VOL. 95, NO. 2, MAY 2005  
pp. 376-380

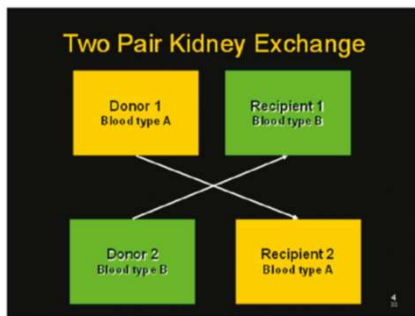
- Matching markets are markets in which you can't just choose what you want (even if you can afford it), you also have to be chosen
- ... a stable matching is one where there are not two people who are not matched to each other but who would both prefer to be matched to each other than who they are matched to.

Nobel Prize Lecture, December 8, 2012 by Alvin E. Roth

10

## Kidney paired donor exchange (KPD)

- First applied in New England hospitals under the New England Program for Kidney Exchange (NEPKE)
- Paired SWAP donation involved anesthetizing both donors simultaneously, to prevent either one from backing out after their recipient had received a kidney from the other donor



From the Nobel Prize Lecture, December 8, 2012 by Alvin E. Roth

11

## KPD Programs in the US

- National Kidney Registry
  - First and largest KPD program in the US
- Alliance for Paired Kidney Donation
- UNOS Kidney Paired Donation Pilot Program
- Local KPD programs

### Our Story

When Jan and Garet's youngest daughter was 10 years old, her kidneys suddenly failed. After the biopsy, they learned that she would never recover her kidney function.

They were in shock and quickly learned that a living donor transplant was her best option. Both Jan and their oldest daughter, Brooke, were tested and ruled out as potential donors because they were blood type incompatible. Garet was blood type compatible, so he was worked up for donation. The transplant surgery was scheduled for a Thursday in the middle of May.

That Monday, they received a call from the transplant center letting them know there was a problem and they needed to return to the transplant center and do another crossmatch test immediately. They took the additional test and waited.



Kidneyregistry.org

12

Do kidneys like plane rides any better than we do?

13

## Shipping of Live Donor Kidneys and Cold Time

- Cold ischemia time (CIT) known to be detrimental to graft function and survival in deceased donor kidneys
- Requiring the donor to travel to the recipient transplant center is a significant hurdle
- What is the impact of shipping live donor kidneys across the country with added CIT ?

14

## Impact of CIT on Live Donor Kidneys

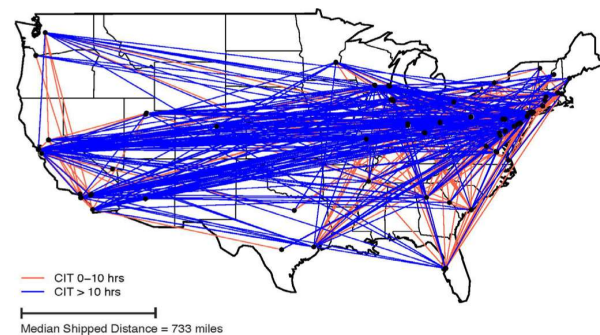
- UNOS/ OPTN data on 38467 live donor transplants (1990-2005)
  - Classified by 2 h CIT groups (0–2, 2–4, 4–6 and 6–8 h)
  - Small increase in DGF between the 0–2 h (4.7%) and 4–6 h (8.3%) groups
  - No difference in 1-year graft function, acute rejection or graft survival in any group with >2 h CIT vs. the 0–2 h group
- Analysis of NKR 2007-2010
  - 56 shipped live donor kidneys
  - Median CIT 7.2 h
  - No cases of DGF

Simpkins CE, *et al.* AJT 2006 Segev DL *et al.* AJT 2011

15

## Impact of CIT on Live Donor Kidneys in KPD

- NKR 2008-2015
  - 1267 shipped vs. 205 non shipped KPD vs. 4800 non shipped non KPD live donor transplants
  - Median CIT 9.3 h vs. 1 h vs. 0.93 h
- 5% increased odds of DGF for each hour of CIT
- No difference in patient or graft survival



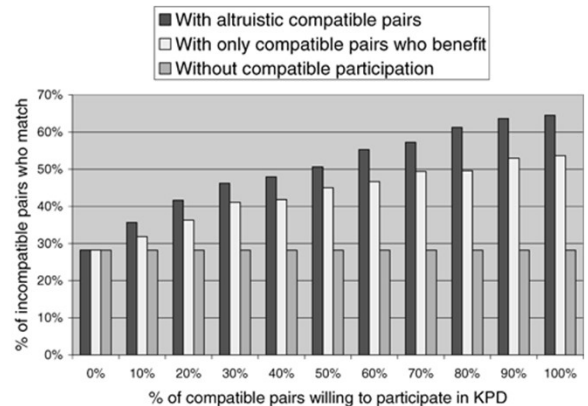
Treat E, *et al.* AJT 2018

16



## Allowing Compatible Pairs in KPD benefits Incompatible Pairs

- Simulation suggested that inclusion of compatible pairs would improve the match rate of incompatible pairs
  - 28% → 64% for single-center program
  - 37% → 75% for national program
- Match rates for even small programs could be improved by including compatible pairs



Gentry SE, et al. AJT 2007

17

## Do Compatible Pairs Benefit from KPD?

- Primary attraction is getting a younger and/or better HLA matched donor
- Simulation of Gentry SE, et al. suggested 34% chance of matching to a donor  $\geq 10$  years younger or avoiding a child-to-mother or spousal combination
  - Plus 17% chance of matching to a similar donor, but one which altruistically facilitates a transplant opportunity for an incompatible pair
  - Majority of compatible pairs could benefit
- Mayo Clinic KPD Experience 2007-2018
  - 54 compatible pairs received a transplant
  - Age/size mismatch (52%) → all received a younger kidney (median 18 y younger, 36 points lower LKDPI)
  - CMV mismatch (18.5%) → 9/10 found a CMV negative donor
  - EBV mismatch (9%) → all found an EBV negative donor
  - Altruistic (20%) → better kidney (median LKDPI 26 points lower)

Basu A, et al. Transplantation 2020

18

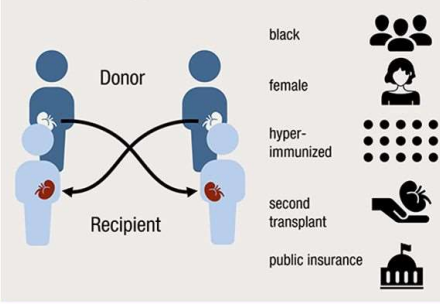
# Patient and Graft outcomes in NKR

## Paired kidney donation compared to living kidney donation: What is the long-term data?



National Kidney Registry facilitates kidney paired donation

paired donation recipients are more likely to be...



	5-year Graft failure	7-year Graft failure	5-year Mortality	7-year Mortality
National Kidney Registry N = 2363	6.4%	8.7%	6.8%	10.9%
Control living donor N = 54,497	7.2%	10.5%	7.0%	11.2%
Control unrelated living donor N = 25,900	7.3%	10.7%	7.1%	11.6%
Control paired donation N = 4635	8.0%	11.5%	7.8%	12.6%

**Conclusions** Even after transplanting patients with greater risk factors for worse post-transplant outcomes, nationalized paired donation results in equivalent outcomes.

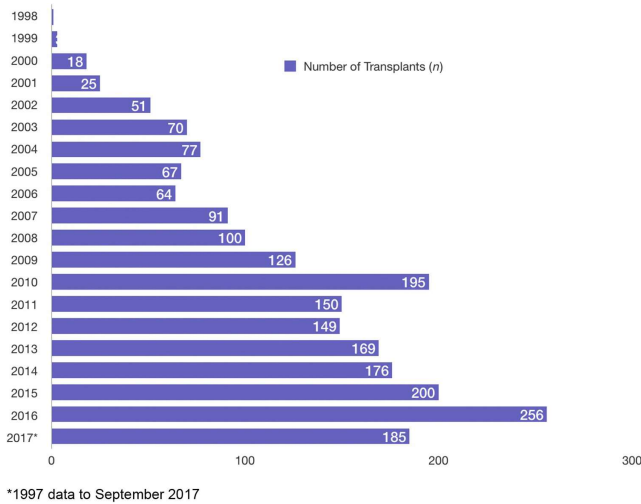
David B. Leeser MD, Alvin G. Thomas, Ashton A. Shaffer, et al. *Patient and Graft Survival after 10 Years of National Kidney Paired Donation*. CJASN doi: 10.2215/CJN.06680619. Visual Abstract by Joel Topf, MD, FACP

19

Can KPD be harnessed to maximize the potential of non-directed donors?

20

## Non-directed (“altruistic”) donors



- Biologically and emotionally unrelated to the recipient
  - 5.6% of live kidney donors in the US in 2019
- Median age 45 years
- 56% female, 92% white
- 51% had associate degrees or higher education

Jan MY, *et al.* Kidney International Reports 2022

21

## Roth Nobel Prize Lecture (continued)

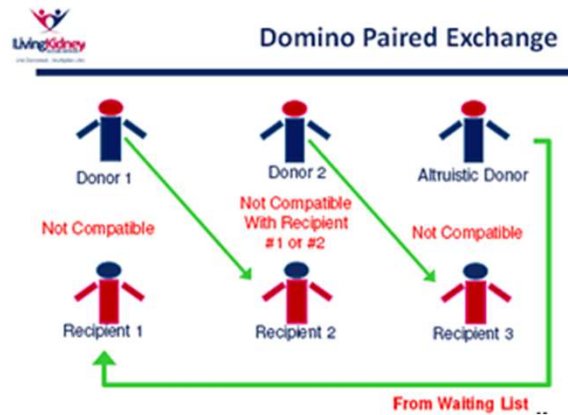
- One question is, “How many transplants can a non-directed donor facilitate?”
- ..a chain initiated by a non directed donor can be arranged so that each patient-donor pair gets a kidney before they give one
- .. the cost of a broken link isn’t nearly as great...
- ..the congestion has been avoided because these chains can now be done non-simultaneously. The marketplace now allows more exchanges, more transplants to be done because you don’t have to assemble all of the operating rooms at the same time

From the Nobel Prize Lecture, December 8, 2012 by Alvin E. Roth

22

## Domino paired donation

- Non-directed donor donates to a recipient in an incompatible pair
  - Vs. donating directly to the list
- “Domino effect” on downstream transplants
- Amplifies the impact of NDD
  - Analysis of UNOS data from 2008-2011
  - 77 NDD who initiated chains resulting in 373 chain transplants

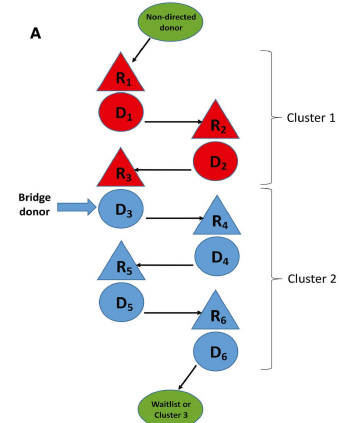


Melcher ML, et al. JAMA Surgery 2013

23

## Non-simultaneous extended altruistic donor (NEAD) chain

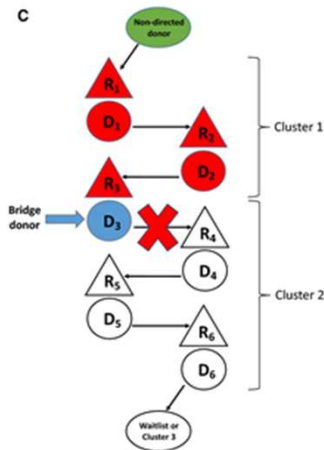
- “Bridge donor” starts a new chain
- Improved transplant logistics
- No need for reciprocal matching
  - Each donor in the chain can be matched with the recipient that leads to the longest or highest quality chain
  - Software can be programmed to find superior age or HLA matches



Cowan N, et al. AJT 2017

24

## Broken chains: Incidence and Impact



- Analysis of NKR transplants 2008-2016
  - 344 chains and 74 loops were completed → 1748 transplants
  - 20 broken chains (5.8%) and 1 broken loop (1.2%) identified
- Most common cause: donor medical issues incurred while acting as a bridge donor (n = 8)
  - Other causes: donors renege (n = 6), kidney declined by the recipient surgeon (n = 4)
- Mean length of chains 4.6 (complete) vs. 4.8 (broken)
- All recipients involved in a broken chain subsequently received a transplant

Cowan N, et al. AJT 2017

25

## Utilization of Deceased Donors to Start KPD Chains

### Kidney Paired Donation Chains Initiated By Deceased Donors

**Cohort**

- Simulations based on actual 2016-2017 DD transplant data from SRTR, US
- Data from the Alliance for Kidney Paired Donation used to simulate KPD pool and DD initiated KPD chains.
- Simulations compared long chains to short chains initiated by DD.

SRTR, Scientific Registry of Transplant Recipients

**Results**

DD Kidney

Long DD initiated KPD Chain

↑ 5%

KPD Transplants

↓ 25%

DD's allocated to KPD pool

Long DD chains compared to short DD chains.

↑

Blood Type O transplants increased

↑

Increased living donors available to waitlist candidates

DD, Deceased donors    KPD, kidney paired donation

**KI REPORTS**  
Kidney International Reports

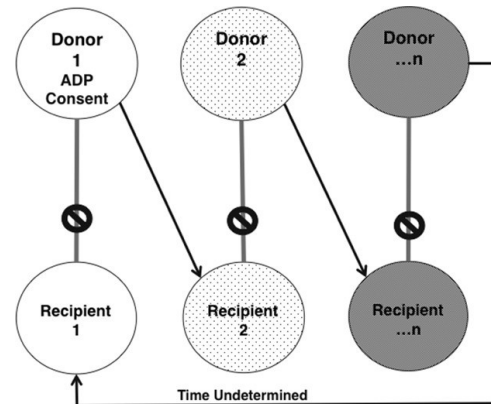
Wang W et al, 2022  
Visual abstract by:  
Krishnam Raju Penmatsa  
MD, DM, DNB

**Conclusion** Allocating fewer than 3% of DD to initiate chains could increase the number of kidney transplants by up to 290 annually. Such use of DDs allows additional transplantation of highly sensitized and Blood Type O KPD candidates. Collectively patients of each blood type, including Blood type O, would benefit from the proposed strategies.

26

## Advanced donation program

- An ADP donor desires to donate by a specific date, but their paired recipient has not yet been matched to a specific donor or scheduled for surgery
- Time-limited donor donates a kidney before paired recipient has an established donor identified



Flechner SM, et al. AJT 2015

27

## ADP “voucher” system

- Emerged as a response to “chronological incompatibility”
- First case of “voucher advanced donation” facilitated by the NKR was in 2014
  - 64-year-old grandfather donated a kidney to a nonrelated individual
  - 4-year-old grandson was provided with an NKR voucher for a future kidney transplant
  - The child was expected to need a transplant in 10-15 years, at which point the grandfather might no longer be eligible to donate
- First 3 “vouchers” → 25 transplants through kidney paired donations across the US

Veale JL, et al. Transplantation 2017

28

## Advanced Donation Program (ADP) Terms

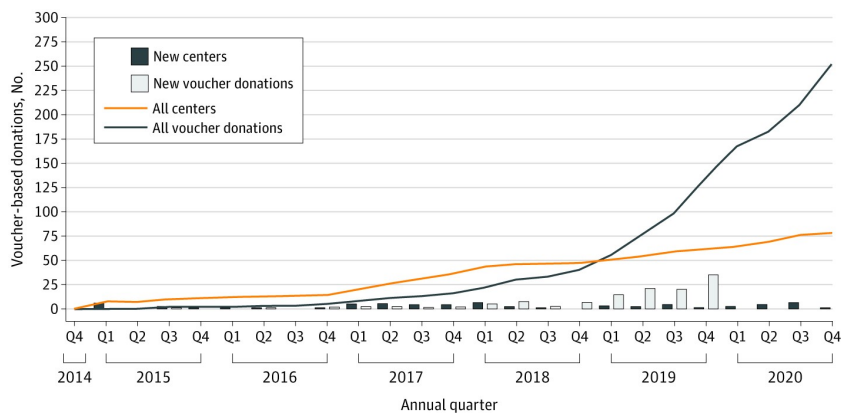
TERM	DEFINITION
<b>Advanced donation program (ADP)</b>	Donors donate BEFORE the intended recipient is transplanted
ADP swap saver	Donor donates to keep a swap intact when their paired recipient gets sick
ADP real-time swap failure repair	Donor donates and the donor's paired recipient does not receive a kidney due to a swap failure
ADP <b>standard voucher</b>	Donor donates before their intended recipient is scheduled for transplant surgery
ADP <b>family voucher</b>	Donor donates before knowing whether their intended recipients will ever need a transplant
<b>Voucher donor</b>	Person donating a kidney and generating 1 or more vouchers
<b>Voucher holder</b>	Person in possession of a voucher
<b>Voucher redemption</b>	Occurs when a voucher holder receives a kidney transplant

Cooper M, et al. AJT 2020

29

## NKR: Growth in voucher-based donations

- A total of 250 voucher-based donations occurred between 2014 and 2020



Veale JL, et al. JAMA Surgery 2021

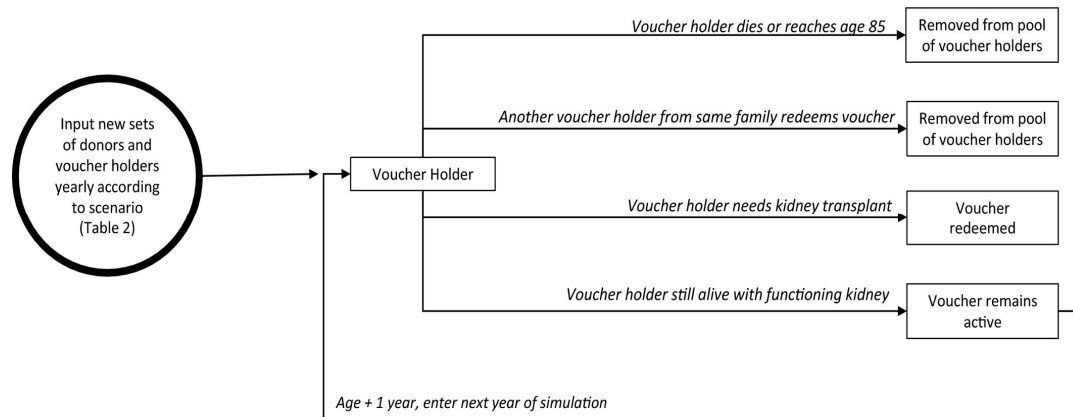
30

How do patterns of growth in the voucher program impact the risk of non-redemption?

31

## 50-year simulation study of the ADP

To estimate the annual number of voucher redemptions vs. number of kidneys available over a 50-year time horizon under several projected scenarios for growth of the program



Cooper M, et al. AJT 2020

32



## Growth scenarios for simulation study of ADP

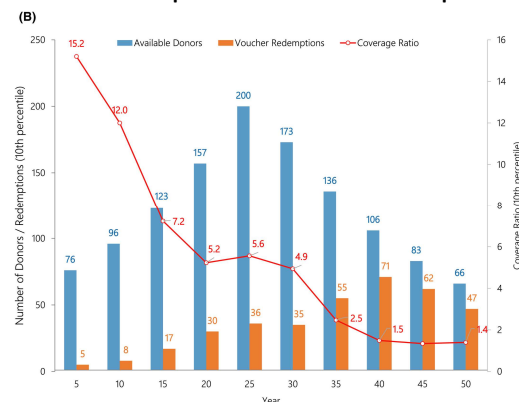
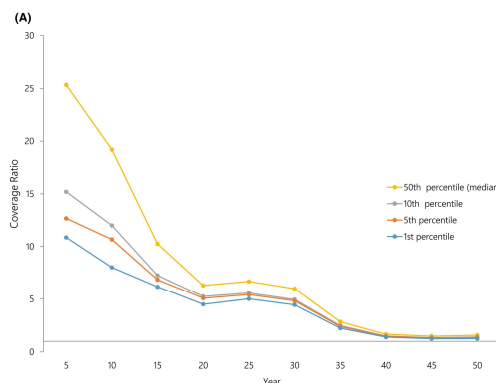
- Rapid Growth: Voucher donors increase by 5% compounded year over year
- Slow Growth: Voucher donors grow slowly with an additional 2-5 voucher donations per year
- Rapid Growth then Rapid Decline: **worst-case scenario** where the number of voucher donors grows rapidly (5% year over year) for the first 25 years then declines rapidly for the next 25 years (same values in reverse)
  - Liabilities increase in the early years but coverage declines in later years when it is more likely that vouchers will be redeemed
- Slow Growth then Slow Decline
- Rapid Growth then Plateau: voucher donors increase at 5% rate each year for the first 25 years then remain constant in years 26-50

Cooper M, et al. AJT 2020

33

## Rapid growth, Rapid decline

- Coverage ratio is the number of available donors per voucher redemption



- “The expanded voucher program should satisfy the likely redemption of vouchers under a range of possible scenarios over a 50-year time horizon”

Cooper M, et al. AJT 2020

34

## Risks of voucher program

- Listed in the consent form  
[http://www.kidneyregistry.org/docs/ADP\\_Consents.pdf](http://www.kidneyregistry.org/docs/ADP_Consents.pdf)
- Risks may be unforeseeable
- *“Advanced Donation Program Obligations: All NKR Member Centers and Partner Centers agree to work with each other in good faith under the leadership of the NKR Surgical Director, should the NKR ever become insolvent and/or cease operations, to provide kidneys for Advanced Donation Program recipients. This obligation is irrevocable, exists in perpetuity, and survives the termination of this contract.”*

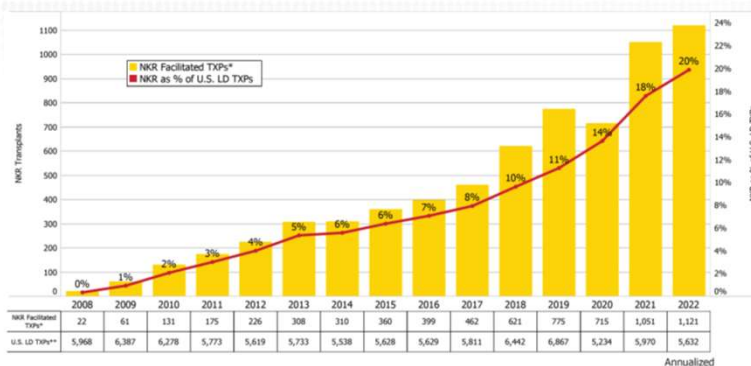
Kidneyregistry.org

35

## National Kidney Registry (NKR) Impact

- Largest KPD organization in the US (kidneyregistry.org)
- Has facilitated 6538 transplants from 2008 to present (as of Nov 1, 2022)

### NKR Facilitated Transplant Growth

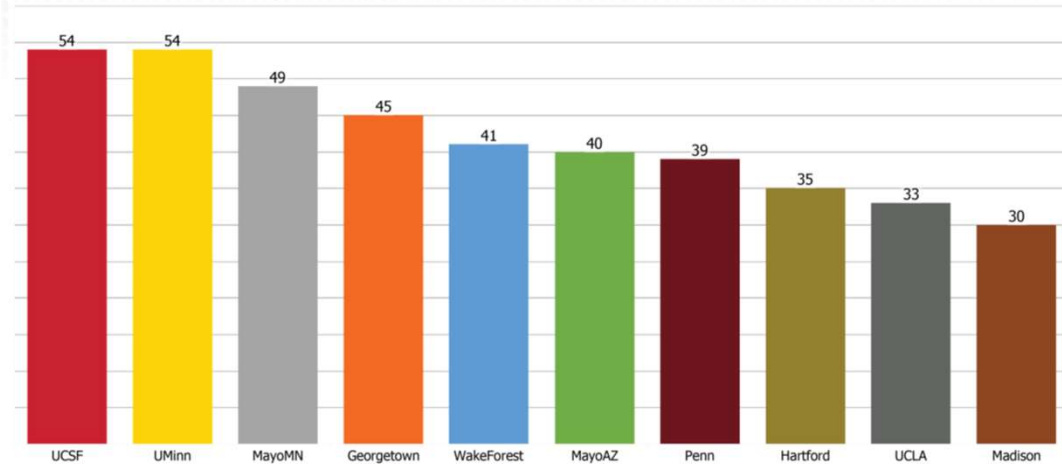
NKR Quarterly Report, 2<sup>nd</sup> quarter 2022

36

## NKR: Center Participation

### Top Centers

NKR Facilitated Transplants 7/1/2021 – 6/30/2022

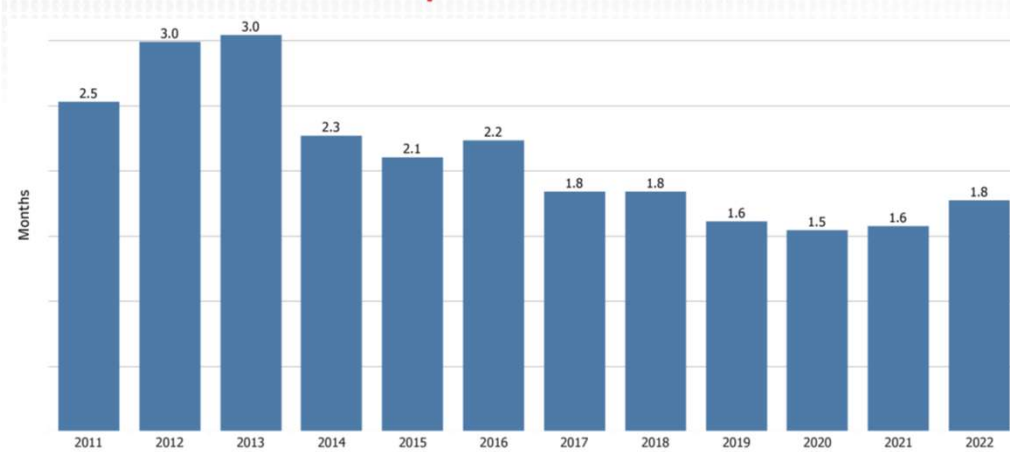


NKR Quarterly Report, 2<sup>nd</sup> quarter 2022

37

## NKR: Expedites Time to Transplant

### Median Wait Time to Transplant

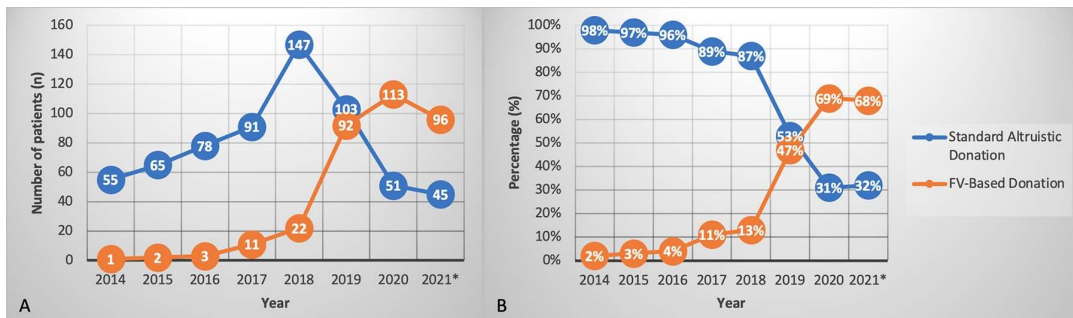


NKR Quarterly Report, 2<sup>nd</sup> quarter 2022

38

## NKR: Increase in Family Voucher Donors

- Voucher-based donation surpassed altruistic donation by 2019
- Helped non directed donation to triple by 2021



**Figure 1:** Number of patients participating in standard altruistic and FV based donation from 2014 to present (A). Percentage of non-directed donation by either standard altruistic or FV-based donation (B). \*Numbers reflect to June 2021.

Capron A, *et al.* Transplantation 2022 [Abstract]

39

## Summary

- Live donor kidney transplant is the preferred option for treatment of ESRD
- Kidney paired exchange programs facilitate and increase transplants in recipients with HLA and ABO-incompatible donors as well as improve graft matching in compatible pairs
- Innovations such as the inclusion of compatible pairs, non directed donor initiated chains, and advance donation can further maximize the pool of live donors for kidney transplant

40