Living Donor Kidney Transplant – The Basics and Beyond

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Disclosures

- I have no relevant financial relationships with any companies related to the content of this course
- I do serve on the Renal Committee of the National Kidney Registry, in an advisory role

Myth 1.

Just be patient, a deceased donor kidney will come your way soon enough

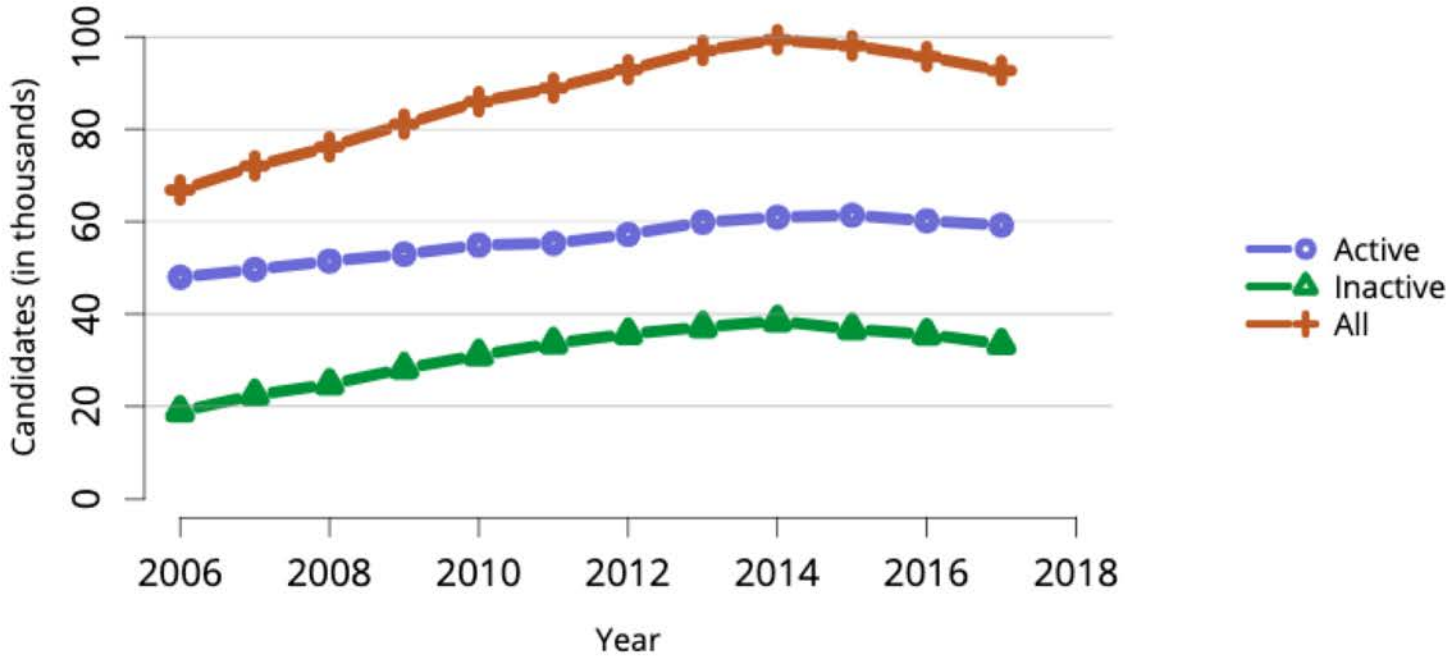


Figure KI 2. Adults listed for kidney transplant on December 31 each year. Candidates concurrently listed at multiple centers are counted once. Those with concurrent listings and active at any program are considered active. Includes kidney and kidney-pancreas listings.

OPTN/SRTR 2017 Annual Report: Kidney.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/ajt.15274

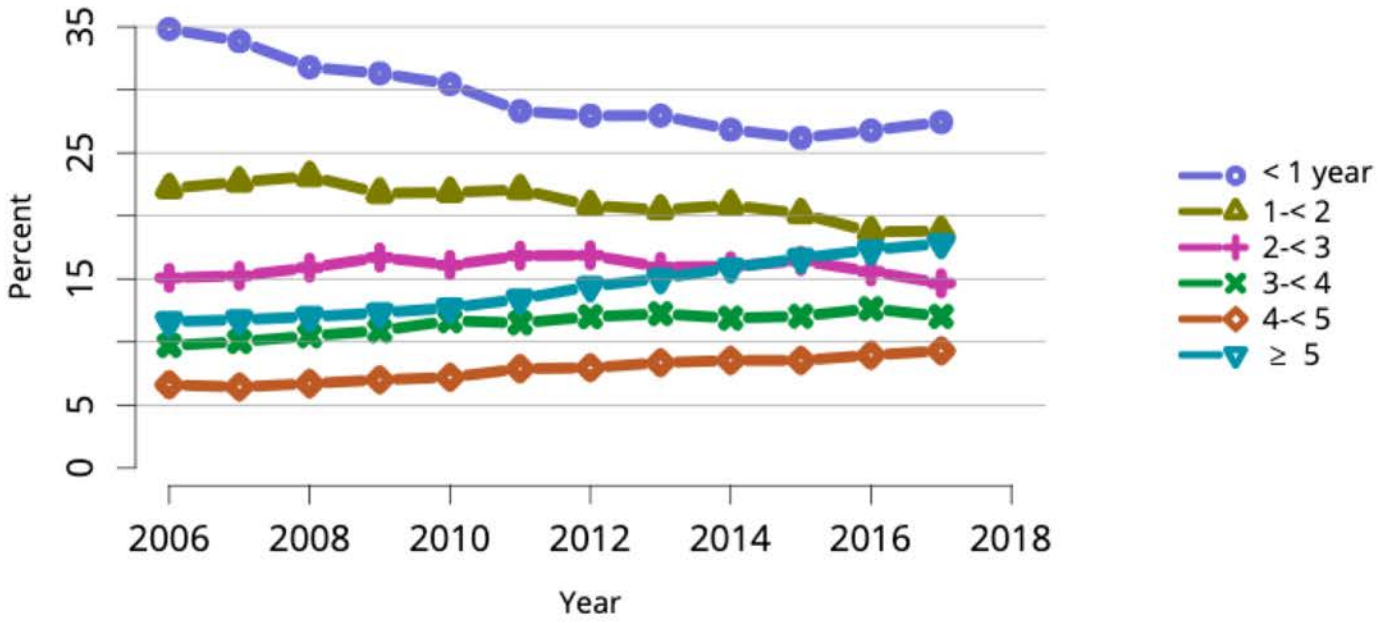


Figure KI 7. Distribution of adults waiting for kidney transplant by waiting time. Candidates waiting for transplant at any time in the given year. Candidates listed concurrently at multiple centers are counted once. Time on the waiting list is determined at the earlier of December 31 or removal from the waiting list. Active and inactive candidates are included.

OPTN/SRTR 2017 Annual Report: Kidney.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/ajt.15274

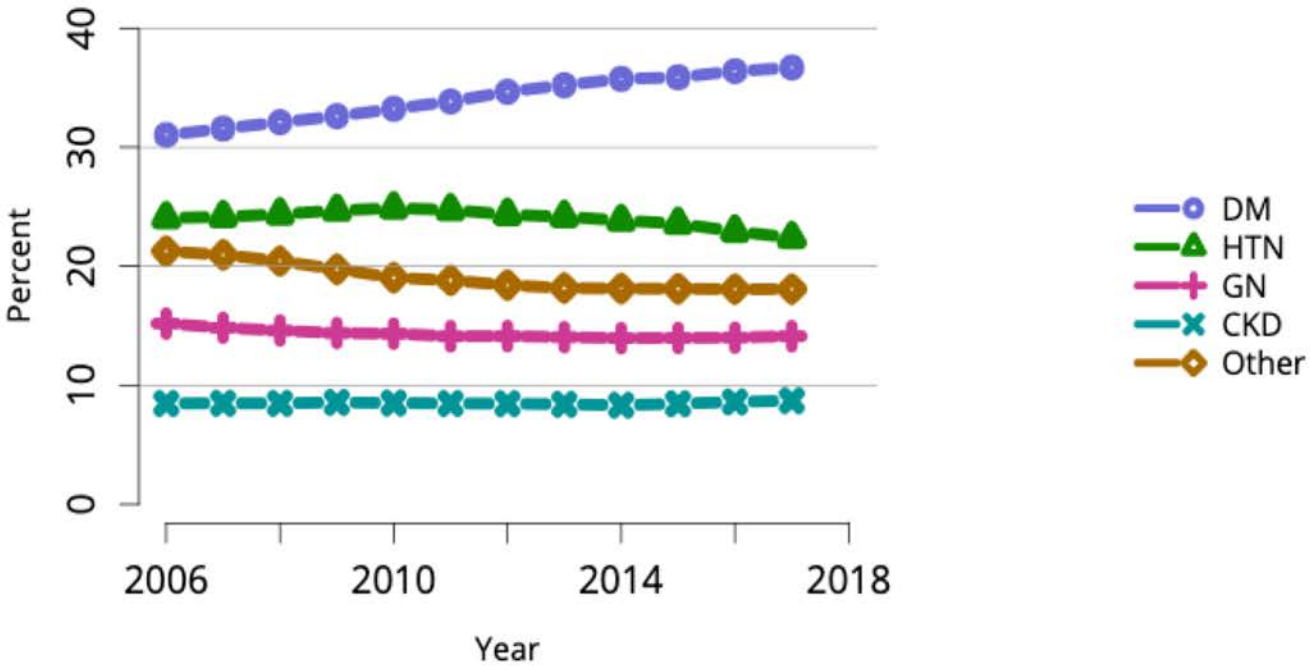


Figure KI 6. Distribution of adults waiting for kidney transplant by diagnosis. Candidates waiting for transplant at any time in the given year. Candidates listed concurrently at multiple centers are counted once. Active and inactive candidates are included. CKD, cystic kidney disease; DM, diabetes. HTN, hypertension. GN, glomerulonephritis.

OPTN/SRTR 2017 Annual Report: Kidney.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/ajt.15274

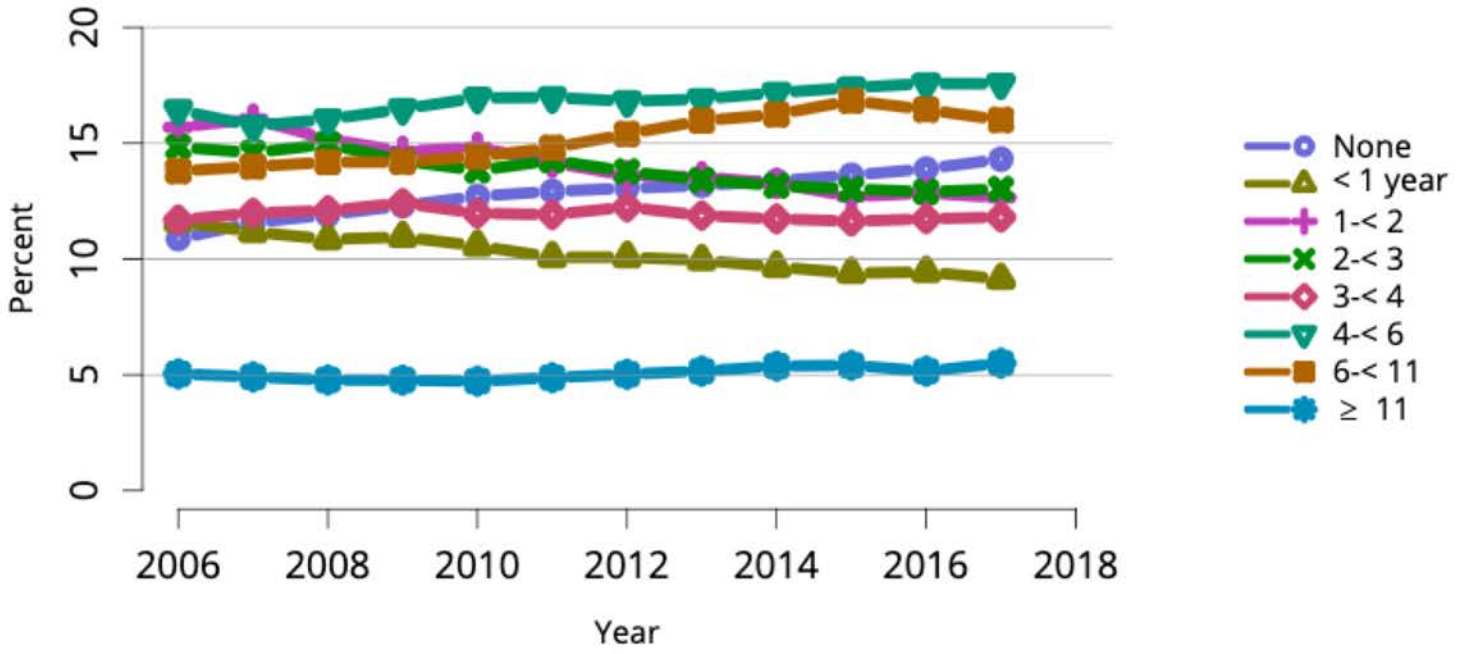


Figure KI 9. Distribution of adults waiting for kidney transplant by time on dialysis. Candidates waiting for transplant at any time in the given year. Candidates listed concurrently at multiple centers are counted once. Time on dialysis begins at the more recent of first ESRD service date and most recent graft failure, and ends at the earlier of December 31 or removal from the waiting list. Active and inactive candidates are included.

OPTN/SRTR 2017 Annual Report: Kidney.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/ajt.15274

Average Wait Times at UCSF

- Blood type O – 8-10 years
- Blood type A – 7-9 years
- Blood type B – 7-9 years
- Blood type AB – 5-7 years
- UCSF is a microcosm of the larger issue of wait list times in California and across the country

Kidney Transplant Decision Aid

Calculate Your Risks

What are your likely outcomes on the kidney transplant waiting list?

Choose the Transplant Program:

University of California San Francisco Medical Center (CA)

☑ Adjust for Program-Specific Transplant Rate

Choose your age:

55

Choose your gender:

- ◉ Male
- ○ Female

Choose your race:

- ○ Asian
- ○ Black
- ○ Native American
- ○ Pacific Islander
- ◉ White
- ○ Multiracial

Choose your ethnicity:

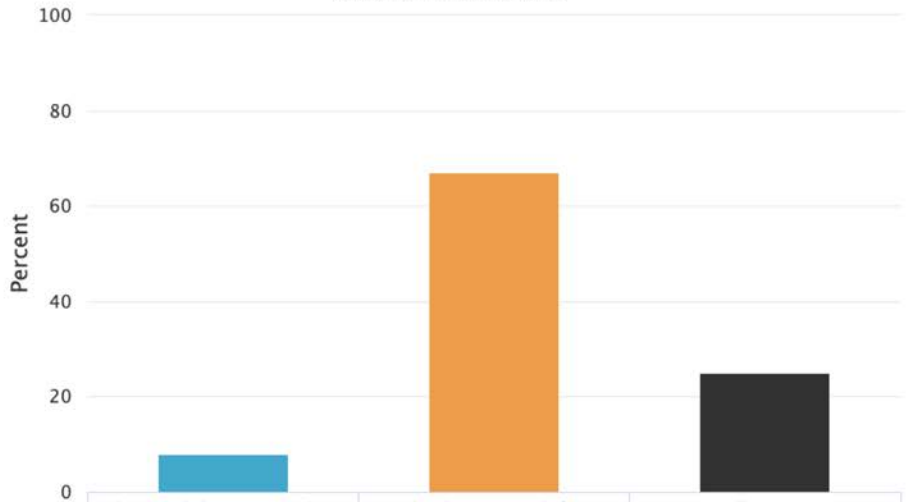
- ○ Latino
- ◉ Not Latino

Enter your height:

Feet: Inches:

Outcomes in 5 Years

University of California San Francisco Medical Center (CA)
Adjusted for Program-Specific Transplant Rate
55-Year-Old White / Not Latino Male
Height: 5' 8" Weight: 150 lbs Blood Type: O cPRA: 0
4 Years on Dialysis
Health Issues: Diabetes
2019-10-19 Version 0.2.0



Of patients like you:
8% will get a deceased-donor transplant
67% will die or become too sick for transplant
25% will still be waiting

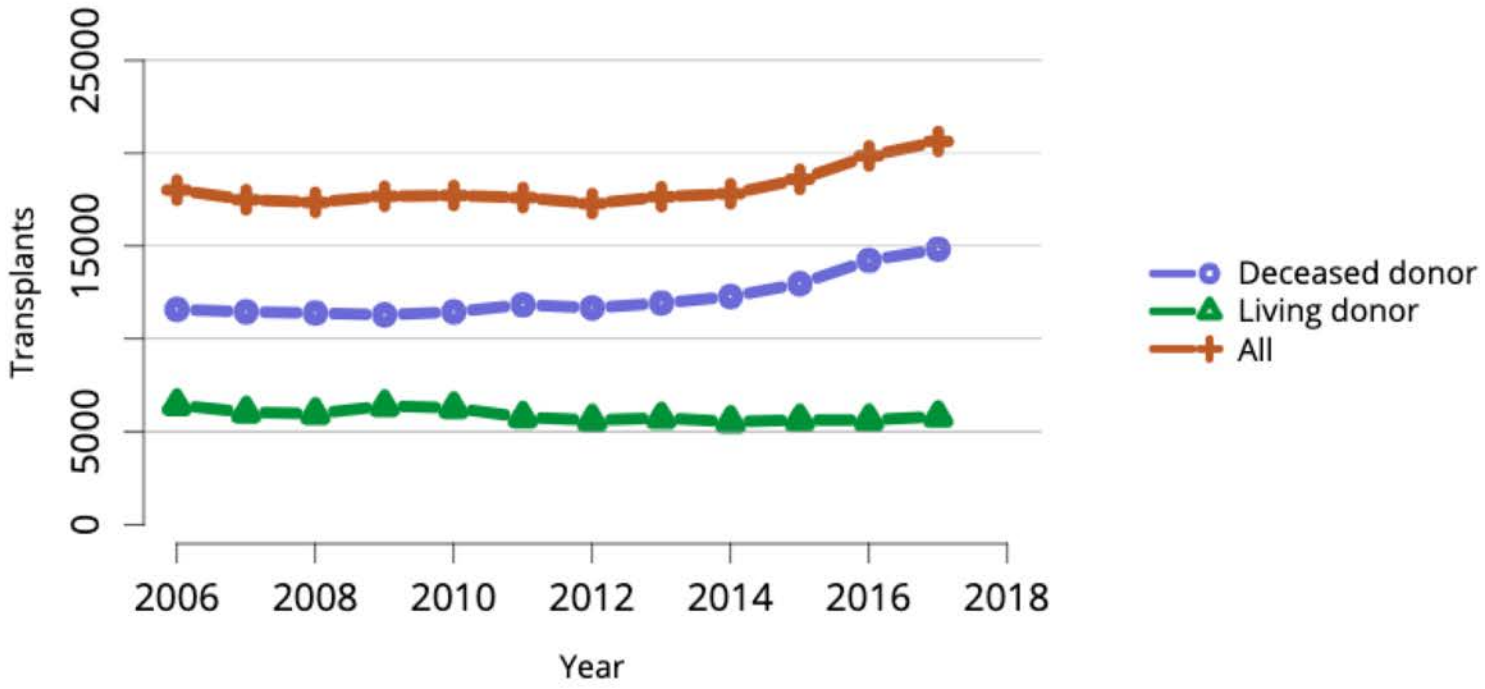


Figure KI 57. Total kidney transplants. All kidney transplant recipients, including adult and pediatric, retransplant, and multi-organ recipients.

OPTN/SRTR 2017 Annual Report: Kidney.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/ajt.15274

Myth 2.

A deceased donor organ is just as good as a living donor kidney

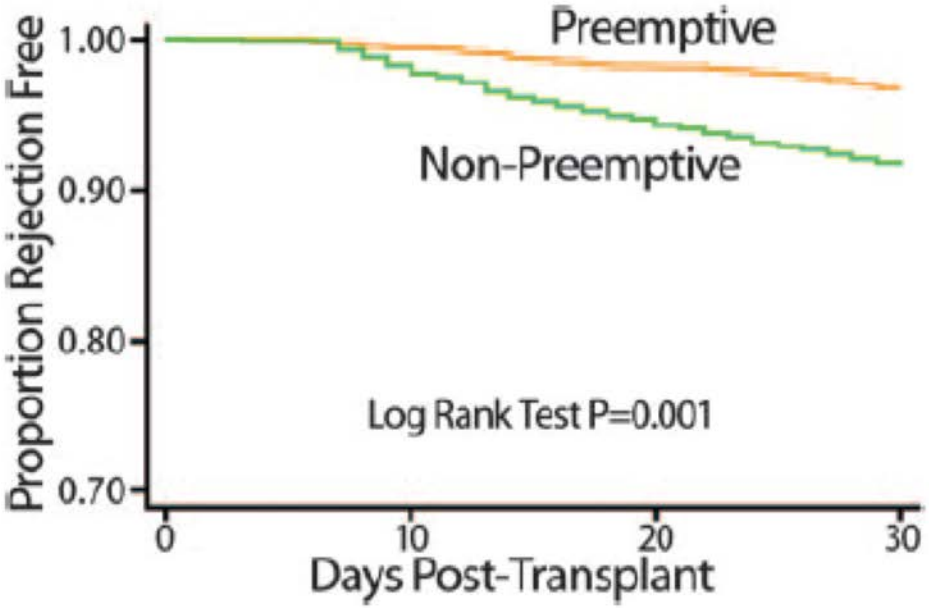
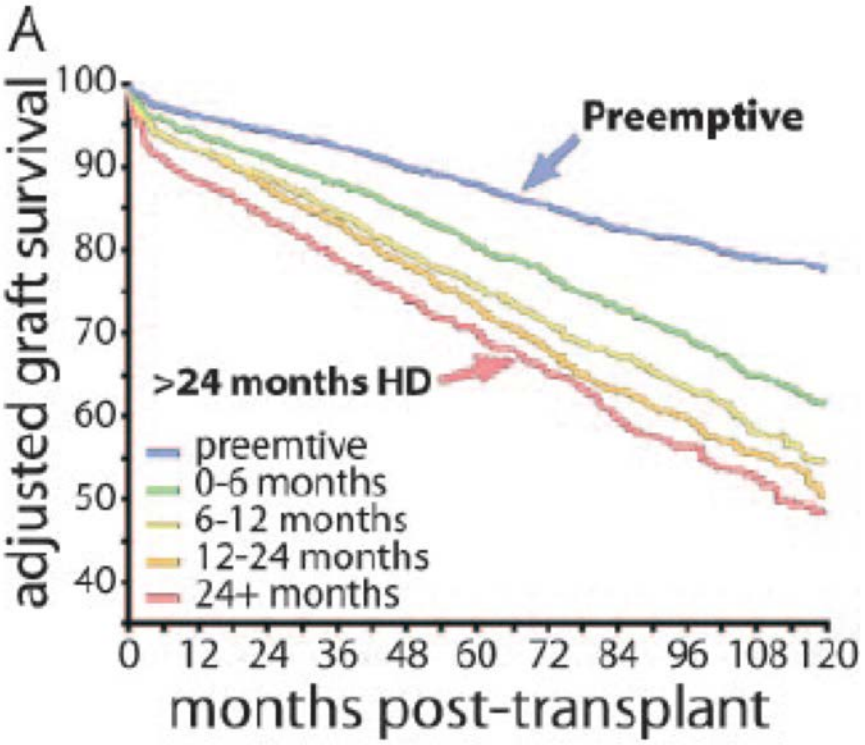
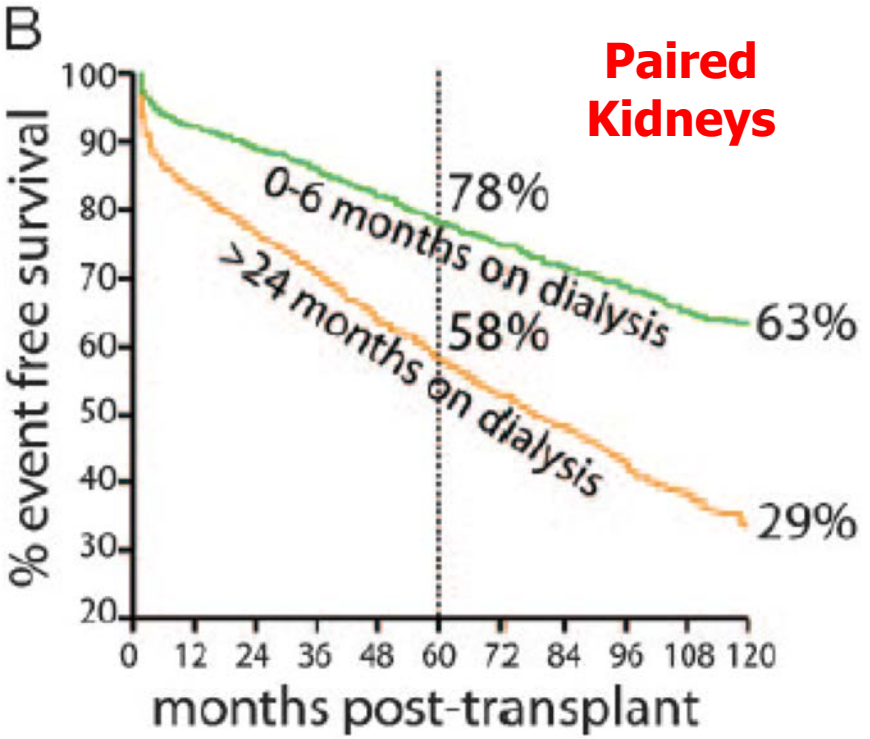


Figure 3. The proportion of recipients with biopsy-confirmed acute rejection according to the use of dialysis before transplantation. Acute rejection episodes are less during the first 30 d in those who receive a preemptive transplant. Reprinted from reference 7, with permission.

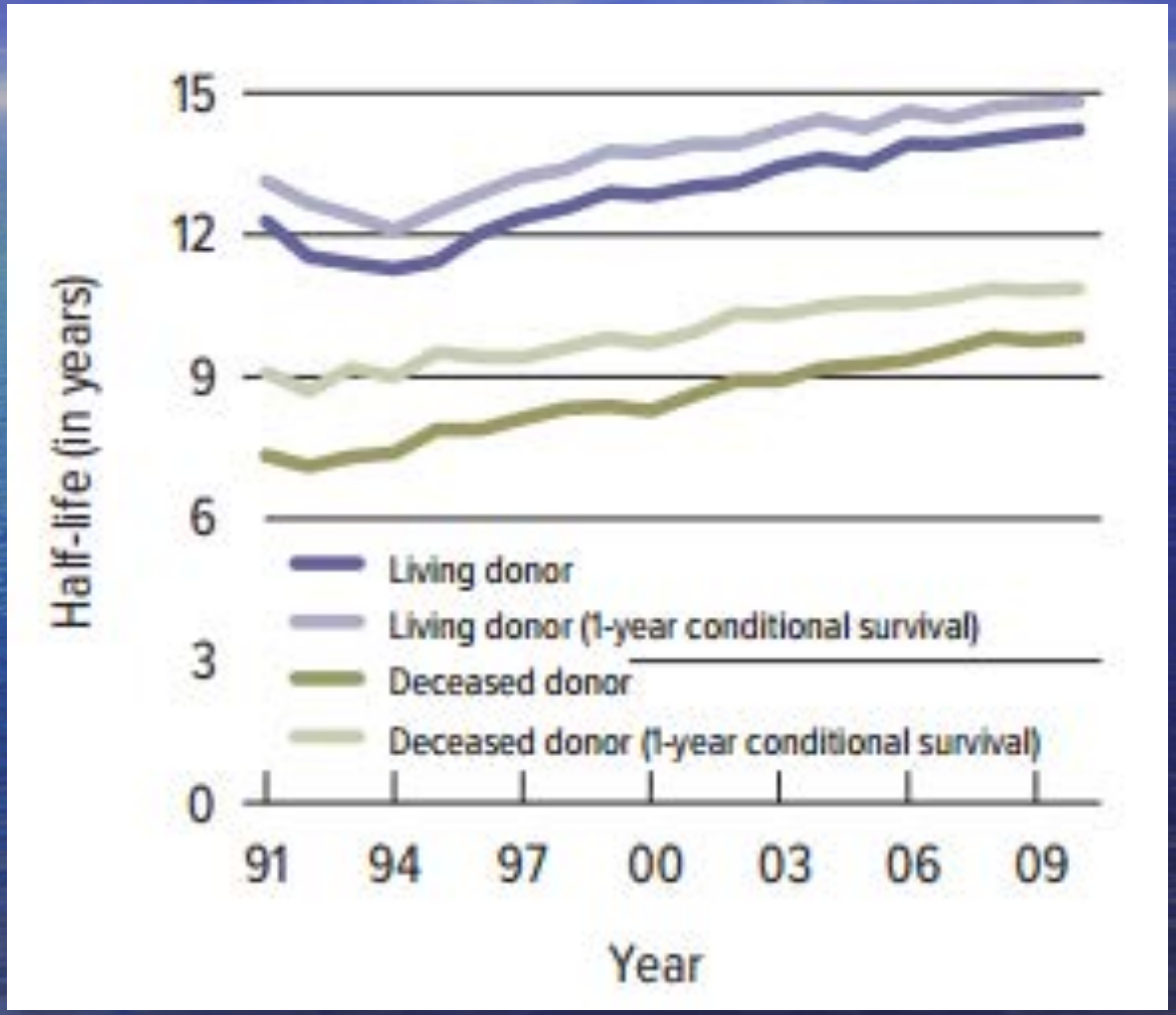
Davis, Delmonico. JASN 2005. 16:2098-2110


A
adjusted graft survival
100
90
80
70
60
50
40
Preemptive
>24 months HD
preemtive
0-6 months
6-12 months
12-24 months
24+ months
0 12 24 36 48 60 72 84 96 108 120
months post-transplant


Davis, Delmonico. JASN 2005. 16:2098-2110


B
Paired Kidneys
% event free survival
100
90
80
70
60
50
40
30
20
0-6 months on dialysis
78%
63%
>24 months on dialysis
58%
29%
0 12 24 36 48 60 72 84 96 108 120
months post-transplant

Allograft Survival



OPTN/SRTR Annual Data Report 2012

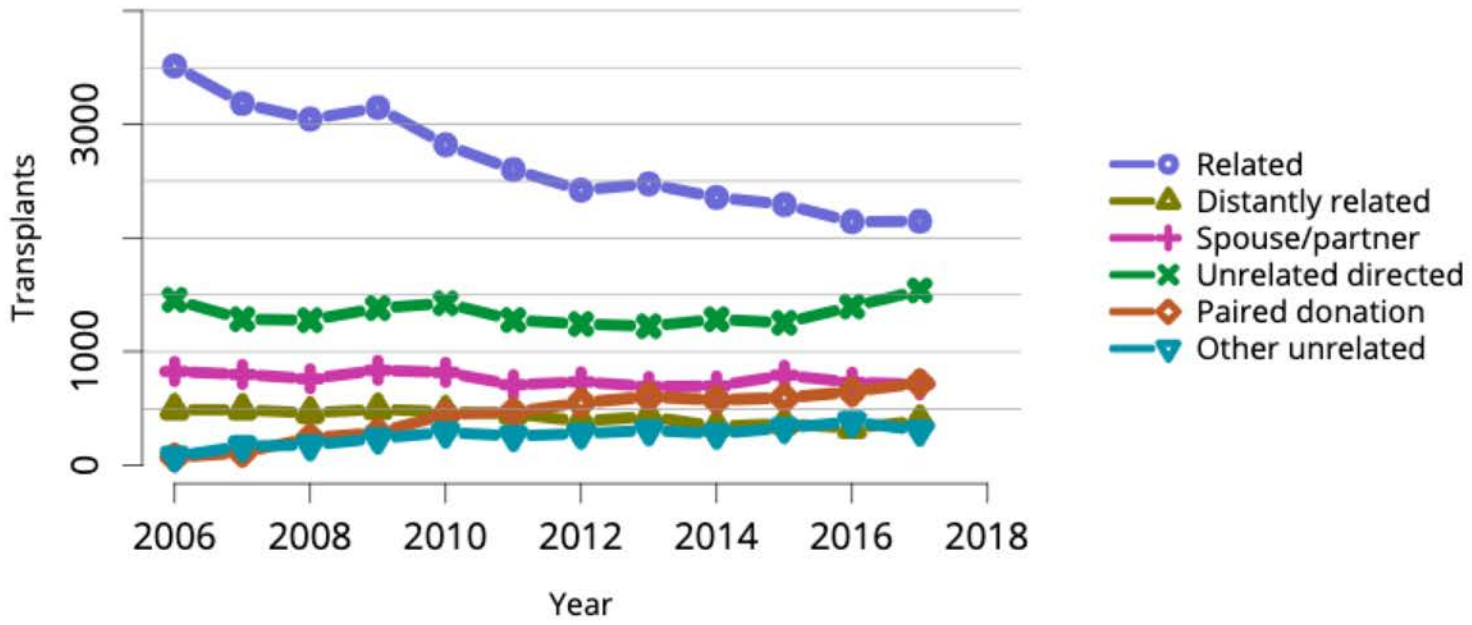


Figure KI 49. Kidney transplants from living donors by donor relation. As reported on the OPTN Living Donor Registration Form.

OPTN/SRTR 2017 Annual Report: Kidney.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/ajt.15274

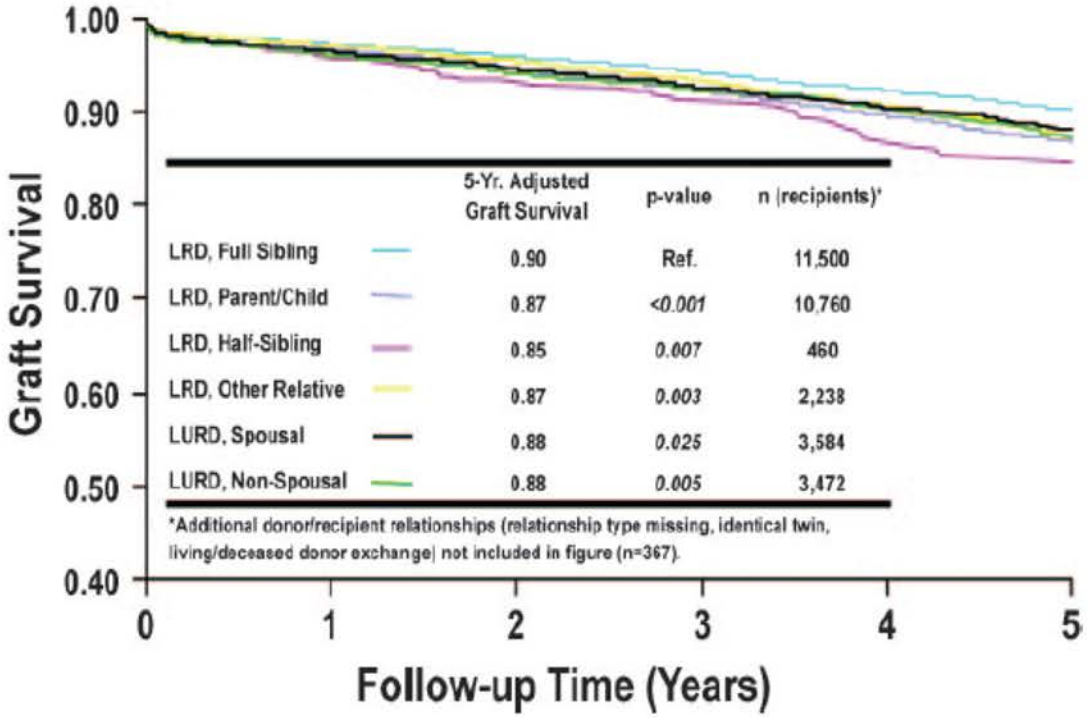


Figure 5. Five-year graft survival according to donor relationship to the recipient. OPTN/SRTR database, Annual Report as of August 1, 2003, Table 5.9b.

Davis, Delmonico. JASN 2005. 16:2098-2110

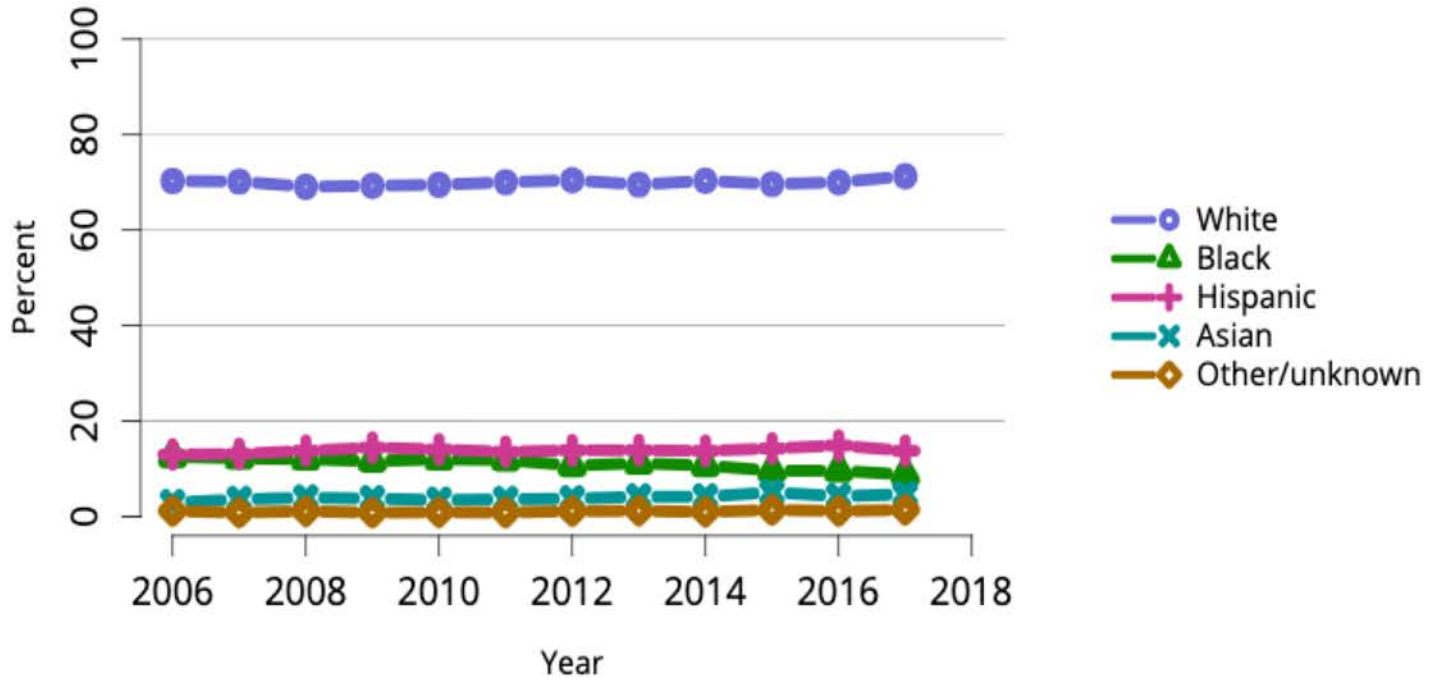


Figure KI 52. Living kidney donors by race. As reported on the OPTN Living Donor Registration Form.

OPTN/SRTR 2017 Annual Report: Kidney.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/ajt.15274

Does Kidney Transplantation With Deceased or Living Donor Affect Graft Survival?

Eghlim Nemati [1]; Behzad Einollahi [1]; Mahboob Lesan Pezeshki [2]; Vahid Porfarziani [1]; Mohamad Reza Fattahi [1,*]

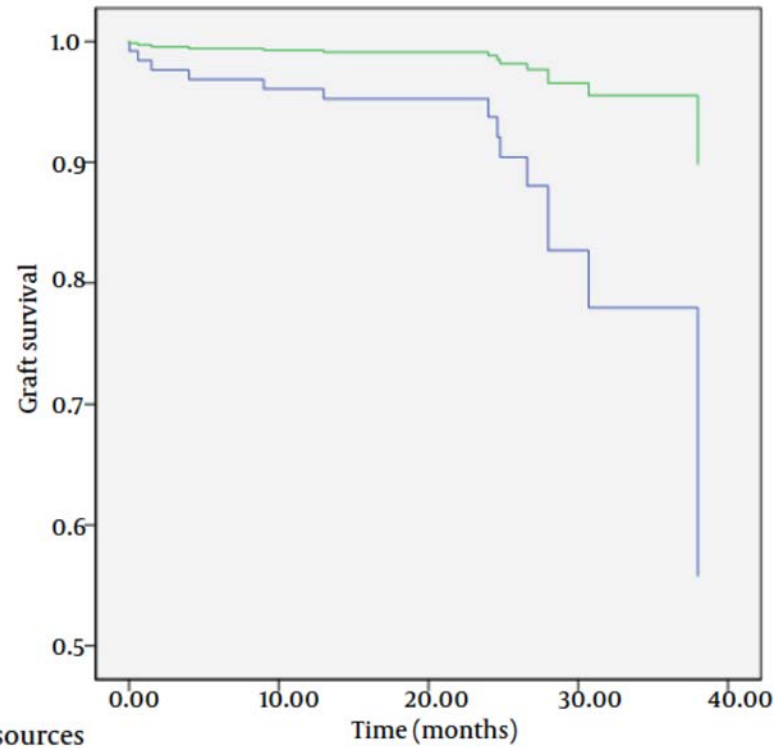
Table 1. Demographic Data of the Recipients in Both Groups [a,b]

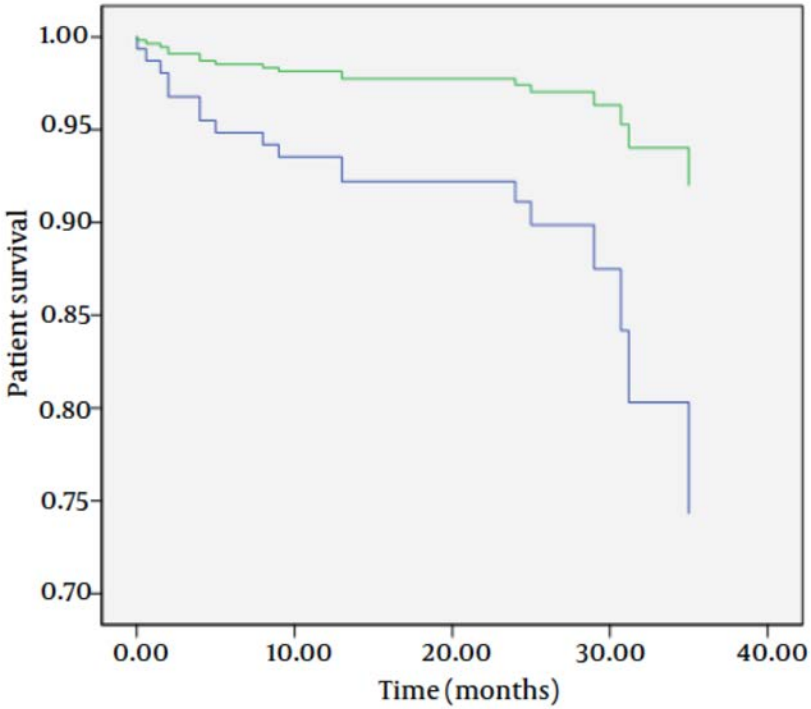
Variables	Overall (n = 218)	LDKT (n = 115)	DDKT (n = 103)	P Value
Gender				0.3
Male	144 (66)	79 (68.7)	65 (63.1)	
Female	74 (34)	36 (31.3)	38 (36.9)	
Age of Recipient, y (range)	43 ± 14 (10-76)	41 ± 14 (10-76)	45 ± 14 (17-71)	0.01
Follow-up, mo	29 ± 10	30 ± 11	22 ± 7	0.000
Graft Loss	14 (6.4)	5 (4.3)	9 (8.7)	0.2
Mortality Rate	18 (8.3)	6 (5.2)	12 (11.7)	0.08
Number of Admissions After Tx				0.2
None	66.5	72.2	60.2	
1	20.2	18.3	22.3	
2	9.6	7.8	11.7	
3	2.3	1.7	2.9	
4	1.4	0	2.9	
Last Serum Creatinine, mg/dL	1.6 ± 1.0	1.4 ± 0.8	1.7 ± 1.1	0.08
Systolic BP, mm Hg	127 ± 15	127 ± 16	126 ± 13	0.4
Diastolic BP, mm Hg	78 ± 7	77 ± 9	79 ± 5	0.2
Hb, g/dL	11.1 ± 1.1	11.0 ± 2.0	11.2 ± 1.8	0.2
TG, mg/dL	128 ± 65	130 ± 71	126 ± 59	0.6
Chol, mg/dL,	143 ± 43	142 ± 39	145 ± 48	0.6
Uric acid, mg/dL	4.8 ± 1.6	4.4 ± 1.5	5.3 ± 1.7	0.000

Table 2. Patient and Graft Survival in Two Groups [a,b]

Survival Rates, y	LDKT	DDKT	P Value (Log Rank)
Graft			0.004
1	97.4	97.0	
3	96.2	67.4	
Patient			0.006
1	95.6	95.1	
3	93.9	45.4	

Nemati et al. Nepho Urol Mon 2014. 6(4):e12182


Donor sources
Deceased
Living
Graft survival
1.0
0.9
0.8
0.7
0.6
0.5
0.00
10.00
20.00
30.00
40.00
Time (months)


Donor sources
Deceased
Living
Patient survival
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.00
10.00
20.00
30.00
40.00
Time (months)

Myth 3.

Being a living kidney donor is unreasonably risky

Once Upron A Time.....

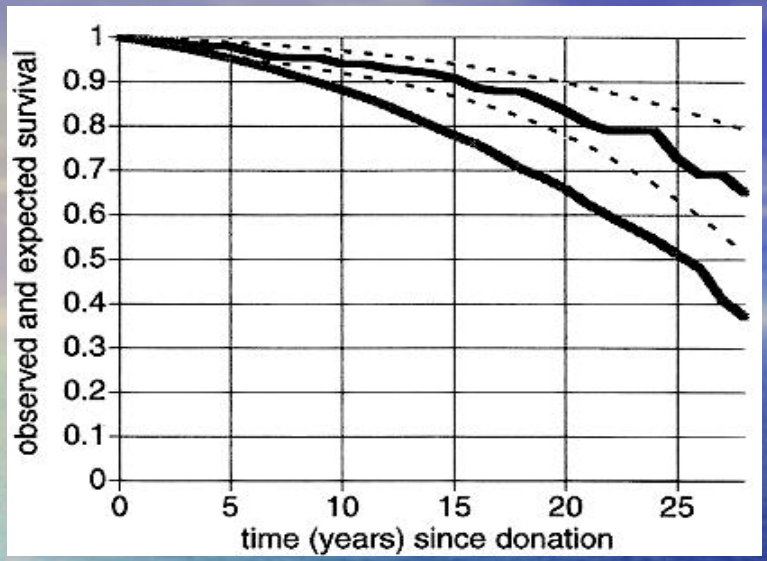
Health of Donor….

- " The health of the donor dominates all other considerations. A major operation on a normal person, not for his own benefit, requires a brusque re-evaluation of traditional surgical thought….moral justification is found in the safety and security of the donor as well as in the expected degree of success when there is no other alternative."

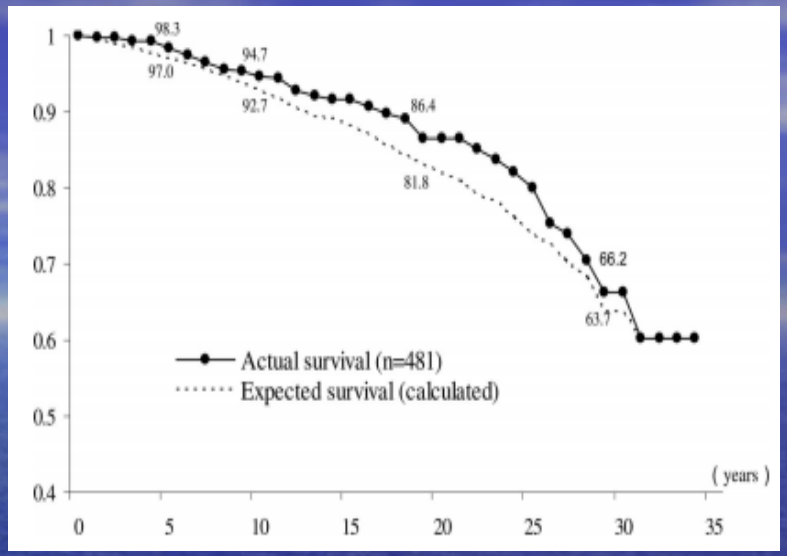
Murray et al. Ann Surg 1958; 148:343-59

Donor vs. Gen Pop Survival Data

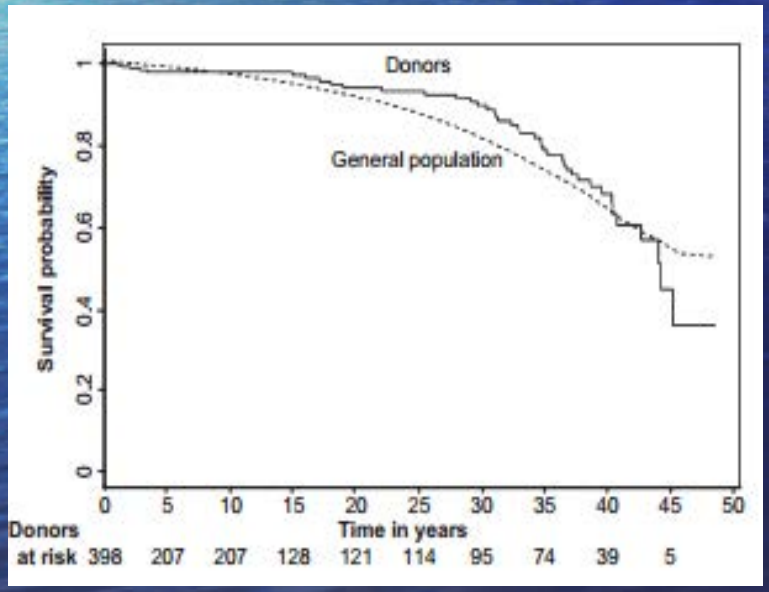
Country Origin	Setting	N=	Years studied	FU (yrs)
Sweden	Single center	430	1964-1994	1-35
Japan	Single center	481	1970-2006	1-35
France	Single center	310	1952-2008	1-53
USA	Single center	3698	1963-2007	1-45



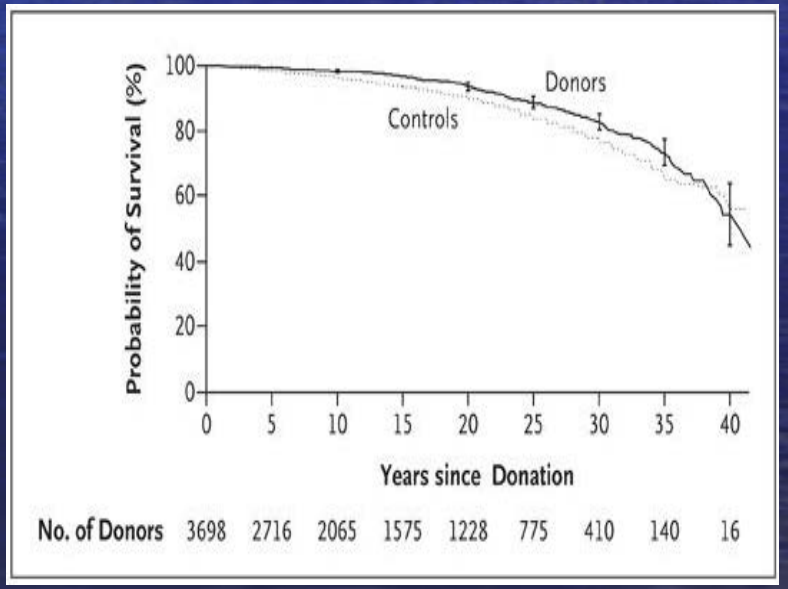
Sweden



Japan



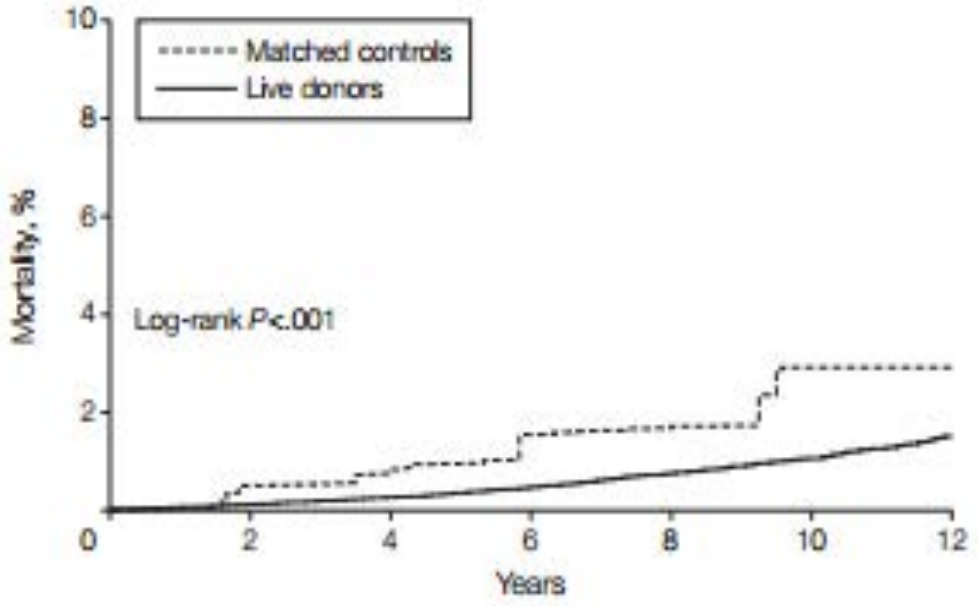
France



USA

Donor vs. Selected "Healthy" Population

Figure 1. Kaplan-Meier Curves Comparing Cumulative Mortality of Live Kidney Donors and Matched Controls for the Entire Cohort of Live Donors



No. at risk

Matched controls	80347	67966	54998	41679	19259	5896	127
Live donors	80347	68230	55282	42154	29657	18960	10436

- 80K + live kidney donors in US, 1994-2009
- Comparison group – selected cohort from NHANES III '88-'94
- Median FU period 6.3 yrs

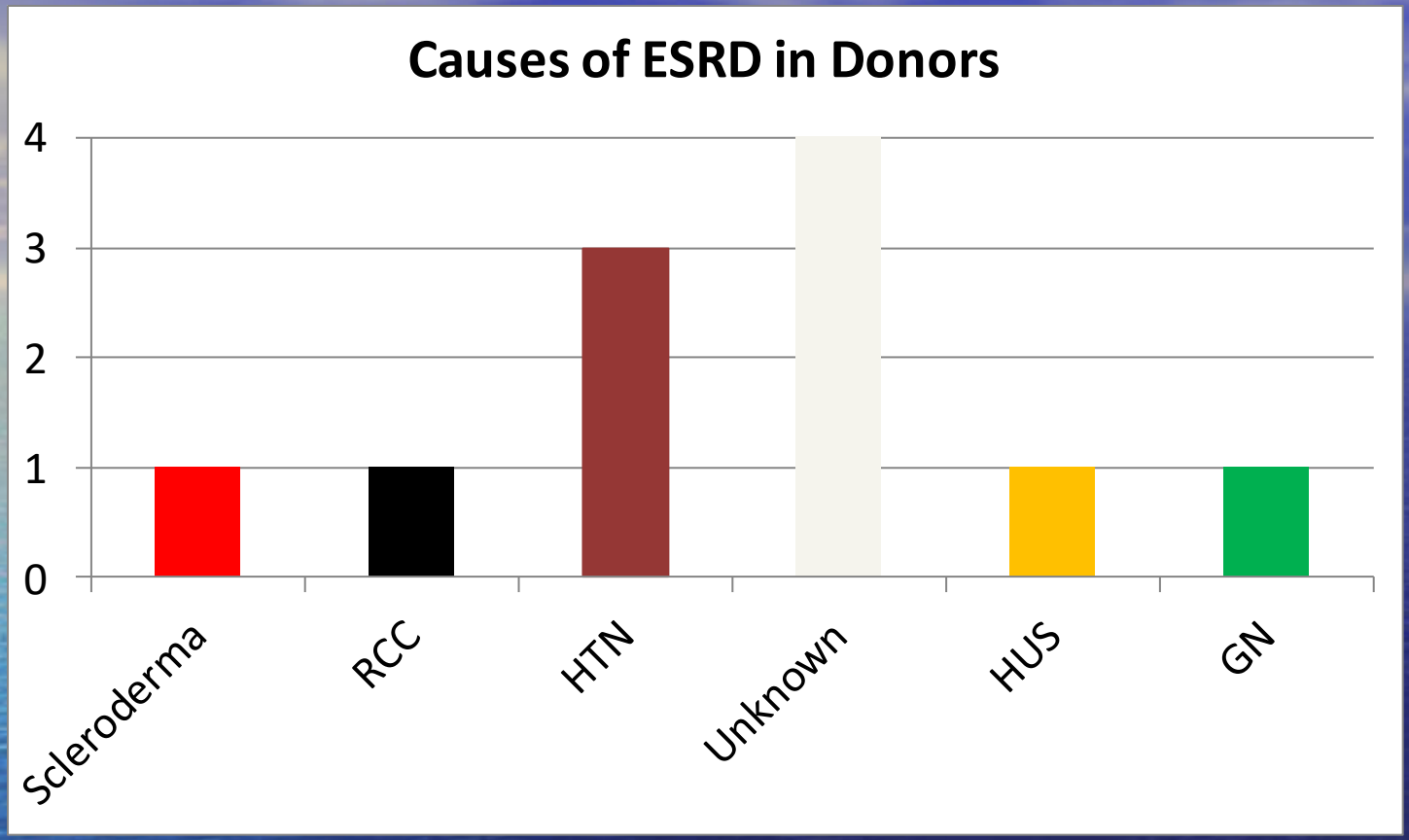
Segev et al. JAMA 2010; 303:959-66

Long-Term Consequences of Kidney Donation

Hassan N. Ibrahim, M.D., Robert Foley, M.B., B.S., LiPing Tan, M.D., Tyson Rogers, M.S., Robert F. Bailey, L.P.N., Hongfei Guo, Ph.D., Cynthia R. Gross, Ph.D., and Arthur J. Matas, M.D.

- 3698 Kidney donors – ’63 through ‘07 @ U Minn
- Cohort of 255 donors also had iohexol GFR and albuminuria measured
- Patient survival of donors compared to life tables from Human Mortality Database
- Rates of ESRD in general population estimated to be 268 cases/million person-yrs (USRDS 2007 annual report)
- NHANES 2003-4 and 2005-6 cohorts were matched by age, sex, ethnicity, and BMI to donors in whom GFR was measured

Ibrahim et al. NEJM 2009; 360:459-69



ESRD Rate	180/ million person-yrs
Female	7/11
Caucasian	8/11
Siblings	7/11 (all ESRD cases were LRRT)

Table 3. **Health Status of Kidney Donors More Than 20 Years after Donation.***

	Kidney Donors with GFR Measurement (N=55)	Controls (N=55)	Kidney Donors without GFR Measurement (N=1035)†	P Value‡
Age (yr)	57.7±9.8	57.7±9.8	61.9±11.6	—
Female sex (%)	64.1	64.1	57.6	—
White race (%)	98	98	98	—
Body-mass index >30 (%)§	32.0	32.0	31.8	—
Blood pressure				
Systolic (mm Hg)	121.3±16.1	128.7±21.3	126.9±15.8	0.02
Diastolic (mm Hg)	72.5±10.5	68.5±17.9	75.8±9.7	0.16
Systolic ≥140 mm Hg or diastolic ≥90 mm Hg (%)	24.5	22.6	23.2	0.80
GFR (ml/min/1.73 m²)¶	62.7±12.6	76.1±16.5	65.2±9.5	<0.001
Urinary albumin-to-creatinine ratio				
Natural-log–transformed value	2.22±1.7	2.28±1.0	NA	0.81
>0.03 (%)	17.3	11.3	NA	0.36
Hemoglobin (g/dl)	13.8±1.3	14.5±1.3	14.0±1.9	<0.001
Glucose (mg/dl)	90.9±9.8	102.3±16.2	100.6±25.9	<0.001
Cholesterol (mg/dl)	186.4±38.1	205.4±35.1	200.5±41.4	0.01
Triglycerides (mg/dl)	112.7±60.3	153.8±80.3	138.1±93.2	<0.01
High-density lipoprotein cholesterol (mg/dl)	50.3±17.4	54.4±16.4	54.7±17.6	0.12
Clinical conditions (%)‖				
Diabetes	5.7	11.3	7.1	0.17
Cancer	11.3	15.1	13.4	0.56
Coronary heart disease	3.8	9.4	4.5	0.17
Cerebrovascular accident or transient ischemic attack	1.9	3.8	1.9	0.56
Use of antihypertensive drugs (%)‖	39.6	37.7	40.4	0.85
Current smoker (%)‖	15.1	11.3	15.7	0.52

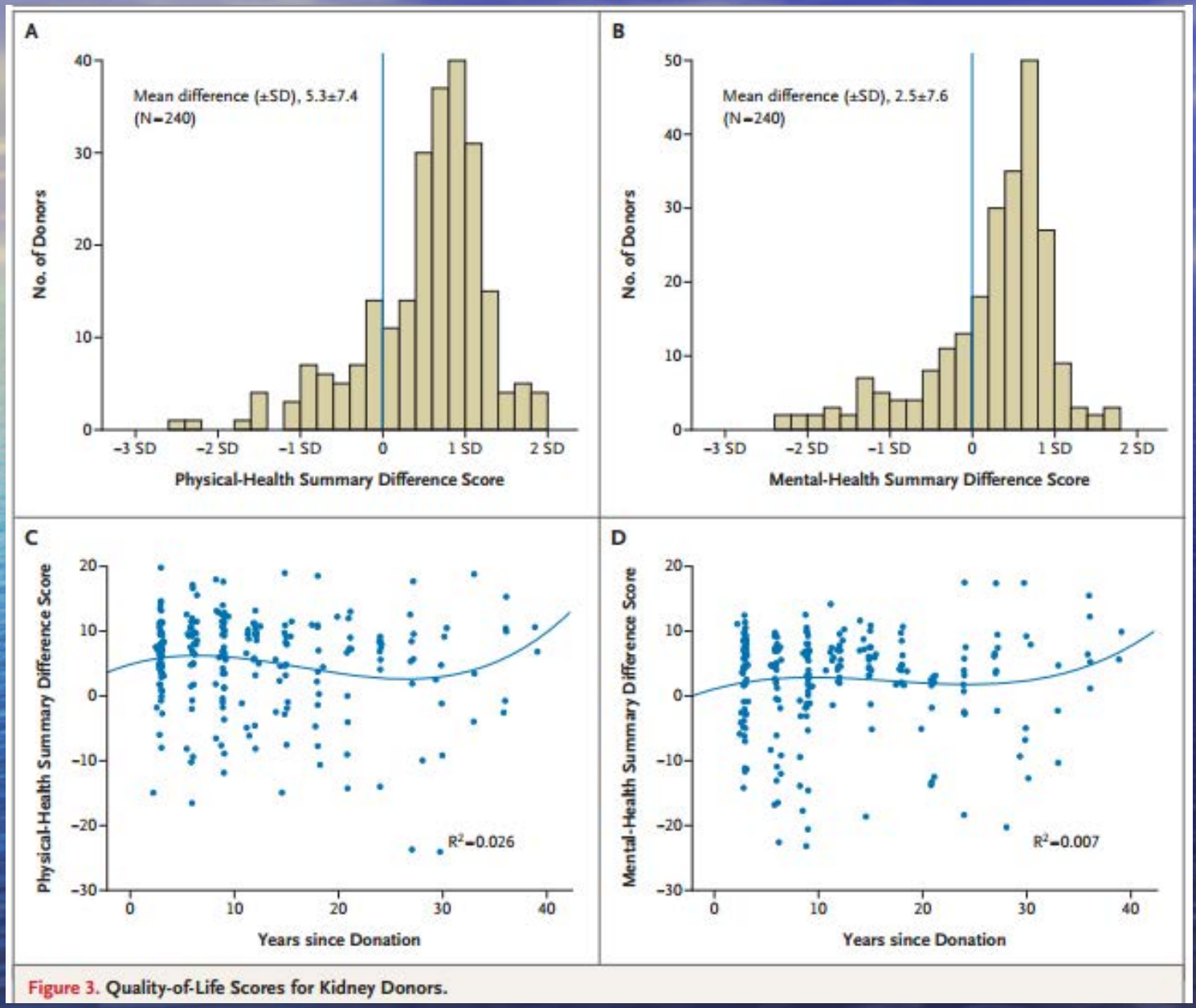


Figure 3. Quality-of-Life Scores for Kidney Donors.

Limitations

- 99% donors were Caucasian
- Increasing acceptance of older donors, those with HTN, obesity
- Relied on patient contact/recall for diagnosis of ESRD
- Control group gleaned from general population, vs. highly selected donor cohort

Along Came Polly

IN THEATERS JANUARY 16

Long-term risks for kidney donors

Geir Mjøen[1], Stein Hallan[2,3], Anders Hartmann[1], Aksel Foss[1], Karsten Midtvedt[1], Ole Øyen[1], Anna Reisæter[1], Per Pfeffer[1], Trond Jenssen[1], Torbjørn Leivestad[4], Pål- Dag Line[1], Magnus Øvrehus[2], Dag Olav Dale[1], Hege Pihlstrøm[1], Ingar Holme[5], Friedo W. Dekker[6] and Hallvard Holdaas[1]

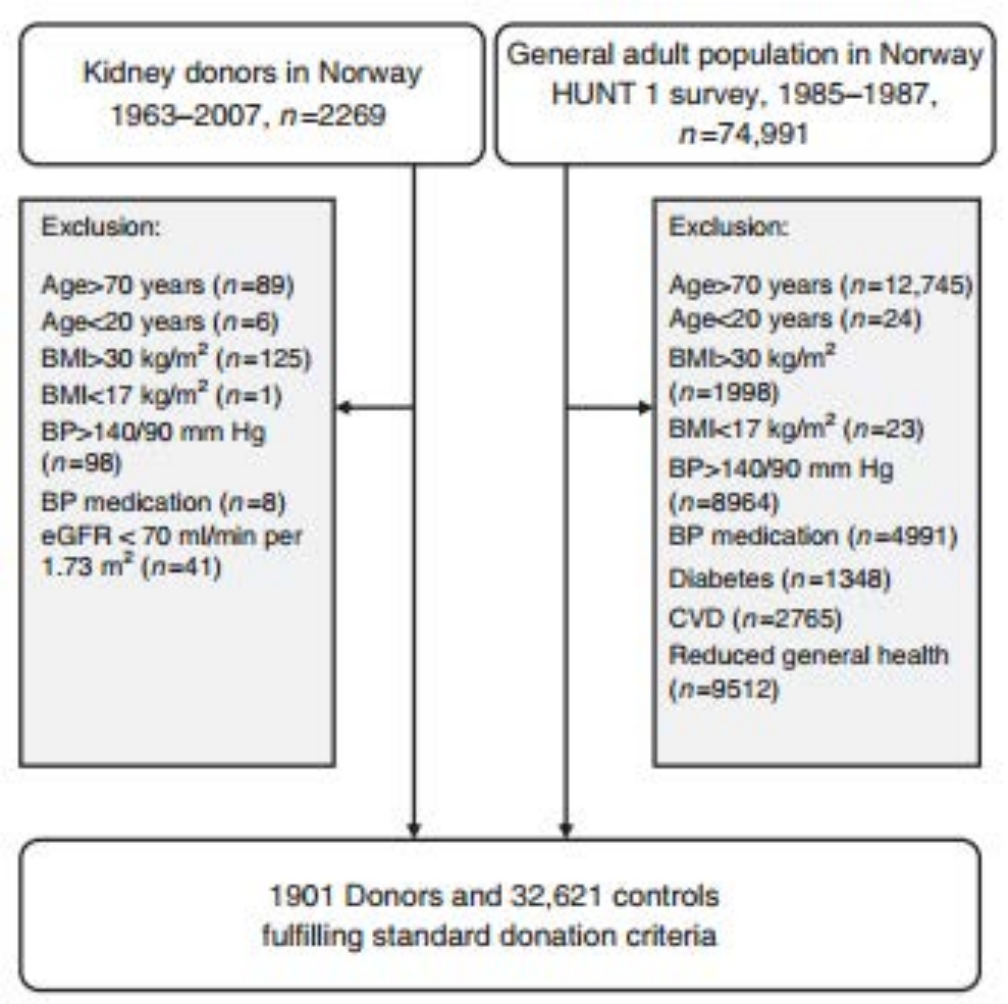


Table 1 | Baseline characteristics of kidney donors and controls

	Kidney donors	Controls
Age, years	46.0 ± 11.5	37.6 ± 11.7
	$n = 1901$	$n = 32{,}621$
Male gender, %	41.0	46.9
	$n = 1901$	$n = 32{,}621$
Current smoking, %	41.5	39.5
	$n = 1375$	$n = 25{,}993$
Systolic BP, mm Hg	123.3 ± 10.0	121.4 ± 10.4
	$n = 1768$	$n = 31{,}398$
Diastolic BP, mm Hg	77.4 ± 7.2	77.2 ± 7.9
	$n = 1768$	$n = 31{,}394$
BMI, kg/m^2	24.2 ± 2.8	23.5 ± 2.6
	$n = 1558$	$n = 31{,}421$

Abbreviations: BMI, body mass index; BP, blood pressure.

Mjoen et al. KI 2014. 86:162-7.

All Cause Mortality

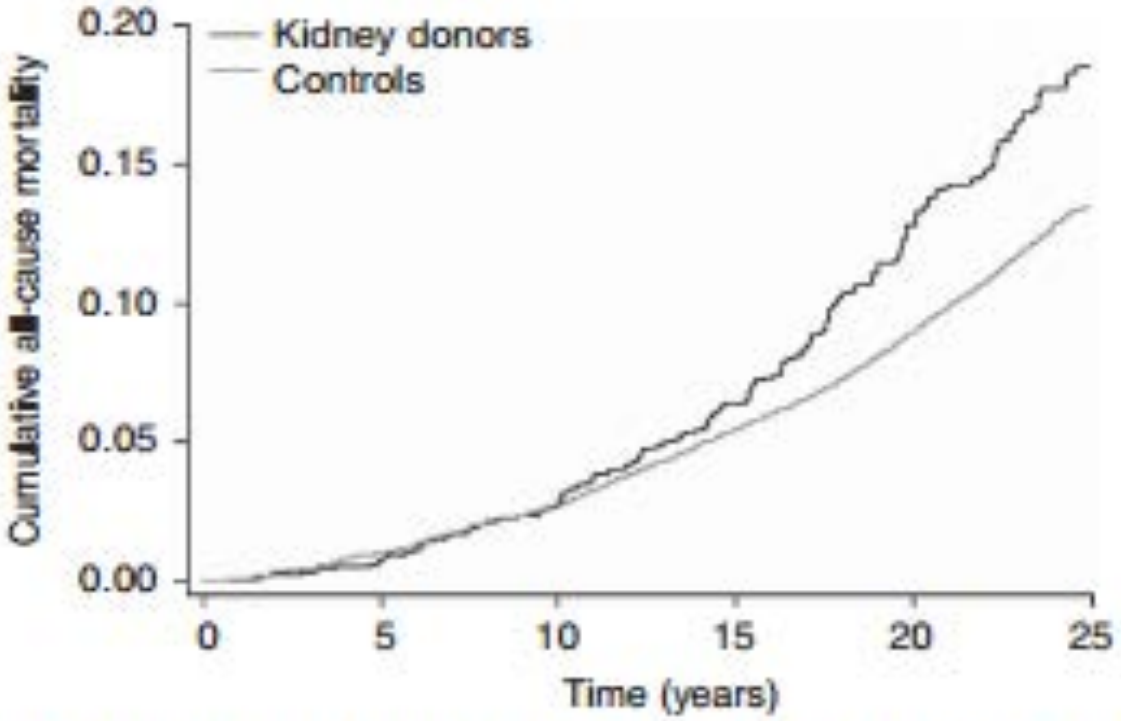


Figure 2 | Cumulative mortality risk in kidney donors and controls, adjusted for year of donation. Controls are matched to donors for age, sex, systolic blood pressure, body mass index, and smoking status.

All-Cause and CV Mortality

Table 2a | Hazard ratio for death by any cause in kidney donors versus controls

	Unadjusted ($n = 27{,}368$–$34{,}522$)	Adjusted 1[a] ($n = 2038/27{,}144$)	Adjusted 2[b] ($n = 2649/34{,}522$)
Kidney donation	2.49 (2.13–2.91, $P < 0.001$)	1.48 (1.17–1.88, $P = 0.001$)	1.30 (1.11–1.52, $P = 0.001$)
Inclusion year	0.95 (0.93–0.97, $P < 0.001$)	0.95 (0.93–0.98, $P < 0.001$)	0.97 (0.95–0.98, $P < 0.001$)
Age, years	1.10 (1.10–1.11, $P < 0.001$)	1.10 (1.10–1.11, $P < 0.001$)	1.10 (1.10–1.11, $P < 0.001$)
Male	1.62 (1.49–1.73, $P < 0.001$)	1.44 (1.32–1.58, $P < 0.001$)	1.52 (1.41–1.65, $P < 0.001$)
Systolic BP	1.04 (1.03–1.04, $P < 0.001$)	1.00 (1.00–1.01, $P = 0.45$)	1.00 (1.00–1.01, $P < 0.24$)
Smoking	1.64 (1.50–1.79, $P < 0.001$)	1.97 (1.80–2.15, $P < 0.001$)	1.91 (1.74–2.10, $P < 0.001$)
BMI	1.12 (1.11–1.14, $P < 0.001$)	1.02 (1.00–1.04, $P = 0.06$)	1.01 (0.99–1.03, $P = 0.21$)

Abbreviations: BMI, body mass index; BP, blood pressure.
[a]Adjusted for age, gender, year of inclusion, systolic BP, smoking, and BMI.
[b]After multiple imputation.

Table 2b | Hazard ratio for cardiovascular death in kidney donors versus controls

	Unadjusted ($n = 27{,}368$–$34{,}522$)	Adjusted 1[a] ($n = 568/27{,}144$)	Adjusted 2[b] ($n = 756/34{,}522$)
Kidney donation	3.18 (2.39–4.23, $P < 0.001$)	1.52 (0.95–2.43, $P = 0.08$)	1.40 (1.03–1.91, $P = 0.03$)
Inclusion year	0.90 (0.87–0.94, $P < 0.001$)	0.92 (0.87–0.98, $P = 0.005$)	0.95 (0.92–0.98, $P = 0.004$)
Age, years	1.13 (1.13–1.14, $P < 0.001$)	1.13 (1.12–1.14, $P < 0.001$)	1.13 (1.13–1.14, $P < 0.001$)
Male	2.23 (1.92–2.60, $P < 0.001$)	2.04 (1.71–2.44, $P < 0.001$)	2.04 (1.75–2.38, $P < 0.001$)
Systolic BP	1.05 (1.05–1.06, $P < 0.001$)	1.01 (1.00–1.02, $P = 0.15$)	1.01 (1.00–1.02, $P = 0.05$)
Smoking	1.82 (1.55–2.14, $P < 0.001$)	2.30 (1.94–2.72, $P < 0.001$)	2.10 (1.75–2.51, $P < 0.001$)
BMI	1.17 (1.14–1.21, $P < 0.001$)	1.05 (1.01–1.08, $P = 0.006$)	1.03 (1.00–1.07, $P = 0.03$)

Abbreviations: BMI, body mass index; BP, blood pressure.
[a]Adjusted for age, gender, year of inclusion, systolic BP, smoking, and BMI.
[b]After multiple imputation.

ESRD Risk in Donors

Table 2c | Cox regression analysis for risk of end-stage renal disease in kidney donors versus controls

	Unadjusted ($n = 25{,}063$–$35{,}222$)	Adjusted 1[a] ($n = 31/34{,}522$)	Adjusted 2[b] ($n = 31/34{,}522$)
Kidney donation	18.99 (8.63–41.76, $P < 0.001$)	11.42 (4.43–29.40, $P < 0.001$)	11.38 (4.37–29.63, $P < 0.001$)
Inclusion year	0.76 (0.70–0.83, $P < 0.001$)	0.91 (0.83–1.00, $P = 0.04$)	0.90 (0.82–0.99, $P = 0.03$)
Age, years	1.04 (1.01–1.07, $P = 0.003$)	1.03 (1.00–1.06, $P = 0.04$)	1.02 (0.99–1.05, $P = 0.13$)
Male	0.94 (0.46–1.91, $P = 0.86$)	1.04 (0.51–2.11, $P = 0.10$)	0.90 (0.43–1.88, $P = 0.77$)
Systolic BP	1.03 (1.00–1.07, $P = 0.14$)	—	1.01 (1.00–1.06, $P = 0.03$)
Smoking	1.09 (0.48–2.46, $P = 0.83$)	—	1.19 (0.51–2.76, $P = 0.68$)
BMI	1.19 (1.02–1.38, $P = 0.03$)	—	1.13 (0.96–1.32, $P = 0.14$)

Abbreviations: BMI, body mass index; BP, blood pressure.

[a]Adjusted for age, gender, and year of inclusion.

[b]After multiple imputation and further adjustments for blood pressure, BMI, and smoking.

- **Absolute risk of ESRD – 9/1901 donors = 0.47%**
- **Median time to ESRD 18.7 yrs**
- **7/9 cases of ESRD was caused by immunologic disease – hereditary component (most were close relatives)**
- **Crude incidence - 302/million person-yrs amongst donors vs. 100/milion person-yrs in Norway population**

Limitations

- 100% donors were Caucasian of Scandivian ancestry
- Most donors were relatives of recipients, not necessarily generalizable to LURT / non-directed donations
- Donors were selected from throughout Norway, while controls belonged to single county exceptionally low mortality rates
- Differing eras (donors 1963-2007) while controls 1984-87, with general mortality having improved between ‘63 and ’84
- Longer FU amongst controls may have affected mortality and ESRD rates

Research

Original Investigation

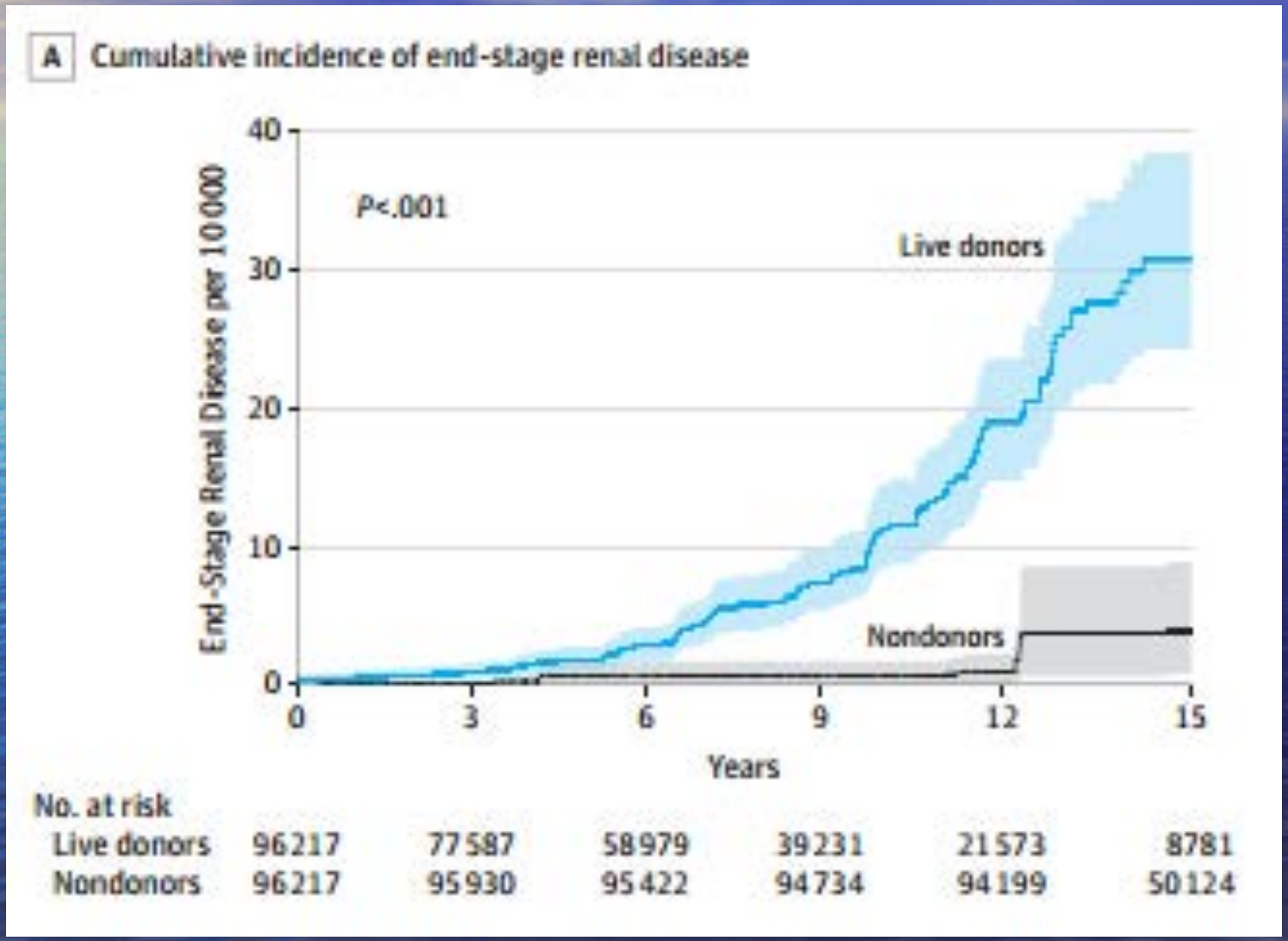
Risk of End-Stage Renal Disease Following Live Kidney Donation

Abimereki D. Muzaale, MD, MPH; Allan B. Massie, PhD; Mei-Cheng Wang, PhD; Robert A. Montgomery, MD, DPhil; Maureen A. McBride, PhD; Jennifer L. Wainright, PhD; Dorry L. Segev, MD, PhD

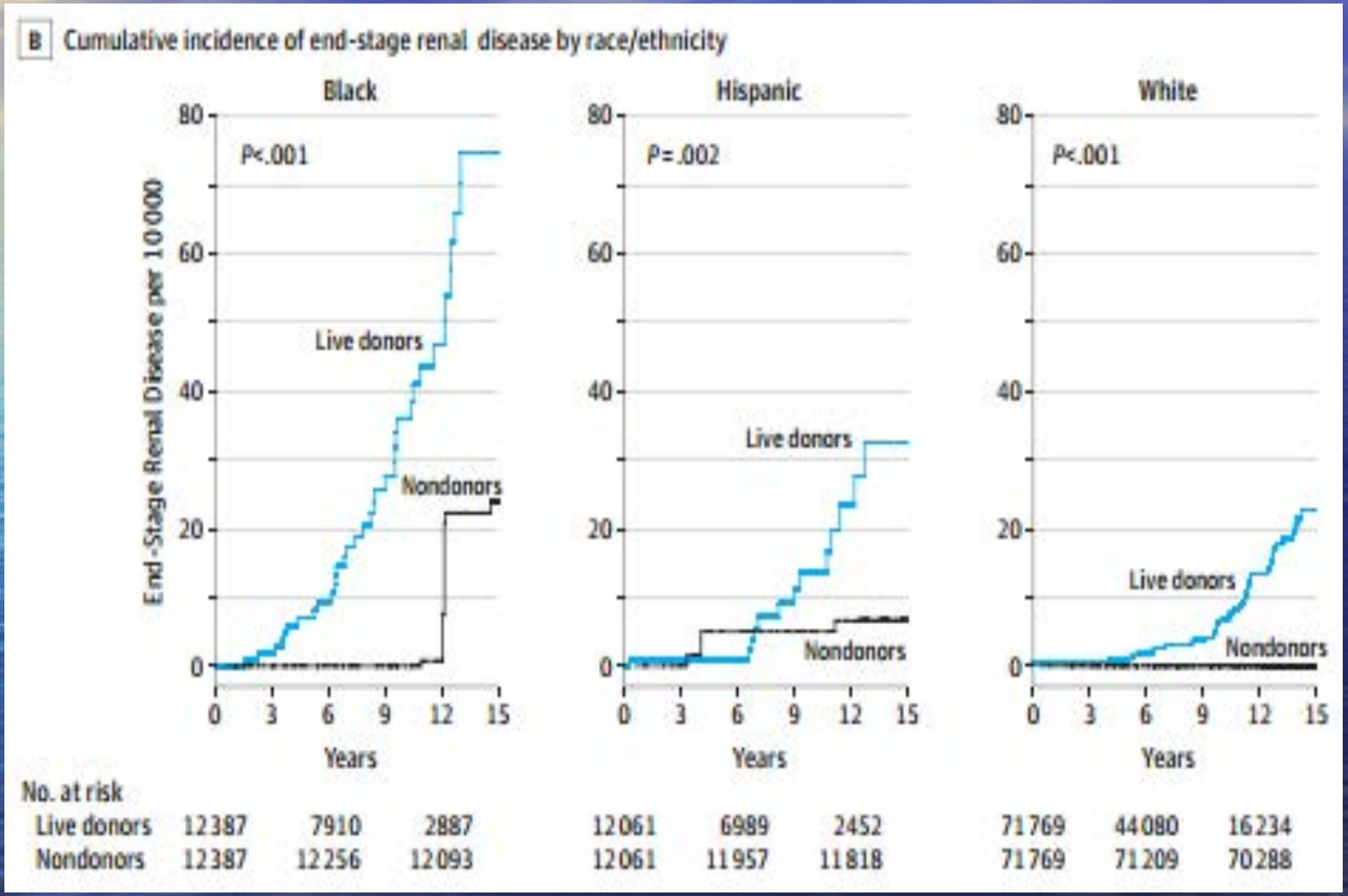
- 96,217 donors from 1994-2011
- 2/3 of live donors were biologically related to recipient
- Repeated matched done with 9364 non-donors, drawn from the NHANES '88-'94 cohort, who had no contraindications to donation
- ESRD defined as initiation of dialysis (CMS 2728), wait-listing for kidney transplant, or receipt of Ktx
- Baseline characteristics were similar, but noted 22% of donors had eGFR < 80 cc/min

Muzaale et al. JAMA 2014; 311: 579-86

Cumulative ESRD incidence



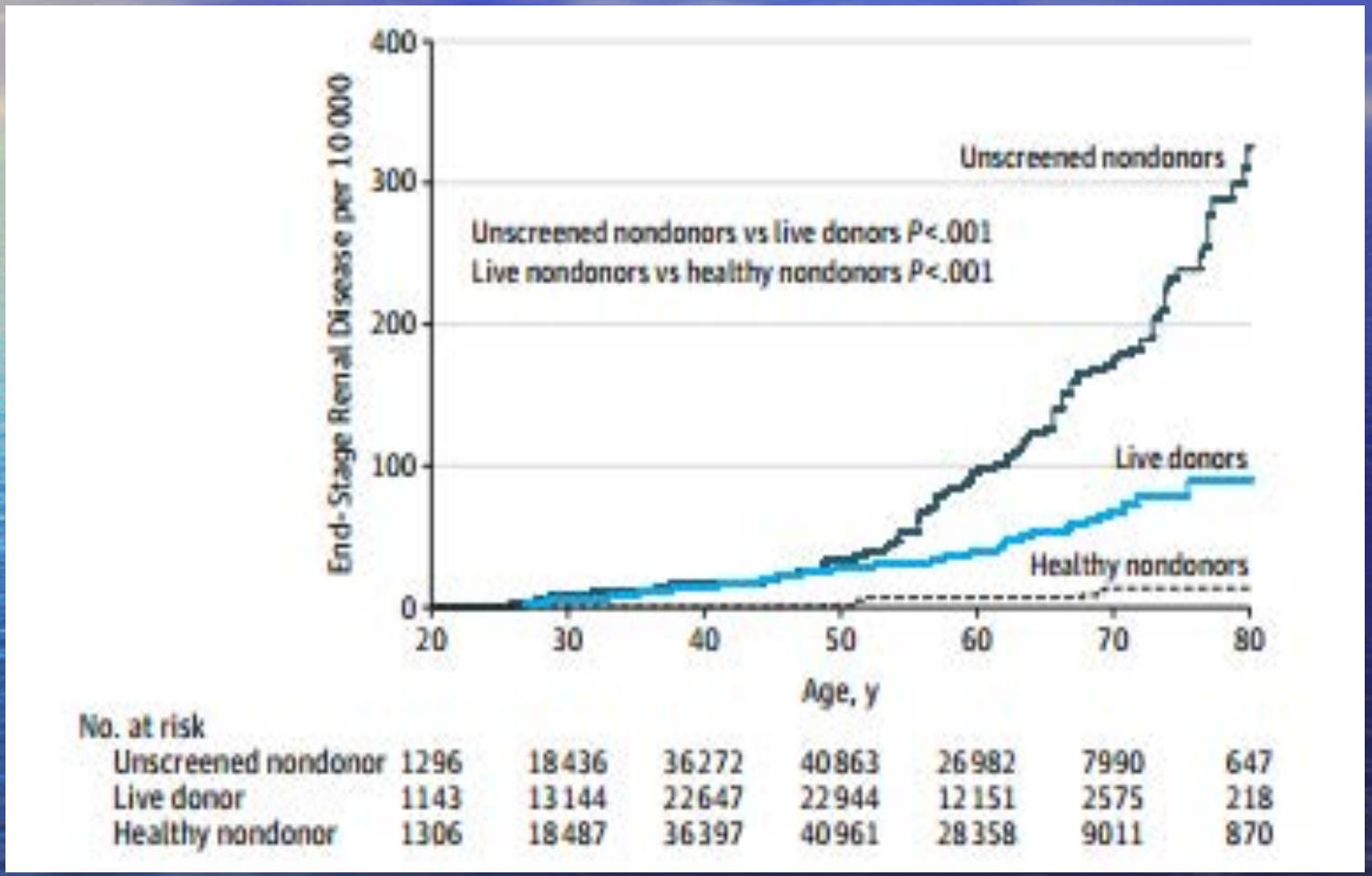
ESRD Incidence Stratified by Ethnicity



Absolute Risk Increases

	Donor (per 10,000)	Non-Donor (per 10,000)	ΔAR (per 10,000)
All	30.8	3.9	26.9
AA	74.7	23.9	50.8
Hispanics	32.6	6.7	25.9
Caucasian	22.7	0	22.7

Life-time Risk of ESRD



No. at risk							
Unscreened nondonor	1296	18436	36272	40863	26982	7990	647
Live donor	1143	13144	22647	22944	12151	2575	218
Healthy nondonor	1306	18487	36397	40961	28358	9011	870

Limitations

- Differing cohorts (donors 1994-2011, controls drawn from '88-94) – recent increased ESRD incidence
- Underestimation of ESRD risk in controls
  - a) Long event free survival repeatedly sampled
  - b) Different competing risks of death
- Increased surveillance for ESRD amongst donors
- Prioritization of previous donors to the waitlist for transplantation (so long as eGFR < 20cc/min)
- Crude vs.15 yr cumulative incidence of ESRD

Incidence	Donors (per 10,000)	Non-Donors (per 10,000)
Crude	10.3	18.2
15 yr cumulative	30.8	3.7

Focus on Absolute Risks

	% donors with ESRD
Mjoen et al.	0.47%
Muzaale et al.	0.1%

Muzaale et al.	15 yr risk %	Lifetime Risk %
Donors	0.0031	0.009
Healthy Controls	0.0004	0.0014
General Pop	N/A	0.033

Myth 4.

You can accept a kidney from any donor who offers

The New England
Journal of Medicine

Volume 280 APRIL 3, 1969 Number 14

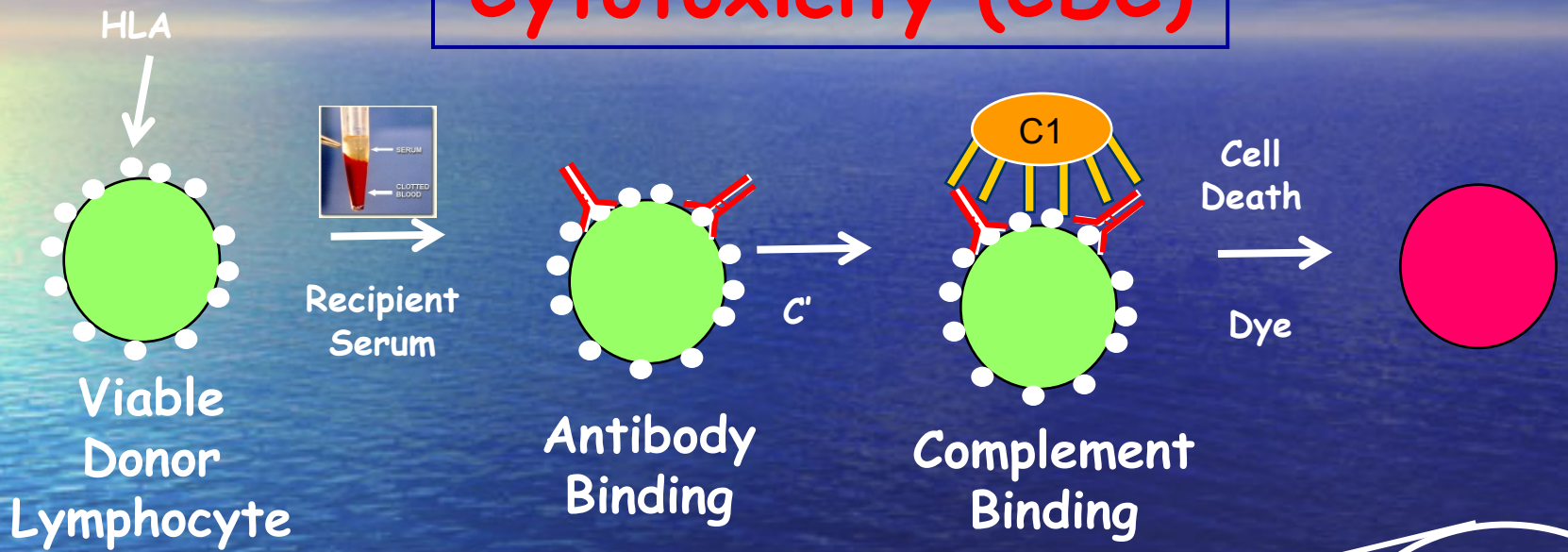
SIGNIFICANCE OF THE POSITIVE CROSSMATCH TEST IN KIDNEY TRANSPLANTATION*

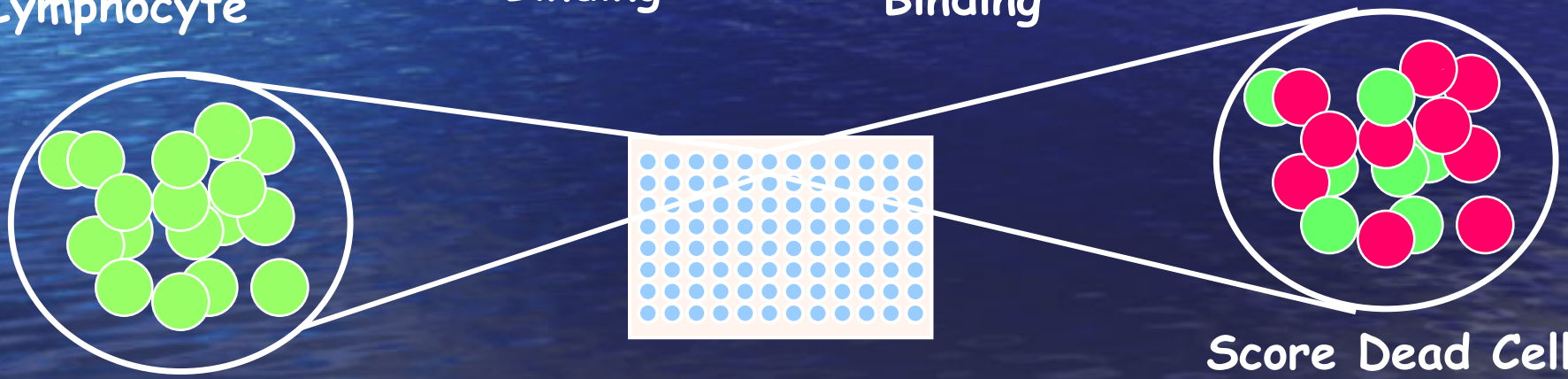
RAMON PATEL, M.R.C.P., AND PAUL I. TERASAKI, PH.D.

Crossmatch Detects HLA Antibodies

Donor Cells and Recipient Serum

Cytotoxicity (CDC)

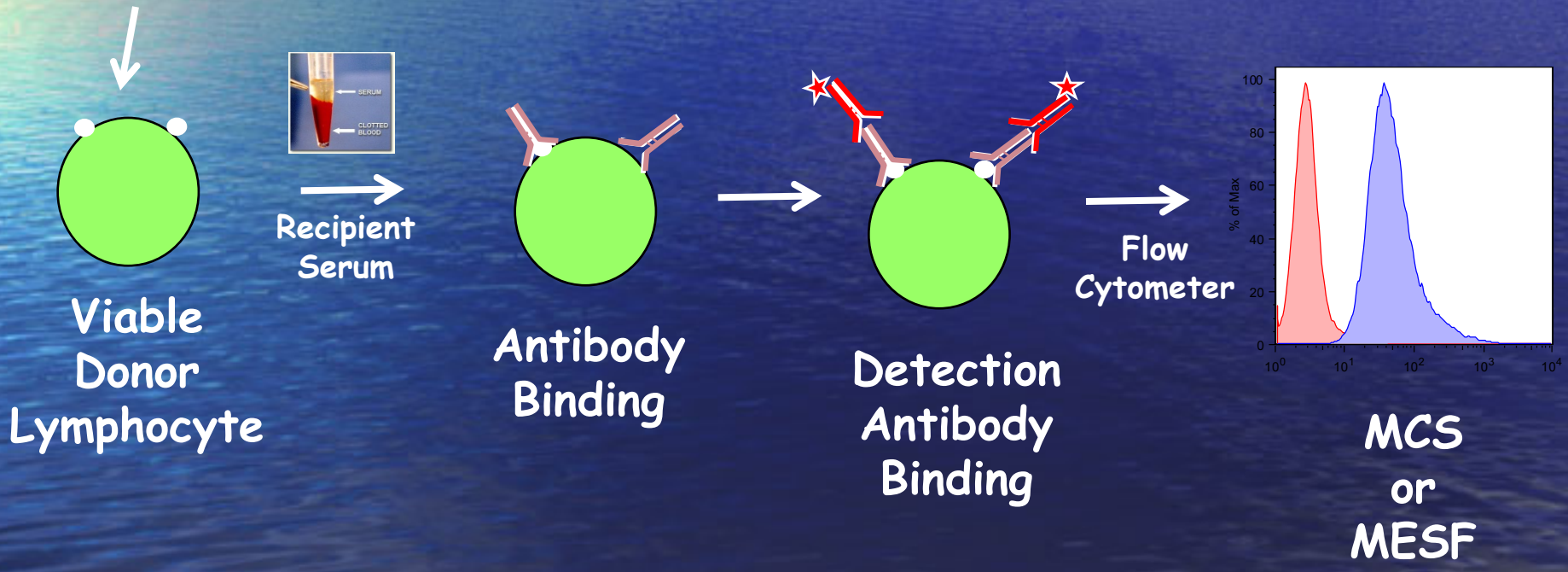




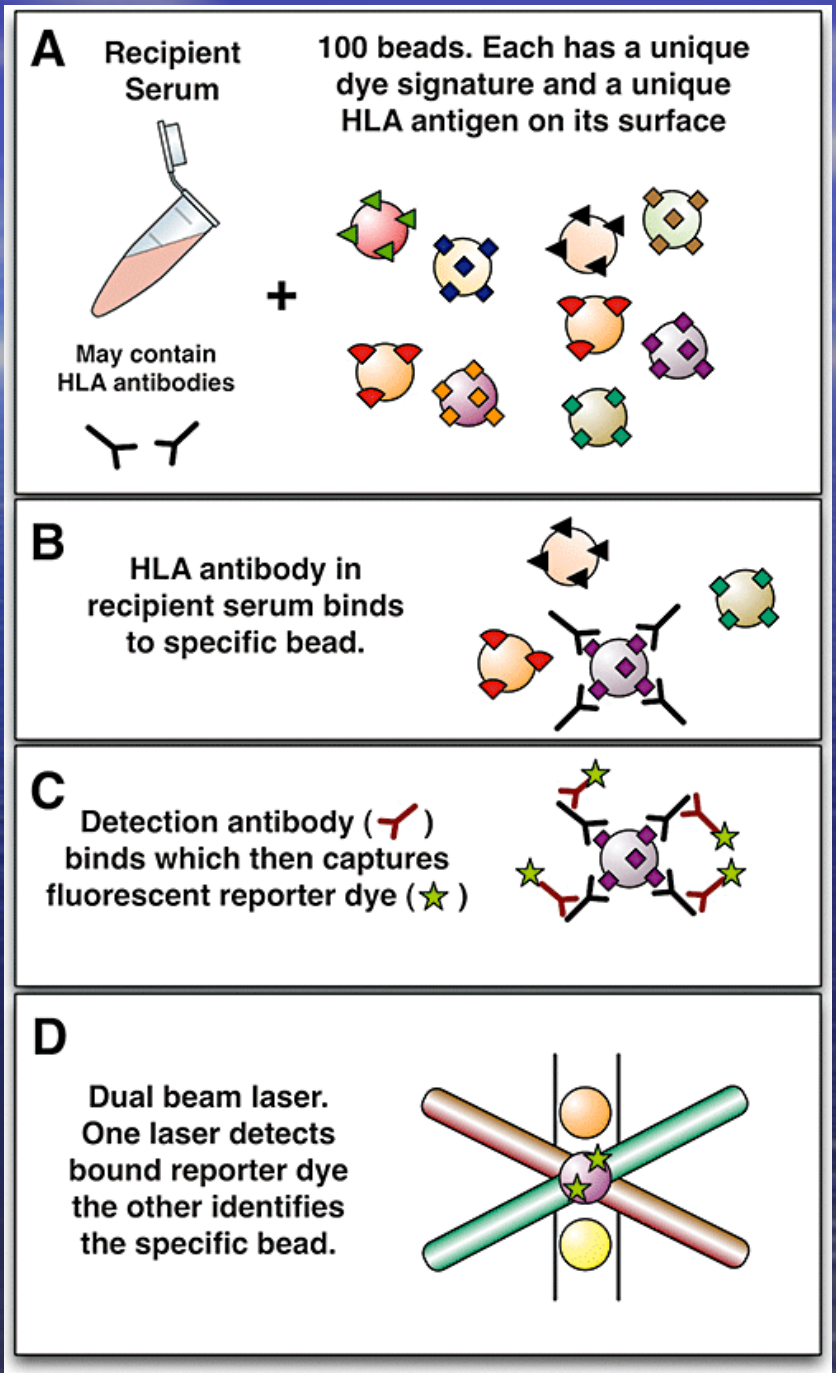
Crossmatch Detects HLA Antibodies

Donor Cells and Recipient Serum

Flow Cytometry Crossmatch



Virtual X-Match



Role of ABO Antigens in Transplantation

Expression of ABO antigens:

High: erythrocytes, vascular endothelium

Medium: gastrointestinal mucosa, bile ducts, urothelium

Low/Absent: glomeruli, hepatocytes

Blood Group (Phenotype)	Genotypes	Antibodies Present in Blood	Reaction When Blood from Groups Below Is Mixed with Antibodies from Groups at Left			
			O	A	B	AB
O	*ii*	Anti-A Anti-B				
A	$I^A I^A$ or $I^A i$	Anti-B				
B	$I^B I^B$ or $I^B i$	Anti-A				
AB	$I^A I^B$	—				

Myth 5.

If you mount a positive crossmatch against your intended donor, then all bets are off

Kidney Paired Donation/Exchange (KPD/E)

- National Kidney Registry (NKR)
- Single Center PKE

National Kidney Registry (NKR) Paired Exchange Program

- NKR founded by Garet Hil, February 2008
  www.kidneyregistry.org
- Built a sophisticated computer software program that facilitates ABO and HLA compatible transplants for those with an incompatible donor
- NKR has facilitated >3600 transplants to date
- >200 patients at UCSF have undergone living donor kidney transplantation through the NKR program

TYPES OF PATIENTS ENROLLED IN NKR

- Incompatible Donor-Recipient pairs
- Compatible pairs
- Patients without a living donor (CHIP)
  - Pediatric patients or those highly sensitized
- Non Directed Donors

Types of Exchanges

2-Way Swap

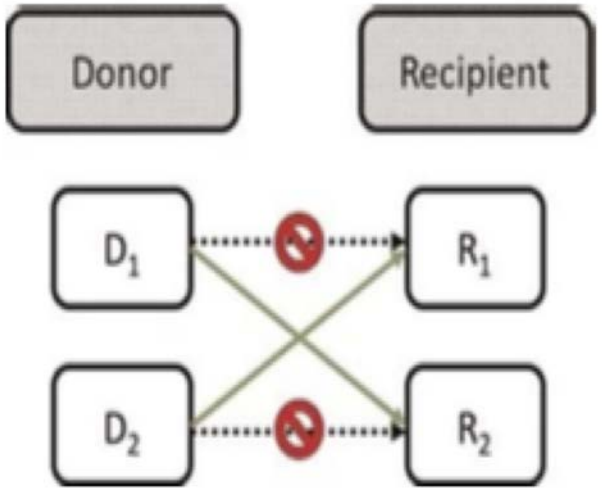
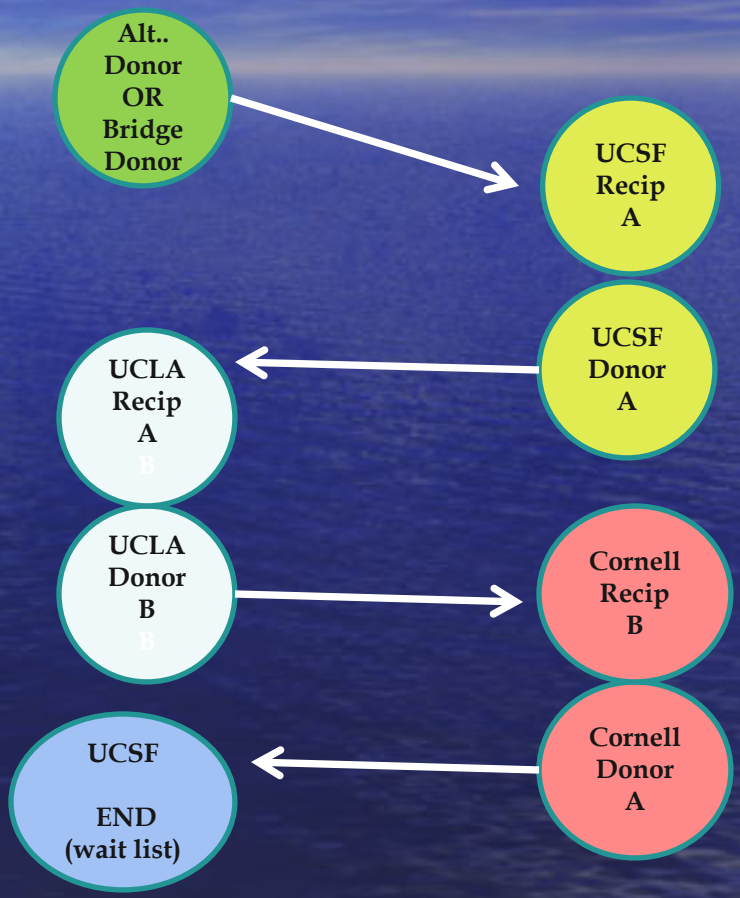


FIGURE 1. Kidney paired donation. A two-way swap is demonstrated, where the donor of the first incompatible pair donates to the recipient of the second incompatible pair and vice versa.

CHAINS



UCSF Medical Center
Transplant Service

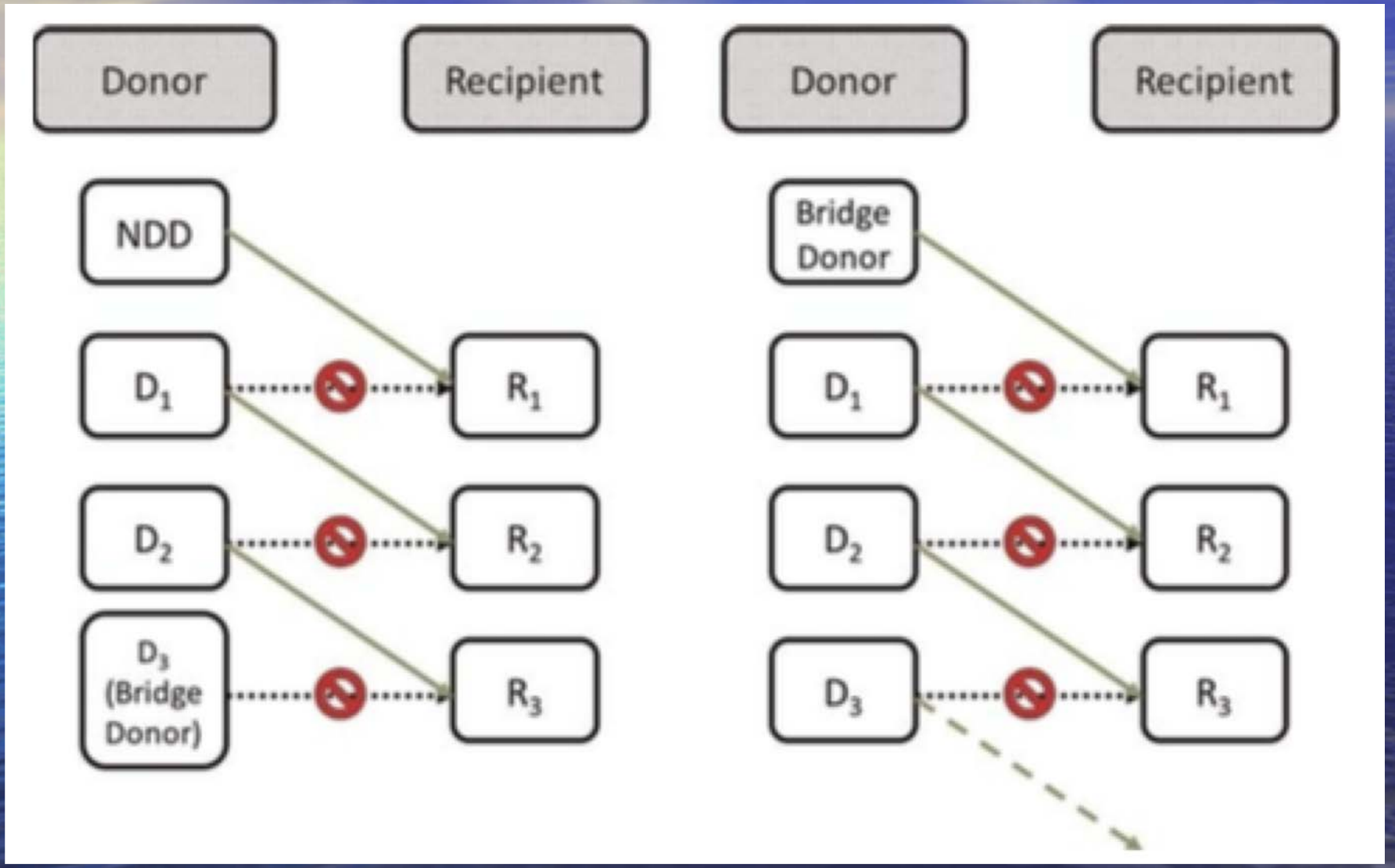
HEALTH

60 Lives, 30 Kidneys, All Linked

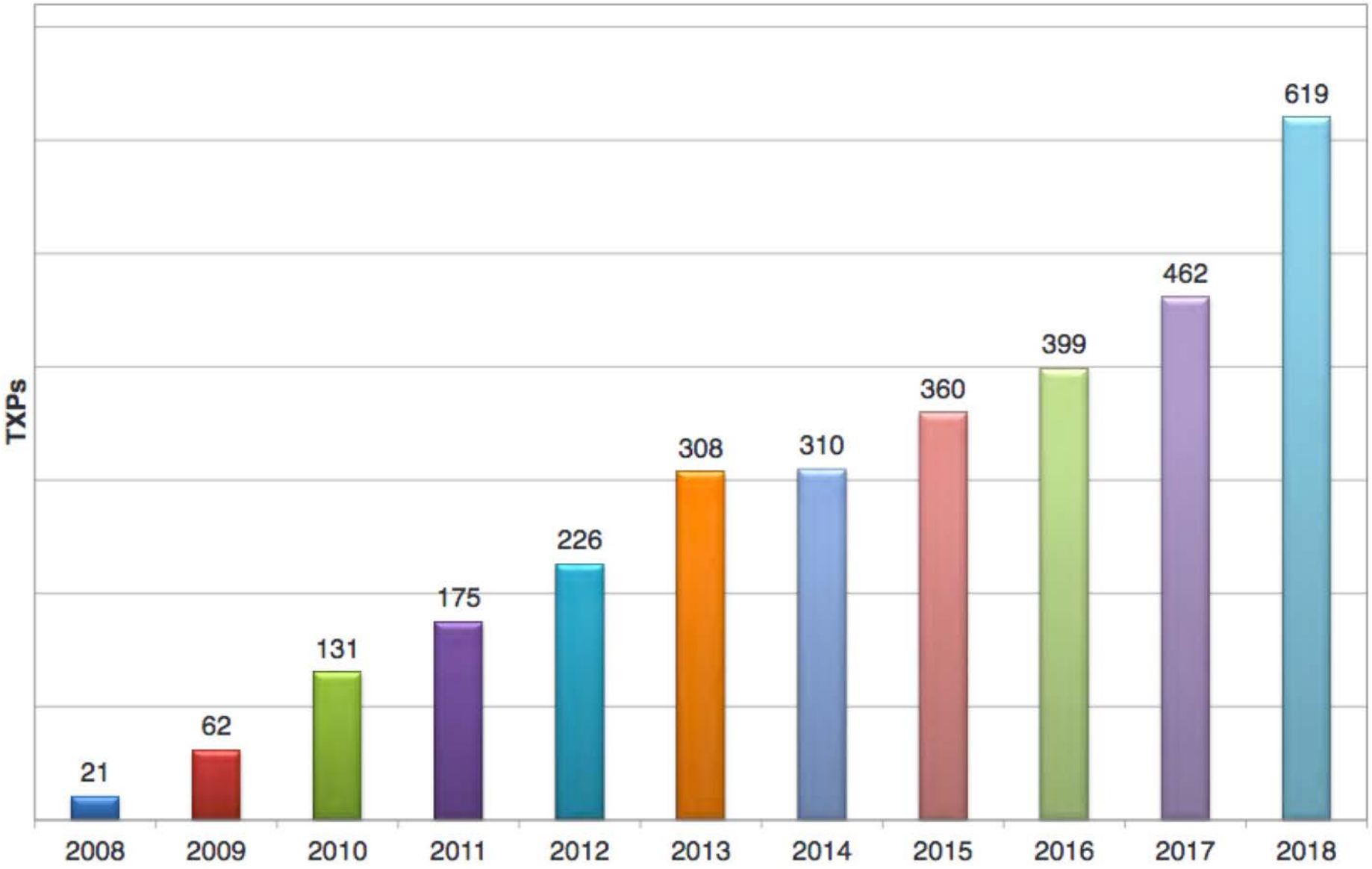
By **KEVIN SACK** FEB. 18, 2012

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.

Bridge Donor Chains

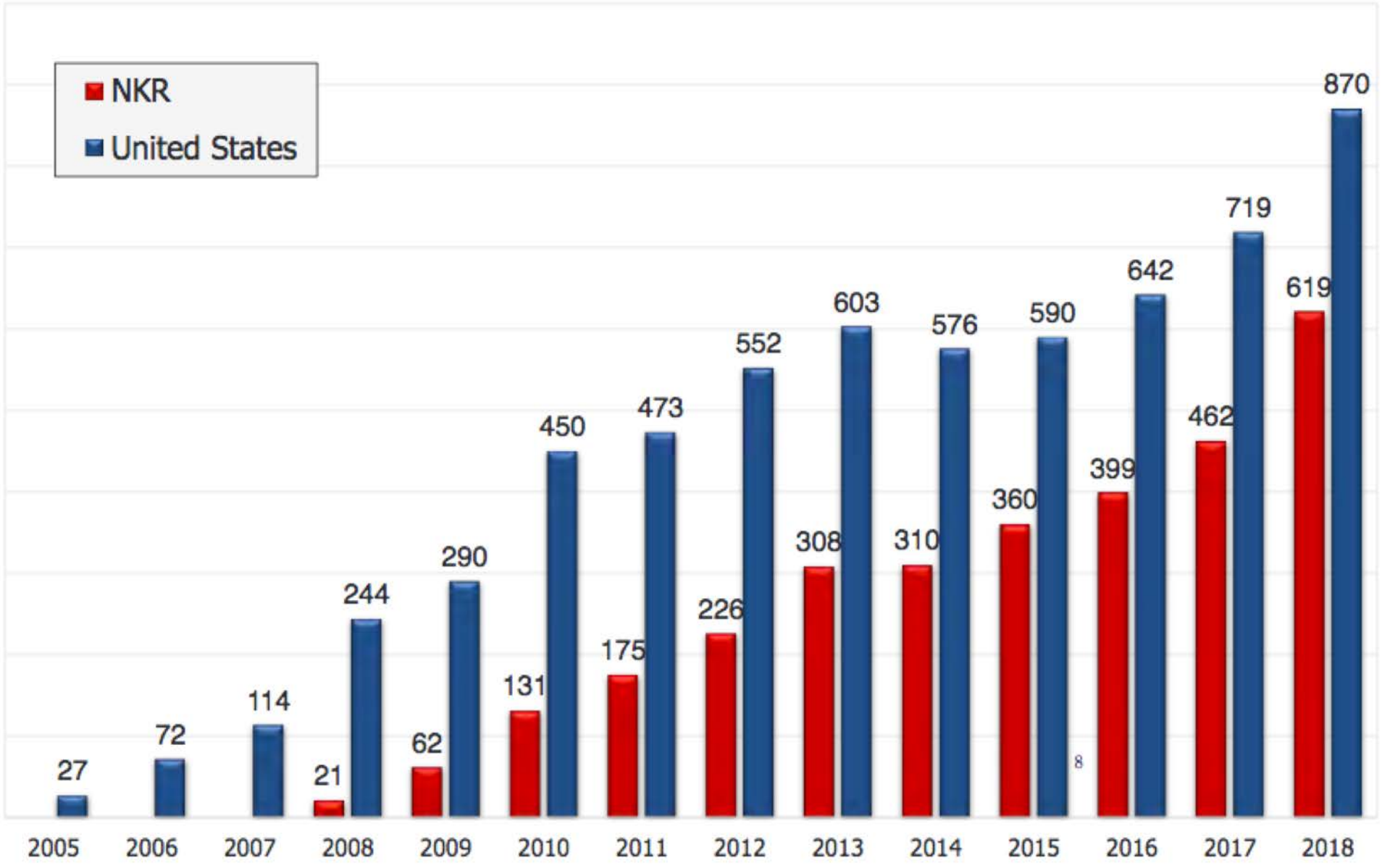


KPD Transplants Facilitated



https://www.kidneyregistry.org/pages/p508/NKR_QtrlyReport_Q4_2018.php

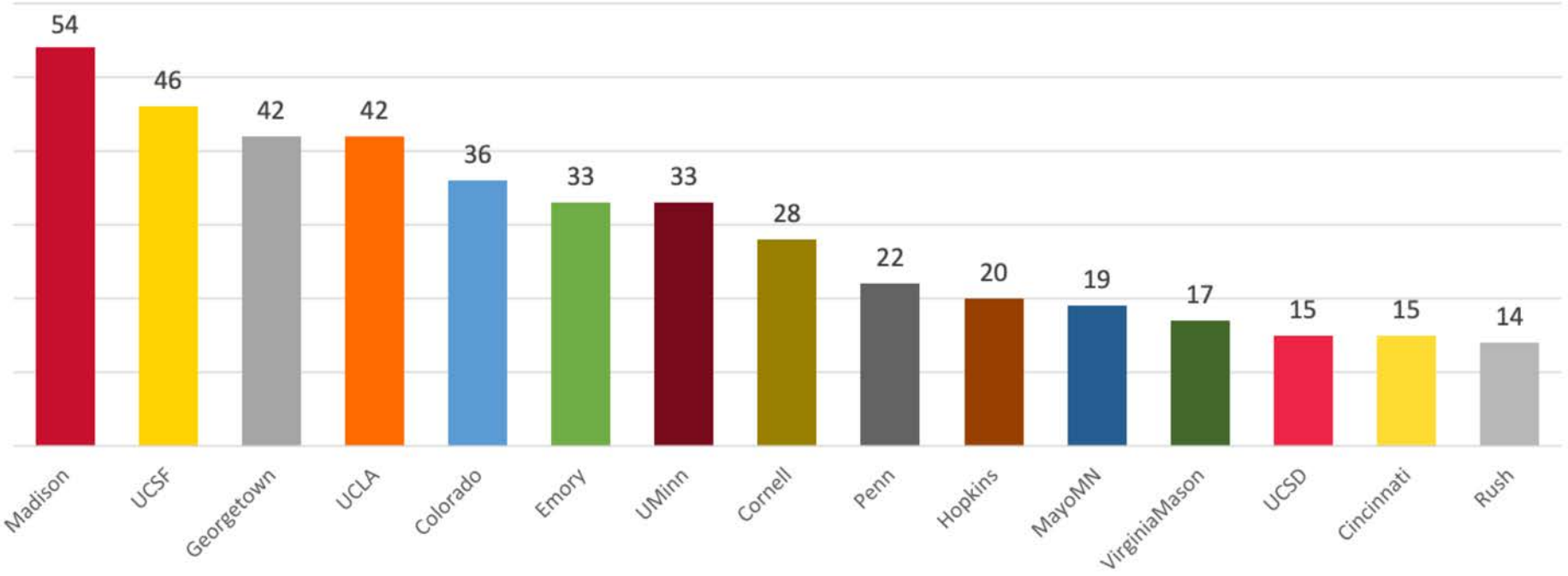
KPD Trends in the US



*Organ Procurement and Transplantation Network. https://optn.transplant.hrsa.gov/ Accessed 10/31/18

Top Centers

Transplants Last 12 Months



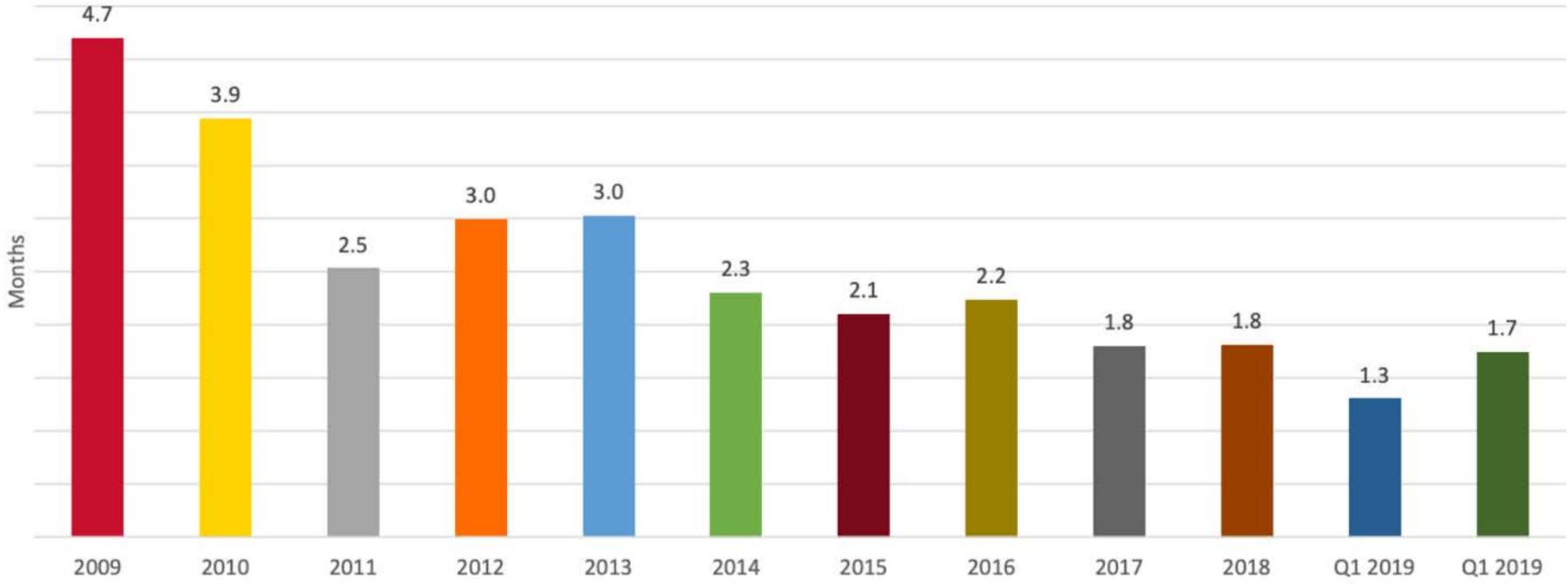
*As of 7/22/19

NATIONAL KIDNEY REGISTRY
FACILITATING LIVING DONOR TRANSPLANTS

https://www.kidneyregistry.org/pages/p534/NKRQ2-2019report.php

Transplanted Patient Median Wait Time

Wait times of patients transplanted during prior 12 months

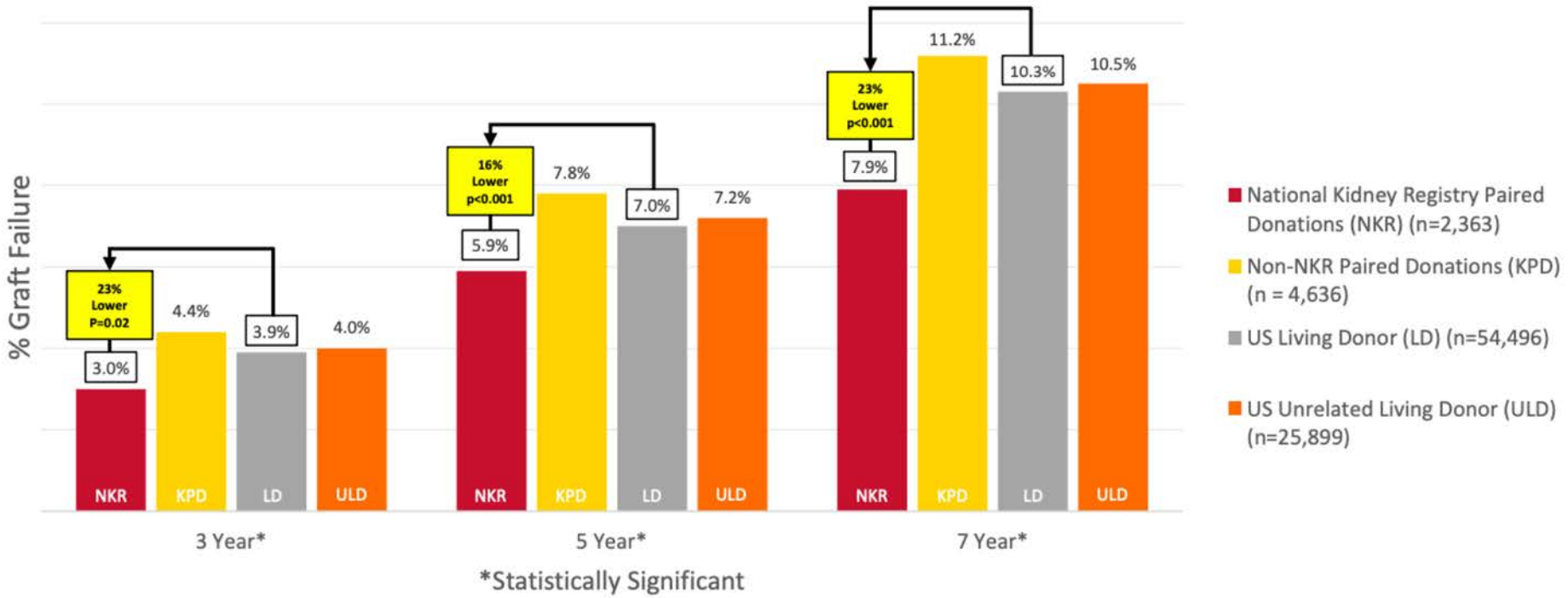


* As of 6/30/19

NATIONAL KIDNEY REGISTRY
FACILITATING LIVING DONOR TRANSPLANTS

https://www.kidneyregistry.org/pages/p534/NKRQ2-2019report.php

Death Censored Graft Failure Comparisons



*Provided courtesy of Johns Hopkins University School of Medicine, Department of Surgery *Not including CHIP patients;*
Kaplan-Meier GS Rates for Transplants Performed: 02/2008-06/2018 with follow-up through 2/28/2019 https://www.srtr.org/ SRTR data as of March, 2019

https://www.kidneyregistry.org/pages/p534/NKRQ2-2019report.php

Myth 6.

Flying living donor kidneys over long distances would damage them

ORIGINAL ARTICLE

Shipping living donor kidneys and transplant recipient outcomes

Eric Treat[1] | Eric K. H. Chow[2,3] | John D. Peipert[4,5] | Amy Waterman[4,5] | Lorna Kwan[6] | Allan B. Massie[2,3,7] | Alvin G. Thomas[2,3] | Mary Grace Bowring[2,3] | David Leeser[8] | Stuart Flechner[9] | Marc L. Melcher[10] | Sandip Kapur[11] | Dorry L. Segev[2,3,7] | Jeffrey Veale[6]

- KPD transplant done through NKR 2/1/08 through 11/30/15
- Data linked to SRTR via UNOS identifiers
- 1267 Shipped KPD kidneys vs. 205 In-center KPD kidneys vs. 4800 non KPD kidneys (at centers not participating in NKR during same period)
- Predictor – Cold Ischemic Time (CIT)
- Primary outcome measure – Delayed Graft Function (adjusted for donor and recipient factors, dialysis vintage, pre-emptive transplant, cause of ESRD, HLA matching, PRA, year of transplant and prior transplants)
- Secondary outcomes – All-Cause Graft Failure, Death Censored Graft Failure, Mortality (SRTR adjustments made)
- Interaction term inserted for donor age > 50 when looking at association between CIT and outcomes

Treat et al. AJT 2018; 18:632-641

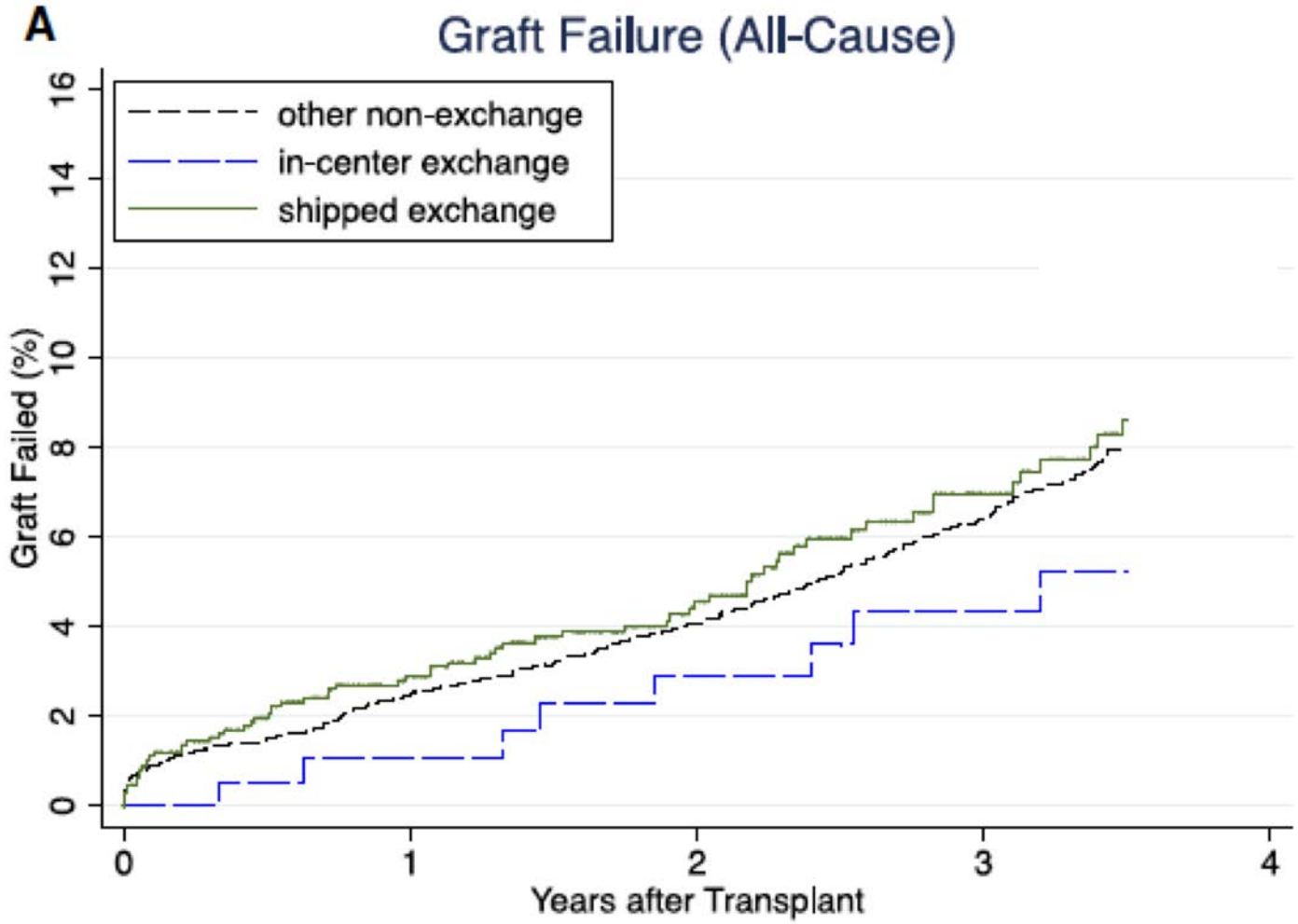
TABLE 1 Study sample characteristics

	Shipped exchange n = 1267	In-center exchange n = 205	*P* value[b]	Other nonexchange n = 4800	*P* value[b]
Cold ischemia time (h)[a]	9.3 (6.9-12.2)	1.0 (0.8-1.5)	<.001	0.9 (0.5-1.0)	<.001
Recipient					
Age, y[a]	50 (39-60)	50 (39-60)	>.9	50 (41-59)	.6
Female	599 (47%)	74 (36%)	<.01	1557 (32%)	<.001
Diabetic	307 (24%)	53 (26%)	.6	1349 (28%)	<.01
Primary diagnosis					
DM	232 (18%)	46 (23%)	.07	1078 (22%)	<.001
GN	412 (33%)	60 (29%)		1401 (29%)	
PKD	158 (12%)	30 (15%)		824 (17%)	
Congenital	48 (3.8%)	1 (0.5%)		108 (2.3%)	
Other	417 (33%)	68 (33%)		1389 (29%)	
Years on RRT[a]	1.4 (0.2-2.9)	1.8 (0.6-3.6)	.048	0.5 (0-1.6)	<.001
Previous transplant	358 (28%)	35 (17%)	.001	504 (11%)	<.001
Preemptive transplant	306 (24%)	40 (20%)	.1	1818 (38%)	<.001
Black (vs nonblack)	211 (17%)	50 (24%)	<.01	554 (12%)	<.001
PRA at transplant					
0	522 (41%)	119 (58%)	<.001	3291 (69%)	<.001
1-10	67 (5.3%)	14 (6.8%)		327 (6.8%)	
11-79	347 (27%)	39 (19%)		661 (14%)	
≥80	324 (26%)	26 (13%)		111 (2.3%)	
Missing	7 (0.6%)	7 (3.4%)		410 (8.5%)	
BMI[a]	27 (23-31)	26 (23-31)	.3	27 (24-31)	<.01
Donor					
Age, y[a]	45 (35-52)	48 (38-56)	<.01	45 (36-53)	.02
Female	789 (62%)	126 (62%)	.8	3217 (67%)	<.01
Black (vs nonblack)	137 (11%)	24 (12%)	.7	385 (8.0%)	<.01
LD KDPI[a]	12.2 (−0.84-25.0)	12.0 (−0.51-31.3)	.4	15.2 (1.86-30.1)	<.001
HLA mismatches					
0	9 (0.7%)	0	.08	17 (0.4%)	<.001
1	29 (2.3%)	3 (1.5%)		38 (0.8%)	
2	81 (6.4%)	10 (4.9%)		207 (4.3%)	
3	198 (16%)	38 (19%)		633 (13%)	
4	340 (27%)	44 (22%)		1348 (28%)	
5	404 (32%)	68 (33%)		1620 (34%)	
6	182 (14%)	41 (20%)		907 (19%)	
Missing	22 (1.7%)	0		30 (0.6%)	
Year of transplant[a]	2013 (2012-2014)	2012 (2010-2014)	<.001	2012 (2010-2014)	<.001

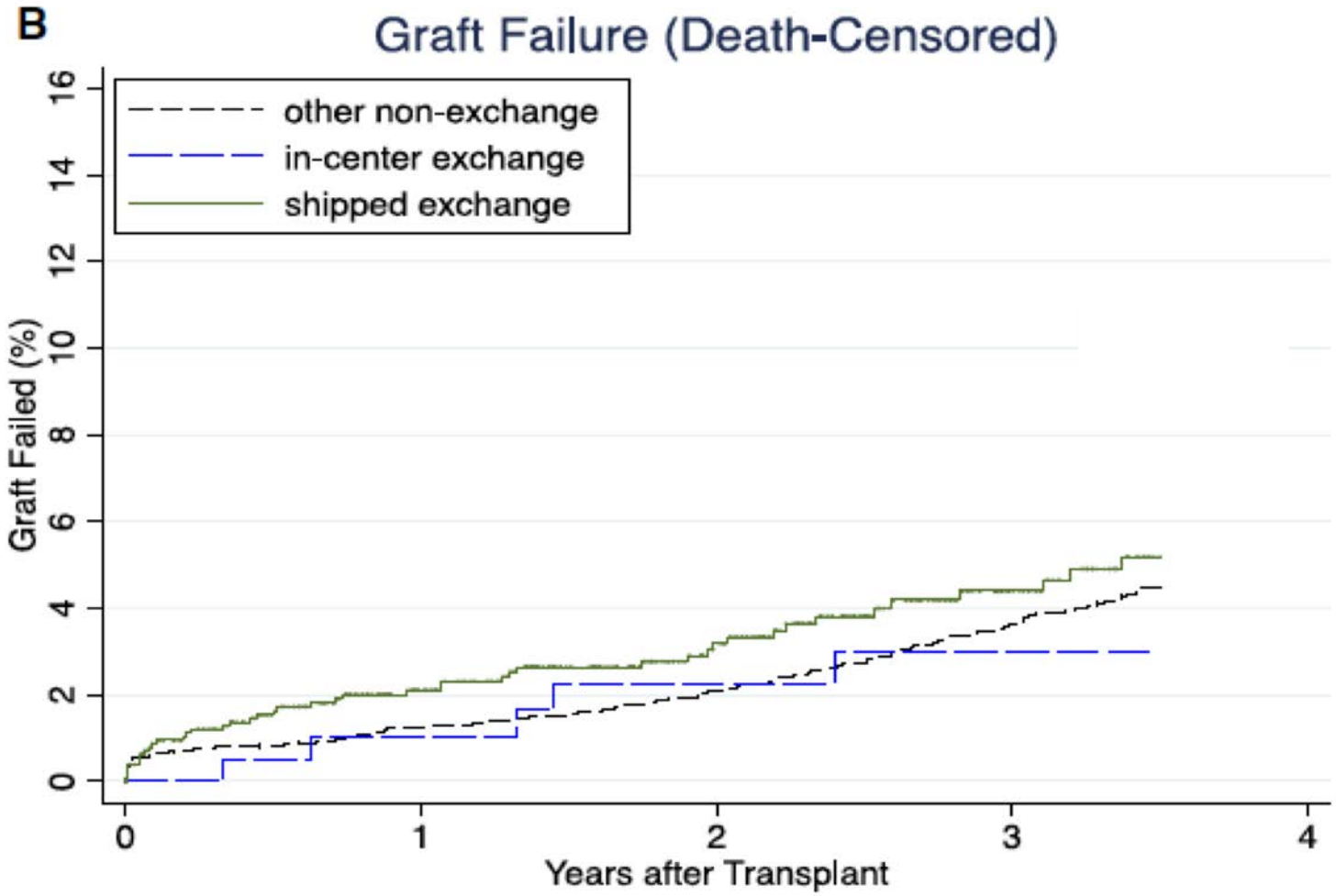
FIGURE 1 Geographic distribution of shipped kidneys. A total of 1267 KPD transplants were shipped. The median shipping distance was 733 miles (1.5-2717 mile range)

TABLE 2 Risk factors for delayed graft function among KPD and non-KPD living kidney donor transplant recipients

	aOR (95% CI)	*P* value
Cold ischemia time (/h)	1.05 (1.02-1.09)	<.01
Black recipient	2.37 (1.71-3.28)	<.001
Female recipient	0.74 (0.54-1.03)	.07
Recipient BMI (centered at 25)	1.00 (1.00-1.00)	.8
Diabetic recipient	1.39 (1.02-1.89)	.04
Primary diagnosis of congenital disease	2.30 (1.07-4.98)	.03
PRA at transplant		
0	REF	-
1-10	0.78	.4
11-79	1.00	>.9
80+	0.93	.8
Preemptive transplant	0.30 (0.19-0.49)	<.001
Previous transplant	1.08 (0.69-1.67)	.7
Years of RRT	1.10 (1.05-1.15)	<.001
LD KDPI	1.01 (1.00-1.02)	<.01
Year of transplant	0.92 (0.86-0.99)	.02



	aHR (95% CI)	*P* value
Cold ischemia time (/h)	1.01 (0.98-1.04)	.4



	aHR (95% CI)	*P* value
Cold ischemia time (/h)	1.02 (0.98-1.06)	.4

	aHR (95% CI)	*P* value
Cold ischemia time (/h)	1.00 (0.96-1.04)	>.9

Myth 7.

The donor and the recipient must undergo surgeries at the same time

Advanced Donation Program (ADP)

- Donor donates ahead of planned surgery for their intended recipient
- Various reasons, usually revolving around specific time frame
- Only centers in good standing are allowed to participate, not likely to cease performing transplant operations
- There are NO GUARANTEES that recipient will match for transplant

American Journal of Transplantation 2015; XX: 1–6
Wiley Periodicals Inc.

Brief Communication

The Incorporation of an Advanced Donation Program Into Kidney Paired Exchange: Initial Experience of the National Kidney Registry

S. M. Flechner[1,*], D. Leeser[2], R. Pelletier[3], M. Morgievich[4], K. Miller[5], L. Thompson[2], S. McGuire[6], J. Sinacore[7] and G. Hil[7]

Flechner et al. AJT 2015. 15:1-6

First 10 ADP Donor-Recip Pairs

Table 4: Characteristics of first ten ADP participants

ADP kidney donor					Paired recipient entered with ADP donor				
Cases	Age (years)	Gender M/F	ABO group		Age (years)	Gender M/F	ABO group	cPRA %	Interval (days)
1	34[1]	F	B	friend	42	M	A	0	10
2	36[2]	M	O	son	68	F	O	58	138
3	52[3]	F	A	spouse	58	M	O	0	14
4	62[3]	F	A	sibling	57	M	B	0	448
5	62[4]	M	A	spouse	60	F	O	96	562
6	47[5]	M	A	friend	73	M	O	0	67
7	54[1]	M	O	friend	67	F	A	98	pending
8	45[5]	M	A	friend	61	M	A	28	176
9	50[1]	F	O	friend	76	F	O	90	pending
10	51[1]	F	O	friend	69	F	A	15	15

Reasons given for entering the ADP:

[1]Return to work, school, business.

[2]Military leave.

[3]Donor recovery to aid in care of recipient.

[4]Future need of paired recipient.

[5]Intercurrent recipient medical or surgical problem.

ADP, Advanced Donor Program; cPRA, calculated percent reactive antibody.

Table 1: Case 1: ADP interval 19 months

Center	Donor	Age (years)	ABO	Center	Recipient	Age (years)	ABO	cPRA	Date
1	D1 ADP	62	A	2	R2	78	A	25	10-18-2011
2	D2	47	A	3	R3	64	A	66	10-18-2011
3	D3	60	B	4	R4	70	B	0	10-19-2011
5	D4	30	O	5	R5	40	O	0	10-8-2013
6	D5	35	A	7	R6	52	A	96.3	10-8-2013
7	D6	51	O	8	R7	56	O	99	10-8-2013
8	D7	23	O	9	R8	65	O	0	10-8-2013
9	D8	36	A	7	R9	37	O	99.7	10-10-2013
7	D9	44	O	10	R10	49	O	98.3	10-10-2013
10	D10	46	O	1	R1	60	O	95.2	10-10-2013

R1 is the paired ADP recipient eventually transplanted.

ADP, Advanced Donor Program; cPRA, calculated percent reactive antibody.

Flechner et al. AJT 2015. 15:1-6

National Kidney Registry

Advanced Donation Program

Informed Consent
Intended Donor

Version 1.4

Intended Donor's Government Issued Photo Identification

The Program: The Advanced Donation Program "ADP" allows a medically and psychosocially acceptable Intended Donor "ID" to donate their kidney via human organ paired donation (more commonly referred to as a swap) before their Intended Recipient "IR" is scheduled to receive a transplant via a swap. The ADP may be preferred by donors or patients due to schedules, availability and/or preferences. Some IR's may have residual kidney function but their diagnosis of chronic renal disease is medically predictive of decreasing renal function eventually requiring renal replacement therapy. Both surgeries must take place at the same transplant center. Once the ID donation has occurred, the IR may be activated by their transplant center for matching within the NKR. The ADP program is unrelated to the U.S. deceased donor system and participation in the ADP program does not confer any wait time points for the IR in the deceased donor system.

Your Situation: I would like to participate in the ADP and I am willing to donate a kidney to an NKR patient and understand that my donation would give my IR a prioritized opportunity to receive a kidney as part of a swap within the NKR.

Information Release: I consent to the disclosure of all my health, medical, and personal information to the NKR for the purpose of participating in the ADP. I authorize the NKR to disclose, disseminate and utilize my health, medical and personal information in conducting the ADP, and I waive any and all privacy law claims that I may or may not have, in the use of this information as part of the ADP.

Risks:

- I may not be able to find a match and donate my kidney through the ADP
- I may become unsuitable for donation at any time in the process
- My surgery may be delayed or cancelled at any time due to unforeseen events
- NKR unexpectedly shutting down operations
- There is no guarantee that my IR will be transplanted through the ADP

Intended Donor Contact Information

Address:	
Primary Phone Number:	Email Address:
Secondary Phone Number:	Donor Center:

Informed Consent Agreed to:

Name (Print):
Signature (Sign):
Today's Date:
SSN:
Donor Alias (Assigned by Center):

Intended Recipient Identification Information

Name:
DOB:
SSN:
Relationship to IR:
Intended Recipient Alias:

Overnight original signed copy to: ***National Kidney Registry • 42 Fire Island Avenue #200 • Babylon, NY 11702***

National Kidney Registry

Advanced Donation Program

Informed Consent
Intended Recipient

Version 1.4

Intended Recipient's Government Issued Photo Identification

The Program: The Advanced Donation Program "ADP" allows a medically and psychosocially acceptable Intended Donor "ID" to donate their kidney via human organ paired donation (more commonly referred to as a swap) before their Intended Recipient "IR" is scheduled to receive a transplant via a swap. The ADP may be preferred by donors or patients due to schedules, availability and/or preferences. Some IR's may have residual kidney function but their diagnosis of chronic renal disease is medically predictive of decreasing renal function eventually requiring renal replacement therapy. Both surgeries must take place at the same transplant center. Once the ID donation has occurred, the IR may be activated by their transplant center for matching within the NKR. The ADP program is unrelated to the U.S. deceased donor system and participation in the ADP program does not confer any wait time points for the IR in the deceased donor system.

Your Situation: I understand that my ID would like to participate in the ADP and donate a kidney to another recipient through the NKR. This donation gives me a prioritized opportunity to receive a kidney as part of a swap, within the NKR.

Information Release: I consent to the disclosure of all my health, medical, and personal information to the NKR for the purpose of participating in the ADP. I authorize the NKR to disclose, disseminate and utilize my health, medical and personal information in conducting the ADP, and I waive any and all privacy law claims that I may or may not have, in the use of this information as part of the ADP.

My Obligation: I understand that I must keep a copy of this form and present it to my transplant center when I return to receive my kidney. Additionally, I am willing to undergo the identity verification process when I return to receive my kidney. I understand that this is non-transferable, and non-assignable.

Patients Risks: There is risk that I may not get transplanted through the ADP due to:

- A sensitization event (e.g. blood transfusion, pregnancy, etc.)
- A situation whereby I become medically unable to go to surgery
- NKR's inability to find an acceptable compatible donor
- NKR unexpectedly shutting down operations
- Other unforeseen circumstances such as an act of nature

Intended Recipient Contact Information

Address:	
Primary Phone Number:	Email Address:
Secondary Phone Number:	Transplant Center:

Informed Consent Agreed to:

Name (Print):
Signature (Sign):
Today's Date:
SSN: DOB:

Intended Recipient Identification Information

Blood Type: [A] [B] [O] [AB] Gender: [M] [F]

Enter HLA Antigens Below:

A-1	A-2	B-1	B-2	DR-1	DR-2

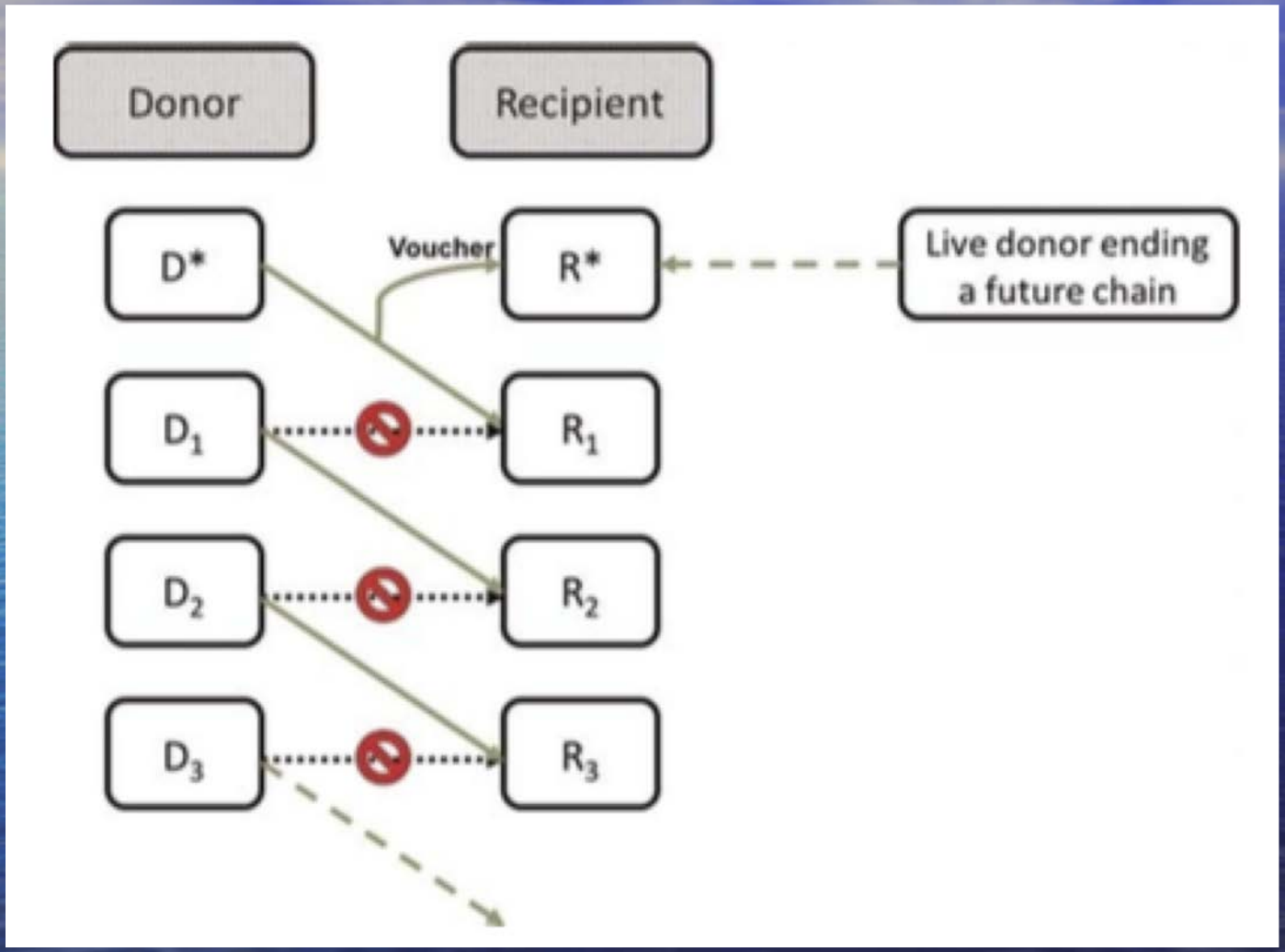
Overnight original signed copy to: ***National Kidney Registry • 42 Fire Island Avenue #200 • Babylon, NY 11702***

Original Clinical Science—General

Vouchers for Future Kidney Transplants to Overcome "Chronological Incompatibility" Between Living Donors and Recipients

Jeffrey L. Veale, MD,[1] Alexander M. Capron, LLB, MA (Hon),[2,3] Nima Nassiri, MD,[3] Gabriel Danovitch, MD,[1] H. Albin Gritsch, MD,[1] Amy Waterman, PhD,[1] Joseph Del Pizzo, MD,[4] Jim C. Hu, MD, MPH,[4] Marek Pycia, PhD,[5] Suzanne McGuire, RN, BSN,[1] Marian Charlton, RN,[4] and Sandip Kapur, MD[4]

Veale et al. Transplantation 2017. 101:2115-9


Donor
Recipient
D*
Voucher
R*
Live donor ending a future chain
D1
R1
D2
R2
D3
R3

Cases – Voucher Program

Case 1

- 4 yo, solitary kidney, CKD anticipated needing Ktx in 10-15 yrs
- 64 yo grandfather wants to donate and allow grandson to receive swap donor kidney in future
- Led to 3 transplants Dec 2014 at UCLA

Case 2

- 10 yo girl, living donor Ktx in 2007, functioning well after 9 yrs
- 54 yo father wants to donate and allow daughter a backup option should her allograft eventually failed
- Led to 8 transplants Aug 2015 at NY Presbyterian-Weil Cornell

Case 3

- Same recip as above
- 60 yo aunt wants to donate and allow niece a second voucher given her young age and likely need for more than 2 transplants
- Led to 14 transplants May 2016 at NY Presbyterian-Weil Cornell

Voucher Program – Key Points

- Overcomes chronologic incompatibility
- No guarantees voucher recipient will get a transplant
- Ensure advanced donor is truly "altruistic"
- Voucher cannot be bartered to another recipient and has no cash value
- If original voucher recipient passes away, then the voucher expires
- Goal of program is to maximize number of facilitated transplants
- Each voucher donor facilitates avg 4.7 transplants

Points of Consideration

- Should the NKR files bankruptcy, all vouchers become void
- Prioritization of voucher holders, based on time voucher held or cPRA levels
- Blood type O recips or highly-sensitized, difficult to match candidates
- Risk of requests exceeding supply of organs

Myth 8.

If a donor donates a kidney then their intended recipient will only be eligible to get a kidney in return

The Washington Post
Democracy Dies in Darkness

Health & Science

A daughter's gift to her mother saves two lives

Erosalyn Deveza, left, was hoping for a life-saving kidney transplant. Then, one day in 2015, her 19-year-old daughter Aliana stumbled onto medical research that would change their lives. (Winni Wintermeyer/For The Washington Post)

https://www.washingtonpost.com/national/health-science/a-daughters-gift-to-her-mother-saves-two-lives/2019/05/11/59dead7c-7277-11e9-9eb4-0828f5389013_story.html?noredirect=on&utm_term=.203b297c5451

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CASE REPORT

AJT

Bi-organ paired exchange—Sentinel case of a liver-kidney swap

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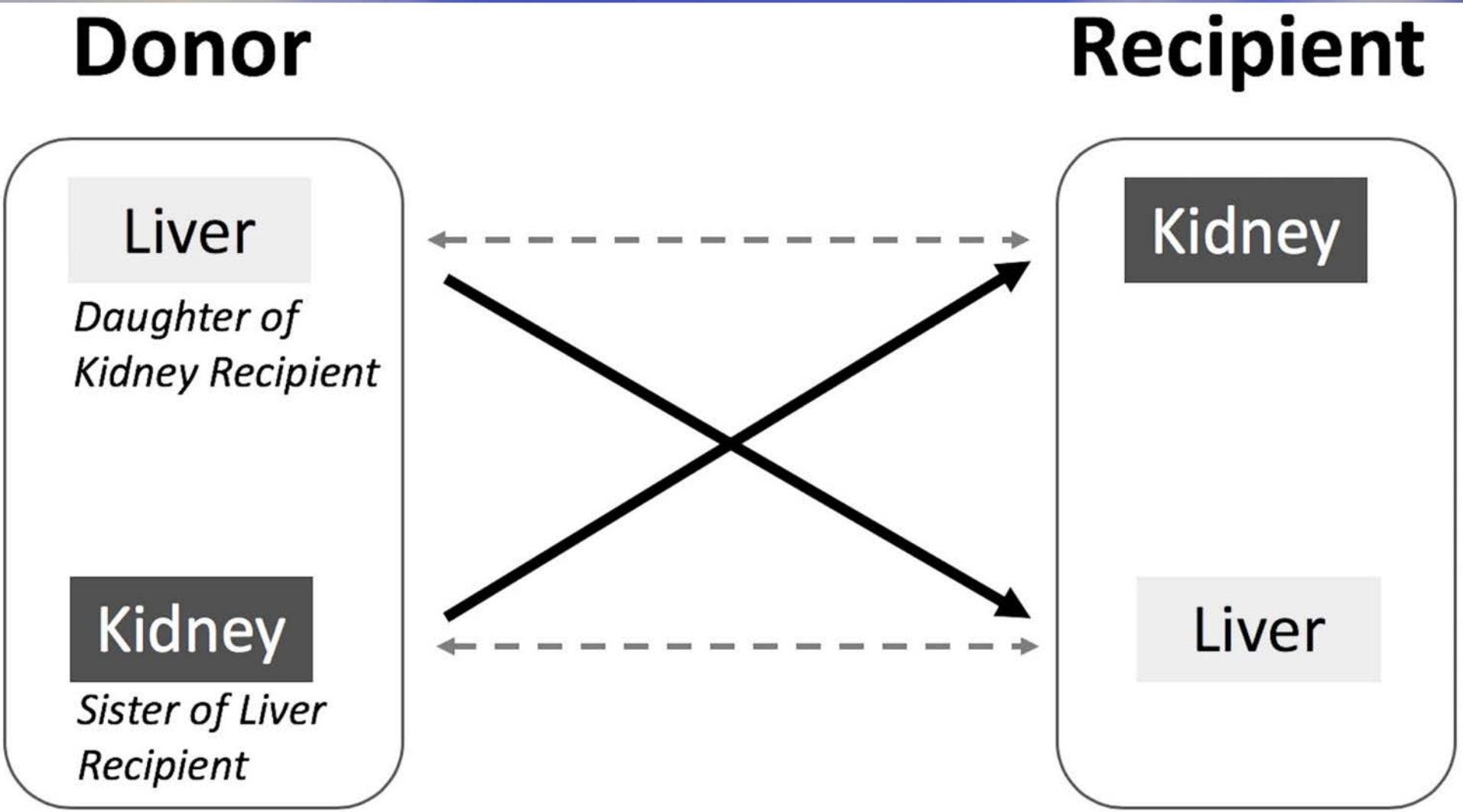
Donor
Recipient
Liver
Daughter of Kidney Recipient
Kidney
Sister of Liver Recipient
Kidney
Liver

Conclusions

- Wait times for a kidney transplant remains long in the US and around the world
- Living donor kidney transplantation offers shorter wait times, makes pre-emptive transplant more likely, improves longevity of allograft
- There may be a higher risk of kidney failure among donors vs. non donors, all things being equal, but that risk is generally considered low
- KPD functions to allow transplantation in immunologically incompatible pairs
- Innovative programs can further enhance transplant options for those difficult-to-match recipients


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