Opportunities in Transplantation

Discard of deceased donor kidneys in the United States

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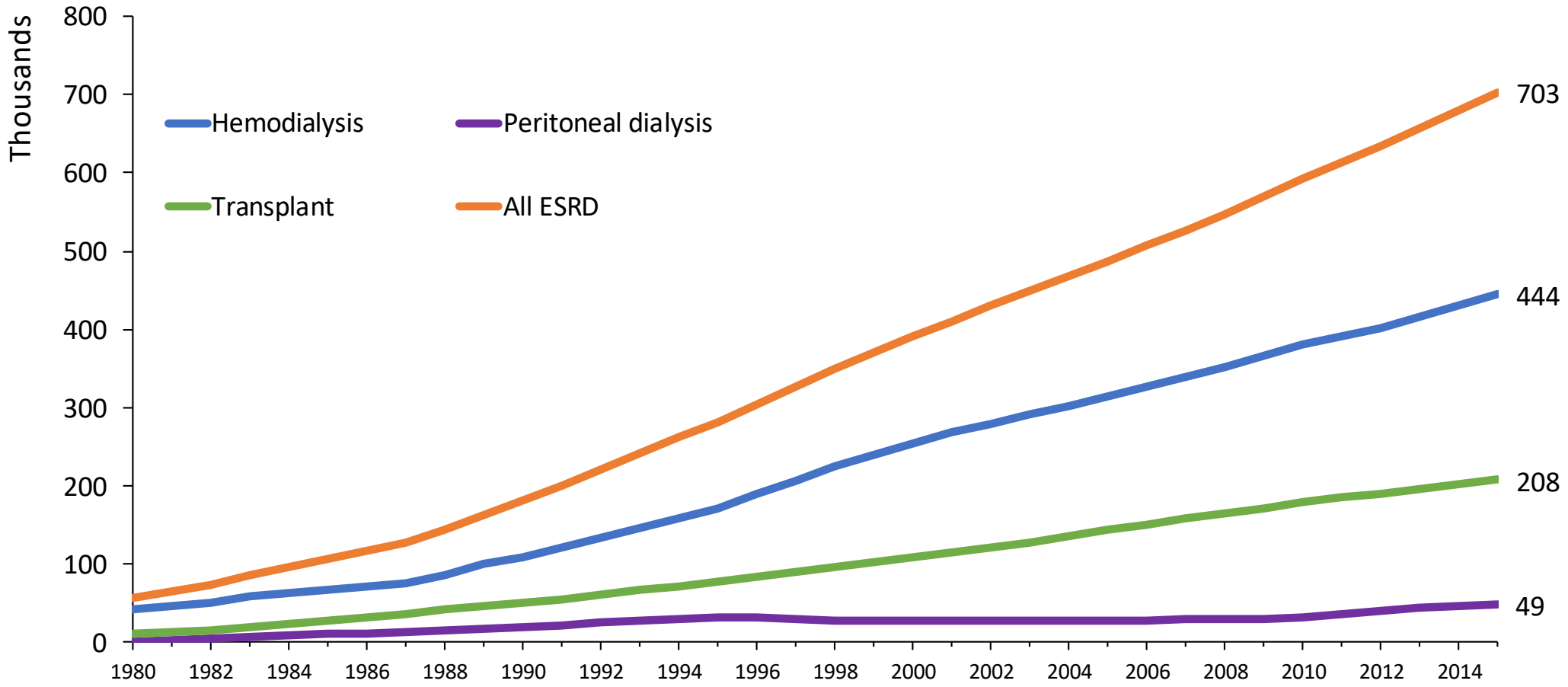
MedStar Georgetown Transplant Institute

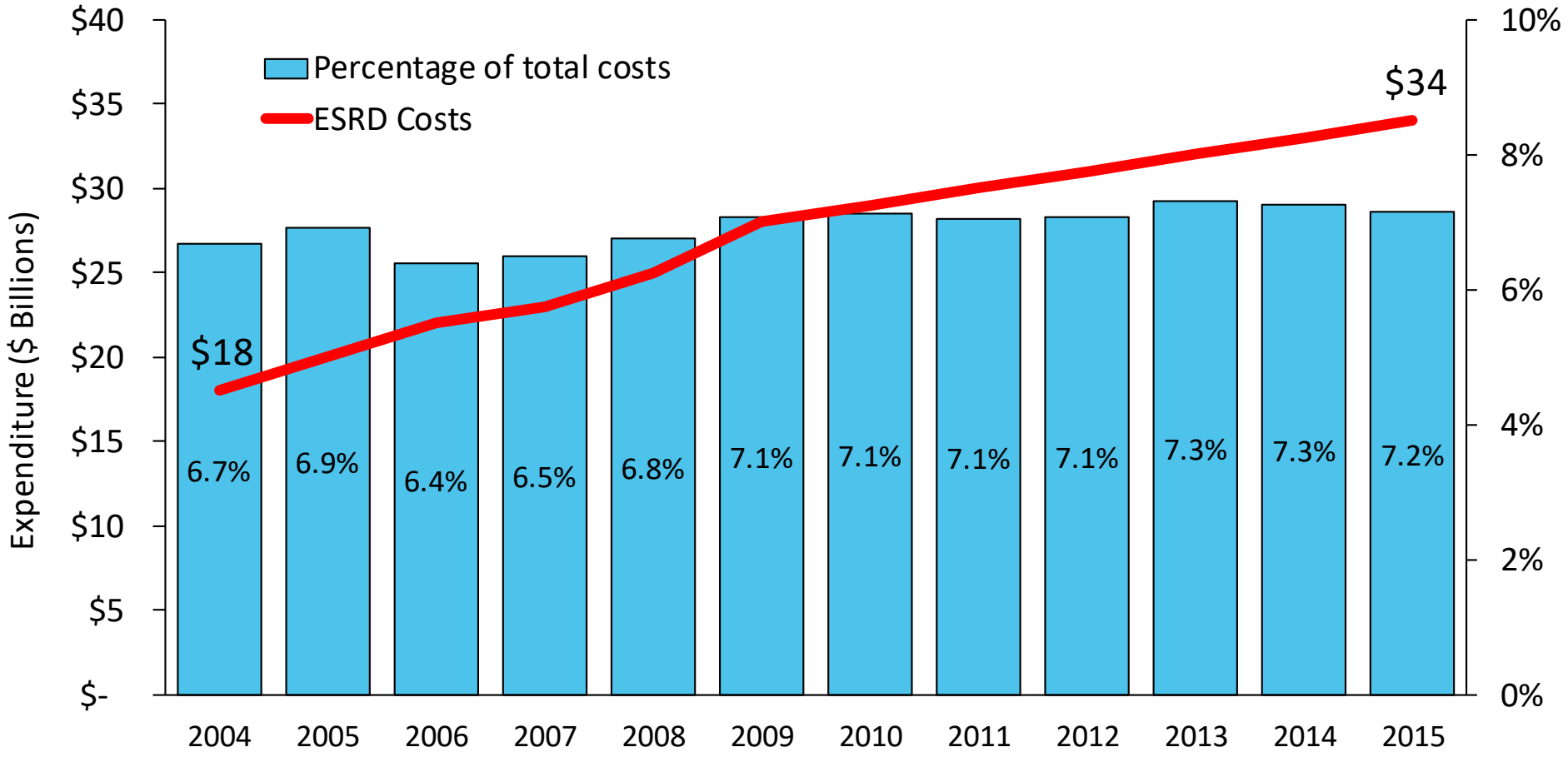
Disclosures

- Deputy Editor, *Kidney International Reports*
- Member, UNOS Data Advisory Committee
- Member, SRTR Visiting Committee
- Member, ASN Quality Committee
- Scientific Advisory Board, Angion Pharmaceuticals

ESRD Prevalence continues to rise



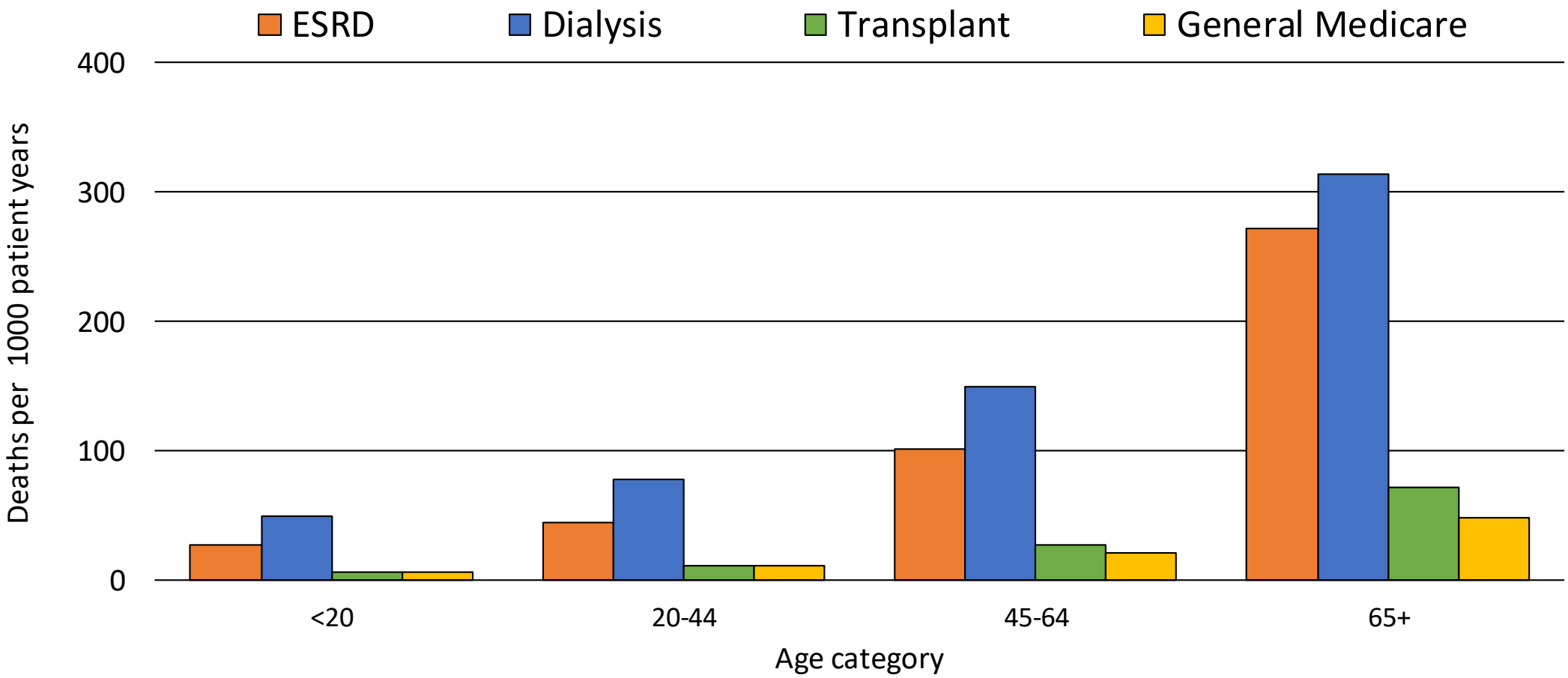
Rising cost of the ESRD program to Medicare



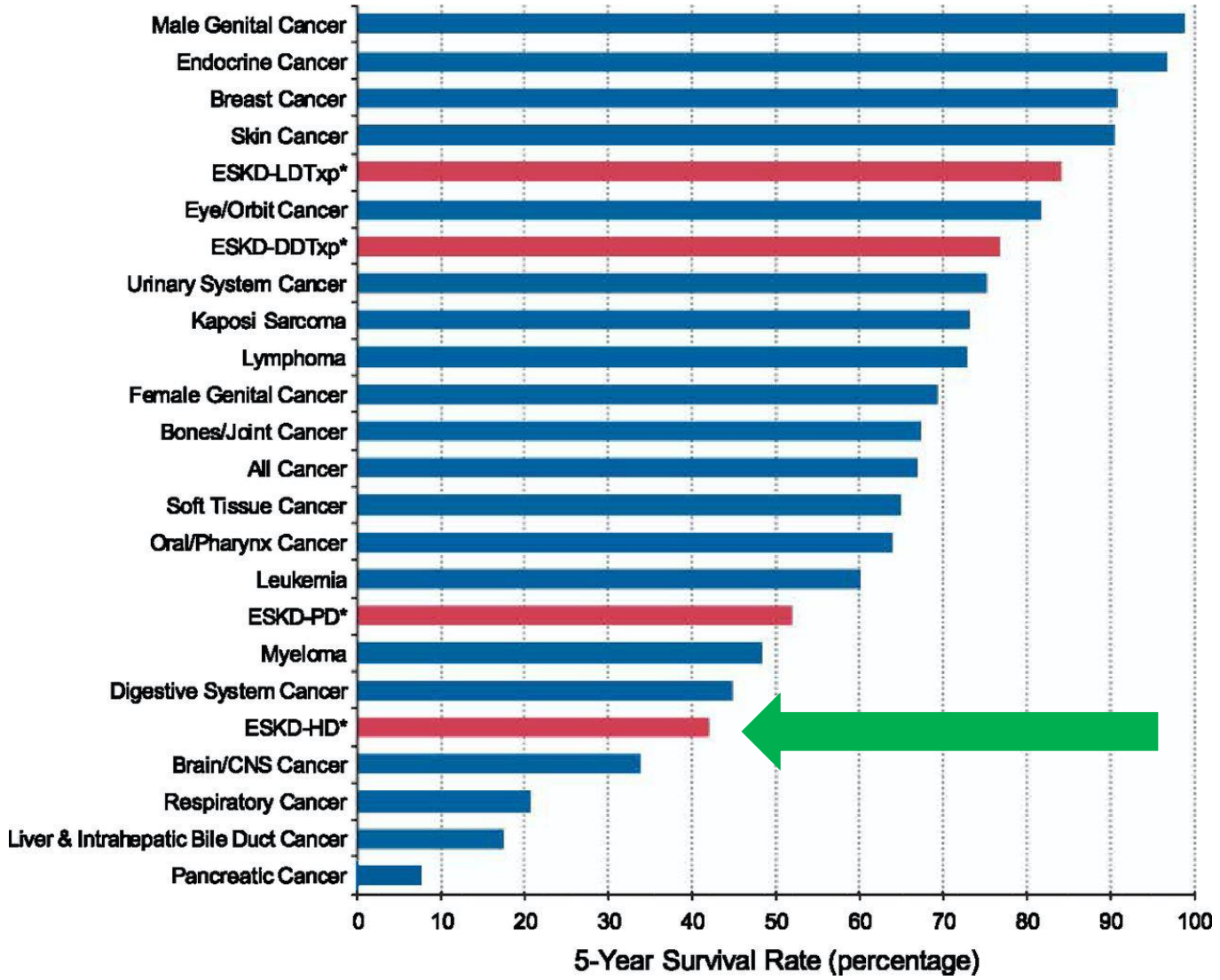
ESRD ~ 1% of the Medicare population

Transplant is the preferred treatment option

All cause mortality among Medicare beneficiaries



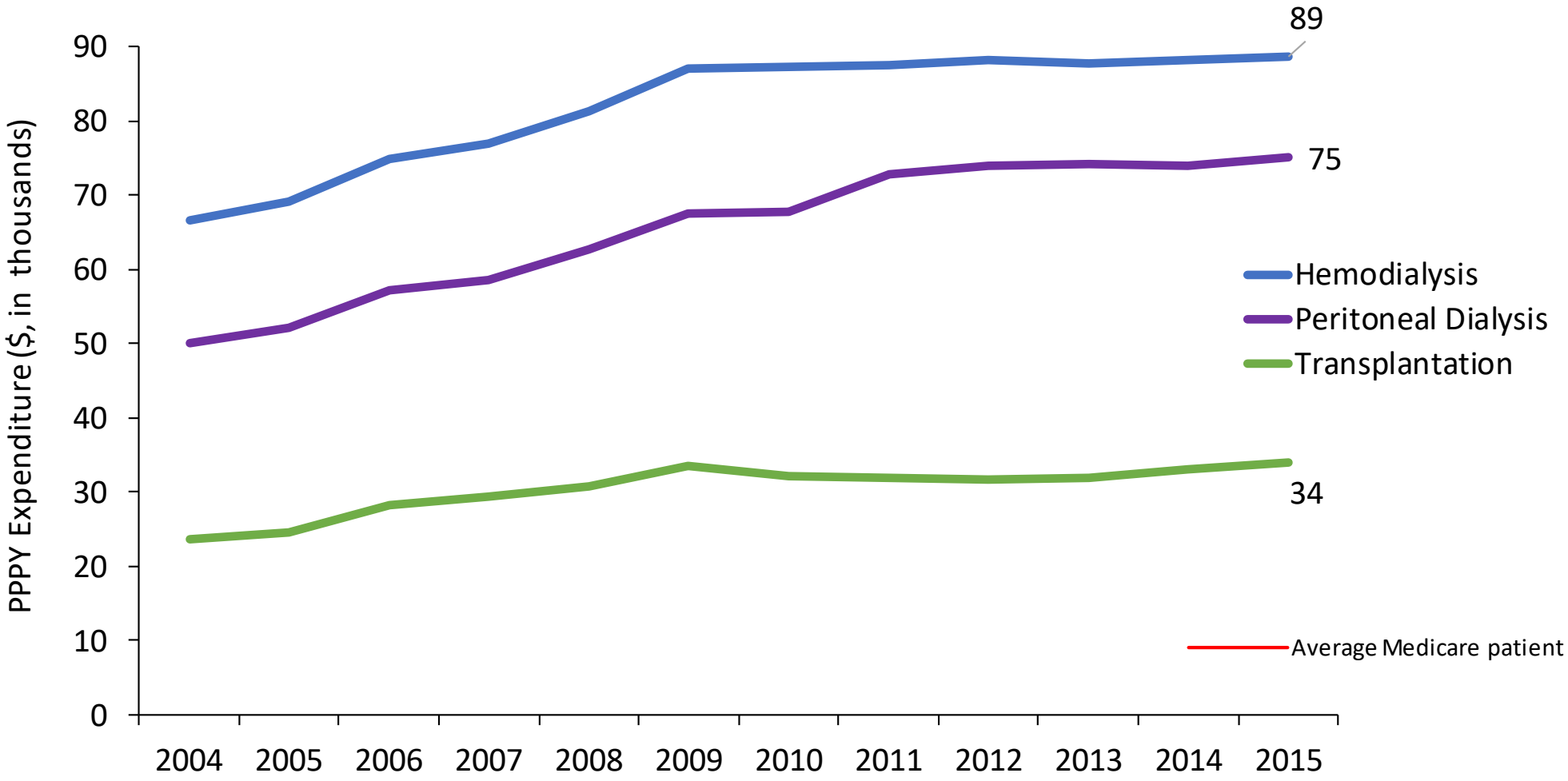
Prevalent ESRD patients from day one, 2011, & general Medicare (non-ESRD) patients with at least one month of Medicare eligibility in 2011. Adj: gender/race



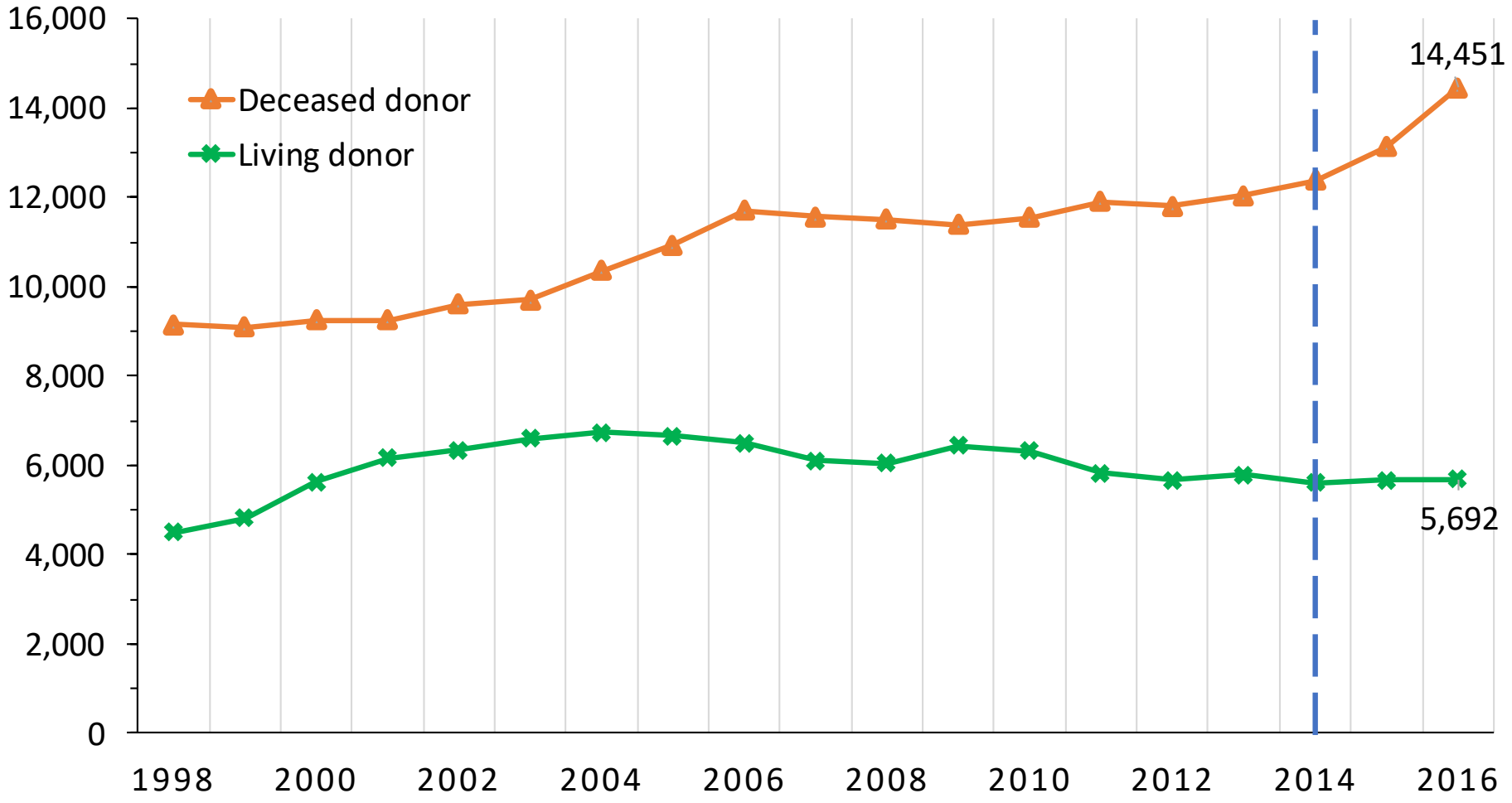
Bonventre et al. CJASN 2019

ESRD Medicare costs by modality

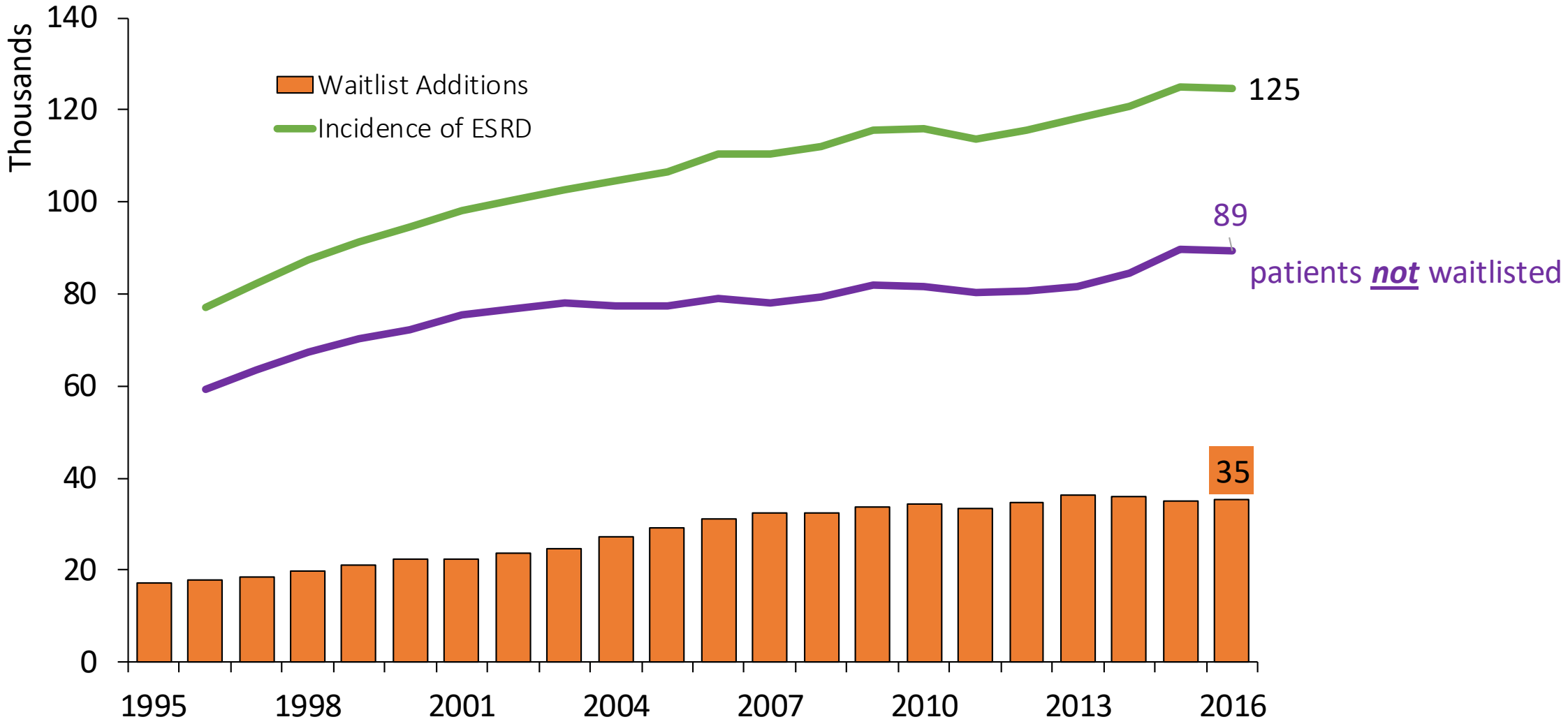
Transplant is by far the cheapest treatment option



Number of transplants being performed annually in the United States



The majority of incident ESRD patients are never waitlisted



USRDS 2018 ADR
UNOS Data 2017

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR MEDICARE & MEDICAID SERVICES

Form Approved
OMB No. 0938-0046

END STAGE RENAL DISEASE MEDICAL EVIDENCE REPORT
MEDICARE ENTITLEMENT AND/OR PATIENT REGISTRATION

A. COMPLETE FOR ALL ESRD PATIENTS *Check one:* ☐ Initial ☐ Re-entitlement ☐ Supplemental

1. Name *(Last, First, Middle Initial)*

2. Medicare Claim Number | 3. Social Security Number | 4. Date of Birth *(mm/dd/yyyy)*

5. Patient Mailing Address *(Include City, State and Zip)* | 6. Phone Number *(including area code)*

7. Sex ☐ Male ☐ Female | 8. Ethnicity ☐ Not Hispanic or Latino ☐ Hispanic or Latino (Complete Item 9) | 9. Country/Area of Origin or Ancestry

10. Race *(Check all that apply)*
☐ White ☐ Asian
☐ Black or African American ☐ Native Hawaiian or Other Pacific Islander*
☐ American Indian/Alaska Native *complete Item 9
Print Name of Enrolled/Principal Tribe _____

11. Is patient applying for ESRD Medicare coverage? ☐ Yes ☐ No

12. Current Medical Coverage *(Check all that apply)*
☐ Medicaid ☐ Medicare ☐ Employer Group Health Insurance
☐ DVA ☐ Medicare Advantage ☐ Other ☐ None

13. Height INCHES _____ OR CENTIMETERS _____

14. Dry Weight POUNDS _____ OR KILOGRAMS _____

15. Primary Cause of Renal Failure *(Use code from back of form)*

16. Employment Status *(6 mos prior and current status)*

Prior	Current	
☐	☐	Unemployed
☐	☐	Employed Full Time
☐	☐	Employed Part Time
☐	☐	Homemaker
☐	☐	Retired due to Age/Preference
☐	☐	Retired (Disability)
☐	☐	Medical Leave of Absence
☐	☐	Student

17. Co-Morbid Conditions *(Check all that apply currently and/or during last 10 years)* *See instructions

a. ☐ Congestive heart failure
b. ☐ Atherosclerotic heart disease ASHD
c. ☐ Other cardiac disease
d. ☐ Cerebrovascular disease, CVA, TIA*
e. ☐ Peripheral vascular disease*
f. ☐ History of hypertension
g. ☐ Amputation
h. ☐ Diabetes, currently on insulin
i. ☐ Diabetes, on oral medications
j. ☐ Diabetes, without medications
k. ☐ Diabetic retinopathy
l. ☐ Chronic obstructive pulmonary disease
m. ☐ Tobacco use (current smoker)
n. ☐ Malignant neoplasm, Cancer
o. ☐ Toxic nephropathy
p. ☐ Alcohol dependence
q. ☐ Drug dependence*
r. ☐ Inability to ambulate
s. ☐ Inability to transfer
t. ☐ Needs assistance with daily activities
u. ☐ Institutionalized
☐ 1. Assisted Living
☐ 2. Nursing Home
☐ 3. Other Institution
v. ☐ Non-renal congenital abnormality
w. ☐ None

18. Prior to ESRD therapy:
a. Did patient receive exogenous eryt
b. Was patient under care of a neph
c. Was patient under care of kidney d
d. What access was used on first outpa
If not AVF, then: Is maturing AVF pre
Is maturing graft pr

19. Laboratory Values Within 45 Days P

LABORATORY TEST	VALUE	DATE	LABORATORY TEST	VALUE	DATE
a.1. Serum Albumin (g/dl)	__ . __		d. HbA1c	__ __ . __%	
a.2. Serum Albumin Lower Limit	__ . __		e. Lipid Profile TC	__ __ __	
a.3. Lab Method Used (BCG or BCP)			LDL	__ __ __	
b. Serum Creatinine (mg/dl)	__ __ . __		HDL	__ __	
c. Hemoglobin (g/dl)	__ __ . __		TG	__ __ __ __	

B. COMPLETE FOR ALL ESRD PATIENTS IN DIALYSIS TREATMENT

20. Name of Dialysis Facility | 21. Medicare Provider Number *(for item 20)*

22. Primary Dialysis Setting
☐ Home ☐ Dialysis Facility/Center ☐ SNF/Long Term Care Facility

23. Primary Type of Dialysis
☐ Hemodialysis (Sessions per week____/hours per session____)
☐ CAPD ☐ CCPD ☐ Other

24. Date Regular Chronic Dialysis Began *(mm/dd/yyyy)* | 25. Date Patient Started Chronic Dialysis at Current Facility *(mm/dd/yyyy)*

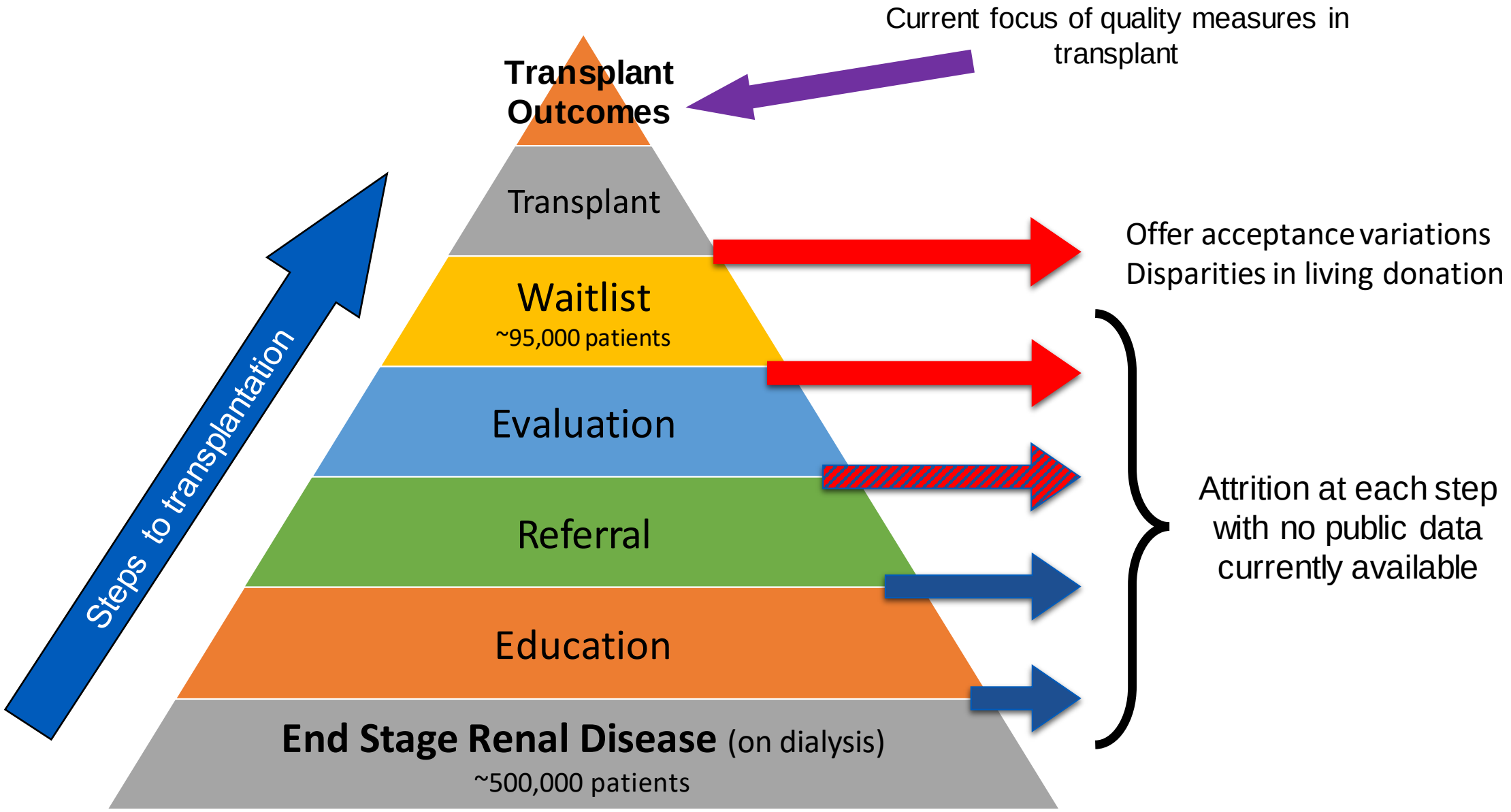
26. Has patient been informed of kidney transplant options? ☐ Yes ☐ No

27. If patient NOT informed of transplant options, please check all that apply:
☐ Medically unfit ☐ Patient declines information ☐ Unsuitable due to age
☐ Patient has not been assessed ☐ Psychologically unfit ☐ Other

FORM CMS-2728-U3 (03/06) 1

26. Has patient been informed of kidney transplant options?
☐ Yes ☐ No

27. If patient NOT informed of transplant options, please check all that apply:
☐ Medically unfit ☐ Patient declines information ☐ Unsuitable due to age
☐ Patient has not been assessed ☐ Psychologically unfit ☐ Other


Current focus of quality measures in transplant
Transplant Outcomes
Transplant
Waitlist
~95,000 patients
Evaluation
Referral
Education
End Stage Renal Disease (on dialysis)
~500,000 patients
Steps to transplantation
Offer acceptance variations
Disparities in living donation
Attrition at each step with no public data currently available

Proportion of ESRD patients waitlisted

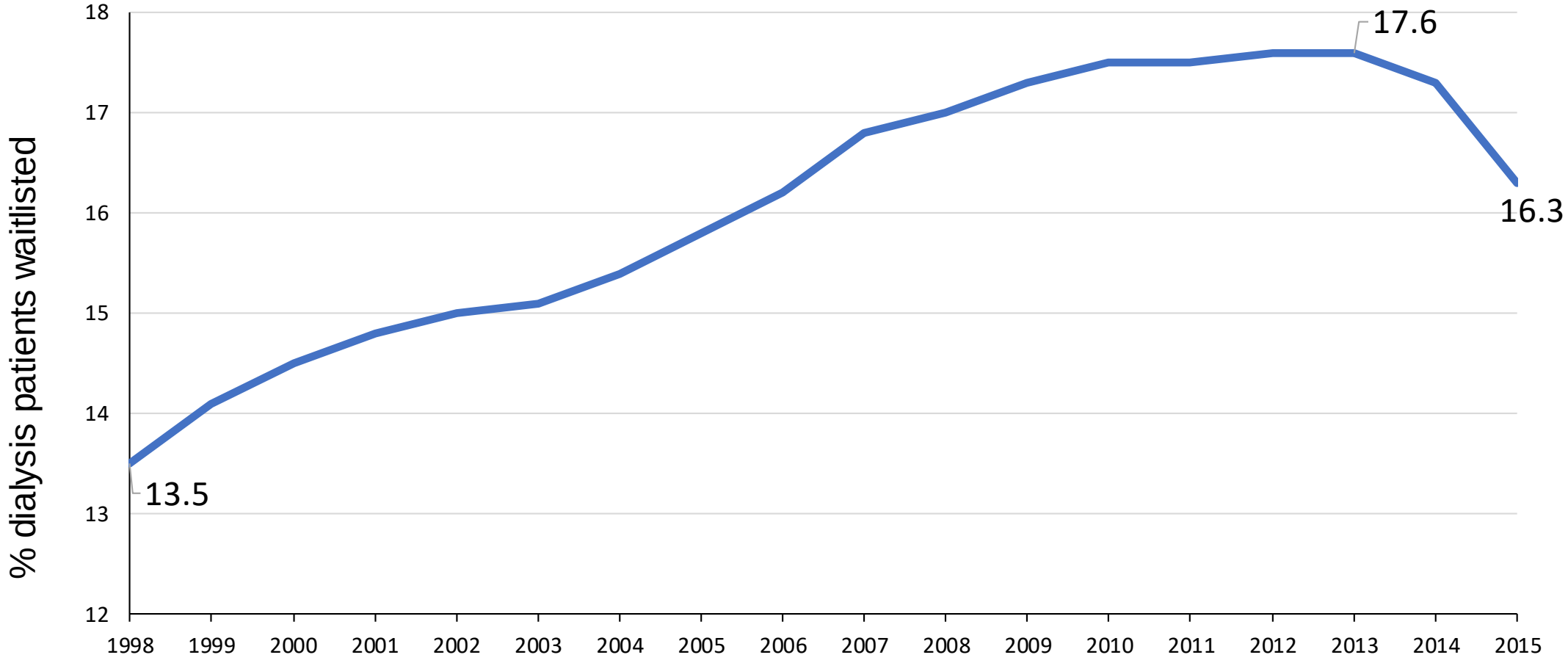
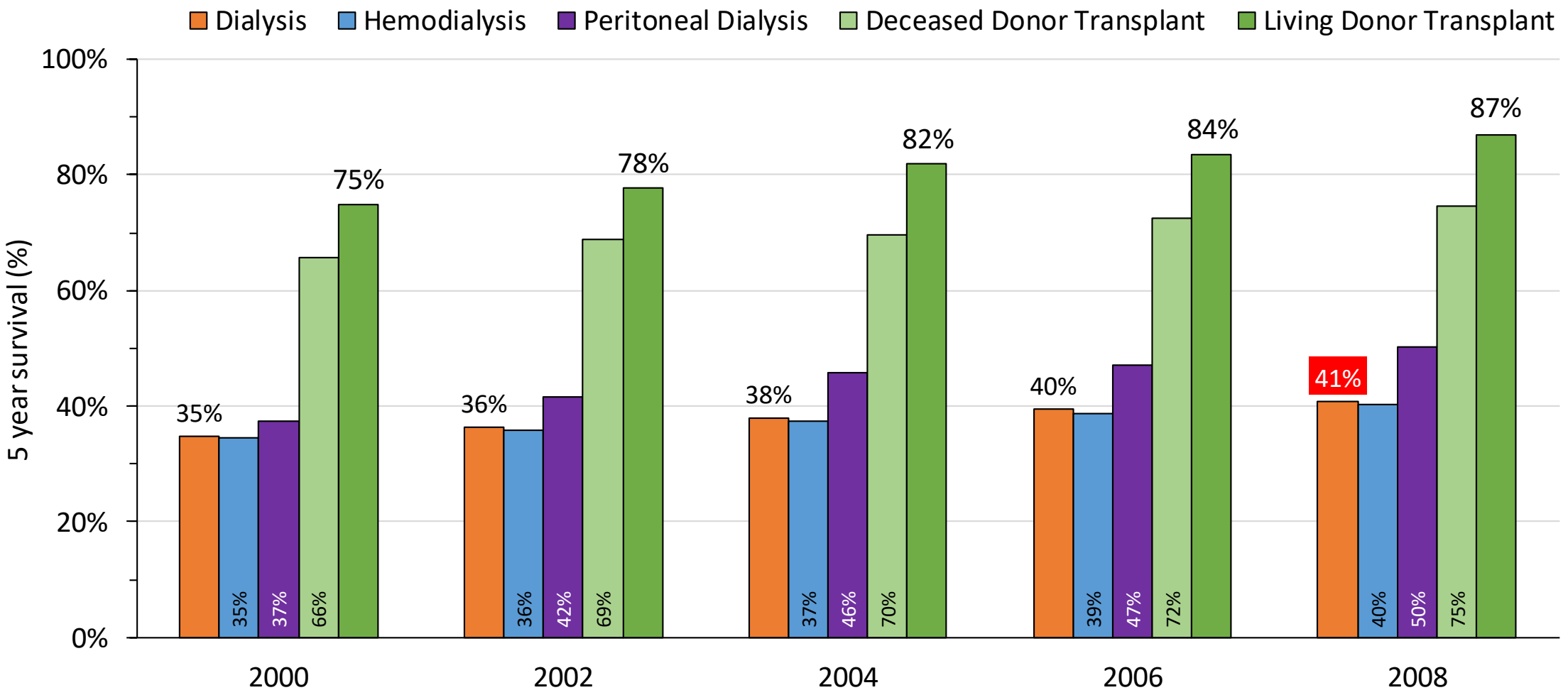


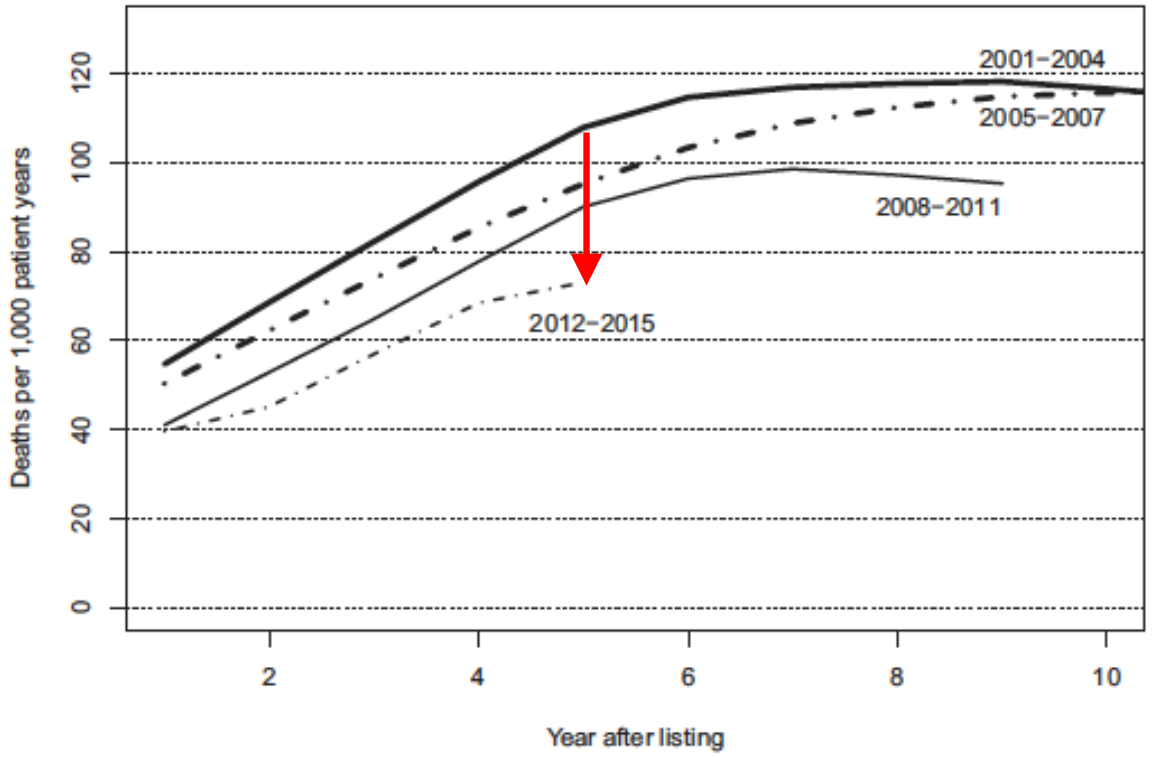
Fig 6.2 USRDS 2018 ADR

5-year survival rates for ESRD by treatment modality

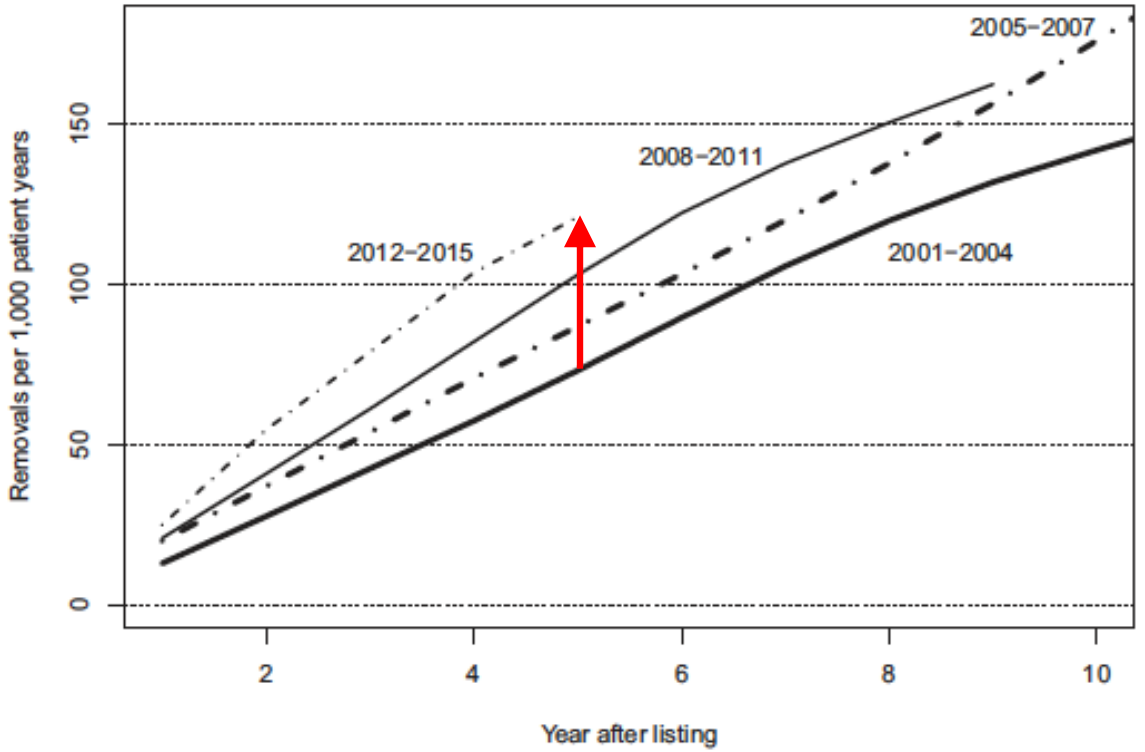


Increasing selectivity of patients are being waitlisted for a transplant

Mortality rates dropping on the waitlist



Removals from the waitlist are increasing



Schold et al. AJT 2018

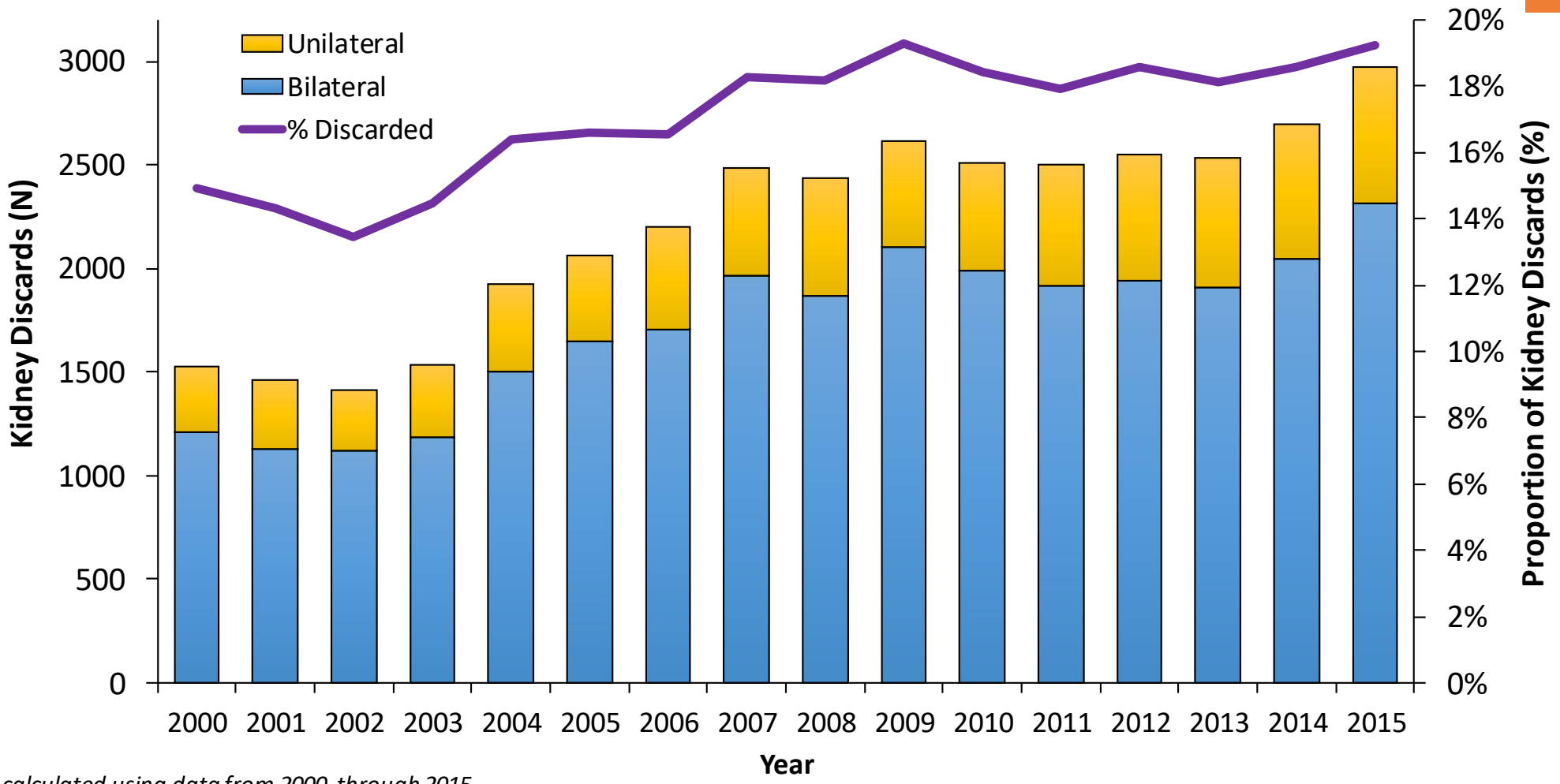
Increasing transplantation rates needs more donors

Perhaps a better first step might be
Improving deceased donor organ utilization

The number of discards is increasing…

and this continues with the new kidney allocation system

3500 discarded kidneys in 2018



Discard data calculated using data from 2000 through 2015

Mohan S et al. Kidney Int. 2018

Why would we not want to use an available deceased donor kidney?

- Significant anatomical abnormality or injury during procurement/ transportation
- Other common reasons cited:
  - Poor quality organ –
    - Patients with AKI, diabetes or other comorbidities
    - Concerning biopsy findings at the time of organ recovery
  - Increased risk of Infectious disease transmission risk
  - Took too long to find a recipient (prolonged cold time)
  - **No recipient located**
- *Are there systemic reasons that impede organ utilization?*

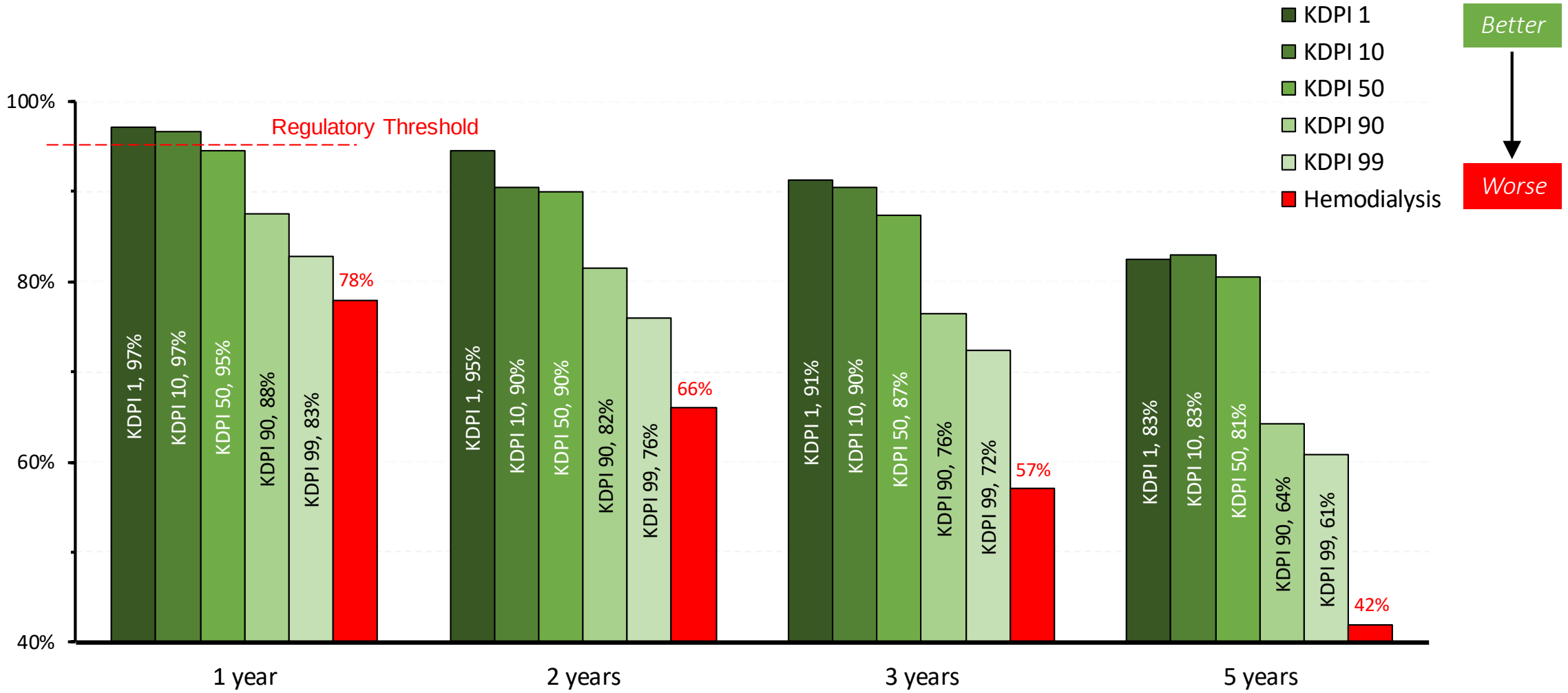
Kidney Donor Profile Index (KDPI)

- Cumulative percentage score
- Measure of expected outcome
- Derived from estimates of the relative risk of allograft failure in an adult recipient. (KDRI)
- Scaled using kidneys procured in the preceding calendar year
- Part of the new kidney allocation system

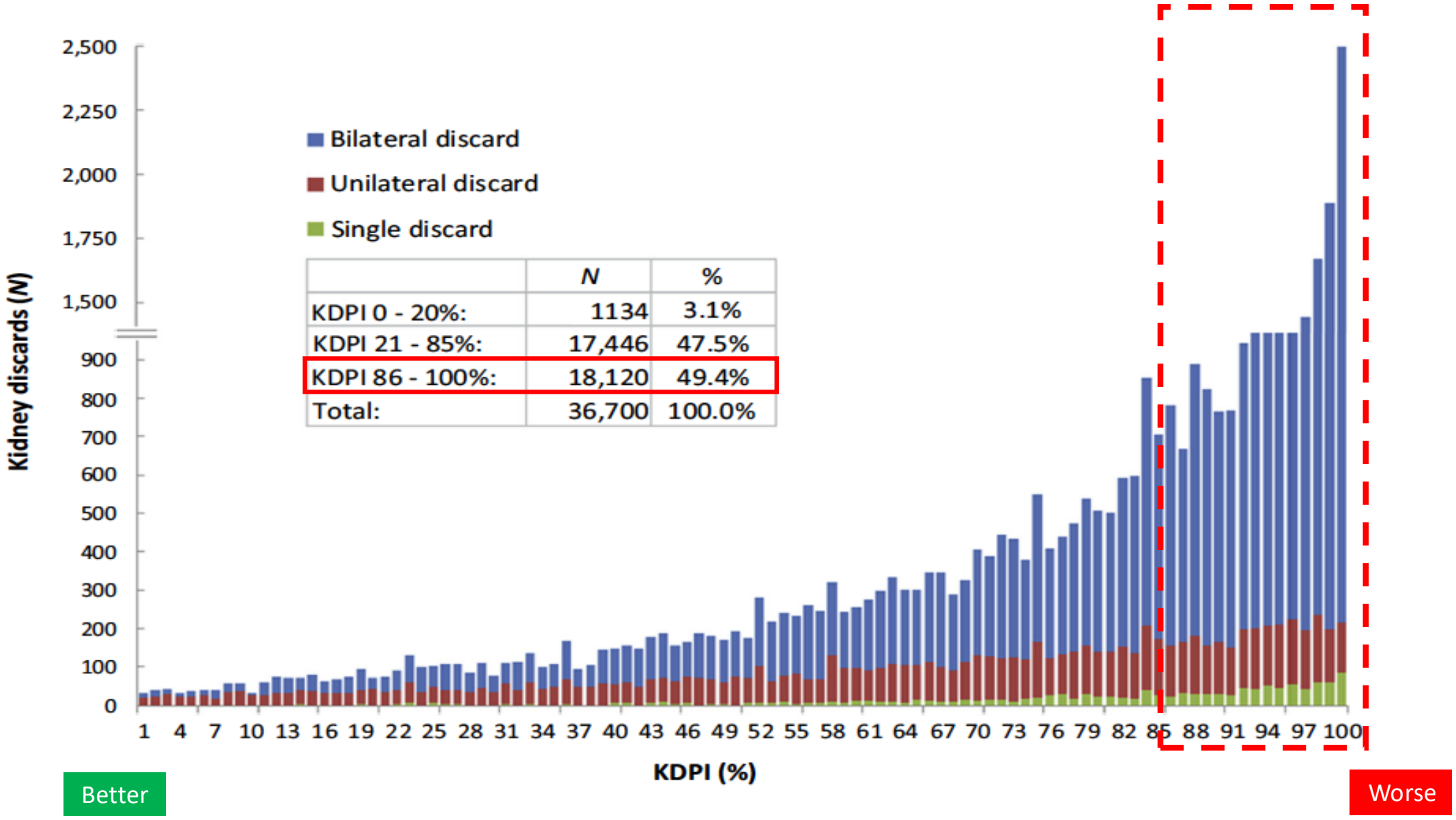
1. Age
2. Height
3. Weight
4. Ethnicity
5. Serum creatinine
6. Hypertension
7. Diabetes
8. HCV status
9. Cause of death
10. Donation after circulatory death

The Kidney Donor Risk Index (KDRI) is an estimate of the relative risk of post-transplant kidney graft failure (in an average, adult recipient) from a particular deceased donor compared to the median (50th percentile) donor

Comparing Graft survival rates with dialysis survival rates



Donor reference population: All deceased kidney donors recovered for transplant in 2016.
Based on OPTN data including primary, adult, deceased donor, kidney alone transplants, as of April 20, 2018.



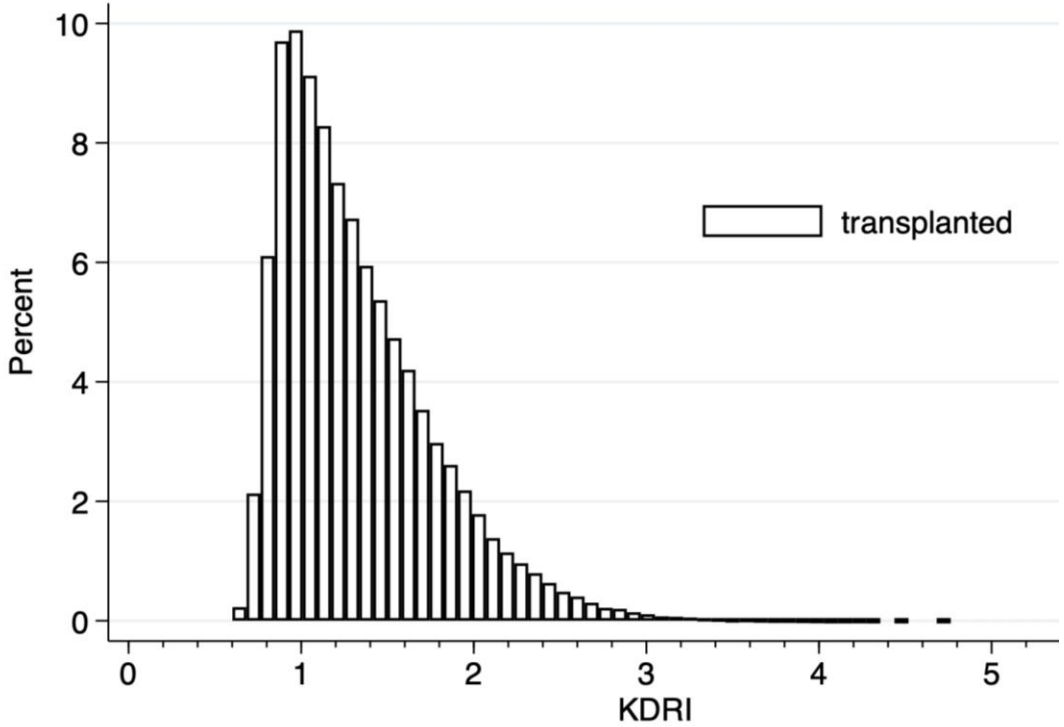
	N	%
KDPI 0 - 20%:	1134	3.1%
KDPI 21 - 85%:	17,446	47.5%
KDPI 86 - 100%:	18,120	49.4%
Total:	36,700	100.0%

Better

Worse

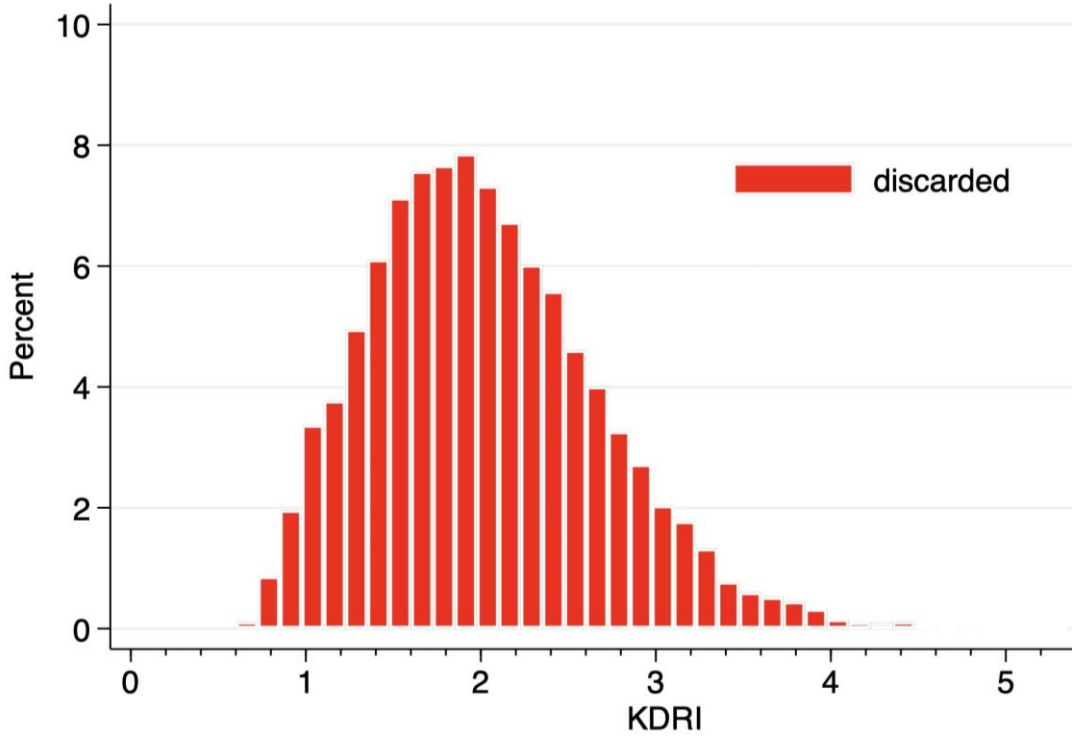
Mohan S et al. Kidney Int. 2018

KDRI for kidneys transplanted and discarded



Better

Worse

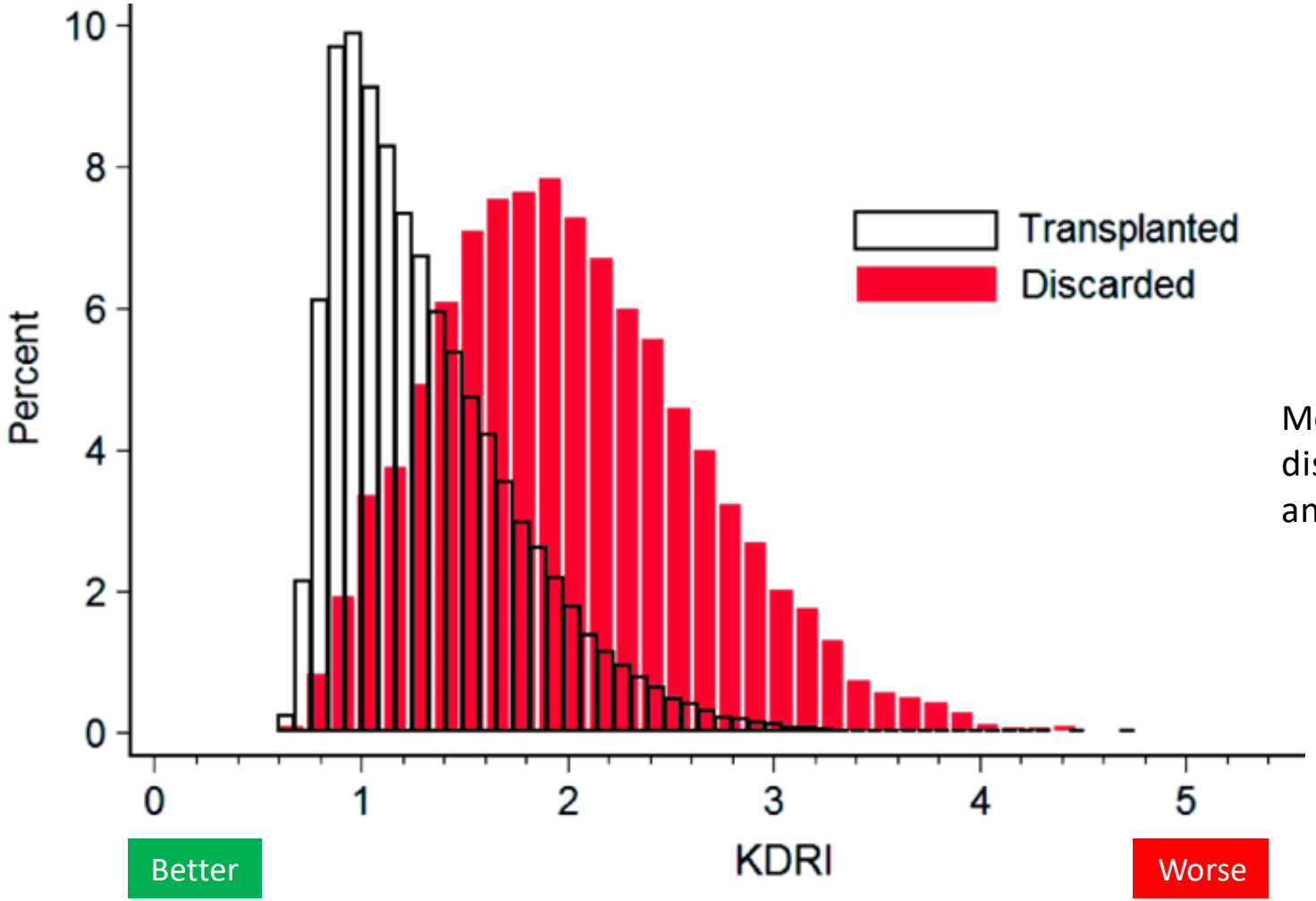


Better

Worse

Calculated using data from 2000 through 2015

Significant overlap in quality of organs transplanted and discarded



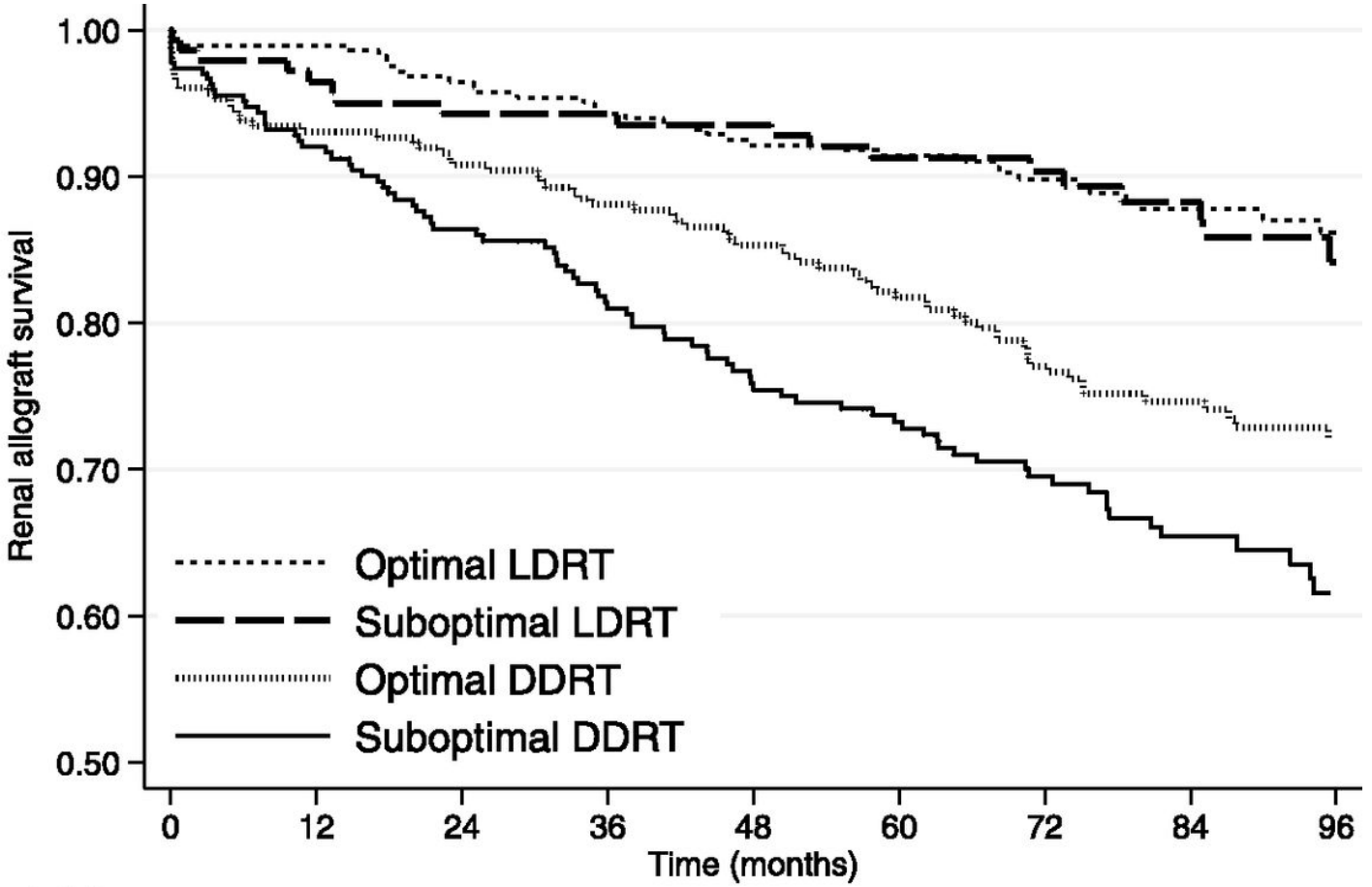
Most common reasons cited for discard are donor characteristics and biopsy findings

Calculated using data from 2000 through 2015

% or mean ± SD	Procured for transplantation (N = 212,305) Transplanted 175,605 (82.7)	Discarded 36,700 (17.3)	*P* value
Donor characteristics			
Age (yr)	36.5 ± 16.5	52.4 ± 16.0	<0.001
Gender (% male)	60.8	52.8	<0.001
BMI (kg/m^2)	26.6 ± 6.6	28.3 ± 7.1	<0.001
African American/black	13.9	16.8	<0.001
Death due to CVA	33.3	58.4	<0.001
Donor Type (% ECD)	14.6	54.2	<0.001
History of diabetes	5.8	20.8	<0.001
History of hypertension	24.1	60.0	<0.001
Clinical infection	47.5	46.4	<0.001
Proteinuria	37.1	46.3	<0.001
Terminal sCr (mg/dl)	1.11 ± 0.91	1.52 ± 1.20	<0.001
Transplant characteristics			
Median KDRI (IQR)	1.12 (0.53)	1.78 (0.75)	<0.001
Median KDPI (%)[a] (IQR)	42 (47)	85 (29)	<0.001
Biopsy performed	36.1	77.1	<0.001

Mohan S et al. Kidney Int. 2018

Reperfusion biopsies are predictive of post transplant outcomes

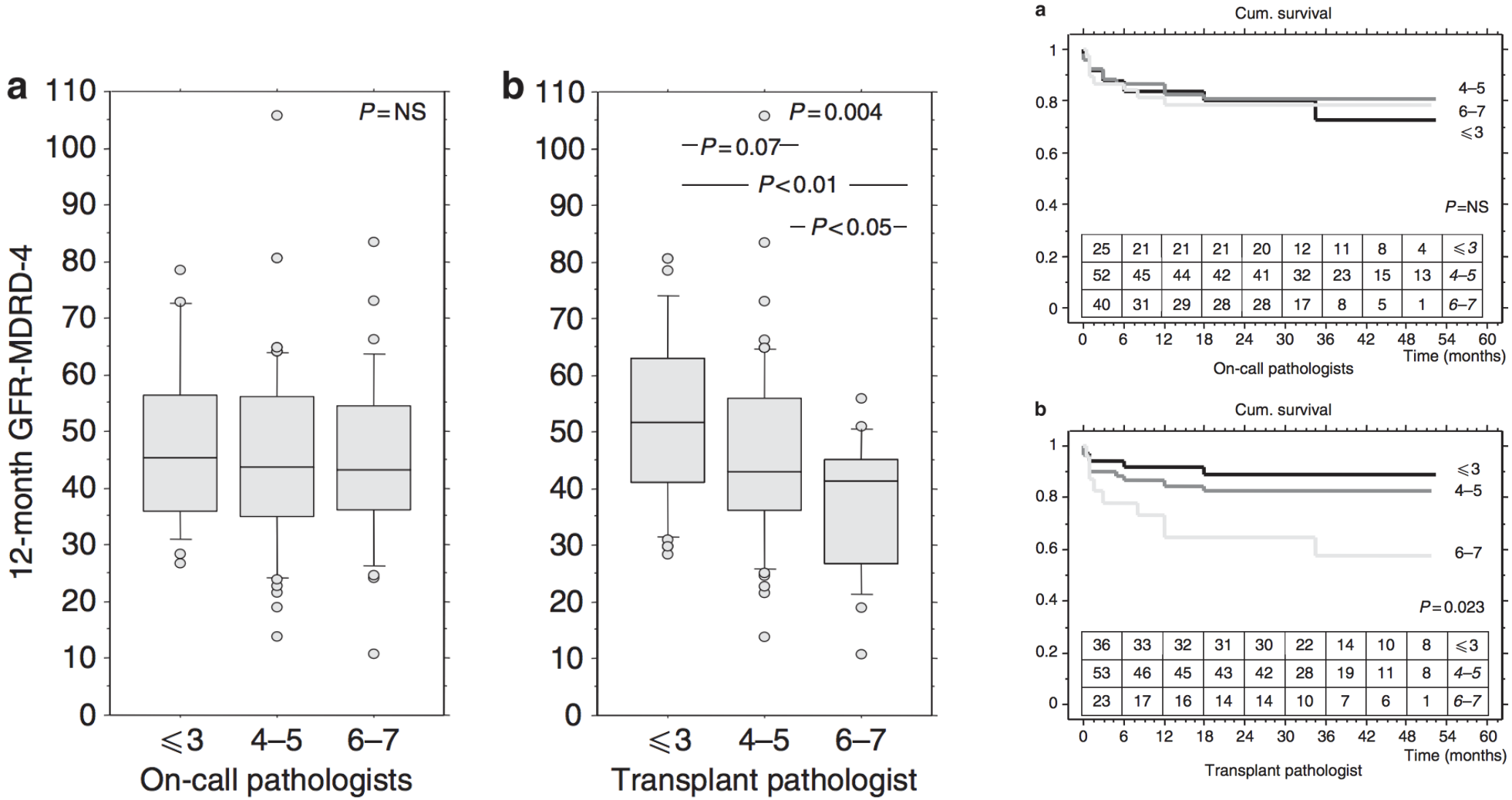


Number at risk

Optimal LDRT	283	280	271	263	255	249	202	144	95
Suboptimal LDRT	144	133	129	127	124	119	95	74	49
Optimal DDRT	278	247	237	226	214	202	174	127	88
Suboptimal DDRT	270	235	211	193	176	164	133	91	60

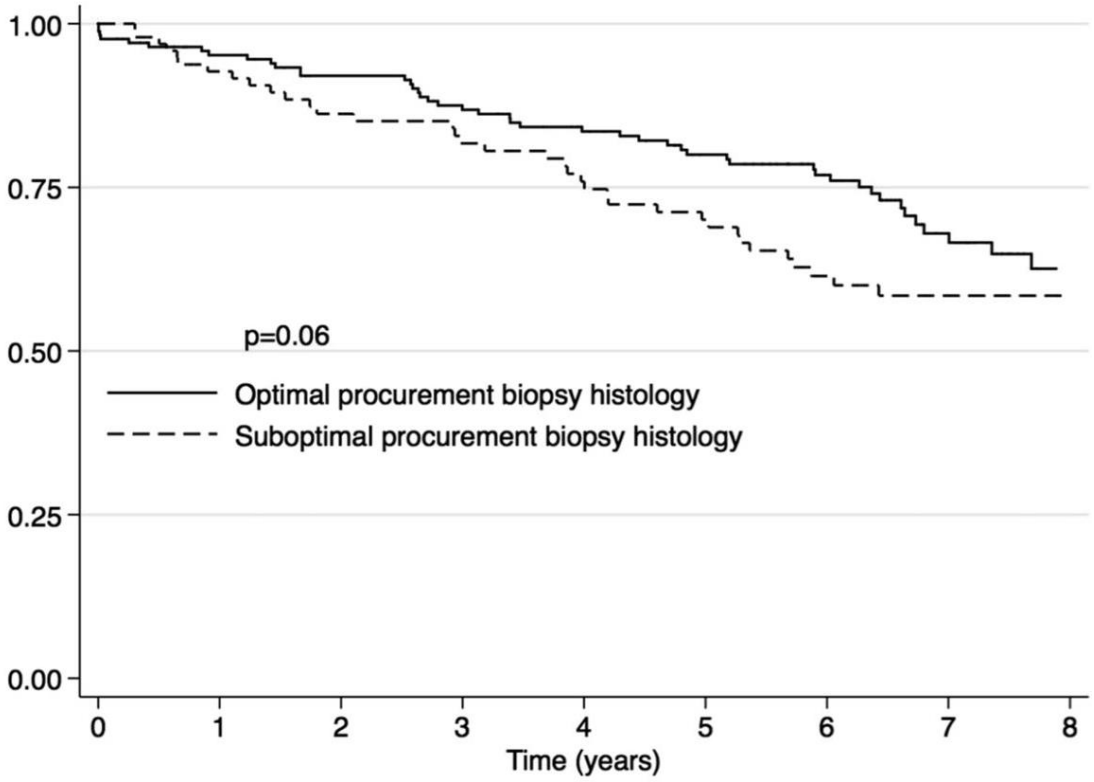
Mohan et al. JASN 2017

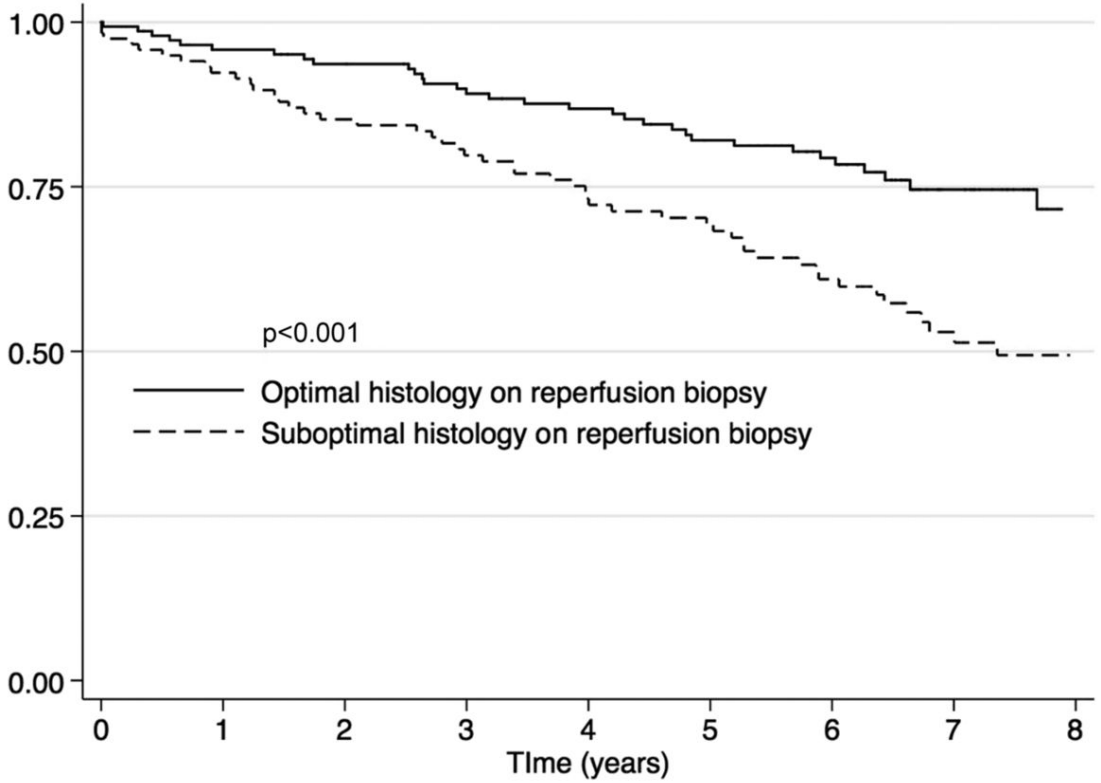
Overnight pathology evaluation of procurement biopsies are non-discriminatory



Azancot et al. Kidney Int 2014

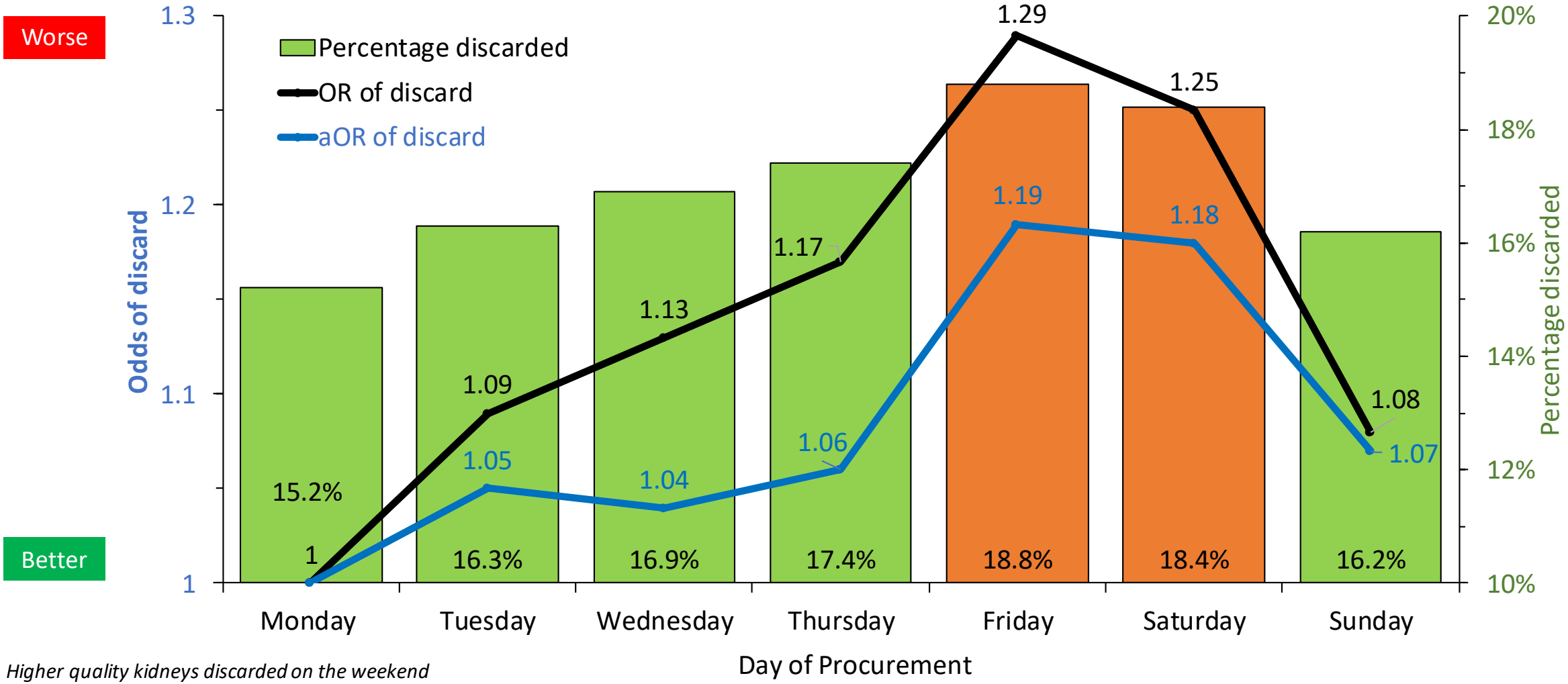
Procurement biopsies are error prone and should not be used to evaluate organ quality





Husain et al. CJASN 2018

Kidneys procured over the weekend are more likely to be discarded even after adjusting for quality

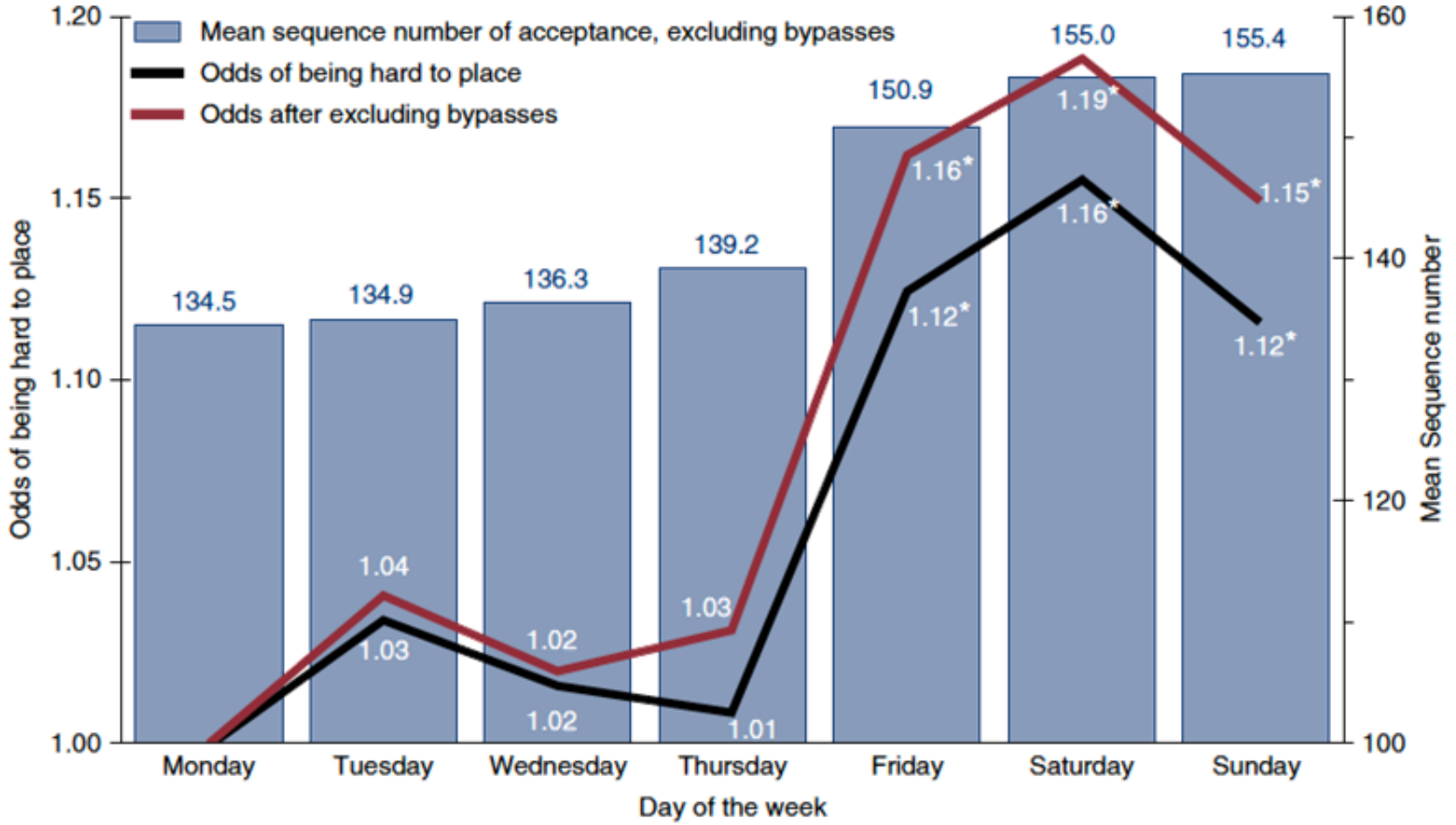


Higher quality kidneys discarded on the weekend
Discard data calculated using data from 2000 through 2013

Kidneys transplanted on the weekend are declined more often before eventually being accepted for transplanted

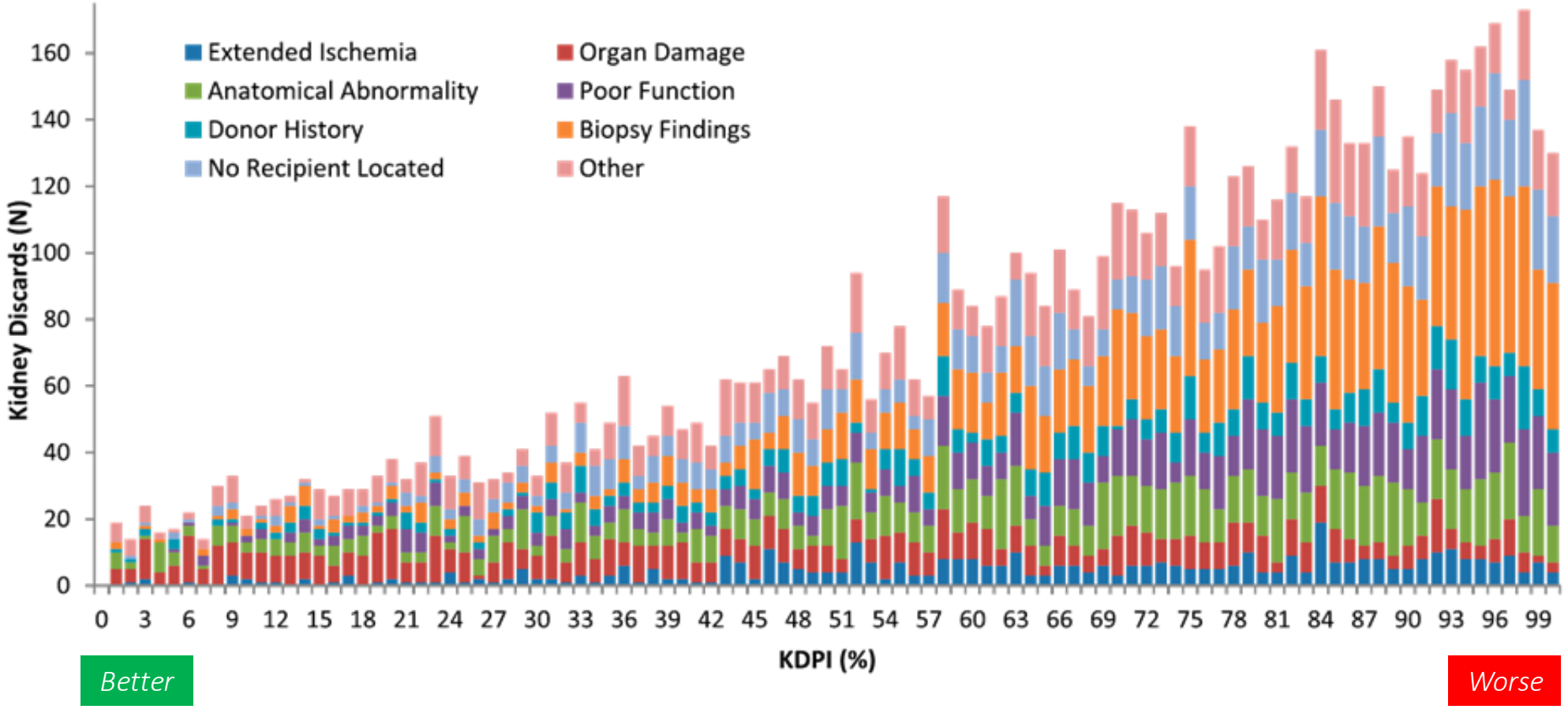
Worse

Better



King K et al. CJASN 2019

Unilateral discards occur across the spectrum of organ quality despite excellent outcomes from the partner kidney from the same donor



Discard data calculated using data from 2000 through 2015

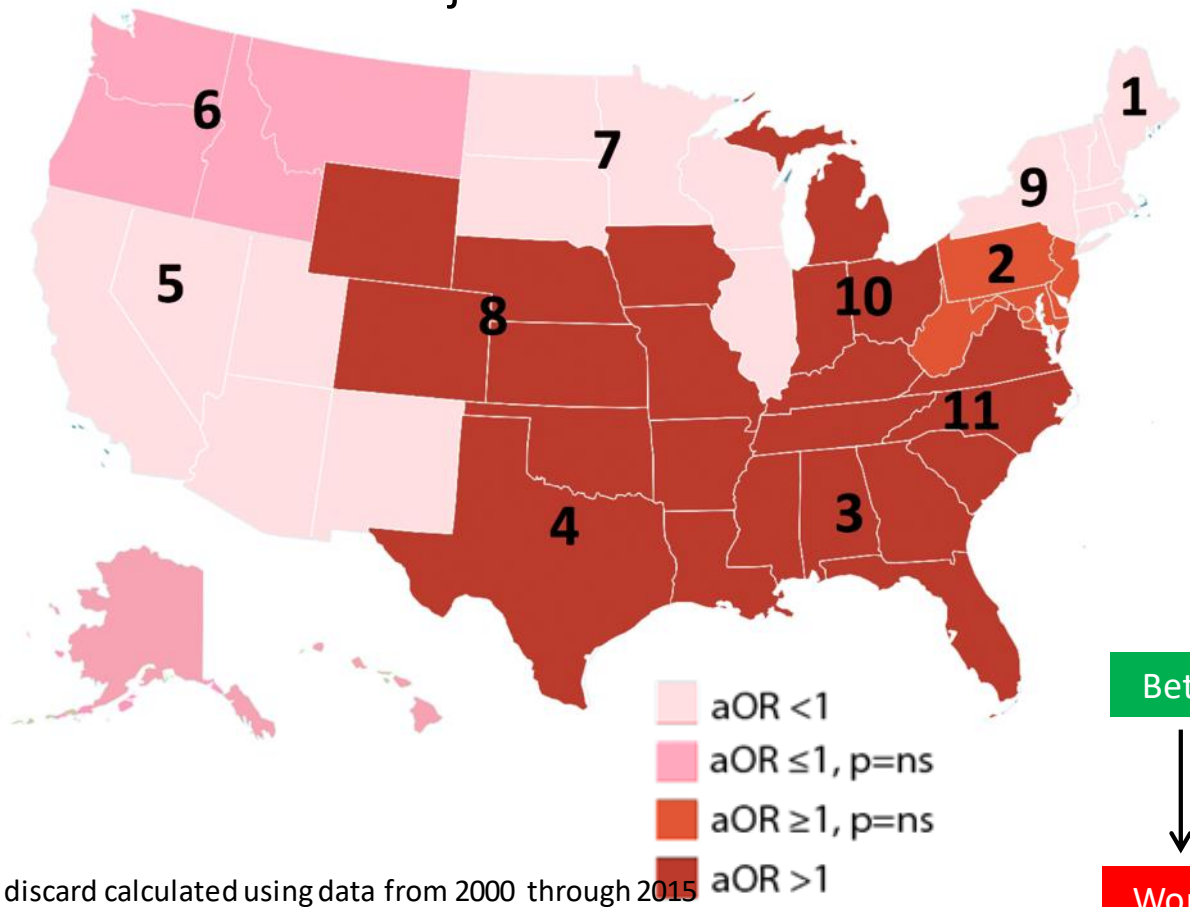
Excellent outcomes with unilateral kidney transplants in the United States

KDPI, %	Observed Single Kidney Graft Survival Rates, %							
	1 yr		2 yr		3 yr		5 yr	
	Unilateral	Bilateral	Unilateral	Bilateral	Unilateral	Bilateral	Unilateral	Bilateral
1	95	95	94	92	81	89	77	79
5	100	93	80	89	78	85	78	75
10	82	94	76	90	69	86	64	76
20	88	95	87	91	86	87	76	78
30	93	93	89	89	83	84	55	74
40	86	93	85	89	77	84	59	70
50	91	92	80	86	73	81	59	70
60	90	89	84	83	79	78	67	66
70	89	88	88	82	85	75	68	61
80	84	87	74	81	67	74	50	61
90	84	83	78	77	70	72	53	56
95	86	86	76	78	67	69	47	50
99	69	80	62	69	52	62	36	43

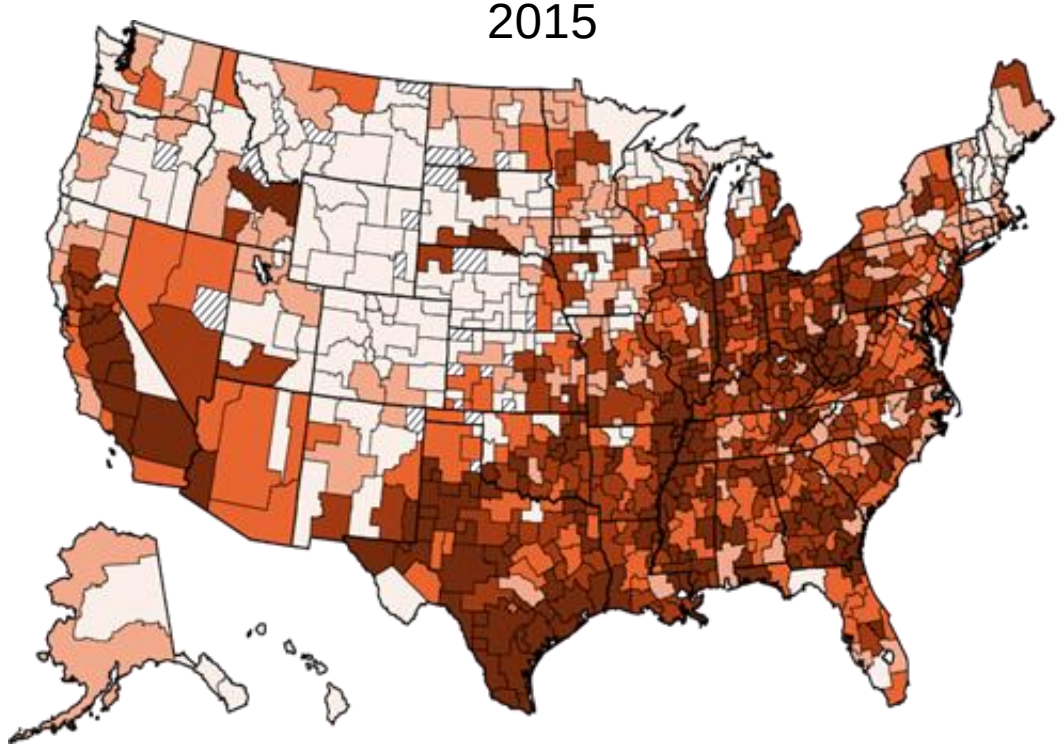
Husain SA et al CJASN 2018

Odds of discard of kidneys is highest in UNOS regions with the highest ESRD incidence

Adjusted Odds of Discard



Unadjusted incidence of ESRD 2011 - 2015



Better

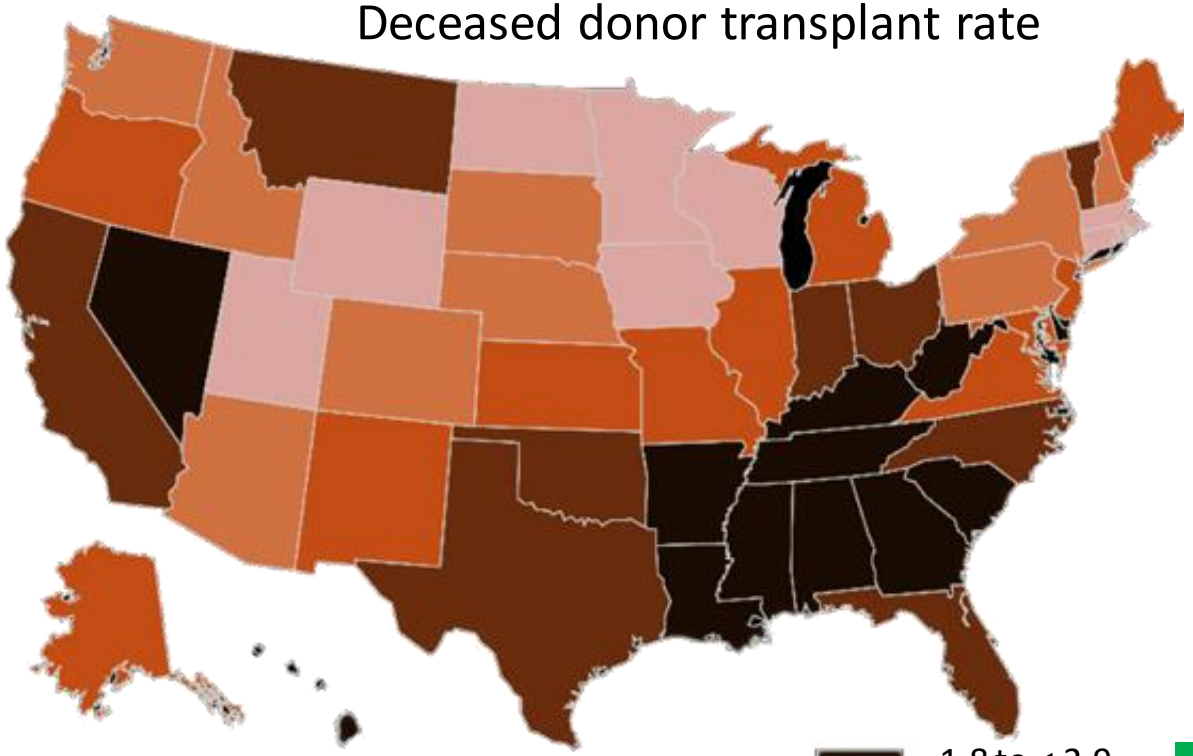
Worse

Odds of discard calculated using data from 2000 through 2015
Annualized transplantation rates calculated from 2000 through 2010

Mohan S et al. Kidney Int. 2018

Odds of discard of kidneys is highest in regions with the lowest transplant rates

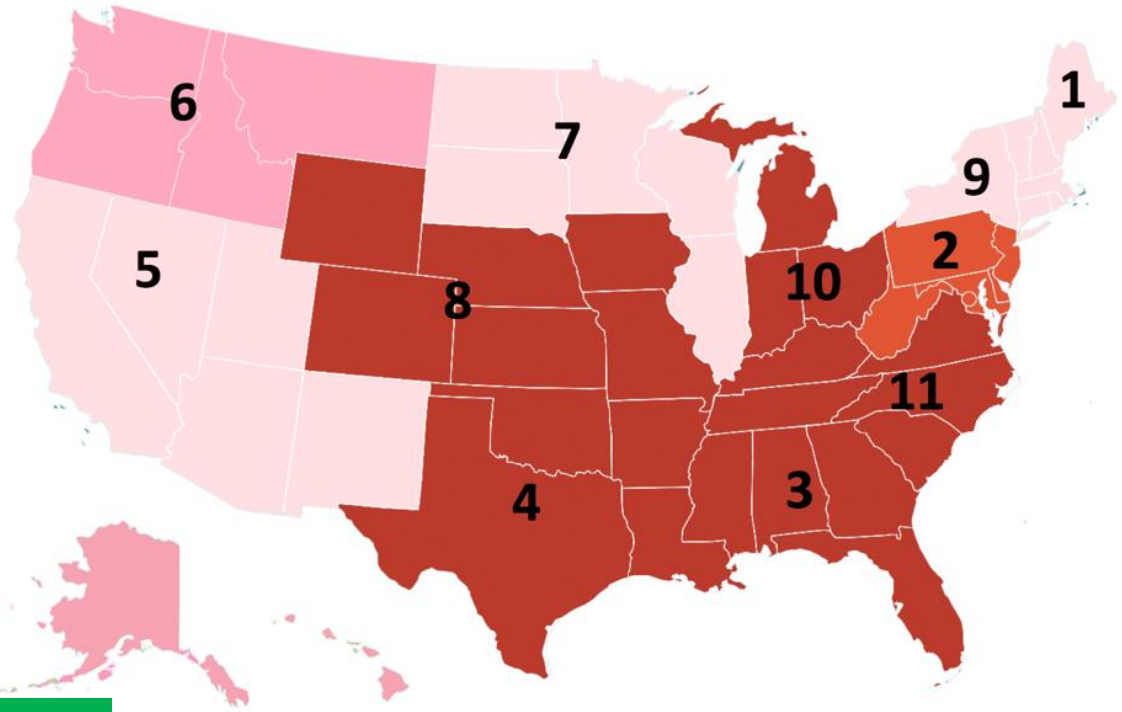
Deceased donor transplant rate



1.8 to < 2.9
2.9 to < 3.4
3.4 to < 4.1
4.1 to < 5
> 5

Odds of discard calculated using data from 2000 through 2015

Adjusted Odds of Discard



Better

Worse

aOR <1
aOR ≤1, p=ns
aOR ≥1, p=ns
aOR >1

So far..

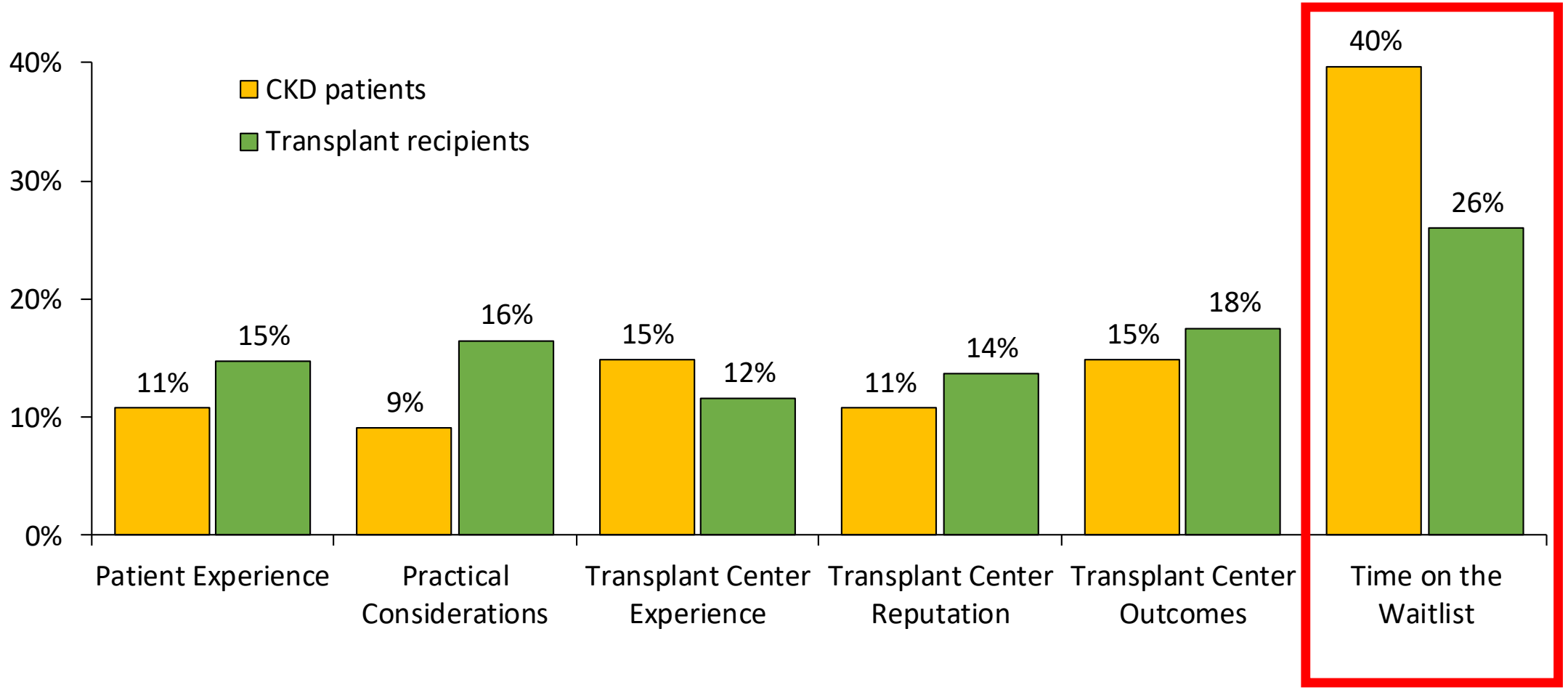
1 in 5 deceased donor kidneys are being discarded

Organ quality does not appear to be driving discards

Significant geographical variation in the discard of organs

Patient preferences

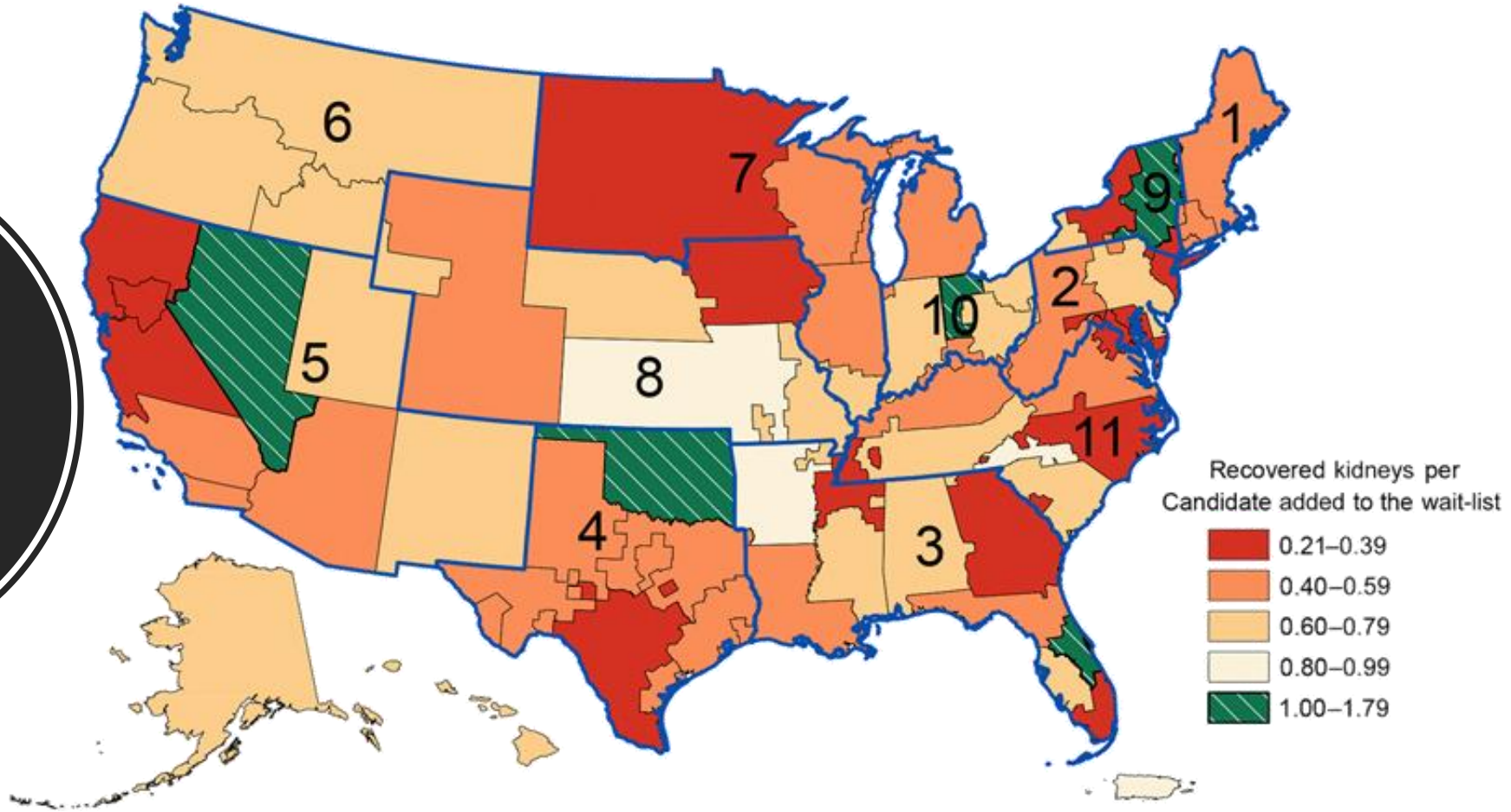
prioritize waitlist over posttransplant outcomes when selecting a transplant center



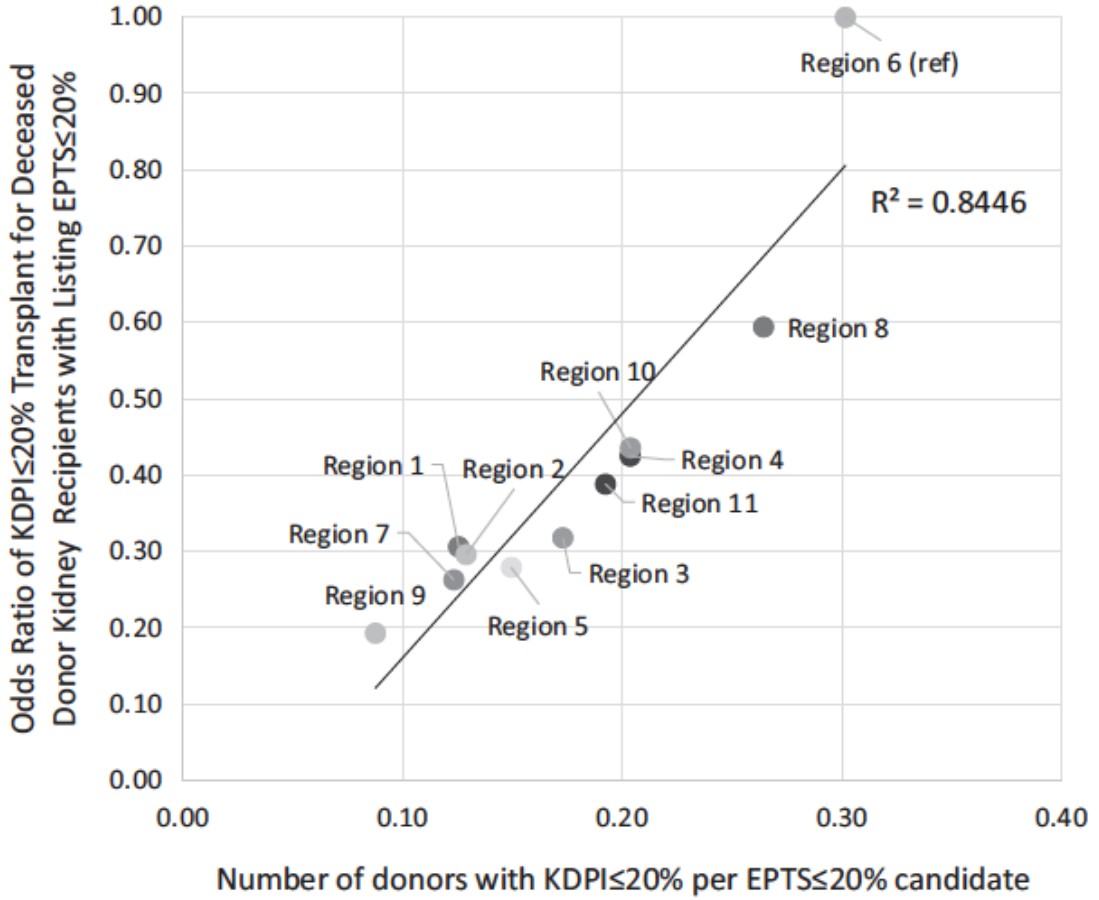
Only published national survey identifying patient centered criteria on selecting a transplant center
Over 500 respondents for survey conducted in 2017

Husain SA et al. Am J Transplant. 2018

Kidneys recovered per candidate



Longevity matching
intent vs reality



Region	1	2	3	4	5	6	7	8	9	10	11
Percent of all donors with KDPI≤20%	16.0	14.1	17.1	21.8	19.0	25.4	15.7	22.5	16.3	18.6	18.9
Number of donors with KDPI≤20% per EPTS≤20% candidate	0.13	0.13	0.17	0.20	0.15	0.30	0.12	0.26	0.09	0.20	0.19

Husain SA et al. Prog Transpl 2019

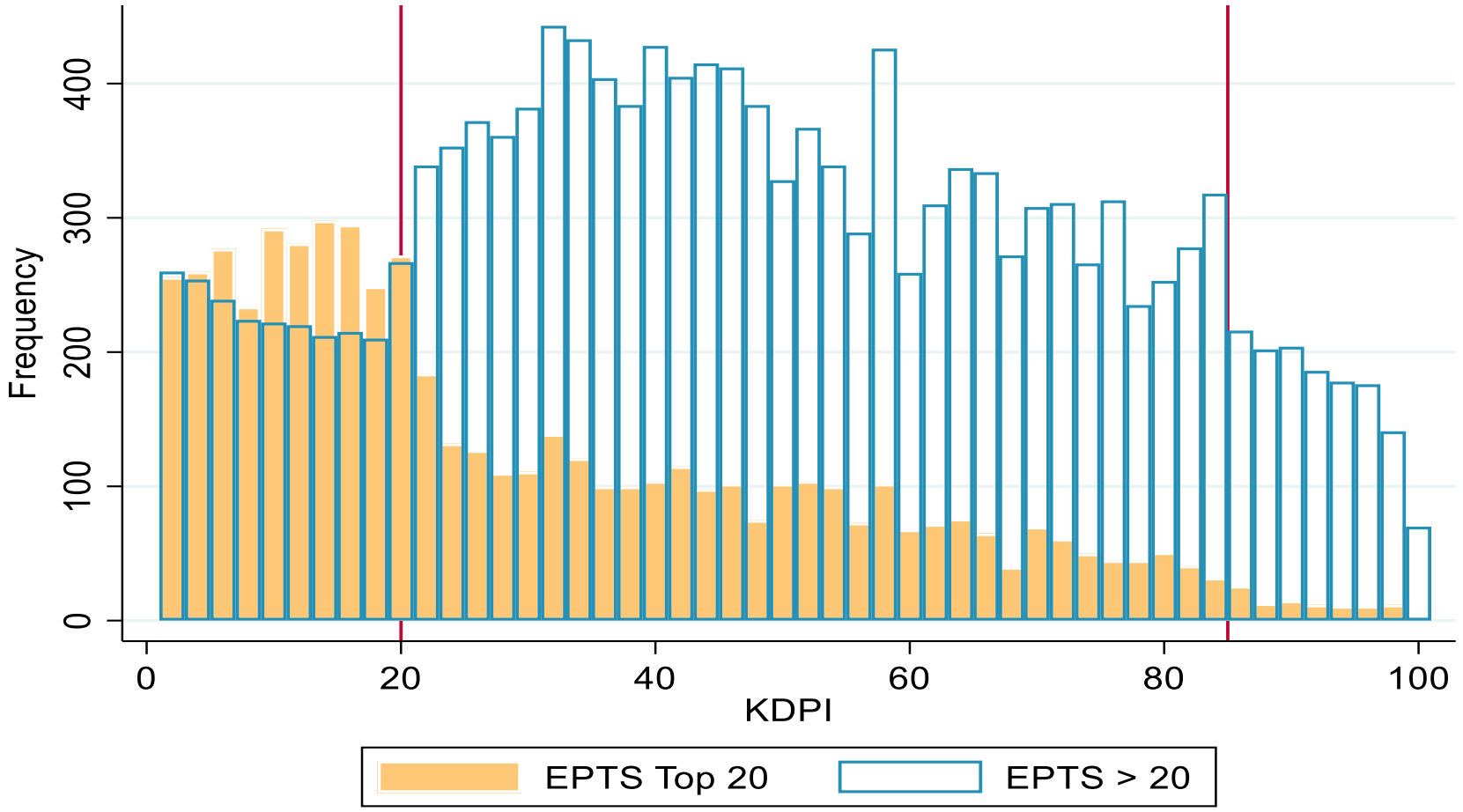
Table 2. Disposition of Top 20 KDPI Organs Transplanted in Recipients With EPTS > 20%, by Region, January 1, 2015, to March 31, 2018.

Region	KDPI ≤ 20% Kidneys Transplanted (n)	n (%) for Recipients With EPTS > 20%[a]	Among KDPI ≤ 20% Kidneys Transplanted in EPTS > 20% Recipients	
			n (%) Used for cPRA > 97%[a]	n (%) Used for Multi-Organ Transplants[b]
1	117	54 (46%)	11 (20%)	28 (52%)
2	543	285 (52%)	68 (24%)	162 (57%)
3	766	399 (52%)	40 (10%)	282 (71%)
4	646	316 (49%)	46 (15%)	212 (67%)
5	772	387 (50%)	62 (16%)	263 (68%)
6	245	87 (36%)	5 (6%)	59 (68%)
7	387	204 (53%)	31 (15%)	147 (72%)
8	425	158 (37%)	19 (12%)	112 (71%)
9	215	98 (46%)	9 (9%)	55 (56%)
10	449	214 (48%)	23 (11%)	141 (66%)
11	581	283 (49%)	53 (19%)	174 (61%)
Overall	5146	2485 (48%)	367 (15%)	1635 (66%)
		$P < .001$	$P < .001$	$P < .001$

Husain SA et al. Prog Transpl 2019

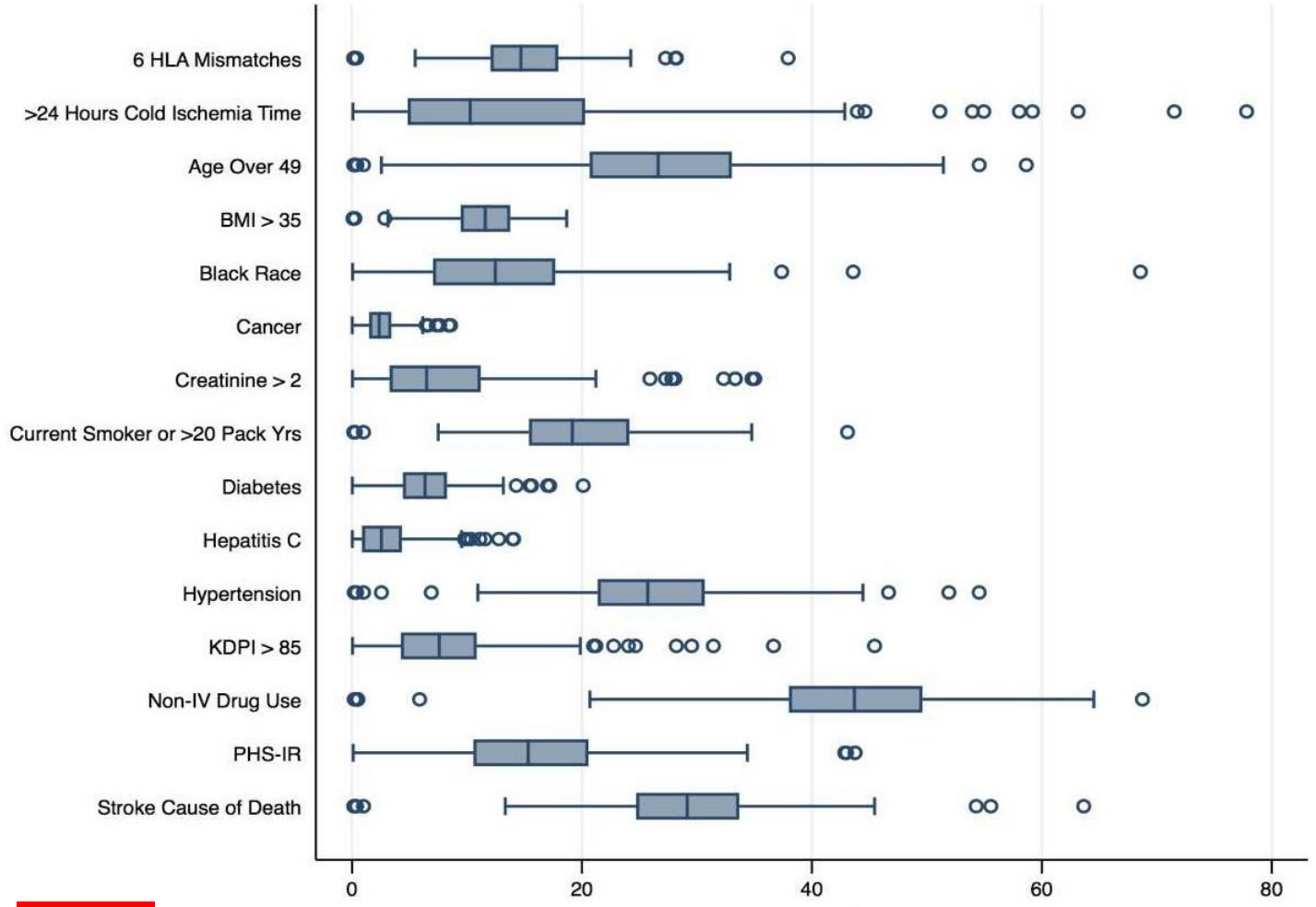
Distribution of KDPI of kidneys accepted by patients

stratified by Top 20 EPTS status



Husain SA et al. Prog Transpl 2019

Variation in the use of donors with unfavorable clinical characteristics



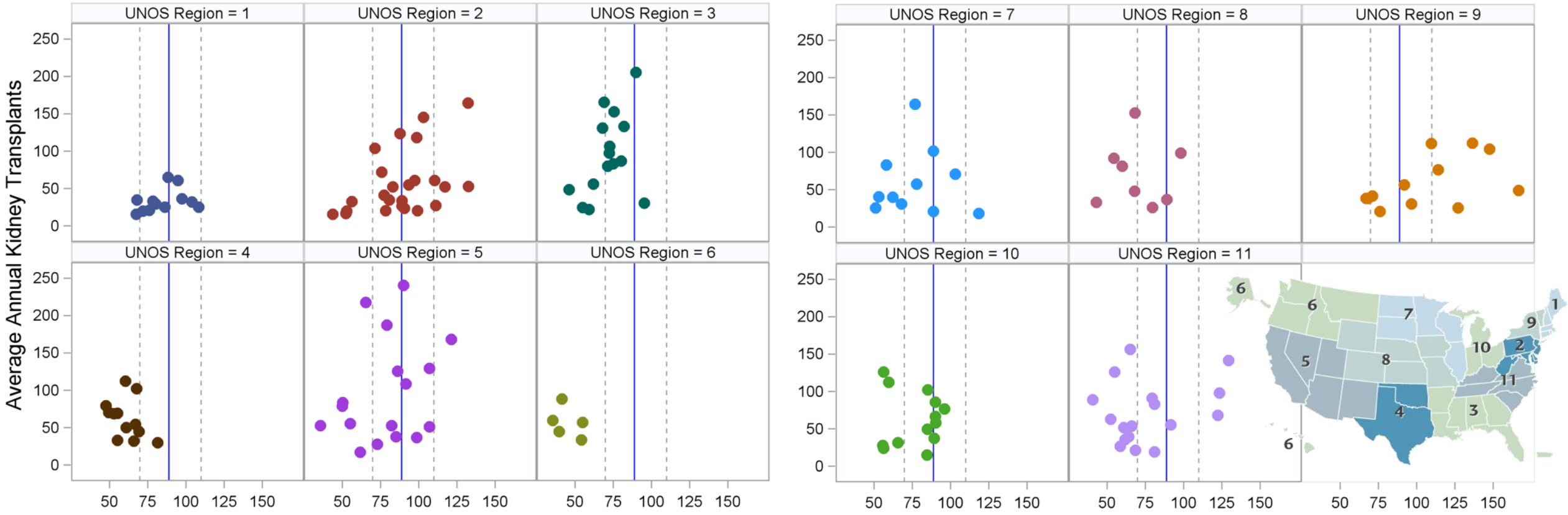
Fewer

Percentage of deceased donors with given characteristic at transplant center

More

Brennan C et al. 2019 In review

Donor Utilization highly variable within UNOS/OPTN regions



Brennan C et al. CJASN 2019

Organ offers

- From 2008 through 2015, 14 million deceased donor kidneys offers were made for kidneys before they were eventually accepted
  - *Excluding discarded organs*
- 76% of patients on the waitlist received at least one offer for a deceased donor kidney
- Only 15.6% of deceased donor kidneys accepted without being declined at least once
- Only 2.6% of all offers were reportedly declined for recipient related reason – i.e most patients are unaware that their centers are turning down organ offers on their behalf

Reasons for deceased donor kidney offer refusal

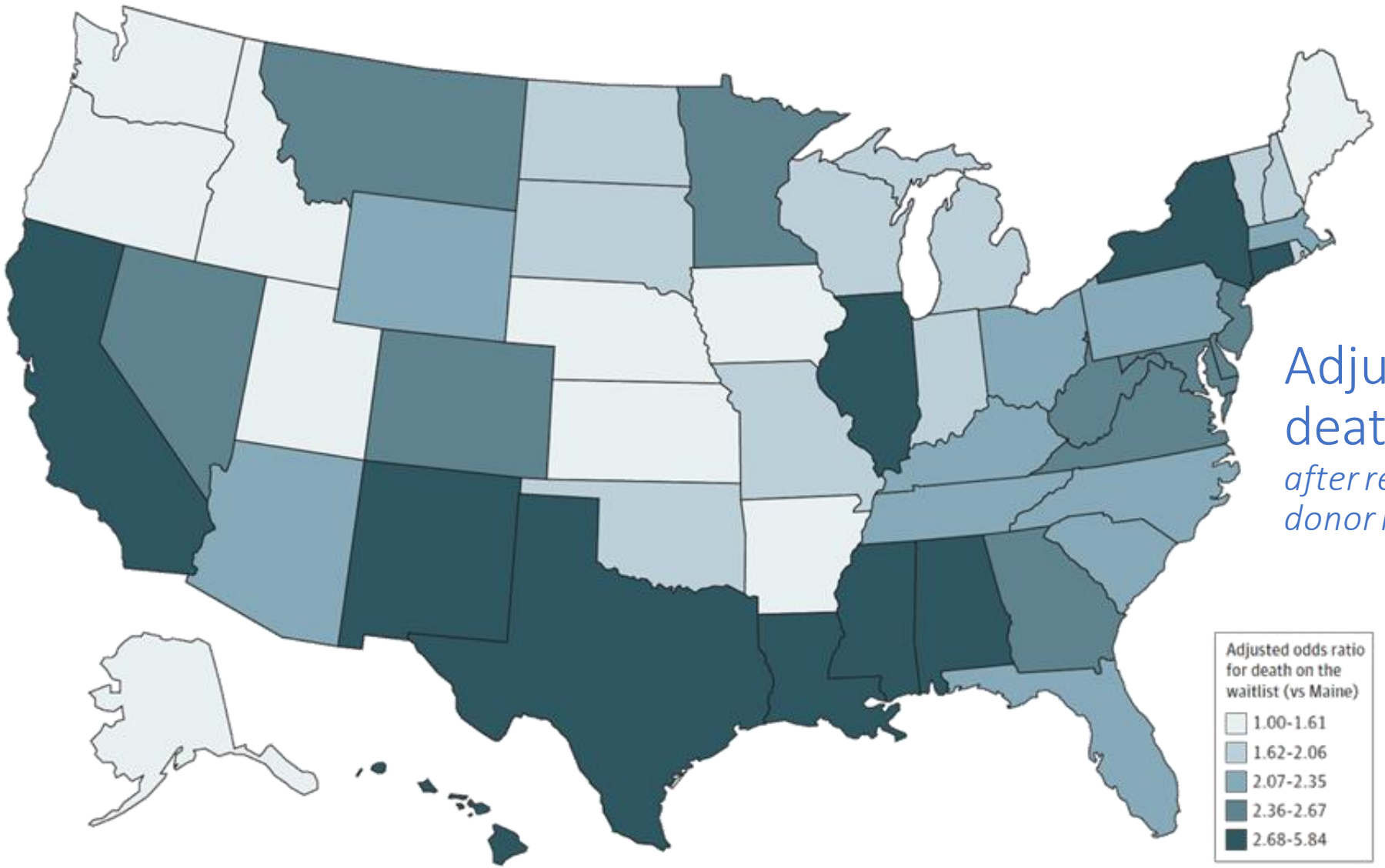
No change over the spectrum of KDPI

	Offer Refusal Category (%)			
KDPI*	**Patient-Related**	**Organ/Donor Quality**	**Logistical**	**Immunologic/ Other**
All	2.6	92.6	0.5	4.3
0 - 10	4.2	87.1	0.6	8.1
11 - 20	4.5	87.9	0.6	7.0
21 - 30	2.8	90.7	0.5	6.0
31 - 40	3.7	91.6	0.5	4.3
41 - 50	2.6	92.9	0.7	3.8
51 - 60	2.4	92.0	0.7	4.9
61 - 70	2.4	93.5	0.4	3.7
71 - 80	2.0	93.3	0.6	4.0
81 - 90	2.3	93.8	0.5	3.5
91 - 100	2.1	94.3	0.4	3.2
Unknown	2.4	90.7	1.0	5.9

** KDPI: Kidney Donor Profile Index, a relative measure for donor quality. Lower KDPI is considered higher donor quality.*

*** Chi-squared p<0.001*

Husain SA et al. 2019 In review



Adjusted odds ratio for death on the waitlist

after receipt of at least 1 deceased donor kidney offer

Husain SA et al. JAMA Netw Open 2019

Consequences of declining kidney offers

Variable[a]	Total	Event Group				
		Died While on Waiting List	Received Allograft From DD	Received Allograft From LD	Removed From Waiting List	Remaining on Waiting List
Started dialysis between wait-listing and event, No. (%)[d]	14 953 (5.3)	750 (2.9)	2059 (2.5)[b]	950 (3.1)	2190 (3.7)	9004 (11.0)
Days between listing and first offer, median (IQR)	48 (13-232)	78 (17-401)	79 (16-426)[b]	34 (11-103)	62 (16-302)	30 (9-104)
Days between first offer and event, median (IQR)[d]	526 (193-1041)	651 (304-1117)	422 (106-909)	188 (83-403)	690 (326-1192)	650 (276-1255)
No. of offers before event, median (IQR)[d]	16 (5-40)	16 (6-41)	17 (6-44)	7 (3-16)	15 (6-37)	21 (8-51)
Days between first and last offers, median (IQR)	386 (122-829)	390 (140-764)	420 (103-907)	144 (40-350)	392 (149-775)[b]	490 (191-984)

Husain SA et al. JAMA Netw Open 2019

Patients who die on the waitlist have often received multiple kidney offers

declined kidneys were subsequently used for patients further down the list

	Total	Died on Waitlist	Removed from Waitlist
N (%)	280,041	25,967 (9.3%)	59,359 (21.2%)
Number of offers before death/removal	16 (5-40)	16 (6-41)	15 (6-37)
Time from first offer to death/removal (days)	526 (193-1041)	651 (304-1117)	690 (326-1192)

Husain SA et al. 2019 In review

So now we also know that

Patients are focused on time to transplant

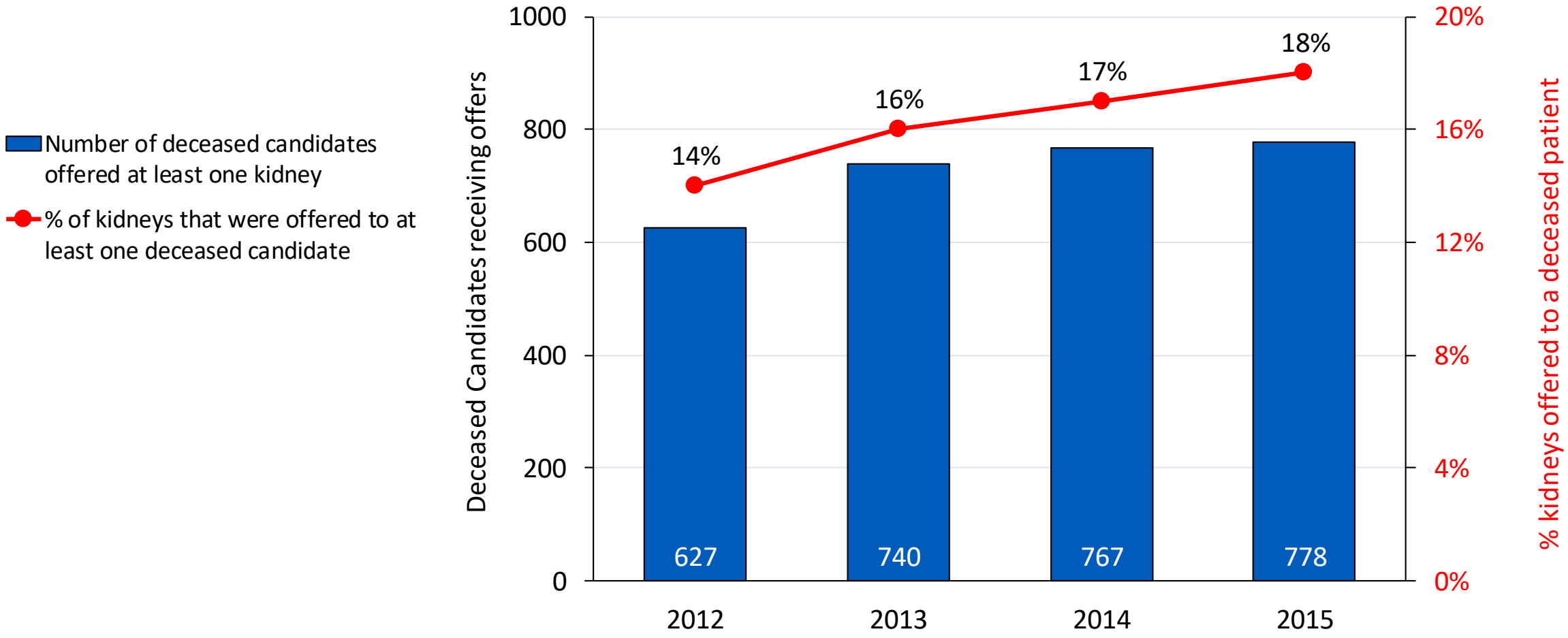
Transplant centers and dialysis don't communicate effectively

Organ offers are frequently declined for unclear reasons

- ✓ *Without patient participation*
- ✓ *Resulting in wide variation in organ acceptance*
- ✓ *Overlooks adverse consequences for patients*

Can this be fixed?

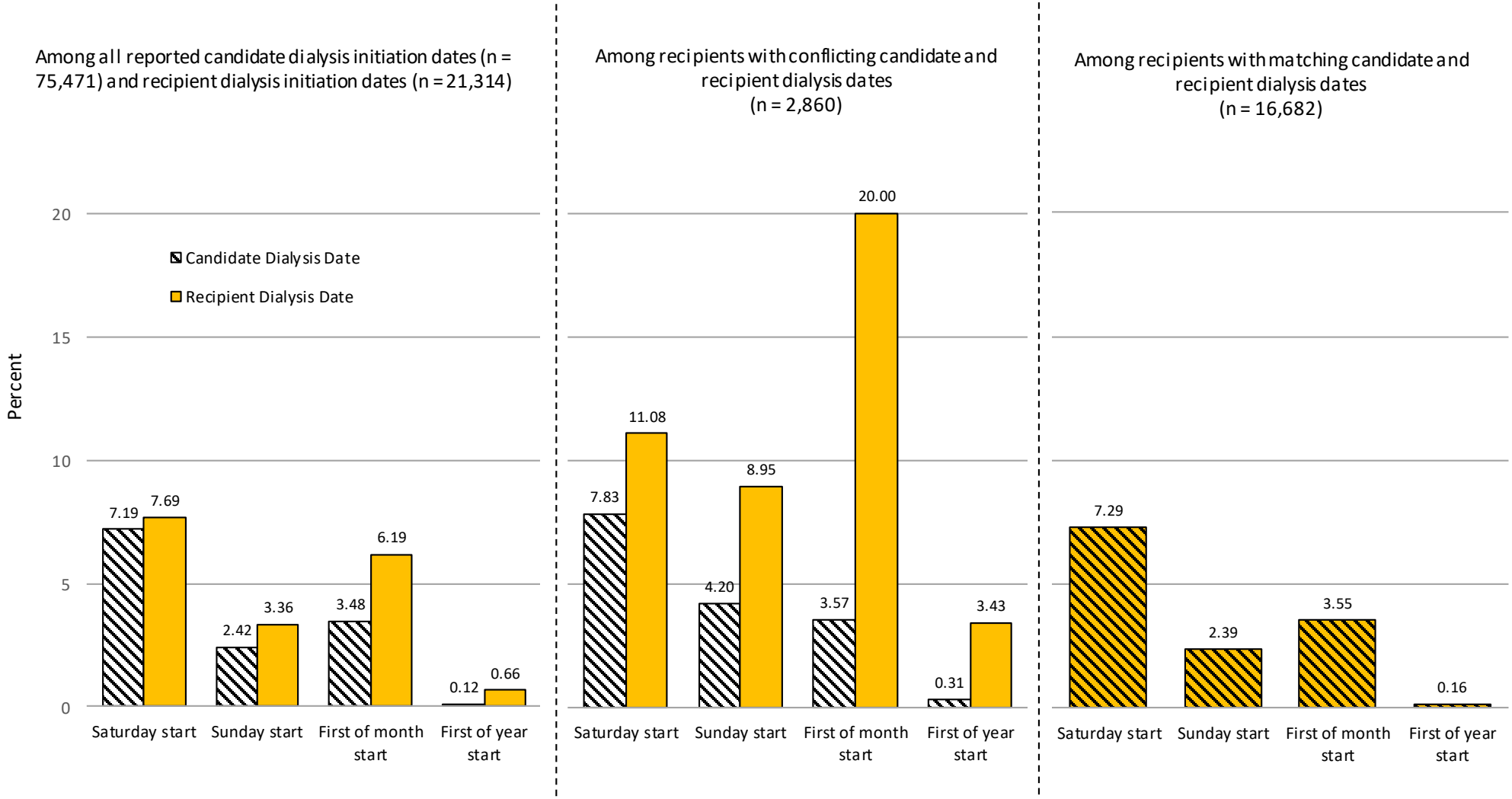
Poor communication between transplant centers and dialysis units



Median of 4 post-death offers (range 1-385, IQR 2-12).
Most (60.4%) offers to deceased candidates occurred >1 month after candidate death

Husain SA et al. Am J Transplant. 2018

Dialysis date errors in the allocation system

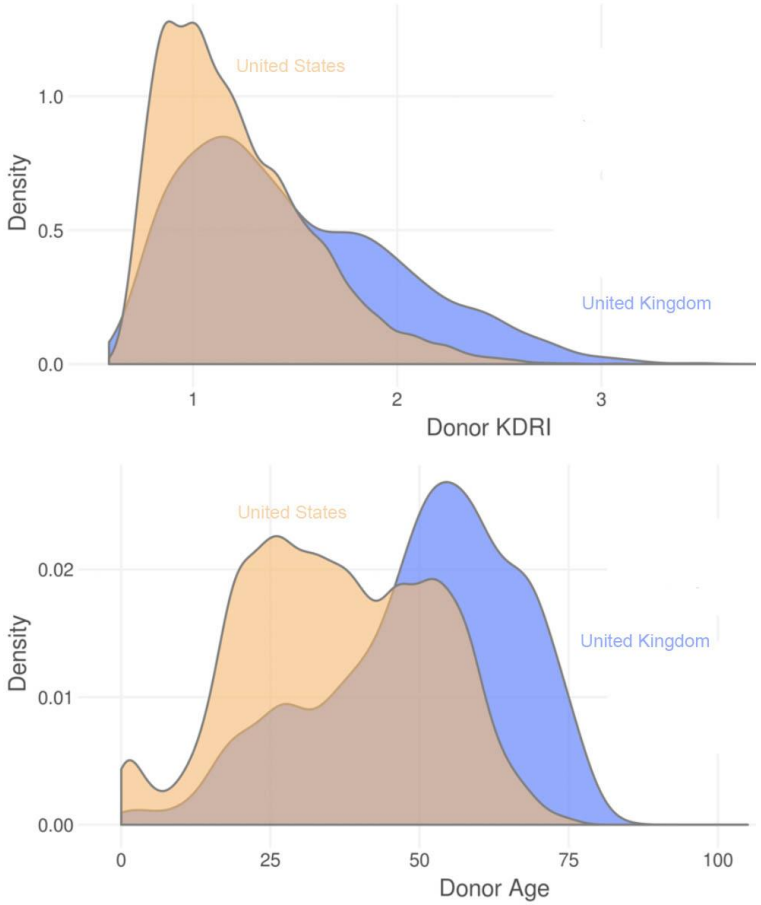


Tsapepas et al. AJT 2019

International Comparisons - UK

	United States	United Kingdom
Recovered (N)	15,144	2,423
Age (years)	36 (24 – 49)	53 (40 – 63)
KDRI (transplanted)	1.13 (0.93 – 1.42)	1.38 (1.03 – 1.83)
Discard rate (overall)	19%	10%
Discard rate (DCD)	81%	59%

Median (IQR) reported for organs procured in 2017



https://atcmeetingabstracts.com/abstract/an-international-comparison-of-kidney-utilization-in-the-united-states-and-united-kingdom-what-can-be-learned/

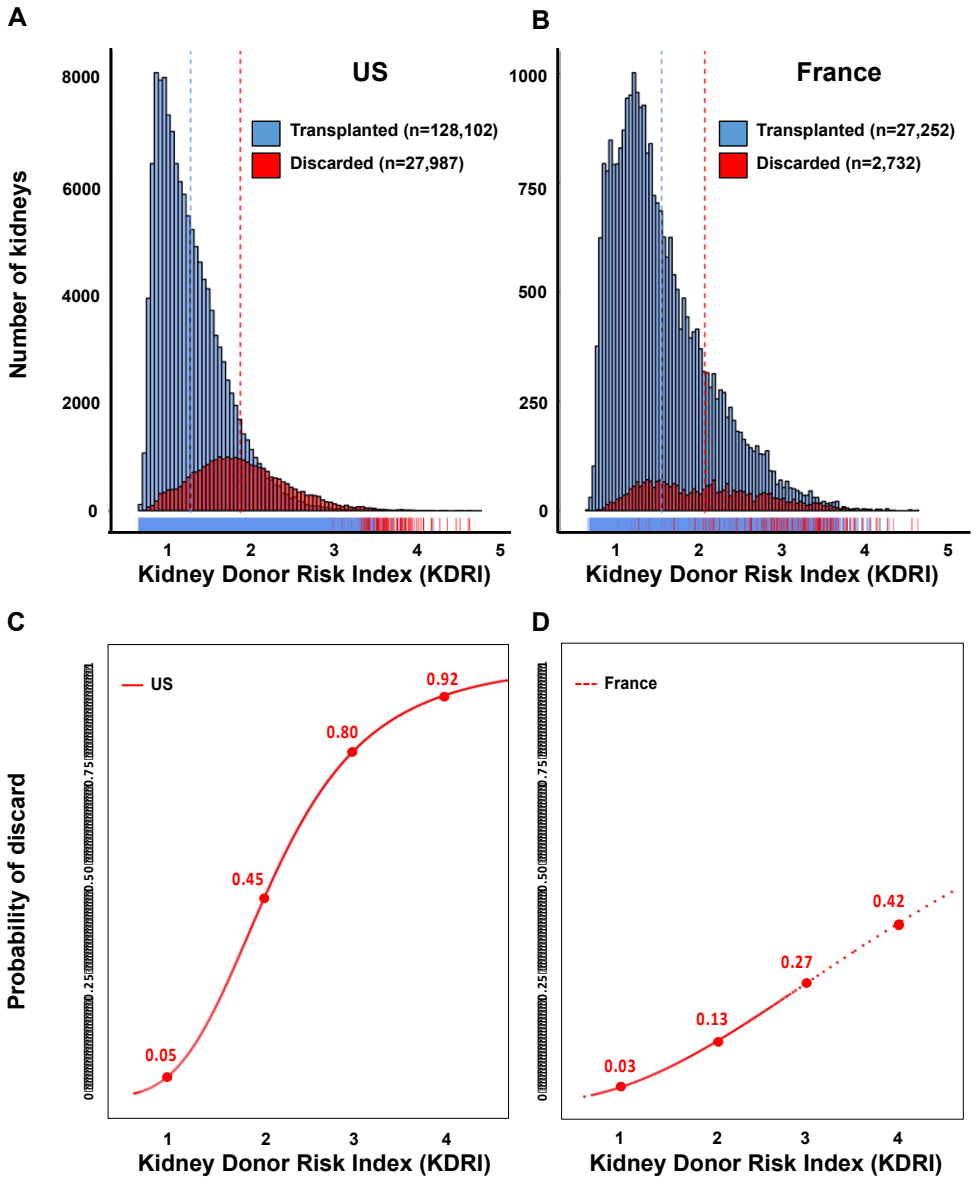
International Comparisons - France

	United States	France
N	156,089	29,984
Age (years)	36.5 (17)	50.9 (17)
KDRI (transplanted in 2004)	1.30 (0.48)	1.37 (0.47)
KDRI (transplanted in 2014)	1.32 (0.46)	1.74 (0.72)
Discard rate (overall)	18%	9%

Mean (SD) reported for organs procured in 2004 - 2014

Using the French criteria, 62% of the kidneys discarded in the US would have been transplanted:

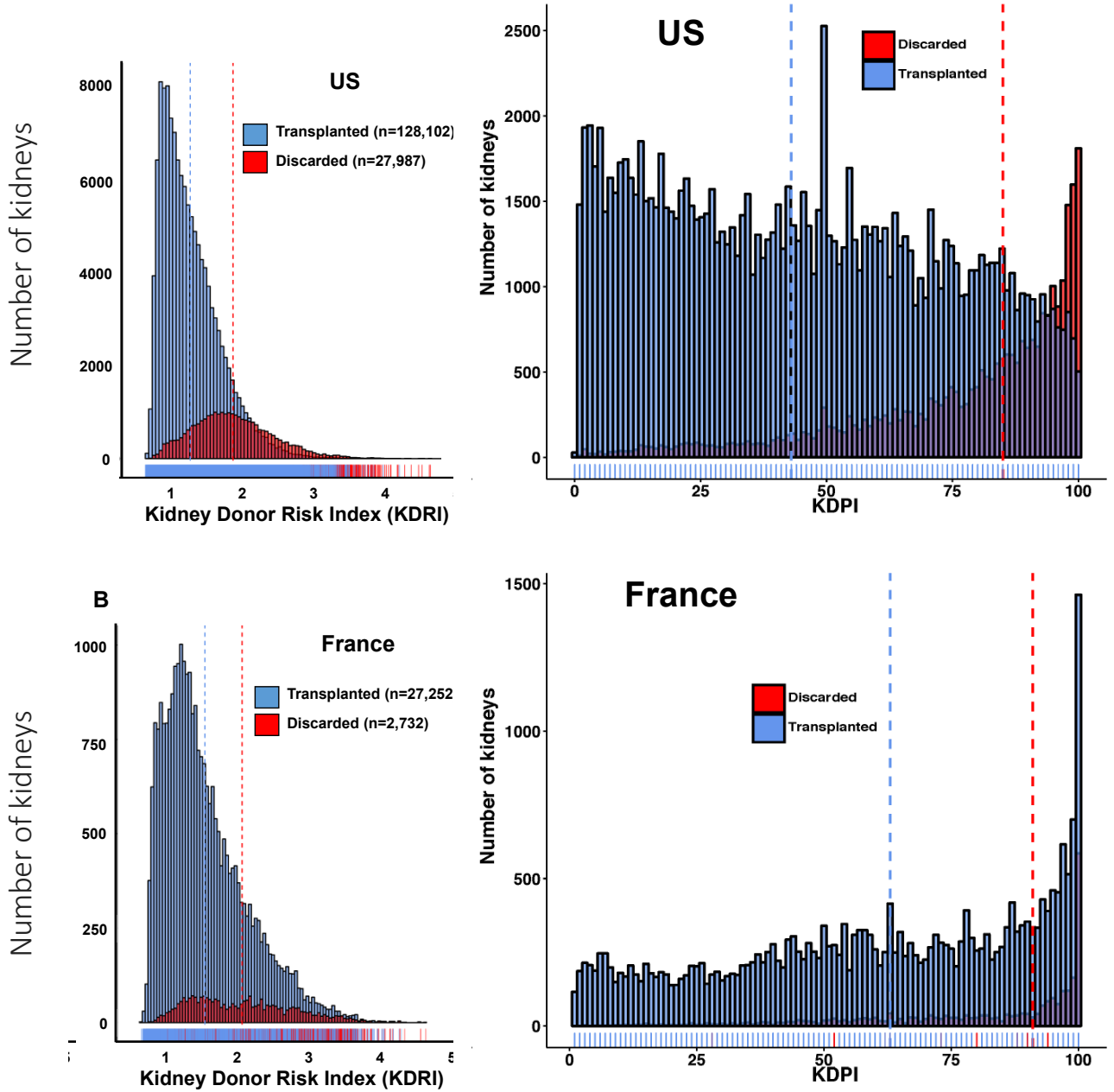
- 17,435 kidneys
- 132,445 allograft life years



https://atcmeetingabstracts.com/abstract/kidney-transplant-outcomes-and-organ-acceptance-practice-patterns-nationwide-analyses-of-the-us-and-france/

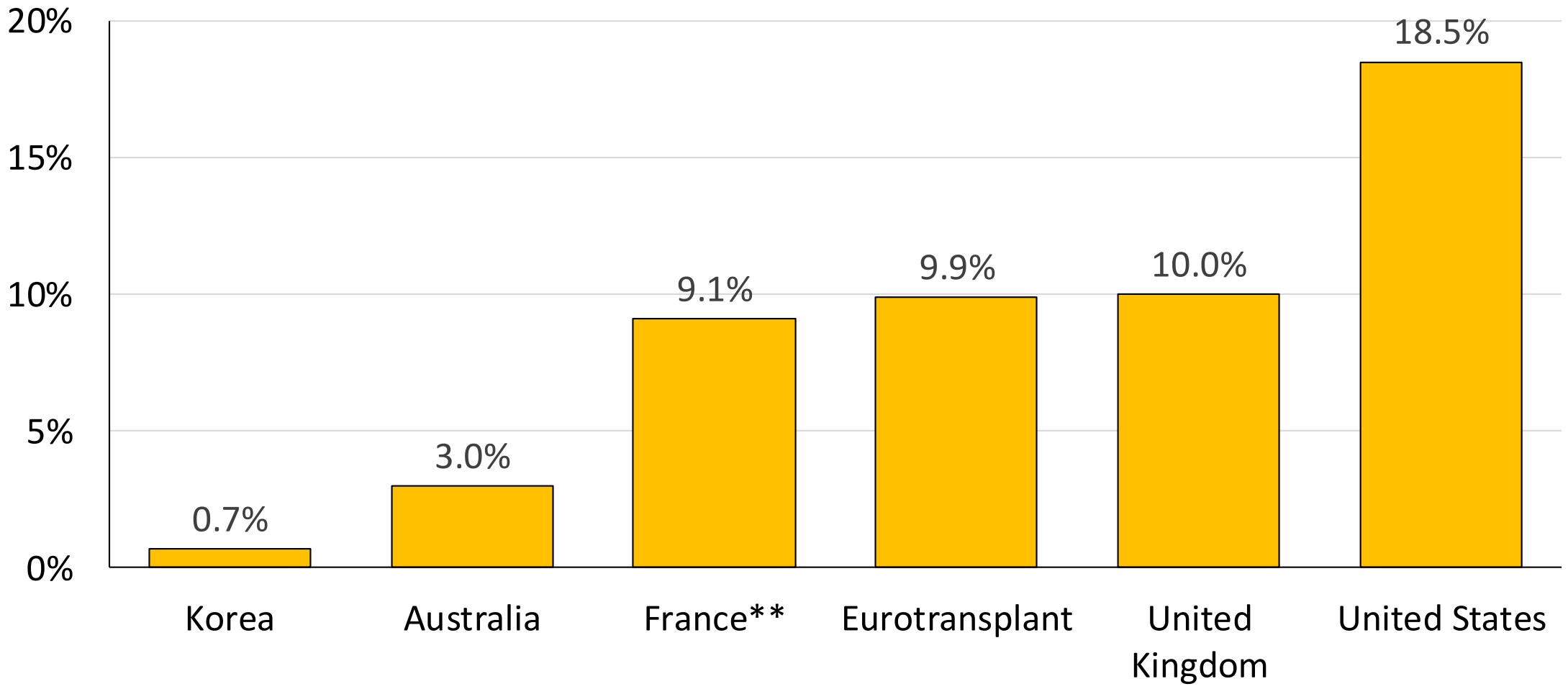
Differences deceased donor kidneys utilization across the KDPI spectrum in France and the U.S.

- Discarded
- Transplanted



2004 – 2014 data

International comparisons - Kidneys discarded in 2014



Kim Hk et al. Transplant Proc 2019
Oubert ATC 2019 and ANZ data 2016

Summary

- 1 in 5 kidneys in the United States is being discarded
  - Majority of kidneys discarded are potentially transplantable
  - Outcomes with less than ideal kidneys far superior to the alternative
- Large variation in practice patterns across transplant centers
  - Variations in the type of kidneys accepted
  - Declined offers clearly associated with adverse outcomes for patients
- Experience with less than ideal kidneys in other countries underscores ability to utilize these kidneys
- Poor communication between dialysis facilities and transplant centers undermines our ability to provide good care for our patients.