Scores in kidney transplantation:
How can we use them?

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M Hazzan (Lille – France)

Contents

Quality of the graft

Extended Criteria Donor (*vs* Standard Criteria Donor)

- Age > 60 years old
- Age 50-59 + 2 of the following criteria:
  - Stroke
  - Hypertension
  - Serum creatinine > 1.5 mg/dl

TABLE 4. Graft survival (death censored) at 3 months, 1 year, and 3 years[a]

Risk status	N (%)	Graft survival (%)		
		3 Mo	1 Yr	3 Yr
RR <1.7	24,756 (85.2)	94.6	90.6	79.4
RR=1.7–2.0	2,125 (7.3)	93.6	86.5	71.7
RR=2.0–2.5	2,054 (7.0)	91.2	82.8	65.6
RR >2.5	133 (0.5)	86.7	78.7	49.4
Expanded donor (RR ≥1.7)	4,312 (14.8)	92.3	84.5	68.0

Does a binary classification really reflect real life?

ECD → **SCD**

Port F, Transplantation 2002

Kidney Donor Profile Index

- Numerical measure of the quality of the graft
- Derived from de Kidney Donor Risk Index[1]
  - KDRI: 14 factors (full KDRI: 10 donor-only factors + 4 donor-recipient factors)
  - KDRI/KDPI: 10 factors (donor-only KDRI)
- Relative risk of graft failure compared to a median donor
  - KDRI = 1.6: Risk of graft failure 60% higher *vs* median donor
- KDPI is mapped to the percentile of its distribution
  - Median donor: 50th percentile

1) Rao PS, Transplantation 2009

Calculation of the KDPI

70000 first Tx from deceased donor (1995-2005)

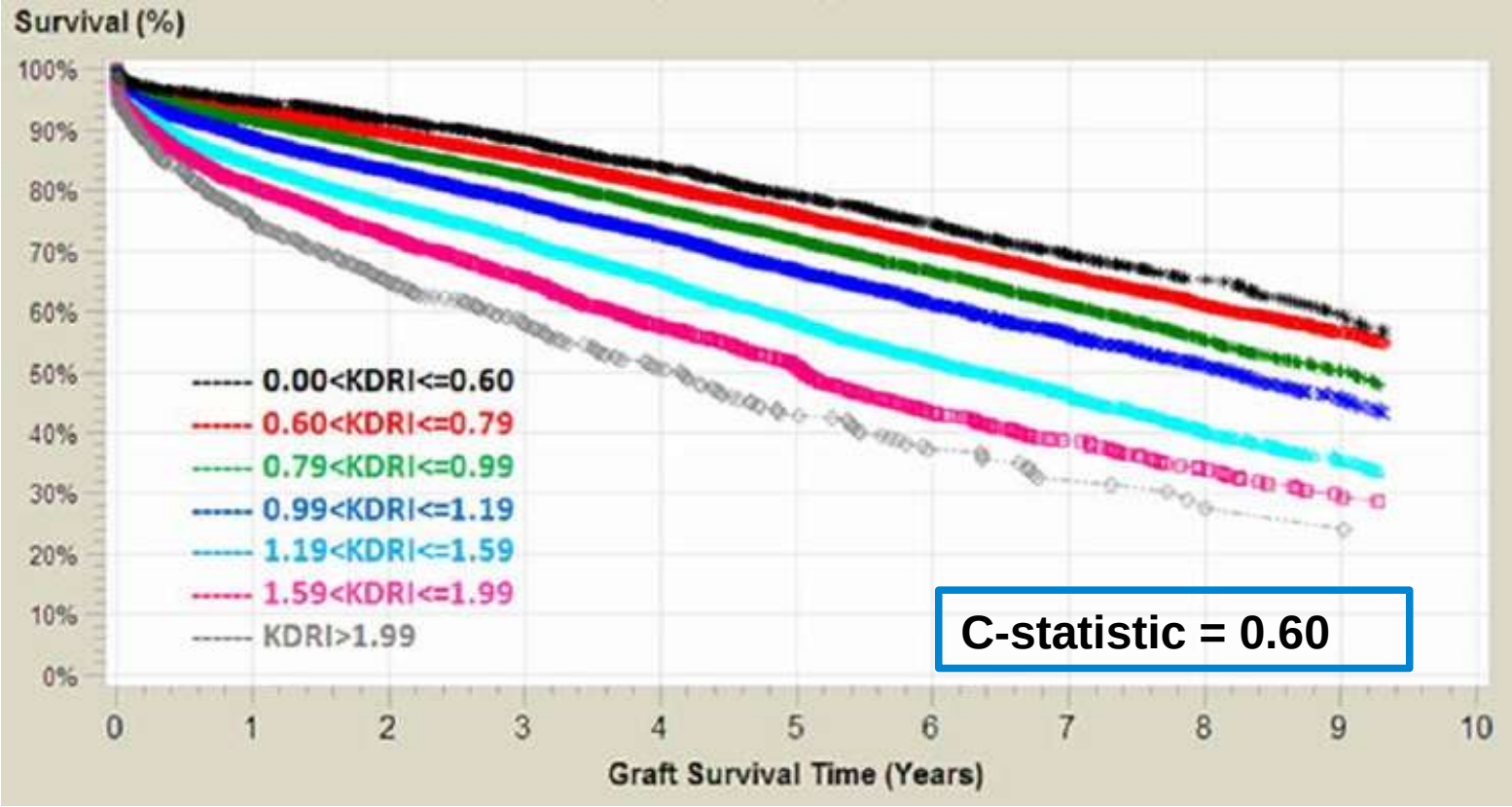
Donor Characteristic	Applies to:	KDRI Coefficient ("Beta")	KDRI "XBeta" Component
Age (integer years)	All donors	0.0128	0.0128*(age-40)
	Donors with age < 18	-0.0194	-0.0194*(age-18)
	Donors with age > 50	0.0107	0.0107*(age-50)
Height (cm)	All donors	-0.0464	-0.0464*(hgt-170)/10
Weight (kg)	All donors w/ weight < 80kg	-0.0199	-0.0199*(wgt-80)/5
Ethnicity	African American donors	0.1790	0.1790
History of Hypertension	Hypertensive donors	0.1260	0.1260
History of Diabetes	Diabetic donors	0.1300	0.1300
Cause of Death	Donors w/ COD=CVA	0.0881	0.0881
Serum Creatinine	All donors	0.2200	0.2200*(creat-1)
	Donors with creat > 1.5 mg/dL	-0.2090	-0.2090*(creat-1.5)
HCV status	HCV positive donors	0.2400	0.2400
DCD Status	DCD donors	0.1330	0.1330

Xbeta=sum(KDRI score component) → KDRI-RAO=exp(XBeta)

Normalization: KDRI-RAO/(scaling factor)* → 1.0 = median donor, range [0.5 – 3.5]

** median KDRI-RAO of the previous calendar year*

Graft survival according to KDRI

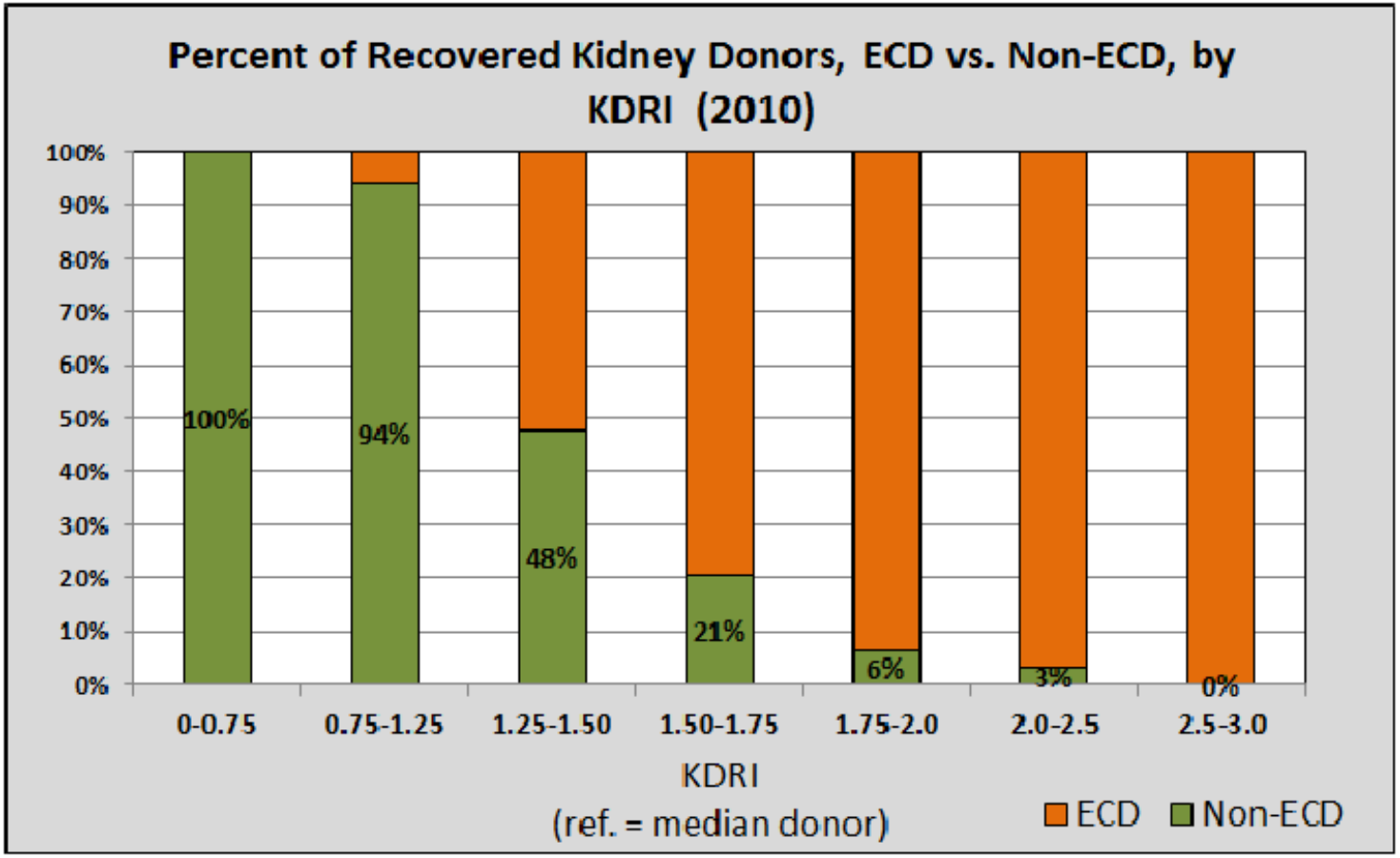


The lower is the better

From ECD/SCD to KDRI

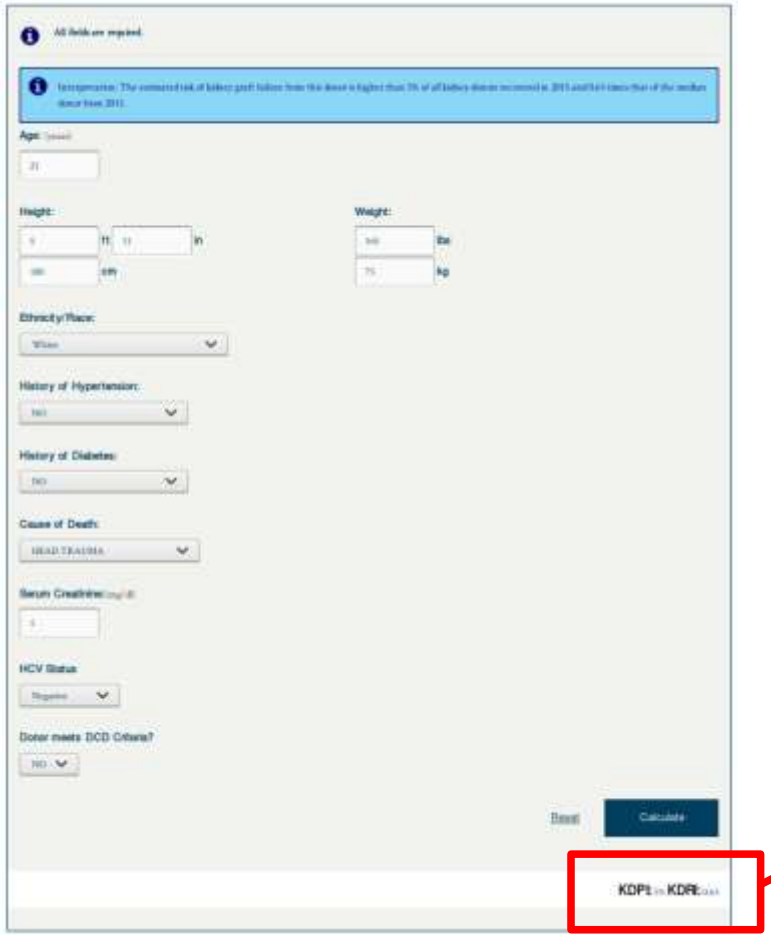
- 4 factors → 10 factors
- Binary score → Continuous score
- Not all ECD are alike
- Some SCD could be ECD

KDRI *vs* ECD/SCD: discrepancies



How to proceed in practice?

https://optn.transplant.hrsa.gov/resources/allocation-calculators/kdpi-calculator/



Interpretation: The estimated risk of graft failure from this donor is higher than 5% (or lower than 95%) of the kidney donors recovered in 2015

KDPI: 5%, KDRI: 0.63

KDPI: what for?

- Longevity matching allocation of the kidneys

- From equity to usefulness
  - To reduce retransplantation rate
  - To improve graft survival

↓

Need for a prognostic score
to estimate the mortality of the recipients

Estimated Post Transplant Survival time

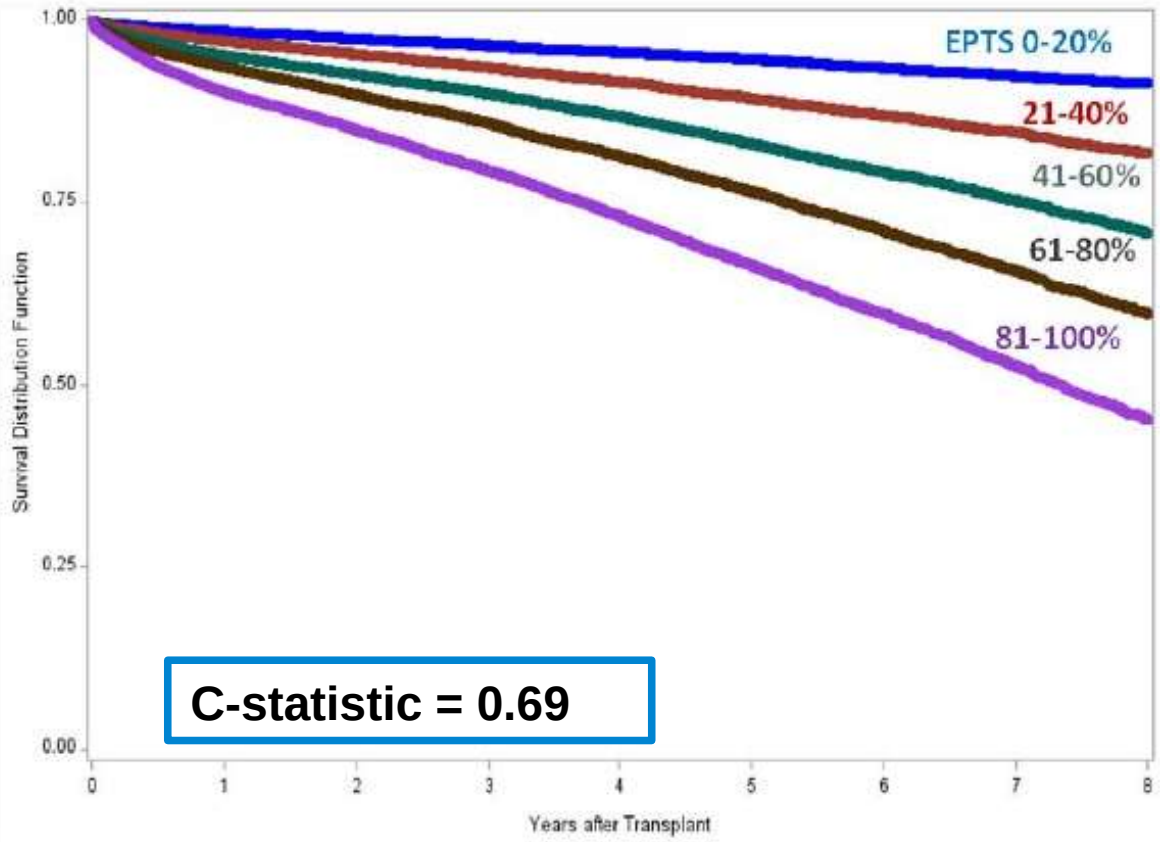
- 4 factors: Age, diabetes, prior transplant, time on dialysis
- Raw EPTS mapped to the percentile of its distribution: EPTS score
- EPTS changes overtime → calculation every day
- https://optn.transplant.hrsa.gov/resources/allocation-calculators/epts-calculator/

Recipient survival according to EPTS

"Raw EPTS" =

0.047 * max(Age - 25, 0) +
-0.015 * Diabetes * max(Age - 25, 0) +
0.398 * Prior Solid Organ Transplant +
-0.237 * Diabetes * Prior Organ Transplant +
0.315 * log(Years on Dialysis + 1) +
-0.099 * Diabetes * log(Years on Dialysis + 1) +
0.130 * (Years on Dialysis = 0) +
-0.348 * Diabetes * (Years on Dialysis = 0) +
1.262 * Diabetes

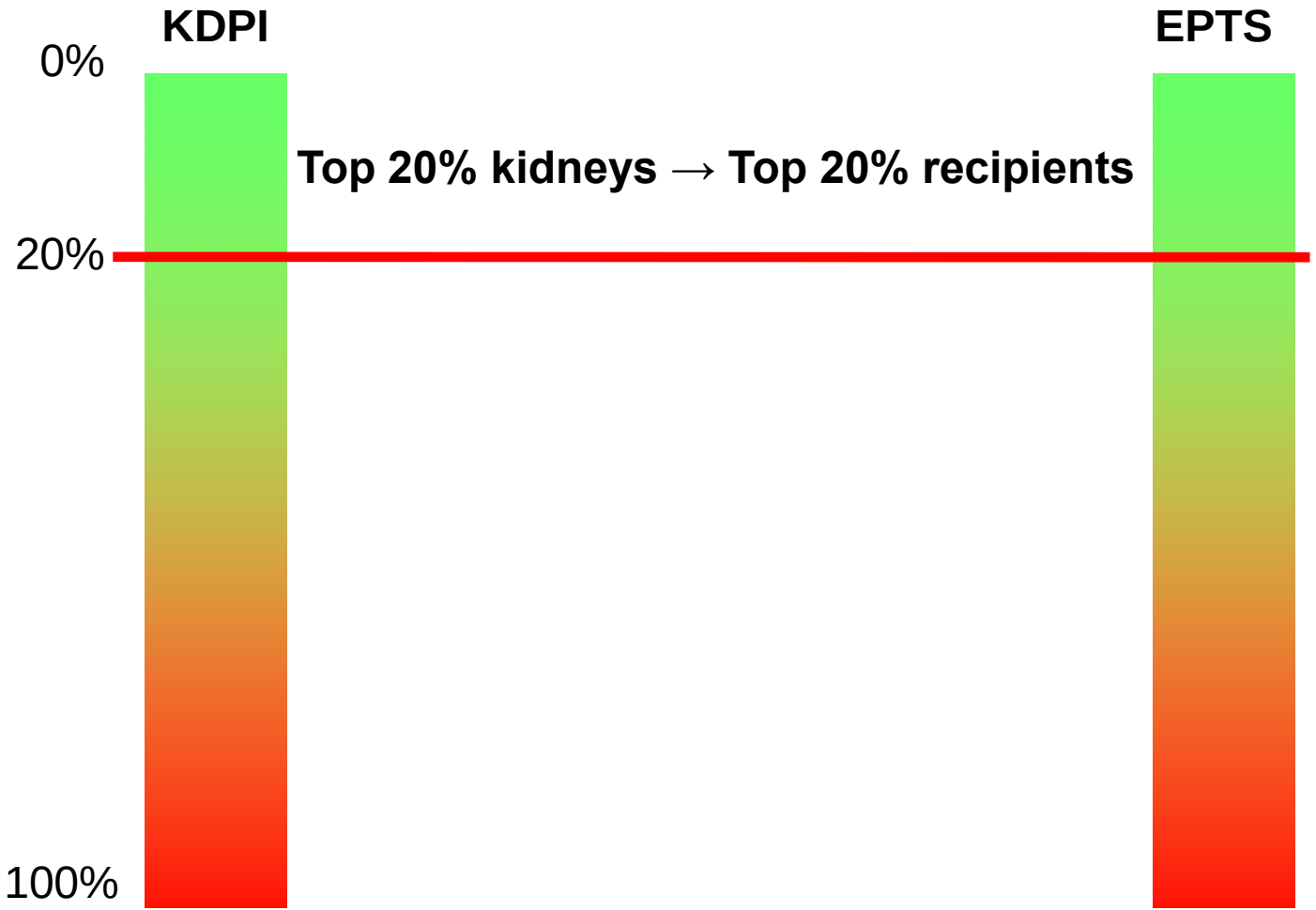
External validation in ANZDATA (Clayton 2014)



C-statistic = 0.69

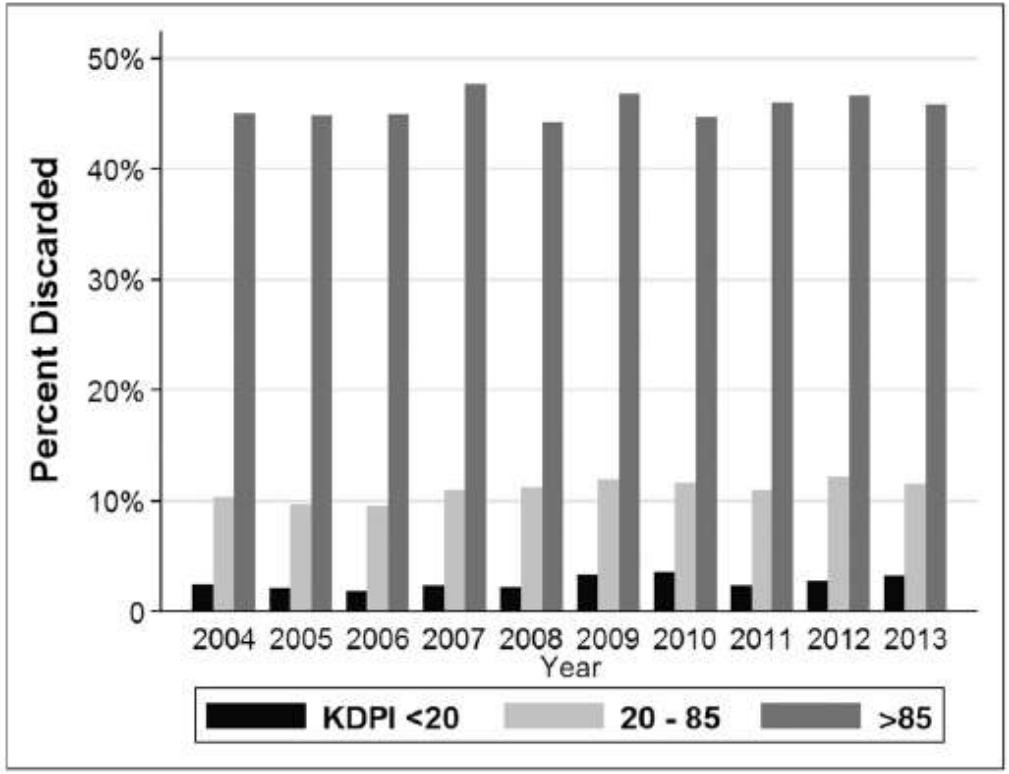
The lower is the better

How KDPI works with EPTS



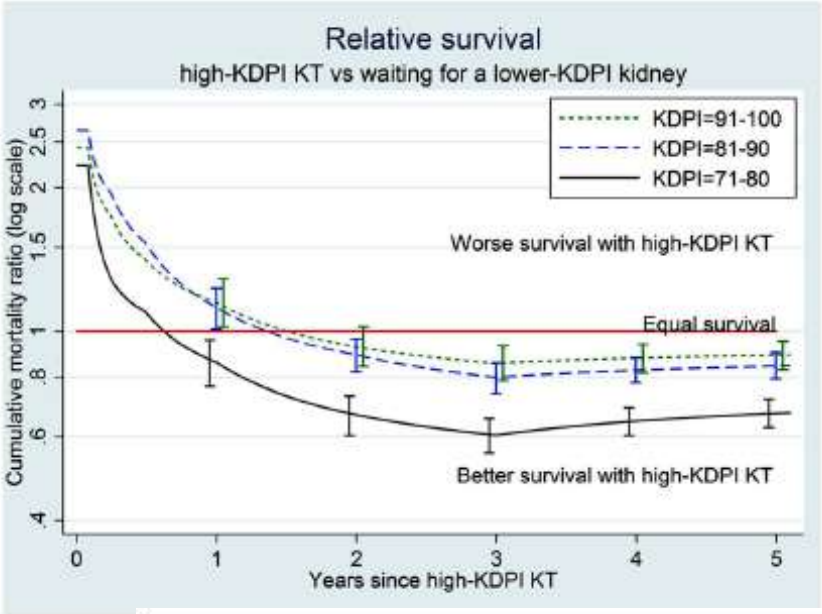
KDPI and discard rates (US data)

Discard rates are high: 17% (up to 50% for KDPI>85)



Reese P, J Am Soc Nephrol 2016

High KDPI gives acceptable results



SRTR data system, n=184277

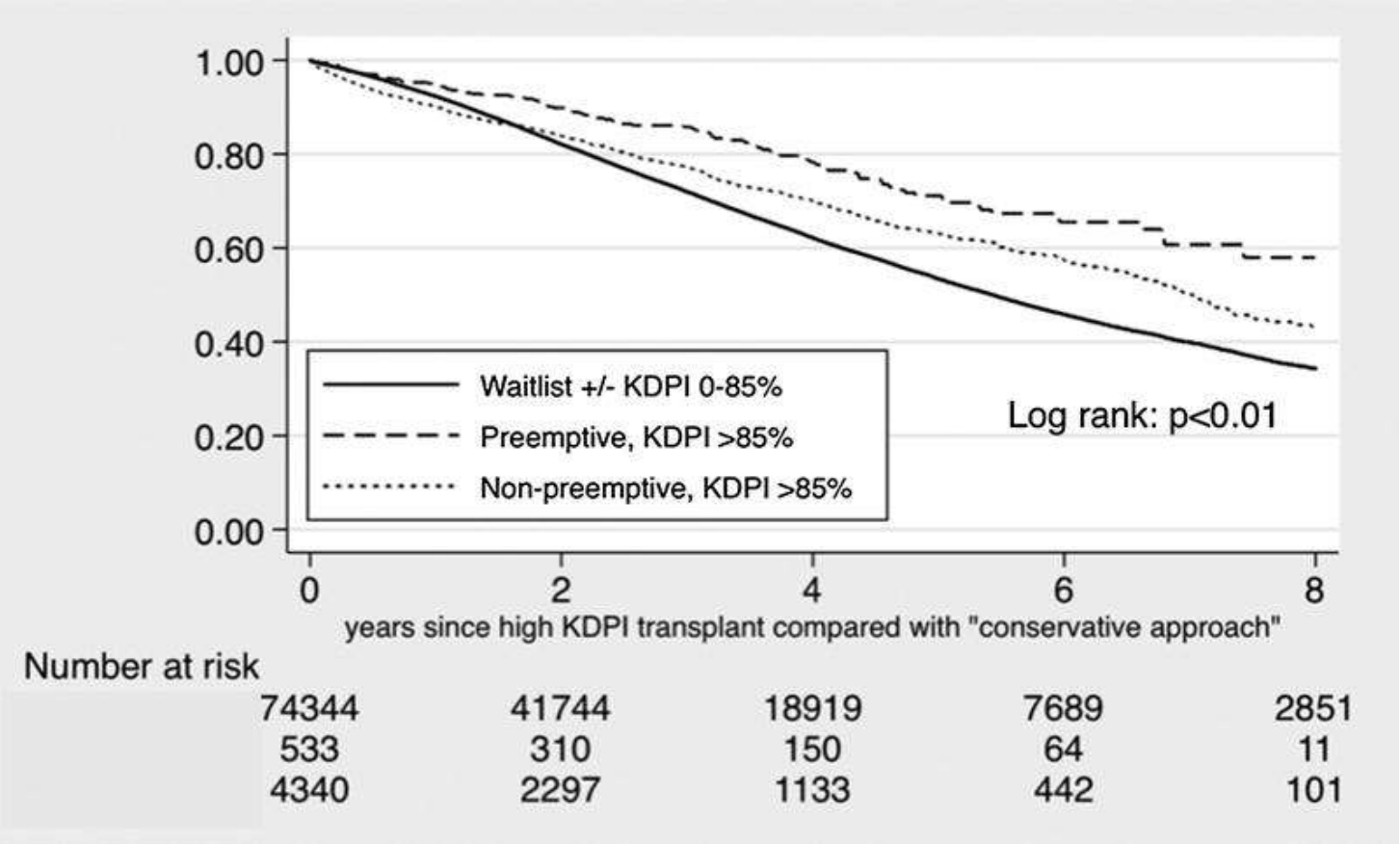
	Time to equal risk (months)	Time to equal survival (months)
KDPI 71–80 vs. waitlist or KDPI 0–70	1.7	7.7
KDPI 81–90 vs. waitlist or KDPI 0–80	6.0	18.0
KDPI 91–100 vs. waitlist or KDPI 0–90	7.2	19.8

	Five-year cumulative mortality ratio of high-KDPI KT		
Subgroup	KDPI 71–80	KDPI 81–90	KDPI 91–100
Age ≤ 50, wait < 33 m, nondiabetic	0.70 0.93 1.18	0.67 0.95 1.27	**1.15 1.68 2.26**
Age ≤ 50, wait < 33 m, diabetic	0.82 1.16 1.62	0.57 0.90 1.34	0.30 0.74 1.36
Age ≤ 50, wait ≥ 33 m, nondiabetic	**0.59 0.71 0.87**	0.80 1.01 1.23	0.97 1.25 1.58
Age ≤ 50, wait ≥ 33 m, diabetic	**0.51 0.69 0.89**	0.67 0.94 1.28	0.46 0.76 1.17
Age > 50, wait < 33 m, nondiabetic	**0.66 0.77 0.88**	0.86 0.98 1.12	0.92 1.07 1.22
Age > 50, wait < 33 m, diabetic	**0.57 0.67 0.79**	0.86 1.00 1.15	0.75 0.89 1.05
Age > 50, wait ≥ 33 m, nondiabetic	**0.54 0.61 0.68**	**0.68 0.76 0.84**	**0.78 0.87 0.96**
Age > 50, wait ≥ 33 m, diabetic	**0.53 0.60 0.68**	**0.75 0.83 0.92**	**0.77 0.86 0.97**

Massie A, Am J Transplant 2014

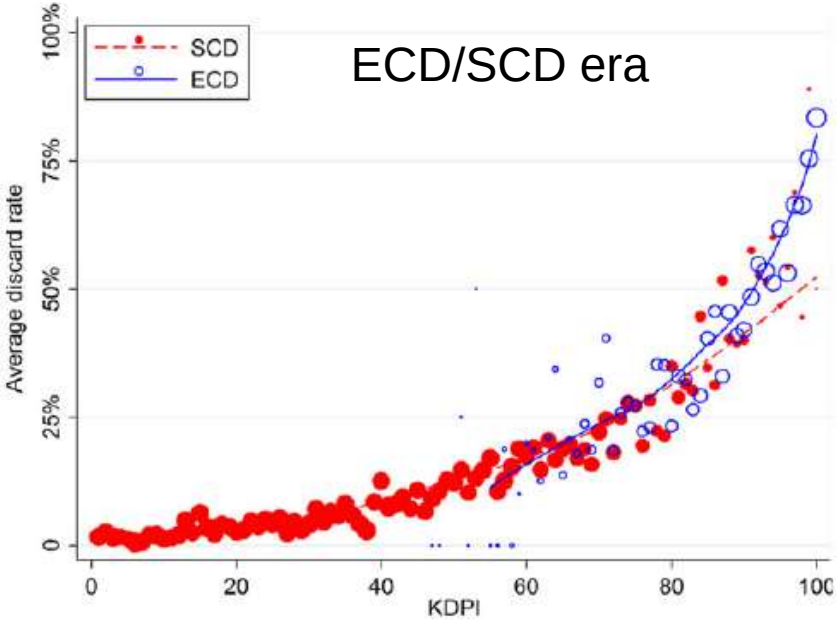
Patients survival after KDPI>85% kidney transplantation

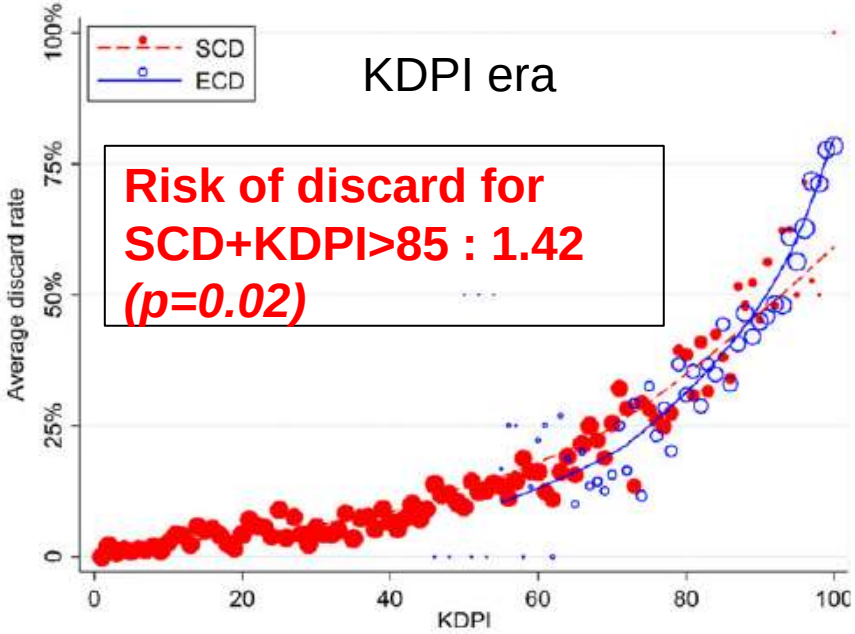
UNOS data 2003-2012. Patients > 60 years old



Jay C, Transplantation 2017

Impact of KDPI on discard rates

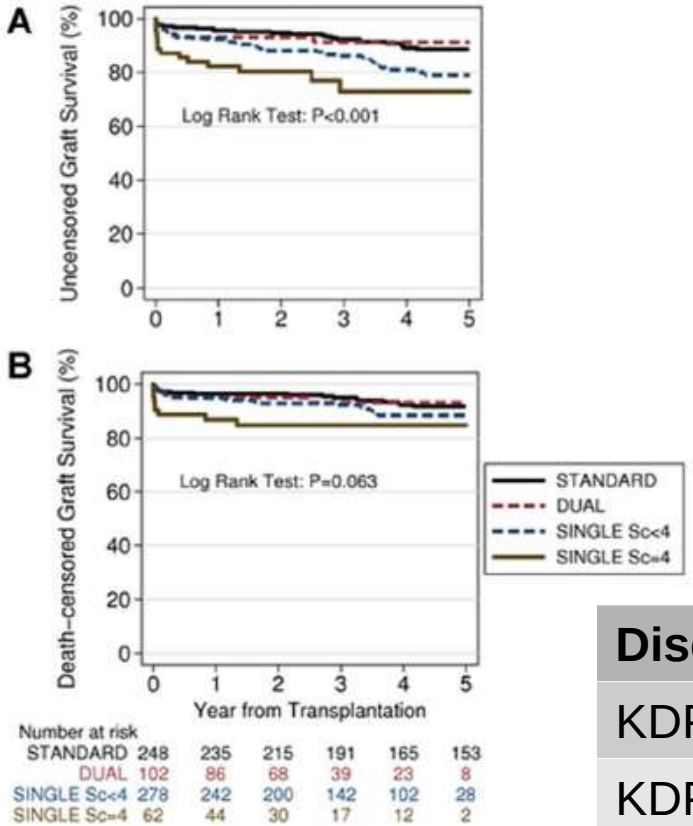


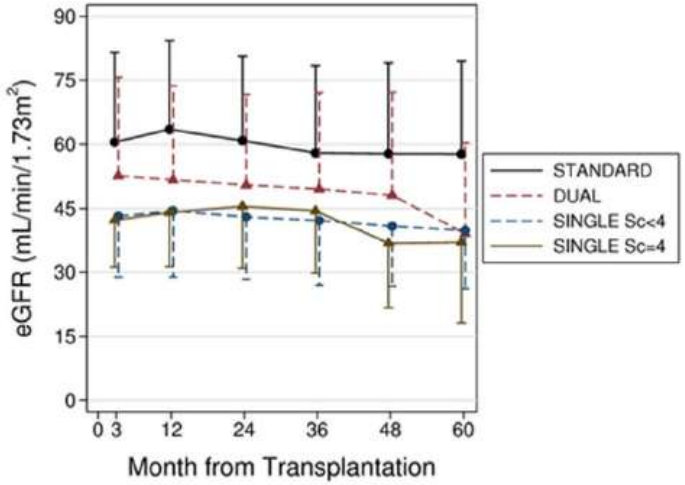


Bae S, Am J Transplant 2016

How to reduce the discard rate: histology + dual Tx

- Marginal donors (>65 yr, eGFR<60, proteinuria>1g/l)
- Day 0 biopsy, Remuzzi score (v[0-3]+i[0-3]+t[0-3]+g[0-3])
  - 〈4 : single Tx
  - [4-6] : dual Tx
  - Left + right>12: discard

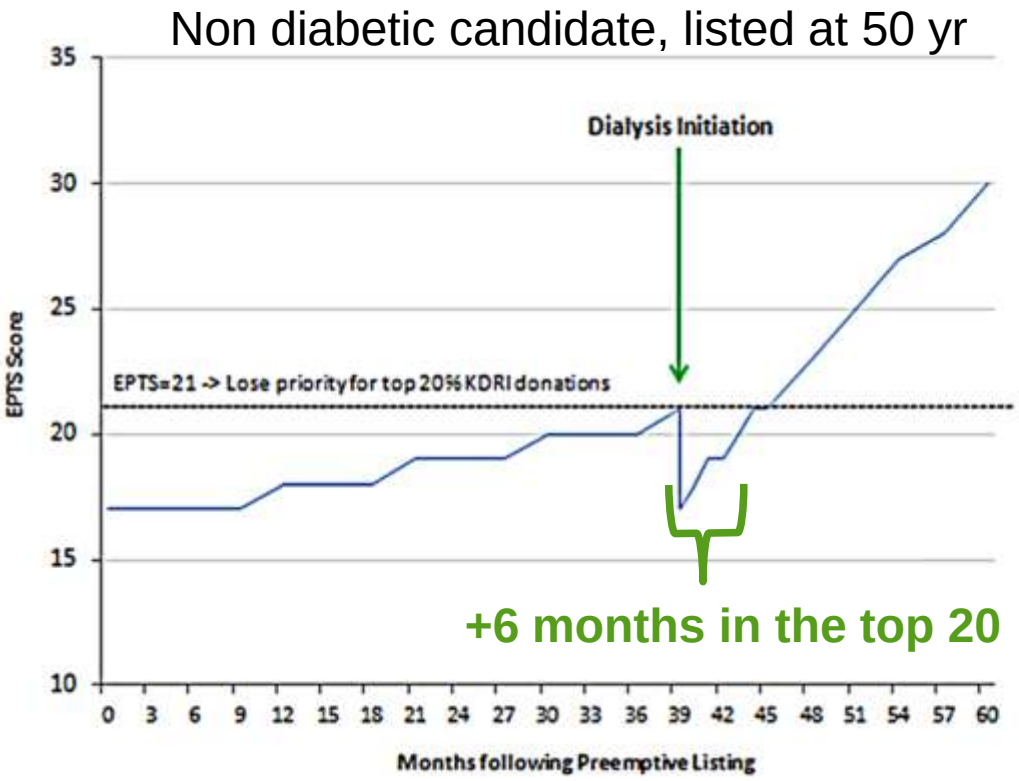


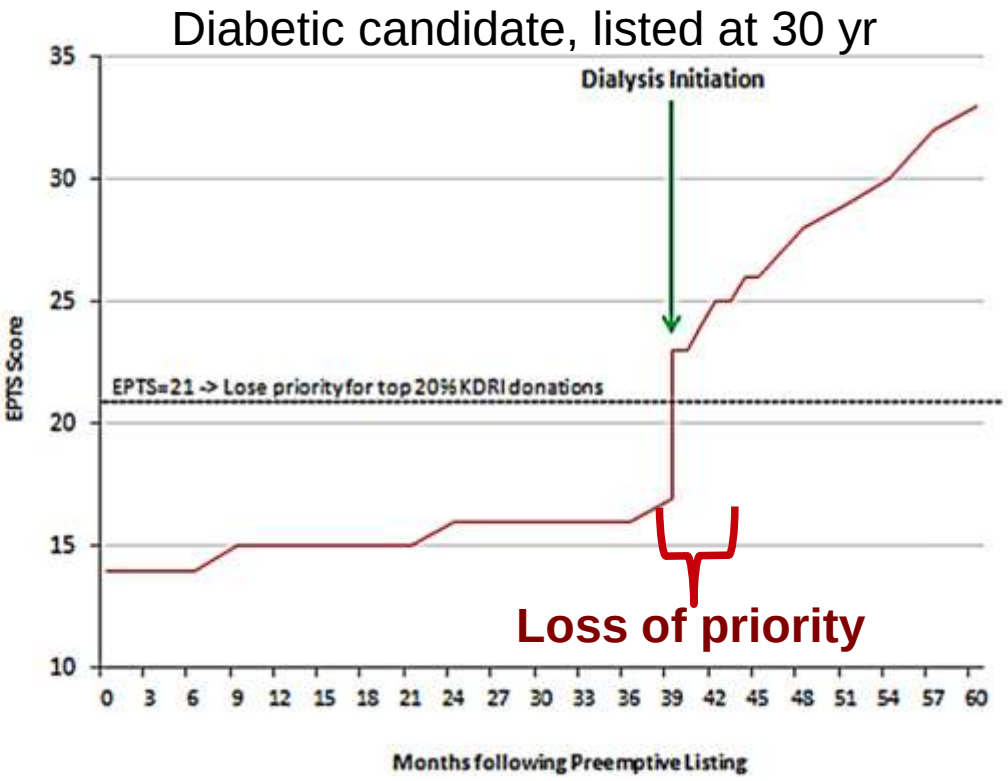


Discard rate	Gandolfini	UNOS
KDPI 80-90	14.9%	36.3%
KDPI 90-100	36.8%	62.5%

Gandolfini I, Transplantation 2014

Scores are not perfect tools





Schold J, Am J Transplant 2014

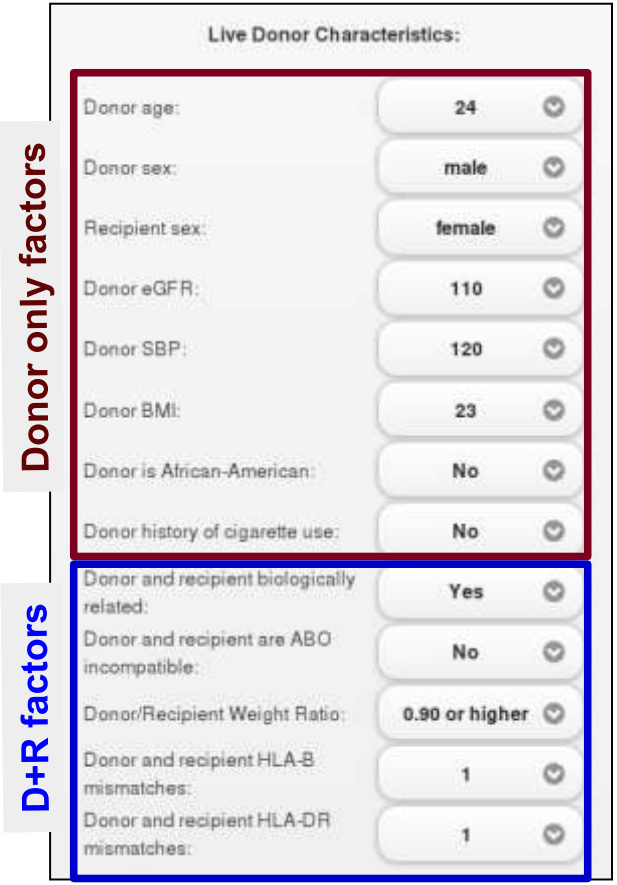
Living Kidney Donor Profile Index

SRTR 2005-2013. 106019 adult first Tx (DD: 69994, LD: 36025)

Formula

$$
\begin{aligned}
LKDPI = & -11.30 + 1.85 * [(age - 50) \text{if } age > 50] \\
& - 0.381 * eGFR + 1.17 * \\
& BMI(+22.34 \text{ if African-American}) \\
& (+14.33 \text{ if history of cigarette use}) + 0.44 * \\
& SBP(-21.68 \text{ if donor and recipient both male}) \\
& (+27.30 \text{ if ABO incompatible})(-10.61 \text{ if unrelated}) \\
& + 8.57 * (\#\text{HLA-B mismatches}) + 8.26 * \\
& (\#\text{HLA-DR mismatches}) - 50.87 * \\
& [\min(D/RWR, 0.9)]
\end{aligned}
$$

Web calculator



Result

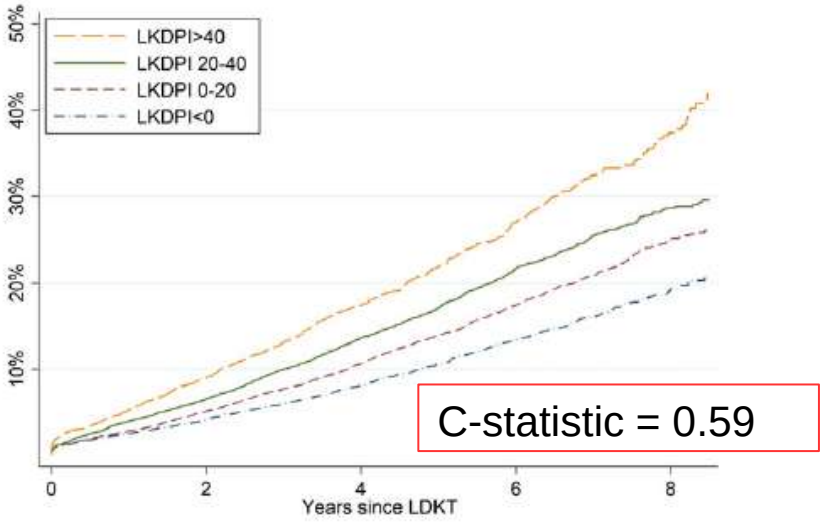
LKDPI = -2

http://www.transplantmodels.com/lkdpi/

Massie A, Am J Transplant 2016

LKDPI *vs* KDPI

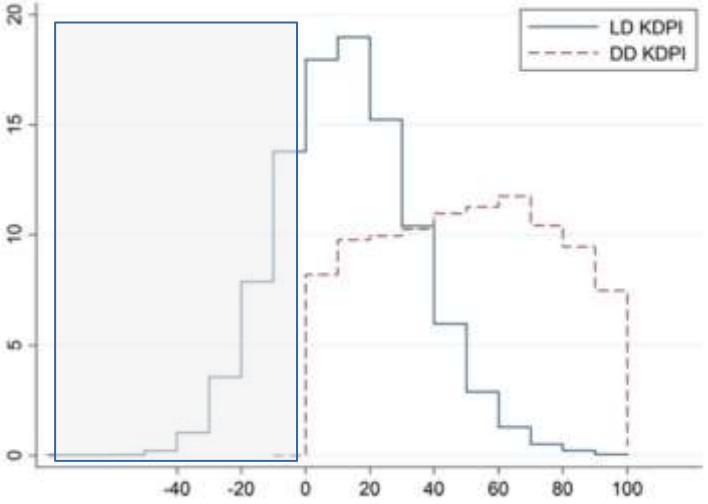
LKDPI is mapped to the risk level predicted by KDPI



Comparison of LKDPI and KDPI

KDPI/LKDPI range	aHR (LDKT)	p
1–20	$_{0.91}1.01_{1.12}$	0.8
21–40	$_{0.85}0.95_{1.06}$	0.3
41–60	$_{0.88}0.99_{1.13}$	0.9
61–80	$_{0.86}1.08_{1.35}$	0.5
81–100	$_{0.47}0.76_{1.22}$	0.3

LKDPI can be negative

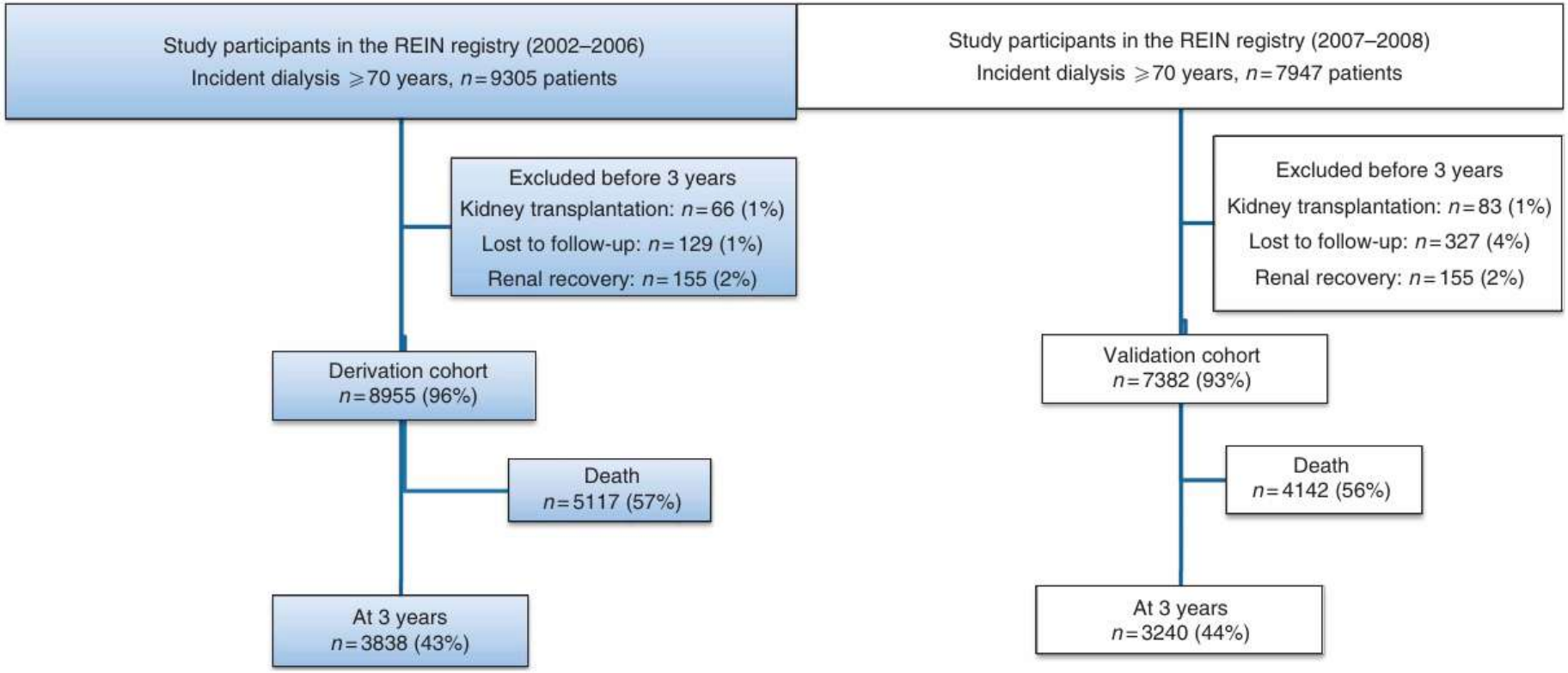


LKDPI, what for?

- To choose between several LD
- To assess kidney paired donation
- To compare LD *vs* DD
- To choose between a marginal LD *vs* a conventional DD

A special score for old candidates

REIN registry. Incident dialysis > 70 years old



Derivation cohort | **Validation cohort**

Dusseux E, Kidney Int 2015

Predicting 3-year mortality rate in dialysis

Multivariate analysis	Derivation Cohort, n = 8955 (20 data set)		
Characteristics	Adjusted OR[a] (95% CI)	β-Coefficient	Points[b]
Sex			
Male	1.13 (1.03; 1.25)	0.126	1
Female	1.0		
Age (years)			
(70–75)	1.0		
(75–80)	1.29 (1.15; 1.45)	0.255	2
(80–85)	1.94 (1.71; 2.19)	0.661	5
⩾85	3.06 (2.60; 3.60)	1.119	9
Diabetes			
Absence	1.0		
Presence	1.24 (1.12; 1.36)	0.211	2
Ischemic heart disease			
Absence	1.0		
Presence	1.25 (1.09; 1.43)	0.220	2
PVD			
No or stage I or II	1.0		
Stage III or IV	1.88 (1.55; 2.29)	0.633	5
Cerebrovascular disease			
Absence	1.0		
Presence	1.16 (1.00; 1.34)	0.146	1
CHF			
No	1.0		
Stage I or II	1.24 (1.10; 1.39)	0.212	2
Stage III or IV	1.75 (1.46; 2.11)	0.562	4
Dysrhythmia			
Absence	1.0		
Presence	1.31 (1.17; 1.46)	0.266	2
Chronic respiratory disease			
Absence	1.0		
Presence	1.32 (1.14; 1.52)	0.276	2
Active malignancy			
Absence	1.0		
Presence	1.79 (1.54; 2.09)	0.584	5
Severe behavioral disorder			
Absence	1.0		
Presence	2.14 (1.62; 2.84)	0.763	6
Mobility			
Walks without help	1.0		
Needs assistance for transfers	1.67 (1.47; 1.90)	0.513	4
Totally dependent for transfers	2.99 (2.34; 3.83)	1.097	9
Body mass index (kg/m²)			
<21 kg/m²	1.42 (1.24; 1.63)	0.352	3
(21–25)	1.16 (1.03; 1.31)	0.151	1
⩾25 kg/m²	1.0		
Temporary CVC at dialysis initiation			
Absence	1.0		
Presence	1.46 (1.32; 1.61)	0.377	3

Risk score	Derivation Cohort: Number at risk, n (%)	Derivation Cohort: Number of deaths, n (%)	Validation Cohort: Number at risk, n (%)	Validation Cohort: Number of deaths, n (%)
⩽6 Points (Q1)	1799 (20)	586 (33)	1552 (21)	466 (30)
(7–9) Points (Q2)	2264 (25)	1068 (47)	1735 (24)	821 (47)
(10–12) Points (Q3)	1610 (18)	976 (61)	1341 (18)	763 (57)
(13–17) Points (Q4)	1643 (18)	1146 (70)	1301 (18)	890 (68)
⩾18 Points (Q5)	1639 (18)	1341 (82)	1453 (18)	1202 (83)
All	8955	5117 (57)	7382	4142 (56)
C index (95% CI)	0.70 (0.69–0.71)		0.71 (0.70–0.72)	

	Validation Cohort: Number at risk	Validation Cohort: Number of deaths
Risk score Q1	N = 1552/7382 (21%)	Total N = 466
0–2 Points	235 (3)	35 (15)
3 Points	219 (3)	54 (25)
4 Points	273 (4)	94 (34)
5 Points	375 (5)	130 (35)
6 Points	450 (6)	153 (34)
Risk score Q2	N = 1275/7382 (17%)	N = 569
7 Points	397 (5)	160 (40)
8 Points	434 (6)	205 (47)
9 Points	444 (6)	204 (46)

How can it be used?

- To systematically evaluate candidates >70 years if score<7 (21%)
- However this score should not be restrictive
- Help decision making for candidates with a score >7
  - Median waiting time
  - Cost: dialysis *vs* transplantation
- This score is moderately predictive (c-statistic = 0.7)

ESRD Risk Tool for Kidney Donor Candidates: big data

7 cohorts (NAHNES, ARIC, VA, ICES KDT, Maccabi, Mount Sinai, Geisinger) - *n=8325115*

↓

Exclusion of high-risk participants
(eGFR<45, diabetes, severe hypertension, albuminuria>300mg/g, history of CD, stroke, heart failure, PAD)

Low-risk subgroup: 4 933 314 → 3900 ESRD events / 31321064 persons-years

↓

Cox model in each group – random effects meta-analysis

↓

Apply equations to LD (n=52998, OPTN 2005-2014)

↓

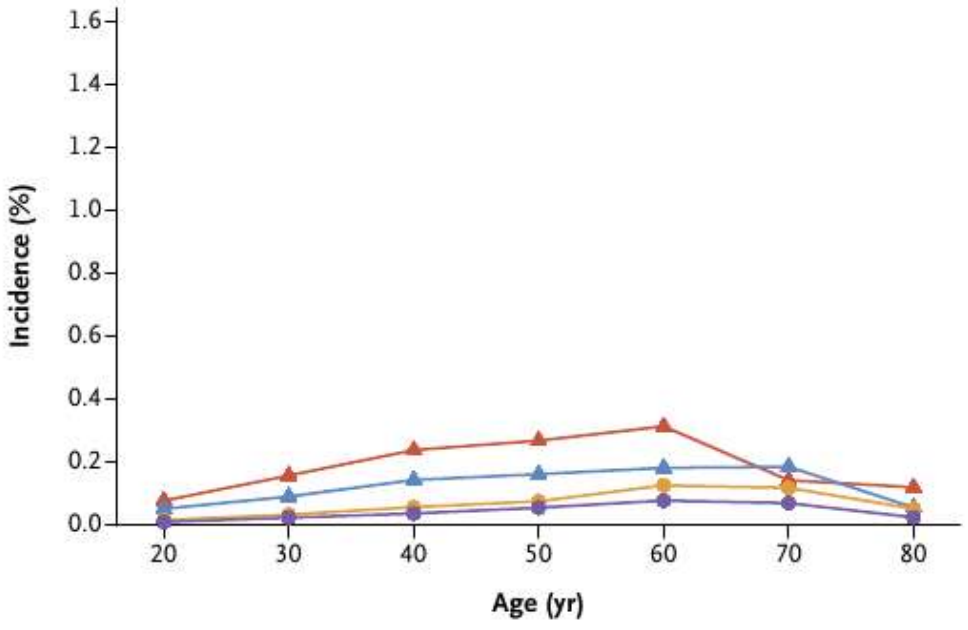
Comparison 15-year risk of ESRD in kidney donors[1]
vs projected risk in a hypothetical matched group (*relative risk*)

1) Muzaale AD, JAMA 2014

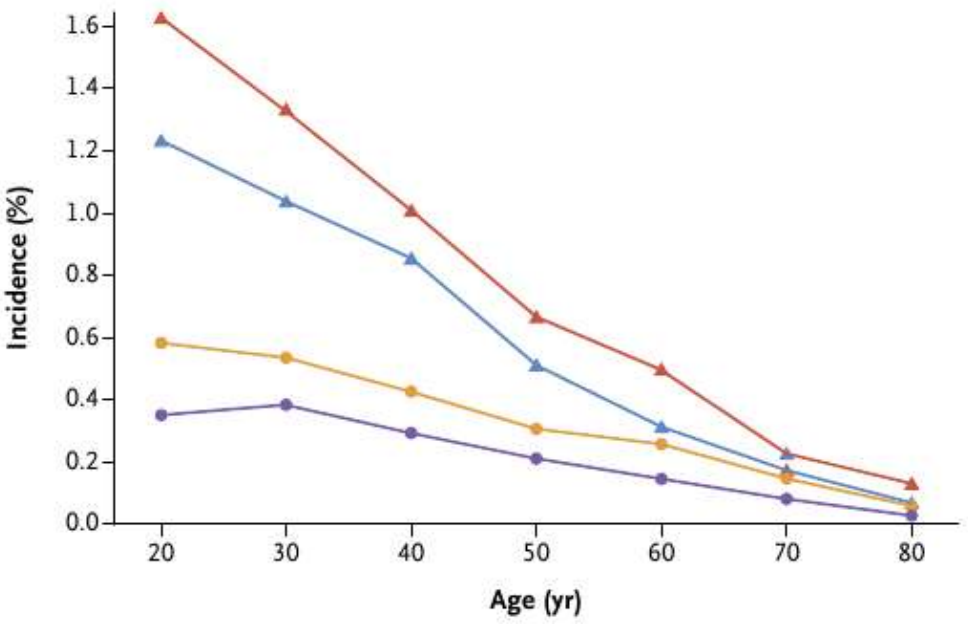
Grams M, N Engl J Med 2016

Projected ESRD-risk

15-Year projected incidence of ESRD



Lifetime projected incidence of ESRD



Black men Black women White men White women

How to calculate ESRD-risk index?

http://www.transplantmodels.com/esrdrisk/

10 factors

Age (18-80yrs)	40
Gender	Female
Race (White or Black)	White
eGFR (mL/min/1.73m²)	90
Systolic Blood Pressure (mmHg)	120
Hypertension Medication	No Medication
BMI (kg/m²)	25
Non-Insulin Dependent Diabetes	No Diabetes
Urine Albumin to Creatinine (mg/g) click on units to change between mg/g and mg/mmol	4
Smoking History	Non-Smoker

Projected Incidence of End-Stage Renal Disease:	
0.04%	0.30%
Pre-Donation 15-Year*	Pre-Donation Lifetime*
?	?
Post-Donation 15-Year**	Post-Donation Lifetime**

blue: < 1%, green: 1-2%, yellow: 2-3%, orange: 3-5%, red: >5%

ESRD-risk post donation is not yet implemented.

The 15-year ESRD risk among donors is estimated between **3.5 to 5.3 times** as high as the projected risk in non donors[1].

1) Muzaale AD, JAMA 2014

The pros and cons of ESRD-risk index?

- **Pros**
  - Rational guide to accept or refuse a donor
  - Enhanced informed consent and shared decision
  - Excellent outcome for older donors (>65)

- **Cons**
  - Lifetime risk, preferred for young donors, is less precise
  - Some factors can appear *after* donation (smoking, obesity)
  - Some factors are not implemented in the model (socio-economic status)
  - The model assumes that the risk is consistent overtime
  - Post donation projected risk is not (yet) estimated

Conclusions

- Scores are helpful
- but their predictive values remain moderate (0.6<c-stat<0.7)
- and they need to be improved (histology, molecular biology?)
- and adapted or validated in different populations
  - Child Donor Index instead of KDPI for paediatric donors
  - US population ≠ European population