Expanding the Donor Pool
ECD/DCD: Evaluation of the Marginal Kidney Donor

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LEADERSHIP IN CANADIAN TRANSPLANTATION

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Disclosure Slide

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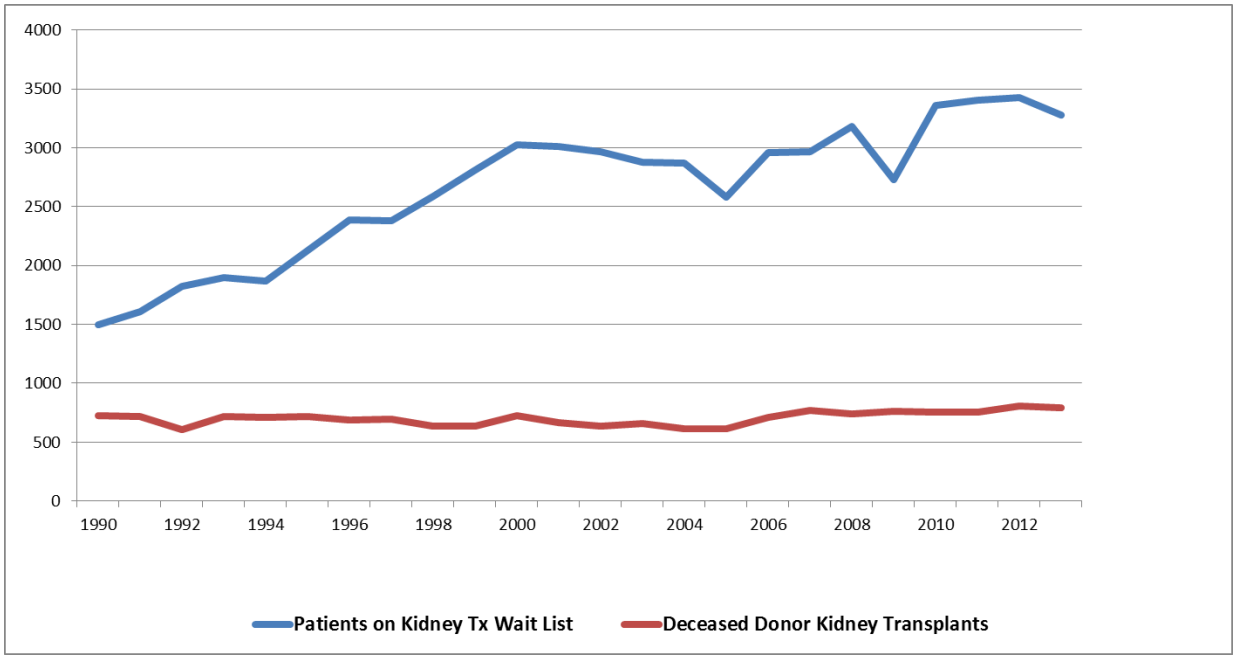
- **Consultant/Speaker Fees: none**

Why are we Discussing this Topic?



Not Enough Donors

or

Not Using the Donors we Have?

(or Both)

CORR Data

Definitions

- **SCD – Standard Criteria Donor**
- **ECD – Expanded Criteria Donor**
- **DCD – Donation after Cardiocirculatory Death**
- **NDD – Neurological Determination of Death (“Brain Death”)**
- **KDRI – Kidney Donor Risk Index**
- **KDPI - Kidney Donor Profile Index**

Definitions

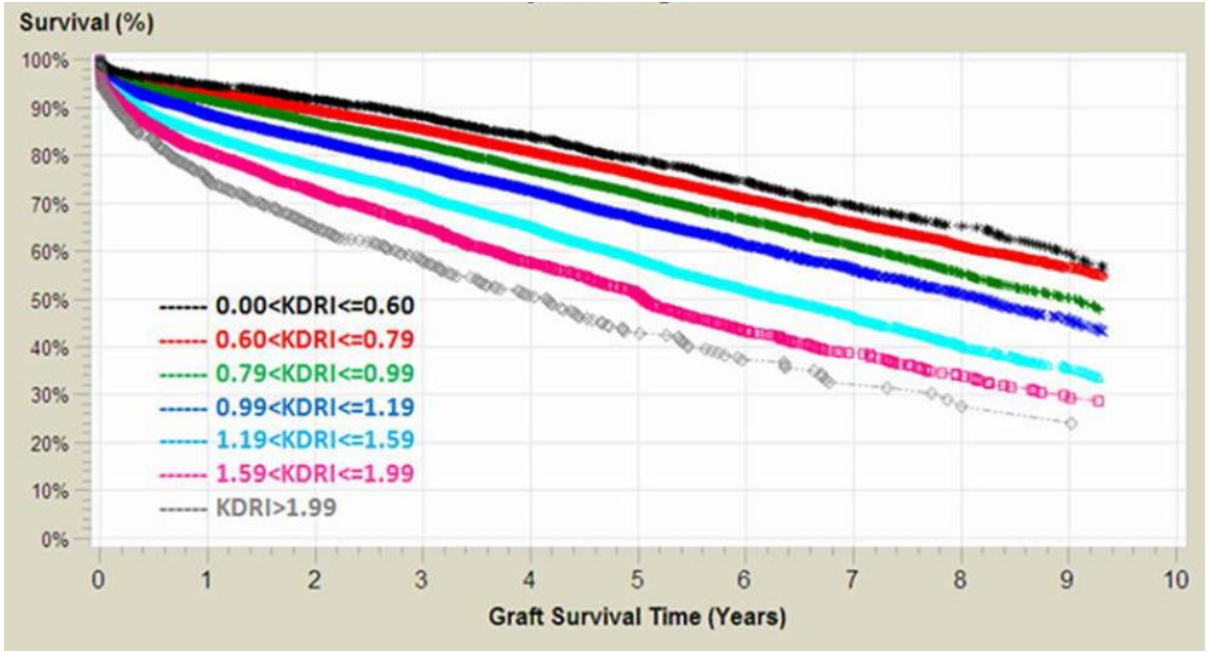
- **ECD – Expanded Criteria Donor**
  - ***Kidneys that have 70% increased risk of graft failure compared to SCD***
    - Age ≥ 60 years
    - Age 50-59 with any 2 of the following criteria
      - Death due to CVA
      - History of hypertension
      - Terminal creatinine ≥ 1.5 mg/dl (133 umol/L)
- **SCD – Standard Criteria Donor**
  - All brain dead deceased donors without any ECD criteria
- **DCD – Donation after Cardiocirculatory Death**
- **NDD – Neurological Determination of Death (“Brain Death”)**

KDRI/KDPI: Kidney Donor Risk Index/Kidney Donor Profile Index

- **KDRI: Risk score based on 10 donor factors**
- **Interpreted as the relative risk of post-transplant graft failure from a specific donor compared to a reference donor (median donor, 50th percentile of score)**
- **Donor with KDRI of 1.28 confers an estimated risk of graft failure that 28% higher than that of the median donor (typically ranges from 0.5 to 3.5)**
- **KDPI is mapping of the RR to a cumulative percentage (0-100%)**
- **Donor with KDPI of 85% has a RR of graft failure that is higher than 85% of all recovered kidneys in the previous year**

- ✓ Age
- ✓ Height
- ✓ Weight
- ✓ Ethnicity
- ✓ History of Hypertension
- ✓ History of Diabetes
- ✓ Cause of Death
- ✓ Serum Creatinine
- ✓ Hepatitis C Virus (HCV)
- ✓ Donation after Circulatory Death

KDRI/KDPI: Kidney Donor Risk Index/Kidney Donor Profile Index



Increasing KDRI Associated with Worse Graft Survival

Why do we need to know how to evaluate marginal kidney donors?

- SCD: 8% discarded
- ECD: 41% discarded

- DCD: 25% discarded
- ECD-DCD: 51% discarded

- Age > 65 years: 60%
- KDPI > 90: 63%

~1500 kidneys/year discarded

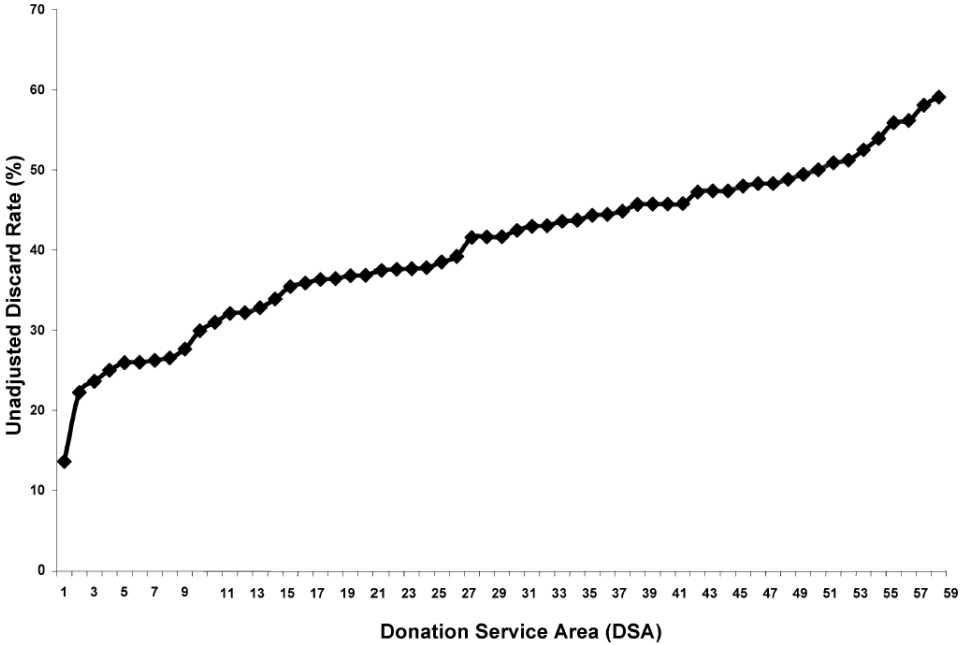
No Canadian Data!!

Clin J Am Soc Nephrol 11: 317–323, 2016.

American Journal of Transplantation 2008; 8: 783–792

World J Surg (2012) 36: 2909. doi:10.1007/s00268-012-1748-0

Discard Rate is Highly Variable for Marginal Donors



Discard rate: 14-60%

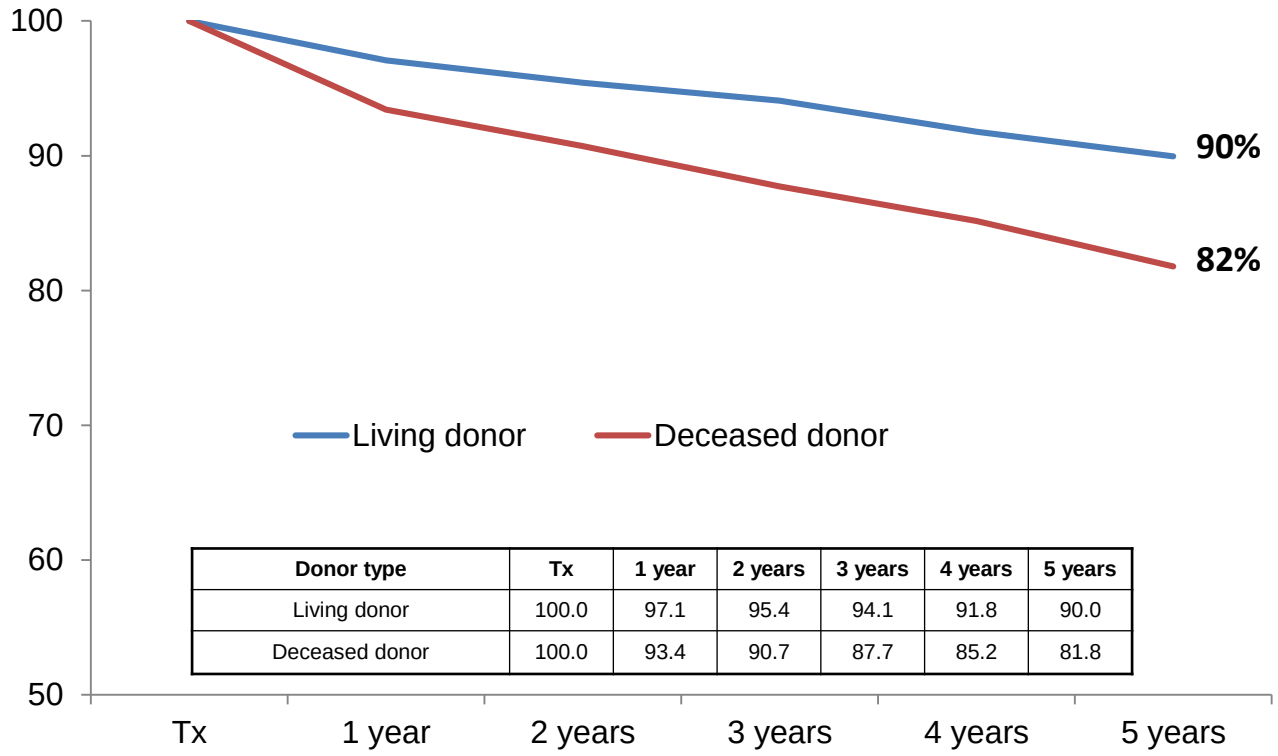
Why would one region routinely discard kidneys that others would transplant?

American Journal of Transplantation 2008; 8: 783–792

Evaluation of the Marginal Kidney Donor

- **Why are Kidneys Discarded?**
  - Anatomic abnormalities
  - Damage during procurement
  - Tumour
  - Poor flush
- **Avoidance of Risk**
  - Risk of transmissable disease
  - ***Risk of premature graft failure:***
    - We need kidneys to function adequately and *long enough*
    - We don't need all kidneys to last forever and that is our problem….
    - We are very conservative and tend to discard kidneys that will most likely function adequately and long enough for certain recipients

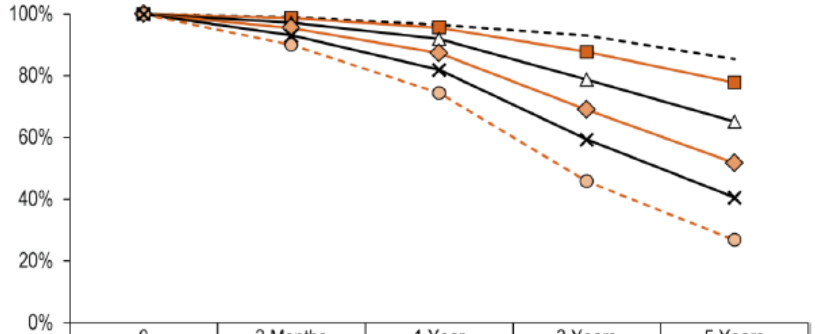
Kidney Transplant Survival



Donor type	Tx	1 year	2 years	3 years	4 years	5 years
Living donor	100.0	97.1	95.4	94.1	91.8	90.0
Deceased donor	100.0	93.4	90.7	87.7	85.2	81.8

CORR 2014

Dialysis Patient Survival in Canada



	0	3 Months	1 Year	3 Years	5 Years
Age 0–17	100	99.0	96.5	93.0	85.4
Age 18–44	100	98.7	95.6	87.7	77.8
Age 45–54	100	97.2	91.9	78.7	65.1
Age 55–64	100	95.5	87.3	69.0	51.7
Age 65–74	100	93.1	82.0	59.4	40.6
Age 75+	99.9	90.0	74.4	45.8	26.8

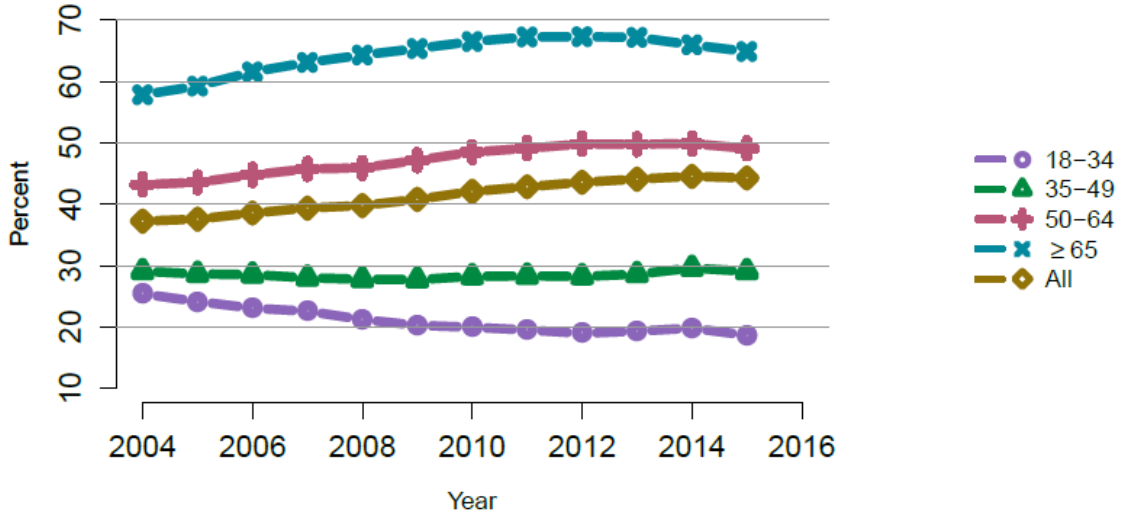
15% of Dialysis patients will die in the first year of treatment.

Only 45% will be alive after 5 years of treatment.

This prognosis is worse than many cancers

CORR 2015 Annual Report

Many Patients Willing to Accept ‘Marginal’ Kidneys

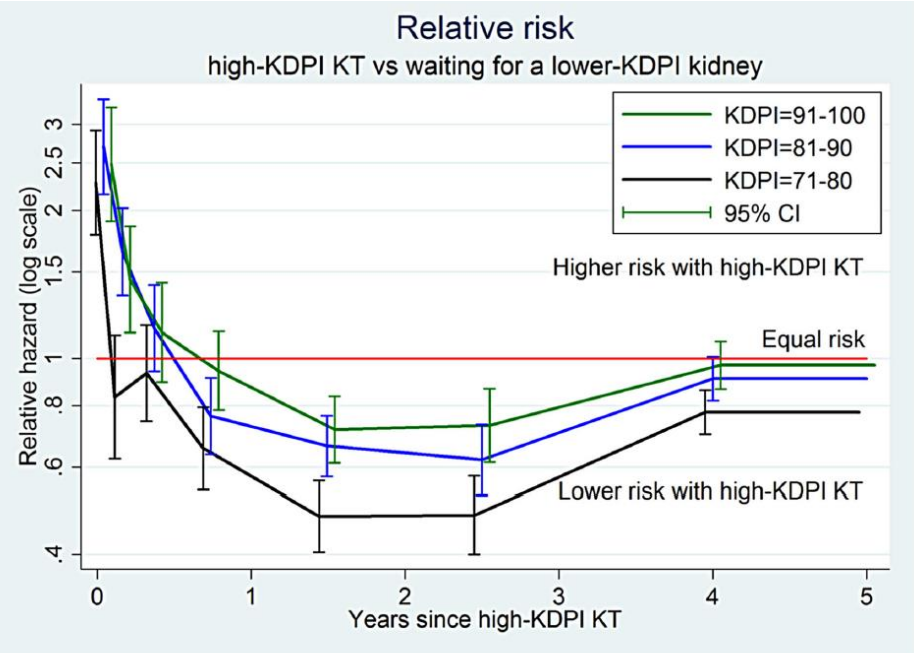


Adults willing to accept an ECD kidney or KDPI >85%

OPTN/SRTR 2015 Annual Data Report: Kidney; AJT 2017; 17: 21-116

Survival Benefit of Primary Deceased Donor Transplantation With High-KDPI Kidneys

A. B. Massie[1,2], X. Luo[1], E. K. H. Chow[1],
J. L. Alejo[1], N. M. Desai[1] and D. L. Segev[1]



Survival Benefit

Patients >50 years old

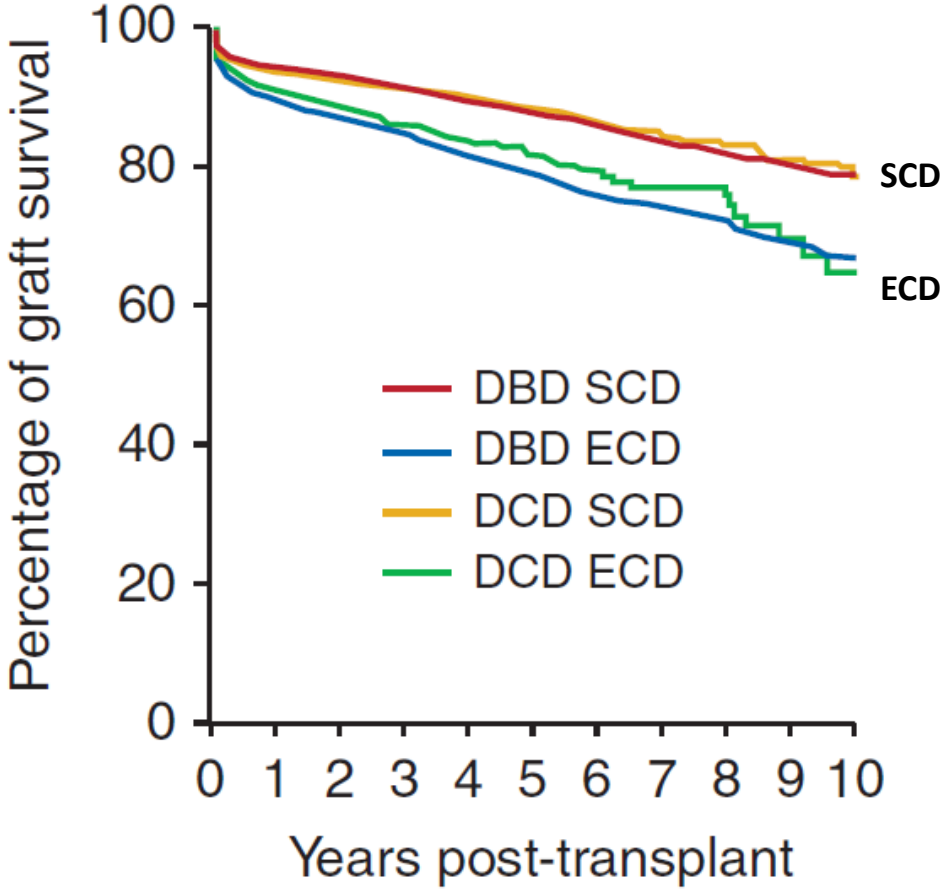
Median wait time at centre >33 months

American Journal of Transplantation 2014; 14: 2310–2316

What Information Can We Use to Evaluate a Marginal Kidney Donor

- Type of Donor
  - DCD vs. NDD
  - ECD vs. Non-ECD
- Clinical Parameters
  - Age
  - GFR
  - Hypertension/Diabetes
  - Cause of Death
- Donor Risk Scores
- Biopsy
- Perfusion Parameters: cold, normothermic *(next talk, Dr. Selzner)*
- Biomarkers: urine, blood, perfusate

Non-ECD DCD Kidneys Should Not Be Considered 'Marginal'

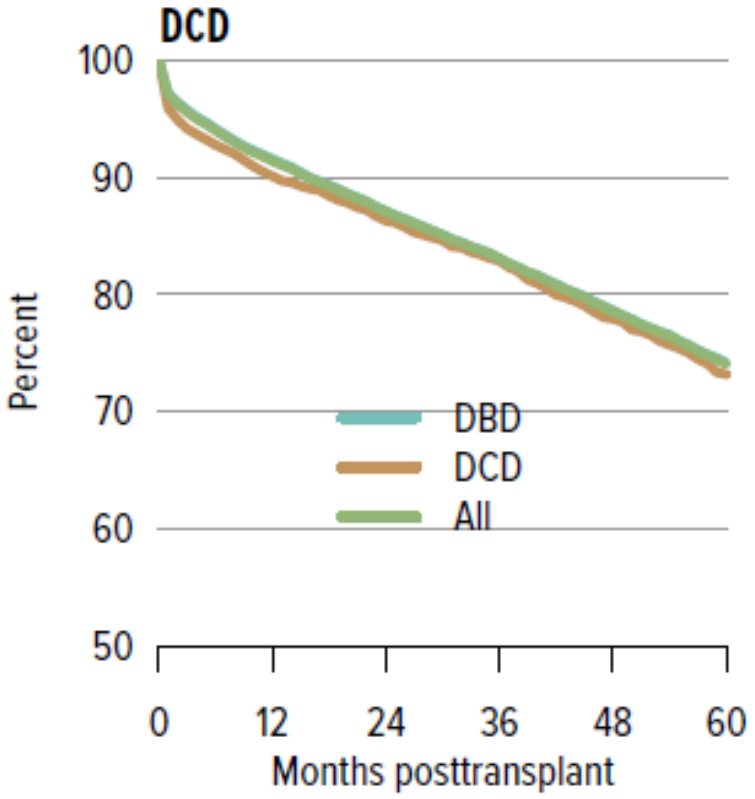


ECD kidneys have decreased survival compared to non-ECD donors

DCD vs DBD does NOT matter

Donation after Cardiocirculatory Death: UK Registry

Graft Survival Identical with DCD and DBD Donors



SRTR 2015

Is the Kidney Biopsy Helpful?

USA: 50.4% of all donors have procurement biopsy (74.8% ECD)

No Canadian data but rarely done in Ontario

Eurotransplant Centres rarely use procurement biopsy (<5%)

Pre-Transplant Kidney Biopsy

Procurement vs. Implantation biopsy

Frozen section vs. Paraffin embedded

“On-call” pathologist interpretation vs. Renal pathologist retrospective review

Wedge vs. Core biopsy

Donor Biopsy Scoring Systems

Table 1. Summary of some commonly used scores in the assessment of donor biopsies

Name (year published)	Variables scored		Predictive value	Reference
Banff schemebased scores	Variables	Points	(a) AUC: 0.79 [29]	(a): [18,22]
(a) Remuzzi (1999)	Global glomerulosclerosis (a–c)	0–3	(b) AUC: 0.76 [29]	(b): [60]
(b) CADI (1994)	Interstitial fibrosis, ci (a–c)	0–3	(c) AUC: 0.74	(c): [56]
(c) Total chronic Banff (2008)	Tubular atrophy, ct (a–c)	0–3		
	Vessel narrowing, cv (a–c)	0–3		
	Mesangial matrix increase, mm (b–c)	0–3		
	Interstitial inflammation, i (b)	0–3		
	Glomerular double contour, cg (c)	0–3		
	Arteriolar hyalinosis, ah (c)	0–3		
Maryland Aggregate Pathology Index (2008)	Variables	Points	AUC: 0.70–0.74	[30]
	Periglomerular fibrosis: present/absent	4		
	Arteriolar hyalinosis: present/absent	4		
	Scar (focus of sclerosis and IFTA ≥10 tubules: present/absent)	3		
	Global glomerulosclerosis ≥15%	2		
	Wall-lumen ratio of interlobular arteries ≥0.5	2		
		5-year graft survival		
	Low risk group (score sum: 0–7)	90%		
	Intermediate risk group (score sum: 8–11)	63%		
	High risk group (score sum: 12–15)	53%		
French clinico-histopathological composite score (2008)	Variables:	Points	AUC: 0.84	[29]
	Global glomerulosclerosis ≥10% (GS)	1		
	Donor hypertension and/or donor serum creatinine ≥150 μmol/l (CP)	1		
		eGFR <25 ml/min at 1 year		
	GS = 0 and CP = 0	5.2%		
	GS = 1 and CP = 0	12.5%		
	GS = 0 and CP = 1	13.5%		
	GS = 1 and CP = 1	35.1%		

Curr Opin Organ Transplant 2013, 18:306–312

Pirani – Remuzzi Score

Glomerular global sclerosis
Based on three sections (the first, middle, and last sections, if available); the number of globally sclerosed expressed as a percentage.
0 none globally sclerosed
1+ <20% global glomerulosclerosis
2+ 20 to 50% global glomerulosclerosis
3+ >50% global glomerulosclerosis

Tubular atrophy
0 absent
1+ <20% of tubuli affected
2+ 20 to 50% of tubuli affected
3+ >50% of tubuli affected

Interstitial fibrosis
0 absent
1+ <20% of renal tissue replaced by fibrous connective tissue
2+ 20 to 50% of renal tissue replaced by fibrous connective tissue
3+ >50% of renal tissue replaced by fibrous connective tissue

Arterial and arteriolar narrowing
For the vascular lesions, if the changes are focal, the most severe lesion present gives the final grade.
0 absent
1+ increased wall thickness but to a degree that is less than the diameter of the lumen
2+ wall thickness that is equal or slightly greater to the diameter of the lumen
3+ wall thickness that far exceeds the diameter of the lumen with extreme luminal narrowing or occlusi

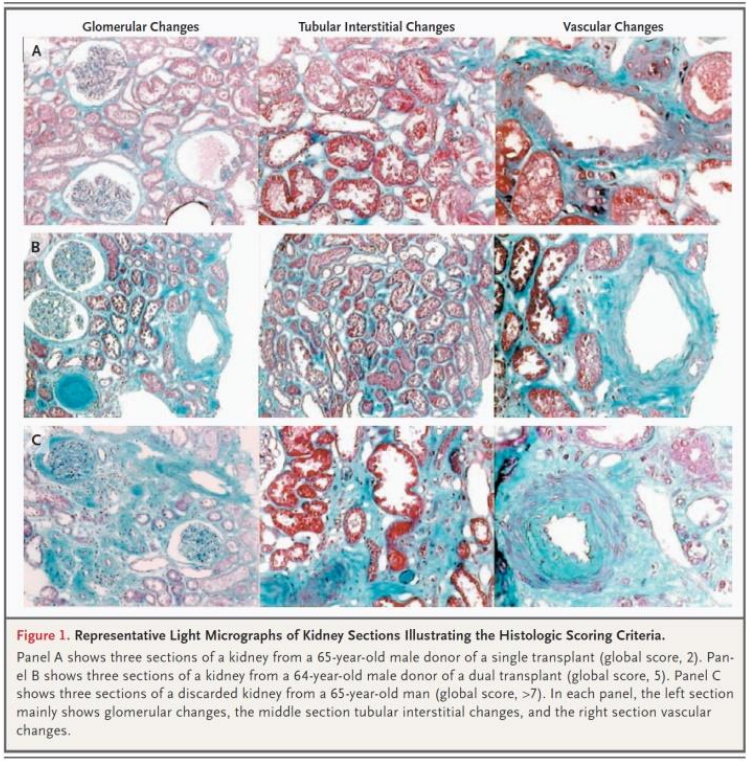


Figure 1. Representative Light Micrographs of Kidney Sections Illustrating the Histologic Scoring Criteria.
Panel A shows three sections of a kidney from a 65-year-old male donor of a single transplant (global score, 2). Panel B shows three sections of a kidney from a 64-year-old male donor of a dual transplant (global score, 5). Panel C shows three sections of a discarded kidney from a 65-year-old man (global score, >7). In each panel, the left section mainly shows glomerular changes, the middle section tubular interstitial changes, and the right section vascular changes.

Score = 2

Score = 5

Score = 7

OUTCOME OF KIDNEY TRANSPLANTATION FROM HIGH-RISK DONORS IS DETERMINED BY BOTH STRUCTURE AND FUNCTION.

Karpinski, Jolanta; Lajoie, Ginette; Cattran, Daniel; Fenton, Stanley; Zaltzman, Jeffrey; Cardella, Carl; Cole, Edward

	High-risk donor: kidney used (n=34)	High-risk donor: kidney not used (n=31)	*P* value
Age (yr)	61±7	63±7	NS[a]
Male	67%	22%	<.001
CrCl (ml/min)	98±30	66±28	<.001
Reasons for biopsy			
Age>60	53%	73%	NS
Hypertension	56%	50%	NS
Vascular disease	29%	23%	NS
Biopsy score			
Overall	4.3±1.7	5.8±1.2	.002
Glomerulosclerosis	0.9	1.25	NS
Tubular atrophy	0.7	1.0	NS
Interstitial fibrosis	0.8	0.9	NS
Vessel	2.0	2.6	<.001

[a] Abbreviations: NS, not significant.

High Risk Donor

Age > 60

DM, Hypertension

Bx: Remuzzi scoring system

Transplantation 67(8):1162; 1999

OUTCOME OF KIDNEY TRANSPLANTATION FROM HIGH-RISK DONORS IS DETERMINED BY BOTH STRUCTURE AND FUNCTION.

Karpinski, Jolanta; Lajoie, Ginette; Cattran, Daniel; Fenton, Stanley; Zaltzman, Jeffrey; Cardella, Carl; Cole, Edward

	CrCl >100 Vessel score <3	**CrCl <100 or Vessel score =3**	**CrCl < 100 Vessel score = 3**	
	Low risk[a] (n=19)	Intermediate risk[b] (n=20)	High risk[c] (n=7)	
DGF	32%	65%	100%	$P=.001$
Dialysis	16%	45%	43%	NS
6 mo Cr	182±41	197±35	317±66	$P<.001$
12 mo Cr	187±51	191±51	320±102	$P<.001$
1 yr Cr>200 μmol/L	42%	38%	100%	$P<.05$[d]
Graft loss	0	20%	43%	$P<.05$[e]

Function and vessel score associated with outcome

Transplantation 67(8):1162; 1999

The Prognostic Utility of Deceased Donor Implantation Biopsy in Determining Function and Graft Survival After Kidney Transplantation

Sandra M. Cockfield,[1] Ronald B. Moore,[2] Gerald Todd,[2] Kim Solez,[3] and Sita Gourishankar[1,4]

- **491 donors; 730 recipients**
- **Implantation biopsy after revascularization in the recipient**
- **Biopsy scored as per Banff scheme for transplanted kidneys**

- **Independent Predictors of Graft Loss**
  - **Repeat transplant: 2.21 (1.33-3.67)**
  - **Old donor age: 1.72 (1.03-2.88)**
  - **Rejection: 3.23 (1.97-5.28)**
  - **Donor CrCL: not significant**
  - **Arteriolar hyalinosis only biopsy finding associated with graft loss: 1.67 (1.03-2.71)**
  - **GS, IF, TA, fibrous intimal thickening not significant**

Transplantation 2010;89: 559–566)

The Kidney Donor Profile Index (KDPI) of Marginal Donors Allocated by Standardized Pretransplant Donor Biopsy Assessment: Distribution and Association With Graft Outcomes

I. Gandolfini[1], C. Buzio[1], P. Zanelli[2], et al

- Biopsy if: age ≥ 65, CrCl < 60, Proteinuria > 1 g/d
  - Core biopsy taken at time of procurement
  - Permanent sections fully stained and read by trained on-call pathologist
  - Graded using Pirani-Remuzzi score
  - Decision to use donor made solely based on biopsy findings: if biopsy score 0-4 then kidneys transplanted as singles

American Journal of Transplantation 2014; 14: 2515–2525

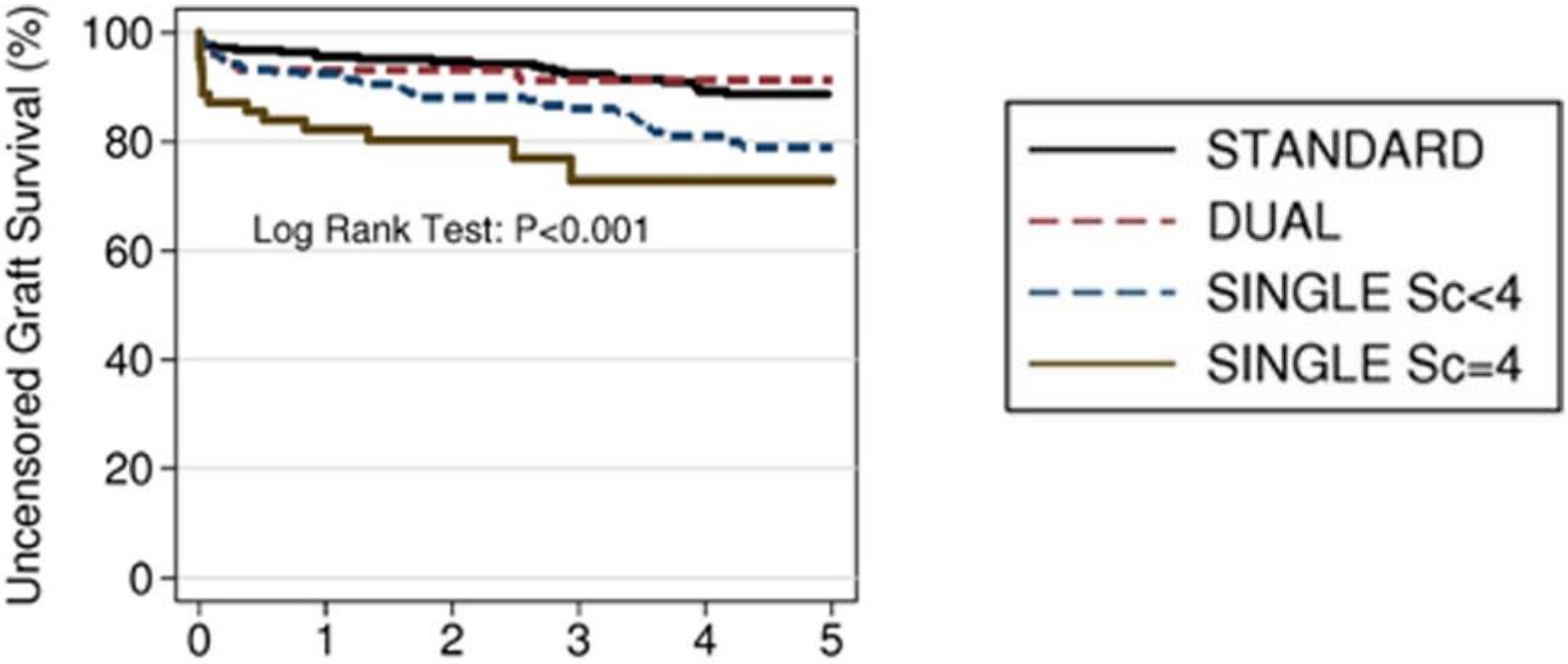
The Kidney Donor Profile Index (KDPI) of Marginal Donors Allocated by Standardized Pretransplant Donor Biopsy Assessment: Distribution and Association With Graft Outcomes

	Marginal		
	DUAL	SINGLE Sc. < 4	SINGLE Sc. = 4
ECD donor, %	85.0	78.0	88.5
KDRI	1.70 (0.31)	1.53 (0.32)	1.57 (0.34)
KDPI	89.3 (9.9)	82.6 (15.1)	83.9 (15.2)
KDPI 80–90, %	18.6	25.7	32.8
KDPI 91–100, %	66.0	41.8	39.3

Lots of High KDPI Kidneys being Transplanted

American Journal of Transplantation 2014; 14: 2515–2525

Excellent Graft Survival Even for High Biopsy-Score Kidneys



American Journal of Transplantation 2014; 14: 2515–2525

Biopsy may Reduce Discard of 'Marginal' Kidneys

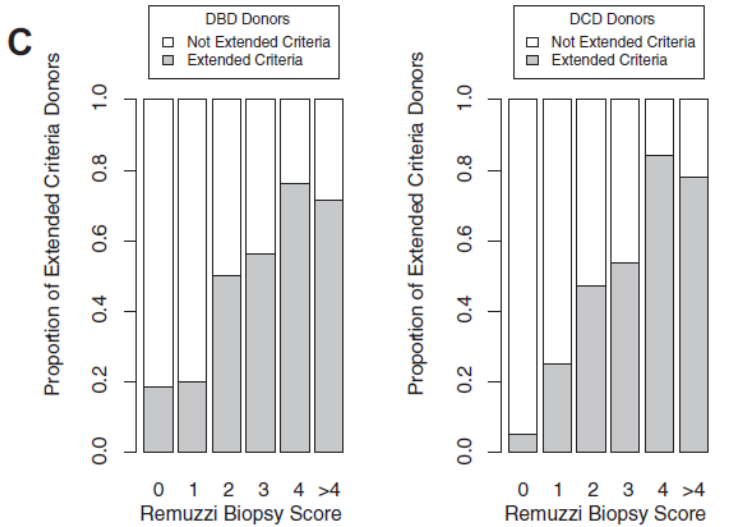
Discard rate in Current Study
15% if KDPI 80-90
37% if KDPI 91-100

Discard rate UNOS Registry
36% if KDPI 80-90
63% if KDPI 91-100

American Journal of Transplantation 2014; 14: 2515–2525

Baseline Donor Chronic Renal Injury Confers the Same Transplant Survival Disadvantage for DCD and DBD Kidneys

V. Kosmoliaptsis[1], M. Salji[1], V. Bardsley[2], Y. Chen[3], S. Thiru[2], M. H. Griffiths[2], H. C. Copley[1], K. Saeb-Parsy[1], J. A. Bradley[1], N. Torpey[4] and G. J. Pettigrew[1,*]



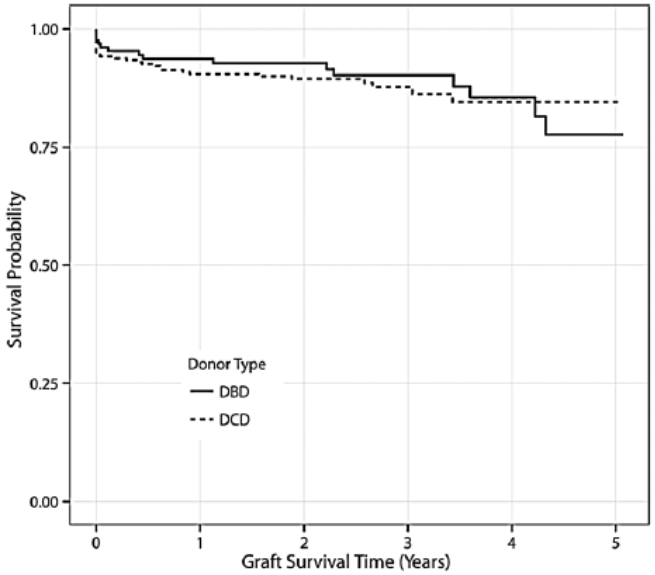
DBD: 44% ECD

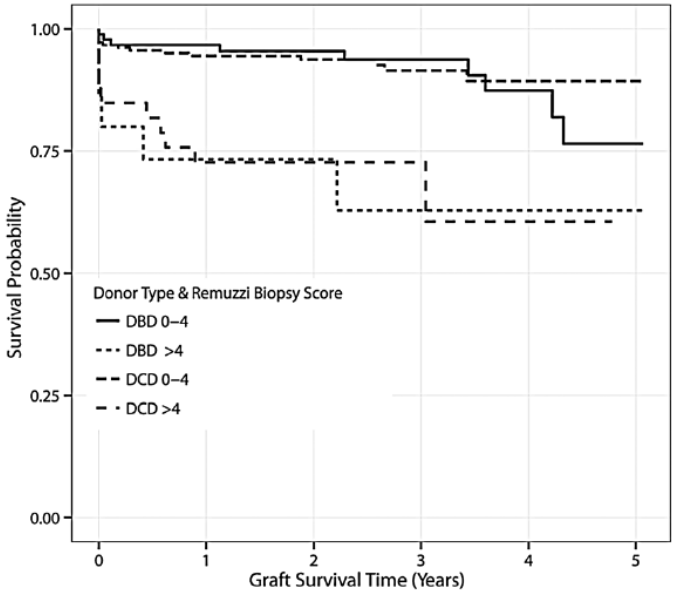
DCD: 46% ECD

ECD kidneys had higher biopsy score regardless of DCD or DBD status

American Journal of Transplantation 2015; 15: 754–763

Baseline Donor Chronic Renal Injury Confers the Same Transplant Survival Disadvantage for DCD and DBD Kidneys





Score ≤ 4
(DBD or DCD)

PNF

Score ≤ 4: 2.6%

Score >4: 12.5%

American Journal of Transplantation 2015; 15: 754–763

Cambridge Transplant Program

Biopsy Score the Only Variable Independently Associated with Graft Survival: DBD or DCD did not Matter

Table 4: Multiple variable Cox regression analysis of kidney allograft survival

Variable	Hazard ratio	95% CI	p-Value
Donor type			
DBD	Reference	–	–
DCD	0.95	0.42–2.17	0.903
Remuzzi biopsy score			
0–4	Reference	–	–
>4	3.88	1.78–8.44	<0.001
Graft number			
First	Reference	–	–
Second/third	1.88	0.52–6.75	0.336
Cold iscaemic time (per hour)	1.01	0.93–1.10	0.823
Recipient sensitization			
Non-sensitized	Reference	–	–
Sensitized[1]	1.23	0.49–3.04	0.657
Donor age (per decade)	1.15	0.69–1.90	0.602
Extended criteria donor (ECD)			
Not ECD	Reference	–	–
ECD	1.86	0.43–8.01	0.406
Donor terminal creatinine (per unit increase)	1.00	0.99–1.01	0.510

American Journal of Transplantation 2015; 15: 754–763

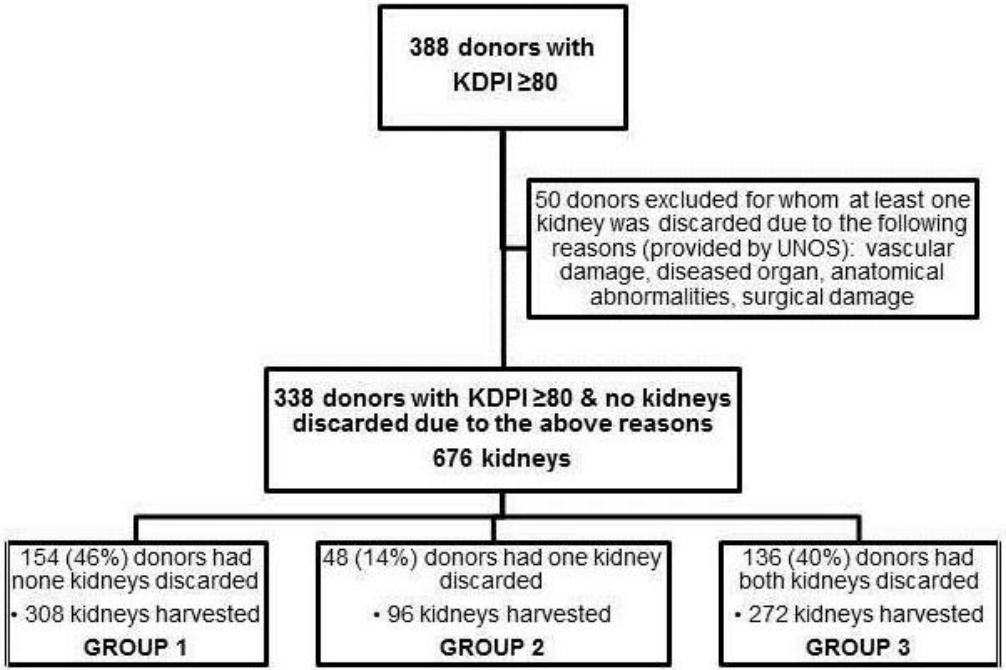
Cambridge Transplant Program

Is the Kidney Biopsy Helpful?

Maybe not always…

Utility of applying quality assessment tools for kidneys with KDPI ≥80

Doshi M, Reese PP, Hall IE, Schröppel B, Ficek J, Formica RN, Weng FL, Hazs RD, Thiessen-Philbrook H, Parikh C



Biopsy: 92%

Discarded: 47%

Discarded:
45% mild findings
55% mod-severe findings

Transplantation 2017; June 101(6):1125-1133

Biopsy and Pump Parameters not Helpful

		GROUP 2 One discarded (N_{kidney}=96)	Transplanted (N_{kidney}=48)	Discarded (N_{kidney}=48)	P (Transplanted vs discarded)
Kidney Biopsy Taken		88 (92%)	44 (92%)	44 (92%)	≈1
ATN**	Absent	40 (77%)	20 (77%)	20 (77%)	≈1
	Mild	4 (8%)	2 (8%)	2 (8%)	
	Moderate/Severe	8 (15%)	4 (15%)	4 (15%)	
Arteriosclerosis	Absent	36 (42%)	17 (40%)	19 (44%)	0.95
	Mild	42 (49%)	22 (51%)	20 (47%)	
	Moderate/Severe	8 (9%)	4 (9%)	4 (9%)	
Fibrosis	Absent	34 (40%)	18 (42%)	16 (19%)	0.8
	Mild	46 (53%)	22 (51%)	24 (28%)	
	Moderate/Severe	6 (7%)	3 (7%)	3 (3%)	
Glomerulosclerosis	Indeterminate or less than 10%	63 (72%)	33 (75%)	30 (68%)	0.69
	11%-20%	18 (20%)	8 (18%)	10 (23%)	
	More than 20%	7 (8%)	3 (7%)	4 (9%)	
Pumped		46 (48%)	23 (48%)	23 (48%)	NA
Pump duration		9.8 [7.0, 13.5]	9.27 (3.64)	12.53 (7.35)	-4.01(6.88) 0.01
Renal resistance, mmHg/mL/min (hour 1)		0.29 [0.22, 0.41]	0.36 (0.38)	0.36 (0.15)	0.01(0.41) 0.12
Pump flow, mL/min (hour 1)		103 [74, 113]	100.62 (33.76)	94.72 (38.20)	7.8(36.43) 0.25
Perfusate collection time		9.13 [6.45, 11.92]	9.46 (5.45)	12.64 (7.15)	-2.44(2.6) 0.03

No differences in biopsy findings or pump parameters between transplanted kidney and mate kidney that was discarded

Transplantation 2017; June 101(6):1125-1133

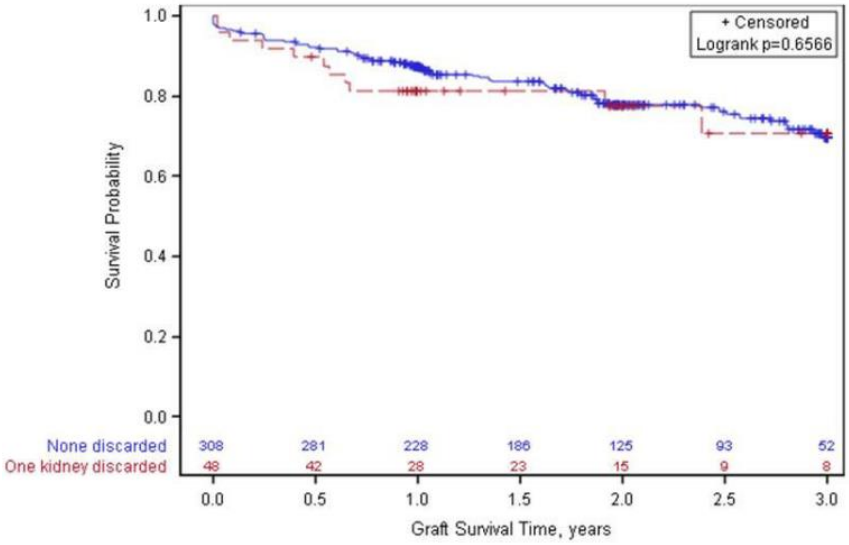
Urine Biomarkers do not seem Helpful

	ALL (N_{donor}=338)	GROUP 1 None discarded (N_{donor}=154)	GROUP 2 One discarded (N_{donor}=48)	GROUP 3 Both discarded (N_{donor}=136)	P (GRP 1 vs. GRP 2)	P (GRP 1 vs. GRP 3)
At least 1 urine biomarker sampled	335 (99%)	152 (99%)	47 (98%)	136 (100%)	0.695	0.182
NGAL, ng/mL	60 [17.5, 199.6]	52.1 [17, 164.85]	61.3 [19.1, 123.9]	81.35 [17.45, 239.1]	0.934	0.116
IL-18, pg/mL	53.38 [22.66, 113.37]	49.16 [19.57, 109.39]	45.64 [21.26, 99.25]	62.61 [28.83, 125]	0.575	0.166
KIM-1, pg/mL	1411.28 [635.59, 3315.15]	1312.83 [644.57, 3305.89]	1374.13 [591.21, 3110.94]	1499.7 [635.36, 3472.53]	0.825	0.634
L-FABP, ng/mL	15.4 [5.2, 60]	12.8 [4.4, 56.4]	11.2 [4.8, 35.6]	19.8 [6.4, 71.2]	0.538	0.122

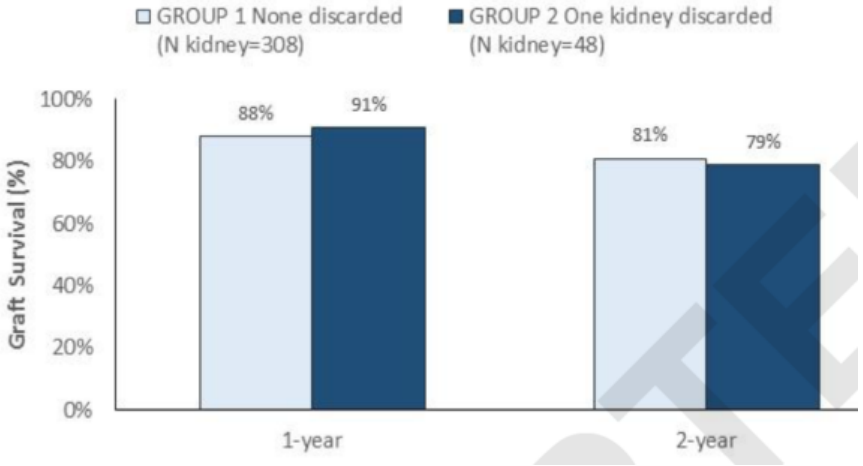
Transplantation 2017; June 101(6):1125-1133

All Outcomes Similar Between Groups

Overall Graft Survival



Death-Censored Graft Survival



aHR for Death-Censored Graft Survival: 1.30 (0.72-2.37)

Transplantation 2017; June 101(6):1125-1133

All Outcomes Similar Between Groups

	GROUP 1 None discarded (N_{kidney}=308)	GROUP 2 One kidney discarded (N_{kidney}=48)	P*
DGF	118 (38%)	21 (44%)	0.477
PNF	11 (4%)	1 (2%)	0.605
6-month acute rejection	25 (8%)	3 (7%)	0.686
1-year death censored graft failure	28 (9%)	5 (10%)	0.769
1-year recipient death	21 (7%)	5 (10%)	0.382
1-year composite outcome (death or graft failure)	38 (12%)	9 (9%)	0.194
2-year death-censored graft failure	41 (13%)	6 (13%)	0.877
2-year recipient death	30 (10%)	6 (13%)	0.560
2-year composite outcome (death or graft failure)	59 (19%)	10 (21%)	0.786
1-year eGFR, mL/min/1.73m^2	41.5 (18)	41.4 (22)	0.977

Transplantation 2017; June 101(6):1125-1133

Kidneys of similar quality are being discarded by some and transplanted by others

Current tools of biopsy, pump parameters and novel biomarkers do not seem to discriminate between kidneys that will and will not work

The reproducibility and predictive value on outcome of renal biopsies from expanded criteria donors

M. Antonieta Azancot[1], Francesc Moreso[1], Maite Salcedo[2], Carme Cantarell[1], Manel Perello[1], Irina B. Torres[1], Angeles Montero[2], Enric Trilla[3], Joana Sellarés[1], Joan Morote[3] and Daniel Seron[1]

- All ECD donors underwent biopsy
- Glomerulosclerosis, interstitial fibrosis, tubular atrophy, intimal thickening, and arteriolar hyalinosis all evaluated using Banff criteria
- Scores from each compartment summed up for overall score
  - Mild damage: score ≤ 3
  - Intermediate: score 4-5
  - Advanced: 6-7
- Biopsies read real-time by on-call pathologist then retrospectively reviewed by trained renal pathologist

Kidney International (2014) **85,** 1161–1168;

The reproducibility and predictive value on outcome of renal biopsies from expanded criteria donors

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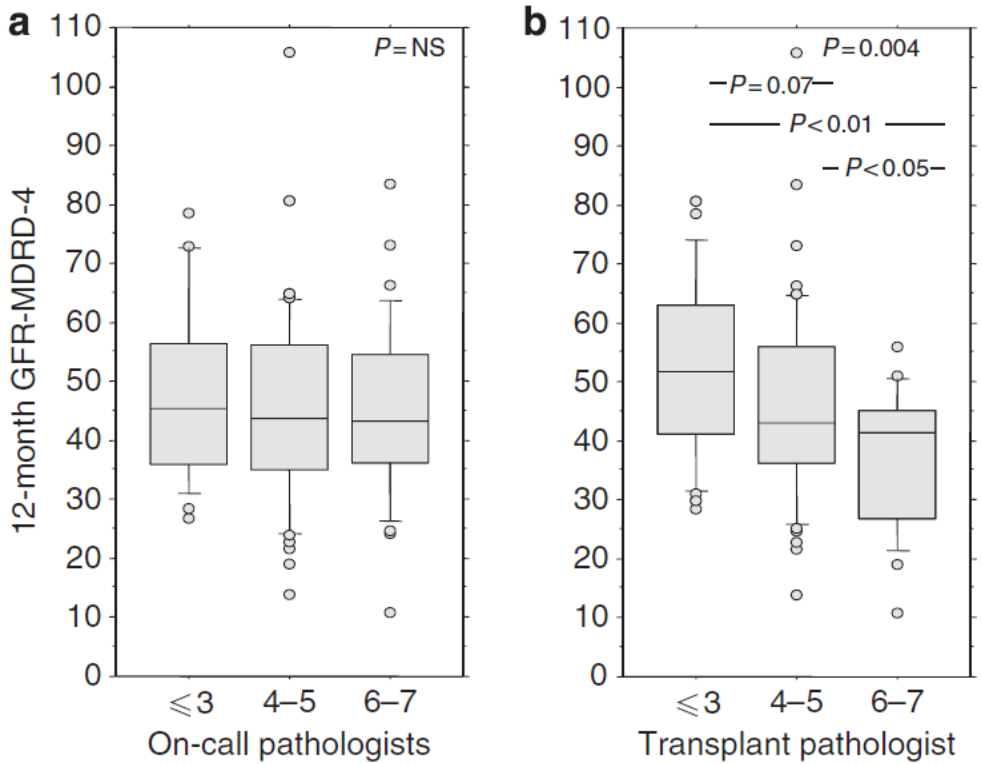
- **Agreement between on-call and renal pathologist**
  - **Glomerulosclerosis: k=0.86 (0.77-0.95)**
  - **Interstitial fibrosis: k=0.31 (0.15-0.46)**
  - **Tubular atrophy: k=0.14 (0.06-0.34)**
  - **Intimal thickening: k=0.37 (0.22-0.51)**
  - **Arteriolar hyalinosis: k=0.25 (0.10-0.39)**

Kappa < 0.4 - poor agreement

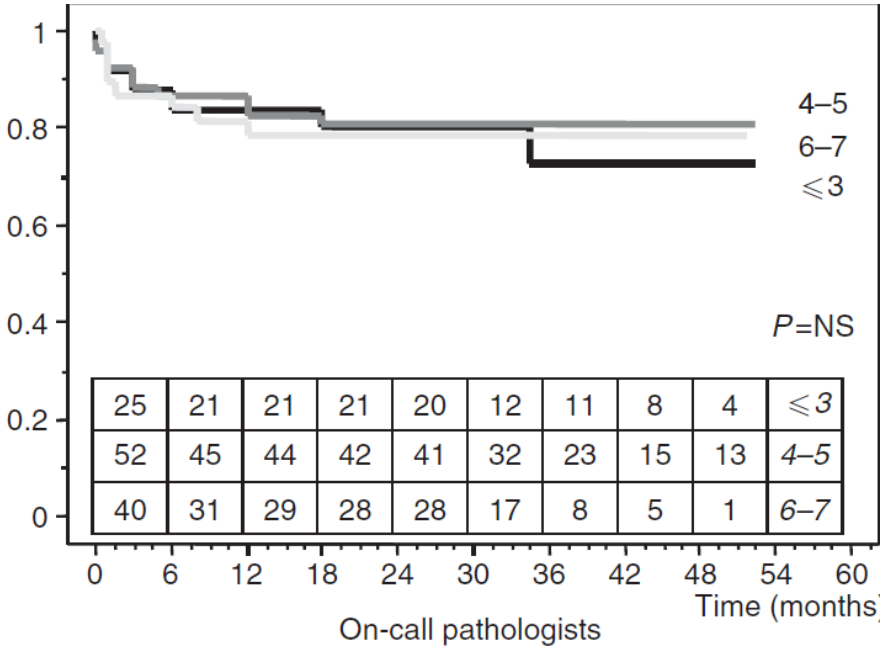
Kidney International (2014) **85,** 1161–1168;

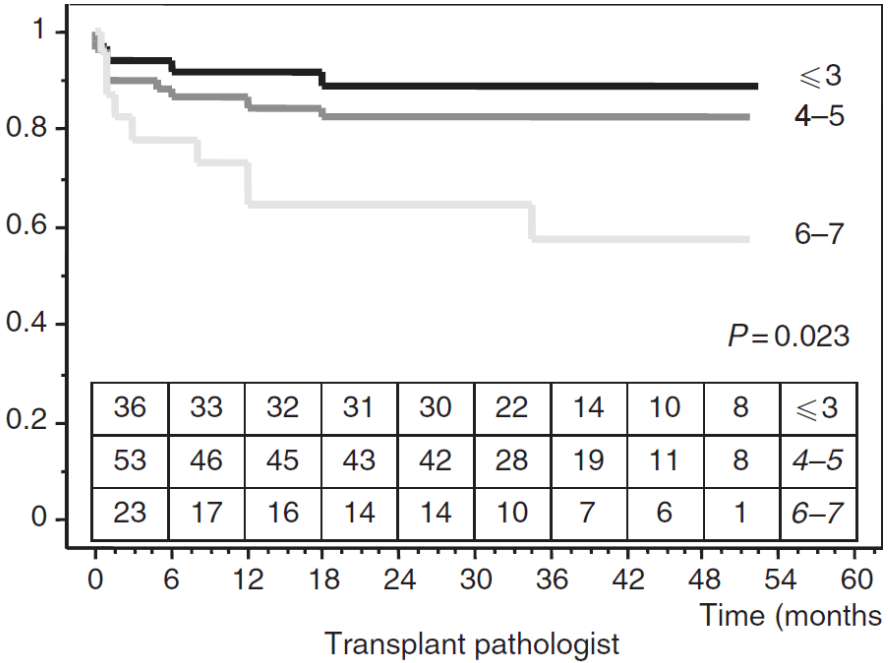
Scoring by On-call Pathologist was Not Associated with 12-Month GFR



Kidney International (2014) **85,** 1161–1168;

Scoring by On-call Pathologist was Not Associated with Composite of Death-Censored Graft Loss or GFR <30

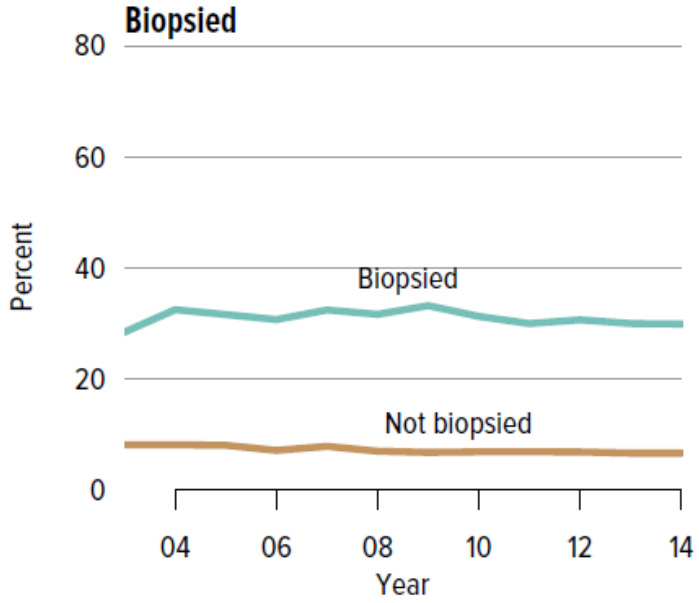




Kidney International (2014) **85,** 1161–1168;

The Role of Procurement Biopsies in Acceptance Decisions for Kidneys Retrieved for Transplant

Bertram L. Kasiske,[*†] Darren E. Stewart,[‡] Bipin R. Bista,[§] Nicholas Salkowski,[*] Jon J. Snyder,[*‖] Ajay K. Israni,[*†‖] Gretchen S. Crary,[¶] John D. Rosendale,[‡] Arthur J. Matas,[**] and Francis L. Delmonico[††]*



Procurement Biopsy: 29.8% discarded

No Biopsy: 6.6% discarded

Clin J Am Soc Nephrol 9: 562–571, March, 2014

SRTR Annual Report 2015

Long term outcomes of transplantation using kidneys from expanded criteria donors: prospective, population based cohort study

Olivier Aubert,[1] Nassim Kamar,[2,3,4,5] Dewi Vernerey,[1] Denis Viglietti,[1,6] Frank Martinez,[7] Jean-Paul Duong-Van-Huyen,[1,8] Dominique Eladari,[1,9] Jean-Philippe Empana,[1] Marion Rabant,[8] Jerome Verine,[10] Lionel Rostaing,[2,3,4,5] Nicolas Congy,[4,11,12] Céline Guilbeau-Frugier,[4,13] Georges Mourad,[5,14] Valérie Garrigue,[5,14] Emmanuel Morelon,[5,15,16] Magali Giral,[5,16,17] Michèle Kessler,[5,16,18] Marc Ladrière,[5,16,18] Michel Delahousse,[1,19] Denis Glotz,[1,5,6] Christophe Legendre,[1,5,7,16] Xavier Jouven,[1,20] Carmen Lefaucheur,[1,5,6] Alexandre Loupy[1,5,7]

Table 4 | Factors associated with kidney allograft loss in the multivariate analysis*

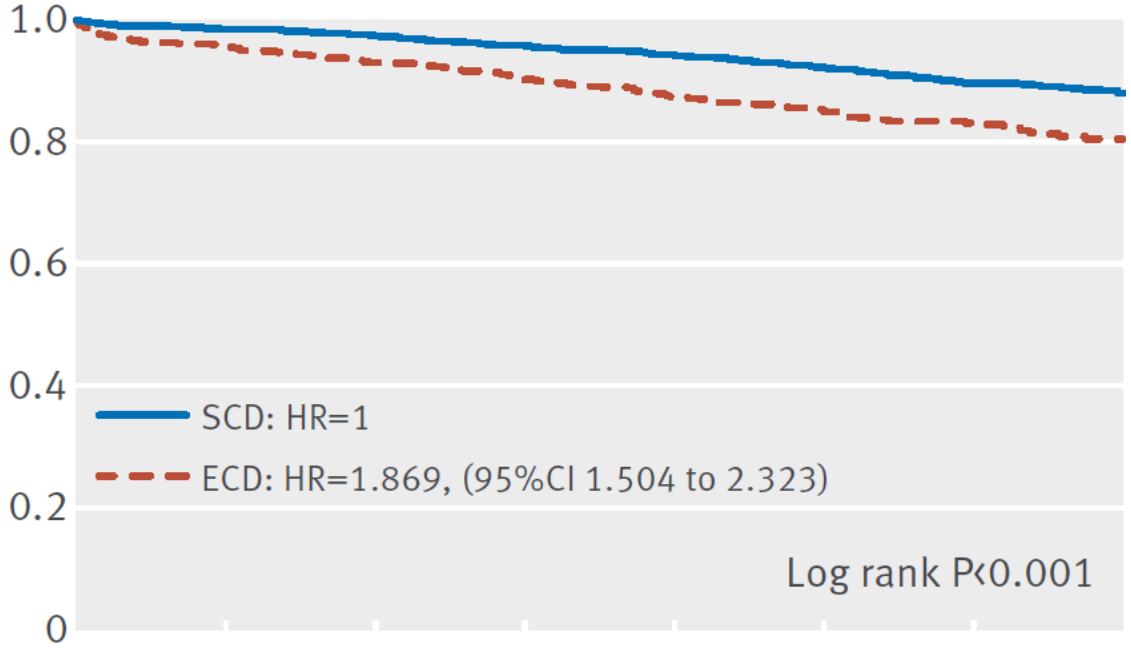
	No of patient/events	Hazard ratio (95% CI)	P	Internal validation hazard ratio 95% CI, BCA
Expanded criteria donor				
No	1835/187	1	<0.001	—
Yes	855/138	1.842 (1.467 to 2.311)		(1.463 to 2.275)
Cold ischaemia time				
<12 h	670/44	1		—
12-24 h	1514/198	1.457 (1.042 to 2.039)	0.017	(1.042 to 2.093)
≥24 h	506/83	1.727 (1.185 to 2.517)		(1.195 to 2.506)
Graft rank				
1	2278/241	1	0.002	—
>1	412/84	1.544 (1.168 to 2.042)		(1.129 to 2.046)
No of HLA A/B/DR mismatches	2690/325	1.095 (1.013 to 1.184)	0.022	(1.013 to 1.182)
Anti-HLA DSA on day 0				
No	2364/241	1	<0.001	—
Yes	326/84	2.988 (2.265 to 3.941)		(2.198 to 3.940)

No biopsy parameters associated with graft loss but CIT was significant

Pre-Implantation Biopsy performed on all donors to establish baseline but not used in decision to accept/decline donor

BMJ 2015; 351:h3557

ECD Death-Censored Graft Survival 80% at 7-Years



Data suggests it might be better to skip the biopsy which will delay decision-making and adds to cold ischemic times

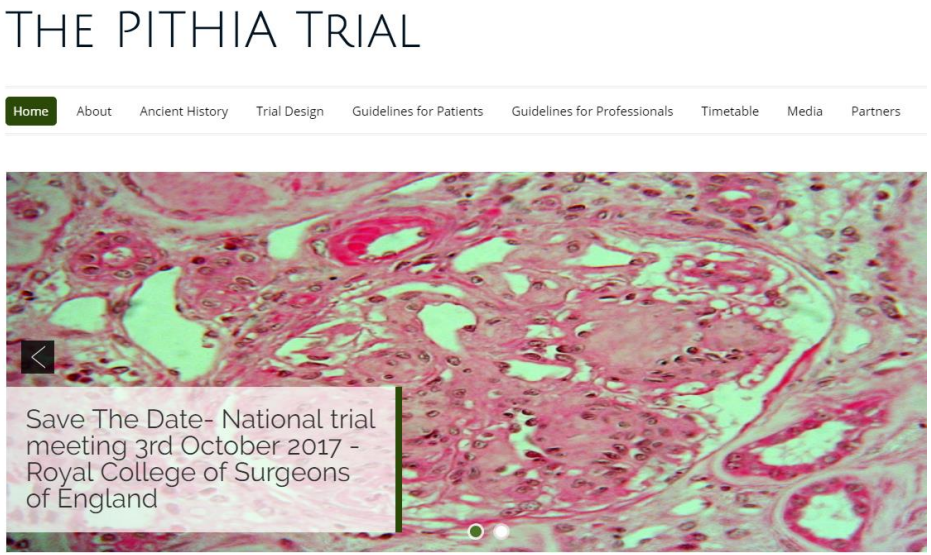
BMJ 2015; 351:h3557

Summary

- There is a high discard rate with marginal kidneys
- Variability in practice suggests that the evidence we are using to make decisions is not ideal
- Non-ECD DCD kidneys have excellent outcomes and should not be considered marginal kidneys – focus on ECD or high KDPI kidneys
- Pre-transplant biopsy scores, especially when considering chronic vascular damage, are associated with outcomes in most studies
- Recent data examining biopsy, perfusion parameters and novel biomarkers together failed to show any advantage of using these tools in high KDPI kidneys

Summary

- There are well recognized limitations of procurement biopsies including reliability of findings, training of those reading the slides etc.
- Many of the positive studies used retrospective review of implantation biopsy rather than real-time reading of procurement biopsy
- Many European centres have excellent ECD results but rarely use biopsy for decision-making
- Moving Forward – variability in practice and data suggests proper RCT could be conducted to assess risks/benefits of procurement biopsy



RCT – stepped wedge design

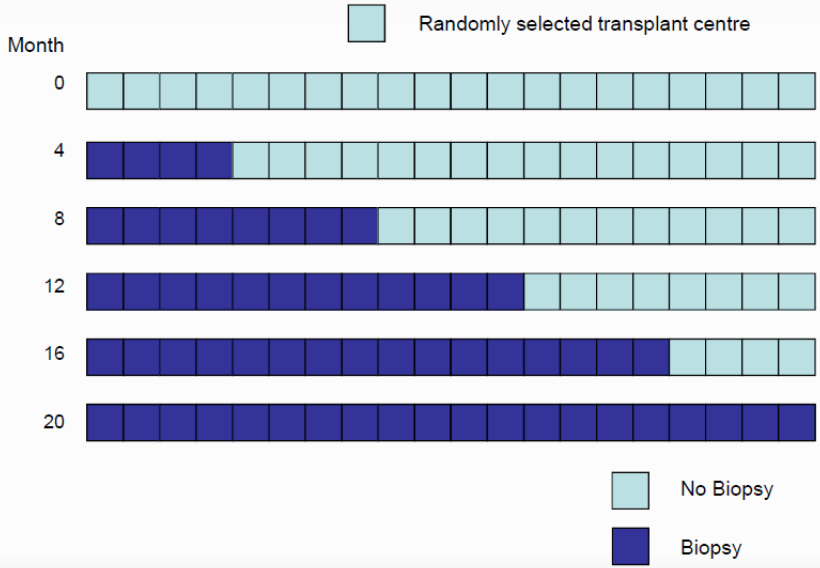
Biopsy: will be done in all donors >65 yrs

Powered to detect a 10% increase in organ utilization

The PITHIA trial

Does having access to a biopsy result increase the number and quality of kidneys for transplantation?

- UK trial
- 20 centres
- Stepped-wedge
- Registry
- Power – 10%
- 4ml/min eGFR
- Economic Analysis
- Feb 2017
- 21 months, + 12



Expanding the Donor Pool
ECD/DCD: Evaluation of the Marginal Kidney Donor

2017 CST/Astellas Canadian Transplant Fellows Symposium

Halifax World Trade and Convention Centre, Halifax, NS

September 25, 2017

Greg Knoll MD MSc

Head, Division of Nephrology, The Ottawa Hospital and the University of Ottawa

Senior Scientist, Ottawa Hospital Research Institute

Professor of Medicine, University of Ottawa

Canadian Society of Transplantation
LEADERSHIP IN CANADIAN TRANSPLANTATION

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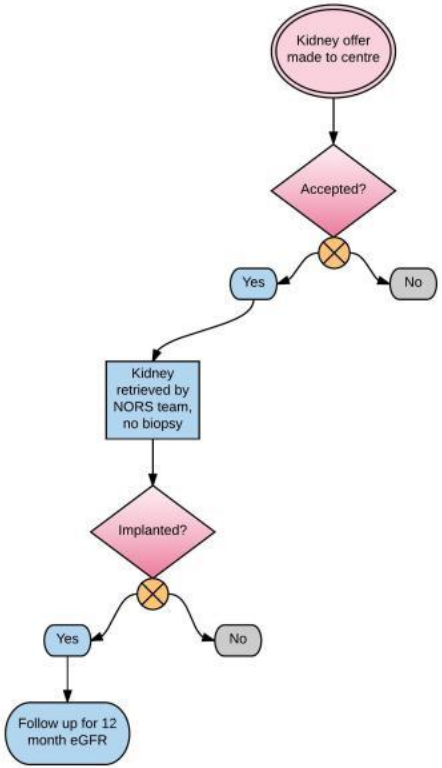
control



The PITHIA trial has two relatively novel elements of trial design: firstly, it is a registry-based, randomised clinical trial. Secondly, it is has a ‘stepped-wedge cluster’ design. These elements should help keep the costs of the trial to a minimum, just a fraction of the costs of a typical national, multi-centre trial. In addition, the trial design aims to minimise the time and effort required by busy clinicians and patients.

Intervention