What The Best Options for Renal Replacement Therapy (RRT)?

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Mrs. K. T.

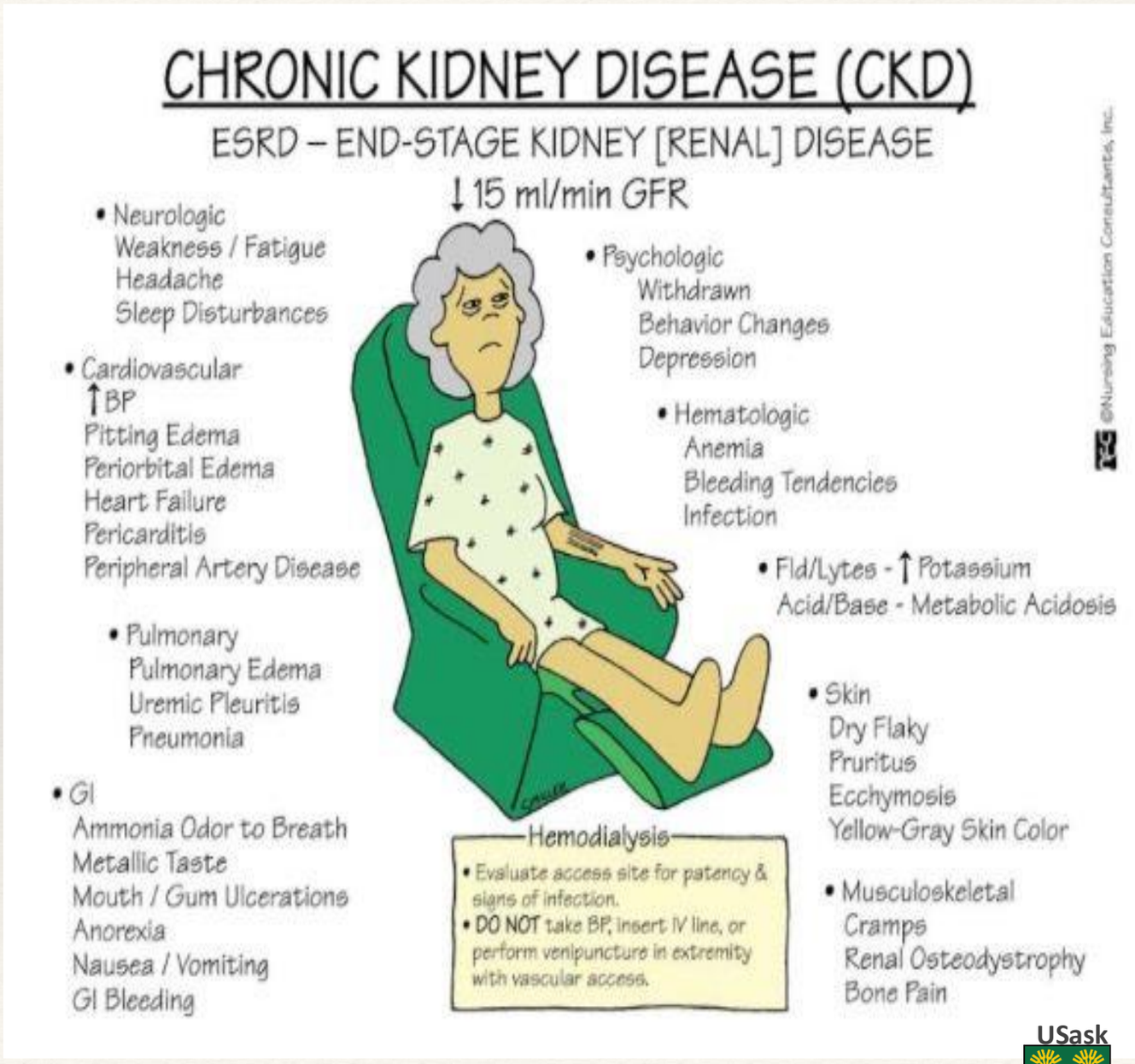
- A 63 Y O F with Advanced CKD (Stage 5: eGFR 16 ml/min/1,73m2) secondary to Diabetic Nephropathy and Hypertensive Nephrosclerosis without Kidney Bx.

- What is the best modalities of RRT for this patient:
  - In centre Chronic Intermittent HD
  - PD: ACPD
  - PD: CCPD
  - Chronic Nocturnal Home HD
  - Pre-emptive Living Donor Kidney Transplant
  - Pre-emptive Deceased Donor Kidney Transplant

Options

The End Stage Kidney Disease Patient

- Dialysis vs. Transplant?
- Living vs. Deceased donor?
- DCC, ECD, SCD?
- Pre-emptive or not?



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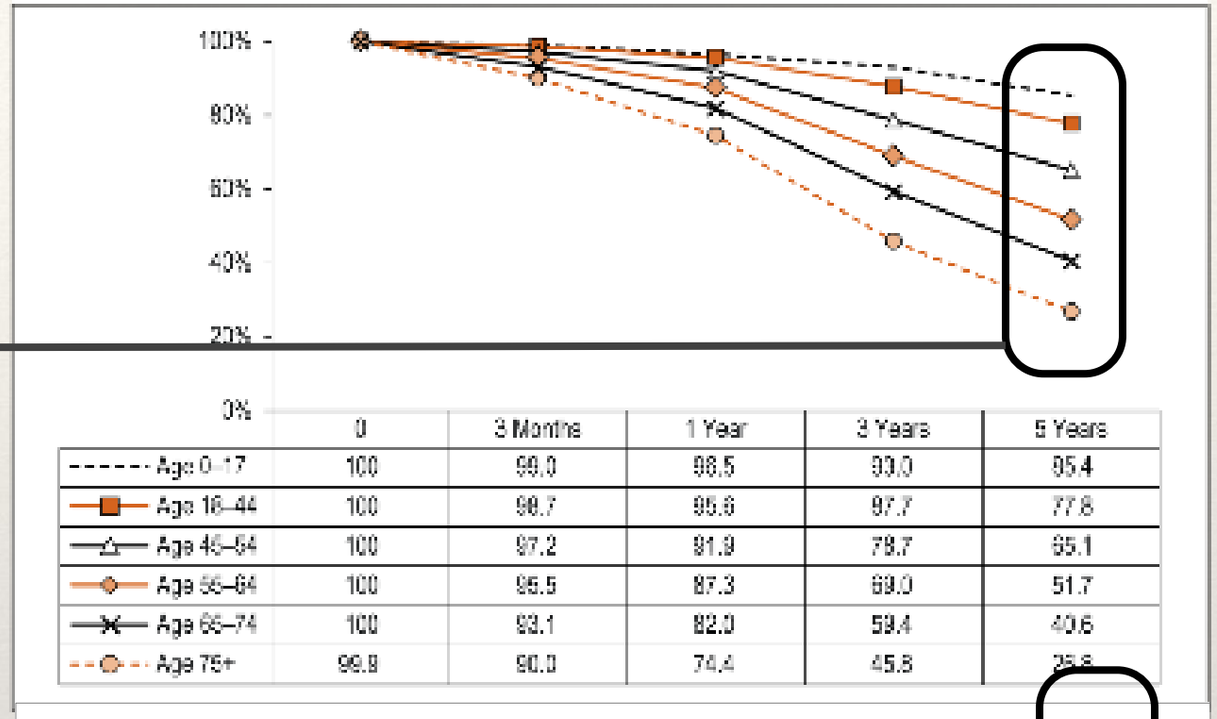
December 23, 1954, Dr. Joseph E. Murray accomplished the impossible

11 December 1963

- First kidney transplant in Saskatchewan
- Second kidney transplant in Canada

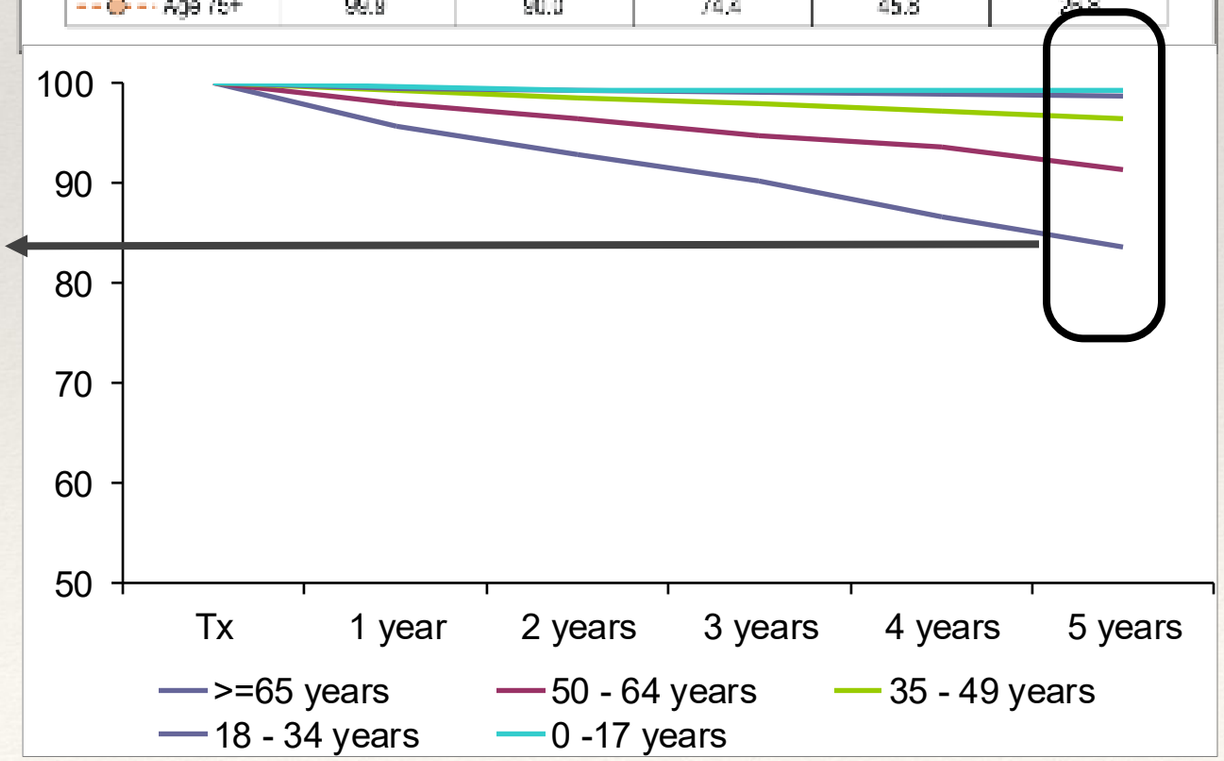
Dialysis or Transplant?

27-85%



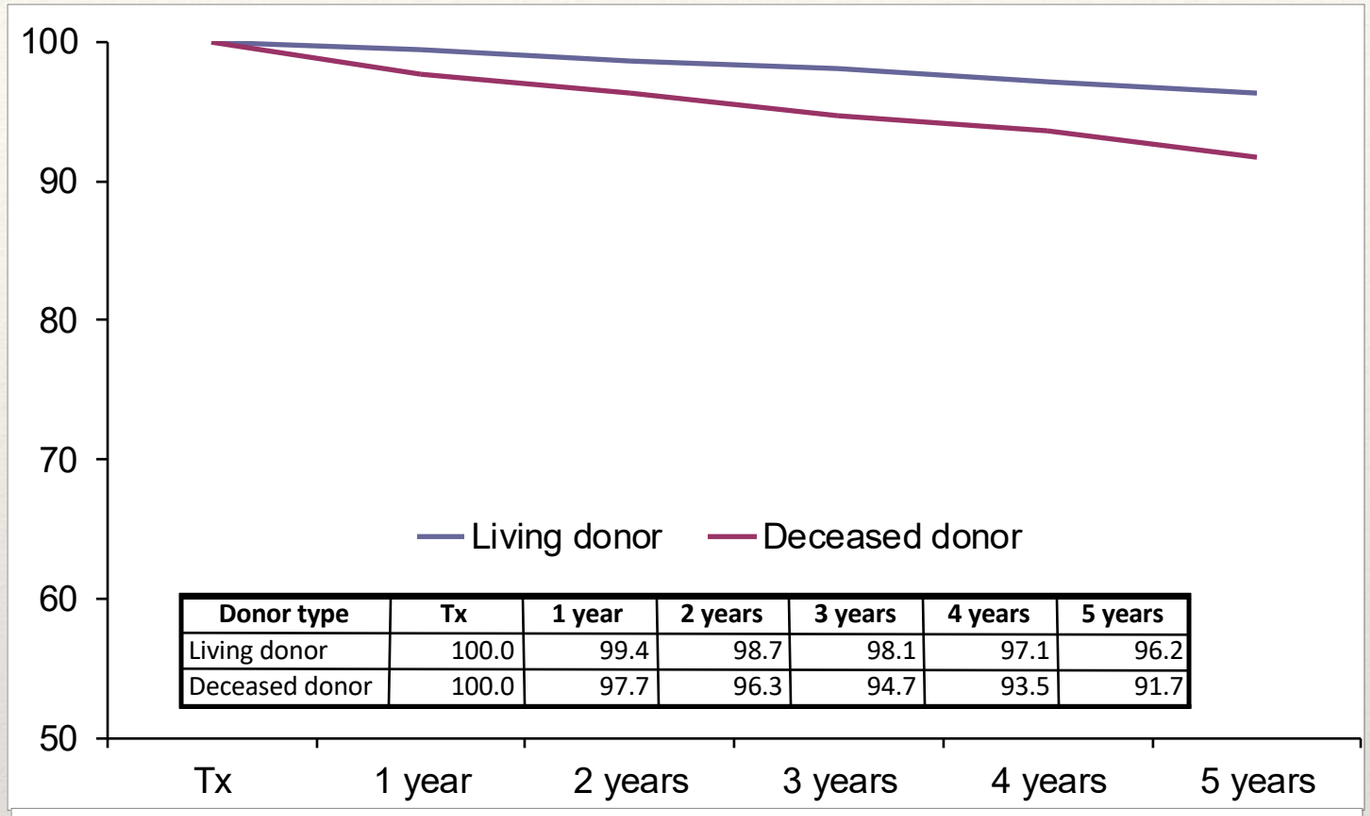
	0	3 Months	1 Year	3 Years	5 Years
Age 0–17	100	99.0	98.5	93.0	85.4
Age 18–44	100	98.7	95.6	87.7	77.8
Age 45–54	100	97.2	91.9	78.7	65.1
Age 55–64	100	96.5	87.3	69.0	51.7
Age 65–74	100	93.1	82.0	59.4	40.6
Age 75+	99.9	90.3	74.4	45.8	29.8

84-99%

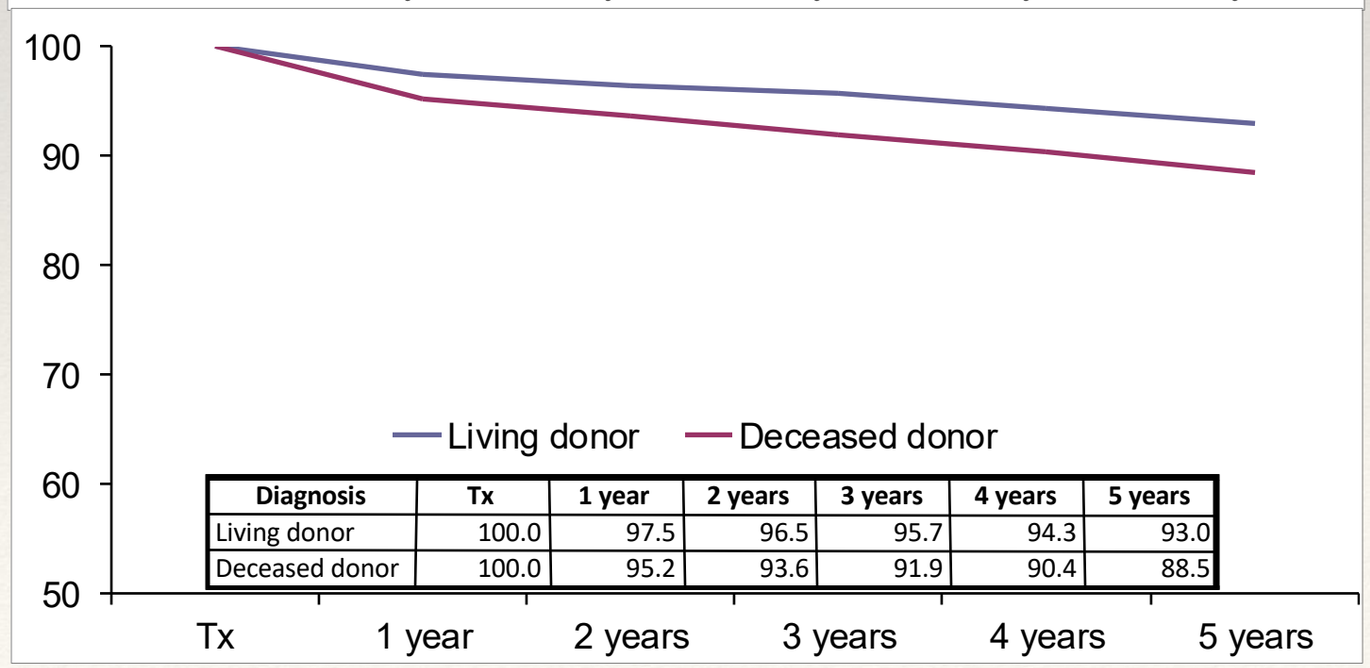


Canadian Organ Replacement Register Annual Report: Treatment of End-Stage Organ Failure in Canada, 2004 to 2013. Report April 2015

The Benefit of Living Donors



Donor type	Tx	1 year	2 years	3 years	4 years	5 years
Living donor	100.0	99.4	98.7	98.1	97.1	96.2
Deceased donor	100.0	97.7	96.3	94.7	93.5	91.7

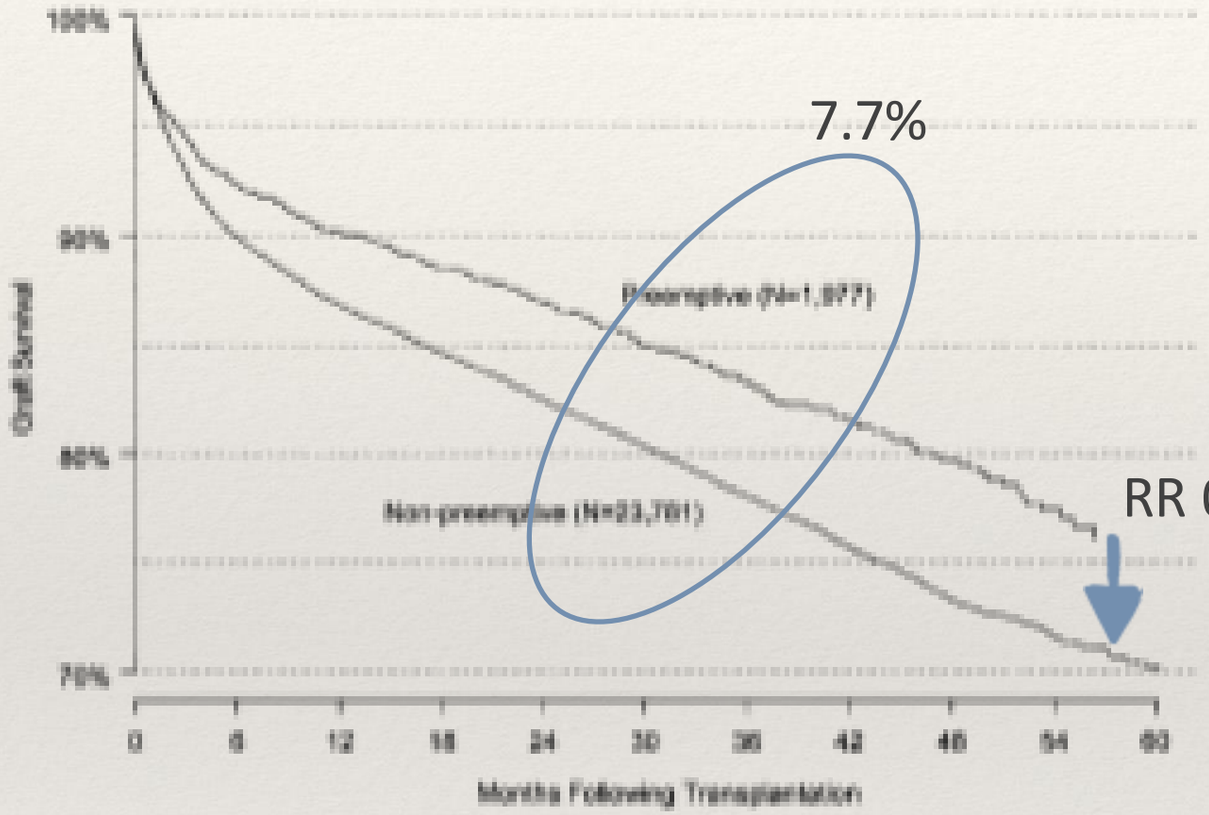


Diagnosis	Tx	1 year	2 years	3 years	4 years	5 years
Living donor	100.0	97.5	96.5	95.7	94.3	93.0
Deceased donor	100.0	95.2	93.6	91.9	90.4	88.5

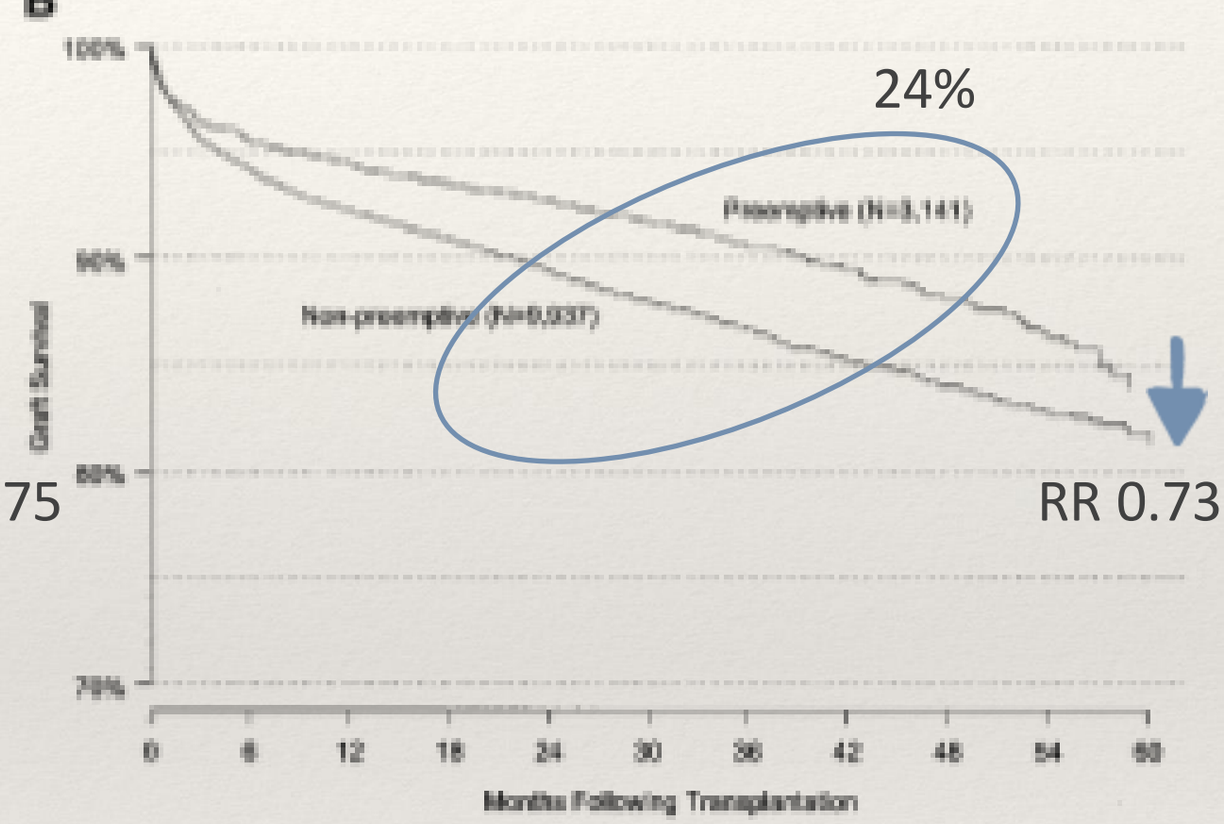
Source
Canadian Organ Replacement Register, 2012, Canadian Institute for Health Information.

Preemptive Transplantation

B Deceased Donor Transplant



B Living Donor Transplant



BERTRAM L. KASISKE, JON J. SNYDER, ARTHUR J. MATAS, MARY D. ELLISON, JOHN S. GILL, and ANNAMARIA T. KAUSZ

Preemptive Kidney Transplantation: The Advantage and the Advantaged

J Am Soc Nephrol 13: 1358–1364, 2002

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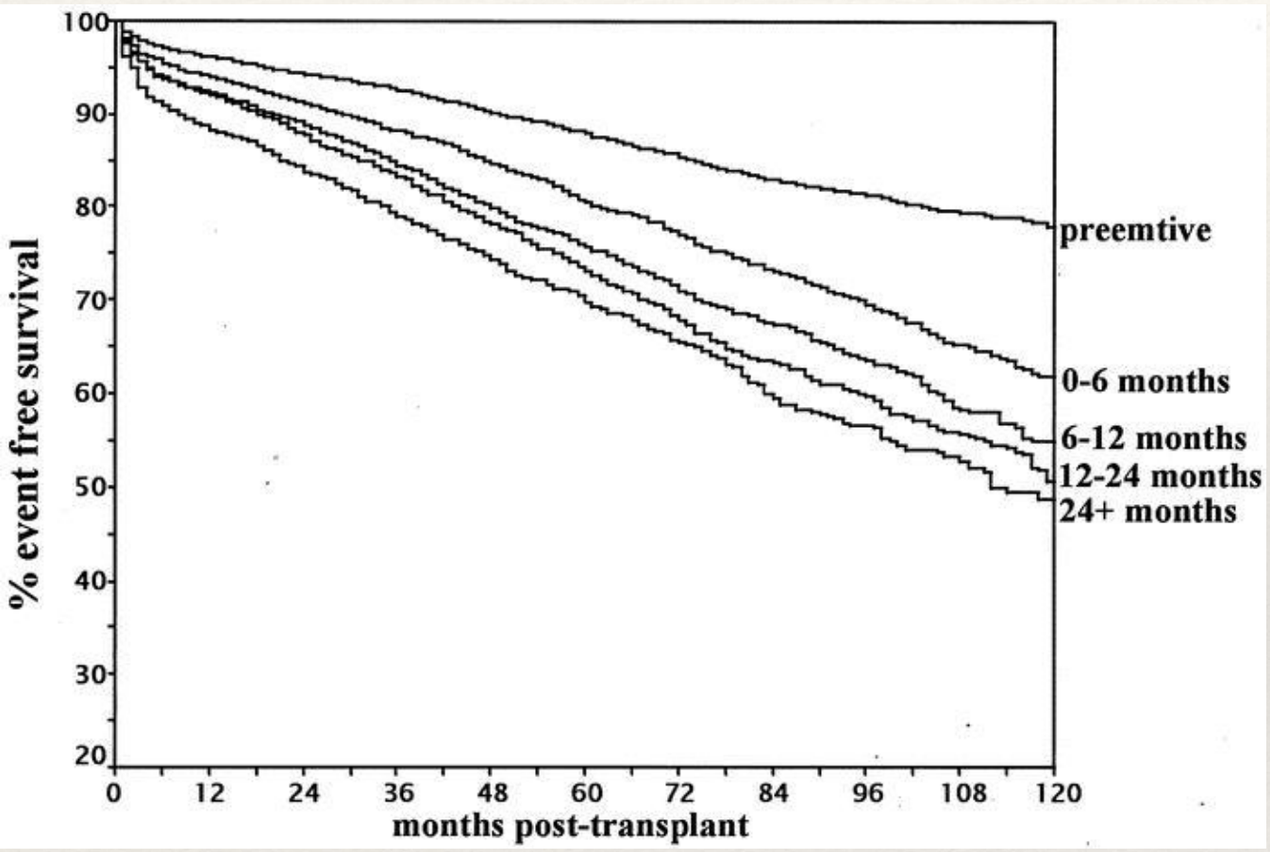
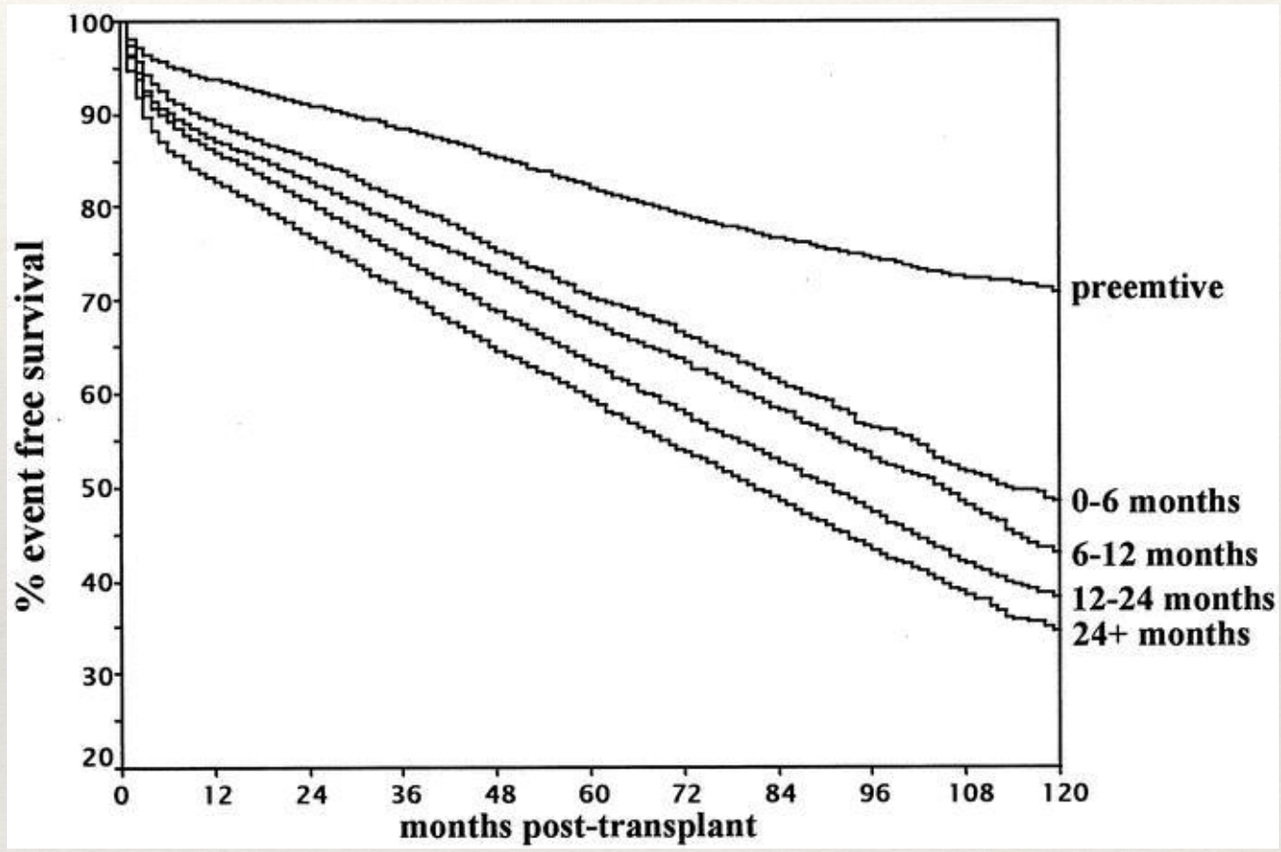
Living and deceased donors graft survival





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How Good is that Kidney?

- DCC: Donation after circulatory death
  - Initial dialysis dependence but long term outcomes similar to SCD
- ECD: Extended criteria donor
  - Donor age>60 or 50-59 with history of renal dysfunction, hypertension, CVA as cause of death
- SCD or ideal donor
- KDPI: Kidney donor profile index:
  - Combines a variety of donor factors into a single number that summarizes the likelihood of graft failure after deceased donor kidney transplant

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Suitability for Transplant

- Renal function
- Age
- Cardiac disease
- Vascular disease
- Pulmonary disease
- Liver disease
- Malignancy
- Psychosocial

Canadian Society of Transplantation consensus guidelines on eligibility for kidney transplantation

Greg Knoll, Sandra Cockfield, Tom Blydt-Hansen, Dana Baran, Bryce Kiberd, David Landsberg, David Rush, Edward Cole, for the Kidney Transplant Working Group of the Canadian Society of Transplantation

CMAJ • November 8, 2005 • 173(10)

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Suitability for Transplant

- Renal function
- Age
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- Vascular disease
- Pulmonary disease
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- Malignancy
- Psychosocial

- Preemptive transplantation is preferred
- Measured or calculated GFR < 20 ml/min *and* there is evidence of progressive renal decline in the prior 6-12 months
- Risk of recurrent disease is not contraindication in most instances
  - SLE & anti-GBM should be quiescent for 6 months *off* cytotoxic agents
  - vasculitis should be quiescent for 12 months *off* cytotoxic agents

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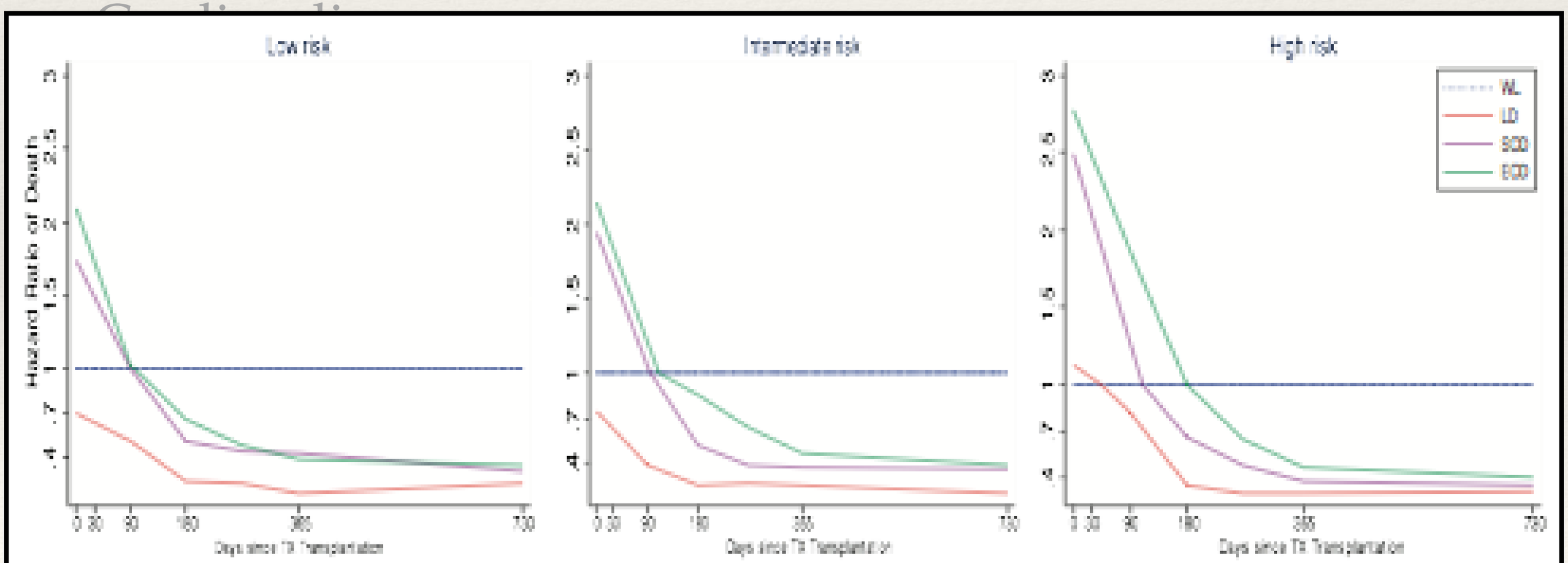
Suitability for Transplant

- Renal function
- Age

Reasonable probability of survival past local transplant waiting times



American Journal of Transplantation, February, 2013.
Quantification of the Early Risk of Death in Elderly Kidney Transplant Recipients
J. S. Gill, E. Schaeffner, S. Chadban, J. Dong, C. Rose, O. Johnston, J. Gill

Suitability for Transplant

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Absolute C/Is to Renal Transplantation

- Recent/ Active Malignancy
- Active infection
- Uncontrolled psychiatric disorders, active drug use, alcoholism
- Absolute non-compliance in dialysis (?)
- Active Smokers (?)

Immunology-ABO

Blood Type Compatibility Chart

Blood Group	Can Recieve From	Can Donate To
A	A·O	A·AB
B	B·O	B·AB
AB	A·B·AB·O	AB
O	O	A·B·AB·O

Kidney Wise

Immunology-HLA

- Major Histocompatibility Complex
  - Found in all vertebrates
- Human Leukocyte Antigen
  - Human version of MHC
  - Class I: HLA A, B, C
    - Activate Killer T Cells
  - Class II: HLA DP, DQ, DR
    - Activate T Helper Cells

Immunology-HLA

- Recipient & Donor HLA (eg: A2, A6, B24, B34, DR7, DR9, DP04, DP06, DQ10, DQ10)
- Recipient HLA antibodies = cPRA (calculated panel reactive antibody)
  - Are these donor specific
- Transfusions, pregnancies, prior transplant

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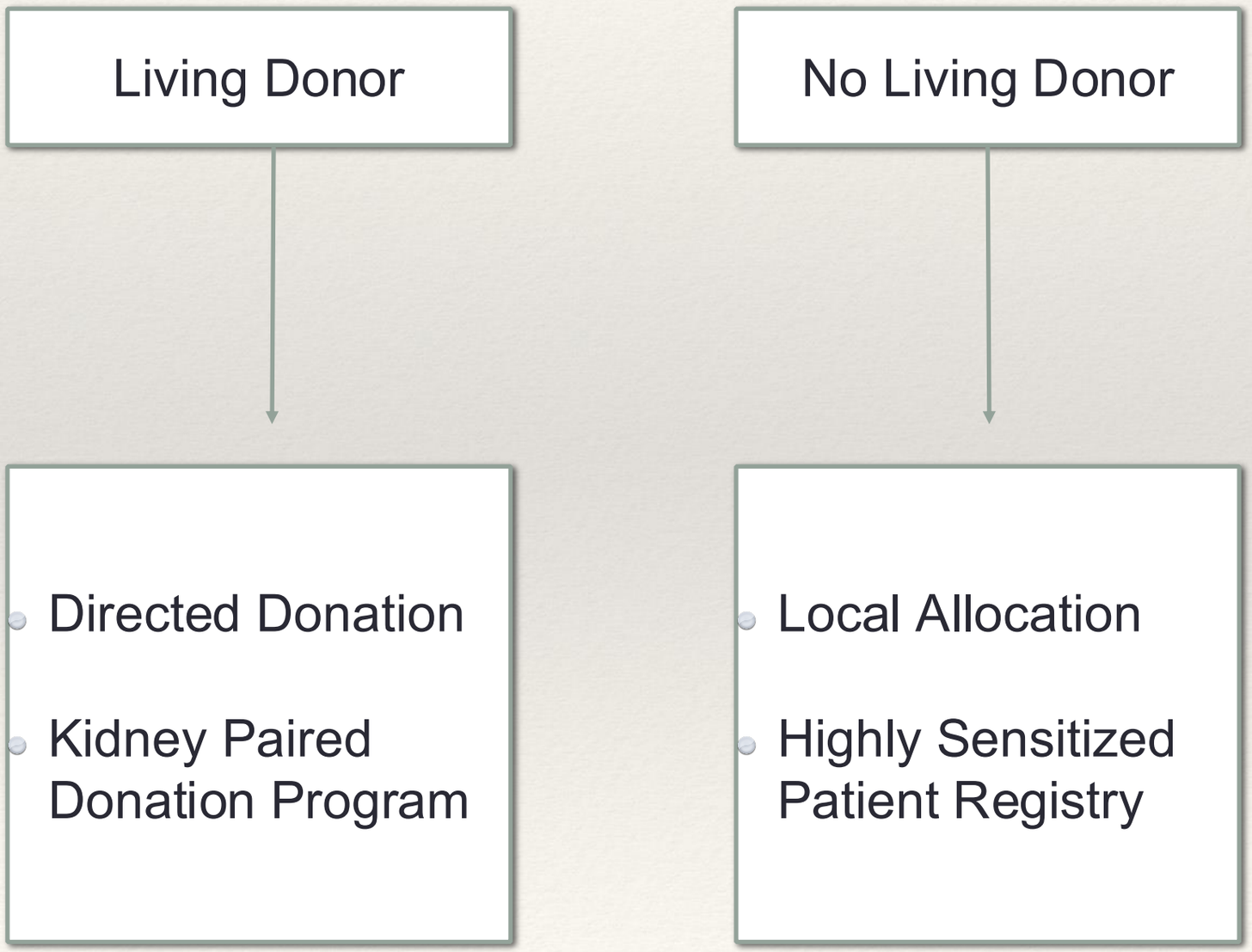
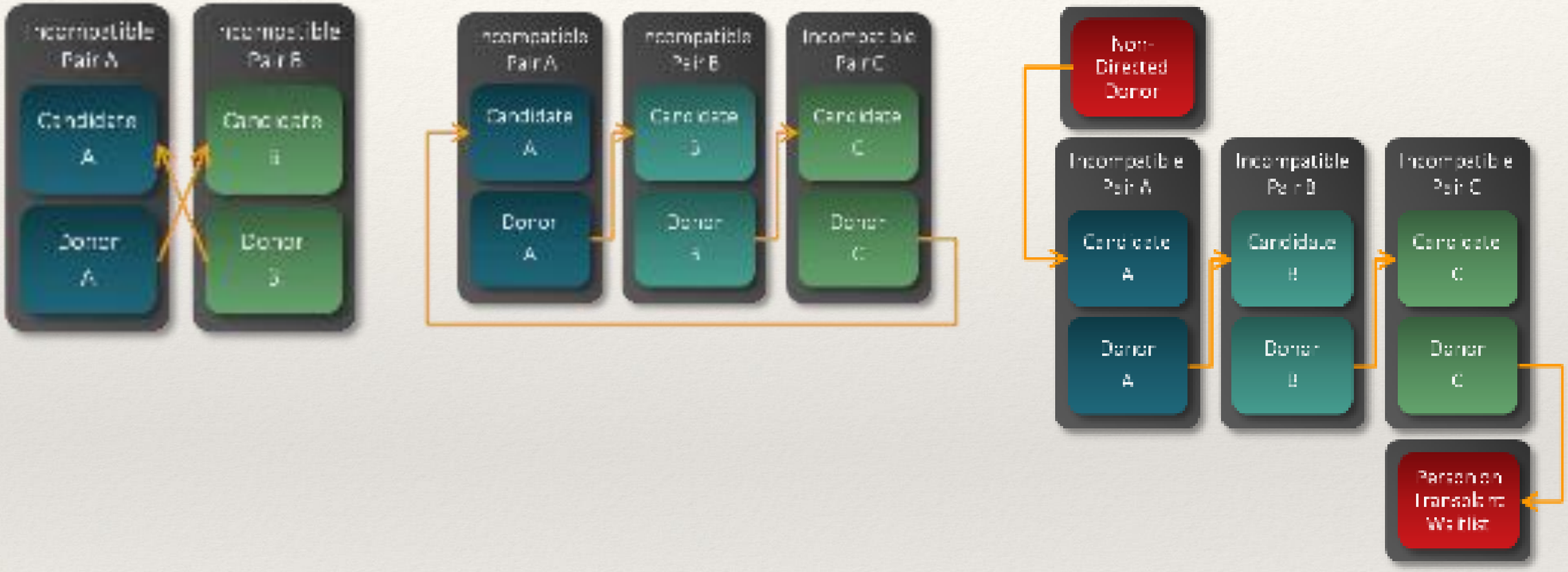
D/R Compatibility

- Step 1: ABO compatibility
- Step 2: HLA compatibility
  - Donor specific HLA antibodies
- Step 3: Crossmatch

Now What?


Living Donor
No Living Donor
Directed Donation
Kidney Paired Donation Program
Local Allocation
Highly Sensitized Patient Registry

Kidney Paired Donation



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Local Allocation

- **Guiding Principles**
  - Medical Urgency
  - Age matching
  - Sensitization
  - Waiting time
  - HLA matching

Highly Sensitized Patient Registry

- October 2013
- National sharing for patients with cPRA > 95%
  - 95% 1 in 20 donors
  - 98% 1 in 50 donors
  - 99% 1 in 100 donors
  - 99.5% 1 in 1000 donors

Case: Mrs. DP

- 52 year old female with ESKD secondary to SLE, blood group B
- Dialysis 17 June 2010
- Transplant 8 Nov 2014
- cPRA 98-100% Antibodies to every HLA B-antigens, except B 8
- Donor's tissue typing was B 8 homozygous
- Retrospectively, 1 in >1700 donor cases in Canada

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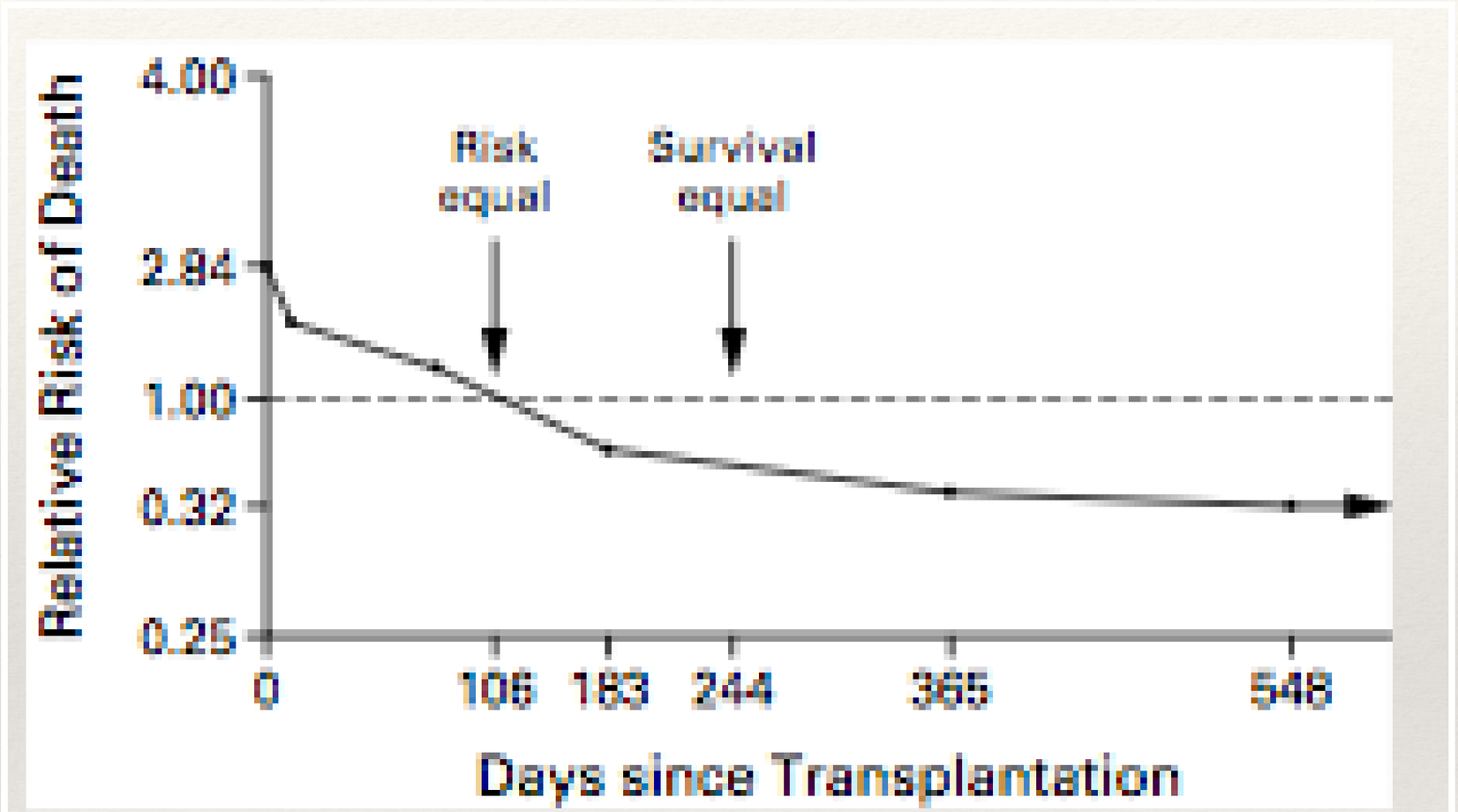
Recipient Risks Post-Transplant

- 1. Post-operative risks
- 2. Chronic immunosuppression
  - CV disease
  - Malignancy
  - Infection
  - Other (DM, HTN, OP & #)

Post-Operative Risks



COMPARISON OF MORTALITY IN ALL PATIENTS ON DIALYSIS, PATIENTS ON DIALYSIS AWAITING TRANSPLANTATION, AND RECIPIENTS OF A FIRST CADAVERIC TRANSPLANT

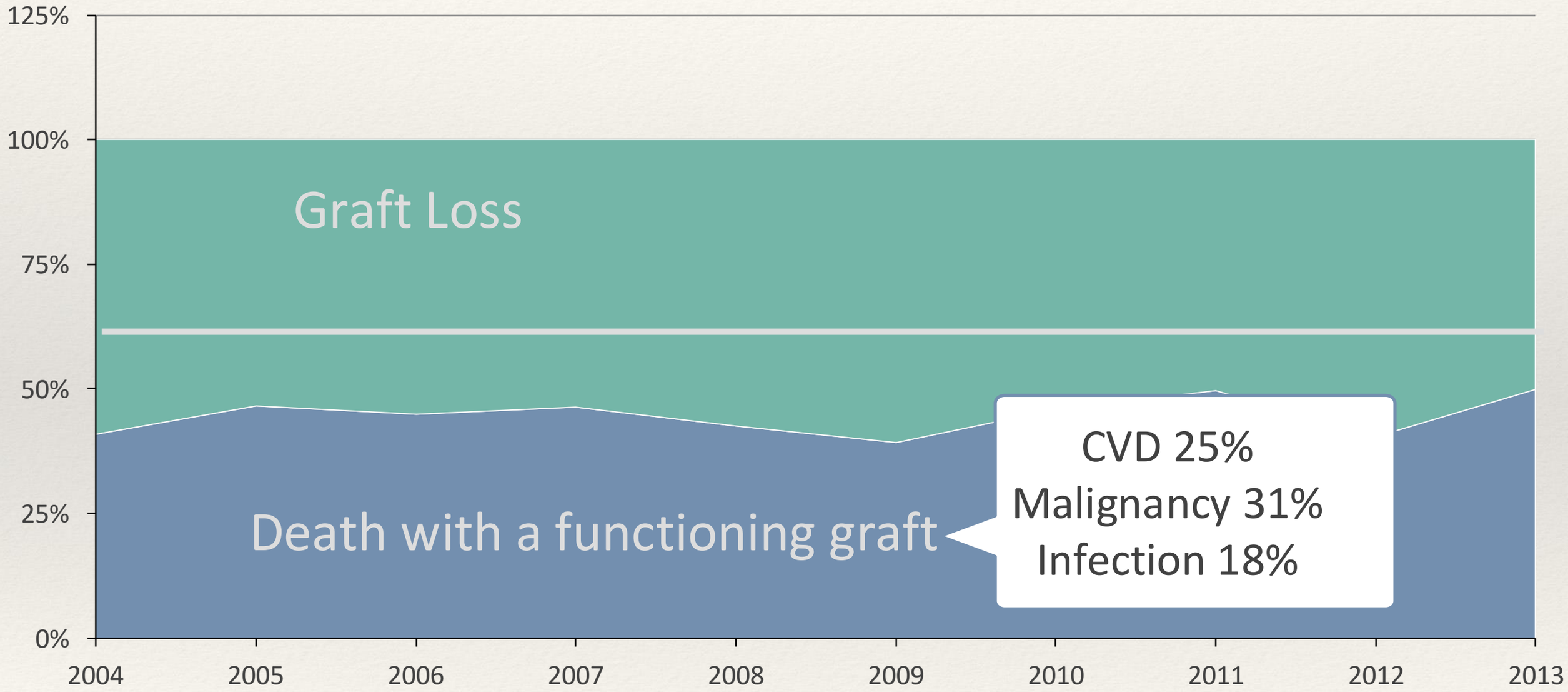
ROBERT A. WOLFE, PH.D., VALARIE B. ASHBY, M.A., EDGAR L. MILFORD, M.D., AKINLOLU O. OJO, M.D., PH.D., ROBERT E. ETTENGER, M.D., LAWRENCE Y.C. AGODOA, M.D., PHILIP J. HELD, PH.D., AND FRIEDRICH K. PORT, M.D.

NEJM 1999 341 (23)

Rejection

- Hyperacute
  - Wrong crossmatch
- Accelerated
  - Within first week
  - Preformed antibodies
- Acute
  - Cell-mediated or Antibody-mediated
  - Interstium, Tubules, Vessels, Glomeruli

Transplant Failure

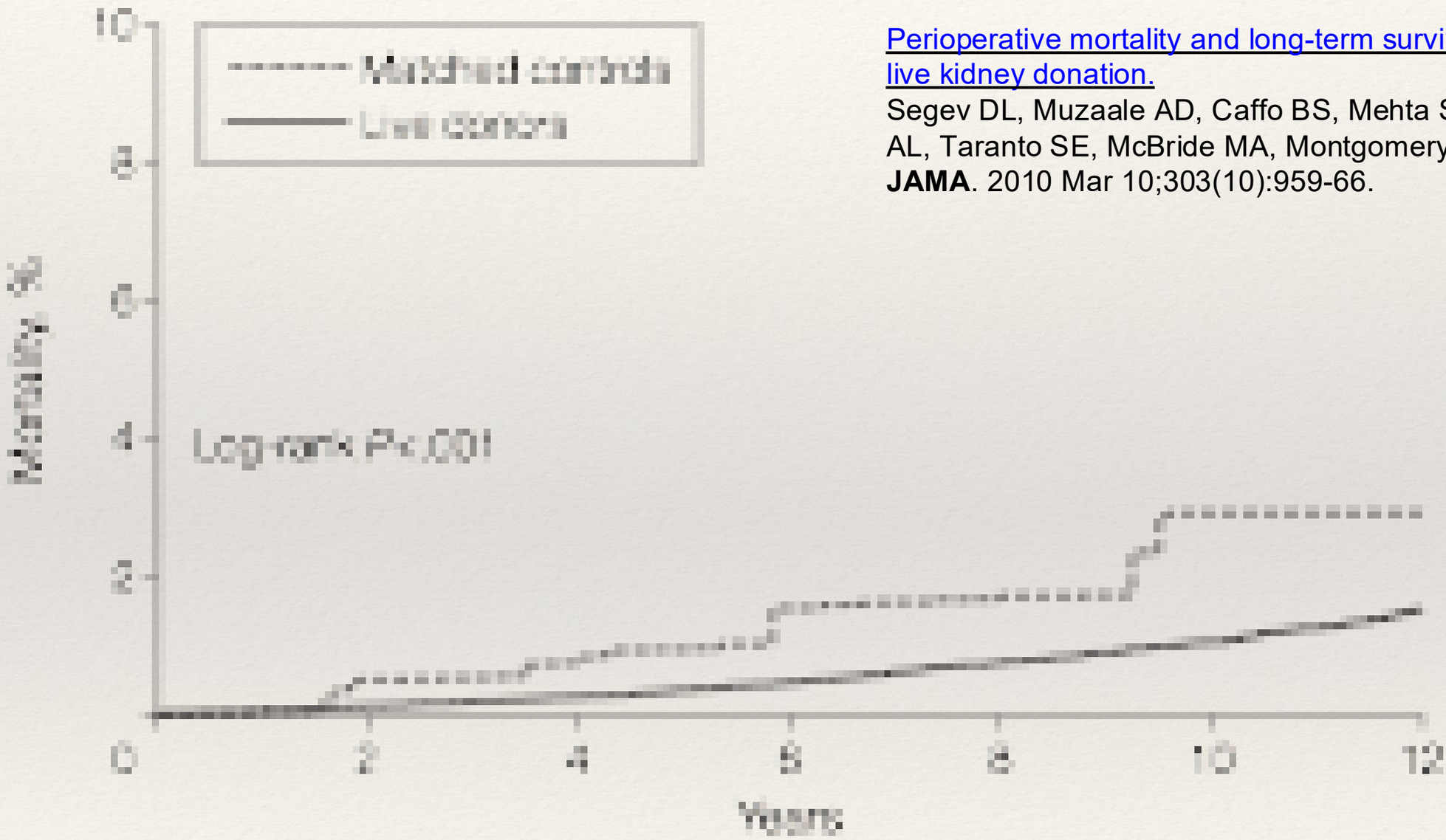


ANZDATA 2014 Report

Risks to Living Donors

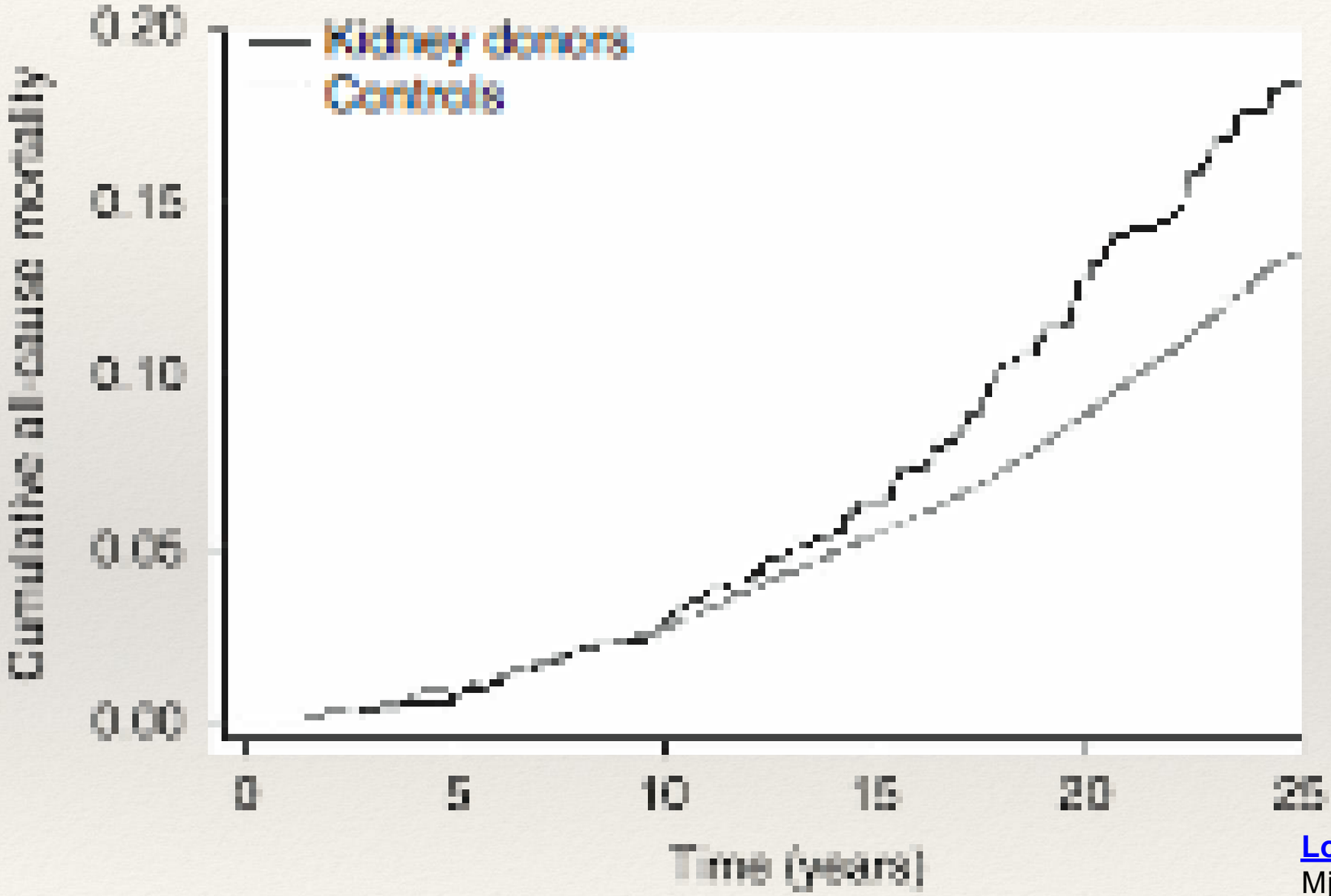
- Does it go against the ethical principle of non-maleficence?

Mortality



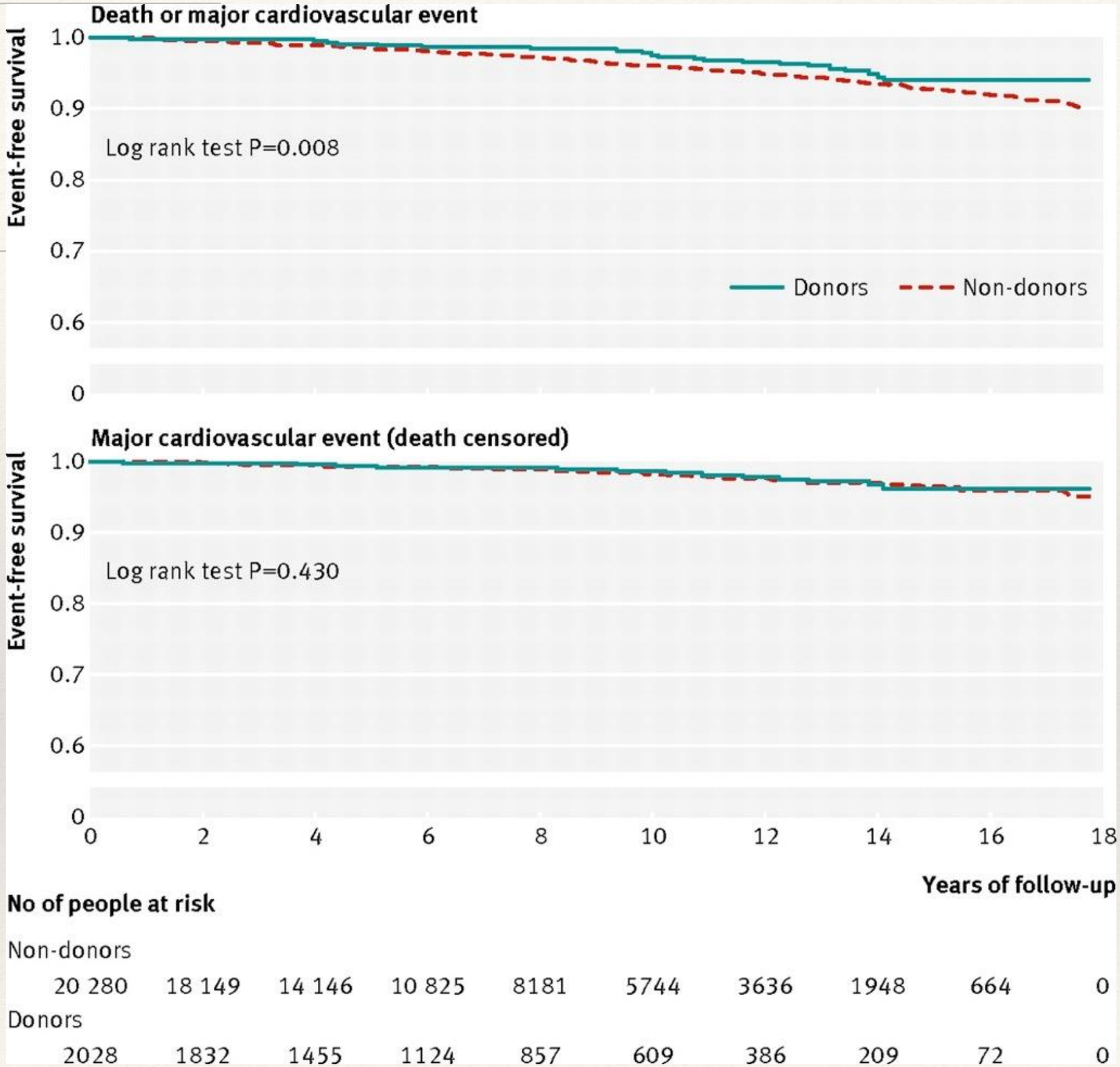
Perioperative mortality and long-term survival following live kidney donation.
Segev DL, Muzaale AD, Caffo BS, Mehta SH, Singer AL, Taranto SE, McBride MA, Montgomery RA.
JAMA. 2010 Mar 10;303(10):959-66.

Mortality



Long-term risks for kidney **donors**.
Mjøen G, Hallan S, Hartmann A, Foss A, Midtvedt K, Oyen O, Reisæter A, Pfeffer P, Jenssen T, Leivestad T, Line PD, Ovrehus M, Dale DO, Pihlstrøm H, Holme I, Dekker FW, Holdaas H.
Kidney Int. 2013 Nov 27.

CV Death



[Cardiovascular disease in kidney donors: matched cohort study.](#)
Garg AX, Meirambayeva A, Huang A, Kim J, Prasad GV, Knoll G, Boudville N, Lok C, McFarlane P, Karpinski M, Storsley L, Klarenbach S, Lam N, Thomas SM, Dipchand C, Reese P, Doshi M, Gibney E, Taub K, Young A; Donor Nephrectomy Outcomes Research Network.
BMJ. 2012 Mar 1;344:e1203.

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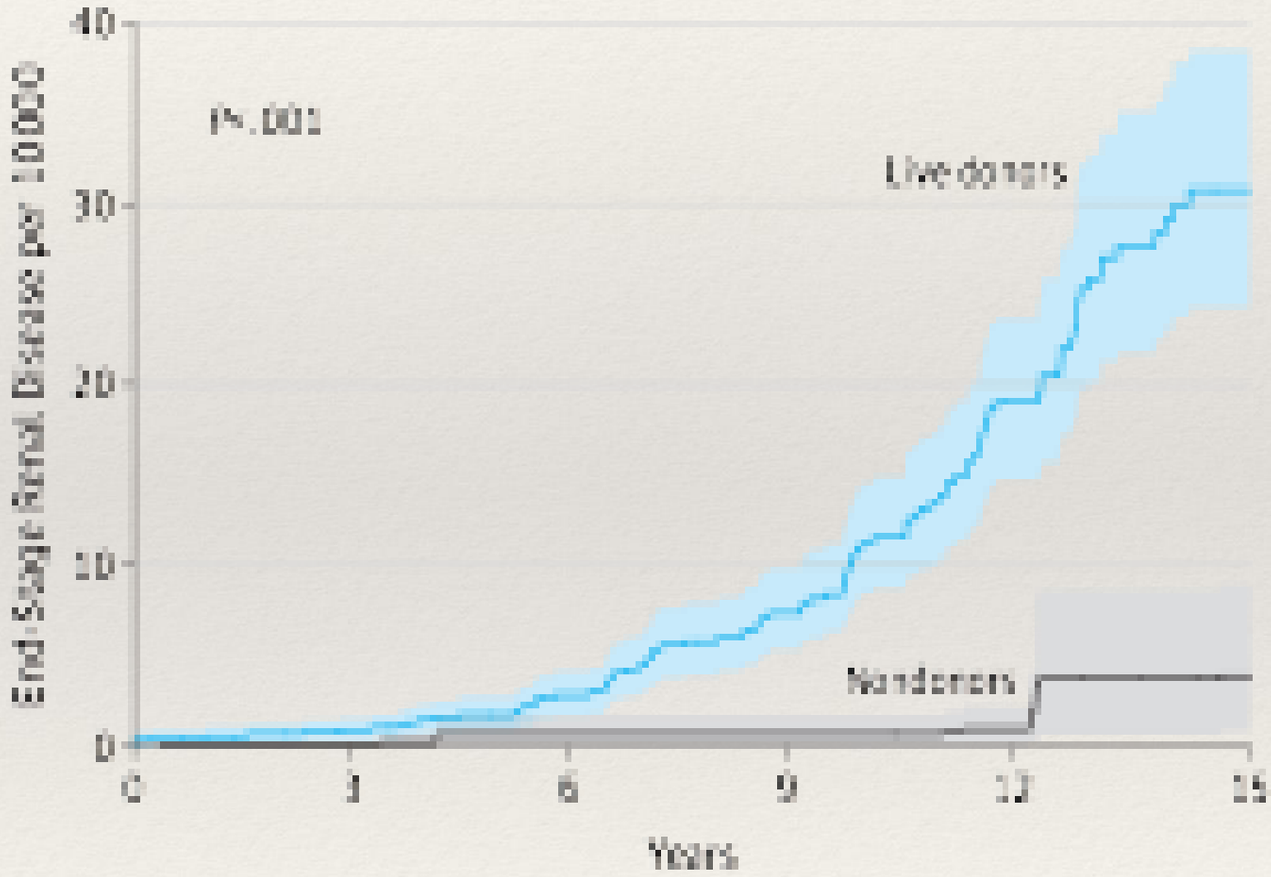
Risk of ESKD

15 year risk

- Donors 3.8 per 1000
- Healthy controls 0.4 per 1000

Lifetime risk

- Donors 9 per 1000
- Healthy controls 1.4 per 1000
- General population 33 per 1000



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, DPhil1; Maureen A. McBride, PhD; Jennifer L. Wainright, PhD; Dorry L. Segev, MD, PhD
JAMA. 2014;311(6):579-586.

est 1989

Saskatchewan Transplant Program

- Provincial program with offices in Saskatoon and Regina
- 3 transplant nephrologists, 4 transplant surgeons
- Nurse coordinators: living donor, assessment patients, listed patients, transplanted patients, tissue/eye
- 3 pharmacists
- ~600 kidney transplant recipients
- Out of province office: liver (81), lung (40), heart (43)

Saskatchewan Health Authority

Questions or Comments