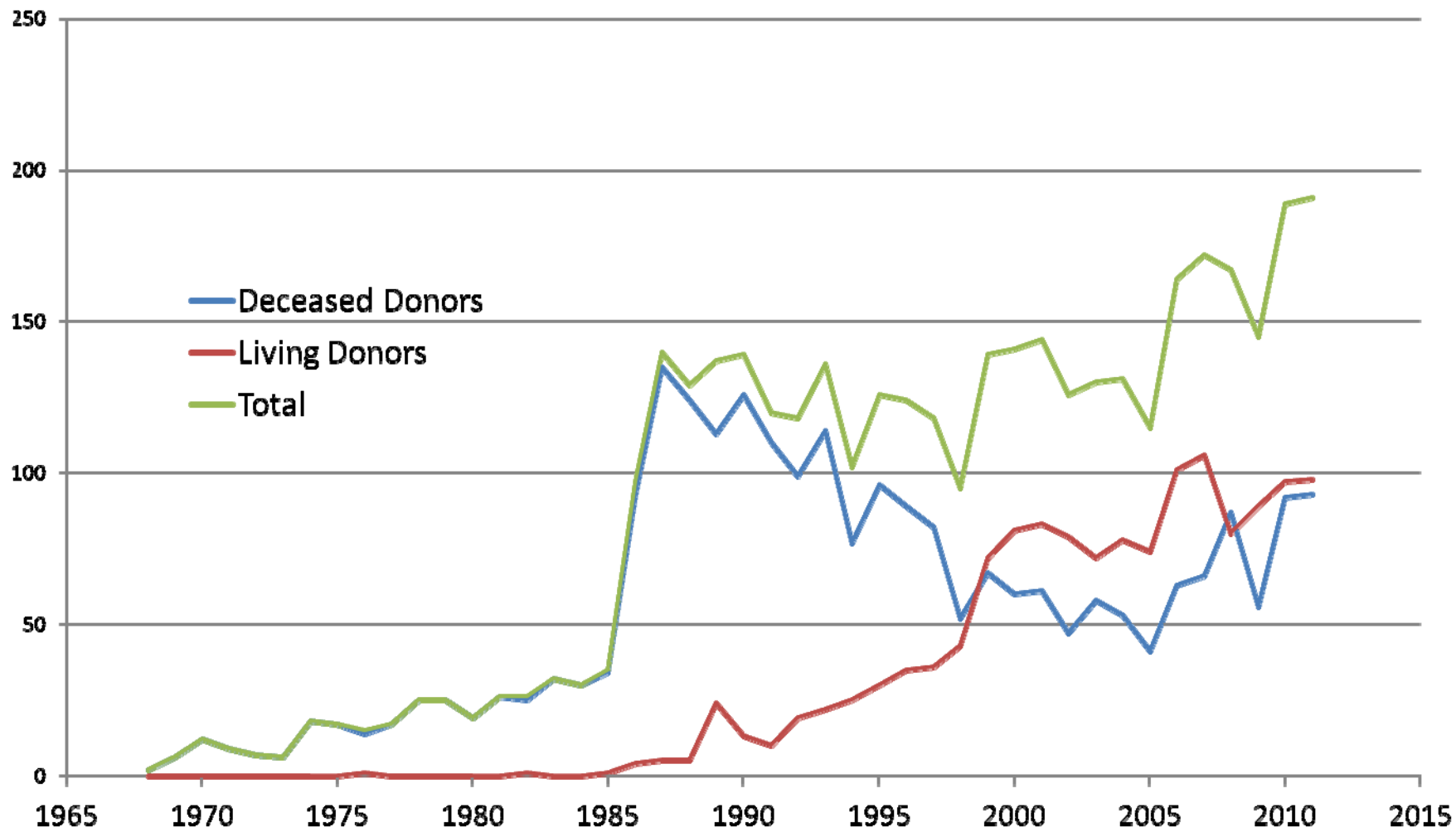


Renal Transplant Past Present and Future
David Landsberg

Outline

- Changing pattern of Donors
 - Types of Donors
 - Allocation
 - Results
- Challenges in the Elderly
- LDPE

Transplants By Year



Terminology

- LD
 - LRD
 - LUD
 - NDAD
- DD
 - SCD
 - ECD
 - NDD
 - DCD

Increasing Deceased Donation

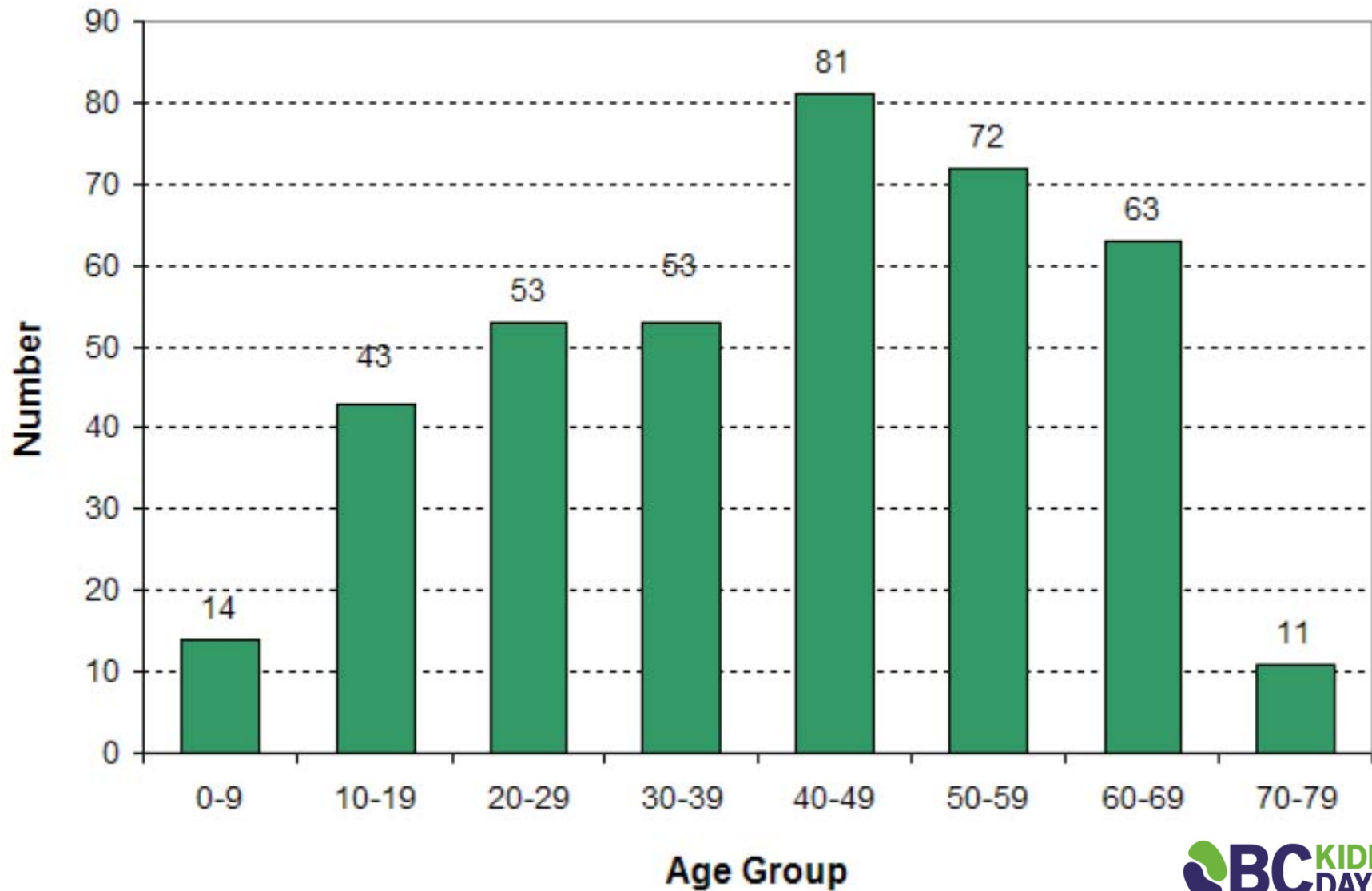
- ECD
- DCD

Definition Of ECD

Port et al Transplantation 2002: 74; 1281-6

- ECD
 - ≥ 50 years with 2/3 (HTN, CVA, Cr >120) or
 - donor age 60+
- ECD associated with a RR risk of graft loss > 1.7 compared to
 - donors aged 10-39 years,
 - with Cr <120 ,
 - no hypertension,
 - Cause of death other than CVA

BC Deceased Donor Age



Deceased Donors Originating in BC, by Age Group

2002 - 2012

Year	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	Total
2011	1	1	7	12	12	10	9	4	56
2010		2	8	8	10	10	9	2	49
2009		4	5	2	7	7	6	1	32
2008	8	4	10	5	10	10	6	1	54
2007		5	6	5	10	4	8		38
2006	1	4	4	4	6	6	9	2	36
2005	1	8	2	4	4	2	3	1	25
2004		2	5	6	7	7	4		31
2003	2	7	4	3	9	8	6		39
2002	1	6	2	4	6	8	3		30
Total	14	43	53	53	81	72	63	11	390

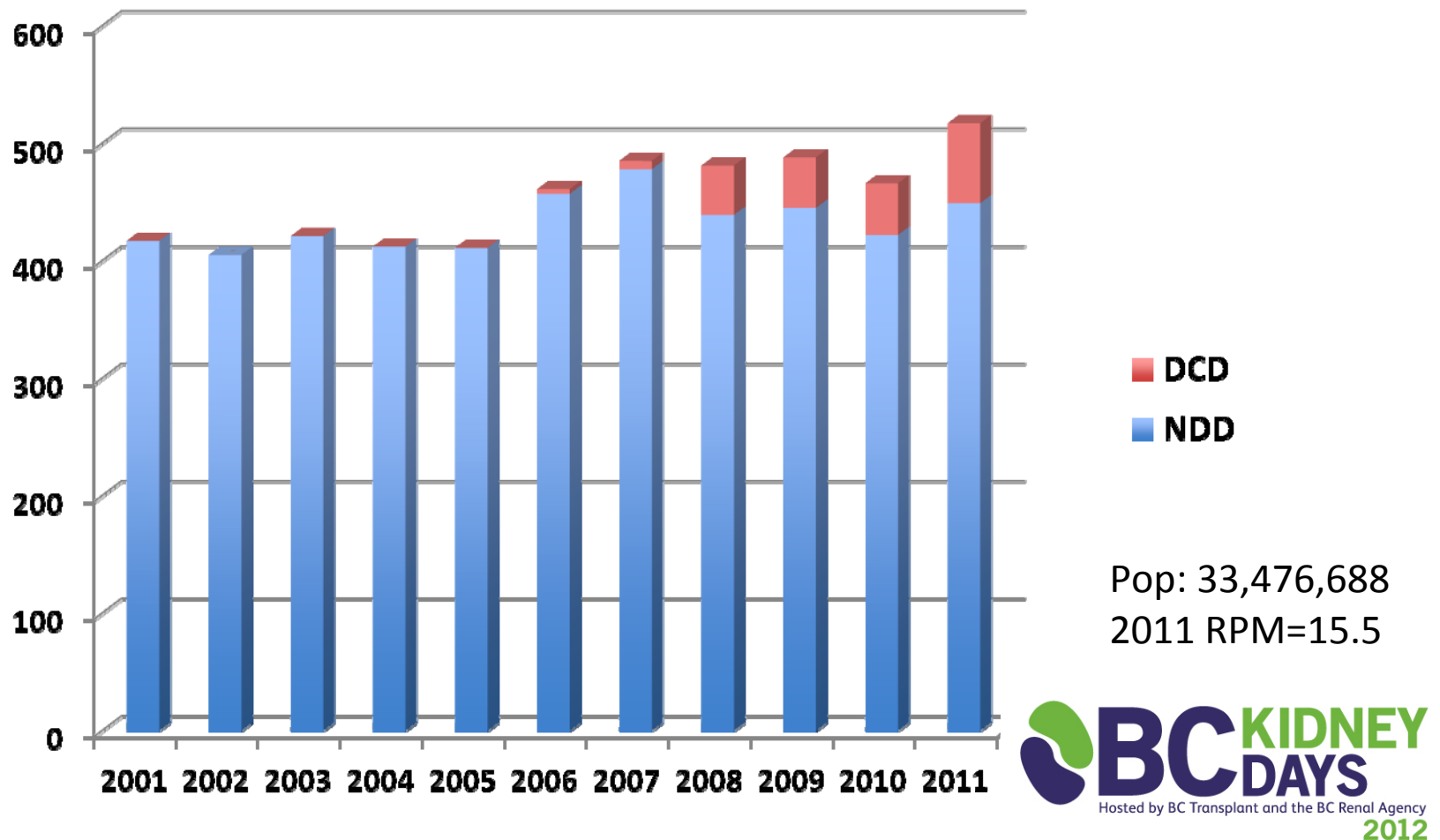
Donation after Cardiac Death (DCD)-Canadian update

- First modern era DCD in Canada happened in June 2006 in Ottawa
- Donor RPM based on Statistics Canada: National census from 2011
- Canadian population in 2011: 33,476,688

Canada deceased donation 2001-2011

2011: 517 DD, NDD=450, DCD=67 (13%)

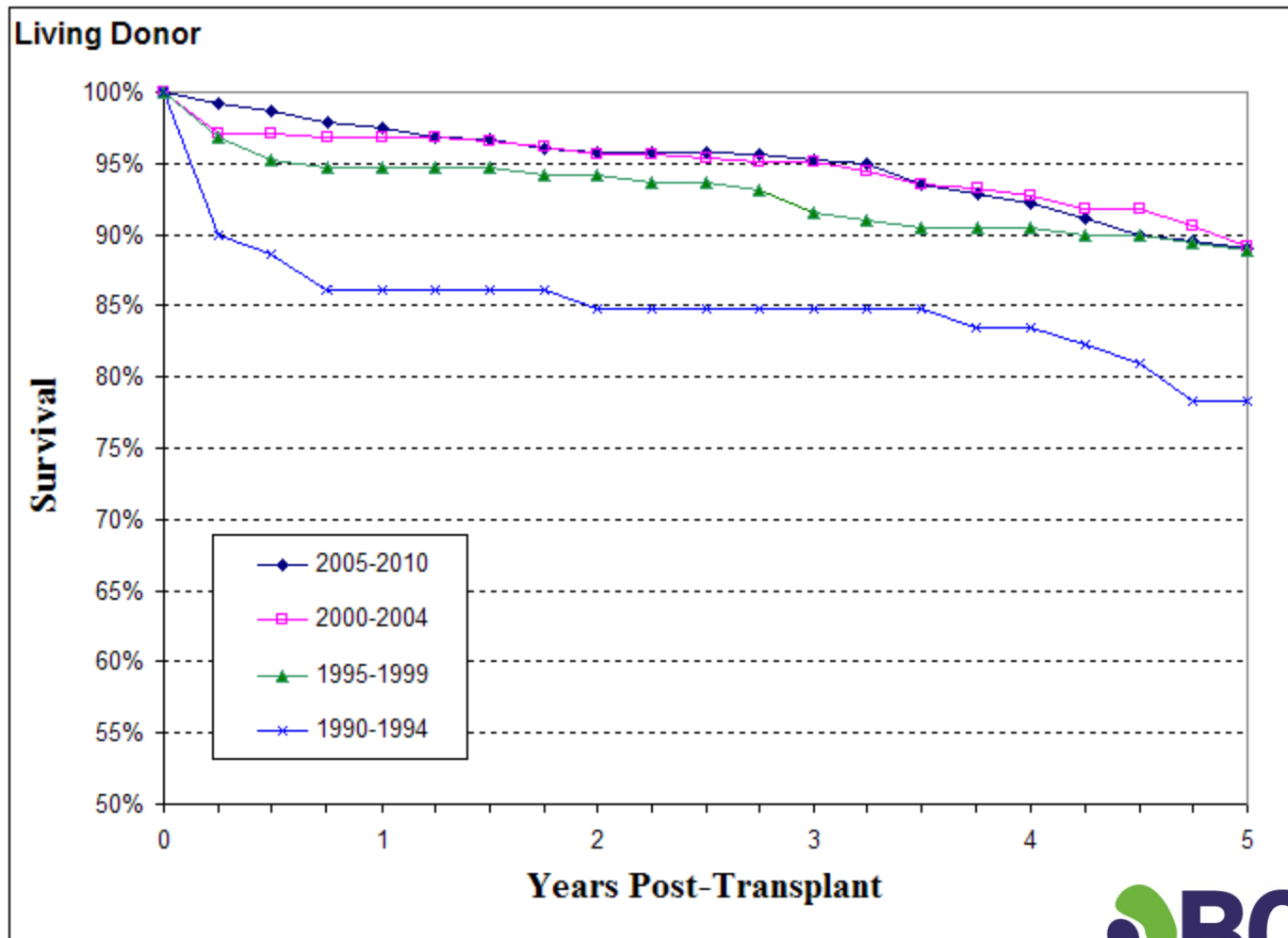
Record year for Canada in both total deceased donation and DCD activity



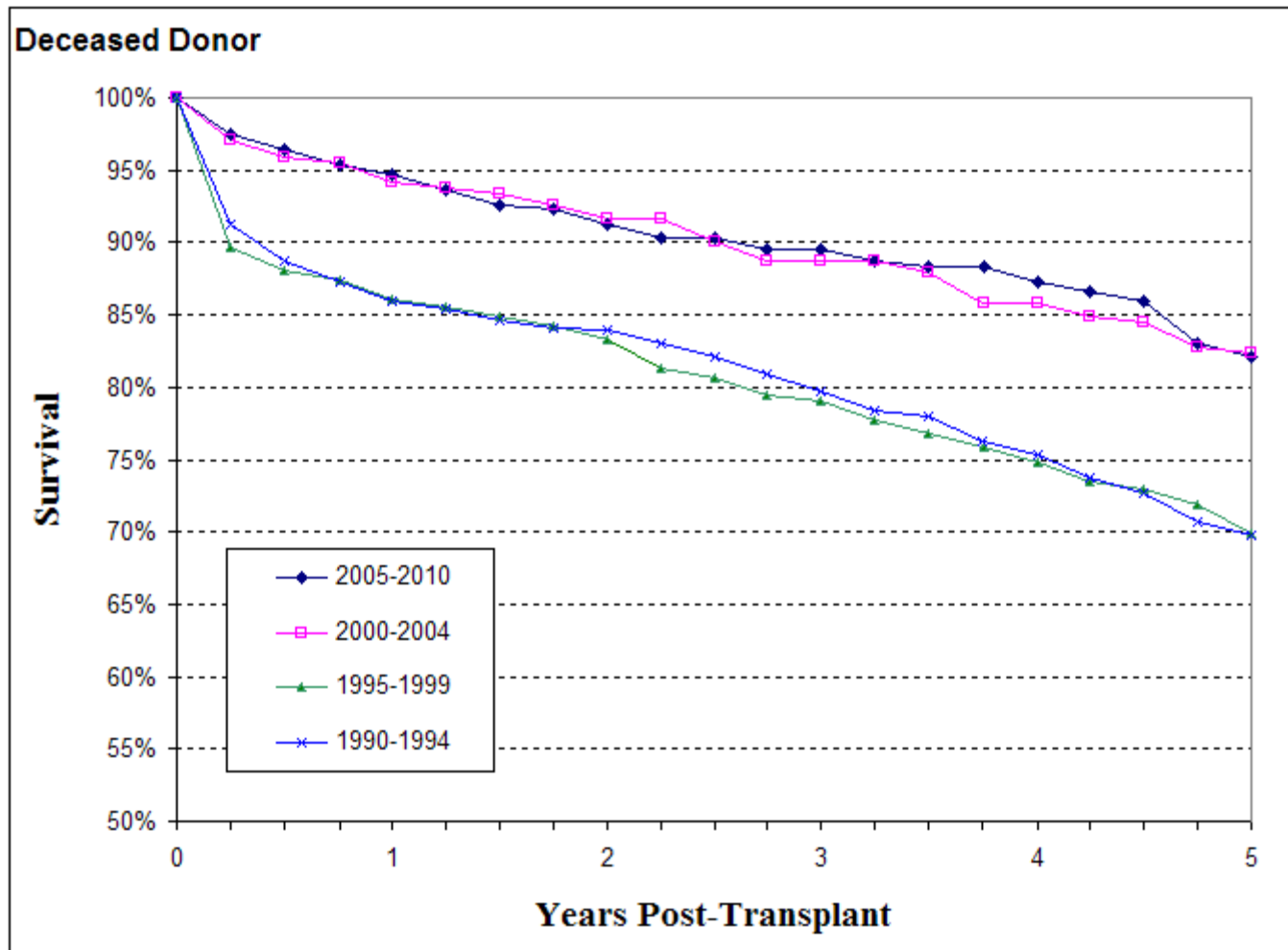
Canadian OPO regions NDD/DCD Donors: 2008-2011

OPO REGION	2008 NDD/DCD	2009 NDD/DCD	2010 NDD/DCD	2011 NDD/DCD
BC	51/2 (3.8%)	32/0	48/1 (2%)	49/7 (8.7%)
EDMONTON	29/1 (3.3%)	20/1(4.7%)	20/1(4.7%)	20/3 (13%)
CALGARY	17/0	17/0	13/0	17/0
SASK	11/0	14/0	15/0	13/0
MAN	14/0	14/0	19/0	9/0
ONT	145/30 (17%)	181/37 (17%)	155/35 (17.5%)	178/42 (20%)
QUEBEC	144/7 (4.6%)	133/5 (3.6%)	112/7 (5.9%)	124/13 (9.5%)
ATL	30/2 (6.3%)	33/0	30/2 (6.3%)	40/2* (4.7%) *NS-25,NB-7. NFLD-10
CANADA	439/42 (8.7%)	445/43 (8.8%)	422/44 (9.4%)	450/67 (13%)

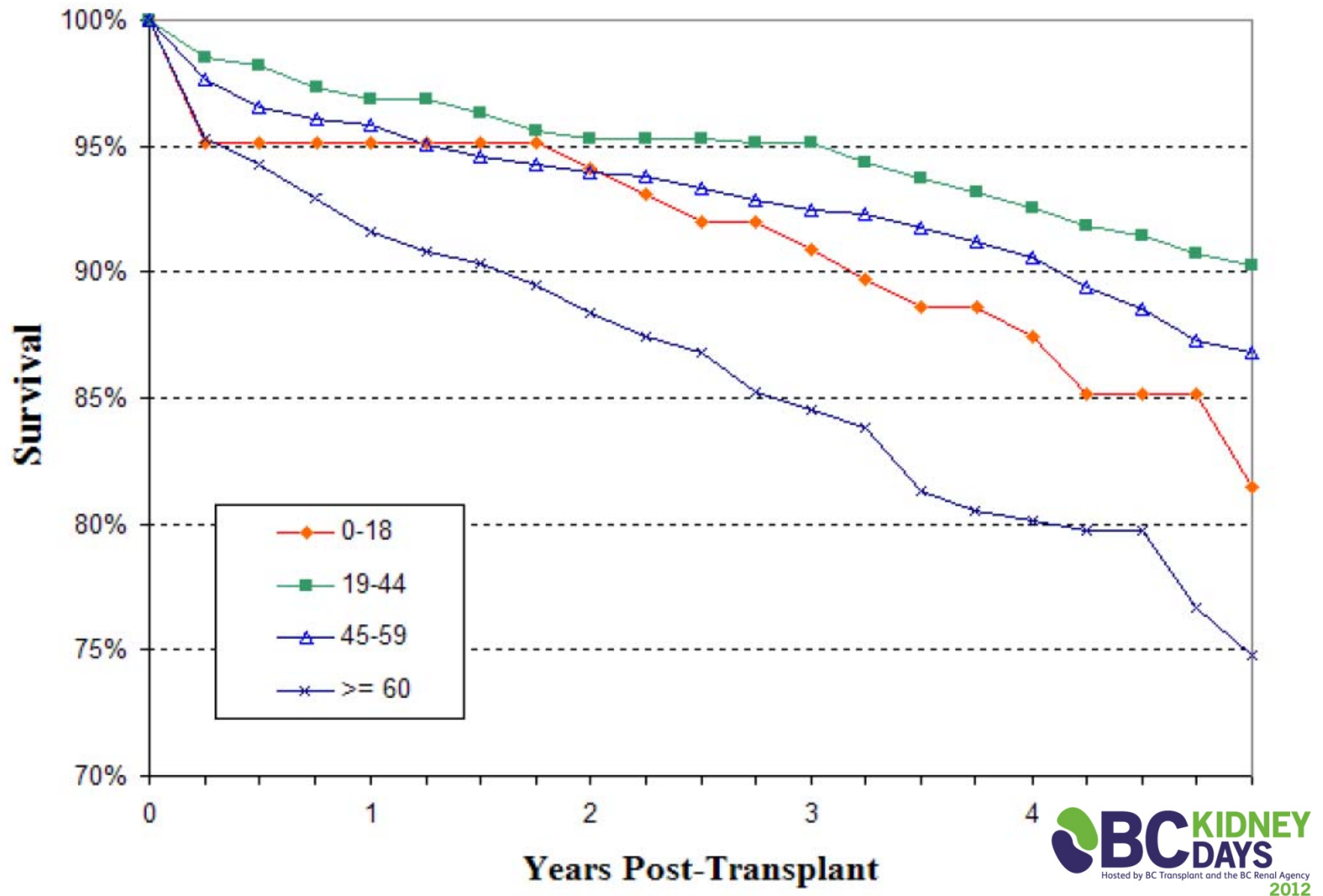
Graft Survival and Year of Transplant



Graft Survival and Year of Transplant



Graft Survival by Age



Donor and Recipient Age

- Young recipients from older donors fail due to graft failure and return to dialysis
- Older recipients from younger donors die with function

Principles of Allocation

- Blood Group
- Medical Priority
- Age Matching
- Wait Time

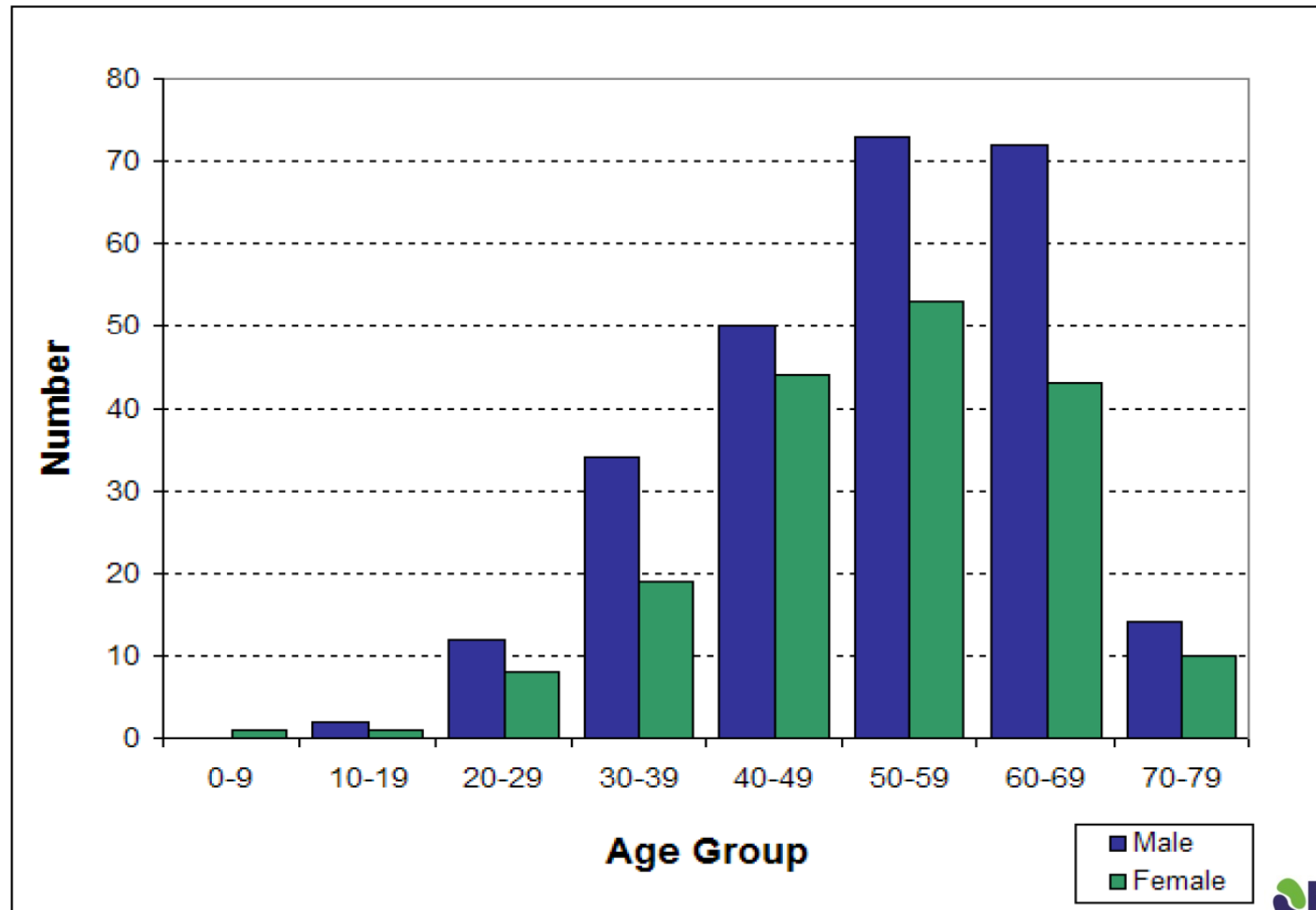
Challenges in the Elderly

- Major cause of failure is death with function
- Cardiovascular disease is leading cause of patient death
- ECD donors have more DGF on this imposes more cardiovascular stress

Transplant Waiting List at Year End, by Age and Gender

Year 2011

Program: All



Transplant Recipients by Age

Year	0-9	10-19	20-29	30-39	40-49	50-59	60-69	>=70	Total
2011	3	8	12	24	36	50	44	15	192
2010	4	8	18	13	30	50	55	11	189
2009	1	4	11	12	39	38	34	6	145
2008		9	15	26	33	46	32	6	167
2007	5	7	17	24	34	49	31	5	172
2006	3	5	21	28	35	42	25	5	164
2005	2	7	10	22	19	37	17	1	115
2004		6	15	18	25	37	26	4	131
2003	2	8	12	24	22	46	15	2	131
2002	4	7	17	24	30	30	16		128
Total	24	69	148	215	303	425	295	55	1534

Burden of Coronary Disease in Renal Transplant Recipients

- Leading cause of death after transplantation is ischemic heart disease
- 36% of patients who die with a functioning graft die from atherosclerotic coronary disease
- Nearly half of deaths in the first 30 days are due to myocardial infarction

Pre Tx Cardiac Assessment

Key Questions

- What screening test best identifies patients with significant CAD?
- What interventions improve outcomes in high risk patients

Changing Views about Screening

- In 2000 screening was widely accepted for many extensive surgeries but experience has shown that risk stratification does little to improve cardiac outcomes especially in asymptomatic patients.
- Today ACC/AHA recommend a conservative approach to screening and only recommend it for a few patient groups.

Screening For Renal Transplant Recipients

- Many now question the routine screening that many transplant programs utilize
- Some advocate only screening symptomatic patients especially in light of role medical therapy versus intervention in asymptomatic patients
- Is this approach justified?

Coronary Artery Disease in a Large Renal Transplant Population: Implications for Management

M. R. Kahn, A. Fallahi, M. C. Kim, R.
Esquitin

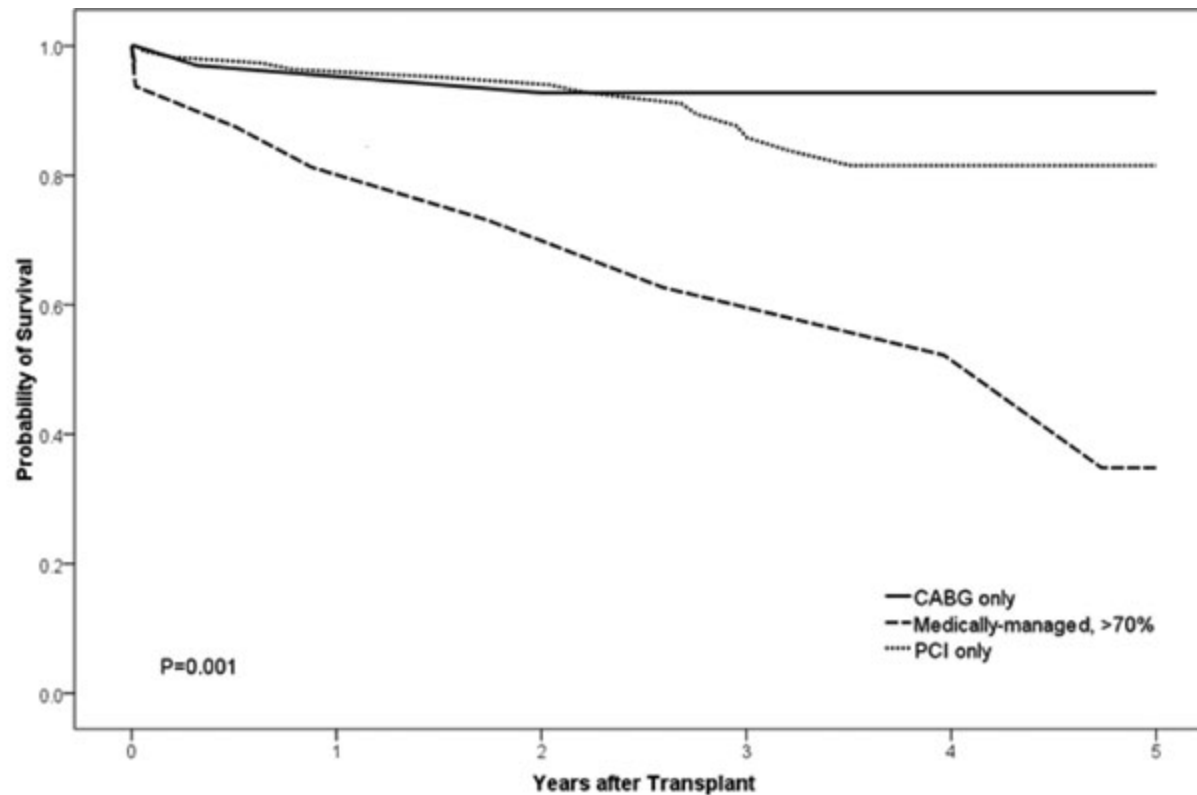
and M. J. Robbins

AJT 2011;11:2665-2674

AJT 2011

- Retrospective analysis of 1460 patients who underwent transplant at a single center between 2000 and Oct 2009.
- As optimal screening strategy unknown a variety were applied so various strategies could be assessed (not randomized)
- As many patients went on to interventions these too could be assessed in light of outcomes

Results in Patients with Critical Disease



At risk, *n*

Medically-managed, >70%	16	12	9	6	5	2
CABG only	38	29	23	18	11	7
PCI only	118	94	77	48	30	24

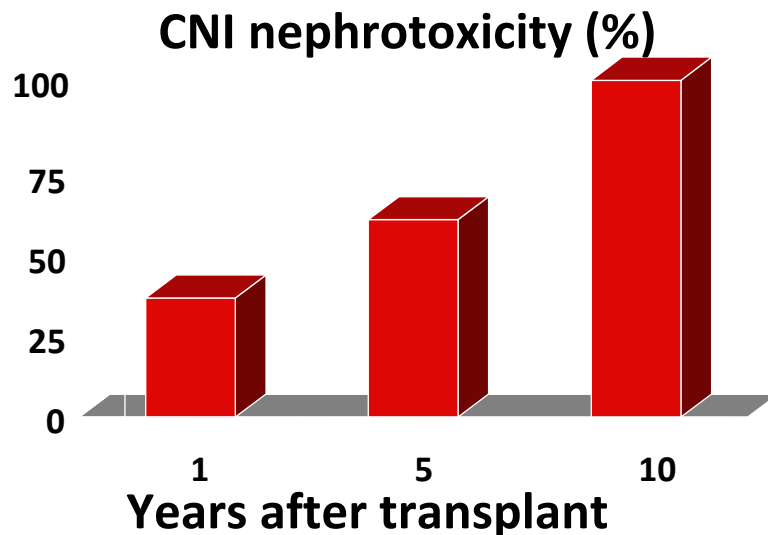
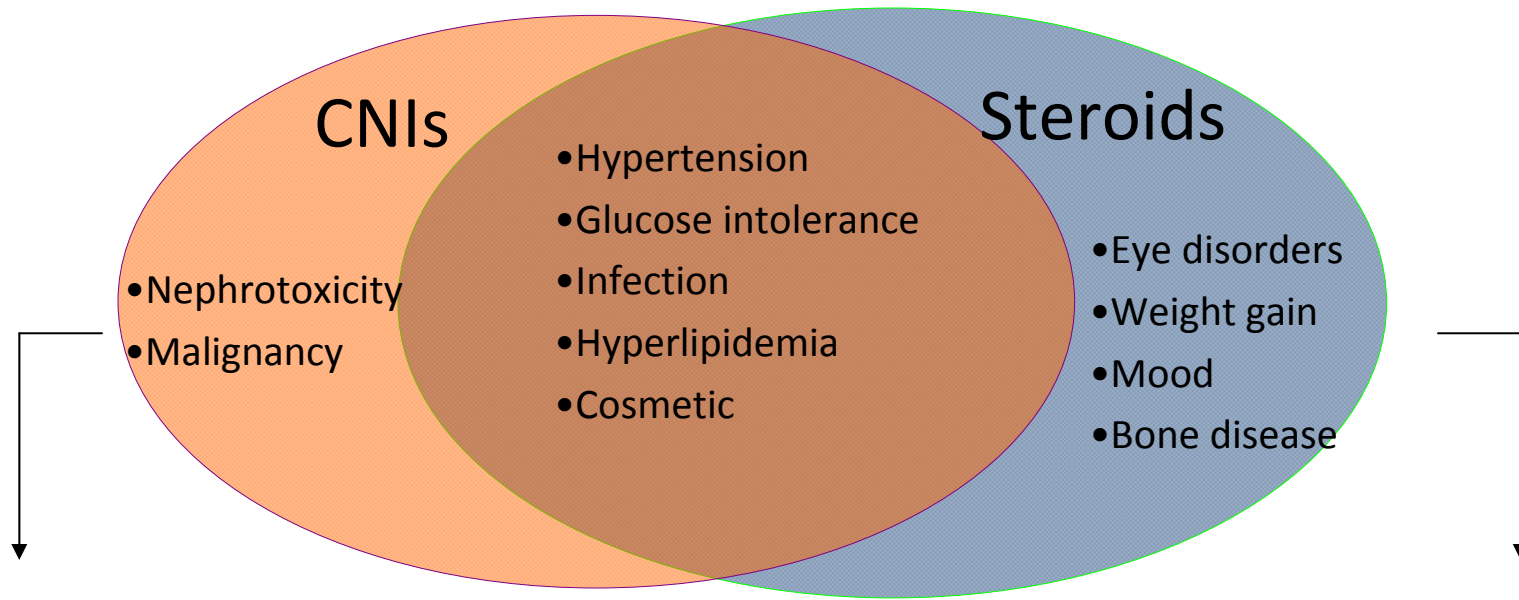
Conclusions

- Even in non diabetics who were asymptomatic there was a high incidence of coronary disease.
- Noninvasive testing does not have the sensitivity or specificity to be useful on it's own
- Intervention alters outcome so that relying on medical management is not a reasonable approach

First Rejection Episodes

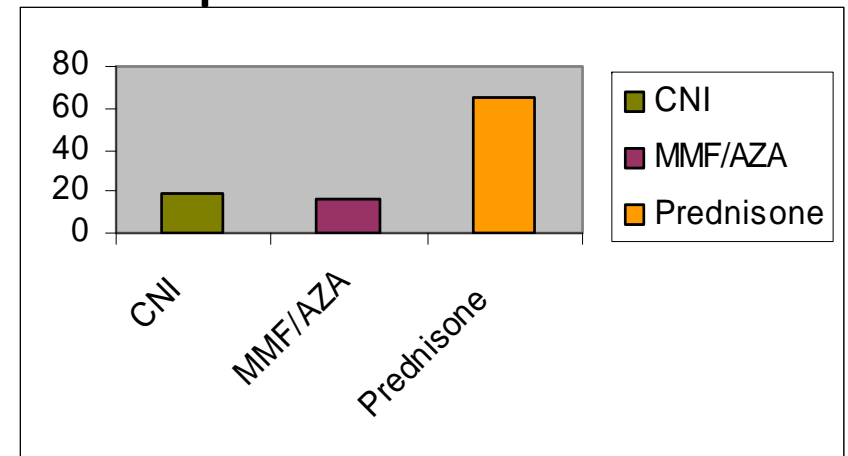
Year	First 90 Days		First 365 Days	
2011	12	6.3%	N/A	
2010	12	6.3%	16	8.5%
2009	14	9.7%	16	11.0%
2008	12	7.2%	16	9.6%
2007	14	8.1%	17	9.9%
2006	14	8.5%	18	11.0%
2005	14	12.2%	18	15.7%
2004	18	13.7%	22	16.8%
2003	17	13.0%	21	16.0%
2002	19	14.8%	25	19.5%
Total	146	9.5%	169	12.6%

Why Minimize/Withdraw Immunosuppression?



Nankivell BJ et al NEJM 2003; 349: 2326.

Patient preference- discontinue:



Prasad GV et al, Clin Transplant 2003; 17: 135

Steroid Withdrawal/Avoidance: Why?

- Diabetes
- Hyperlipidemia
- Bone disease
- Cataract formation
- Weight gain
- Patient quality-of-life (skin changes, edema, neurological/psychological effects)

Midtvedt K, et al, JASN, 15, 2004, 3233

Vanrenterghem Y et al, Transplantation, 70, 2000, 1352

Opelz G et al, Am J Transplant 2005; 5: 720

Rogers CC et al, Transplantation, 80, 2005, 26

RATIONALE FOR INDIVIDUALIZING IMMUNOSUPPRESSION

Too Much

- Cardiovascular Disease
- Infection
- Neoplasia
- Nephrotoxicity



Too Little

- Allograft Rejection

INDIVIDUALIZING IMMUNOSUPPRESSION BASED ON IMMUNOLOGIC RISK

PRE-TRANSPLANT
IMMUNOMODULATION

INDUCTION ANTIBODY
THERAPY

TRIPLE THERAPY
MAINTENANCE

MINIMIZATION PROTOCOLS

HIGH RISK

HIGHLY SENSITIZED

NON-PRIMARY TRANSPLANT

AFRICAN AMERICAN/HISPANIC
ETHNICITY

CADAVERIC DONOR SOURCE

POOR HLA MATCH

LOW RISK

NONSENSITIZED

ASIAN/CAUCASIAN ETHNICITY

THE ELDERLY

LIVING DONOR SOURCE

GOOD HLA MATCH

Current Immunosuppressive Low Risk Protocol

- Basilixumab 20mg. Day 0 and 4
- MMF 1 gram bid
- CNI
- Perioperative Steroids

Current High Risk Immunosuppressive Protocol

- Thymoglobulin (7.5 mg/kg.)
- Steroids
- MMF
- Tacrolimus

Increasing Living Donation Living Donor Paired Exchange Program (LDPE)

LDPE Registry Match Cycles

13 Match Cycles completed to date

2009	2010	2011	2012
Jan	Feb	Mar	Feb
Feb	May	June	June
May	Aug	Oct	Oct 15
Oct	Nov		



LDPE ... AS OF October 10, 2012

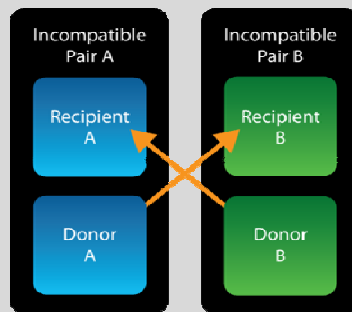
Scheduled Match Cycles	13
Pairs Registered	362 (141 in last MC)
Recipients Registered	342 (135 in last MC)
NDADs Registered	35 (3 in last MC)
<hr/>	
Transplants Completed	144
Registered Recipient Transplants	118
Wait List Transplants	26
<hr/>	
Transplants Scheduled	10 (3 Chain(s))
Matches under review	4 (1 Chain(s))

Next Match Cycle: October 15, 2012

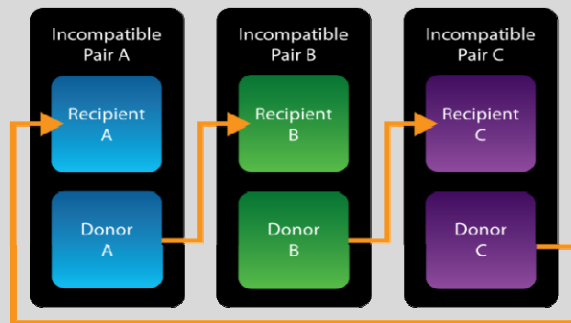
POWER OF DOMINO EXCHANGE

Of the 144 transplants completed to date:

14 from Paired Exchanges

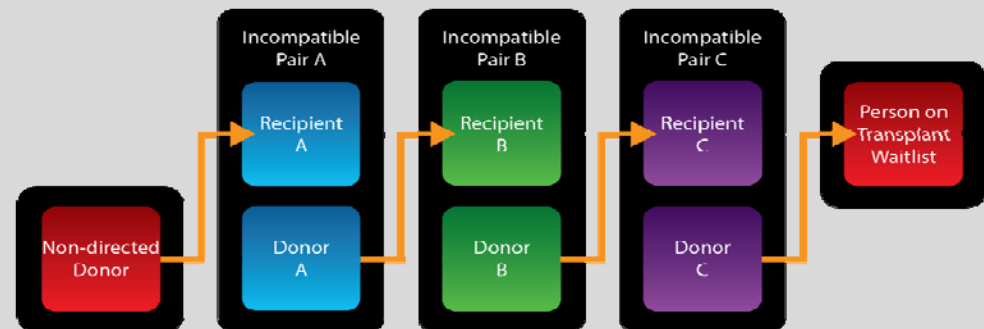


37 from N-Way Exchanges



11 chains of 3, 4 or 5 exchanges

93 from Domino Exchanges



27 dominos of 1 to 5 transplants each

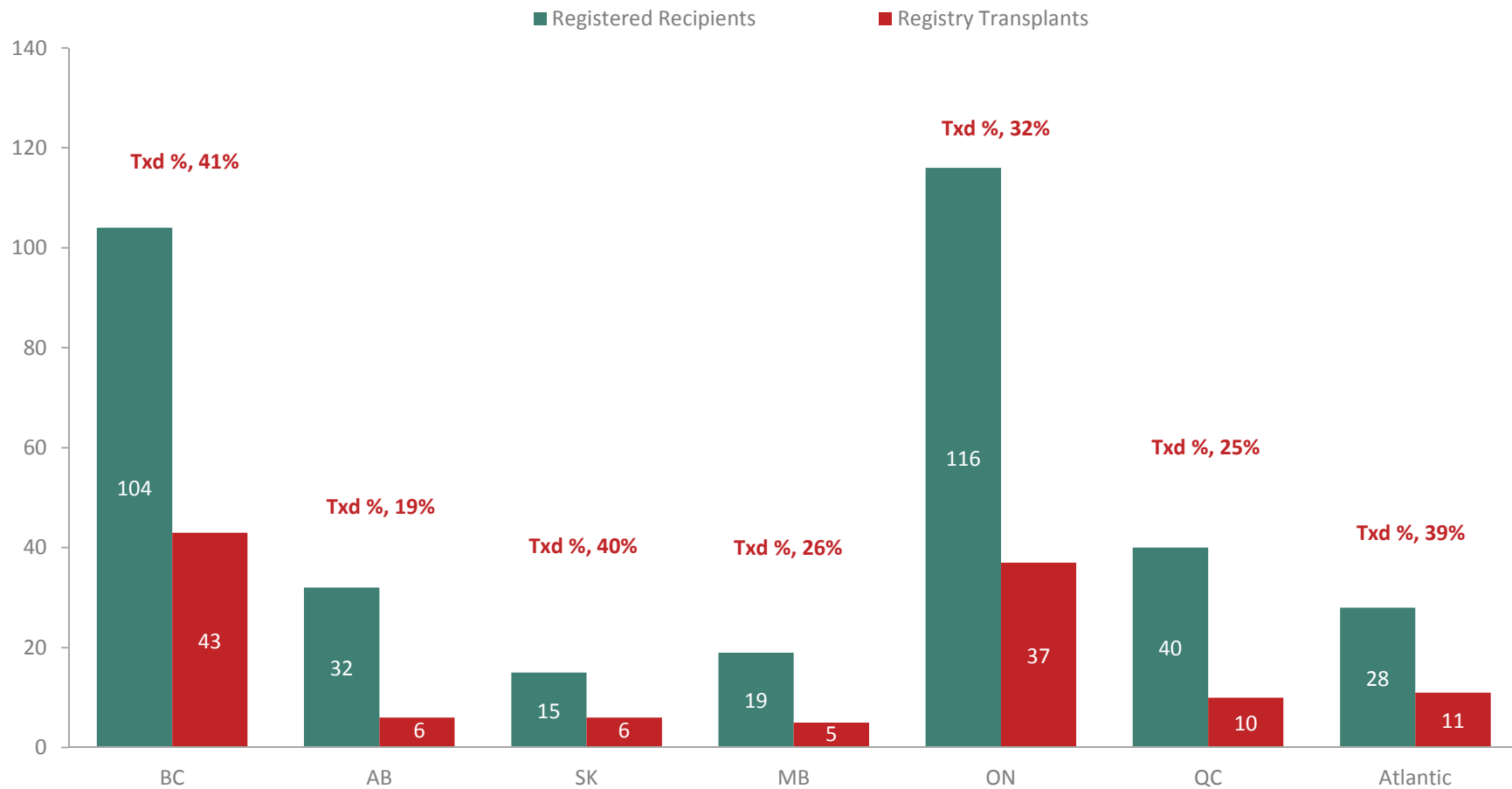
TRANSPLANTED RECIPIENTS BY PROVINCE

Recipient Transplant Program	Registered Recipients	Wait List Recipients	Provincial Totals		
Vancouver General	16	3	BC	49	34%
St. Paul's Hospital	27	3			
University of Alberta	4	1	AB	9	6%
Foothills Medical Centre	2	2			
St. Paul's Hospital - SK	6	2	SK	8	6%
Health Sciences Centre	5	0	MB	5	3%
London Health Sciences	2	0	ON	50	35%
Toronto General Hospital	12	8			
St. Michael's Hospital	13	2			
The Hospital for Sick Children	1	0			
The Ottawa Hospital	9	3			
Hospital Maisonneuve-Rosemont	1	0	QC	11	8%
McGill University	1	1			
C.H, Universitaire de Sherbrooke	1	0			
Notre Dame	7	0			
Queen Elizabeth II Hospital - NB	2	0	Atlantic	12	8%
Queen Elizabeth II Hospital - NS	4	0			
Queen Elizabeth II Hospital - PEI	1	0			
Queen Elizabeth II Hospital - NL	3	0			
Western Memorial Regional - NL	1	1			
TOTAL	118	26		144	100%

Includes all Registered Recipients and Registry Transplants up to and including Match Cycle 12

REGISTERED AND TRANSPLANTED RECIPIENTS

Transplants vs Registered Recipients



Includes all Registered Recipients and Registry Transplants up to and including Match Cycle 12

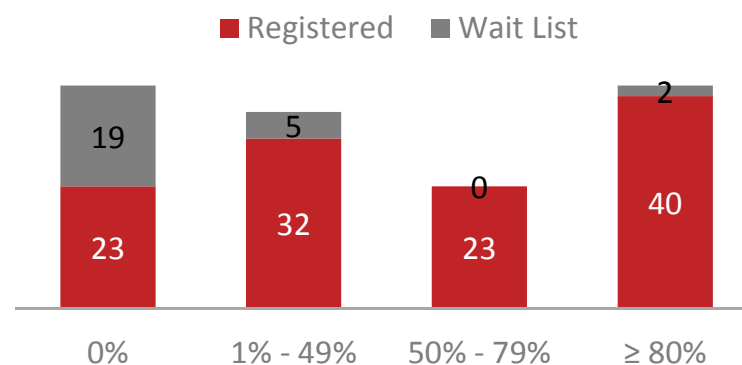
TRANSPLANTED RECIPIENTS BY PRA

Registry Recipients

PRA Percentage	#	%
0%	23	19%
1% - 49%	32	27%
50% - 79%	23	19%
≥ 80%	40	34%
Total	118	100%

Wait List Recipients

PRA Percentage	#	%
0%	19	73%
1% - 49%	5	19%
50% - 79%	0	0%
≥ 80%	2	8%
Total	26	100%



Includes all Registered Recipients and Registry Transplants up to and including Match Cycle 12

Next Steps for High PRA Patients

- National Highly Sensitized Wait List
- National Sharing for Highly Sensitized Patients

The Future

- Both deceased and living donor transplant numbers will grow
- More pre-emptive LD transplants
- More transplants in the elderly with acceptable results
- More highly sensitized patients transplanted