

Expanded Criteria Donor: Revisited?

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Overall AIM of ECD Policy

Increase organ utilization

Objectives

- Review the definitions of ECD
- ECD allocation options
- Evidence supporting the use ECD

Definition of ECD

- Potential Low Function
 - Heart beating (i.e. older donor)
 - Non-heart beating (Deceased Cardiac Donor)
- Potential High Risk to Recipient
 - Infection (HCV, HBV, others)
 - Cancer (primary brain, historic cancer)
- Bought kidneys?

Many ECD Definitions

- United Network Organ Sharing (UNOS)
- Deceased Donor Score
- Donor Histology
- Donor Age

UNOS criteria

Risk of Graft Loss 1.7 times higher than a standard donor kidney

- >60 year old donor
- 50-60 age donor and 2 of the following 3
 - Hypertension
 - Serum Creatinine $132 \mu\text{mol/L}$ at any time
 - CVA as cause of death

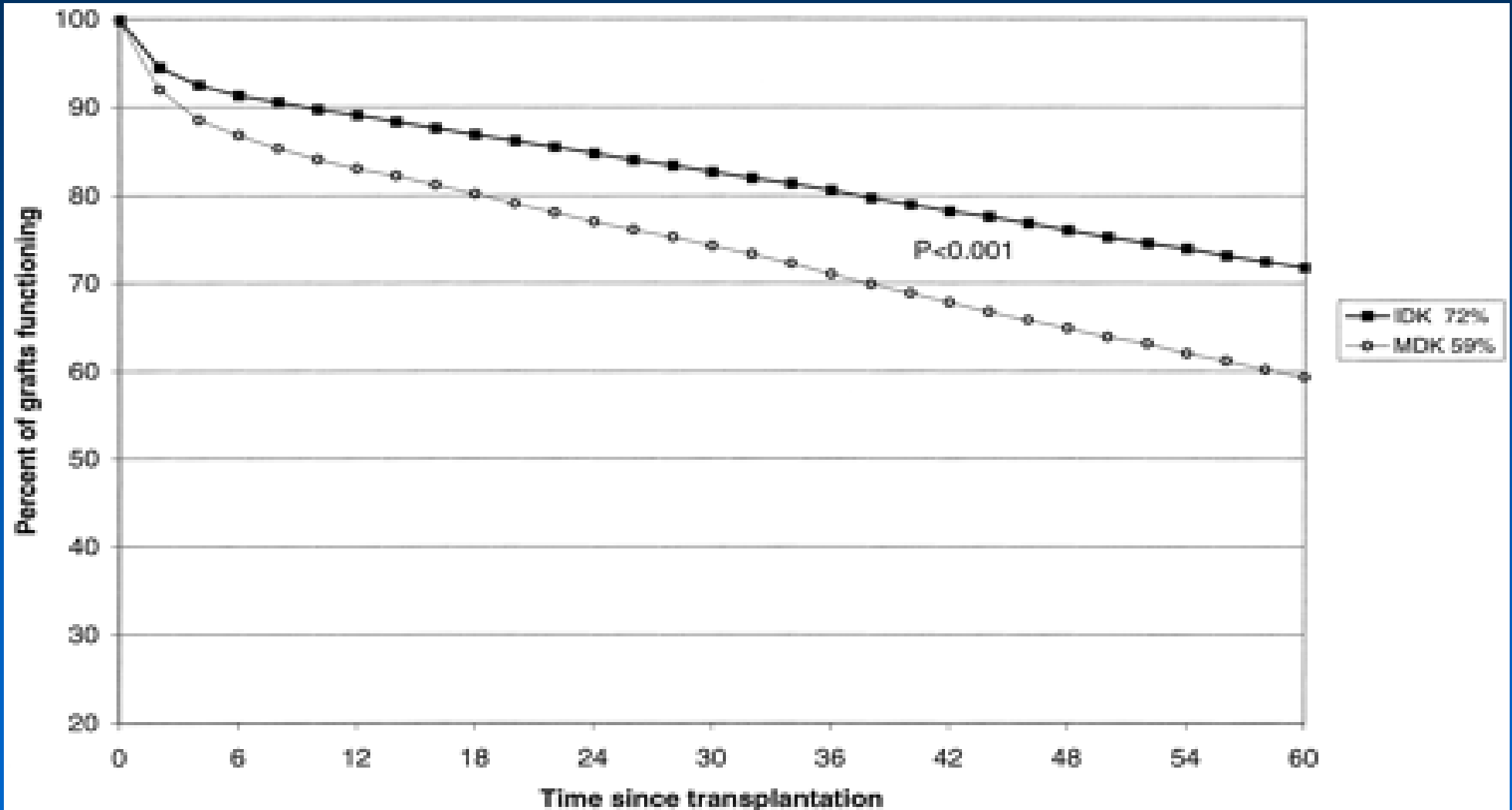
Current discard rate 40% of these donors

Current utilization is 15% of all transplanted kidneys

Definition of Standard Donor

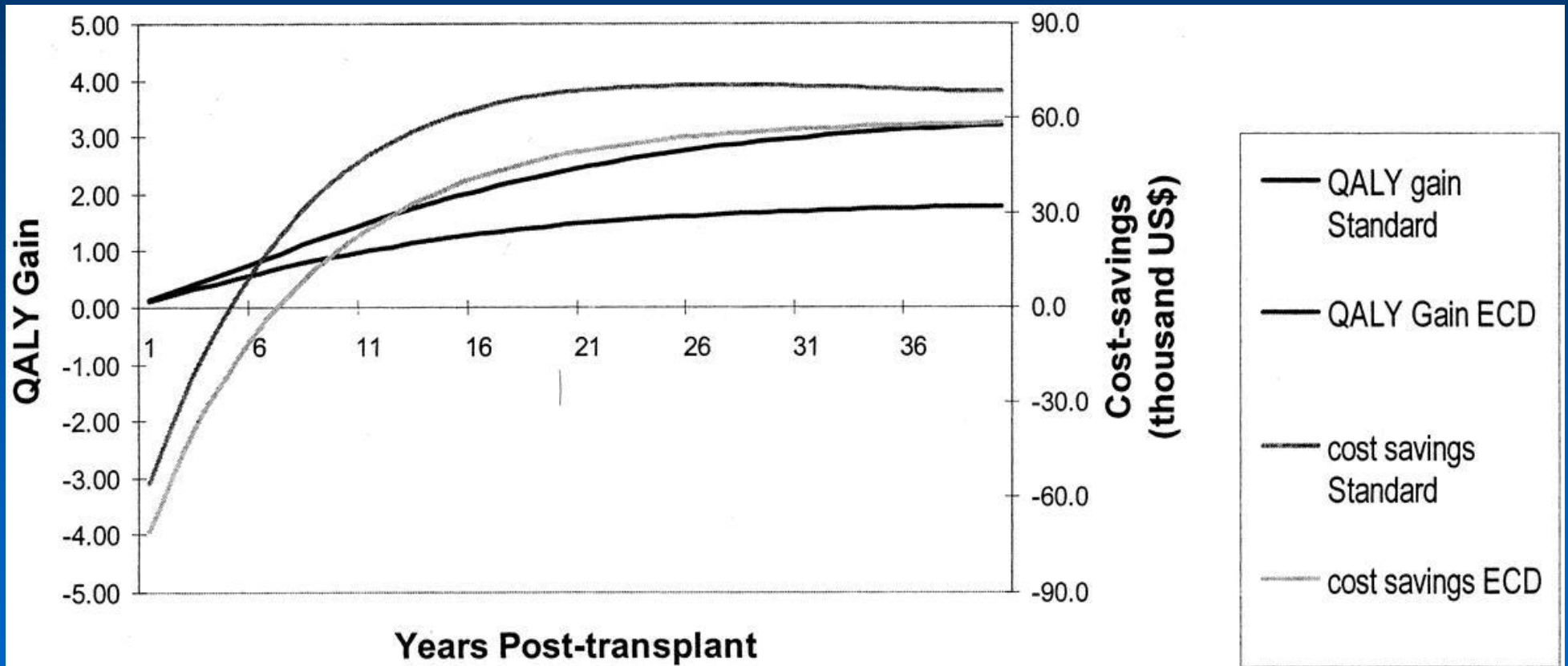
- Donor age 10-39
- Death Non-CVA
- No hypertension
- Terminal creatinine $<132 \mu\text{mol/L}$

ECD vs SD Graft Survival (Ojo JASN 2001)



Cost Savings ECD and SD vs Dialysis

(Schnitzler Transplantation 2003)



UNOS Implementation (Oct 2002)

- Identify willing ECD kidney recipients
- Consent potential recipients
- Minimal cold time

<http://www.unos.org/downloadables/ExpandedCriteriaDonorKidneyPolicyBrochureProf10072002Final.pdf>

Information on Consent

- Expect increase in delayed graft function
- Expected decrease in graft survival
- Expected decrease in waiting time
- Expected increase in survival compared to waiting.
- Benefit of transplant prior to increased morbidity

Sample consent AJT 2003;3 (suppl 4):124-5

UNOS Problems

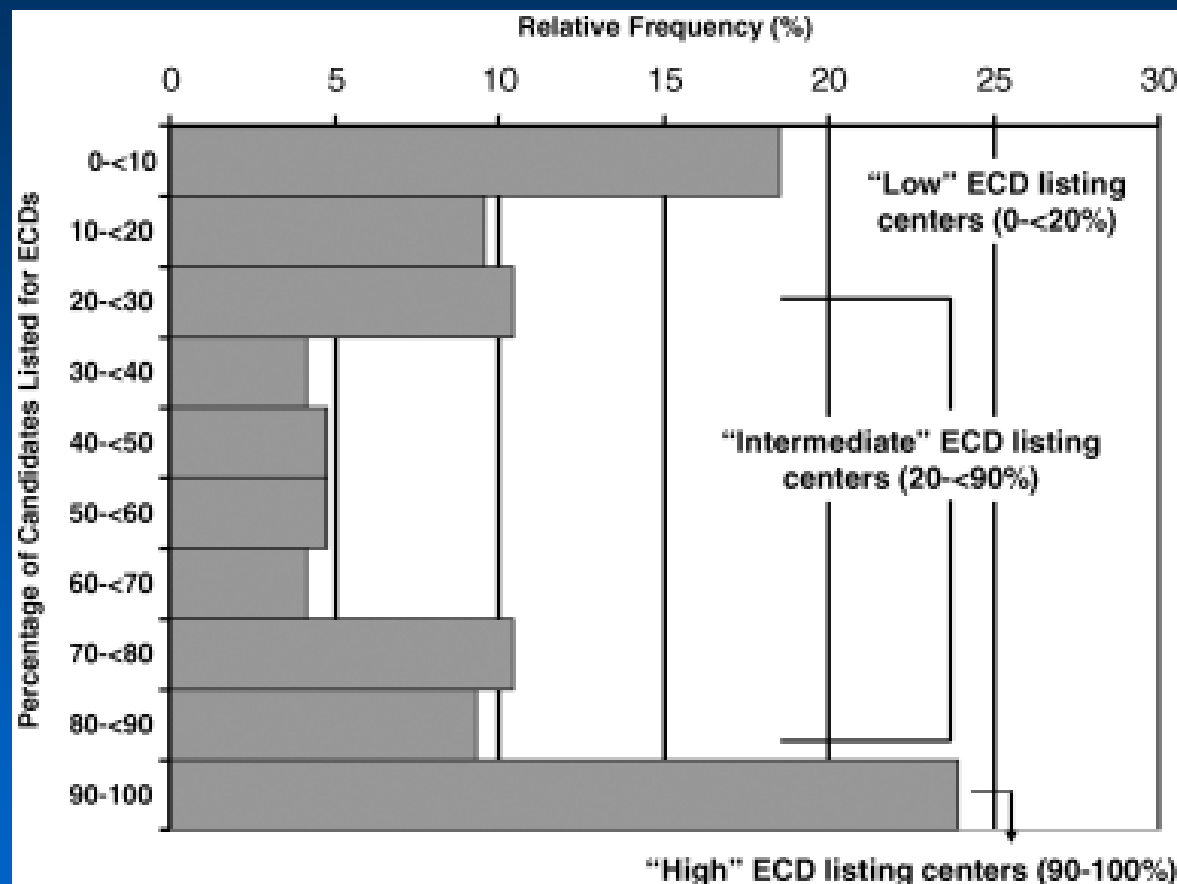
Many kidneys discarded that should be used
(WTC 2006 pg 140)

	Graft Loss	Discard Rate
Donor with PVD	0.87	3.49
Urine protein	1.10	2.20
Donor age 65-69	1.19	6.98
Cysts	0.58	1.81
Resistance (pump)	1.16	5.67

- Re-evaluation of criteria (CVA death vs Hypertension/Creatinine)

UNOS Problems

Schold et al AJT 2006;6:1689



Some centers have few awaiting ECD
Some centers have almost all on ECD lists

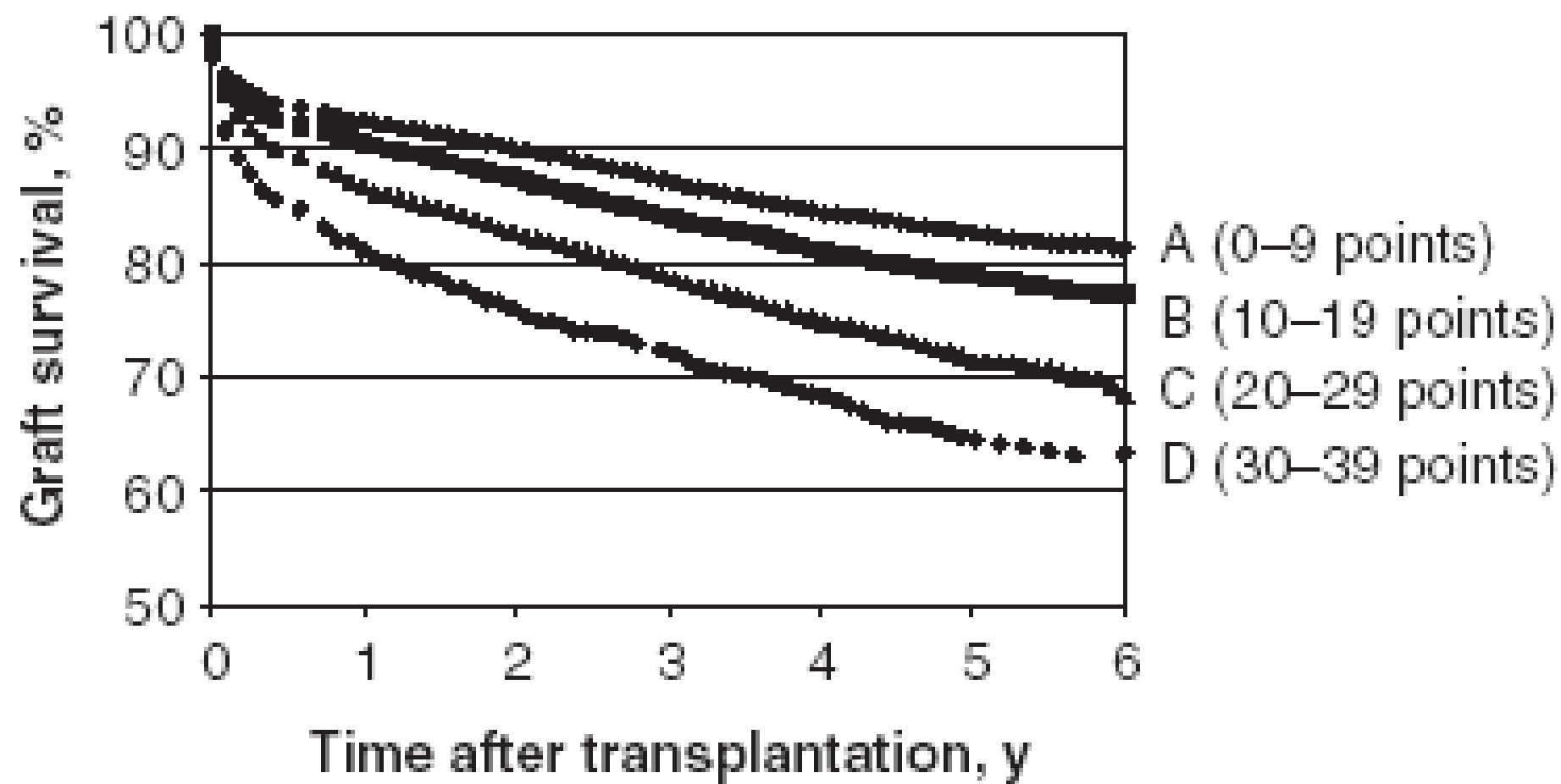
Deceased Donor Criteria

Nyberg et al AJT 2003

- Donor Age 0-25 points
- Hypertension 0-5
- Donor CrCl 0-4
- CVA death 0-3
- HLA MM 0-3

Total 0-39

Nyberg et al.



Histologic Criteria

Remuzzi et al NEJM 2006;354:343

- Donors > age 60 (recipients >50 age or difference <10 years)
- 16 gauge needle (40-50 glomeruli)
- Evaluate vessels, glomeruli, tubules and interstitium
- Score 0-3 each component
- Total score (0-12)
 - >6 discard
 - 4-6 dual kidney
 - ≤ 3 single kidneys

Criteria Comparison

Luis et al WTC 2006 pg 143

n=95

	Graft Survival	Creatinine
	At 1 year	
■ <u>Histologic</u>		
• 0-3	87%	1.30 ± 0.44
• 4-6	85%	1.45 ± 0.56
■ Deceased Donor Score		
• A	96%	0.95 ± 0.24
• B	93%	1.55 ± 0.44
• C	73%	1.64 ± 0.60

Criteria Comparison

Rossini et al WTC 2006 pg 236

n=167 transplants

Concordance Score

■ Histologic	0.64 ± 0.08
■ DDS	0.73 ± 0.08
■ Integrated	0.81 ± 0.08

Integrated score = DDS (0-39) + 13*Glom score (0-3)

Cut point 34 (5 year GS 97% vs 67%)

Old for Old (>64 to >64)

Fritsche et al Am J Transplant. 2003;3:1434

- 43% increase in transplantation of the elderly with reduced wait time (WTC 2006 pg 141)

	<u>Old for Old</u>	<u>Traditional Allocation</u>
• R Age	68±3	64±3 years
• D Age	71±4	45±15 years
• CIT	7.8 ±3.4	14.2 ±5.5 h
• HLA MM	4.2 ± 1.2	1.6 ± 1.7
• PSurvival	85%	89%
• GSurvival	84%	87%

UNOS vs Eurotransplant

Cecka et al AJT (ATC 2004)

- 1500 cadaver kidneys discarded in US annually
- 37% of 61-65 y/o donor kidneys discarded in US vs 7% in ET
- 54% of >65 y/o donors kidneys discarded in US vs 8% in ET
- Eurotransplant Senior Program >65 y/o donor kidneys to >65 y/o recipients

What should be our plan?

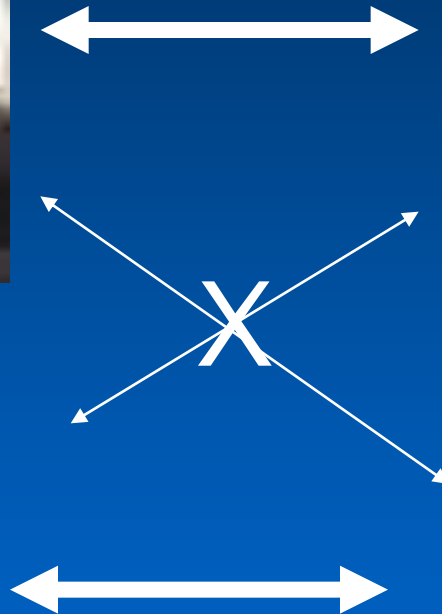
Avoid “ECD”

Rather ‘Optimized
Allocation’

Optimized Matching



Optimized Matching



Remaining Life Years Remaining Miles to Travel

Vancouver to St John's

Gander to St John's

Optimized Matching

Vancouver to St John's



Gander to St John's



Our Current Plan

'Now Under Review'

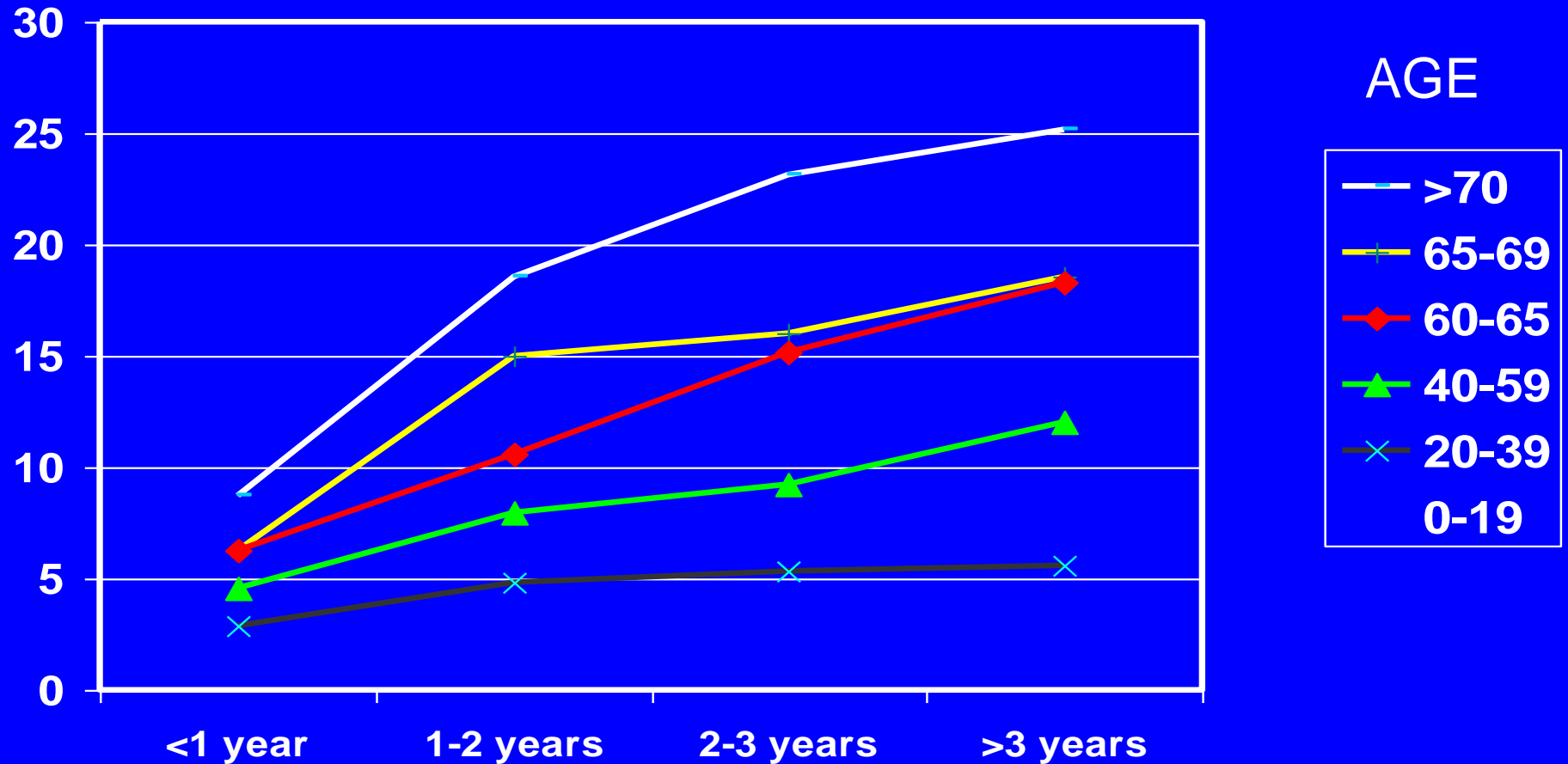
- Retrieve All kidneys
- Visibly scarred kidneys should be discarded.
- Biopsy some deceased donors kidneys
 - > age 65
 - > age 55 and donor CrCl <70 ml/min
 - Discard advanced arteriolar sclerosis or interstitial fibrosis (use 16 g needle)
- Allocate to
 - Older (>59) or diabetic
 - Avoid the sensitized
 - Minimize cold ischemic time
 - Avoid large weight or age mismatches

Still Some Angst

Analysis of Outcomes

Mortality Rate On Wait List

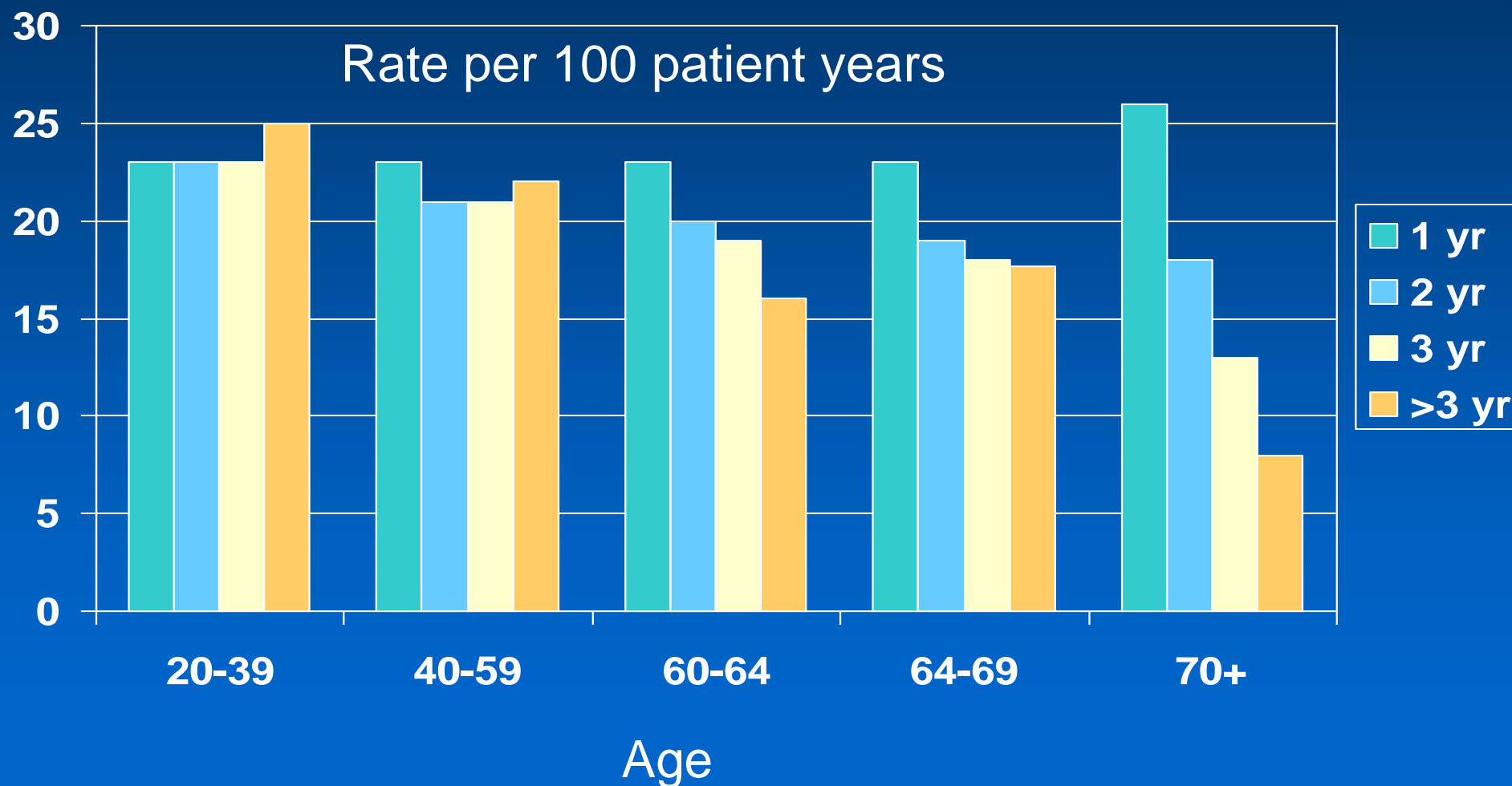
Per 100 patient years



Gill et al Kidney Int 2005

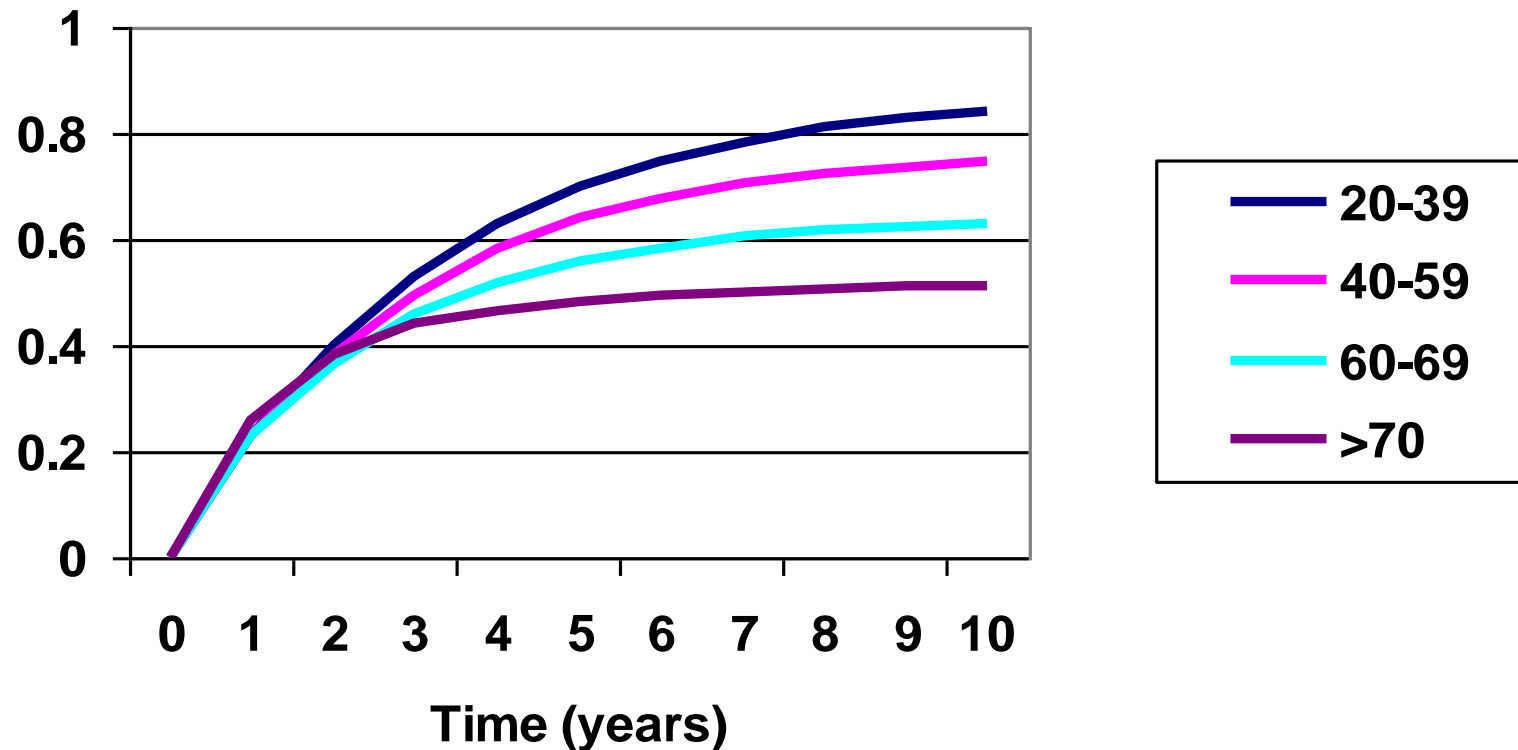
Transplant Rates by Time on List

Gill et al AJT 2005;5 (Suppl 11):261



Probability of Transplantation

Cumulative probability
Overestimated since it ignores removal from the list



The ECD in deceased donor renal transplantation.

JAMA 2005;294:2726

- Cohort of >109,000 ESRD patients 1/95-12/02
- Compared transplanted outcomes from wait list to death for standard and ECD recipients.
- RR for mortality with ECD kidney (vs SD)
 - $RR=1$ Implies ECD and SD equivalent
 - $RR<1$ Implies ECD better than SD
 - $RR>1$ Implies ECD worse than SD

The ECD in deceased donor renal transplantation.

JAMA 2005;294:2726

	Short Wait (<3.5 yrs)	Long Wait
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Age 40-59	0.90	0.71 (0.60-0.85)*
Age 60+	0.92	0.63 (0.50-0.78)*
DM	0.77 (0.64-0.94)*	0.74 (0.59-0.924)*

The ECD in deceased donor renal transplantation.

JAMA 2005;294:2726

■ Net Benefit

- Long waiting times
 - Diabetes mellitus and >40 years of age
- Short waiting times
 - Diabetes mellitus

The ECD dilemma in cadaveric renal transplantation.

Schnitzler MA et al Transplantation 2003

- Selected subsets revealed differences in wait times that equated QALYs for ECD and standard donors:
 - Average 3.2 years
 - African Am. 4.4 years
 - Age under 30 4.0 years;
 - Age over 60 11 months.

Future Allocation Solutions

Optimized Solution

WTC 2006 pg 322

Recipient Score (1-4 grade based on DM, Age, IHD, Dialysis time)

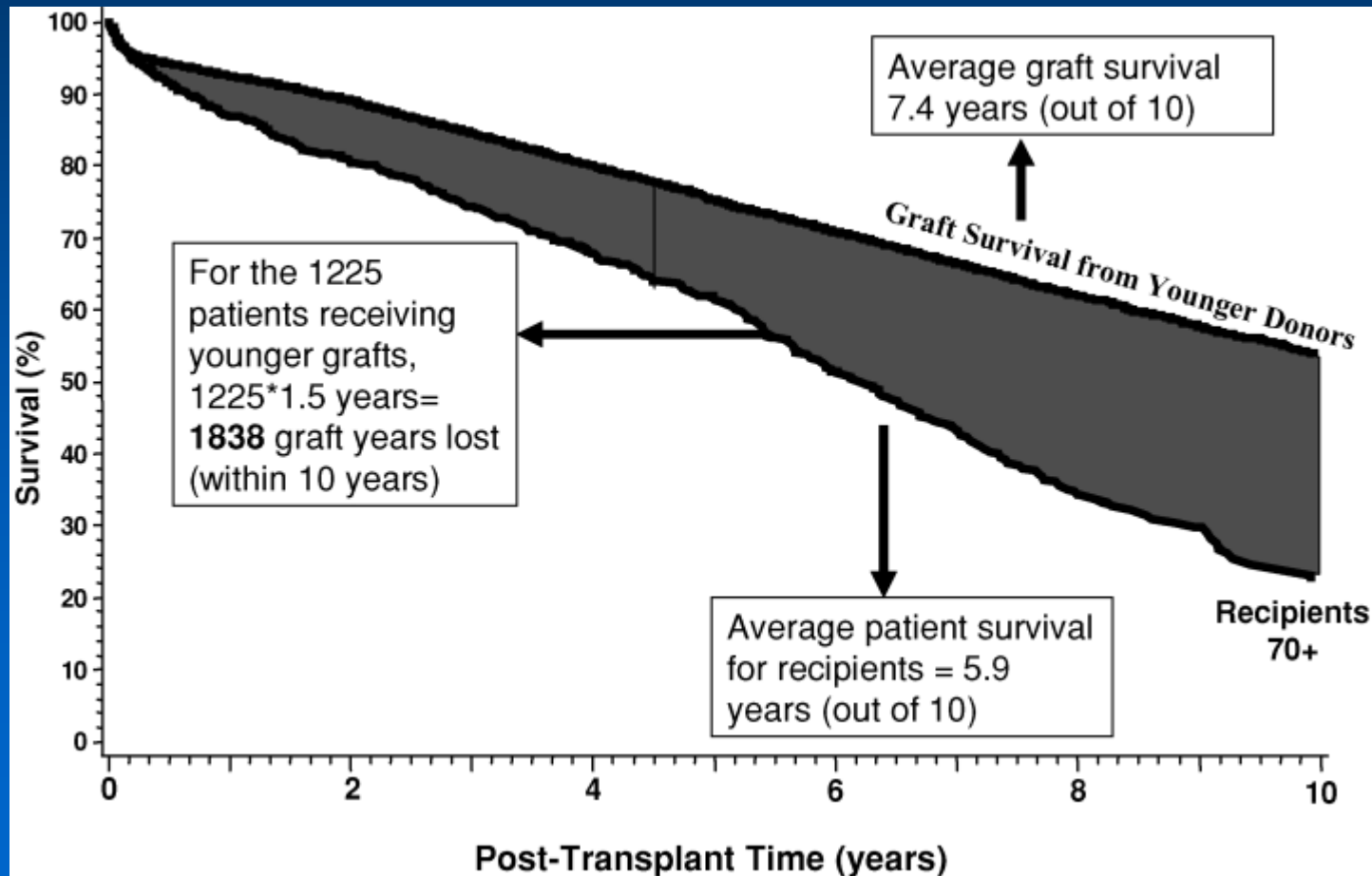
Deceased Donor Score

	A	B	C	D
1	+3	-8	-13	-15
2	+20	+10	+4	+0.4
3	+24	+14	+8	+4.5
4	+27	+16	+11	+7

Graft Survival minus Patient Survival in %

Maximizing Value

Meier-Kriesche et al AJT 2005;5:1725



Matching Recipient and Graft Survival

Baskin-Bey et al Transplantation 2006; 82:10

TABLE 3. Renal years according to age group and Deceased Donor Score

Recipient age (years)	Recipient renal years	Donor renal years			
		A	B	C	D
<18	10808	1126	446	68	0
18–39	36446	6736	4206	1971	65
40–49	25647	8290	5990	2801	120
50–59	23950	8173 ^a	8062 ^a	5666	400
60–69	11689	3667 ^b	3802 ^b	3376 ^b	844 ^b
≥70	2117	569 ^c	583 ^c	648 ^c	317 ^c
Total	110656	28561 +	23090 +	14530 +	1746 = 67926

2002 calculation of renal years = number of transplants × survival (recipient or graft). Recipient survival was substituted for the original graft survival data (see Fig. 5); in these marked areas, graft survival superceded recipient survival. Our model attempts to preclude this occurrence.

^a Corrected graft survival used for calculation: 13.90 years.

^b Corrected graft survival used for calculation: 9.70 years.

^c Corrected graft survival used for calculation: 7.20 years.

Matching Recipient and Graft Survival

Baskin-Bev et al Transplantation 2006: 82:10

TABLE 4. Optimized expected renal year supply for 2002

Recipient age (years)	Deceased Donor Score	N	Median graft survival (years)	Median recipient survival (years)	Optimized renal years
<18	A	193	8.8	26.7	1698
18–39	A	1365	10.9	26.7	14879
40–49	A	782	15.1	18.9	11808
40–49	B	575	12.2	18.9	7015
50–59	B	1502	17.1	13.9	25684
50–59	C	221	11.4	13.9	2519
60–69	C	1205	13.0	9.7	11689
≥70	C	73	18.0	7.2	526
≥70	D	221	7.2	7.2	1591
Total		6137			77409

**+10,000
Renal Years**

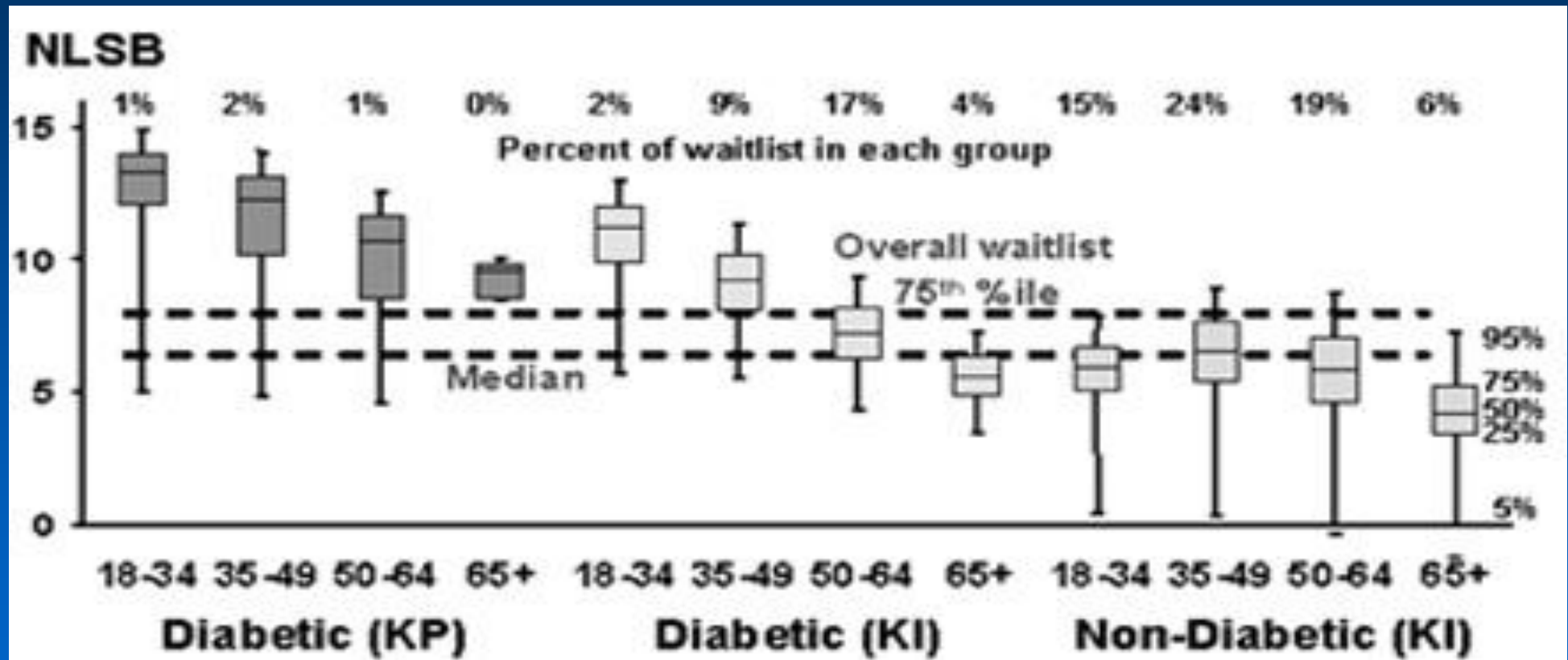
Calculation summary: 110,656 years of renal function to meet demand in 2002; 67,926 years of renal function supplied by deceased donors in 2002 (real); 77,409 years of renal function supplied by deceased donors in 2002 (optimized data); + 9483 additional years of renal function saved by optimization; 13.96% increased by optimization; 22.19% deficit reduced by optimization.

THE NET LIFETIME SURVIVAL BENEFIT

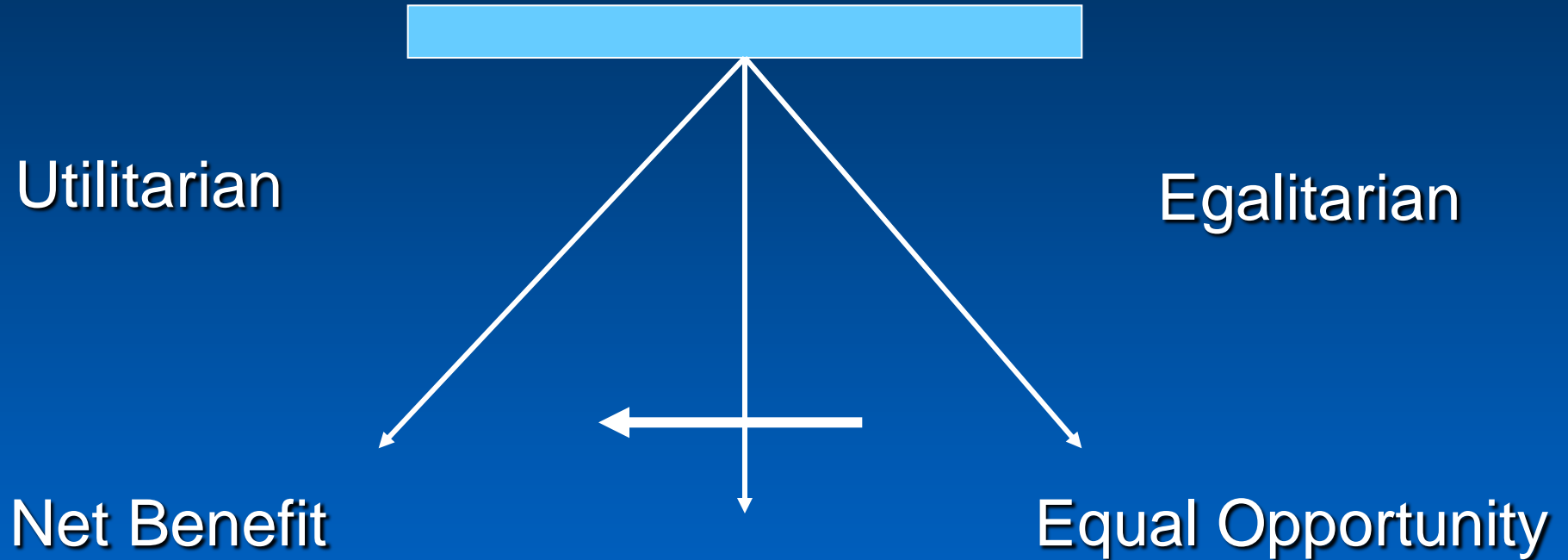
KP McCullough et al WTC Abstract #217

- UNOS rethinking allocation of Standard Donors
 - More utility based
- For every donor kidney
 - The net gain in life expectancy is calculated
 - Cox model, years 4-10 with a Weibull model, Models included candidate age, albumin, BMI, years of ESRD, peak PRA, previous transplant, primary diagnosis, KI v. KP, and diabetes mellitus.

THE NET LIFETIME SURVIVAL BENEFIT



Competing Ethical Principles



Other Organs

ECD Liver Organs

Decrease Wait List mortality

WTC 2006 #603

■ ECD Definition

- >14 hours of cold ischemia time
- AST>150 Na>170 Macrosteatosis >30%
(Liver Transpl 2005;11:1184)
- Non-heart beating donors
- Split liver
- Hepatitis C or B donor

Liver Allocation

- Recipient Scoring System
 - MELD (Model for End Stage Liver Disease)
 - PELD
- ECD Allocation (under review WTC Abstracts)
 - Avoid in Combined Kidney/Liver (#609)
 - Avoid MELD <15 (#607)
 - Avoid in high risk MELD >31 (#1000)
 - Avoid intermediate MELD 15-26 (#1001)

Conclusions

- Maximize use of donor organs
- ECD definitions and allocation will change
 - A Canadian approach is under review (Oct 26)
- Optimized Solution (rather than ECD)
 - Keep it simple
 - Size limitations
 - 65+ to 65+ versus ≥ 60 to ≥ 60 or DM)

Having Enough Patients on the Wait List

Examination of the Wait List

- <14% of adult Halifax program dialysis population on wait list
- 16% of Canada and USA

Access to the Transplant Wait List

Am J Transplant. 2006 Sep 4; [Epub ahead of print]

Kiberd B, Boudreault J, Bhan V, Panek R.

■ Aim:

- To examine policy that all patients with ESRD are considered for transplantation

■ Hypotheses

- That only about 20% are referred
- That burden of comorbidity impacts on referral status
- That a proportion of patients would not be referred despite relatively low comorbidity

Access to the Wait List

Am J Transplant. 2006 Sep 4; [Epub ahead of print]

- 113 consecutive ESRD patients from 4/05-4/06
 - 92 hemodialysis, 13 PD, 8 pre-emptive transplant
 - Age 62 ± 15 (25-85)
 - Diabetes Mellitus 35%
 - Cancer 20%
 - CHF 34%
 - IHD 35%
 - Stroke 14%

Access to the Wait List

AJT in Press 2006

- Comorbidity Indices
 - Charlson
 - 14 weighted health states
 - ESRD
 - 12 weighted health states

Access to the Wait List

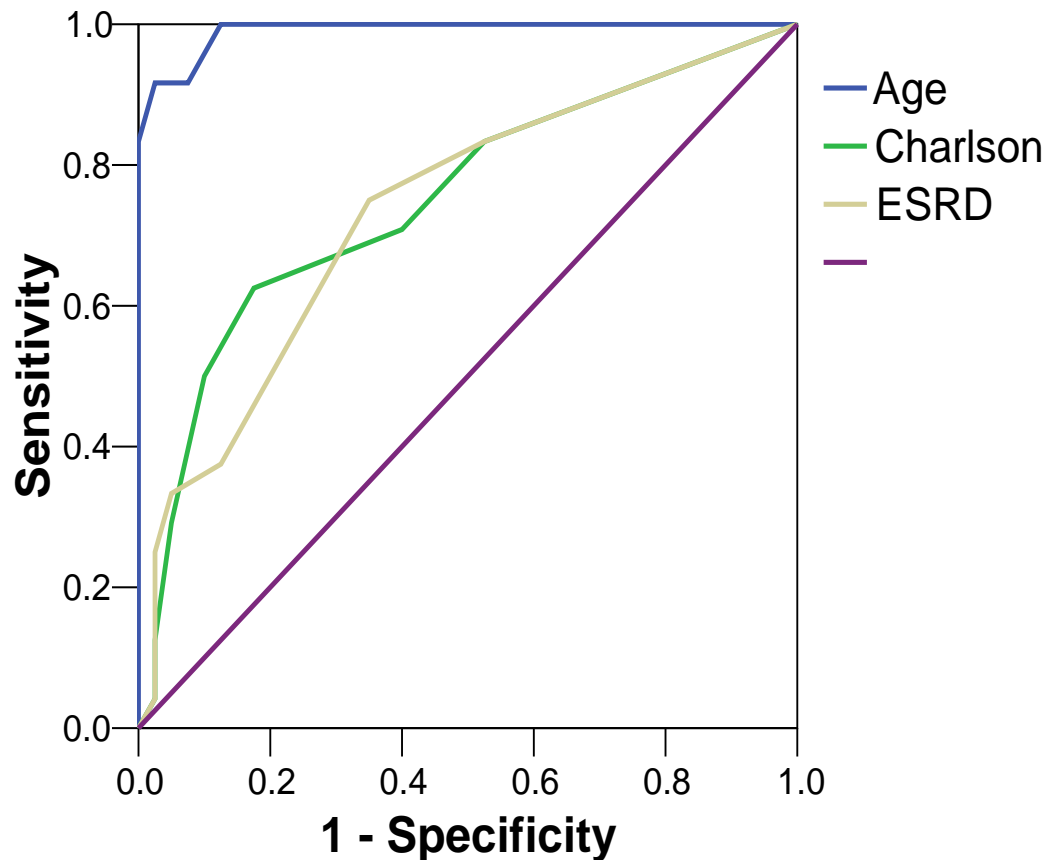
AJT in Press 2006

- 47 (42%) Referred for transplantation
- 48 (43%) Contraindication
 - Canadian Guidelines 2005 CMAJ
 - Cancer-13, CV event -15, Active Disease-20
- 26 (23%) Not referred and No contraindication

Patients with No Contraindication

	Referred N=39	Not Referred N=26	prob
Age in years	50±12	75±7	0.000
Diabetes Mellitus	12 (31%)	13 (50%)	
Cancer	3 (7.7%)	6 (23%)	
IHD	7 (21%)	9 (35%)	
CHF	6 (12%)	11 (42%)	0.016
Albumin (g/L)	35±5	32±6	0.049
Charlson Index	3.3±1.6	5.1±2.1	0.000
ESRD index	1.4±1.8	3.3±2.5	0.001

ROC Curve for Referral



Concordance Statistic

Age 0.99 (0.97-1.00)

Charlson 0.76 (0.61-0.89)

ESRD 0.75 (0.62-0.87)

If no contraindications

Almost everyone <65 is referred

Almost no one >70 is referred

Our Findings

- Higher referral rate than expected
- Are acceptable candidates being discriminated against by age?