

Risky Business: Considerations for Using ECD and DCD Kidneys

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Alan Leichtman, MD

**Division of Nephrology and the Kidney Epidemiology and Cost Center
University of Michigan**

**Scientific Registry of Transplant Recipients, Arbor Research Collaborative for Health
Ann Arbor, MI**

**Gift of Life Michigan
Ann Arbor, MI**

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Disclosure Information

**I have no financial relationships to disclose
beyond my affiliations**

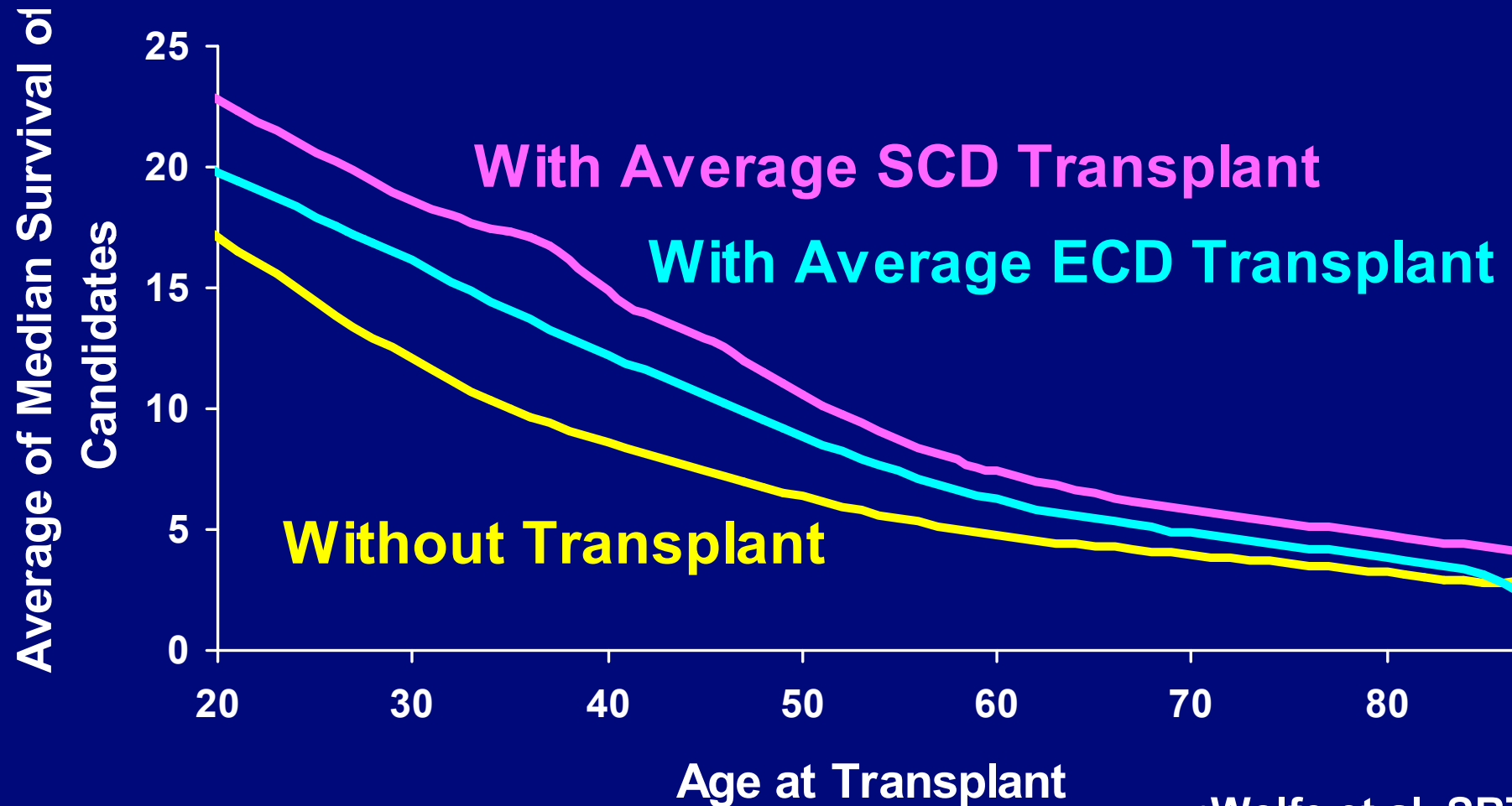
**I will not discuss off label or investigational
uses of pharmaceutical agents or medical
devices during this presentation**

Bottom Line

- **Nearly all waitlisted chronic renal failure patients are predicted to live longer with a kidney transplant than without (dialysis alone)**
- **Kidney transplantation provides:**
 - **Not only a better quality of life, but also**
 - **Longer life**
 - **Reference: Wolfe et al NEJM 1999**

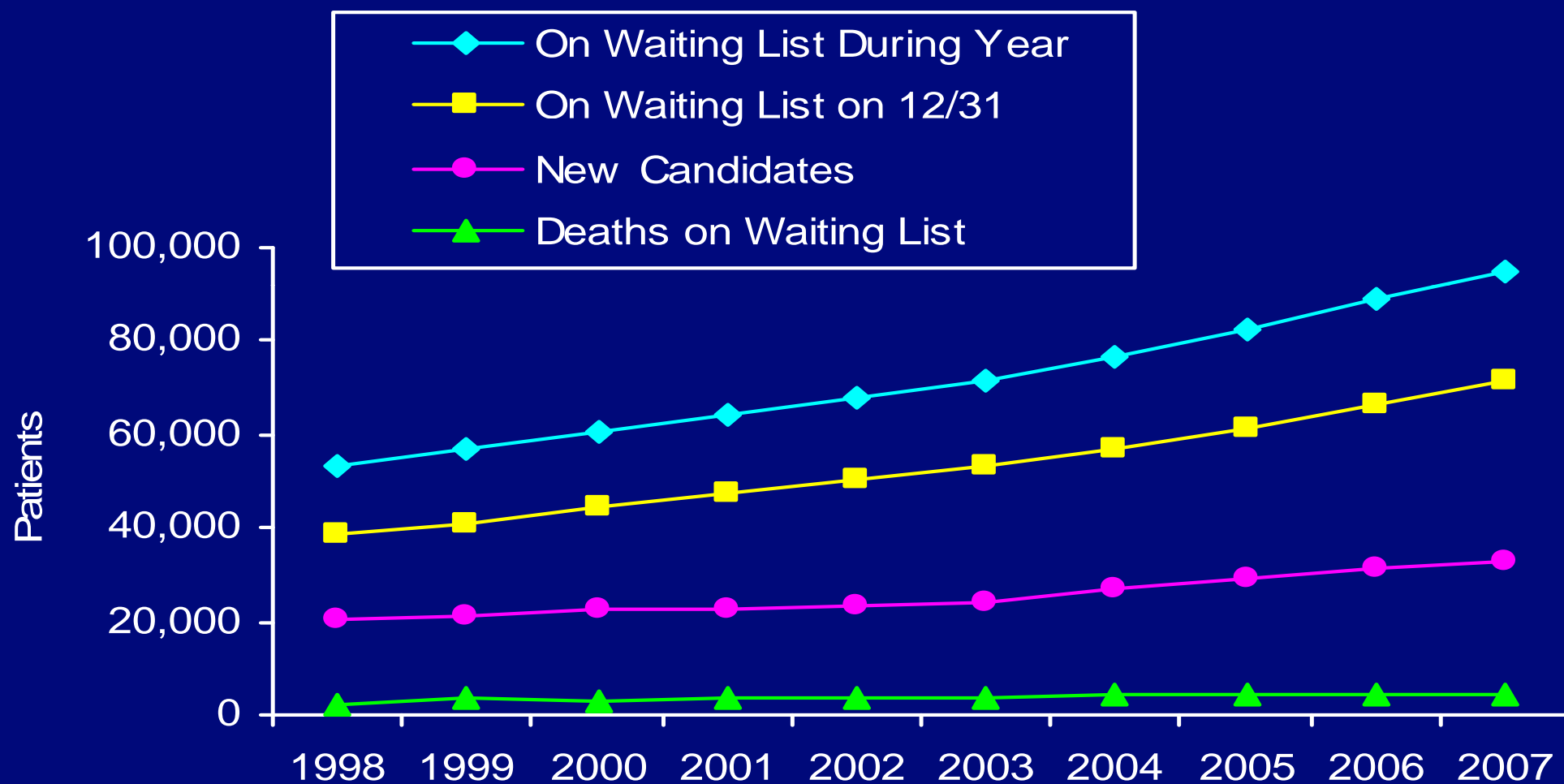
Median Expected Survival by Age

Active Kidney Candidates, 1/1/2004

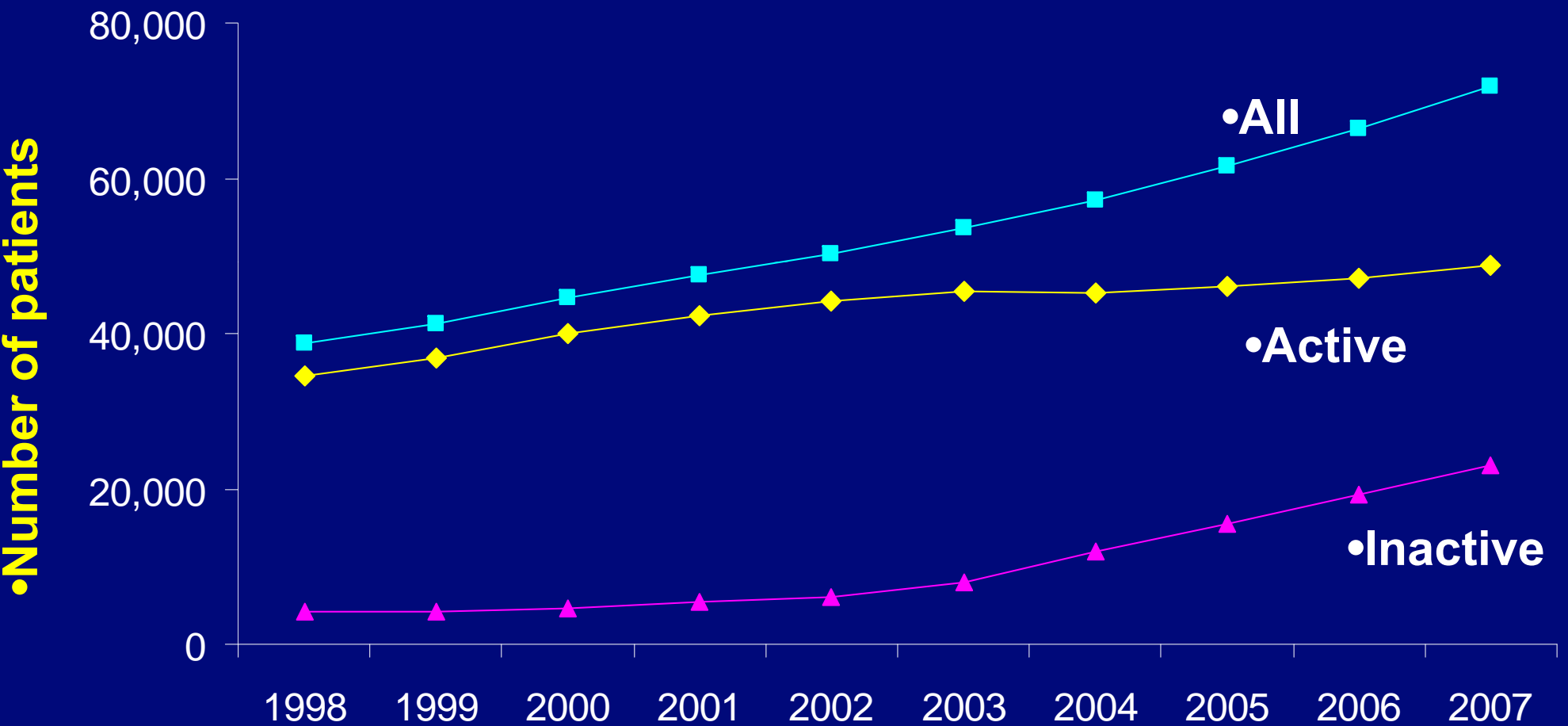


- Wolfe et al, SRTR
- simulation models

•Number of New and Prevalent Kidney Waiting List Candidates and Deaths on the US Waiting List, 1998 to 2007

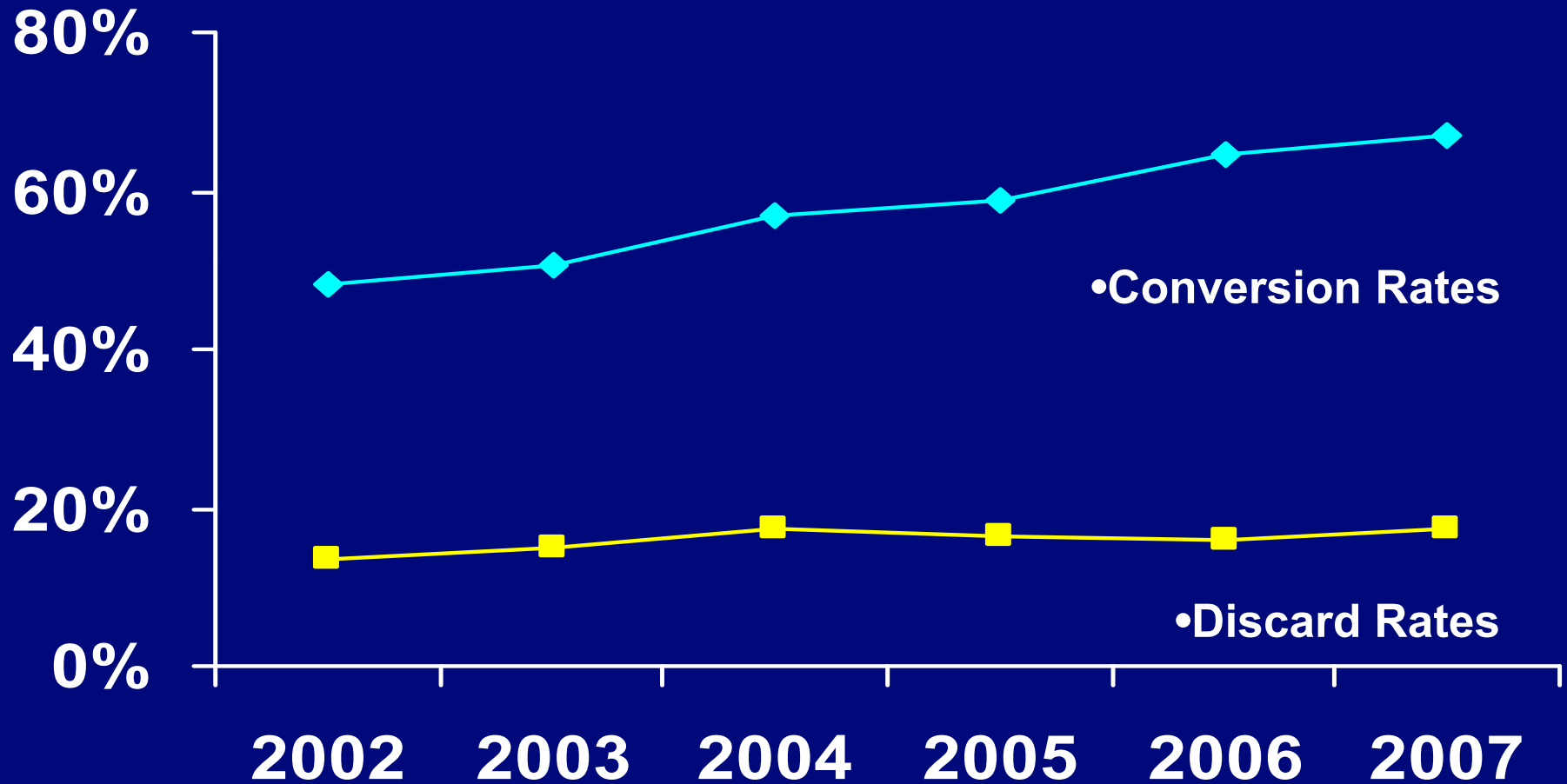


•Active Status Kidney Waiting List Patients at Year-End, 1998-2007



Source: 2008 OPTN/SRTR Annual Report, Tables 5.1a and 5.1b

•Average Conversion and Discard Rates for All OPOs, 2002-2007

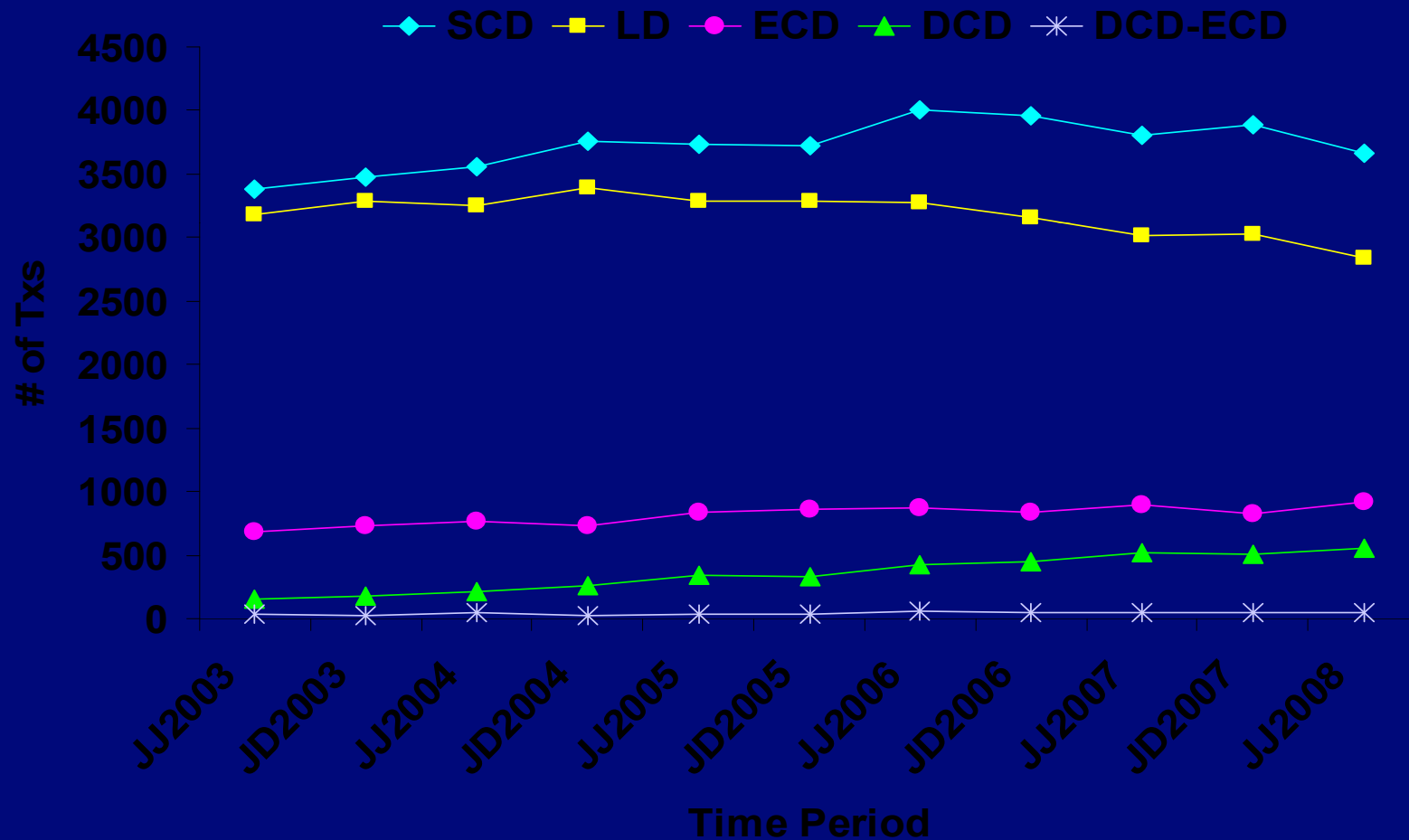


•HRSA Collaboratives began in April 2003

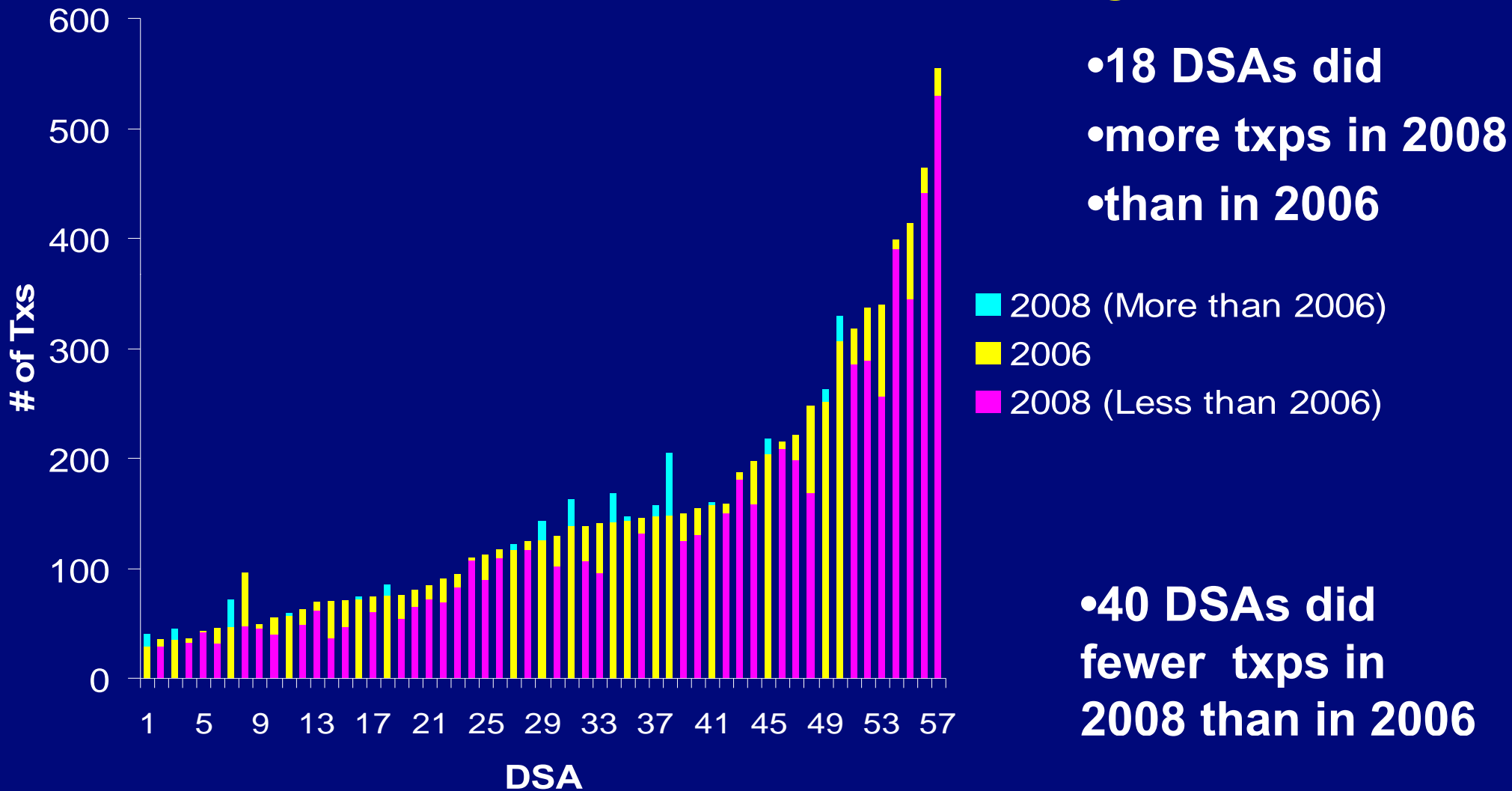
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Source: SRTR analysis, July 2008

National Kidney Transplants by Organ Type for 2003-2008



- **Kidney Transplants from Jan-June**
- **in 2006 compared to 2008 by DSA**



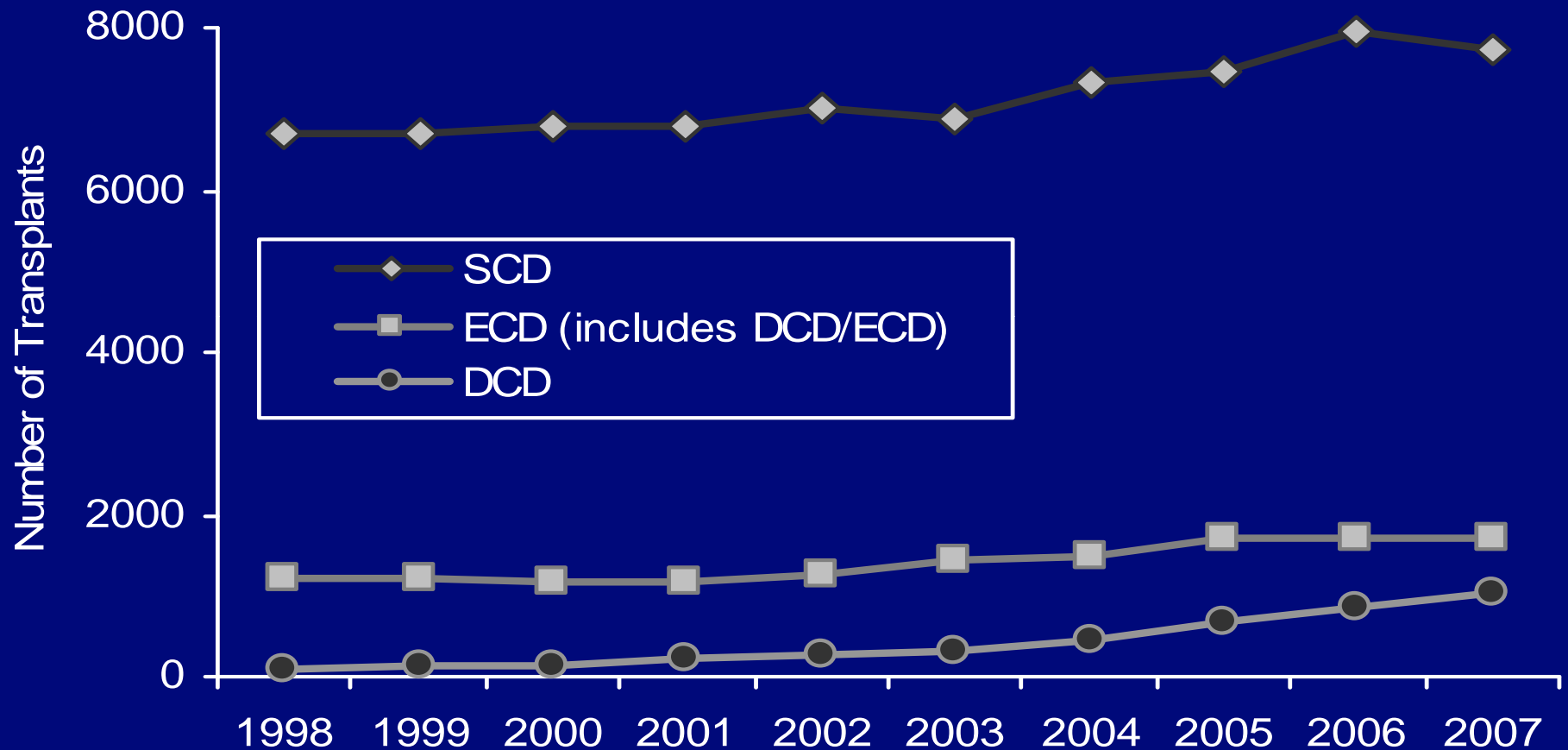
What Do All These Initials Stand For

- **DCD**
 - Donor after Cardiac Death
 - Controlled or uncontrolled
- **DBD**
 - Donor after Brain Death
 - Conventional deceased donor
- **ECD**
 - Expanded Criteria Donor
- **SCD**
 - Standard Criteria Donor
 - DBD that does not meet the ECD definition

Creates Four Categories of Deceased Donors

- DBD that does not meet the ECD definition (SCD) ~ 75%
- DCD that does not meet the ECD definition ~ 10% and growing
 - Allocated by the same algorithm
 - Have similar outcomes
- DBD that meets the ECD definition (DBD-ECD) ~ 14%
- DCD that meets the ECD definition (DCD-ECD) < 1%
 - Allocated by a different algorithm
 - DCD-ECD has worse outcomes

**•Figure 3. SCD, ECD, and DCD Kidney Transplants,
•1998-2007**



•HRSA Collaboratives began in April 2003

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•Source: 2008 OPTN/SRTR Annual Report, Table 5.4

DCD

Uniform Determination of Death Act (UDDA)

- The National Conference of Commissioners on Uniform State Laws formulated the Uniform Determination of Death Act (UDDA) in 1980 .
- The UDDA states that: "An individual who has sustained either
 - irreversible cessation of circulatory and respiratory functions, or
 - irreversible cessation of all functions of the entire brain, including the brain stemis dead.
- This definition was approved by the American Medical Association in 1980 and by the American Bar Association in 1981. Today all fifty states and the District of Columbia follow the UDDA as a legal standard of death.
- Twice reviewed and supported by IOM

Maastricht Criteria for DCD Donors

Category	Description	Type
I	Dead on Arrival	Uncontrolled
II	Unsuccessful Resuscitation	Uncontrolled
III*	Awaiting Cardiac Arrest	Controlled
IV	Cardiac Arrest After Brain Death	Controlled

Candidates for DCD Donation

- **Patients with severe unrecoverable neurological injury**
 - Intracranial hemorrhage, stroke, anoxia, trauma
- **Patients without neurological injury**
 - Unrecoverable cardiopulmonary diseases
 - Degenerative neuromuscular diseases
- **Do not meet criteria for brain death**
- **No chance for survival off the ventilator**
- **Do not have other exclusionary diagnoses**
- **Family and physicians elect to withdraw support (48% of ICU deaths in the US)**

Ethical Axioms

- Recovery team should not interact with the patient or family until after an independent decision to withdraw care has been made
- Recovery team should not assume care of the patient until after death has been declared (2-5 minutes of asystole)
- No treatments should be given or avoided in order to allow potential organ donation, all treatment should be aimed at helping the patient until the point of withdrawal of support
 - What is good for the patient is good for the organs
 - Retrieval of organs for transplantation should not cause the death of a donor (“Dead Donor Rule”)

What Organs Can Be Used From DCD?

- **Kidneys**
 - Results are the same as from brain dead donors
- **Livers**
 - Results are not as good as ideal brain dead donors, but are equivalent to livers from donors that are older than 60
- **Lungs**
- **Pancreas**
- **Occasionally hearts**

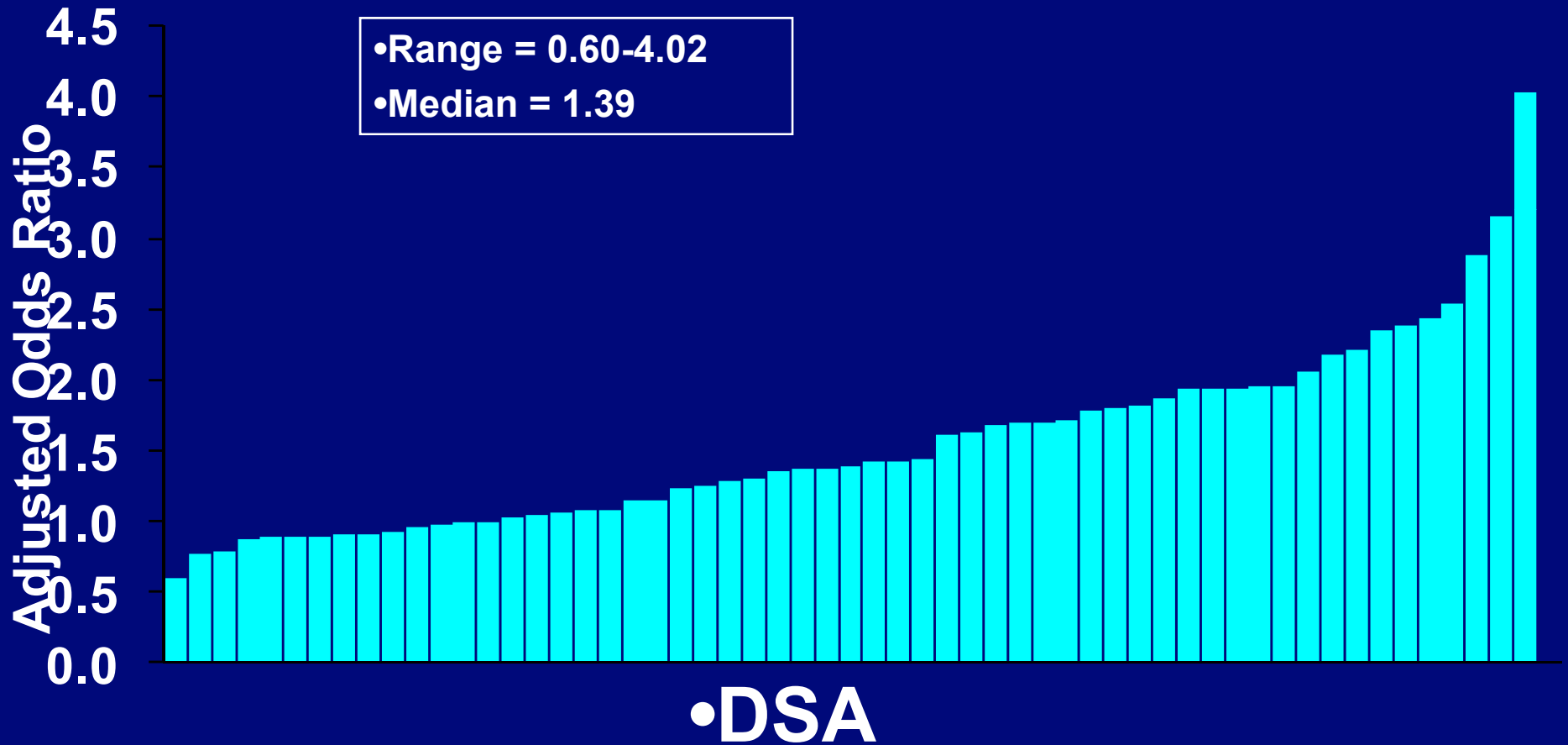
How Are (non-ECD) DCD Kidneys Allocated

- **Just like (non-ECD) DBD kidneys**
- **Non-ECD DBD and DCD kidneys represent 85% DD kidney transplants**
 - **5% - kidney plus life saving organ**
 - **15% - zero HLA-A,B,DR mismatched kidney or simultaneous kidney pancreas candidates**
 - **no sharing of zero HLA-A,-B-DR kidneys to candidates with PRA <20%, projected to decrease to 8%)**
 - **65% - HLA mismatched candidates based upon a menu of priorities**

Current Allocation Priorities for Mismatched Deceased Donor Kidney

- Prior living donors
- Paybacks
- Pediatric candidates have first priority for donors under the age of 35 years
- Point System
 - Time waiting (1 point per year, fraction of a point for partial year)
 - Prior sensitization (4 points for Panel Reactive Antibody level $\geq 80\%$)
 - HLA-DR Similarity (2 points zero HLA-DR MM, 1 point for a one HLA-DR MM)

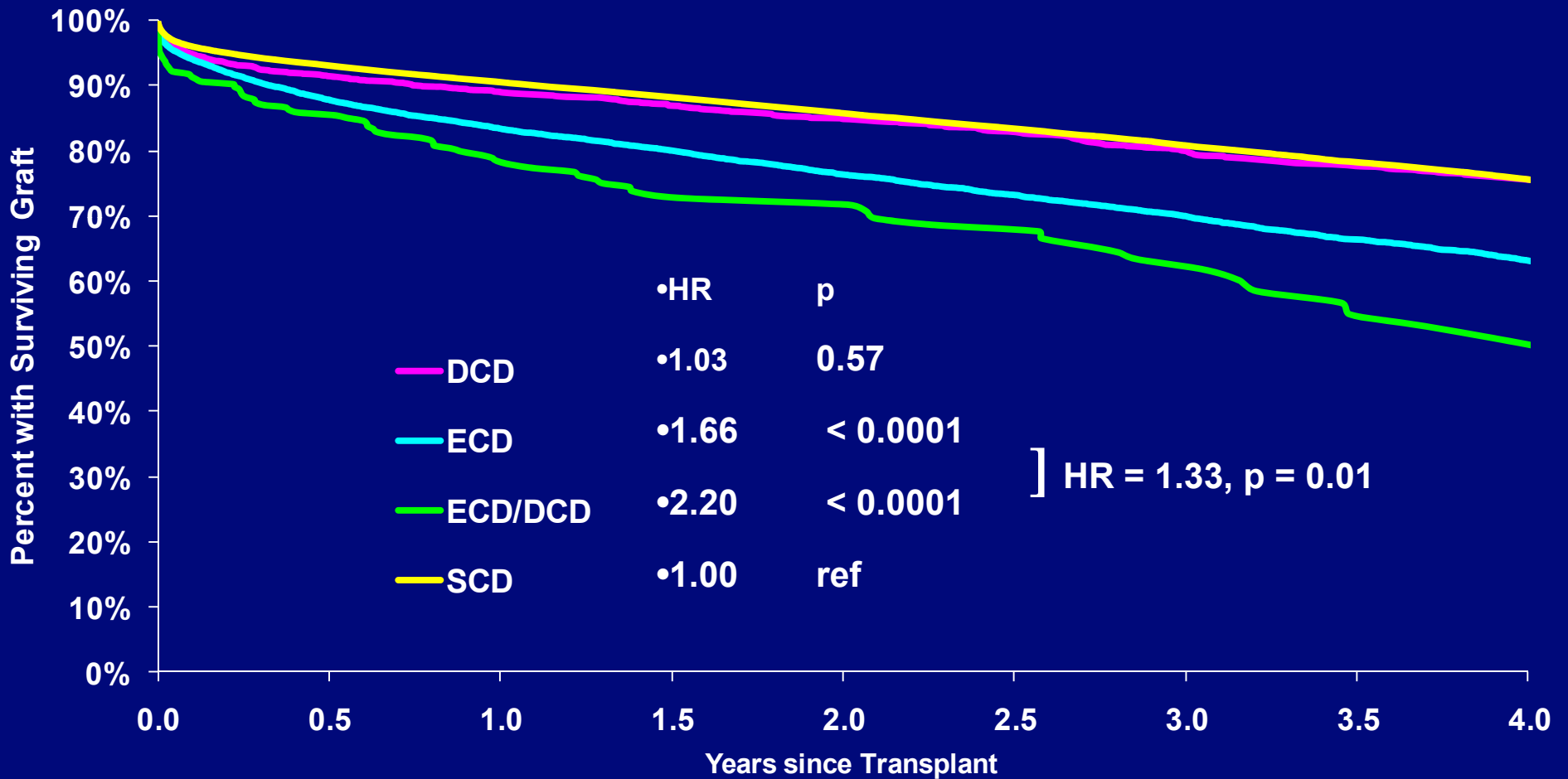
Adjusted Odds Ratio of Discard for Non-ECD Kidneys by DSA, 2004 – 2007



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•Source: SRTR analysis, October 2008.

Graft Survival by DCD, ECD Status 1/1/97 – 5/30/05



ECD

Definition of ECD Kidney

- **Defined as a kidney from any deceased donor**
 - **Age greater than or equal to 60 years, or**
 - **Age 50-59 years with any two or more of:**
 - **terminal creatinine greater than 1.5 mg/dl**
 - **cerebrovascular accident (CVA) as cause of death**
 - **history of hypertension**
 - **Implemented October 30, 2002**

What is an ECD Kidneys?

- Kidneys that meet this definition have a 40% chance of discard.
- ECD kidney transplants have a relative risk of allograft failure that is ≥ 1.7 , when compared to a reference group of
 - nonhypertensive, deceased-donors, between the ages of 10 and 39 years, whose cause of death was not a cerebral vascular accident, and whose terminal creatinine was ≤ 1.5 mg/dl

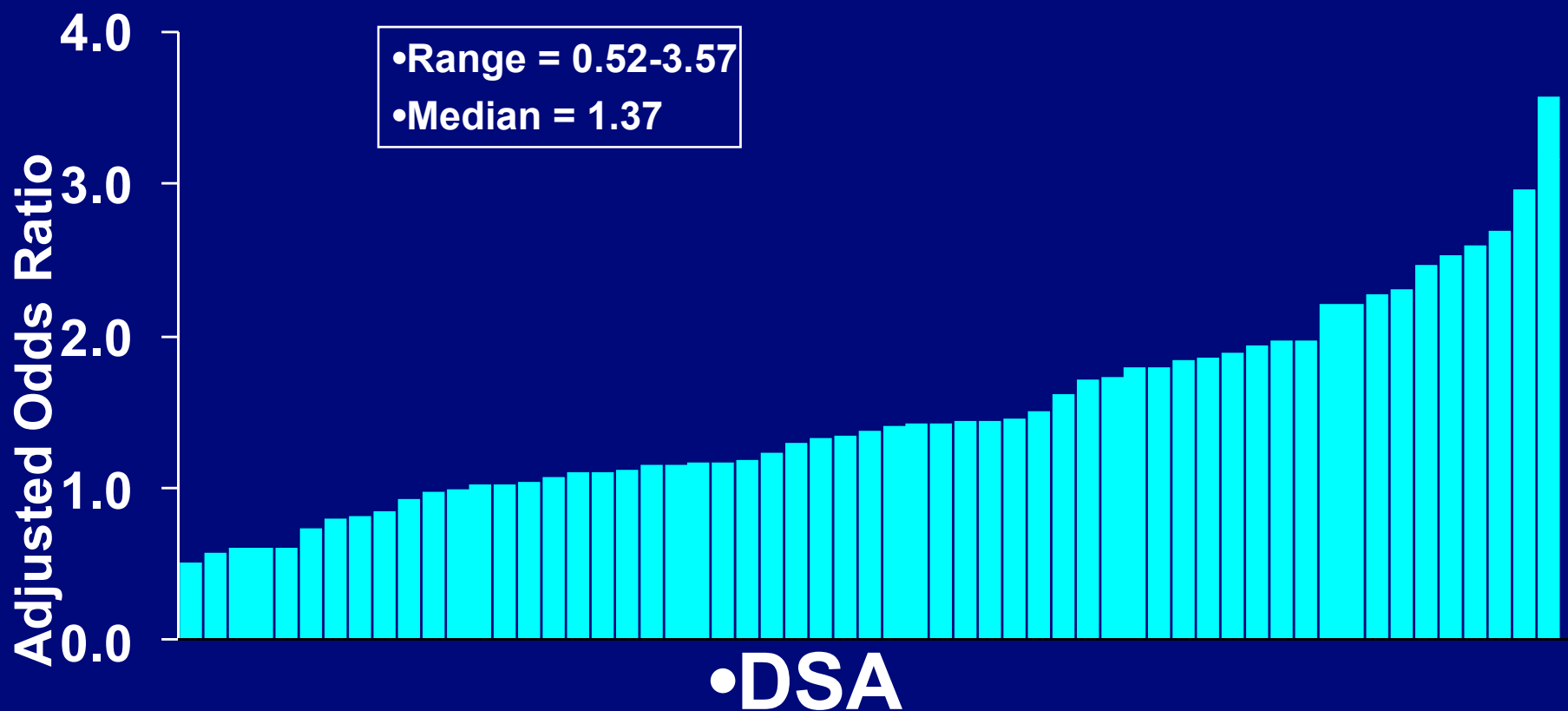
ECD Kidney Allocation System

- **Except in the situation of zero HLA-mismatch, ECD kidneys are allocated by waiting time alone**
- **Goals of the ECD allocation system**
 - **Improve overall access to deceased donor kidney transplantation**
 - **Expedite the placement of ECD kidneys**
 - **Increase number of ECD transplants performed**

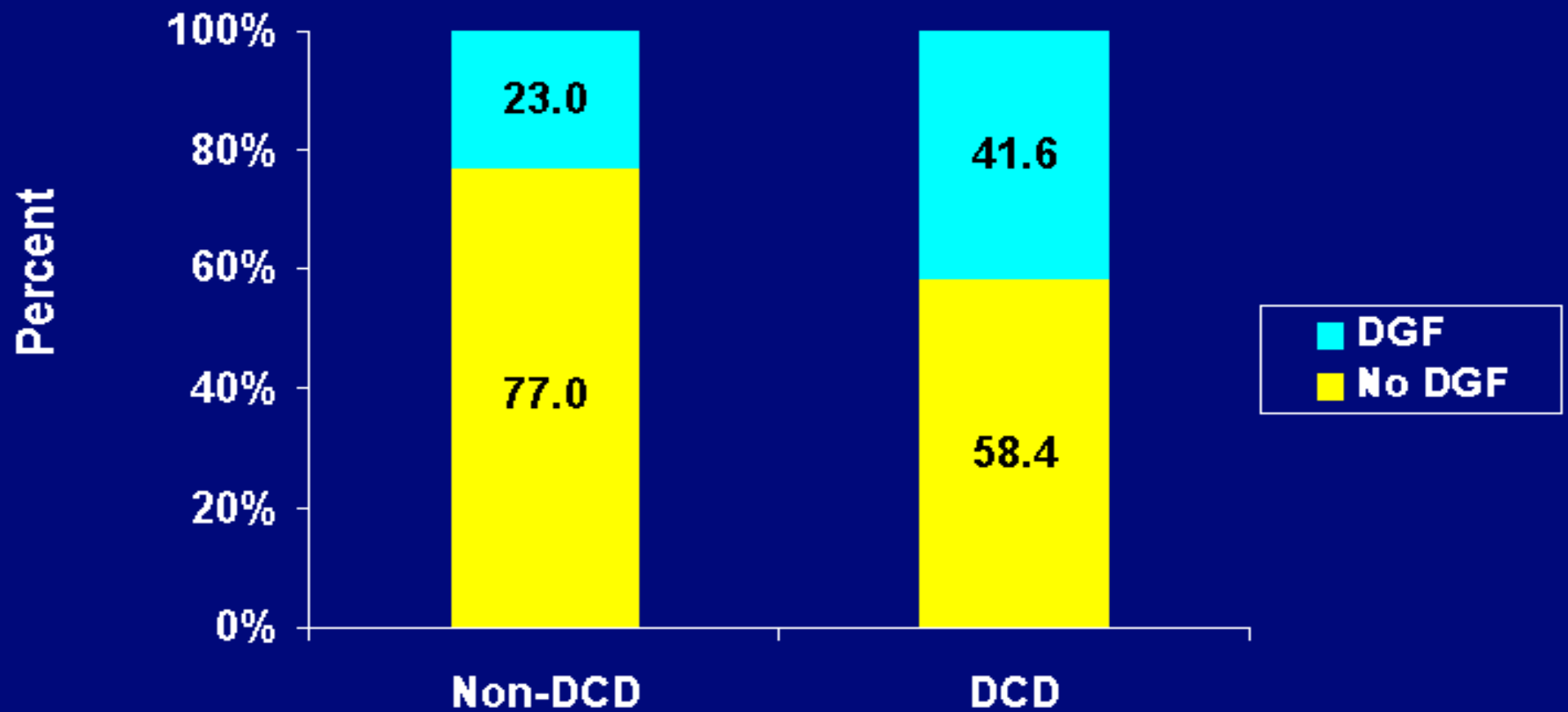
Elements of the ECD Kidney Allocation System

- Identification and consent of candidates for ECD kidneys prior to receiving an ECD designation
- Pre-procurement tissue typing
- Abbreviated time period (2 hours) for placement of zero antigen mismatched kidneys
- Allocation of mismatched kidneys by waiting time alone (4 hours for local placement)
- System has not met expectations

Adjusted Odds Ratio of Discard for ECD Kidneys by DSA, 2004 – 2007



Delayed Graft Function (DGF) for DCD vs. Non-DCD Kidneys, 2000-2004



There were 454/41,218 non-DCD and 27/1,635 DCD kidneys with missing DGF information.

Discard, DGF and Graft Failure for ECD Kidneys

Characteristic	Odds of Discard N=8145		Odds of DGF N=4748		RR of Graft Failure N=4763			
	AOR	p-value	AOR	p-value	RR	p-value		
Diabetes (ref= no diabetes)	1.84	<.0001	1.07	0.4462	1.14	0.1892		
Male (ref= female)	1.33	<.0001	1.20	0.0099	0.98	0.7788		
Biopsy-- %	Not done	1.00	ref	1.00	ref	1.00	ref	
	0-5%	0.50	<.0001	1.16	0.0888	0.92	0.3083	
	6-10%	0.90	0.3349	1.26	0.0450	0.81	0.1939	
	Glomeruloscler osis	11-15%	1.40	0.0047	1.15	0.3505	1.21	0.1518
	16-20%	3.01	<.0001	1.59	0.0102	0.78	0.3373	
	20+%	6.83	<.0001	1.17	0.3961	1.37	0.1530	
ECD RR Group	1.70-1.99	1.00	ref	1.00	ref	1.00	ref	
	2.00-2.39	1.77	<.0001	1.00	0.9726	1.19	0.1032	
	2.40+	2.71	<.0001	1.12	0.2085	1.50	< 0.0001	

DGF and Graft Failure models: Adjusted for factors in table as well as recipient age, sex, race, cause of ESRD, PRA and cold ischemia time and HLA mismatch

Factors That Predict Discard of ECD Kidneys are Poorly Predictive of Allograft Failure

Donor Characteristic	AOR Discard	HR Graft Failure
DCD (ref=non-DCD)	3.06	1.18
Not Pumped (ref=pumped)	1.68	1.09
Diabetes (ref=no diabetes)	1.76	1.20
Glomerulosclerosis 6-10% (ref=no biopsy)	1.55	1.18
Glomerulosclerosis 11-15% (ref=no biopsy)	2.45	1.25
Glomerulosclerosis 16-20% (ref=no biopsy)	4.34	1.29
Glomerulosclerosis 20+% (ref=no biopsy)	10.62	1.22
COD CNS Tumor (ref=head trauma)	2.04	0.99
Hypertension (ref=no hypertension)	1.61	1.16
Age 45-54 (ref=18-44)	1.63	1.12
Age 55-64 (ref=18-44)	3.31	1.45
Age 65 or higher (ref=18-44)	11.59	1.80
Pump resistance 0.349+ (ref=0.186-0.25)	2.73	0.95
GFR 0-62.1 (ref = 62.2 – 85.8)	1.86	1.07
HBV Surface Ag +	4.55	1.28
HBV Core +	1.54	1.06
HCV +	7.08	1.43
HTLV +	16.53	2.16

*all AOR > 1.5 and significant;

Deceased donor kidneys recovered between 10/25/1999 and 1/1/2005

Factors Predictive of Discard

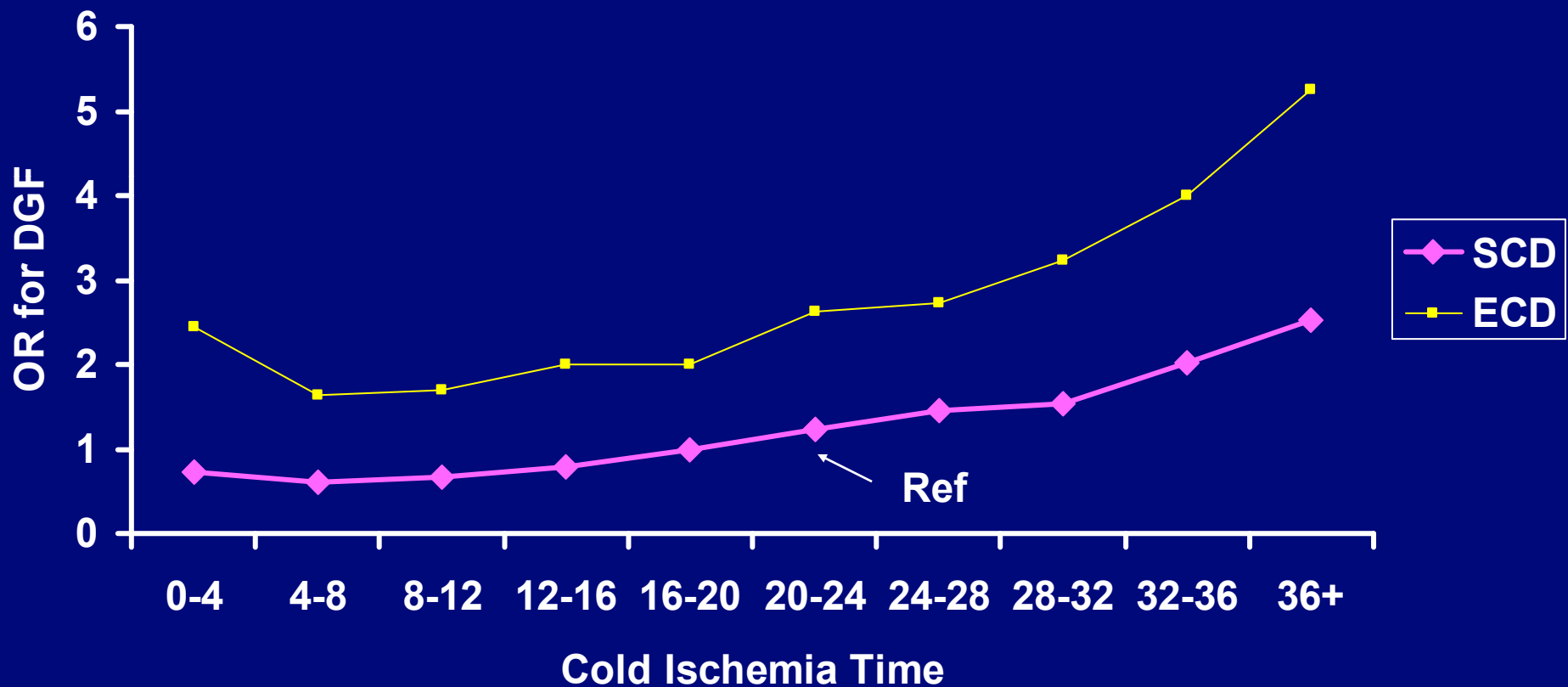
Multivariate analysis of risk factors for ECD kidney discard, 5 factors were statistically significant in the study:

- 1) frozen initial biopsy interpretation showing **10-19% glomerulosclerosis** vs. 0% GS (p=0.0132, OR=2.07),
- 2) frozen initial biopsy interpretation showing **≥ 20% glomerulosclerosis** vs. 0% GS (p<0.0001, OR=4.61),
- 3) **final pump resistance > 0.4** vs. 0.0 – 0.2 (p=0.0049, OR=2.95),
- 4) **donor age ≥ 70** vs. age 50-59 (p=0.0020, OR=3.27),
- 5) **presence of cysts** (p=0.0003, OR=1.89)

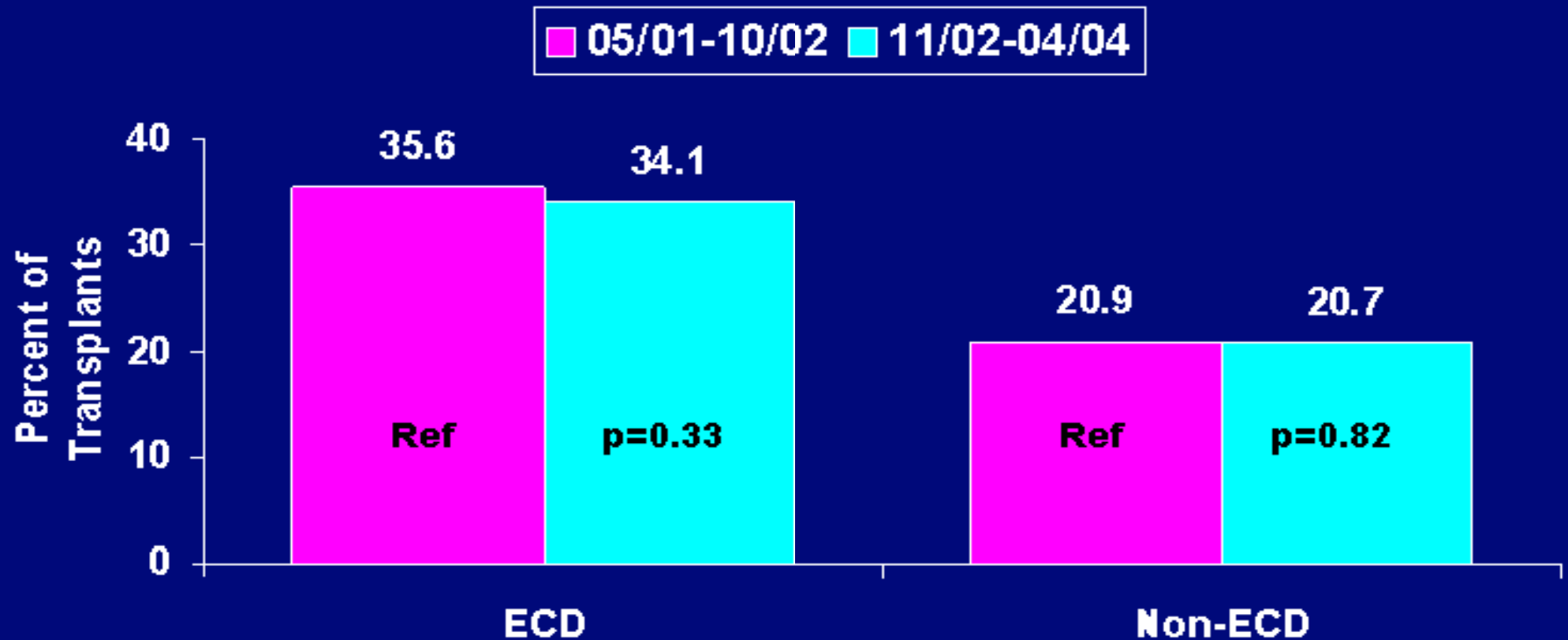
Factors Predictive of Discard are Poorly Predictive of Outcomes

- Of the 5 factors predictive of discard
 - None was predictive of DGF, or length-of-stay.
- Only donor age ≥ 70 years vs. 50-59 years (p=0.0245, HR=2.38) was predictive of death-censored graft loss or of graft loss counting death as an event (p=0.0341, HR=1.91).
- The allograft survival for 309 kidneys transplanted at 1 year: 83.4%.

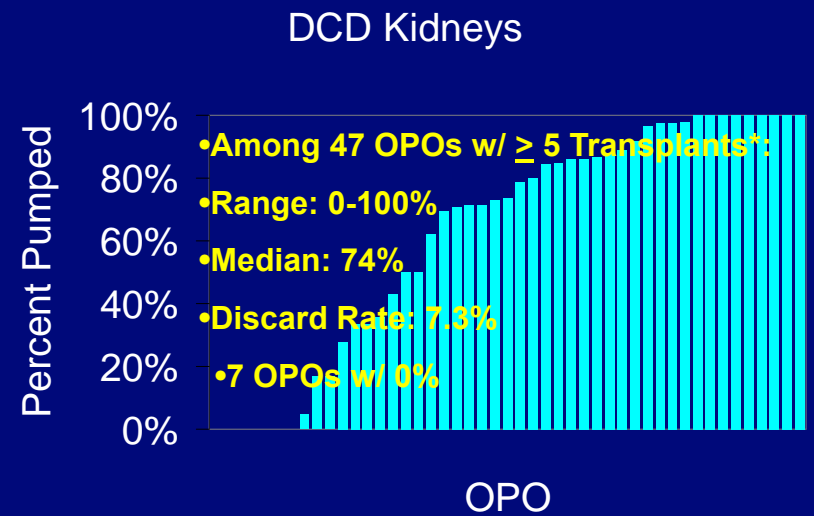
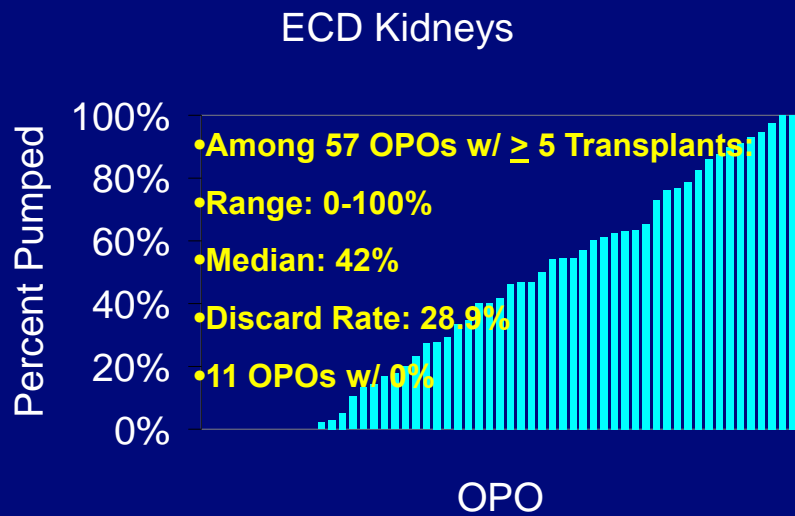
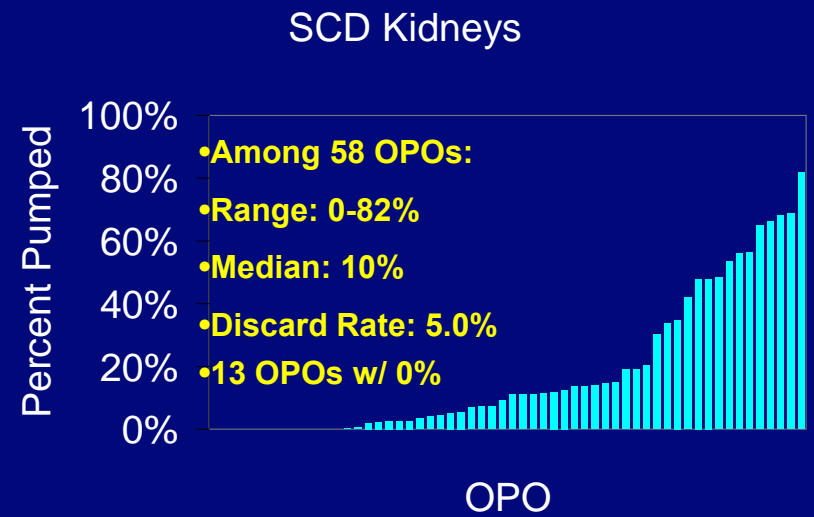
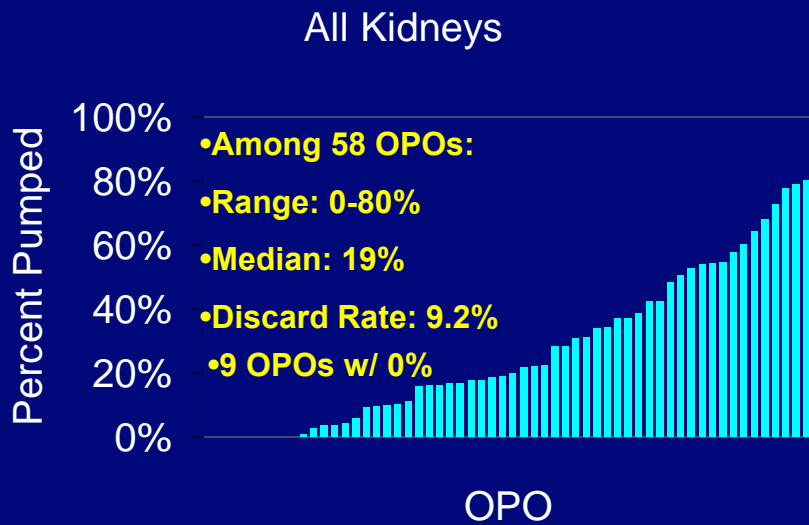
Odds of DGF by Cold Ischemia Time for SCD and ECD Kidneys



Delayed Graft Function Pre- and Post-ECD Policy Implementation



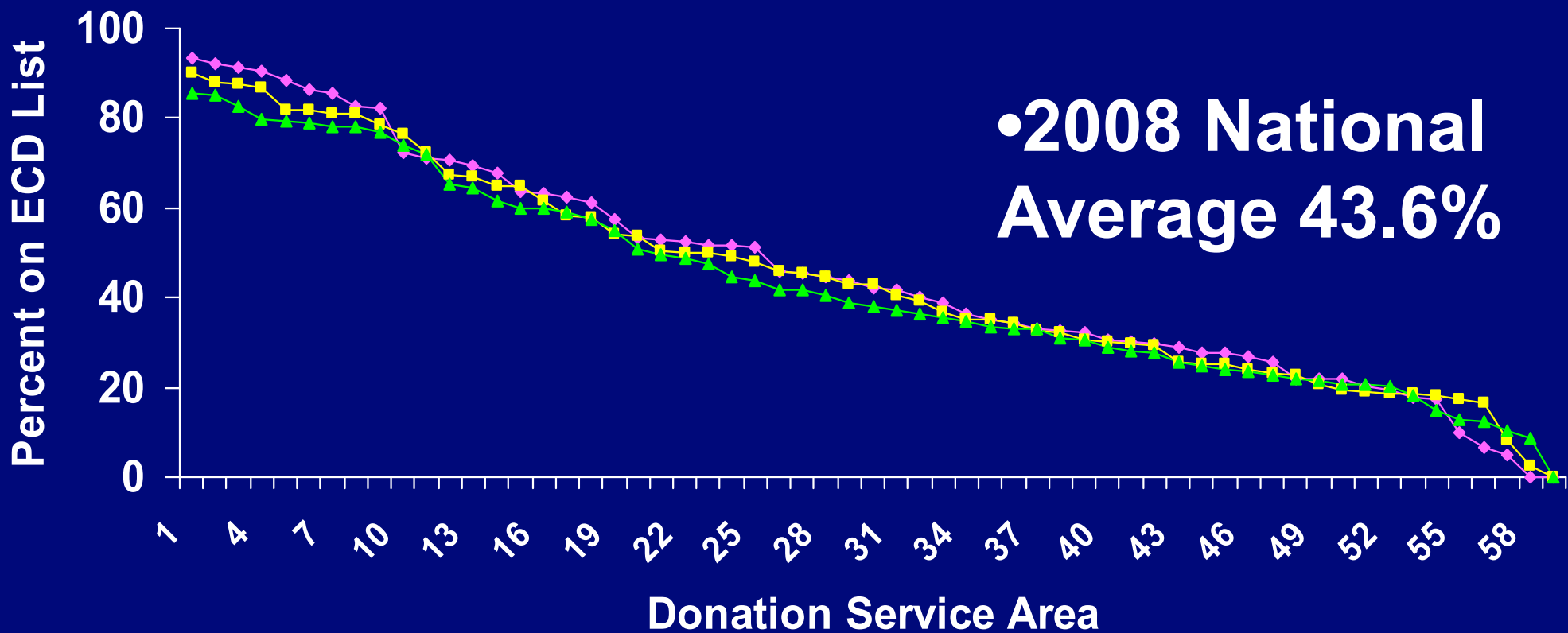
Pulsatile Perfusion by OPO and Organ Type*



*Non-preemptive kidney-only transplants 7/1/07 – 6/30/08

Percent of Candidates on ECD List By Donation Service Area

As of 10/31/2004 As of 10/31/2006 As of 06/30/2008



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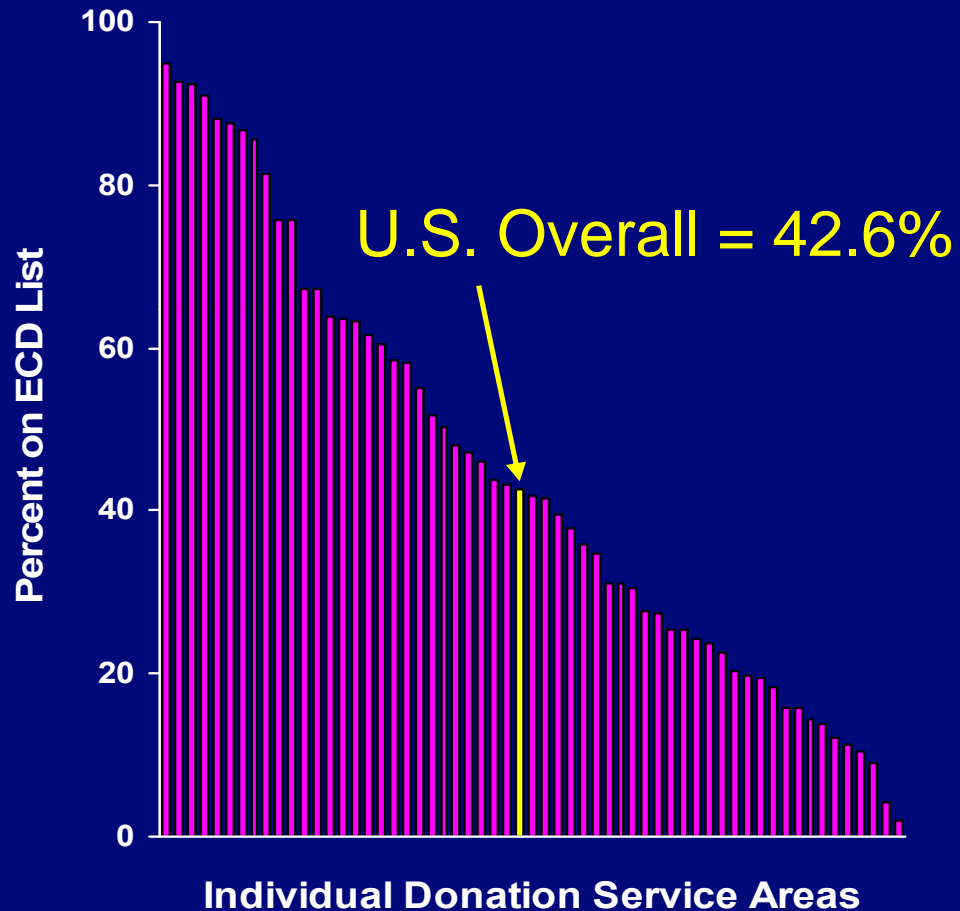
Source: SRTR analysis, October 2008

Who is Likely to be on the ECD List?

Candidate Characteristic	%	OR*	p-value
Age (years)			
0-17	11.5	0.17	<0.0001
18-39	32.4	1.00	Ref
40-49	38.3	1.41	<0.0001
50-59	45.9	2.32	<0.0001
<u>≥</u> 60	57.1	4.77	<0.0001
Female (ref = Male)	42.0	0.97	0.1390
Diabetic (ref = Non-Diabetic)	48.3	1.35	<0.0001
Race			
White/non-Hispanic	43.3	1.00	Ref
African American	46.2	1.05	0.0604
Asian	29.4	1.04	0.4574
Hispanic	39.4	0.90	0.0035
Other	41.0	1.13	0.1472
Peak PRA			
0-29	42.9	1.00	Ref
30-79	44.7	1.12	0.0019
<u>≥</u> 80	44.2	1.17	0.0002
Time on list (per year)		0.99	0.1426

*Also adjusted for DSA effect, ethnicity, previous transplant; as of 12/31/05

Effect of ECD Designation on Access to a Deceased Donor Kidney Transplant



- As of 11/1/05, after adjusting for differences in patient and DSA characteristics, patients on the ECD waiting list on 11/1/02 were **41%** more likely to receive any kidney transplant than those not on the ECD list (OR=1.41; $p < 0.0001$).
- Among recipients who had been listed for ECD kidneys, **30.1%** received an ECD transplant, and **70.6%** a non-ECD transplant.

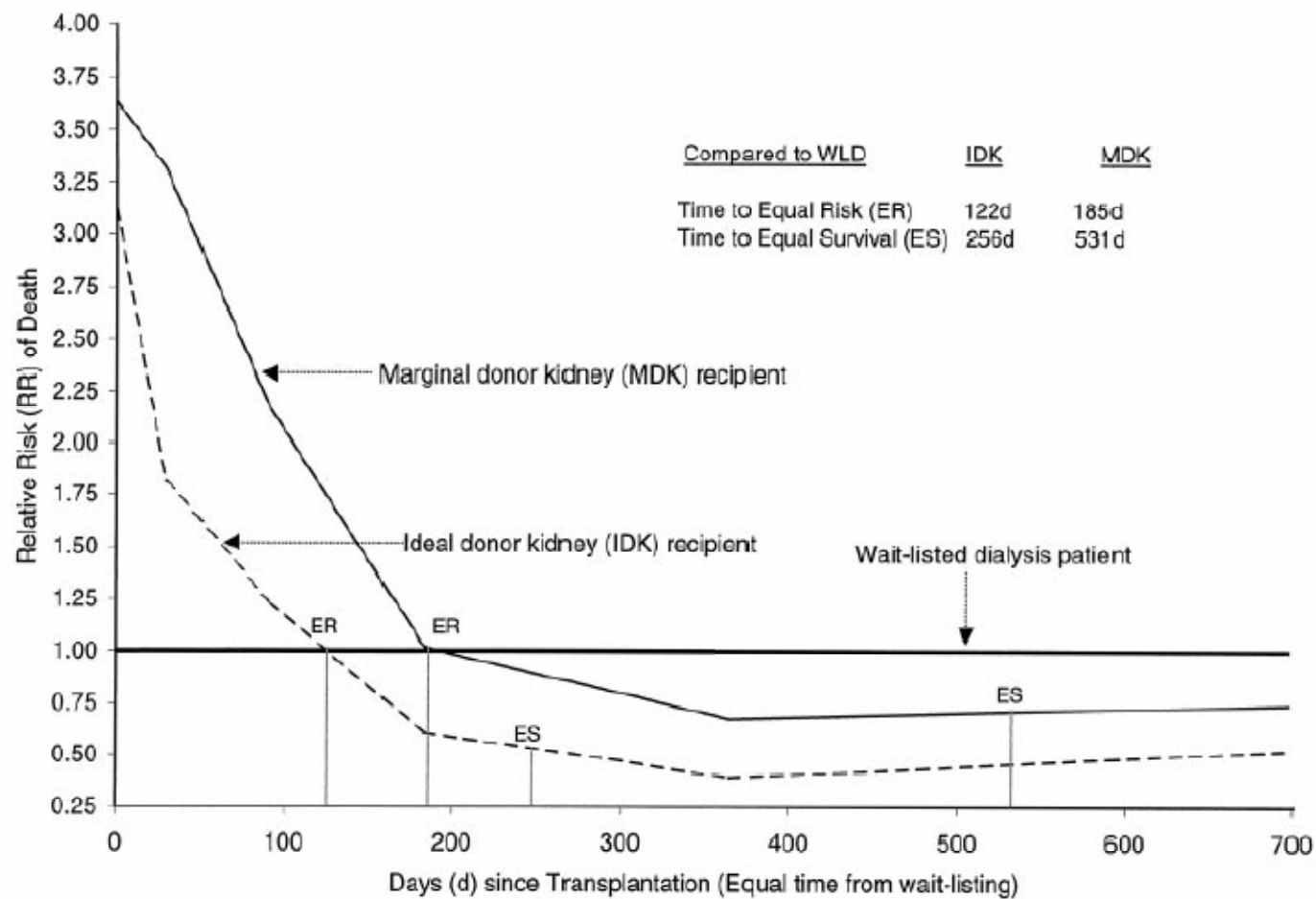
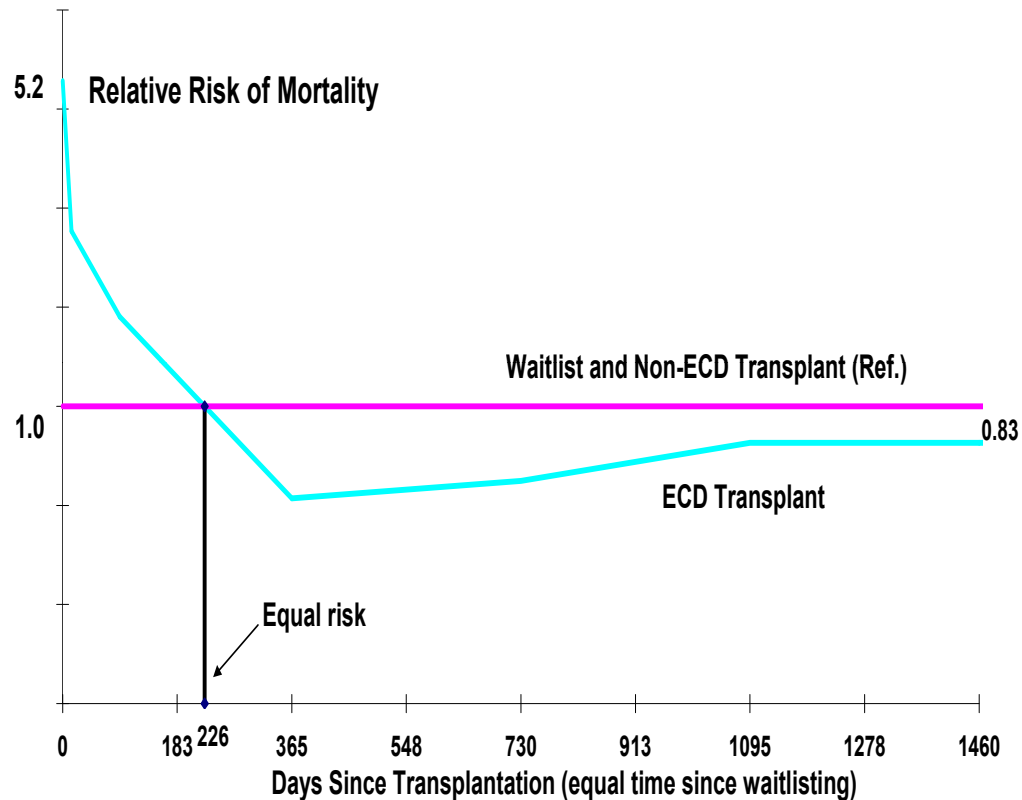


Figure 2. Mortality risks in two groups of cadaveric renal transplant recipients relative to wait-listed dialysis patients.

Accept an ECD kidney now or wait for an SCD?



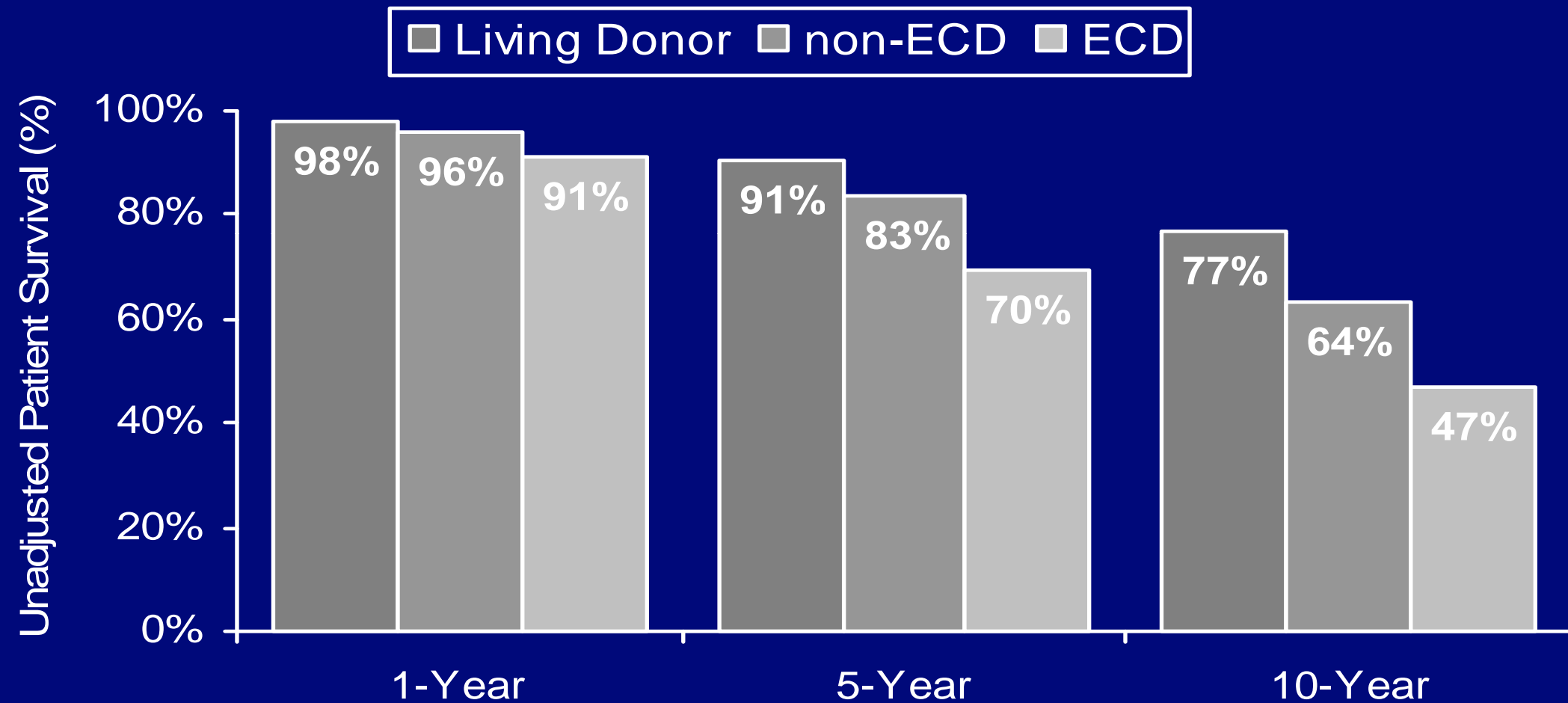
Who Benefits?

Candidates age >40

- Long (>1350d) OPO WT
 - All adult candidates
- Short (<1350d) OPO WT
 - Diabetic only

Tradeoff = additional time waiting vs. inferior donor quality

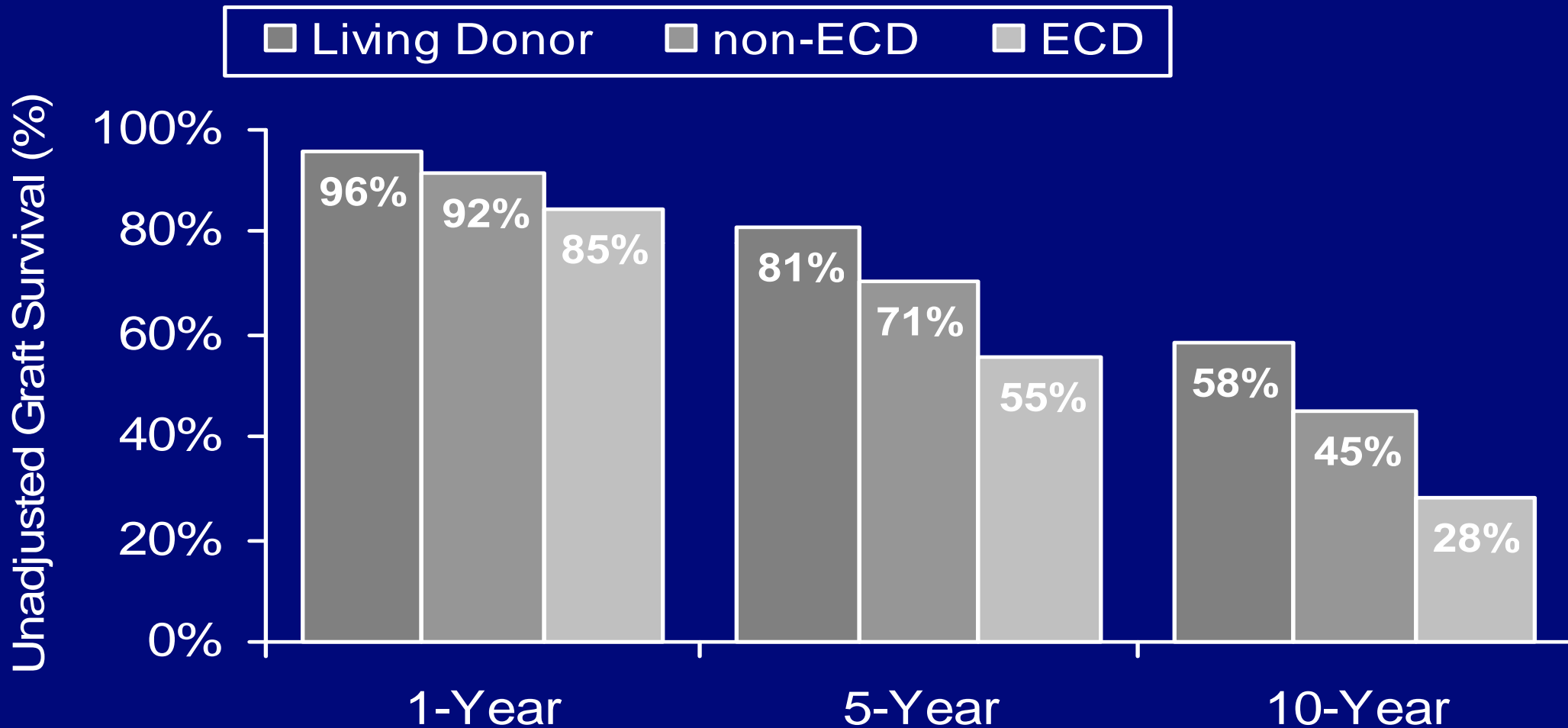
Unadjusted 1-Year (2005-2006), 5-Year (2001-2006), and 10-Year (1996-2006) Kidney Recipient Survival, by Donor Type



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•Source: 2008 OPTN/SRTR Annual Report, Tables 5.14a, b, d.

Unadjusted 1-Year (2005-2006), 5-Year (2001-2006), and 10-Year (1996-2006) Kidney Graft Survival*, by Donor Type



●* Death is included as an event.

●Source: 2008 OPTN/SRTR Annual Report, Tables 5.10a, b, d.

ECD Candidate

ECD kidneys should be directed towards

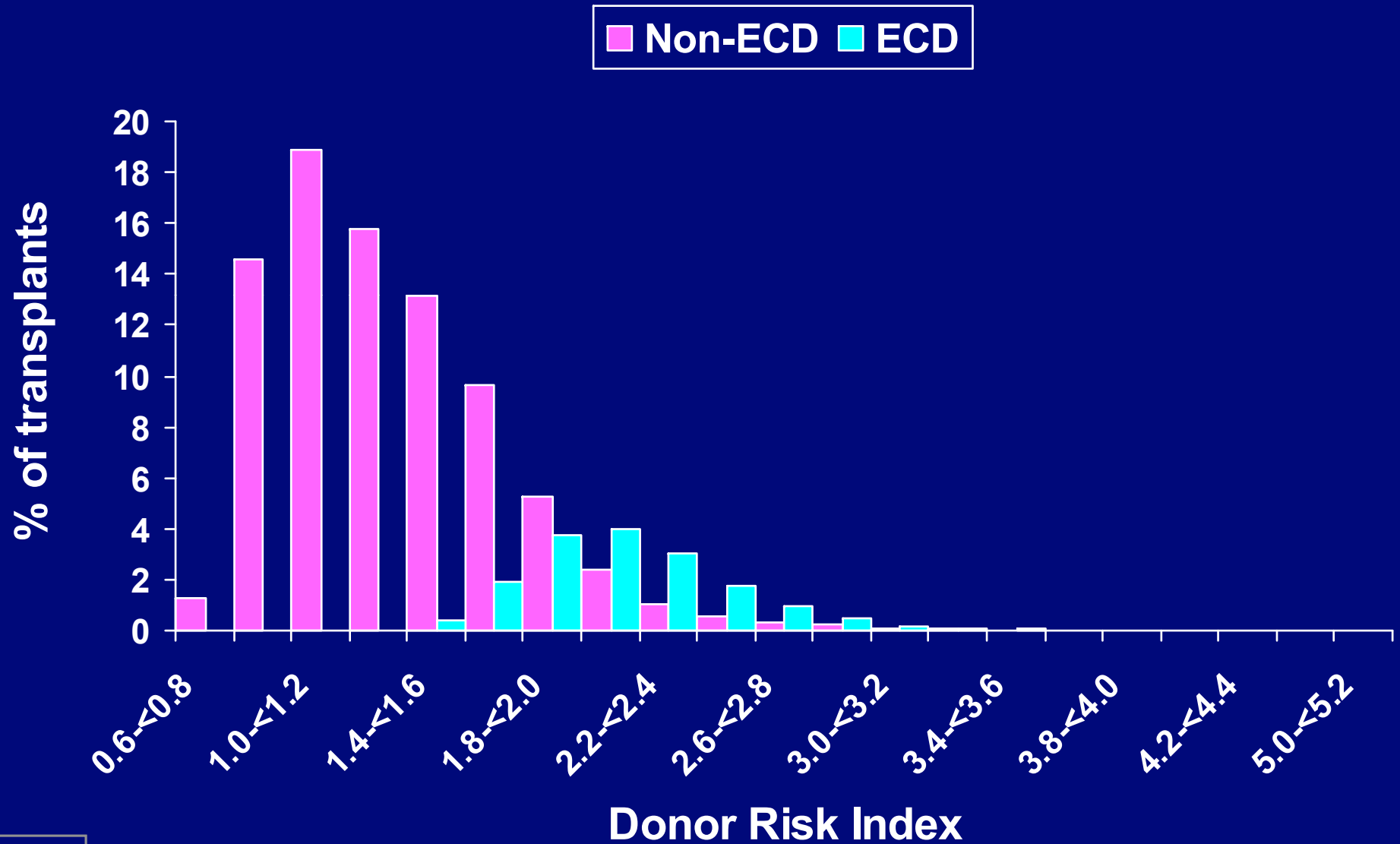
- **any candidate over 60 years of age,**
- **any diabetic candidate over 40 years of age,**
- **any candidate with failing vascular access,**
- **or any candidate whose expected waiting time exceeds their life expectancy.**

outcome of deliberations by the workgroup entitled

“Expanded Criteria Donor Kidneys: Who Should Get Them?”

“A National Conference To Analyze the Wait List for Kidney Transplantation”, Philadelphia, March 2002.

Histogram of KDRI by ECD Status



Mostly ECD Definition/Allocation has been a “Good System”

- There are some problems
 - Makes some pretty good kidneys look bad
 - Makes some marginal kidneys look good
 - Too many candidates/too few candidates
 - Since ECD kidneys are allocated by waiting time, candidates wait a long time for a less than optimal kidney
 - Candidates in “short waiting time DSAs” may benefit more from waiting for and accepting a SCD kidney
 - Higher rates of Delayed Graft Function (DGF) despite expedited placement

Risky Business: Considerations for Using ECD and DCD Kidneys

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October 29, 2009***

Alan Leichtman, MD

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