

# Kidney Transplant Outcomes In Elderly Patients

Simin Goral MD

University of Pennsylvania Medical Center  
Philadelphia, Pennsylvania

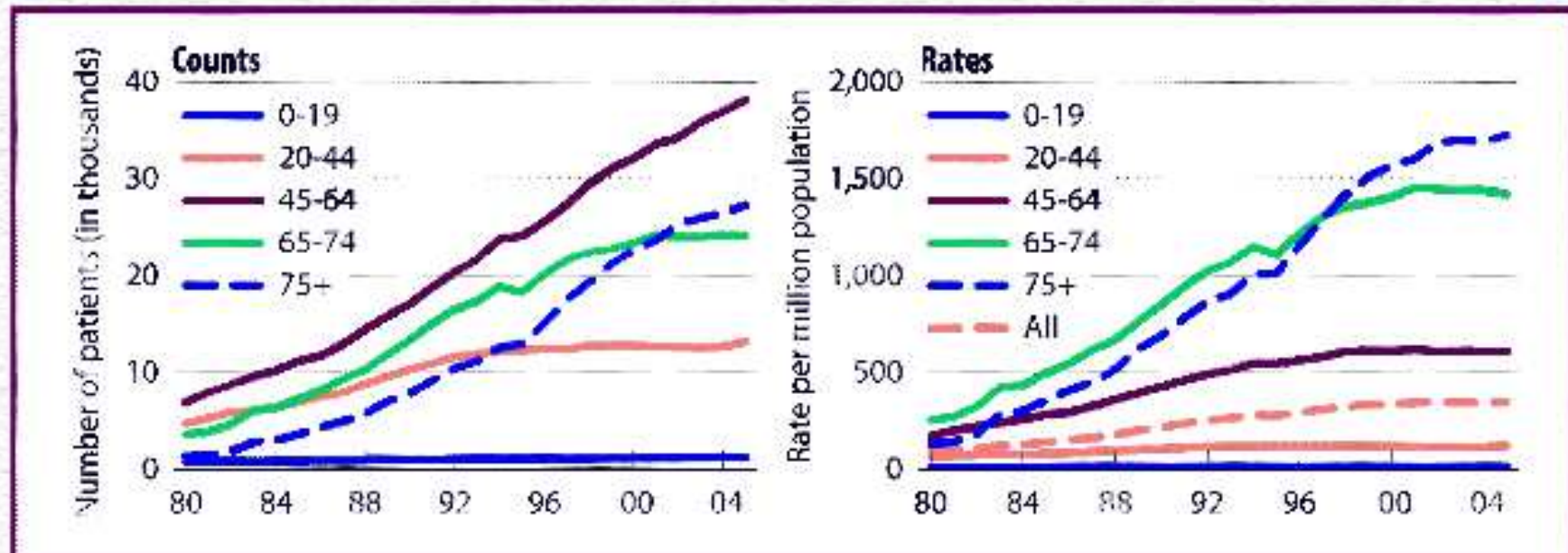
# Case Discussion

- 70 year old Asian male, neuropsychiatrist, works full time
- ESRD due to FSGS, BMI 20.4
- HTN, CABGx5 vessel 10 years ago, on PD for 3 months, blood transfusion+
- Prostate cancer: diagnosed 8 months ago, Gleason score 7, treated with cryoablation, most recent PSA is less than 0.1
- PRA: weakly positive

# ESRD in the US

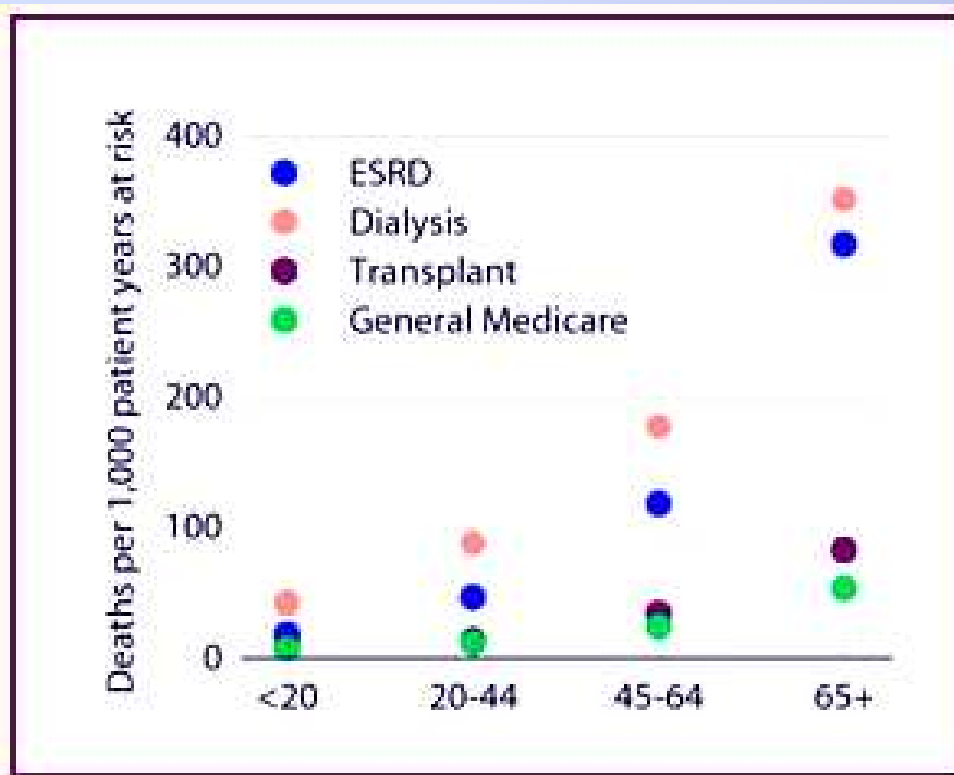
- More than 106,000 new patients began therapy for ESRD in 2005; the median age 64.6.
- Prevalent dialysis population 341,000
- Fastest growth is among patients **age 45-64**, but rising more quickly among those **age 65 and older**
- By 2020: incident population 150,000, prevalent population 800,000, and dialysis population 534,000

# Incident ESRD Patients: Rates Adjusted for Gender and Race



USRDS 2007 Annual Data Report

# All Cause Mortality Rates by Age, 2005



- Age 65 or older: mortality rates are 6 times higher than in the general population
- For elderly patients on dialysis, 5-year survival is less than 30%
- The factors influencing survival: race, comorbid conditions such as HTN and DM, cardiovascular diseases, PVD, impairment of vision and ambulation

*2007 USRDS Annual Data Report*

# Kidney Transplantation

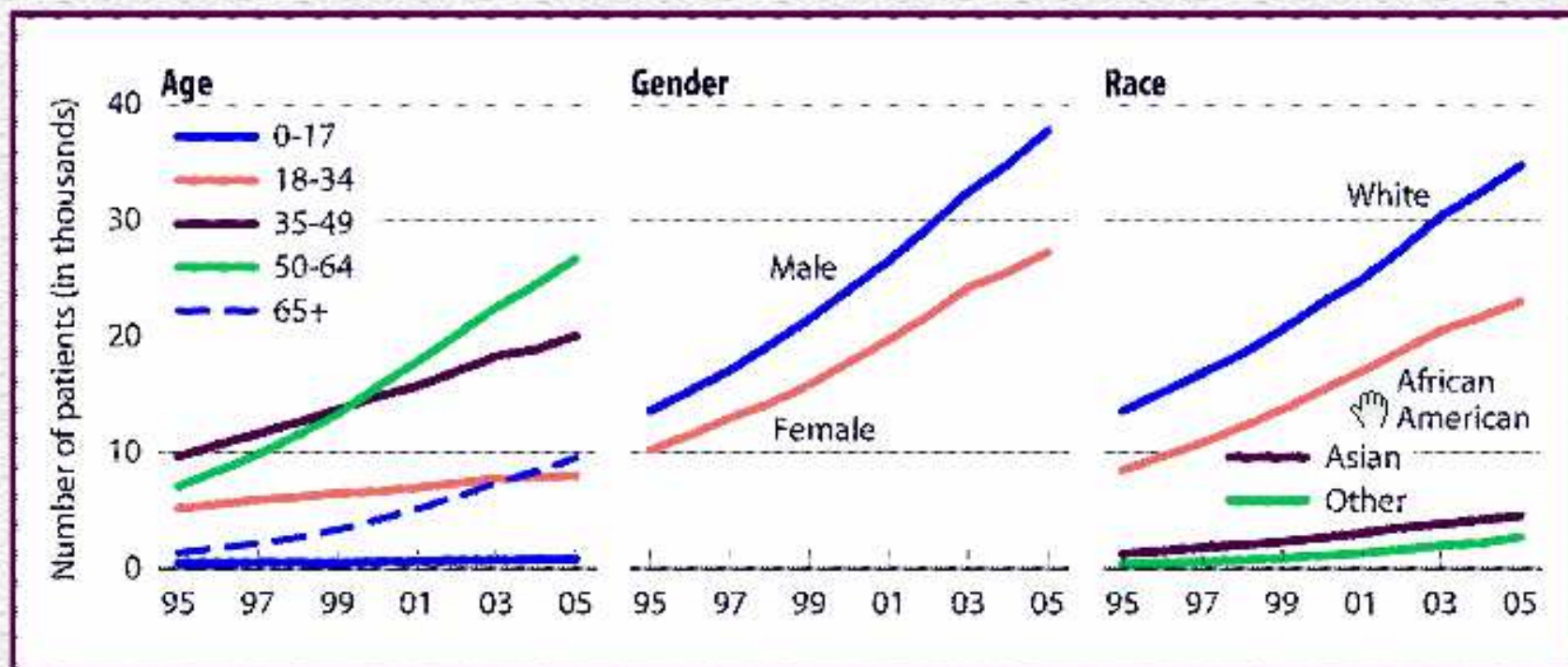
- The prevalent transplant population in 2005: 143,693
- The number of patients on the waiting list for deceased donor (DD) kidney transplant: 70,778-competing for approximately 11,000 kidneys

*USRDS 2007 Annual Data Report*

# Waiting List by Age

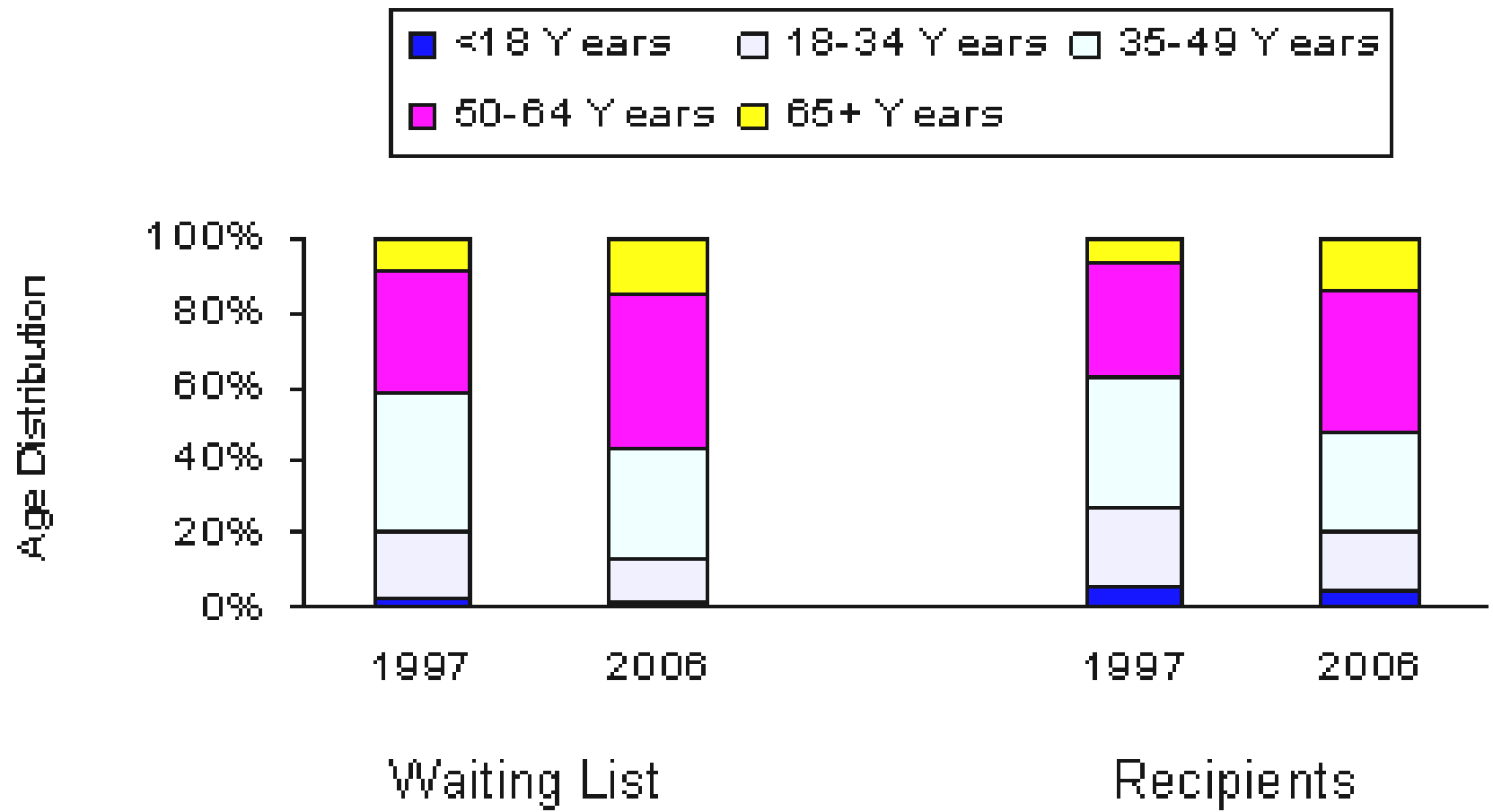
- At the end of 2006:
  - **59%** of all candidates were **50 yo** or older
  - **14%** were **65 yo or older**
  - In 1997: 43% >50 yo and 7% >65 yo
- Increase in the number of older patients on the waiting list

# Wait List Patient Counts



USRDS 2007 Annual Data Report

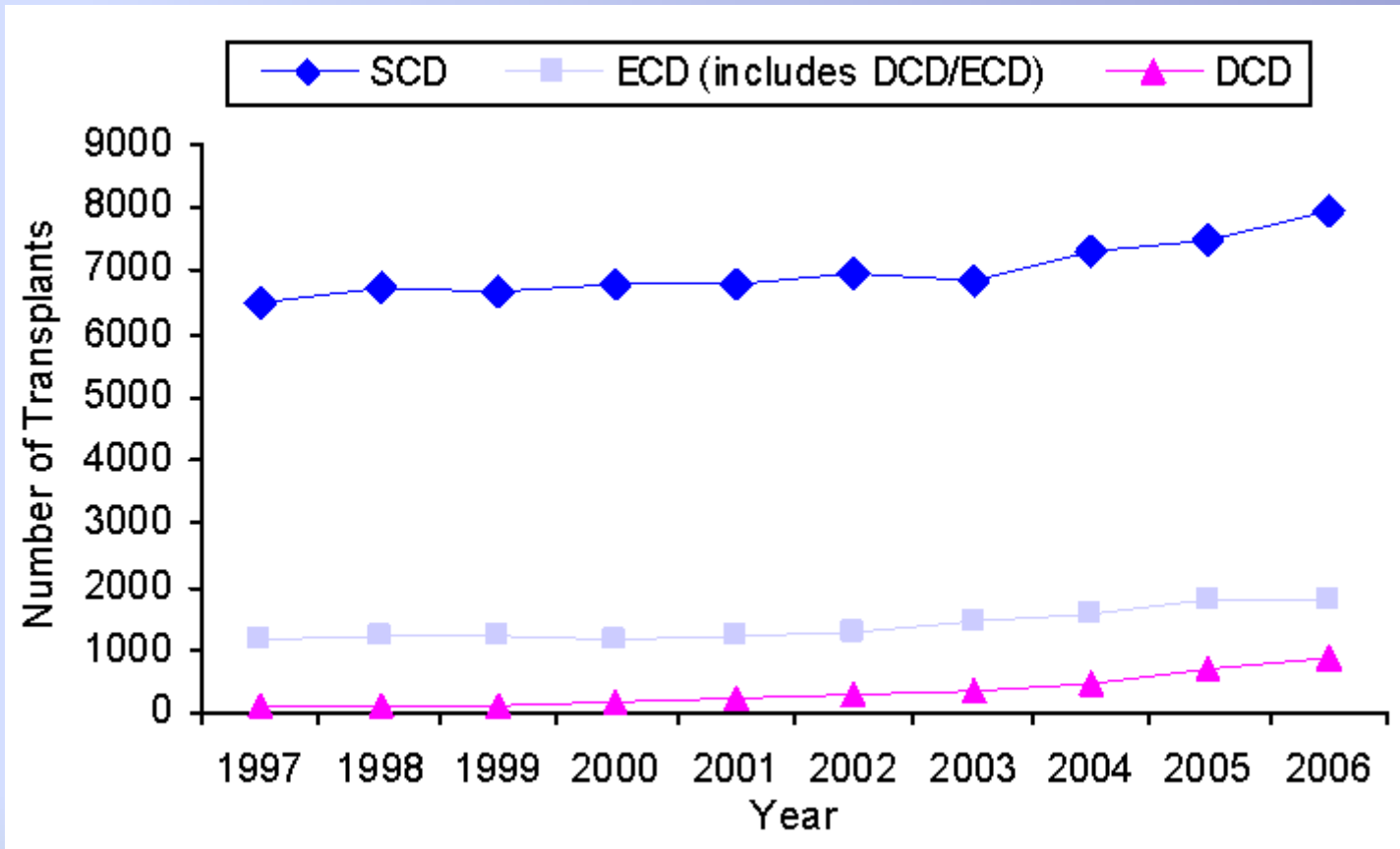




# Kidney Transplantation

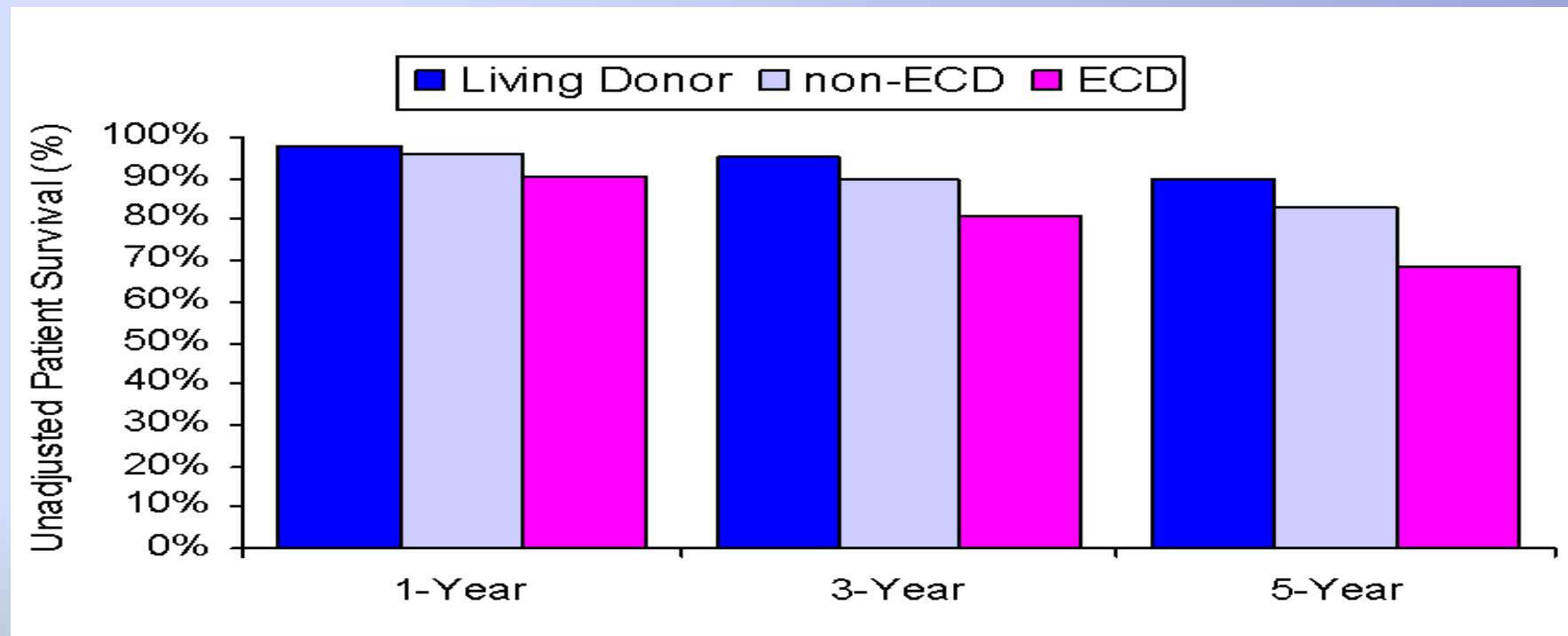
- The **best** treatment option for all patients with ESRD regardless of sex, race, age or cause of ESRD
  - Increase in life expectancy
  - Increase in quality of life
  - Decrease in healthcare costs
- No formal upper age limit
- The demand for kidney transplantation exceeds the supply of transplantable organs
- Waiting times are quite long

# DD Transplants: SCD, ECD, and DCD, 1997-2006

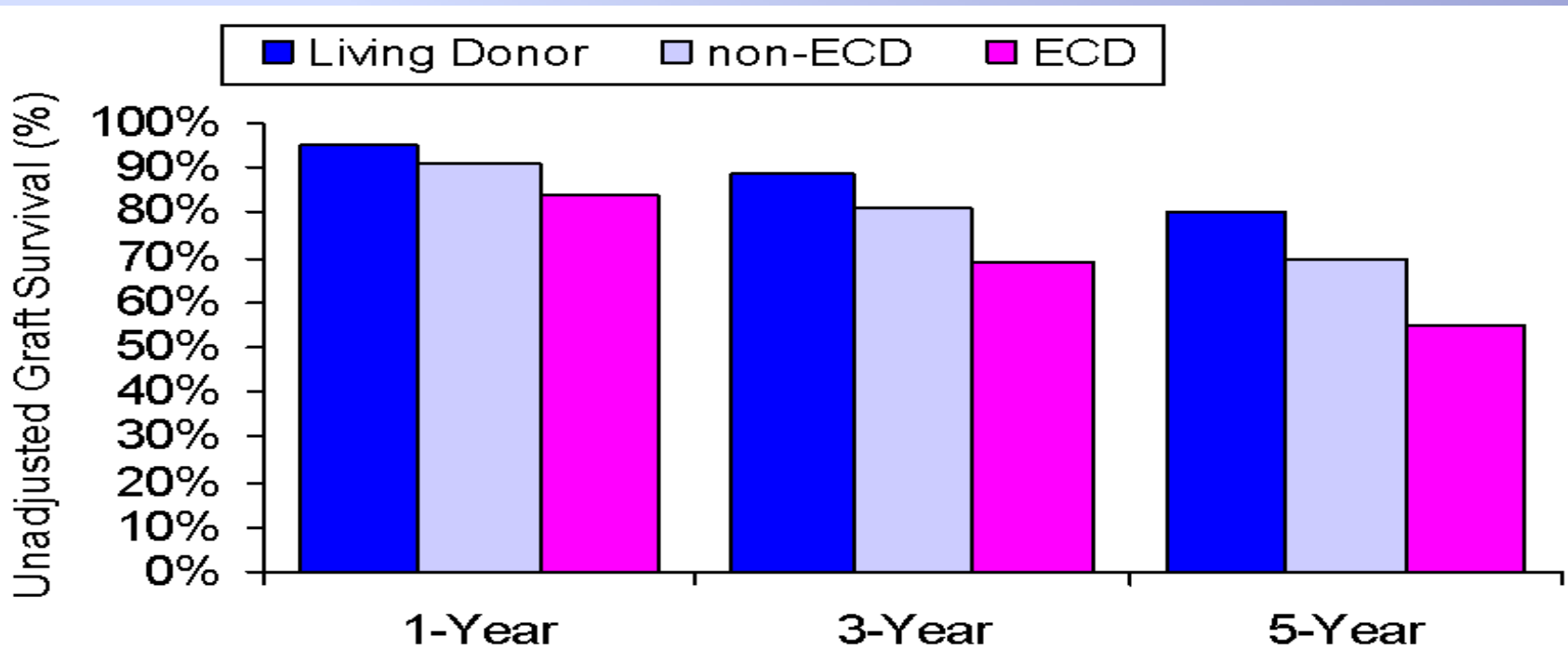


*2007 OPTN/SRTR Annual Report*

# Unadjusted 1-yr, 3-yr, and 5-yr Patient Survival , by Donor Type: 2000-2005



# Unadjusted 1-yr, 3-yr, and 5-yr Graft Survival , by Donor Type: 2000-2005



\*Death is included as an event.

# Transplantation in the Elderly: Concerns

- Shorter life expectancy-need to have a transplant early after wait-listing
- Shorter life expectancy-shorter graft survival
- Accelerated atherosclerosis leading to more cardiovascular events (myocardial infarction, stroke and peripheral vascular disease) and death
- Frail with multiple comorbid conditions

# Transplantation in the Elderly: Concerns

- Longer initial hospitalization
- Safety of chronic immunosuppression-HTN, salt and water retention, hyperlipidemia, infections and malignancy
- Use of ECD kidneys in this population: Is there increased risk of morbidity and mortality with ECD kidneys in the elderly?

# Survival Advantage

- 1991-1996: age older than 60 (on dialysis: 38.8%, on the waiting list: 15%, DD kidney tx: 13%)
- Mortality rate for patients on dialysis who were on the waiting list was about half of all patients on dialysis: selection of healthier patients for waiting list
- In pts 60-74 yo, the cumulative survival rate improved after the first year posttransplant, projected increase in the life span of 4 years and a decrease in the long-term risk of death of 61%
  - 60-64 yo: 4.3 years
  - 65-69 yo: 2.8 years
  - 70-74 yo: 1.0 year

*Wolfe RA, et al. NEJM 1999*



# Studies-Review

- 114 patients, age >60 (25 pts>70), 54% received ECD kidneys; **less waiting time**, mean f/u 27 months, **similar PS and GS** compared to younger groups
- 110 patients, age >60, **lower acute rejection rate** in the elderly group compared to younger pts (age 50-59 yo), median f/u 22 months, **more death in the elderly group-mainly due to infection, cardiovascular disease and malignancy**

*Moore PS, et al. Surgery 2007 (from Wake Forest University)*

*Mendonca HM, et al. Clin Transplant 2007 (from Sao Paulo, Brazil)*

# Studies-Review

- 301 patients-old group (age >70 yo) vs 513 patients-senior group (age 60-69 yo) vs 512 patients-control group (age 45-54 yo), transplanted 1990-2005, from Norway
- Less preemptive and LRD transplants in both elderly groups, older donors in the “old” group, **higher incidence of death with a functioning graft** (45%, 31%, 13%-control group)
- No difference in **5-year graft survival** when censored for death
- Leading reasons for death: **cardiovascular disease and infections**

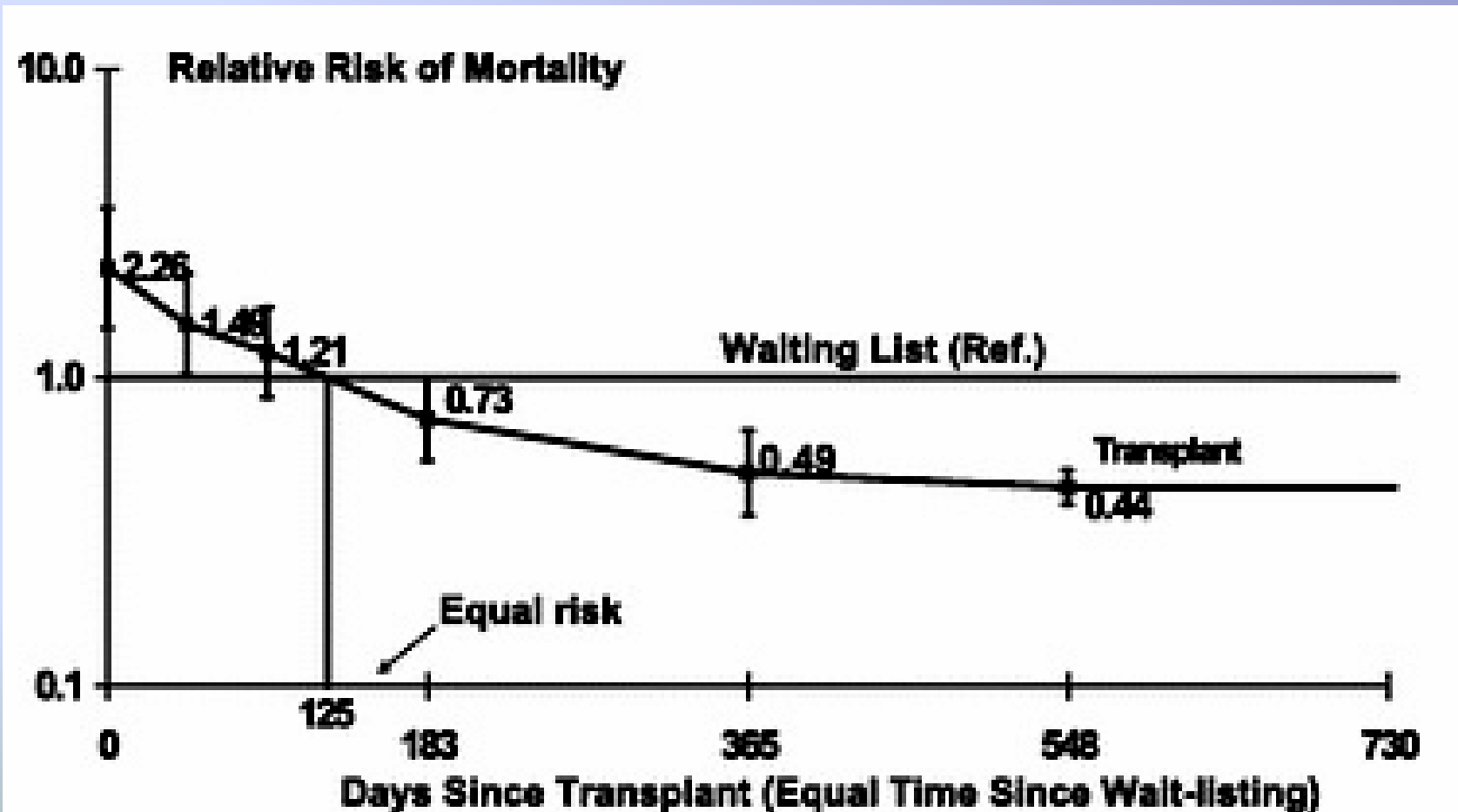
*Heldal K, et al. Nephrol Dial Transplant 2007*

# Studies-Review

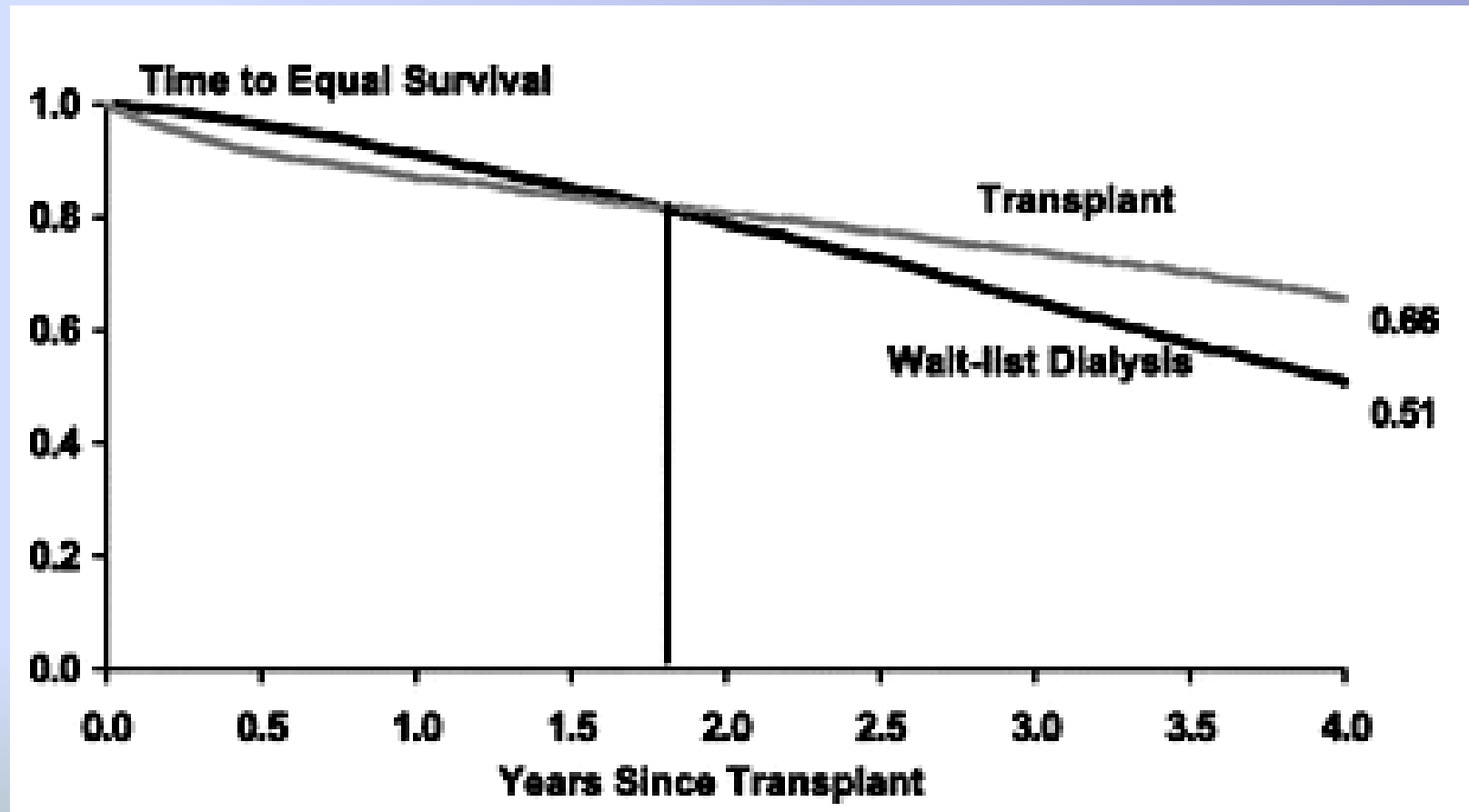
- SRTR data, observational: 5667 elderly pts (>70 and older at the time of listing) initially wait-listed from 1/1990 to 12/2004
  - 2078 pts (36.7%) received DD kidney tx (688-33%-had ECD kidneys)
  - 360 (6.4%) LRD tx
  - 1849 (32.6%) died without transplant
  - 1380 (24.4%) were alive but on the waiting list (last f/u 12/2005)
- They excluded pts who received a kidney tx before they started dialysis

*Rao P, et al. Transplantation 2007*

# Relative Risk of Death for 2078 DD Kidney Tx Recipients vs 5667 Wait-Listed Patients



# Cumulative Survival Curves (DD Recipients vs Wait-Listed Dialysis Patients)



*Rao P, et al. Transplantation 2007*

# Graft Survival Rates

**TABLE 3.** Unadjusted graft survival among deceased donor and living donor kidney transplant recipients at 1, 2, and 3 years

Transplant type	Transplant recipients		Graft survival, including death as an event (95% CI)		
	N	%	1 yr	2 yr	3 yr
Deceased donor	2078	85.2	80.9 (79.1–82.7)	73.9 (71.8–75.9)	66.9 (64.6–69.2)
Living donor	360	14.8	90.1 (86.6–93.4)	84.2 (80.2–88.5)	79.3 (74.6–84.4)

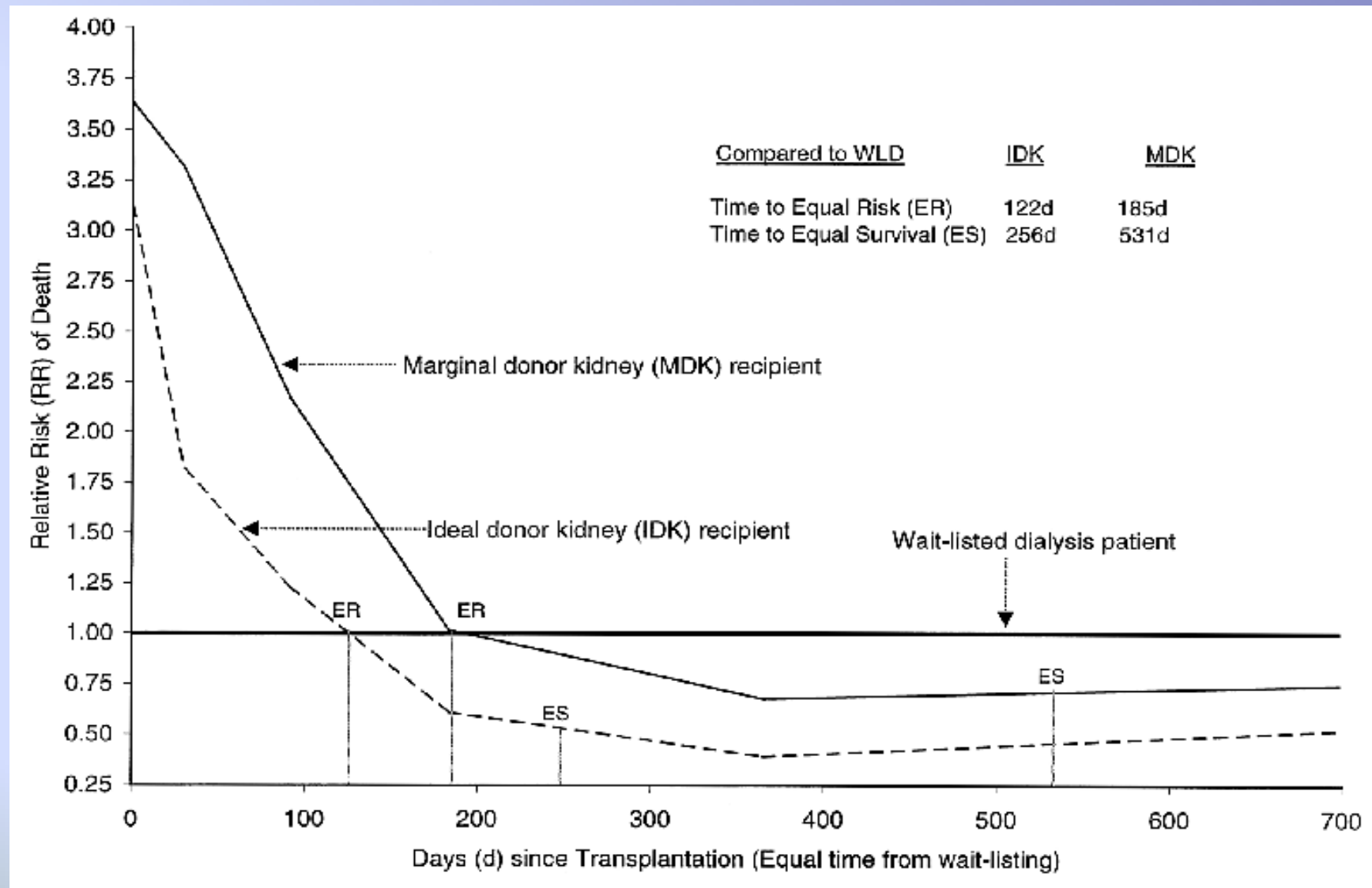
**TABLE 4.** Unadjusted death-censored graft survival among deceased donor and living donor kidney transplant recipients at 1, 2, and 3 years

Transplant type	Transplant recipients		Death-censored graft survival (95% CI)		
	N	%	1 yr	2 yr	3 yr
Deceased donor	2078	85.2	90.4 (89.1–91.7)	88.0 (86.5–89.6)	85.2 (83.5–87.1)
Living donor	360	14.8	95.8 (93.6–98.0)	93.6 (90.9–96.5)	93.1 (90.1–96.1)

# Studies-Review

- Largest study (pts>70 yo), BUT registry data
- The survival benefit of kidney transplantation in ESRD patients older than the age of 70, especially in patients with HTN and DM
- Transplantation was associated with a 41% lower risk of death-recipients with ECD kidneys had 25% lower mortality risk compared to waiting list patients on dialysis

*Rao P, et al. Transplantation 2007*



- Recipients of aged 55-64 yrs had the greatest survival benefit of 7.3 yrs with a marginal donor kidney (1992-1997) *Ojo AO, et al. J Am Soc Nephrol 2001*



# Use of ECD Kidneys in the Elderly

- Retrospective cohort study using SRTR, SS Death Master File and CMS data: 1/1995-12/2002
  - Long-term relative mortality risk was 17% lower for ECD recipients
  - Significant ECD survival benefit in patients older than 40 yrs, both sexes, non-Hispanics, all races, unsensitized patients and patients with DM or HTN
  - In OPOs with long median waiting times (>3.7 years), ECD recipients had a 27% lower risk of death
- ECD kidneys SHOULD be offered to candidates >40 yrs in OPOs with long waiting times and only to diabetics in OPOs with shorter waiting times

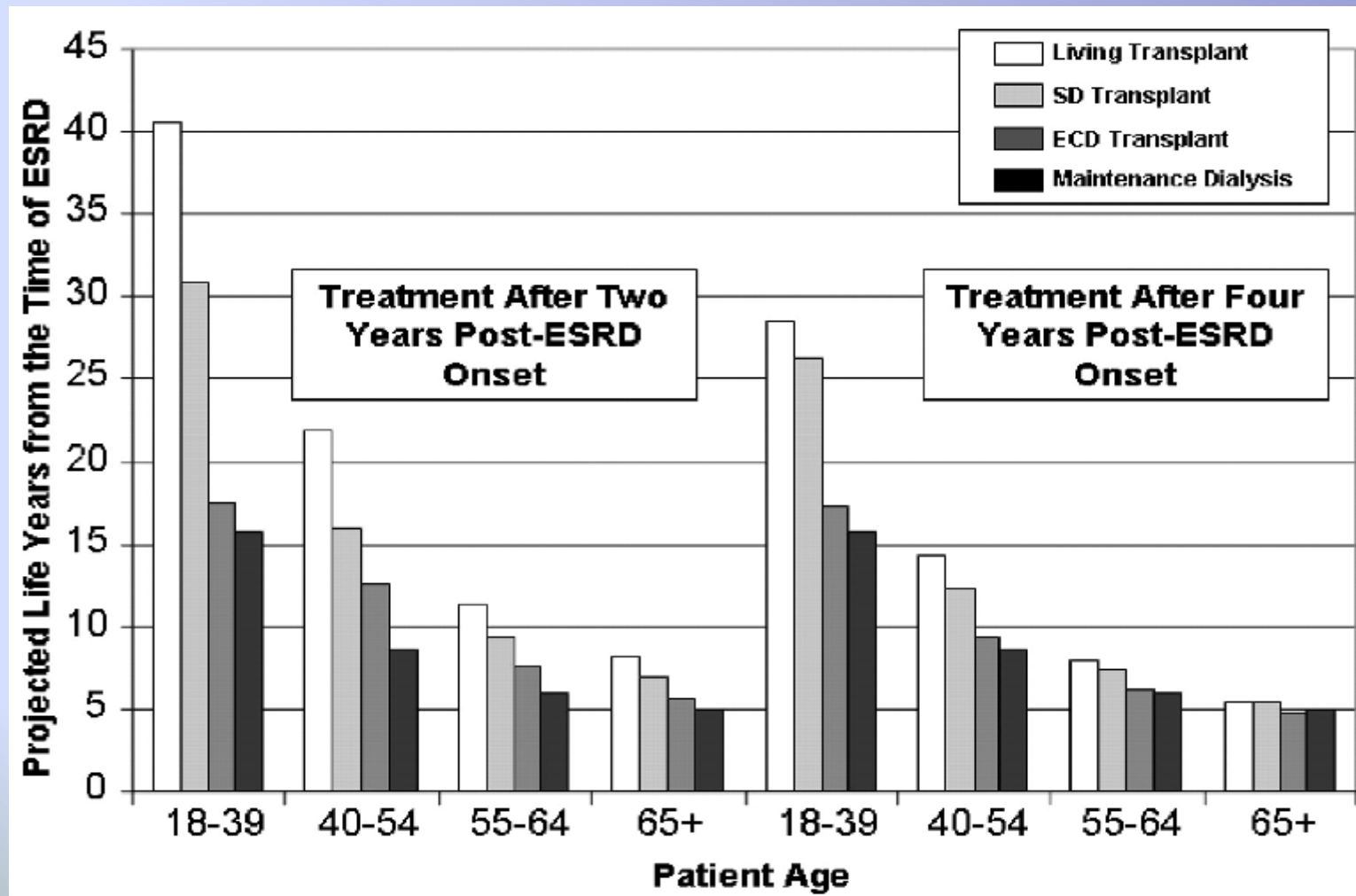
*Merion RM, et al. JAMA 2005*

# Marginal Kidneys-Shorter Waiting Time

- SRTR database, all adult solitary renal transplant candidates and recipients registered from 1995 and 2004
- Younger patients (age 18-39 yo): longer life expectancy with a living donation or an SCD kidney after 4 years on dialysis compared to an ECD kidney after 2 years on dialysis
- Older patients (>65 yo): life expectancies with an ECD kidney after 2 years on dialysis comparable to an SCD kidney or living donation after 4 years of dialysis

*Schold JD and Meier-Kriesche HU Clin J AM Soc Nephrol 2006*

# Projected Life Expectancy after ESRD onset by Recipient Age and Treatment Modality

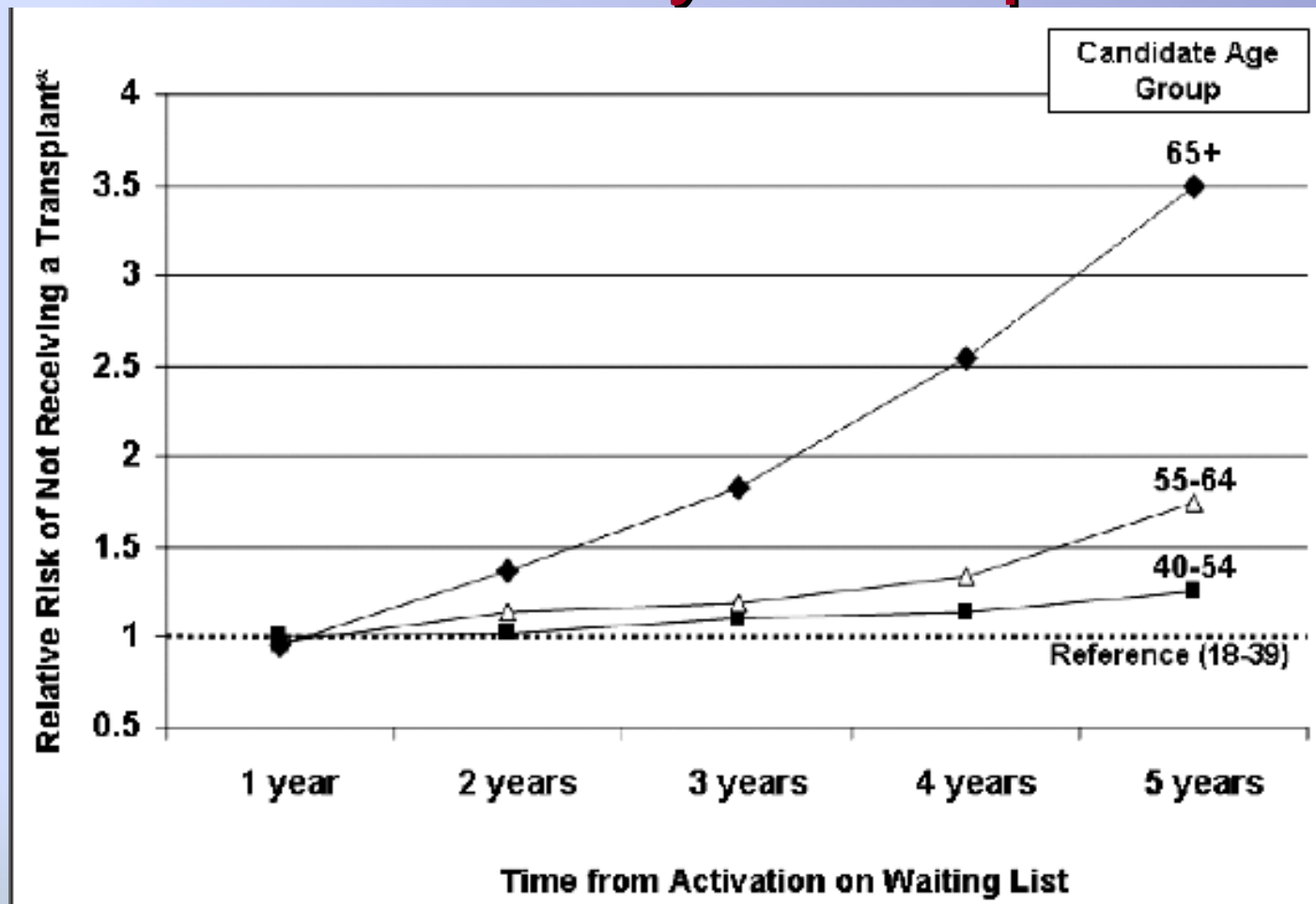


Schold JD and Meier-Kriesche HU Clin J AM Soc Nephrol 2006

# Marginal Kidneys-Shorter Waiting Time

- 47,5% of candidates were on the ECD donor list
- Increased age, black race, elevated PRA, and diagnoses of DM and HTN: increased likelihood of listing for ECD kidney
- As waiting time accumulated, the relative likelihood of a transplant for older candidates diminished

# Relative Risk of NOT Receiving a DD Kidney Transplant



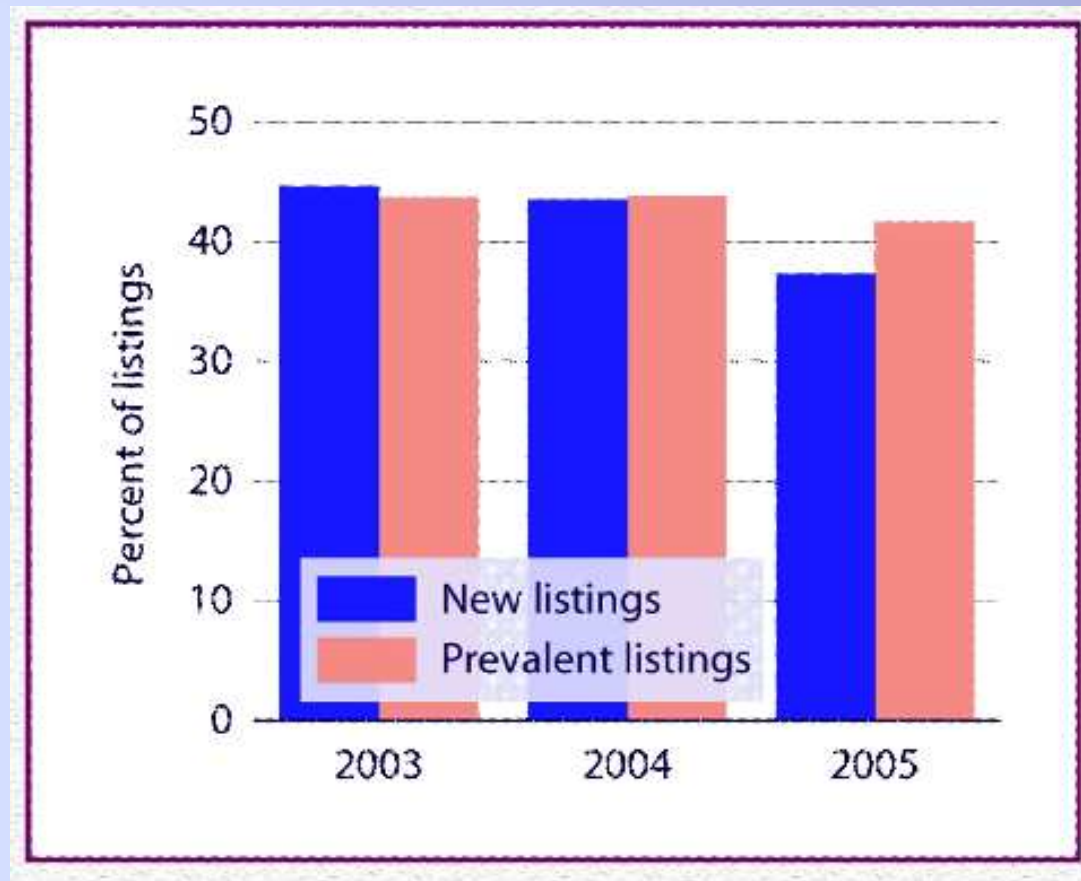
Schold JD and Meier-Kriesche HU Clin J AM Soc Nephrol 2006

# Studies-Review

- Among recipients >60 yo (n-315), patients survival was worse than for younger recipients but no differences in graft or death-censored graft survival
- Recipients >60 yo who received kidneys from donors >60 yo or older had worse outcomes compared to those receiving donor kidneys less than 60 years old

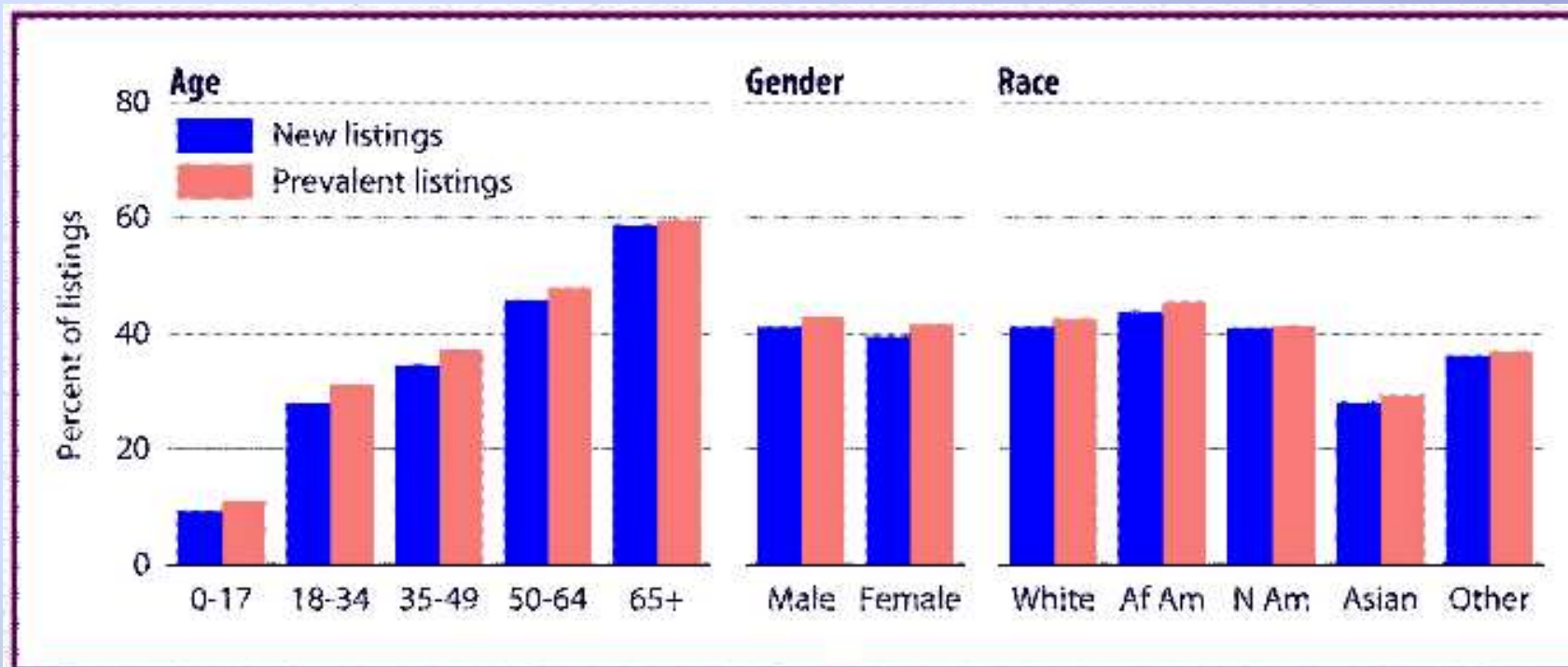
*Foley DP, et al. Clin Transpl 2005*

# Listings Willing to Accept an ECD Kidney



*USRDS 2007 Annual Data Report*

# Listings Willing to Accept an ECD Kidney by Age, 2004-2005



*USRDS 2007 Annual Data Report*

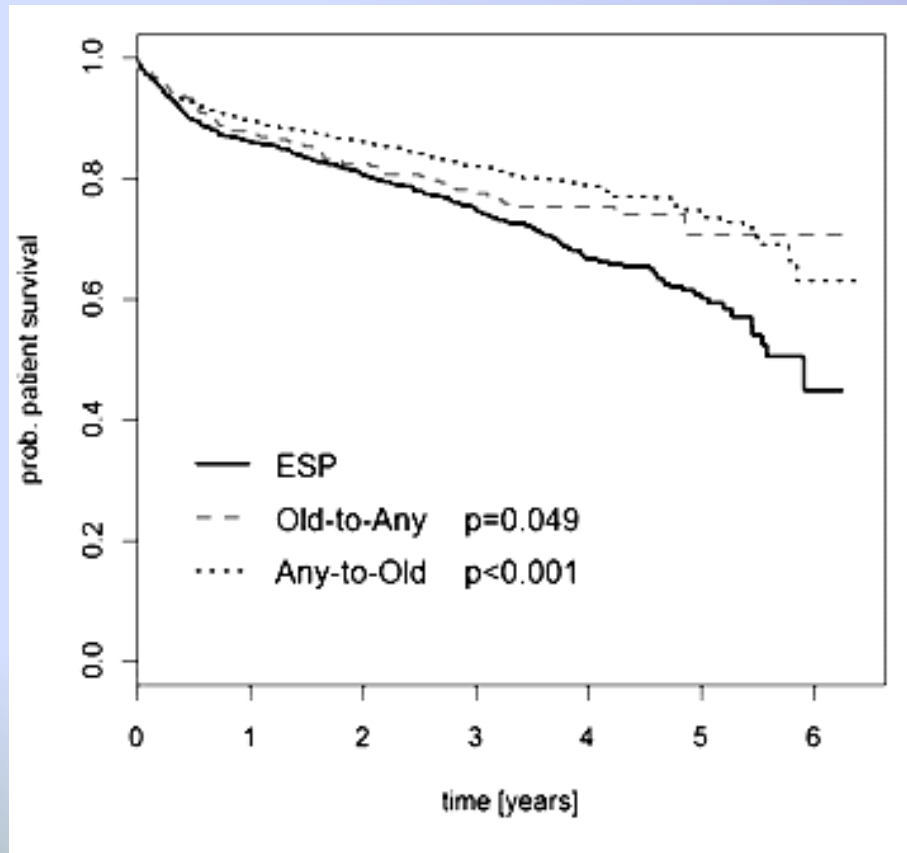


# Eurotransplant Senior Programme (ESP)

- Established in 1999, 7 countries
- Eurotransplant: 12,000 patients on dialysis and 4000 DD kidneys available each year
- To reduce the waiting time of elderly patients and to achieve a higher efficiency in the use of kidneys from elderly donors
- Matches are made between DD  $\geq 65$  yo and recipients  $\geq 65$  yo, PRA less than 5%
- Regional allocation based on waiting time and blood group

# Eurotransplant Senior Programme (ESP)

*Frei U, et al. Am J Transplant 2008*

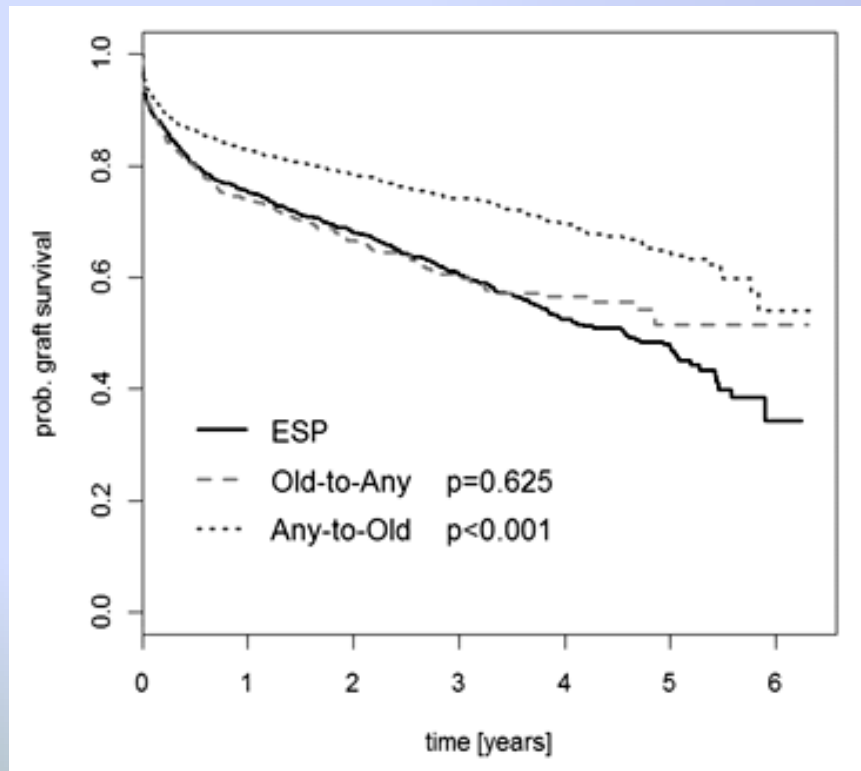


Patient Survival

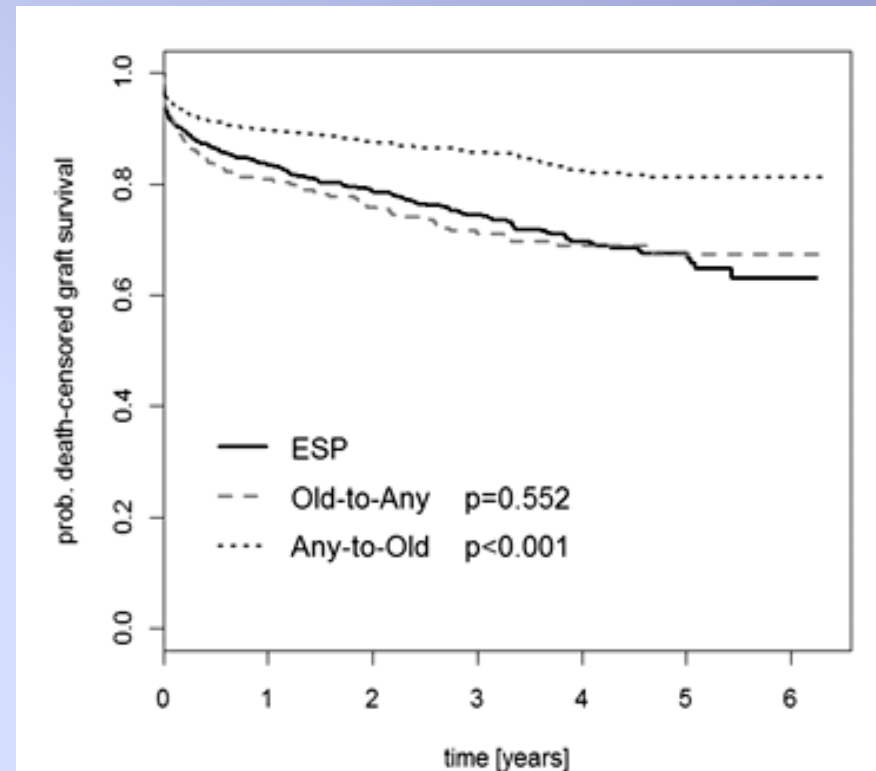
- 1406 patients >65 yo from 7 countries
- Mean donor age 70.2 yo
- Induction with T-cell depleting agents in 20.8% of patients
- Shorter cold ischemia time (mean CIT: 11.9 h vs >17h)

# Eurotransplant Senior Programme (ESP)

*Frei U, et al. Am J Transplant 2008*



Graft Survival



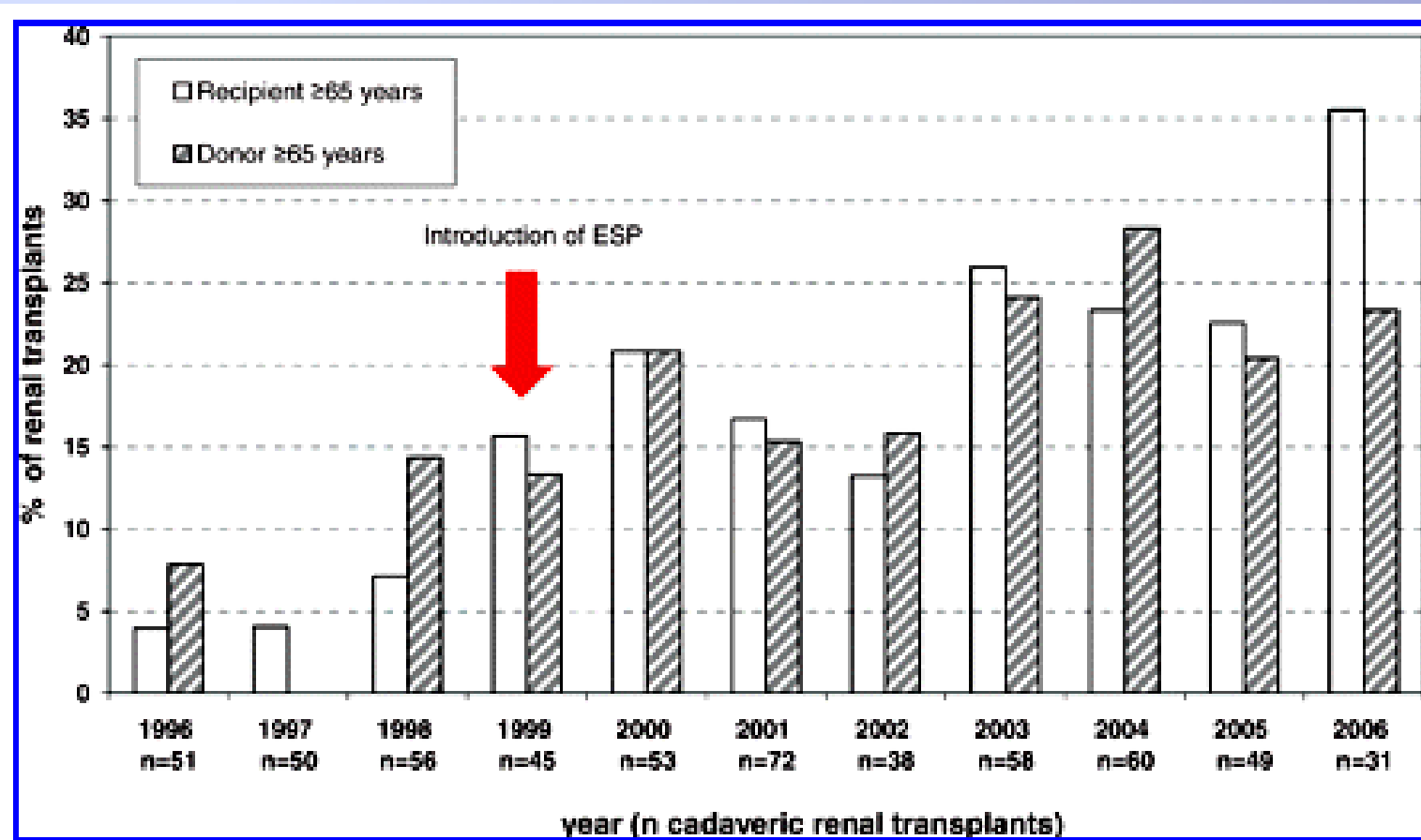
Death-censored Graft Survival

# Eurotransplant Senior Programme (ESP)

- 73 patients in ESP and 51 patients as controls (>60 years old)-Germany
- Induction therapy with basiliximab (80% vs 29%)
- Immunos: Csa (74%) or TAC (33%) + AZA (33-41%) or MMF (80% vs 61%) + steroids (99%)

*Bentas W, et al. Nephrol Dial Transplant 2008*

# Proportion of Transplant Recipients and Donors $\geq 65$ Years Old



*Bentas W, et al. Nephrol Dial Transplant 2008*

# Intraoperative Arterial Vascular Calcifications

	ESP <i>n</i> (%) patients	ETKAS <i>n</i> (%) patients	<i>P</i>
<b>Donor</b>			
Mild	18 (25)	5 (10)	0.003
Moderate	6 (8)	1 (2)	
Pronounced	2 (3)	0	
Total	26 (36)	6 (12)	
<b>Recipient</b>			
Mild	17 (23)	11 (22)	0.017
Moderate	13 (18)	0	
Pronounced	4 (6)	2 (4)	
Total	34 (47)	13 (26)	

# Eurotransplant Senior Programme (ESP)

- Less time on dialysis (42 mo vs 77 mo)
- Higher frequency of **arteriosclerosis** of both donors and recipients
- Prolonged mean **anastomosis time**
- More **postoperative complications** in the ESP group
- Similar GS and PS rates (up to 5 years)
- 13 patients died during follow-up of  $39.5 \pm 24$  mo, all with a functioning graft

# Kidney Transplant Outcomes in Elderly Patients: A Single Center Experience

- Retrospective analysis, 1/2000-4/2006
- **Group I:** patients  $\geq 60$  yr old at the time of transplant (n= 214)
- **Group II:** patients 40-59 yr old at the time of transplant (n= 436)
- **Group III:** patients  $\geq 60$  yr old at the time of listing who remained on the waiting list (n= 250)
- 34 pts  $>70$  yrs of age (18 of them ECD kidney recipients, 16 SCD recipients)
- Immuno: TAC 90% + MPA + steroids

*Sahin S, et al. ATC 2008 Toronto, abstract# 698*



	<b>Elderly ECD Recipients</b>		<b>Elderly SCD Recipients</b>		<b>Elderly on the waiting-list</b>	
	<b>n: 71</b>	<b>33%</b>	<b>n: 143</b>	<b>67%</b>	<b>n: 250</b>	<b>%</b>
<b>Age(yrs) (range)</b>	64.4(60-80)		63.9(60-78)		65 (60-90)	
<b>Gender (F/M)</b>	22/49		48/95		92/158	
<b>Ethnicity</b>						
Caucasian	45	63.4	94	65.7	130	52
African-American	22	31*	34	23.8*	100	40*
Asian	4	5.6	8	5.6	5	5
Other	x	x	7	4.9	15	6
<b>Etiology of ESRD</b>						
Diabetes**	24	33.8**	42	29.4**	101	40.4**
Hypertension	12	16.9	19	13.3	45	18
Glomerulonephritis	13	18.3	31	21.7	25	10
ADPKD	9	12.7	15	10.5	12	4.8
Others	13	18.3	36	25.1	67	26.8

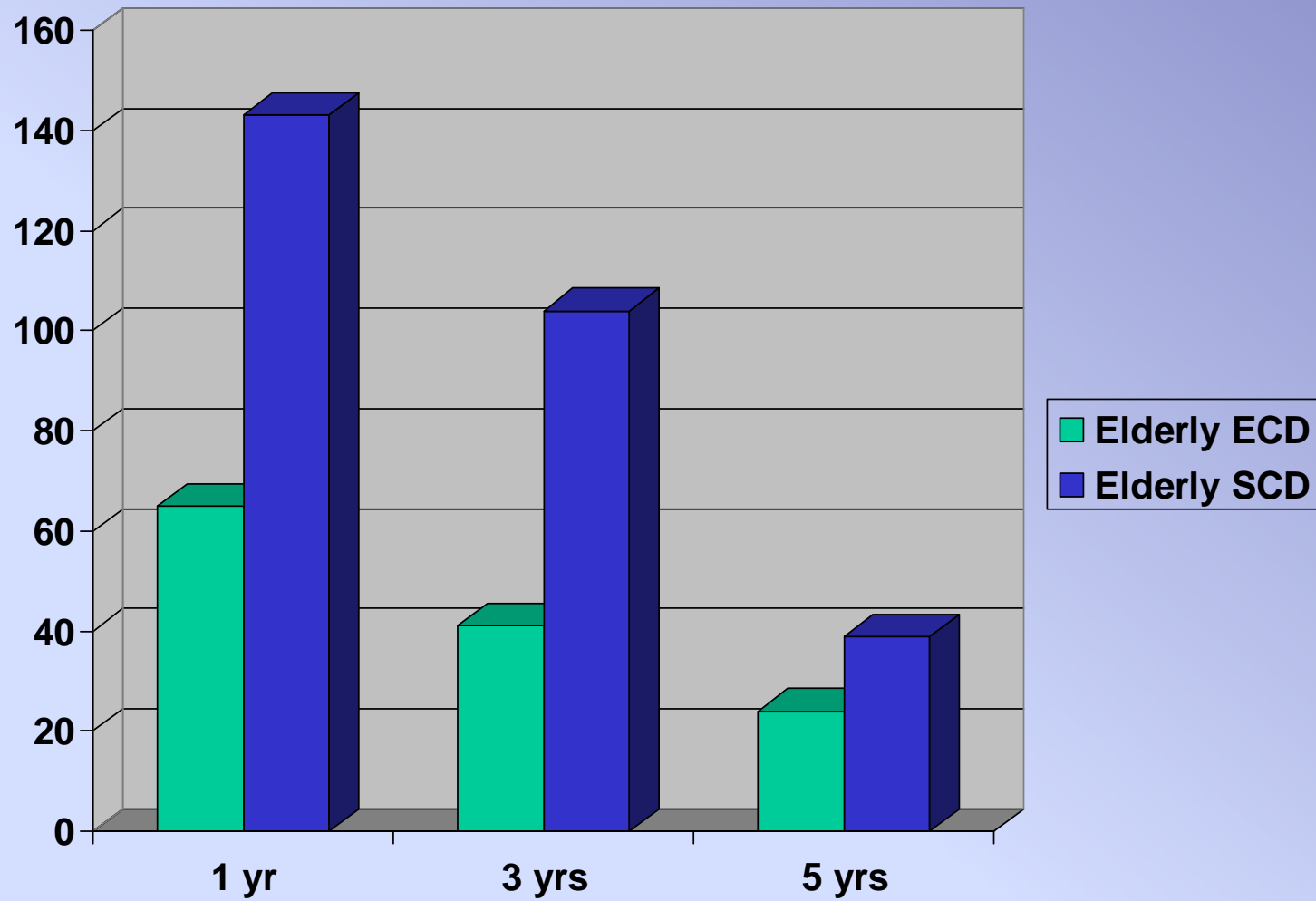
*Sahin, S, et al. ATC 2008 Toronto, abstract# 698*

	Elderly ECD Recipients		Elderly SCD Recipients	
	n: 71	%	n: 143	%
<b>Prior transplantation</b>	1	1.4	7	4.9
<b>PRA</b>				
<20	60	84.5	130	90.9
20-80	7	9.8	7	4.9
>80	4	5.7	6	4.2
<b>Waiting time (days)</b>	857*		1043.5*	
<b>BMI</b>	28.4		27.9	
<b>DGF*</b>	16	22.5**	18	12.6**
<b>Cold ischemia time (min)</b>	892		1010	
<b>Donor age**</b>	64.6*		39.3*	
<b>Induction protocol</b>	66	93	133	93

*Induction: majority rabbit anti-thymocyte globulin/few pts with basiliximab*

\*\* $p=0.03$ , \*  $p<0.001$  Less waiting time, more DGF, older donors in the ECD group

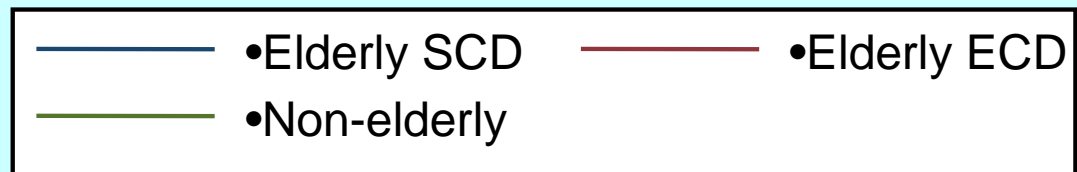
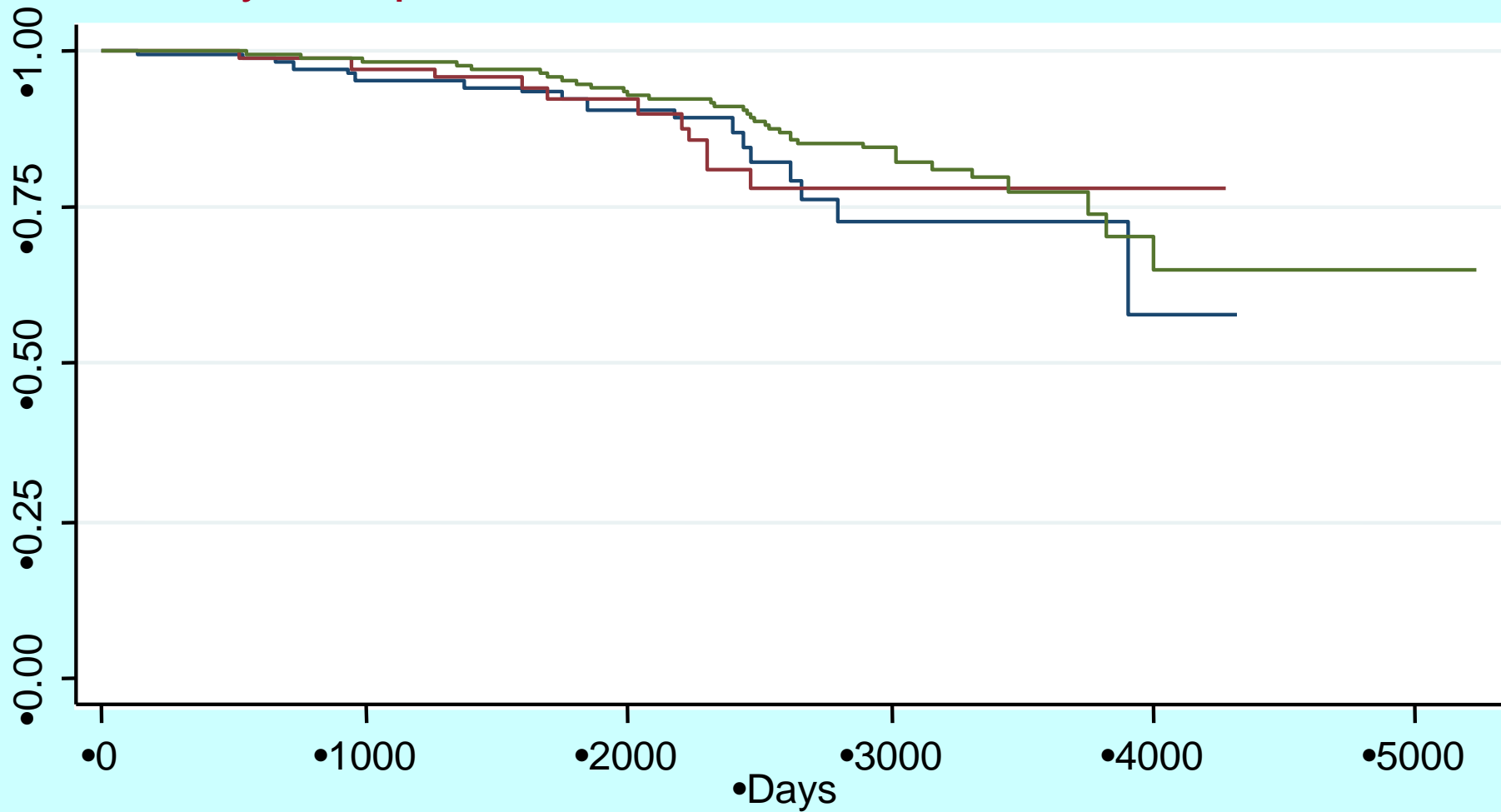
*Sahin S, et al. ATC 2008 Toronto, abstract# 698*



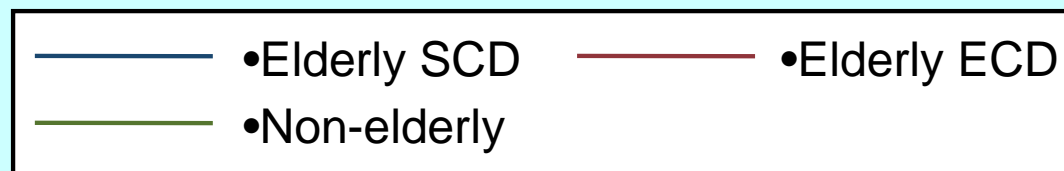
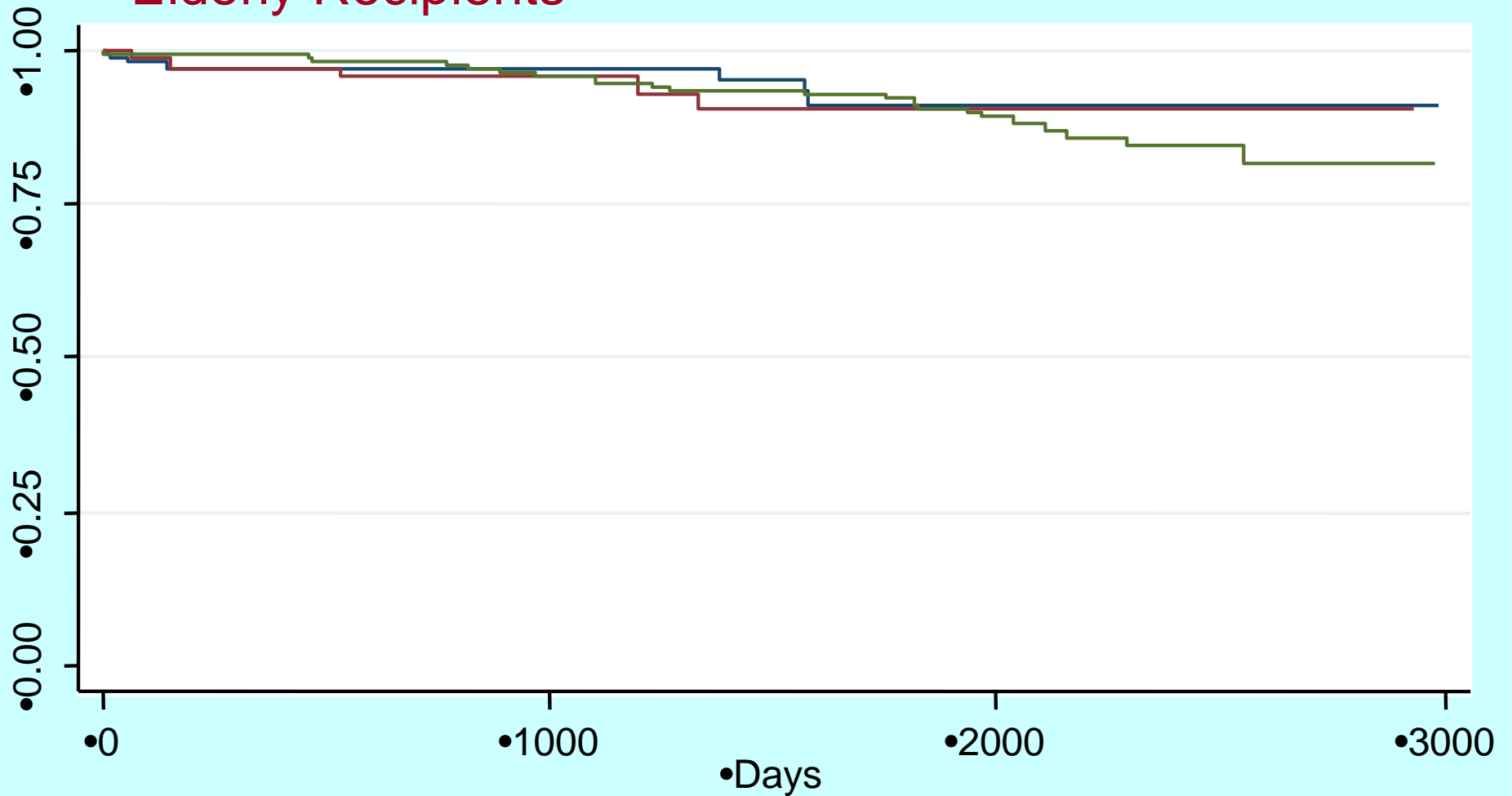
Elderly ECD    65 pts            41 pts            24 pts

Elderly SCD    143 pts            104 pts            39 pts

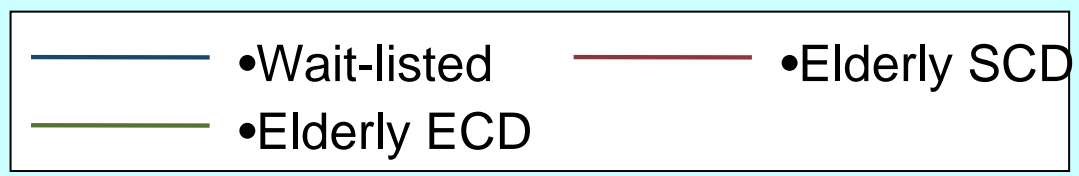
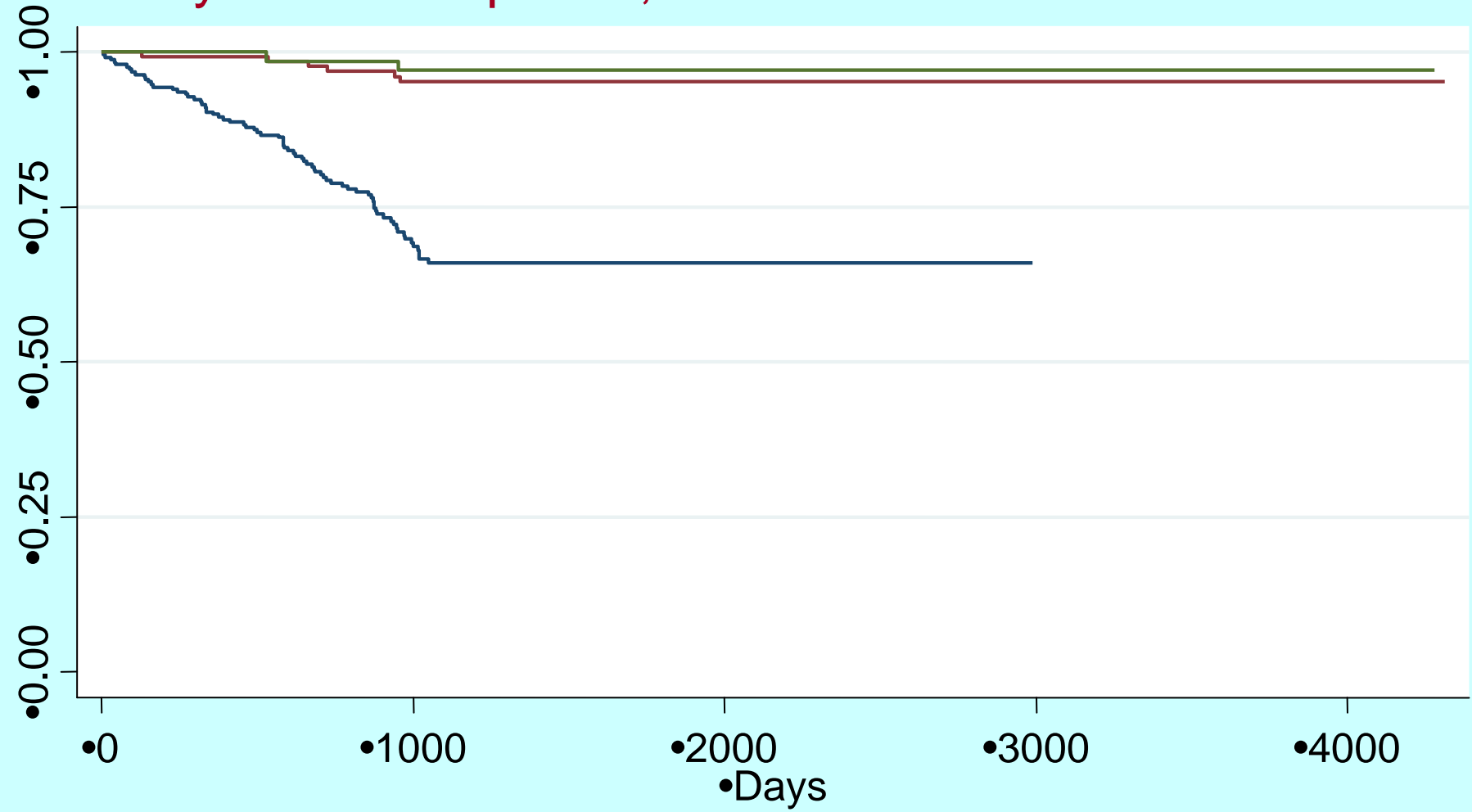
# Patient Survival for Elderly SCD, Elderly ECD and non-Elderly Recipients



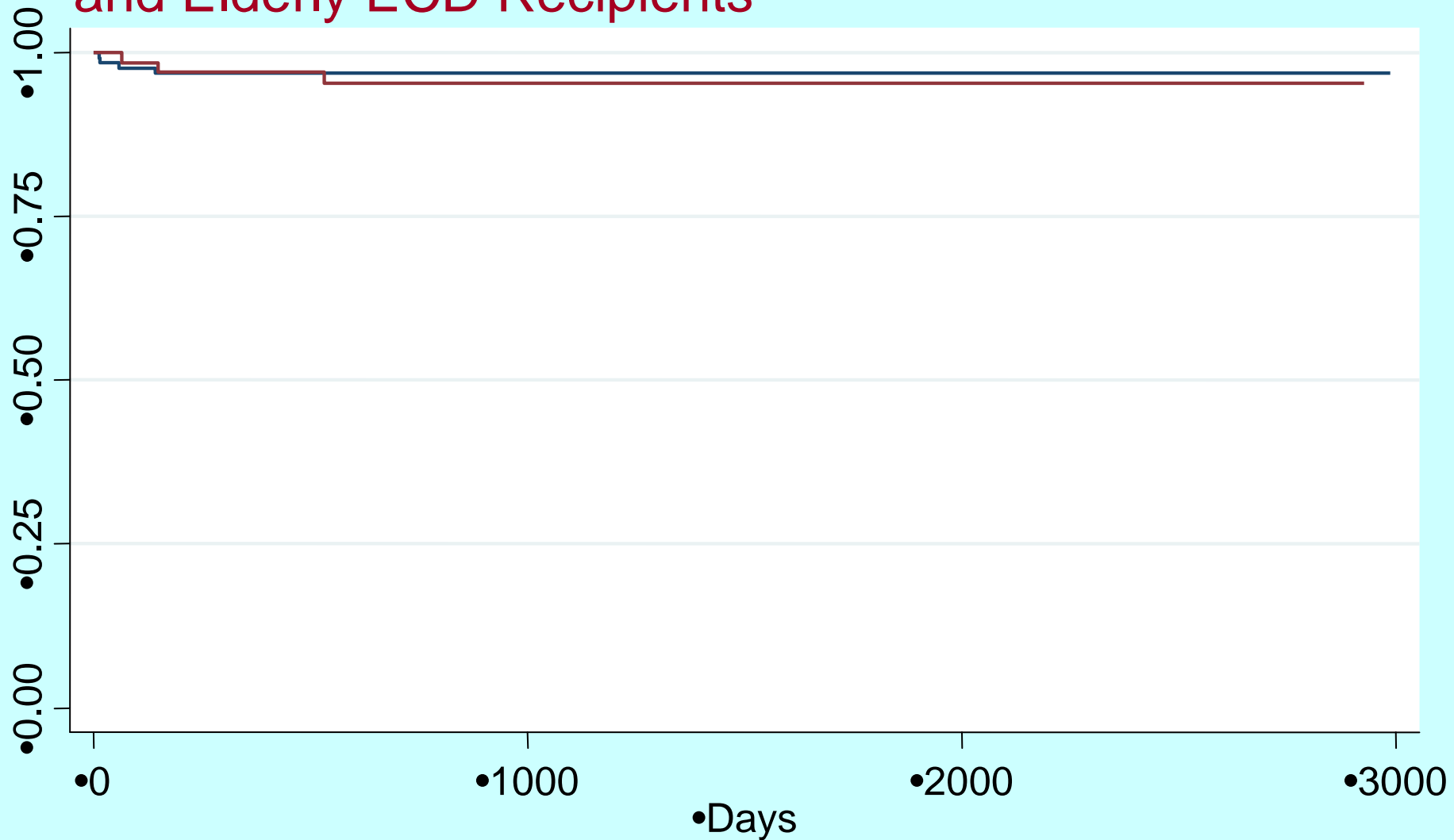
# Graft Survival in Elderly SCD, Elderly ECD, and non-Elderly Recipients



# Unadjusted Patient Survival for Elderly SCD Recipients, Elderly ECD Recipients, and Wait-Listed Candidates



# Unadjusted Graft Survival for Elderly SCD Recipients and Elderly ECD Recipients



— Elderly SCD — Elderly ECD

	<b>1-year PS</b>	<b>3-year PS</b>	<b>1-year GS</b>	<b>3-year GS</b>
<b>Elderly ECD</b>	100%	97%	94.1%	90%
<b>Elderly SCD</b>	99.2%	95%	96.7%	95%
<b>Young ECD+SCD</b>	99.7%	98.1%	98.8%	94.4%

Waiting List: 1-year PS 89.9%, 3-year PS 55.9%



<b>Death</b>	<b>Elderly wait-listed candidates (≥60 yr)</b>	<b>Elderly transplant recipients (≥60 yr)</b>	<b>Younger transplant recipients (40-59 yr)</b>
<b>Total deaths</b>	108 (43.2%)	34 (15.8%)	46 (10.5%)
<b>Cause of death</b>			
<b>Cardiovascular</b>	16	3	6
<b>Infection</b>	3	5	3
<b>Malignancy</b>	7	5	4
<b>Liver disease</b>	1		
<b>Cerebrovascular</b>	3	1	1
<b>Multisystem organ failure</b>	4		
<b>Respiratory failure</b>	4		
<b>Pulmonary emboli</b>	1		1
<b>Others</b>	Elective surgical procedure 1, bleeding from access 1		GI bleeding 1, trauma 1
<b>Unknown</b>	67	20	29

<b>Malignancy</b>	<b>Elderly ECD Recipients (n:71) 12 solid organ tm + 5 skin ca (23.9%)</b>	<b>Elderly SCD Recipients (n:143) 15 solid organ tm + 13 skin ca (19.6%)</b>
<b>Solid organ</b>		
<b>Lung</b>	3	4
<b>Prostate</b>	4	2
<b>RCC</b>	2	3
<b>GIS</b>	2	2
<b>Bladder</b>	1	-
<b>Endocrine</b>	-	1
<b>PTLD</b>	-	3
<b>Skin ca</b>		
<b>BCC</b>	3	8
<b>SCC</b>	2	5

# Elderly Transplants-Outcomes

- Acute rejection: 9 elderly patients (4%) vs 57 young patients (13%)
- Death:
  - **Group I:** 34 died (12 in the ECD group- 10 death with a functioning graft; 22 in the SCD group-18 death with a functioning graft)
  - **Group II:** 46 died-12 ECD, 9 DFG and 34 SCD-30 DFG
  - **Group III:** 108 in 250 patients (43.2%) died

*Sahin S, et al. ATC 2008 Toronto, abstract# 698*

# Conclusion-UPENN Experience

- In our center, patients >60 yo who received a kidney transplant (ECD and SCD) with our standard IS had excellent graft and patient survival rates comparable to 40-59 yo patients transplanted at the same time
- Our study demonstrated that elderly patients experienced significant survival benefit with kidney transplantation compared to patients remained on the waiting list
- Use of ECD kidneys in elderly patients did not appear to jeopardize outcomes
- Our data support the rising trend of accepting older aged tx candidates and suggest that these older pts can tolerate current IS therapy without high rate of serious adverse events

*Sahin S, et al. ATC 2008 Toronto, abstract# 698*

# Modifiable Factors Predicting Patient Survival in Elderly Recipients

- Multicenter, population-based, retrospective cohort study from Canada, >60 years or older, 1/1985 and 6/2000
- 256 patients (25% received kidneys from older donors->51 yo)
- Factors associated with PS: **active smoking at transplantation, high BMI, and long time on dialysis before transplantation**-all modifiable

*Cardinal H, et al. Kidney Int 2005*

- Pretransplant h/o **nonskin malignancy** and **peripheral vascular disease**, and **current smoking** history: risk factors for decreased GS and PS

*Doyle S, et al. Kidney Int 2000*

- Poor functional capacity predicts a poor outcome

*Yange AF. Et al. Clin Transpl 2006*

# Risks of Kidney Transplantation in Elderly Patients

- Risk for infection or chronic graft dysfunction-not decreased
- Higher mortality after transplantation, mostly due to CVD, infections and malignancy
- Increased likelihood of DGF, especially in ECD kidneys-ways to minimize DGF

# Benefits of Kidney Transplantation in Elderly Patients

- Best results with LRD transplants
- Survival advantage compared to patients on dialysis-positive in most studies though less than younger patients
- Quality of life benefits, better compliance than younger patients
- Lower immunosuppression requirements and less acute rejection
- Modifiable risk factors to improve results
- Less use of induction therapy with T-lymphocyte depleting agents-choice of induction-controversial-Is it necessary?

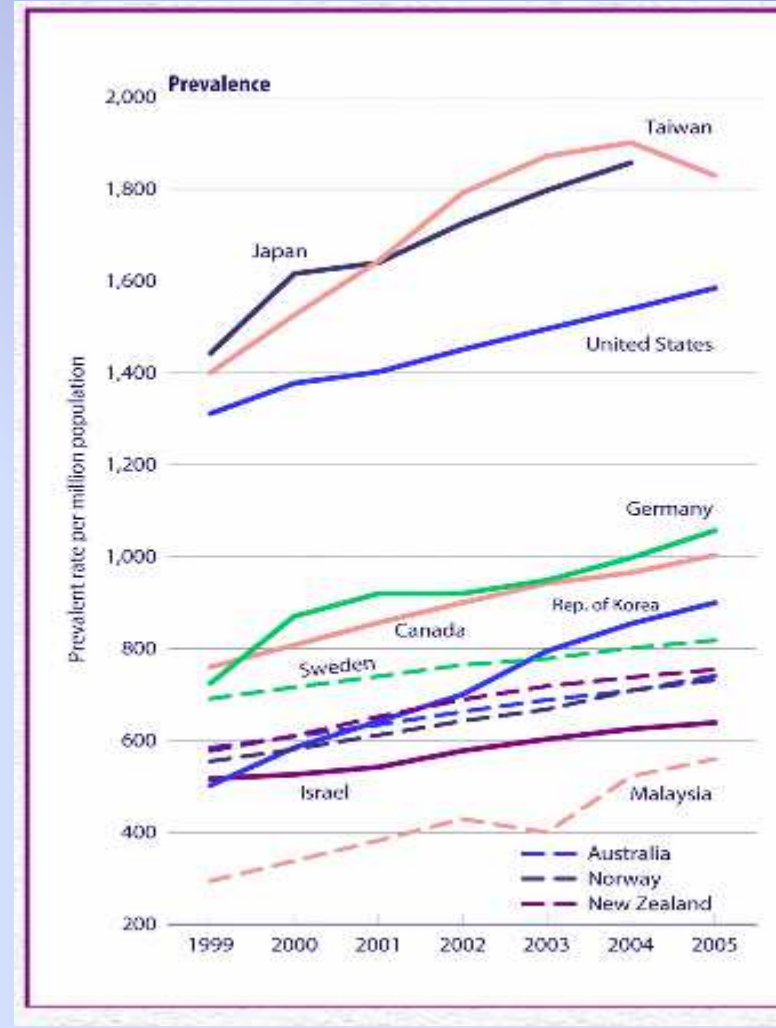
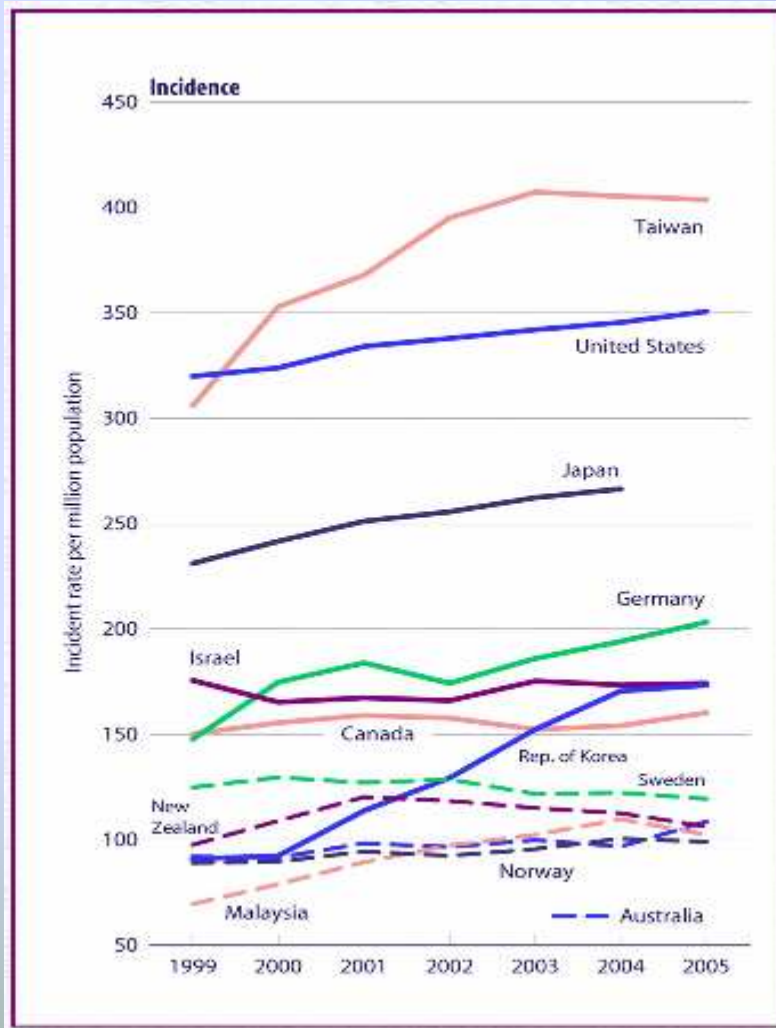
# Kidney Transplantation in Elderly Patients

- Majority of older patients are not candidates for kidney transplantation
- Patient selection: careful assessment of risk factors to select patients who would benefit the most
- Special considerations during evaluation: strict standard malignancy screening, evaluation of heart disease and PVD, assessment of cognitive abilities and capacity to ambulate
- “Old for old” concept and discussion of ECD kidney transplants in the elderly





# Incidence and Prevalence of ESRD per Million Population



# Transplant Rates (per Million Population), by Age, 2005

