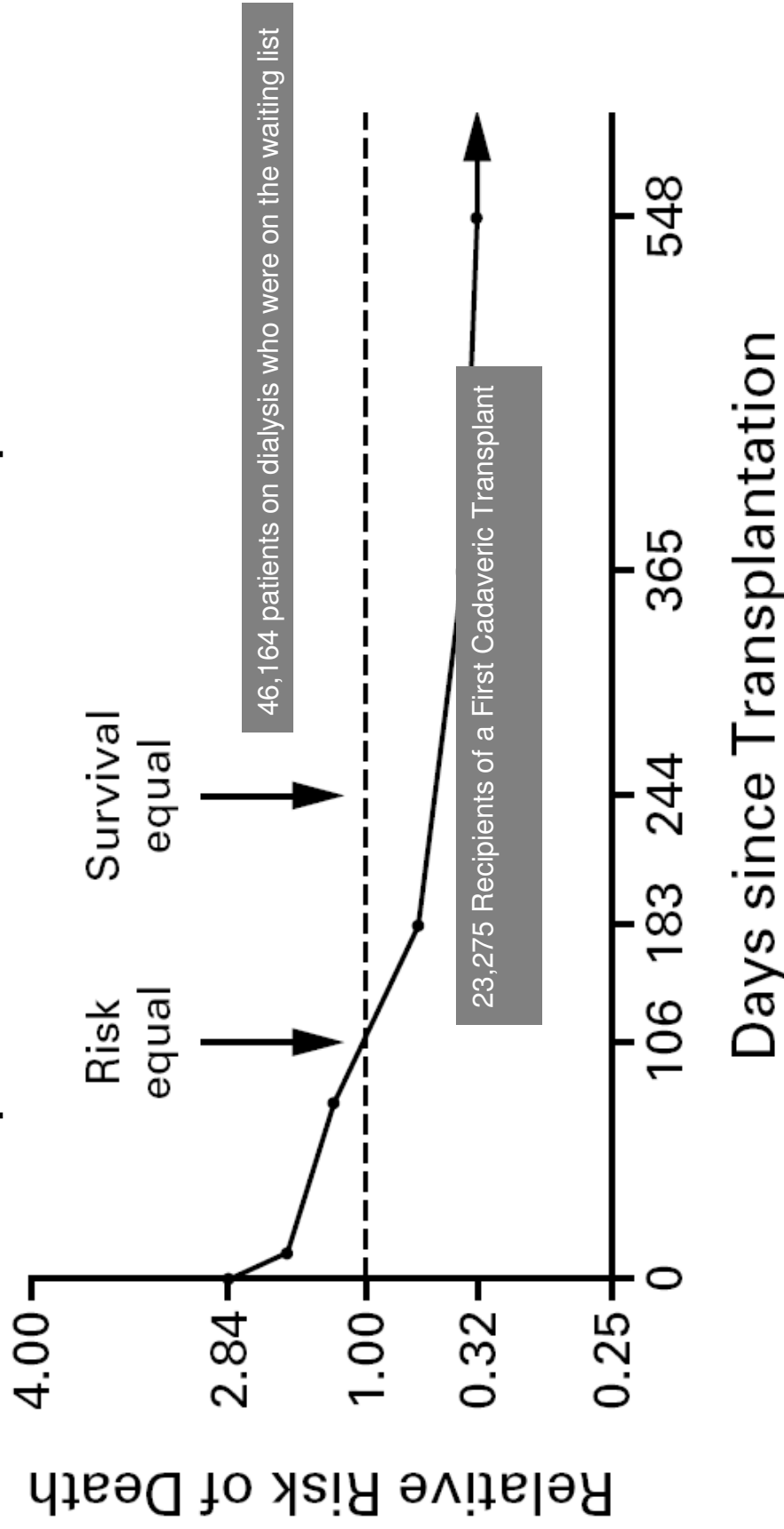# ¿La edad es un factor limitante para el acceso al trasplante?
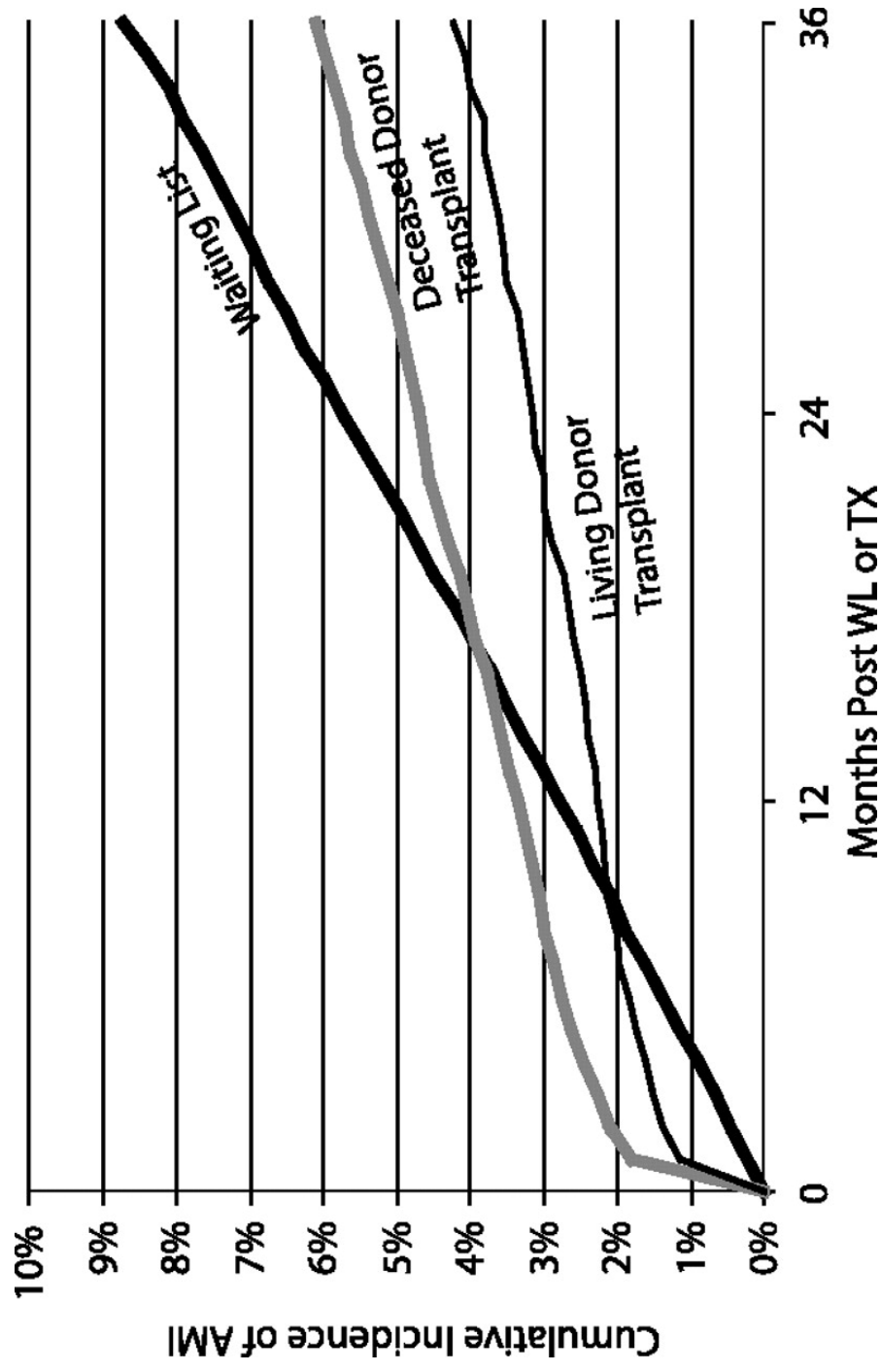
Federico Oppenheimer

Servei de Nefrologia I Trasplantament Renal
Hospital Clínic de Barcelona
oppen@clinic.ub.es

Más supervivencia con trasplante que con diálisis (de los pacientes en lista de espera)

Adjusted Relative Risk of Death among 23,275 Recipients of a First Cadaveric Transplant

46,164 patients on dialysis who were on the waiting list

23,275 Recipients of a First Cadaveric Transplant

Risk equal

Survival equal

Relative Risk of Death

4.00 2.84 1.00 0.32 0.25

Days since Transplantation

0 106 183 244 365 548

Cumulative (Kaplan-Meier) incidence of acute myocardial infarction (AMI) on the waiting list and after kidney transplantation

Waiting List

Deceased Donor Transplant

Living Donor Transplant

Cumulative Incidence of AMI

10%
9%
8%
7%
6%
5%
4%
3%
2%
1%
0%

0   12   24   36

Months Post WL or TX

Kasiske et al. J Am Soc Nephrol 2006

Outcome among Recipients of First Cadaveric Transplants, According to Characteristics at the Time of Initial Placement on the Waiting List

Group	Relative Risk 18 Mo after Transplantation (95% CI)†	P Value	Time at Which Risk of Death Equals That in Reference Group	Time at Which Likelihood of Survival Equals That in Reference Group	Projected Years of Life (in Reference Group) without Transplantation†‡	Projected Years of Life with Transplantation‡
			days after transplantation			
All recipients of first cadaveric transplants	0.32 (0.30–0.35)	<0.001	106	244	10	20
Age						
0–19 yr	0.33 (0.12–0.87)	0.03	3	5	26	39
20–39 yr	0.24 (0.20–0.29)	<0.001	11	57	14	31
40–59 yr	0.33 (0.29–0.37)	<0.001	95	251	11	22
60–74 yr	0.39 (0.33–0.47)	<0.001	148	369	6	10
Sex						
Male	0.34 (0.30–0.38)	<0.001	110	255	10	19
Female	0.30 (0.26–0.34)	<0.001	94	220	11	23
Race						
Native American	0.50 (0.27–0.96)	0.04	123	304	9	14
Asian	0.43 (0.25–0.75)	0.003	161	673	15	23
Black	0.52 (0.44–0.62)	<0.001	109	305	13	19
White	0.28 (0.25–0.30)	<0.001	100	220	9	19
Cause of end-stage renal disease						
Diabetes	0.27 (0.24–0.30)	<0.001	57	146	8	19
Glomerulonephritis	0.39 (0.31–0.48)	<0.001	130	360	11	18
Other	0.38 (0.33–0.43)	<0.001	137	353	12	20

Projected years of life for patients on dialysis and transplant recipients from the moment of listing for transplantation

All Patients	Years of Life on Dialysis	Years of Life with a Kidney Transplant
Male	5.84	17.19
Female	5.63	16.13
Primary renal disease	5.99	16.98
Glomerulonephritis	6.37	17.40
Interstitial nephritis	8.90	21.31
Multisystem disease	5.39	14.16
Diabetes	2.92	8.60
Other	5.36	12.27
Age, yr		
18 to 34	27.22	41.50
35 to 49	6.71	18.03
50 to 59	5.12	11.18
60 to 64	4.32	7.84
≥65	3.69	7.60

¿Existe un límite de edad para el trasplante?

Transplantation versus haemodialysis in elderly patients

Table 2. Multivariate analysis of survival (Cox regression)

	n	Univariate risk	Multivariate risk	P value
Group				
HD	369	1	1	–
Tx	108	0.47	0,51	0.02
Sex				
Males	290	1	1	–
Females	187	0.59	0.57	0.006
Age group				
55–59	210	1	1	–
60–64	187	1.19	1.07	0.75
65–70	80	1.88	1.87	0.013
FAD				
Normal	256	1	1	–
Limited	207	1.32	1.32	0.15
Special care	14	3.51	3.71	0.0015
CV				
Without	416	1	1	–
With	61	1.49	1.33	0.30

FAD, functional autonomy degree; CV, ischaemic heart disease, cardiomyopathy, cardiac arrythmia or stroke.

Pacientes Registro Catalán
Inicio tto. 1984 – 1993
Edad 55-70 años al inicio tto.
Pacientes en lista espera
Nefropatías estándar

- 395 pacientes HD
- 157 pacientes Tx

Mejor supervivencia Tx
después del 2º año

Supervivencia similar en
grupo de edad 65-70 años:
   A 5 años: HD 67%
                  Tx 66%

¿Existe un límite de edad para el trasplante?

Renal Transplantation in Elderly Patients Older Than 70 Years of Age: Results From the Scientific Registry of Transplant Recipients
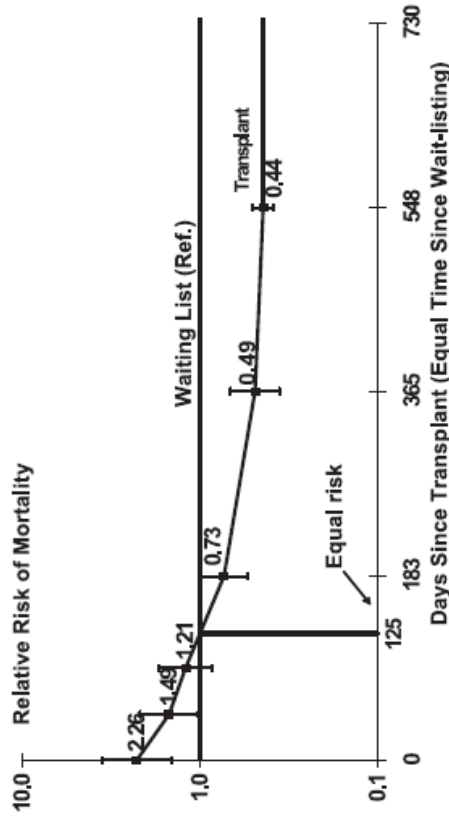

FIGURE 1. Mortality RR (95% CI) for 2078 first deceased donor kidney transplant recipients versus 5667 wait-listed dialysis patients older than 70 years of age.
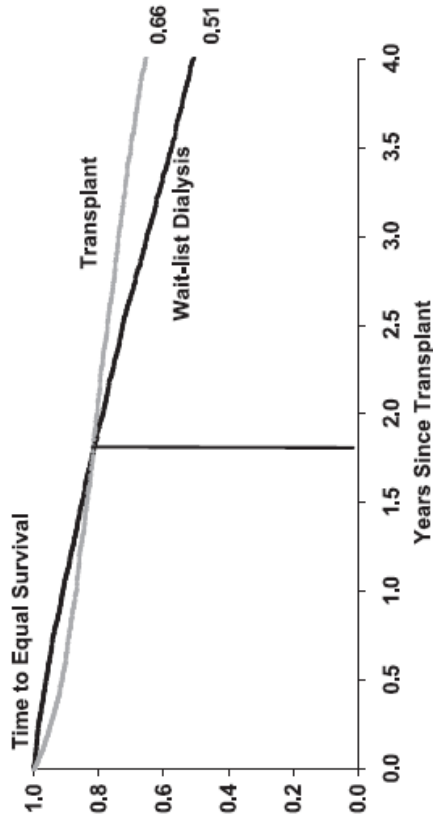

FIGURE 2. Cumulative survival curves for elderly deceased donor transplant recipients and elderly wait-listed dialysis patients.
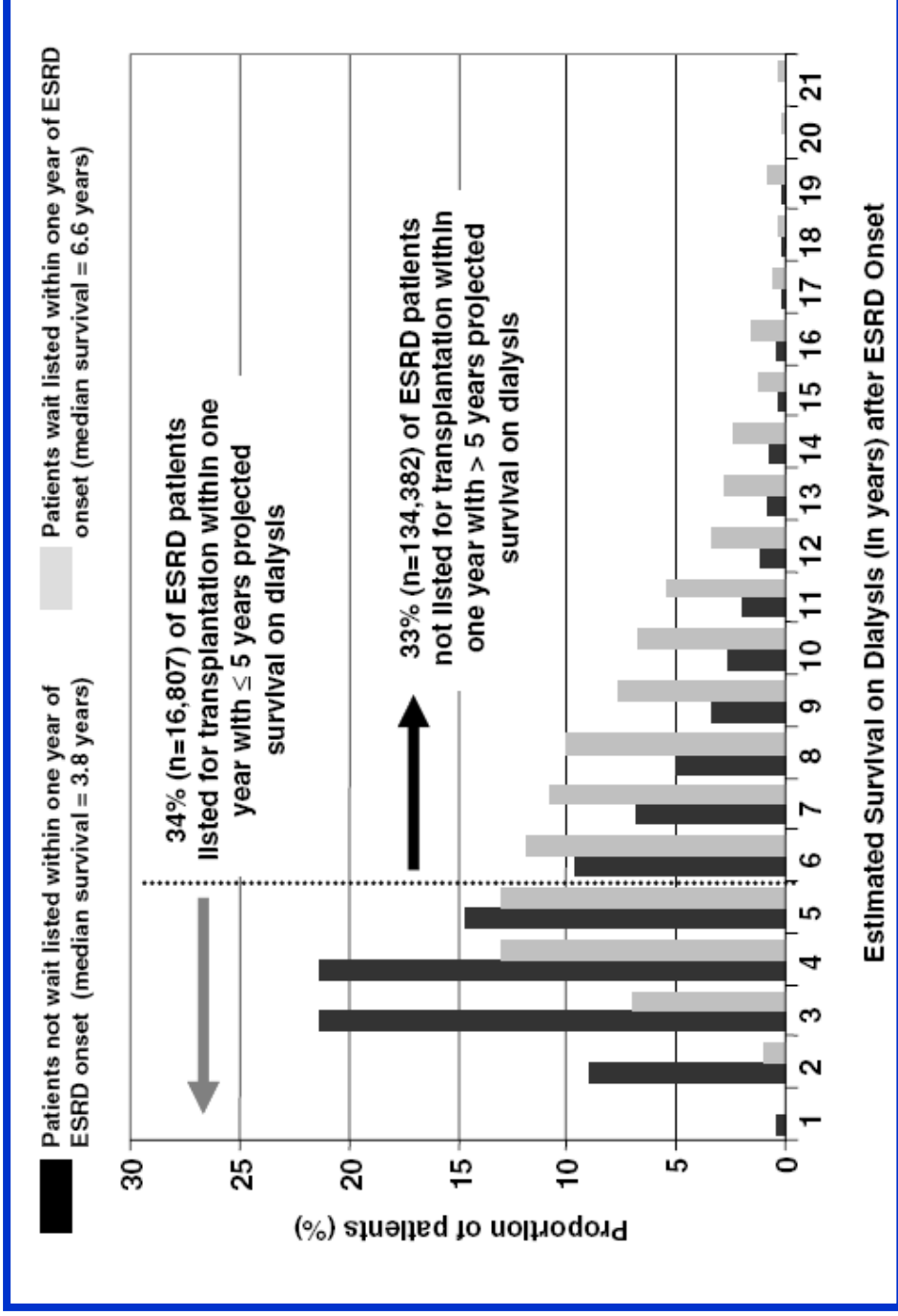
Registro USA 1990 -2004
5667 pacientes mayores de 70 años al entrar en lista de trasplante
  2078 Tx cadáver
  360 Tx donante vivo
  1849 fallecen en diálisis
  1380 permanecen en diálisis

Renal Transplantation in Elderly Patients Older Than 70 Years of Age: Results From the Scientific Registry of Transplant Recipients

- Elderly patients on the waiting list experience significant survival benefit with kidney transplantation.

- The benefit is observed among patients whose life expectancy is expected to exceed 1.8 yr and is most striking for patients with ESRD caused by diabetes and/or hypertension.

- Deceased donor transplantation (both ECD and non-ECD) also confers a survival benefit.

- The recipients of ECD kidneys had a 25% reduction in mortality risk compared with those on the waiting list.

Rao et al, Transplantation 2007

The Overlapping Risk Profile Between Dialysis Patients Listed and Not Listed for Renal Transplantation

Projected survival following ESRD onset

Patients not wait listed within one year of ESRD onset (median survival = 3.8 years)

Patients wait listed within one year of ESRD onset (median survival = 6.6 years)

34% (n=16,807) of ESRD patients listed for transplantation within one year with ≤ 5 years projected survival on dialysis

33% (n=134,382) of ESRD patients not listed for transplantation within one year with > 5 years projected survival on dialysis

Estimated Survival on Dialysis (in years) after ESRD Onset

Proportion of patients (%)

The Overlapping Risk Profile Between Dialysis Patients Listed and Not Listed for Renal Transplantation
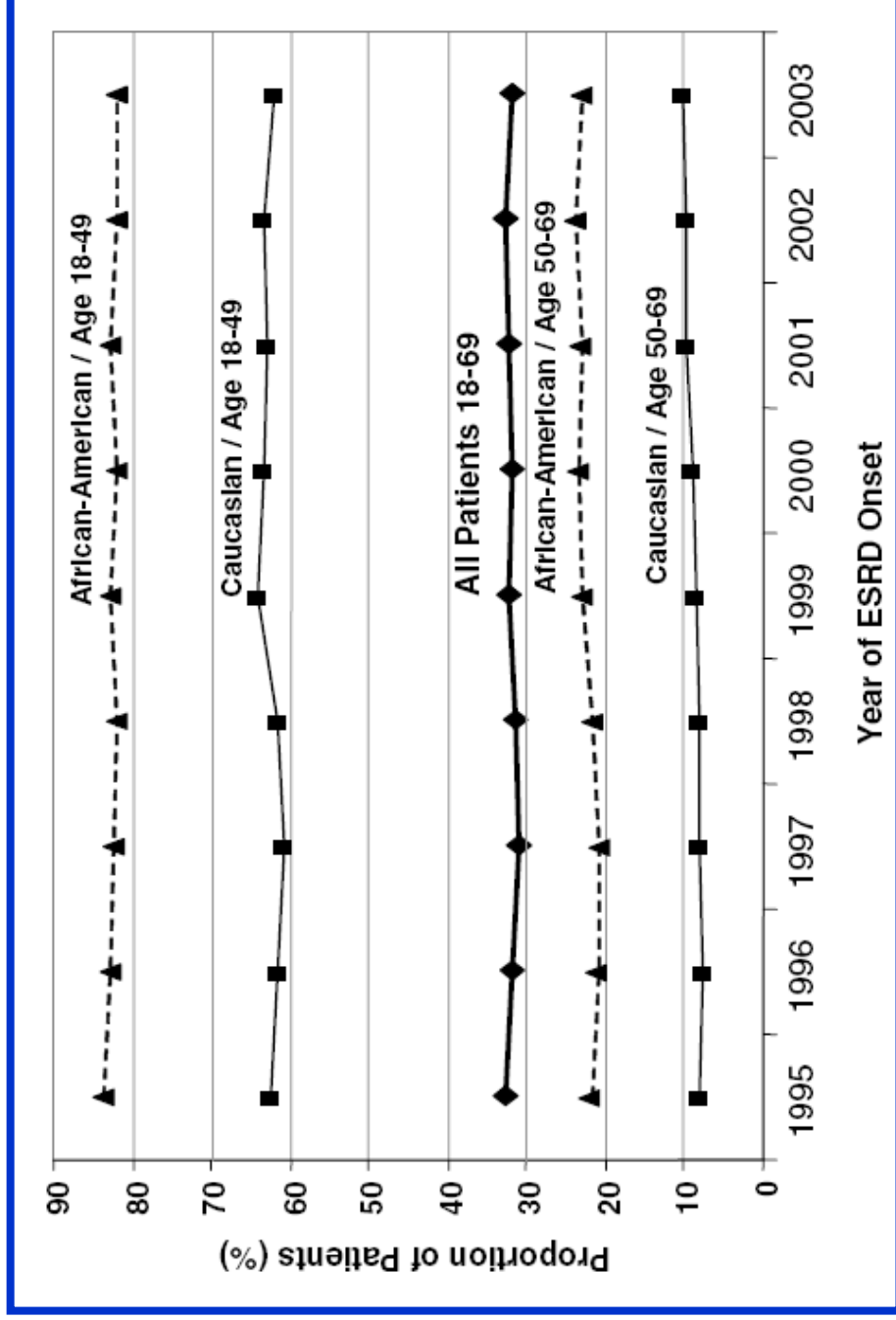
Proportion of patients with *greater than* 5-year life expectancy among patients not listed for transplantation within 1 year

Schold et al, Am J Transplant 2007

# Deceased donor transplantation in the elderly—are we creating false hope?

Kathryn K. Stevens[1], Y. Mun Woo[1], Marc Clancy[1], John D. McClure[2], Jonathan G. Fox[1] and Colin C. Geddes[1]

Table 2. Outcome of dialysis patients (1992–2008) on the basis of whether they were or were not on the kidney transplant waiting list

Age category (years), n	1 (18–34.9)	2 (35–49.9)	3 (50–64.9)	4 (65–74.9)	5 (≥75)
Total	134	207	415	438	319
Listed for transplant	114 (85%)	152 (73%)	162 (39%)	31 (7%)	3 (1%)
Transplanted (live/deceased)	105 (92%)	95 (63%)	75 (46%)	10 (32%)	0
Listed but not transplanted	9 (8%)	57 (37%)	77 (54%)	21 (68%)	3 (1%)
Deceased on waiting list	2 (2%)	27 (18%)	42 (26%)	7 (23%)	1 (33%)
Not listed	20 (15%)	55 (27%)	253 (61%)	407 (93%)	316 (99%)
Assessed but not listed[a]	6 (30%)	25 (45%)	65 (26%)	17 (4%)	0
Not listed and now deceased	10 (50%)	34 (62%)	207 (82%)	344 (85%)	260 (82%)
Alive and not listed	6 (30%)	17 (30%)	34 (13%)	52 (13%)	39 (12%)
Lost to follow up	4 (20%)	4 (7%)	12(5%)	11 (3%)	17 (6%)

[a]Put forward for formal assessment but following this not deemed fit enough to be put onto the waiting list.

Time to first deceased donor transplant from start of RRT (censored for death, date lost to follow up and live donor transplant) for patients who were wait listed for transplantation.
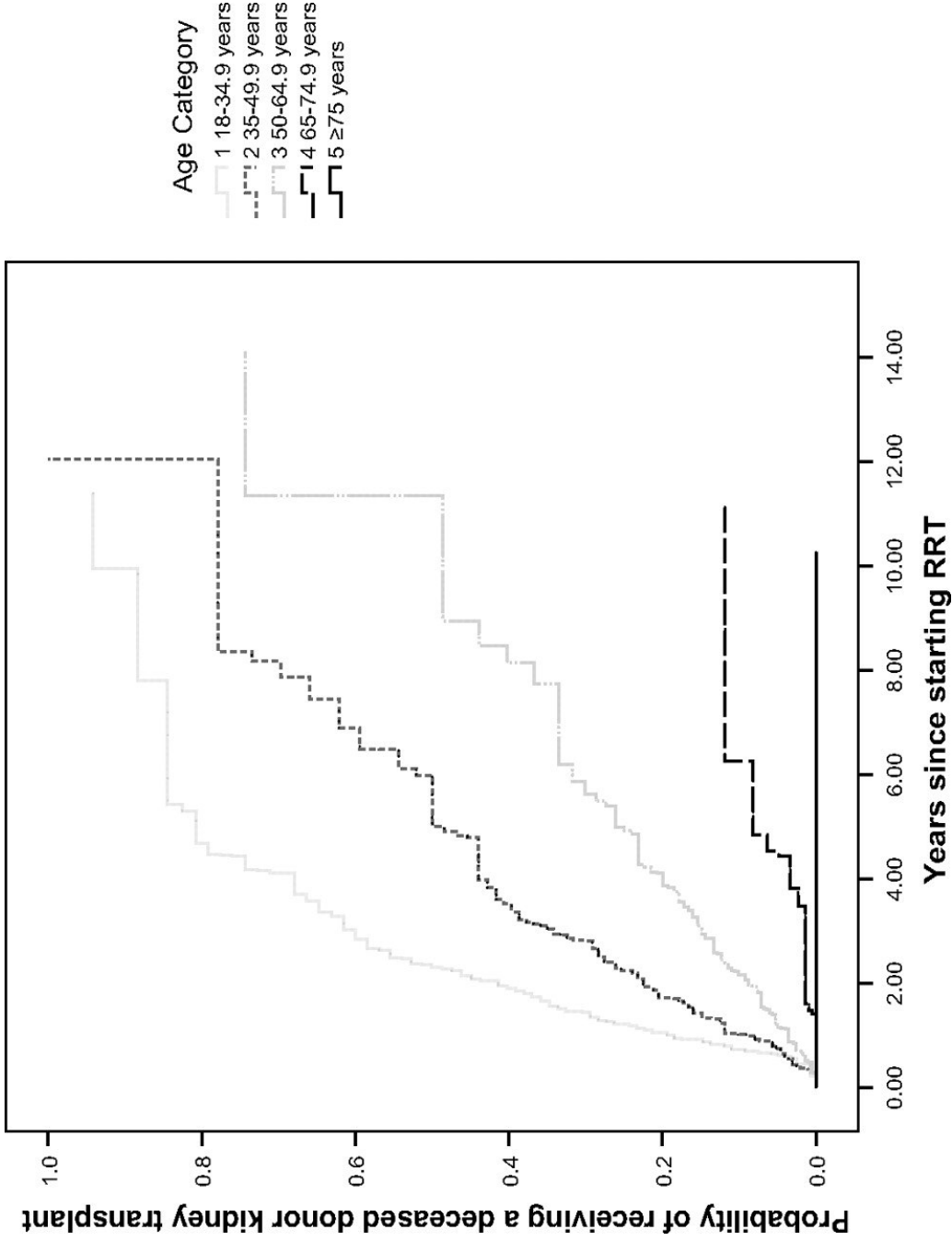
Stevens K K et al. Nephrol. Dial. Transplant. 2011;ndt.gfq826

NDT
Nephrology Dialysis Transplantation

The Impact of Recipient History of Cardiovascular Disease on Kidney Transplant Outcome

Table 4. The Results of Cox Model Evaluating the Association of CVD With the Recipient Survival Stratified by Recipient History of Diabetes Status*

| | Recipient Survival | | | |
| | Diabetic Recipients | | Non-Diabetic Recipients | |
	HR (95% CI)	p Value	HR (95% CI)	p Value
Cardiovascular disease	1.30 (1.21–1.40)	<0.001	1.52 (1.42–1.64)	<0.001
Cardiac arrest	1.16 (0.72–1.88)	0.533	1.61 (0.95–2.73)	0.075
Congestive heart failure	1.30 (1.19–1.43)	<0.001	1.53 (1.36–1.71)	<0.001
Unstable angina	1.32 (1.24–1.41)	<0.001	1.35 (1.24–1.46)	<0.001
Dysrrhythmia	1.15 (0.88–1.51)	0.303	1.68 (1.36–2.07)	<0.001
Ischemic heart disease	1.22 (1.10–1.35)	<0.001	1.44 (1.26–1.64)	<0.001
Myocardial infarction	1.18 (0.99–1.41)	0.070	1.51 (1.24–1.83)	<0.001
Peripheral vascular disease	1.28 (1.18–1.40)	<0.001	1.70 (1.49–1.95)	<0.001
Coronary artery disease†	1.29 (1.20–1.39)	<0.001	1.43 (1.32–1.55)	<0.001

Table 3. The Results of Cox Model Evaluating the Association of CVD With the Allograft Survival Stratified by Recipient History of Diabetes Status*

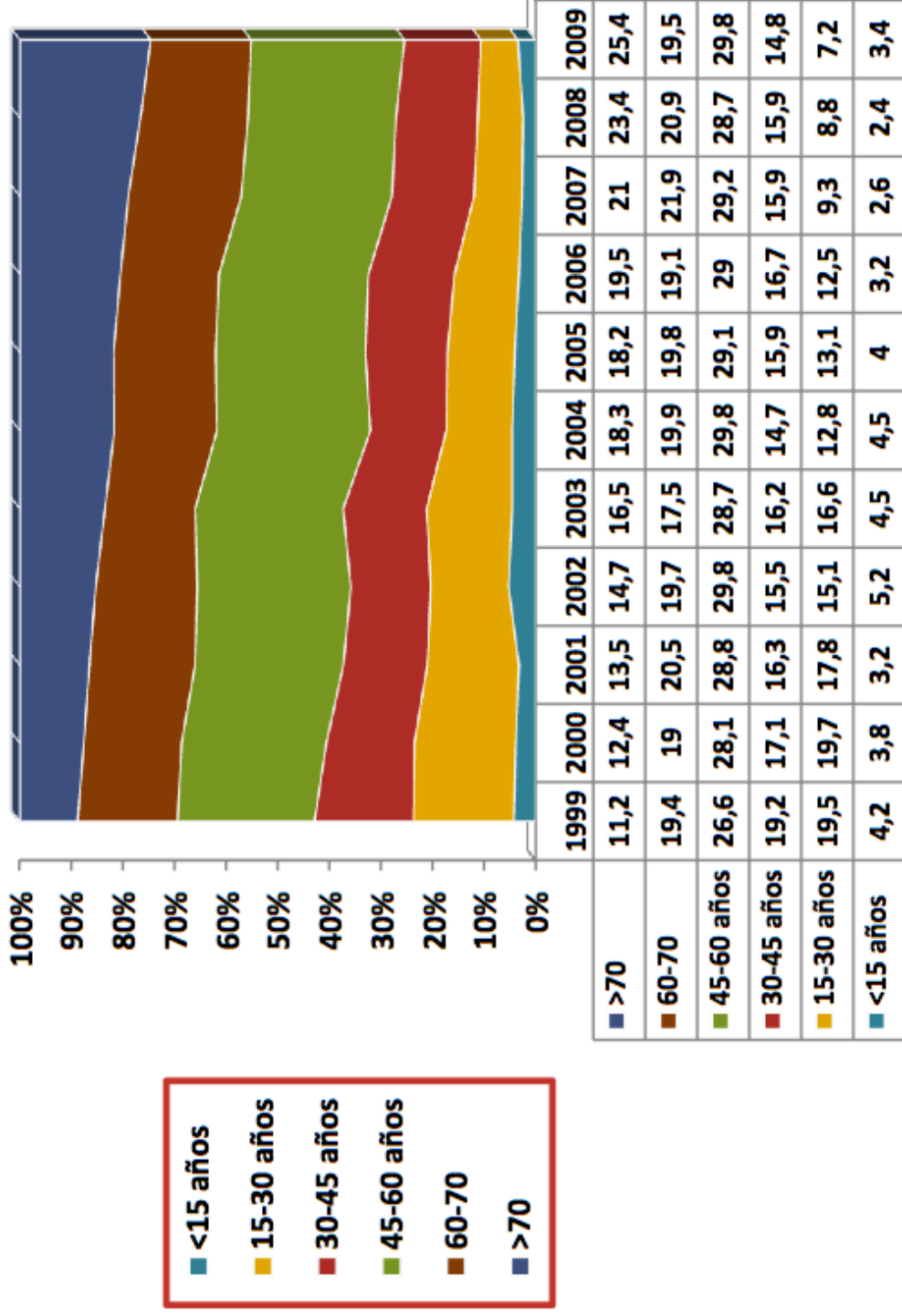| | Graft Survival | | | |
| | Diabetic Recipients | | Non-Diabetic Recipients | |
	HR (95% CI)	p Value	HR (95% CI)	p Value
Cardiovascular disease	1.03 (0.93–1.13)	0.579	1.18 (1.09–1.27)	<0.001
Cardiac arrest	1.42 (0.74–2.74)	0.294	1.35 (0.75–2.45)	0.317
Congestive heart failure	1.17 (1.03–1.33)	<0.05	1.12 (0.99–1.27)	0.074
Unstable angina	0.97 (0.87–1.07)	0.514	1.08 (0.98–1.20)	0.108
Dysrrhythmia	1.73 (1.23–2.43)	<0.005	1.05 (0.79–1.40)	0.727
Ischemic heart disease	1.04 (0.89–1.21)	0.652	1.01 (0.84–1.21)	0.946
Myocardial infarction	0.92 (0.70–1.24)	0.634	1.01 (0.77–1.33)	0.940
Peripheral vascular disease	0.98 (0.86–1.11)	0.746	1.27 (1.07–1.51)	<0.01
Coronary artery disease†	1.01 (0.91–1.12)	0.898	1.10 (1.00–1.21)	<0.05

Donor Age

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
>70	11,2	12,4	13,5	14,7	16,5	18,3	18,2	19,5	21	23,4	25,4
60-70	19,4	19	20,5	19,7	17,5	19,9	19,8	19,1	21,9	20,9	19,5
45-60 años	26,6	28,1	28,8	29,8	28,7	29,8	29,1	29	29,2	28,7	29,8
30-45 años	19,2	17,1	16,3	15,5	16,2	14,7	15,9	16,7	15,9	15,9	14,8
15-30 años	19,5	19,7	17,8	15,1	16,6	12,8	13,1	12,5	9,3	8,8	7,2
<15 años	4,2	3,8	3,2	5,2	4,5	4,5	4	3,2	2,6	2,4	3,4

Legend:
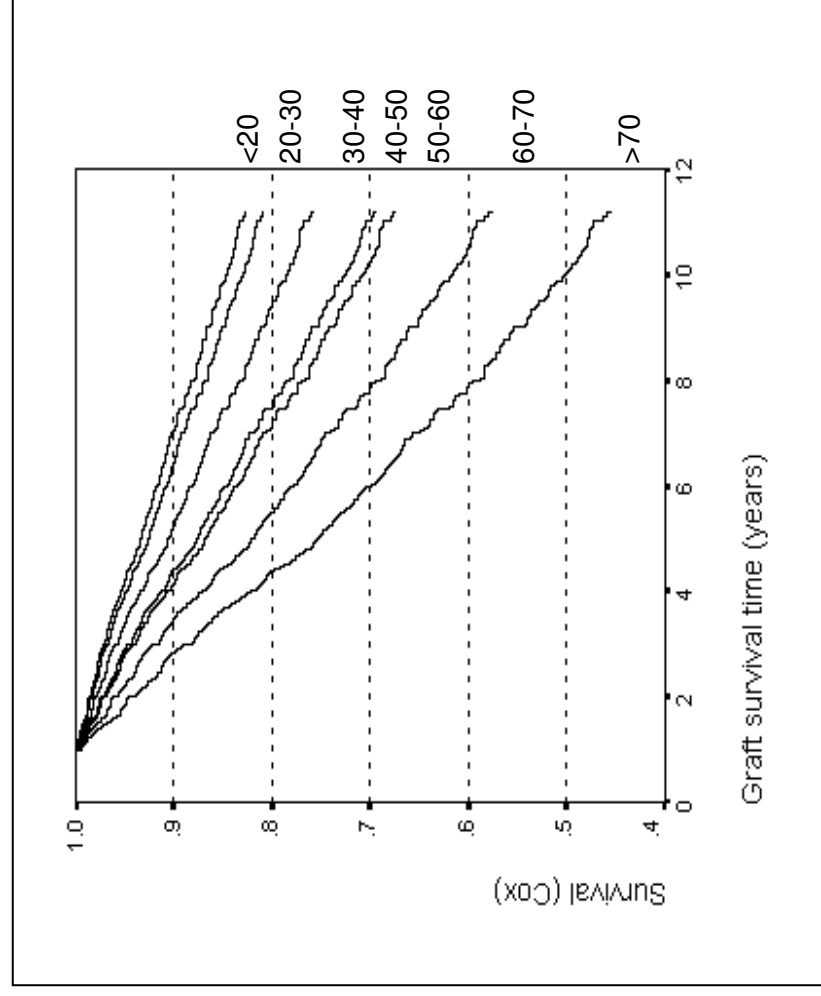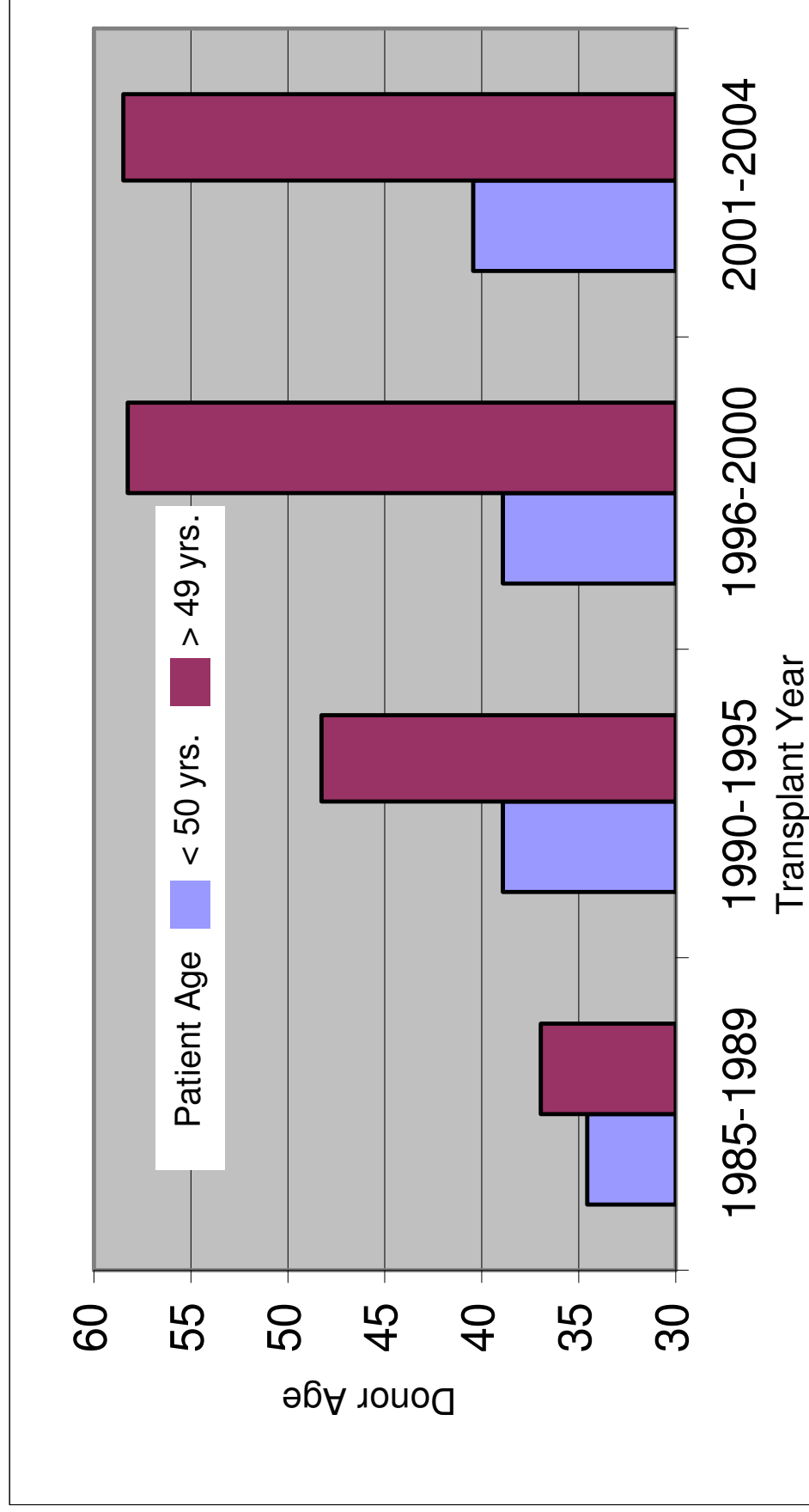- <15 años
- 15-30 años
- 30-45 años
- 45-60 años
- 60-70
- >70

Figura 9: Grupos de edad de donantes de órganos. España 1999-2009.

The impact of Donor Age on Graft Survival

RISK FACTORS FOR CHRONIC ALLOGRAFT NEPHROPATHY IN SPAIN BETWEEN 1990 – 1998.

Old for Old Kidney Allocation

CLÍNIC
BARCELONA
Hospital Universitari

Eurotransplant Kidney Allocation System (ETKAS)

Allocation factors	Points	
	Minimum	Maximum
HLA-A, B, DR Mismatch	0	400
Mismatch probability	0	100
Waiting period	0.09 points per day	
Distance between donor/transplantation center	0-104-208-300	
Ratio between national import/export	0	200
Extra points		
Extremely urgent	500 points extra	
Children	Double points if they have the same HLA as the donor	
Age of the pattient		
0–5 years	Bonus of 1095 extra waiting days, or 99 points extra	
6–10 years	Bonus of 365 extra waiting days, or 33 points extra	
11–16 years	Bonus of 730 extra waiting days, or 66 points extra	

ETKAS se implantó en 1996 para corregir los problemas de acumulación de hipersensibilizados en las listas, prolongación de los tiempos de espera, etc

ETKAS se complementa con dos iniciativas para favorecer el trasplante de pacientes hiper-inmunizados:

The Highly Immunized Trial (HIT)
The Acceptable Mismatch (AM) program

Programa adicional:
Eurotransplant Senior Program (old for-old)

Prospective Age-Matching in Elderly Kidney Transplant Recipients
## A 5-Year Analysis of the Eurotransplant Senior Program

Table 2: Selected efficacy and safety results for ESP and comparator groups

Outcome	ESP (n = 1406)	Old to any (n = 446)	Any to old (n = 1687)	p-Value*,†,‡
Median waiting time 1999–2000 (years/range)	3.94 (0.2–9.0)	3.61 (0.9–13.5)	3.89 (0.2–13.4)	NS‡
Median waiting time 1999–2004 (years/range)	3.55 (0.2–13.5)	3.79 (0.3–15.0)	4.64 (0.1–13.8)	<0.001†
Cold ischemia time (h ± SD)	11.9 ± 5.2	17.8 ± 6.8	17.5 ± 6.4	<0.001‡
CIT < 8 h (%)	25.7	6.2	5.0	<0.001‡
CIT > 12 h (%)	43.1	81.6	81.2	<0.001‡
Initial graft function (%)	63.0	55.5	63.8	
Delayed graft function (%)	29.7	36.2	30.9	0.03*
Never functioning graft (%)	7.3	8.3	5.0	
SCr at 2 weeks (μmol/L ± SD)	186 ± 166	210 ± 189	153 ± 181	<0.007‡
SCr at 6 months (μmol/L ± SD)	159 ± 84	167 ± 91	127 ± 71	<0.001‡
AR at any time (%)#	29.1	24.3	20.1	<0.001†
SAE-infections any time posttransplant (%)	51.0	50.4	39.8	
SAE-CV event any time posttransplant (%)	15.2	11.7	14.0	<0.001†
SAE-malignancy any time posttransplant (%)	10.3	7.3	9.0	

CIT = cold ischemia time; – = no statistical test performed; AR = acute rejection; SCr = median serum creatinine; SAE = serious adverse event; CV = cardiovascular disease.
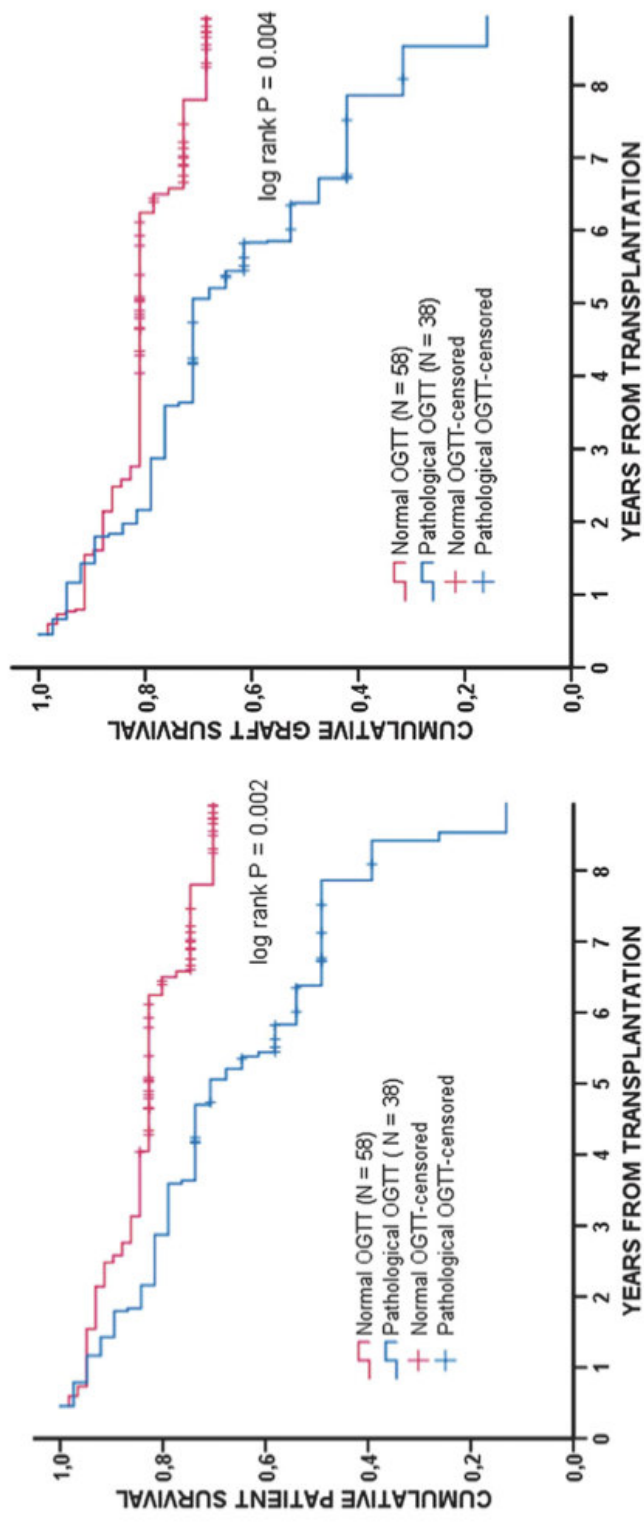
#Analysis performed in 'updated population'; *ESP vs. old-to-any; †ESP vs. any-to-old; ‡ESP vs. both comparator groups.

Graft Survival in Elderly Patients
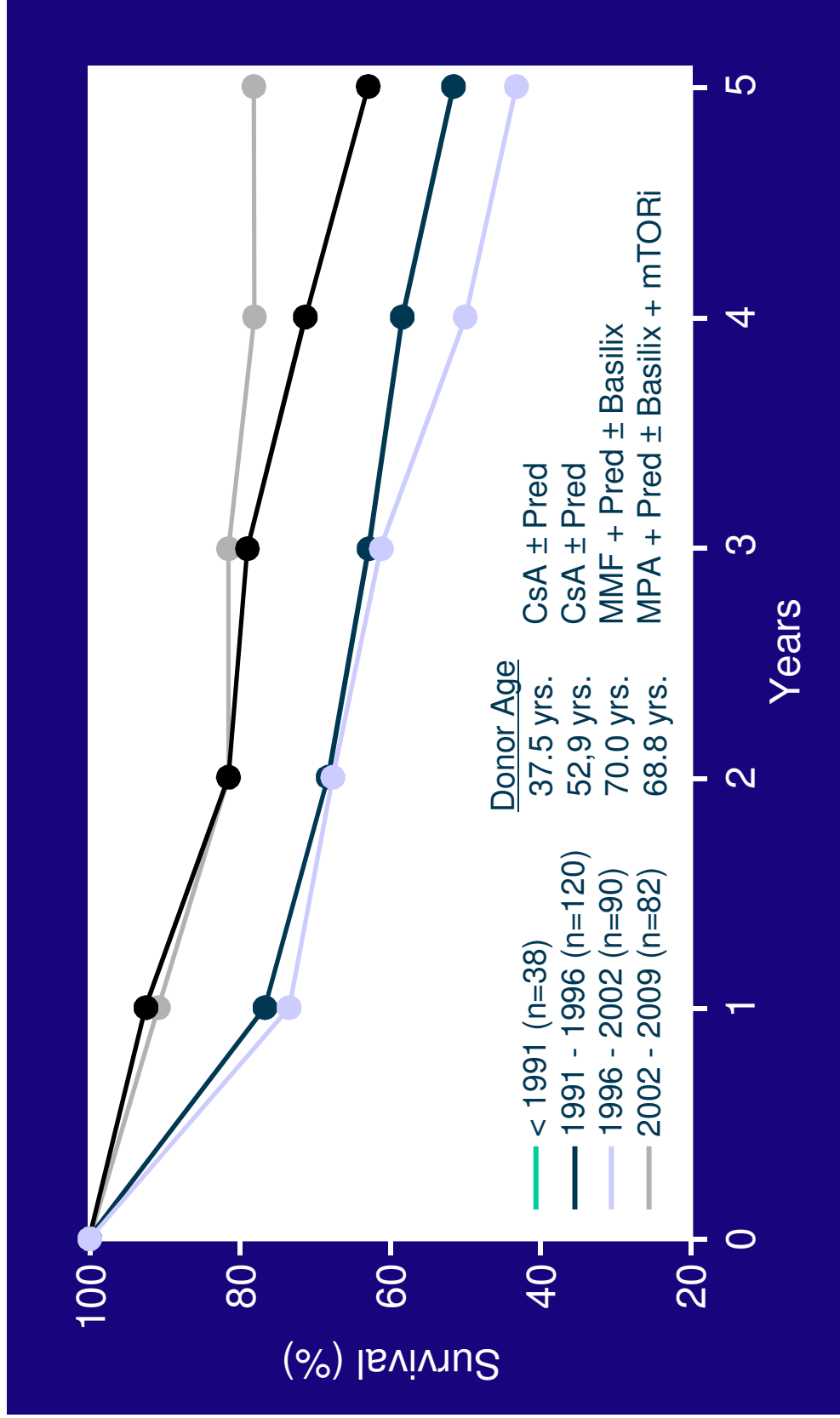
Risk variables associated with the outcome of kidney recipients >70 years of age in the new millennium

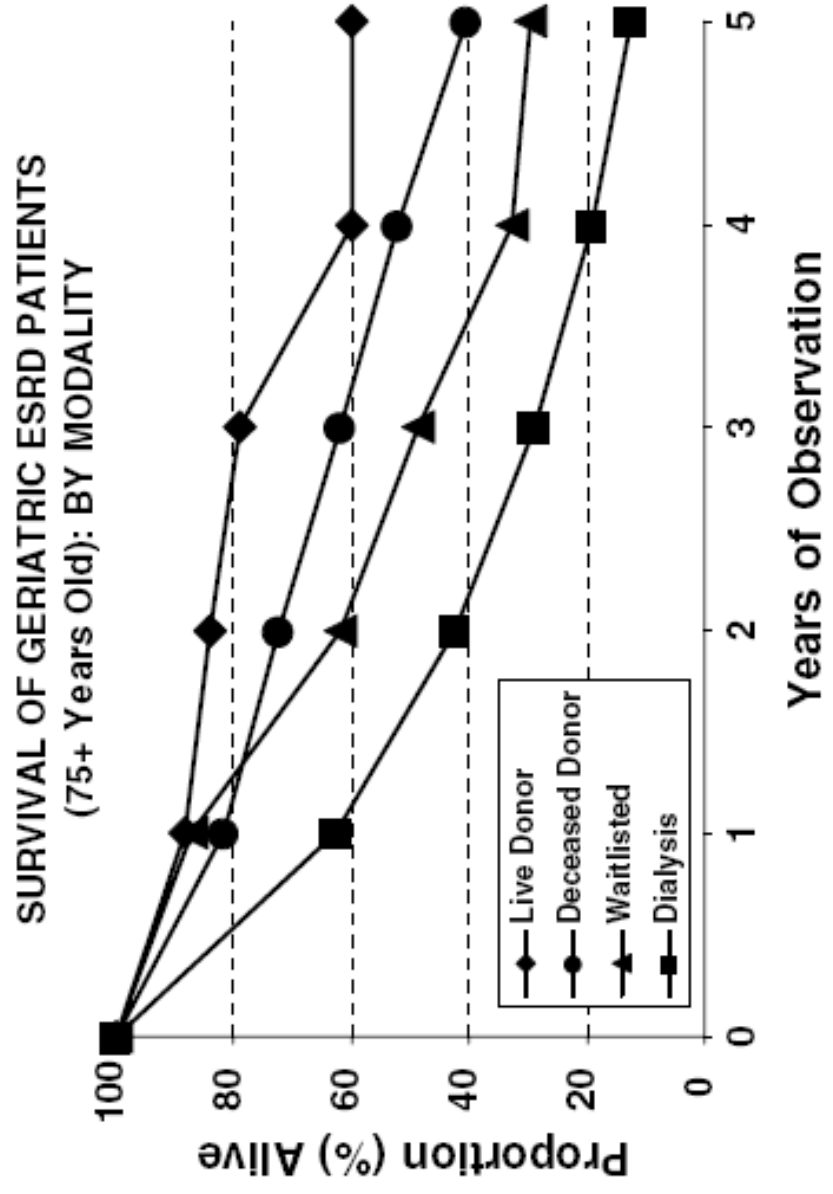Kristian Heldal[1,2,3], Anders Hartmann[2,3], Torbjørn Leivestad[4], Aksel Foss[5] and Karsten Midtvedt[2]

Risk variables associated with the outcome of kidney recipients >70 years of age in the new millennium

Kristian Heldal[1,2,3], Anders Hartmann[2,3], Torbjørn Leivestad[4], Aksel Foss[5] and Karsten Midtvedt[2]

Table 2. Comparison of clinical characteristics of recipients grouped according to result of OGTT at 10 weeks after kidney transplantation

	Normal OGTT, $N = 58$	Pathological OGTT, $N = 38$	P-value
Age at transplantation; median [range]	72.3 [70.1–80.1]	74.2 [70.0–79.9]	0.011
Donor age; median [range]	54.0 [4–81]	55.8 [4–82]	NS
Donor aged ≥ 60 years	18 (31%)	18 (47%)	NS
Living donor	10 (17%)	7 (18%)	NS
Cold ischemia time (hours); median [range]	12.0 [1–25]	12.5 [1–25]	NS
HD pre-transplant	36 (62%)	24 (63%)	NS
PD pre-transplant	16 (28%)	9 (24%)	NS
Pre-emptive transplant	6 (10%)	5 (13%)	NS
Time on dialysis (years); median [range]	1.3 [0–4.4]	1.3 [0–3.8]	NS
Pre-transplant ischemic heart disease	17 (29%)	13 (34%)	NS
Charlson Comorbidity Index; median [range]	3.0 [2–7]	3.0 [2–9]	NS
Any HLA-DR mismatch	36 (62%)	18 (47%)	NS

Live and deceased donor kidney transplantation in patients aged 75 years and older in the United States

SURVIVAL OF GERIATRIC ESRD PATIENTS
(75+ Years Old): BY MODALITY

Live Donor
Deceased Donor
Waitlisted
Dialysis

Proportion (%) Alive

Years of Observation

Conclusiones

El trasplante renal en pacientes de edad avanzada mejora las probabilidades de supervivencia

La diabetes y la morbilidad cardiovascular se asocian a un peor pronóstico de supervivencia del paciente y del injerto

El empleo de donantes marginales y en menor medida el trasplante de donante vivo son probablemente la única fuente de donantes en pacientes de edad avanzada

Muchas gracias por su atención