

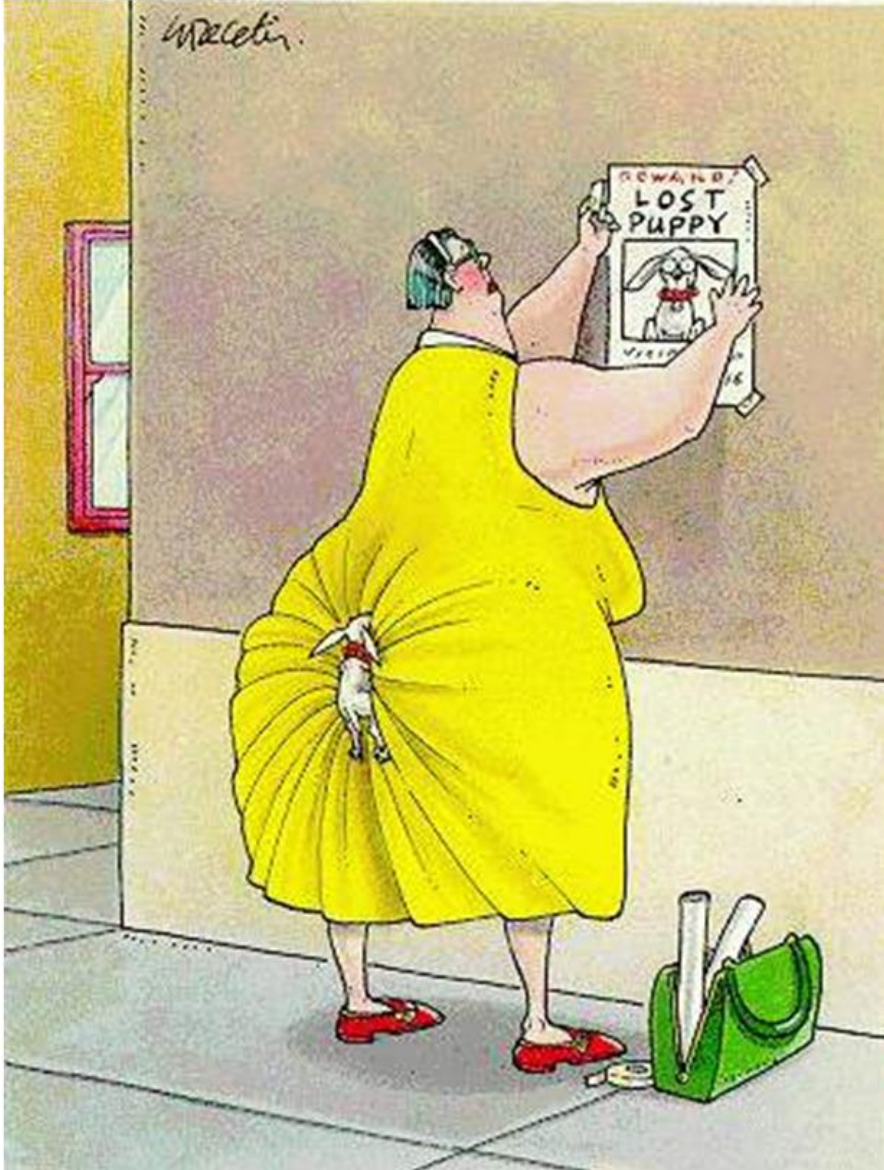
# Extending the boundaries of transplantation: considering more marginal recipients?

**UK Living Kidney Donor Network Meeting  
Thursday 24<sup>th</sup> January 2019**

**Gareth Jones**

**UCL Centre for Nephrology, Royal Free NHS Foundation Trust,  
London, UK**

# Missing the obvious ....



...or just not sure  
where to look!

# Transplanting the unexpected

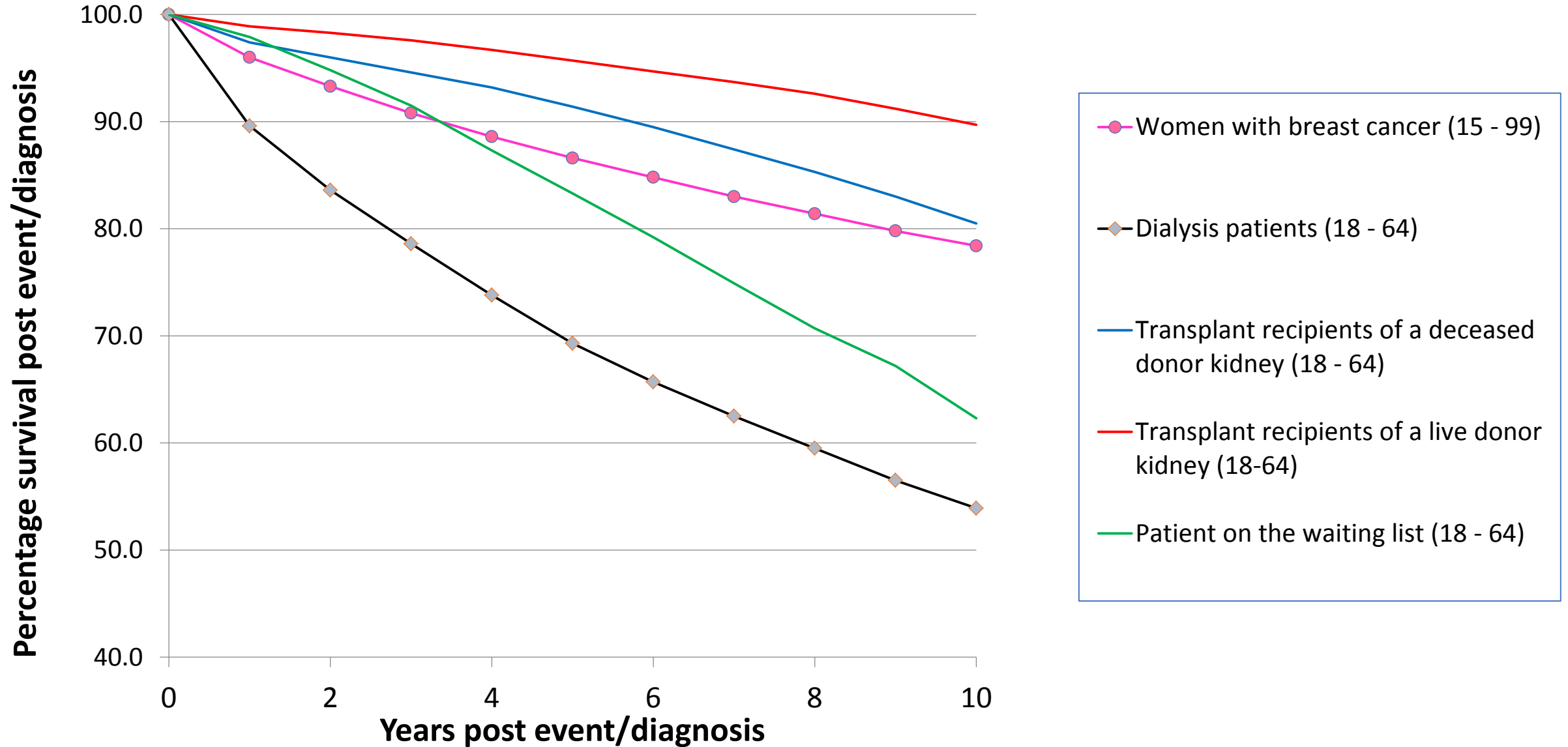
Why ?

When ?

Where ?

Who ?

# Why - live donor transplantation



# Transplanting the unexpected

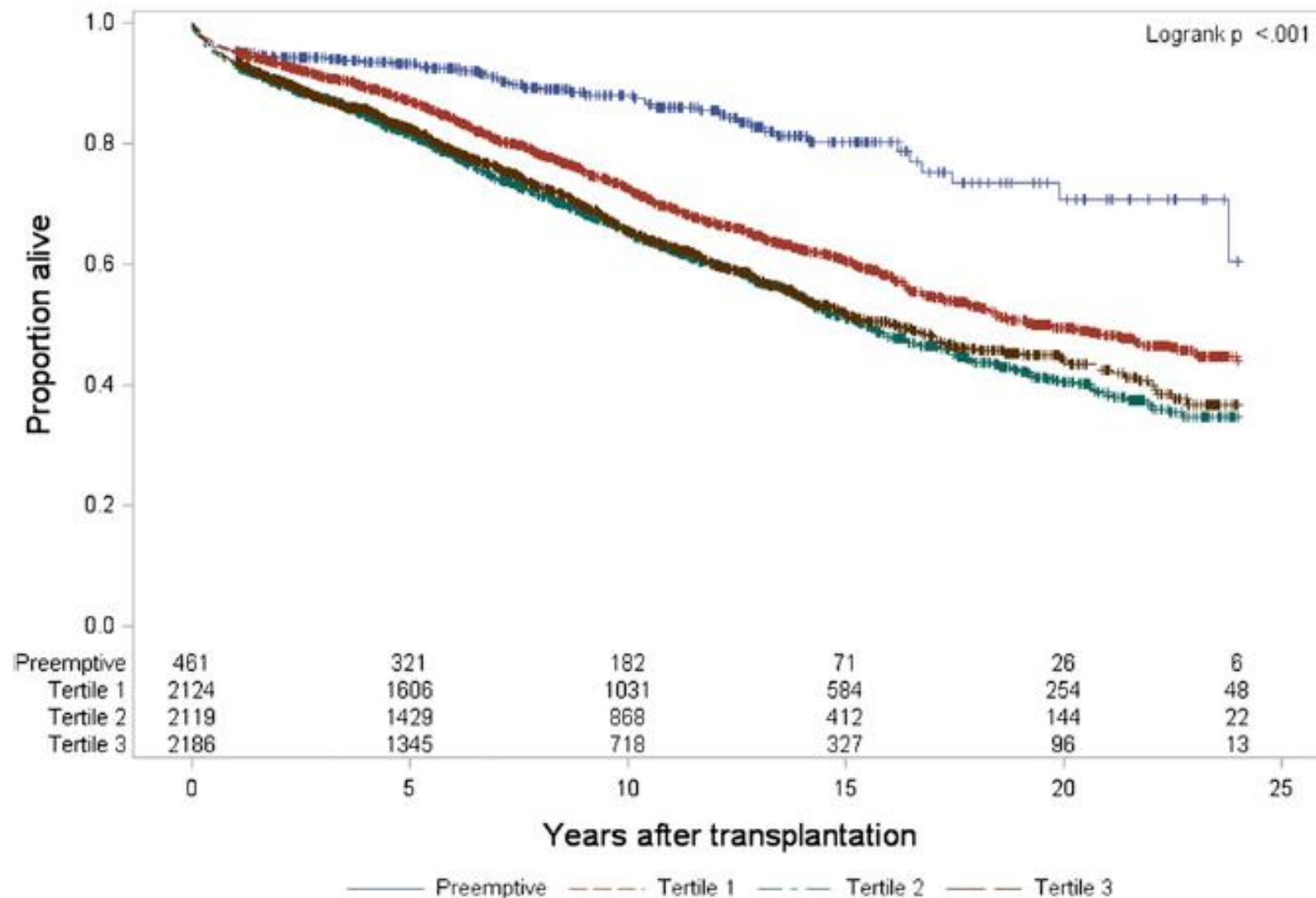
Why ?

**When ?**

Where ?

Who ?

# Dialysis Vintage and Outcomes after Kidney Transplantation: A Retrospective Cohort Study



N = 6967

Tertile 1 – dialysis < 1.5 yrs

Tertile 2 – dialysis 1.5 – 3 years

Tertile 3 – dialysis > 3 years

# Transplanting the unexpected

Why ?

When ?

**Where ?**

Who ?



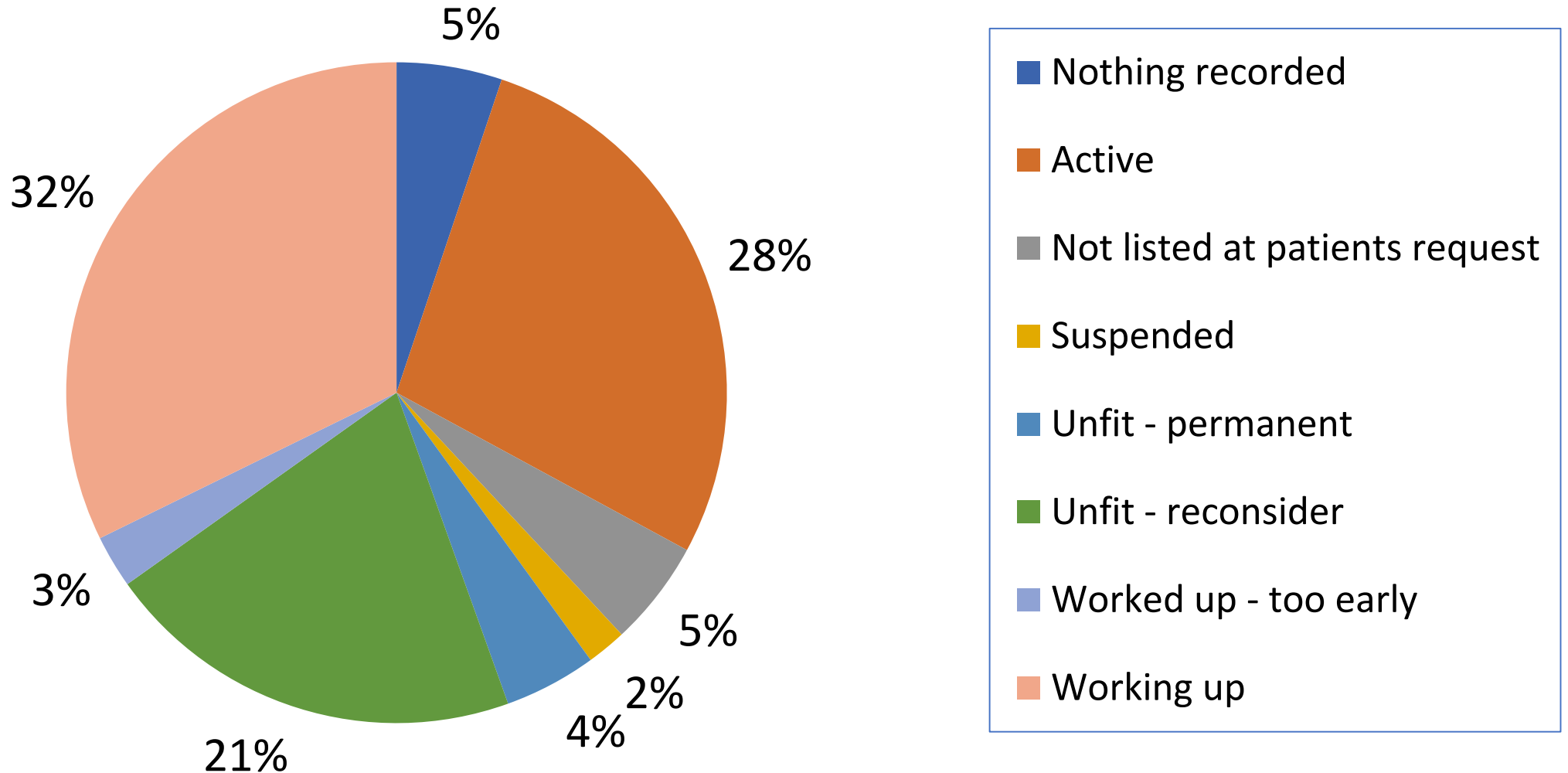
# Hobby horse alert !



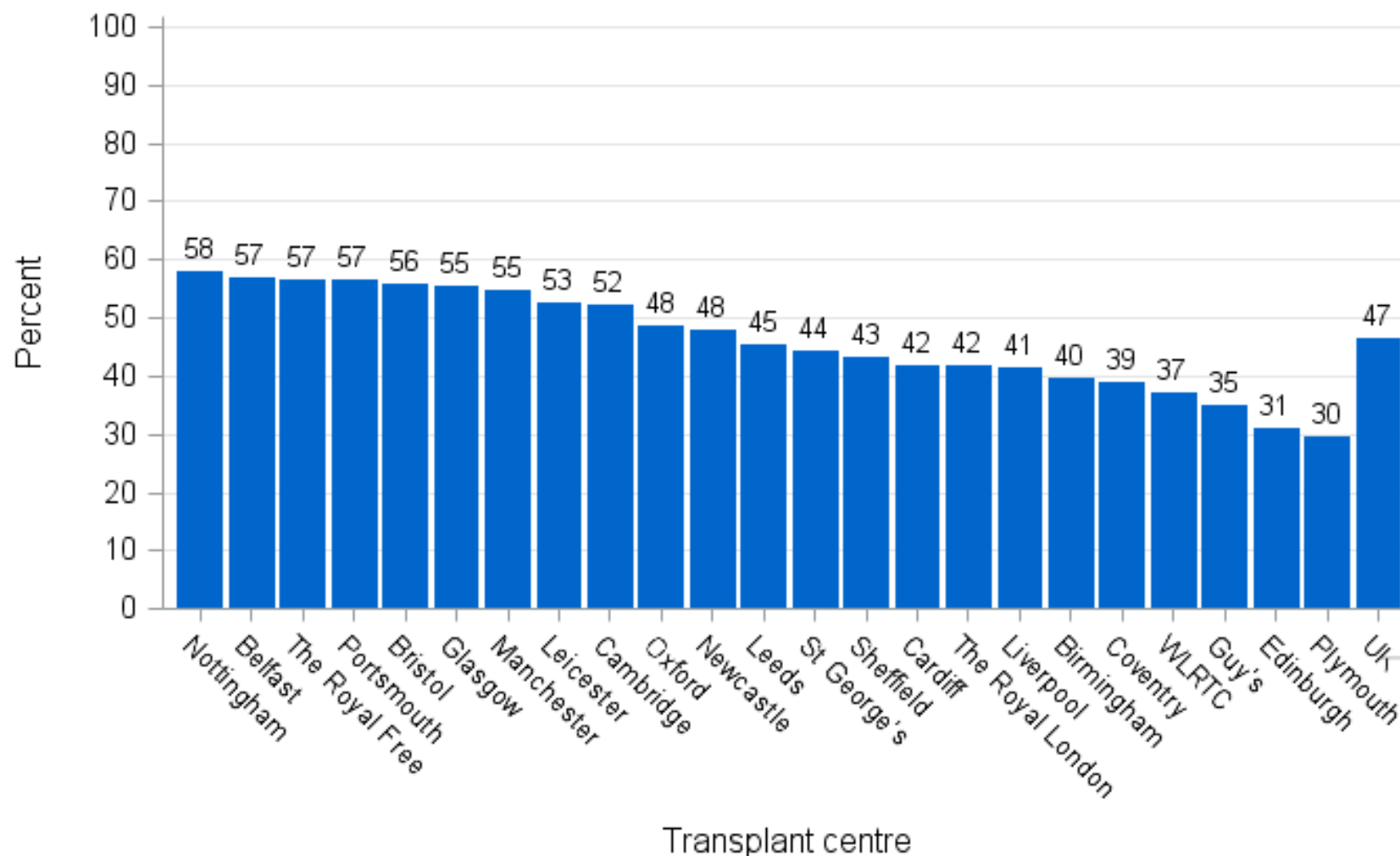


# Where should we be looking

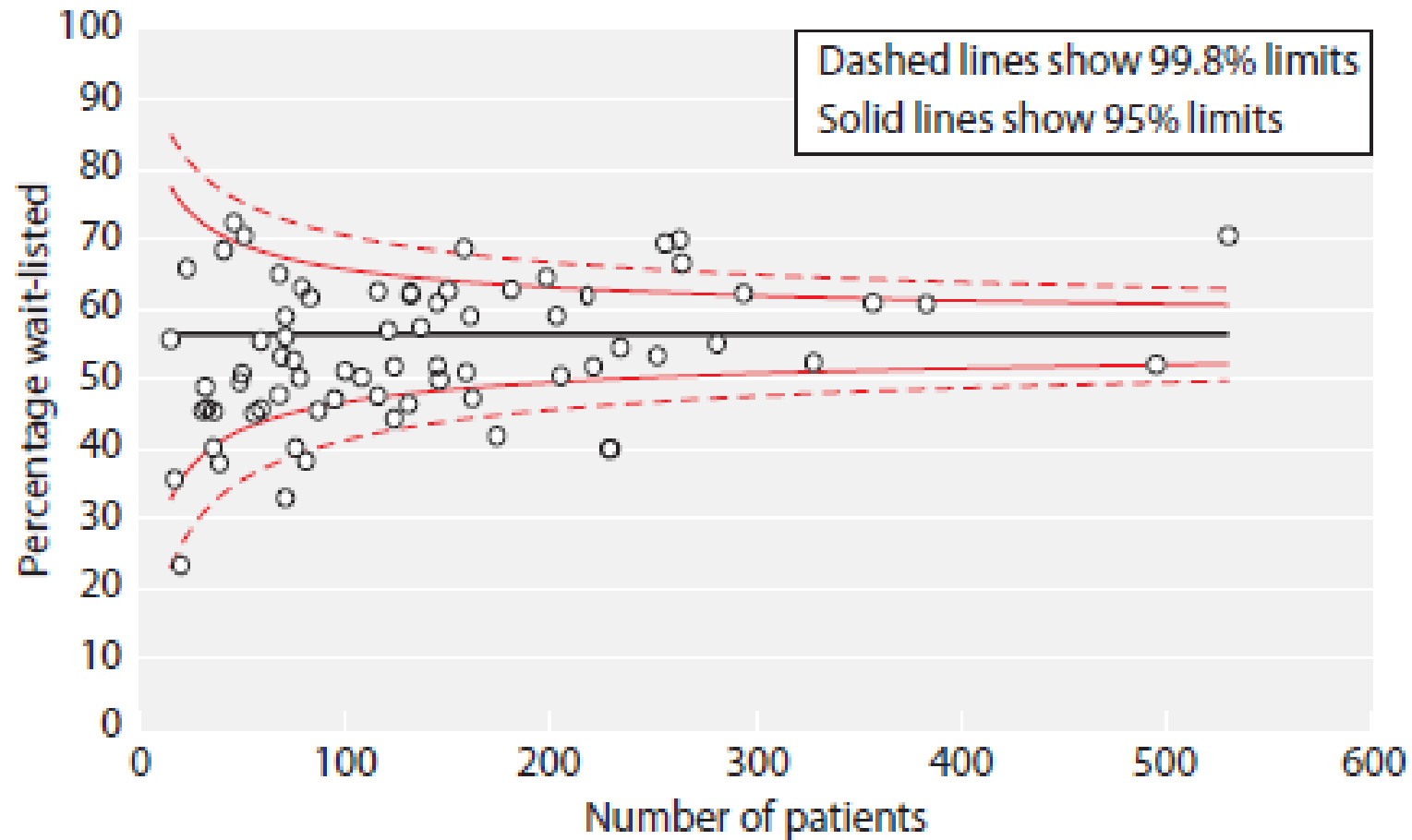
## Transplant listing status of LCC patients under 65 with eGFR under 15ml/min



**Figure 3.12**      **Adult pre-emptive listing rates by centre,  
registrations between 1 April 2016 and 31 March 2017**



# Waitlisting in UK



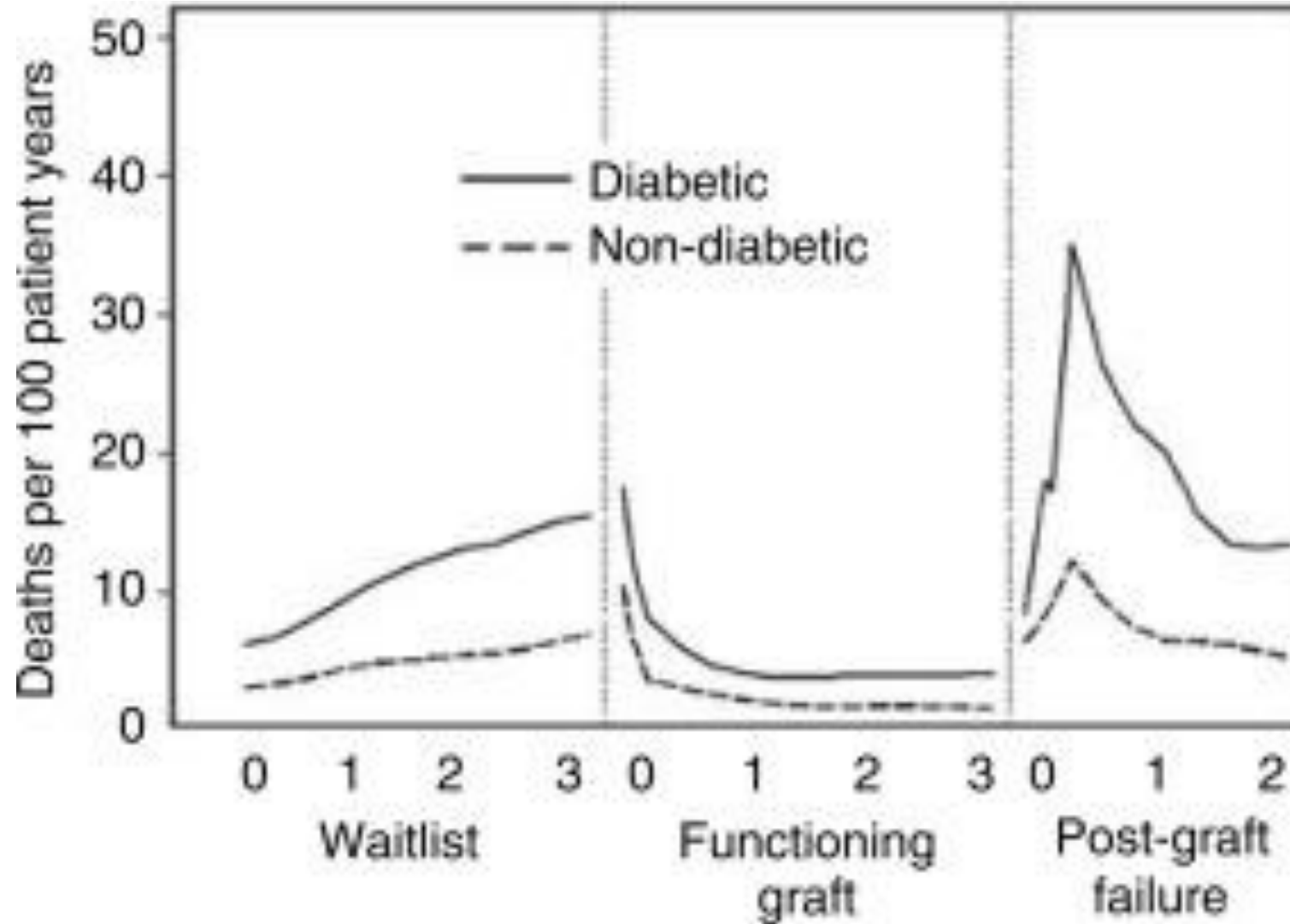
**Fig. 9.1.** Proportion of incident 2011–2013 RRT patients wait-listed prior to, or within two years of starting RRT, by renal centre

# Failing grafts



*I have seen the light !*

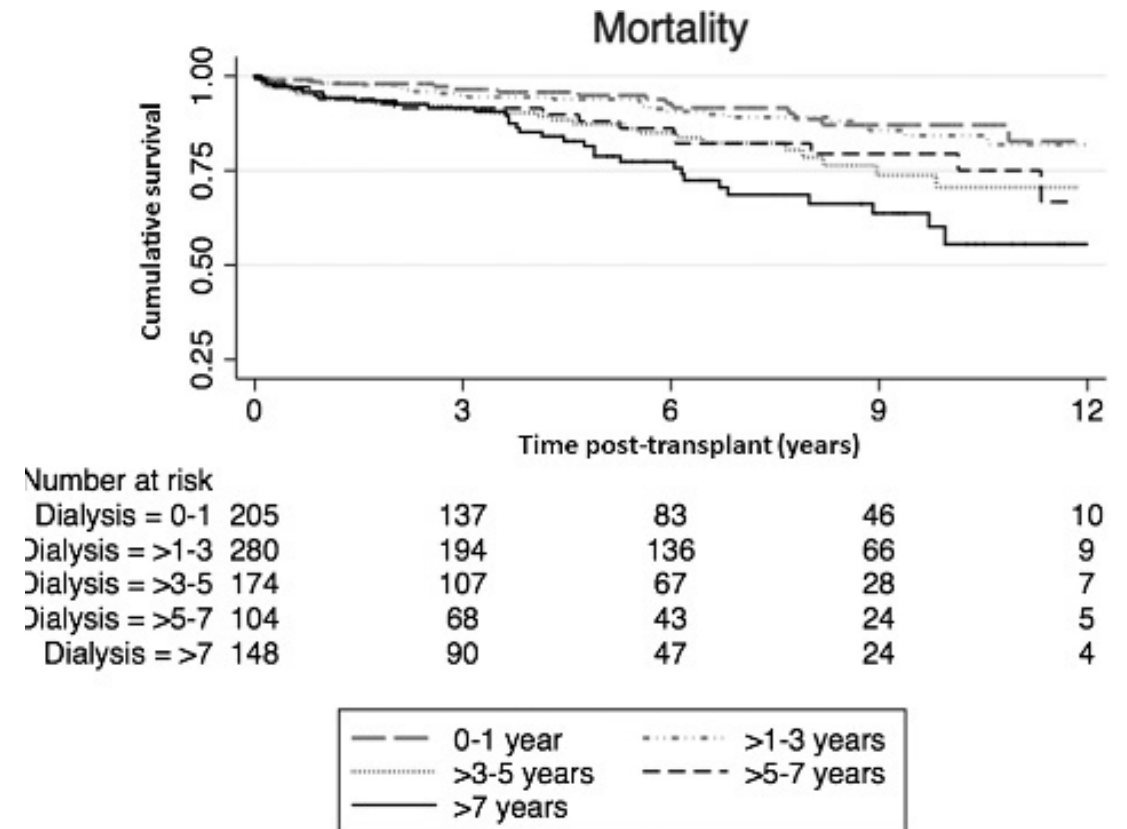
# The failing transplant



# Mortality and retransplantation

- In US only 15-20% are relisted
- Post adjustment for comorbidity  
- only half are relisted in UK
- HR for death is 4 cf native failure
- In UK, median survival post failure
  - 34 mo if relisted in 6 /12
  - 18 mo if not

## Waiting Time Between Failure of First Graft and Second Kidney Transplant and Graft and Patient Survival



# Transplanting the unexpected

Why ?

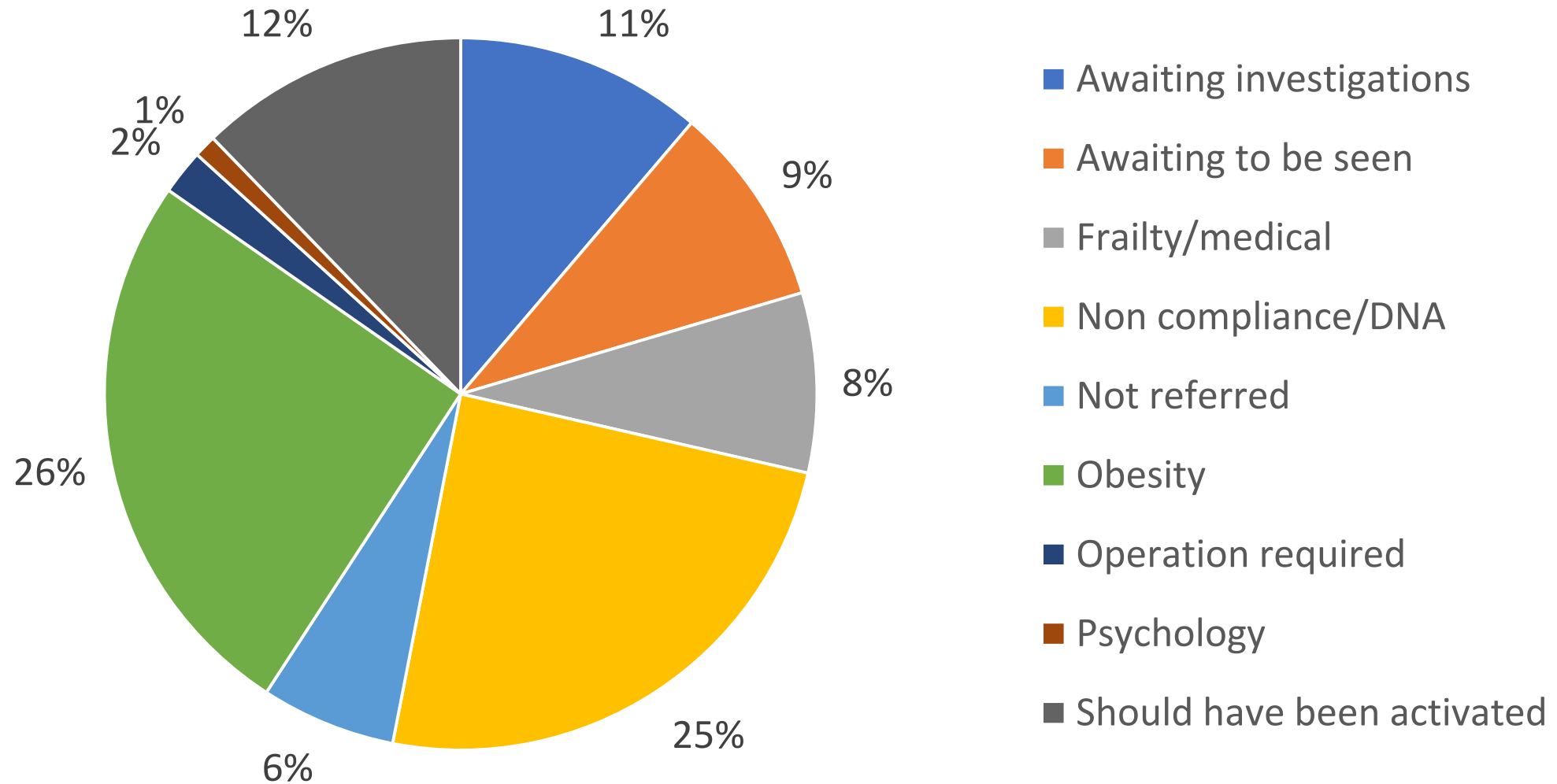
When ?

Where ?

**Who ?**



# Why are patients not pre-emptively listed?



Median BMI of Obese group = 42

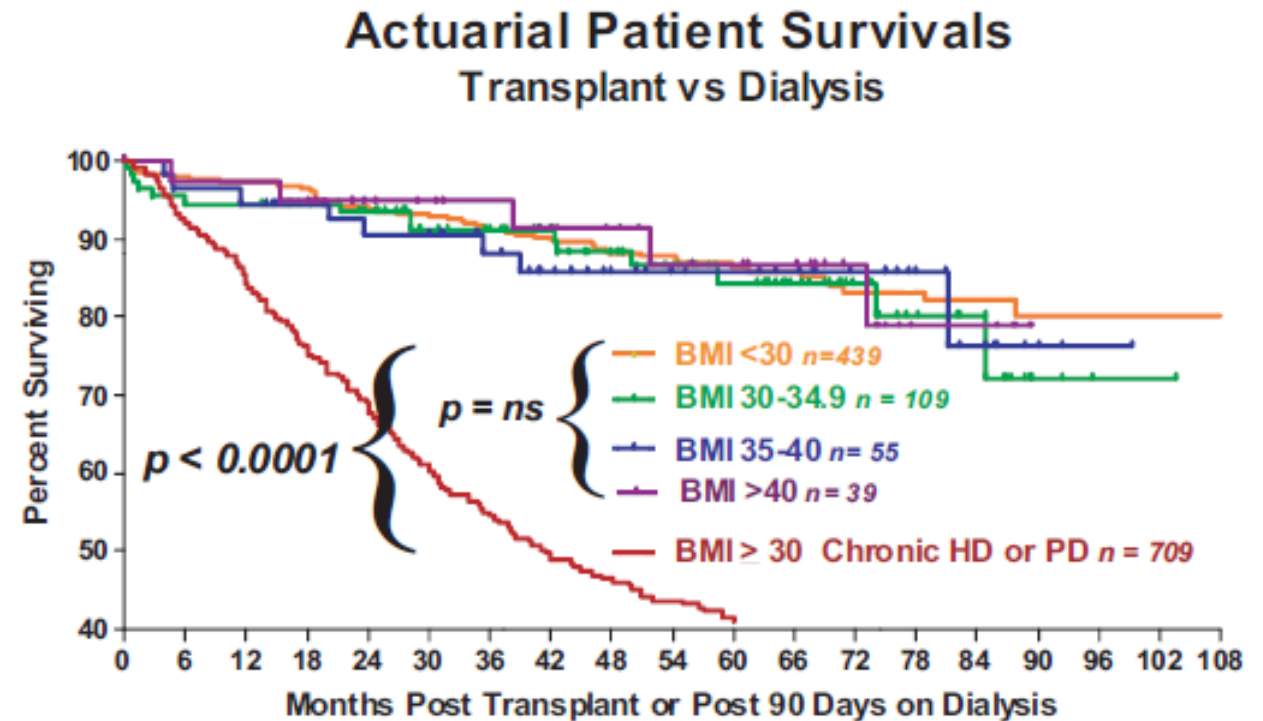
# Kidney transplantation in the morbidly obese: complicated but still better than dialysis

- 642 renal transplant patients
  - BMI under 30
  - BMI 30 – 34.9
  - BMI over 35
- Compared to dialysis cohort
  - BMI over 30

Table 2. Overall outcomes

	Group 1 n = 439	Group 2 n = 109	Group 3 n = 94
Graft survival at 1 yr (%)	94	92	87
Graft survival at 3 yr (%)	83	87	73
Patients survival at 1 yr (%)	97	95	95
Patients survival at 3 yr (%)	91	88	91
Median anastomosis time (min)	31	33	34
Median length of stay (d)	6	6	6
Median cold ischemia (h)	9	12	13
Delayed graft function (%)	17	33	32
Any surgical wound infection (%)	3.8	5.5	15.7*
Deep wound infection	1.7	2.8	9.2*

\*p < 0.01 for both Groups 1 and 2 vs. Group 3.



# The Survival Benefit of Kidney Transplantation in Obese Patients

**Table 3:** Risk of death in transplant recipients compared to wait-listed patients with the same body mass index 1 year after transplantation

	SCD recipients	ECD recipients	LD recipient
BMI < 18.5	0.33 (0.26, 0.41)	0.30 (0.21, 0.42)	0.35 (0.24, 0.52)
BMI 18.5–24.9	0.34 (0.30, 0.39)	0.37 (0.32, 0.42)	0.20 (0.15, 0.26)
BMI 25.0–29.9	0.32 (0.28, 0.37)	0.43 (0.38, 0.50)	0.30 (0.22, 0.47)
BMI 30.0–34.9	0.32 (0.26, 0.39)	0.42 (0.35, 0.51)	0.23 (0.17, 0.32)
BMI 35.0–39.0	0.34 (0.26, 0.46)	0.39 (0.24, 0.52)	0.28 (0.14, 0.50)
BMI ≥ 40.0	<b>0.52</b> (0.37, 0.72)	<b>0.54</b> (0.33, 0.78)	<b>0.34</b> (0.19, 0.59)

# The Survival Benefit of Kidney Transplantation in Obese Patients

**Table 3:** Risk of death in transplant recipients compared to wait-listed patients with the same body mass index 1 year after transplantation

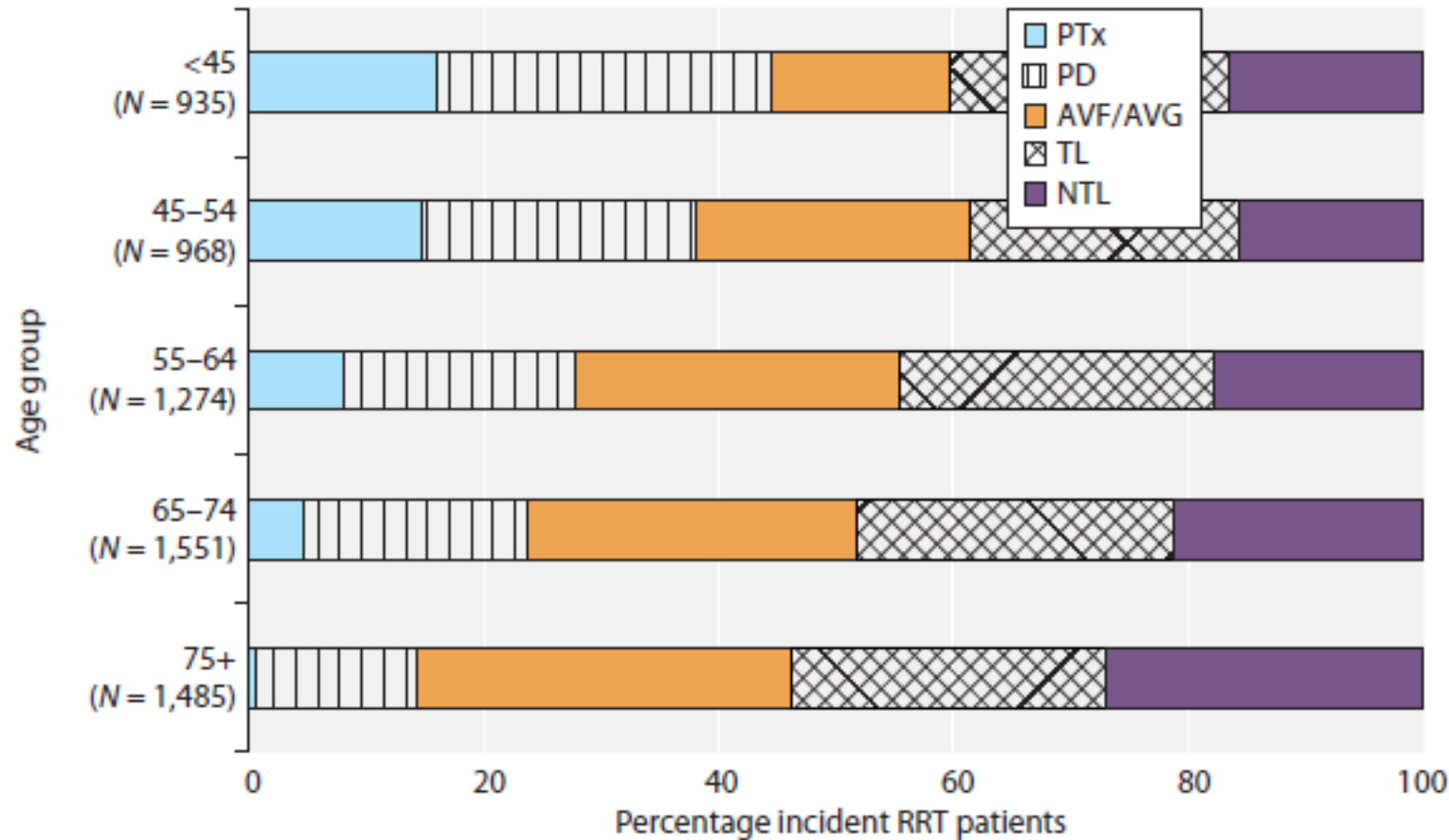
	SCD recipients	ECD recipients	LD recipient
BMI < 18.5	0.33 (0.26, 0.41)	0.30 (0.21, 0.42)	0.35 (0.24, 0.52)
BMI 18.5–24.9	0.34 (0.22, 0.50)	0.27 (0.22, 0.40)	0.32 (0.15, 0.50)

**Table 5:** Time (days) to equal risk of death and equal survival\* in transplant recipients compared to wait-listed patients with the same body mass index

	<18.5 (n = 13 714)	18.5–24.9 (n = 67 260)	25–29.9 (n = 64 655)	30–34.9 (n = 37 453)	35–39.9 (n = 16 070)	≥40 (n = 9 346)
Death rate on waiting list per 100 patient years	5	5	6	6	6	6
Days to equal risk of death						
SCD	68	50	70	80	85	145
ECD	135	95	90	160	150	200
LD	55	Immediate	33	57	60	65
Days to equal survival						
SCD	118	100	137	210	179	245
ECD	216	226	210	331	257	387
LD	116	Immediate	75	121	135	157

Age

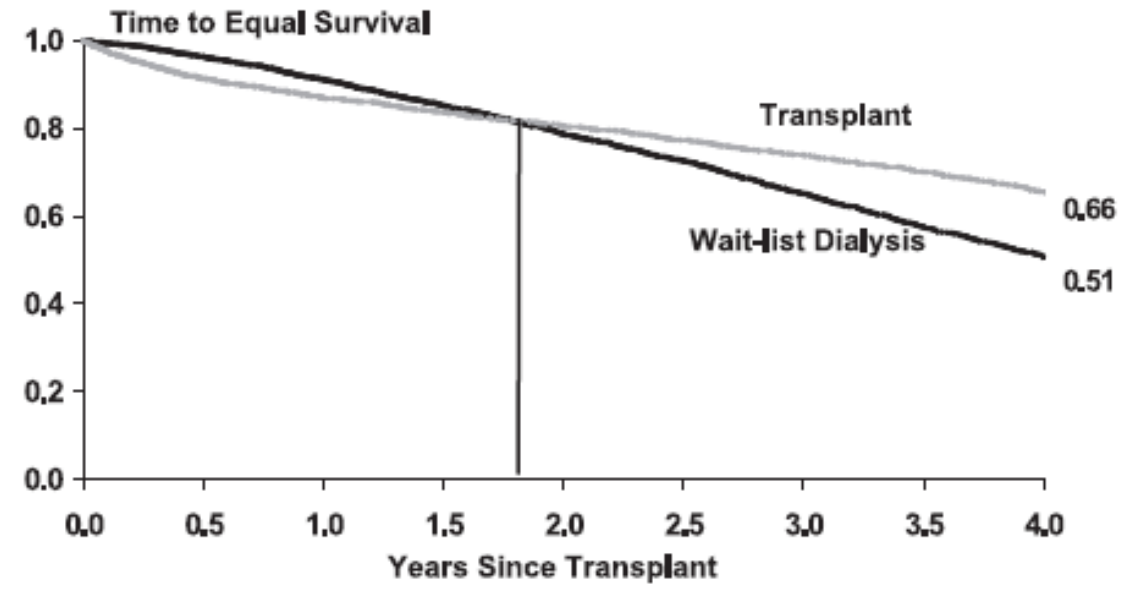
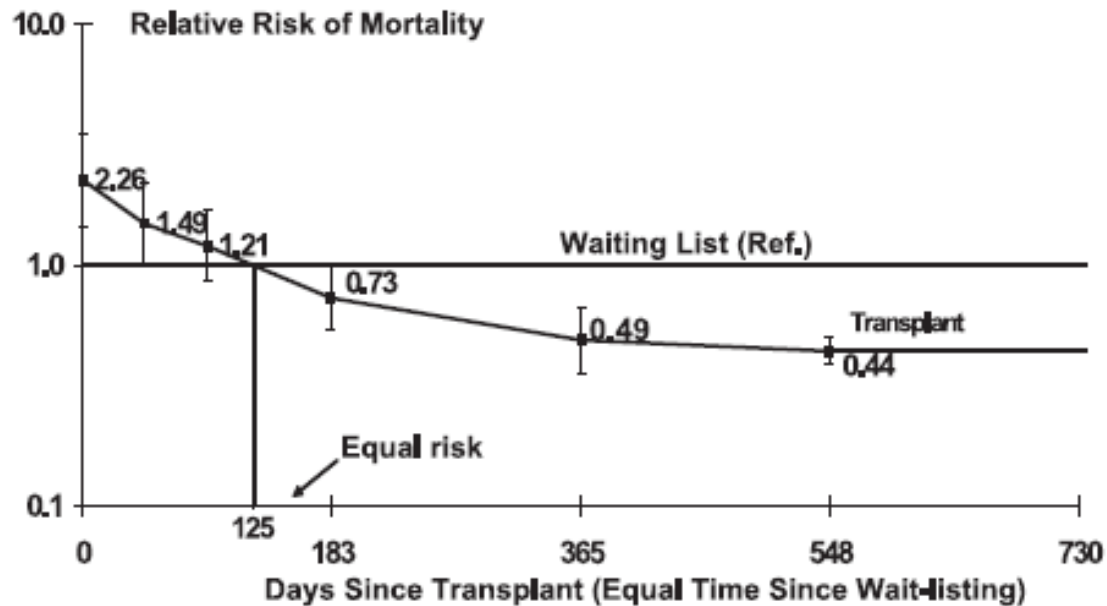
# The older recipient



**Fig. 10.2a.** Incident RRT approach for patients in the 2016 Multisite Dialysis Access Audit, stratified by age

Number of patients in each group in brackets. PTx – pre-emptive transplant; PD – peritoneal dialysis; AVF – arteriovenous fistula; AVG – arteriovenous graft; TL – tunnelled line; NTL – non-tunnelled line; RRT – renal replacement therapy

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



Transplanted patients had a 41% lower overall risk of death of waitlisted ESRF due to diabetes and hypertension – greatest benefit



# Survival and donor type

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

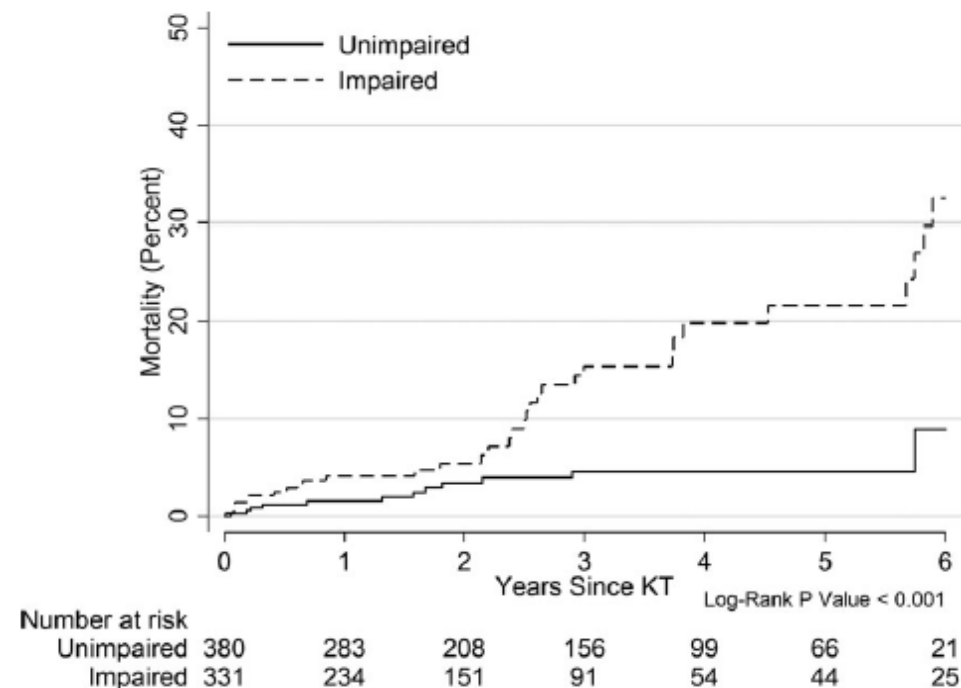
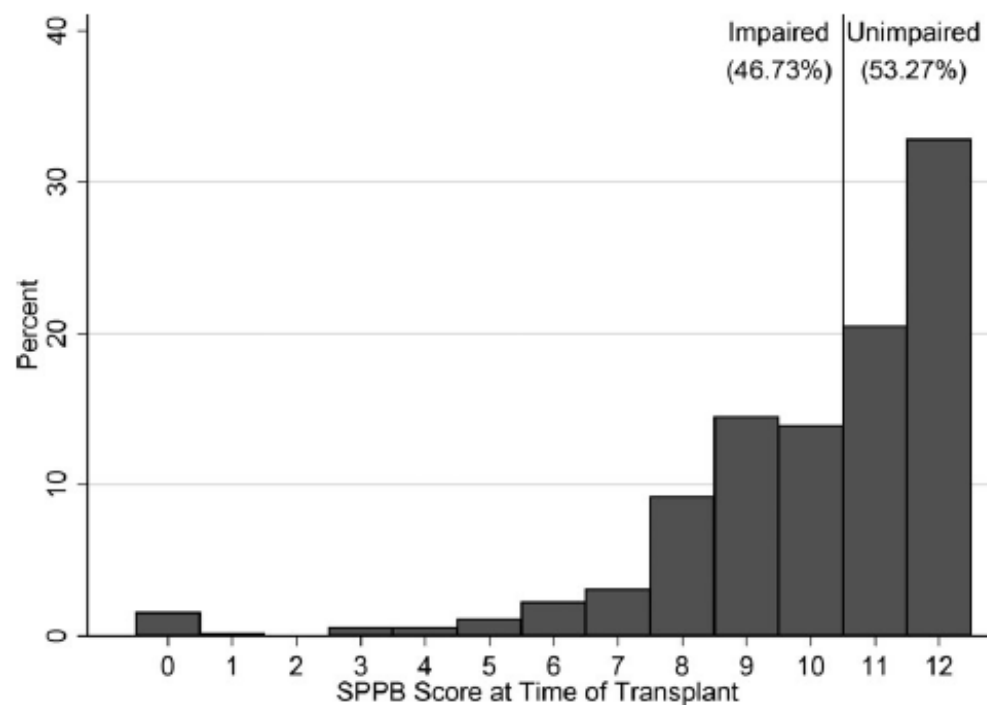
Transplant type	Transplant recipients		Graft survival, including death as an event (95% CI)		
	N	%	1 yr	2 yr	3 yr
Deceased donor	2078	85.2	80.9 (79.1–82.7)	73.9 (71.8–75.9)	66.9 (64.6–69.2)
Living donor	360	14.8	90.1 (86.6–93.4)	84.2 (80.2–88.5)	79.3 (74.6–84.4)

**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)

# Pre-Kidney Transplant Lower Extremity Impairment and Post-Kidney Transplant Mortality

- 719 KT recipients
- Frailty score (Fried)
- Short Physical Performance Battery (max score 12)
  - Standing balance
  - Walking speed
  - Chair stands
- Mean age of 51.6 (Range 18.7 – 86)
  - Impaired 56.3
  - Non impaired 47.5



**Table 2:** Risk of mortality for KT recipients by short physical performance battery (SPPB) impairment

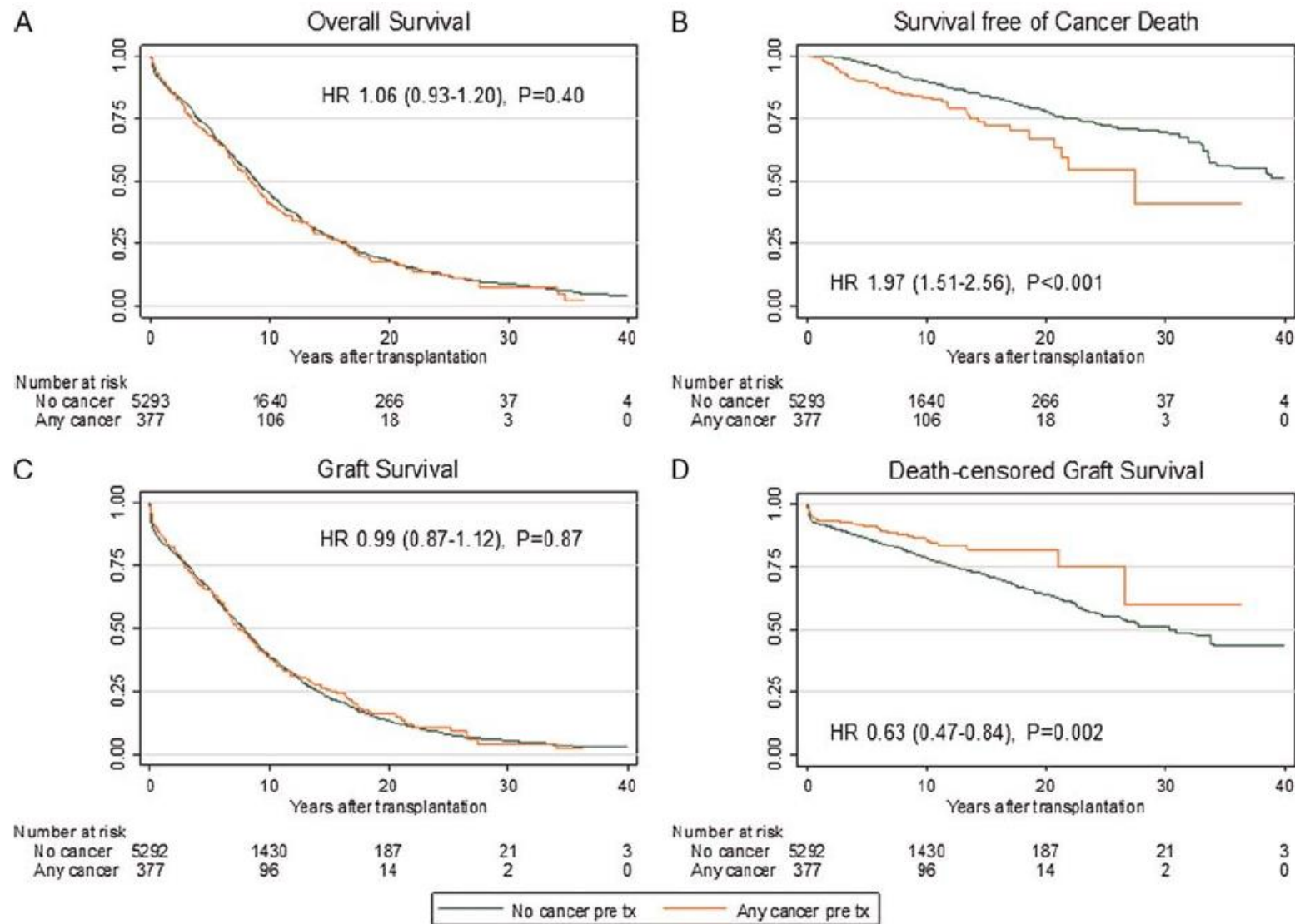
	1-year (%)		3-year (%)		5-year (%)	
	Unimpaired	Impaired	Unimpaired	Impaired	Unimpaired	Impaired
Overall	1.5	4.1	4.5	14.8	4.5	20.6
Age, y						
18–44	0.7	0.0	0.7	14.4	0.7	14.4
45–64	2.8	4.5	6.9	9.0	6.9	16.7
≥65	0.0	3.9	8.5	27.1	8.5	27.1

The risks (cumulative incidences) are expressed as % and estimated using a Kaplan-Meier approach.

Nastasi et al AJT 2017

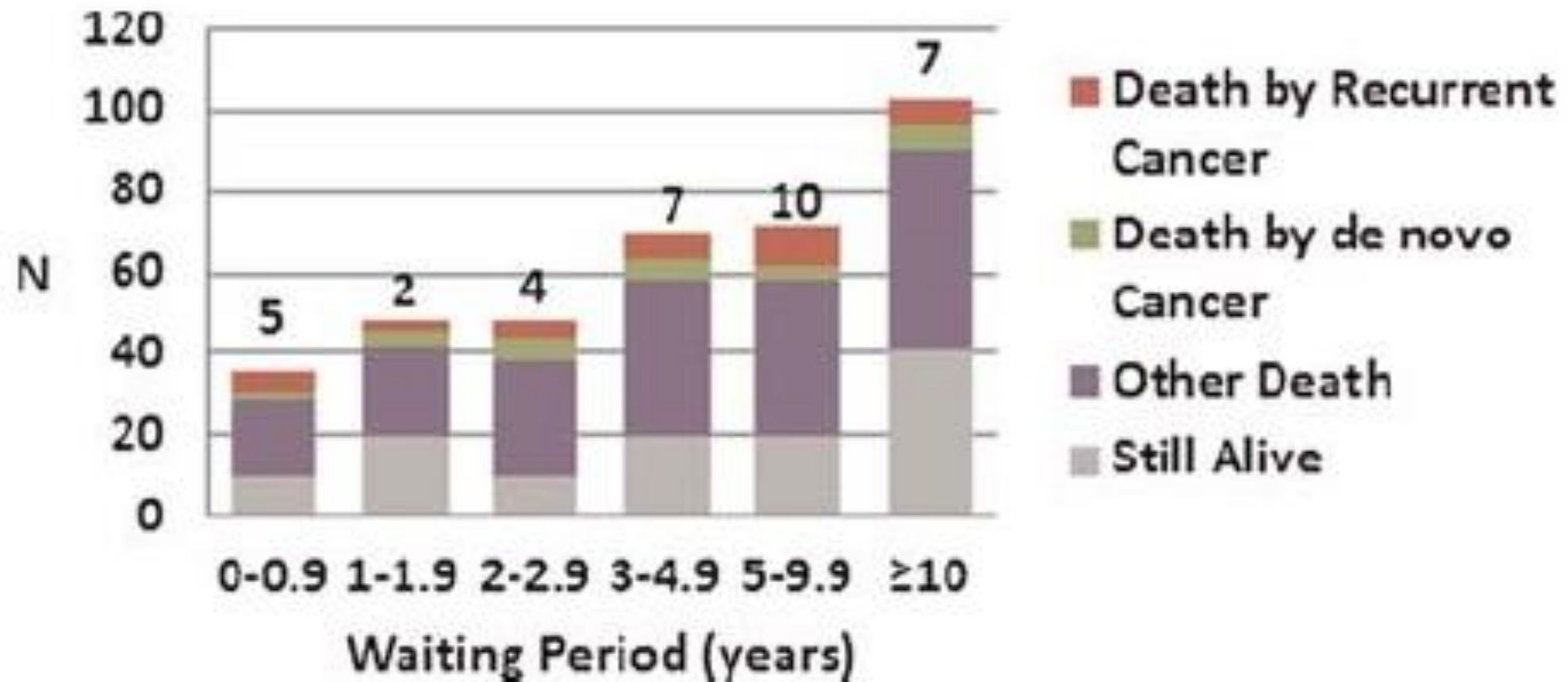
# Cancer

# Association Between Pretransplant Cancer and Survival in Kidney Transplant Recipients



# Waiting time and cancer

## Outcome, by Waiting Period



# CTS data

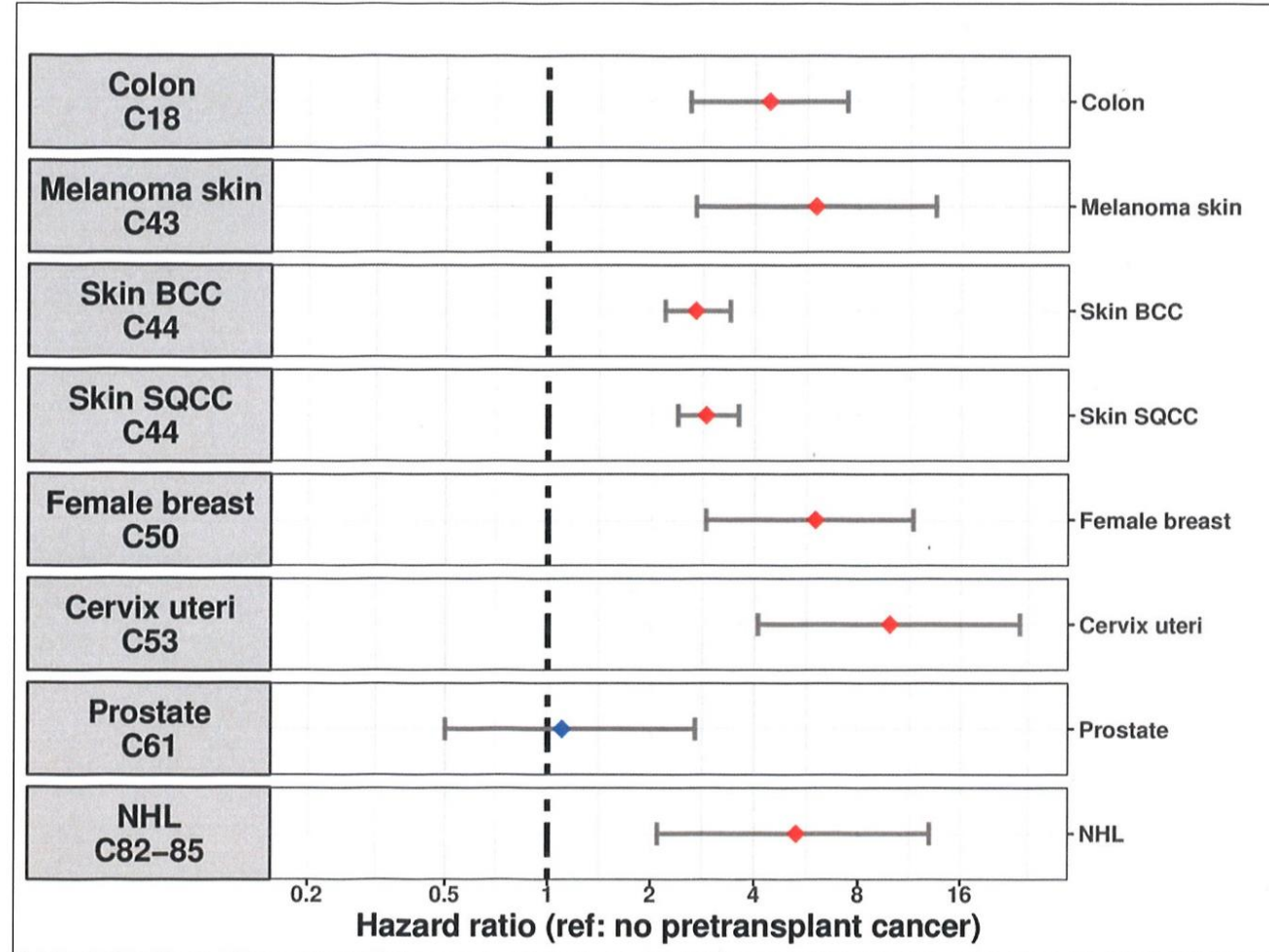


Figure 3

270,000 transplant recipients. 4000 had a previous cancer



# CARI guidance

- **Nil**

- Superficial Bladder Cancer (2D).
- In situ Cancer of the Cervix (2D).
- Non-metastatic Non-Melanoma Skin Cancers (2D).
- Prostatic Cancer microscopic (2D).
- Asymptomatic T1 Renal Cell Carcinoma with no suspicious histological features (2D).
- Monoclonal Gammopathy of Undetermined Significance (2D).

- **2 years**

- Invasive Bladder Cancer (2D).
- In situ Breast Cancer (2D).
- Stage A and B Colorectal Cancer (2D).
- Lymphoma (2D).
- In situ Melanoma (2D).
- Prostatic Cancer (2D).
- Testicular Cancer (2D).
- Thyroid Cancer (2D).
- Wilm's Tumour (2D).

- **5 years**

- Stage II Breast Cancer (2D).
- Extensive Cervical Cancer (2D).
- Colorectal Cancer stage C (2D).
- Melanoma (2D).
- Symptomatic Renal Cell Carcinoma (2D).

Malignancy	Europe	United States
Incidental renal cell carcinoma	No	No
Basal cell carcinoma	No	No
Bladder carcinoma in situ	1 year	No
Cervical carcinoma in situ	2 year	Not specified
Lymphoma	2 years	2 years
Prostate	1–2 years	2 years
Thyroid	2 years	2 years
Testicular	2 years	2 years
Symptomatic renal	2 years	2 years
Invasive cervix	4–5 years	Not specified
Invasive bladder	>5 years	2 years
Colorectal	>5 years	0–5 years*
Mamma	>3 years	2–5 years
Malignant melanoma	>2 years	2–5 years

\* stage-dependent

# Who else should be considered

- Other common issues that are not a barrier to transplantation
  - MGUS
  - Hepatitis B
  - Hepatitis C
  - HIV
  - Poor LV function from fluid loading

# Conclusions

- Pre-emptive evaluation of patients
  - Native
  - Failing transplant
- Obese patients are difficult to transplant
  - Survival benefit over dialysis
  - Live donor transplant may be better
- Age is not a barrier to transplantation (or living donation)
  - Physical functionality may be a better test
- Cancer is not a barrier to transplantation
  - Prostate
  - Asymptomatic Pt1 renal cancer



# UCL

CENTRE FOR NEPHROLOGY

**ROYAL** FREE  
TRANSPLANTATION