Joint Meeting of Assurance Medical Society and Select 74

Renal Diseases

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Oxford Kidney Unit

Kidney disease

- ***Acute and reversible***

  Acute renal failure
  e.g. after trauma
  Acute obstruction
  e.g. kidney stone
  Acute infection

- ***Chronic and irreversible***

  Primary renal disease

  Secondary
  congenital
  traumatic
  inflammatory
  neoplastic

Chronic kidney disease

- ***Can be***
  a primary renal disease e.g. nephritis
  or
  secondary to a systemic disorder e.g. diabetes
- Is usually progressive
- ***May***
  end in kidney failure and death
  or
  contribute to premature death e.g. hypertension

Detection of chronic kidney disease

- History of associated conditions
- Urine abnormalities
  proteinuria > 300mg/24 hours
  microscopic haematuria
- Raised blood pressure
- Simple biochemical test – plasma creatinine
- Simple imaging – ultrasound
- Renal biopsy

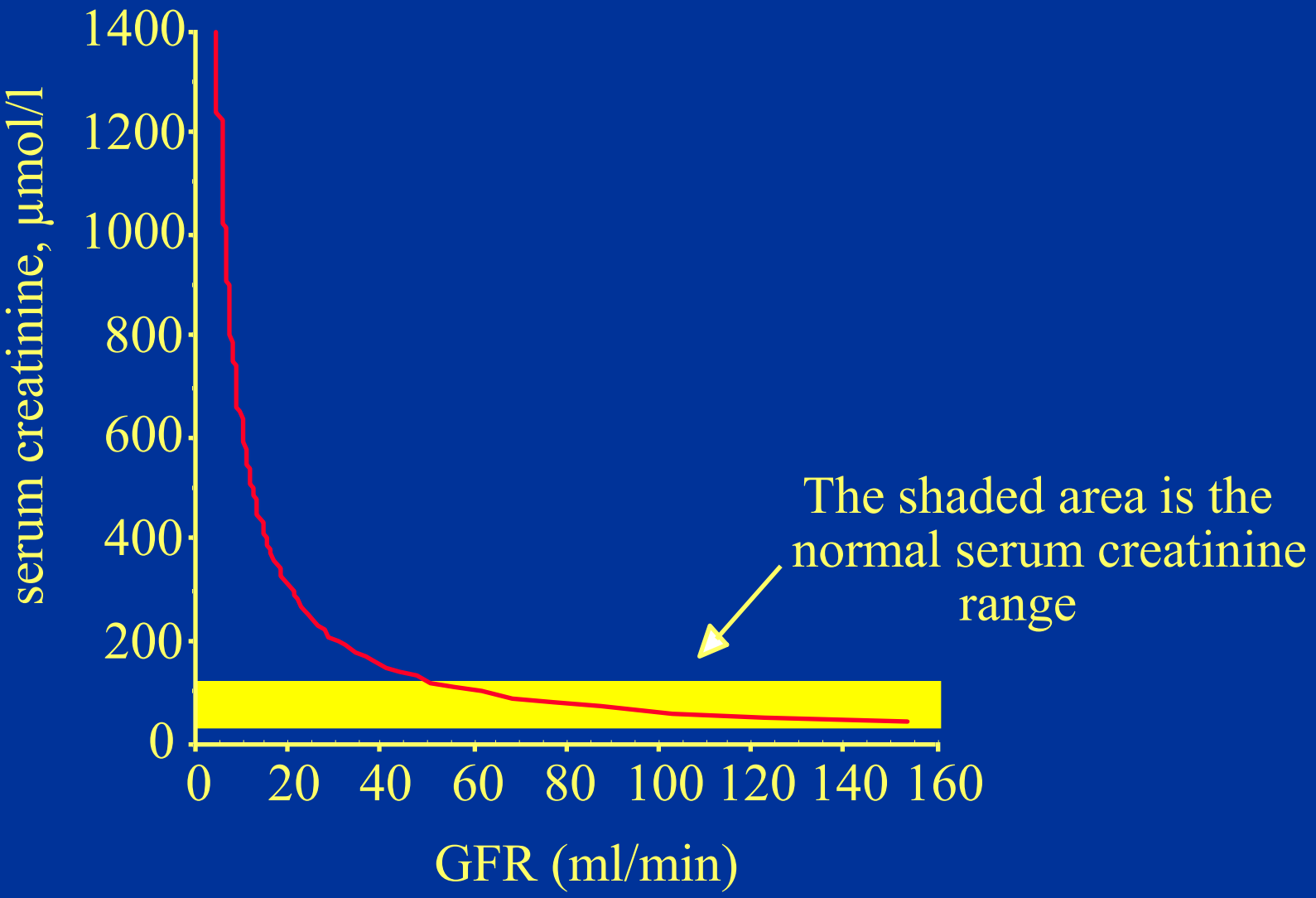
Interpreting the creatinine

- Related to muscle mass and GFR
- Quick calculation of Cr Clearance

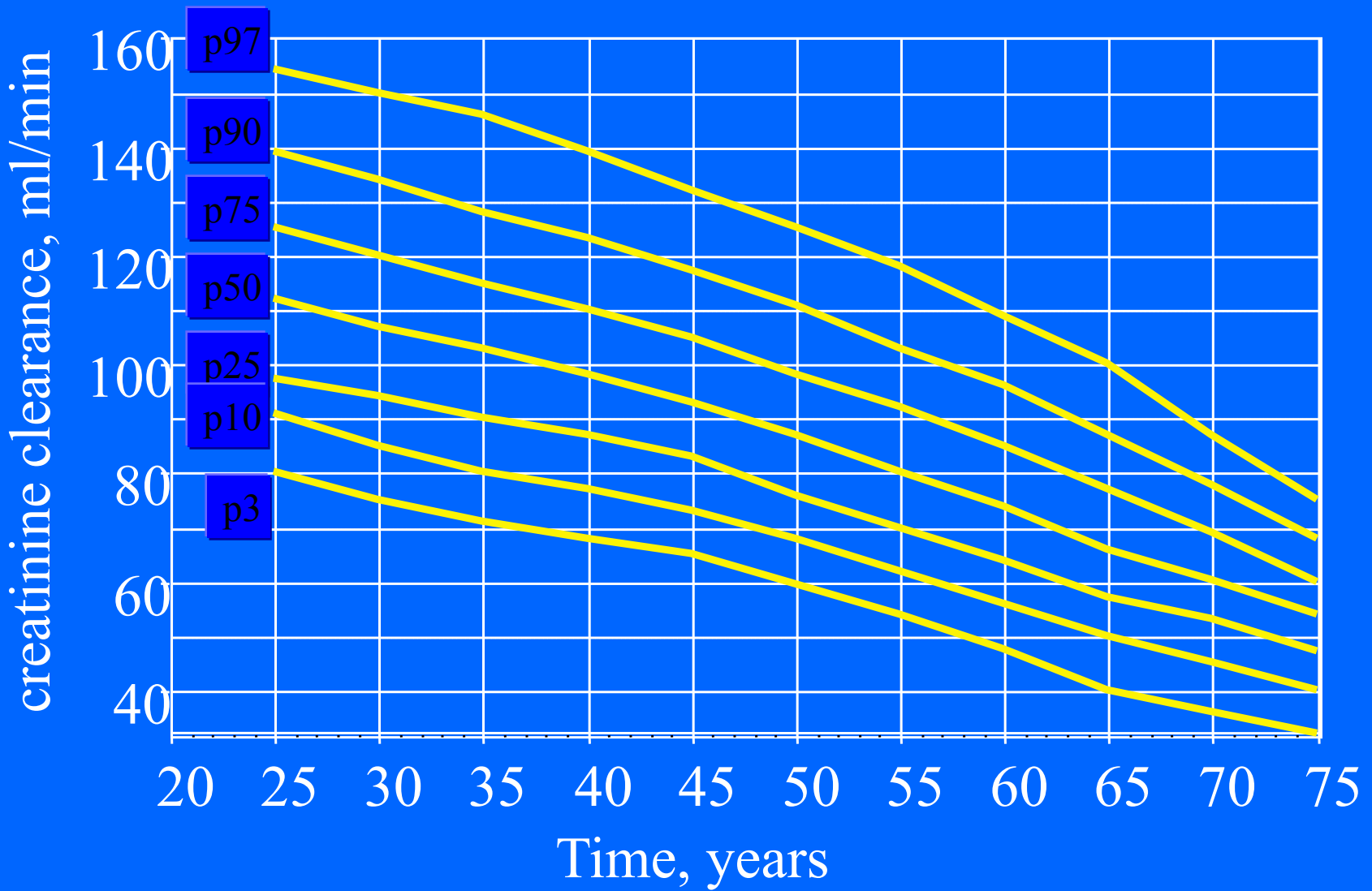
$$\frac{(140\text{-age}) \times \text{wt (kg)}}{\text{creat (umol)} \times 0.82}$$

- Allow for age and gender

Relationship between GFR and creatinine



Creatinine clearance by age normal males



Stages of Chronic Kidney Disease

Stage	Description	GFR*	Prevalence
1	With normal GFR	>90	3.3%
2	Mild reduction	60-89	3.0%
3	Moderate reduction	30-59	4.3%
4	Severe reduction	15-29	0.2%
5	Kidney failure	<15 or RRT	0.2%

* mls/min/1.7m

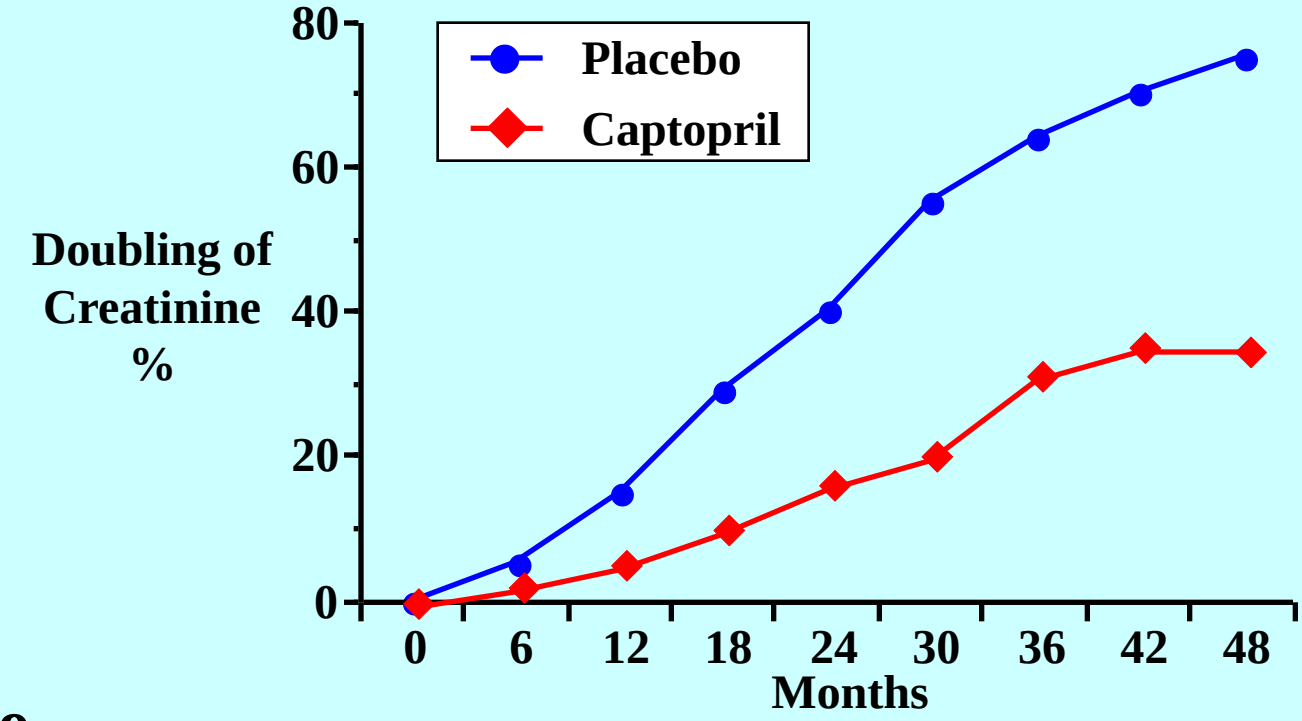
Chronic kidney failure - definition

Loss of renal function that is:

- Substantial (usually > 50% loss)
- Clinically relevant (complications)
- Irreversible
- Progressive

"SCIP"

ACEI and progression of DM-N



n=409

Overt proteinuria

Cr > 132 µmol/l

Response in all pts irrespective of BP

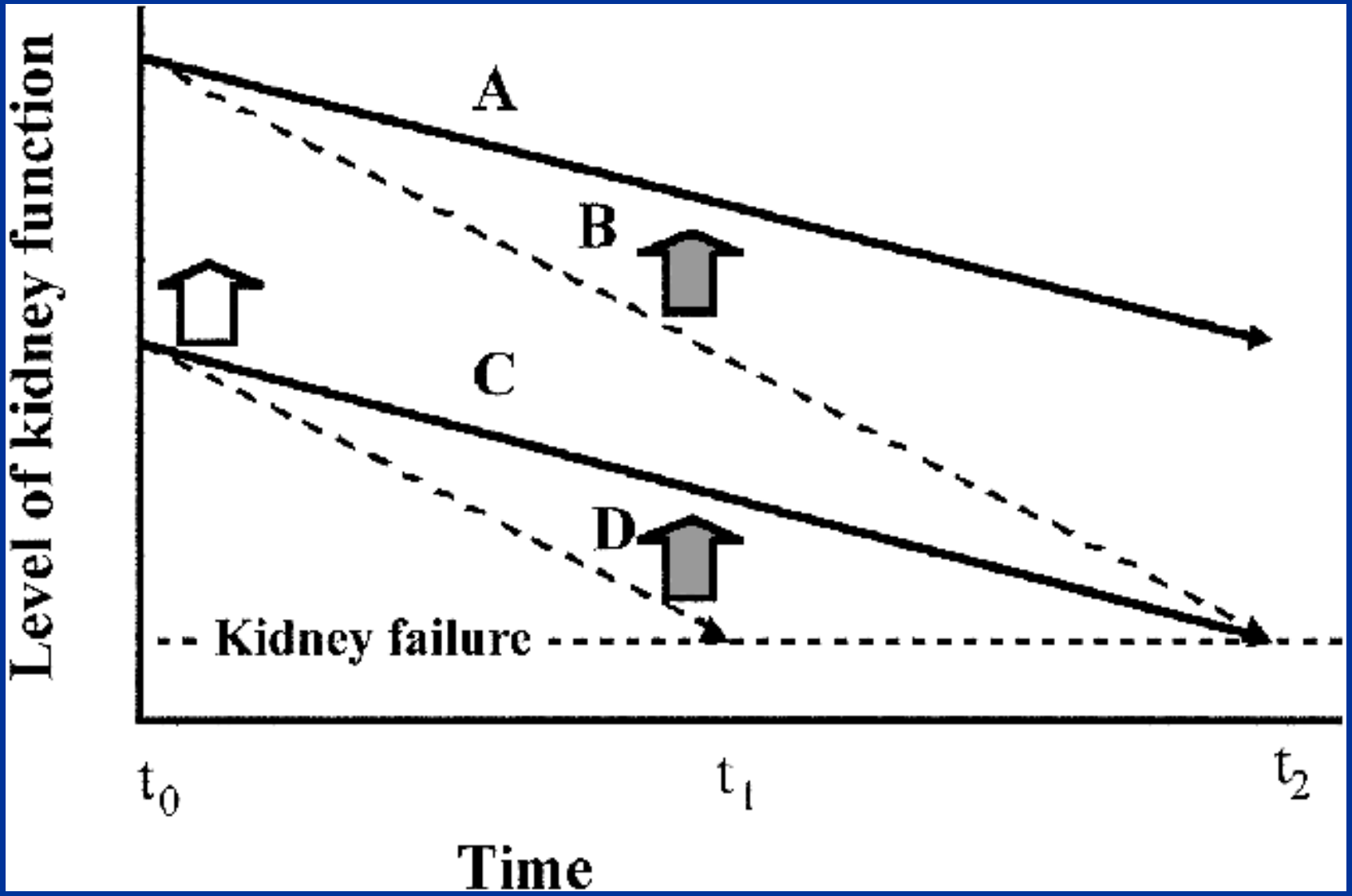
from Lewis, EJ, Hunsicker, LG, Bain, RP, Rohde, RD
N Engl J Med 1993 329:1456

Degrees of CRF

Mild	>40%-60% *	silent
Moderate	20-40%	hypertension
Severe	5-20%	symptomatic
Endstage	<5%	very ill

* % predicted median GFR

Plotting the progression of renal failure

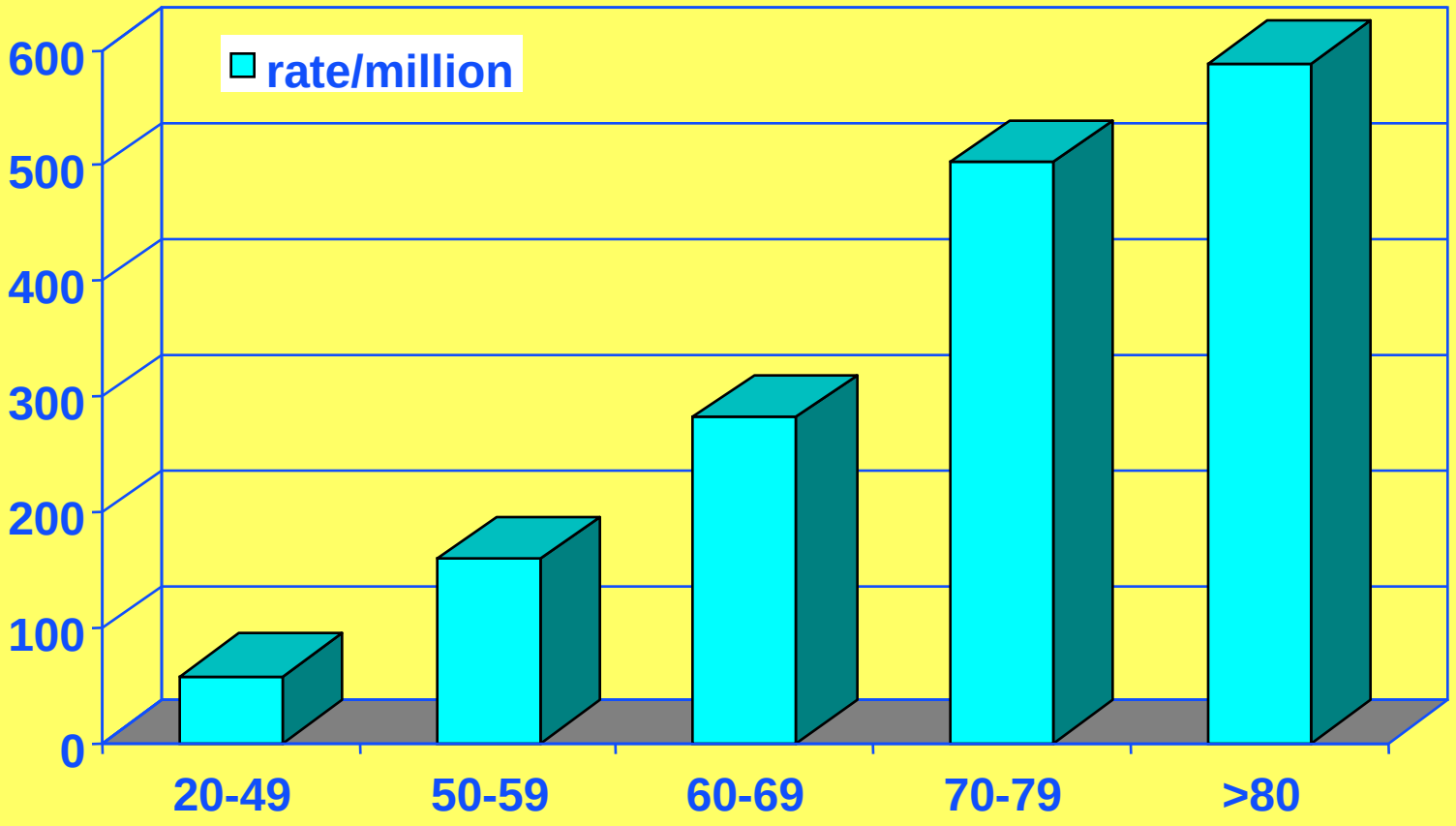


Incidence of ESRF

- 80 – 120 pmp per annum
- Higher in the socially deprived
- Higher in ethnic minorities –blacks and Asians
- 40% > 65 years of age. Median 61 years

"The deprived, the elderly, the minorities"

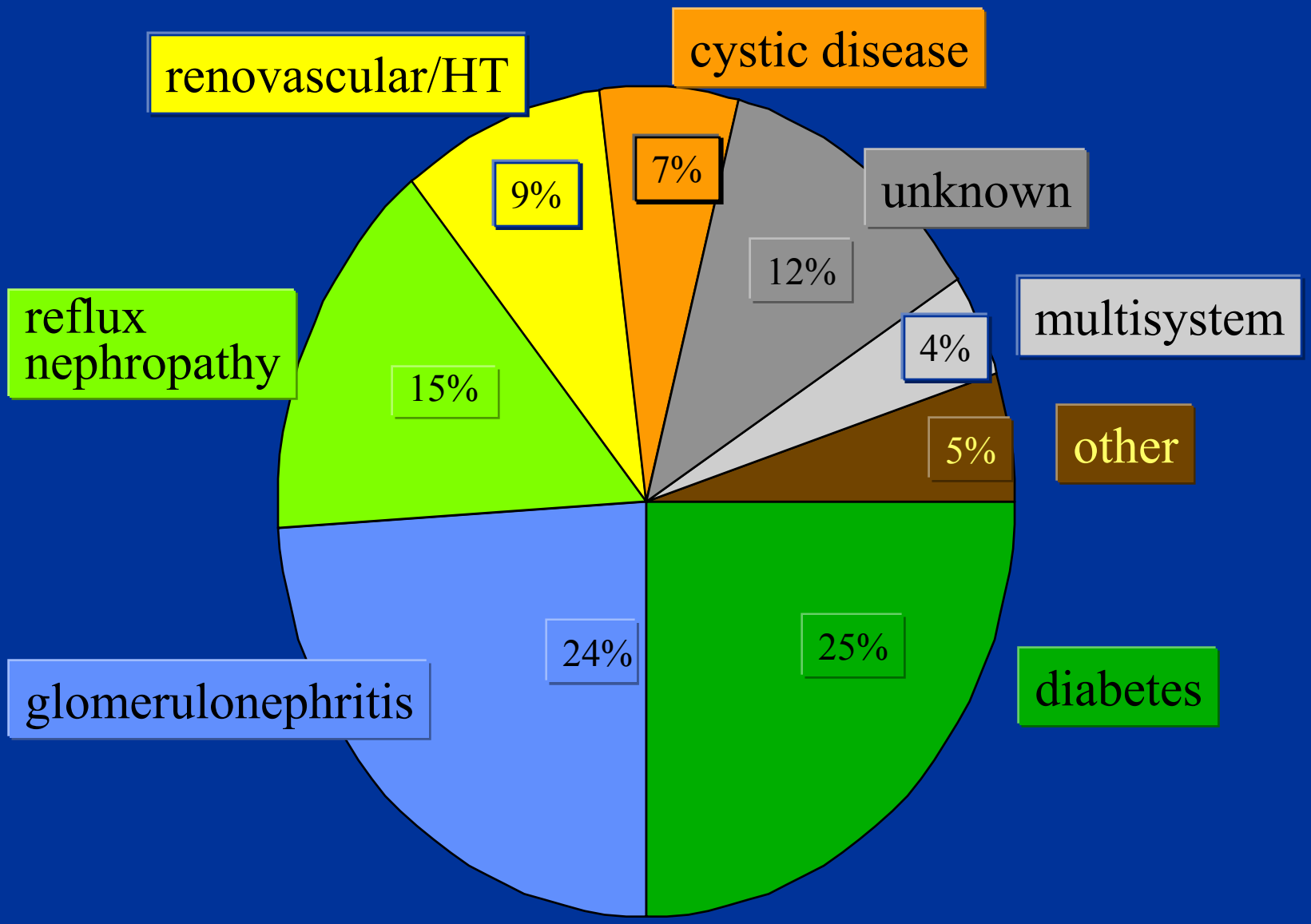
Age related incidence of ESRF



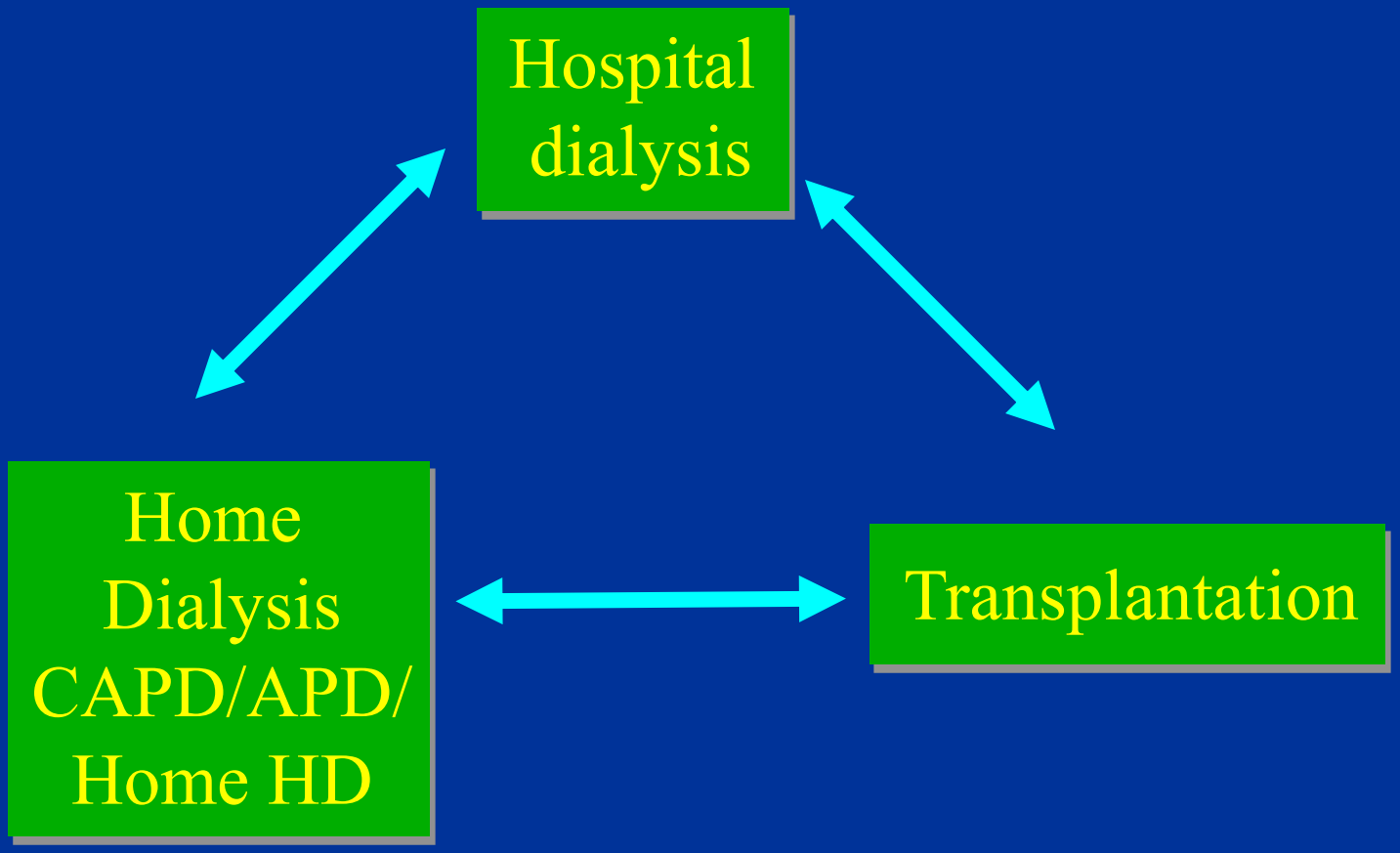
Prevalence of ESRF

- ~ 800 per million population
- 45% will be transplanted
- Steady state not reached

Causes of end-stage renal failure



Patients with chronic Renal failure



Costs - annual, inclusive of VAT!

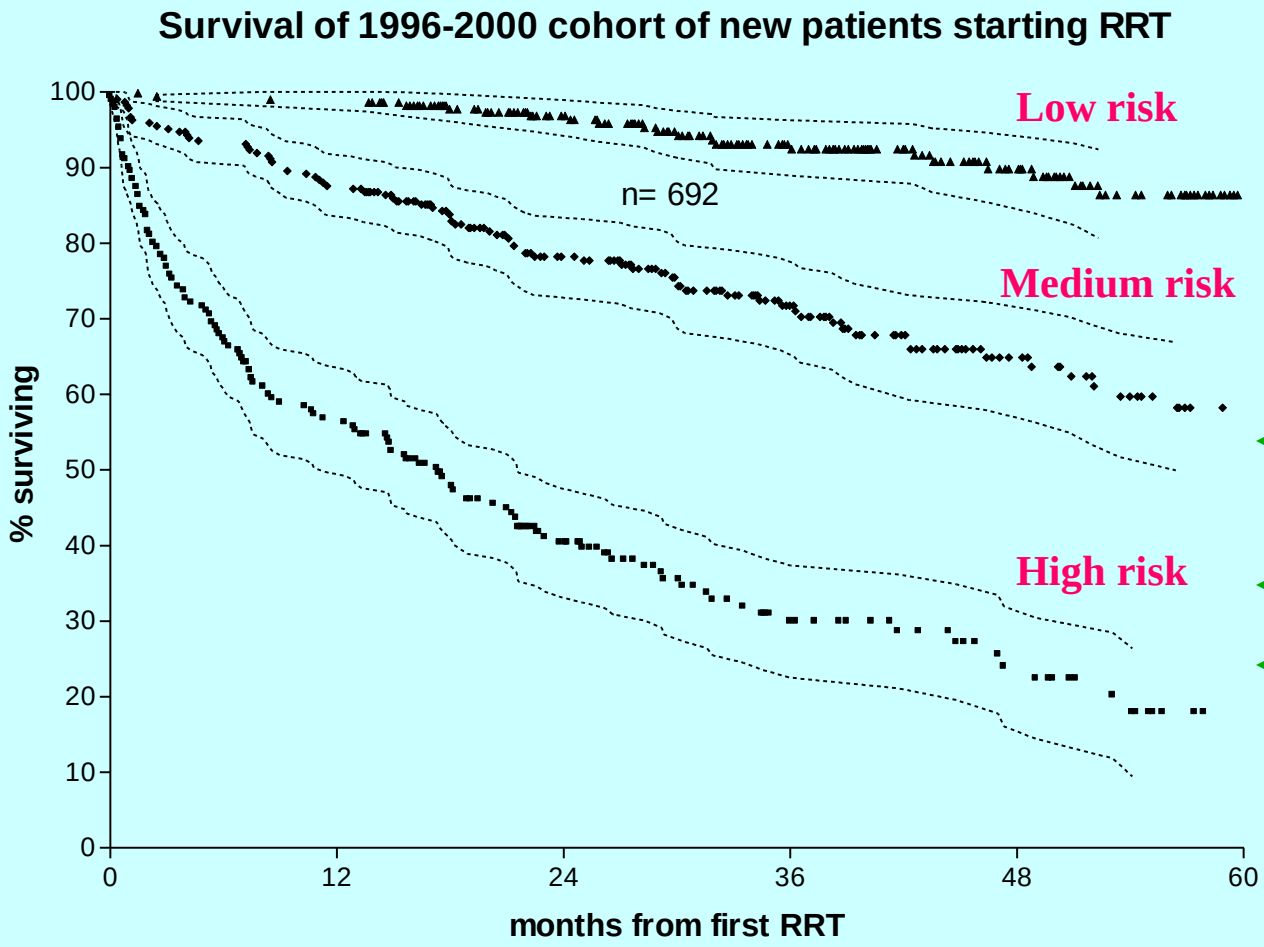
- **Haemodialysis** ~ £25,000
  at home ~£15,000
- **CAPD** ~ £20,000
- **APD** ~ £22,000
- **Transplant**
  First year ~£25,000
  thereafter ~ £5,000

Risk groups - Khan et al

- LOW: < 70 years and no co-morbid illness
- MEDIUM: 70-80 years
  < 70 years with co-morbidity
- HIGH: > 80 years
  or any age with 2 other organ dysfunctions
  diabetes and cardiac disease
  visceral malignancy

Median survival by risk group

- ***Standard***: non diabetics < 55y = **14 years**
- ***Medium***: non diabetics 55-64 = **7 years**
  diabetics <55
- ***High***: non-diabetics >65
  diabetics >55 = **3.5 years**



Comparison *

← Myocardial infarct 55%

← Bowel cancer 35%

← Heart failure 25%

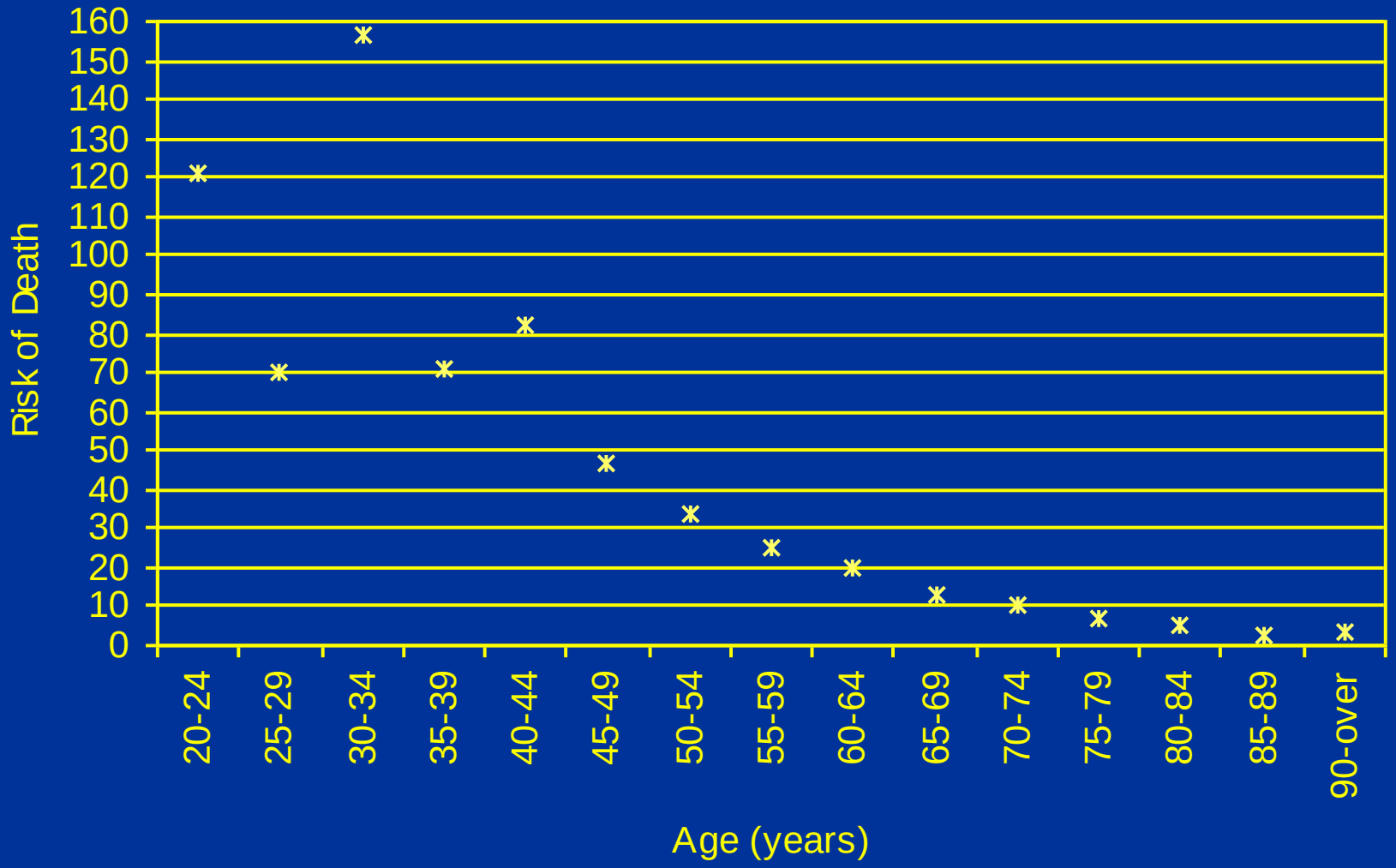
*** 5 year survival after first hospital admission**

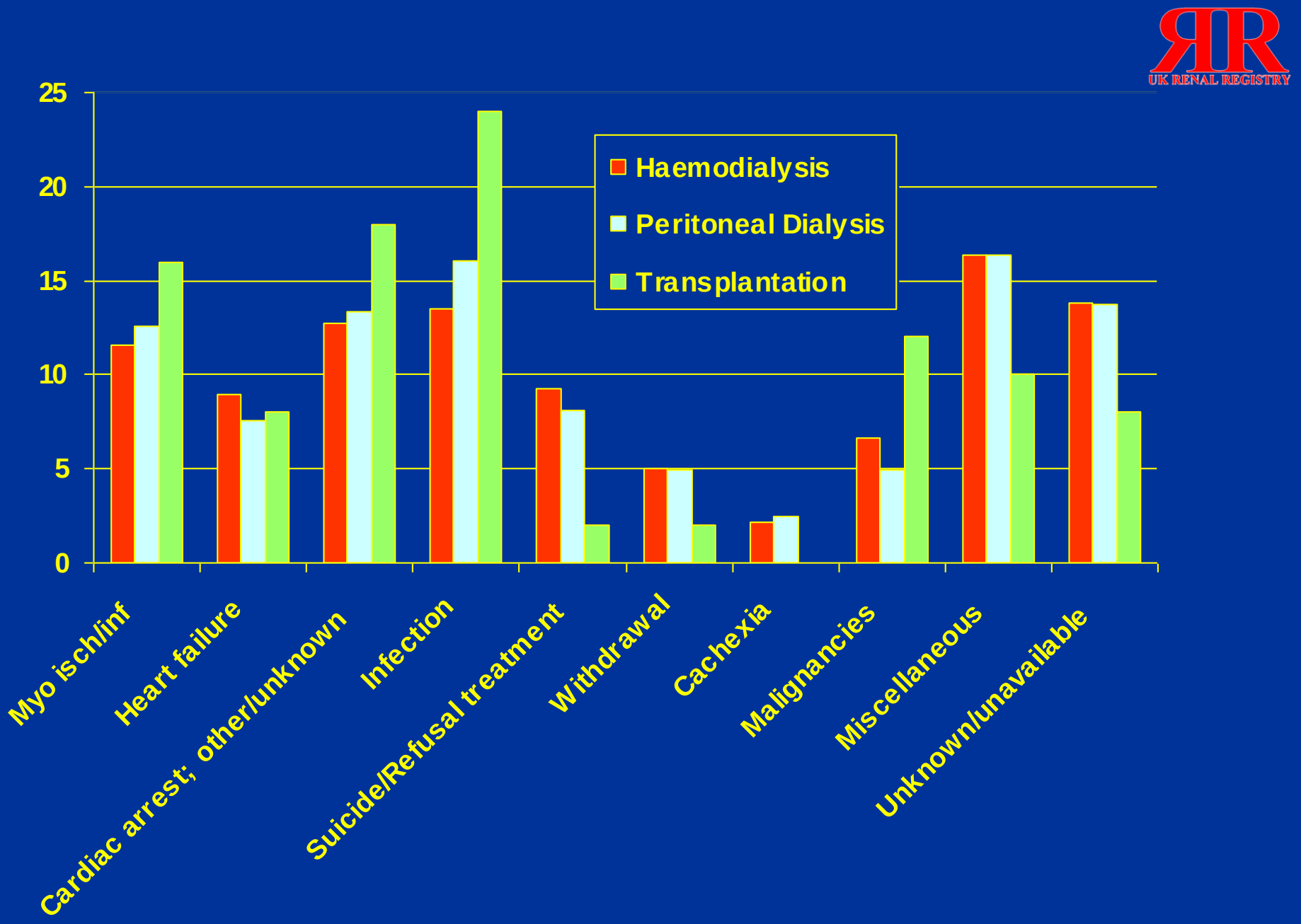
Death rate by primary diagnosis

Diagnosis	Deaths/100 patient years	Compared to GN
Amyloid	27.1	1.79
Polycystic	11.7	0.78
Diabetes	27.4	1.82
G'nephritis	15.1	1.0
Cancer	49.7	3.29
Pyelonephritis	15.9	1.05
Renal vascular	21.8	1.44

Renal Registry 2002

Relative Risk of Death in ERF Patients compared with the General Population of E&W




UK RENAL REGISTRY
25
20
15
10
5
0
Haemodialysis
Peritoneal Dialysis
Transplantation
Myo isch/inf
Heart failure
Cardiac arrest; other/unknown
Infection
Suicide/Refusal treatment
Withdrawal
Cachexia
Malignancies
Miscellaneous
Unknown/unavailable

Causes of death

	Dialysis (952)	Transplant (111)
Cardiac	42%	32%
Infection	13%	13%
Withdrawal	21%	Not applicable
Malignancy	5%	25%

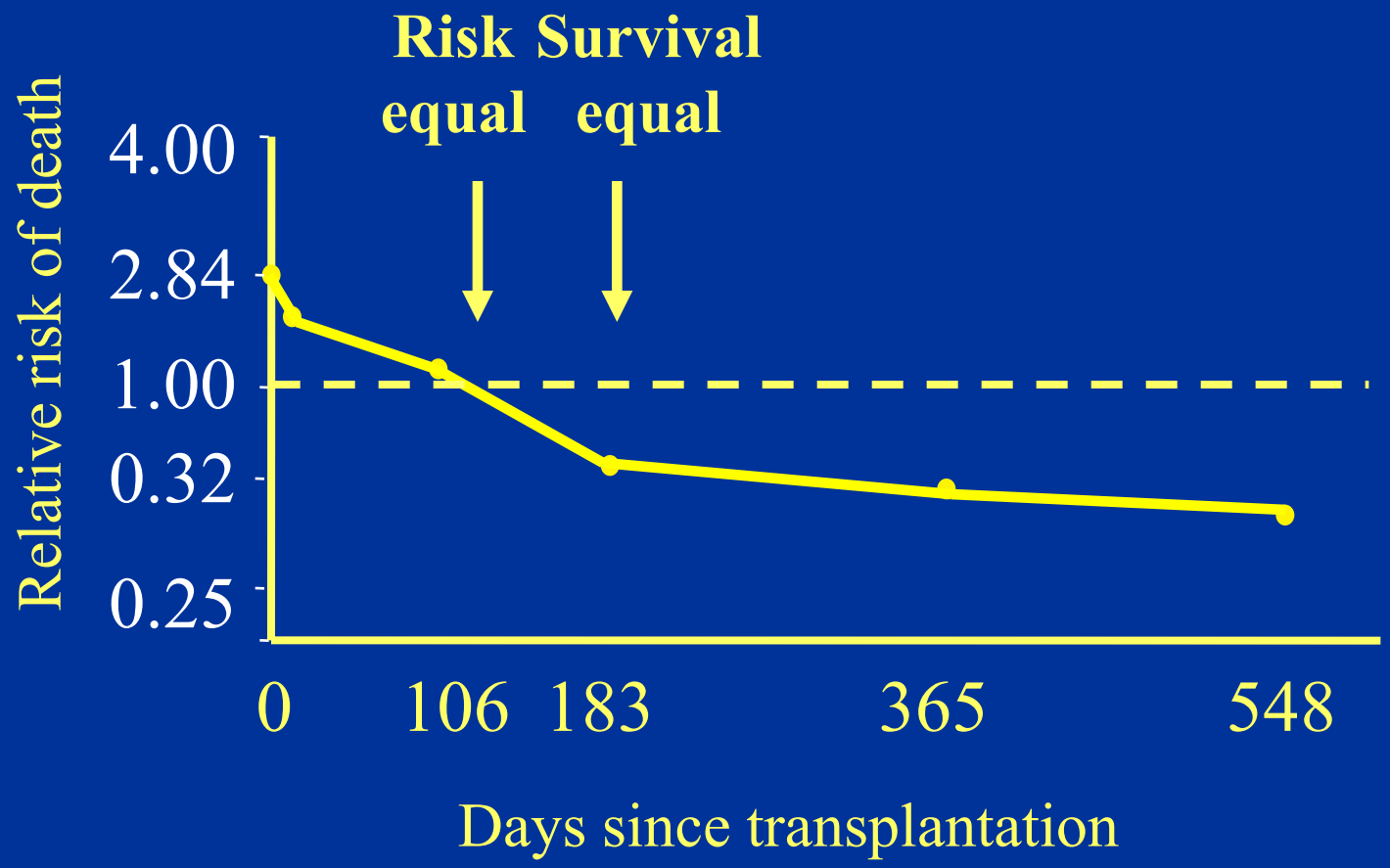
ANZDATA 1999

Cardiovascular relative risk compared with the general population

Age	Any RRT	Txp	diabetic	non-diabetic
35-44	70	40	320	34
45-54	20	12	62	14
55-64	12	8	22	11
65-74	5	10	13	5

From EDTA Registry

Adjusted relative risk of death among 23,275 1st CAD recipients cf. 46,164 on dialysis



Wolfe et al, NEJM, 1999

Annual death rates 1991-1997 USRDS (deaths per 100 patient years)

Variable	All dialysis	Transplant *candidates*	Transplant *recipients*
All patients	16.1	6.3	3.8
Diabetics	19.9	10.8	5.6
Non-diabetics	13.3	4.3	3.0

Specific topics

- Proteinuria
- Polycystic kidney disease
- Diabetes mellitus
- IgA nephropathy

Proteinuria

- normal up to 150mg/24 hours
  (<75mg/L–300mg/L)
- usually detected with urine dipstick
  sensitivity = 100mg/L
  NB mainly albumin-not Bence-Jones protein
  false positives rare-radiocontrast media
  colour blindness
- noting SG on dipstick helps interpretation

Casual proteinuria is common and may not need investigation

Study (dipstick positive)	Prevalence(%)
schoolchildren	0.6-6.4
10 studies, n=50,000	weighted mean, 2.2
young adults	
male forces recruits	0.9-5.6
college students	5.0-26.0
adults	1.7-3.0
incl. microalbuminuria	up to 10.0
adults, > 60yr	6.6-10
> 80yr	16.1

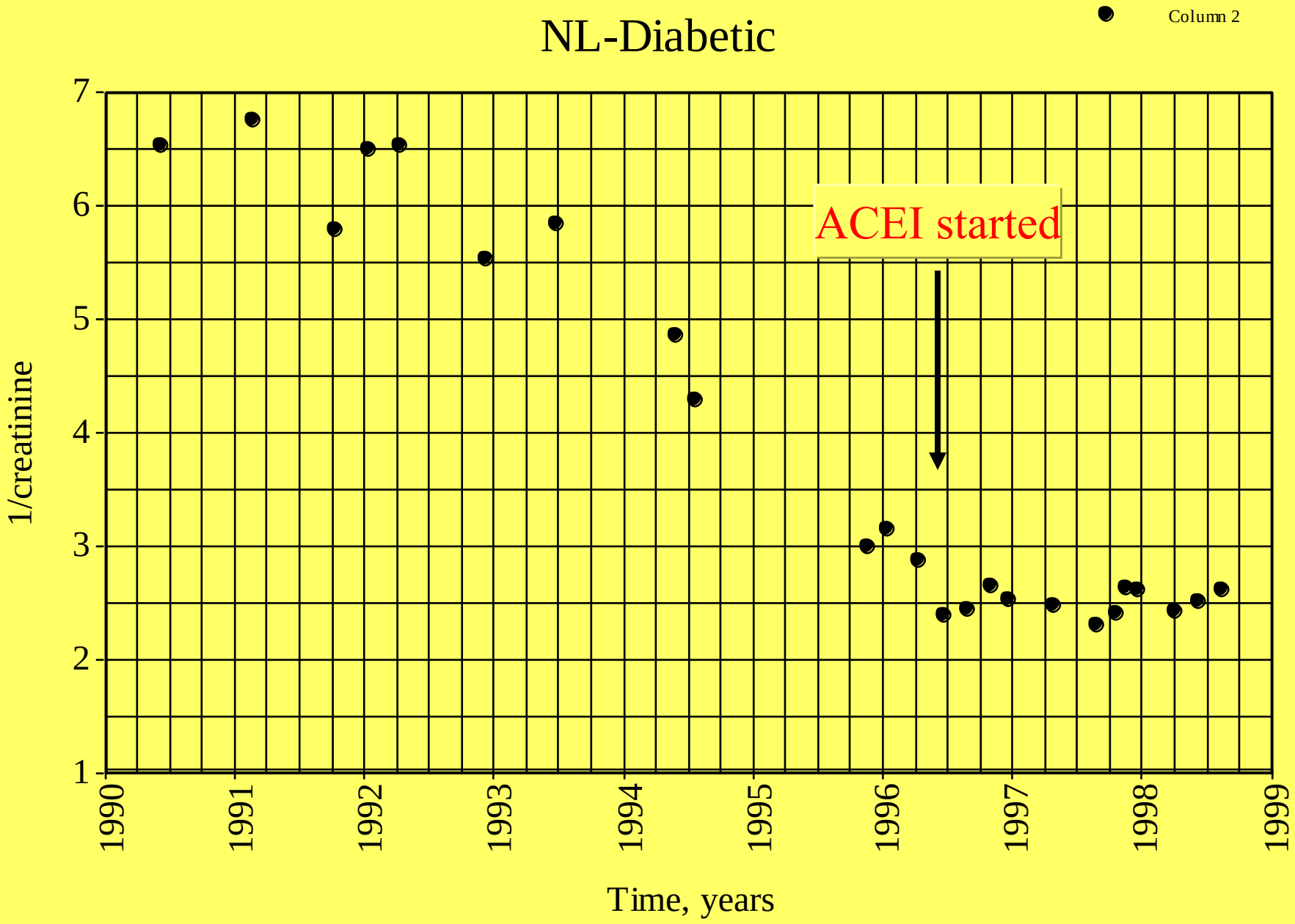
Outcome of ‘mild’ proteinuria (< 1g/day) (normal renal function & no HT)

- Framingham study (>5000 patients, 16yr)

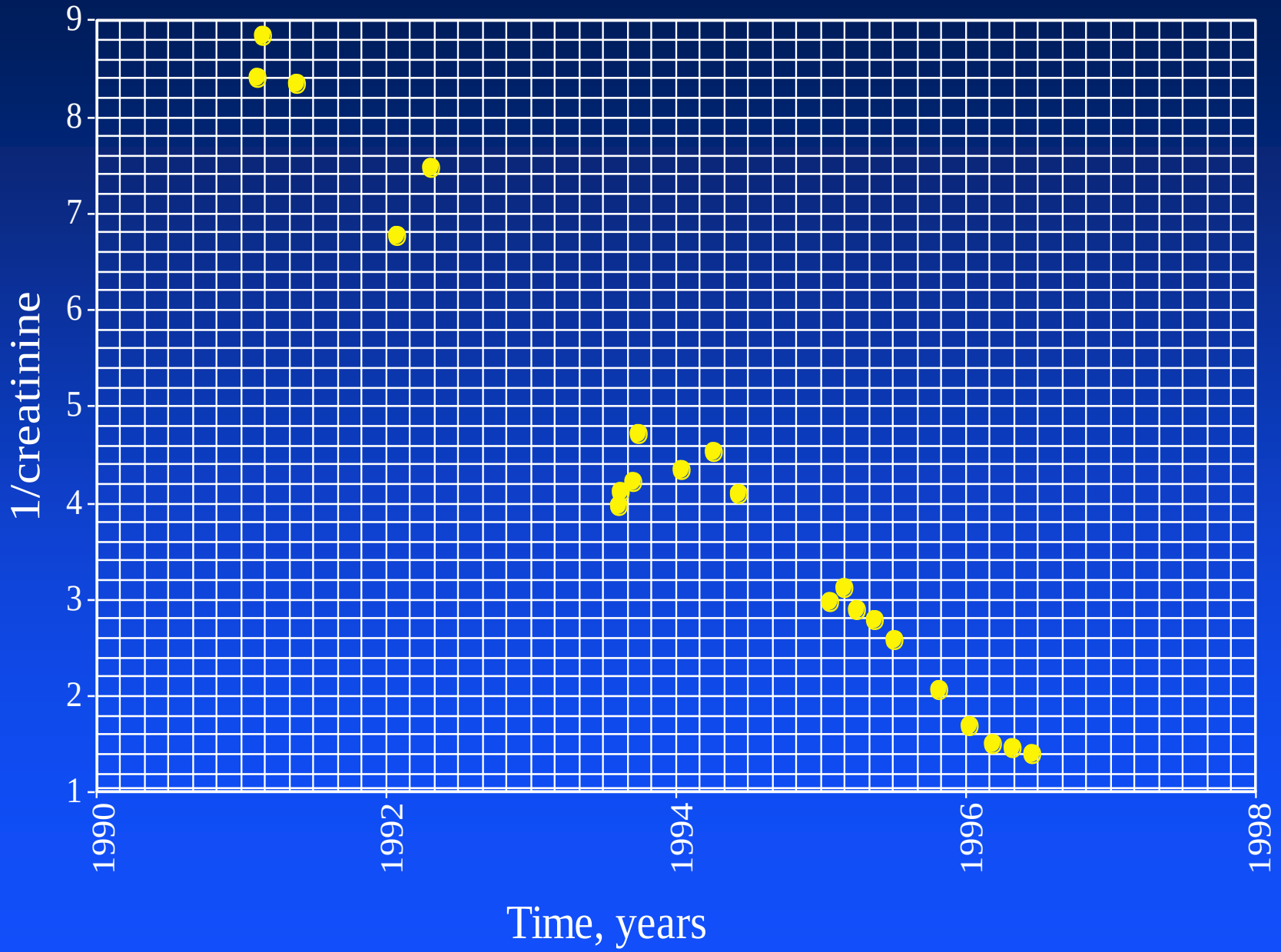
  proteinuria associated with 3-fold increase in mortality but only with HT and/or diabetes and none developed renal impairment

Risk of renal failure in subjects with mild renal impairment or proteinuria

- Impossible to predict without a diagnosis
  after obstruction – low risk
  diabetics and ADPKD – high risk
- Look at the function vs time plot
- Effect of treatment


NL-Diabetic
Column 2
ACEI started
1/creatinine
Time, years
7
6
5
4
3
2
1
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999

DM chronic GN •



Bad prognostic signs

- Diseases known to progress
- Heavy proteinuria > 3g/day
- Hypertension
- Rising creatinine
- Smoking
- Male gender
- Small kidneys on ultrasound
- Chronic interstitial changes on biopsy

Adult polycystic kidney disease

- 1:1000
- 4-10% of patients on RRT
- less common in blacks

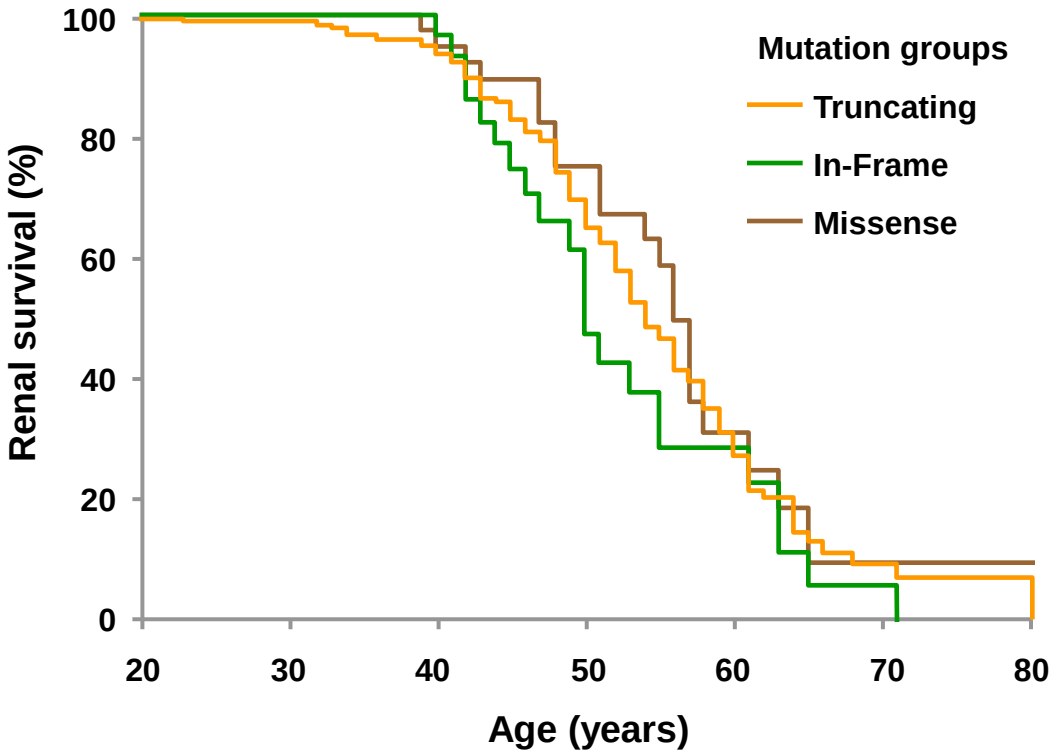
Presentation and manifestations

- Positive family history - screening
- Flank pain 20% - cysts, haemorrhage, obstruction and infection
- Bleeding 20%
- Infection 20% males 70% females
- Calculi
- Hypertension
- Subarachnoid haemorrhage – berry aneurysms
- ESRF

Genetics

- Autosomal dominant
- Type 1 chromosome 16
- Type 2 chromosome 4 (milder phenotype)
- Often sporadic

The effect of the type of lesion on renal survival



mayo

CP986604-3

Diabetes mellitus

- **Type 1 IDDM**

  nephropathy
  in 40% at 40 years

  Probably less now

- Type 2 NIDDM
  (10-15x more common)

  nephropathy
  25% at 20 years
  5% at diagnosis
  5% will require RRT

Risk of nephropathy in Diabetes mellitus Type 2 (UKPDS)

Event	Risk per year
Micro-albuminuria	2% per annum
Micro to macro-albuminuria	2.8% per annum
Macro to renal impairment	2.3% per annum
Death in those with CRF	19.2%

IgA nephropathy

aka:

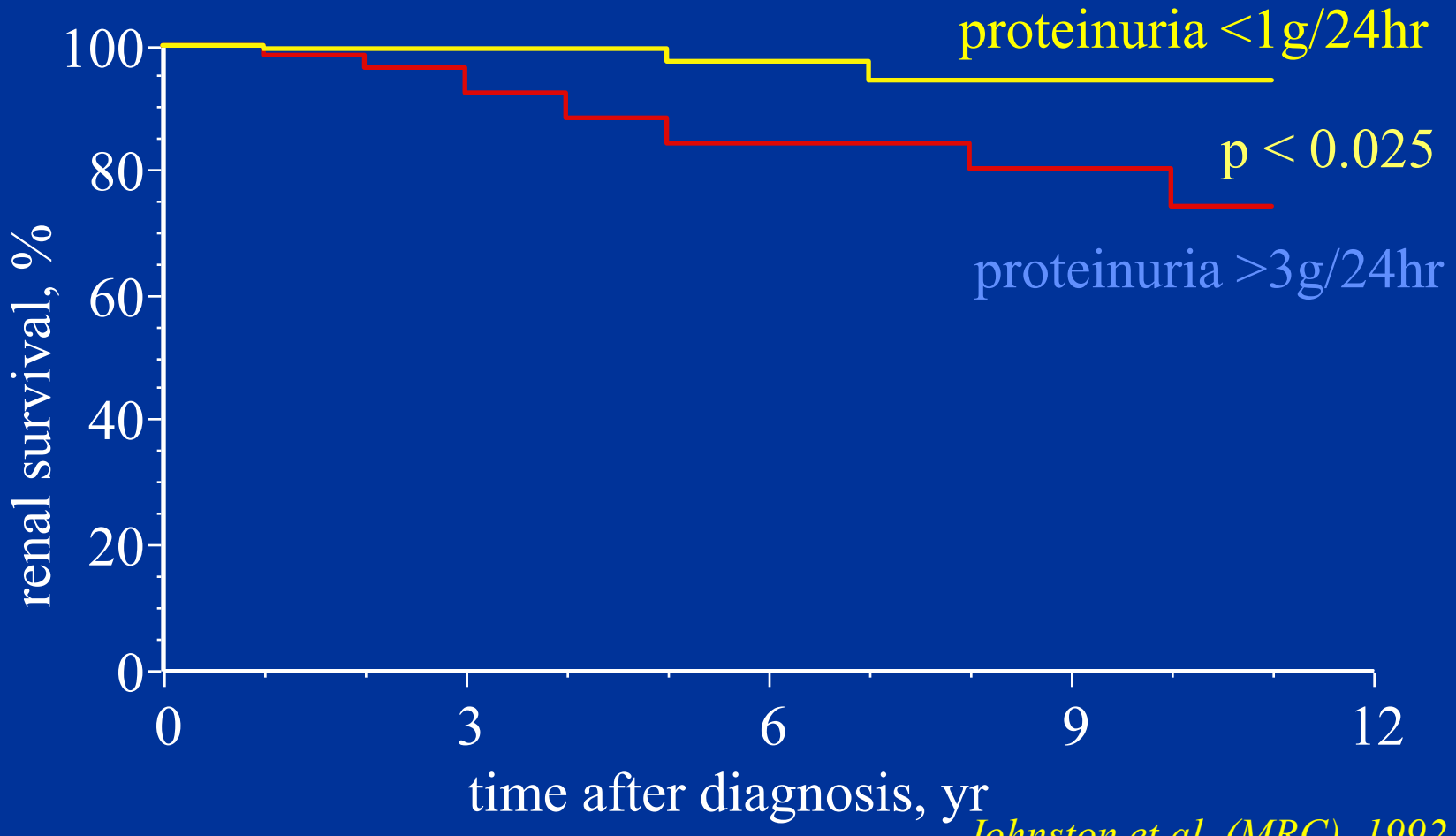
Berger's Disease or Mesangial IgA Disease

- Most common glomerulonephritis
- Precisely defined immunohistology
- Presentation:
  - Microscopic haematuria (ascertainment)
  - Macroscopic haematuria (synpharyngitic)
  - Hypertension
  - Renal impairment (rarely acute)
  - Nephrotic syndrome rare

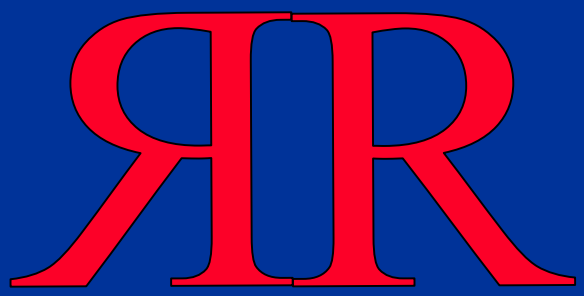
Prognosis of IgA disease

- ESRF in 20-30% at 20 years from diagnosis
- Predictors of poor outcome
  - Male gendder
  - Young age at onset
  - Persistent micro haematuria
  - Absence of macro haematuria
  - Hypertension
  - Heavy proteinuria

Kaplan-Meier plot of renal survival of patients with IgA nephropathy by proteinuria



Johnston et al, (MRC), 1992



UK Renal Registry

www.renalreg.com

UK Renal Registry

Southmead Hospital

Bristol

England

BS10 5NB

Useful data sources

- USRDS *www2.usrds.org*
- US transplant data *www.unos.org*
- EDTA/ERA *www.era-edta-reg.org*
- UK Renal Registry *www.renalreg.com*
- UK Transplants *www.uktransplant.org.uk*