Alport syndrome 2015

Manchester

Neil Turner

Cecil Alport

1880-1959

1905 MBChB Edin
1922 London
1927 Syndrome

Alport 2015

- What is Alport Syndrome?
- How rare is it?
- Is there a treatment for it?

Alport Syndrome

- Kidney disease
- Deafness
- Eye changes

Kidney disease and deafness

- Alport syndrome
- BOR Syndrome
- MYH9 diseases
- Mitochondrial DNA problems
- Others ...


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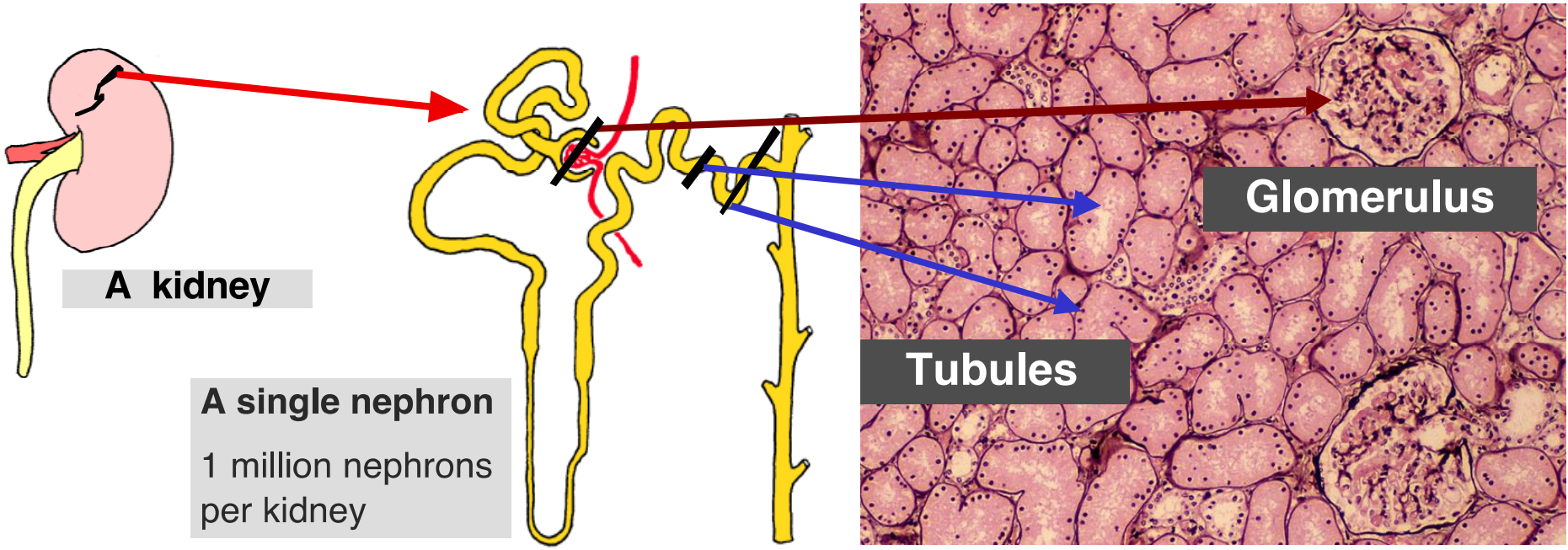
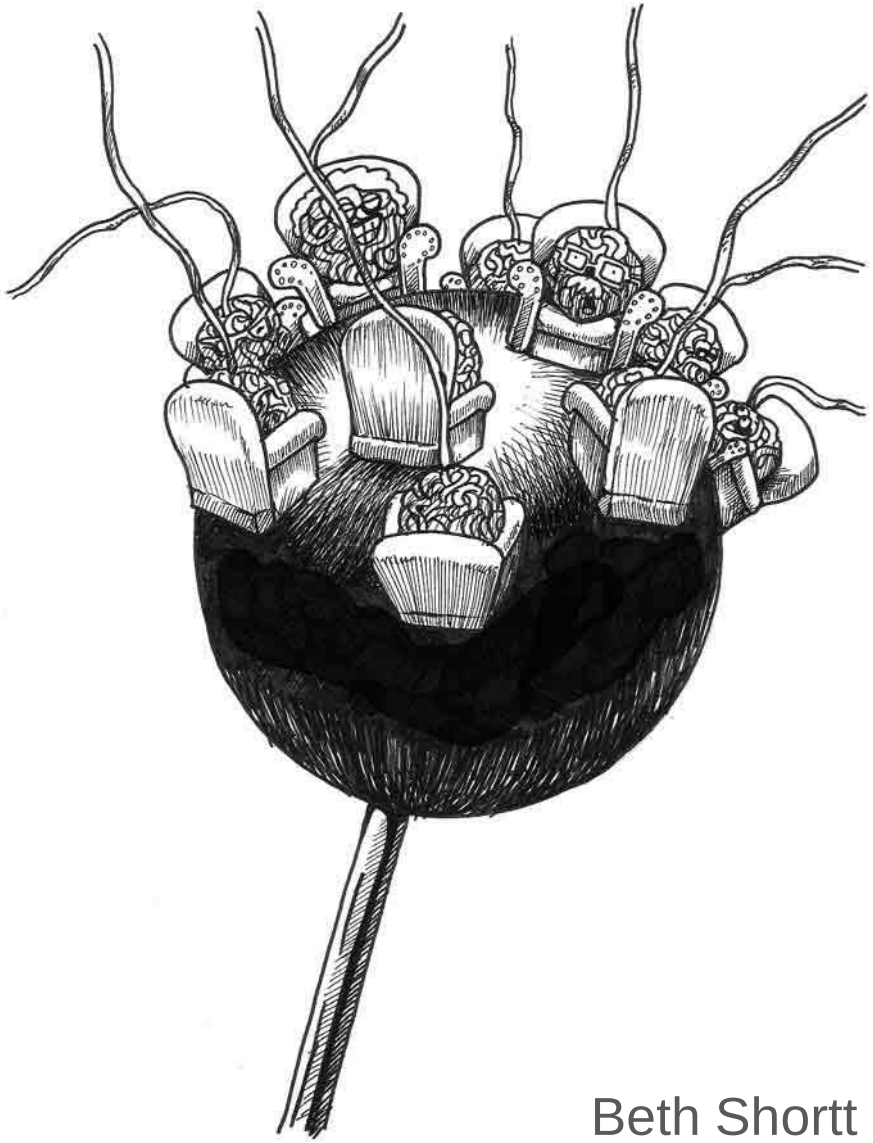
What happens in Alport Syndrome

What happens in Alport Syndrome



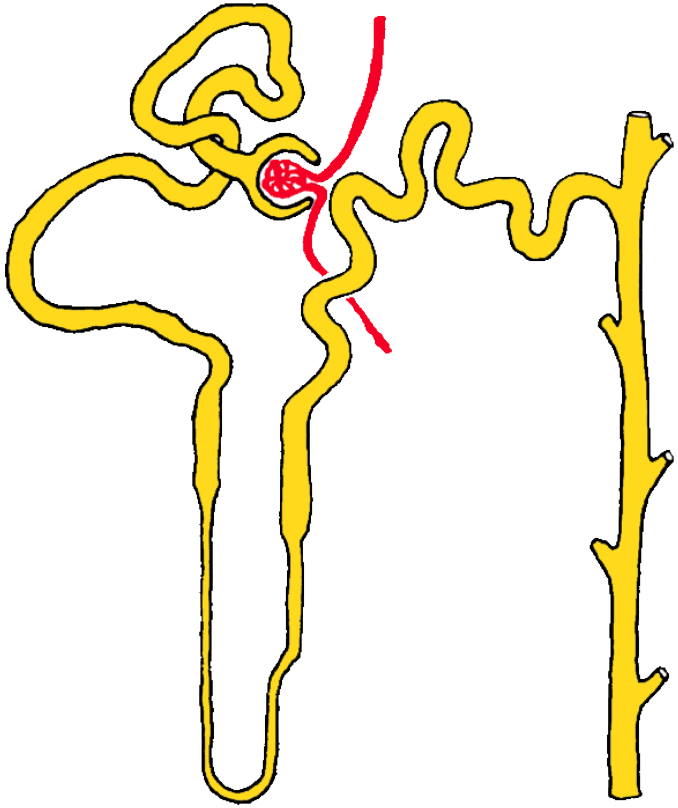
The glomerulus



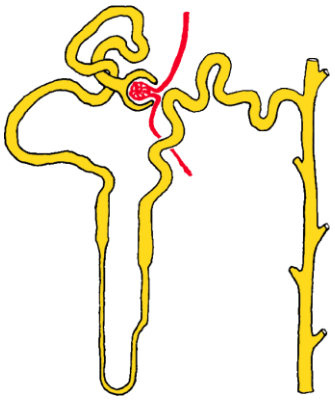
Beth Shortt

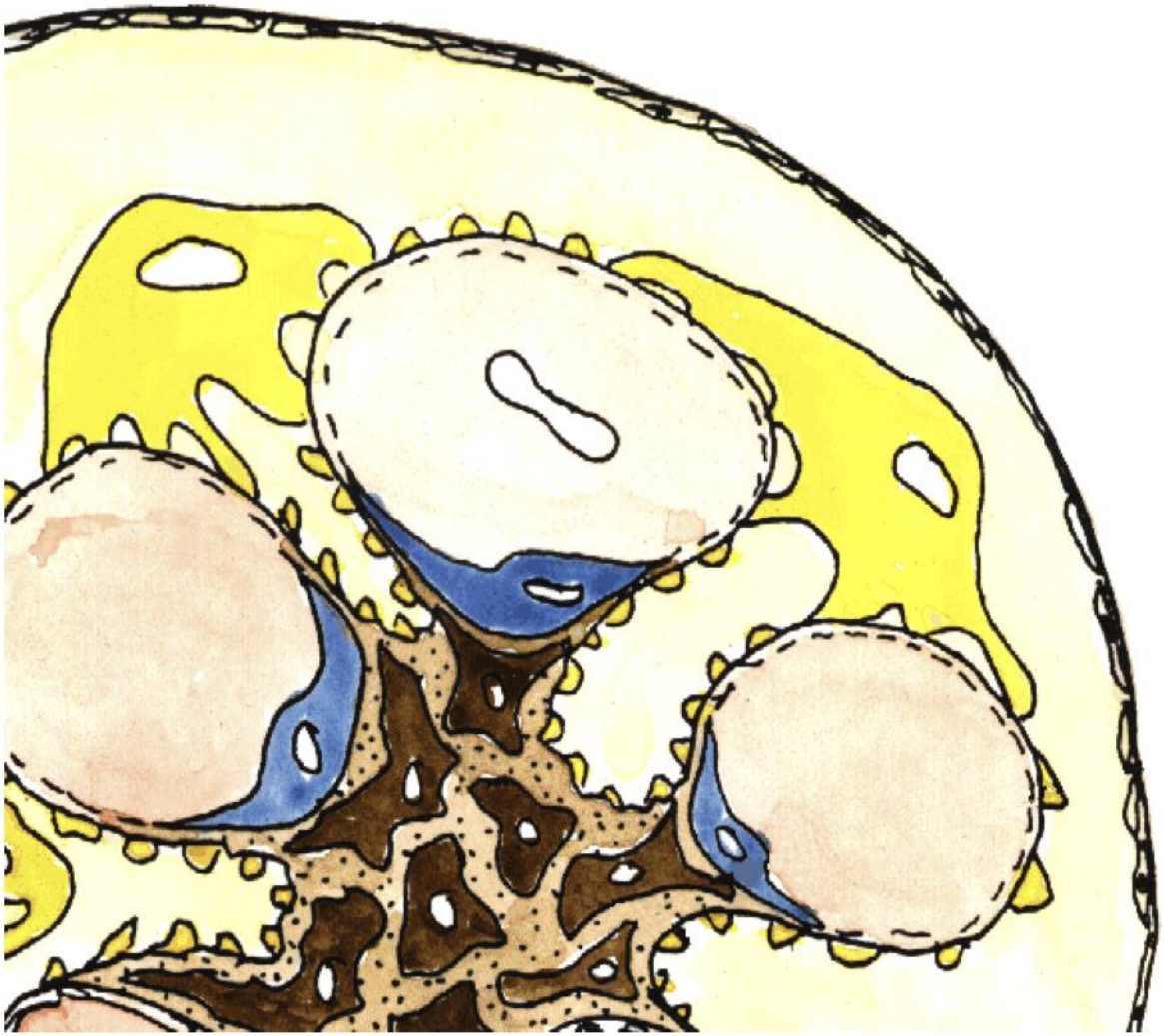
10 on a pin

1 million per kidney

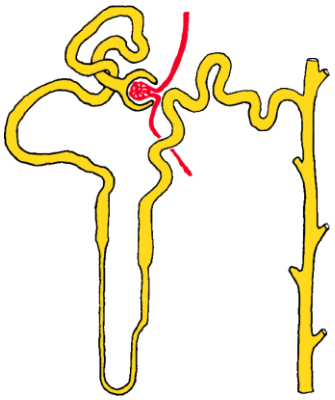


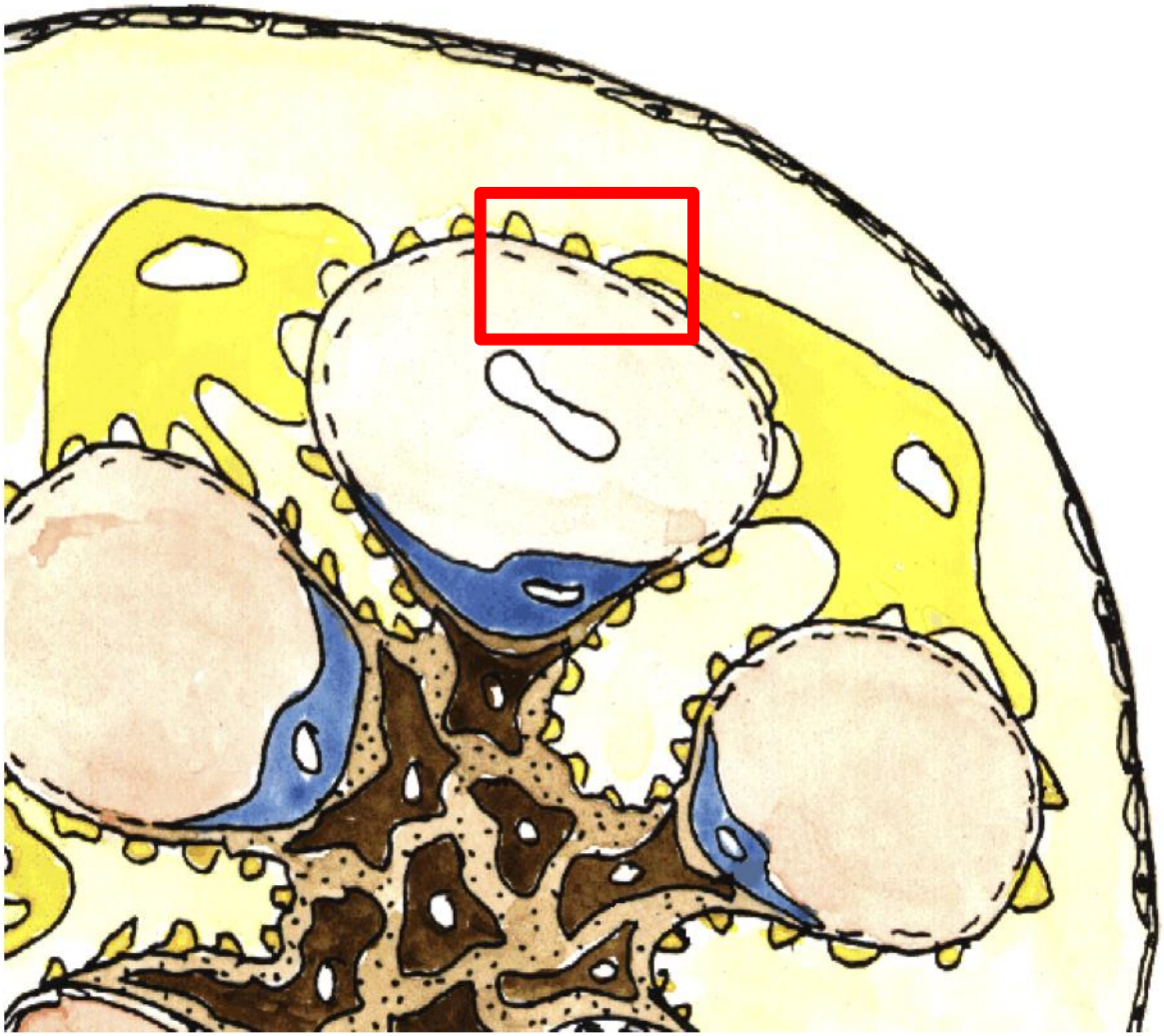
The GBM and filtration barrier

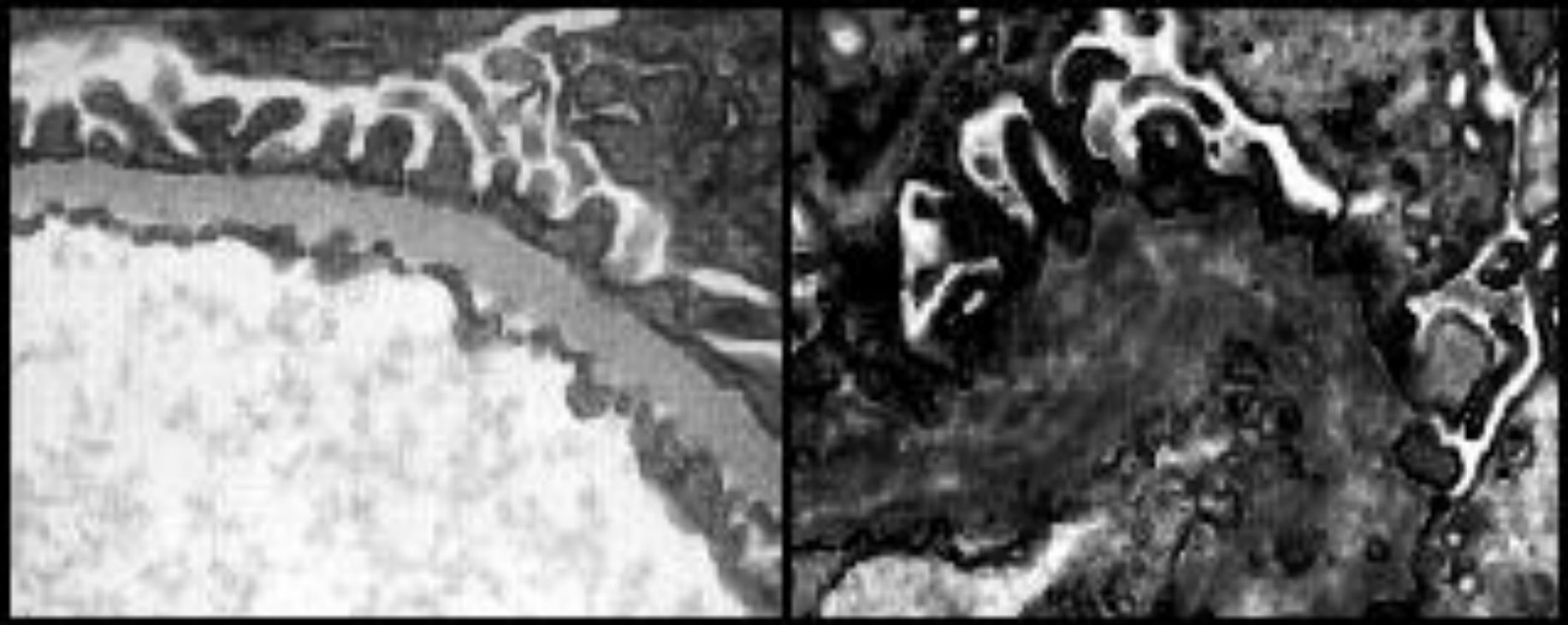




The GBM and filtration barrier

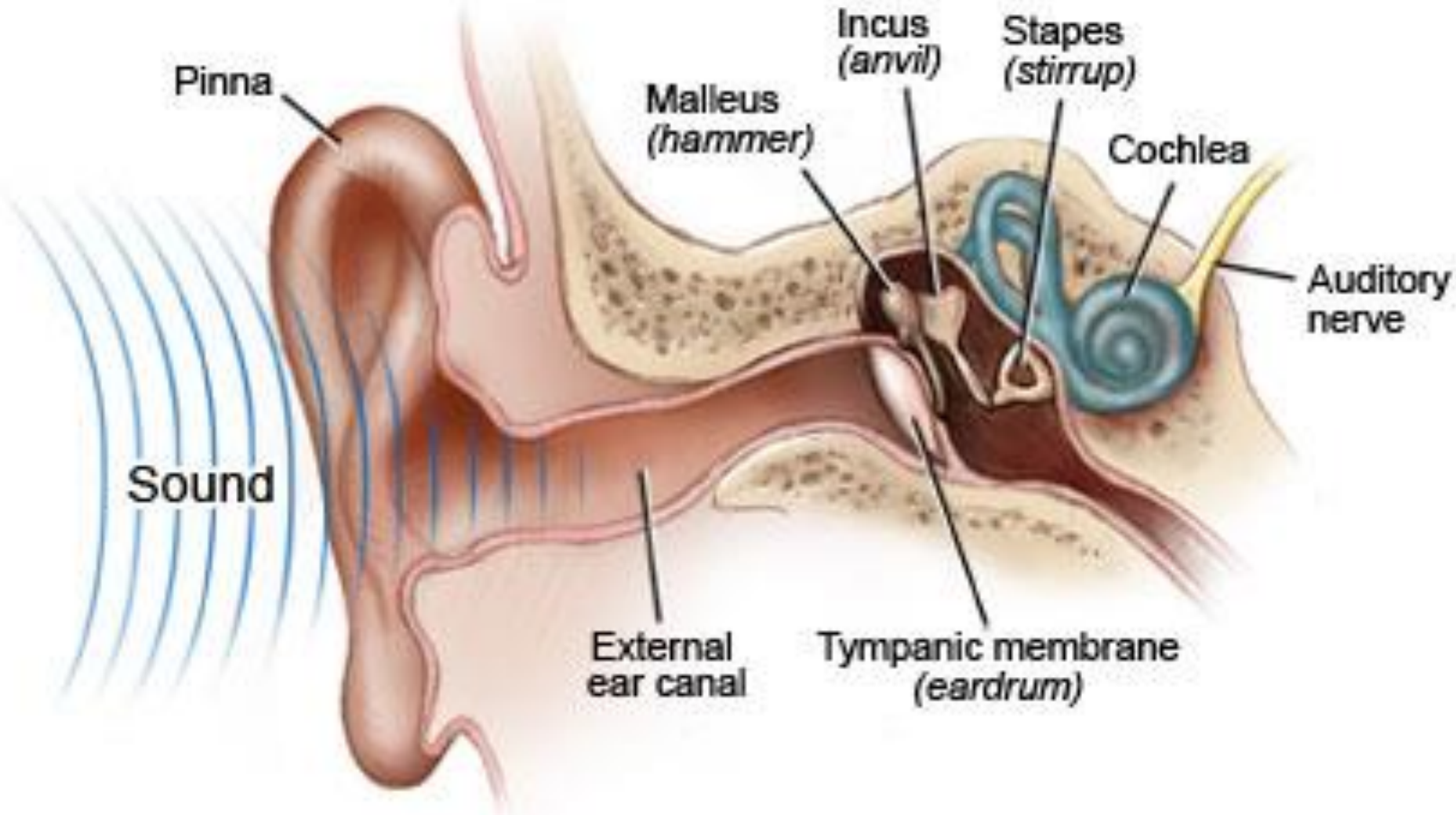


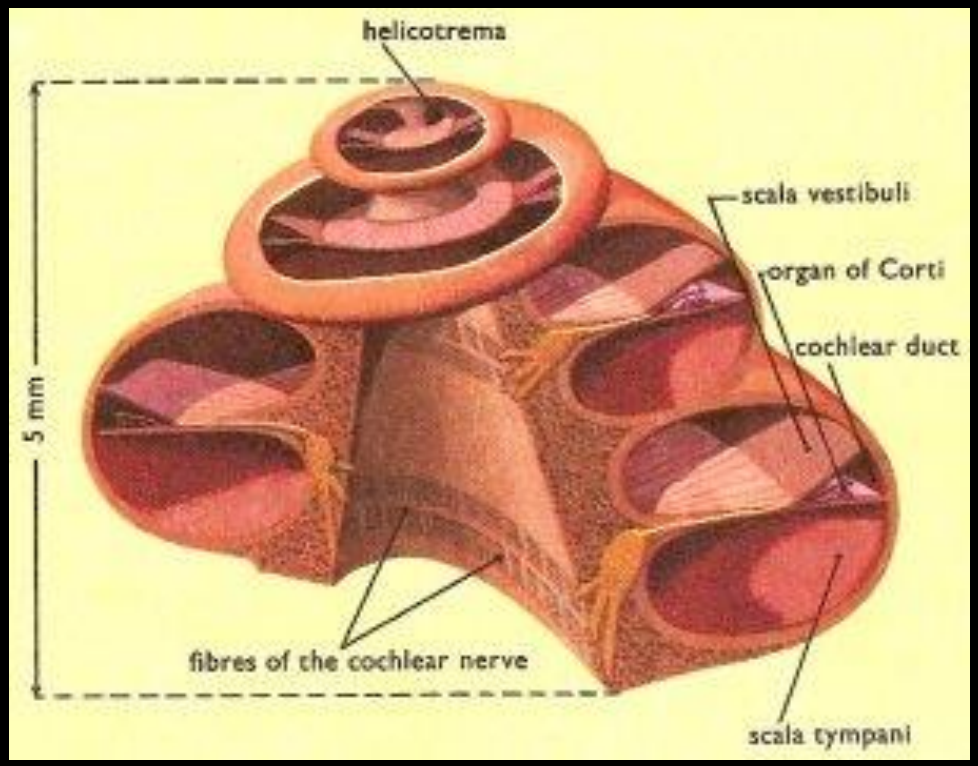


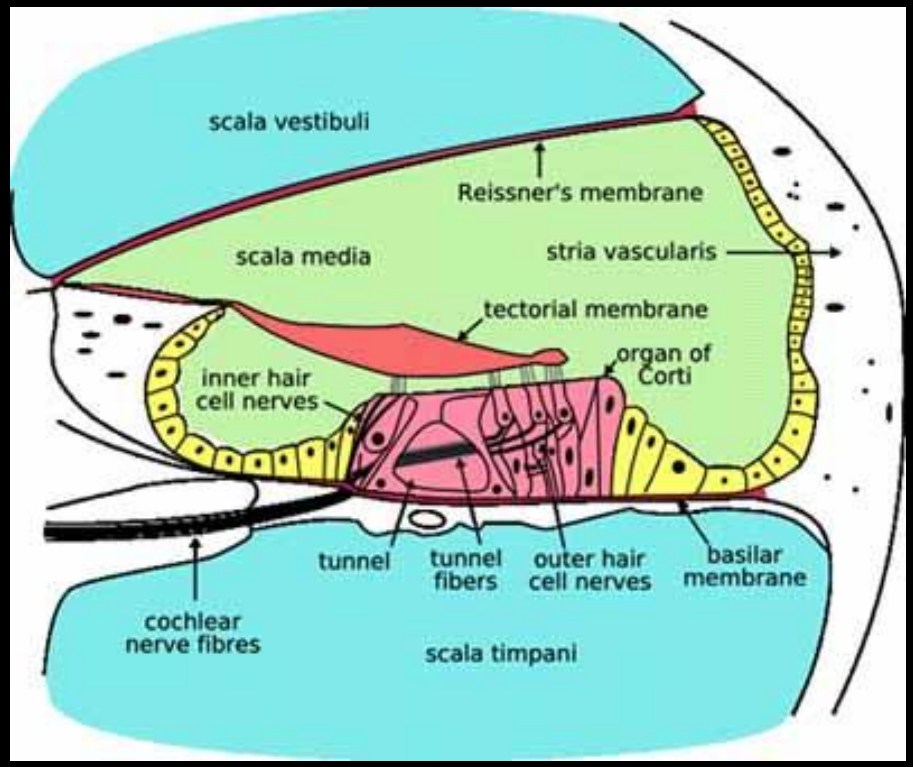


Normal and Alport GBM

Normal Hearing




helicotrema
scala vestibuli
organ of Corti
cochlear duct
5 mm
fibres of the cochlear nerve
scala tympani


scala vestibuli
Reissner's membrane
scala media
stria vascularis
tectorial membrane
organ of Corti
inner hair cell nerves
tunnel
tunnel fibers
outer hair cell nerves
basilar membrane
cochlear nerve fibres
scala timpani

Kidney disease in Alport's

- Haematuria (blood in urine)
- Proteinuria (protein in urine)
- Creatinine rises (GFR falls)

Speed varies

What happens

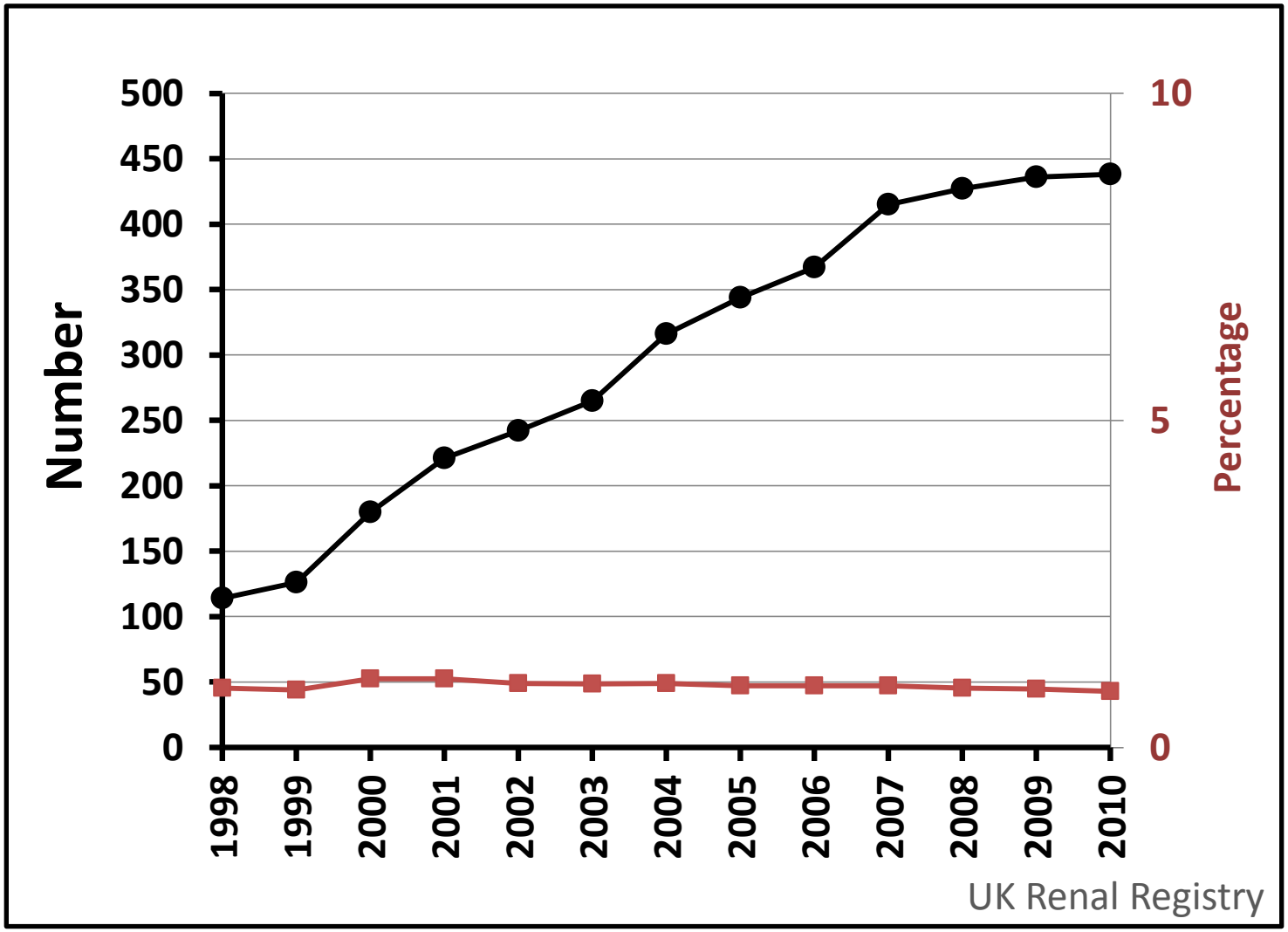
	Age
Haematuria	0
Proteinuria	5-15
GFR slips	15-35
Need dialysis	15-70 (35)

Alport 2015

- What is Alport Syndrome?
- **How rare is it?**
- Is there a treatment for it?

How many have Alport Syndrome in the UK?

Patients with Alport Syndrome on RRT in the UK



How many have Alport Syndrome in the UK?

450-500 on dialysis/ transplanted

450-500 not on RRT

Carriers – 2000? (underestimate)

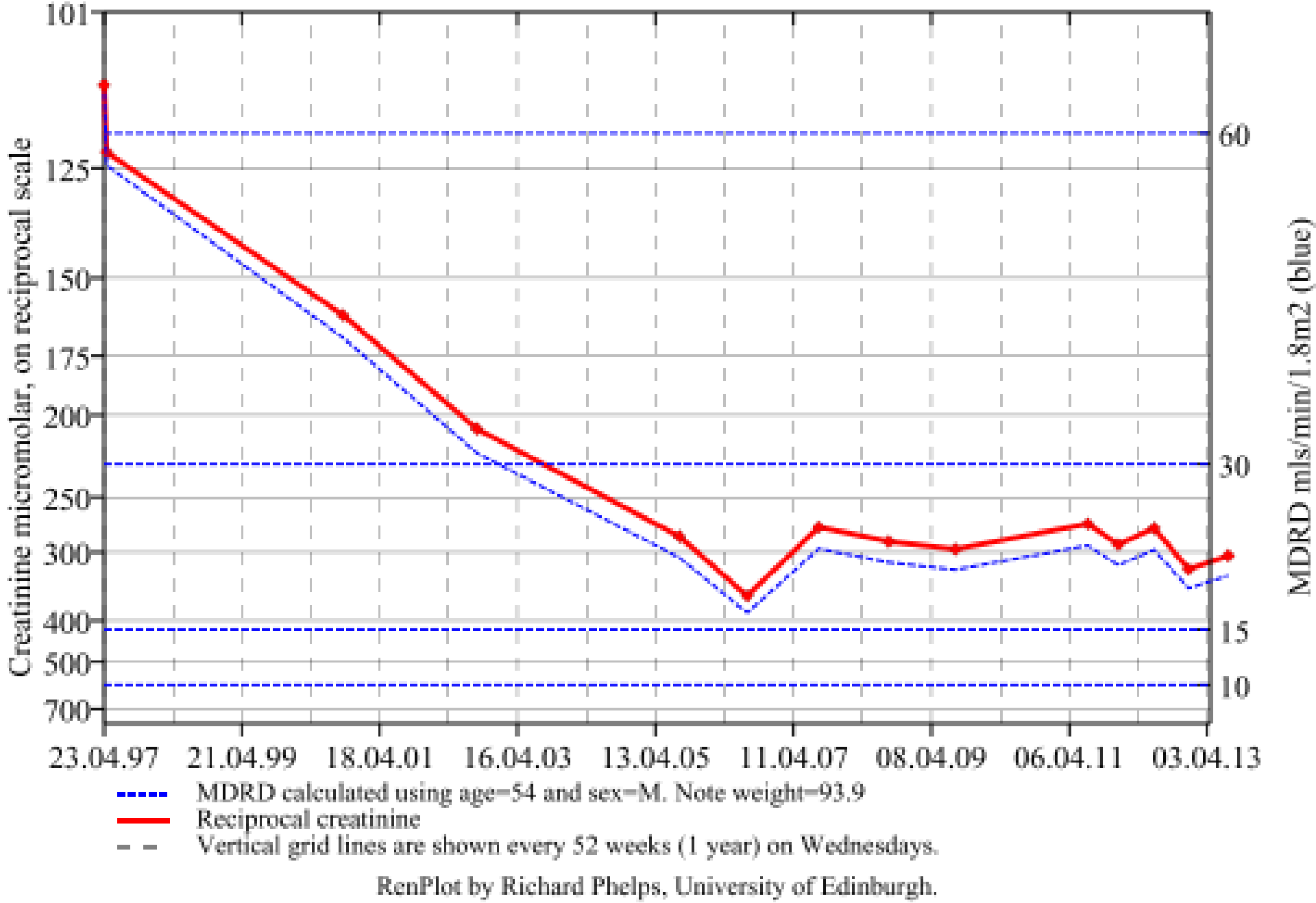
Total – maybe 3000?

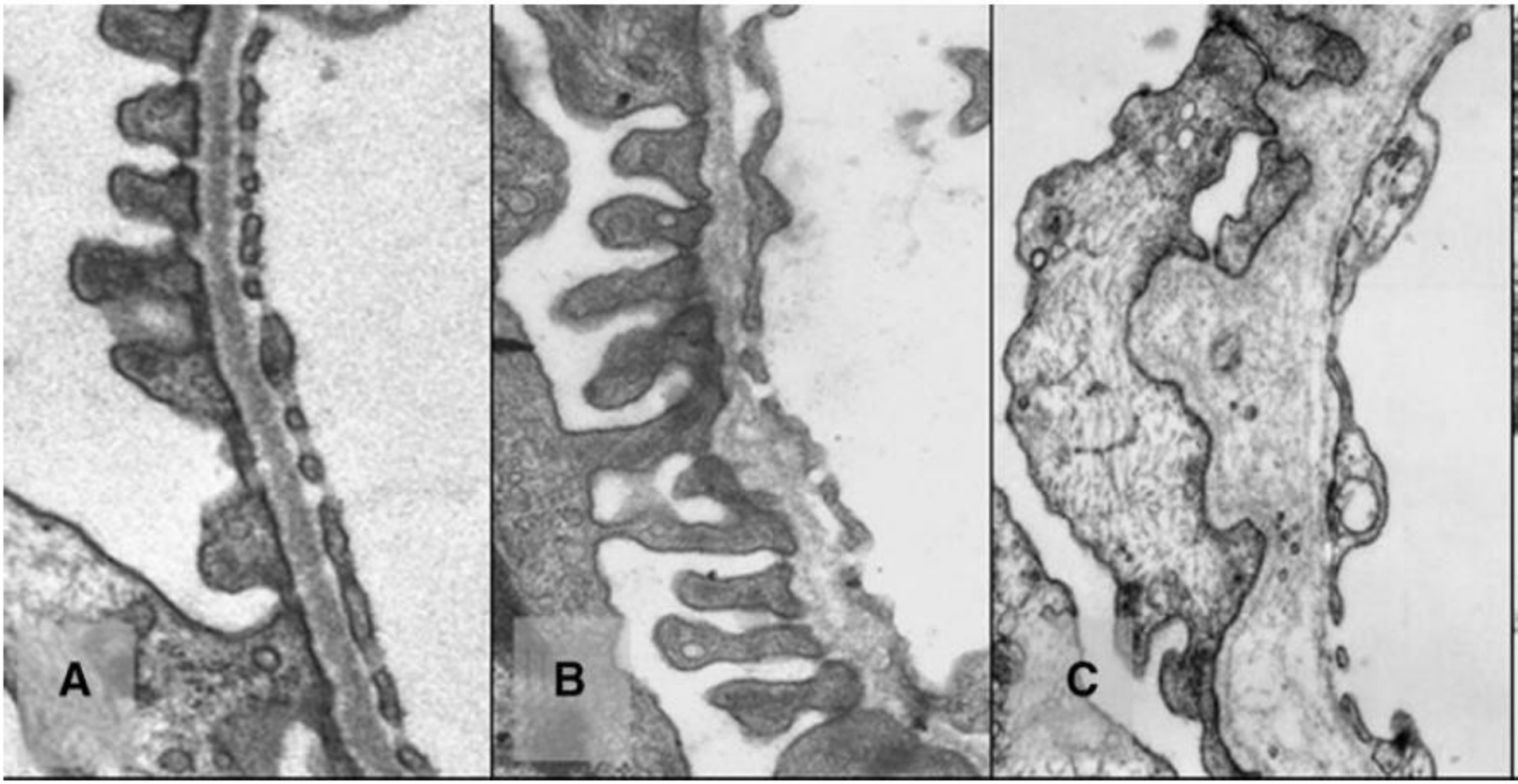
15 per year start RRT in the UK

6-7 on RRT per renal unit

Alport 2015

- What is Alport Syndrome?
- How rare is it?
- **Is there a treatment for it?**

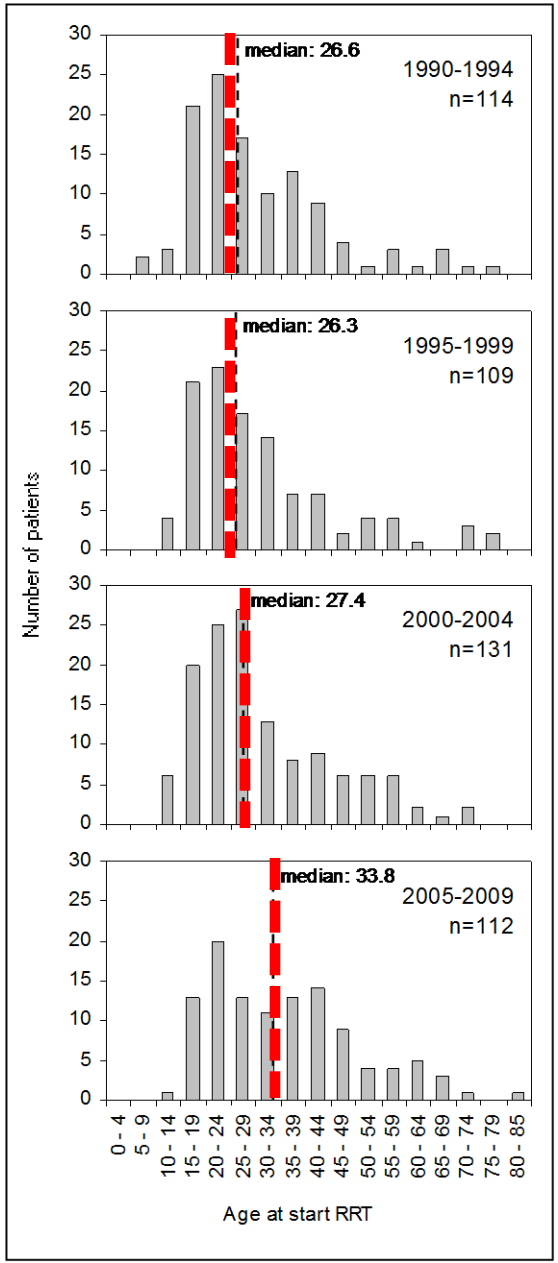

Creatinine micromolar, on reciprocal scale
101
125
150
175
200
250
300
400
500
700
MDRD mls/min/1.8m2 (blue)
60
30
15
10
23.04.97
21.04.99
18.04.01
16.04.03
13.04.05
11.04.07
08.04.09
06.04.11
03.04.13
MDRD calculated using age=54 and sex=M. Note weight=93.9
Reciprocal creatinine
Vertical grid lines are shown every 52 weeks (1 year) on Wednesdays.
RenPlot by Richard Phelps, University of Edinburgh.

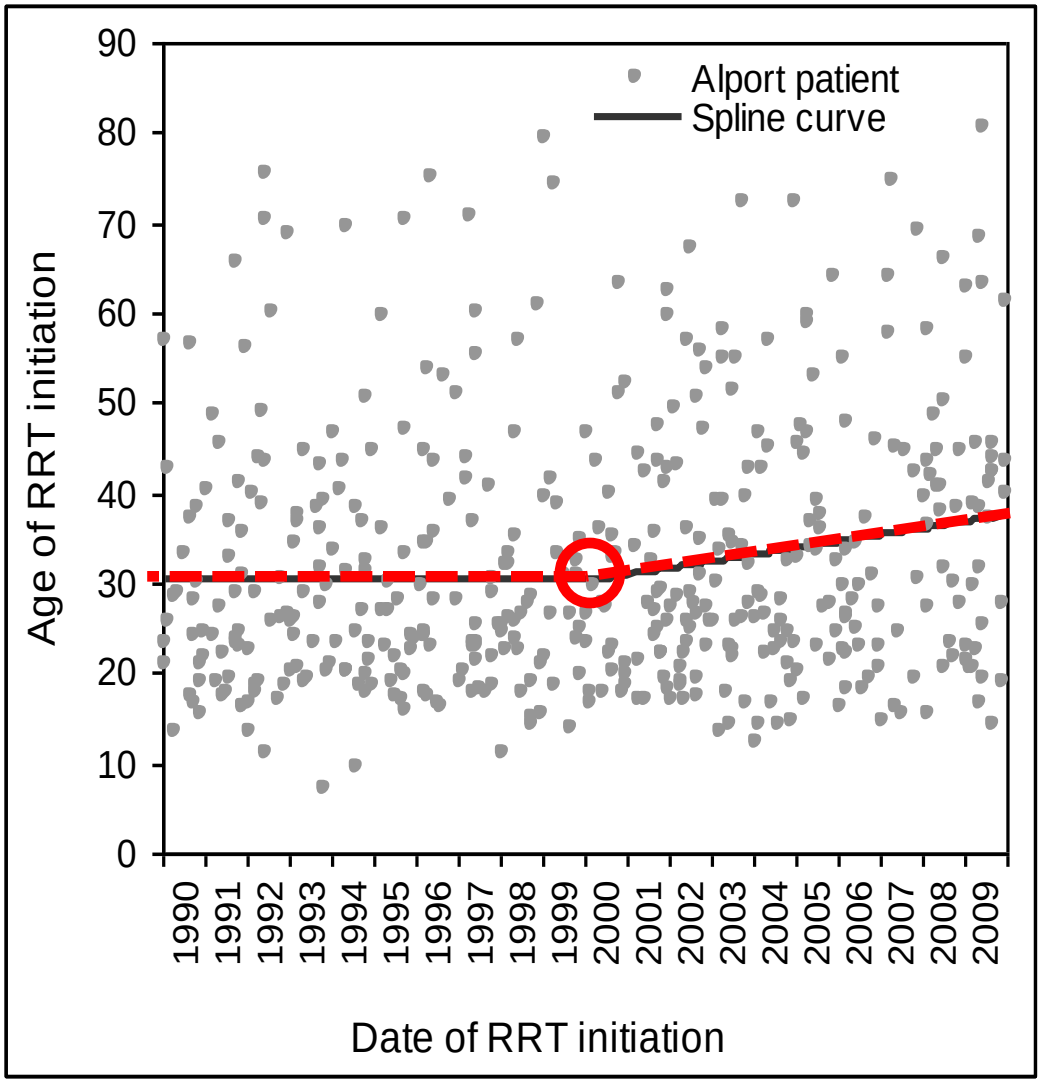


Gross 2008

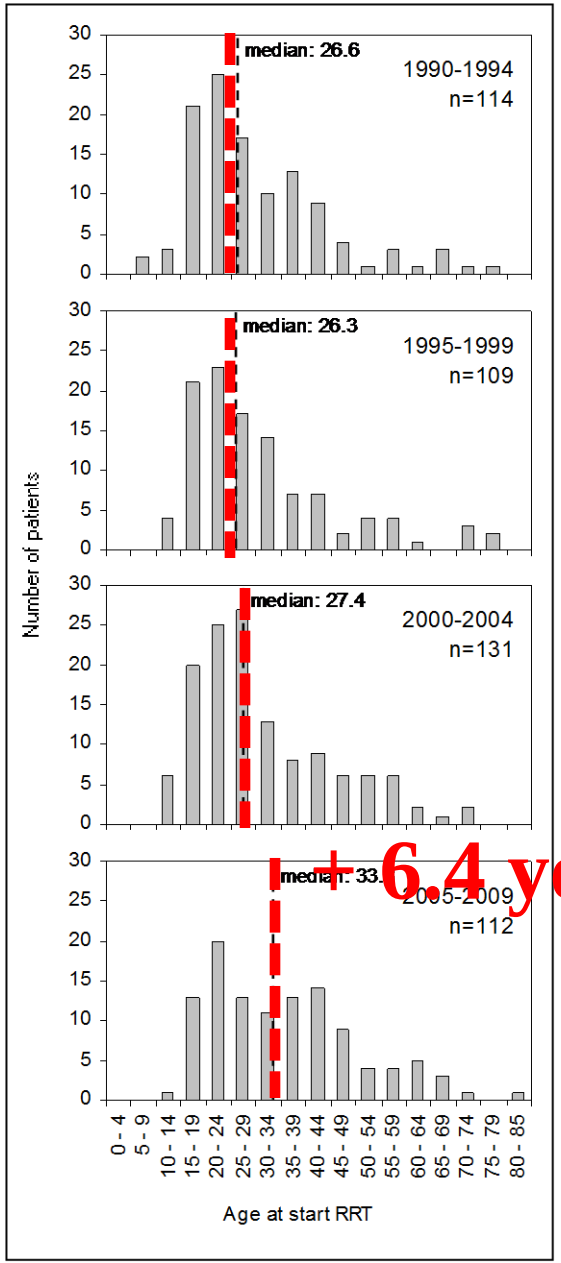
ACE inhibitors

- Work in animals (mice, dogs)

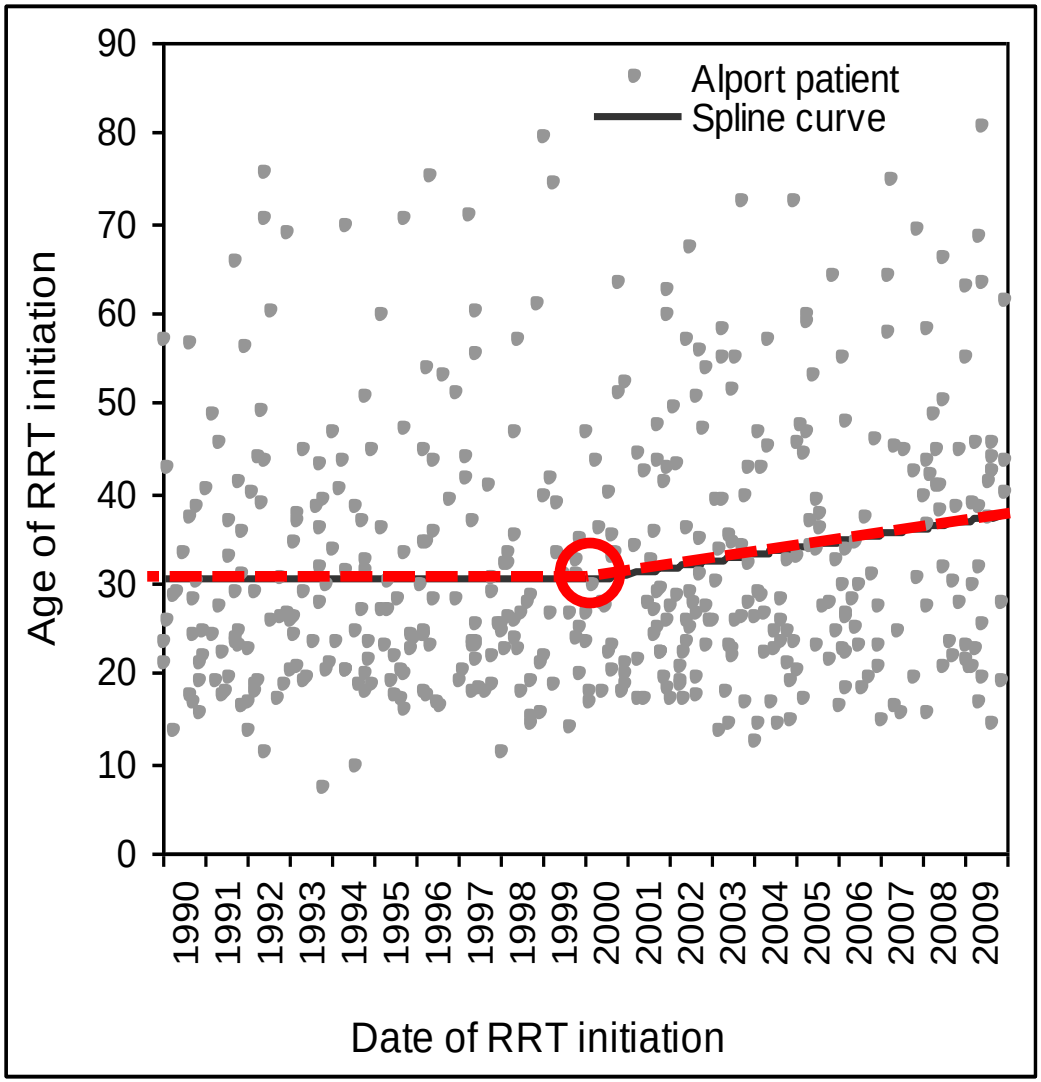




Oliver Gross, *CJASN*

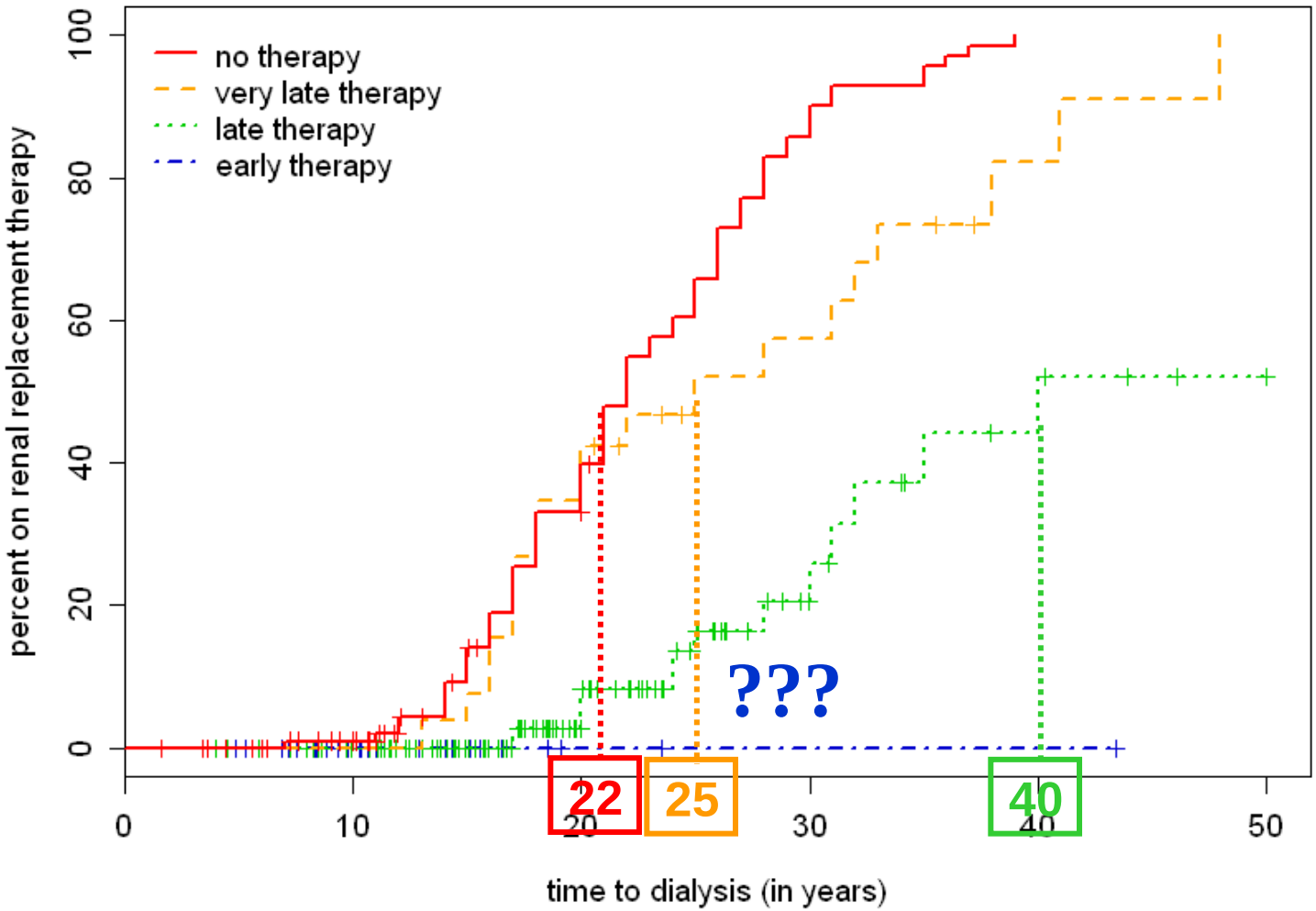


+6.4 years



Oliver Gross, *CJASN*

Earlier treatment is better?



no. at risk

no therapy	109	105	96	75	50	29	10	5	0	0	0
very late therapy	26	26	26	25	17	10	8	5	2	1	0
late therapy	115	113	105	84	52	31	15	9	7	4	3
early therapy	33	32	20	8	2	1	1	1	1	0	0

Gross, *Kidney Int 2012*

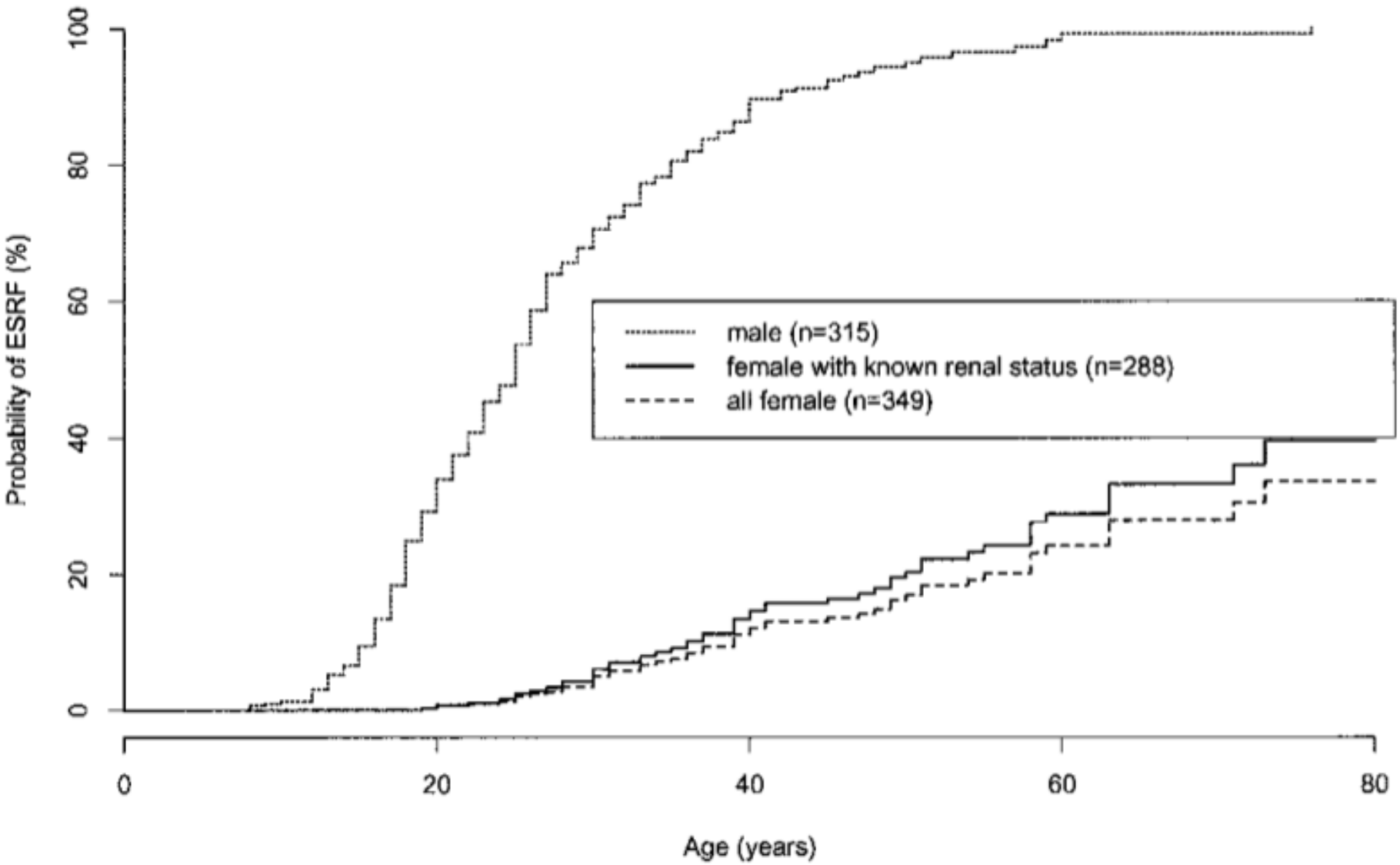
ACE inhibitors

- Work in animals (mice, dogs)
- Work in humans

ACE inhibitors now

Anyone with proteinuria

- ‘Carrier’ or fully affected


Probability of ESRF (%)
100
80
60
40
20
0
male (n=315)
female with known renal status (n=288)
all female (n=349)
0
20
40
60
80
Age (years)

Jais 2003

ACE inhibitors

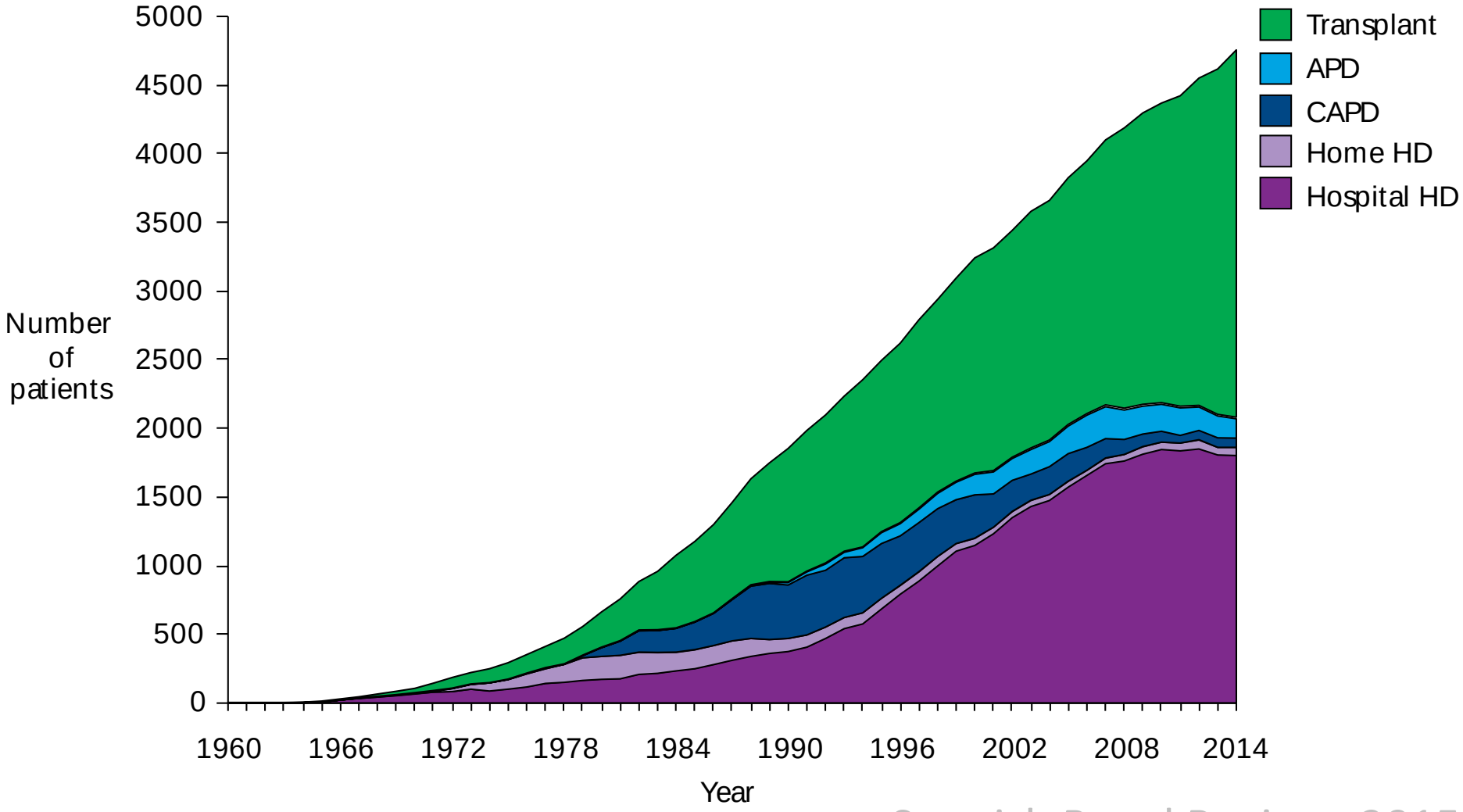
- Work in animals (mice, dogs)
- Work in humans
- There are other candidate drugs

ACE inhibitors

- Work in animals (mice, dogs)
- Work in humans
- There are other candidate drugs
  - Lower proteinuria?
  - Reduce scarring?
  - Stabilise GBM?

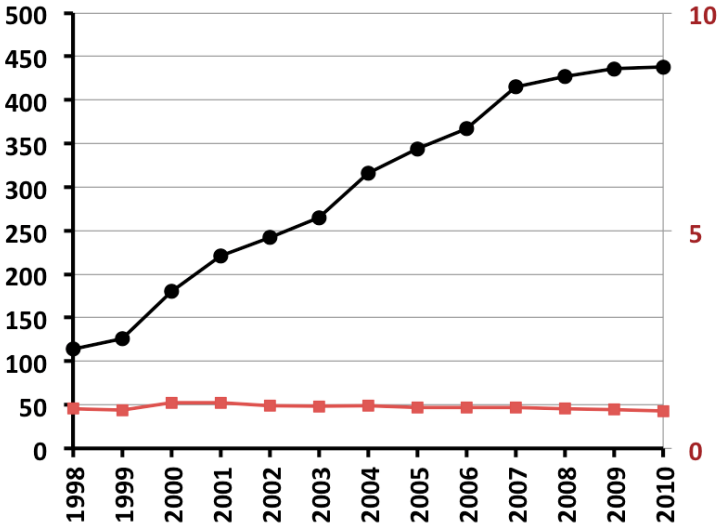
Linda Phillips
Nancy Spaeth

All patients on dialysis/transplanted



Scottish Renal Registry 2015

The challenge



- Improve
- Prevent
- Find the next treatments

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Eye changes