

The organs of the human body were created to perform ten functions among which is the function of the kidney to furnish the human being with thought.

Leviticus Rabba 3 Talmud Berochoth 6₁b



Outline & Objectives

Renal sessions

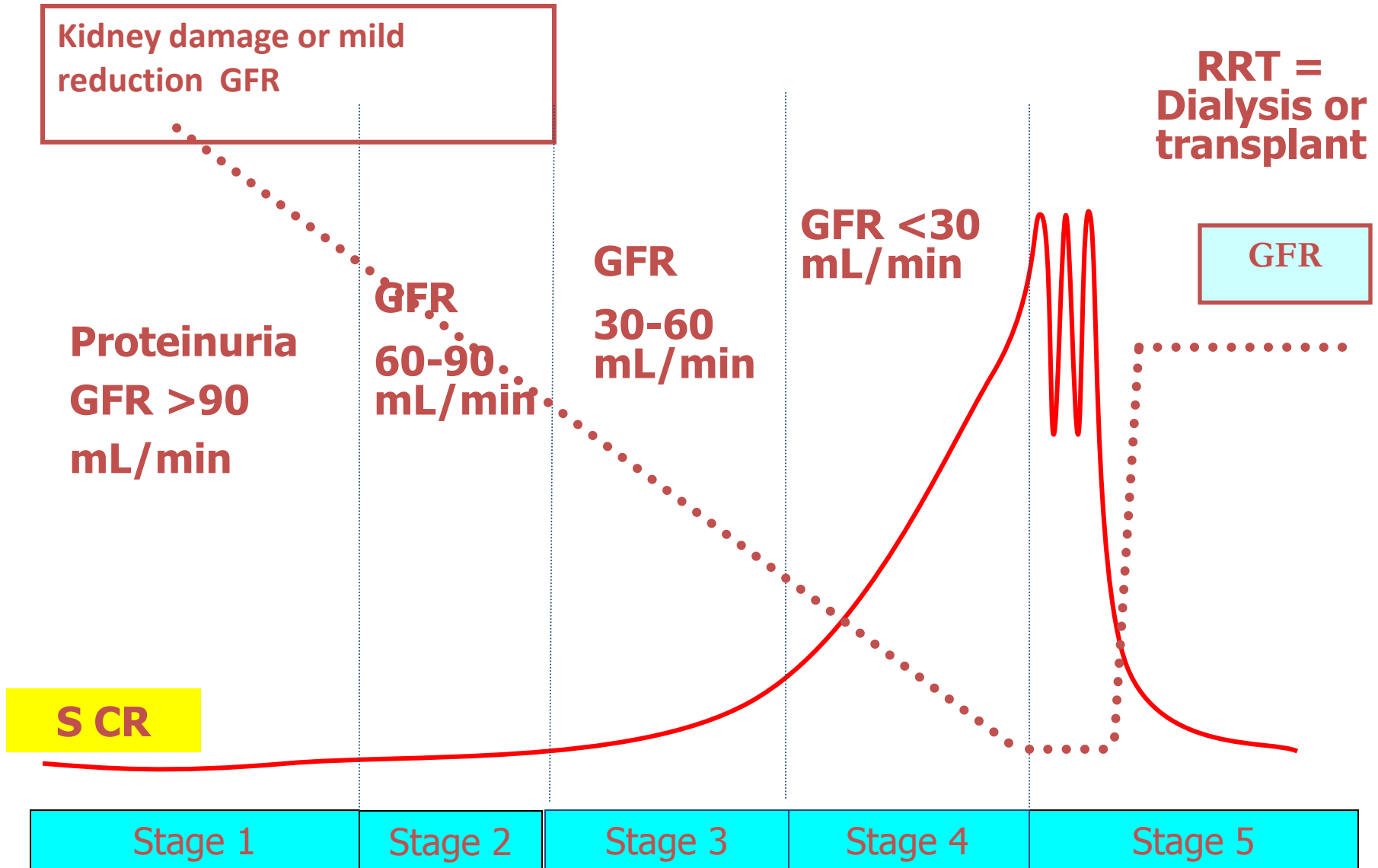
- Identification of CKD – impending epidemic?
- What do CKD patients die of?
Why are they at a higher cardiovascular risk?
Progression?
- eGFR Real or lab changes (Sunday)
Importance of proteinuria (Sunday)
- Combined urological session Stephen Marks.
Haematuria, Kidney stones, UTIs



Chronic Kidney Disease

Stage	Description	GFR (ml/min)
1	Kidney damage (proteinuria) with normal or increased GFR	>90
2	Kidney damage with mild decrease in GFR	60 to 89
3	Moderate decrease in GFR	30 to 59
4	Severe decrease in GFR	15 to 29
5	Kidney failure	< 15 or RRT

Stages of CKD— a clinical continuum



Chronic Kidney Disease (CKD)

Data from AusDiab

**Australia
or NZ**

Healthy Adult Community

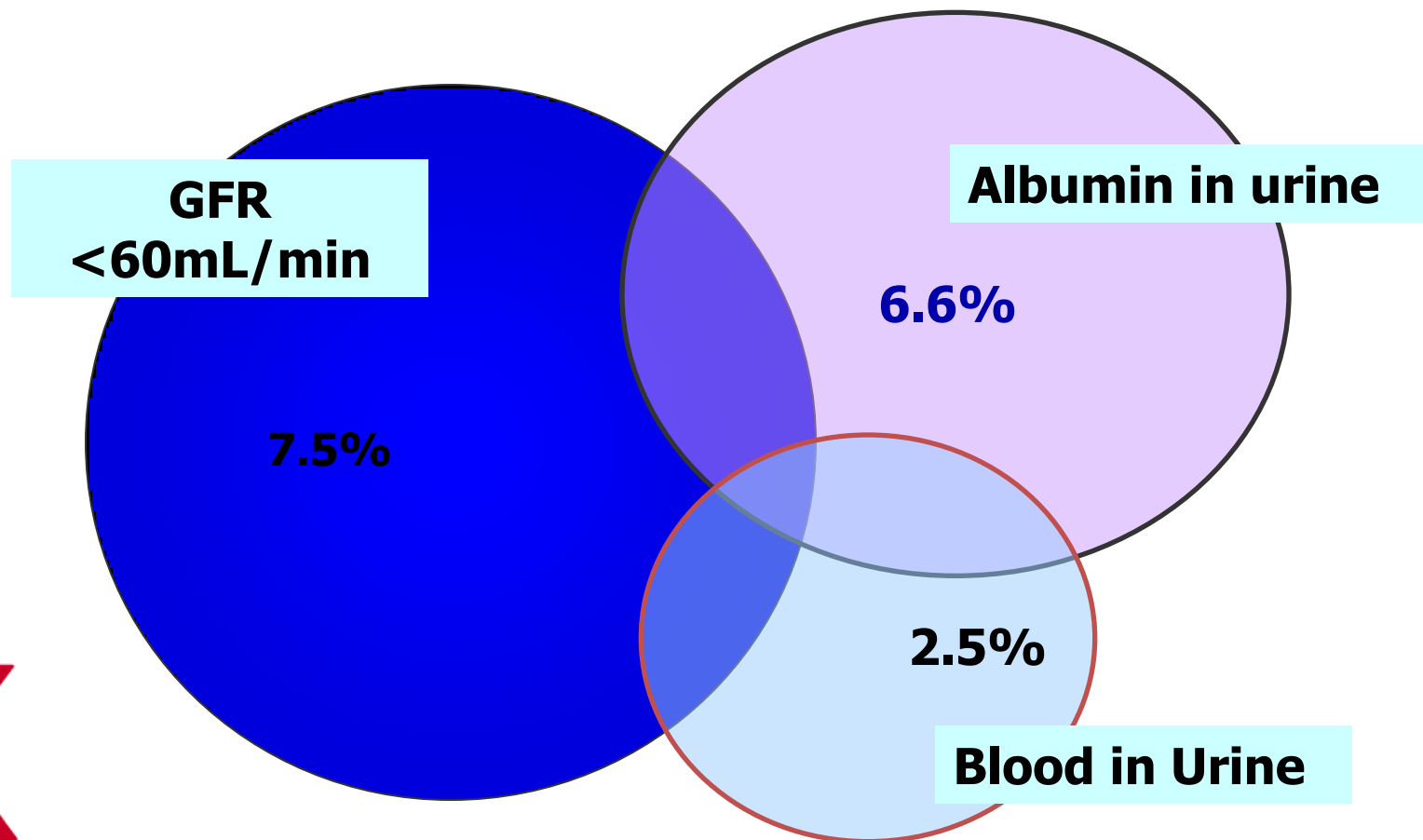
**Increased risk
– 1:3**

CKD – 1:7

**Dialysis or
Transplant 1:1400**

How much CKD in Australia?

*16% of Adults >25yrs have protein or blood in urine or moderately severe reduction in kidney function**



AusDiab Study- Prevalence of CKD

	GFR<60ml/min	GFR 30-59 ml/min	GFR < 30 ml/min
All patients%	11.2 (8.6-13.2)	10.9(8.4-13.3)	0.3 (0.2-0.5)

Table 3. Prevalence of renal impairment according to age and gender*

	GFR <60 mL/min 1.73 per m ^{2b}	GFR 30 to 59 mL/min 1.73 per m ²	GFR <30 mL/min 1.73 per m ²
All men	9.3 (7.3, 11.4)	9.1 (7.0, 11.1)	0.3 (0.1, 0.4)
25 to 44 yr	—	—	—
45 to 64 yr	1.8 (1.0, 2.6)	1.8 (1.0, 2.6)	0.0 (0.0, 0.0)
≥65 yr	51.8 (47.1, 56.5)	50.3 (45.6, 55.0)	1.5 (0.6, 2.3)
All women	13.0 (9.6, 16.4)	12.6 (9.4, 15.8)	0.4 (0.1, 0.7)
25 to 44 yr	0.0 (0.0, 1.0)	0.0 (0.0, 1.0)	—
45 to 64 yr	3.2 (1.9, 4.4)	3.2 (1.9, 4.4)	—
≥65 yr	57.2 (51.4, 63.0)	55.3 (49.2, 61.4)	1.9 (0.7, 0.5)
All subjects	11.2 (8.6, 13.8)	10.9 (8.4, 13.3)	0.3 (0.2, 0.5)
25 to 44 yr	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	—
45 to 64 yr	2.5 (1.6, 3.3)	2.5 (1.6, 3.3)	0.0 (0.0, 0.0)
≥65 yr	54.8 (50.2, 60.0)	53.1 (48.7, 57.5)	1.7 (1.1, 2.4)

* Data are percent prevalence (95% confidence interval).

^b GFR defined as glomerular filtration rate calculated by the Cockcroft-Gault method and corrected for body surface area, mL/min 1.73 per m².

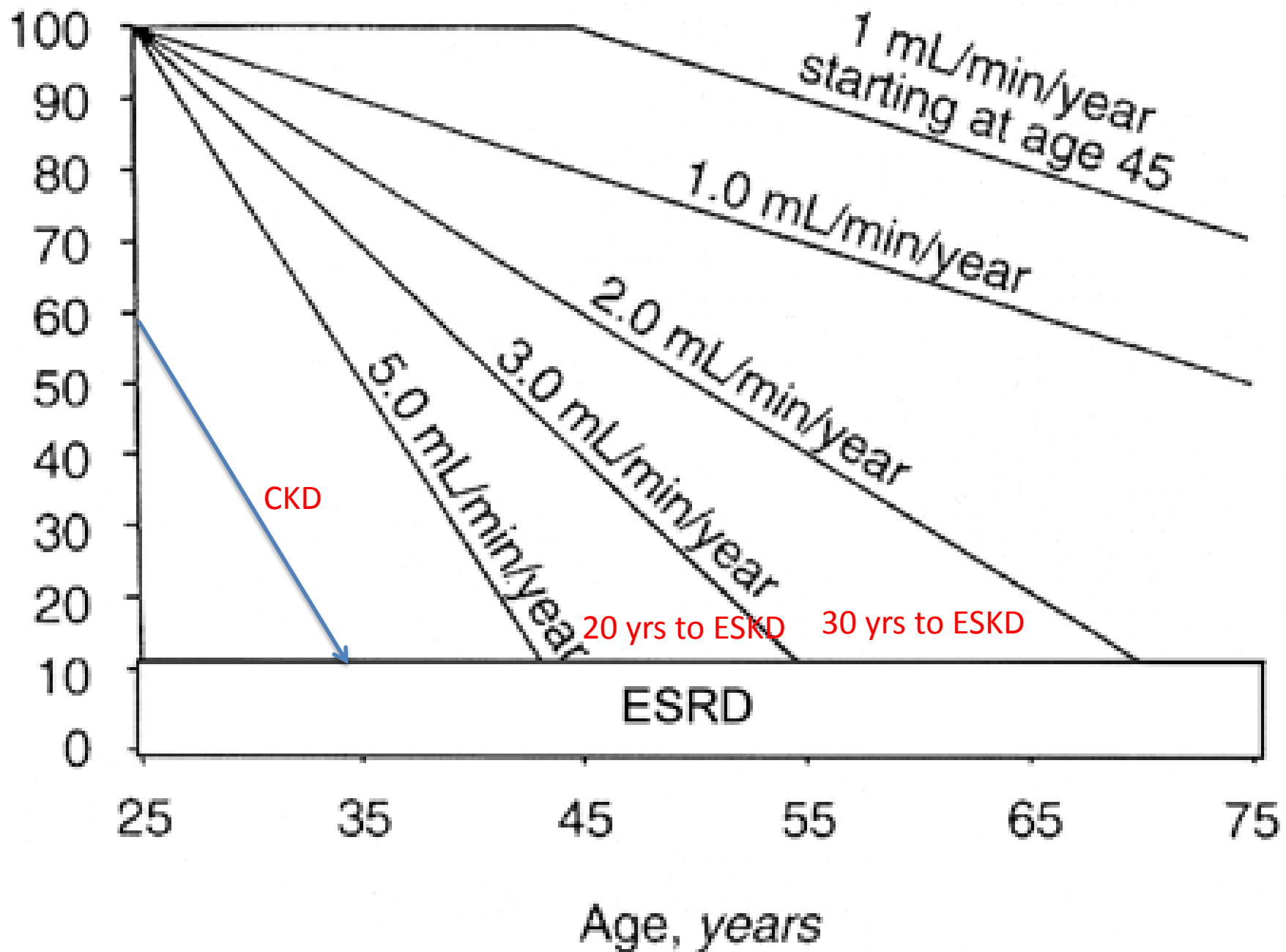
Estimated 1/3 adults at increased risk of CKD

AusDiab Survey April 2001

High risk subgroups:

1. Diabetes
 - 7.5% diabetic (only ½ knew it)
 - 23% abnormal GT
2. Hypertension 29% (only ½ knew it)
3. Smokers 23%
4. Age > 65 yrs
5. Aboriginals & Torres St Islanders (Maori and Pacific Islanders)
6. Family history of kidney disease etc
7. Obese

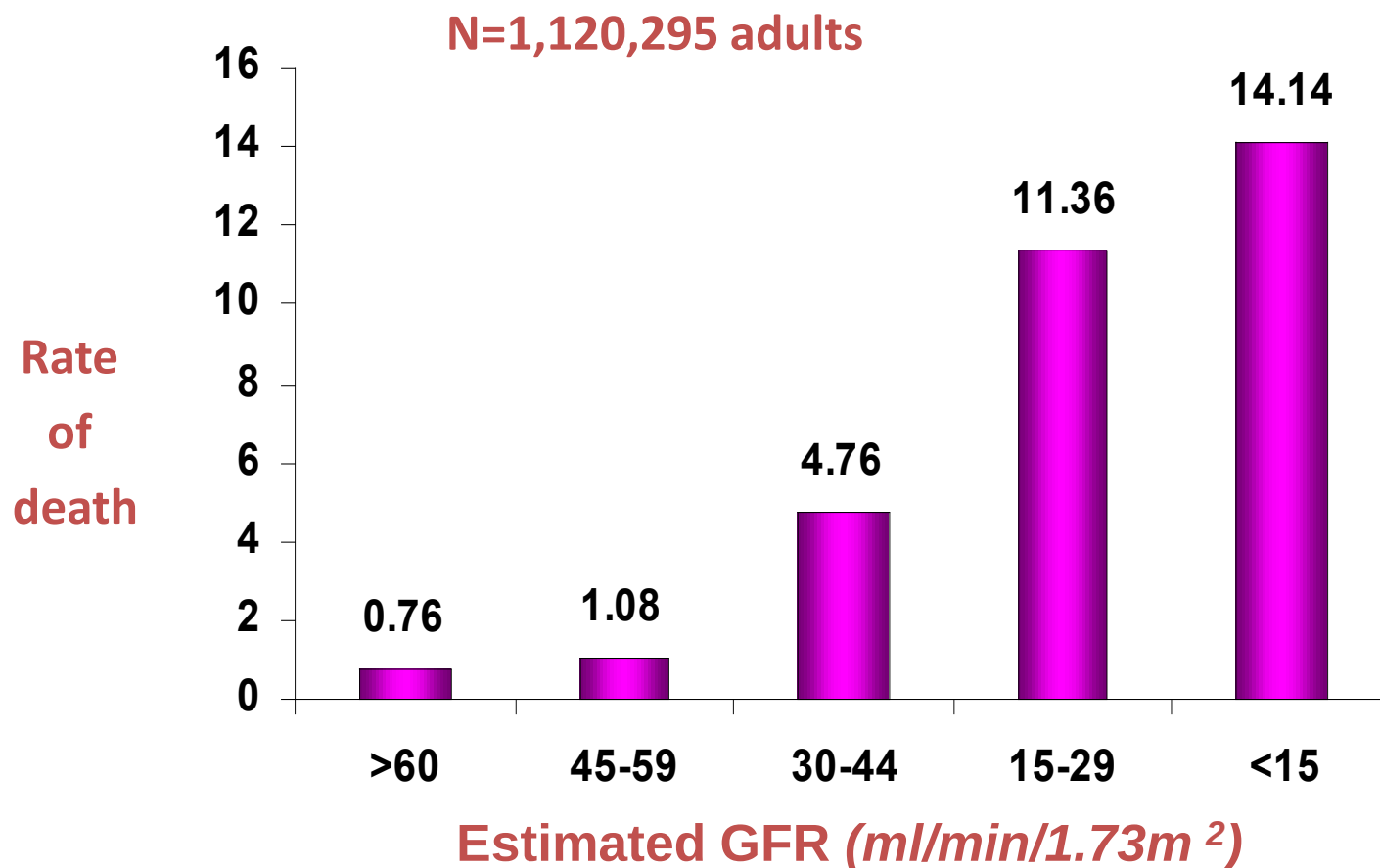
GFR, mL/min/1.73 m²



With 1:3 at risk and 1:7 with actual evidence of CKD why are so few seen with end stage kidney failure?

ESKD = ESRF = RRT

CKD predicts rate of all cause death (age standardized/100 person years) – HMO population

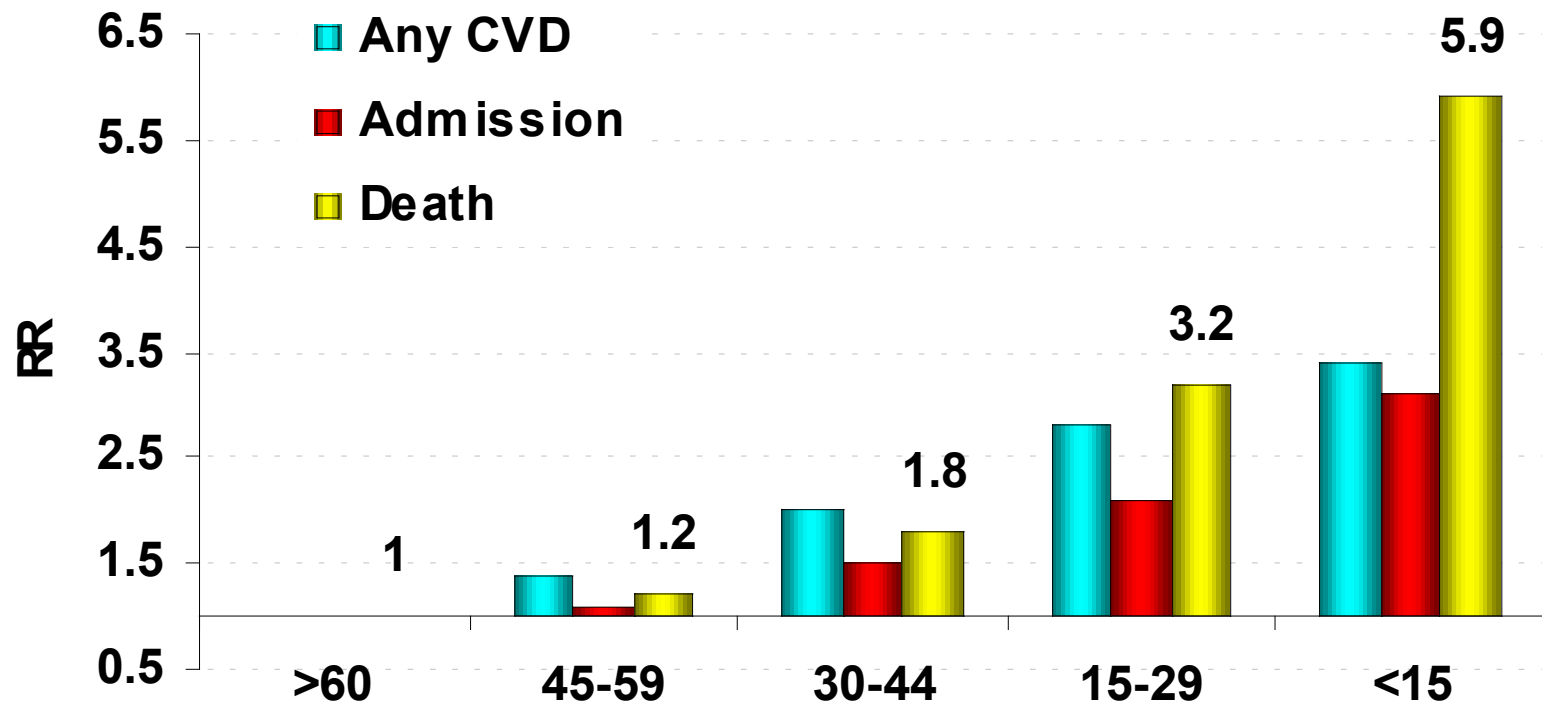


Median Follow-up = 2.8 yrs

Go et al., *N Engl J Med*, 2004

Adjusted Risk Ratio showing independent and significant inverse relationships to eGFR

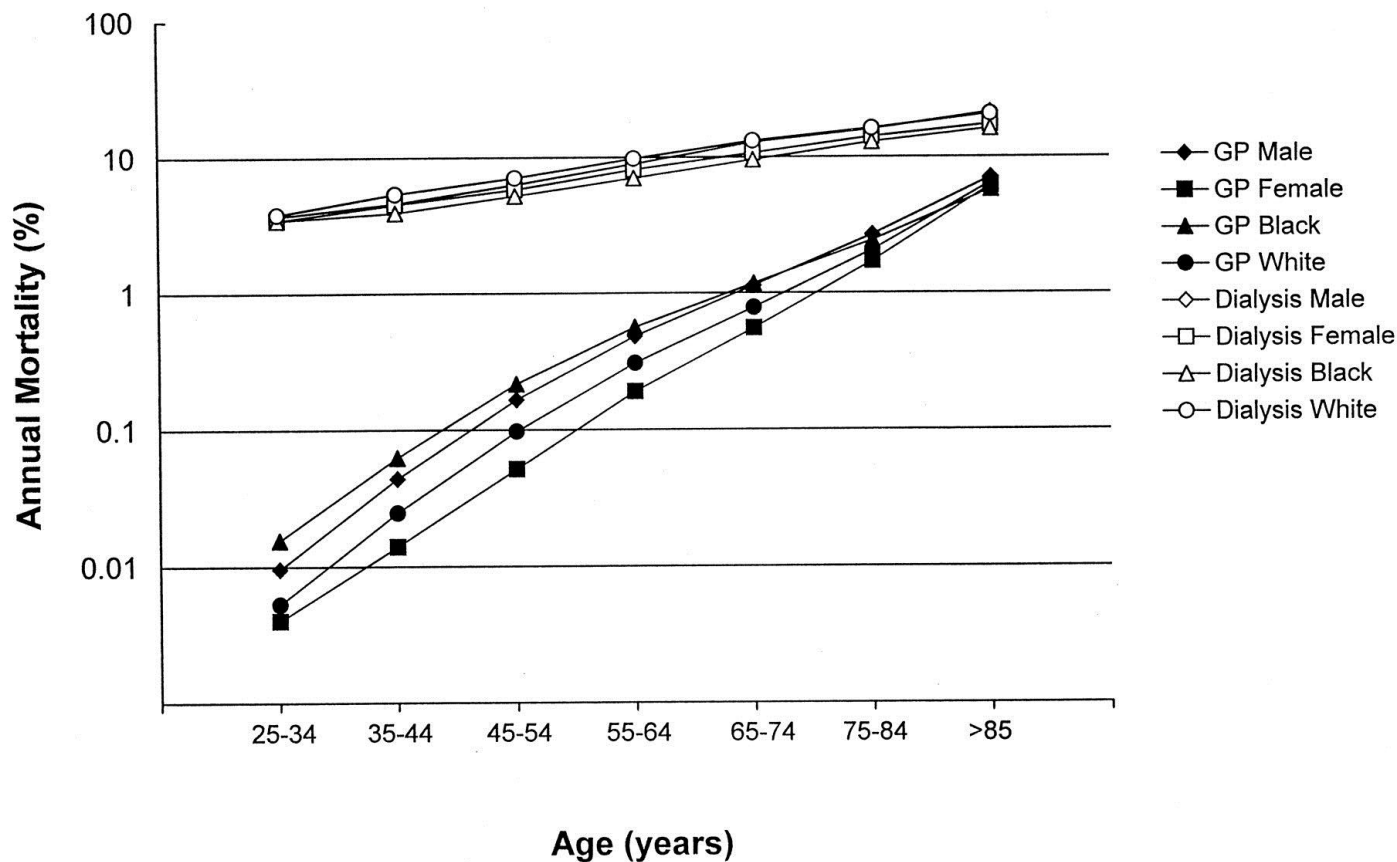
N=1,120,295 adults



Median Follow-up = 2.8 yrs

Go et al., *N Engl J Med*, 2004

Cardiovascular disease mortality by age, race, and gender in the general population and dialysis population



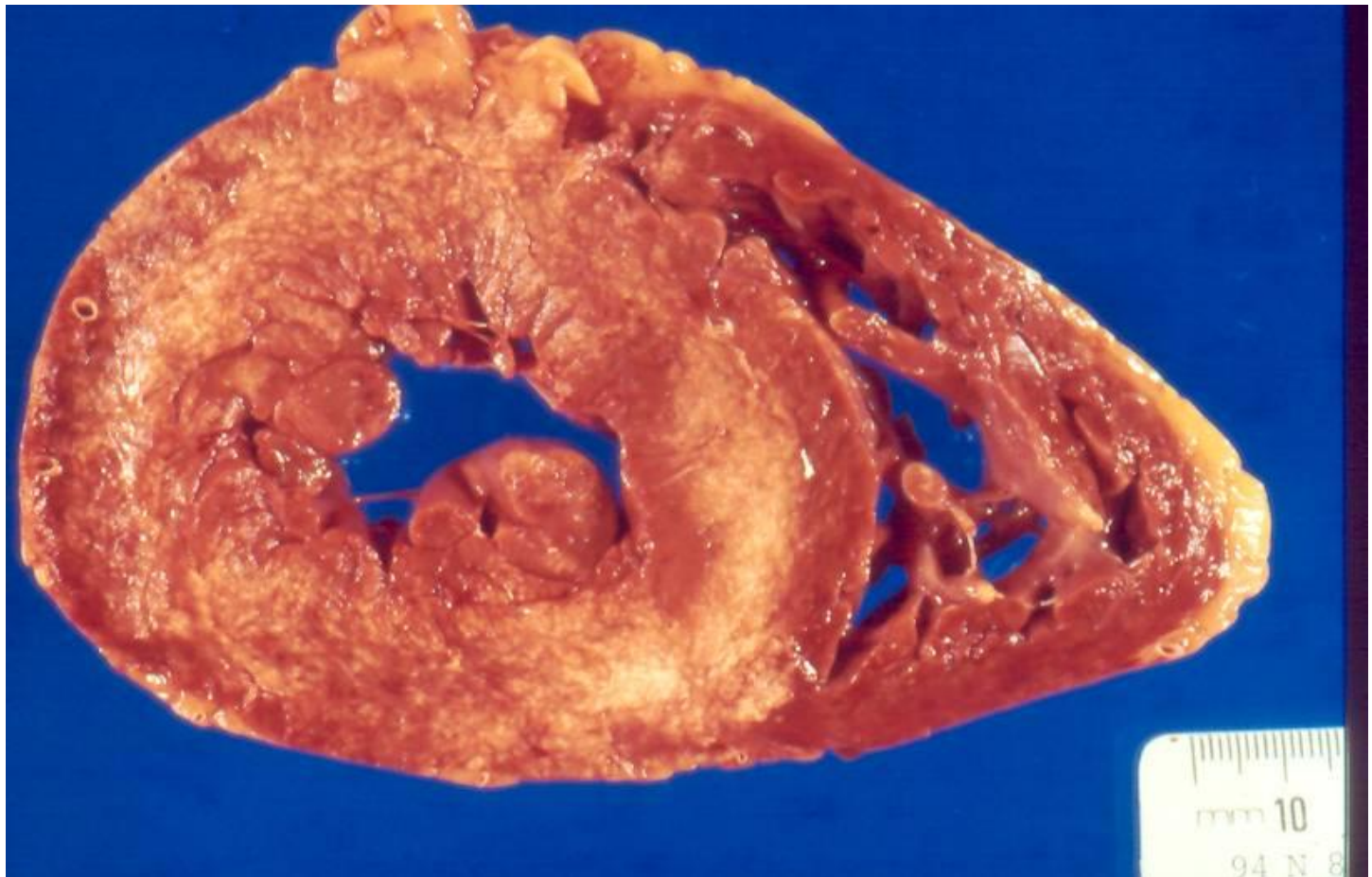
PARFREY, P. S. et al. J Am Soc Nephrol 1999;10:1606-1615

Prevalence of LVH in kidney failure

Renal Insufficiency	CCr ml/min	Prevalence LVH
General Population		17%
Mild	75-50	27%
Moderate	50-25	31%
Severe	<25	45%
Start Dialysis		75%

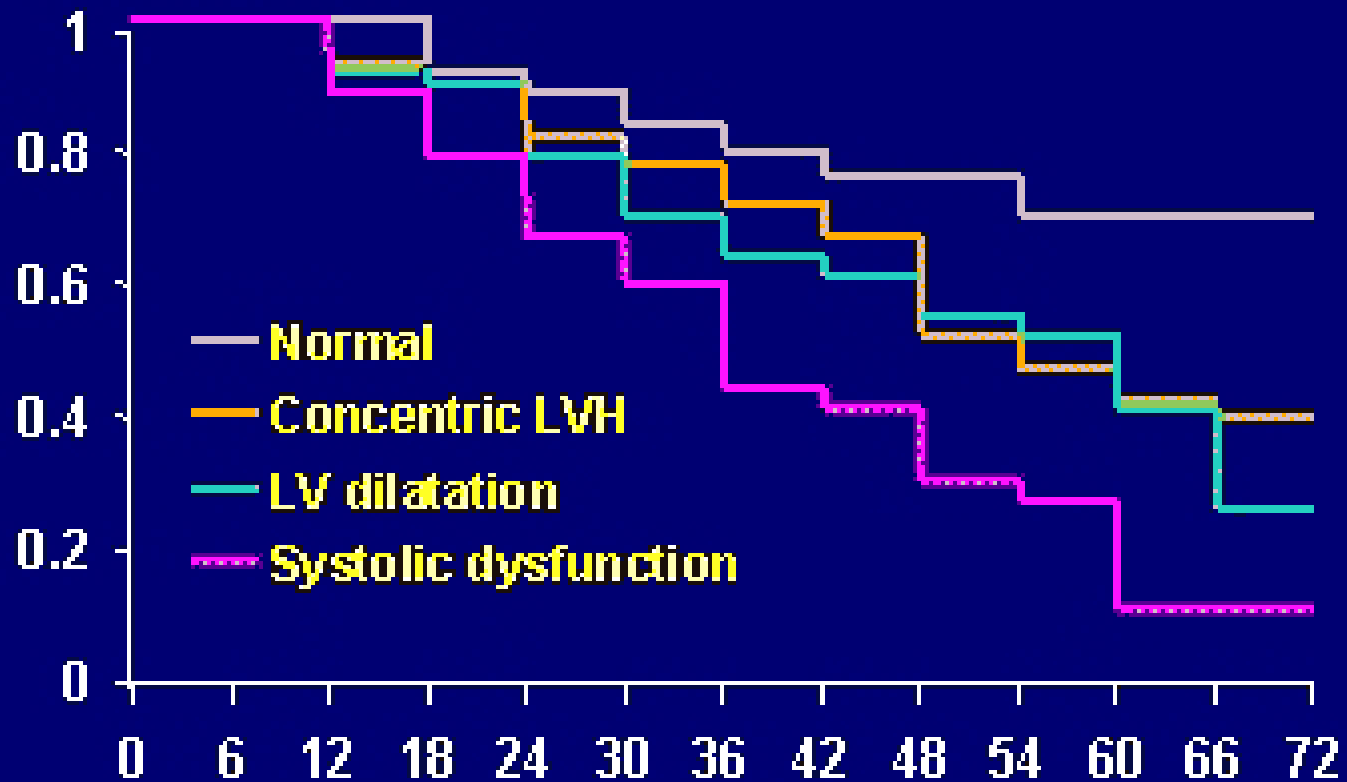
Levin et al, AJKD 1999;34:125-134

Intramycocardial fibrosis and calcification



LV disease predicts survival on dialysis

Survival probability



Parfrey and Foley, 1999

Months

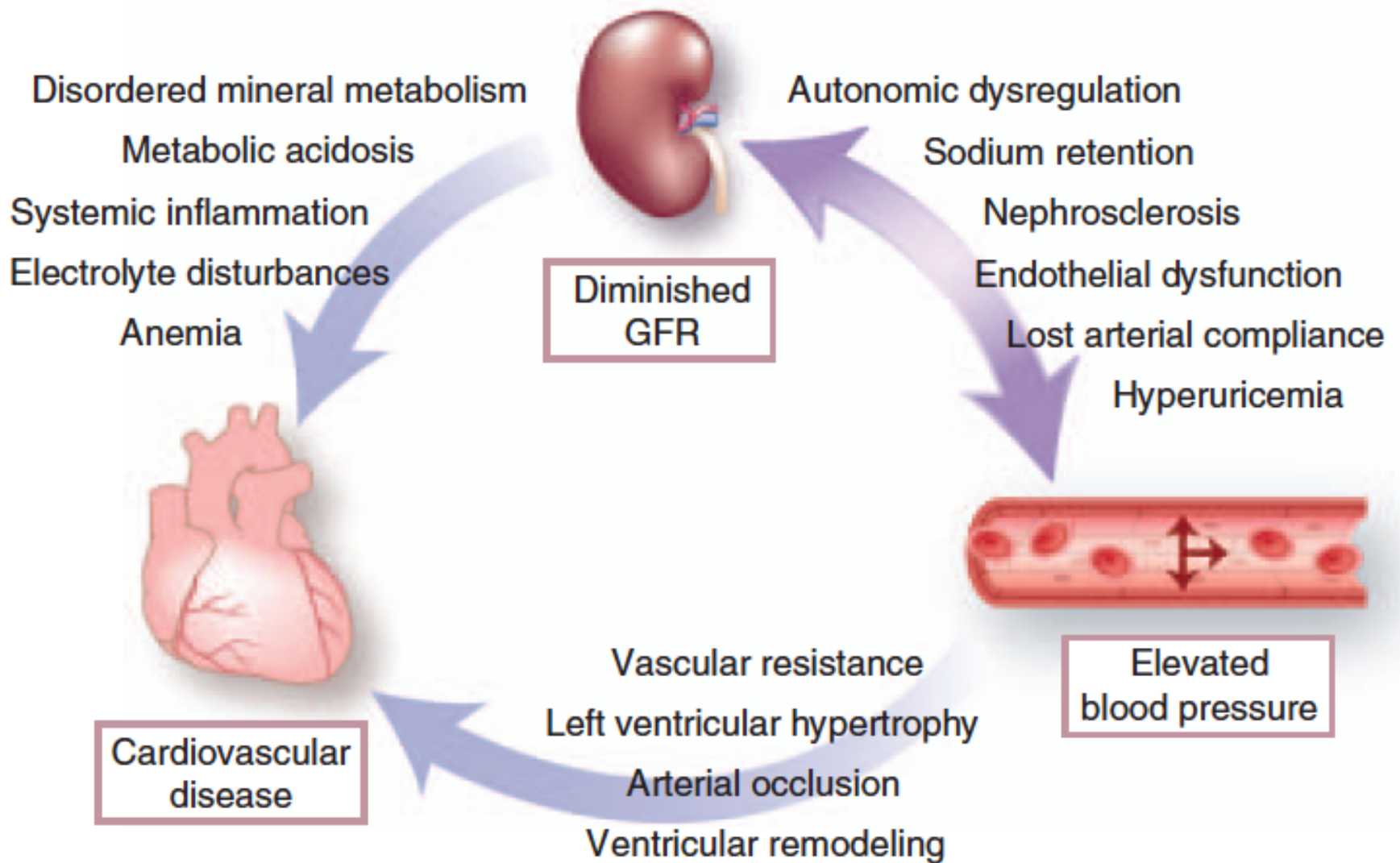
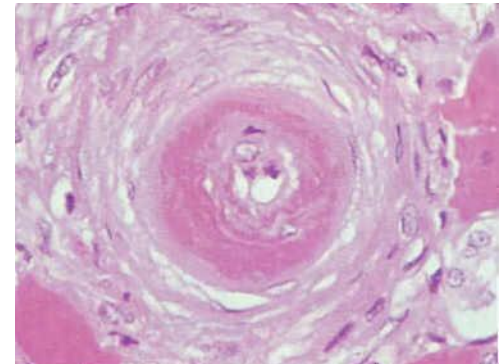
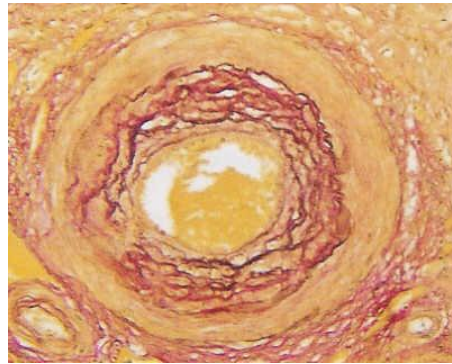
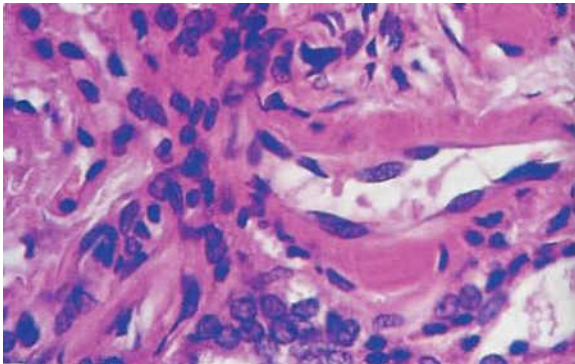


Figure 1 | Joint contribution of CKD and hypertension to cardiac risk. CKD, chronic kidney disease; GFR, glomerular filtration rate.

CKD & CVD

- Annual CVD checks
- Do you assess CKD as part of this?
- eGFR, proteinuria, hypertension

Hypertension and the Kidney

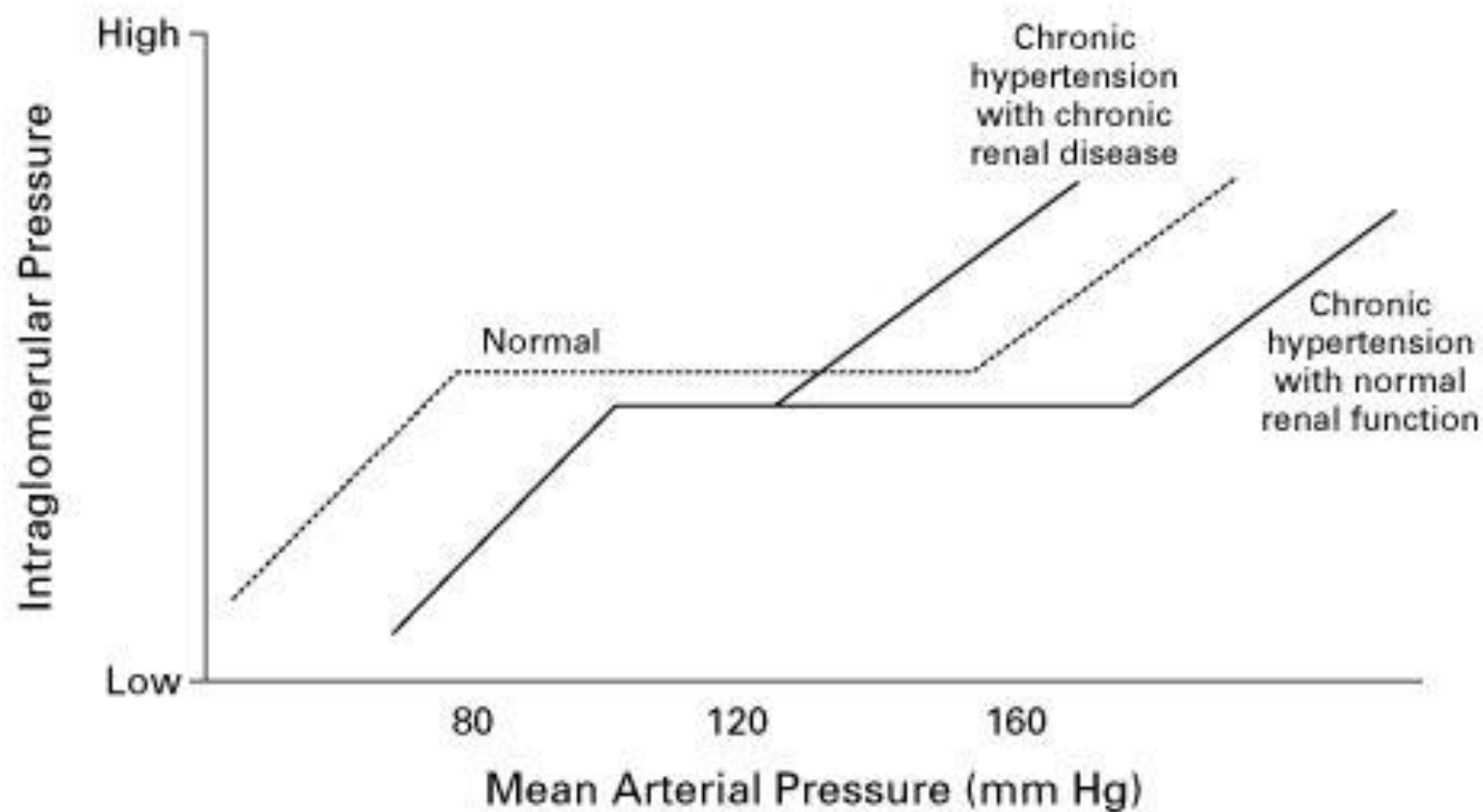


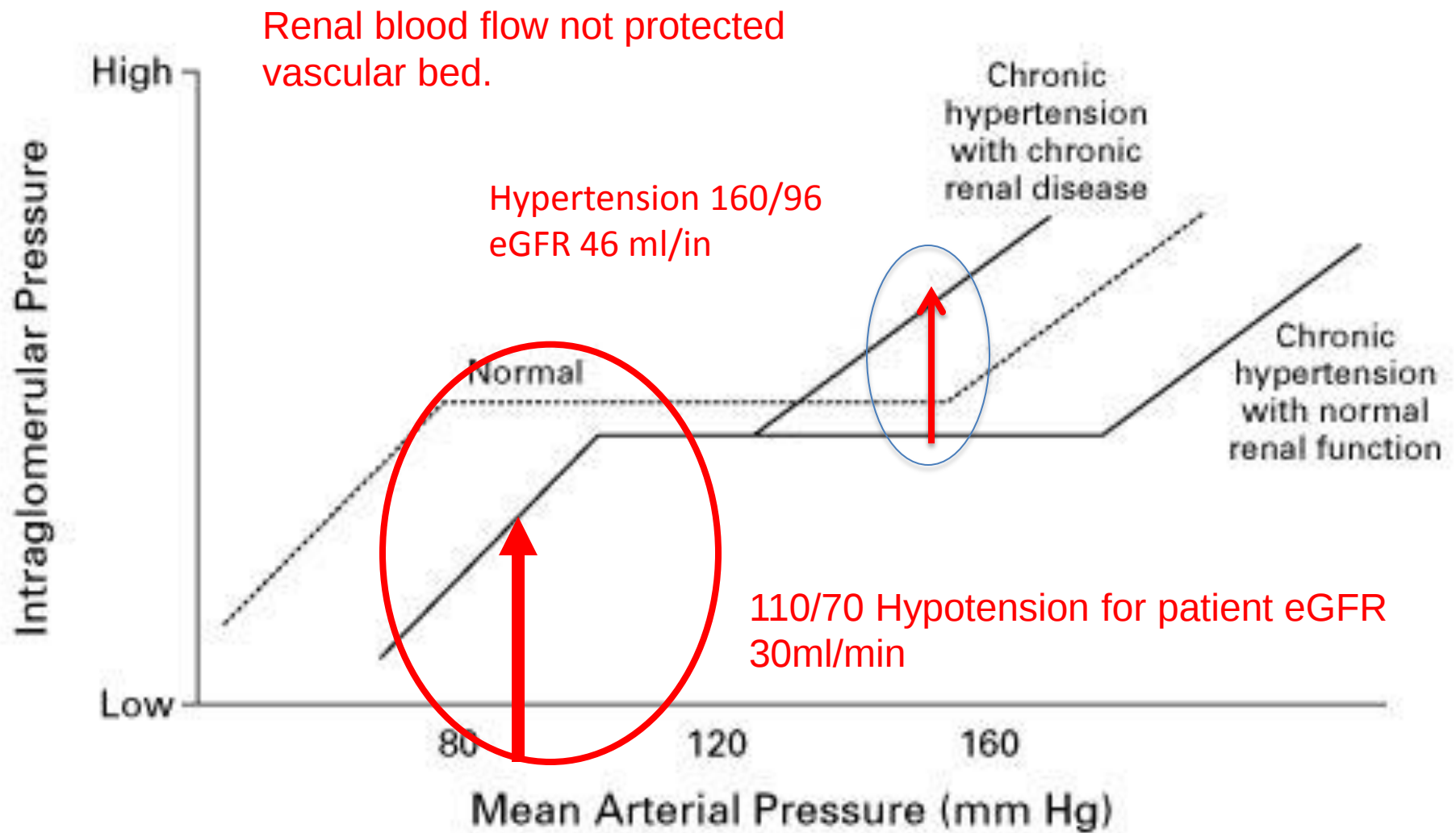
Progressive Nephropathy

- Initial insult seems to be followed by progressive decline.
- Role of loss of auto-regulation and transmission of systemic pressure to glomeruli.

Progressive Nephropathy

- Overall in CKD
 - Lose the protective vasodilation or vasoconstriction
 - Kidney senses these highs and lows in perfusion pressure
 - Creatinine does rise and fall as you correct this
 - (a linear relationship almost)
 - Pre-glomerular pressure response lost and post-glomerular compensation lost

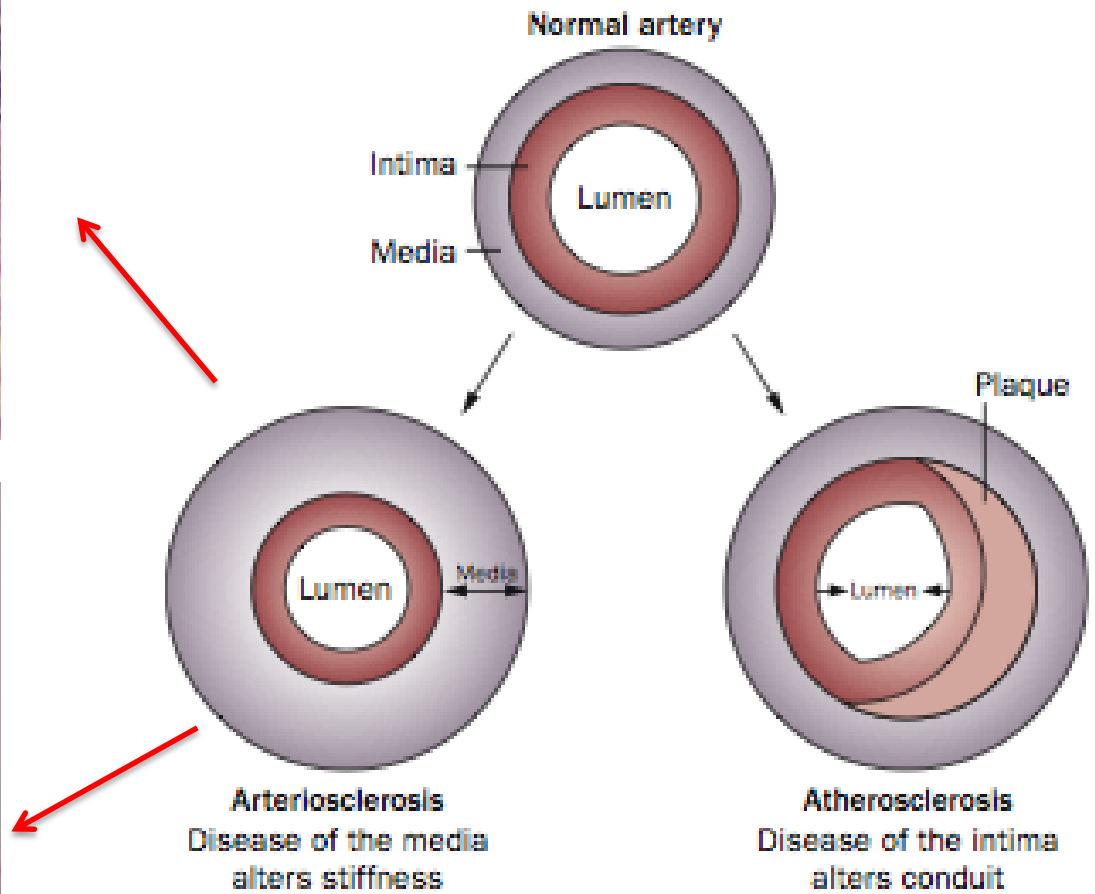
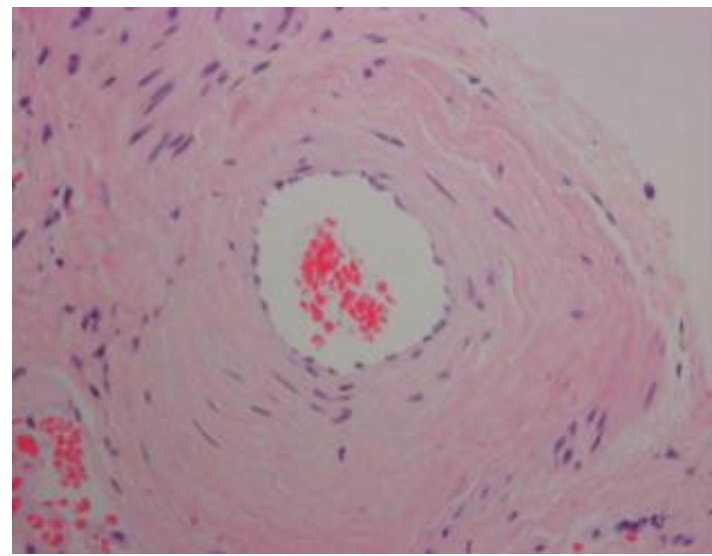
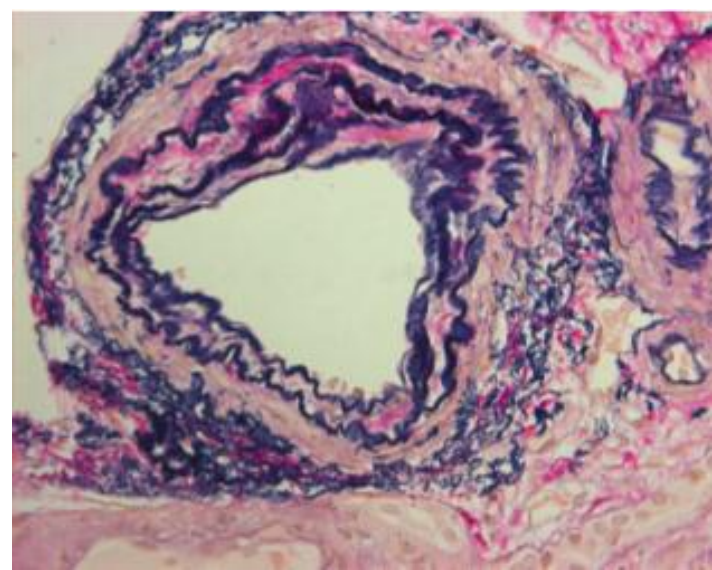




Arteries stiffen

- Long standing arterial pulsation:
- Medial degeneration
- Direct effects on matrix proteins, collagen and elastin
 - Elastin fibres break – reduplication
 - Detachment smooth muscle fibres
 - Increased VSMC
- Calcification
 - Oxidative stress AGE add to stiffness

Thickened media
Reduplication of elastic lamina



Intimal hyperplasia

Arterial Stiffness:

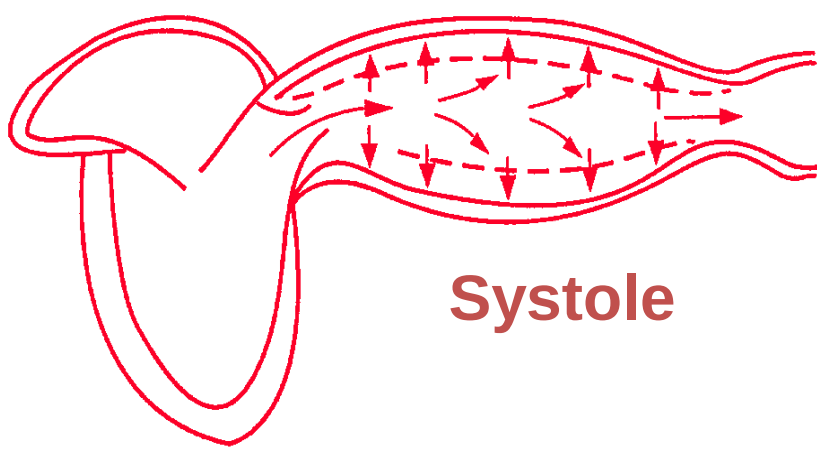
Functional changes:

- Reduction in endothelial mediated vasodilation
- Changes in smooth muscle function
Note SMVC hypertrophy attempt to modify increased collagen

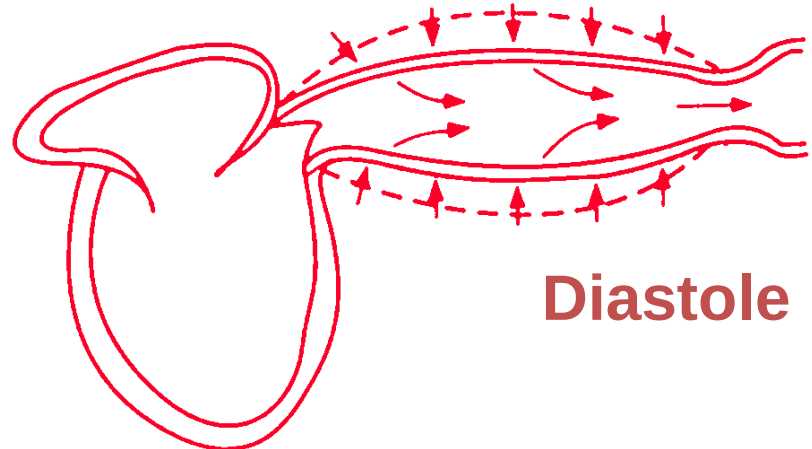
Age mediated changes

- Age mediated increases in stiffness progress more rapidly in central arteries than peripheral arteries.
Increases in Aortic PWV reflect vessel stiffness
Changes are independent of MAP
Valid in an older age group.

Arteriosclerosis and Pulse Wave Velocity

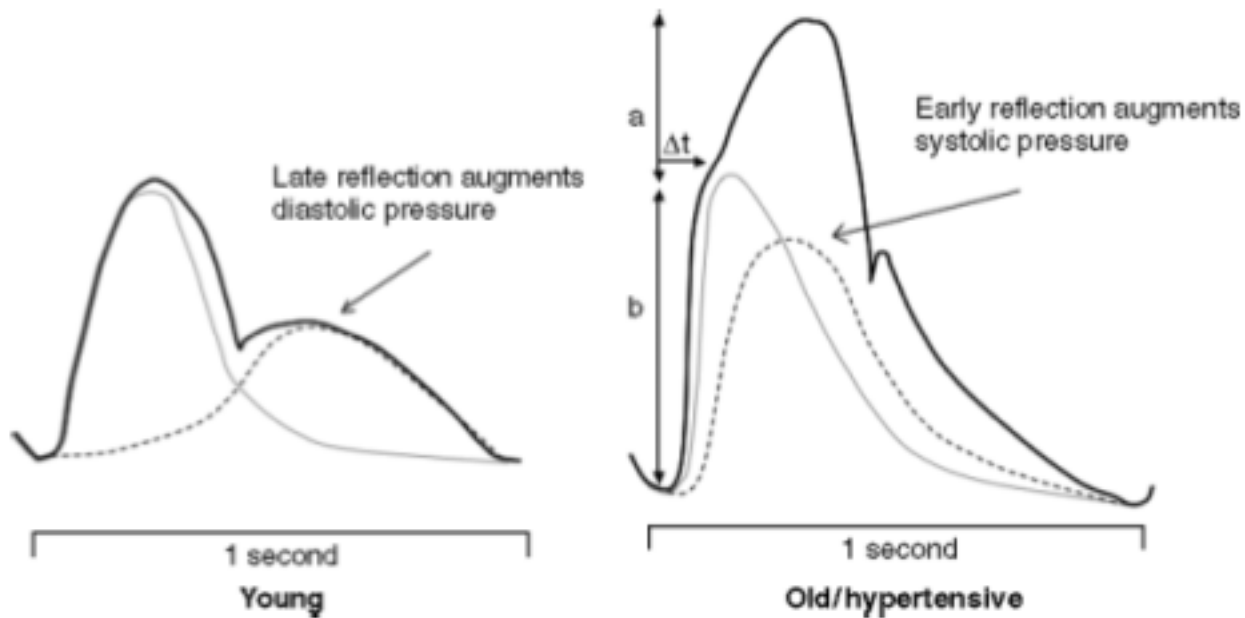


Systole



Diastole

Pulse Wave Forms



Shape – force felt by artery.

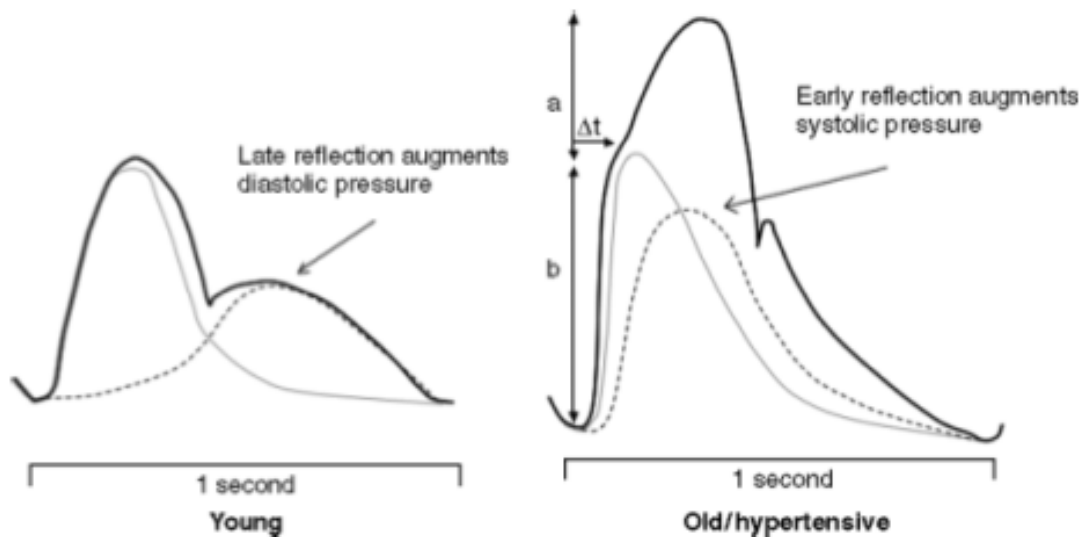
Older stiff vessel – reflected wave early

↑SBP ↓DBP

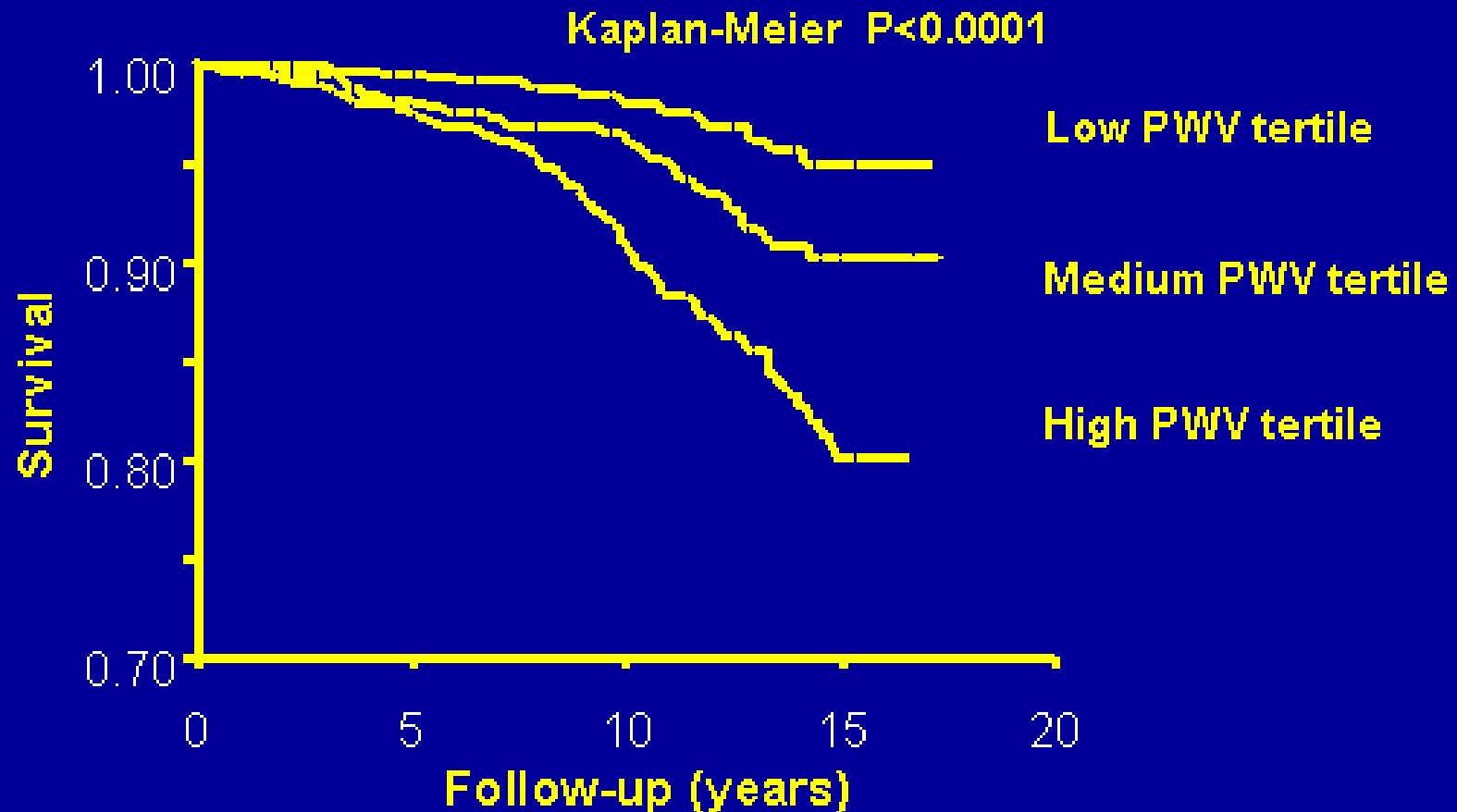
Increased pressure – Heart brain kidney

Impact of vascular stiffness

- Heart
 - impaired diastolic perfusion
 - diastolic dysfunction
 - additional impact of coronary calcification

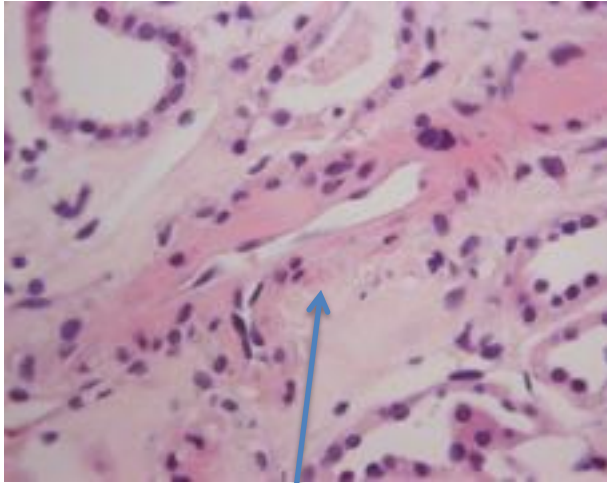


Aortic stiffness and all-cause mortality in general population (Laurent et al Hypertension 2001)

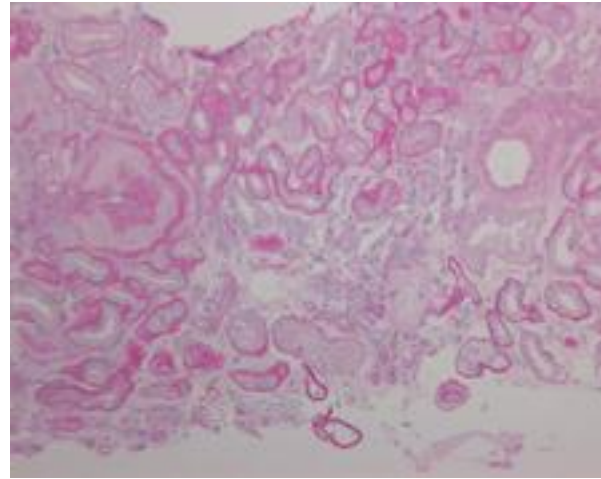


Impact of vascular stiffness

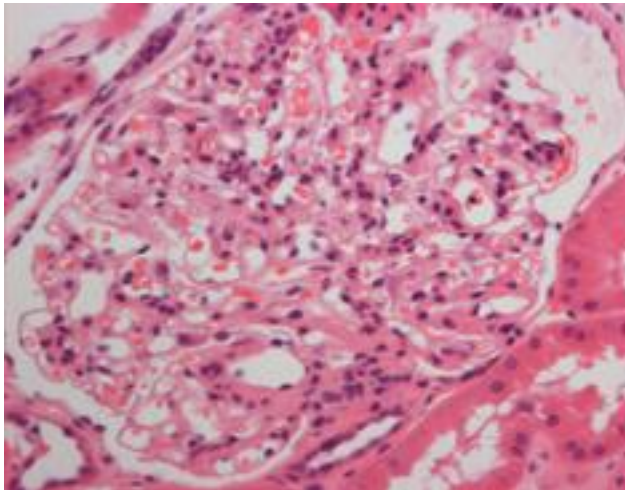
- Heart
 - impaired diastolic perfusion
 - diastolic dysfunction
 - additional impact of coronary calcification
- Brain
 - increased risk stroke
- Kidneys
 - arteriolosclerosis, glomerulosclerosis



Arteriolosclerosis

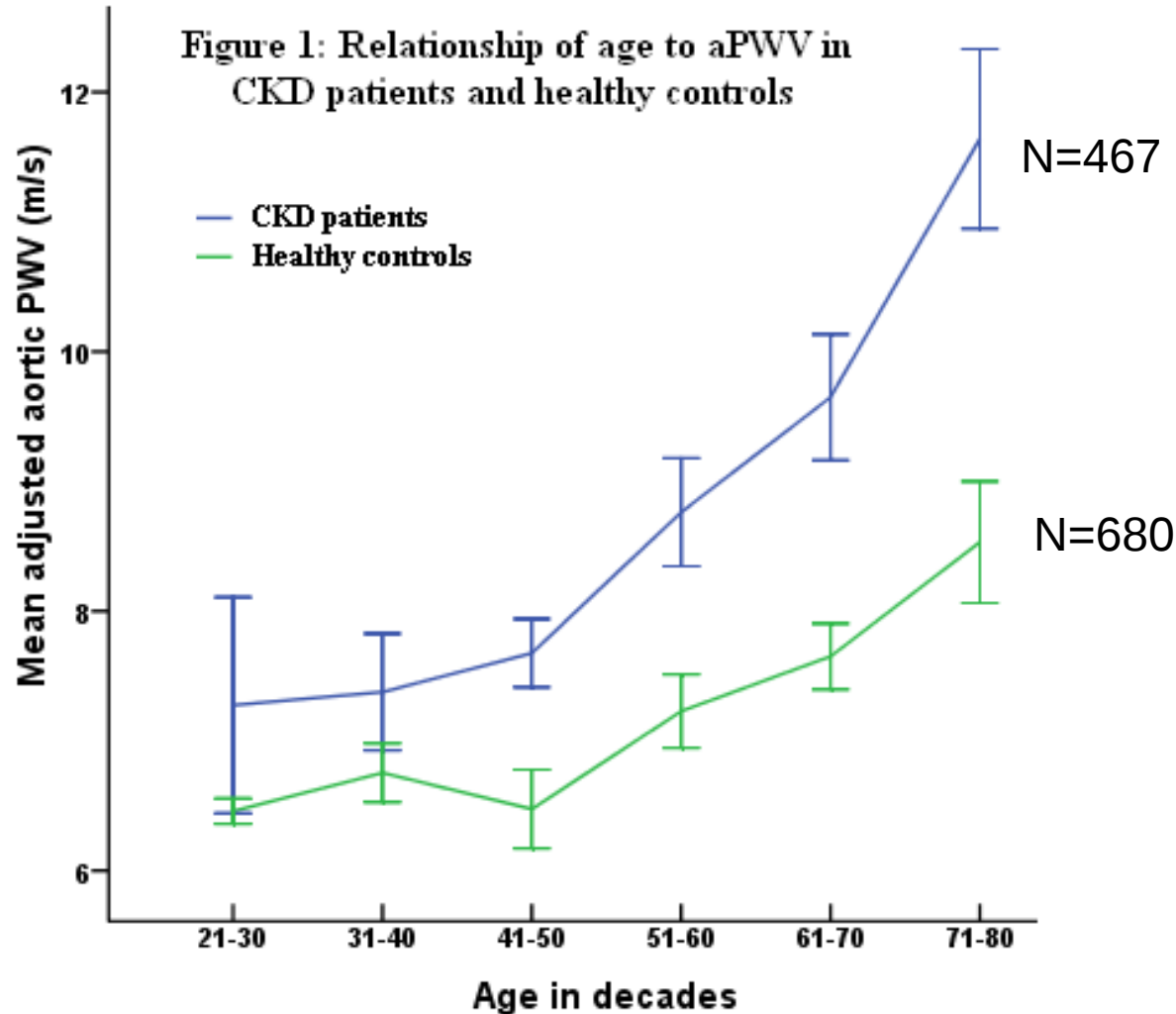


Interstitial fibrosis
glomerulosclerosis and
tubular atrophy



Compensatory
glomerular hypertrophy

Arteries stiffen prematurely in CKD



Tomlinson L (on behalf of the UREKA collaboration)
unpublished data not for distribution

Kidneys reflect vascular injury

- In patients with CKD Stage 3
Hypertensive nephrosclerosis is the major aetiology.
- Impact of proteinuria – marker of endothelial injury (Sunday)
- Blood pressure control – main focus of therapy.

Take Home Points

- Hypertension is a major component of Kidney disease
- Contributes to progression of CKD.
- Most patients with CKD die of CVD
10 – 20 x risk of CV event
- Proteinuria and hypertension are major prognostic factors – require more aggressive treatment.
- Frequently require 3 drug therapy – drug type.

“Once in a while
You may come across a place
where everything
is as close to perfection
as you will ever need”

“Place” Brian Turner



“Old age is a disease which we can not cure.” Seneca
(c. 4 BC - 65 AD)