

Chronic Kidney Disease – an update

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Talk Outline

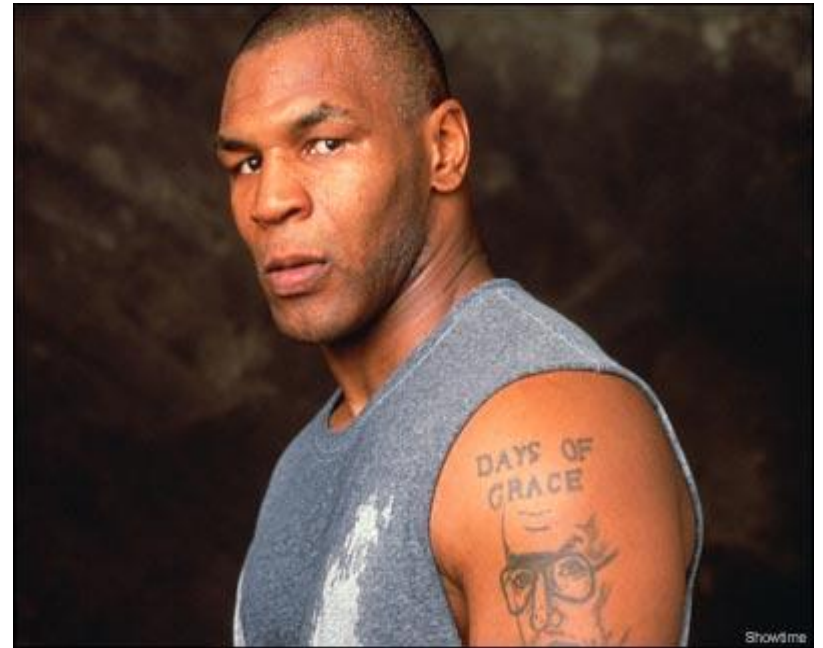
- eGFR and CKD staging NICE guideline
- Approach to CKD
- Cardiovascular risk
- Management of Diabetic Nephropathy
- Clinical cases

So who has the better kidney function?



Creatinine $120\mu\text{mol/l}$
eGFR = 39 ml/min/1.73m²

CKD 3



Creatinine $120\mu\text{mol/l}$
eGFR = 77 ml/min/1.73m²

Normal kidney function!!

Kidney function prediction equations

Cockcroft and Gault equation

$$\text{Estimated creatinine clearance (Cl}_{Cr}) = \frac{(140 - \text{age}) \times \text{weight} \times 1.2}{SCr} \times (0.85 \text{ if female})$$

where age is expressed in years, SCr in $\mu\text{mol/l}$, and weight in kg^{10}

6-variable MDRD¹⁵

$$170 \times (S_{Cr}/88.4)^{-0.999} \times \text{age}^{-0.176} \times (\text{SU}/0.357)^{-0.170} \times (\text{SAIb} \times 10)^{+0.318} \times (0.762 \text{ if female}) \times (1.180 \text{ if black})$$

where S_{Cr} = serum creatinine in $\mu\text{mol/l}$, SU = serum urea in mmol/l , SAlb = serum albumin in g/l , and age is expressed in years

4-variable MDRD¹⁶

$$186.3 \times (S_{Cr}/88.4)^{-1.154} \times \text{age}^{-0.203} \times (0.742 \text{ if female}) \times (1.21 \text{ if black})$$

where S_{Cr} = serum creatinine in $\mu\text{mol/l}$, and age is expressed in years

Modified 4-variable MDRD (traceable by isotope dilution mass spectrometry)

$$F \times 175 \times (S_{Cr}/88.4)^{-1.154} \times \text{age}^{-0.203} \times (0.742 \text{ if female}) \times (1.21 \text{ if black})$$

where F = correction factor, S_{Cr} = serum creatinine in $\mu\text{mol/l}$, and age is expressed in years

KDOQI:

Kidney and dialysis quality initiative is a set of guidelines produced by the US National Kidney Foundation

UK CKD NICE Classification

Stage ^a	GFR (ml/min/1.73m ²)	Description
1	≥ 90	Normal or increased GFR, with evidence of kidney damage
2	60–89	Slight decrease in GFR, with other evidence of kidney damage
3A	45–59	Moderate decrease in GFR, with or without other evidence of kidney damage
3B	30–44	
4	15–29	Severe decrease in GFR, with or without other evidence of kidney damage
5	< 15	Established renal failure

- Evidence of kidney damage:
- Proteinuria / microalbuminuria
 - Haematuria
 - Structural abnormalities
 - E.g. Horseshoe kidney

^a Use suffix (p) to denote presence of proteinuria when staging CKD

CKD KDIGO/NICE Classification- 2013/14

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min/1.73m ²) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

- A2 equivalent to the old term of microalbuminuria
- Based on CKD-EPI equation rather than MDRD
- Categories rather than stages

KDIGO- NICE Classification

- Recommend using eGFR-Cystatin C-creatinine for those with no other evidence of CKD and eGFR between 45-59mls/min/1.73m².
- If Cystatin C based eGFR normal (and no albuminuria/structural abnormalities) then don't label these people as having CKD

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*So how do I approach
somebody with CKD*



Chronic Kidney Disease

**Pre-Renal
causes**

**Intrinsic Renal
causes**

**Post-Renal
causes**

Glomerular Disease

Tubulo-interstitial disease

Inherited
disease

Vascular
Disease

Chronic
Glomerulonephritis

Systemic Disease:
Diabetes
Hypertension
SLE

Chronic pyelonephritis
Reflux nephropathy
Interstitial Nephritis
(NSAIDS, penicillin,
sarcoid, TB)

Polycystic
Kidney Disease,
Alports

**Atherosclerotic
renovascular
disease**

Clinical approach to CKD

Is this acute or chronic kidney disease?



Historical creatinine
Small kidneys on ultrasound → CKD (except diabetes) Repeat eGFR within 14 days if no previous result

Is this drug related CKD?



Nephrotoxics – e.g. NSAIDs, Lithium, sulphasalazine Check if recently started diuretics, ACE-I/ARBs

Is this pre-renal CKD?

Volume depletion – diuretics, vomiting, diarrhoea, liver disease

Is this obstructive CKD?

Obstructive symptoms

Most causes of CKD can be identified by looking at the history, urine dipstick and drug list with clinical evaluation

Is this a glomerulonephritis?



Active urine dipstick in absence of infection

Is this diabetic or renovascular disease?



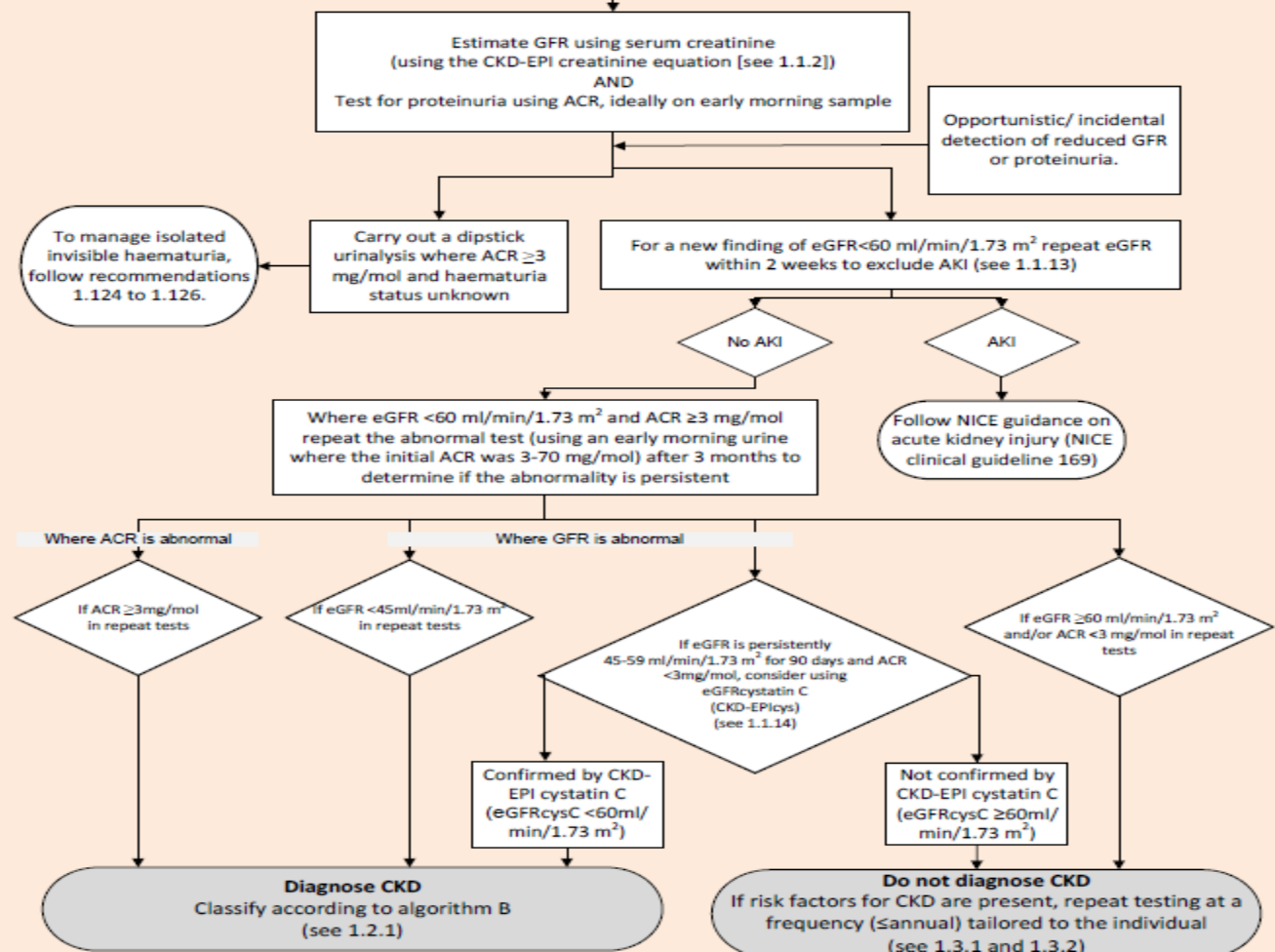
Diabetic nephropathy likely if proteinuria. May also have retinopathy. Haematuria unusual.
Asymmetric kidneys on US, worsening kidney function on ACE-I/ARB, presence of vascular disease → likely atherosclerotic renovascular disease

Offer testing for CKD using eGFRcreatinine and ACR to people with any of the following risk factors:

- diabetes
- hypertension
- acute kidney injury
- cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease or cerebral vascular disease)
- structural renal tract disease, recurrent renal calculi or prostatic hypertrophy
- multisystem diseases with potential kidney involvement - for example, systemic lupus erythematosus
- family history of end-stage kidney disease (GFR category G5) or hereditary kidney disease
- opportunistic detection of haematuria.

Monitor eGFR at least annually in people prescribed drugs known to be nephrotoxic.

(see 1.1.27 and 1.1.28)

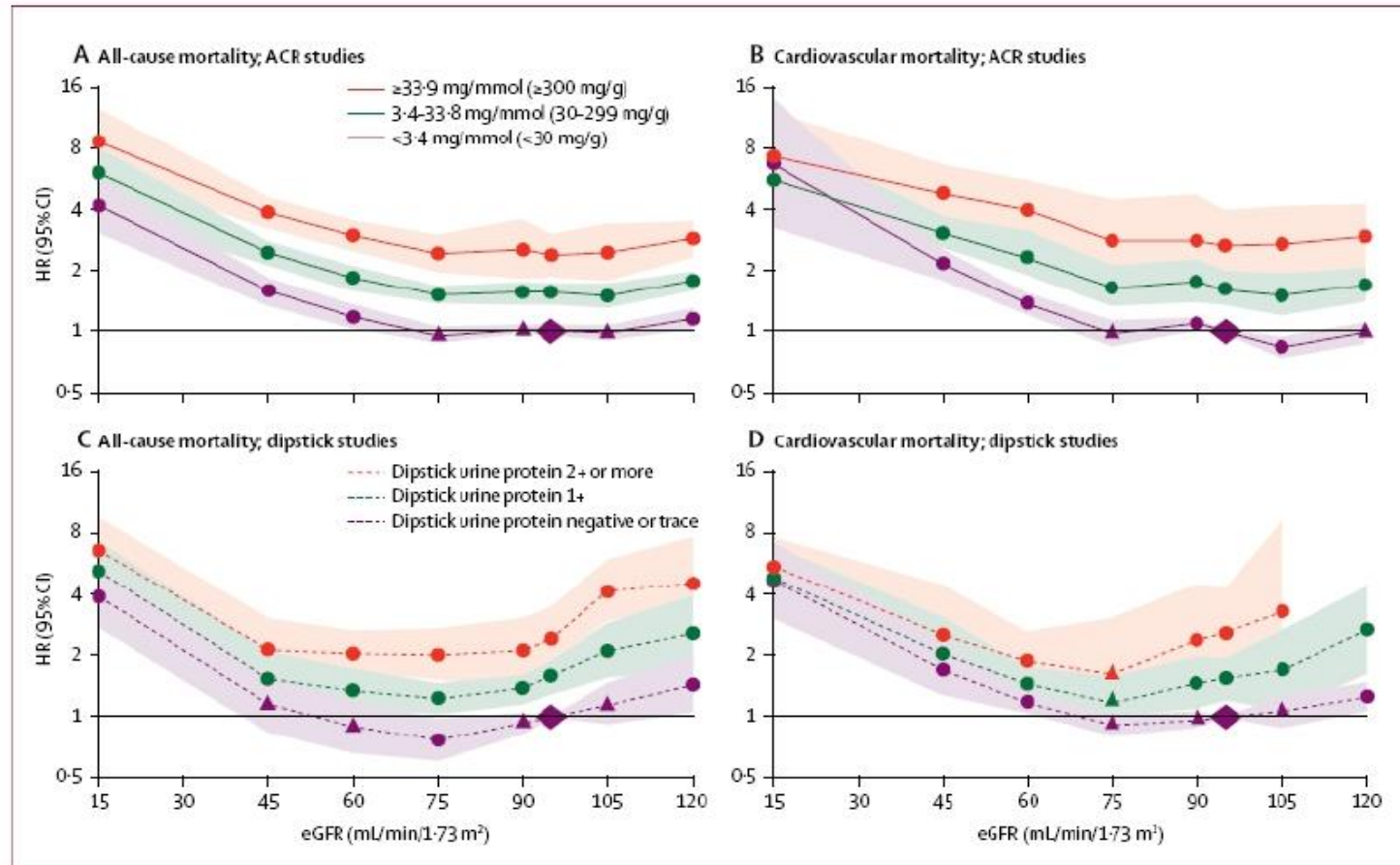


Update 2014

So why is proteinuria important?



Increasing albuminuria and adverse outcomes



**KDIGO CKD prognosis consortium,
The Lancet May 2010**

Albuminuria – the terminology

- **Microalbuminuria:** Negative dipstick but elevated ACR
 - $ACR = 70 \text{ mg/mmol} \approx PCR = 100 \text{ mg/mmol}$
 - $PCR = 100 \text{ mg/mmol} \approx 1\text{gram}/24 \text{ hour urinary protein excretion}$
 - Can use ACR or PCR

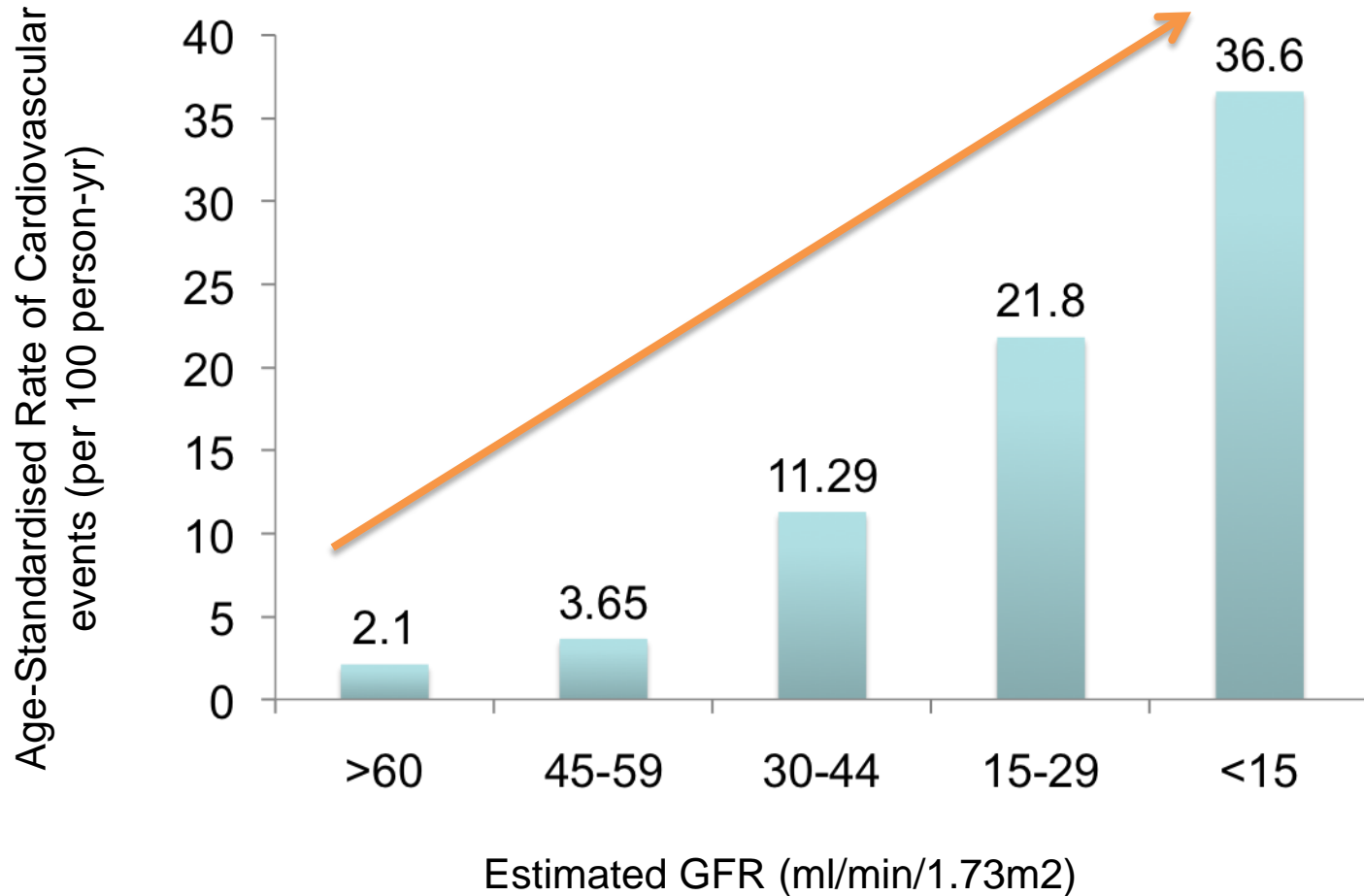
Urinary protein concentration equivalents

	Dipstick	Urinary PCR, mg/mmol (urine protein mg/L)	Urine Total Protein excretion mg/24 h (g/24 h)	Urinary ACR, mg/mmol	Urinary Albumin excretion, µg/min (mg/24 h)
Normal	Negative	< 15 (<100)	<150 (<0.150)	<2.5 (males), <3.5 (females)	<20 (<30)
Microalbuminuria	Negative	< 15 (<100)	<150 (<0.150)	≥2.5-30 (males), ≥3.5-30 (females)	20-200 (30-300)
‘Trace’ protein	Trace	15-44 (100-299)	150-449 (0.150- 0.449)		
Clinical proteinuria (‘macroalbuminuria’)	1+	45-149 (300- 999)	450-1499 (0.450-1.499)	>30	> 200 (>300)
	2+	150-449 (1000- 2999)	1500-4499 (1.500-4.499)		
Nephrotic range proteinuria	3+	≥450 (≥3000)	≥4500 (≥4.500)		

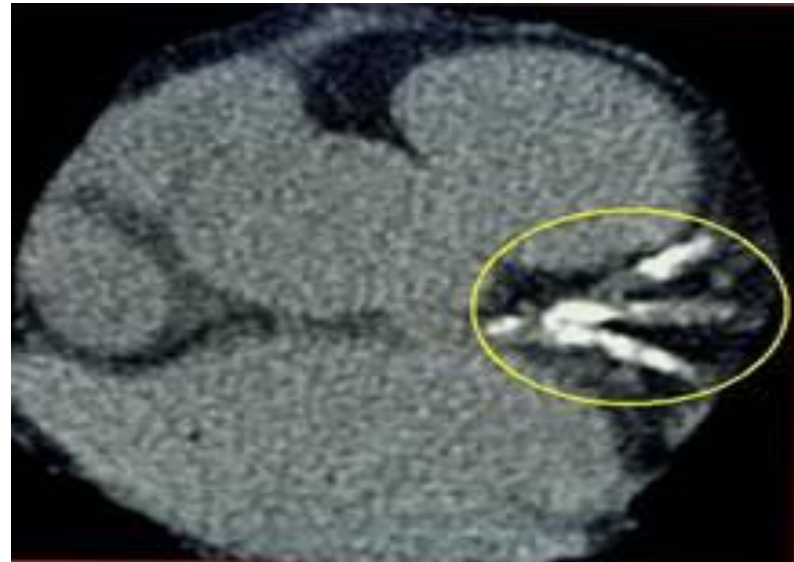
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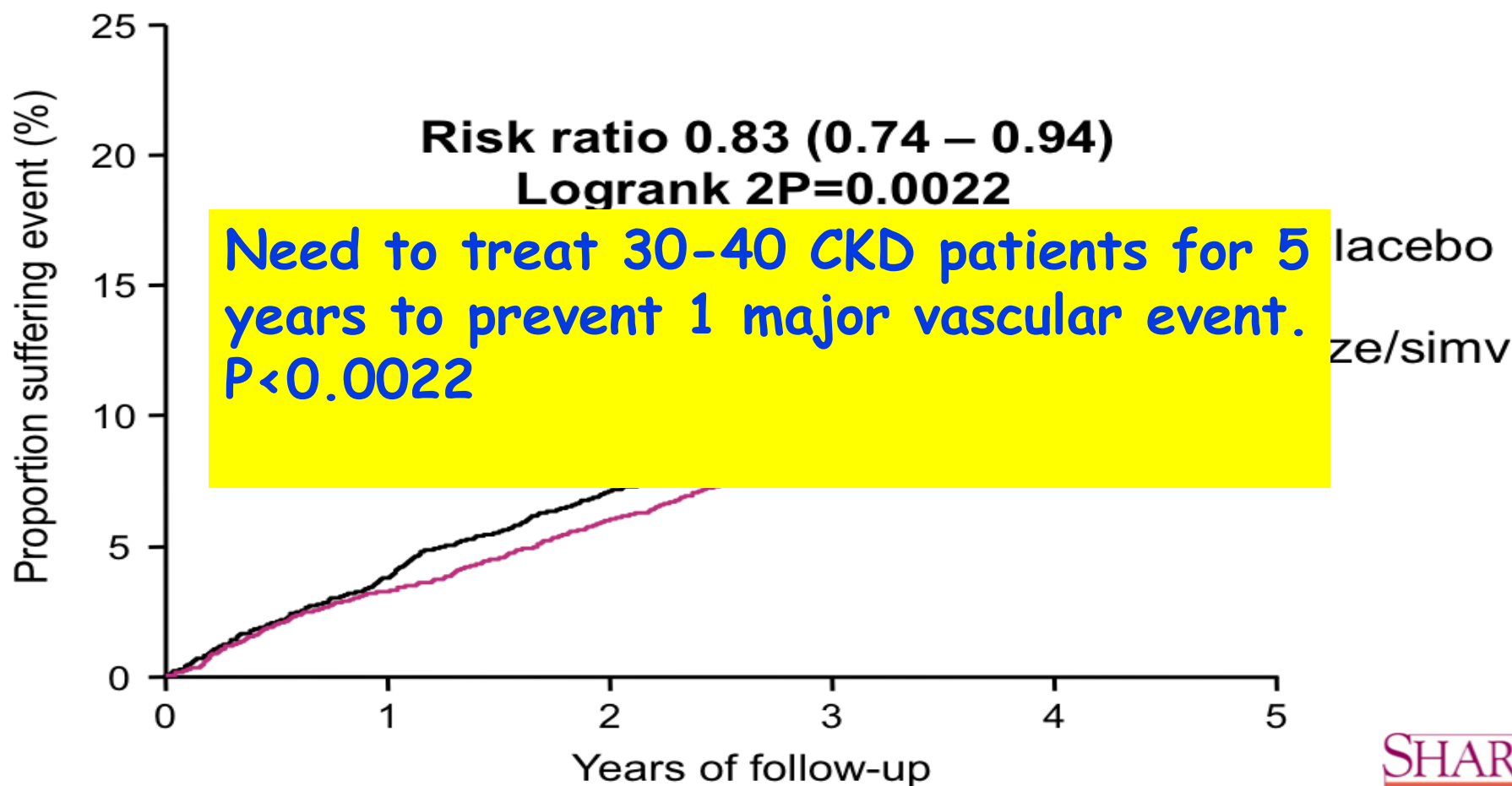
Increased cardiovascular risk in CKD



Vascular calcification in CKD



SHARP – impact of lipid reduction on major vascular events



*So how do I manage CKD
and diabetic CKD - in a
nutshell?*



Diabetic Nephropathy – how to manage

- Assess the patient to make sure this is diabetic nephropathy – proteinuria, evidence of retinopathy
- Control BP – if possible
- Control lipids
- Glycaemic control – if possible
- Smoking, exercise, salt restriction
- **MONITOR!!!!**

So what are the BP targets in diabetes?



BP targets in CKD and Diabetes – the guidelines

- People with diabetes and hypertension should be treated to a systolic blood pressure goal of **<140/80 mmHg**. **American Diabetes Association**
- Lower systolic targets, such as **<130 mmHg**, may be appropriate for certain individuals, such as younger patients, if it can be achieved without undue treatment burden. **American Diabetes Association**

BP targets in CKD and Diabetes – the guidelines

- Target < 140/90 – **KDIGO/NICE guidelines (1B)**
- If ACR > 2.5mg/mmol (males) or 3.5mg/mmol (females) the target BP <130/80 **KDIGO/NICE guidelines (2D)**
- Use ACEi/ARB if ACR between 3-30 mg/mmol **KDIGO/NICE guidelines (2D)**
- Use ACEi/ARB if ACR >30 mg/mmol **KDIGO/NICE guidelines (1B)**

•

BP targets in diabetic CKD – personal view!

- Target of $< 140/90$ or less will be appropriate in many type 2 diabetics
- $130/80$ in those with type 1 diabetes
- ACEi/ARBs benefit those in Type 1 diabetes and Type 2 with heavy proteinuria
- Non diabetics: $<140/90$.
- Non-diabetics with proteinuria (PCR >100): $130/80$

Individualise care... and targets



So what do I monitor and how often?



Stages of CKD^a and frequency of eGFR testing

Stage ^b	eGFR (ml/min/1.73 m ²)	Description	Typical testing frequency ^c
1	≥ 90	Normal or increased GFR, with other evidence of kidney damage	12 monthly
2	60–89	Slight decrease in GFR, with other evidence of kidney damage	
3A	45–59	Moderate decrease in GFR, with or without other evidence of kidney damage	6 monthly
3B	30–44		
4	15–29	Severe decrease in GFR, with or without other evidence of kidney damage	3 monthly
5	< 15	Established renal failure	6 weekly

Check FBC in CKD 3B,4,5 – target Hb 10.5-12.5

Check calcium/phosphate in CKD 3B,4,5

Proteinuria - annual

May want to check PTH and vitamin D in 4,5

*Who do I need to refer
and discuss with a
nephrologist*



Criteria for referral

- Advanced – CKD 4/5... but many elderly with stable CKD 4 don't need referral
- Deteriorating and heavy proteinuria (ACR>70 and not due to diabetes)
- ACR>30 + haematuria
- Sustained decrease in GFR of 25% or more, and a change in GFR category or sustained decrease in GFR of 15 ml/min or more within 12 months
- Sustained Rapidly declining eGFR requires referral

Referral advice

- **Many patients meet the NICE criteria but may not need referral but just advice**
- Email advice: sht-tr.CKDEnquiry@nhs.net

What do I write in referral?

- A clinical question!!
- Drug history, historical and current creatinine
- BP
- Urine dipstick and proteinuria
- Ultrasound (maybe)

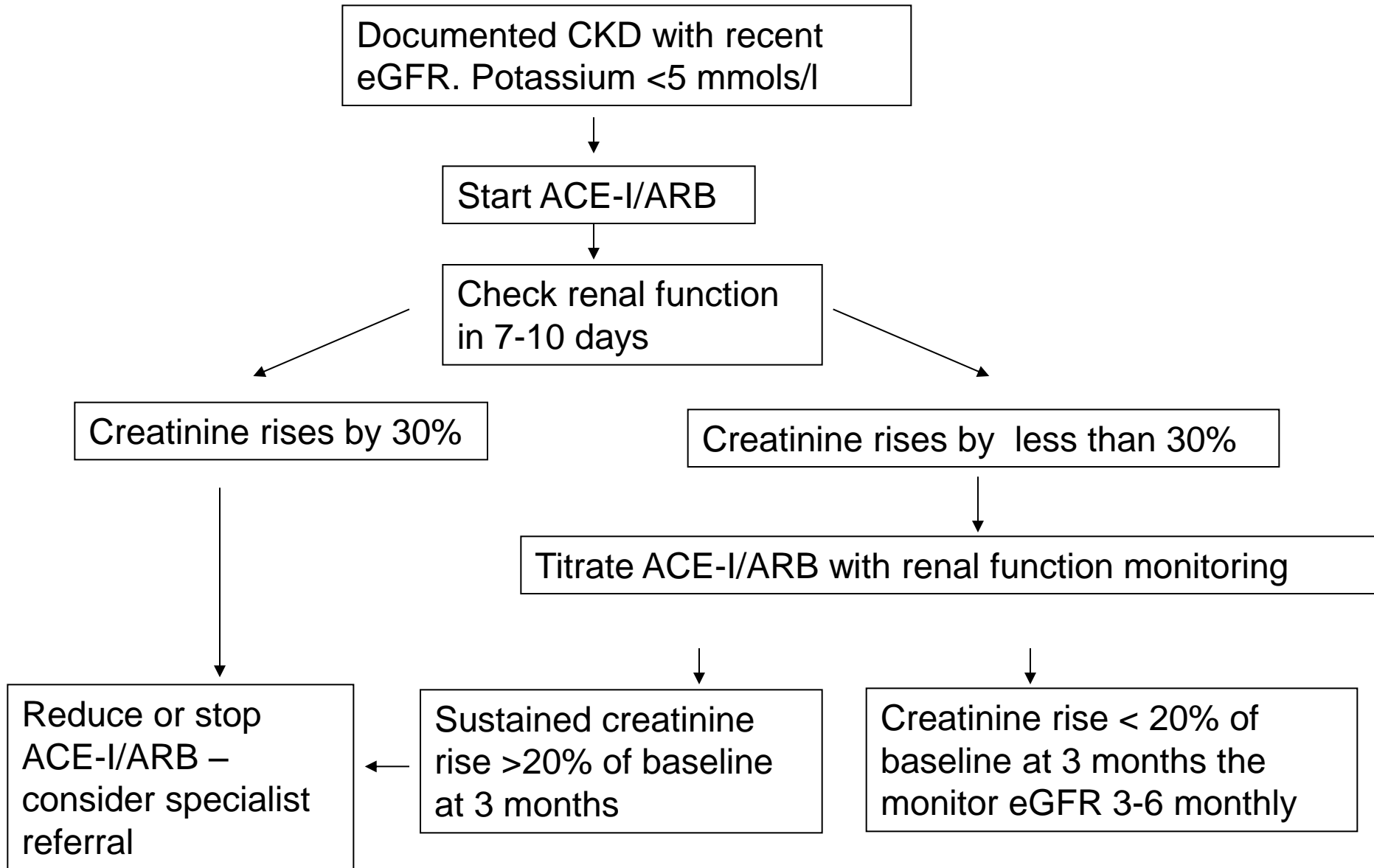
*So who should I give an
ACE-Inhibitor to*



ACE inhibitors in CKD

- ACEi/ARBs are good agents for BP control
- More effective when used with salt restriction or diuretic
- Benefit most in those with heavy proteinuria
- Care in those with vascular disease
- 'Sick day rules' – i.e. don't take when unwell

Algorithm for ACE-I/ARB use in CKD



*What about oral hypoglycaemics
in CKD4?*



Hypoglycaemics in CKD 4

- Metformin cant be used when $GFR < 30$ – not nephrotoxic but risk of lactic acidosis
- Gliclazide is safe
- Linagliptin – no dose reduction
- Sitagliptin – reduce dose to 50 mg od if eGFR 30-50mls/min and 25mg od if eGFR < 30mls/min
- Saxagliptin – 2.5 mg od in CKD 3, caution in CKD 4

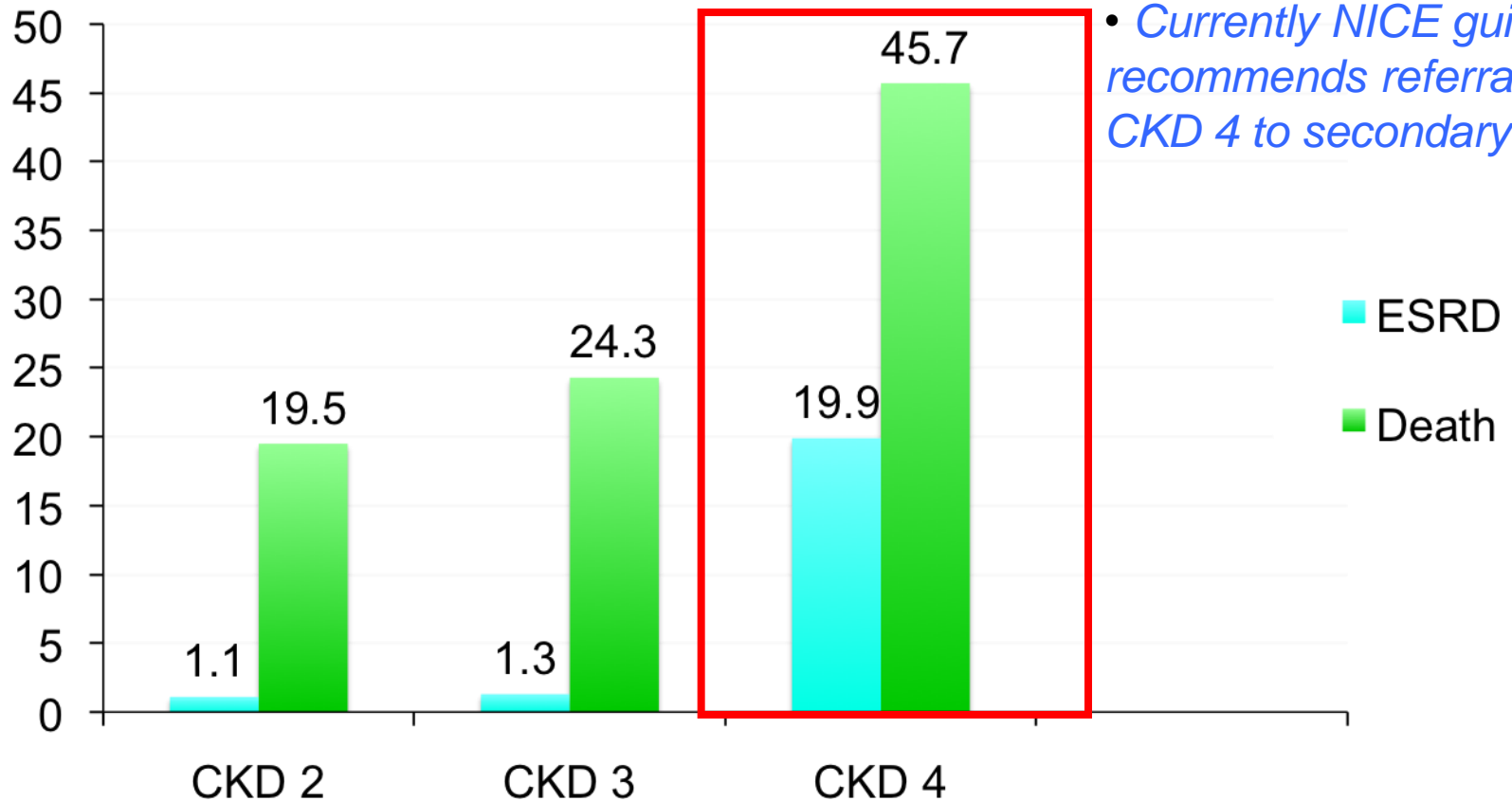
*My patient is really worried
about ending up on dialysis –
who do I tell them?*



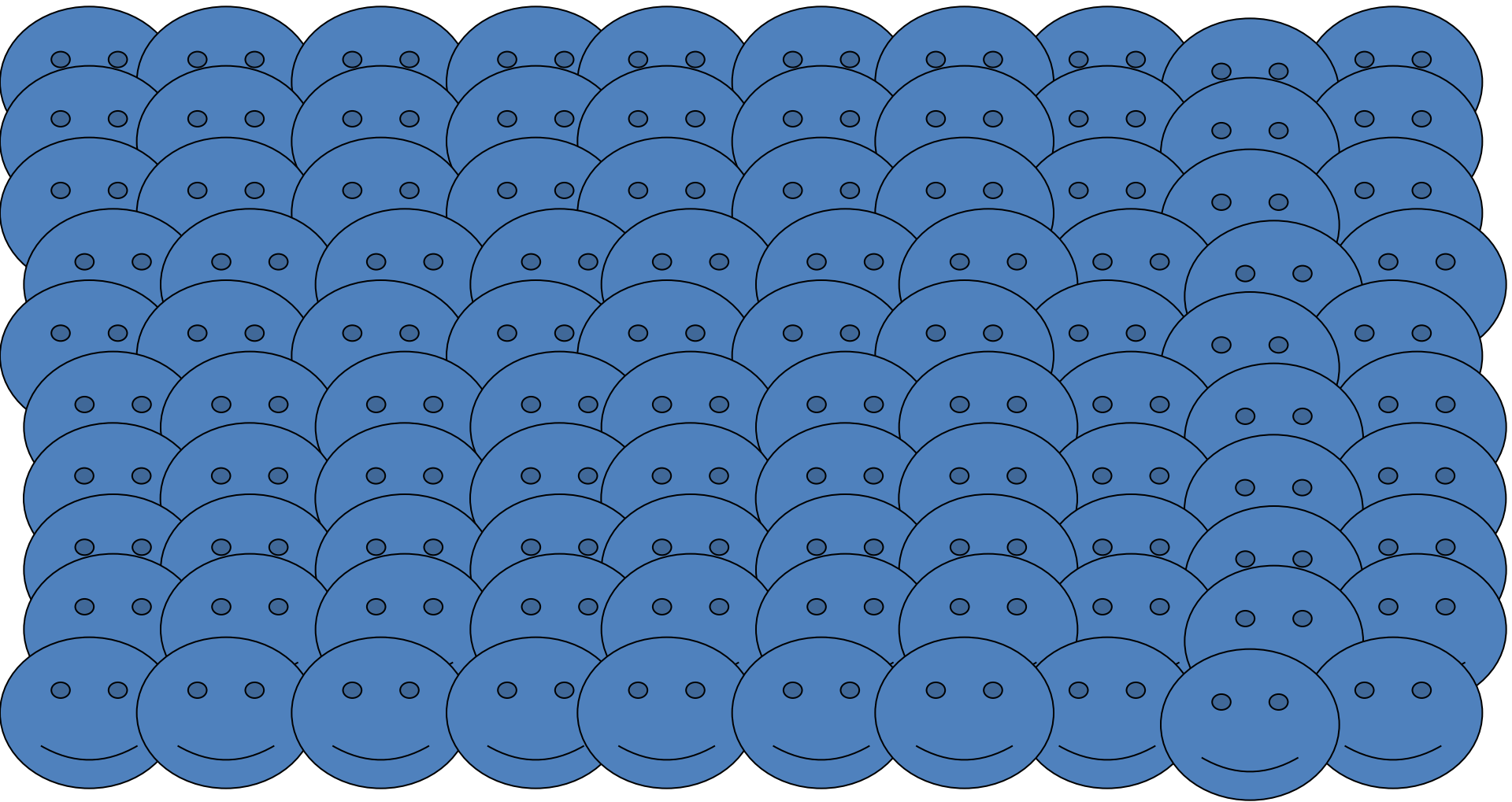
Death – the key outcome in CKD

27,998 CKD patients – outcomes at 66 months

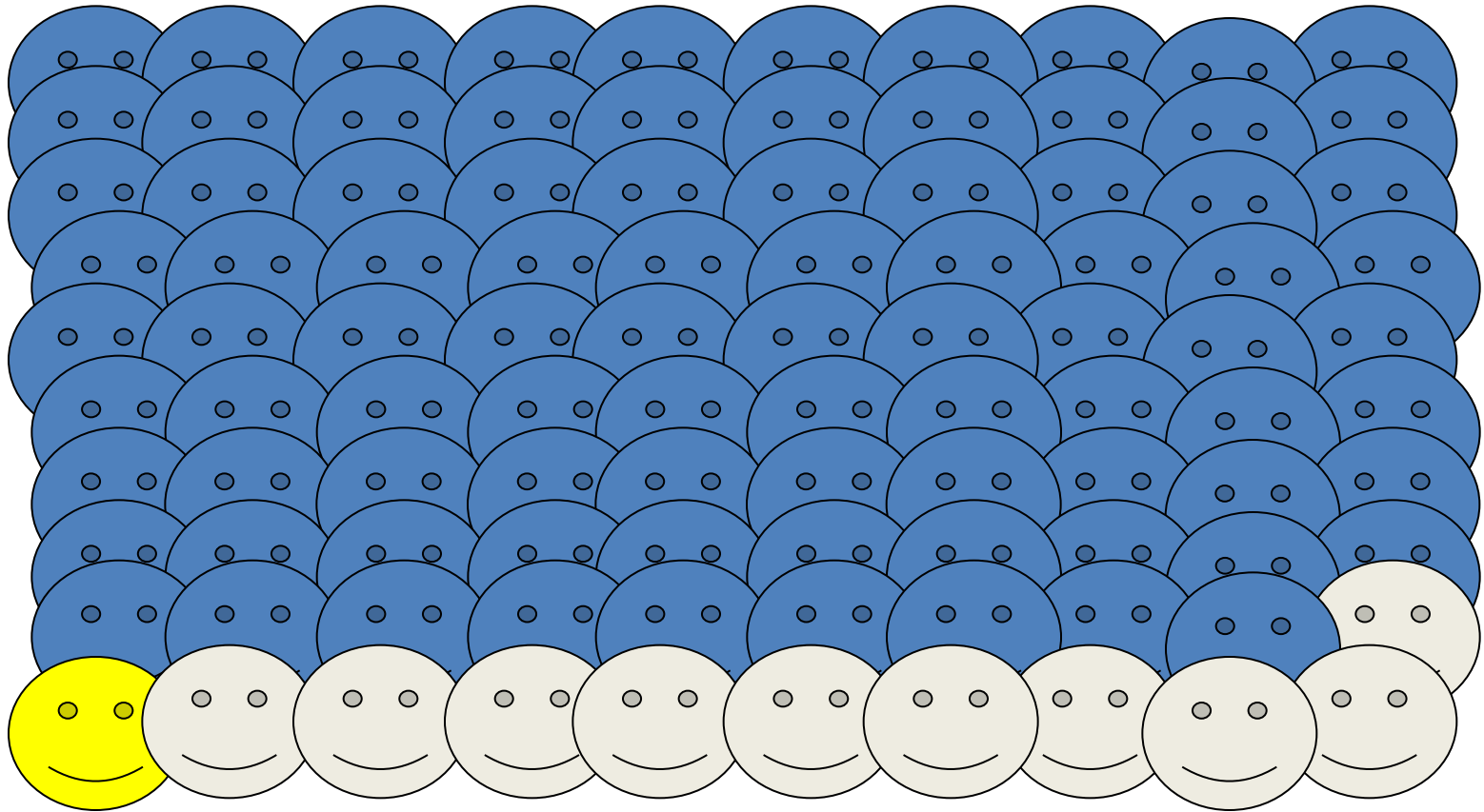
• % patients



• *Currently NICE guidance recommends referral of CKD 4 to secondary care*



100 patients with eGFR < 60
(Monday afternoon in Outpatients)



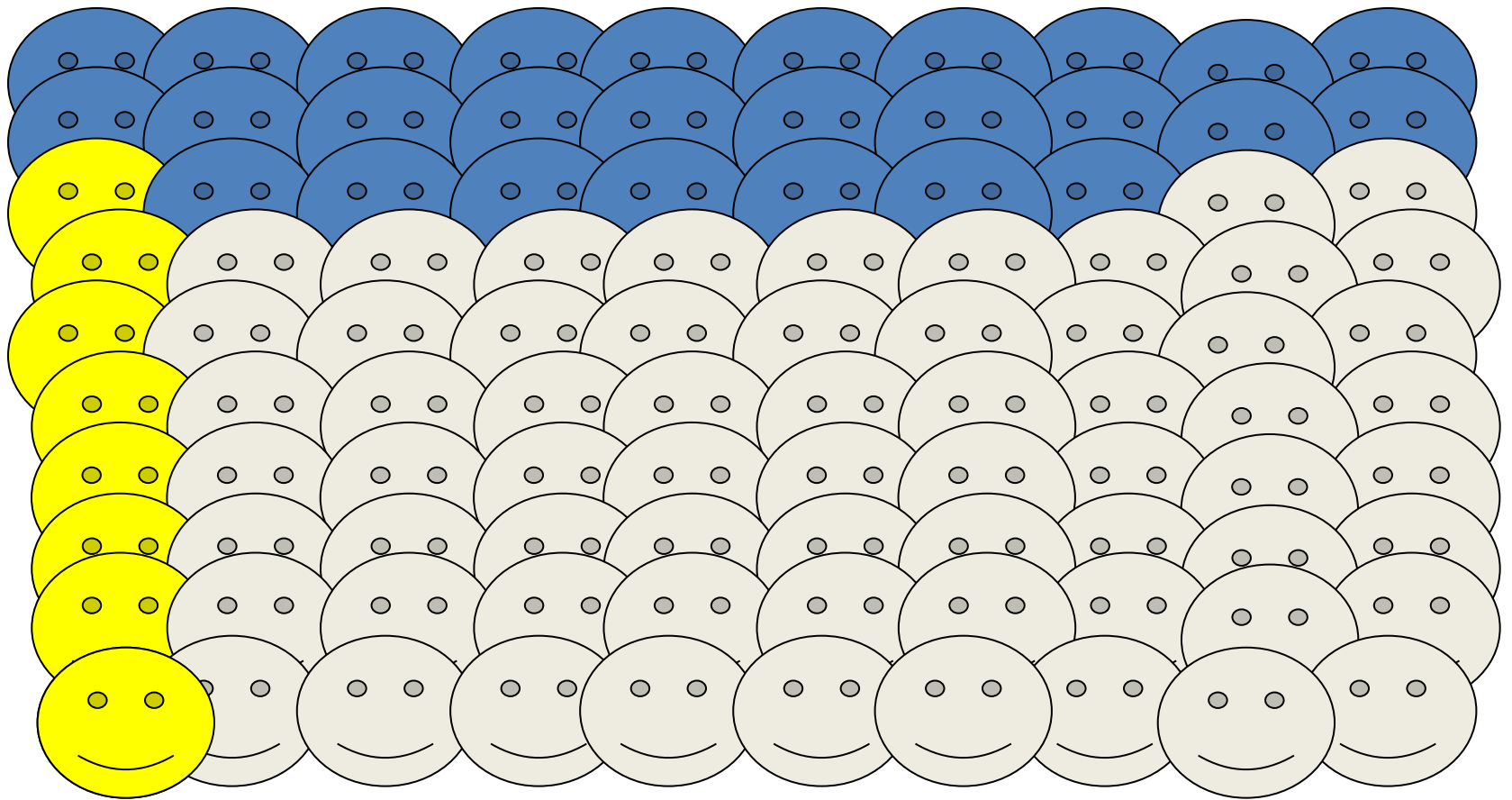
1 year later



Renal replacement therapy



Death



10 years later



Renal replacement therapy



Death

What did he say?



Conclusion

- Management of CKD and diabetic nephropathy focussed on BP control (140/80 good enough in most cases)
- Lipids, smoking, glycaemia, lifestyle, salt
- ACEi/ARBs use is fine but patients should be monitored
- **USE ADVISORY SERVICE** – many elderly with CKD4 don't need to see a nephrologist

Useful Links

- <http://www.sheffield-kidney-institute.org/education-and-training/primary-care-nephrology>
- Email advice: sht-tr.CKDEnquiry@nhs.net