



Primary Care  
Cardiovascular  
Society

Driving primary care to deliver  
the best in cardiovascular health

# CKD and CVD – a deadly combination

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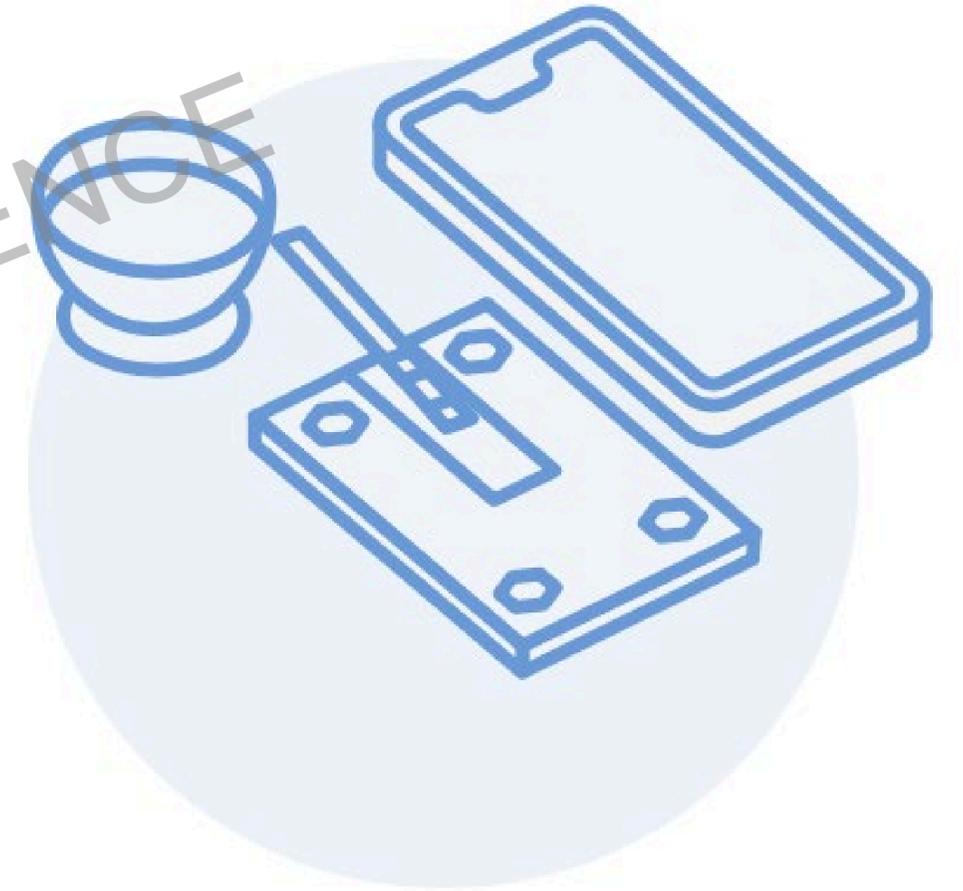
UK Clinical Director, Healthy.io

Wales, April 2023

## Declarations:

AstraZeneca|Novartis|Bayer|Amgen|Medtronic|Omron

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# Today's talk:

CKD as a risk factor for CVD

The importance of ACR testing [Prev/Sev/Risk]

How to improve outcomes

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Progression of CKD by GFR and Albuminuria Categories				Albuminuria categories		
				Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mol	≥300 mg/g ≥30 mg/mmol
GFR categories (ml/min/1.73m <sup>2</sup> ) Description and range	G1	Normal to high	≥90			
	G2	Mildly decreased	60-90			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	15			

Green: low risk (if no other markers of kidney diseases, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk

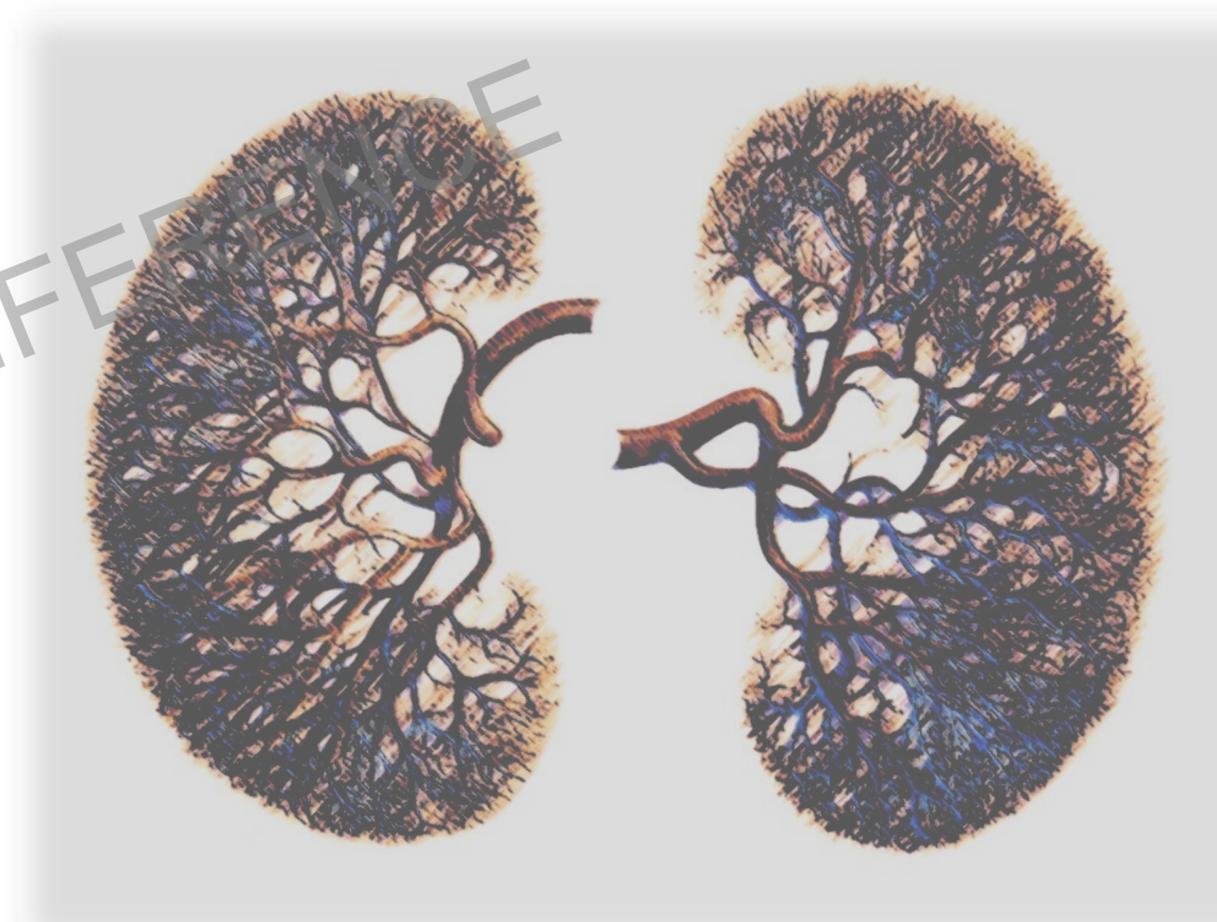
				risk: Red, very high risk		
				Green: low risk (if no other markers of kidney diseases, no CKD); Yellow: moderately increased risk; Orange: high risk		
GFR category	G2	Kidney failure	15			
	G3a	Severely decreased	15-29			

# What is Chronic Kidney Disease?

“The presence of kidney damage,  
mainly albuminuria

and/or

decreased kidney function (estimated  
glomerular filtration rate [eGFR] <60  
mL/min/1.73 m<sup>2</sup>) for at least 3 months”



# Diagnosing and Classifying CKD [NICE, CKD 2021]:

Requires **both** blood testing [eGFR] and urine testing [ACR] to investigate patients for CKD

**Key:**

- Low risk
- Medium risk
- High risk
- Very high risk

**Albuminuria [ACR]**  
Increased kidney damage

**A1** | <30mg/g, <3mg/mmol      **A2** | 30-300mg/g, 3-30mg/mmol      **A3** | >300mg/g, >30mg/mmol

**GFR** | ml/min/1.73m<sup>2</sup>  
Decreased kidney function

	A1   <30mg/g, <3mg/mmol	A2   30-300mg/g, 3-30mg/mmol	A3   >300mg/g, >30mg/mmol
<b>G1</b> >90	Low risk	Medium risk	High risk
<b>G2</b> 60-89	Low risk	Medium risk	High risk
<b>G3a</b> 45-59	Medium risk	High risk	Very high risk
<b>G3b</b> 30-44	High risk	Very high risk	Very high risk
<b>G4</b> 15-29	Very high risk	Very high risk	Very high risk
<b>G5</b> <15	Very high risk	Very high risk	Very high risk

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; UACR, urine albumin-creatinine ratio  
Adapted from: KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International. 2013;3(1):136–150.

# Who should be tested for CKD?

NICE NG203, CKD

1.1.21: Offer testing for CKD using eGFR and ACR to adults with any of the following risk factors:

- diabetes
- hypertension
- previous episode of acute kidney injury
- cardiovascular disease
- structural renal tract disease inc. stones, prostate disease
- gout
- multisystem diseases – e.g. SLE
- family history of end-stage renal disease (GFR category G5) or hereditary kidney disease

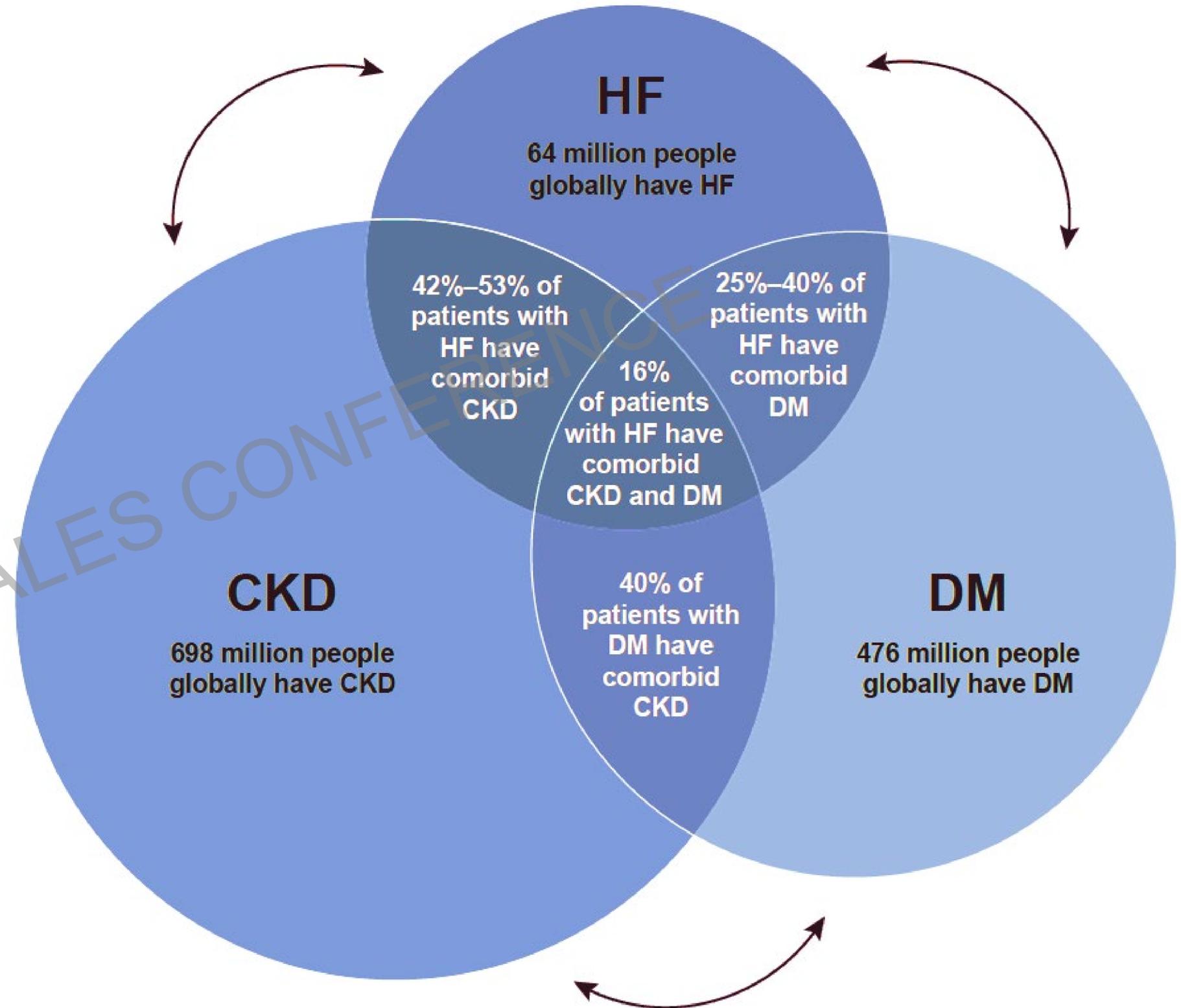


# Heart Failure in Patients with Diabetes and Chronic Kidney Disease: Challenges and Opportunities

## Review Article

Cardiorenal Med 2022;12:1–10  
DOI: 10.1159/000520909

Received: May 17, 2021  
Accepted: November 6, 2021  
Published online: November 19, 2021

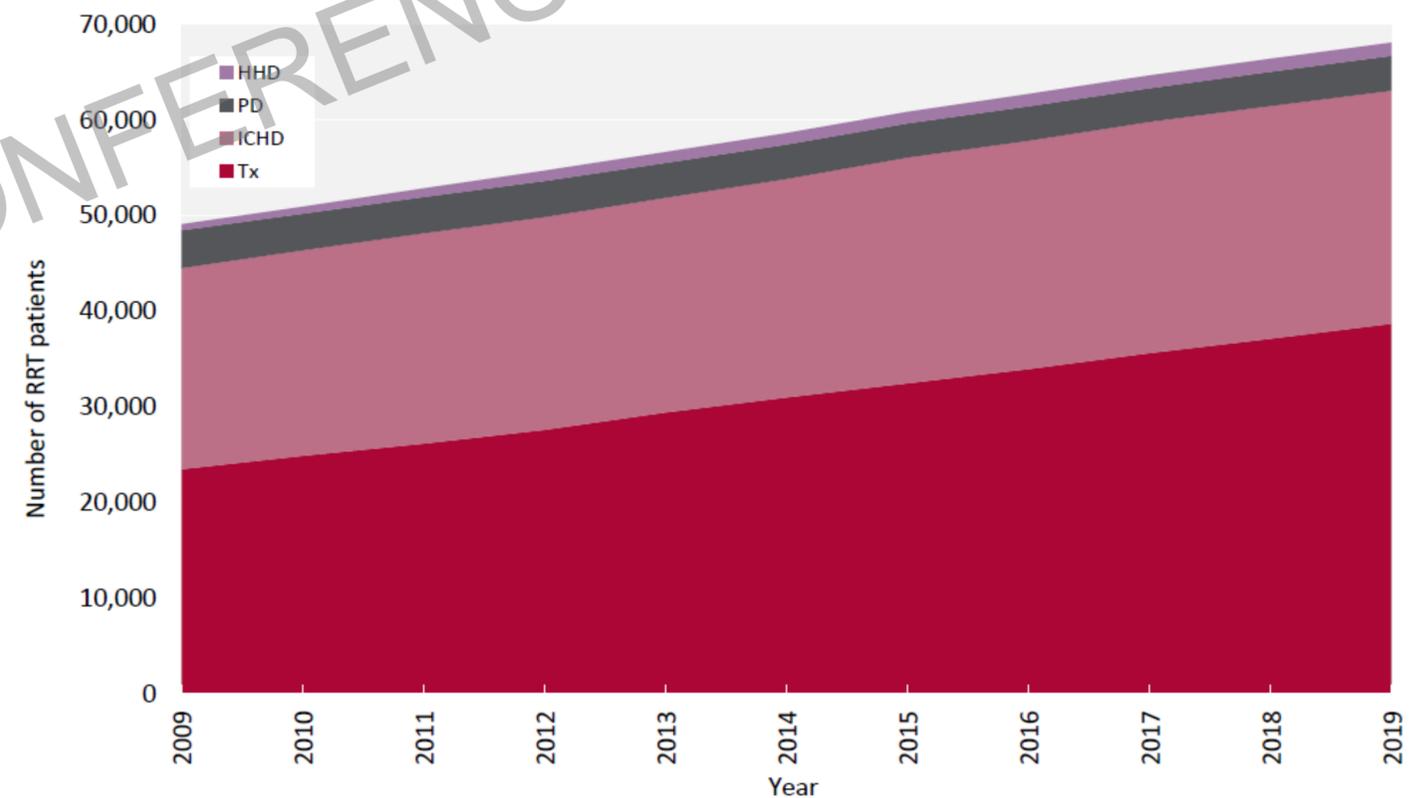


# CKD Epidemic<sup>1-4</sup>:

- Global prevalence of CKD has risen by 87% between 1990–2016
- Estimated further increase of 17% in prevalence of CKD by 2030
- 3<sup>rd</sup> fastest growing cause of death
- 5<sup>th</sup> ranked cause of death by 2040
- UK: 2020 (3.63 million) 2030 (4.38 million) (Xie et al., 2018)
- 34% of CKD cases are undiagnosed
- Higher rates of CKD in under-served communities
- South Asians with diabetes 10x more likely to get kidney failure than Caucasians with diabetes

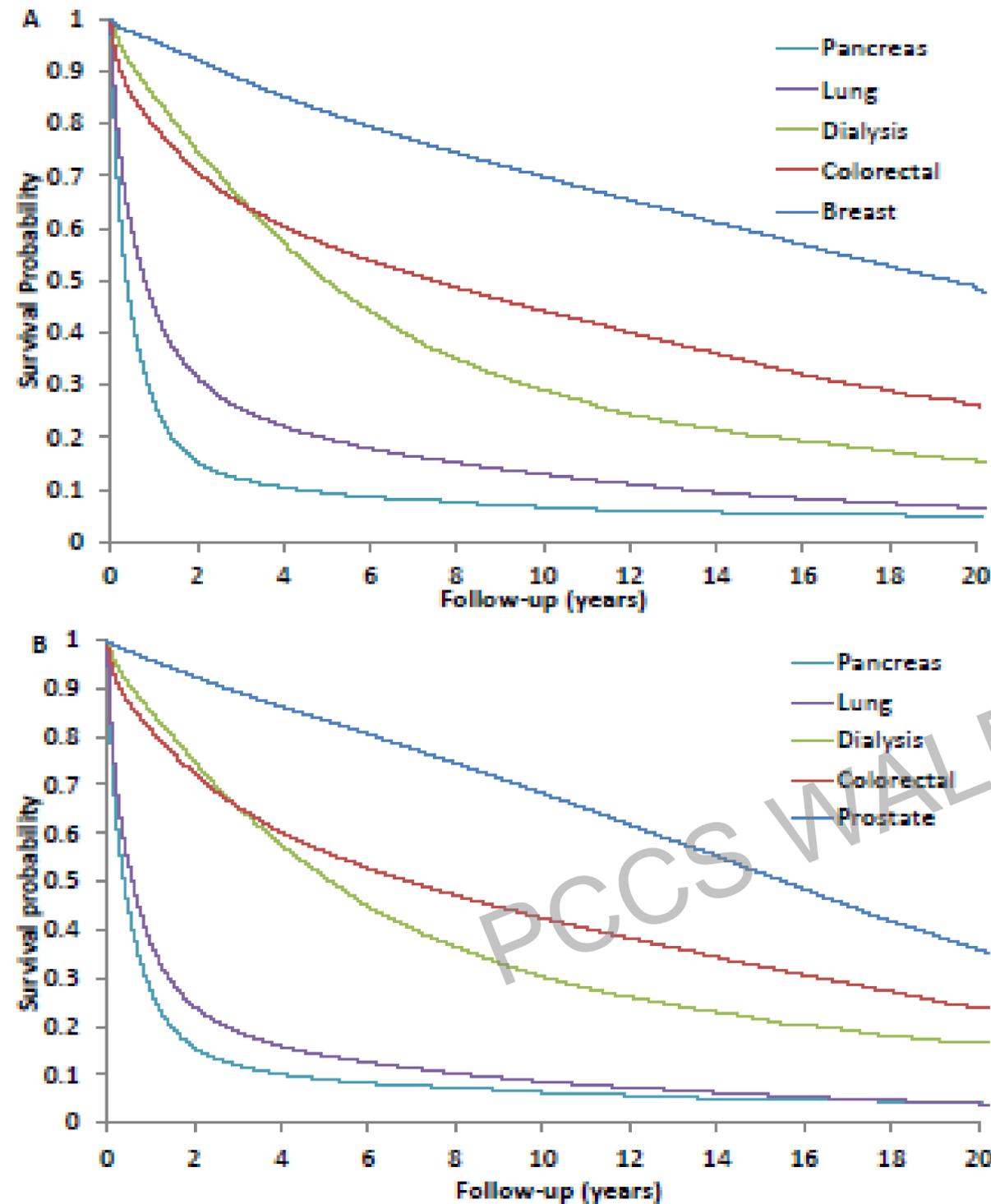


**Growth of prevalent adult renal replacement therapy patients in the UK between 2009 and 2019<sup>2</sup>**



CKD, chronic kidney disease.

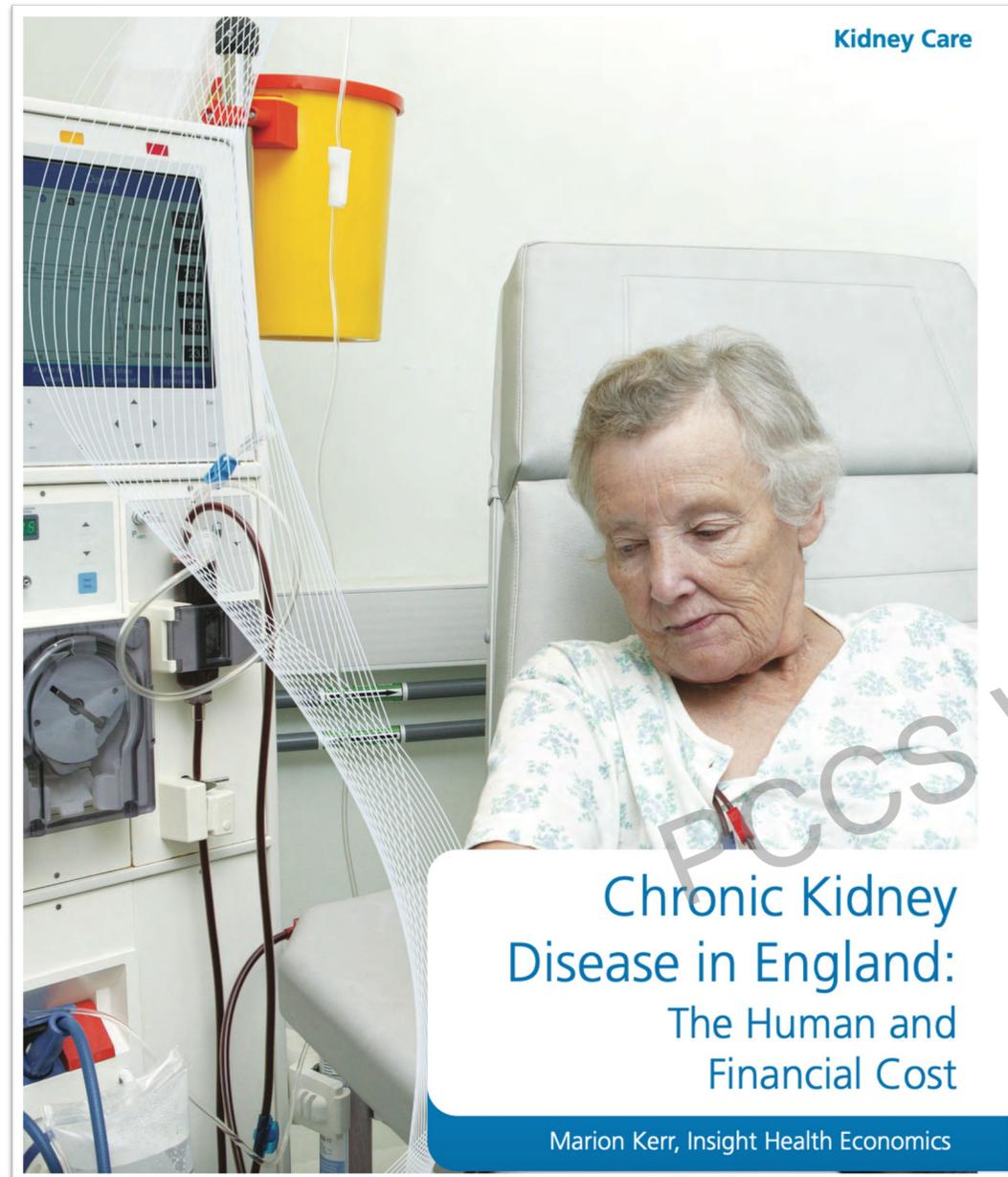
1. Xie Y et al. Kidney Int. 2018 Sep;94(3):567–581; 2. The Renal Association. UK Renal Registry 23<sup>rd</sup> Annual Report. [https://ukkidney.org/sites/renal.org/files/23rd\\_UKRR\\_ANNUAL\\_REPORT.pdf](https://ukkidney.org/sites/renal.org/files/23rd_UKRR_ANNUAL_REPORT.pdf). Accessed December 2022; 3. Ke C et al. BMC Nephrol 2022;23:17 doi: 10.1186/s12882-021-02597-3; 4. London School of Hygiene & Tropical Medicine. National CKD Audit. 2017 [National Chronic Kidney Disease Audit \(NCKDA\) | LSHTM](https://www.nckda.org.uk/). Accessed April 2023.



**Figure 1.** Survival probabilities for all-cause mortality in (A) female maintenance dialysis patients and patients with cancer (log-rank  $P < 0.001$ ) and (B) male maintenance dialysis patients and patients with cancer (log-rank  $P < 0.001$ ).

**End Stage Kidney Disease has worse survival rates than colorectal, prostate and breast cancer**

# Health Economics of CKD:



- **NHS England spent an estimated £1.45 billion on CKD in 2009–10:** equivalent to £1 in every £77 of NHS expenditure. This spending estimate covers both treatment directly associated with CKD (renal care and prescribing to prevent disease progression), and also treatment for excess non-renal problems such as strokes, heart attacks and infections in people with CKD.
- **There were an estimated 7,000 extra strokes and 12,000 extra myocardial infarctions in people with CKD in 2009–2010,** relative to the expected number in people of the same age and sex without CKD. The cost to the NHS of health care related to these strokes and MIs is estimated at £174–178 million.
- **People with CKD have longer hospital stays** than people of the same age without the condition, even when they go into hospital for treatments unrelated to CKD. We estimate that the average length of stay is 35% longer for people with CKD, and that the cost to the NHS of excess hospital bed days for patients with CKD was £46 million in 2009–10.

CKD, chronic kidney disease.

NHS England. Chronic kidney disease in England: the human and financial cost. 2012 <https://www.england.nhs.uk/improvement-hub/publication/chronic-kidney-disease-in-england-the-human-and-financial-cost/>. Accessed April 2023.



SCAN ME

# The association of CKD with Cardiovascular Disease

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# **NICE**impact *cardiovascular disease prevention*

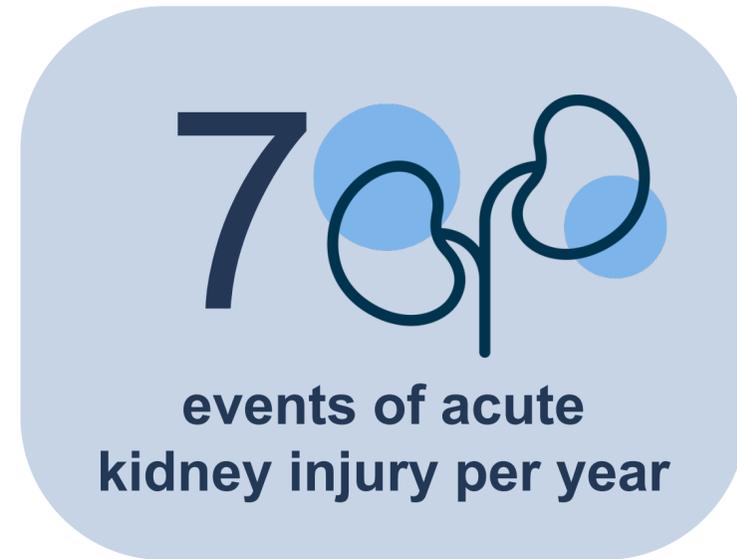
**1.2 million people with CKD are undiagnosed  
[=undiagnosed + uncoded].**

**Effective coding and management of CKD can reduce emergency admission to hospital.**

**Primary care is responsible for a number of key interventions in early-stage CKD.**

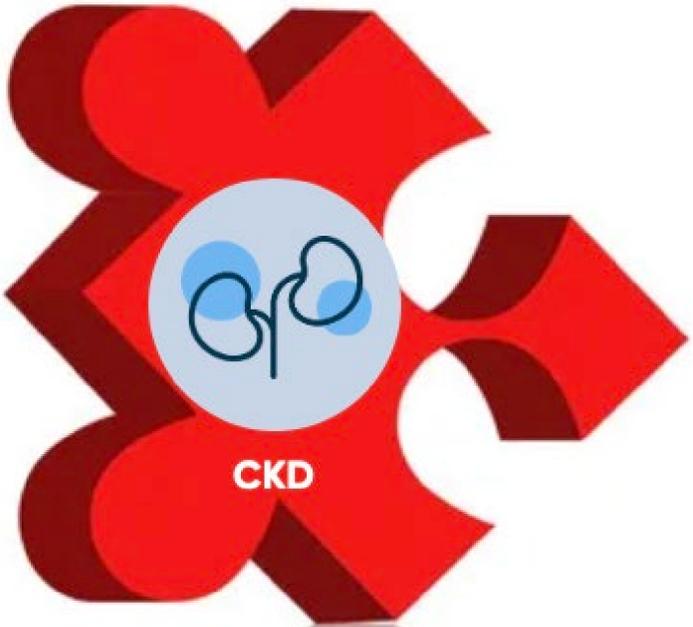
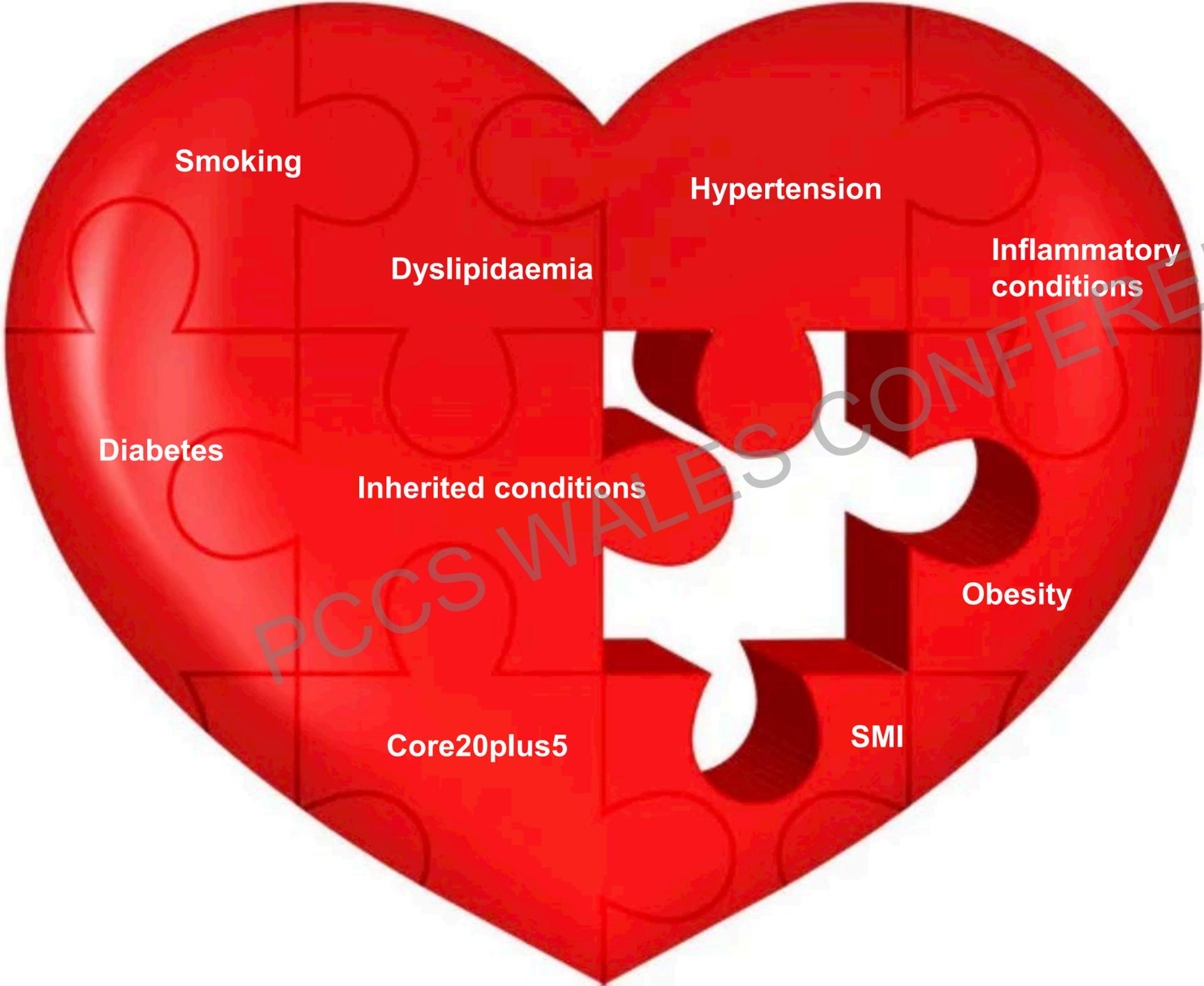
**Many of those with CKD have poor blood pressure control and poor proteinuria control**

# For every 100 patients with moderate to severe CKD:



SCAN ME

# CKD is an under-recognised risk factor for CVD

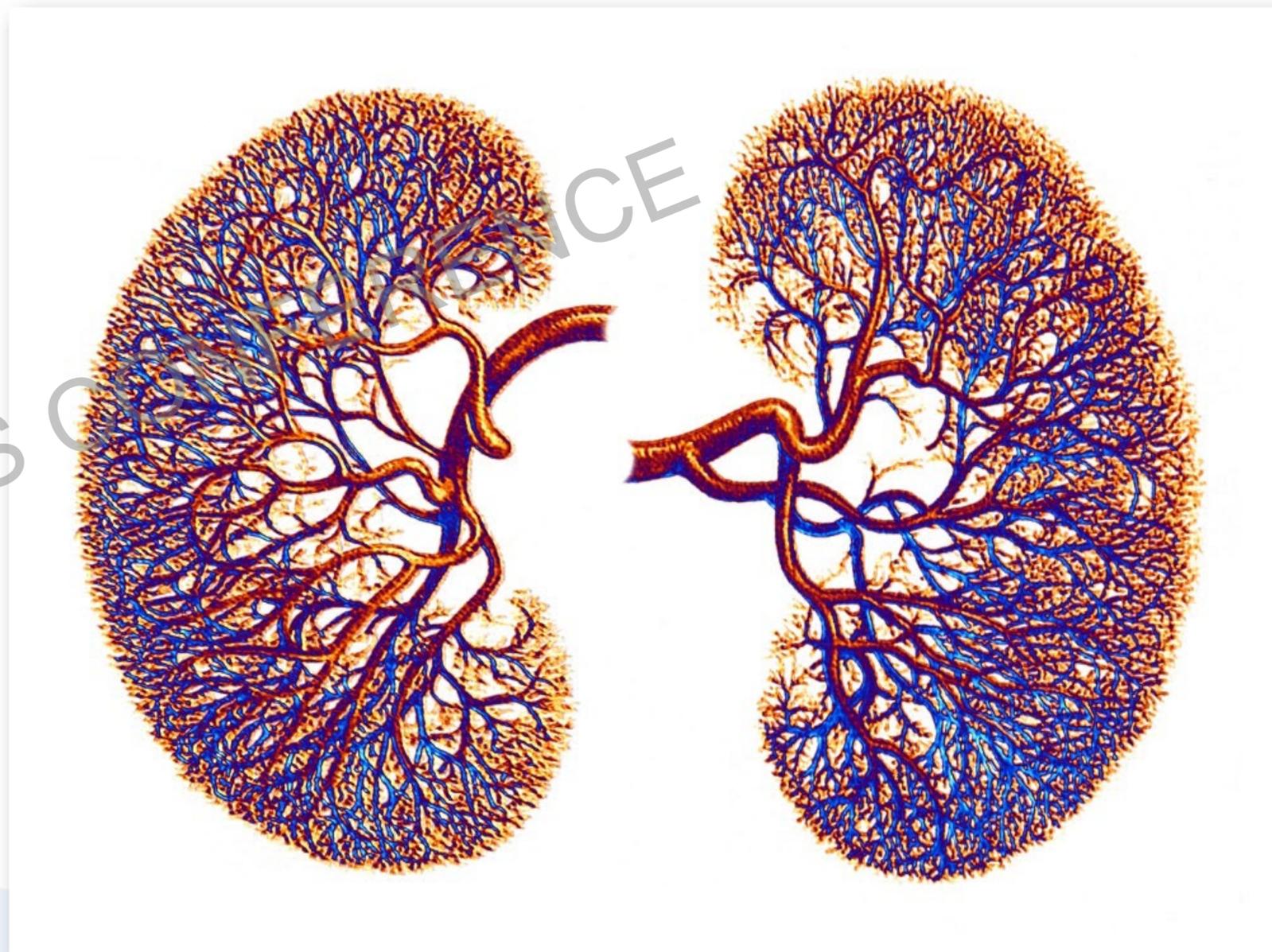


CKD, chronic kidney disease; SMI, severe mental illness.  
1. NICE CKS 2020 CVD risk assessment and management: What are the risk factors? [Risk factors for CVD | Background information | CVD risk assessment and management | CKS | NICE](#). Accessed April 2023; 2. NHS England. Core20PLUS5 (adults) – an approach to reducing healthcare inequalities [NHS England » Core20PLUS5 \(adults\) – an approach to reducing healthcare inequalities](#). April 2023.

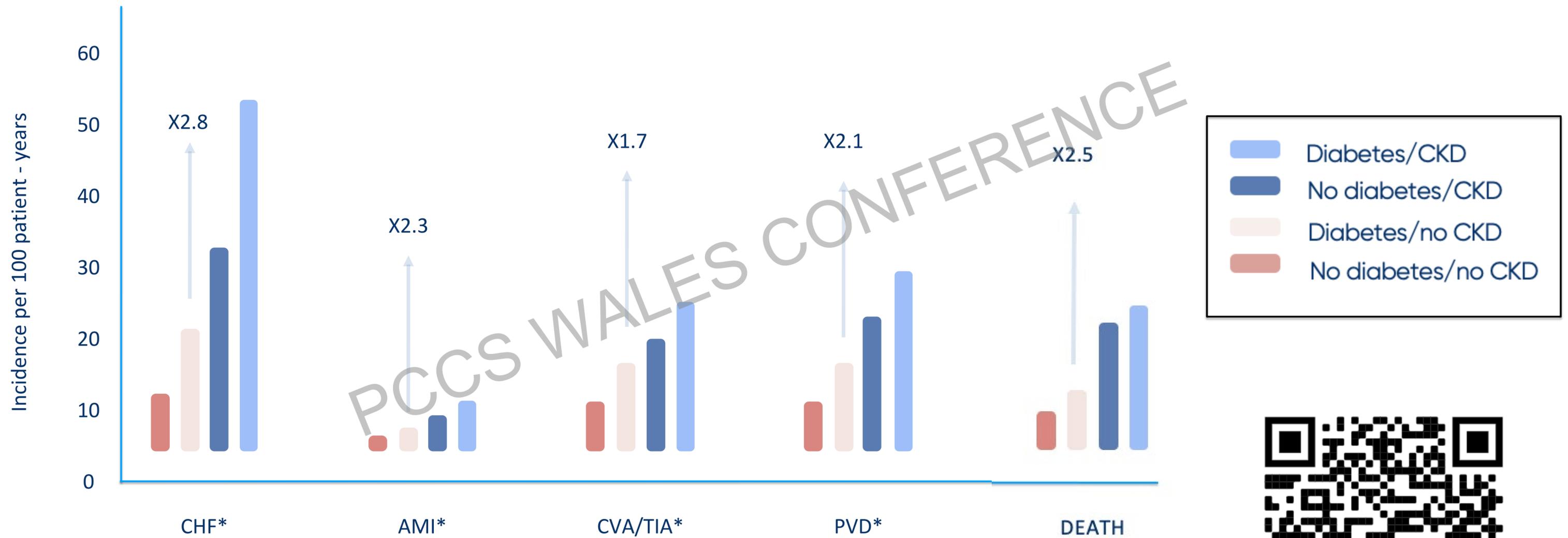
# Kidney vasculature is a **lens** into the body's cardiovascular health:<sup>1-4</sup>

- Approximately 10 km of capillaries in both kidneys
- 180L plasma filtered by kidneys in 24 hours
- 20-25% cardiac output
- CKD is a cardiovascular risk state<sup>1</sup>
- Patients with CKD are 20x more likely to die from CVD than renal failure

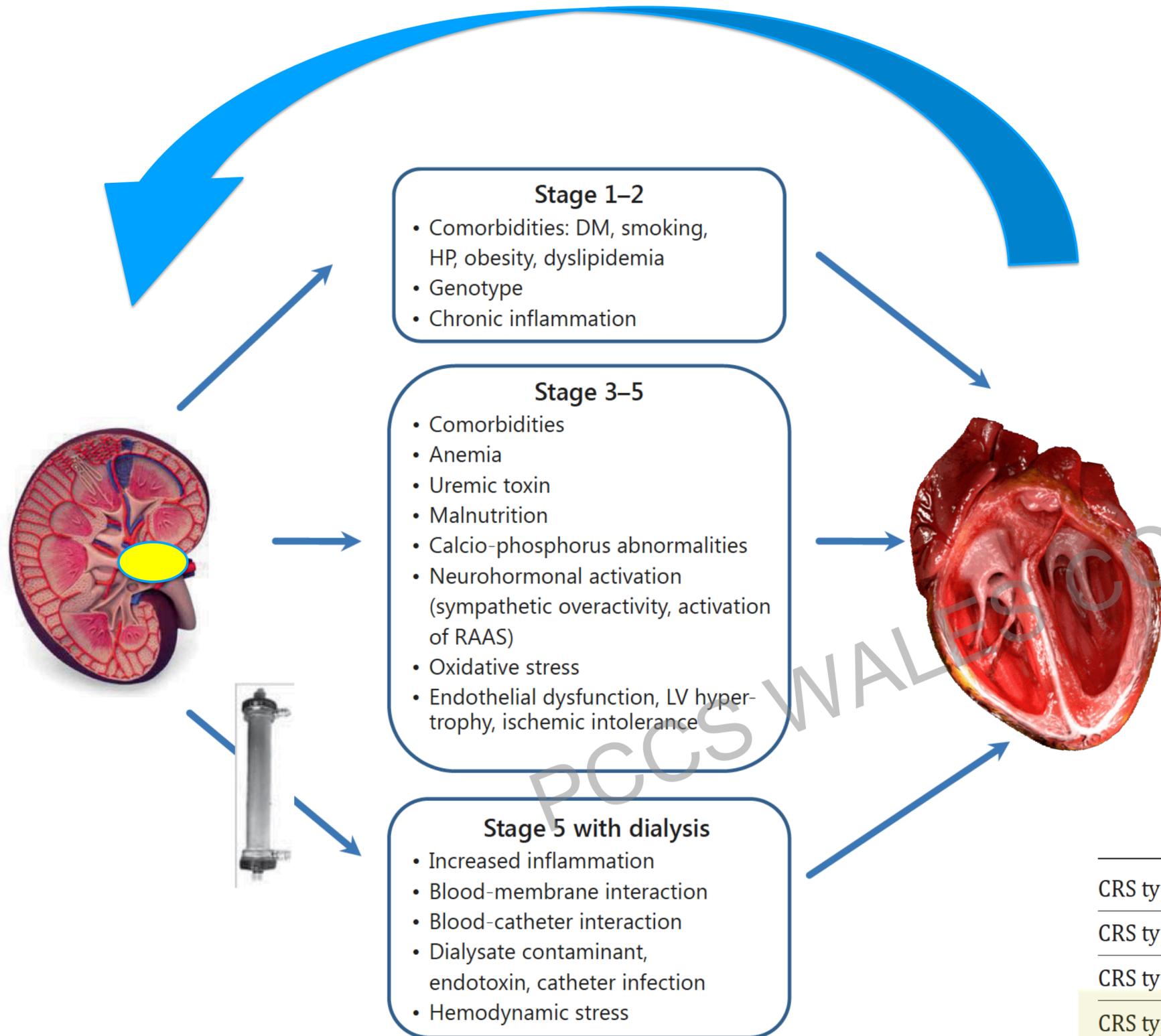
**CKD must be considered one of the strongest risk factors for the development of CVD<sup>2</sup>**



# CKD and diabetes: a deadly combination



# Cardiorenal syndromes



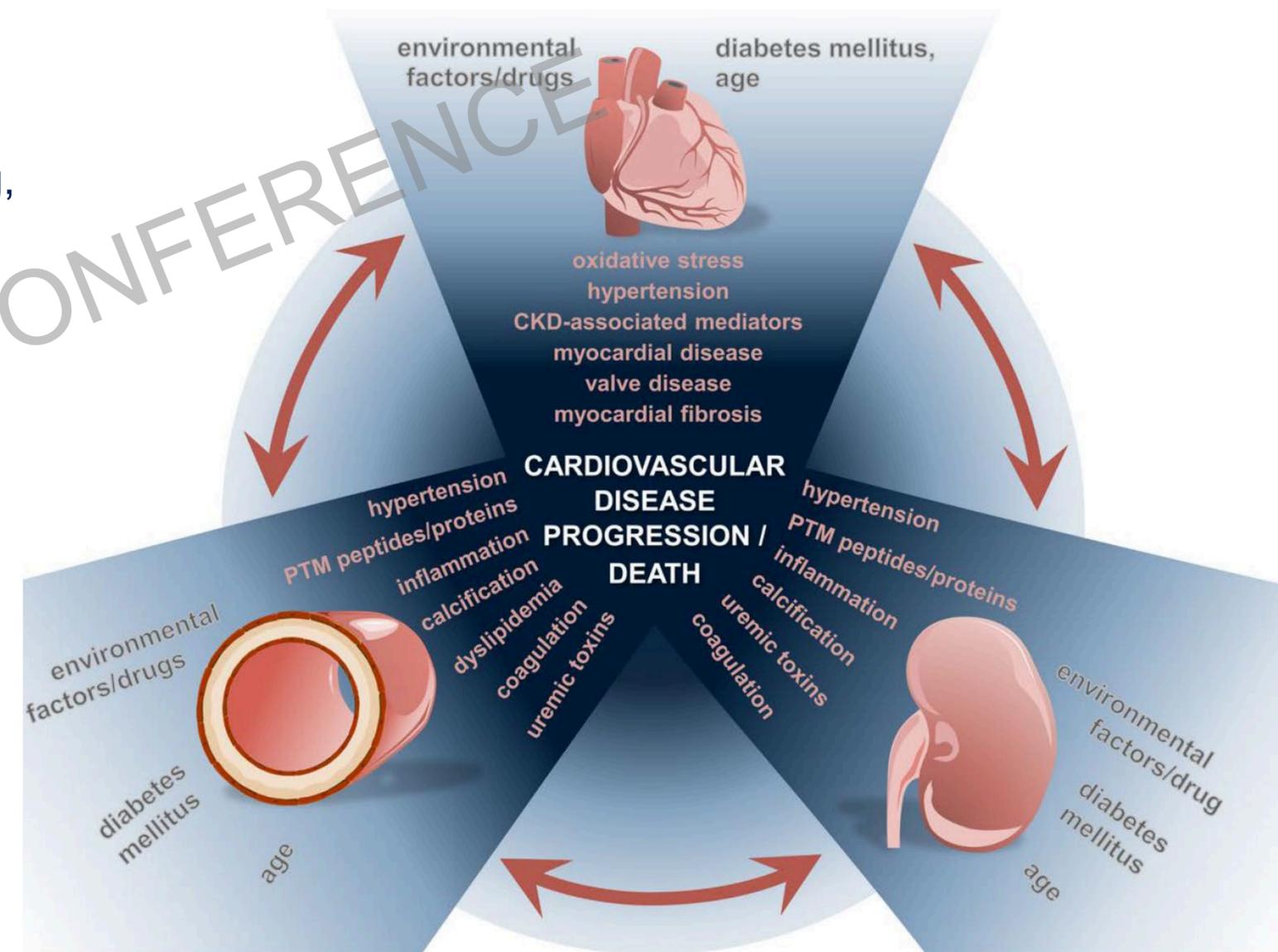
- Hypertension
- Valve disease
- Heart failure, LVH, cardiomyopathy, myocardial fibrosis
- AF
- CAD
- Stroke
- Sudden cardiac death – fatal arrhythmias [2/3 advanced CKD -59X popn adjusted risk]

CRS type 1	Acute worsening of heart function causing acute kidney injury and/or dysfunction
CRS type 2	Chronic abnormalities in cardiac function leading to progressive CKD
CRS type 3	Sudden worsening of renal function causing acute cardiac injury and/or dysfunction
CRS type 4	Condition of primary CKD leading to a reduction in cardiac function (ventricular hypertrophy, diastolic dysfunction) and/or increased risk of cardiovascular events
CRS type 5	Systemic disorders (e.g. sepsis) that concurrently induce cardiac and kidney injury and/or dysfunction

# Why does CKD cause cardiovascular complications?

## CKD increases CVD for the following reasons:

- Traditional CAD risk factors also damage the kidney e.g. smoking, dyslipidaemia, HTN, diabetes etc
- Activation of Renin – Aldosterone System
- Arterial stiffening
- Instability of atherosclerotic plaque in uraemia
- Renal anaemia
- Cardiac remodelling inc. LVH (30-80%) and fibrosis
- Marked accelerated vascular (45x) and valve calcification esp. aortic (40% CKD3, almost all CKD5)
- Chronic inflammation – endothelial dysfunction and NO production.

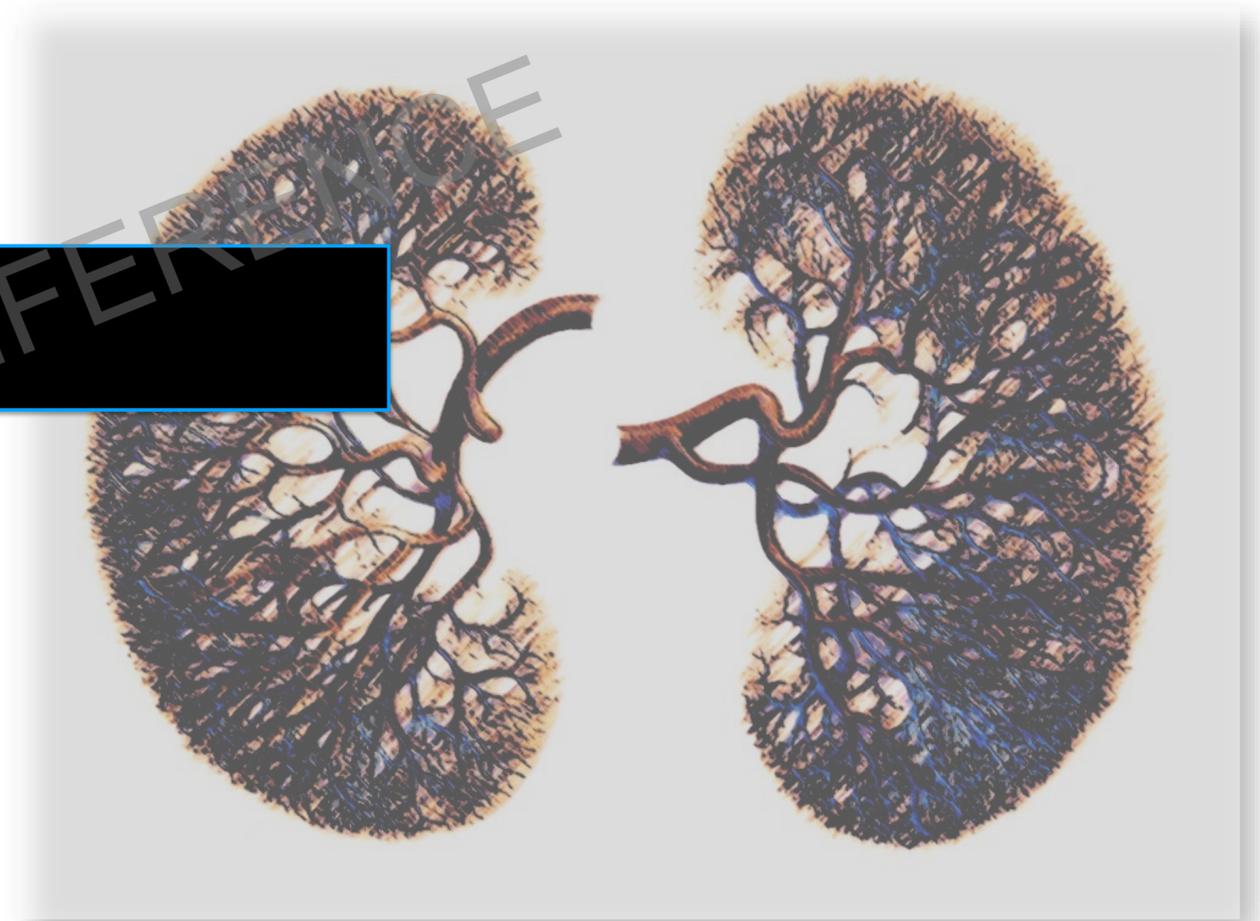


# What is Chronic Kidney Disease?

“The presence of kidney damage,  
mainly albuminuria

**Duplicate slid?**

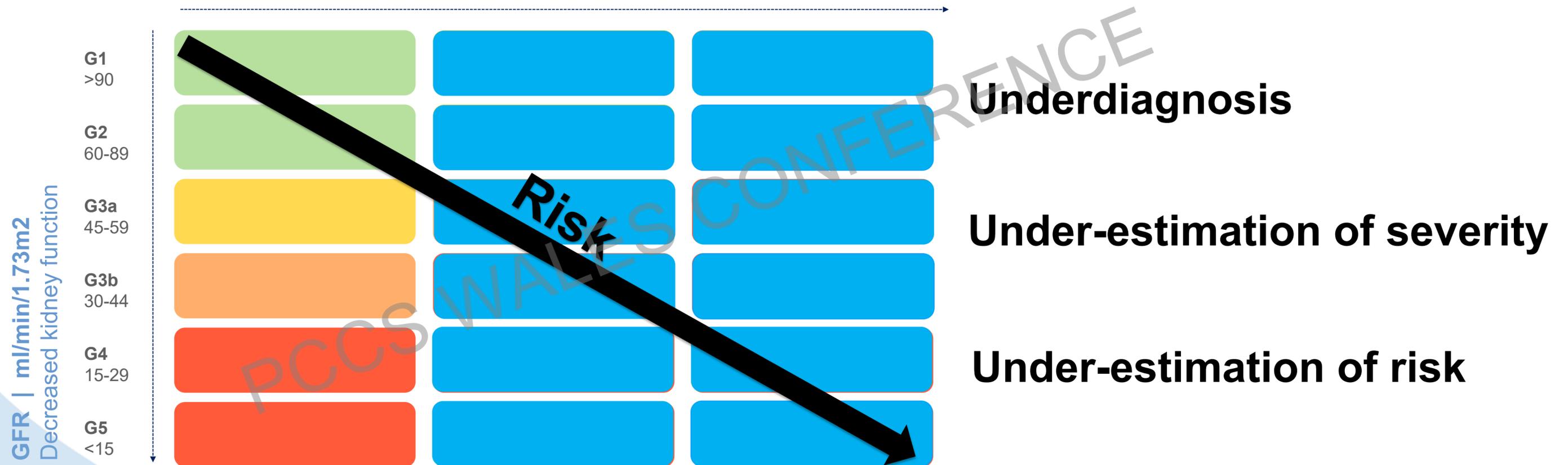
decreased kidney function (estimated  
glomerular filtration rate [eGFR] <60  
mL/min/1.73 m<sup>2</sup>) for at least 3 months”



# What happens if we don't check the urine for albuminuria?<sup>1,2</sup>

Albuminuria [ACR]  
Increased kidney damage

A1 | <30mg/g, <3mg/mmol    A2 | 30-300mg/g, 3-30mg/mmol    A3 | >300mg/g, >30mg/mmol



Key

Low risk

Medium risk

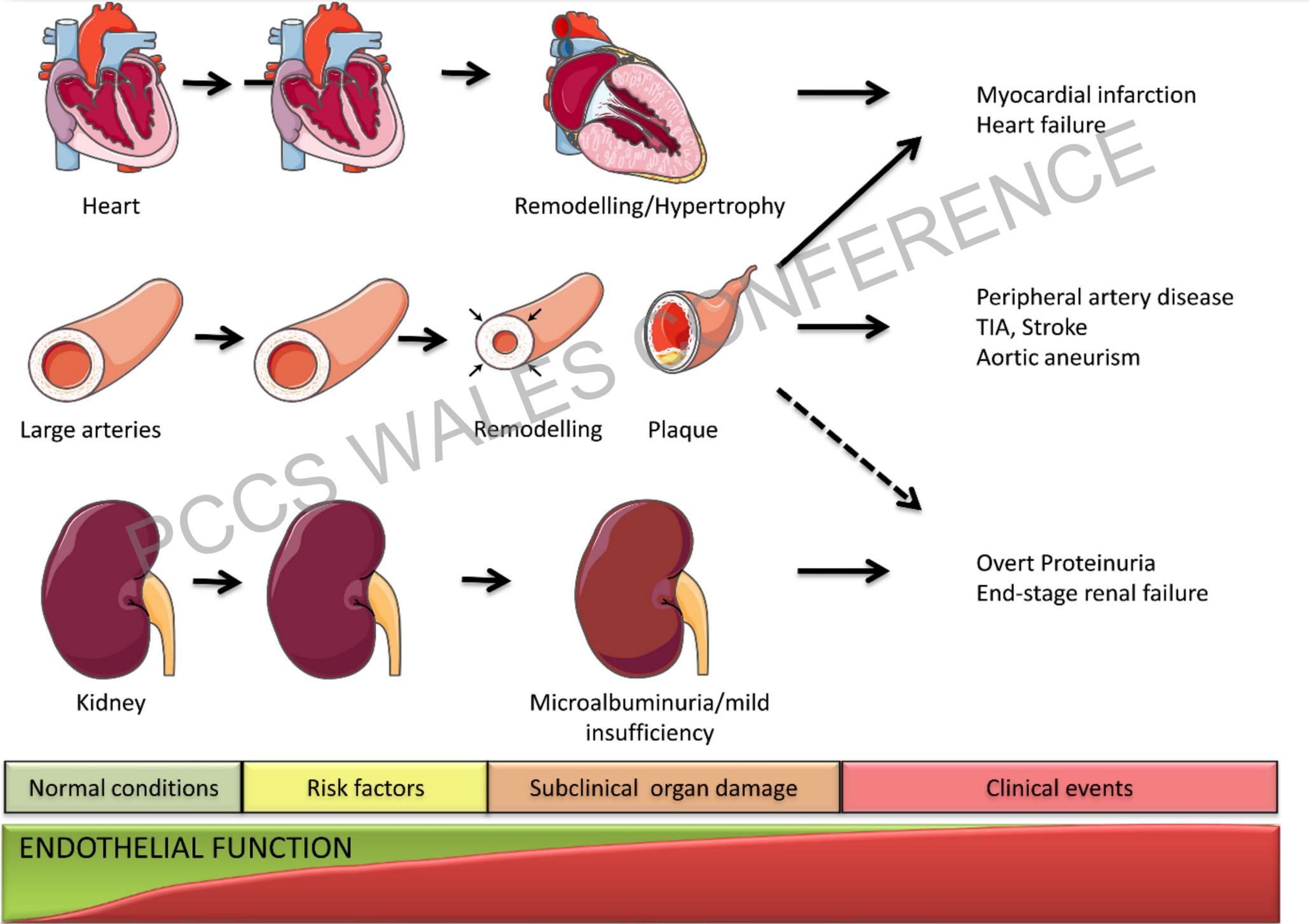
High risk

Very high risk

ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease; CVD, cardiovascular disease.

1. Adapted from NICE Guidelines NG203 2021 <https://www.nice.org.uk/guidance/ng203>. Accessed December 2022; 2. Adapted from KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney International Supplements 2022;102(5S):S1-S127.

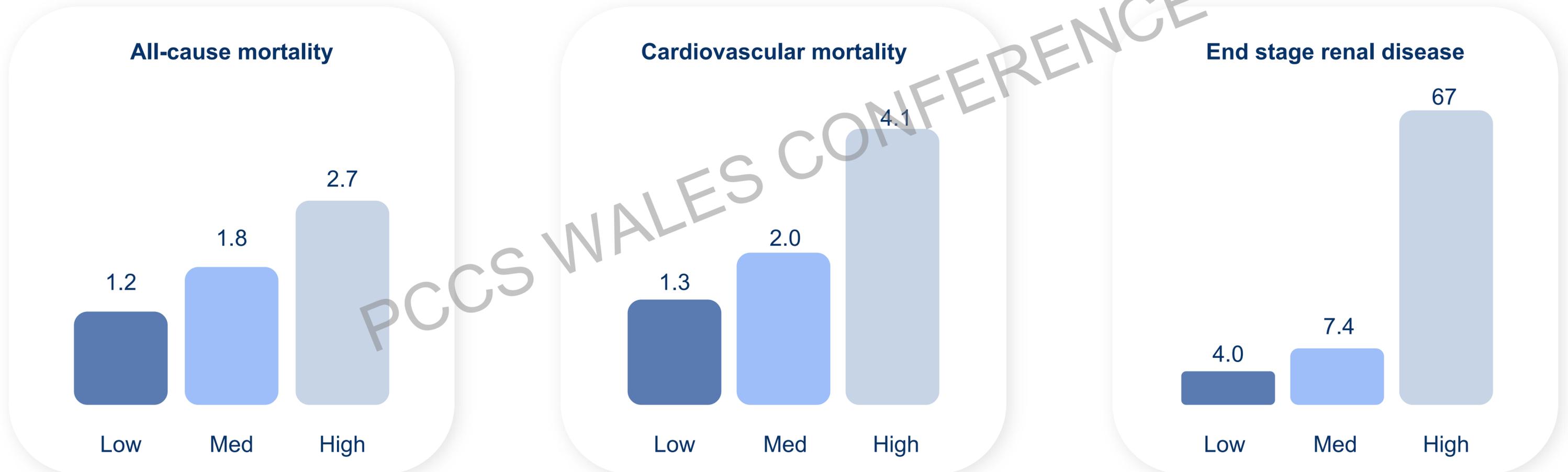
# Albuminuria is an early marker of cardiovascular disease



Versari D et al. Diabetes Care 2009;32:S314-S321.

# Albuminuria is a strong independent risk predictor for End-Stage Renal Disease (ESRD), CVD and death

Adjusted Hazard Ratio for cohort with eGFR stage 3, by ACR level



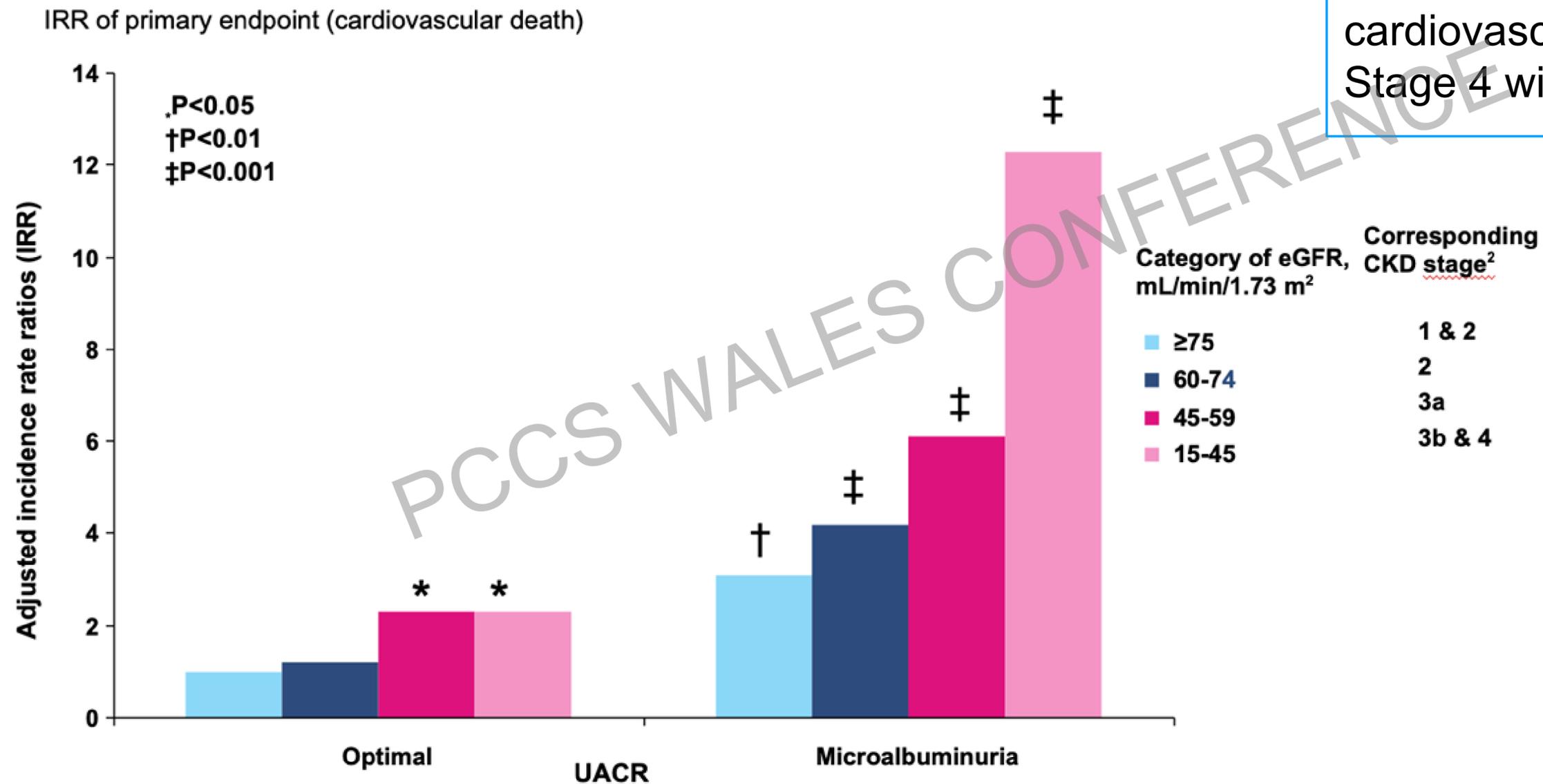
\*Low=ACR <3 mg/mmol, Med=ACR 3–30 mg/mmol; High=ACR >30 mg/mmol.

ACR, albumin-to-creatinine ratio; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate.

Adapted from Levey AS, et al. The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. *Kidney Int.* 2011; 80:17–28.

# Risk is intensified with microalbuminuria

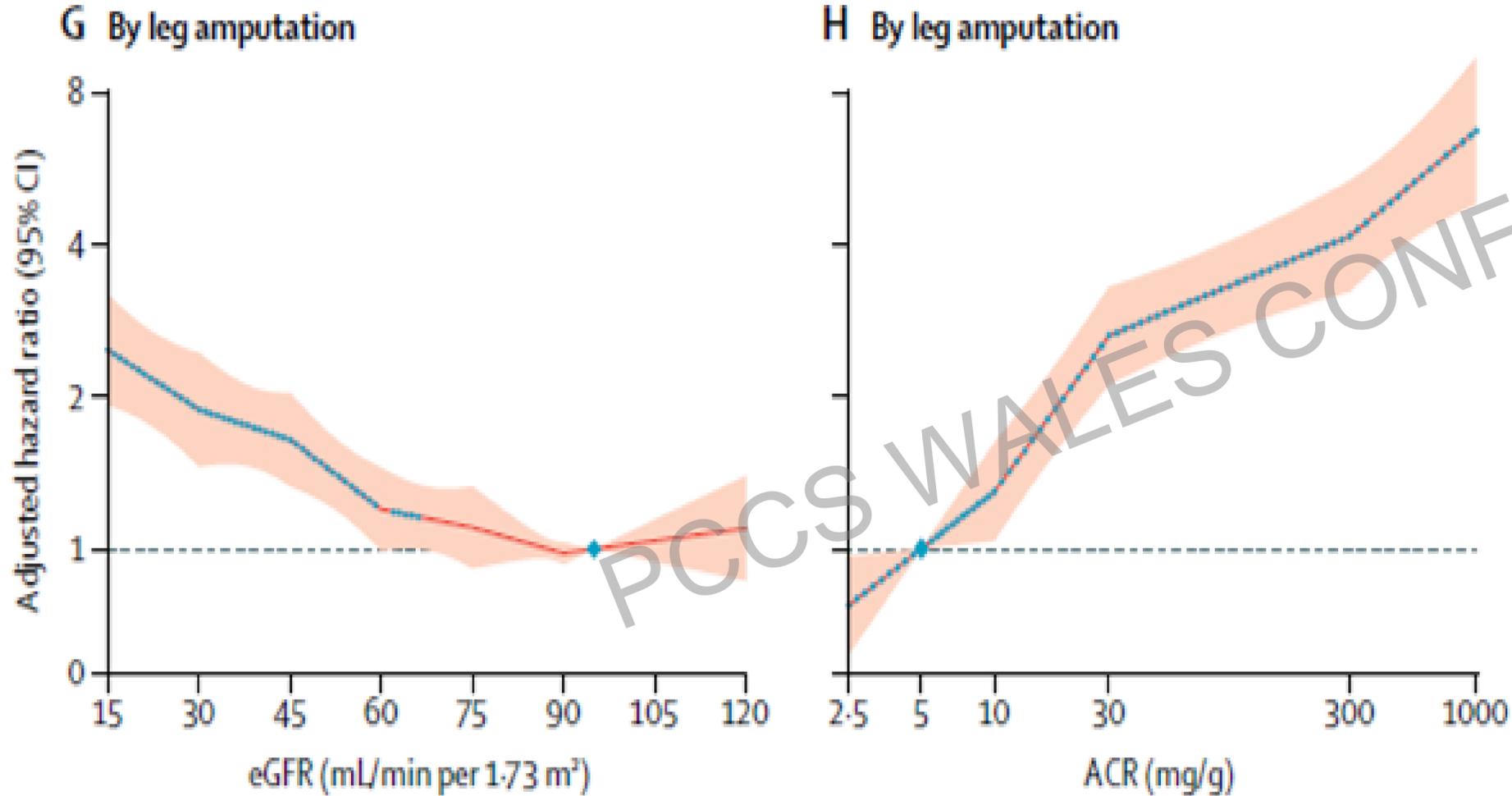
Microalbuminuria with eGFR >75 mL/min/1.73m<sup>2</sup> is associated with higher risk of cardiovascular death than CKD Stage 4 without albuminuria



1. Adapted from Hallan et al. *Archives Internal Medicine* 2007 167;22;2490-2496

2. NICE Management of CKD: NICE

# Risk of leg amputation in Diabetic Kidney Disease

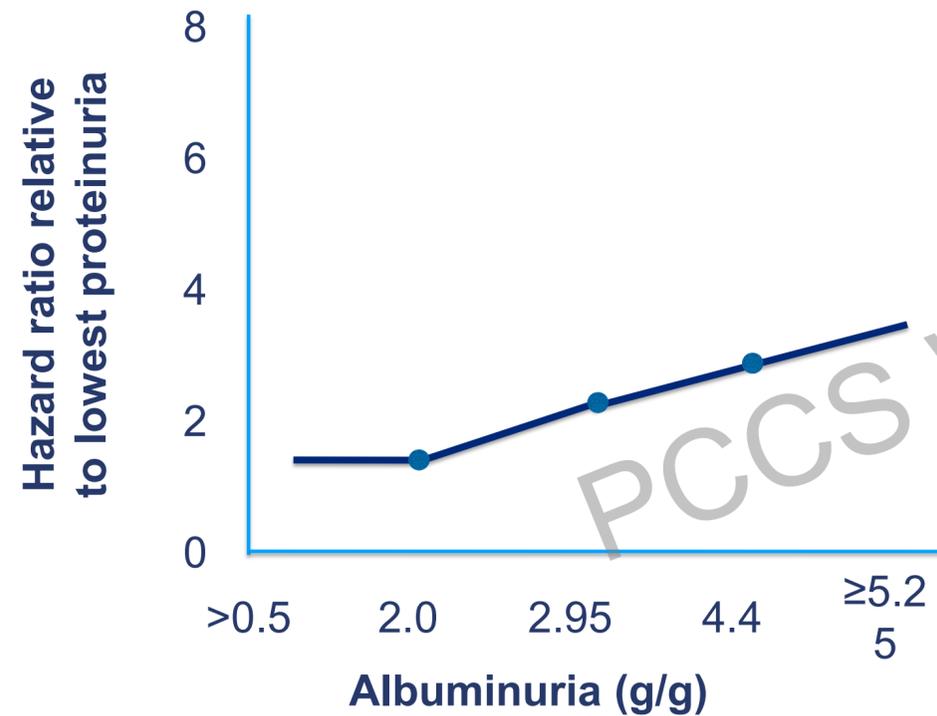


Amputation risk is significantly higher with declining eGFR, and rising albuminuria.

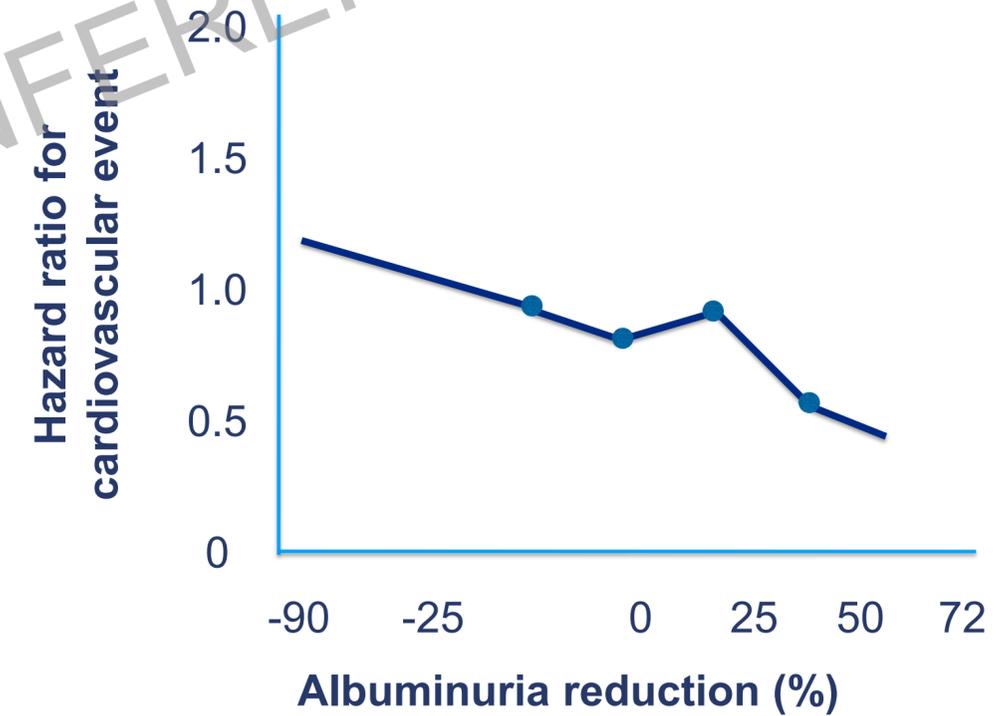
ACR, albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate. Matsushita K, et al. Lancet Diabetes Endocrinol. 2017;5:718-728.

# Cardiovascular events are more common with albuminuria and less likely to occur if albuminuria is reduced

CV Endpoint



CV Endpoint



\*1513 patients with diabetic nephropathy treated with losartan vs placebo  
De Zeeuw D, et al. Circulation 2004;110:921–927. (Posthoc analysis of RENAAL trial)

## Summary

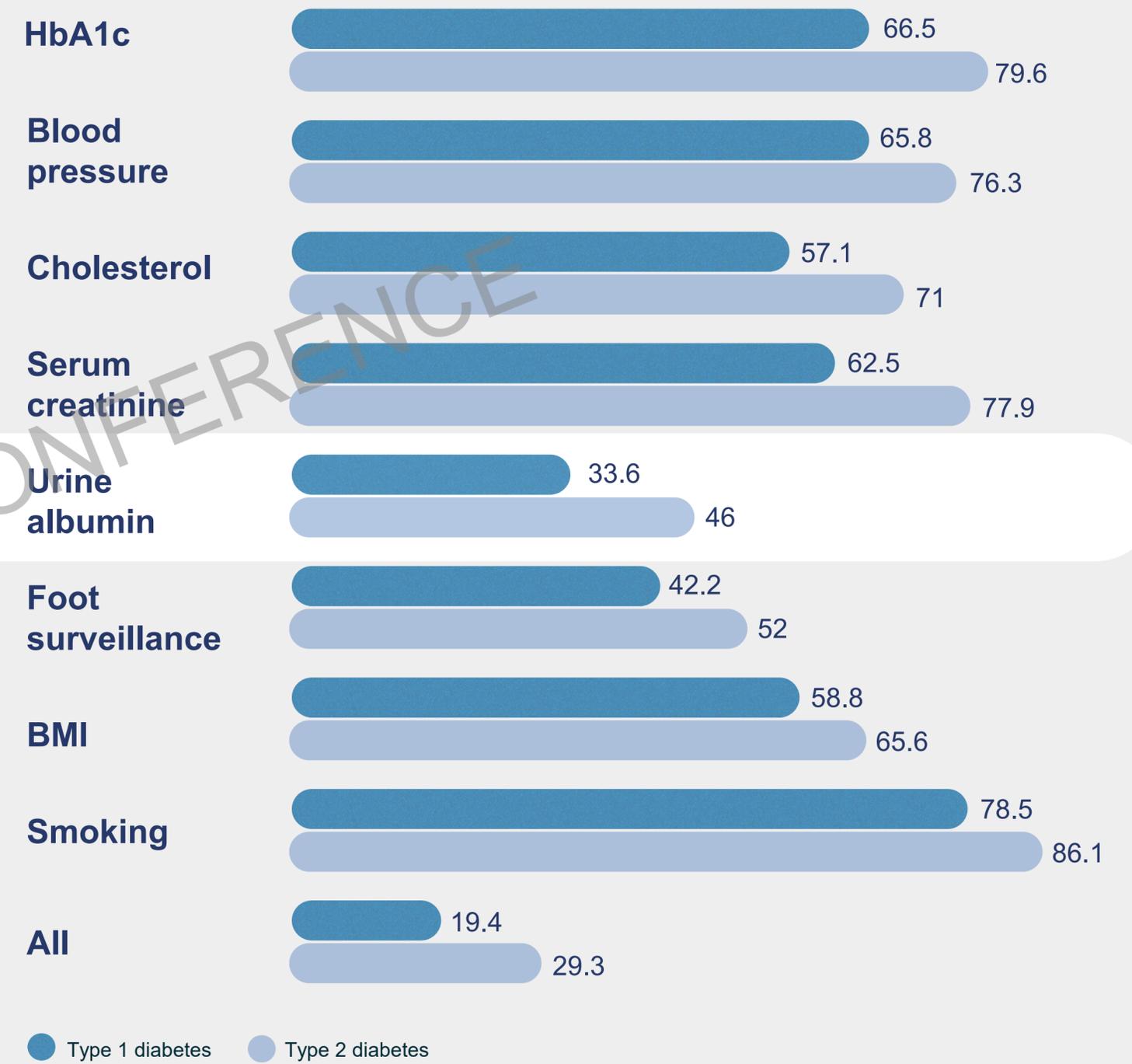
- 1 CKD is a strong predictor of adverse cardiovascular outcomes
- 2 CKD is a greater risk factor for CVD than diabetes
- 3 Testing for eGFR alone is not enough – albuminuria is strong independent predictor of CVD and renal failure
- 4 Failure to test for albuminuria underestimates prevalence, severity of CKD and risk
- 5 Treatment of albuminuria significantly improves outcomes
- 6 Coding patients with CKD can reduce admissions and death
- 7 It is important to look for CKD in at risk patients [NICE]

**Why is ACR testing adherence so poor?**

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# Clear guidance, but low compliance

National uptake of ACR testing compared with other care processes for people with diabetes.



# Why don't patients complete their test?

## Clinician factors



- Do we take the test seriously enough?
- Do we check to see its been done at reviews?
- Contractual levers
- Workload

## Patient factors



- How easy is it to get a test done?
- How much do they really know about it?

# Identification and management in primary care

## Identification

- CKD coding
- Case finding for unidentified CKD using eGFR and ACR
- Inequalities

## Management

- Education – Cardiovascular health / lifestyle / modifiable risk-factors

## Medical Optimisation

- Blood Pressure Optimisation
- Lipid lowering therapy [QOF]
- Maximum Renin Angiotensinogen Aldosterone inhibition [Stop-ACEi study]
- Sodium Glucose Transporter-2 inhibitor and finerenone
- Optimise LTC
- Frailty/EOL

# Why should we code for CKD?

Significant number of patients uncoded

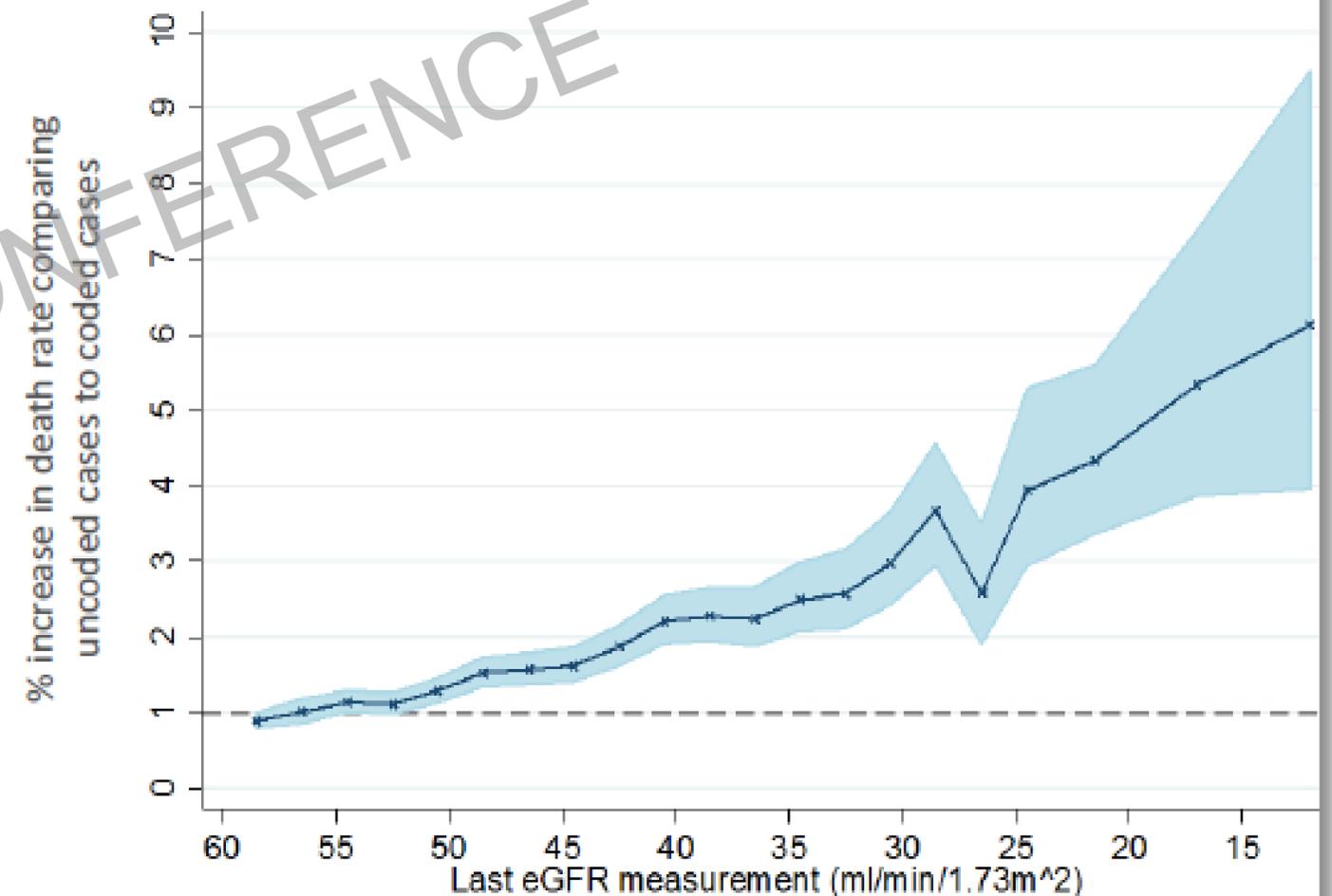
CQC may look at coding as a quality marker

Uncoded patients with CKD have worse outcomes than coded patients (CKD audit, 2017)

- x2 mortality
- higher admissions

Coding facilitates audit of care through CKD<sub>PREVENT</sub> e.g. Proportion of patients with CKD Stage 3-5 prescribed lipid lowering therapy

Comparison of death rates between uncoded and coded patients with biochemical CKD stages 3-5



# KFRE<sup>1,2</sup>

- Kidney failure risk equation
- Adopted for UK population. - [www.kidneyfailurerisk.co.uk/](http://www.kidneyfailurerisk.co.uk/)
- Gives 5 year risk of end stage renal failure
- 5% referral threshold
- Challenges
  - Doesn't give CVD risk
  - What happens > 5 years
  - Impact of treatment on KFRE
  - Why not optimise in primary care?

# Finerenone for treating chronic kidney disease in type 2 diabetes

Technology appraisal guidance [TA877] Published: 23 March 2023

## 1 Recommendations

- 1.1 Finerenone is recommended as an option for treating stage 3 and 4 chronic kidney disease (with albuminuria) associated with type 2 diabetes in adults. It is recommended only if:
- it is an add-on to optimised standard care; this should include, unless they are unsuitable, the highest tolerated licensed doses of:
    - angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) and
    - sodium–glucose cotransporter-2 (SGLT2) inhibitors and
  - the person has an estimated glomerular filtration rate (eGFR) of 25 ml/min/1.73 m<sup>2</sup> or more.
- 1.2 This recommendation is not intended to affect treatment with finerenone that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

### Why the committee made these recommendations

Standard care for chronic kidney disease in people with type 2 diabetes includes ACE inhibitors and ARBs, with SGLT2 inhibitors being added if needed. Finerenone would be added to ACE inhibitors and ARBs if they are not working well enough. It could be offered before, after, or with SGLT2 inhibitors.

## Referral criteria

1.5.5 Refer adults with CKD for specialist assessment (taking into account their wishes and comorbidities) if they have any of the following:

- a 5-year risk of needing renal replacement therapy of greater than 5% (measured using the 4-variable Kidney Failure Risk Equation)
- an ACR of 70 mg/mmol or more, unless known to be caused by diabetes and already appropriately treated (see recommendations 1.6.6 and 1.6.7)
- an ACR of more than 30 mg/mmol (ACR category A3), together with haematuria
- a sustained decrease in eGFR of 25% or more and a change in eGFR category within 12 months
- a sustained decrease in eGFR of 15 ml/min/1.73 m<sup>2</sup> or more per year
- hypertension that remains poorly controlled (above the person's individual target) despite the use of at least 4 antihypertensive medicines at therapeutic doses (see also [NICE's guideline on hypertension in adults](#))
- known or suspected rare or genetic causes of CKD
- suspected renal artery stenosis. **[2021]**

# Referral in frailty

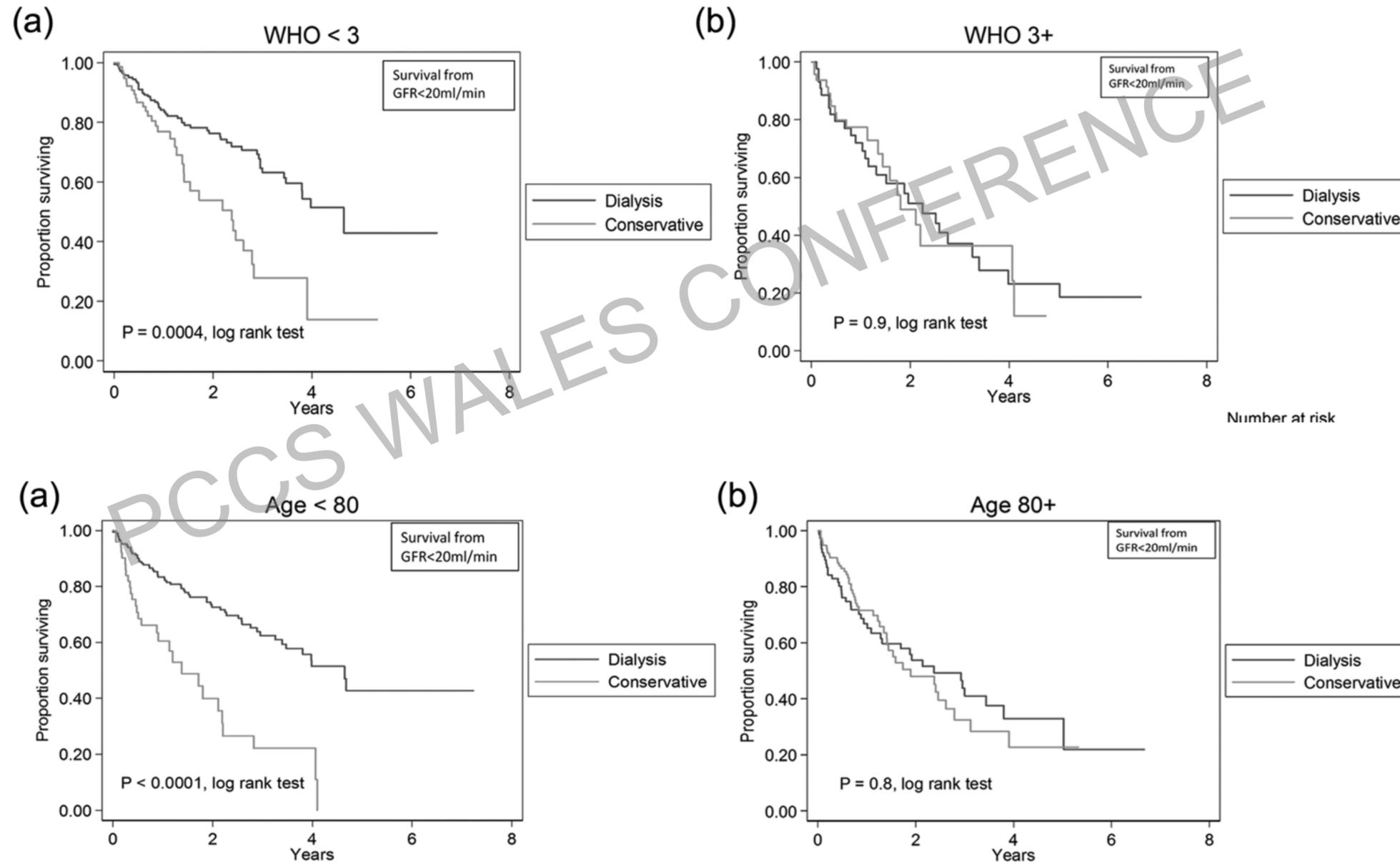
## Comparison of survival analysis and palliative care involvement in patients aged over 70 years choosing conservative management or renal replacement therapy in advanced chronic kidney disease

Palliative Medicine  
0(0) 1-11  
© The Author(s) 2013  
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sagepub.co.uk/journalsPermissions.nav  
DOI: 10.1177/0269216313484380  
pmj.sagepub.com  
SAGE

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Lynne Russon *Sue Ryder Wheatfields Hospice, Leeds, UK; Leeds Teaching Hospitals NHS Trust, Leeds, UK*



# Quality improvement ideas in CKD

## Population health



- Code patients with CKD
- Actively look for patients at risk of having CKD using eGFR and ACR
- Ensure patients with CKD are auscultated for valve disease
- Have a high index of suspicion for heart failure

## Management



- Ensure patients with CKD esp with albuminuria are optimised
- Optimise CVD risk at an early stage
- Optimise secondary prevention
- Identify frailty early

## Summary slide 2

- 1 CKD is a stronger predictor of CVD outcomes than diabetes
- 2 CKD is under coded and under diagnosed primary care. This increases risk of admission/death.
- 3 It is important to look for CKD in at risk patients [NICE] by checking both eGFR and ACR
- 4 Albuminuria is a strong independent risk factor for CVD
- 5 Treatment of CKD improves outcomes - by looking at the underlying cause, lifestyle factors, and optimising with ACEi/ARBs, SGLT2i, finerenone, statins and BP control
- 6 Identify frailty early

# Q&A

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