Chronic kidney disease: Primary care's key role

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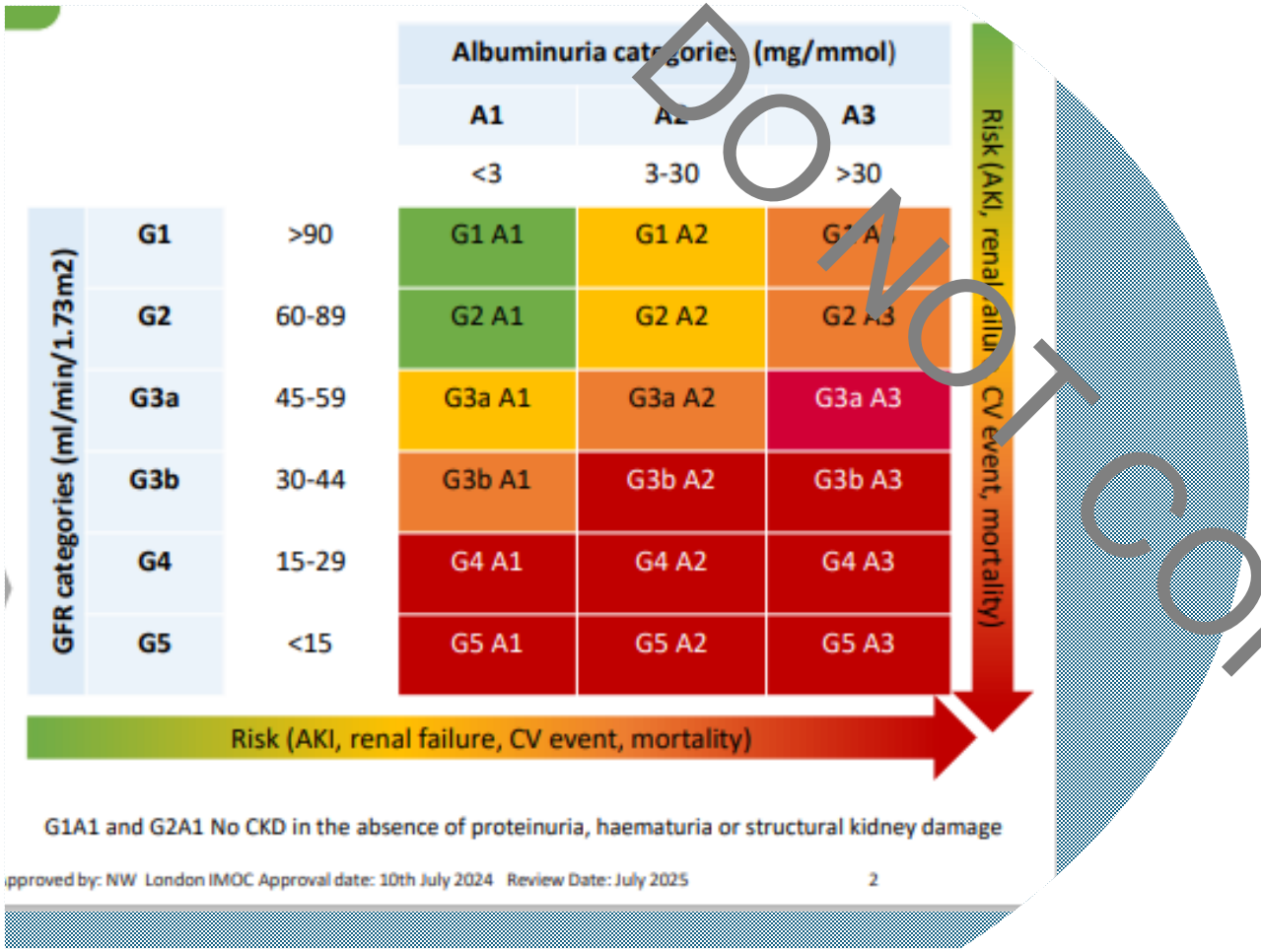
Declarations

- Receipt of research grants
- Preparation of educational materials
- Attendance at drug advisory boards
  - Boehringer Ingleheim
  - Lilly
  - Astra Zeneca
  - Menarani
  - Bayer
  - Novo Nordisk
  - Proteomics International

Summary and Objectives

- The growth in CKD (driven by the increasing numbers of people with diabetic kidney disease) constitutes a major healthcare emergency
- Over the last 10 years there have been significant advances in relation to treatment of chronic kidney disease
- In this presentation I will provide a clearer understanding of
  - Who is at risk and who to screen
  - How to effectively and safely optimise the person with diabetes and CKD
  - Familiarise yourselves with resources available to support yourselves and your patients.

Definitions



Chronic Kidney Disease

CKD is defined as abnormalities of kidney structure or function, present for a minimum of 3 months, with implications for health. (1)

Kidney Health Check

Blood (eGFR)
Urine ACR
Urine dip haematuria (≥ 1+)
Blood pressure

1 -KDIGO-2024-CKD-Guideline.pdf

‘Public health emergency’: 2023 Kidney Research UK report highlights the increasing burden of CKD

>10% of the UK population (7.2 million people) are estimated to have CKD, and this number is growing over time

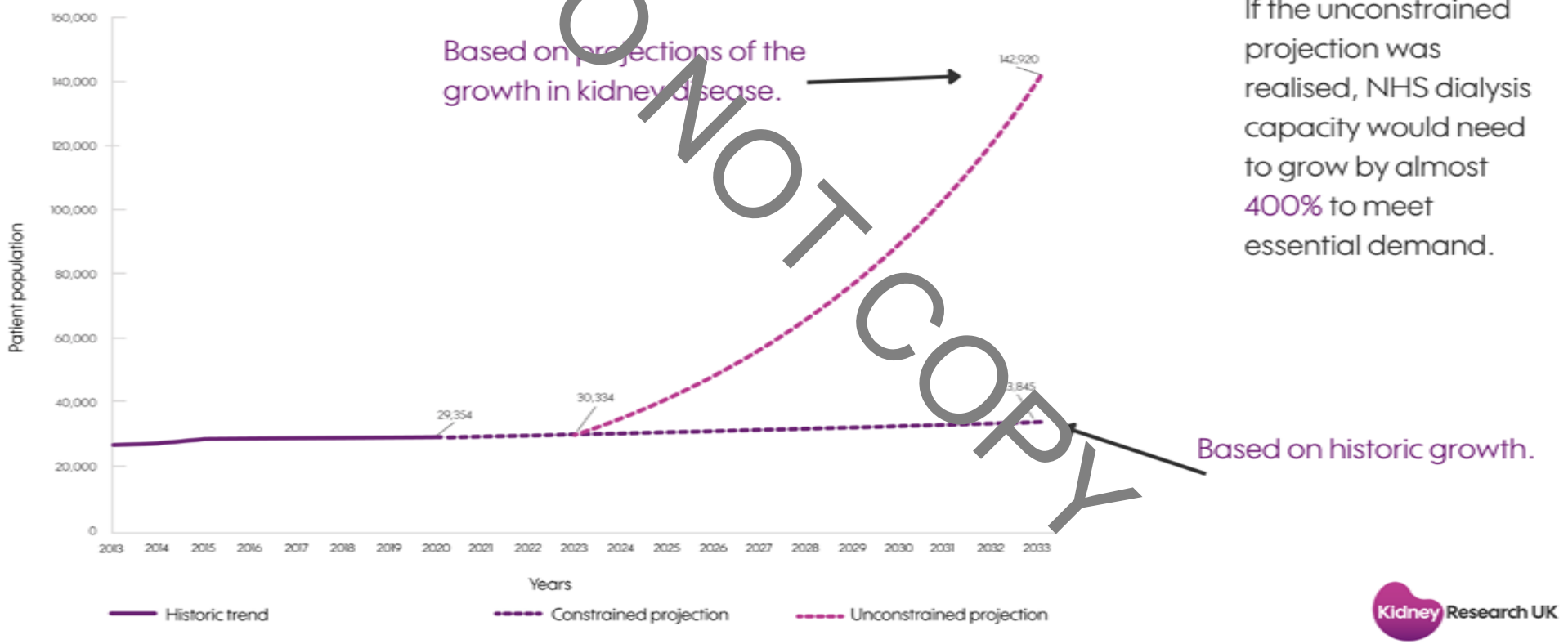
CKD is the tenth biggest killer worldwide today, projected to be the fifth leading cause of lost life years by 2040

£ Total annual UK economic burden of kidney disease is £7 billion; this cost could nearly double over the next 10 years, largely driven by increasing demand for dialysis*

***This is the unconstrained view, which estimates the number of people who may need dialysis based on how quickly people progress through the stages of kidney disease, and factors in all potential unmet need.**
CKD: chronic kidney disease.

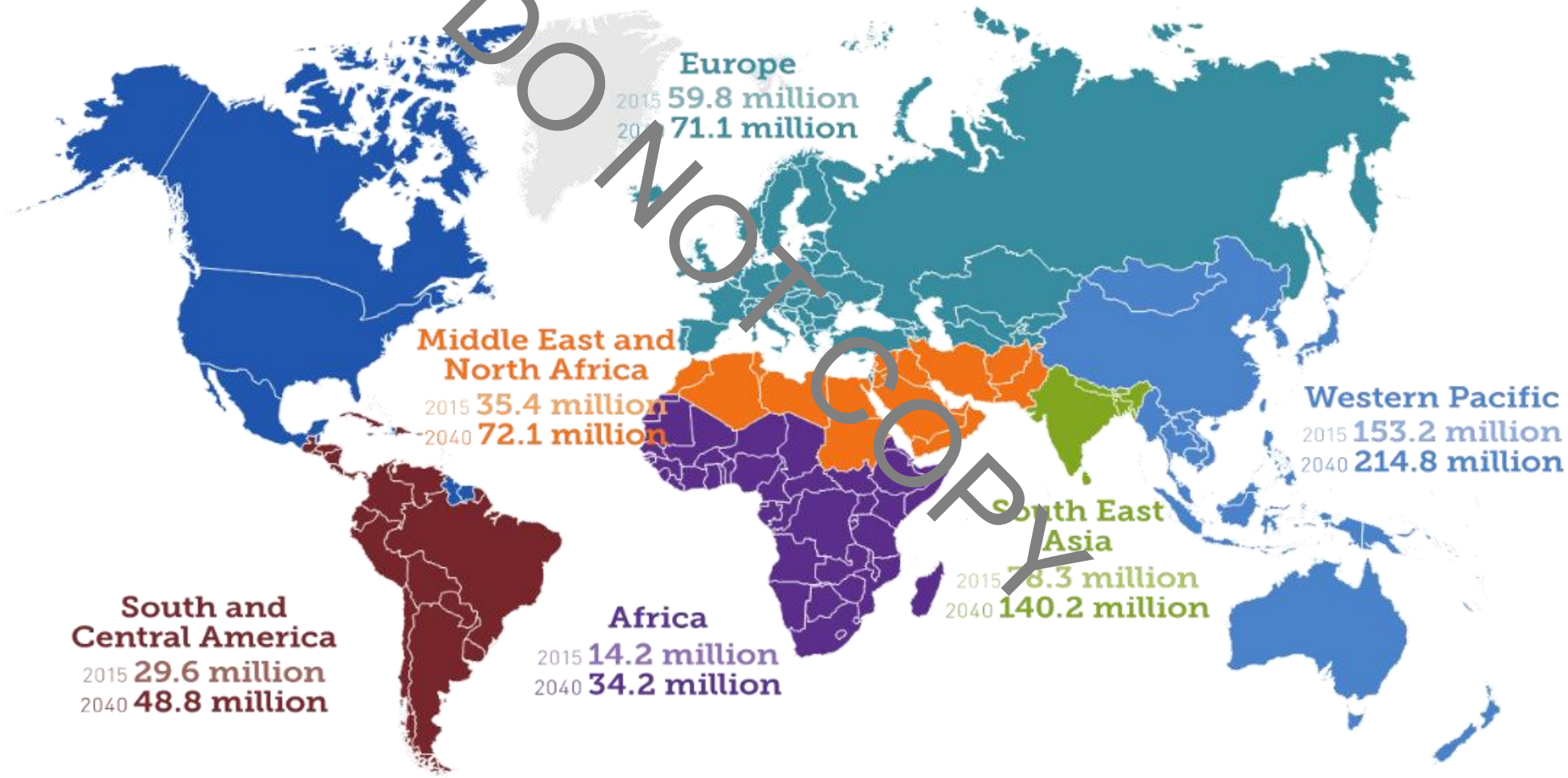
Kidney Research UK. *Kidney disease: a UK public health emergency. The health economics of kidney disease to 2033*. 2023.
Available at: https://www.kidneyresearchuk.org/wp-content/uploads/2023/06/Economics-of-Kidney-Disease-full-report_accessible.pdf (accessed November 2023).

Around 30,000 adults and children were on dialysis for kidney failure in 2023. This could grow to as much as 143,000 by 2033.



Kidney Research UK A Public Health Emergency 2023

Global estimates of diabetes

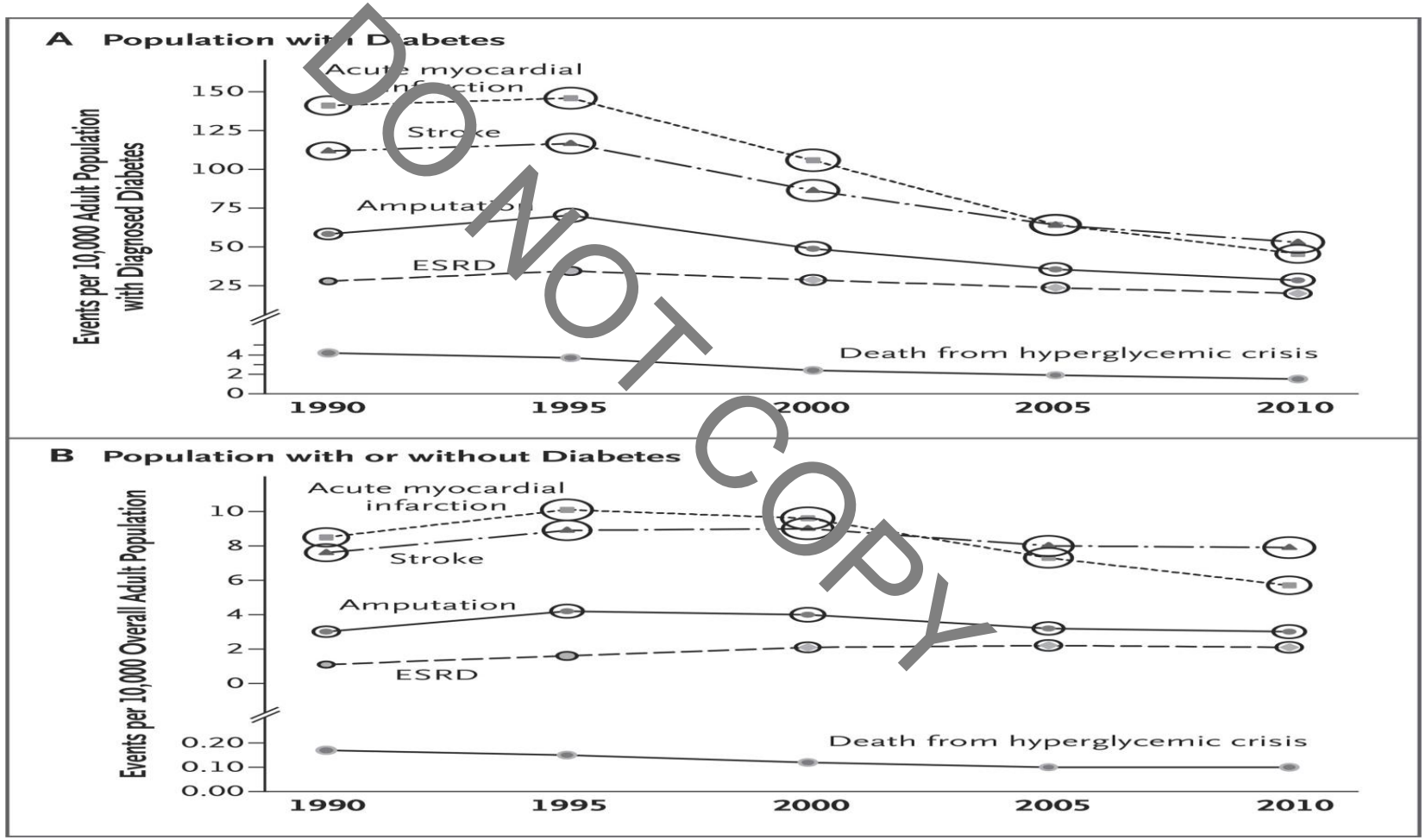


HOLISTIC MULTI DISCIPLINARY CARE

Diabetes Atlas, 7th ed. http://www.diabetesatlas.org/resources/2015-atlas.html. Last accessed October 2017.

Changes in Diabetes-Related Complications in the United States, 1990–2010

Imperial College Healthcare NHS Trust



Gregg et alN Engl J Med 2014; 370:1514-1523

Management of DKD: 2025

Management of CKD: 2025

RECOGNISE

TREAT

1. ACE inhibitor/ARB
2. SGLT2 inhibitors
3. BP targeting
4. Finerenone (DKD)
5. GLP1 Receptor Agonists
6. Glycaemic control

FOUNDATION

REDUCE CV RISK

- Lipids and Lifestyle changes

ENGAGE

- Patient engagement
- Social factors

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CKD, chronic kidney disease; CV, cardiovascular; SGLT2, sodium-glucose cotransporter-2.

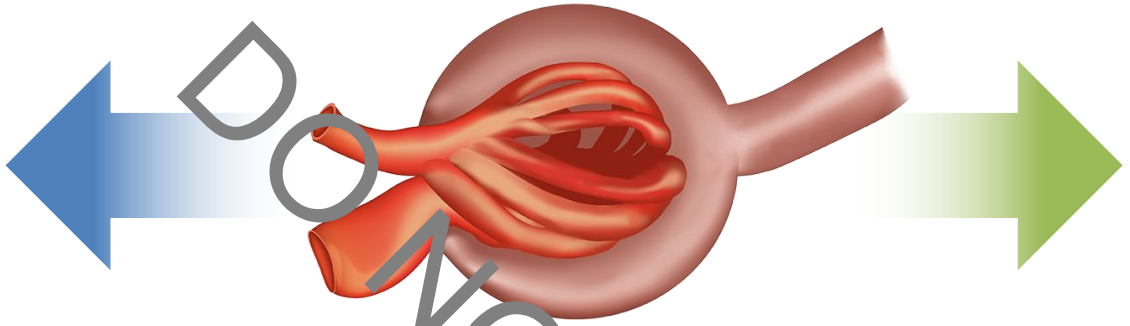
Recognition

Recognition – The Kidney Health Check

Imperial College Healthcare NHS Trust

Reduced eGFR

Creatinine clearance is reduced



Albuminuria

Protein leaks through glomerular basement membrane[1]

eGFR is an important indicator of CV risk and progression[2]

but

eGFR testing alone does not give a true picture of a patient's risk of worsening outcomes such as DKD progression and MACE

- eGFR: estimated glomerular filtration rate; CV: cardiovascular; DKD: diabetic kidney disease; MACE: major adverse cardiovascular events.

- Reidy K, et al. J Clin Invest 2014;124:2333-40.
- NICE Guideline CG182. Chronic kidney disease in adults: assessment and management. July 2014. [Accessed July 2020]. www.nice.org.uk/guidance/cg182

Who should be screened? – Reveal the hidden boxes

art
or

gout

Recommendations | Chronic kidney disease: assessment and management | Guidance | NICE

Who should be screened?

Diabetes

Yearly

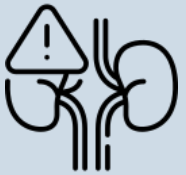
Hypertension

Yearly, or up to 5 yearly if BP well controlled

Cardio Vascular Disease

Ischaemic heart disease, chronic heart failure, peripheral vascular disease or cerebral vascular disease

Acute kidney Injury



Yearly for 3 years

Multisystem diseases

eg arthritis, lupus, HIV, psoriasis, gout

Structural renal tract disease

e.g. prostate hypertrophy, renal calculi

Incidental haematuria or proteinuria

Family Hx of kidney failure

Eg. Polycystic kidney disease

Recommendations | Chronic kidney disease: assessment and management | Guidance | NICE

Primacy of Lifestyle Intervention

Six pillars of lifestyle medicine

Eat

Predominantly whole food, plant-based diet emphasising nutrient density and appropriate caloric intake. Personalized nutritional plans consider cultural preferences and specific metabolic needs.

Avoidance of Harmful Substances

Support for reducing or eliminating tobacco, excessive alcohol, and other substances with negative cardiometabolic effects.

Connect

Fostering meaningful relationships and community engagement. Group-based interventions and peer support to enhance treatment adherence and outcomes.

Move

Regular movement combining cardiovascular exercise, strength training, and flexibility work. Tailored to individual capability and gradually increased to meet recommended guidelines.

Sleep

Optimising sleep duration and quality through evidence-based sleep hygiene practices. Addressing sleep disorders that impact cardiometabolic health.

Relax

Techniques to reduce psychological stress including mindfulness, meditation, and cognitive behavioral approaches. Focus on building resilience against chronic stressors.

These pillars work synergistically within the CRM pathway, with interventions tailored based on individual assessment results. Patients are empowered to select priority areas for change, supported by appropriate clinical resources and behavior change techniques to build sustainable healthy habits.

How Early is Early?

Chronic Kidney disease – Referral algorithm

North West London Integrated Care System

Clinical Assessment

Is patient unwell? — Yes → Manage acute illness
Is this acute kidney injury (AKI)?
Repeat eGFR within 1 week, refer urgently if declining

no

Test results

Persistent haematuria (≥1+)?
- yes >50 yrs → **Urology referral** → Is malignancy excluded? → Yes
- yes <50 yrs

no

ACR >70? — Yes

no

eGFR fall of ≥ 25% AND /OR ≥15ml/min within 12 months — Yes

no

5 year risk of Renal Failure

KFRE >5% at 5 years
Click here to calculate KFRE — Yes

no

Clear cause of CKD? — No – seek advice

Yes

Referral to nephrology **NOT** required
Manage CKD in primary care → Most patients with CKD 4/5 should be followed in secondary care
HOWEVER – if RRT not indicated (e.g. frail elderly), management of advanced CKD in primary care may be more appropriate

Urgent Nephrology referral

- Suspected multisystem disease with evidence of renal involvement.
- Acute kidney injury (without an obvious cause manageable in primary care).
- Newly diagnosed eGFR < 15.
- Nephrotic syndrome .
- Accelerated hypertension.
- Severe hyperkalaemia (>6.5mmol/L).

Nephrology Advice/ referral

ADVICE

Email advice for primary care healthcare staff in North West London: ICHC-tr.ckdadvice@nhs.net nephrology consultant response within 24 hours Monday- Friday
If your query is regarding a patient already under nephrology please contact imperial.renalsecretaries@nhs.net

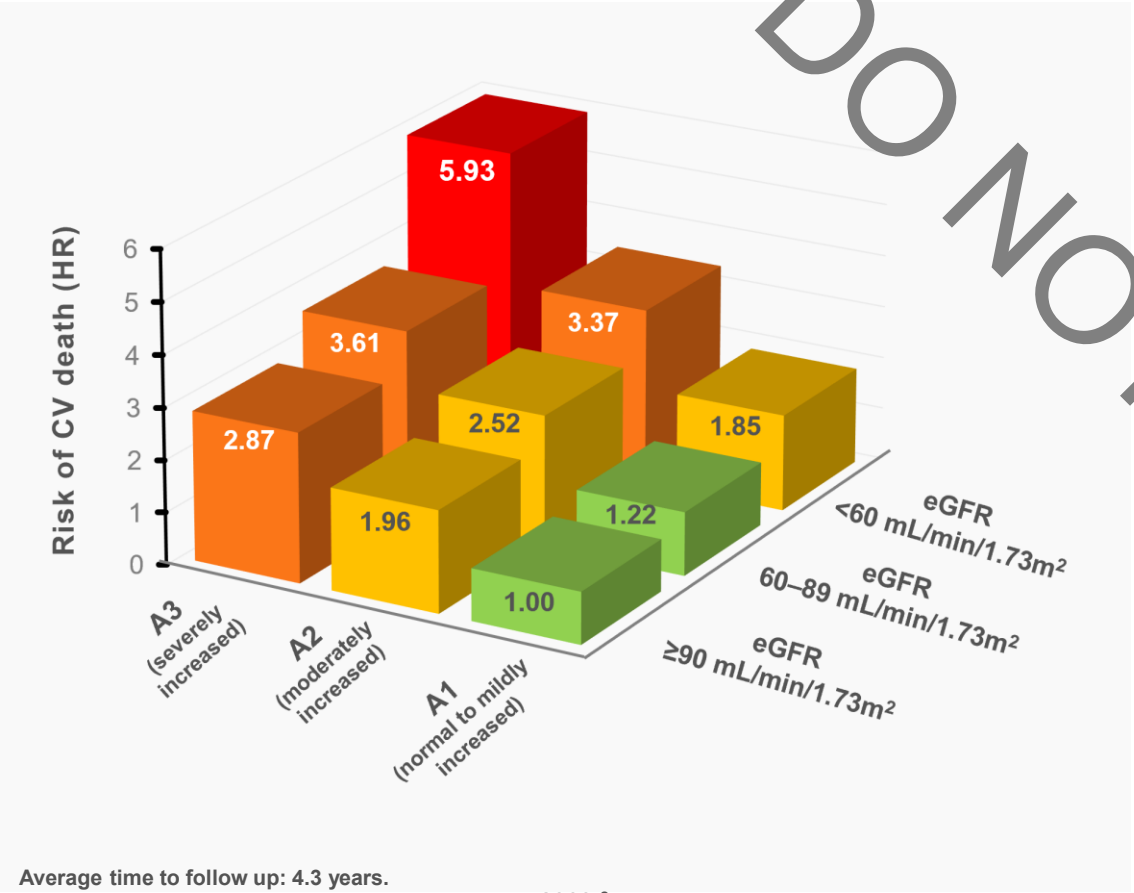
REFERRAL

Minimum information for referral: Dates and results of previous creatinine / eGFR measurement, medical history, drug history, current BP, urine dipstick and ACR if dipstick positive.

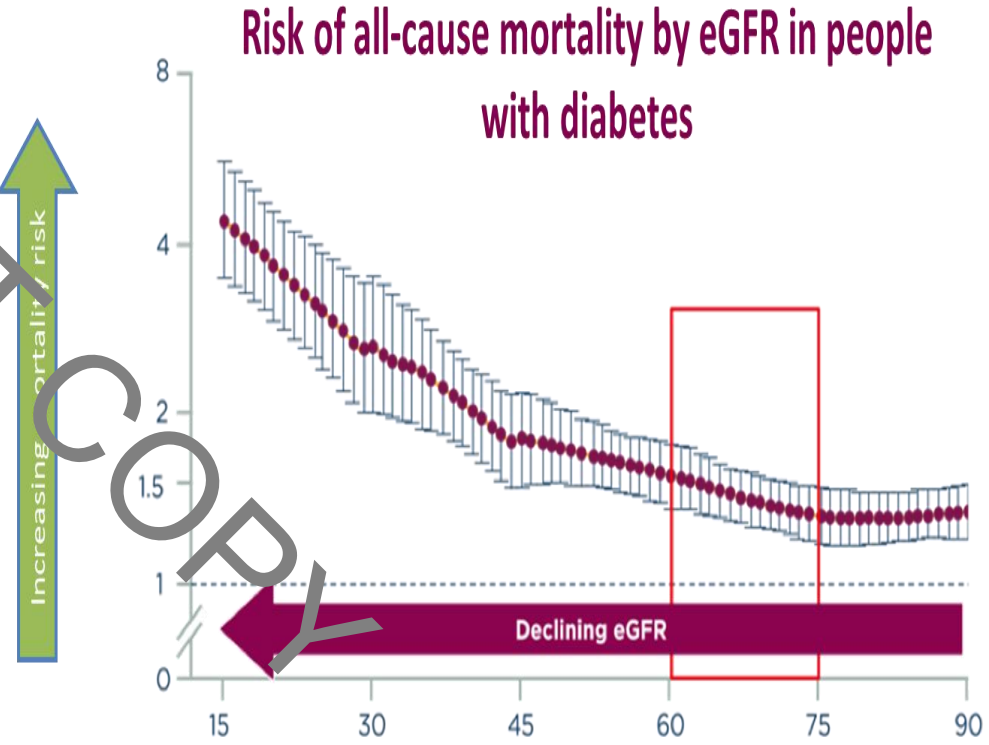
Single point of referral ERS (NWL Kidney Care Virtual Clinic)

- If transfer to nephrology not required clinical entry with recommendation on EMIS/SystmOne within 48 hours
- If transfer to nephrology, location of nephrology clinic visible on ERS.

How Early is Early



Average time to follow up: 4.3 years.
American Society of Nephrology, Ninomiya T *et al.* 2009.[2]



Fox C *et al. Lancet* 2012;380:1662-1673

Inflammatory and Cardiovascular Events in CKD: The Multi-Ethnic Study of Atherosclerosis (MESA)

A

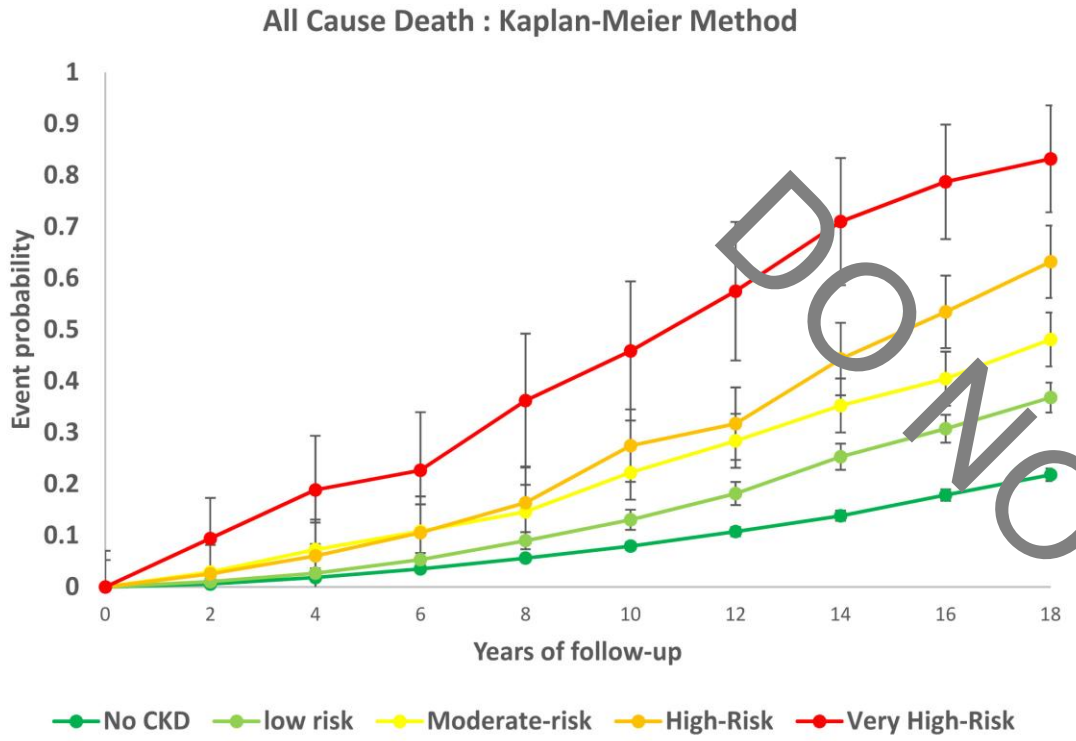
Combination categories of eGFR and UACR		UACR categories (mg/g)			
		A1a (< 10 mg/g)	A1b (10–29 mg/g)	A2 (30–299 mg/g)	A3 (≥ 300 mg/g)
eGFR categories (ml/min/1.73m²)	G1 (≥ 90)	1a	1b	2	3
	G2 (60–89)	1a	1b	2	3
	G3a (45–59)	3	3	3	4
	G3b (30–44)	3	3	4	4
	G4 (15–29)	4	4	4	4
	G5 (< 15)	4	4	4	4

B

Modified CKD risk categories	Definitions eGFR (ml/min/1.73m²) UACR (mg/g)
No CKD (1a; dark green)	eGFR ≥60 and UACR <10
Low-risk (1b; light green)	eGFR ≥ 60 and UACR 10–29
Moderate-risk (2, yellow)	eGFR ≥60 and UACR 30–299
High-risk (3, orange)	(eGFR 30-59 and UACR <30) or (eGFR 45–59 and UACR 30–299) or (eGFR ≥60 and UACR ≥300)
Very High-risk (4, red)	eGFR < 30 or (eGFR 30–44 and UACR 30–299) or (eGFR 30–59 and UACR ≥ 300)

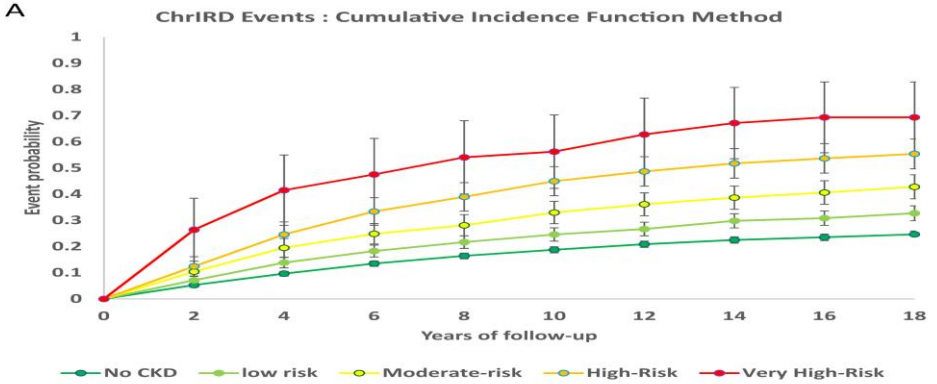
- In this study, the authors used a large community-based sample from the Multi-Ethnic Study of Atherosclerosis to evaluate the likelihood of, and risks associated with, inflammatory conditions with worsening kidney function. They studied a novel diagnostic entity called **chronic inflammation–related disease (ChrIRD)** encompassing several infectious and noninfectious inflammatory conditions. Over 19 years of follow-up, they demonstrated progressively higher risk of ChrIRD with worsening kidney function. The risks of ChrIRD are apparent in individuals with low levels of proteinuria and exceed cardiovascular disease at most stages of kidney function.

American Journal of Kidney Diseases 2025 86178-191.e1DOI: (10.1053/j.ajkd.2025.03.020)



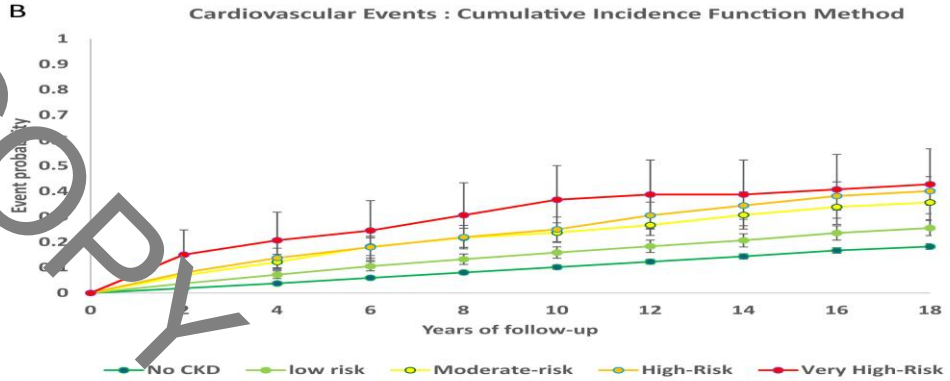
Years of follow-up	No CKD	low risk	Moderate-risk	High-Risk	Very High-Risk
4	4669	1139	467	306	48
8	4485	1079	424	276	40
12	4231	974	365	221	28
16	3874	810	298	164	15
18	1245	233	72	34	3

A



Years of follow-up	No CKD	low risk	Moderate-risk	High-Risk	Very High-Risk
4	4325	1029	407	261	34
8	3742	825	303	177	15
12	3316	689	239	122	8
16	2893	552	179	84	3
18	946	168	44.5	19	1

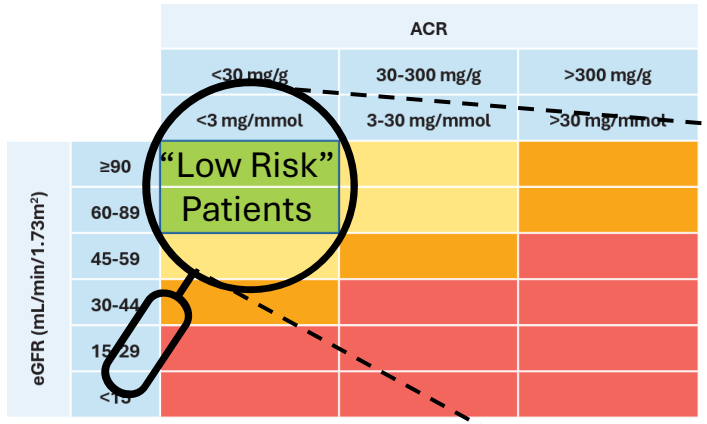
B

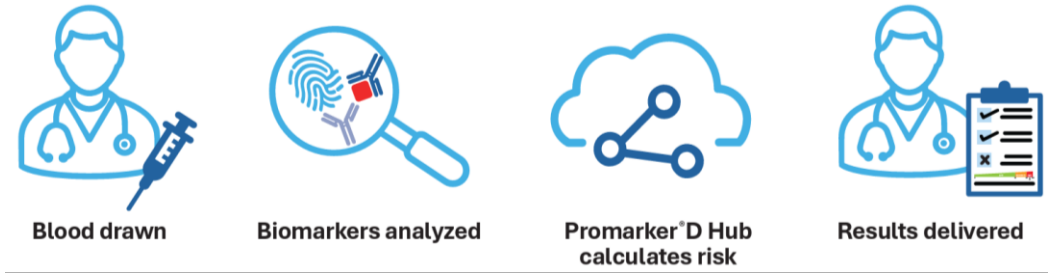


Years of follow-up	No CKD	low risk	Moderate-risk	High-Risk	Very High-Risk
4	4481	1067	426	276	38
8	4066	905	334	219	25
12	3648	762	268	168	16
16	3139	606	202	108	8
18	961	166	47	23	1

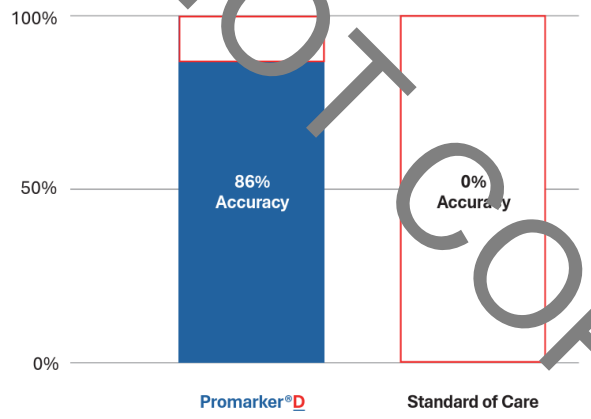
American Journal of Kidney Diseases 2025 86178-191.e1DOI: (10.1053/j.ajkd.2025.03.020)

PromarkerD – a Prognostic CKD Test for T2D



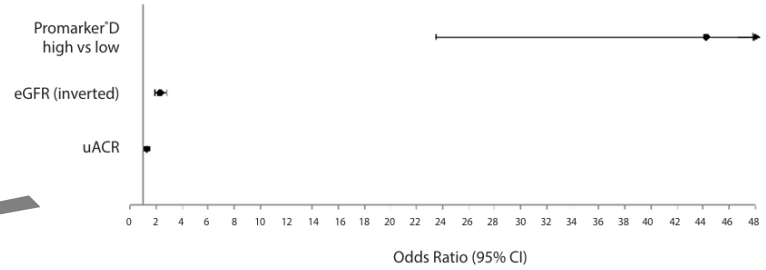


Promarker®D correctly identified 86% of low risk patients who progressed to CKD at four year follow-up



Lui et al evaluated PromarkerD in a study of 949 T2D participants in the 'green zone' at T=0, showing no/low evidence of CKD. The test accurately predicted 86% of patients who progressed of patients at T=4 years. Standard diagnostics (eGFR and ACR) failed to identify any of those who progressed.

Comparison of Promarker®D and SOC for predicting incident CKD or eGFR decline ≥40%



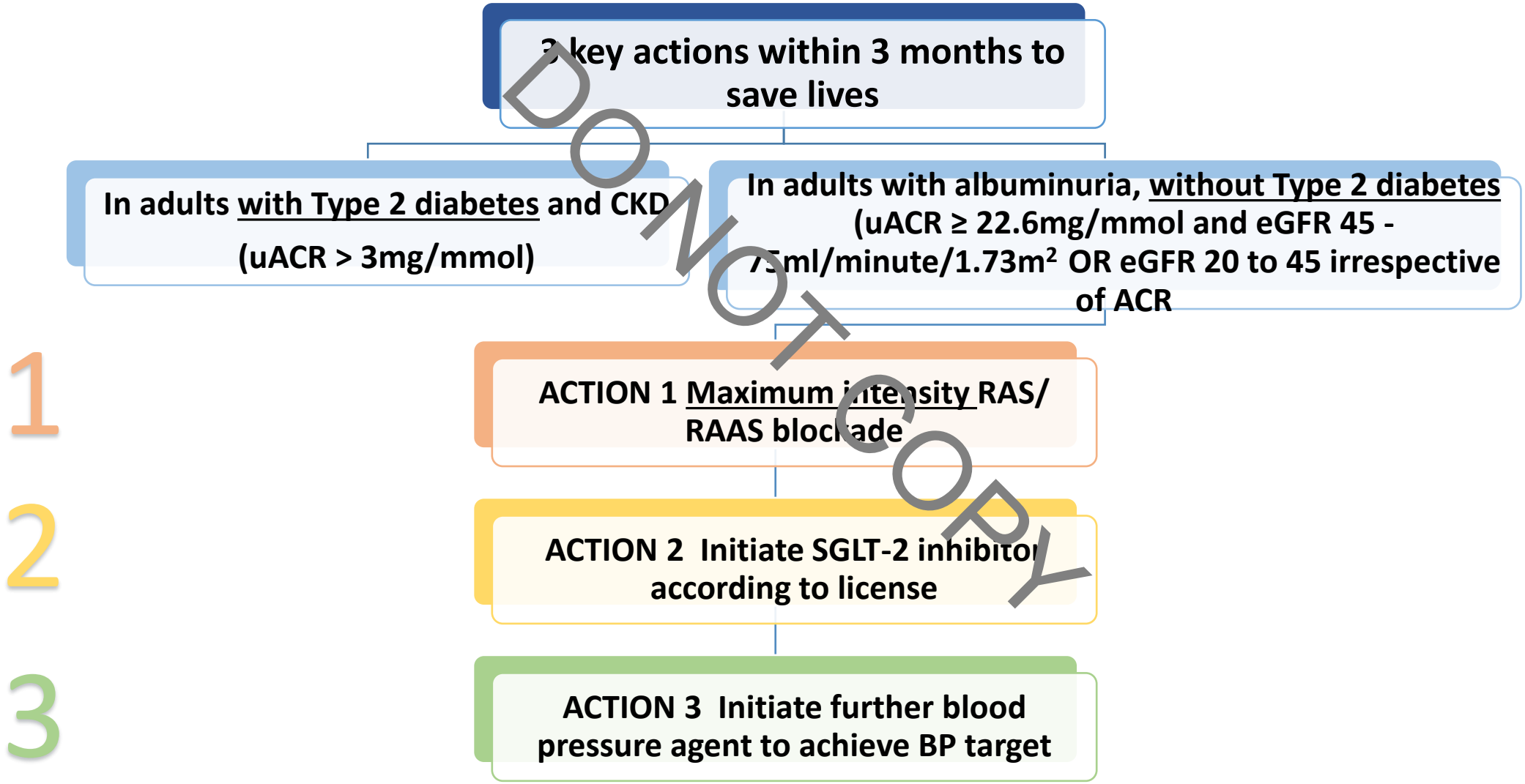
Peters et al reported an Odds Ratio of 44.3 (95% CI, 24.0-83.5) for PromarkerD (high vs low) as compared to 2.3 for eGFR and 1.3 for ACR.

REFERENCES
Lui, JKC et al. (2025). Analytical and clinical performance of a novel immunoassay-based test system to predict diabetic kidney disease. Journal of Applied Laboratory Medicine.

Peters et al., 2025. Next-Generation PromarkerD vs. Standard of Care for Assessing Kidney Function Decline in Type 2 Diabetes. American Diabetes Association Late-Breaking Poster. June 20-23. Chica go, IL. Diabetes 13 June 2024; 74 (Supplement_1): 1862–LB. doi.org/10.2337/db25-1862-LB

How Quickly is Quickly?

London Kidney Network "3in3" Initiative



Guidelines Emphasise Optimising RAASi Therapy for Patients With CKD and HF[1-3]

Chronic Kidney Disease	Heart Failure	
KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of CKD[1]	**2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic HF[2]**	**2022 AHA/ACC/HFSA Guideline for the Management of HF[3]**
RASi (ACEi or ARB) should be administered using the **highest approved dose that is tolerated** to achieve the benefits described because the proven benefits were achieved in trials using these doses[a]	ACEi and MRA are recommended for patients with HFrEF to reduce the risk of HF hospitalisation and death (1A)[b] Sacubitril/valsartan is recommended as a replacement for an ACEi in patients with HFrEF to reduce the risk of HF hospitalisation and death (1B)[c] RAASi[d] therapy should be up-titrated to the **highest tolerated doses**	In patients with HFrEF, titration of guideline-directed medication dosing, including RAASi,[e] to achieve **target doses** showed to be efficacious in RCTs is recommended, to reduce cardiovascular mortality and HF hospitalisations, unless not well tolerated (1A)[f]

[a]In the KDIGO 2024 CKD guideline, this is a practice point that are consensus-based statements representing the expert judgement of the Work Group and are not graded. Users should consider the practice point as expert guidance and use it as they see fit to inform the care of patients;[1] [b]Recommendation (1A) in the 2021 ESC guideline: Class I = evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective and Level of evidence A = data derived from multiple RCTs or meta-analyses;[2] [c]Recommendation (1B) in the 2021 ESC guideline: Class I = evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective and Level of evidence B = data derived from a single RCT or large non-randomised studies;[2] [d]RAASi therapy includes ACEi, ARNI, and MRA. ARBs can be used if intolerant to ACEi or ARNI;[2] [e]RAASi therapy includes ACEi, ARB, ARNI, and MRA (spironolactone or eplerenone);[3] [f]Recommendation (1A) in the 2022 AHA/ACC/HFSA guideline: Class 1 = Strong (benefit >>> risk) and Level of Evidence A = High-quality evidence from more than 1 RCT; meta-analyses of high-quality RCTs; one or more RCTs corroborated by high-quality registry studies.[3]

ACC = American College of Cardiology; ACEi = angiotensin-converting enzyme inhibitor; AHA = American Heart Association; ARB = angiotensin II receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; CKD = chronic kidney disease; ESC = European Society of Cardiology; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; HFSA = Heart Failure Society of America; KDIGO = Kidney Disease: Improving Global Outcomes; MRA = mineralocorticoid receptor antagonist; RAASi = renin-angiotensin-aldosterone system inhibitor; RASi = renin-angiotensin system inhibitor; RCT = randomised controlled trial.

1. KDIGO CKD Work Group. *Kidney Int.* 2024;105(4S):S117-S314; 2. McDonagh TA et al. Article and supplementary data. *Eur Heart J.* 2021;42(36):3599-3726; 3. Heidenreich PA et al. *J Am Coll Cardiol.* 2022;79(17):e263-e421.

Hyperkalaemia Is a Barrier to Maximum RAASi Dose

Following a hyperkalaemia event in patients who received maximum RAASi dose, **RAASi down-titration or discontinuation** occurred[a]

of the time in **mild hyperkalemia** (K^+ 5.1–5.4 mmol/L; 23,556 events)

of the time in **moderate-to-severe hyperkalemia** (K^+ ≥5.5 mmol/L; 11,608 events)

A retrospective study of US Humedica database from 2007 to 2012

Note: Study of electronic health records (N >200,000) of patients with various comorbidities (including cardiorenal ones) who were ≥5 years of age with ≥1 outpatient RAASi prescription, and ≥2 serum K^+ readings.

[a]An event-level analysis was done to examine RAASi dose changes following hyperkalaemia events in patients on maximum RAASi dose where maximum = labelled dose; down-titration = submaximum dose of any RAASi lower than the labelled dose; discontinued = absence of RAASi prescriptions for a period of >390 days subsequent to prior prescription. RAASi included ACEi, ARB, direct renin inhibitor, and select MRA.

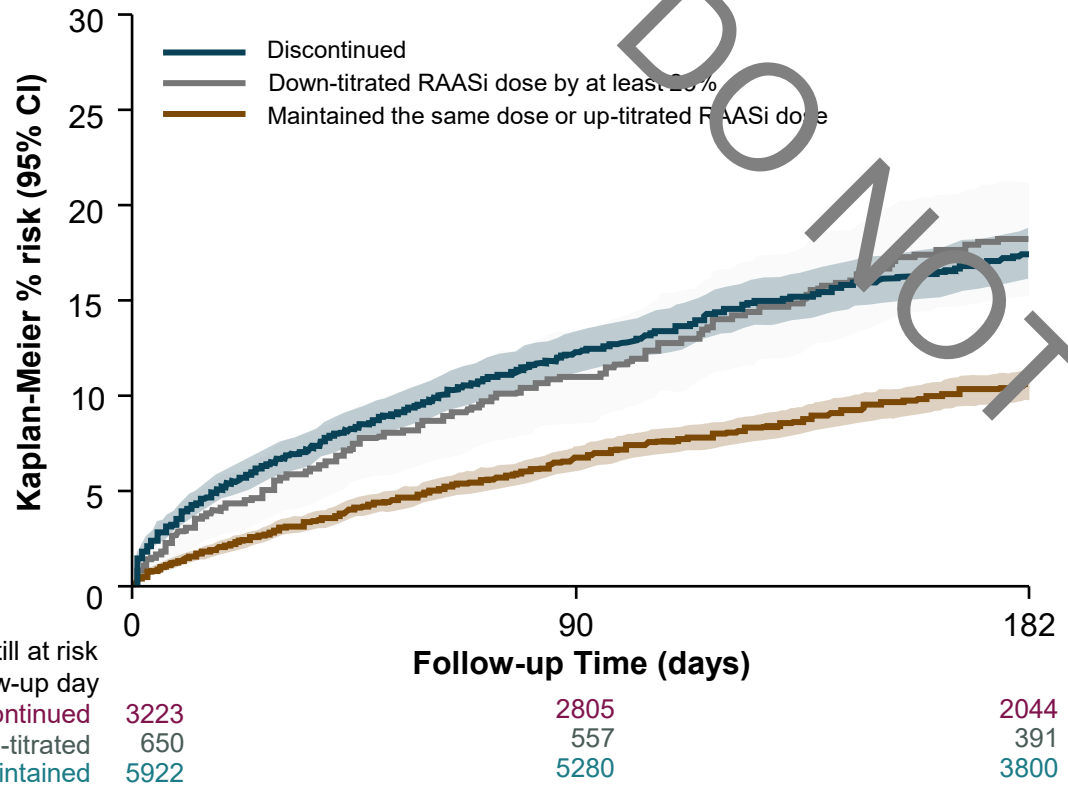
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; K^+, potassium; MRA, mineralocorticoid receptor antagonist; RAASi, renin-angiotensin-aldosterone system inhibitor; US, United States.

Epstein M, et al. *Am J Manag Care*. 2015;21(Suppl 11):S212-S220.

RAASi Down-titration and Discontinuation Was Associated With Increased Risk of Morbidity in Cardiorenal Patients

Risk of the composite outcome of progression to ESKD[a] and HF-related hospitalisations[b]

Change in RAASi following a hyperkalaemia event (US data)



55% increased relative risk with RAASi **discontinuation**

51% increased relative risk with RAASi **down-titration**

compared to the risk with **RAASi maintenance**[c]

Adapted from Kanda E, et al. *BMC Nephrol.* 2023.

Note: An observational study that utilised the US claims and EHR data from July 2019 and September 2021 in 15,488 adult patients with CKD Stage 3 or 4 and/or HF who experienced an index hyperkalaemia event (ICD-10 or ICD-9 diagnosis codes) and had ≥1 filled RAASi prescription within 6 months before the index hyperkalaemia event. RAASi included ACEi, ARB, ARNI, and MRA.

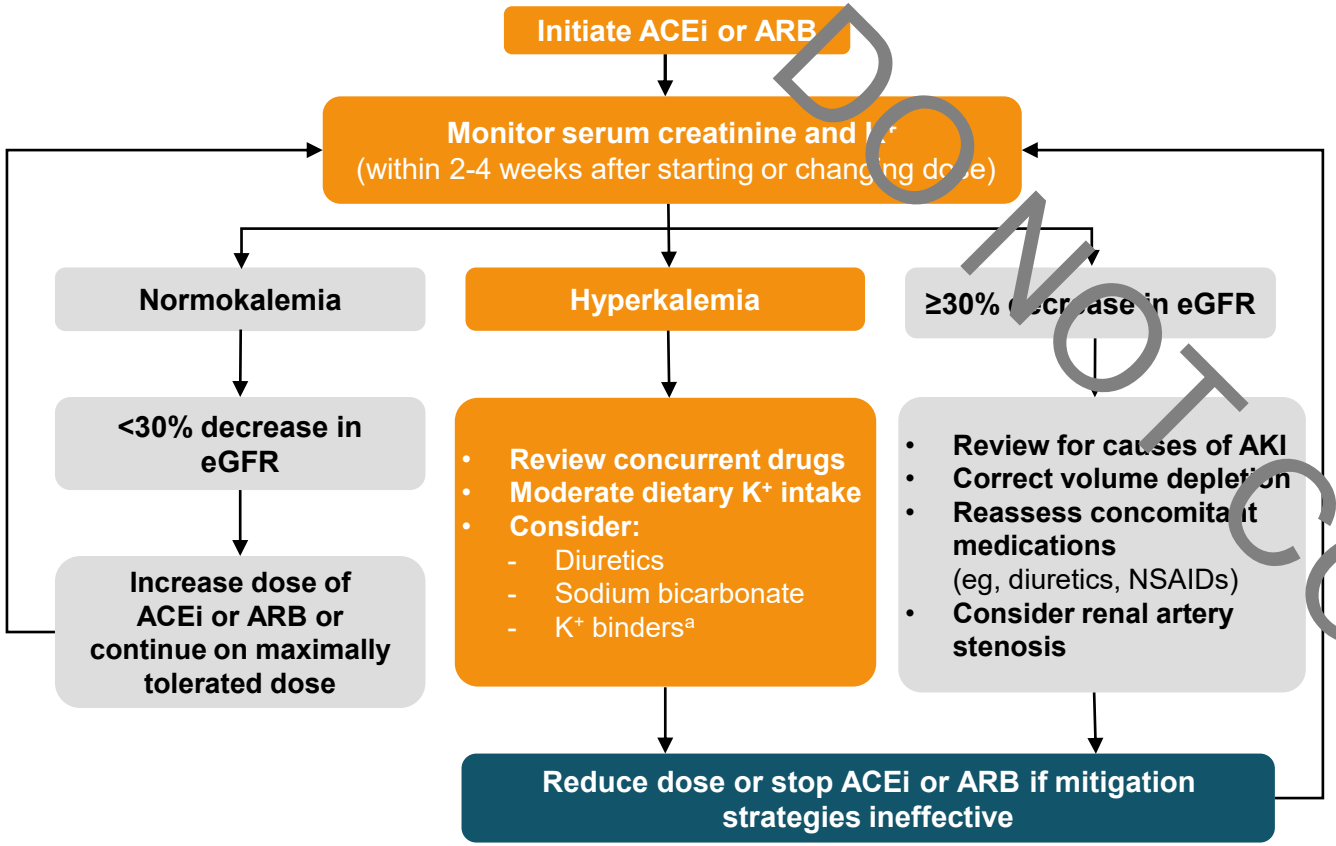
[a]Initiation of haemodialysis or a diagnosis of ESKD or CKD Stage 5 in any position recorded in hospital, emergency, or outpatient setting; [b]Hospitalisations with HF or emergency visits for HF; [c]p<0.001 for each comparison. Adjusted for age, sex, history of hyperkalaemia, diabetes, HF, CKD including stage, and baseline use of ACEi, ARB, ARNI, and MRA.

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; CI, confidence interval; CKD, chronic kidney disease; EHR, electronic health record; ESKD, end-stage kidney disease; HF, heart failure; ICD, International Classification of Diseases 9th or 10th revisions; MRA, mineralocorticoid receptor antagonist; RAASi, renin-angiotensin-aldosterone system inhibitor; US, United States.

Kanda E, et al. *BMC Nephrol.* 2023;24(1):18.

The 2024 KDIGO CKD Guideline Provides A Stepwise Approach To Hyperkalaemia Management and States Reducing RAASi Only After Other Measures Have Failed[1]

Algorithm for monitoring potassium and eGFR after ACEi/ARB initiation



Actions to hyperkalemia[b] management in CKD

1st line: Address correctable factors

- Review non-RAASi medications (e.g. NSAIDs, trimethoprim)
- Assess dietary potassium intake (dietary referral) and consider appropriate moderation of dietary potassium intake

2nd line: Medications

- Appropriate use of diuretics
- Optimise serum bicarbonate levels
- Licensed potassium exchange agents[c]

3rd line: Last resort

- Reduce dose or discontinue RASi/MRA (discontinuation is associated with increased cardiovascular events. Review and restart RAASi or MRA at a later date if patient condition allows)

Note: RASi includes ACEi or ARB. [a]Such as SZC and patiromer; [b]K^+ >5.5 mmol/L; [c]SZC, patiromer, and sodium/calcium polystyrene sulfonates.

ACEi, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin II receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; K^+, potassium; KDIGO, Kidney Disease: Improving Global Outcomes; MRA, mineralocorticoid receptor antagonist; NSAIDs, nonsteroidal anti-inflammatory drugs; RAASi, renin-angiotensin-aldosterone system inhibitor; RASi, renin-angiotensin system inhibitor; SZC, sodium zirconium cyclosilicate.

KDIGO CKD Work Group. *Kidney Int*. 2024;105(Suppl 4S):S117–S314.

UK+ CARDIORENAL PROTECTION FORUM

UK Hyperkalaemia Steering Group:

Overcoming hyperkalaemia as a barrier to RAASi therapy optimisation in individuals with cardiorenal disease

GB-70272 September 2025

This Steering group work was initiated and funded by AstraZeneca

AstraZeneca

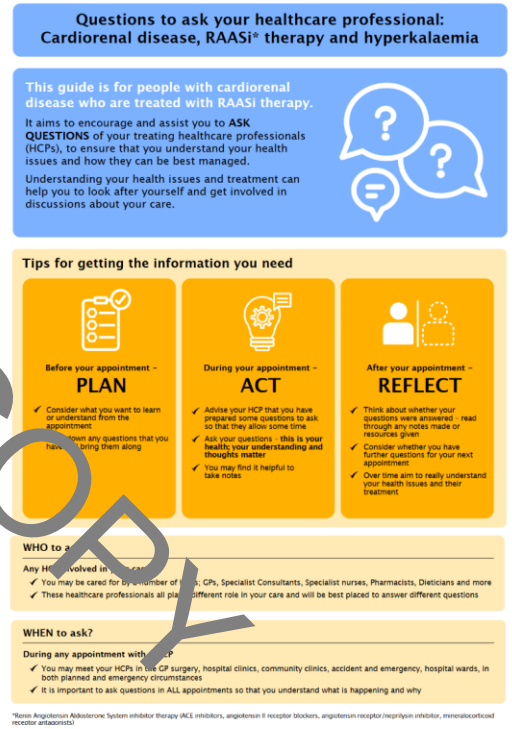
Eleven practicing cardiorenal experts from across the UK

Name	Role
Andrew Frankel	Nephrologist, London
Stephen Wheatcroft	Cardiologist, Leeds
Barbara Byrne	Heart failure specialist nurse, London
Darren Green	Nephrologist, Manchester
Kate Bramham	Nephrologist, London
Mandie Welch	Heart failure specialist nurse, South Wales
Ruby Chumber	Renal pharmacist, Advanced practitioner, Nottingham
Sarah Davies	GP, Cardiff
Simon G Williams	Cardiologist, Manchester
Ahmet Fuat	GP, Co Durham
William Priestman	GP, Leicester

Focus: Overcoming hyperkalaemia as a barrier to RAASi therapy optimisation in individuals with cardiorenal disease

Four key areas of suboptimal and variable practice identified:

- **RAASi optimisation**
- **Definition and management of acute hyperkalaemia**
- **Secondary to primary care communications**
- **Patient education**



Questions to ask your healthcare professional: Cardiorenal disease, RAASi* therapy and hyperkalaemia

This guide is for people with cardiorenal disease who are treated with RAASi therapy.

It aims to encourage and assist you to **ASK QUESTIONS** of your treating healthcare professionals (HCPs), to ensure that you understand your health issues and how they can be best managed.

Understanding your health issues and treatment can help you to look after yourself and get involved in discussions about your care.

Tips for getting the information you need

Before your appointment – PLAN

- Consider what you want to learn or understand from the appointment
- Write down any questions that you have and bring them along

During your appointment – ACT

- Advise your HCP that you have prepared some questions to ask so that they allow some time
- Ask your questions – **this is your health; your understanding and thoughts matter**
- You may find it helpful to take notes

After your appointment – REFLECT

- Think about whether your questions were answered – read through any notes made or resources given
- Consider whether you have further questions for your next appointment
- Over time aim to really understand your health issues and their treatment

WHO to a…

Any HC… involved in…

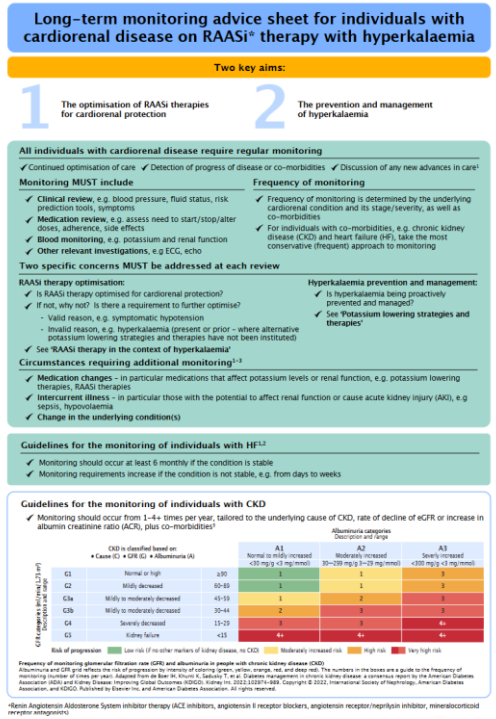
- You may be cared for by a number of … GPs, Specialist Consultants, Specialist nurses, Pharmacists, Dieticians and more
- These healthcare professionals all play a different role in your care and will be best placed to answer different questions

WHEN to ask?

During any appointment with your …

- You may meet your HCPs in the GP surgery, hospital clinics, community clinics, accident and emergency, hospital wards, in both planned and emergency circumstances
- It is important to ask questions in ALL appointments so that you understand what is happening and why

*Renin Angiotensin Aldosterone System inhibitor therapy (ACE inhibitors, angiotensin II receptor blockers, angiotensin receptor/neprilysin inhibitor, mineralocorticoid receptor antagonists)



Long-term monitoring advice sheet for individuals with cardiorenal disease on RAASi* therapy with hyperkalaemia

Two key aims:

1 The optimisation of RAASi therapies for cardiorenal protection

2 The prevention and management of hyperkalaemia

All individuals with cardiorenal disease require regular monitoring

✓ Continued optimisation of care ✓ Detection of progress of disease or co-morbidities ✓ Discussion of any new advances in care[1]

Monitoring MUST include

- ✓ **Clinical review**, e.g. blood pressure, fluid status, risk prediction tools, symptoms
- ✓ **Medication review**, e.g. assess need to start/stop/alter doses, adherence, side effects
- ✓ **Blood monitoring**, e.g. potassium and renal function
- ✓ **Other relevant investigations**, e.g ECG, echo

Frequency of monitoring

- ✓ Frequency of monitoring is determined by the underlying cardiorenal condition and its stage/severity, as well as co-morbidities
- ✓ For individuals with co-morbidities, e.g. chronic kidney disease (CKD) and heart failure (HF), take the most conservative (frequent) approach to monitoring

Two specific concerns MUST be addressed at each review

RAASi therapy optimisation:

- ✓ Is RAASi therapy optimised for cardiorenal protection?
- ✓ If not, why not? Is there a requirement to further optimise?
  - Valid reason, e.g. symptomatic hypotension
  - Invalid reason, e.g. hyperkalaemia (present or prior – where alternative potassium lowering strategies and therapies have not been instituted)
- ✓ See **'RAASi therapy in the context of hyperkalaemia'**

Hyperkalaemia prevention and management:

- ✓ Is hyperkalaemia being proactively prevented and managed?
- ✓ See **'Potassium lowering strategies and therapies'**

Circumstances requiring additional monitoring[1–3]

- ✓ **Medication changes** – in particular medications that affect potassium levels or renal function, e.g. potassium lowering therapies, RAASi therapies
- ✓ **Intercurrent illness** – in particular those with the potential to affect renal function or cause acute kidney injury (AKI), e.g sepsis, hypovolaemia
- ✓ **Change in the underlying condition(s)**

Guidelines for the monitoring of individuals with HF[1,2]

- ✓ Monitoring should occur at least 6 monthly if the condition is stable
- ✓ Monitoring requirements increase if the condition is not stable, e.g. from days to weeks

Guidelines for the monitoring of individuals with CKD

- ✓ Monitoring should occur from 1–4+ times per year, tailored to the underlying cause of CKD, rate of decline of eGFR or increase in albumin creatinine ratio (ACR), plus co-morbidities[1]

CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A)		Albuminuria categories Description and range A1 Normal to mildly increased <30 mg/g <3 mg/mmol	A2 Moderately increased 30–299 mg/g 3–29 mg/mmol	A3 Severely increased ≥300 mg/g ≥3 mg/mmol
G1	Normal or high	≥90	1	1	3
G2	Mildly decreased	60–89	1	1	3
G3a	Mildly to moderately decreased	45–59	1	2	3
G3b	Mildly to moderately decreased	30–44	2	3	3
G4	Severely decreased	15–29	3	3	4+
G5	Kidney failure	<15	4+	4+	4+

GFR categories (ml/min/1.73 m²) Descriptions and range

Risk of progression: Low risk (if no other markers of kidney disease, no CKD) Moderately increased risk High risk Very high risk

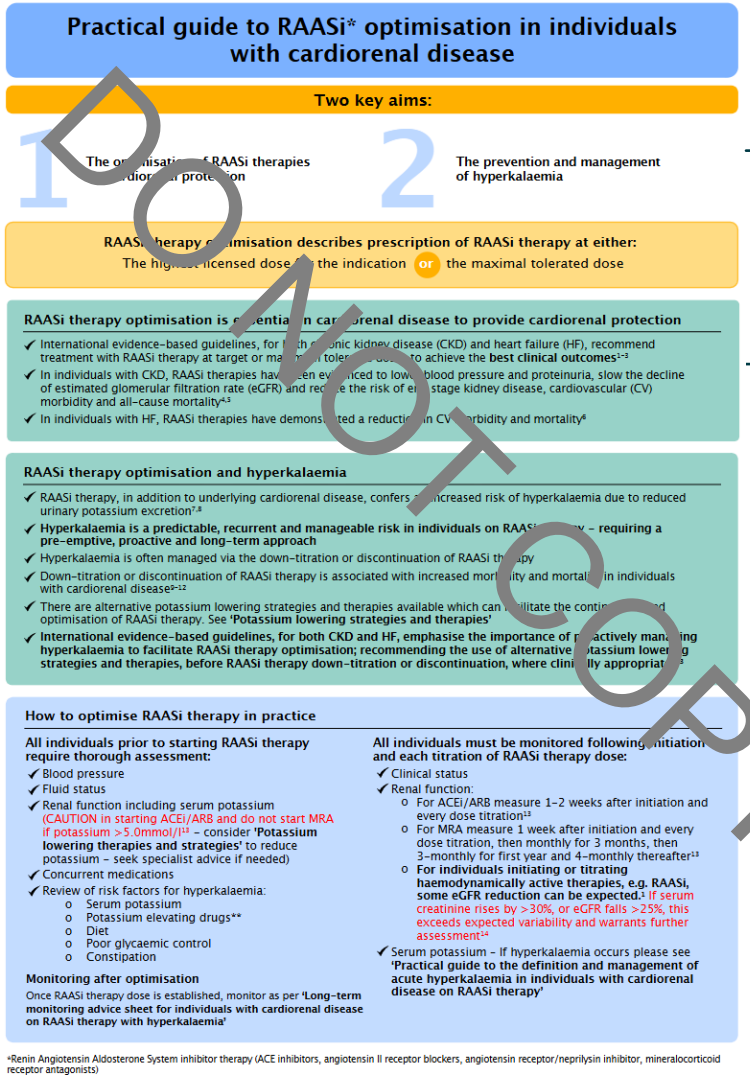
Frequency of monitoring glomerular filtration rate (GFR) and albuminuria in people with chronic kidney disease (CKD)

Albuminuria and GFR grid reflects the risk of progression by intensity of coloring (green, yellow, orange, red, and deep red). The numbers in the boxes are a guide to the frequency of monitoring (number of times per year). Adapted from de Boer IH, Khunti K, Sadusky T, et al. Diabetes management in chronic kidney disease: a consensus report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int. 2022;102(5):974–989. Copyright © 2022, International Society of Nephrology, American Diabetes Association, and KDIGO. Published by Elsevier Inc. and American Diabetes Association. All rights reserved.

*Renin Angiotensin Aldosterone System inhibitor therapy (ACE inhibitors, angiotensin II receptor blockers, angiotensin receptor/neprilysin inhibitor, mineralocorticoid receptor antagonists)

The steering group created a range of practical resources for use in clinical practice

Practical guide to RAASi therapy optimisation in individuals with cardiorenal disease



Practical guide to RAASi* optimisation in individuals with cardiorenal disease

Two key aims:

1 The optimisation of RAASi therapies for cardiorenal protection

2 The prevention and management of hyperkalaemia

RAASi therapy optimisation describes prescription of RAASi therapy at either:
The highest licensed dose for the indication OR the maximal tolerated dose

RAASi therapy optimisation is essential in cardiorenal disease to provide cardiorenal protection

- ✓ International evidence-based guidelines, for both chronic kidney disease (CKD) and heart failure (HF), recommend treatment with RAASi therapy at target or maximal tolerated dose to achieve the **best clinical outcomes**[1-3]
- ✓ In individuals with CKD, RAASi therapies have been evidenced to lower blood pressure and proteinuria, slow the decline of estimated glomerular filtration rate (eGFR) and reduce the risk of end-stage kidney disease, cardiovascular (CV) morbidity and all-cause mortality[4,5]
- ✓ In individuals with HF, RAASi therapies have demonstrated a reduction in CV morbidity and mortality[6]

RAASi therapy optimisation and hyperkalaemia

- ✓ RAASi therapy, in addition to underlying cardiorenal disease, confers an increased risk of hyperkalaemia due to reduced urinary potassium excretion[7,8]
- ✓ **Hyperkalaemia is a predictable, recurrent and manageable risk in individuals on RAASi therapy – requiring a pre-emptive, proactive and long-term approach**
- ✓ Hyperkalaemia is often managed via the down-titration or discontinuation of RAASi therapy
- ✓ Down-titration or discontinuation of RAASi therapy is associated with increased morbidity and mortality in individuals with cardiorenal disease[9-12]
- ✓ There are alternative potassium lowering strategies and therapies available which can facilitate the continued optimisation of RAASi therapy. See **'Potassium lowering strategies and therapies'**
- ✓ **International evidence-based guidelines, for both CKD and HF, emphasise the importance of proactively managing hyperkalaemia to facilitate RAASi therapy optimisation; recommending the use of alternative potassium lowering strategies and therapies, before RAASi therapy down-titration or discontinuation, where clinically appropriate**[1-3]

How to optimise RAASi therapy in practice

All individuals prior to starting RAASi therapy require thorough assessment:

- ✓ Blood pressure
- ✓ Fluid status
- ✓ Renal function including serum potassium (CAUTION in starting ACEi/ARB and do not start MRA if potassium >5.0mmol/l[13] – consider **'Potassium lowering therapies and strategies'** to reduce potassium – seek specialist advice if needed)
- ✓ Concurrent medications
- ✓ Review of risk factors for hyperkalaemia:
  - o Serum potassium
  - o Potassium elevating drugs**
  - o Diet
  - o Poor glycaemic control
  - o Constipation

Monitoring after optimisation

Once RAASi therapy dose is established, monitor as per **'Long-term monitoring advice sheet for individuals with cardiorenal disease on RAASi therapy with hyperkalaemia'**

All individuals must be monitored following initiation and each titration of RAASi therapy dose:

- ✓ Clinical status
- ✓ Renal function:
  - o For ACEi/ARB measure 1-2 weeks after initiation and every dose titration[13]
  - o For MRA measure 1 week after initiation and every dose titration, then monthly for 3 months, then 3-monthly for first year and 4-monthly thereafter[13]
  - o **For individuals initiating or titrating haemodynamically active therapies, e.g. RAASi, some eGFR reduction can be expected.**[5] If serum creatinine rises by >30%, or eGFR falls >25%, this exceeds expected variability and warrants further assessment[14]
- ✓ Serum potassium – If hyperkalaemia occurs please see **'Practical guide to the definition and management of acute hyperkalaemia in individuals with cardiorenal disease on RAASi therapy'**

*Renin Angiotensin Aldosterone System inhibitor therapy (ACE inhibitors, angiotensin II receptor blockers, angiotensin receptor/neprilysin inhibitor, mineralocorticoid receptor antagonists)

The 2 key treatment aims – RAASi therapy optimisation and prevention/management of hyperkalaemia - are highlighted throughout the resources

It is essential for primary and secondary care colleagues to understand the importance and practicalities of RAASi therapy optimisation - and to pre-empt hyperkalaemia as a barrier

Scan to access this material and other useful resources.

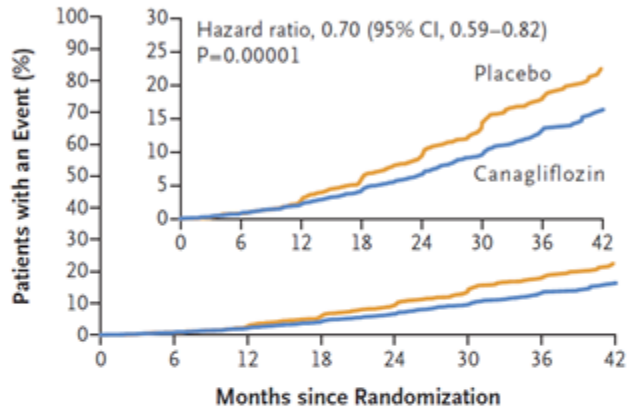
SGLT2is are Primary Care drugs
The Statin of the 21st Century?

Imperial College Healthcare NHS Trust

Renal Outcomes Trials – primary cardiorenal outcomes

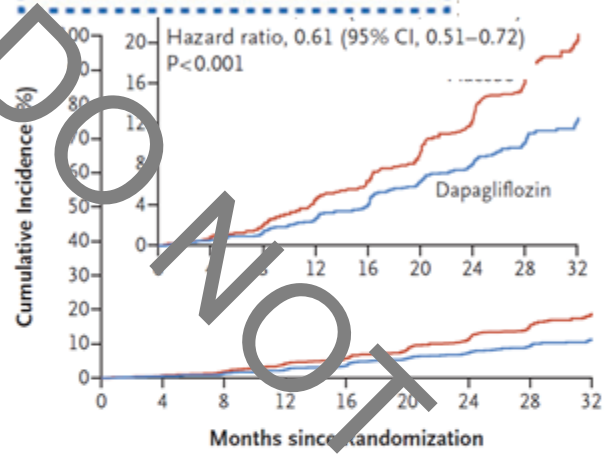
CREDENCE (DKD only)
eGFR ≥30 to <90 mL/min/1.73 m²
and UACR ≥300 mg/g

A



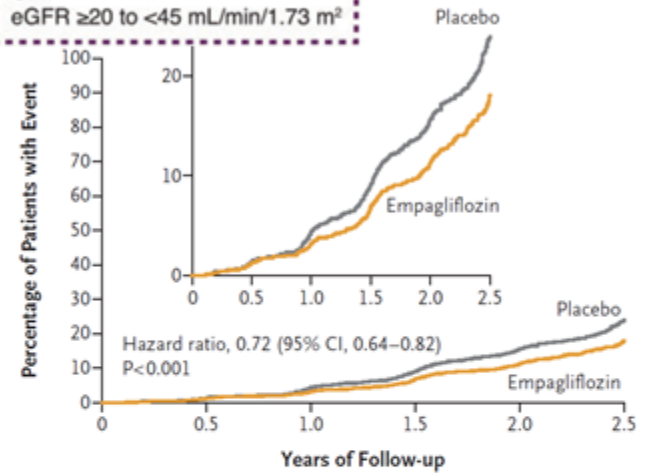
No. at Risk								
Placebo	2199	2178	2132	2047	1725	1129	621	170
Canagliflozin	2202	2181	2145	2081	1786	1211	646	196

DAPA-CKD (CKD)
eGFR ≥25 to <75 mL/min/1.73 m²
and UACR ≥200 mg/g



No. at Risk								
Placebo	2152	1993	1936	1858	1791	166	1232	774	270
Dapagliflozin	2152	2001	1955	1898	1841	170	1288	831	309

EMPA-KIDNEY (CKD)
eGFR ≥45 to <75 mL/min/1.73 m²
and UACR ≥200 mg/g
OR
eGFR ≥20 to <45 mL/min/1.73 m²



No. at Risk						
Placebo	3305	3250	3129	2243	1496	592
Empagliflozin	3304	3252	3163	2275	1538	624

The primary outcomes for all above studies were composite renal outcomes.

CREDENCE:	ESKD, CV or renal death, doubling serum creatinine*	HR **0.70** (95% CI, 0.59 to 0.82) ARR: 18 fewer events per 1000 patient-years
DAPA-CKD:	ESKD, CV or renal death, GFR decline ≥50%	HR **0.61** (95% CI, 0.51 to 0.72) ARR: 29 fewer events per 1000 patient-years
EMPA-KIDNEY:	ESKD, CV or renal death, GFR decline ≥40%	HR **0.72** (95% CI, 0.64 to 0.82) ARR: 21 fewer events per 1000 patient-years

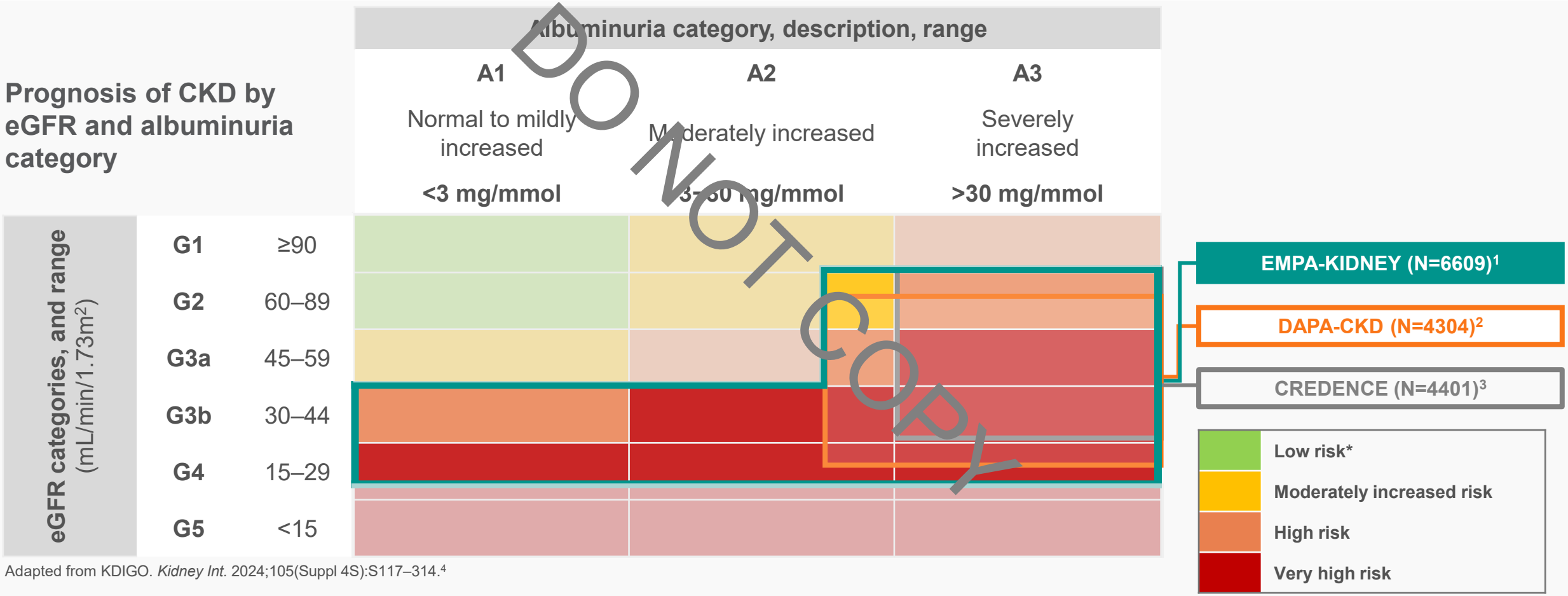
Studies have different populations, designs and endpoints so should not be directly compared.
Refer to source data for all ARRs and other detail.[1-4]

ARR: absolute risk reduction
HR: hazard ratio

1. Perkovic et al. 2019.
2. Heerspink et al 2020.
3. Herrington et al 2023.

* doubling serum creatinine is approximately equivalent to a GFR decline of 57% [Levey 2014]

SGLT2 inhibitor Primary Renal Trials



Adapted from KDIGO. *Kidney Int.* 2024;105(Suppl 4S):S117–314.[4]

***If no other markers of kidney disease, no CKD.[4] Unit conversions are approximate.**
CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; G: grade; SGLT2i: sodium-glucose co-transporter-2 inhibitor.

1. The EMPA-KIDNEY Collaborative Group. *N Engl J Med.* 2023;388:117–127; 2. Heerspink HJL *et al. N Engl J Med*. 2020;383:1436–1446; 3. Perkovic V *et al. N Engl J Med*. 2019;380:2295–2306; 4. KDIGO CKD Work Group. *Kidney Int.* 2024;105(4S):S117–314.

What are the key considerations when prescribing SGLT2is?

Indication	Educate the patient and inform primary care[1]
Hypoglycaemia	When used in combination with an SU or with insulin in T2D patients with HbA1c <58 mmol/mol AND eGFR >45 mL/min/1.73m^2,[1] UKKA recommend reducing the SU or insulin dose by 50% or 20%, respectively[2]
Volume depletion	Exercise caution in patients in whom a drop in blood pressure could pose a risk, such as patients with known CVD, patients on anti-hypertensive therapy with a history of hypotension or patients aged 75 years and older[1]

Please consult the Summary of Product Characteristics for further details regarding adverse events, monitoring requirements, contraindications and interactions prior to initiating empagliflozin.

CVD: cardiovascular disease; eGFR: estimated glomerular filtration rate; SU: sulphonylurea; T2D: type 2 diabetes; UKKA: UK Kidney Association.

1. Jardiance® (empagliflozin) Summary of Product Characteristics; 2. Roddick AJ *et al. BMC Nephrol*. 2023;24:310.

What are the key considerations when prescribing SGLT2is?

Urinary tract/genital infection

Highlight the need to maintain good personal hygiene

- Temporary interruption of empagliflozin should be considered in patients with complicated urinary tract infections

Fournier's gangrene

Rare (≥1/10 000 to <1/1000), but serious and potentially life-threatening; advise patients to seek medical attention if they experience a combination of pain, tenderness, erythema or swelling in the genital or perineal area, with fever or malaise

- If Fournier's gangrene is suspected, empagliflozin should be discontinued and prompt treatment should be instituted

Ketoacidosis

Counsel patients on sick-day guidance and ketoacidosis (including euglycaemic)

- In patients where ketoacidosis is suspected or diagnosed, treatment with empagliflozin should be discontinued immediately

Please consult the Summary of Product Characteristics for further details regarding adverse events, monitoring requirements, contraindications and interactions prior to initiating empagliflozin.
Jardiance® (empagliflozin) Summary of Product Characteristics.

Characteristics of finerenone & currently available MRAs[1]

Imperial College Healthcare NHS Trust

Characteristic[1]	Spironolactone	Eplerenone	Finerenone
Mineralocorticoid receptor class	Steroidal	Steroidal	Non-steroidal
Potency	High	Low	High
Selectivity	Low	Medium	High
Metabolites	Multiple active metabolites	No active metabolites	No active metabolites
Half-life	Long (≥24 h)	Medium to short (3-6 h)	Short (2-3 h)
Tissue distribution in rodents	Concentrated in the kidney (>6 : 1)	Concentrated in the kidney (3 : 1)	Balanced (1 : 1)

Finerenone is highly selective for the mineralocorticoid receptor, with no relevant affinity for the glucocorticoid , androgen, estrogen or progesterone receptors[2]

Finerenone has not been compared to currently available MRAs in phase 3 clinical trials
The clinical consequences of differences between the characteristics described is therefore unknown

1. Kolkhof P *et al*. Handb Exp Pharmacol 2017; 243: 271-305. 2. Frampton JE. Drugs 2021; 81(15): 1787-94.

FIDELIO - Primary Renal Composite Endpoint

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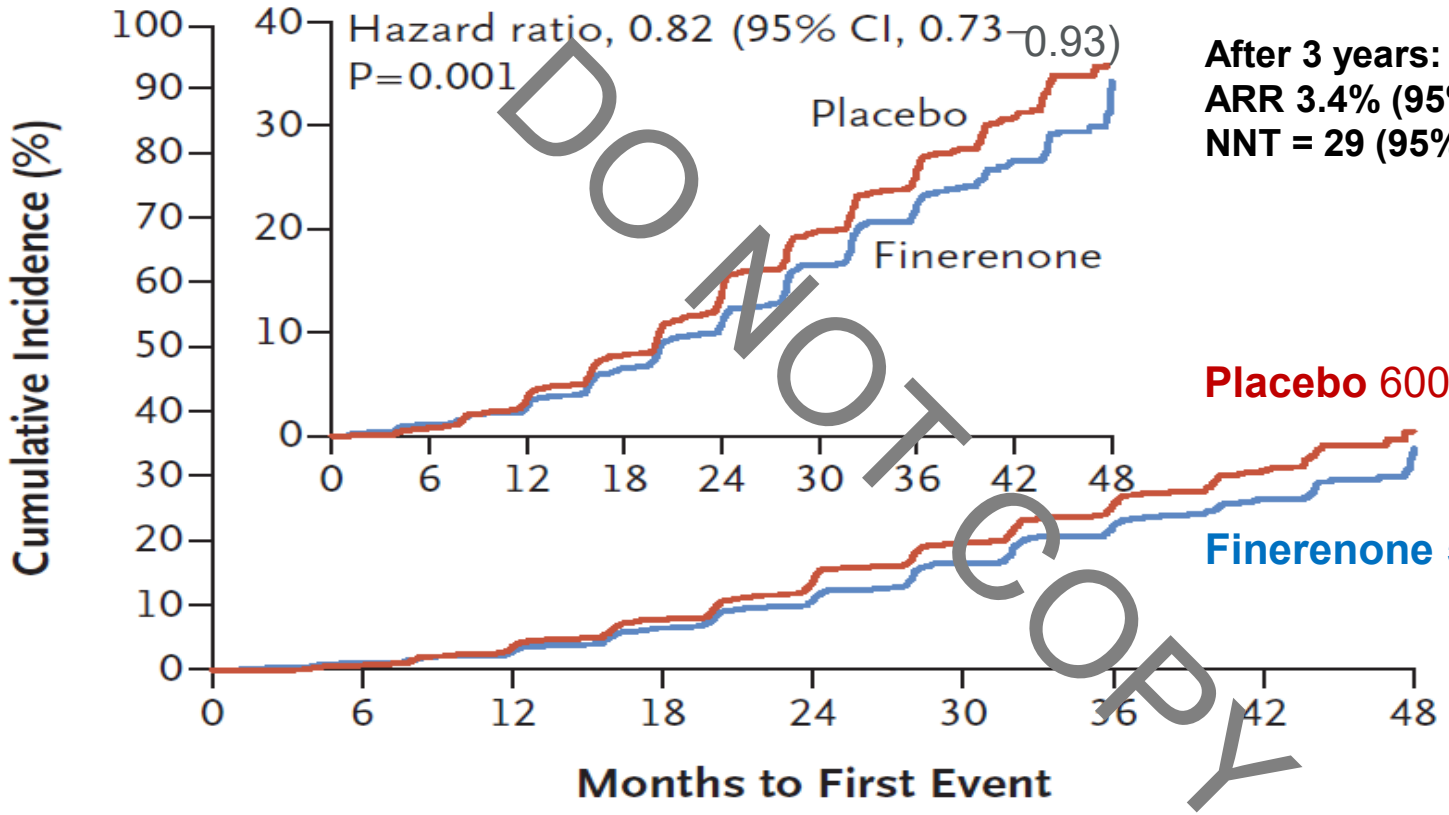
Kidney failure*, sustained ≥40% decrease in eGFR from baseline over a period of at least 4 weeks, or death from renal causes#



After 3 years:
ARR 3.4% (95% CI, 0.62-6.2)
NNT = 29 (95% CI 16-166)

Placebo 600/2841 (21.1%)‡

Finerenone 504/2833 (17.8%)‡

‡Median follow up 2.6 years

No. at Risk

Placebo	2841	2724	2586	2379	1758	1248	792	453	82
Finerenone	2833	2705	2607	2397	1808	1274	787	441	83

*ESKD or an eGFR <15 ml/min/1.73 m^2; #Events were classified as renal death if: (1) the patient died; (2) KRT had not been initiated despite being clinically indicated; & (3) there was no other likely cause of death;

ARR, absolute risk reduction; CI, confidence interval; ESKD, end-stage kidney disease; HR, hazard ratio; NNT, number needed to treat

Adapted from Bakris GL et al., N Engl J Med 2020; 383:2219-2229

Finerenone Initiation Criteria (NICE 2024)

- Adult patient
- Type 2 DM
- GFR 25 to 60
- Treated with an appropriate dose of ACEi/Ag2RB and SGLT2i or intolerant to one of these
- Persistent Albuminuria (ACR >3)
- K < 5

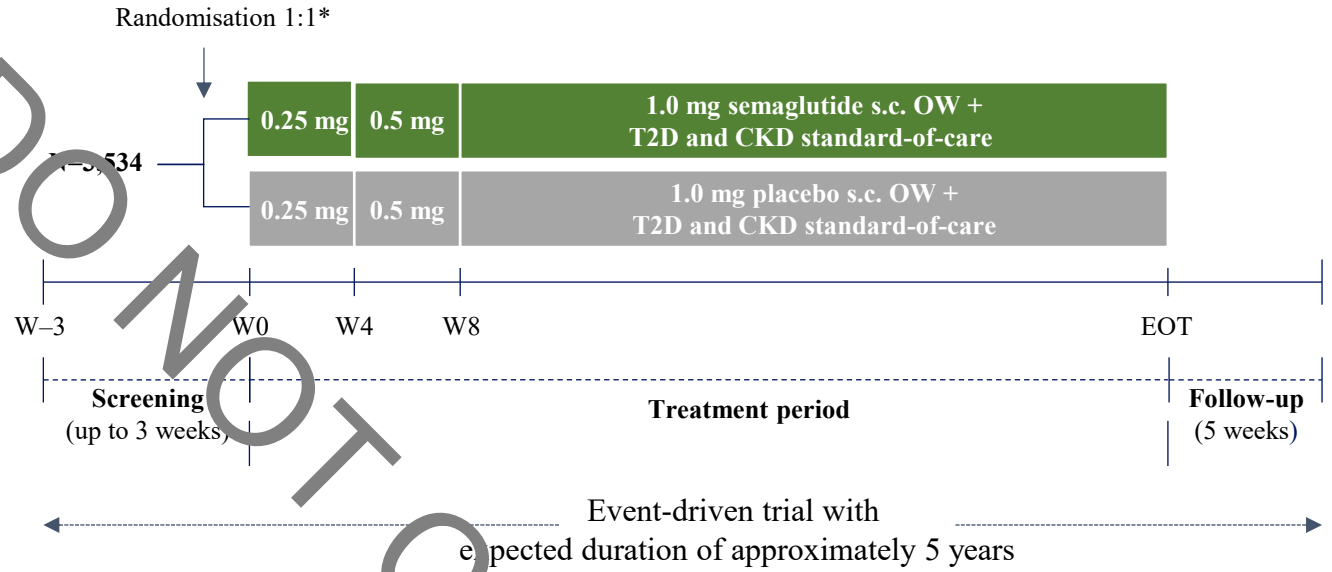
There is more coming down the line!

FLOW trial design

Adults with CKD and T2D

- Age ≥18 years†
- HbA_{1c} ≤10% (≤86 mmol/mol)
- eGFR ≥50 to ≤75 mL/min/1.73 m^2 and UACR >300 to <5,000 mg/g

  OR
- eGFR ≥25 to <50 mL/min/1.73 m^2 and UACR >100 to <5,000 mg/g
- On background RAAS blockade



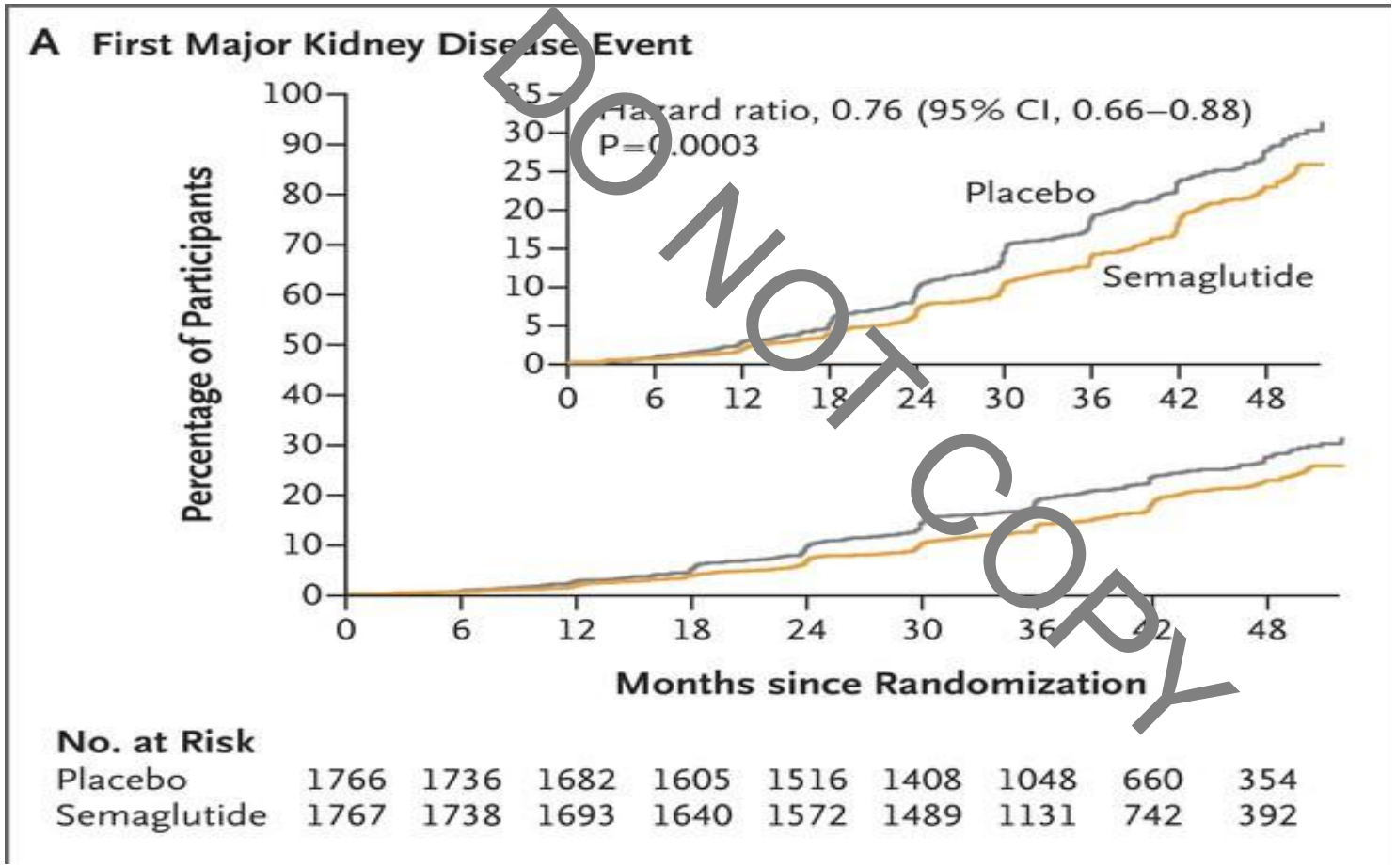
Trial information

- Randomised, double-blind, parallel-group, multinational phase 3b trial
- Eligibility criteria designed to select broad population with CKD and T2D and at risk for progression of CKD
- Number of participants with eGFR ≥60 mL/min/1.73 m^2 at randomisation was capped at 20% to ensure predominance of participants with moderate-to-severe CKD

Adapted from Figure 2.
*†≥20 years in Japan; *Stratified by sodium-glucose cotransporter-2 inhibitor use (yes/no).*
CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; EOT, end of treatment; N, number of participants; OW, once-weekly; RAAS, renin-angiotensin-aldosterone system; s.c., subcutaneous; UACR, urine albumin-to-creatinine ratio; W, week.
Rossing P et al. Nephrol Dial Transplant. 2023; https://doi.org/10.1093/ndt/gfad009

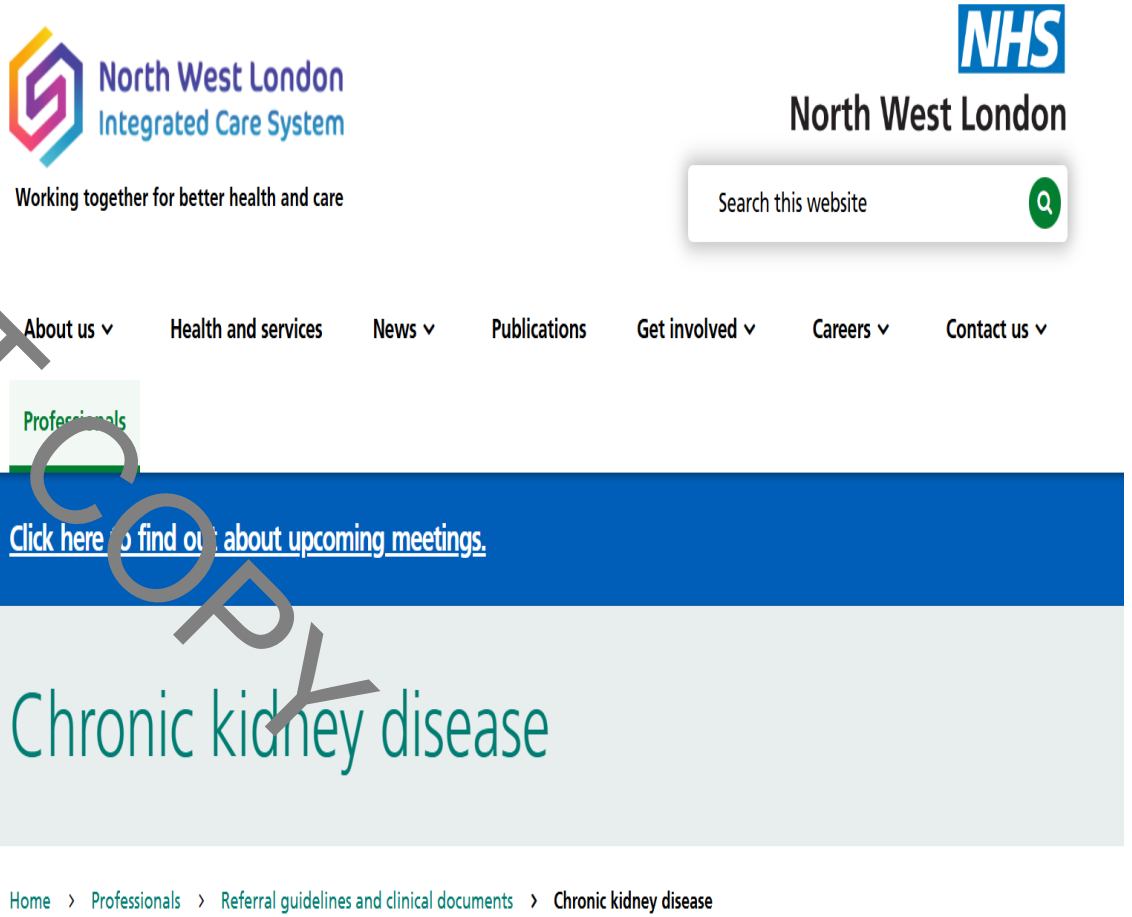
Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes

Imperial College Healthcare NHS Trust



Vlado Perkovi et al **Published May 24, 2024**
DOI: 10.1056/NEJMoa2403347

https://www.forkidneyssake.com/



www.nwlondonics.nhs.uk/ckdguidelines

Summary and Objectives

- The growth in CKD (driven by the increasing numbers of people with diabetic kidney disease) constitutes a major healthcare emergency
- Over the last 10 years there have been significant advances in relation to treatment of chronic kidney disease
- In this presentation I will provide a clearer understanding of
  - Who is at risk and who to screen
  - How to effectively and safely optimise the person with diabetes and CKD
  - Familiarise yourselves with resources available to support yourselves and your patients.