# **CKD 2024**

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# Dr Andrew Frankel Declarations



- Receipt of research grants
- Preparation of educational materials
- Attendance at drug advisory boards
  - Boehringer Ingleheim
  - Lilly
  - Astra Zeneca
  - NAPP
  - VP UK
  - Bayer
  - GSK



# **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 has been significant advances in relation to the medical treatment of chronic kidner disease
- New treatments will provide little benefit unless they are effectively rolled out and utilised to intervene early in the course of DKD.
- This healthcare challenge requires a significant change in the way that we design and deliver healthcare around individuals with diabetic kidney disease.

# '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

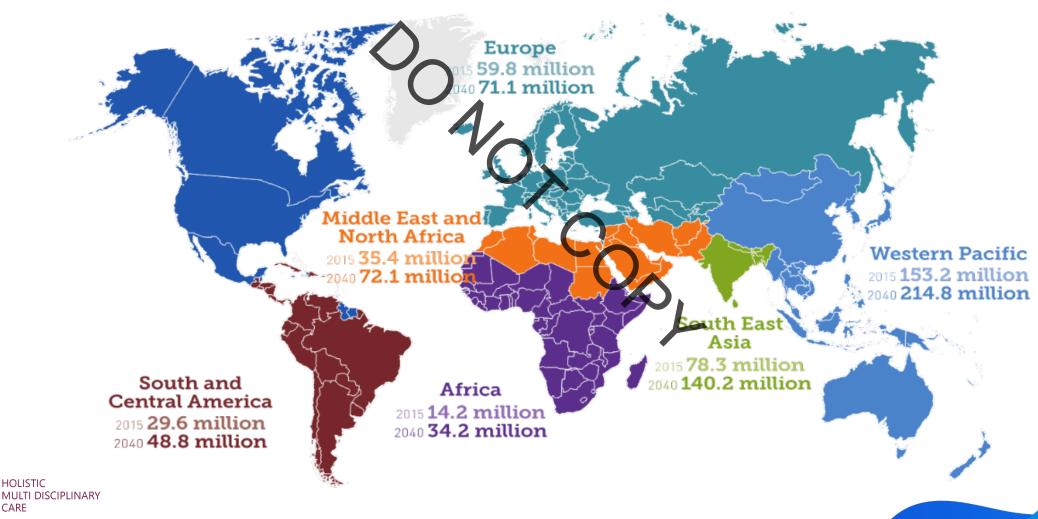


Total annual UK economic burden of kidney disease is £7 billion; this cost could nearly double over the next 10 years, largely driven by increasing demand for dialysis\*

CKD: chronic kidney disease.

<sup>\*</sup>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.

# Global estimates of diabetes

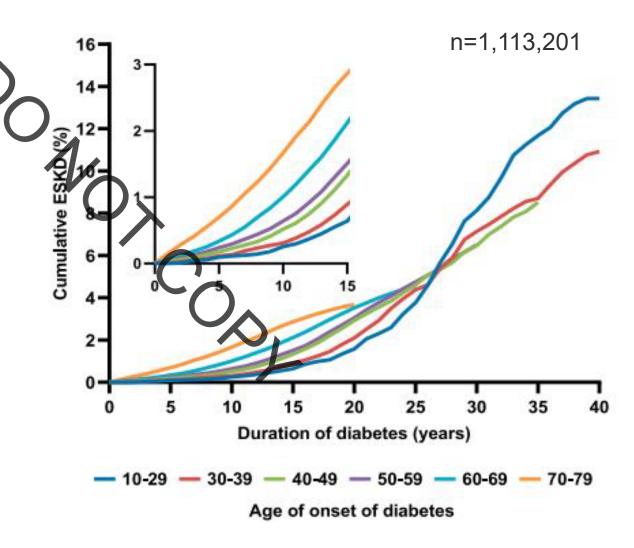




# Age of onset of T2DM and long-term risk of ESKD

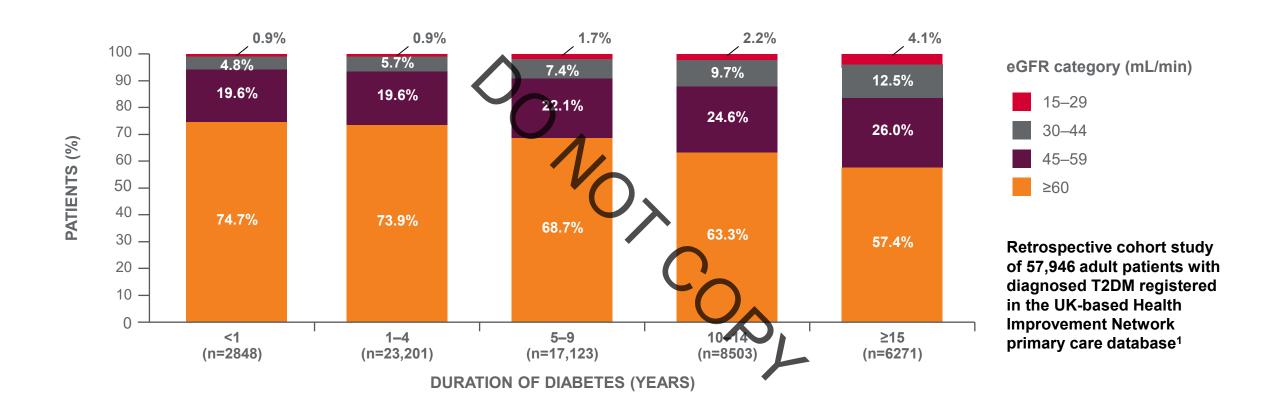
#### **Treated and untreated ESKD**

- Cumulative incidence of ESKD by duration of T2DM stratified by age of onset of diabetes
- Inset shows the first 15 years of diabetes



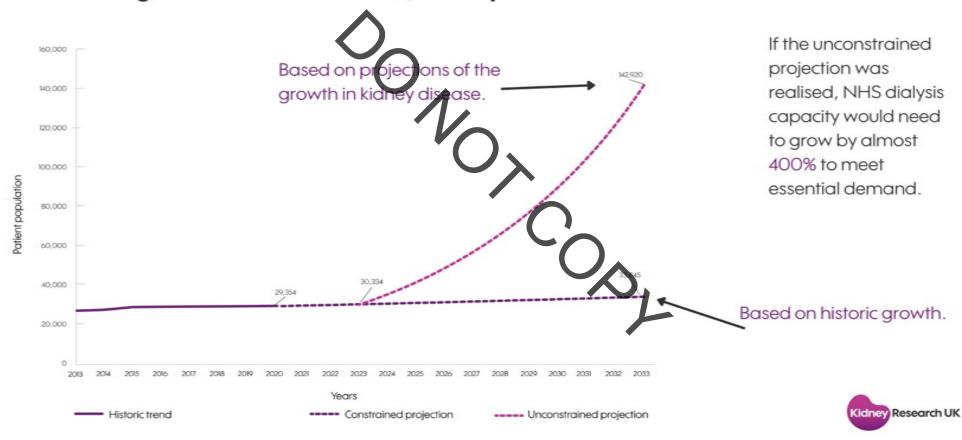


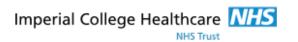
# Renal decline with duration of T2DM



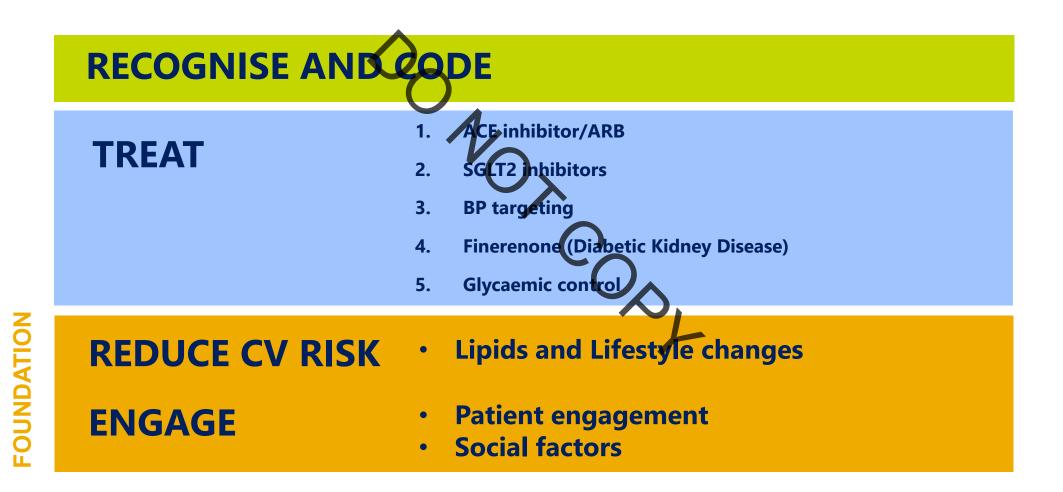
A longer duration of type 2 diabetes is associated with a lower eGFR<sup>1</sup>

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.





# Management of CKD: 2024



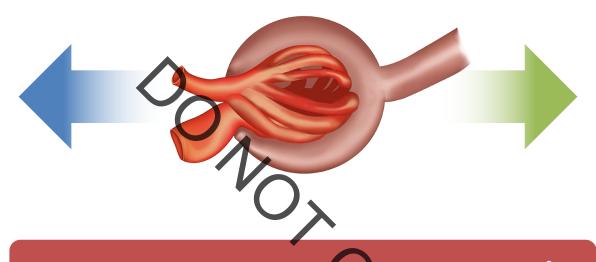




#### Reduced eGFR

Creatinine clearance is reduced





eGFR is an important indicator of CV risk and progression<sup>2</sup>
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

#### Albuminuria

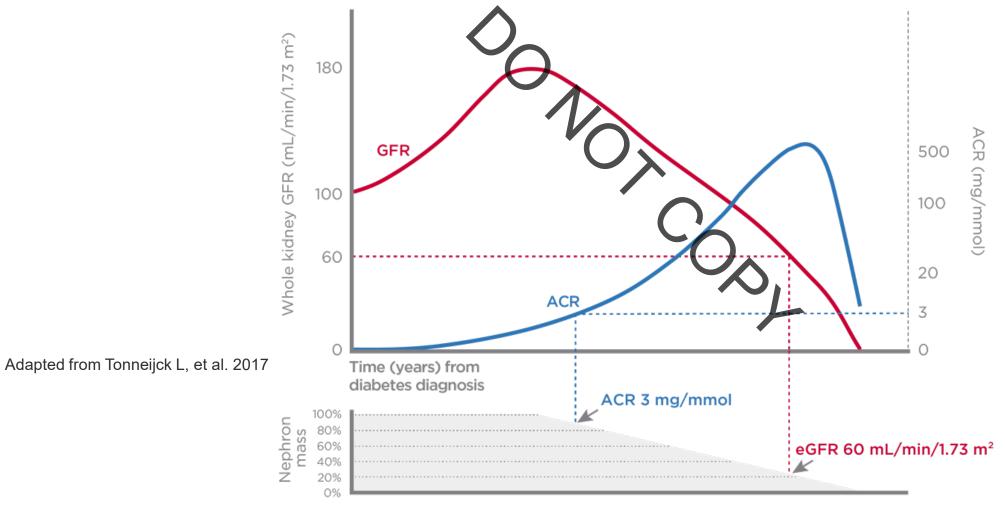
Protein leaks through glomerular basement membrane<sup>1</sup>







# **ACR** testing can detect early signs of Diabetic Kidney Disease(DKD) before England significant nephron loss has occurred - why wait?



#### Imperial College London



# **CKD Annual Screening Summary : Patients with Clinical Risk** factors in 2010 screened annually for CKD

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Fully CKD screening : uACR\_eGFR\_Urine dip

eGFR alone

uACR\_+ eGFR

Partially screened : uACR alone

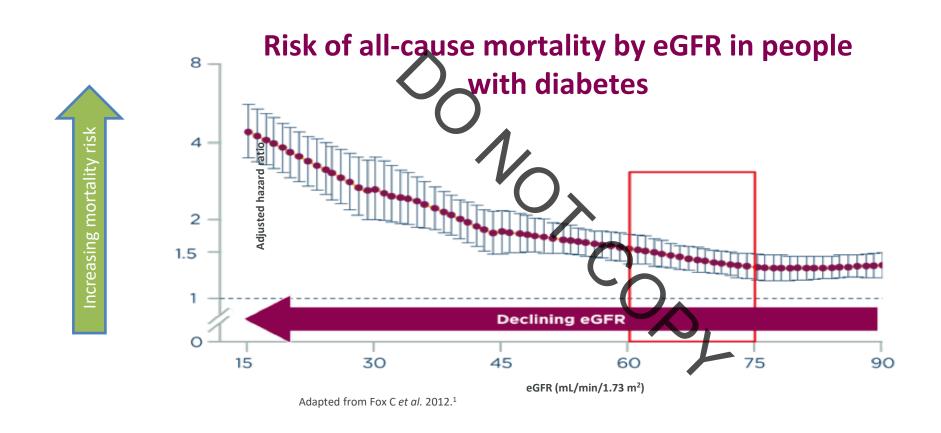
Urine Dip alone

eGFR + Urine dip

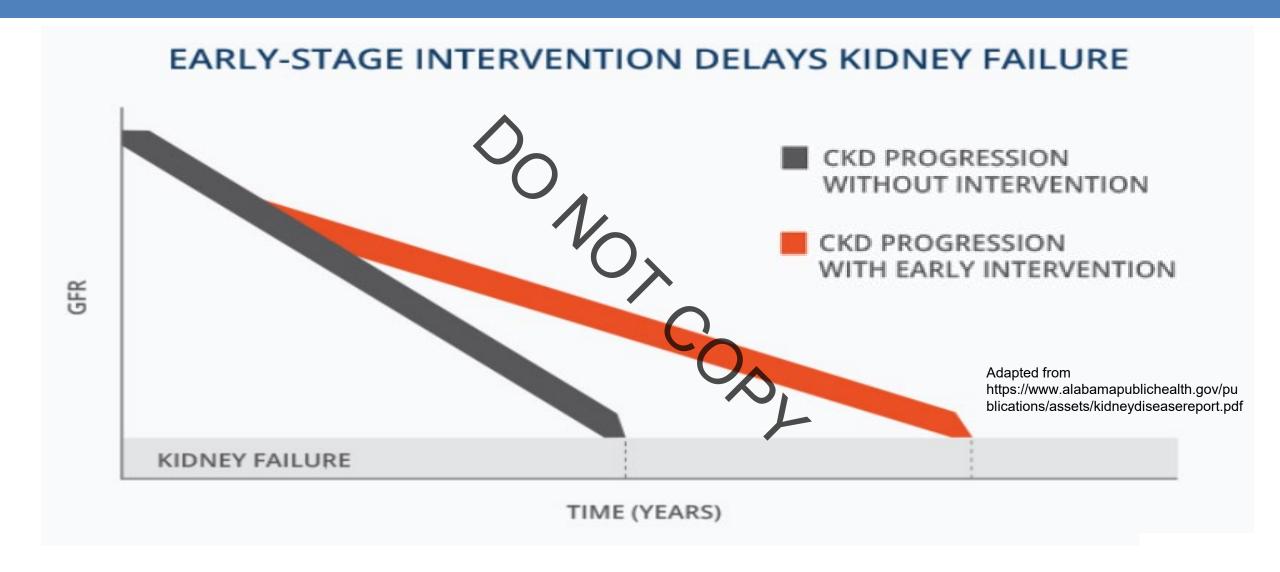
# How early is early



# In diabetes, even a modest decline of eGFR (≤75 mL/min/1.73 m2) is associated with an increased risk of death¹



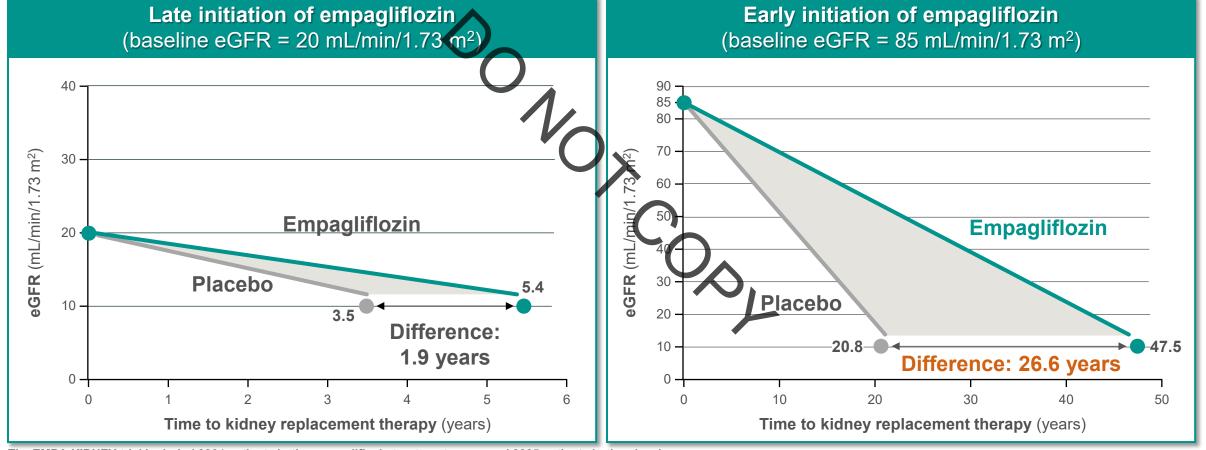
## The earlier the intervention the greater the benefit accrued over time



## EARLY intervention with empagliflozin is key for patients with CKD

Potential impact on time to kidney replacement therapy compared to placebo with early and late initiation of empagliflozin in the EMPA-KIDNEY trial

(Extrapolated data from the EMPA-KIDNEY trial. Based on hypothetical transformation of chronic eGFR slopes into time to kidney failure, defined as eGFR = 10 mL/min/1.73 m<sup>2</sup>)



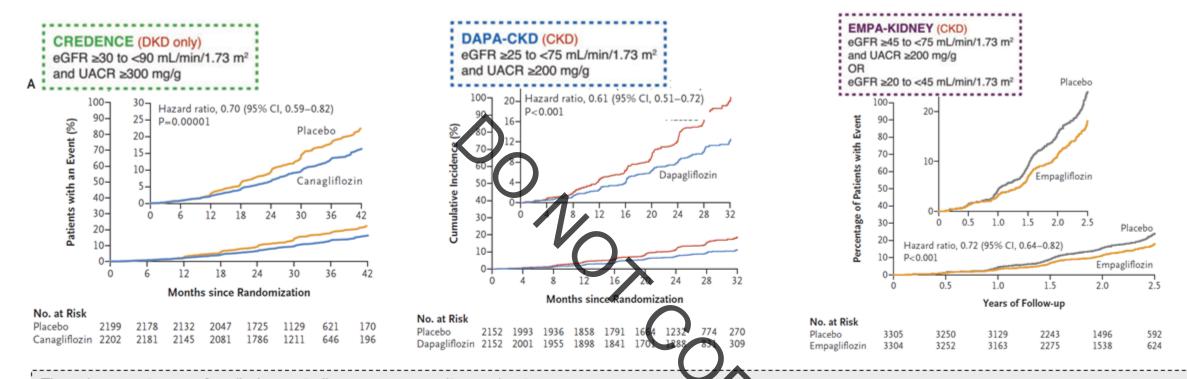
The EMPA-KIDNEY trial included 3304 patients in the empagliflozin treatment group and 3305 patients in the placebo group.

Graphical representation of representative chronic eGFR slopes from baseline to kidney failure, i.e., to the need for kidney replacement therapy. Hypothetical lines have been traced starting from extremes of the baseline eGFR inclusion criteria values (20 and 85 mL/min/1.73 m²) to eGFR 10 mL/min/1.73 m², corresponding to chronic eGFR slopes of participants on placebo and on empagliflozin within each baseline eGFR subgroup.

CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate.

Fernández-Fernandez B, et al. Clin Kidney J. 2023;16(8):1187-1198.

## Renal Outcomes Trials – primary cardiorenal outcomes



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

CREDENCE:

DAPA-CKD: ESKD, CV or renal death, GFR decline ≥50%

EMPA-KIDNEY: ESKD. CV or renal death. GFR decline ≥40%

ESKD, CV or renal death, doubling serum creatinine\* HR 0.70 (95% Cl, 0.59 to 0.82) ARR: 18 fewer events per 1000 patient-years

HR <u>0.61</u> (95% CI, 0.51 to 0.72) ARR: 29 fewer events per 1000 patient-years

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

Perkovic et al. 2019.

<sup>2.</sup> Heerspink et al 2020.

Herrington et al 2023

#### **UKKA Guideline: SGLT-2i and Kidney Disease Update 2023**

# UK Kidney Association

# QUICK REFERENCE GUIDE FOR IMPLEMENTATION IN PEOPLE WITH CKD WITH OR WITHOUT TYPE 2 DIABETES

SGLT-2 inhibition t		Urinary Albumin-to-creatinine ratio (mg/mmol)			
cardiovascu		<25	≥25		
	≥60	†	Recommended		
	≥45 <60	Suggested (in type 2 diabetes)	Recommended		
eGFR (mL/min/1.73m²)	≥20 <45	Recommended	Recommended		
	<20	Suggested	Suggested		
	Dialysis	Not recommended‡	Not recommended‡		

<sup>\*</sup> People with type 1 diabetes, polycystic kidney disease, or kidney transplant excluded from the definitive trials.

<sup>†</sup> In this guideline we do not make recommendations on the use of SGLT-2 inhibition to reduce kidney disease progression for people with eGFR ≥60 mL/min/1.73m² and uACR <25 mg/mmol as this is outside the scope of this guideline. However, we support the use of SGLT-2 inhibitors in this population for relevant indications, including treatment of people with heart failure and reduction of cardiovascular risk in people with type 2 diabetes at high cardiovascular risk. 

‡ We recommend further research in people on kidney replacement therapy to establish the role of SGLT-2 inhibition in these populations.

## What do we need to consider when prescribing an SGLT2i?



#### Indication

Educate the patient on the indication that the SGLT2i is being prescribed for



#### Hypoglycaemia

When used in combination with a sulphonylurea or with insulin, a lower dose of the sulphonylurea or insulin may be considered to reduce the risk of hypoglycaemia



#### **Volume depletion**

• Exercise caution in patients in whom a drop in blood pressure could pose a risk, such as patients with known cardiovascular disease, patients on anti-hypertensive therapy with a history of hypotension or patients aged 75 years and older

## What do we need to consider when prescribing SGLT2i?



#### **Urinary tract infection/genital infection**

Highlight the need to maintain good personal hygiene



#### **Ketoacidosis**

- Counsel patients on sick-day guidance and ketoacidosis (including euglycaemic)
- Advise patients not to start low carbohyd ate or ketogenic diets

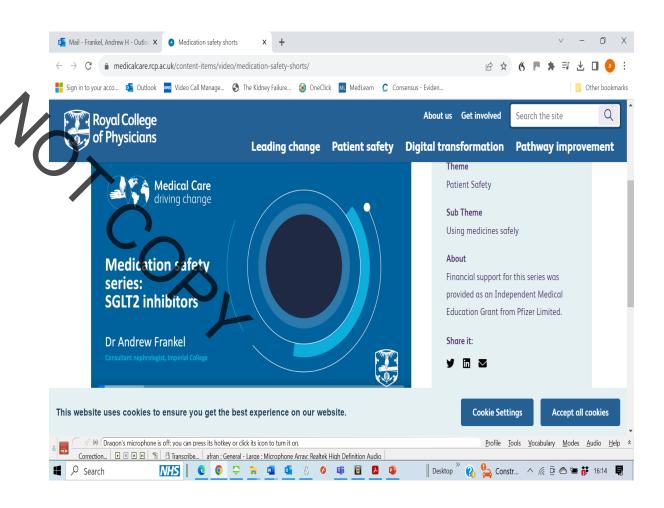


#### Fournier's gangrene

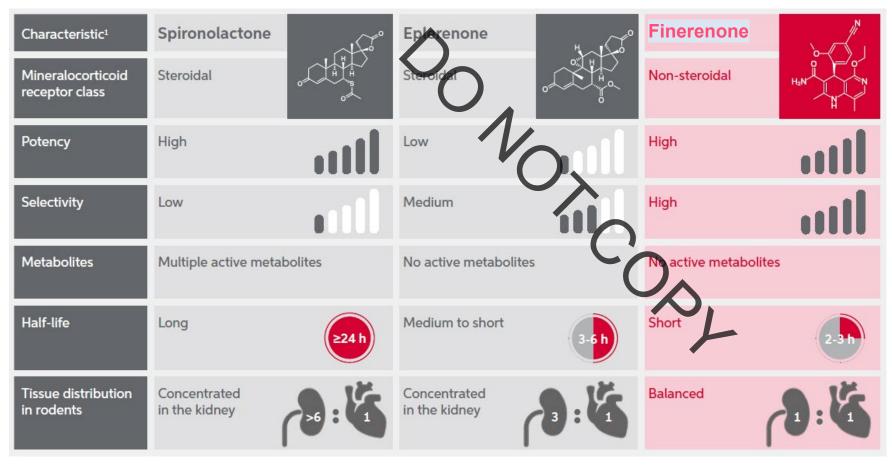
- Rare, but serious and potentially life-threatening
- Advise patients to seek medical attention if they experience a combination of pain, tenderness, erythema or swelling in the genital or perineal area, with fever or malaise

# RCP Medication safety shorts SGLT2 inhibitors

 https://medicalcare.rcp.ac.uk/contentitems/video/medication-safety-shorts/



# Characteristics of finerenone & currently available MRAs<sup>1</sup>



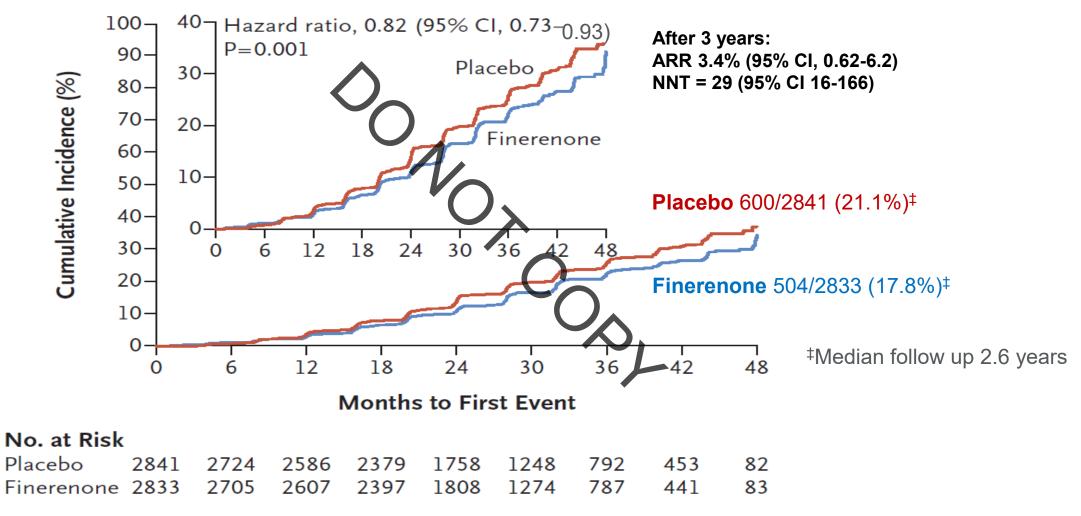
Finerenone is highly selective for the mineralocorticoid receptor, with no relevant affinity for the glucocorticoid, androgen, estrogen or progesterone receptors<sup>2</sup>

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

## **FIDELIO - Primary Renal Composite Endpoint**

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



<sup>\*</sup>ESKD or an eGFR <15 ml/min/1.73 m<sup>2</sup>; \*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

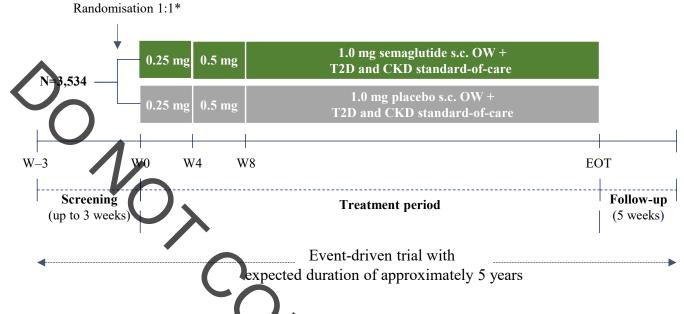
**FLOW trial design** 

#### Adults with CKD and T2D

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

#### OR

- eGFR  $\ge$ 25 to <50 mL/min/1.73 m<sup>2</sup> and UACR >100 to <5,000 mg/g
- On background RAAS blockade



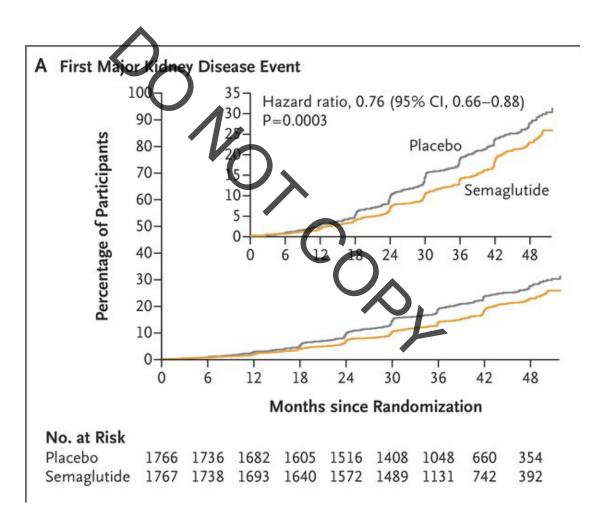
#### **Trial information**

- 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 m² at randomisation was capped at 20% to ensure predominance of participants with moderate-to-severe CKD

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

Authors: Vlado Perkovi et al Published May 24, 2024

DOI: 10.1056/NEJMoa2403347



#### Imperial College London



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Urine Dip alone

eGFR + Urine dip

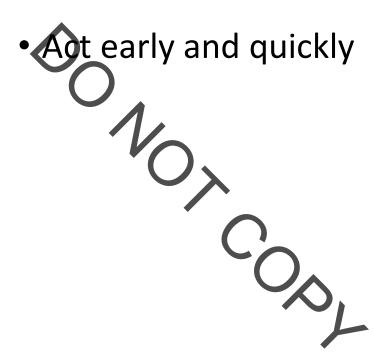
# **Solutions**



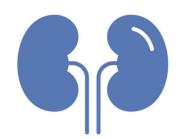


# **Solutions**

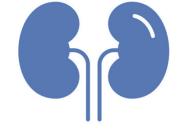








# The London Kidney Network initiative





#### 3 key actions within 3 months to save lives (3in3)

**LKN CKD Optimisation Pathway** 

## In adults with Type 2 diabetes and CKD

GFR 20-90ml/min







London Kidney Network, June 2024

#### **ACTION 1 (Month 1)**

Maximum intensity RAS/ RAAS blookade

Start ACE-inhibitor or ARB and titrate to maximum tolerated licensed dose (NICE, NG203) within one month. Ensure the patient is on a high intensity static, unless contraindicated.

#### **ACTION 2 (Month 2)**

**Initiate SGLT-2 inhibitor according to license** 

Consider/ counsel on risks of diabetic ketoacidosis (which may be euglycaemic), sick day rules, risk of UTI/fungal infections. Consider adjusting sulfonylureas/insulin where eGFR >45ml/min and HbA1c < 58mmol/mol to mitigate risk of hypoglycaemia.

#### **ACTION 3 (Month 3)**

Initiate further blood pressure agent to target 140/90mmHg unless uACR >70mg/mmol (then 120-129/80mmHg).

If BP remains above target initiate 2<sup>nd</sup> line BP agents as per NICE guidance (*NG203/NG136*)

In patients with GFR 25-60ml/min, uACR>3mg/mmol and potassium<5mmol/l; consider Finerenone as add on therapy

# **Solutions**



- Step out of your comfort Zone
- Support Primary Care

# **Discover-NOW program**

Over the past 10 years, there has been considerable work undertaken to integrate CKD management between primary and secondary care: nowever, a step change was recognized to be necessary.

The Discover-Now program was designed to:

#### **UNDERSTAND**

The current pathway for the management of people with CKD in North West London

The barriers that prevent optimal management for those at risk of or with CKD

#### **PRODUCE**

Utilities that support primary care in circum, coding, optimization, and the activation and education of those living with CKD

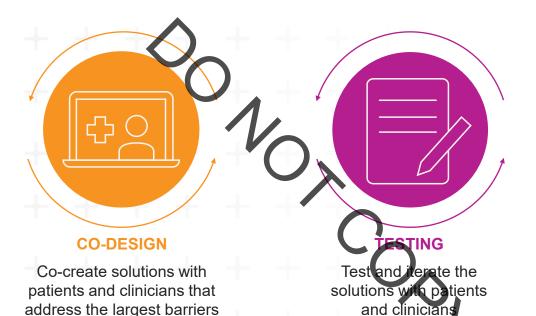




# Discover-NOW used a multidisciplinary approach to address the primary care pathway challenges impacting patient care



Map the current CKD pathway to identify barriers to identification and optimization



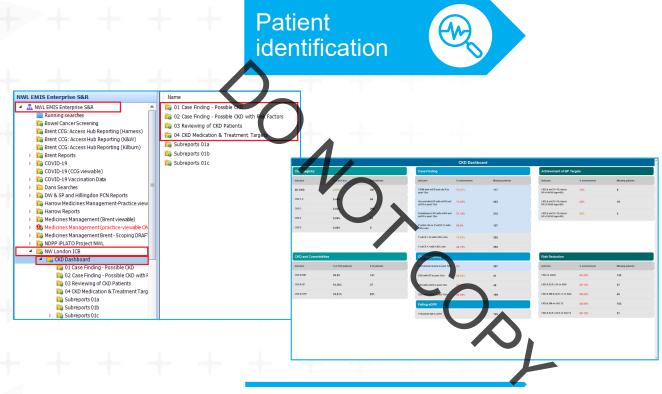


Roll out the solutions to primary care and evaluate their impact

Analysis of screening, coding, and management practices over past 10 years using Discover-NOW dataset



# The North West London CKD toolkit for primary care and patients



Priority patient EPR searches | 45 PCNs

Population health and patient-level dashboard 27 PCNs





The North West London CKD toolkit for primary care and patients

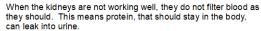
Jersian 2 published 183 24 Review 2027

#### The Urine ACR Test **Checking Kidney Health**

There are two tests that detect chronic kidney disease (CKD): eGFR blood test and urine Albumin Creatinine Ratio (ACR) test This leaflet is about the urine ACR test

#### What iobs do our kidneys do?

The job of our kidneys is to filter waste products and extra water from our bodies, which produces urine.





#### What does a urine ACR test show?

Testing urine will show us if there is any protein leakage which would be a sign that the kidneys are not working as well as they should. This can happen even if the kidney function test (blood test) is normal.

#### How often should I be having these tests?

If you have any of the conditions below, you should have your urine tested at least once a year or as advised by your doctor.

This is because these conditions put you at higher risk of developing chronic kidney disease:

- Type 2 diabetes
- Heart failure
- ☐ High blood pressure ☐ Family history of kidney disease



#### The urine ACR test – what to do step by step

- (1) Collect a urine sample pot from your GP practice.
- (2) Take a sample of your urine. An early morning urine sample is best if possible.
- (3) Ensure the pot is labelled with your name, date of birth and the date the sample was taken
- ig(4ig) Return the urine sample to your GP practice reception on the same day

If you have any further questions, please contact your GP practice



Practice staff UACR training video

Patient information leaflet

Patient-designed text message



The North West London CKD toolkit for primary care and patients

CKD Education kit V2. Pub 0 2/20 24 Rv 0 3/2027 Page 4/4 Comms Ref 930

Imperial College Healthcar



#### Know your kidneys

"Know your kidneys" is an interactive group video call for people living with chronic kidney disease (CKD). The session will help you to understand CKD and gain confidence to manage your health. To access the session, you have a session will be considered to the confidence of the c "Know your kidneys" is an interactive group video call for people living with will need either a desktop computer, laptop, iPad or phone, and either Chrome or Safari internet browser. You will also need your NHS number, if you don't know it find out on https://www.nhs.uk/nhs-services/online-

#### Step by step guide to register and join "KNOW YOUR KIDNEYS"

#### How to register

Step 1 Scan the QR code above. Alternatively, type the following link in your browser https://www.nwlondonics.nhs.uk/CKD. This will open the chronic kidney disease page where you can register for the session and access further education materials (videos, leaflets and booklets) available in different languages.

Step 2 Under the green tab "Register to know your kidneys education session" chose the date most convenient for you to attend by clicking "register here" next to the chosen date.

Step 3 After selecting your preferred date a registration page will open. Please fill in the details: patient's name, email address and NHS number. When you have filled in your details click the 'Register now' button.

Step 4 You are now registered. Next, log in to your email account and confirm that you have received an email invitation to the online session. The email will be sent from Microsoft Teams

#### How to join

Step 1 Log in five minutes before the session starts. Open the invitation in your email and

Step 2 A new window will open asking "how do you want to join your TEAMS meeting?". Click 'Continue on this browser.

Step 3 You now have access to the session. During the session, if you want to ask a question, please click the hand icon, or alternatively you can type your question into the chat box.

#### Chronic kidney disease educational videos

What causes CKD?

CKD: what should Leat?

CKD:: what are the treatments?















Primary care referral route to virtual education session

CKD education pack

Automated coding guidance from pathology labs | 31 PCNs



#### **What is Chronic Kidney Disease?**



Chronic Kidney Disease (also called CKD) is a long-term condition where the kidneys do not work as well as they should.

With CKD, waste products can build up in the body and the kidneys may also leak blood and protein into your urine (wee). CKD is mostly caused by high blood pressure and diabetes - there are other causes which you may need to discuss

In most cases, a new CKD diagnosis has no symptoms. However, CKD does increase the risk of cardiovascular disease, such as heart attack and stroke.

Many people with CKD can live normal lives. Although kidney damage cannot be reversed, it will not worsen for many people, particularly if caught and managed well at an early stage. However, it is worth bearing in mind that a small number of patients will need a kidney transplant or dialysis.

#### What can I do to help stop CKD from getting worse?



Make sure you have your blood pressure, urine and blood checked as often as your GP or nurse recommends.



Speak with your doctor or pharmacist to understand what your medication is for and how to take it



Stop smoking



Try to be active - even a little exercise helps



Eat a healthy diet that is low in salt

#### Where can I find out more information about CKD?

- ✓ www.londonkidneynetwork.nhs.uk/preventing-progression
- ✓ www.kidneycareuk.org information (different language options) and support
- ✓ www.kidney.org.uk information and support

If you have any further questions, please contact your GP practice







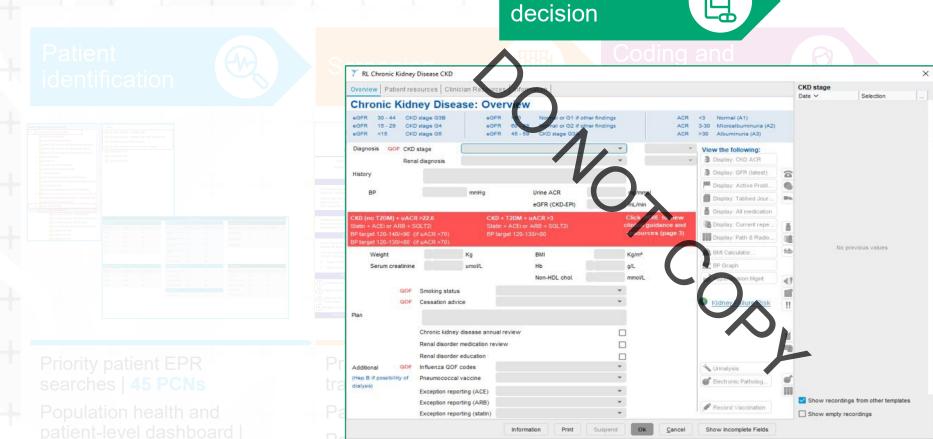


Champion:

Change

The North West London CKD toolkit for primary care and patients

Treatment



Review template for patients 31 PCNs with CKD and comorbidities | 45 PCNs



# **Solutions**



- Make Friends
- Work together around the patient

# Cardiorenal-metabolic care – the problem

- Care for people with CVD, renal and diabetes is too frequently siloed
- Focus on advanced disease rather than earlier intervention
- Individuals with CRM disorders attend multiple clinics in primary and/or secondary care
- Inefficiency
  - Duplication of effort and resources
  - Patient fatigue
  - Education focussed on individual disorders rather than on the combined disorder

CVD

RENAL

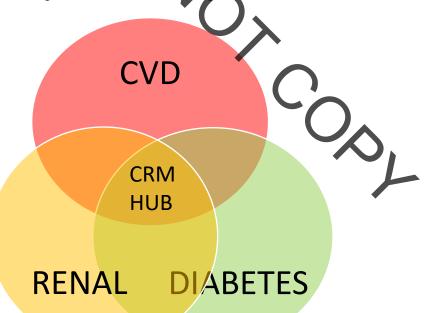
DIABETES



# Cardio-renal metabolic hub — The NWL Model

- The aim is to prevent onset and prevent progression of additional longterm conditions for patients with a diagnosis of one condition
- Establish a community-based multidisciplinary hub

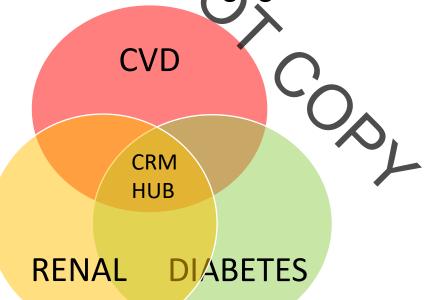
• Integrated care – primary, secondary and community clinicians





# Cardio-renal metabolic hub - Foundation

- Build on agreed clinical pathways
- Implemented by a Multiprofressional Multidisciplinary Workforce
- Efficient and Effective Secondary Care Support (21st Century)
- Embed Education, Activation and Engagement within Hub





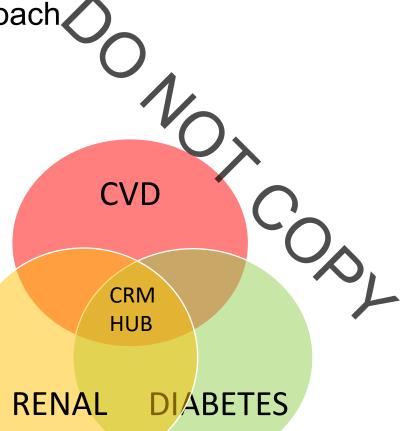
# Cardio-renal metabolic hub – Delivery Tools

Time for consultation

Health Coaching approach

Expert patients

Social prescribing





## Cardio-renal metabolic hub – Outcomes

#### For Individuals with the disorder

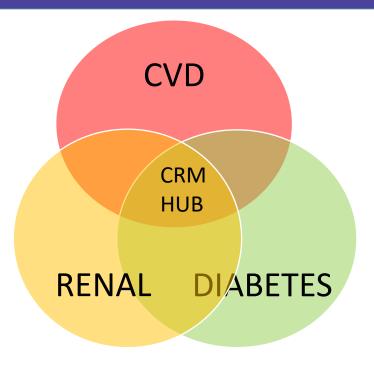
 Altered disease trajectory - prevent the development of a second condition for those already diagnosed with diabetes, CKD or a CVD condition

#### For organisations

- Satisfied clinicians
- Increased efficiency better utilisation of resources
- Financial savings due to efficiencies
- Increased clinician skills and broadening in thinking (i.e. multiple T conditions)

#### For the health system

- Reduced demand on secondary care due to patients managing their conditions earlier in the pathway
- Increasing individuals to stay in work or return to work
- Decrease in long term cost of healthcare
- Reduced demand on in- centre haemodialysis (3Ps)







# **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 has been significant advances in relation to treatment of chronic kidney disease
- New treatments will provide little benefit unless they are effectively rolled out and utilised to intervene early in the course of DKD.
- This healthcare challenge requires a significant change in the way that we design and deliver healthcare around individuals with diabetic kidney disease.