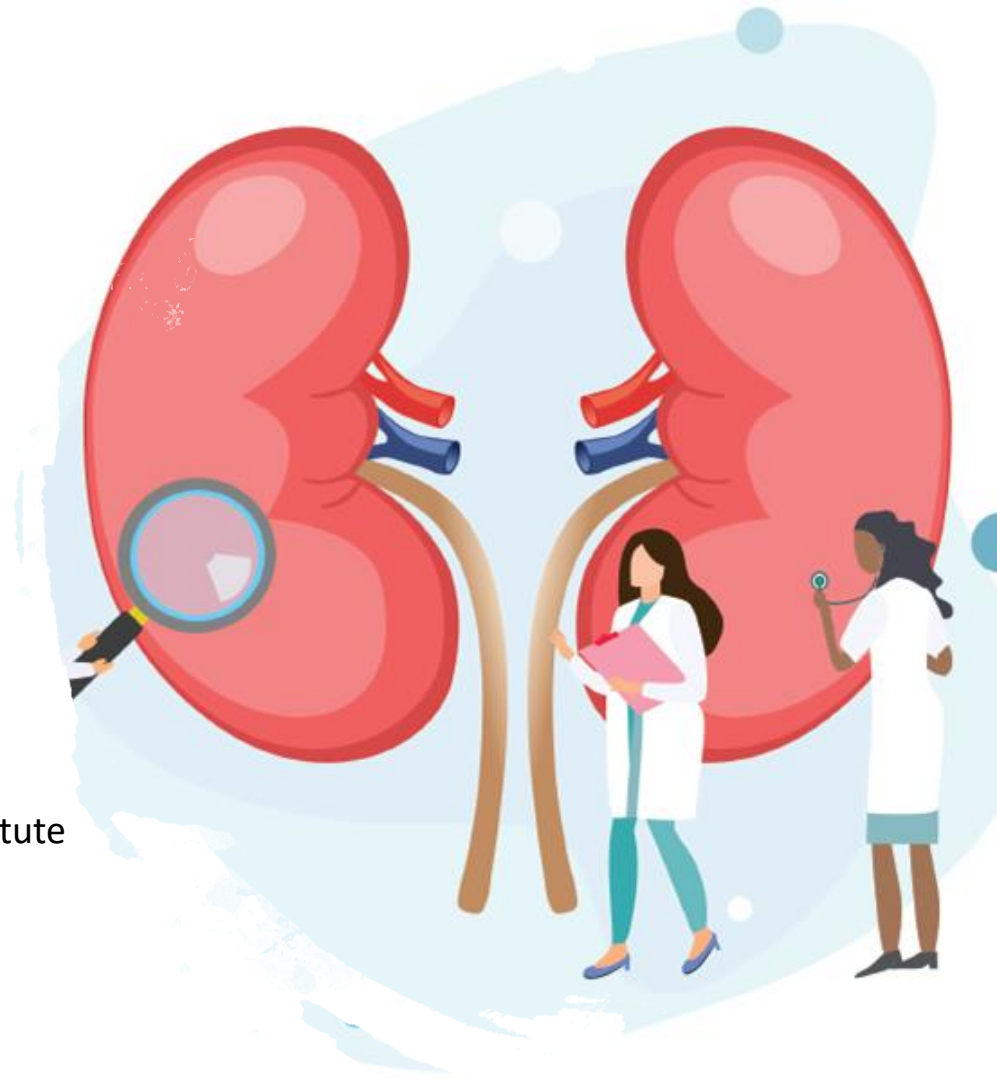


# CKD – teaching update

Dr Pann Ei Hnyinn Si (MRCP, PhD)  
Consultant Nephrologist, Sheffield Kidney Institute  
Honorary Clinical Lecturer (SCHARR)  
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# Outline

- Why is CKD important
- CKD classification and how to approach patient
- KFRE
- CKD Management
- Cases



# Why is CKD important?

## Epidemiology of chronic kidney disease: an update 2022

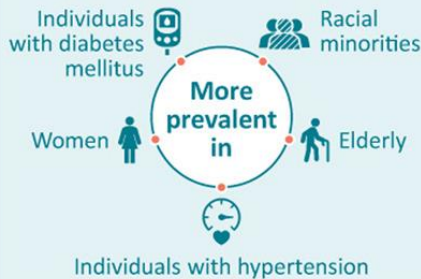
**kidney**  
INTERNATIONAL  
supplements



Extremely common

**843,6** Million  
in 2017

Approximately **1 in 10**



Increasing death rate

**+41.5%** 1990 to 2017



Rank in cause of death

**Large burden** in  
low- and middle-income countries



Among the **top 10 causes** of death  
in Singapore, Greece, and Israel

Kovesdy, 2022

### CONCLUSION

Chronic kidney disease (CKD) occurs frequently and has devastating consequences. This should prompt major efforts to develop preventative and therapeutic measures that are effective. The aim of these measures should be lowering the incidence of CKD and slowing its progression.

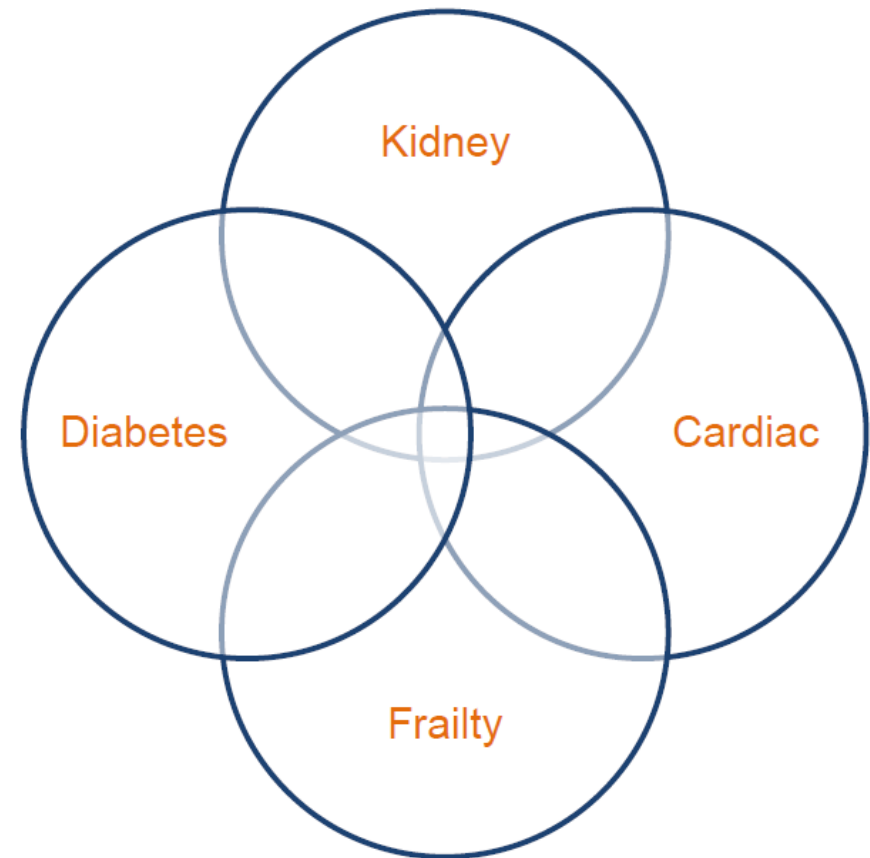


# CKD rarely in isolation

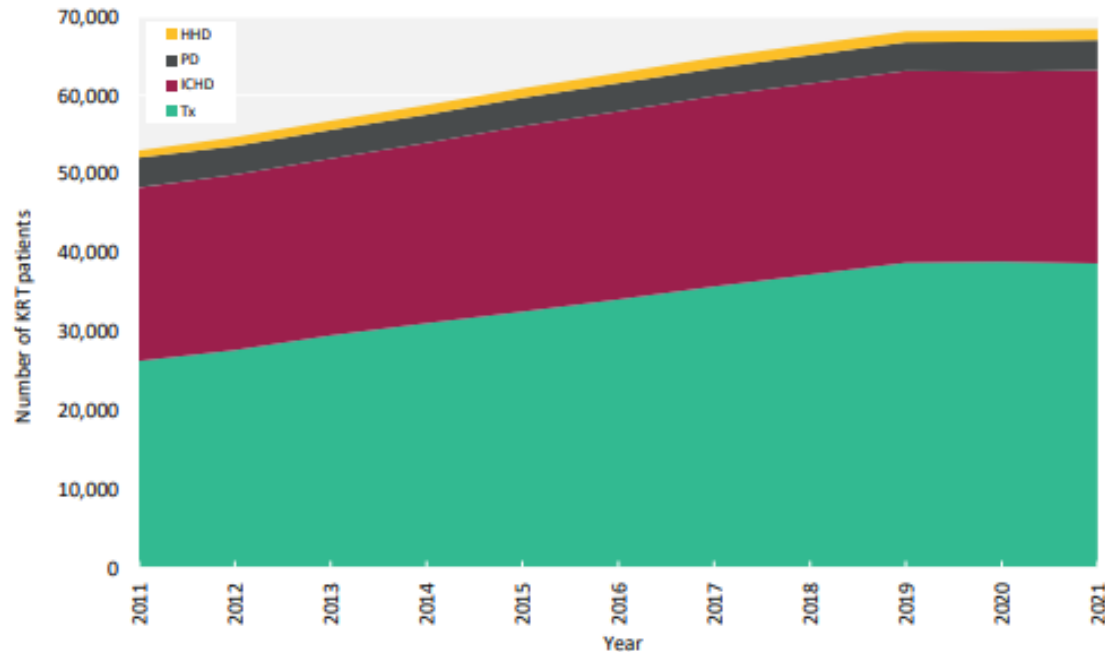
**6%** overall population prevalence with a focus on management, not prevention

**Referrals outside of NICE guidelines and low discharge rates back to primary care**

**80%** of patients have three or more significant co-morbid diagnoses

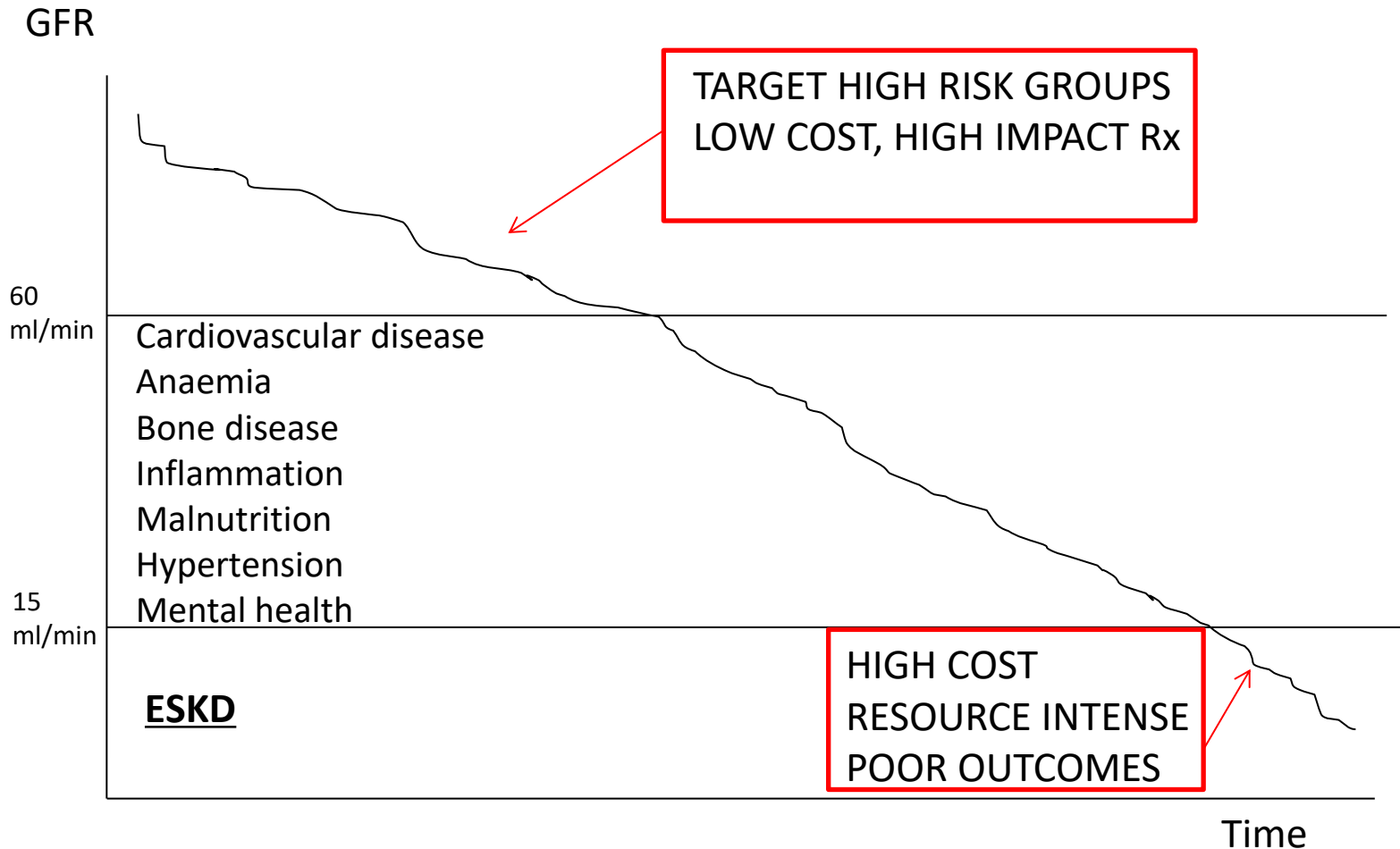


# How common is Renal Replacement Therapy in the UK?

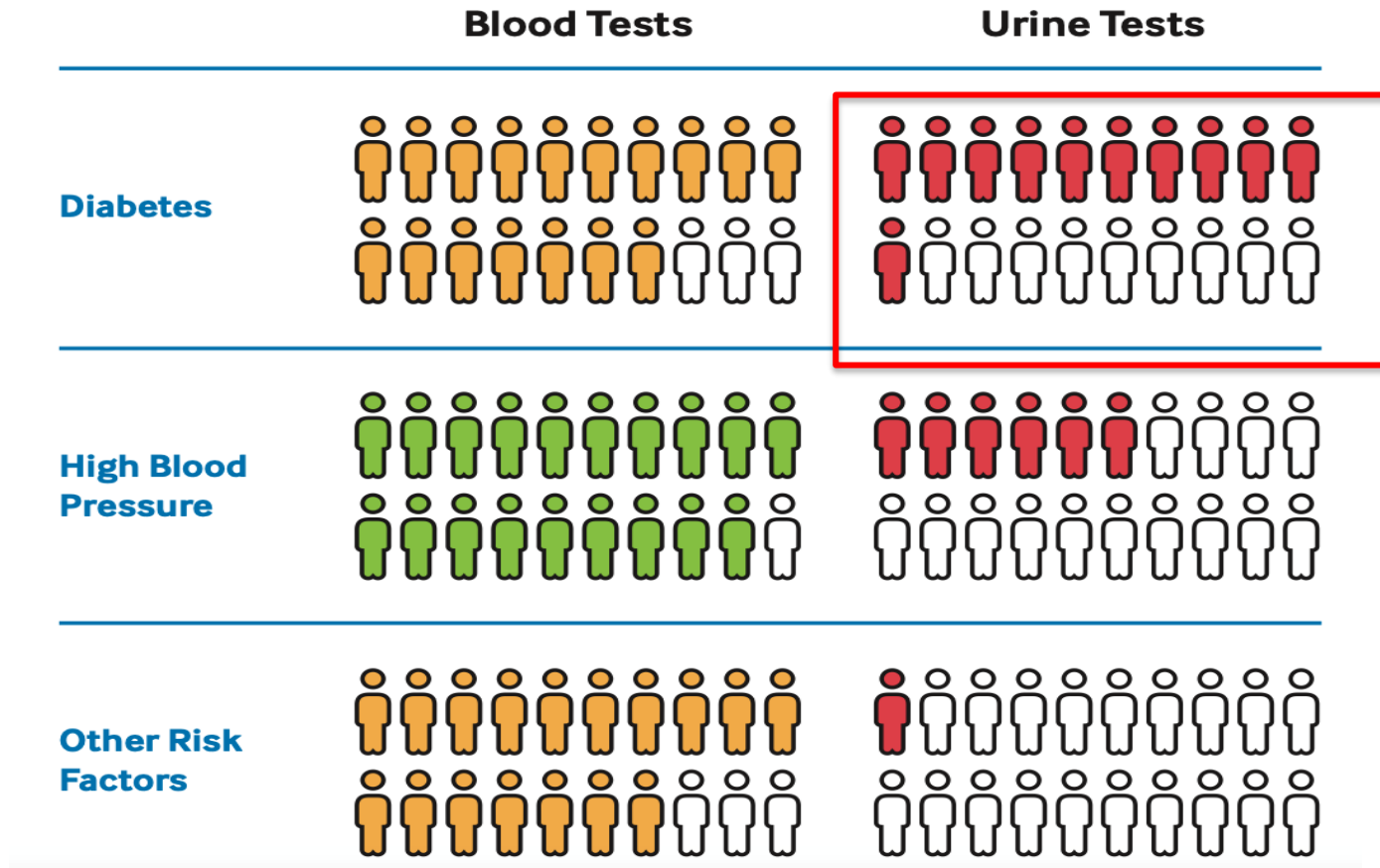


**Figure 3.7** Growth in numbers of prevalent adult KRT patients by treatment modality between 2011 and 2021

# Why intervene early in CKD?



# CKD diagnosis – missed opportunities



Need to embed urine ACR + KFRE in CKD monitoring

# Outline

- Why is CKD important
- CKD classification and how to approach patient
- CKD Management
- Cases





# Classification of CKD

**Prognosis of CKD by GFR  
and Albuminuria Categories:  
KDIGO 2012**

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



# What predicts progression to ESKD?

- BP
- Proteinuria
- eGFR at presentation
- Age
  - Young more likely to reach ESKD
  - Elderly more likely to die



# Chronic Kidney Disease

Pre-Renal causes

Intrinsic Renal causes

Post-Renal causes

Glomerular Disease

Tubulo-interstitial disease

Inherited disease

Vascular Disease

Chronic Glomerulonephritis

Systemic Disease:  
Diabetes  
Hypertension  
SLE

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

Polycystic Kidney  
Disease, Alports

Atherosclerotic  
renovascular disease



# How to screen?

- eGFR
- Urinalysis
- Albumin : Creatinine ratio – ACR\*
  
- **Kidney Failure Risk Equation**
  
- \*NB ACR not valid on samples from a catheter, ileal conduit, with infection or pyuria




# What is the risk of kidney failure

 **35** mg/mmol  
URINE ALBUMIN

 **M**  
SEX

 **45**  
AGE

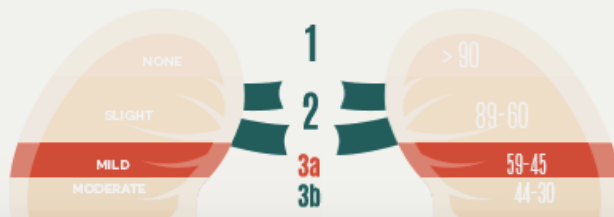
 **58** mL/min/1.73 m<sup>2</sup>  
EGFR

## ASSESSMENT

### STAGE 3a

MILD DECREASE IN FUNCTION

CKD STAGES



ESTIMATED GLOMERULAR  
FILTRATION RATE

Patient risk of progression to kidney failure requiring dialysis or  
transplant:

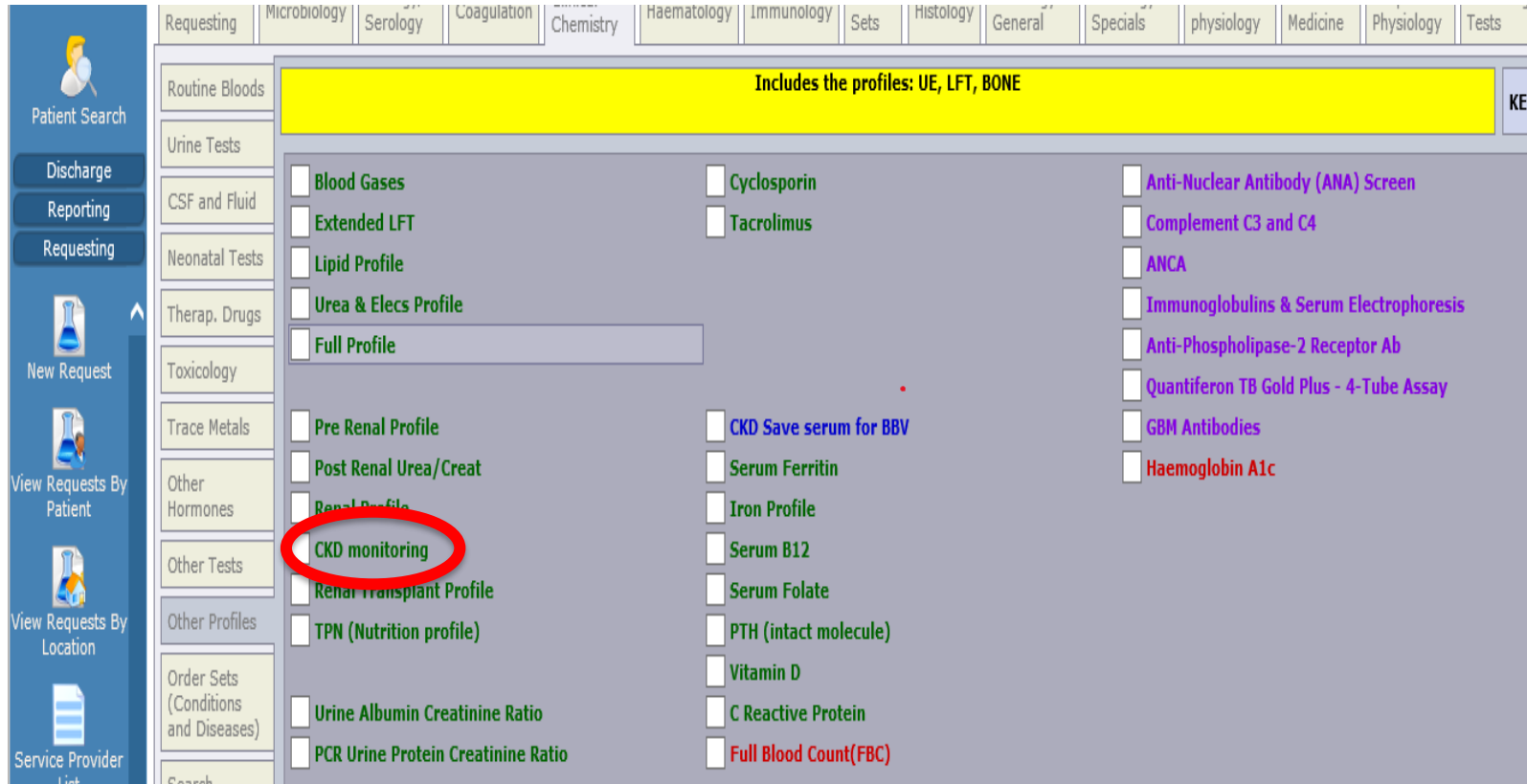
AT 2 YEARS

0.3 %

AT 5 YEARS

1.0 %

# Kidney Failure Risk Equation - ICE requesting



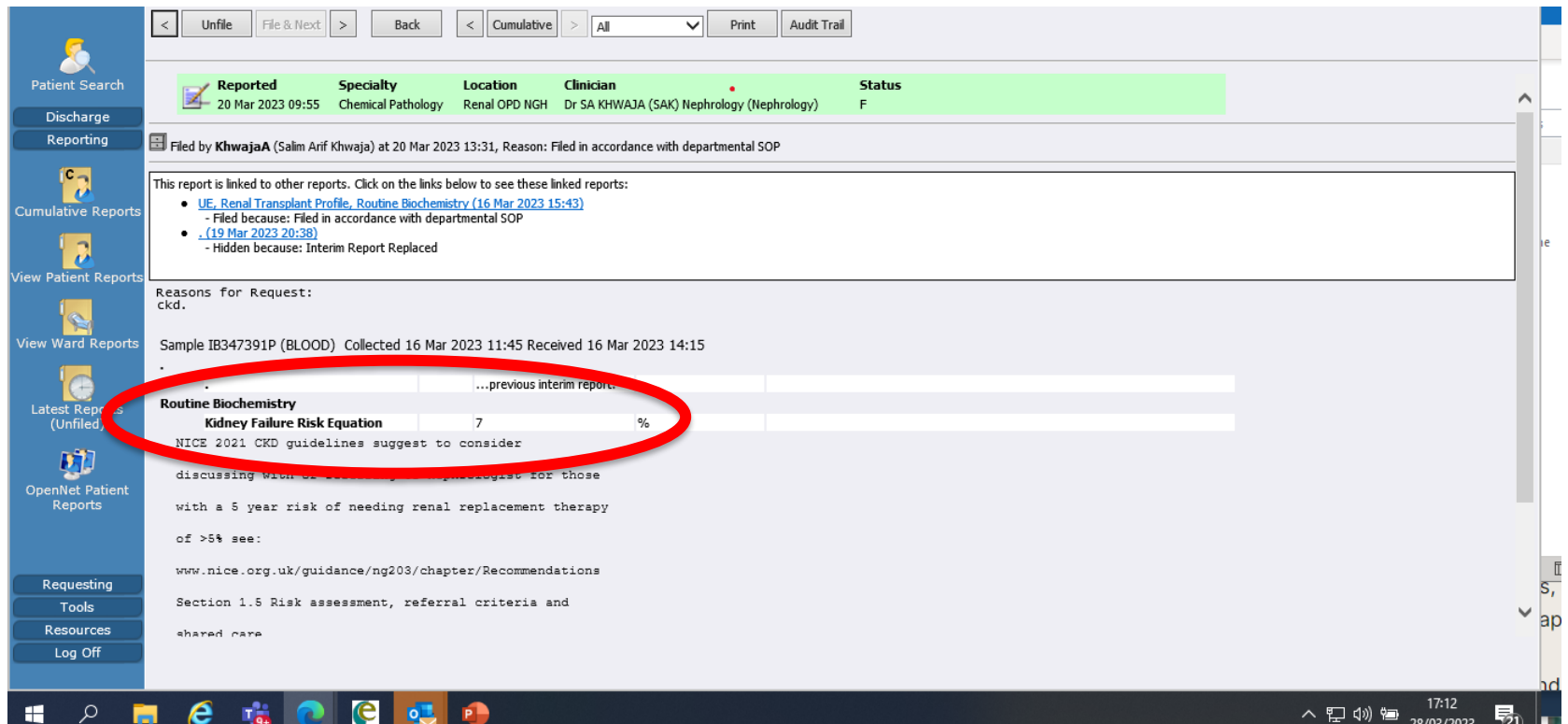
The screenshot displays the ICE interface for requesting tests. The top navigation bar includes: Requesting, Microbiology, Serology, Coagulation, Chemistry, Haematology, Immunology, Sets, Histology, General, Specials, physiology, Medicine, Physiology, Tests.

The left sidebar contains: Patient Search, Discharge, Reporting, Requesting, New Request, View Requests By Patient, View Requests By Location, Service Provider List.

The main content area shows a grid of test profiles. A yellow banner at the top indicates: "Includes the profiles: UE, LFT, BONE". The "CKD monitoring" option is circled in red. Other visible options include: Blood Gases, Extended LFT, Lipid Profile, Urea & Elecs Profile, Full Profile, Pre Renal Profile, Post Renal Urea/Creat, Renal Profile, Renal transplant Profile, TPN (Nutrition profile), Urine Albumin Creatinine Ratio, PCR Urine Protein Creatinine Ratio, Cyclosporin, Tacrolimus, Anti-Nuclear Antibody (ANA) Screen, Complement C3 and C4, ANCA, Immunoglobulins & Serum Electrophoresis, Anti-Phospholipase-2 Receptor Ab, Quantiferon TB Gold Plus - 4-Tube Assay, GBM Antibodies, Haemoglobin A1c, CKD Save serum for BBV, Serum Ferritin, Iron Profile, Serum B12, Serum Folate, PTH (intact molecule), Vitamin D, C Reactive Protein, and Full Blood Count(FBC).

CKD Monitoring tab on ICE – renal profile and urine ACR; automatically reports a KFRE score

# Kidney Failure Risk Equation - ICE reporting



The screenshot displays a clinical reporting interface. At the top, there are navigation buttons: Unfile, File & Next, Back, Cumulative, All, Print, and Audit Trail. Below this is a table with columns: Reported, Specialty, Location, Clinician, and Status. The table contains one row with the following data: Reported: 20 Mar 2023 09:55, Specialty: Chemical Pathology, Location: Renal OPD NGH, Clinician: Dr SA KHWAJA (SAK) Nephrology (Nephrology), Status: F.

Below the table, it says "Filed by KhwajaA (Salim Arif Khwaja) at 20 Mar 2023 13:31, Reason: Filed in accordance with departmental SOP".

A box contains the text: "This report is linked to other reports. Click on the links below to see these linked reports:" followed by a list of links and their reasons for being linked.

Below this, it says "Reasons for Request: ckd." and "Sample IB347391P (BLOOD) Collected 16 Mar 2023 11:45 Received 16 Mar 2023 14:15".

The main content area shows a table with the following data:

Routine Biochemistry	Value	Unit
Kidney Failure Risk Equation	7	%

The row for "Kidney Failure Risk Equation" is circled in red. Below the table, there is text: "NICE 2021 CKD guidelines suggest to consider discussing with a renal physician or nephrologist for those with a 5 year risk of needing renal replacement therapy of >5% see: www.nice.org.uk/guidance/ng203/chapter/Recommendations Section 1.5 Risk assessment, referral criteria and shared care".

The bottom of the screen shows a Windows taskbar with various application icons and a system tray with the time 17:12 and date 28/03/2023.

# CKD Management





# 4 pillars to save lives for adults with CKD

Pillar 1: RAAS Blockage and rapid titration

Pillar 2: SGLT2i

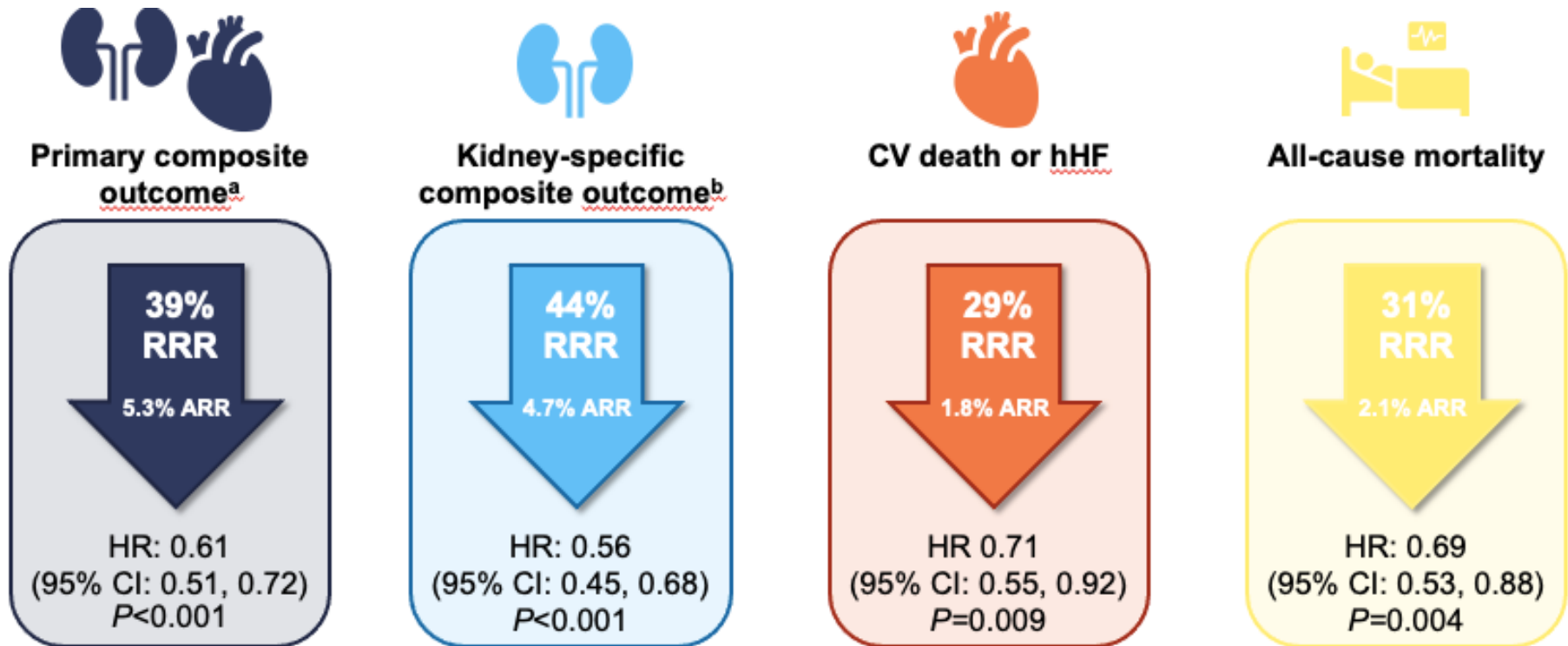
Pillar 3: Optimise BP and other cardiovascular risk factor

- Statin – Atorvastatin 20mg should be offered for primary prevention
- Aspirin
- Weight loss and smoking cessation

Pillar 4: Finerenone

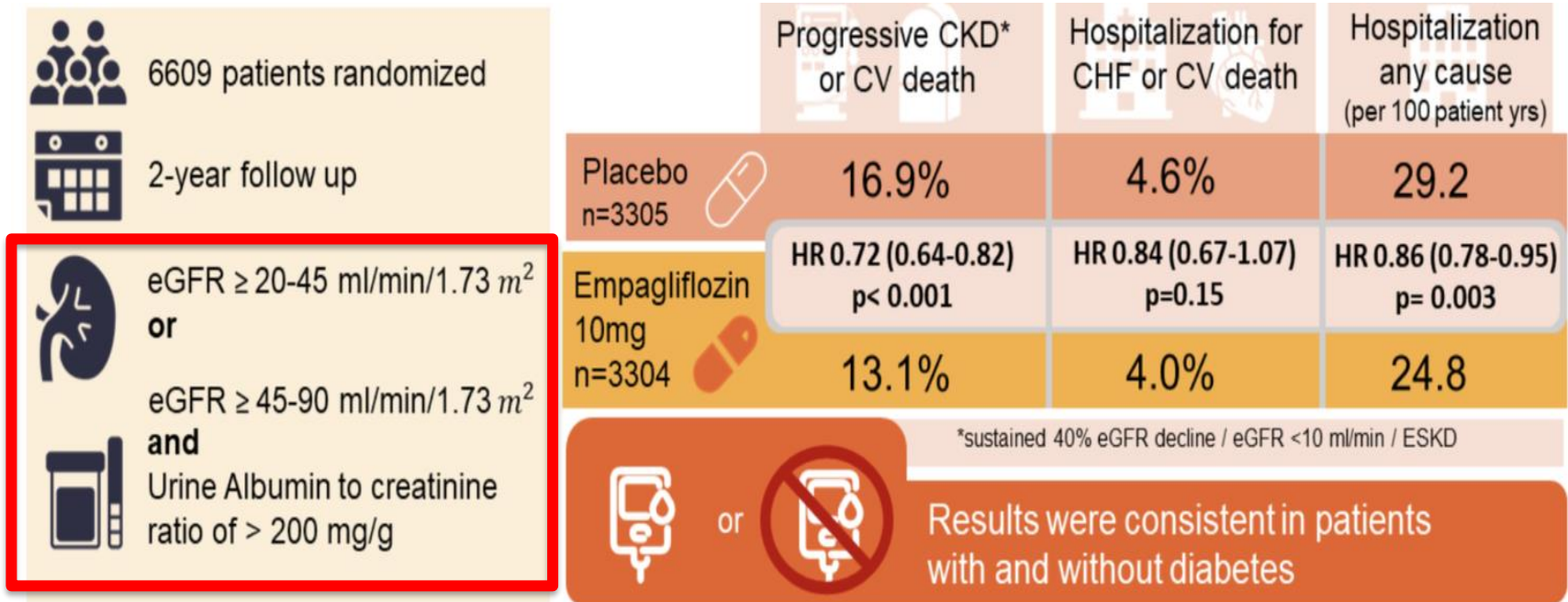
GLP1a

# Dapagliflozin and trial outcomes



Age 61+/-12

# Empa-CKD Outcomes



Age 64+/-14

# CKD Management –SGLT2is

Dapagliflozin is recommended as an option for treating chronic kidney disease (CKD) in adults. It is recommended only if:

- it is an add-on to optimised standard care including the highest tolerated licensed dose of angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs), unless these are contraindicated, and

people have an estimated glomerular filtration rate (eGFR) of 25 ml/min/1.73 m<sup>2</sup> to 75 ml/min/1.73 m<sup>2</sup> at the start of treatment and:

- have type 2 diabetes or
- have a urine albumin-to-creatinine ratio (uACR) of 22.6 mg/mmol or more.

Empagliflozin is recommended as an option for treating chronic kidney disease (CKD) in adults, only if:

- it is an add-on to optimised standard care including the highest tolerated licensed dose of angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs), unless these are contraindicated, and
- people have an estimated glomerular filtration rate of:
  - 20 ml/min/1.73 m<sup>2</sup> to less than 45 ml/min/1.73 m<sup>2</sup> or
  - 45 ml/min/1.73 m<sup>2</sup> to 90 ml/min/1.73 m<sup>2</sup> and either:
    - a urine albumin-to-creatinine ratio of 22.6 mg/mmol or more, or
    - type 2 diabetes.



Low Risk Prescribe SGLT2is	Moderate Risk Prescribe with caution	High Risk Do not prescribe SGLT2is
<p>Monotherapy when metformin is contraindicated or not tolerated</p> <p>Dual therapy in combination with metformin or other oral agents</p> <p>Triple therapy in combination with other oral agents</p> <p>Combination with insulin</p> <p>Established CVD</p> <p>Prior stroke</p> <p>History of HF</p> <p>No history of LLA</p> <p>No history of PAD</p> <p>Age &lt; 75 years</p> <p>ACR &lt; 3 mg/mmol</p> <p>eGFR ≥ 60 mL/min/1.73 m<sup>2</sup>*</p> <p>Overweight or obese (BMI &gt; 25 kg/m<sup>2</sup>)</p> <p>Vulnerable to the effects of hypoglycaemia</p> <p>No liver impairment</p>	<p>History of PAD</p> <p>Osteoporosis or history of fractures</p> <p>Frail/elderly (age &gt; 75 years)</p> <p>History of foot ulceration</p> <p>CKD stage 3a (eGFR 45–60) or CKD stage 3b (eGFR 30–45) with ACR &gt; 30 mg/mmol†</p> <p>Receiving loop diuretics</p> <p>High HbA1c levels (&gt; 86 mmol/mol or 10%)</p> <p>Systemic steroid therapy</p> <p>Ketogenic diet (&lt; 5% carbohydrate content)</p> <p>BMI &lt; 25 kg/m<sup>2</sup></p> <p>Recurrent UTIs</p> <p>Long-term catheter</p> <p>Men with benign prostatic hypertrophy</p> <p>Mild to moderate liver impairment (Child-Pugh score A/B)</p>	<p><b>Diabetes contraindications:</b></p> <p>History of DKA</p> <p>Rapid progression to insulin (within 1 year of diagnosis)</p> <p>Latent autoimmune diabetes of adulthood (LADA)</p> <p>Ketosis-prone T2DM</p> <p>Type 1 Diabetes (diagnosed or suspected)</p> <p>Genetic diabetes</p> <p>Diabetes due to pancreatic disease</p> <p>Existing/active diabetic foot ulcers</p> <p>Previous LLA</p> <p><b>Non-diabetes contraindications:</b></p> <p>Falling disorders</p> <p>Cognitive impairment</p> <p>Acute illness</p> <p>Alcoholism likely to increase the risk of falls and metabolic disturbances</p> <p>Recent major surgery</p> <p>Pregnancy, planning pregnancy or breastfeeding</p> <p>History of Fournier's gangrene</p> <p>Severe hepatic impairment (Child-Pugh score C)</p>



# CKD Management – Finerenone

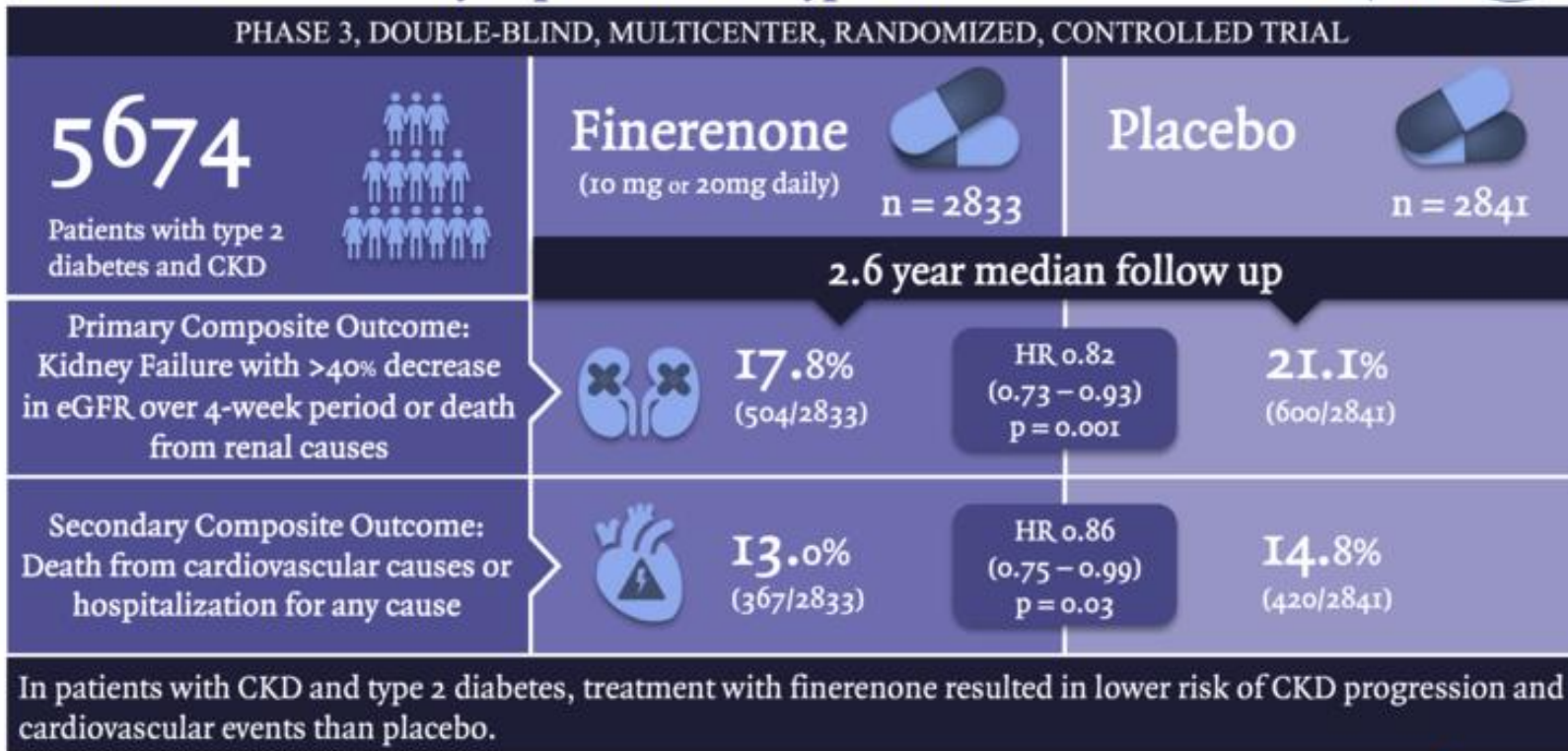
## 1 Recommendations

- 1.1 Finerenone is recommended as an option for treating stage 3 and 4 chronic kidney disease (with albuminuria, that is, an albumin to creatinine ratio that is persistently 3 mg/mmol [30 mg/g] or more) 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.



# CKD Management – Finerenone

Does finerenone slow progression of CKD and reduce cardiovascular mortality in patients with type 2 diabetes?



Reference: Bakris GL, Agarwal R, Anker S, Pitt B, et al. Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes. NEJM

VA by Dhwanil Patel @ilheartkidneys

# CKD Management – Semaglutide

## Semaglutide for CKD in Patients with Type 2 Diabetes: “FLOW”ing with the Semaglu“TIDE”



### METHODS



International, double-blind, placebo-controlled 28 countries






**Type 2 DM and CKD:**  
 GFR 50-75 ml/min +  
 ACR 300-5000 mg/g  
 or



GFR 25-<50 ml/min +  
 ACR 100-5000 mg/g



Median follow-up,  
 3.4 years

	 Major kidney disease events	 Death from any causes	 Adverse event leading to discontinuation
<b>Placebo</b> n = 1766	7.5 events per 100 patient-years	279 (15.8%)	211 (11.9%)
	<b>HR 0.76</b> (95% CI, 0.66-0.88)	<b>HR 0.80</b> (95% CI, 0.67-0.95)	
<b>Semaglutide</b> n = 1767	5.8 events per 100 patient-years	227 (12.8%)	233 (13.2%)

Major kidney disease events- kidney failure, ≥50% reduction in GFR, death from CV or kidney-related causes

HR= Hazard ratio

**Reference:** Perkovic,V et al. Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes. NEJM, May 2024.

VA by Anjana Gopal  @anjanagopal9

**Conclusion:** Semaglutide reduced the risk of clinically important kidney outcomes and death from cardiovascular causes in patients with type 2 diabetes and chronic kidney disease.





# Case Study

- 45 year old type 2 DM with hypertension and obesity
- eGFR 58 mls/min. ACR 35mg/umol. BP 142/78
- On Metformin 1g bd, ramipril 2.5mg, amlodipine 5mg aspirin and atorvastatin
- What are the next steps in management?
  - Optimise Ramipril
  - Add SGLT2i
  - Add finerenone
  - Liaise with diabetes re GLP1Ra

# Case Study


- 78 year old female, hypertensive with history of smoking and peripheral vascular disease. Urine dipstick was negative for protein and blood. BP=150/90. Last year eGFR 35mls/min.
- Now 28mls min. In view of progression of kidney disease please can you see. Rx: Aspirin, Simvastatin, Ramipril, Bendroflumethazide
  - What is the likely diagnosis?
  - How would you manage?
  - What is the risk of kidney failure?

# What is the risk of kidney failure

 **3** mg/mmol  
URINE ALBUMIN

 **F**  
SEX

 **78**  
AGE

 **28** mL/min/1.73 m<sup>2</sup>  
EGFR

## ASSESSMENT

# STAGE 4

SEVERE DECREASE IN FUNCTION

CKD STAGES



ESTIMATED GLOMERULAR  
FILTRATION RATE

Patient risk of progression to kidney failure requiring dialysis or  
transplant:

AT 2 YEARS

**0.9 %**

AT 5 YEARS

**3.4 %**

## Case Study- suggested management

- No nephrological indication for ACEI as no proteinuria and high risk of renovascular disease. **Therefore trial stop ACEI**
- High risk of cardiovascular death - already on aspirin/statin
- **Add Empagliflozin 10mg day**
- **eGFR<30mlsmin – control BP <140 systolic – switch to loop diuretic**

# CKD Management –SGLT2is

Dapagliflozin is recommended as an option for treating chronic kidney disease (CKD) in adults. It is recommended only if:

- it is an add-on to optimised standard care including the highest tolerated licensed dose of angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs), unless these are contraindicated, and
- people have an estimated glomerular filtration rate (eGFR) of 25 ml/min/1.73 m<sup>2</sup> to 75 ml/min/1.73 m<sup>2</sup> at the start of treatment and:
  - have type 2 diabetes or
  - have a urine albumin-to-creatinine ratio (uACR) of 22.6 mg/mmol or more.

Empagliflozin is recommended as an option for treating chronic kidney disease (CKD) in adults, only if:

- it is an add-on to optimised standard care including the highest tolerated licensed dose of angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs), unless these are contraindicated, and
- people have an estimated glomerular filtration rate (eGFR) of:
  - 20 ml/min/1.73 m<sup>2</sup> to less than 45 ml/min/1.73 m<sup>2</sup> or
  - 45 ml/min/1.73 m<sup>2</sup> to 90 ml/min/1.73 m<sup>2</sup> and either:
    - a urine albumin-to-creatinine ratio of 22.6 mg/mmol or more, or
    - type 2 diabetes.



## CKD – Case study

- 81 year old Type 2 diabetic, hypertensive. female recently moved to your practice. BP= 132/90. Routine bloods show creatinine 180  $\mu\text{mol/l}$  with eGFR 26. uACR = 5mg/ $\mu\text{mol}$ . HbA1C = 52. Frail
- Creatinine = 150 in 2019.
- On Aspirin, atorvastatin, ramipril, Linagliptin
  - What is the risk of kidney failure?
  - Would you do anything else?

## CKD – Case study

- Tell the patient she has slowly progressive CKD
- In theory may benefit from an SGLT2i (+/- finereone) – but perfectly acceptable to leave alone as risk of kidney failure alone

# Case Study

- 72 yr old female. History of type 2 diabetes, heart failure and diabetic retinopathy.
- eGFR = 35 mls/min. ACR=150.
- BP=158/88.
- Treatment: aspirin, atorvastatin, metformin, ramipril and doxazosin
  - Whats the likely diagnosis and risk of kidney failure?
  - What should you do?



# Case Study

- Likely diagnosis – diabetic nephropathy – in view of retinopathy
- High risk of progression to end-stage disease – proteinuria, diabetes, poor BP. Therefore tertiary referral appropriate
- Start SGLT2i – CKD and heart failure
- Ensure Metformin dose correct – lactic acidosis

 **150** mg/mmol  
URINE ALBUMIN

 **F**  
SEX

 **72**  
AGE

 **35** mL/min/1.73 m<sup>2</sup>  
EGFR

ASSESSMENT

# STAGE 3b

MODERATE DECREASE IN FUNCTION

CKD STAGES

ESTIMATED GLOMERULAR  
FILTRATION RATE



Patient risk of progression to kidney failure requiring dialysis or transplant:

AT 2 YEARS

**2.9 %**

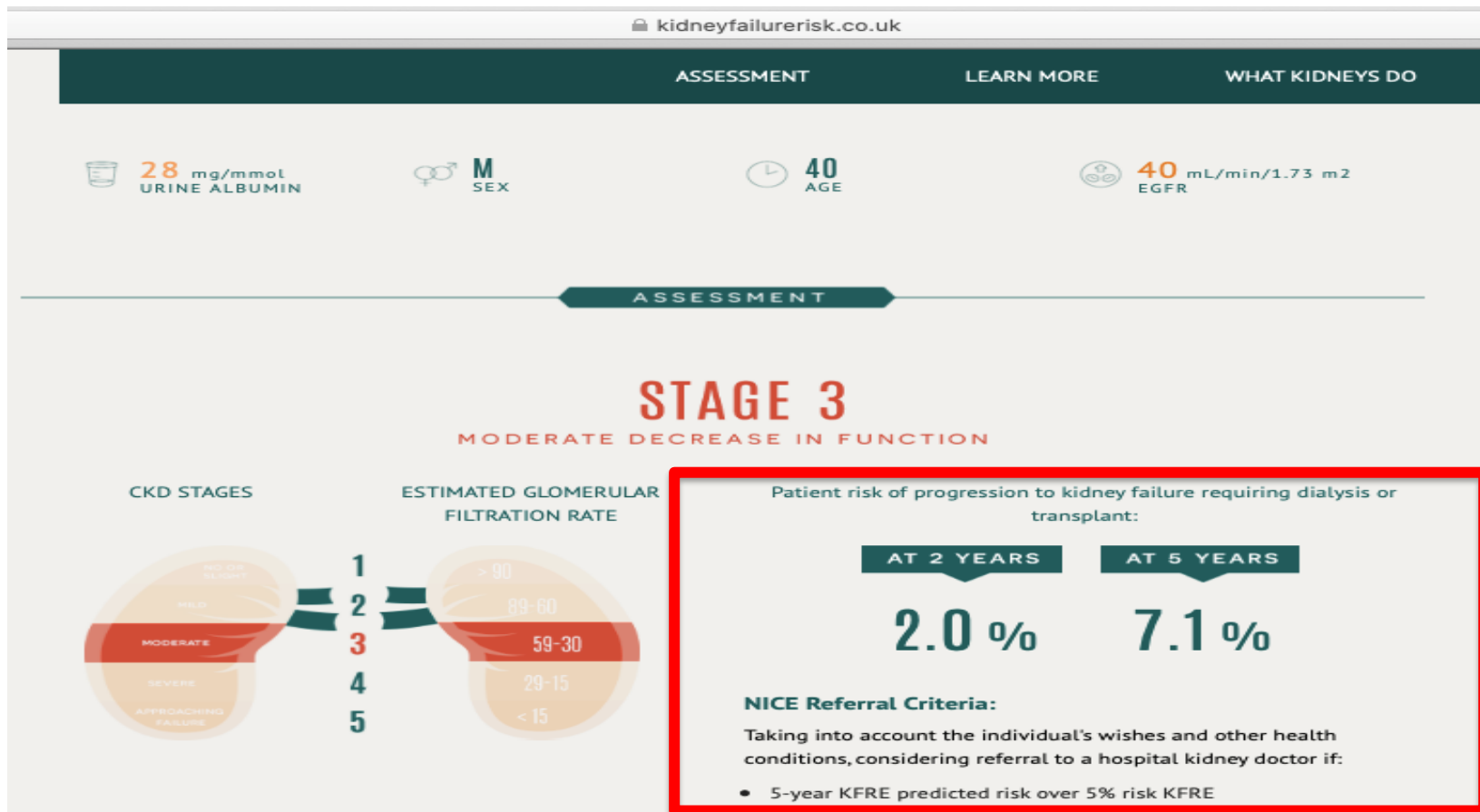
AT 5 YEARS

**10.0 %**

## CKD – Case study

- Very well 30 year old male comes to you as part of an insurance medical. On no medication. Urinalysis 1+ haematuria. ACR = 28mg/umol. eGFR = 40mls/min.
- No historical creatinines. BP =130/80
- What would you do next?

# Kidney Failure Risk Equation<sup>1</sup>



1. <https://kidneyfailure risk.co.uk/>

## CKD – Case study

- Repeat creatinine and dipstick within 7-10 days.
- Repeat bloods and urine unchanged
- Likely IgA nephropathy – start SGLT2i and refer to nephrology

# NICE referral criteria

- Patients with eGFR  $<30$  ml/min , but if  $>30$  ml/min, referral will depend on below criteria.
- 5-year KFRE  $>5\%$  (5 year risk of needing RRT )
- UACR  $>70$  mg/mmol
- UACR  $>30$  with associated microscopic haematuria
- Sustained decline in eGFR  $>25\%$  or more within 12 months
- Sustained decline in eGFR  $>15$ ml/min within 12 months
- Suspected RAS
- Poorly controlled HTN ( $>4$  anti HTN)
- Suspected genetic cause of CKD



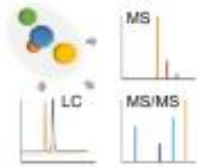
# We can't prescribe our way out of CKD

## Non-adherence to cardiometabolic medication as assessed by LC-MS/MS in urine and its association with kidney and cardiovascular outcomes in type 2 diabetes mellitus



Guidelines recommend a combination of drugs to prevent cardiovascular and kidney complications in patients with T2DM

Non-adherence is an important barrier in clinical practice



Biochemical adherence testing with LC-MS/MS in urine: non-invasive, direct and objective



1125 patients from the PROVALID study (median follow-up 5.10 years)



Baseline urine samples tested for 79 cardiometabolic drugs via LC-MS/MS



Cardiovascular endpoint: Myocardial infarction, stroke, cardiovascular death



Kidney endpoint: eGFR decline, progression of albuminuria, ESKD, kidney death



Totally adherent: 56.3%  
Partially non-adherent: 42.0%  
Totally non-adherent: 1.7%



Adherence: highest to antiplatelet and glucose-lowering drugs, lowest to lipid-lowering drugs



Worse cardiovascular outcome with non-adherence to antiplatelet drugs (HR 10.13 [95% CI 3.06, 33.56])



Worse kidney outcome with non-adherence to antihypertensive drugs (HR 1.98 [95% CI 1.37, 2.86])

Denicolò et al 2024

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<https://creativecommons.org/licenses/by/3.0/>

**Conclusion:** This analysis shows, via a direct and objective adherence measure, that non-adherence to cardiometabolic drugs is common in type 2 diabetes mellitus and negatively affects kidney and cardiovascular outcomes



# Key messages

- **When monitoring CKD routinely use the ‘CKD Monitoring’ request on ICE**
- NICE recommend to discuss patients (with eGFR <60mls/min) with nephrology if Kidney Failure Risk (Equation) >5% at 5 years
- SGLT2is are foundational treatments in both diabetic and non-diabetic kidney disease





# Key messages

- Finereone for T2DM with an eGFR between 25-60mls/min and ACR >3
- Think GLP1RAs for diabetics with CKD – especially for obese
- If you want to do virtual CKD MDTs , please contact us.

