Chronic Kidney Disease Updates

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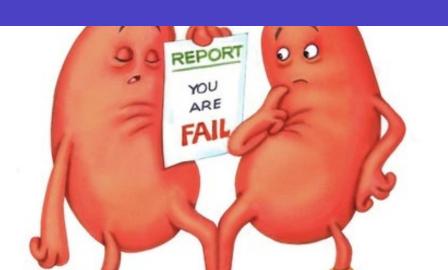


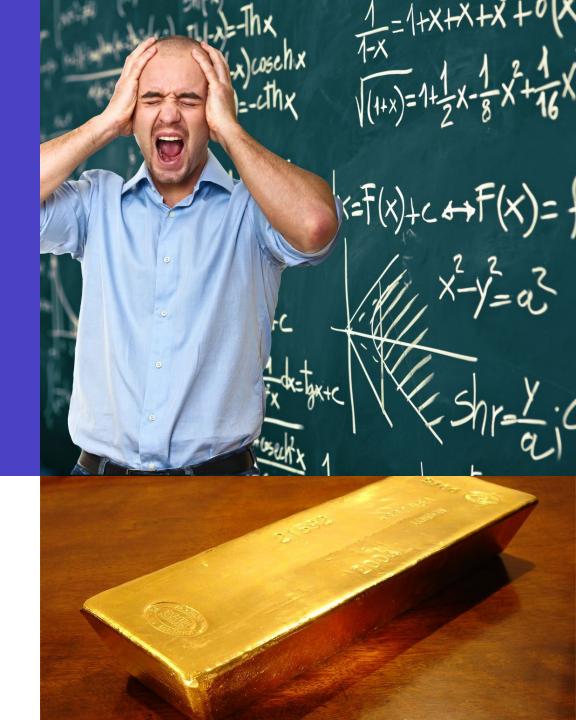


Agenda

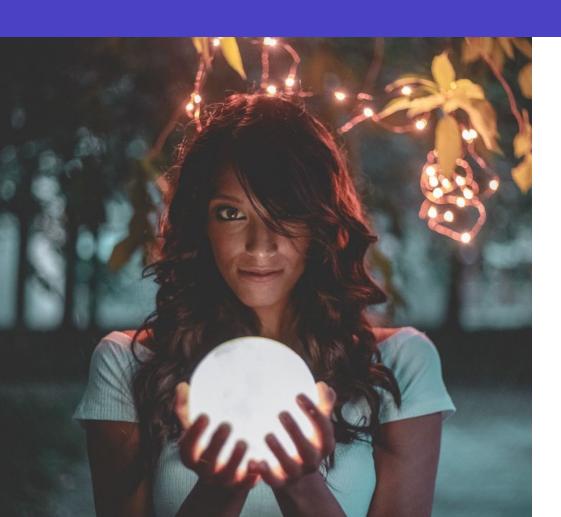
- KFRE
- SGLT2i
- Finerenone
- CKD Cases

Kidney Failure Risk Equation (KFRE)





Kidney Failure Risk Equation (KFRE) - What is it?



- Risk Prediction Model
- First outlined by Tangri et al in 2011
- Ideal model: accurate, easy-to-implement, highly generalizable
- Relies solely on info available to lab

Why KFRE?

Measure	NICE Criteria	Recalibrated KFRE			Hybrid criteria	
		≥3%	≥5%	≥15%	KFRE \geq 5% or eGFR $<$ 30 ml/min/1.73 m ²	KFRE \geq 5% or ACR \geq 70 mg/mmol
Sensitivity	5.5%	4.4%	6.8%	16.7%	5.2%	6.6%
	(4.1 to 7.2)	(3.3 to 5.8)	(5.0 to 9.1)	(11.0 to 23.8)	(3.8 to 7.0)	(5.0 to 8.5)
Specificity	99.7%	99.7%	99.7%	99.6%	99.7%	99.8%
	(99.6 to 99.8)	(99.6 to 99.8)	(99.6 to 99.8)	(99.5 to 99.7)	(99.6 to 99.8)	(99.7 to 99.8)
Baseline referrals	879	1,084	615	144	803	836
	(5.6%)	(6.9%)	(3.8%)	(0.9%)	(5.1%)	(5.3%)
ESRD not referred at baseline	41	41	47	65	47	34
	(46.1%)	(46.1%)	(52.8%)	(73.0%)	(52.8)	(38.2%)
Mean age if eligible, years	76.3	76.3	75.2	70.3	77.3	73.8
	(75.4 to 77.2)	(75.5 to 77.1)	(74.1 to 76.3)	(67.6 to 72.9)	(76.3 to 78.2)	(72.9 to 74.8)
Female referrals	58.4%	55.9%	54.3%	47.2%	59.4%	52.8%
	(55.1 to 61.6)	(52.9 to 58.9)	(50.4 to 58.3)	(39.0 to 55.4)	(56.0 to 62.8)	(49.4 to 56.1)
Mean referral eGFR,	32.7	30.5	27.7	21.6	27.5	34.0
ml/min/1.73 m ²	(31.9 to 33.5)	(30.0 to 30.9)	(27.1 to 28.3)	(20.5 to 22.7)	(27.1 to 28.0)	(33.1 to 34.9)
Mean referral ACR, mg/mmol	77.3	50.6	64.8	130.8	50.5	86.0
	(69.7 to 84.9)	(45.0 to 56.2)	(56.2 to 73.4)	(103.4 to 158.2)	(43.7 to 57.3)	(78.3 to 93.8)

Sensitivity refers to the percentage of patients referred who developed ESRD within 5 years of follow-up. Specificity refers to the percentage of patients not initially referred who did not go on to develop ESRD. Figures in parentheses for 'baseline referrals' and 'ESRD not referred at baseline' refer to percentage of all individuals in cohort not previously seen in renal secondary care. All other figures in parentheses refer to 95% confidence intervals. n = 15,830 for eligibility assessment cohort, with 89 ESRD cases.

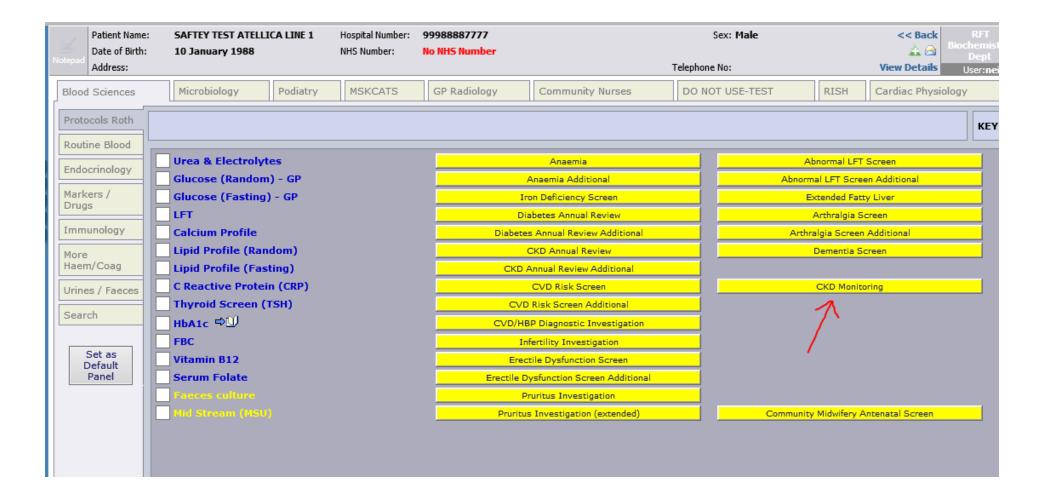
ACR, albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate; ESRD, end stage renal disease; KFRE, Kidney Failure Risk Equation; NICE, National Institute of Health And Clinical Excellence.

https://doi.org/10.1371/journal.pmed.1002955.t003

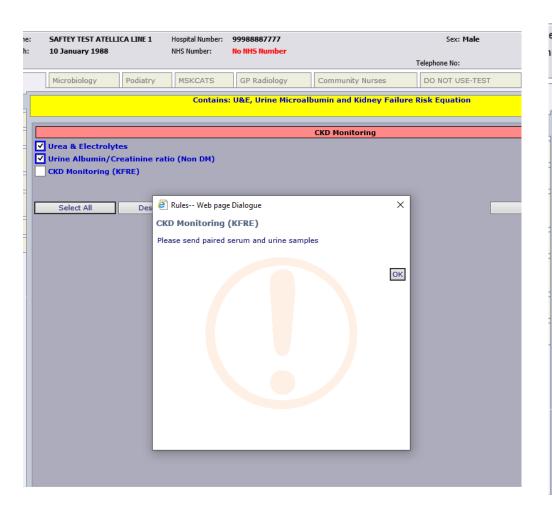
Referral criteria

- 1.5.5 Refer adults with CKD for specialist assessment (taking into account their wishes and comorbidities) if they have any of the following:
 - a 5-year risk of needing renal replacement therapy of greater than 5% (measured using the 4-variable Kidney Failure Risk Equation)
 - an ACR of 70 mg/mmol or more, unless known to be caused by diabetes and already appropriately treated (see recommendations 1.6.6 and 1.6.7)
 - an ACR of more than 30 mg/mmol (ACR category A3), together with haematuria
 - a sustained decrease in eGFR of 25% or more and a change in eGFR category within
 12 months
 - a sustained decrease in eGFR of 15 ml/min/1.73 m² or more per year
 - hypertension that remains poorly controlled (above the person's individual target)
 despite the use of at least 4 antihypertensive medicines at therapeutic doses (see also
 NICE's guideline on hypertension in adults)
 - known or suspected rare or genetic causes of CKD
 - suspected renal artery stenosis. [2021]

How to KFRE?

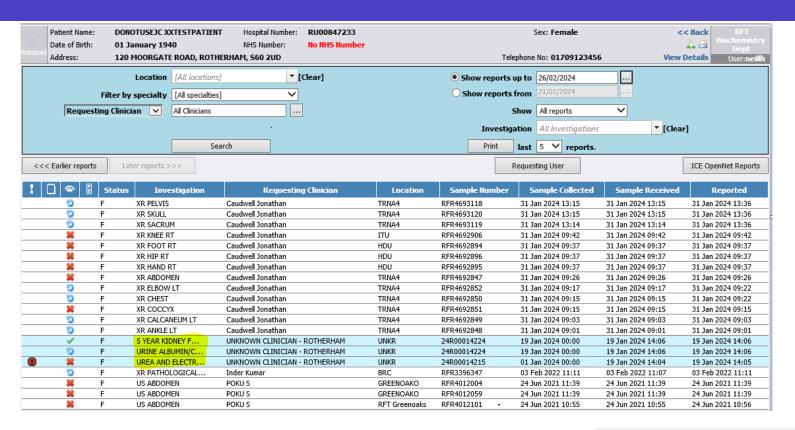


How to KFRE?



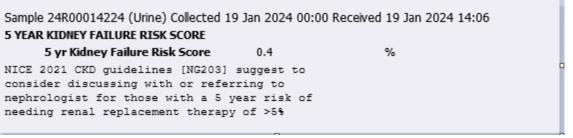


How to KFRE?



Note from labs:

- Do not request U&E and uACR separately - won't calculate KFRE
- If you request CKD monitoring and send both samples within 30 days of each other, a KFRE will be calculated (must be SAME request)



KFRE - Take home points

- KFRE is a validated tool to quantify risk of needing kidney replacement over 5 years
- It will only be reported if eGFR < 60ml/min
- NICE guidelines now advise referral for anyone with KFRE >5% rather than all patients with eGFR < 30ml/min
- It does NOT account for competing risk of death therefore in elderly, comorbid patients where risk of death from other cause is higher, it may be reasonable to use advice and guidance first

SGLT2i

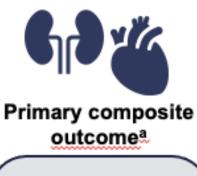
Empagliflozin and Dapagliflozin

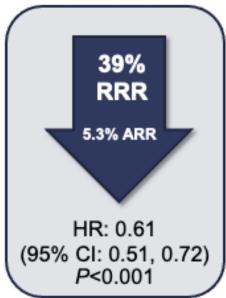






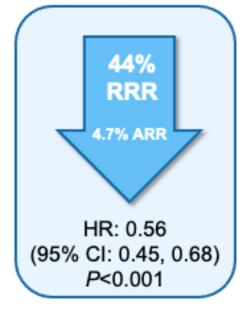
Dapagliflozin outcomes



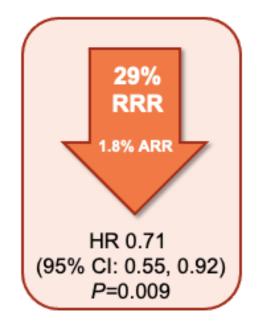




Kidney-specific composite outcome^b











Empagliflozin outcomes



6609 patients randomized



2-year follow up



eGFR \geq 20-45 ml/min/1.73 m^2 or

eGFR \geq 45-90 ml/min/1.73 m^2 and



Urine Albumin to creatinine ratio of > 200 mg/g

		Progressive CKD* or CV death	Hospitalization for CHF or CV death	Hospitalization any cause (per 100 patient yrs)
ı	Placebo n=3305	16.9%	4.6%	29.2
ı	Empagliflozin 10mg n=3304	HR 0.72 (0.64-0.82) p< 0.001	HR 0.84 (0.67-1.07) p=0.15	HR 0.86 (0.78-0.95) p= 0.003
		13.1%	4.0%	24.8
1		*sustained	40% eGFR decline / eGFR <10	ml/min / ESKD



Results were consistent in patients with and without diabetes

NICE SGLT2i

- 1.1 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 m² to less than 45 ml/min/1.73 m² or
 - 45 ml/min/1.73 m² to 90 ml/min/1.73 m² and either:
 - a urine albumin-to-creatinine ratio of 22.6 mg/mmol or more, or
 - type 2 diabetes.

National Institute for Health and Care Excellence

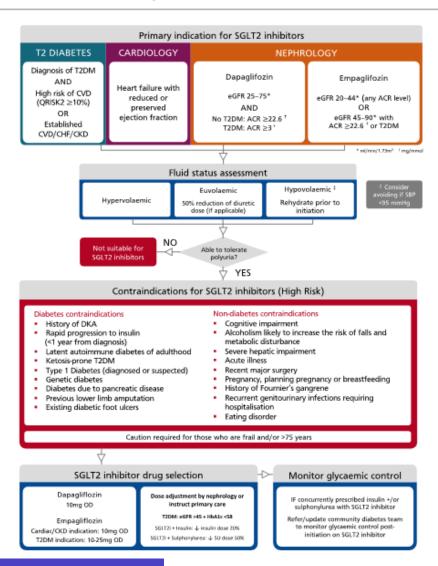
Dapagliflozin is recommended as an option for treating chronic kidney disease (CKD) in adults. It is recommended only if:

- 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 m² to 75 ml/min/1.73 m² 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.

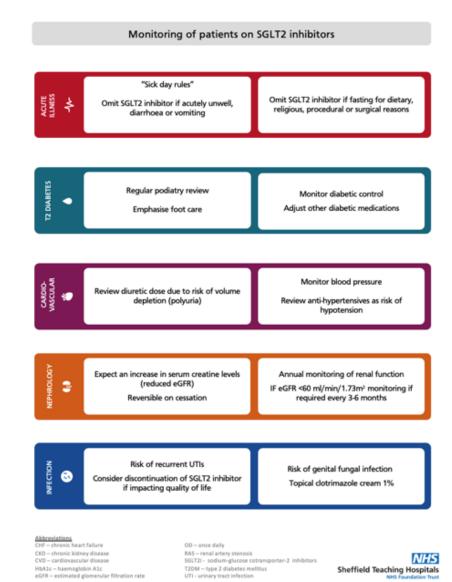
2 Summary and Guideline

2.1 Flowchart

Stepwise Multi-speciality Outpatient Approach to the Prescription of SGLT2 inhibitors



Stepwise Multi-speciality Outpatient Approach to Prescription of SGLT2 inhibitors



Finerenone

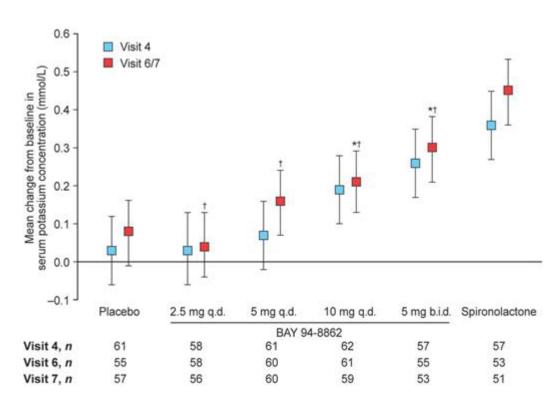
The New Kid on the Block







What is it?

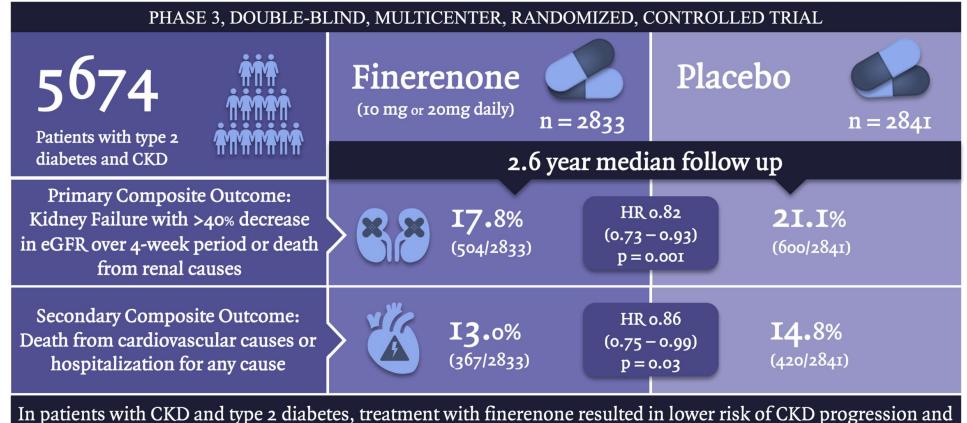


- Non-steroidal MRA
- Main concern with steroidal MRA is hyperkalaemia
- Finerenone more potently blocks MR than spironolactone and eplerenone
- For the same benefit in reducing BNP, albuminuria, causes lower incidence of hyperkalaemia

Finerenone outcomes

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

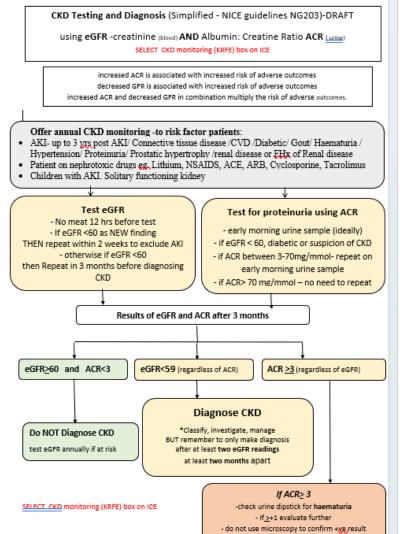
cardiovascular events than placebo.

NICE Finerenone

- 1.1 Finerenone is recommended as an option for treating stage 3 and 4 chronic kidney disease (with albuminuria) associated with type 2 diabetes in adults. It is recommended only if:
 - it is an add-on to optimised standard care; this should include, unless they are unsuitable, the highest tolerated licensed doses of:
 - angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers
 (ARBs) and
 - sodium–glucose cotransporter-2 (SGLT2) inhibitors and
 - the person has an estimated glomerular filtration rate (eGFR) of 25 ml/min/1.73 m² or more.

		Current Finerenone dose	
		10mg	20mg
Current Serum Potassium	≤4.8mmol/L	Increase to 20mg once daily	Continue 20mg once daily
	>4.8- 5.5mmol/L	Continue 10mg once daily	Continue 20mg once daily
	>5.5mmol/L	Withhold. Consider to Re-start at 10 mg once daily when serum potassium ≤ 5.0 mmol/L.	Withhold. Consider to re-start at 10 mg once daily when serum potassium ≤ 5.0 mmol/L.

BEST CKD Pathway



Stage	eGFR (ml/min/1.73m2)	Description	e-GFR testing		Proteinuria annually	FBC	Ca, PO4	Vit D
			ACR<30	ACR>30				
1	≥ 90	Normal or increased GFR -with other evidence of kidney damage	12 monthly		٧	×	×	×
2	60-89	Slight decrease in GFR - with other evidence of kidney damage	•		٧	×	×	х
3A	45-59	Moderate decrease in GFR - With or without other evidence of kidney	12 monthly	6 monthly	٧	×	×	×
3B	30-44	damage	6 monthly		٧	FBC Target	Ca, PO4	×
4	15-29	Severe decrease in GFR -With or without other evidence of kidney damage	6 monthly	4 monthly	٧	Hb10.5 -12.5		Vit D an may be PTH offer Significant ergocaldine
5	<15	Established renal failure	3 monthly		٧	1		if vijiQ reduced

Progressive CKD Criteria

- need three eGFR spread over at least 3 months
- Fall in eGFR of 25% AND change in eGFR category in 12 months OR sustained fall in eGFR of 15ml/min/yr.

Risk Factors associated with CKD Progression

AKI- previous episodes, African, African-Caribbean, Asian , CVD, diabetes, hypertension, NSAIDs – chronic use, proteinuria, smoking, urinary outflow obstruction- if chronic an untreated

CKD and Anaemia (Hb < 110g/l)

 if eGFR > 60ml/min consider/investigate other causes of anaemia other than CKD
 if eGFR 30-60ml/min CKD possible cause, still exclude other cause of anaemia
 if e-GFR < 30ml/min CKD most likely cause of anaemia

 DO NOT use transferrin saturation/ferritin alone to assess iron deficiency status in CKD
 if Iron treatment given, ferritin should not rise > 500 mcg/l

BP Targets - (see Hypertension pathway)

- <140/90 if CKD and ACR <70 mg/mmol
- <130/80 if CKD and ACR >70 mg/mmol Type 1 diabetic
- if ACR> 30mg/mmol- offer ACE inhibitors or Angiotensin-receptor blocker (ARB)
- -if ACR >3 mg/mmol AND patient Type 1/ Type 2 Diabetes .-offer ACE /ARB
- ACE inhibitors- check U+E 7-10 days post / stop when ill/ stop if K +>6 or Cr rise >30 %.

- Ultrasound consider if eGFR <30 ml/min, LUTS, EHX polycystic kidney/ accelerated progress of CKD
- Statins for all CKD patients (cannot use QRISK)
- Antiplatelet meds offer for secondary prevention of CVD- be aware of increased risk
 of bleeding
- . SGLT2 inhibitors Empagliflozin / Dapagliflozin
- SGLT2i can be started in primary care but worth noting that empagliflozin also now NICE approved and has slightly broader reach than Dapagliflozin
- -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
- · for empagliflozin use in CKD- Check TA942 in NICE Guidelines
- https://www.nice.org.uk/quidance/ta942/chapter/1-Recommendations
- Check TA775 for dapagliflozin use in CKD Check TA775 in NICE Guidelines https://www.nice.org.uk/guidance/ta775/chapter/1-Recommendations

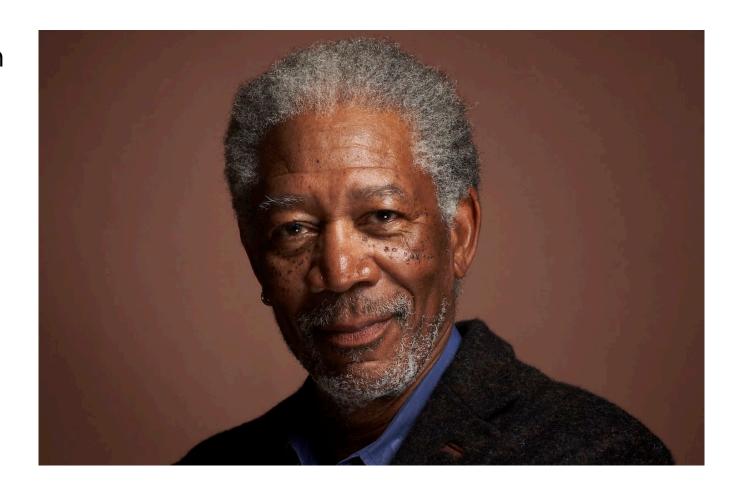
Referral Criteria to Secondary Care

- Advanced CKD 4/5. However many elderlies with stable CKD 4 do not need referral.
- A 5-year risk of needing renal replacement therapy of greater than 5% (measure using the 4-Variable Kidney Failure Risk Equation)
 The Kidney Failure Risk Equation
- · Deteriorating and heavy proteinuria (ACR>70 and not due to diabetes)
- ACR>30 mg/mmol + hematuria
- · Sustained decrease in GFR of 25% or more, and a change in GFR category
- Sustained Rapidly declining eGFR of 15ml/min or more/ year.
- Consider Referral if resistant hypertension despite four antihypertensive
- · Known / suspected rare or genetic cause of CKD.
- Suspected renal artery stenosis
- · Refer patients with CKD and renal outflow obstruction to urology services.
- Consider discussing management with a <u>specialist_via</u> Advice & Guidance in ERS if there are concerns but the person with CKD does not need to see a specialist.

Main message: SELECT CKD monitoring (KRFE) box on ICE 24/2/2024



- 85 year old Morgan Freeman
- BG:
 - Obstructive Uropathy
 - Hypertension
 - LVSD EF 30%
 - OA
 - Frail
- Current eGFR 26ml/min



• Background of AKI in 2015 due to obstruction - had a TURP

Kidney function recovered to eGFR 28ml/min then

• Hb 120

• BP 126/70

- Prescribed drugs:
 - Bisoprolol 5mg OD
 - Ramipril 5mg OD
 - Atorvastatin 20mg OD
 - Aspirin 75mg OD
 - Tamsulosin 400 micrograms OD
 - Co-codamol 8/500 2 tabs QDS
 - Furosemide 40mg OD
- No OTC NSAID use

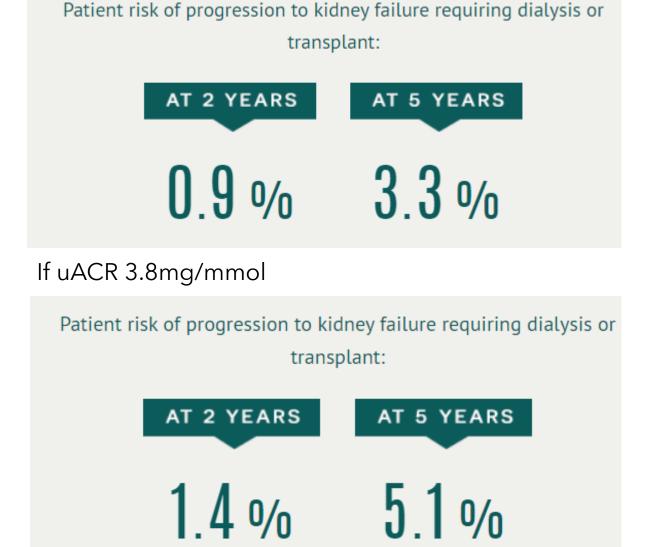
What next?

- Urine dipstick: 1+ blood, -ve protein
- Urine ACR: 1.4mg/mmol
- US abdomen: 2 x 9.6cm kidneys, thin cortices, 2 simple cysts on right kidney, 1 on left. No ongoing obstruction

• Refer?

 Remember ACR can vary with time - best to check early morning sample to minimise risk of dilute sample

Consider competing risks



- 36 year old Rebecca Ferguson
- Type 2 diabetes
- Laser treatment in right eye

- eGFR 46ml/min
- HbA1c 67mmol/mol (previously 70-80 for years)
- BP 138/88



- Current medications:
 - Tresiba OD
 - Novorapid TDS
 - Metformin 1g BD
 - Ramipril 5mg OD
 - Amlodipine 10mg OD
 - Atorvastatin 20mg OD

What next?

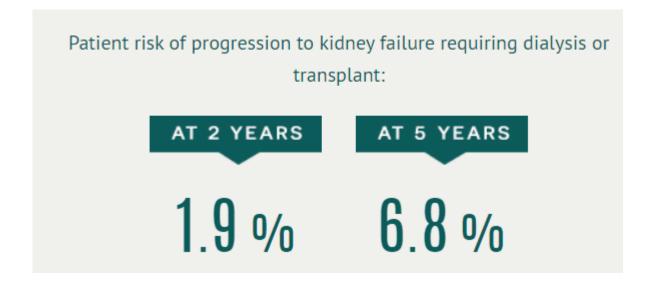
- ACR 158mg/mmol
- No blood
- Albumin 38

• ?Ultrasound

Indications for renal ultrasound in adults

- 1.2.5 Offer a renal ultrasound scan to all adults with CKD who:
 - have accelerated progression of CKD (see recommendation 1.3.5)
 - have visible or persistent invisible haematuria
 - have symptoms of urinary tract obstruction
 - have a family history of polycystic kidney disease and are older than 20
 - have a GFR of less than 30 ml/min/1.73 m² (GFR category G4 or G5)
 - are considered by a nephrologist to need a renal biopsy. [2008, amended 2014]

• Refer?



- Things to do while waiting for appointment?
 - Maximise ACEi
 - Start SGLT2i while waiting for appointment
- Be aware, both of these cause a slight decline in KF, but confer longer term reno-protection

- 74 year old Meryl Streep
- BG:
 - Hypertension
 - Smoker
 - BMI 34
- BP 158/92
- eGFR 45ml/min (Creat 108umol/L)
- 2 years ago eGFR 55ml/min (Creat 92umol/L)



- Current medications:
 - Amlodipine 10mg OD
 - Bendroflumathiazide 2.5mg OD
- Not taking NSAIDs

• What next?

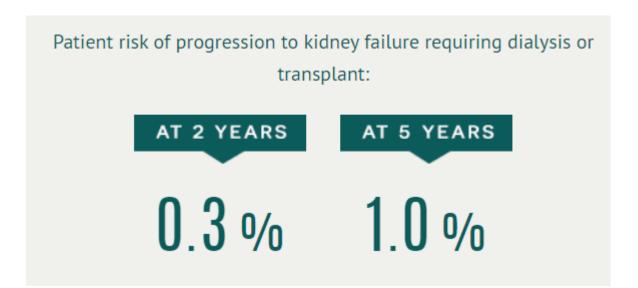
- Urine dipstick Blood 2+ Protein 1+ Leuk 2+
- Urine ACR 20mg/mmol

• MSU - negative

• Ultrasound: Both kidneys 10.5cm

• Refer?

- Repeat urine dip after 6 weeks:
 - Blood 1+ Protein 1+ Leuk 2+
 - Urine ACR 10mg/mmol
 - MSU -ve
- Repeat urine dip after 6 more weeks
 - Bloods 2+ Protein 1+ Leuk 2+
 - Urine ACR 13mg/mmol
 - MSU -ve

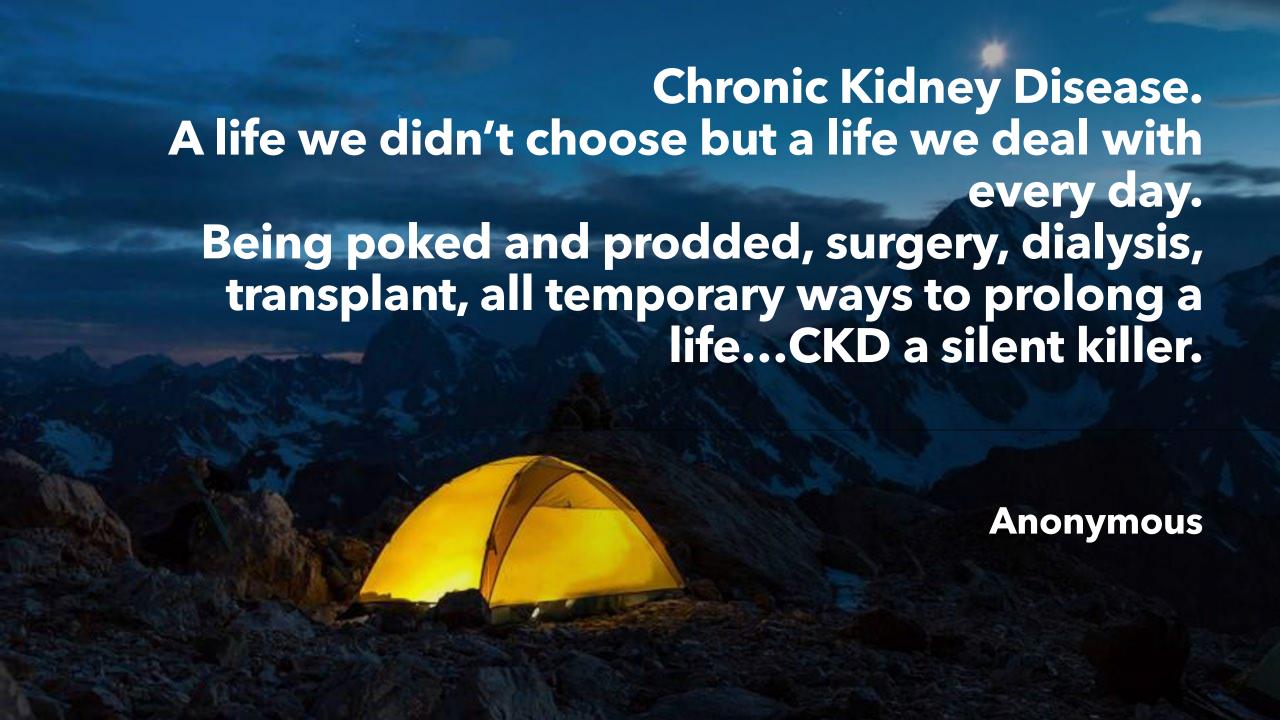


UROLOGY!

- What else?
- Lifestyle: Advise weight loss, exercise, stopping smoking
- Start ACEi for BP management
- Start atorvastatin 20mg OD
- Consider Empagliflozin when eGFR <45ml/min

NICE's guideline on hypertension in adults recommends using clinic blood pressure for monitoring response to lifestyle changes or medical treatment (see recommendation 1.4.15).

- 1.6.1 In adults with CKD and an ACR under 70 mg/mmol, aim for a clinic systolic blood pressure below 140 mmHg (target range 120 to 139 mmHg) and a clinic diastolic blood pressure below 90 mmHg.
 [2021]
- 1.6.2 In adults with CKD and an ACR of 70 mg/mmol or more, aim for a clinic systolic blood pressure below 130 mmHg (target range 120 to 129 mmHg) and a clinic diastolic blood pressure below 80 mmHg. [2021]
- 1.1.9 Do not use a risk assessment tool for people who are at high risk of CVD, including people with:
 - type 1 diabetes (see the <u>section on primary prevention of CVD for people with type 1</u> <u>diabetes</u>)
 - an estimated glomerular filtration rate less than 60 ml per minute per 1.73 m² and/or albuminuria (see the <u>section on primary and secondary prevention of CVD for people</u> <u>with chronic kidney disease [CKD]</u>)
- 1.8.1 Offer atorvastatin 20 mg for the primary or secondary prevention of CVD to people with CKD.[May 2023]
- 1.8.2 If the lipid target for primary or secondary prevention of CVD (see <u>recommendation 1.6.1</u> and <u>recommendation 1.7.1</u>) is not met and eGFR is 30 ml per minute per 1.73 m² or more, increase the dose of atorvastatin. [May 2023, amended December 2023]





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Thank you

