Chronic Kidney Disease

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Common queries

- Declining eGFR; when to worry
- Proteinuria; which level is significant

- ACEin/ARB usage
- Furosemide usage
- Renal cysts
- Very frail / elderly with renal impairment

CKD for primary care
- distilled to one page

Chronic kidney disease (CKD) for primary care - identification; monitoring; referral; management

offer testing with eGFR, urine diptest & ACR for

- diabetes
- hypertension
- acute kidney injury in primary or secondary care
- cardiovascular disease
- structural renal tract disease
- multisystem diseases with potential kidney involvement
- family history of end-stage or hereditary kidney disease
- opportunistic detection of haematuria

Offer a renal ultrasound scan to all with CKD and

- accelerated progression of CKD (eGFR >60 and decline >10 ml/min on < 3 years)
- visible or persistent invisible haematuria (>40 refer to urology; <40 monitor for CKD
- symptoms of urinary tract obstruction
- FH of polycystic kidney disease and > 20 years old
- an eGFR of less than 30 ml/min

Key Points

1. ACR test at least 1x/yr
2. Patients with an eGFR <60 ml/min should be on the practice CKD register
3. Patients with an eGFR <30 ml/min +/or an ACR 30 mg/mmol should have a care plan agreed with secondary care nephrology

Frequency/year of monitoring by stage of CKD

eGFR (ml/min) \ ACR (mg/mmol)		ACR Category		
		A1 <3 (normal)	A2 3-30 (high)	A3 30+ (v high)
eGFR category	G1 (90+)	1	1	1+
	G2 (60-89)	1	1	1+
	G3a (45-59)	1	1	2
	G3b (30-44)	1-2	2	2+
	G4 (15-29)	2	2	3
	G5 (<15)	4	4+	4+

Referral to kidney team

1. **stage 4-5 CKD (an eGFR <30 ml/min)**
2. **Acute Kidney Injury (sudden (days-weeks)) eGFR decline >25% from baseline)**
3. **decline in eGFR (months-years) from baseline of >25% and a change in CKD stage**
4. **blood & protein in urine on diptest in the absence of infection confirmed on retesting**
5. **ACR >30 mg/mmol, even if the eGFR is normal**
6. **CKD and hypertension despite 4 agents**
7. **Where indicated for Hb <110 g/L and eGFR <45 ml/min (see below)**

Management

Blood Pressure

- <140/85 if ACR <30 mg/mmol and no diabetes (<150/90 if >80 years old)
- 120-129/<80 if diabetes or ACR >30 mg/mmol
- ACEi or ARB as first line if one of: <55 years old, diabetes, ACR >30mg/mmol

Diabetes

- Target HbA1c to 48 - 58 mg/mmol

CVD prevention

- Offer Atorvastatin 20 mgs nocte to all patients with stage 3-5 CKD as primary prevention
- Use all other conventional indications for primary and secondary prevention (e.g. Aspirin)

Anaemia

- Check Hb if eGFR <45 ml/min. If Hb <110g/L check haematinics and address deficiency including iron (ferritin <100 ug/mmol).
- If Hb <110 g/L after supplementation discuss with nephrology.

Vitamin D and bone

- Where vitamin D supplementation is required prescribe cholecalciferol or ergocalciferol to patients with stage 1-3 CKD. CKD 4-5 and vitamin D deficiency – discuss with nephrology
- Offer bisphosphonates if indicated to patients with CKD except for stage 4 and 5

Communication

- Most people with CKD are at very low risk of dialysis, you can calculate this risk for the patient at kidneyfailurerisk.com/
- Agree with the patient a care plan to include frequency of eGFR and ACR monitoring
- It may help to explain that kidney damage can indicate some 'wear' on the blood supply in the kidneys and therefore care should be taken around management of CVD risk and diabetes

Chronic kidney Disease (CKD) staging

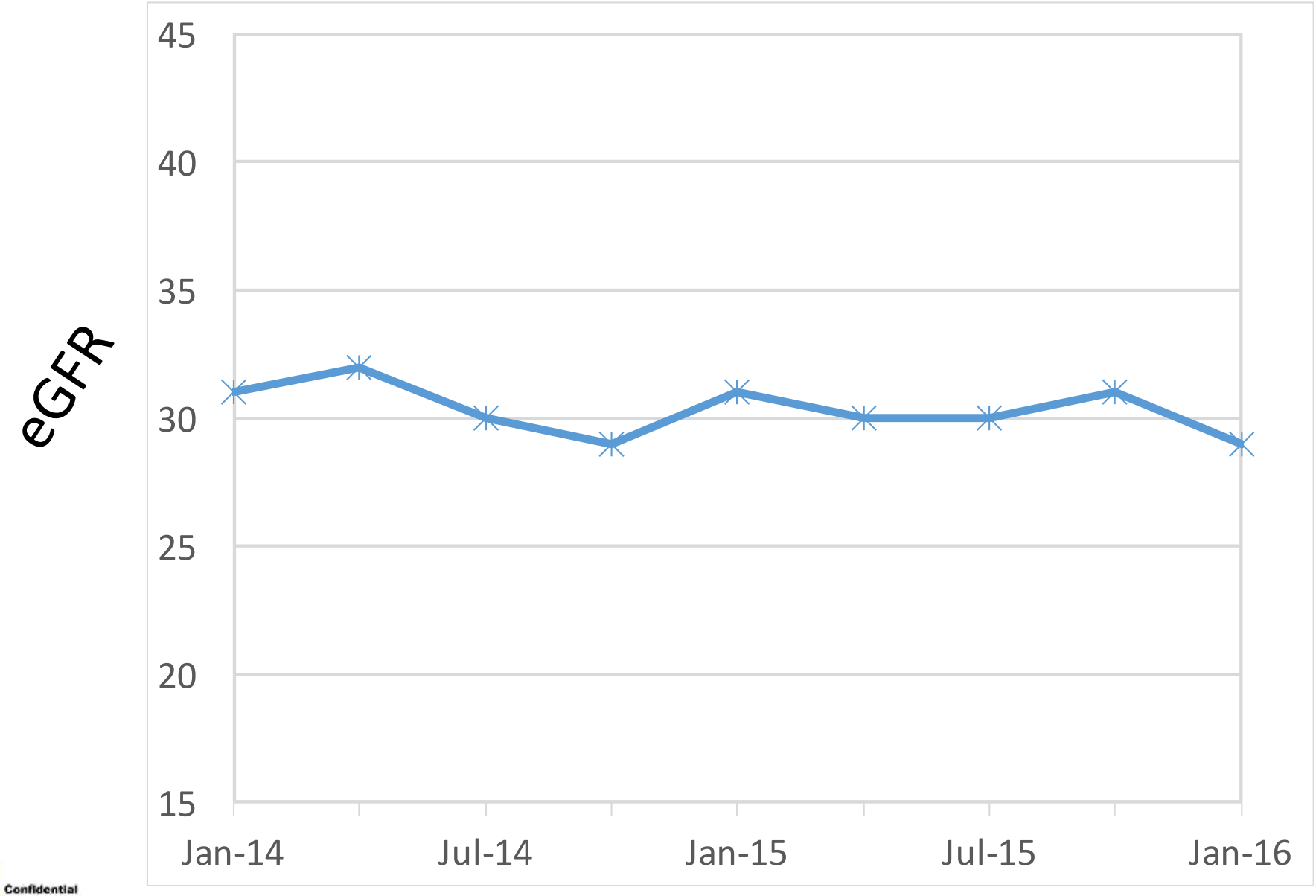
GFR stage	ml/min	GFR term
G1	≥90	normal or high
G2	60–89	normal or mild
G3a	45–59	mild to moderate
G3b	30–44	moderate to severe
G4	15–29	severe
G5	<15	kidney failure
Albuminuria	**UACR mg/mmol**	**Albuminuria**
A1	<3	normal
A2	3–30	high (micro)
A3	>30	very high (macro)

How do you explain kidney function testing to a patient?

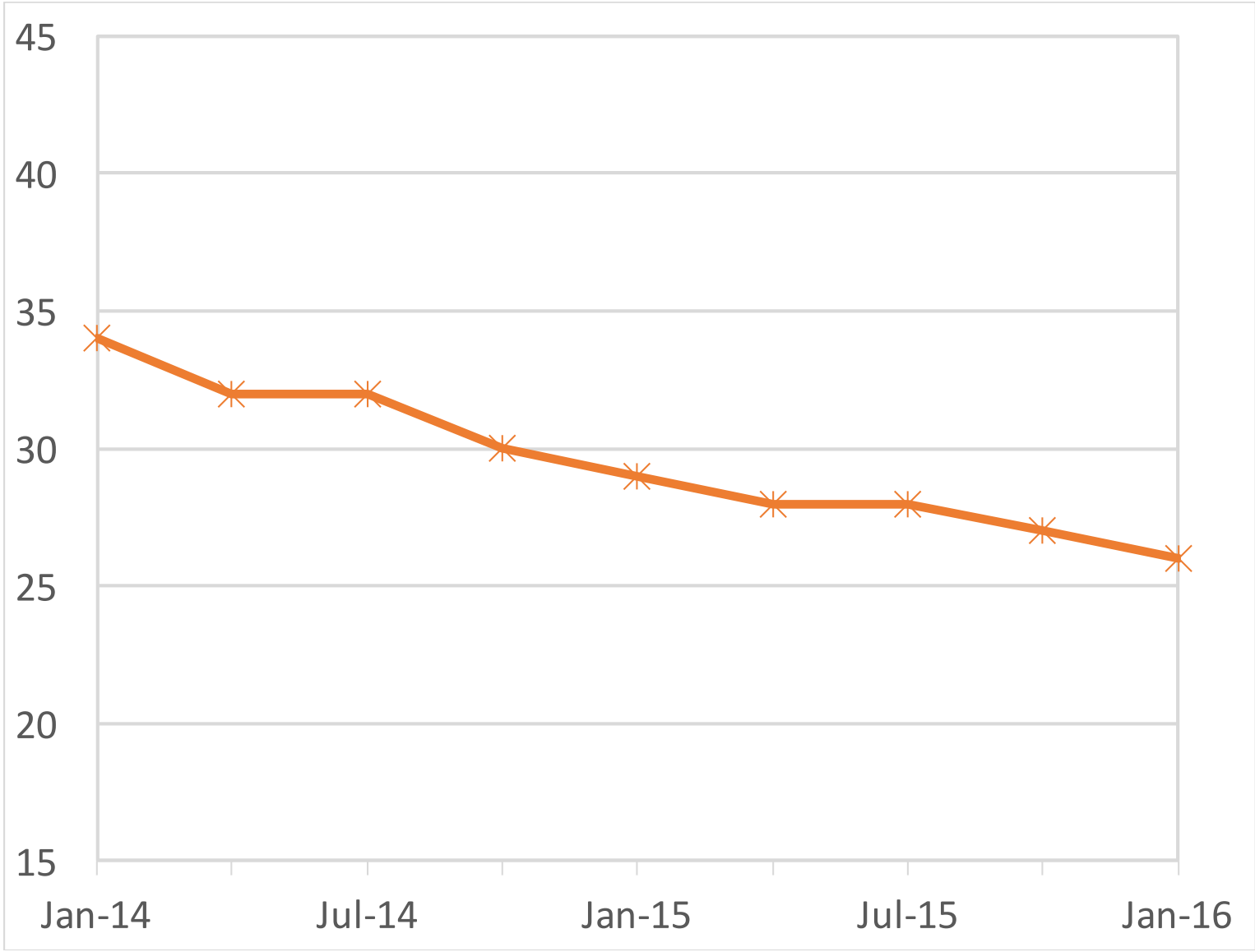
eGFR

ACR

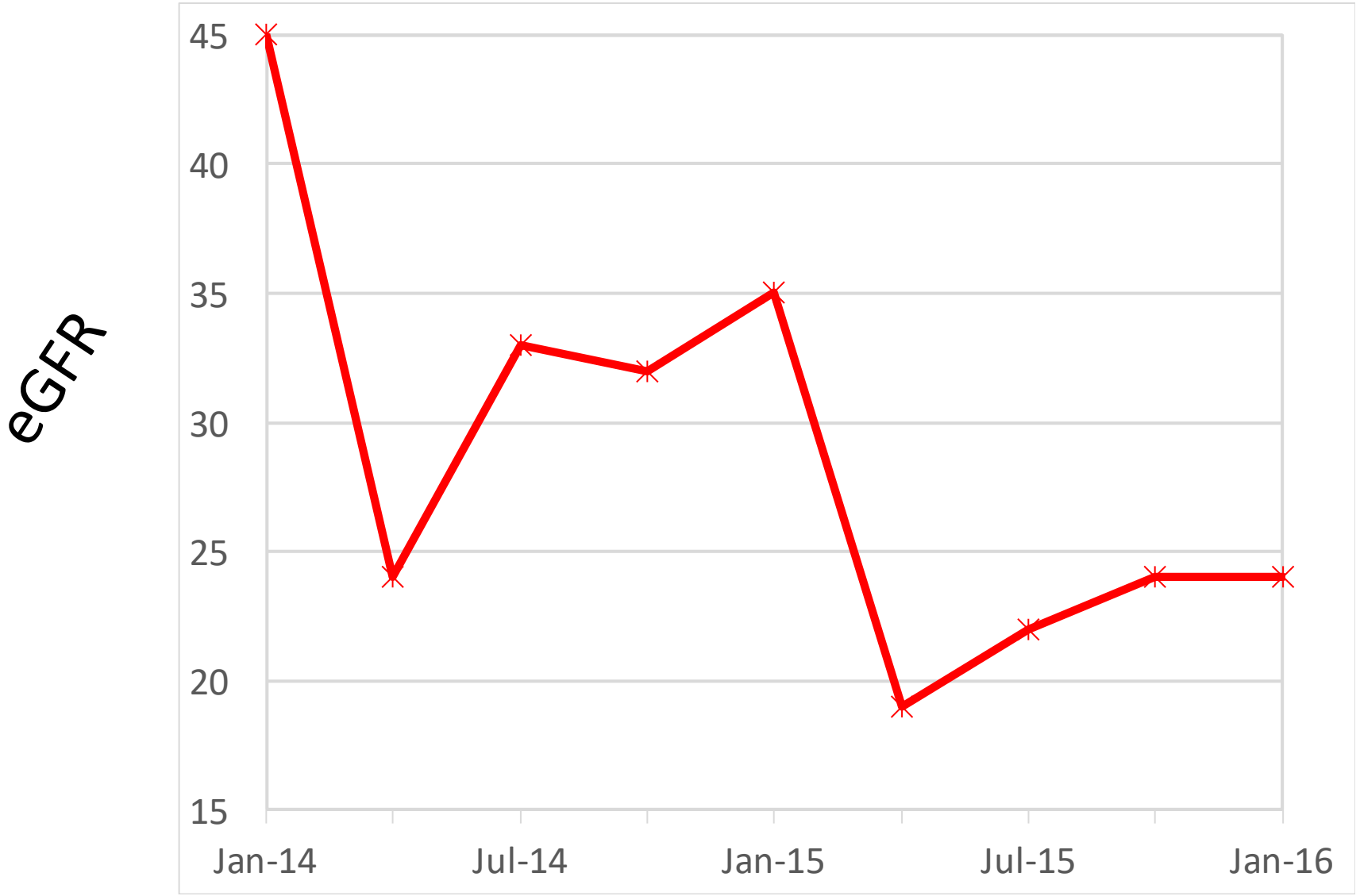
CKD - Slow Progressor



Proteinuric CKD (fast progressor)



Acute Kidney Injury on CKD

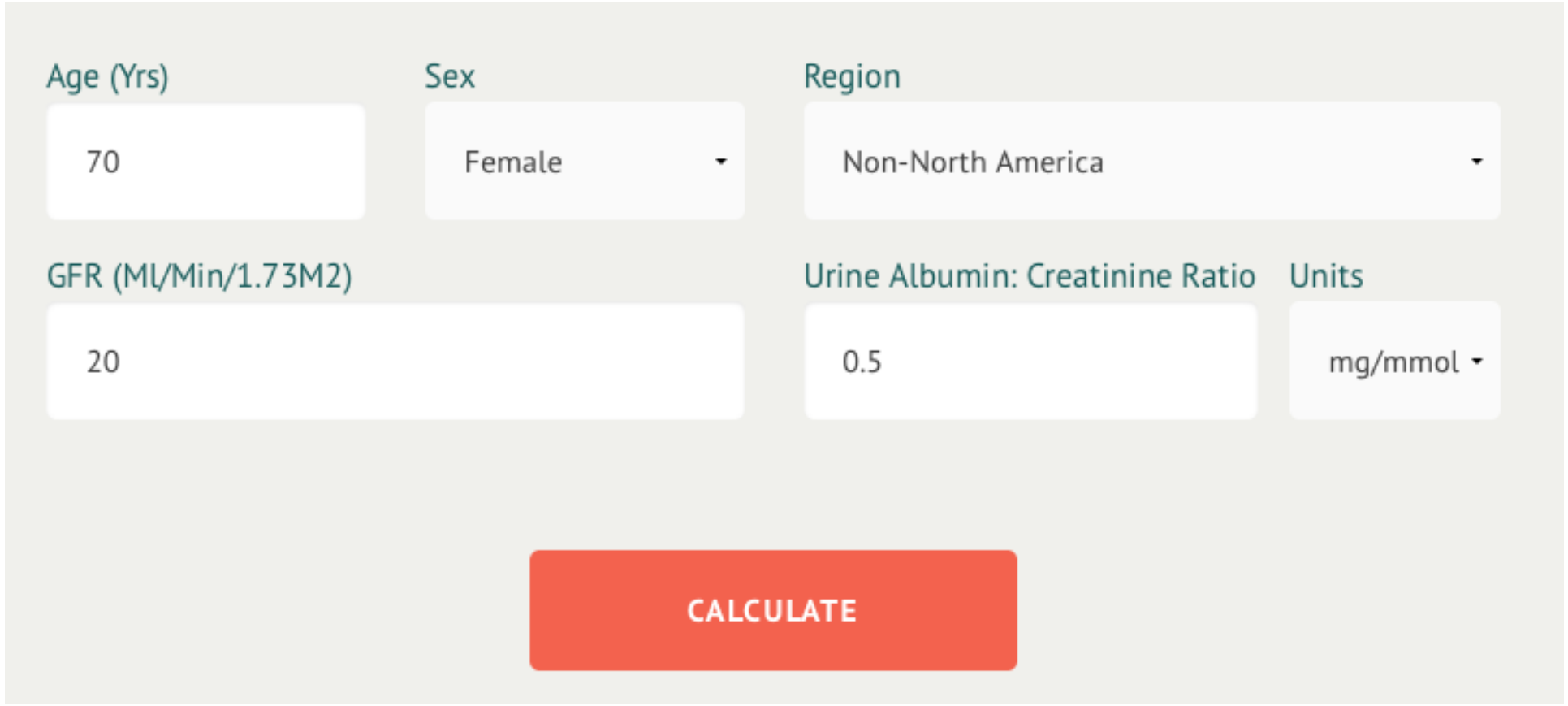


70 year female; eGFR 20, ACR 0.5 mg/mmol

Risk of end-stage renal failure at 2-years?

1. 1.7%
2. 7%
3. 17%
4. 37%

http://kidneyfailurerisk.com



0.5
URINE ALBUMIN-CREATININE RATIO

F
SEX

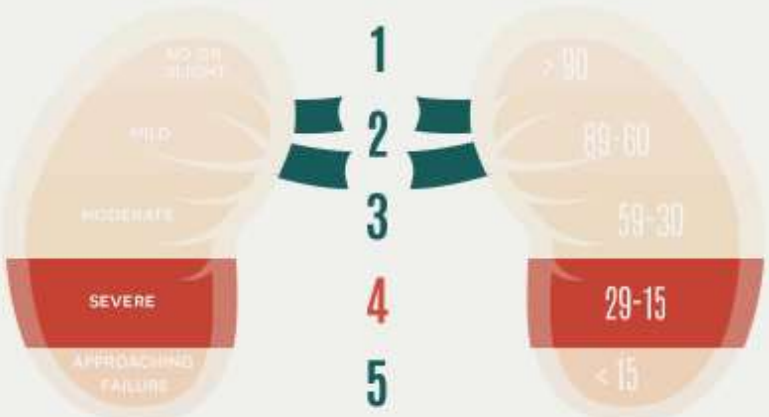
70
AGE

20
GFR

ASSESSMENT

STAGE 4

SEVERE DECREASE IN FUNCTION



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

AT 2 YEARS	AT 5 YEARS
1.7 %	6.44 %

0–5 % IS LOW RISK 5–15 % IS INTERMEDIATE RISK 15 % IS HIGH RISK

PRINT YOUR RESULTS

DOWNLOAD YOUR RESULTS

40-year male; eGFR 20, ACR 100 mg/mmol
Risk of end-stage renal failure at 2-years?

1. 1.7%
2. 7%
3. 17%
4. 37%

100
URINE ALBUMIN-CREATININE RATIO

M
SEX

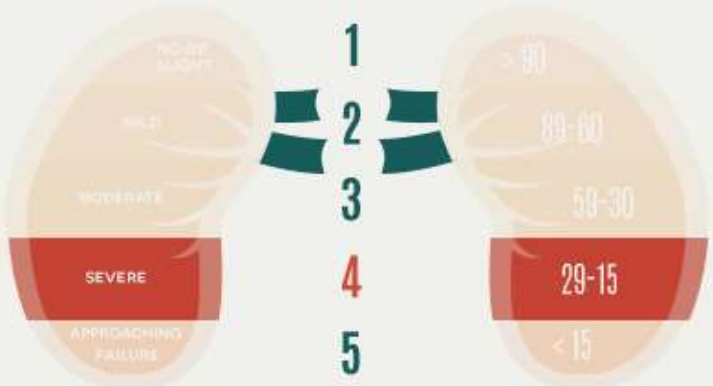
40
AGE

20
GFR

ASSESSMENT

STAGE 4

SEVERE DECREASE IN FUNCTION



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

AT 2 YEARS	AT 5 YEARS
37.19 %	83.48 %

0–5 % IS LOW RISK 5–15 % IS INTERMEDIATE RISK 15 % IS HIGH RISK

PRINT YOUR RESULTS

DOWNLOAD YOUR RESULTS

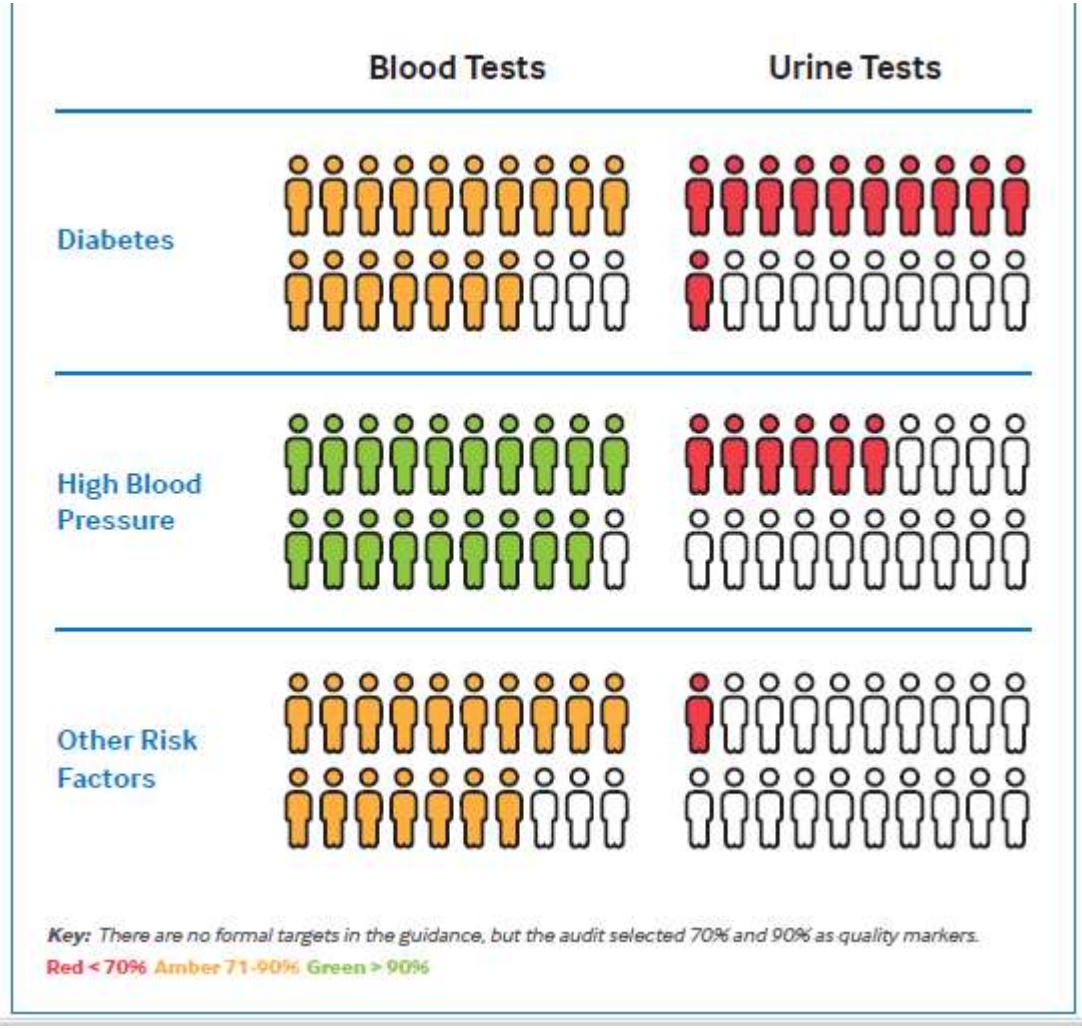
An ACR of 100 = an AER of 1g/d

	Normal	High	Very high
ACR (mg/mmol)	<3	3-30	>30
PCR (mg/mmol)	<15	15-50	>50
AER (mg/day)	<10	10-300	>300
PER (mg/day)	<50	50-500	>500
Urine diptest	-ve to trace	Trace to 1+	>1+

A quality improvement programme for chronic kidney disease

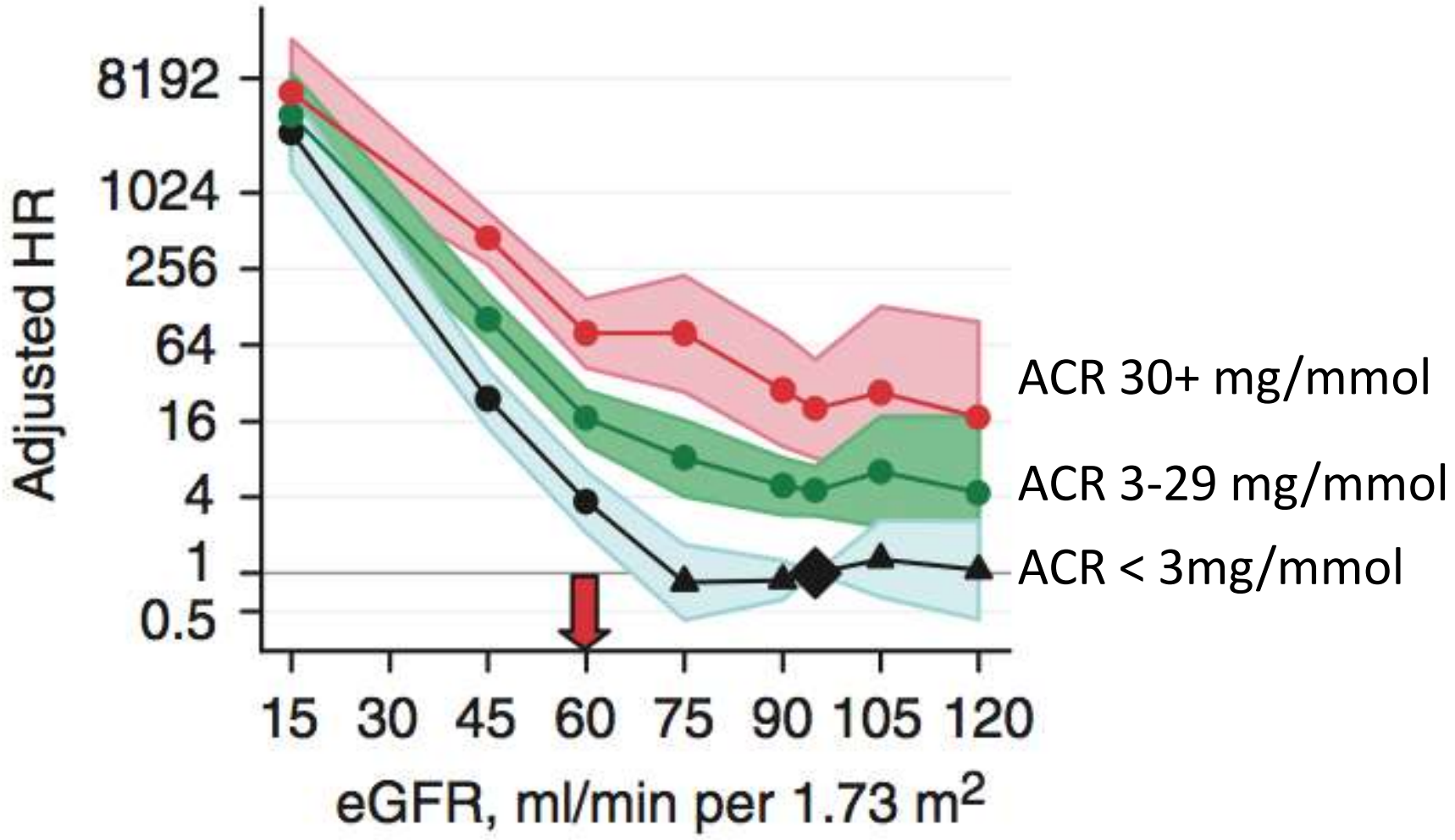
National CKDAudit

data from 911 practices (74% of Welsh and 86% of English practices, 2015-2016)



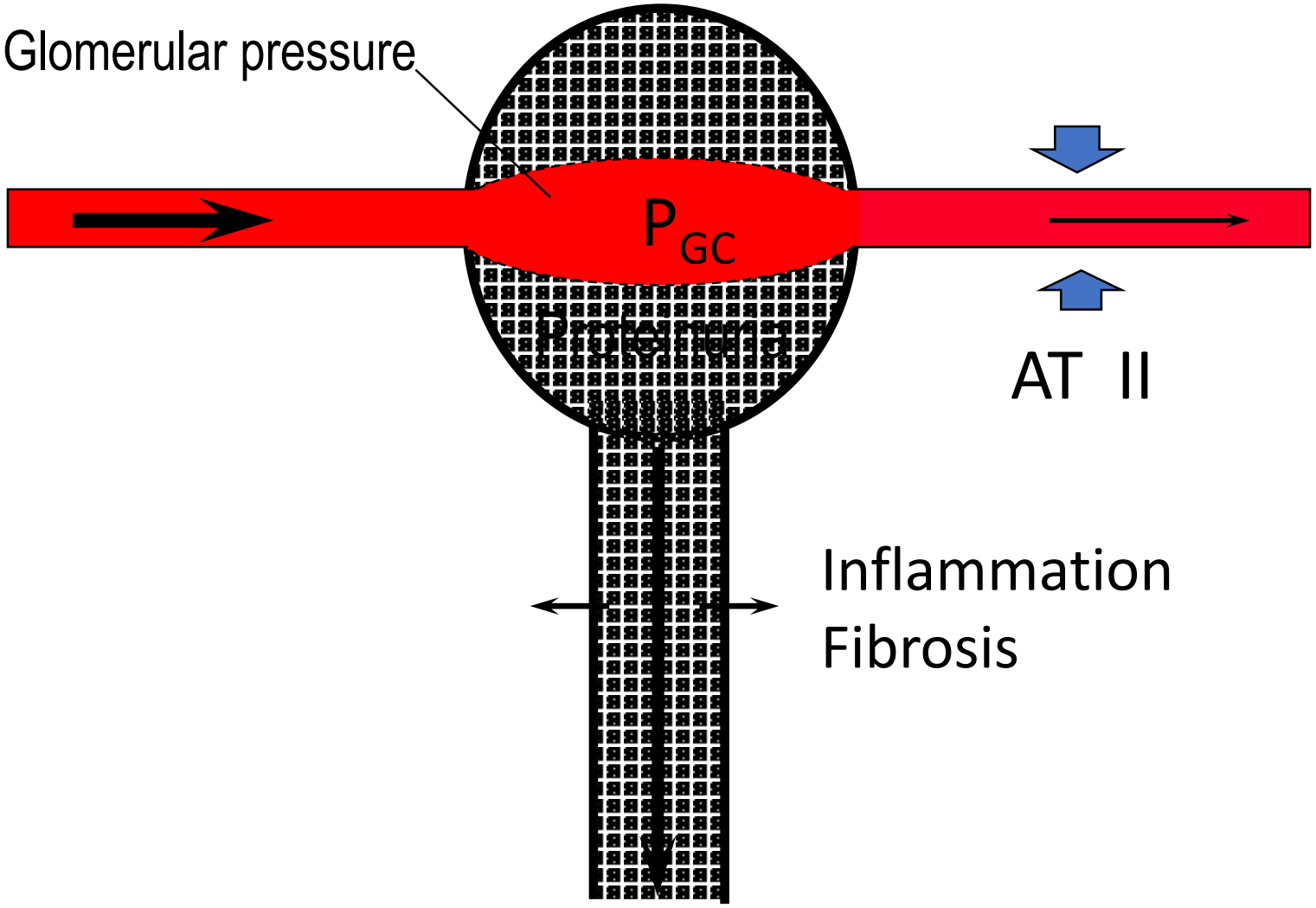
86% of people with diabetes for have an annual eGFR but **only 54% have urine tests**

Risk of ESKD in respect of eGFR and proteinuria

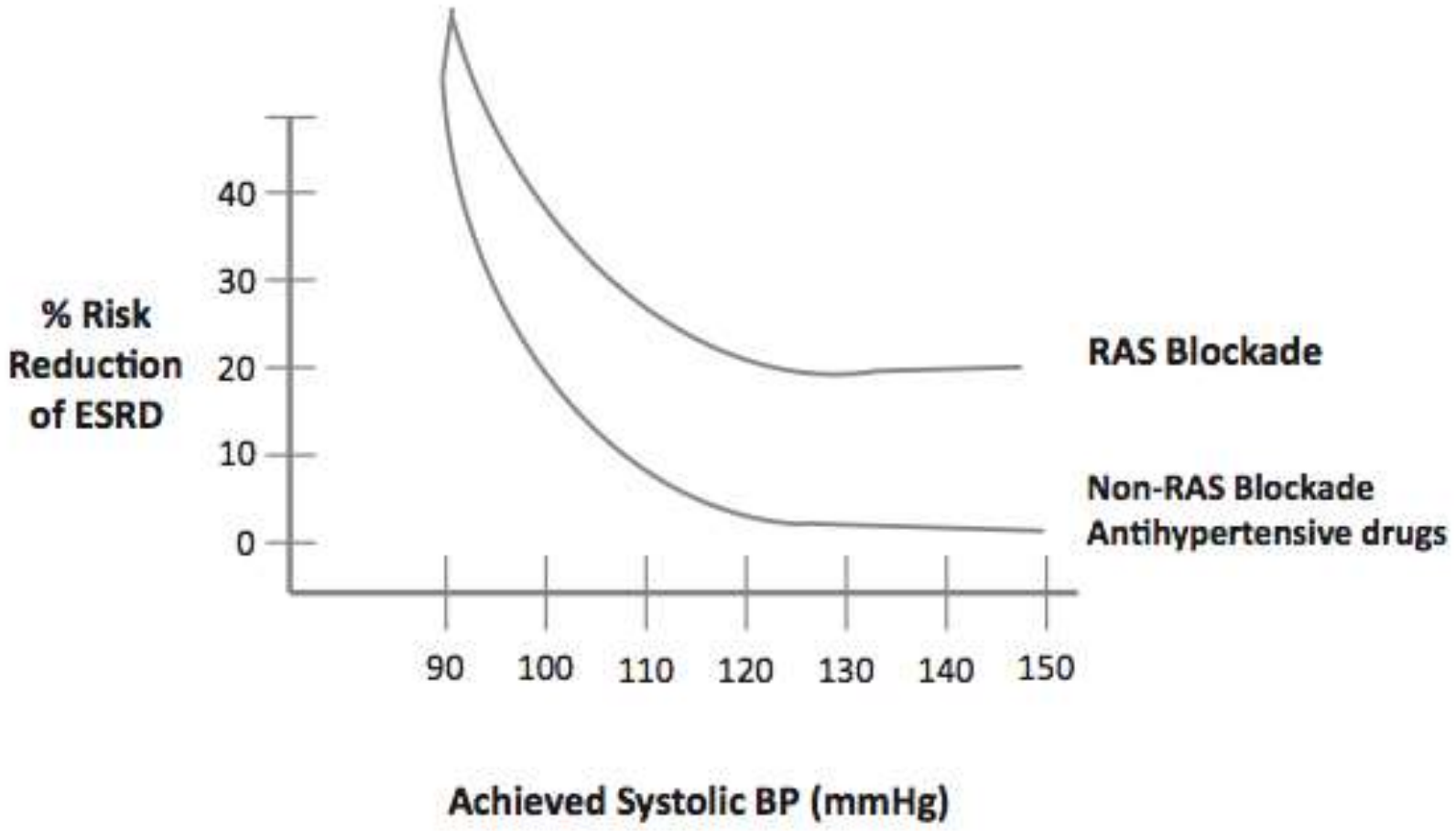


Adapted from Levey et al KI 2011

High intraglomerular pressure promotes proteinuria



In high risk groups ACEi/ARBs provide a 20% risk reduction in ESKD



From Weir, NephSap; Vol 5 No 10, 2011

Evidence base for pre-dialysis CKD

Therapy	Comment
ACEi/ARB	Include normotensive if ACR>3mg/mmol
	Target BP <130/80
HbA1c <60 mg/mmol	Care with older people and low HBA1c
Statin (for CVD primary prevention)	Not dialysis

Diabetes drugs

	Kidney function	Comment
Metformin	> 30 ml/min eGFR	?eGFR <30ml/min
Sulphonylurea	>30 ml/min	Hypoglycaemia
DDP-4i	OK	
SGLT-2	>30 ml/min	Don't start if eGFR<45
Thiazolidinediones	OK	Not on dialysis
GLP-1 receptor antagonists	>30 ml/min	

ABCD guideline – Managing hyperglycaemia in patients with diabetes and diabetic nephropathy-chronic kidney disease

- Sodium glucose co-transporter-2 (SGLT2) inhibitors: recommendations

- Clinical trial data has shown:
  - Canagliflozin and empagliflozin reduce cardiovascular outcomes in patients at high cardiovascular risk
  - Patients with eGFR 60 to <90 mL/min/1.73 m^2 gain cardiovascular benefit

"…we recommend that this drug class be considered over other glucose-lowering therapies for patients with stage 2 chronic kidney disease (CKD)"

- Data has also shown SGLT2 inhibitors improve renal endpoints, including:
  - changes in serum creatinine and eGFR
  - the need for end-stage renal replacement therapy

SGLT2 inhibitors (currently canagliflozin and empagliflozin) are recommended to help improve renal outcomes for patients with T2DM and high cardiovascular risk

Frequent self-monitoring of blood glucose isn't necessary for patients with type 2 diabetes and CKD who are treated with SGLT2 inhibitors unless they are also being treated with other medicines that can cause hypoglycaemia (e.g. sulfonylureas and insulins)

Association of British Clinical Diabetologists. Managing hyperglycaemia in patients with diabetes and diabetic nephropathy-chronic kidney disease. 2018. [Accessed May 2019].
https://abcd.care/sites/abcd.care/files/site_uploads/Images/ABCD%E2%80%93RA_Managing%20glycaemia%20guideline_Recommendations%20summary.pdf

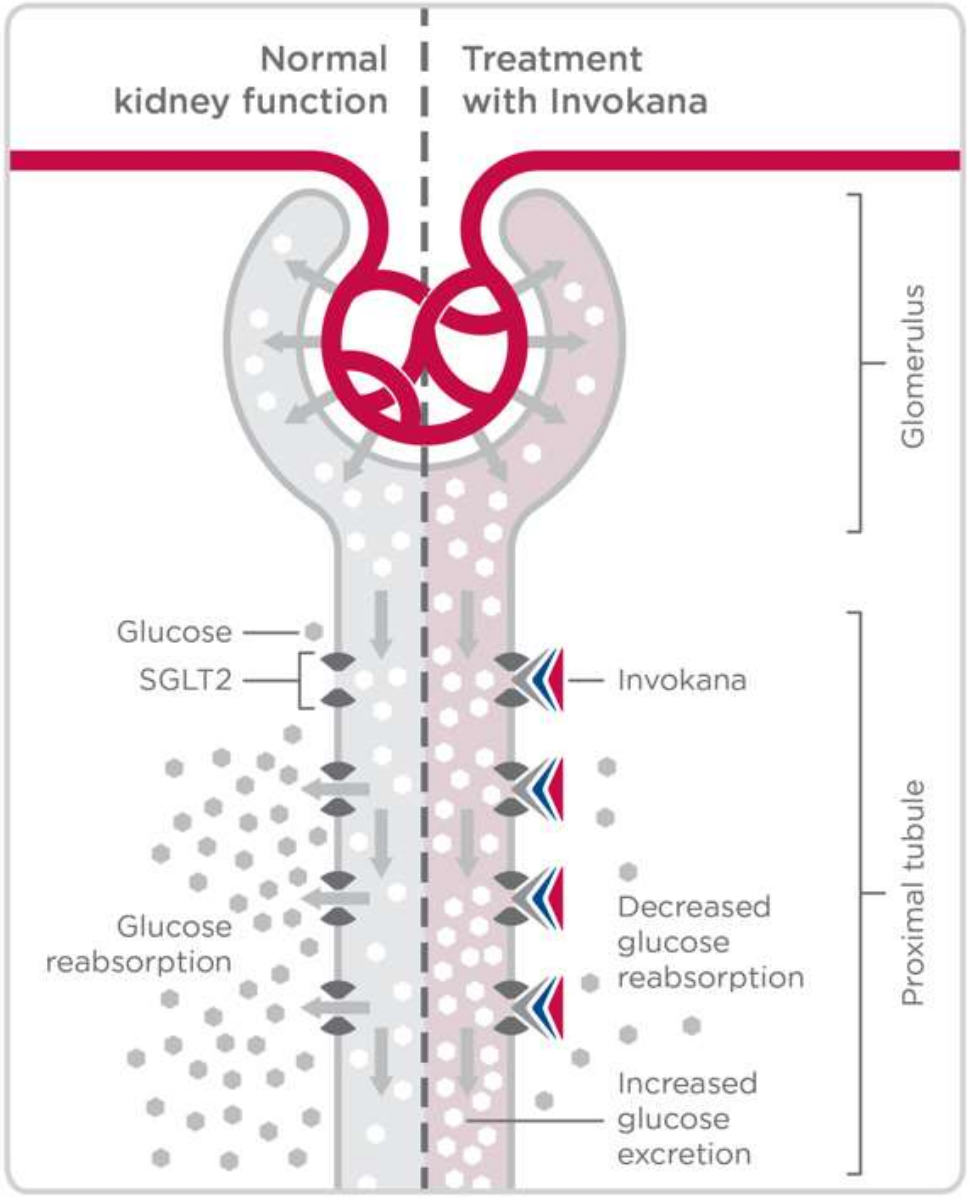
NAPP DIABETES

CREDENCE

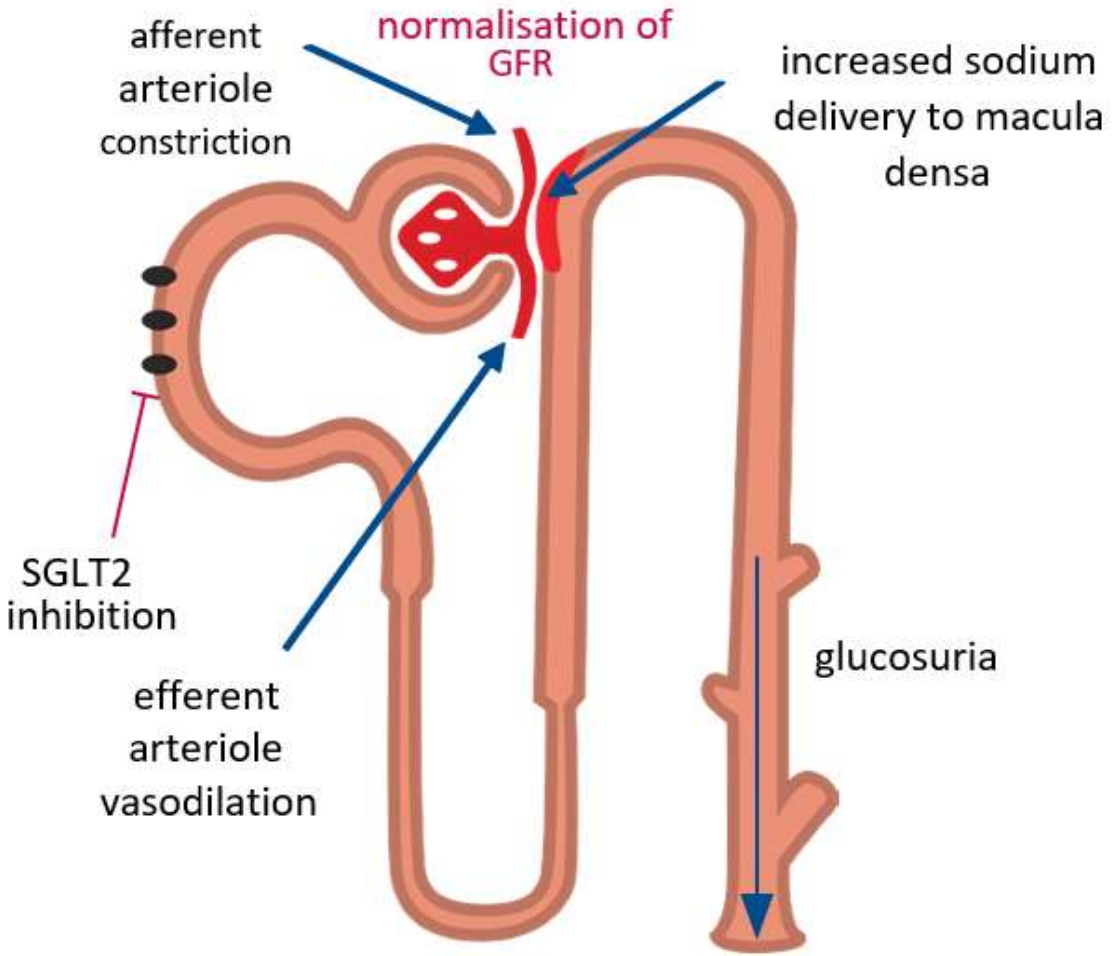
Canagliflozin and renal outcomes in type 2 diabetes and nephropathy

Perkovic V, Jardine MJ, Neal B, Bompoint S, Heerspink HJL, Charytan DM, et al.,

N Eng J Med. 2019. Apr 14

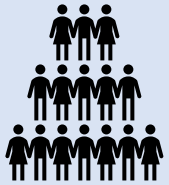


SGLT2 inhibition has multiple effects including decreasing glomerular hyperfiltration



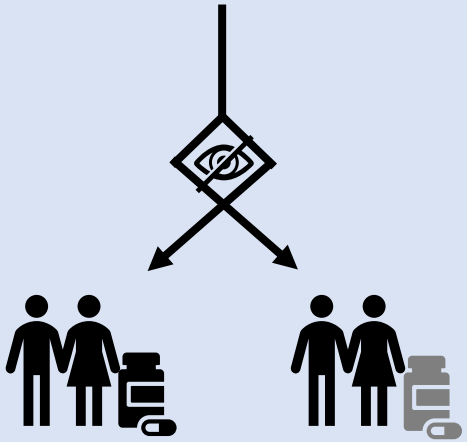
Does canagliflozin (SGLT2i) improve renal outcomes for type 2 diabetic patients with CKD and proteinuria?

Study design



GFR 30-90
>30 years
HbA1c 6.5-12%
uACR >300-5000
Stable max ACE/ARB

N=4401



Canagliflozin
N=2202

Placebo
N=2199

Participant characteristics

Age 63 years ± 9.2
33.9% women

GFR 56.2 ml/min/1.73m² ±18.2

HbA1c 8.3% ± 1.3

uACR 927 mg/g
± 463-1833 (105 ml/mmol)

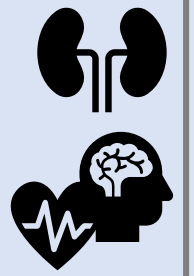
BP 140/78 mmHg
± 15.6/9.4

Primary outcome

Composite: ESRD, doubling serum creatinine, GFR <15, renal or CV death

Canagliflozin

43.2 per 1000 patient/yr



Placebo

61.2 per 1000 patient/yr

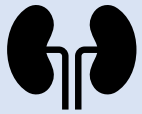
HR = 0.7 (0.59-0.82)

NNT = 21 (15-38)

Does canagliflozin (SGLT2i) improve renal outcomes for type 2 diabetic patients with CKD and proteinuria?

Secondary outcomes

ESRD, doubling serum creatinine or renal death



HR 0.66 (0.53-0.81)

Cardiovascular outcomes

HR 0.74 (0.63-0.86)

Death any cause

HR 0.83 (0.68-1.02)

Adverse effects

Fractures
HR 0.98
(0.7-1.37)

Amputation
HR 1.11
(0.79-1.56)

Genital mycotic infection

HR 9.3 (2.83-30.6) ♂
HR 2.1 (1.0-4.45) ♀

UTI
HR 1.08
(0.9-1.29)

DKA
HR 10.8
(1.39-83.65)

Discussion

1. Adds to body of data supporting flozins in reducing adverse outcomes in diabetic KD
2. Timely incorporation into current guidelines
3. Safety for stage 4-5 CKD
4. Amputation risk: CANVAS HR 1.9 and fracture risk: CANVAS HR 1.26
5. Surveillance advice for dehydration and mycotic infection
6. Unwanted side effects: Osmotic diuresis and dehydration and ketoacidosis
7. Further SGLT2i studies to report in 2019-2022 (VERTIS CV, DAPA-CKD, SCORED and EMPA-KIDNEY)

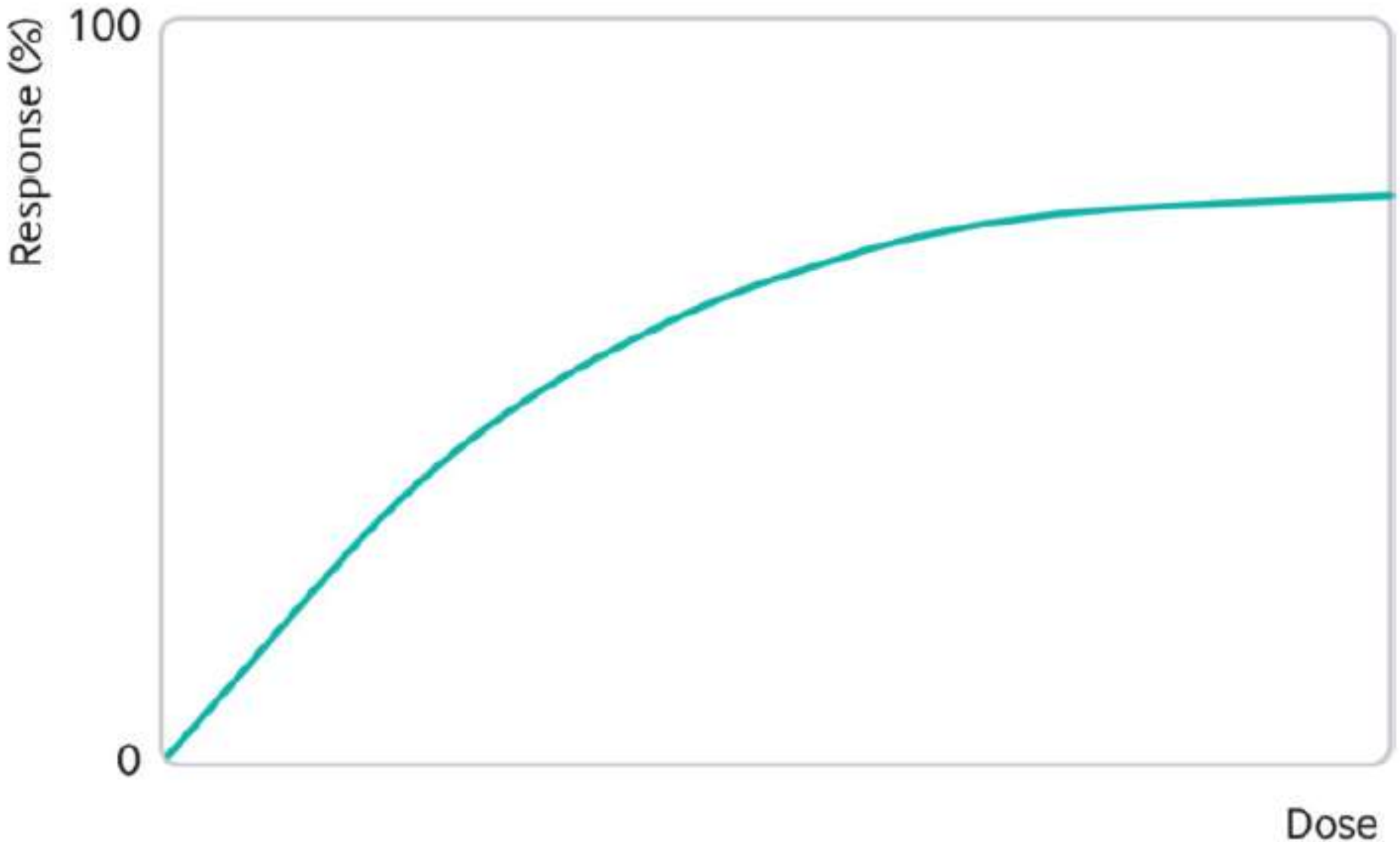
Diuretic dosing

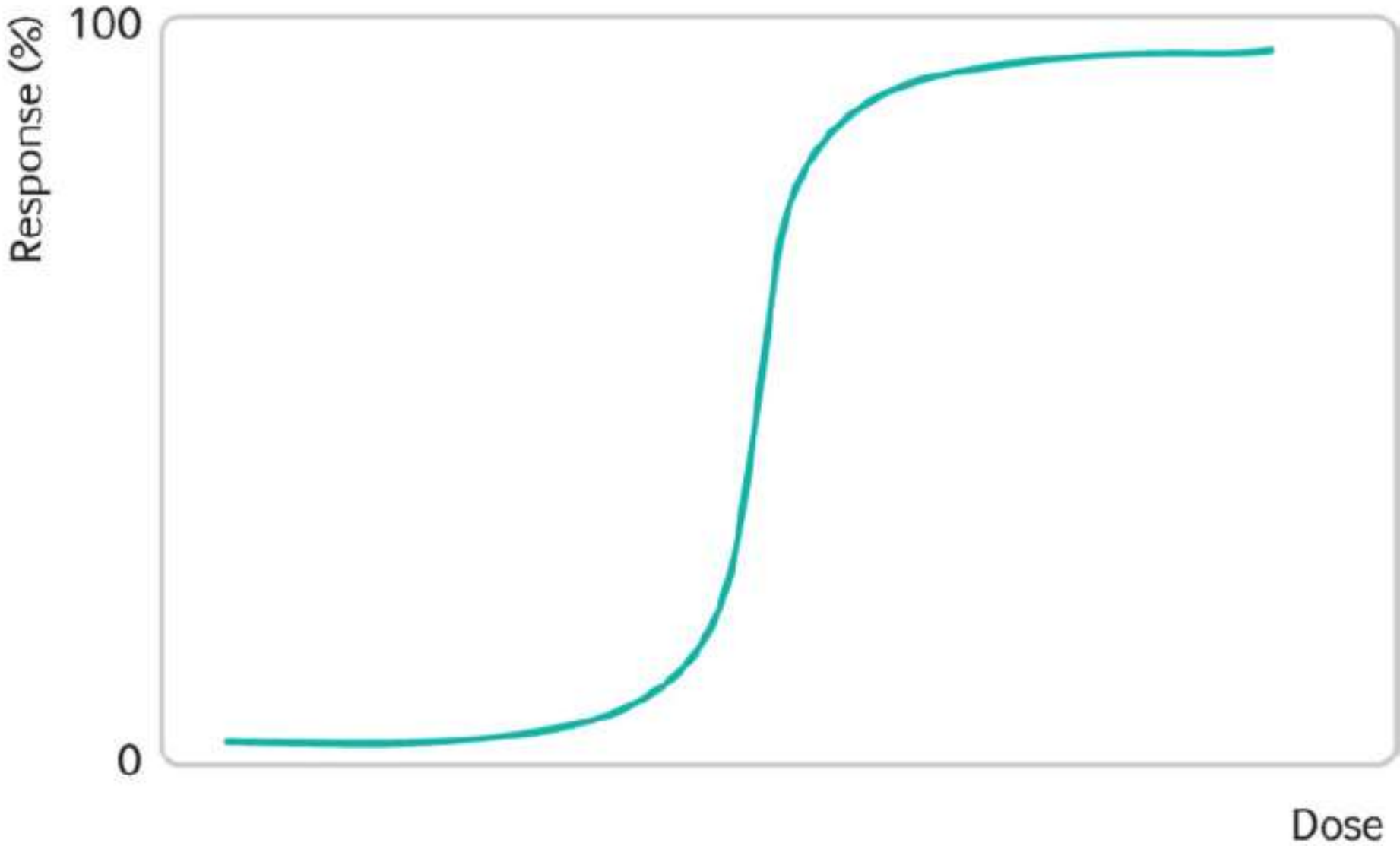
- A 65 year old man with known heart failure attends the surgery with worsening peripheral oedema and breathlessness

- He is on treatment that includes an ACE inhibitor at maximum dose and furosemide at 80mg once daily

- His last eGFR was 24 ml/min/1,.73m^2 two months ago, which is stable compared with previous readings

How do you manage this patient?


Response (%)
100
0
Dose


Response (%)
100
0
Dose

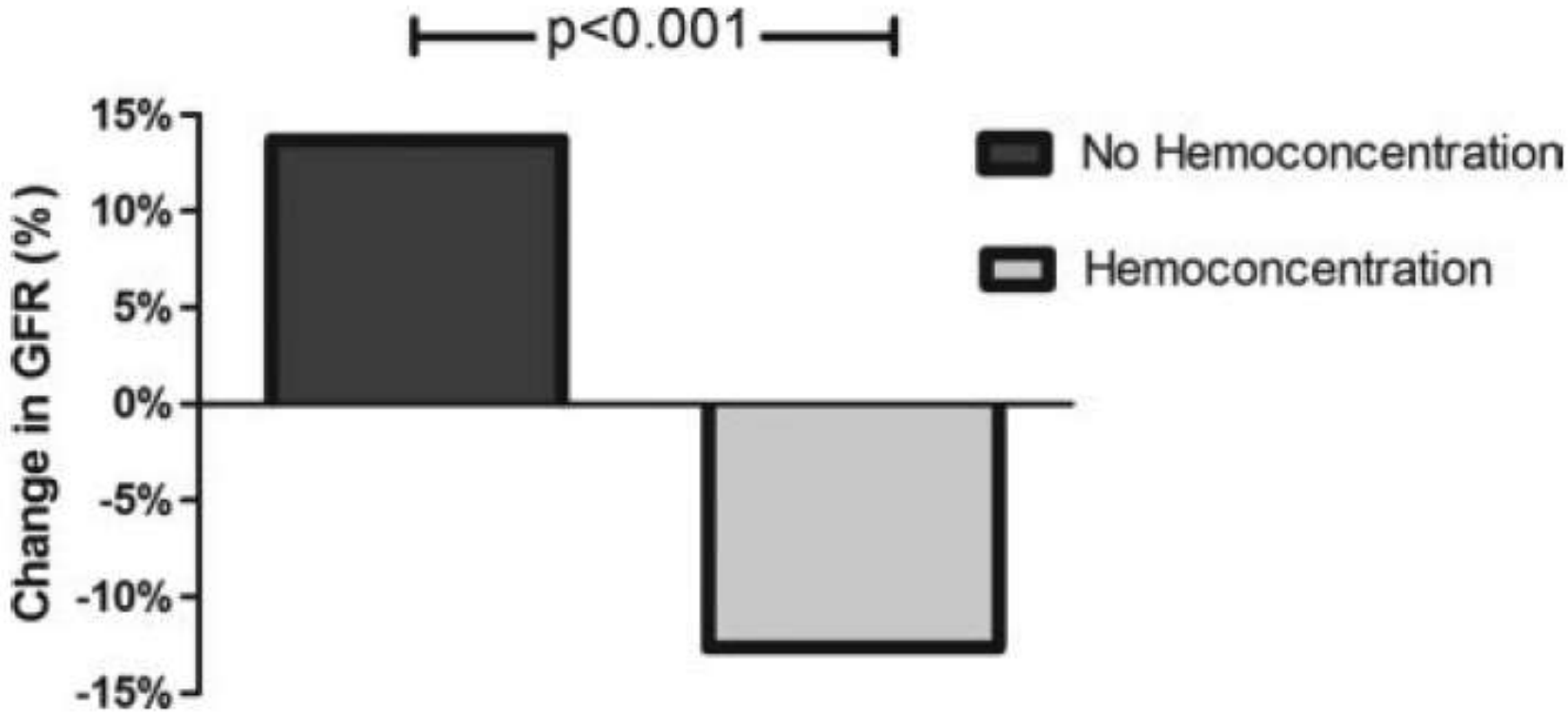
Loop diuretics are threshold dose drugs, therefore increase the single dose rather than split an increased dose

Should you stop the diuresis if creatinine is increasing?

Potential Effects of Aggressive Decongestion During the Treatment of Decompensated Heart Failure on Renal Function and Survival

Jeffrey M. Testani, MD; Jennifer Chen, BS; Brian D. McCauley, BS;
Stephen E. Kimmel, MD, MSCE; Richard P. Shannon, MD

Circulation. 2010;122:265-272;



You may need a very big diuretic dose in renal impairment

- The drug's intratubular concentrations (not serum concentrations) determine if the therapeutic threshold is reached
- Larger doses may be needed with renal impairment and/or proteinuria
- Tolerance can develop over time at a given dose and a given level of kidney function

As needed dosing or regular dosing?

How to determine if the dose is working?

- When does the patient urinate?
- How long does the effect last?

- Polyuria unrelated to dosing indicates not working

- Nocturia = ineffective daytime diuresis

- Daily weights

Practical management

- As needed = self management
- Check weights daily and use medication based on those weights
- Weights and symptoms can be used for patient activation

RAASi

- A fall in eGFR (and rise in creatinine) is very common after initiation of RAAS inhibitors
- A progressive fall in GFR on RAAS inhibition suggests primary renal disease, including extra-renal and intra-renal vascular disease
- For patients with HFrEF, the benefit of RAAS inhibitors is the same in patients with and without worsening renal function during RAAS inhibition
- A moderate, asymptomatic decline in renal function is not an indication to stop RAAS inhibitors

- **There is unequivocal evidence that inhibitors of the RAAS improve survival in patients with HFrEF**
- **All such patients should be offered RAAS inhibitors**
- **There is no such evidence for patients with HeFpEF**

	Recommendations for RAAS inhibitors	
	HFPEF (assuming no other prognostic indication)	**HFREF**
Increase in serum creatinine by <30%	Consider stop ACEI/ARB Review MRA according to fluid status	Continue unless symptomatic hypotension
Increase in serum creatinine 30-50%	Stop RAAS inhibitor	Consider reducing dose or temporary withdrawal*
Increase in serum creatinine >50%	Stop RAAS inhibitor	Temporarily stop RAAS inhibitor*
Severe renal dysfunction e.g. eGFR <20	Stop RAAS inhibitor	Stop RAAS inhibitor if symptomatic uraemia irrespective of baseline function

RAASi and kidneys – clinical considerations

- Compare to baseline renal function (review series of results).
- Assess fluid status: if intravascularly depleted (JVP not visible, postural drop in BP, no oedema) consider cautious IV fluids.
- Interpret blood pressure in the context of usual values (low BP does not necessarily mean patient needs fluid).
- Reduce/withdraw RAASI if symptomatic hypotension.
- Repeated clinical and biochemical assessment is vital.
- Presence of moderate or severe hyperkalaemia may over ride recommendations based on change in renal function.
- In severe renal dysfunction assess for symptoms or uraemia.

K >5.4 mmol/l??

- Check for over-diuresis/hypovolaemia
- Non-selective beta-blockers can increase potassium. Review indication
- Stop K supplements
- Stop amiloride, triamterene
- Stop NSAIDs
- Stop trimethoprim
- Stop sodium substitutes
- Check for digoxin toxicity
- Provide low K diet advice
- ?Potassium lowering agents

Serum K^+	Mild hyperkalaemia 5.5-5.9 mmol/L	Moderate hyperkalaemia 6.0-6.4 mmol/L	Severe hyperkalaemia >6.5 mmol/L
Patient clinically well, no AKI	Increase frequency of biochemical monitoring, but do not stop RAASi	Stop RAAS inhibitor(s), repeat test Re-start at lower dose once K^+<5.5 Re-start one drug at a time, with biochemical monitoring, if the patient was previously on a combination of ACEI or ARB plus MRA	Admit to hospital for immediate K^+-lowering treatment Stop RAAS inhibitor(s). Repeat blood test 24h later. Re-start at lower dose once K^+<5.5 Re-start one drug at a time,
Patient clinically unwell with sepsis or hypovolaemia and/or AKI	Withhold RAASi until sepsis/hypovolaemia corrected, then re-start	Withhold RAAS inhibitor(s) until sepsis/hypovolaemia corrected, then re-start once K^+<5.5	Withhold RAAS inhibitor(s) until sepsis/hypovolaemia corrected then re-start once K^+<5.5. Re-start one drug at a time
Patient clinically unwell with decompensated heart failure with/without AKI	Do not withhold RAASi. Treat congestion with loop diuretics or combination of loop and thiazide diuretics	Reduce dose of RAAS inhibitor(s) and monitor frequently. Treat congestion with loop diuretics or combination of loop and thiazide diuretics	Withhold RAAS inhibitor(s) and re-start at lower dose when serum K^+ < 6.0 Re-start one drug at a time,

RAAS inhibition

With-hold if potassium rises above 6.0 mmol/L, or creatinine rises more than 30%, RAAS

Towards end of life, consider stopping RAAS inhibitors.

RAAS inhibition has no known prognostic benefit in heart failure with preserved ejection fraction

RAAS inhibition for reno-protection is limited to patients with proteinuria

Fluid overload, Diuretics, RAAS

- Baseline: Blood pressure and weight

- Use diuretics to the dose required for management
  - High doses may be needed
  - A decline in renal function is not an indication to reduce dose if the patient remains congested
  - ACEi/ARB – what to do and when
  - MRA – take care; HFpEF vs HFrEF

When to refer (NICE)

- **Take into account individual's wishes and comorbidities**
- GFR <30 ml/min/1.73 m^2 (GFR G4 or G5)
- ACR ≥ 70 mg/mmol, unless known to be due to diabetes & already treated
- sustained drop GFR ≥ 25% + change in GFR category or
- sustained drop GFR ≥ 15 ml/min/1.73 m^2 or more within 12 months
- Others: 4+ drug hypertension or suspected
- <u>When to refer KFRE – risk of ESRF >3% at 5-years</u>