Office Management of Reduced GFR

Practical advice for the management of CKD

CKD Online Education – CME for Primary Care – April 27, 2016

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No relevant disclosures

Objectives

- Review current guidelines for evaluation, diagnosis and classification of CKD

- Caveats for interpretation of GFR

- Measurement, significance and treatment of Proteinuria

- Common electrolyte, hematologic and mineral metabolism abnormalities in CKD and how to treat them in primary care.

- Who should I refer? Who will progress?

The majority of people with CKD will be managed in general practice, not by specialists…

- Approximately **1 in 10** adults in Canada have CKD
- **Most patients** with abnormal kidney function will die without reaching end stage kidney disease
    - Risk of progression depends on cause of kidney disease, GFR, age, and level of proteinuria
- Renal replacement therapy is associated with significant mortality and loss of quality of life
- By identifying CKD earlier, interventions that improve CV outcomes and delay progression of CKD can be initiated in a timely manner

Prognosis of patients who reach end stage kidney disease

- The **average life expectancy** of a patient on dialysis is 5 years (2 years if >75 yrs old)

- The average life expectancy of a patient who starts dialysis in their late 20's is about 20 years

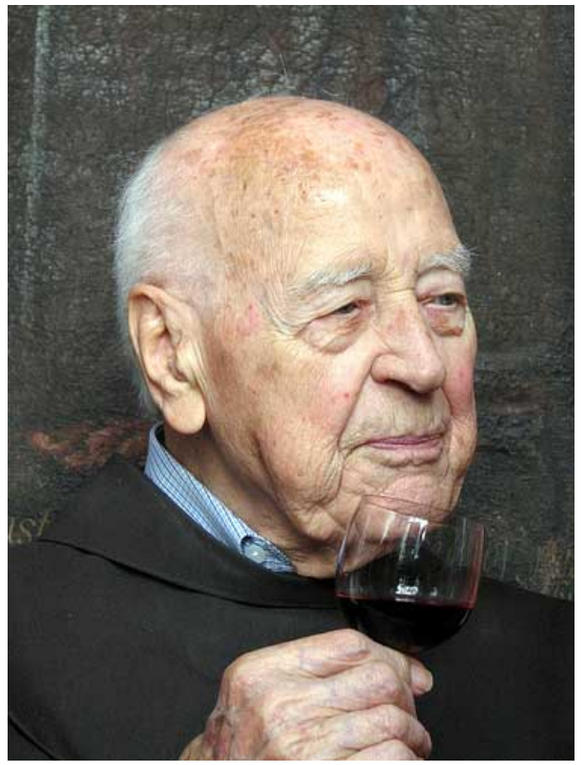
- A transplant increases a 30 yr old dialysis patient's life expectancy by 20 yrs beyond projected life expectancy with dialysis

The Patient with early stage CKD is 5 to 10 times more likely to die from a cardiovascular event than progress to ESRD

Foley RN et al. Chronic kidney disease and the risk for cardiovascular disease, renal replacement, and death in the United States Medicare population, 1998 to 1999. J Am Soc Nephrol 2005; 16:489-95

Identifying those who will progress – consider the following patients

- Risk of progression to dialysis
- GFR 30 ml/min
- 0.9% over 2 years
- 2.8% over 5 years



- Risk of progression to dialysis
- GFR 30 ml/min
- 5.3% over 2 years
- 16.6% over 5 years

- Risk of progression to dialysis
- GFR 30 ml/min
- 25% over 2 years
- 61.4% over 5 years

Screening for CKD — **only** for the populations at risk

- Diabetes
- Hypertension with or without CVD
- Family history of kidney disease
- Specific high-risk ethnic groups
  - First nations, Pacific Islanders, African descent, Asians

Screen at risk populations every 1-2 years depending on clinical circumstances using serum creatinine and random urine tests.

Investigation

- Estimated glomerular filtration rate (eGFR) is the best marker for CKD and is computed from the serum creatinine
    - Labs in BC automatically report eGFR when serum creatinine is ordered
    - **modest fluctuation in creatinine/eGFR are common and need to be contextualized — do not diagnose CKD based on one test!**
    - CKD diagnosis requires TIME, and thus persistence of abnormalities

CKD is classified by **eGFR** and amount of **albuminuria**

GFR category	GFR (ml/min/1.73 m²)	Terms
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	<15	Kidney failure

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.
*Relative to young adult level
In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

In the absence of kidney damage, an eGFR >60 is not kidney disease!

Diagnosis and staging of CKD

- CKD defined as “eGFR <60 mL/min for > 3 months, **or** evidence of kidney damage (pathological abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies)

    - If CKD — always do **urinalysis, ACR**

- Values between 60-100 mL/min in the absence of urine abnormalities or structural abnormalities **do not** indicate CKD

- A renal mass or complex cyst on ultrasound requires referral to a UROLOGIST

- Caution with overinterpretation of “medical renal disease” on ultrasound

Use of eGFR when > 60 mL/min

- DL is a 52 yr old man with well controlled hypertension. His eGFR has “fallen” from 89 mL/min —> 72 mL/min —> 65 mL/min over 2 years. His urinalysis is unremarkable, his ACR is < 2. Your next course of action is to:

1. Refer him to a nephrologist as you are concerned about his rapid decline of renal function

2. Continue to follow but reassure patient, realizing that GFR estimates are much less accurate at higher levels of GFR

Decreased accuracy of GFR estimates at higher levels of eGFR

- Several possible explanations
  - greater biologic and measurement variability of GFR at higher values
  - limitations of generalizing an equation developed in one population to another population

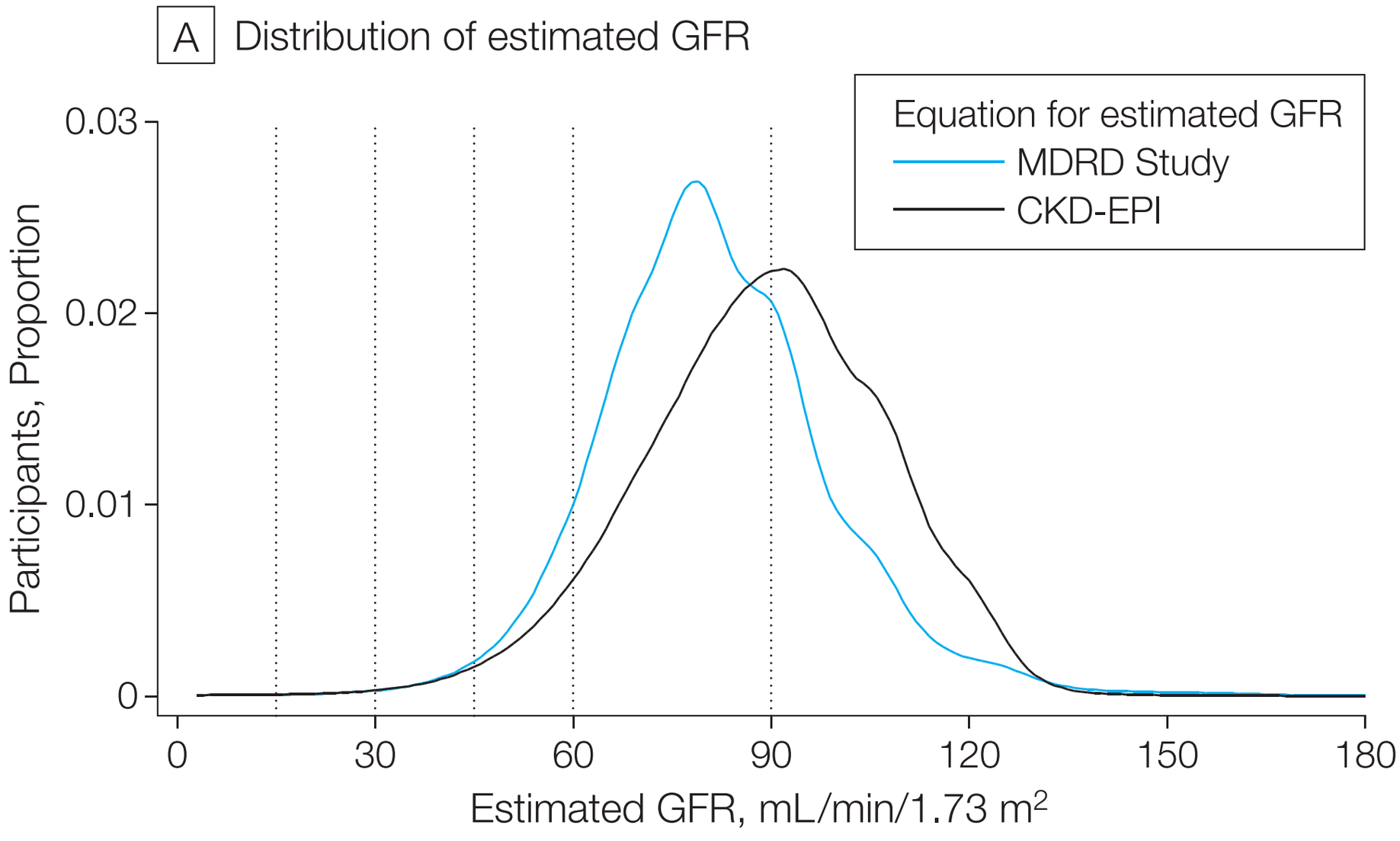
Serial GFR measurements are meant to follow CKD—they are not as accurate in patients without kidney disease!

The CKD-EPI equation classifies less people as having CKD

- Uses the same variables (age, gender, creatinine and race)
- Is more accurate, especially at higher GFR (> 60 mL/min)
- Classifies fewer individuals as having CKD
- compared with the MDRD equation, 24.4% of patients were re-classified to a **higher** GFR category

Levey AS et al, JAMA 2012;307(18): 1941-1951

The CKD-EPI equation classifies less people as having CKD

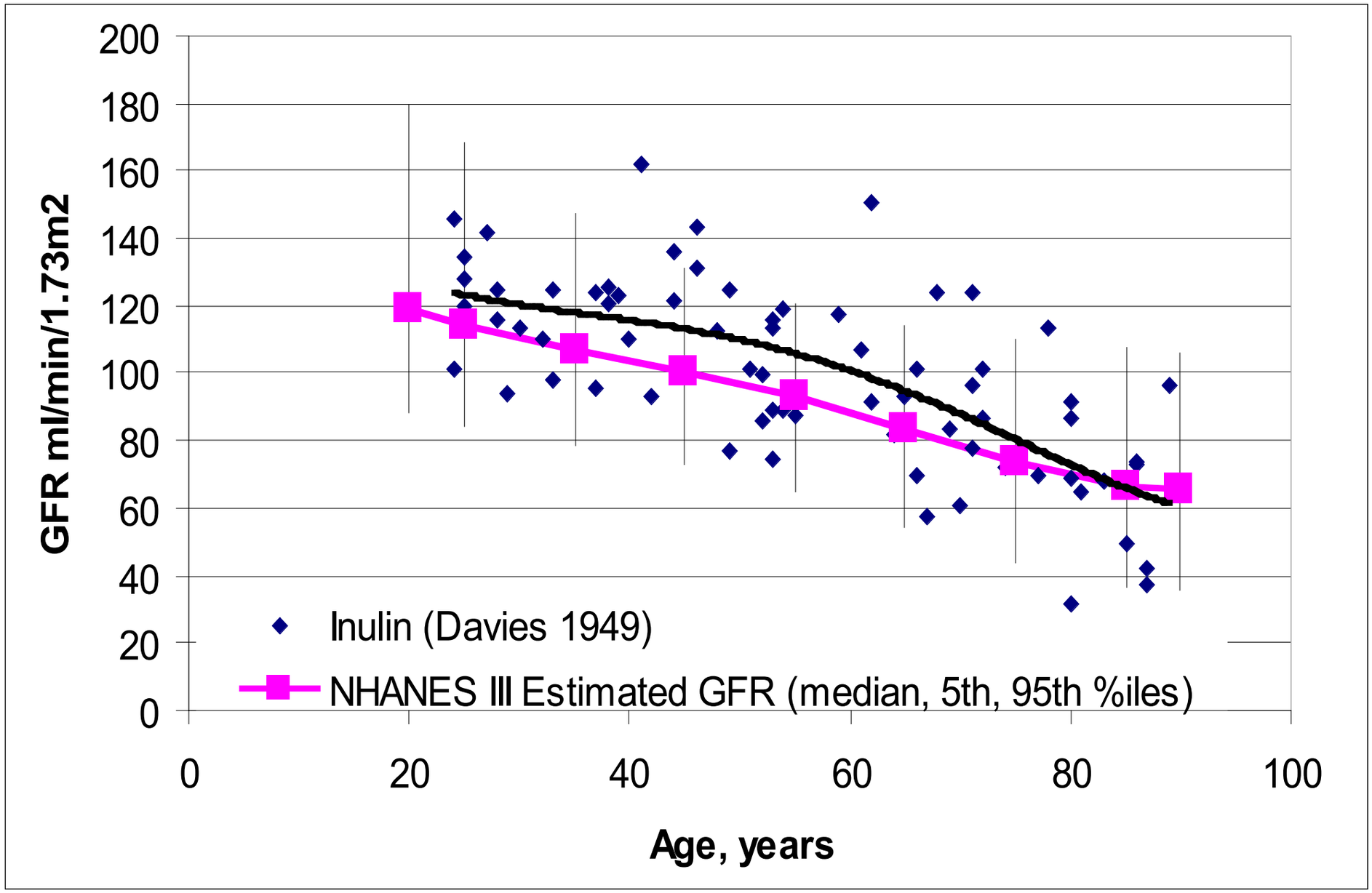


True or False?

eGFR measurements can be used as a reliable estimate of kidney function in elderly patients

False

Age and eGFR


GFR ml/min/1.73m2
200
180
160
140
120
100
80
60
40
20
0
0
20
40
60
80
100
Age, years
Inulin (Davies 1949)
NHANES III Estimated GFR (median, 5th, 95th %iles)

Caveats and practical interpretations of eGFR

- Age caveats
    - Age >75 — accuracy questionable and may **underestimate** true kidney function. Values 45-60 mL/min may be normal variation in the absence of other conditions
    - Age >85 — equation very problematic and risk of progression much less.
    - Caution persists with medications, dye, and risk of AKI with severe illness

True or False?

There is virtually no role for 24-hour urine collections for the evaluation of proteinuria

True

How to measure proteinuria

- Dipstick tests—pick up 300mg albumin or an ACR of 30 or higher
- Urine ACR—test of choice
  - **Confirm ACR >3 with at least 2 more samples (need 2 of 3 positive)**
    - Remember, albuminuria has large day to day variation and TRANSIENT PROTEINURIA may be due to poor BP control, glucose control, CHF, exercise, UTI
- 24 hr urine—UNNECESSARY in primary care

Urine ACR is the test of choice for measuring urine protein

	ACR (mg/mmol)	**Dipstick**	**mg/day**
A1 - Normal	<3	Negative	<30mg/d
A2 -Moderate increase	3-30	Negative, +1	30-300mg/d
A3 -Severe increase	> 30	+2, +3	> 300mg/d

True or False?

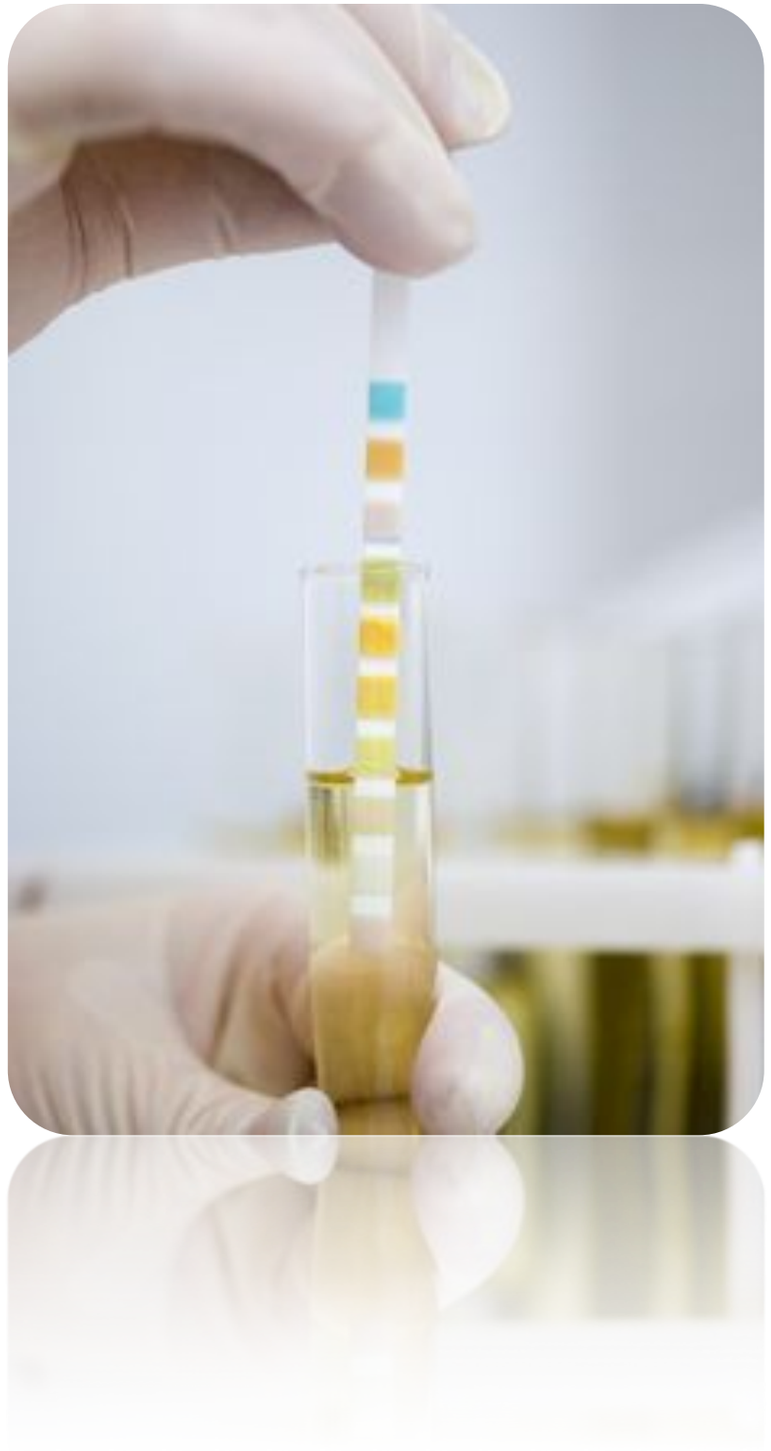
A patient with a GFR of 45 mL/min and an ACR of 1.0 mg/mmol (normal) has a similar risk of adverse events (cardiovascular and renal) as a patient with a GFR of 70 mL/min and an ACR of 15 mg/mmol

True

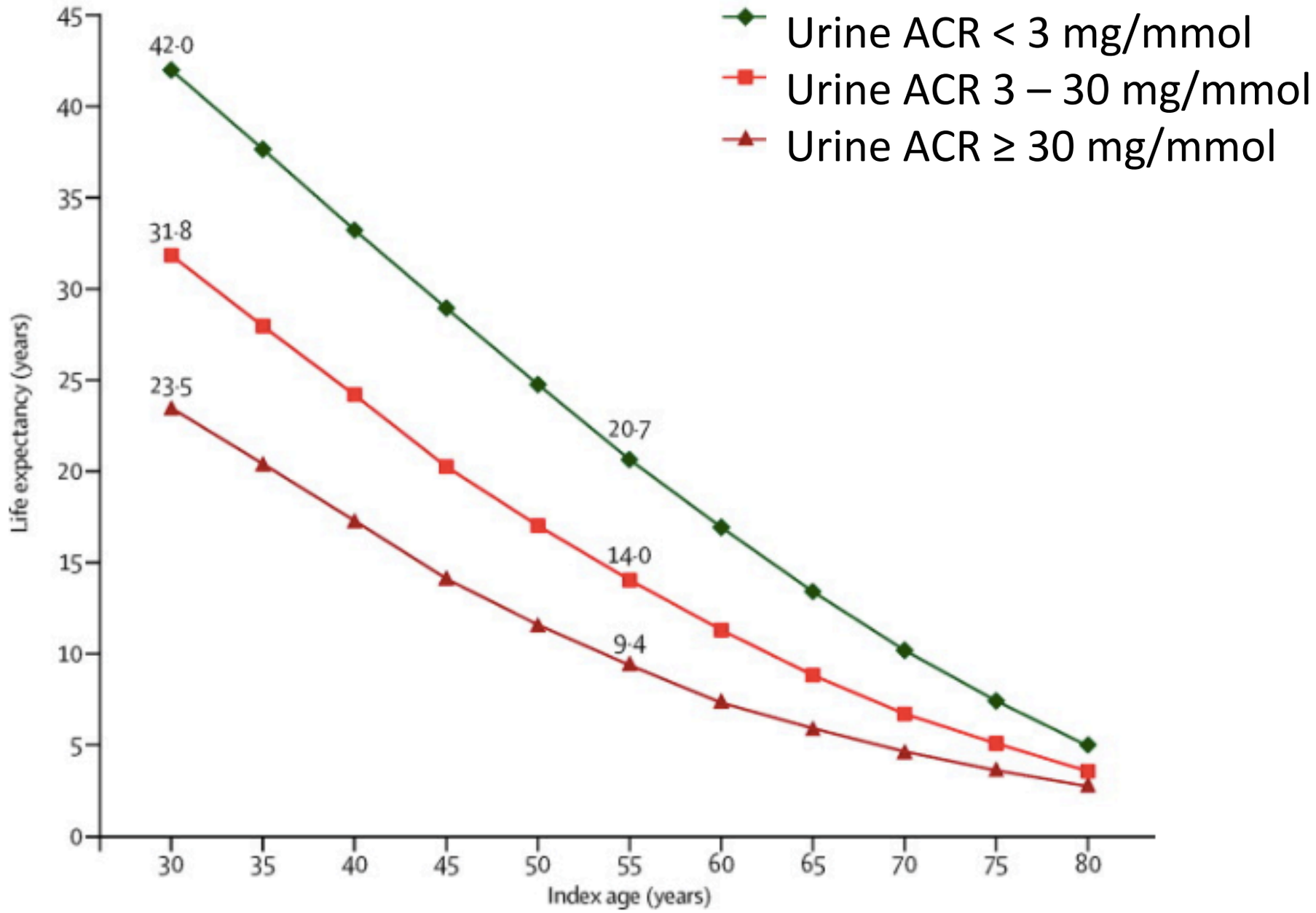
Proteinuria, a bad thing since 400BC

Proteinuria predicts adverse outcomes in CKD

- Identifies people at increased risk of:
  - Cardiovascular events
  - Mortality
  - CKD progression

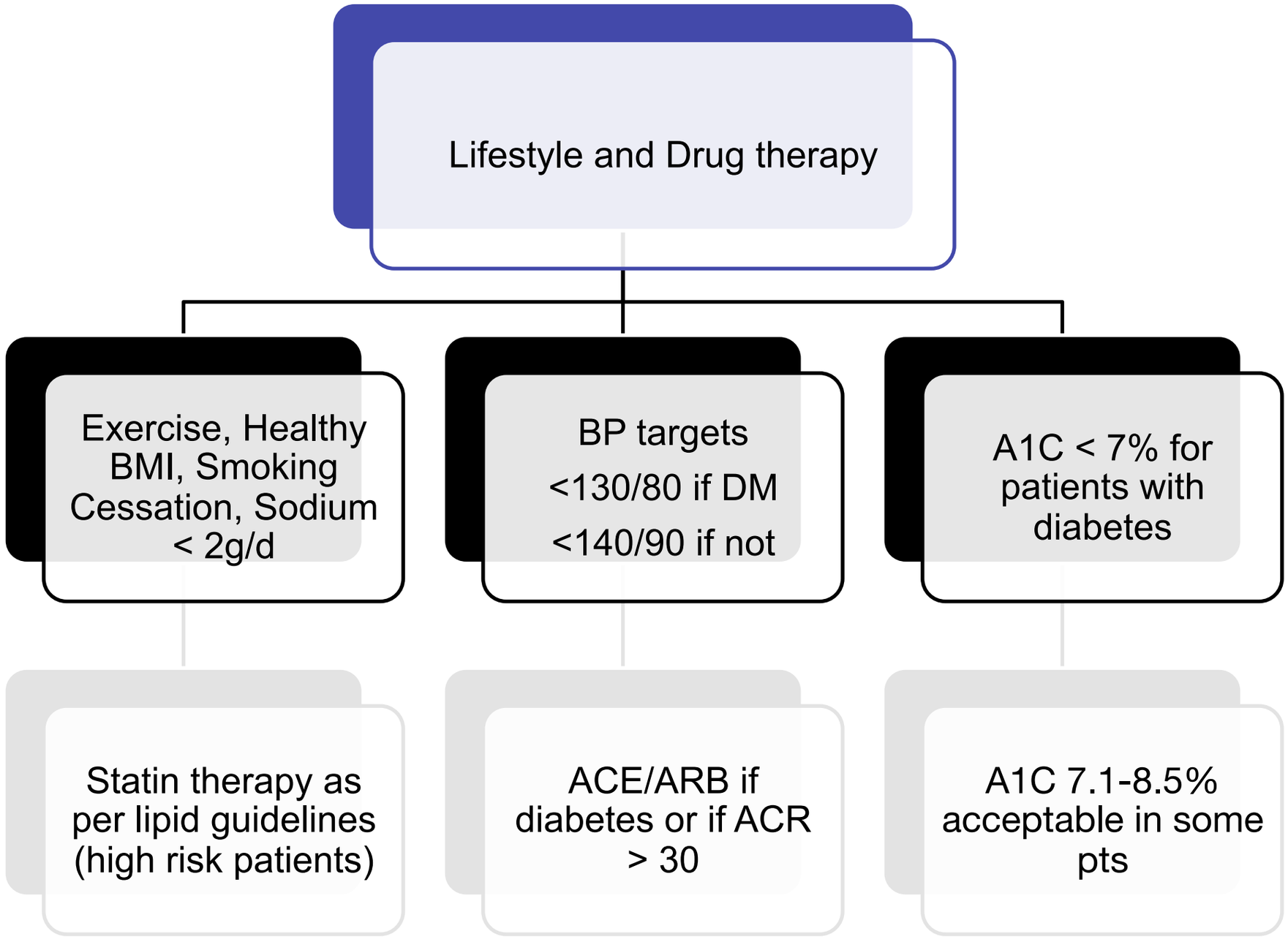


Albuminuria predicts shorter life expectancy due to CVD deaths



Gansevoort et al, Lancet 2013;382:339-52

CKD guidelines 101 – Treatment of CKD



How should you treat this patient?

Mr. Smith is a 70 yr old man with dyslipidemia and PVD. His BP is 130/80, eGFR 70mL/min. He is on statin therapy. An ACR is done and is 21 - 25 mg/mmol (normal <3) on 3 occasions. His U/A is normal.

You should:

(a)Continue to optimize his other CV risk factors, counsel to avoid precipitants of AKI (no NSAIDS) and follow ACR and renal function q 6-12 mo

(b)Do the above plus start ACE-I or ARB as his ACR is significantly elevated

(c)Do (a) and (b) and refer to nephrology as ACR is significantly elevated

When to treat with an ACE or ARB?

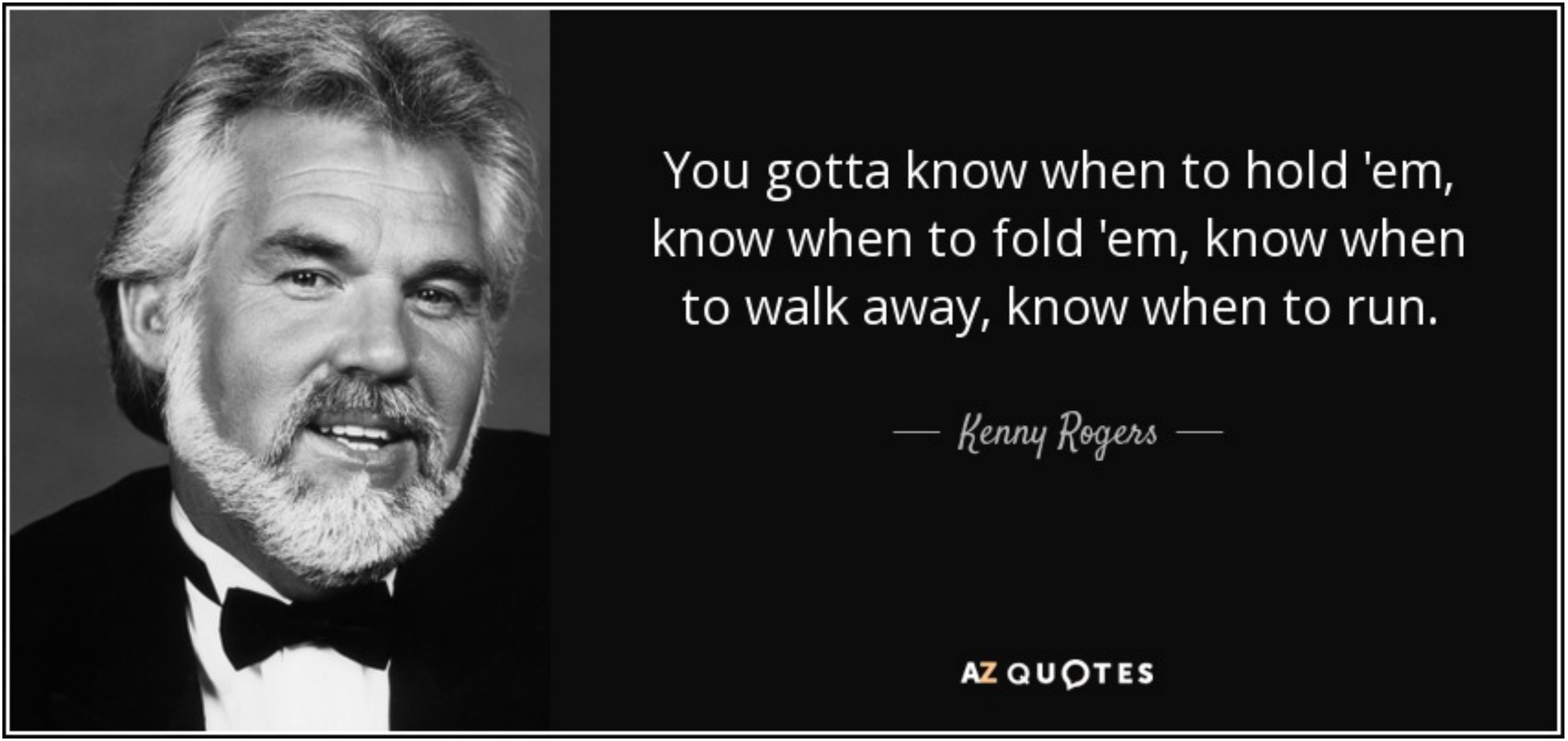
	ACR <3	**ACR 3-30**	**ACR >30**
DM, no HTN	No	Yes	Yes
DM, HTN	Yes	Yes	Yes
No DM, No HTN	No	**No**	Yes
No DM, HTN	No	Yes	Yes

Pharmacologic choices to treat proteinuria

- ACE-I or ARB – yes
- Combination of ACE or ARB — no
- Antiproteinuric effect is enhanced by a **low Na^+ diet** or a diuretic

Is is ever to late to start an ACE-I or ARB in CKD?

- Never too late - no “eGFR cutoff” below which patients do not benefit from these medications
    - but stage 4 and 5 CKD are at higher risk of complications – closer monitoring required
- Accept up to 20-30% rise in creatinine – **this is expected!**
- CHECK creatinine and potassium at baseline and within 1 – 2 weeks of starting or uptitrating an ACEi or ARB


You gotta know when to hold 'em, know when to fold 'em, know when to walk away, know when to run.
— Kenny Rogers —
AZ QUOTES

Is there a specific “target” level for proteinuria reduction

- Reduce urine ACR to < 30 mg/mmol or “as low as possible”
  - Higher is worse, but sometimes not able to get it lower
- Stabilize eGFR – < 1-2 mL/min loss per year
- Educate patients to
  - avoid nephrotoxins (dye, NSAIDS)

If acute illness/ECFV contraction → Hold ACEi, ARB, diuretic, metformin

Management of CKD complications – anemia, potassium, mineral metabolism, acidosis

Anemia management

- 75 year old female, HTN, CKD with eGFR 50 mL/min
  - Hb 108, ferritin 258
  - FIT normal, endoscopy and colonoscopy 3 years ago normal

- How to manage?
  - **Check transferrin saturation → 0.18**
  - **Start po iron ferrous fumarate 300mg po qhs**

Anemia management — not all about the EPO

- Anemia common in CKD
  - No absolute rules of what “is in proportion/out of proportion” to level of kidney function, look at trends, however unusual to have Hb < 100 if eGFR > 45 mL/min
  - Ferritin unreliable, measure tsat and aim for 0.25 at least, may require IV iron to get there
  - Ferrous fumarate 300mg po qhs → up to 900mg po qhs
  - Consider referring for ESA’s in patients with Hb **below 90 -100** after iron stores have been replenished

Managing high potassium

- 72 yr old man, Type 2 DM, HTN, Increased lipids, BMI 30
- GFR 30 mL/min, ACR 200, Hb 110
- On CCB, ACE-I, Metformin, ASA, Lipitor
- K with recent bloodwork 5.9 (previously 5.5), not hemolysed
- What would you tell him to do?
  - **Dietary history and repeat value**
  - **If still >5.5, if BP not optimal, could try a thiazide diuretic, if BP OK, try Kayexalate 15g po 3x/week, repeat in 1-2 weeks**

Treatment of potassium in CKD

- Incidence increased in patients with diabetes and on offending meds (ACE/ ARB, Spironolactone)
    - Stable potassium up to 5.5 mmol/L acceptable
    - Very responsive to dietary intervention
    - If good indication for ACE-I, continue the ACE-I or titrate down to lower dose
    - Can add potassium wasting diuretic if indicated
    - Resins – Kayexalate 15g PO 3x/week or Ca Resonium 30g PO 3x/wk

Management of Calcium, Phosphorus, PTH in CKD — less is more

- No need to routinely measure if GFR > 30-45 mL/min

- Vitamin D — PTH elevation often due to vit D deficiency

  - **Vitamin D 1000 u/day if GFR >30 mL/min and suspected deficiency**

- Calcium and Phosphate — Generally stays in normal range in early CKD

  - **Dietary phosphate restriction +/- use of phosphate binders (usually not required in primary care)**

- Target PO4 and calcium normal range

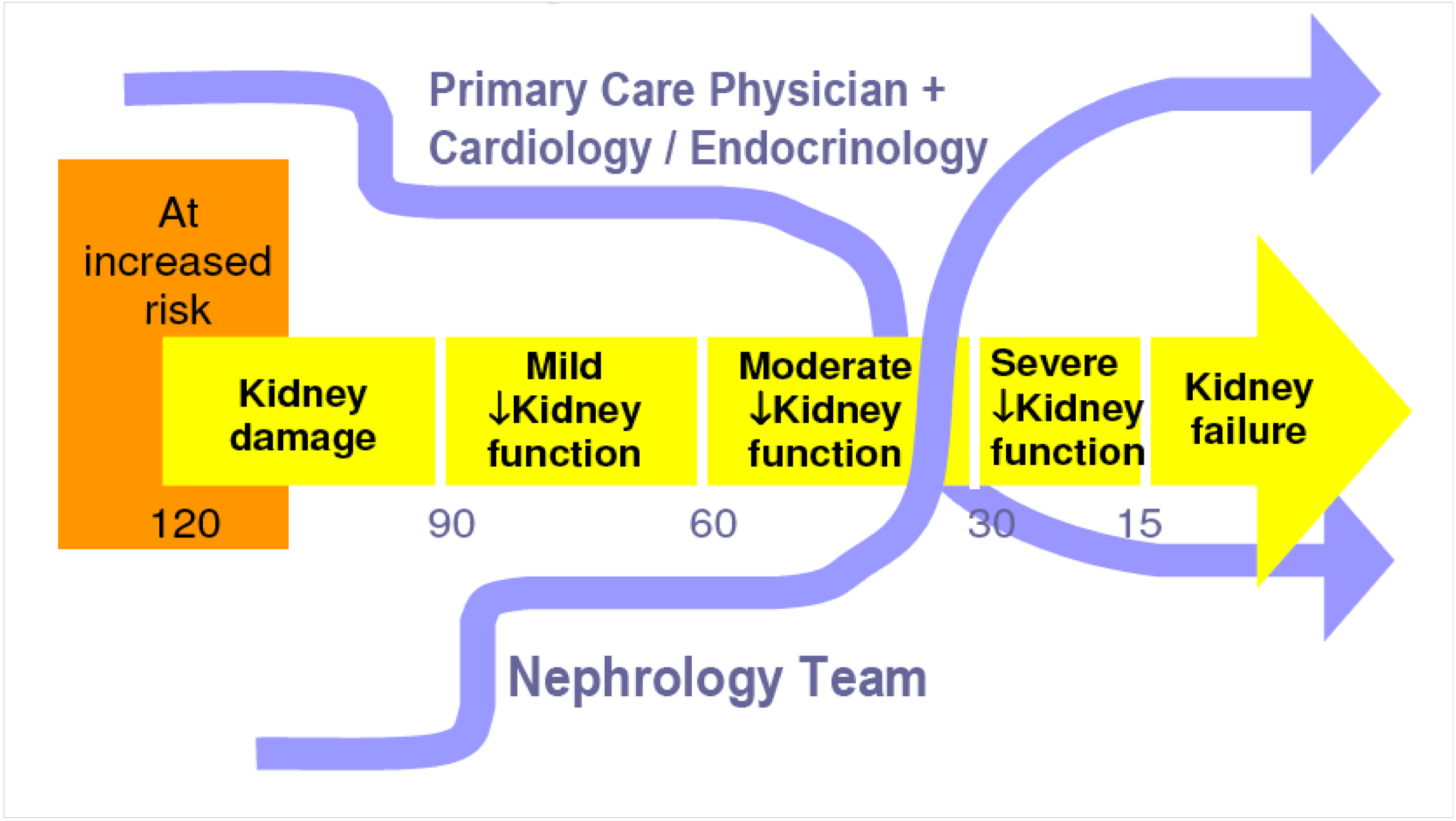
- Optimal PTH level unknown, mild increases ok, watch trend to see if consistently rising

Treatment of acidosis in CKD

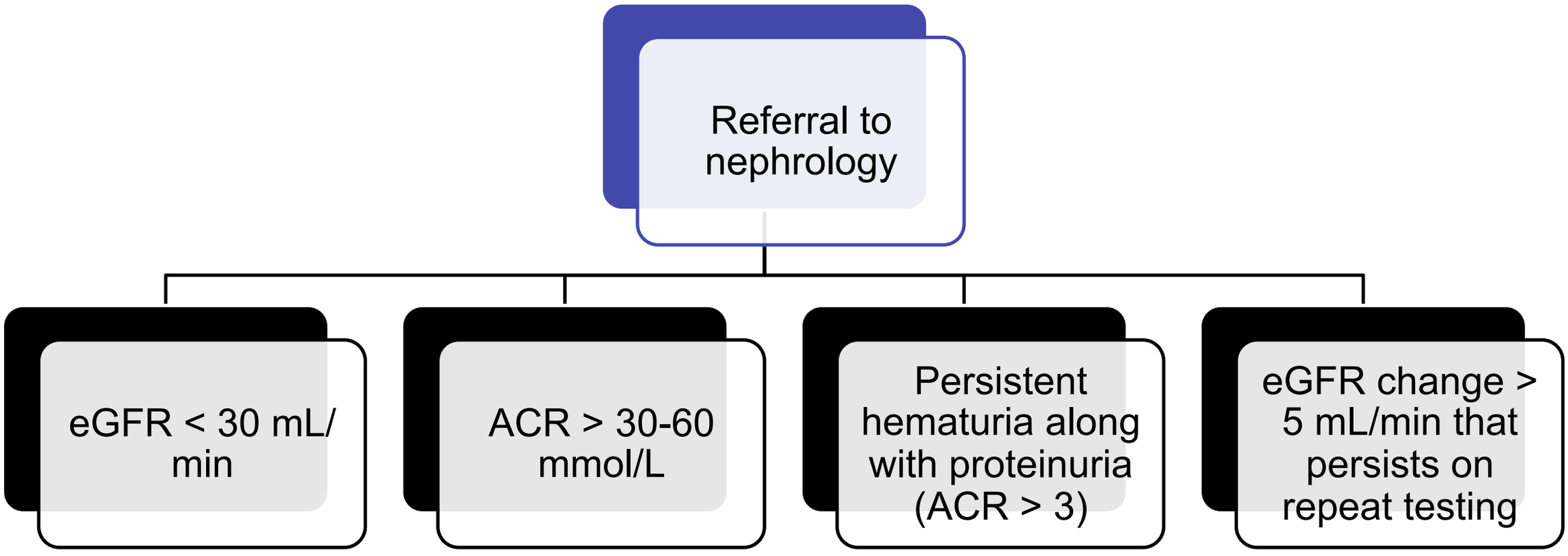
Treatment of acidosis in CKD

- Patients with CKD and bicarbonate < 22 mmol/L should be treated with oral bicarbonate supplementation to maintain serum bicarbonate in the normal range
- Improves nutritional status
- Slows progression of CKD
- Caution if tendency to volume overload (but can still try)

Co-managment of patients with CKD



CKD guidelines 101 – Referral for CKD



Also consider if:
CKD and refractory HTN
Abnormalities in K
Recurrent/refractory stones
Hereditary kidney disease

Referral is recommended for....

- Acute kidney failure/ abrupt sustained change
- eGFR < 30 mL/min (CKD stage 4 and 5) contextualized within age and other parameters
- Progressive decline of eGFR not readily explained or requiring qualification
- Urine albumin to creatinine ratio (ACR) > 30 mg/mmol on repeated measures
- Inability to achieve treatment targets
- Other — Reassurance, explanation

Referral decision making by GFR and Albuminuria

			Urine ACR categories Description and range		
			A1	**A2**	**A3**
			Normal to mildly increased	Moderately increased	Severely increased
			<3mg/mmol	3-30mg/mmol	>30mg/mmol
G1	Normal or high	≥90		Monitor	Refer*
G2	Mildly decreased	60-89		Monitor	Refer*
G3a	Mildly to moderately decreased	45-59	Monitor	Monitor	Refer
G3b	Moderately to severely decreased	30-44	Monitor	Monitor**	Refer
G4	Severely decreased	15-29	Refer*	Refer*	Refer
G5	Kidney failure	<15	Refer	Refer	Refer

And in all patients — CV risk reduction, BP control, DM control, avoid precipitants of AKI

Summary

- CKD is common
- Moderate reduction in eGFR should be seen as a **CVD risk factor** and does not require referral in most cases
- Identifying those who are likely to have progressive kidney disease will help refer appropriately to nephrology
    - eGFR 30-60 ml/min and minimal proteinuria have a lower risk of progression and can usually be managed in the primary care setting

Questions?

BCRenal
an agency of the Provincial Health Services Authority

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