Management of CKD in pre dialysis stage

Introduction

- Chronic kidney disease (CKD) is an important and common noncommunicable condition globally.
- Chronic kidney disease (CKD) is a common condition that refers to a long-term loss of kidney function.
- It is often asymptomatic in its early stages and early detection is important to reduce future risk
- It tends to be diagnosed in the presence of other comorbidities (particularly hypertension, diabetes, and cardiovascular disease).
- Effective identification and management are necessary in order to prevent CKD progression and cardiovascular events, reduce the risks associated with acute kidney injury (AKI).

Fraser SD et al. Pragmat Obs Res. 2016;7:21-32

Chronic kidney disease

- The National Kidney Foundation defined CKD as either kidney damage or GFR <60 mL/min per 1.73 m2 for ≥3 months.
- In 2012, Kidney Disease: Improving Global Outcomes (KDIGO) re-defined CKD as abnormalities of kidney structure or function, present for more than 3 months, with implications for health.
- In national and international guidelines, CKD is defined and staged according to measures of kidney function that allow for a degree of risk stratification using commonly available markers.

Fraser SD et al. Pragmat Obs Res. 2016;7:21-32

Prevalence of CKD world wide

- CKD, with its high prevalence, morbidity and mortality, is an important public health problem.
- In the 2015 Global Burden of Disease Study, kidney disease was the 12th most common cause of death, accounting for 1.1 million deaths worldwide.
- CKD ranked as the 17th leading cause of global years lost of life, an 18.4% increase since 2005.
- Between 2005 and 2015, the prevalence of diabetic kidney disease increased by 39.5% globally

Neuen BL et al. BMJ Glob Health 2017;2:e000380

Prevalence of CKD in india

- The reported prevalence of CKD in different regions of india ranges from <1% to 13%, and recently, data from the International Society of Nephrology's Kidney Disease Data Center Study reported a prevalence of 17%
- Because of challenges in access to care, over 50% of patients with advanced CKD are first seen when the eGFR is <15 ml/min per 1.73 m^{2}..
- Parts of the states of Andhra Pradesh, Odisha, and Goa have high levels of CKD of unknown etiology (CKDu), which is a chronic interstitial nephropathy with insidious onset and slow progression .

Varghese S et al. Clin J Am Soc Nephrol. 2018; 13: 802–804.

Stages of CKD

GFR category	GFR (mL/min per 1.73 m2)	Description
G1	≥90	Normal or ↑ GFR
G2	60–89	Mild ↓ GFR
G3a	45–59	Mild-to-moderate ↓ GFR
G3b	30–44	Moderate-to-severe ↓ GFR
G4	15–29	Severe ↓ GFR
G5	<15 or dialysis	Kidney failure

Tang SC et al. Nephrology (Carlton).2019 Mar;24 Suppl 1:9-26

Chronic kidney disease risk factors

Susceptibility factors

- Old age
- Family history of CKD
- Reduced renal mass
- Light weight upon birth
- Black population and other ethnic minorities
- High blood pressure
- Diabetes
- Obesity
- Low socioeconomic level

Martinez Castelao A et al. Nefrologia. 2014;34(2):243-62

Chronic kidney disease risk factors

- **Initiating factors:**
- Autoimmune diseases
- Systemic infections
- Urinary infections
- Kidney stones
- Obstruction of the lower urinary tract
- Nephrotoxic drugs, mainly NSAIDs
- High blood pressure
- Diabetes

Martinez Castelao A et al. Nefrologia. 2014;34(2):243-62

Chronic kidney disease risk factors

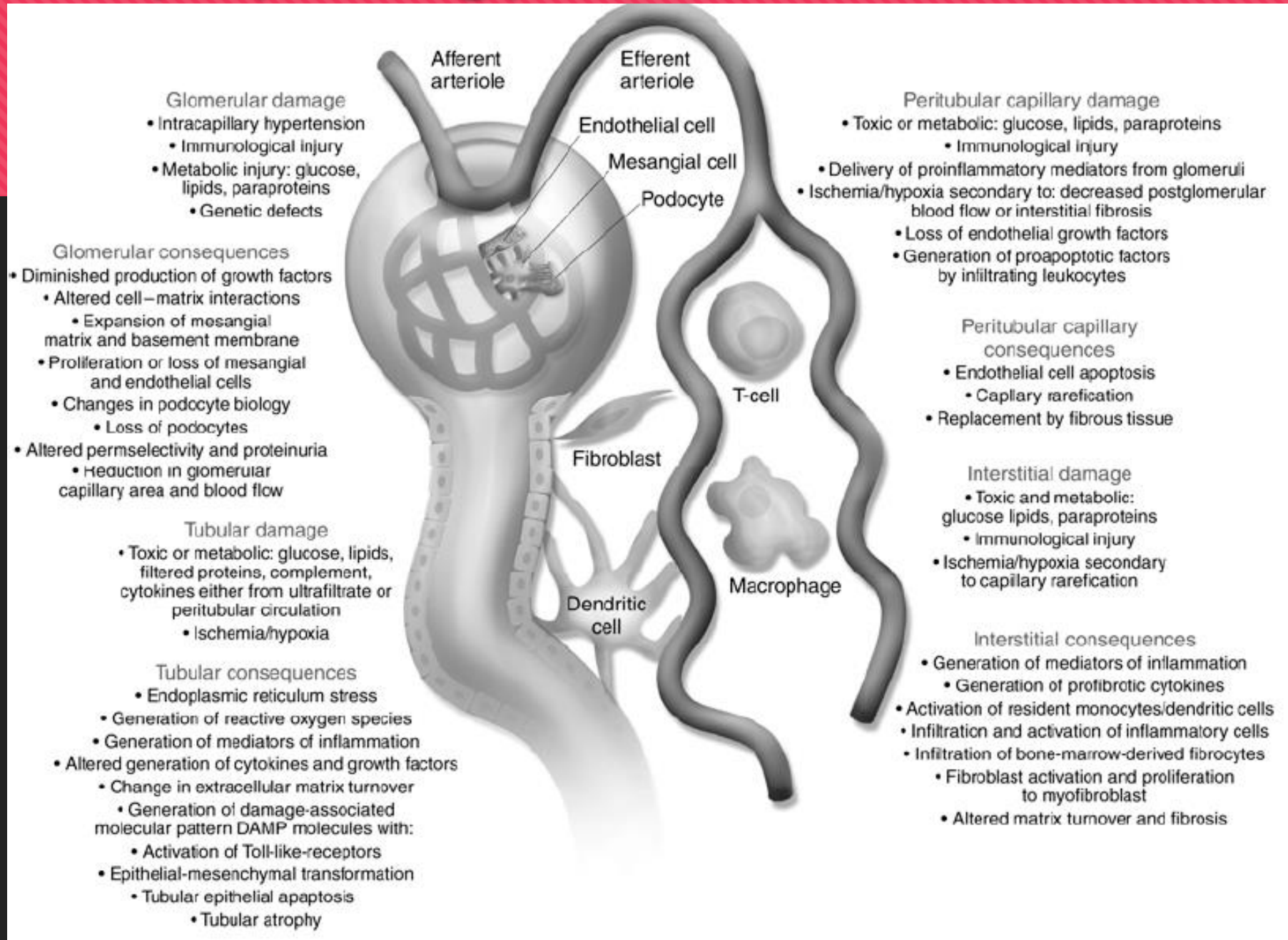
End stage factors

- Low dialysis dose (Kt/V)
- Temporary vascular access for dialysis
- Anaemia
- Hypoalbuminaemia
- Late referral to Nephrology

Kt/V: K = urea clearance in the dialyser, t = time, V = urea distribution volume. The resulting figure is used to quantify the sufficiency of dialysis dose

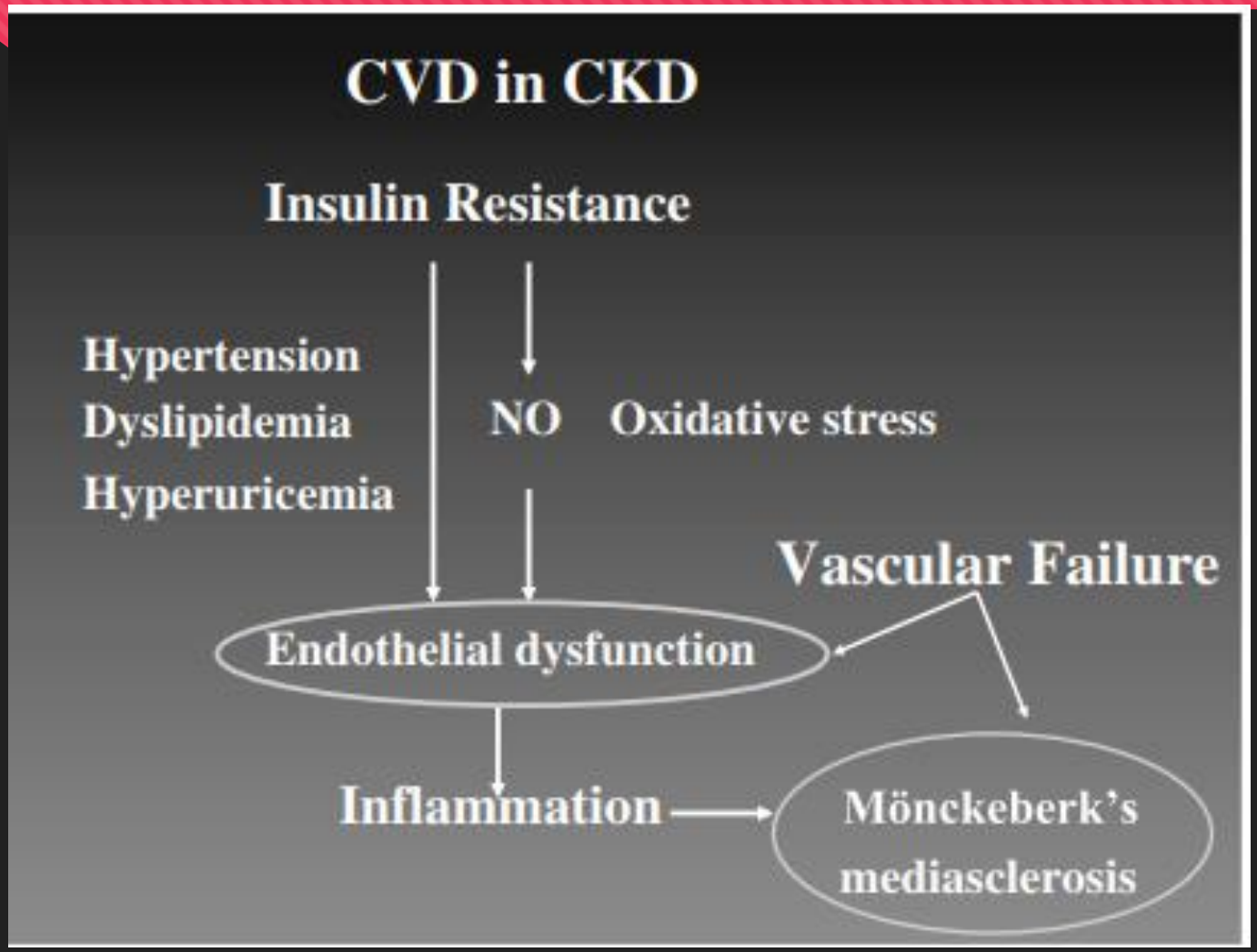
Martinez Castelao A et al. Nefrologia. 2014;34(2):243-62

Pathophysiology of CKD



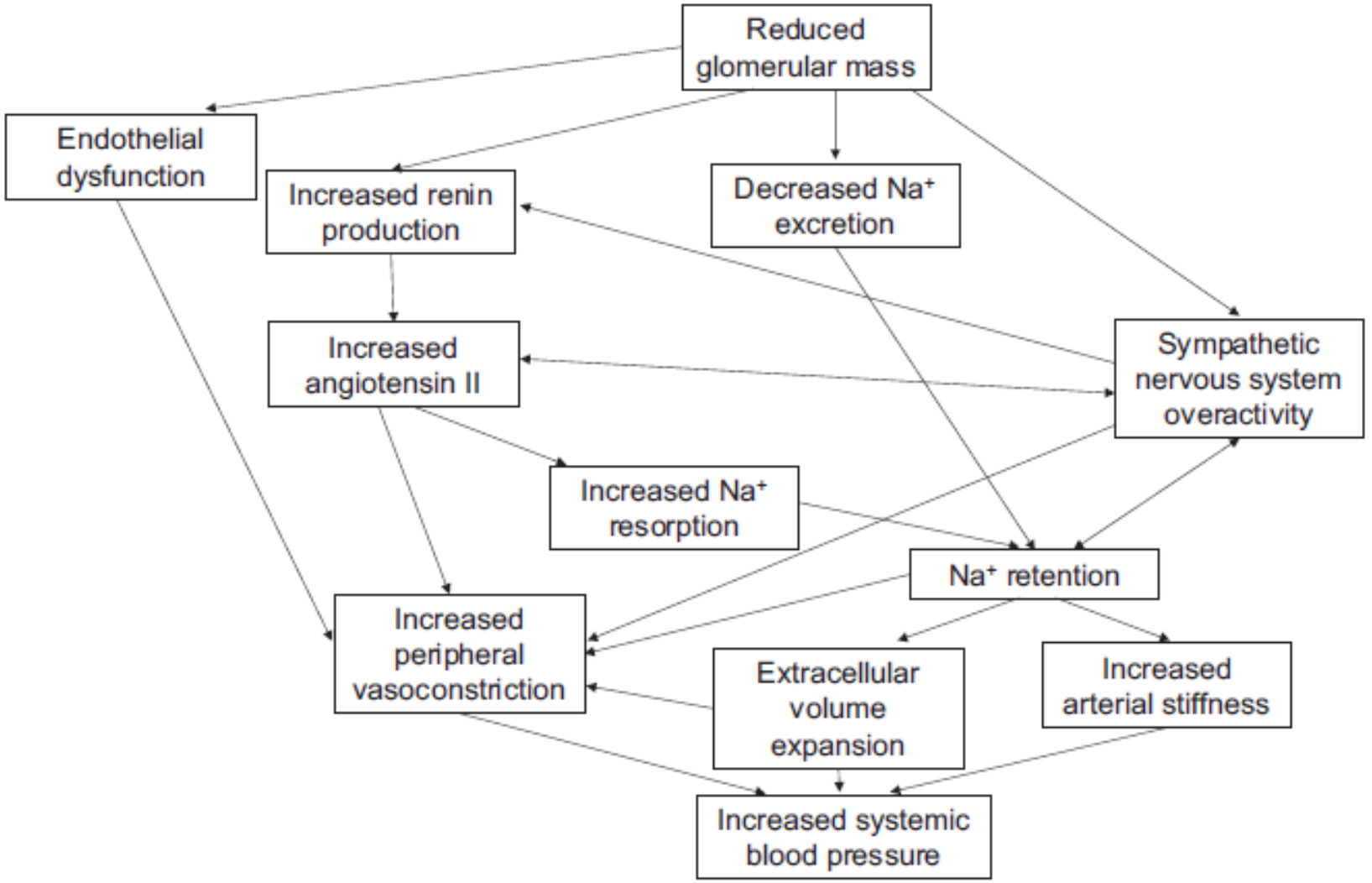
Matovinovic MS . EJIFCC. 2009 Apr; 20(1): 2–11

Pathophysiology of cardiovascular disease in patients with Chronic Kidney Disease



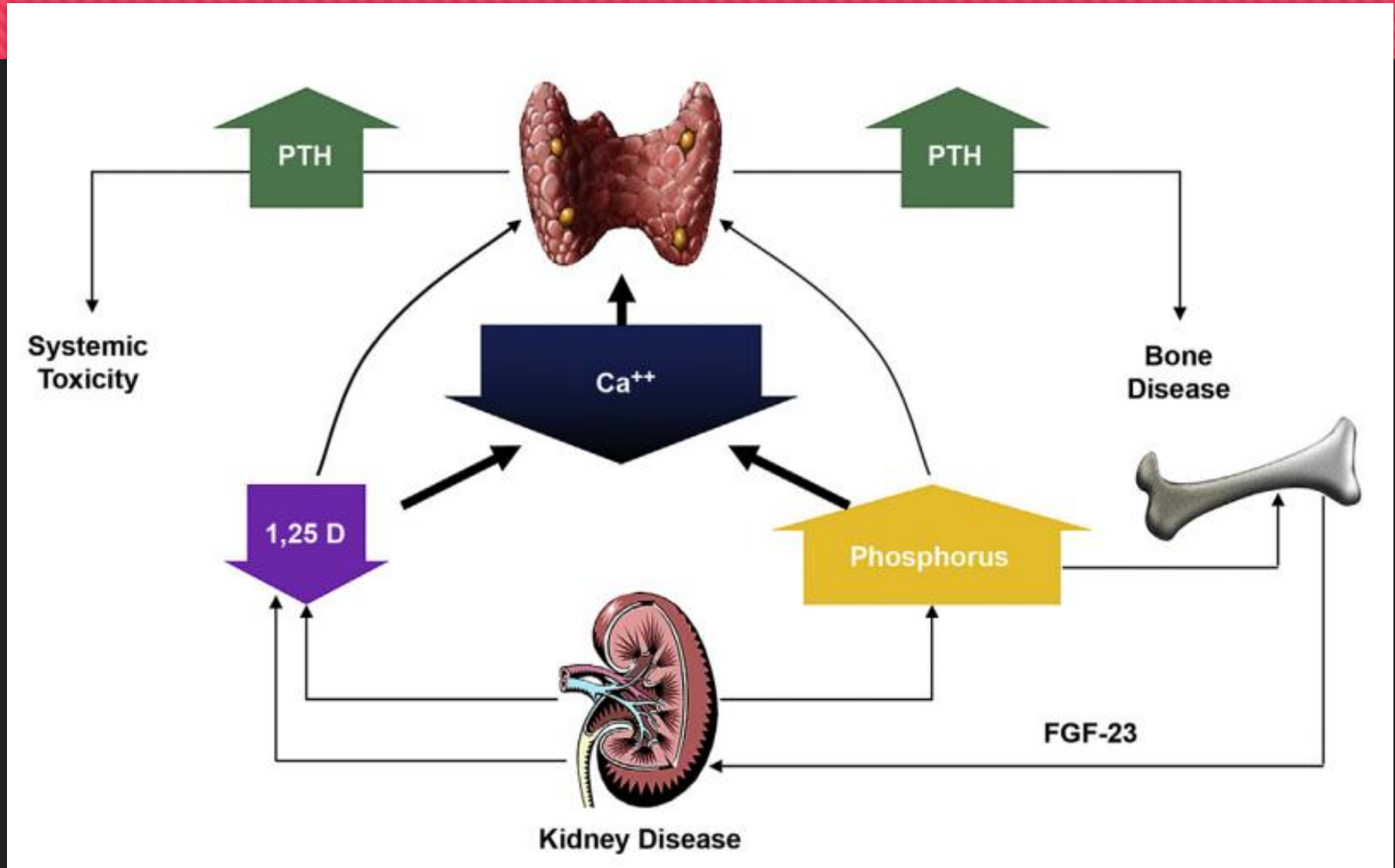
Kobayashi S. Renal Replacement Therapy. 2016 ;2(1):55.

Pathophysiologic mechanisms of hypertension in chronic kidney disease



Ku E et al. Am J Kidney Dis.2019; 74(1):120-131.

Pathophysiological mechanism of chronic kidney disease-mineral bone disorders



1,25 D - 1-a-hydroxylation of 25-hydroxy vitamin D;
Ca11- ionized calcium;
FGF-23 - fibroblast growth factor
PTH- parathyroid hormone

Beto J et l. J Ren Nutr. 2019 Jan;29(1):2-15.

Clinical features of CKD

- Fatigue
- Lethargy
- Cognitive dysfunction
- Symptoms of neuropathy
- Uremic pruritus
- Sleep disturbances
- Anorexia
- Nausea
- Restless legs

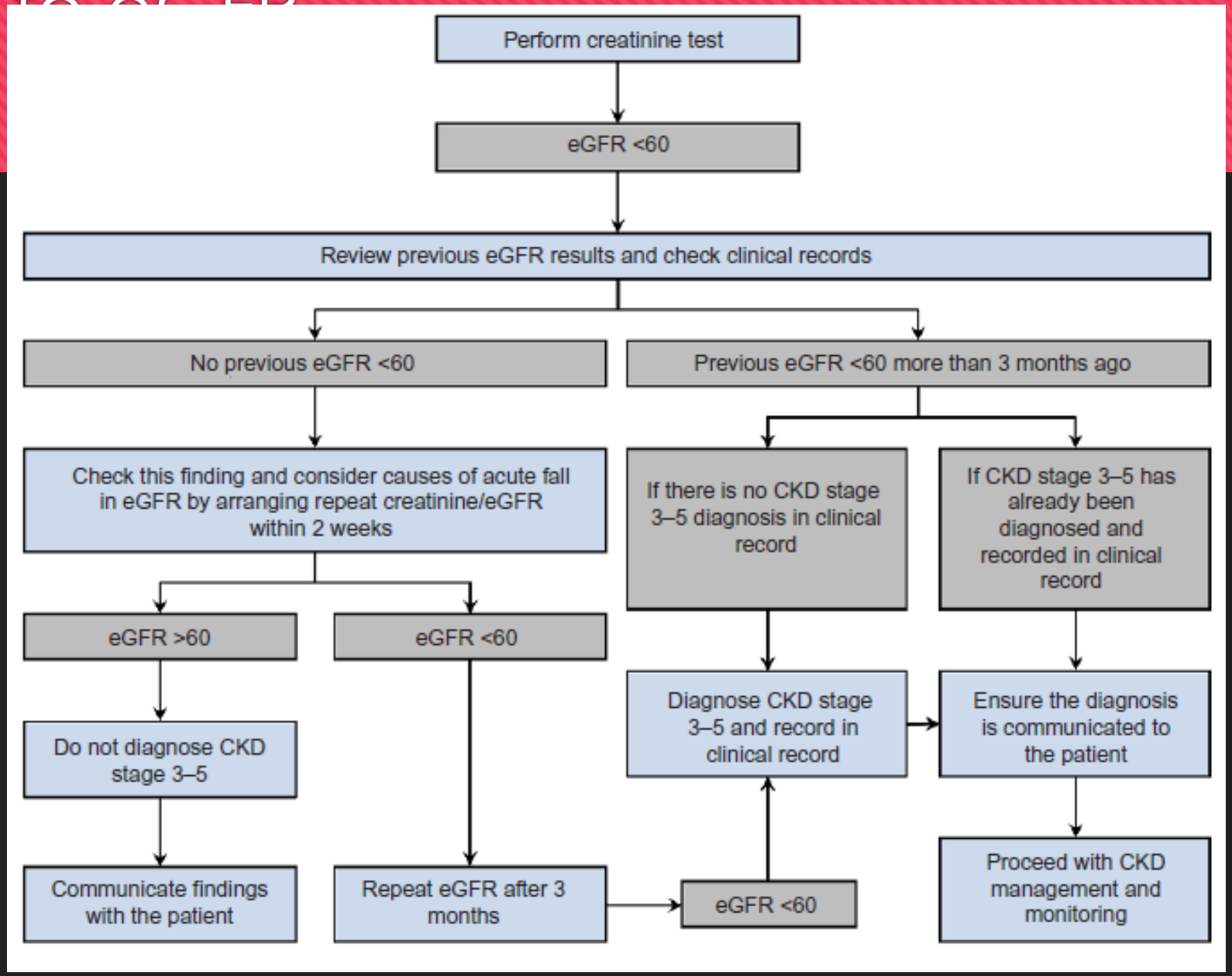
Cabrera VJ et al. Clin J Am Soc Nephrol. 2017;12(4):687-693.

Diagnostic criteria for CKD

- One of the following needs to be present for at least 3 months:
- a) Decreased eGFR (<60 mL/min/1.73 m2)
- b) One or more marker of kidney damage:
- i. Albuminuria (urinary albumin-to-creatinine ratio [ACR] ≥30 mg/g [3 mg/mmol])
- ii. Structural abnormalities (from imaging)
- iii. Urine sediment abnormalities (hematuria, red or white blood cell casts, oval fat bodies or fatty casts, granular casts, and renal tubular epithelial cells)
- iv. Electrolyte and other abnormalities due to tubular disorders
- v. Histological abnormalities
- vi. Previous history of kidney transplantation

NICE Clinical Guidelines . *Chronic Kidney Disease: Early Identification and Management of Chronic Kidney Disease in Adults in Primary and Secondary Care*. London: National Institute of Health and Care Excellence; 2014.

Clinical decision pathway in CKD diagnosis in relation to eGFR



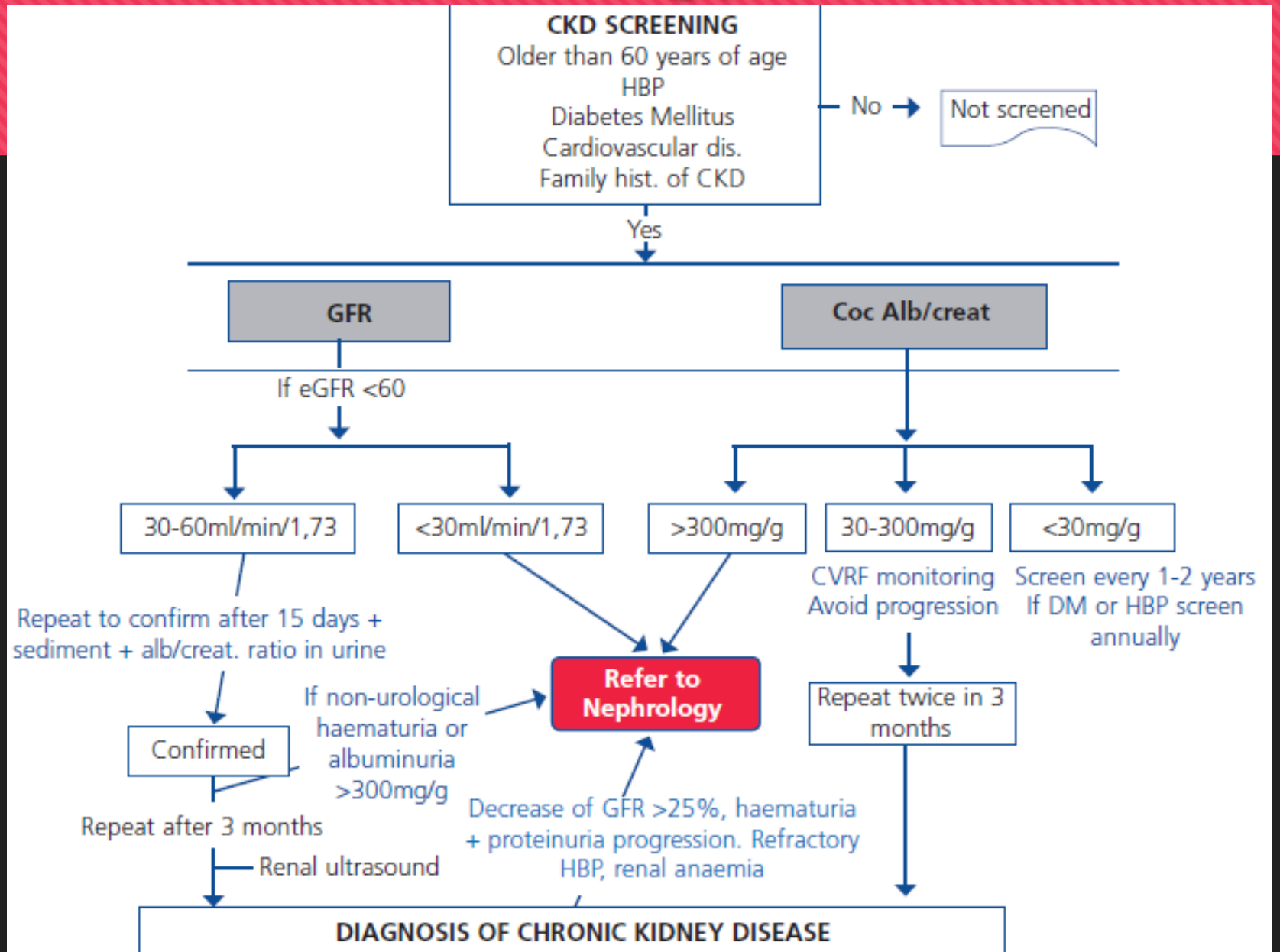
Fraser SD et al. Pragmat Obs Res. 2016;7:21-32

Referal for Nephrology

- CKD 4 or higher
- Anticipation of the need of initiation of renal replacement therapy within 1 year
- AKI or abrupt sustained fall in GFR
- Significant proteinuria, for example >1 g/24 h
- Urinary red cell casts, for example RBC >20 per high power field sustained and not readily explained.
- CKD and hypertension refractory to treatment with four or more anti-hypertensive agents
- Persistent abnormalities of serum potassium not otherwise explained
- Recurrent urinary tract infections
- Hereditary kidney disease, for example autosomal dominant polycystic kidney disease (ADPKD)

Tang SC et al. Nephrology (Carlton).2019 Mar;24 Suppl 1:9-26

Referal to nephrology



Martinez Castelao A et al. Nefrologia. 2014;34(2):243-62

Referal to nephrology

DIAGNOSIS OF CHRONIC KIDNEY DISEASE

CKD stage	eGFR (ml/min/1,73 m²)	Albuminuria stage		
		A1 (< 30mg/g)	A2 (30-300mg/g)	A3 (Proteinuria) (> 300mg/g)
1	> 90	No CKD unless there is haematuria, imaging abnormalities or pathological abnormalities		
2	60-89			
3a	45-59		*	
3b	30-44			
4	15-29			
5	< 15			

■ Referral to Nephrology

■ Monitoring by Primary Care

■ *Monitoring by Primary Care, more frequent monitoring (every 3-6 months). Referral to Nephrology if there is progression of albuminuria in two consecutive tests or an albumin/creatinine ratio of around 300mg/g or if the eGFR is 30-45ml/min/1.73m² in <70 years of age.

Martinez Castelao A et al. Nefrologia. 2014; 34(2):243-62

Markers of kidney injury

- Albuminuria (albumin excretion rate (AER) ≥30 mg/24 h
- albumin-creatinine ratio (ACR) ≥30 mg/g (≥3 mg/mmol))
- Urine sediment abnormalities, especially renal tubular cells, red blood cells (RBC)/white blood cell casts, dysmorphic RBC
- Electrolyte and other abnormalities due to tubular disorders
- Abnormalities detected by histology
- Structural abnormalities detected by imaging
- History of kidney transplantation

Tang SC et al. Nephrology (Carlton).2019 ;24 (1):9-26

Albuminuria categories in CKD

Albuminuria category	AER (mg/24 h)	ACR (approximately) in mg/mmol	ACR (approximately) in mg/g	**Description**
A1	<30	<3	<30	Normal or mild ↑
A2	30-300	3-30	30-300	Moderate ↑
A3	>300	>30	>300	Severe ↑

Tang SC et al. Nephrology (Carlton).2019;24 (l) 1:9-26

Number of annual visits for monitoring

CKD stage	FGe (ml/min/1,73 m²)	Albuminuria stage		
		A1 (< 30mg/g)	A2 (30-300mg/g)	A3 (Proteinuria) (>300mg/g)
1	> 90	1 if CKD	1	2
2	60-89	1 if CKD	1	2
3a	45-59	1	2	3
3b	30-44	2	3	3
4	15-29	3	3	4 or more
5	< 15	4 or more	4 or more	4 or more

■ Monitoring by Nephrology.

■ Monitoring by Primary Care or other specialties

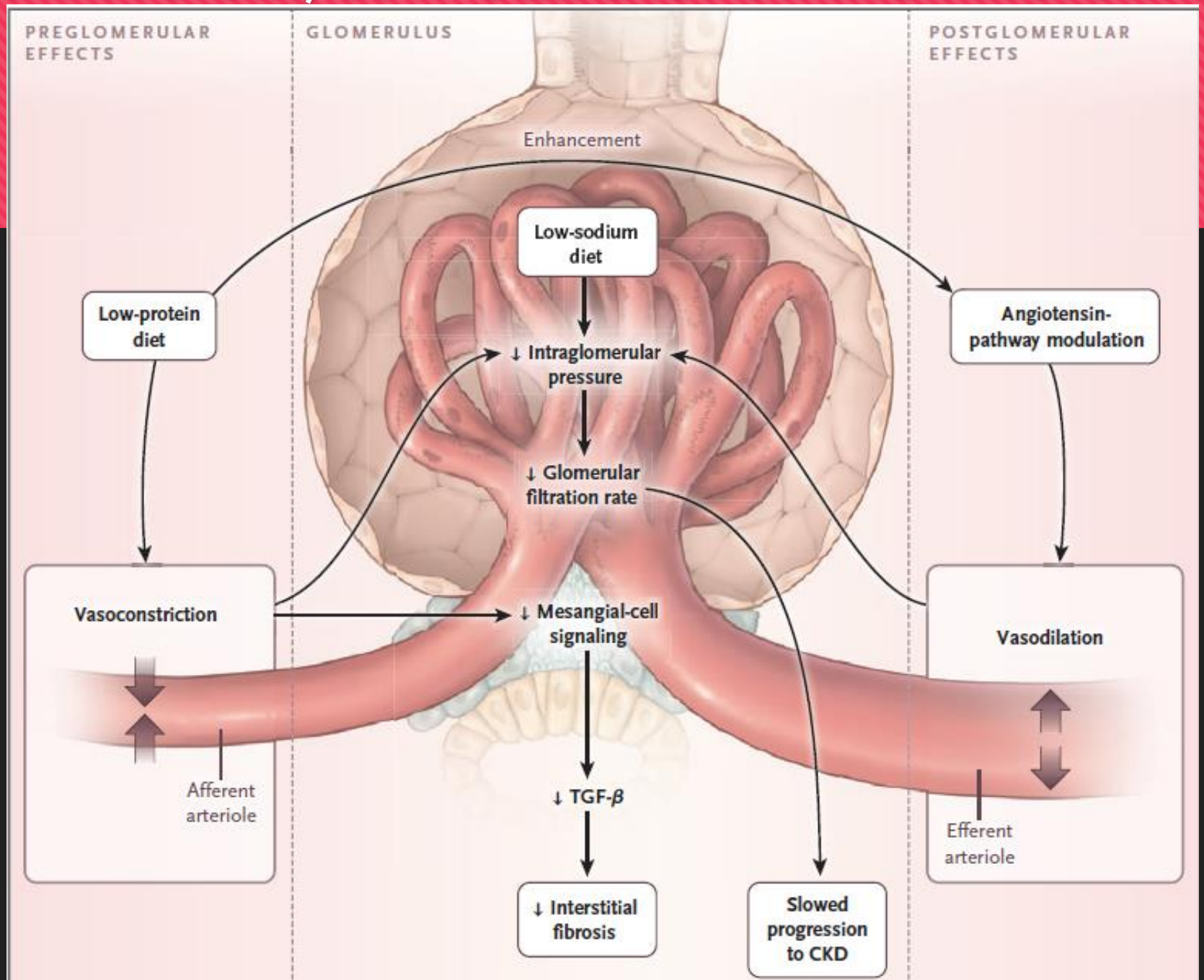
CKD: chronic kidney disease, eGFR: estimated glomerular filtration rate.

Martinez Castelao A et al. Nefrologia. 2014;34(2):243-62

General management strategies

- The management of progression of CKD is aimed at tackling a myriad of factors known to be associated with progression.
- These measures have been shown to modify cardiovascular health and CKD concomitantly or separately.
- Addressing CV risk factors may indirectly and directly impact CKD progression, and vice-versa.
- Strategies include general lifestyle measures, salt restriction, BP control and blockade of the renin-angiotensin-aldosterone system.
- In addition, control of other metabolic parameters such as blood sugar, lipid, anaemia, bone metabolism, uric acid and acidosis are also important

Effect of low Protein, Low-Salt Diet on the Afferent Arteriole



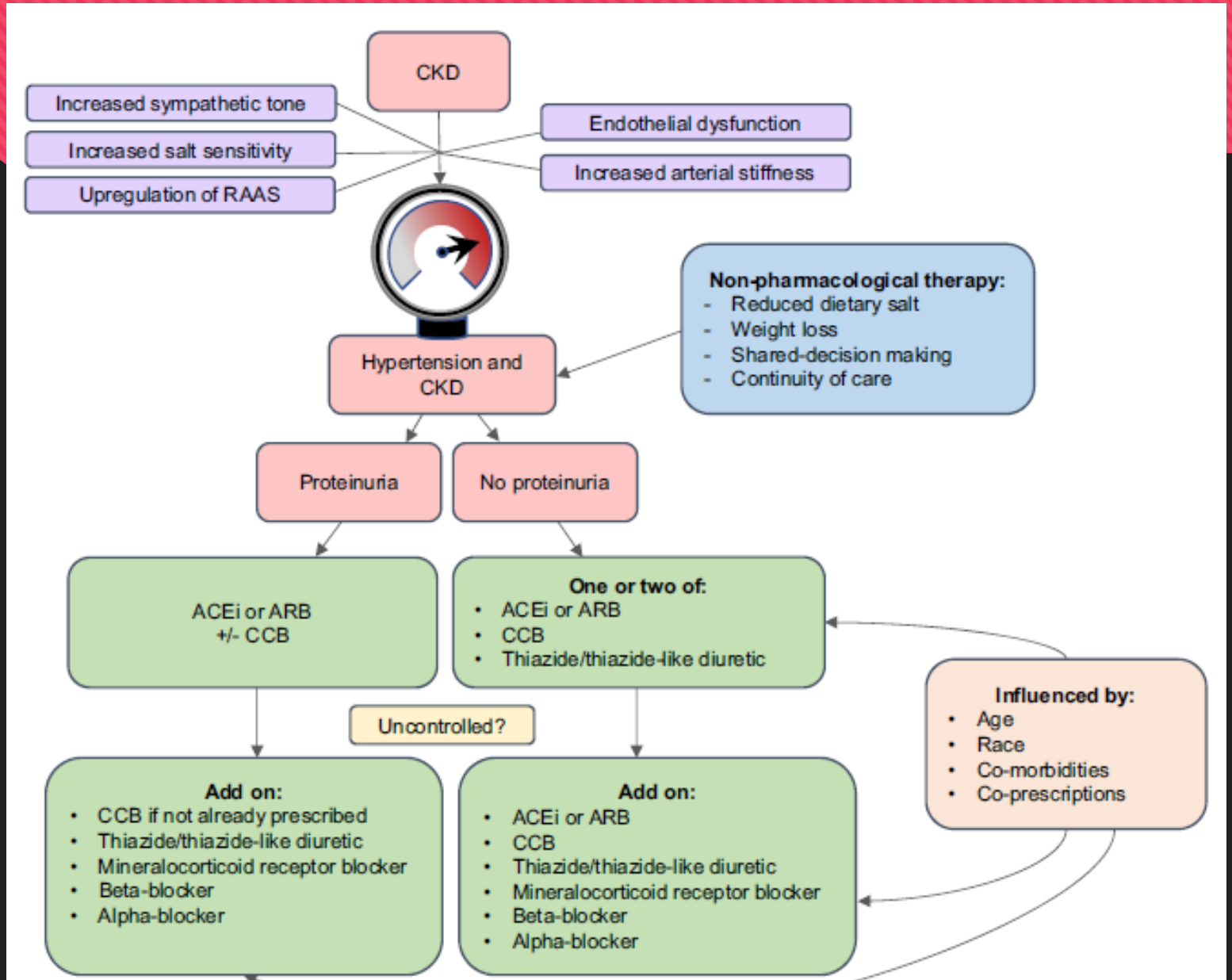
Kalanter Zadeh K et al. N Engl J Med 2017;377(18):1765-1776

Recommended Dietary and Nutrient Intake in Adults, According to the CKD Stage

Dietary Constituent	Normal Kidney Function with Increased CKD Risk	Mild-to-Moderate CKD†	Advanced CKD†	Transition to Dialysis†	Ongoing Dialysis or Any Stage with Existing or Imminent PEW
Protein (g/kg/day)	<1.0; increase proportion of plant-based proteins	<1.0 (consider 0.6–0.8 if eGFR <45 ml/min/1.73 m^2 or rapid progression)	0.6–0.8, including 50% HBV protein, or <0.6 with addition of EAA or KA	0.6–0.8 on nondialysis days and >1.0 on dialysis days	1.2–1.4; may require >1.5 if hypercatabolic state develops
Sodium (g/day)‡	<4 (<3 in patients with hypertension)§	<4; avoid intake of <1.5 if hyponatremia likely	<3; avoid intake of <1.5 if hyponatremia likely	<3	<3
Potassium (g/day)¶	4.7 (same as recommended for general population)	4.7 unless frequent or severe hyperkalemia excursions likely	<3 if hyperkalemia occurs frequently during high-fiber intake	<3 if hyperkalemia occurs frequently during high-fiber intake	<3; target high-fiber intake
Phosphorus (mg/day)‖	<1000; minimize added inorganic phosphorus in preservatives and processed foods	<800; minimize added inorganic phosphorus and encourage consumption of more plant-based foods	<800; minimize added inorganic phosphorus and encourage consumption of more plant-based foods	<800; minimize added inorganic phosphorus; consider phosphorus binder	<800; minimize added inorganic phosphorus; add phosphorus binder as needed
Calcium (mg/day)	1000–1300 (adjusted for age)	800–1000	800–1000	800–1000 or less	<800
Fibers, alkali, and plant-based foods (g/day)	25–30; target higher proportion (>50%) of plant-based foods (e.g., DASH diet)	25–30 or more; higher proportion (>50%) of plant-based foods	25–30 or more; consider >70% plant-based foods	25–30 or more	25–30 or more; suggest avoiding strict vegan diet
Energy (kcal/kg/day)**	30–35; adjust to target weight reduction if BMI >30††	30–35; increase proportion with LPD	30–35; increase proportion with LPD	30–35	30–35; target higher intake if PEW present or imminent
Fats	Mostly monounsaturated and polyunsaturated lipids, including n–3 fatty acids	Mostly monounsaturated and polyunsaturated lipids, including n–3 fatty acids; increase proportion with low-protein intake	Mostly monounsaturated and polyunsaturated lipids, including n–3 fatty acids; increase proportion with low-protein intake	Mostly monounsaturated and polyunsaturated lipids, including n–3 fatty acids	Mostly monounsaturated and polyunsaturated lipids, including n–3 fatty acids

Kalanter Zadeh K et al. N Engl J Med.2017;377(18):1765-1776

Pathogenesis and management flow-chart of hypertension in chronic kidney disease



Pugh D et al. Drugs 2019; 79(4): 365–379

Blood pressure targets in CKD over time

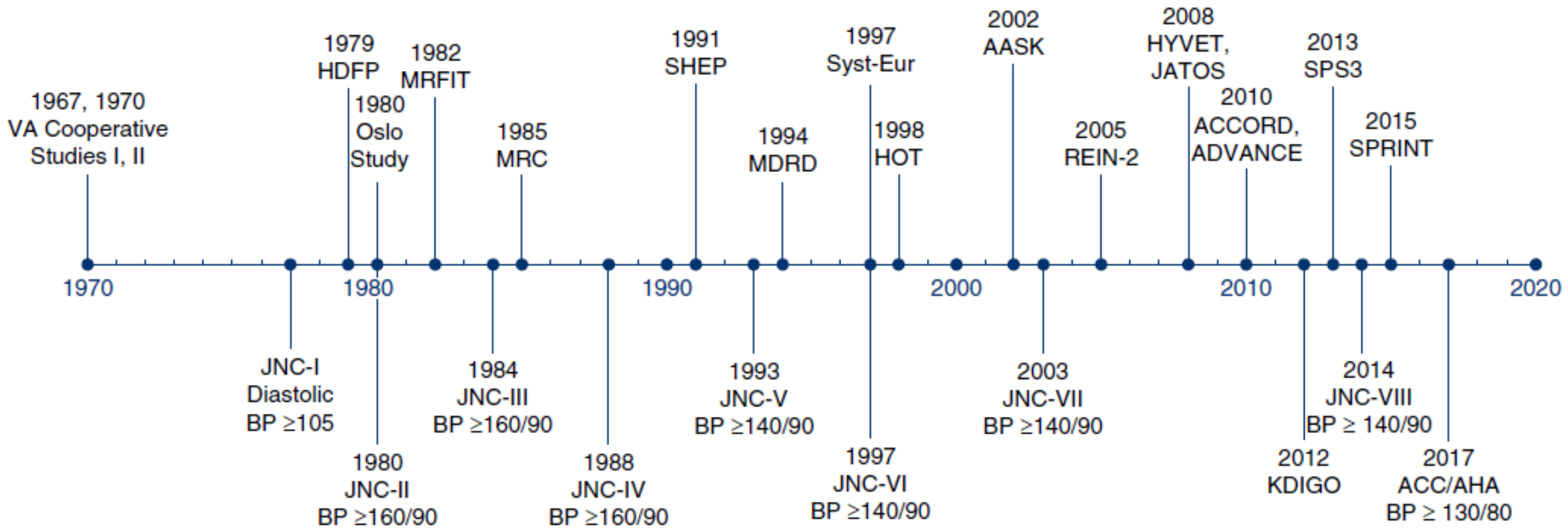


Figure 1. | The Definition of Hypertension per United States BP Guidelines has Changed Over Time. Above timeline: major hypertension trials from 1960 to 2018 (6,34–37,39,55–66). Below timeline: guideline and definition of hypertension, from 1960 to 2018 (3–5,9–11,14,67–69). ADVANCE, The Action in Diabetes and Vascular Disease: Preterax and Diamicron Controlled Evaluation trial; ALLHAT, The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; HDFP, The Hypertension Detection and Follow-up Program; HOT, The Hypertension Optimal Treatment study; HTN, Hypertension; HYVET, The Hypertension in the Very Elderly Trial; JATOS, The Japanese Trial to Assess Optimal Systolic BP in Elderly Hypertensive Patients; KDIGO, Kidney Disease Improving Global Outcomes; MRC, Medical Research Council; MRFIT, Multiple Risk Factor Intervention Trial; SHEP, The Systolic Hypertension in the Elderly Program; SPS3, The Secondary Prevention of Small Subcortical Strokes trial; Syst-Eur, The Systolic Hypertension in Europe trial; UKPDS, The United Kingdom Prospective Diabetes Study; VA, Veterans Affairs.

Chang AR et al. Clin J Am Soc Nephrol. 2019 ;14(1):161-169

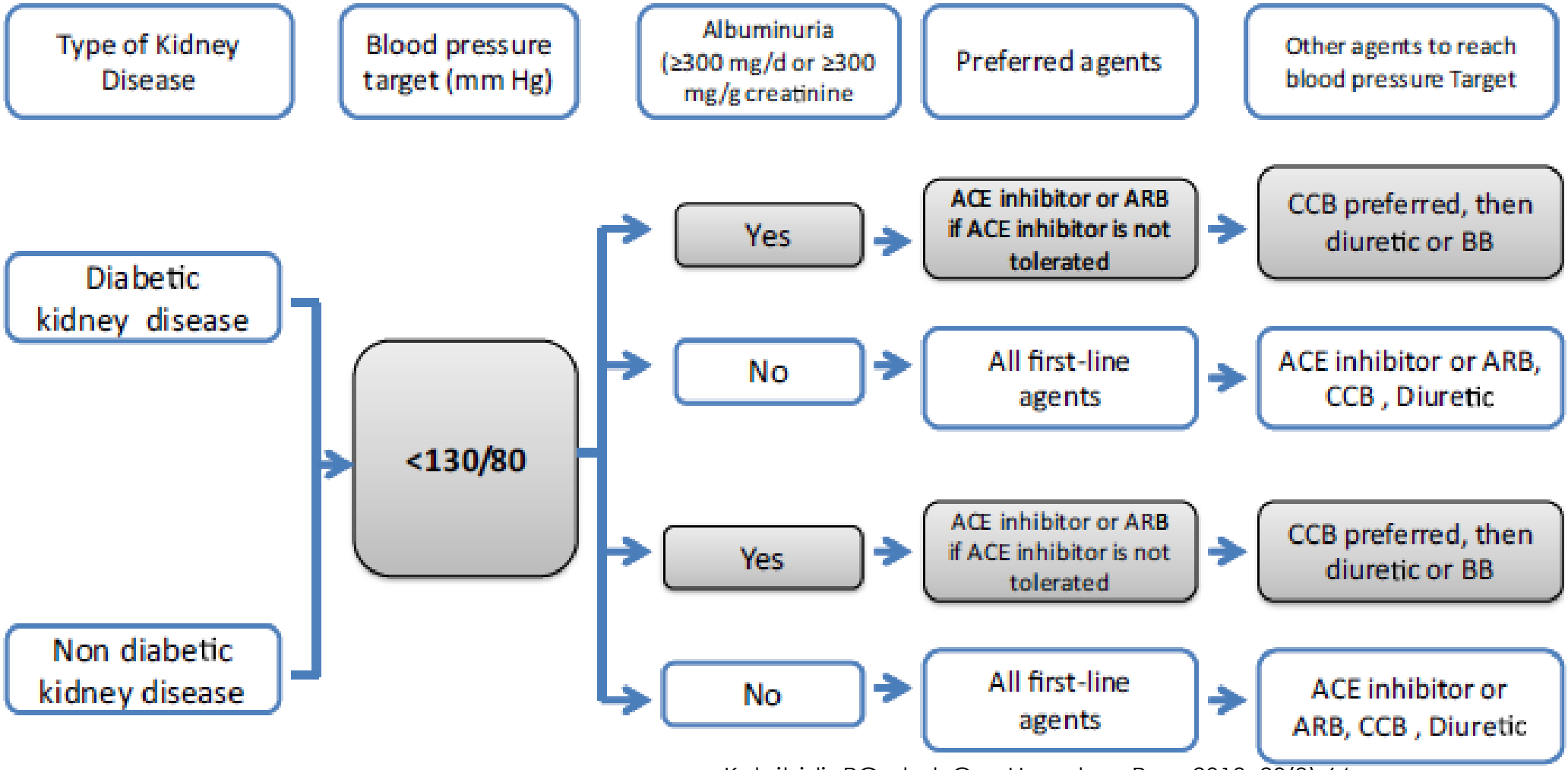
manage hypertension in patients with CKD and albuminuria

	2017 ACC/AHA	2013 ESH/ESC	2018 ADA	2012 NKF KDOQI
Type of CKD considered	Albuminuria ≥ 300 mg/d or ≥ 300 mg/g creatinine	Overt proteinuria	Urinary albumin-to-creatinine ratio ≥ 300 mg/g creatinine or 30–299 mg/g creatinine	Urine albumin excretion of 30 to 300 mg or > 300 mg per 24 h
Recommended BP target (mm Hg)	Lowering < 130/80	Lowering SBP to < 140 Lowering < 130/80 mmHg in individuals with overt proteinuria	Lowering < 140/90 Lowering < 130/80 mmHg, for individuals at high risk of cardiovascular disease	Lowering ≤ 130/80
Recommended initial antihypertensive treatment	ACE inhibitor or ARB if ACE inhibitor is not tolerated	ACE inhibitor or ARB	ACE inhibitor or ARB If one class is not tolerated, the other should be substituted	ACE inhibitor or ARB
Other comments	A 10 to 25% increase in serum creatinine may occur in some patients with CKD as a result of RAAS therapy	RAS blockade is more effective in reducing albuminuria than other antihypertensive agents and is also effective in preventing incident microalbuminuria	Patients and clinicians should engage in a shared decision-making process to determine individual BP targets Bedtime dosing: moving at least one antihypertensive medication to bedtime.	The antihypertensive and antialbuminuric effects ACE inhibitor or ARB are complemented by dietary sodium restriction or administration of diuretics.

ACC/AHA American College of Cardiology/American Heart Association; ACE inhibitors, angiotensin-converting enzyme inhibitors; *ADA*, American Diabetes Association; *ARBs*, angiotensin II receptor blockers; *CKD*, chronic kidney disease; *ESH/ESC*, European Society of Hypertension/European Society of Cardiology; *RAS*, renin angiotensin system; *NKF*, National Kidney Foundation

Kalaitzidis RG et al. Curr Hypertens Rep. 2018

Accepted combinations of antihypertensive agent for BP management in CKD patients



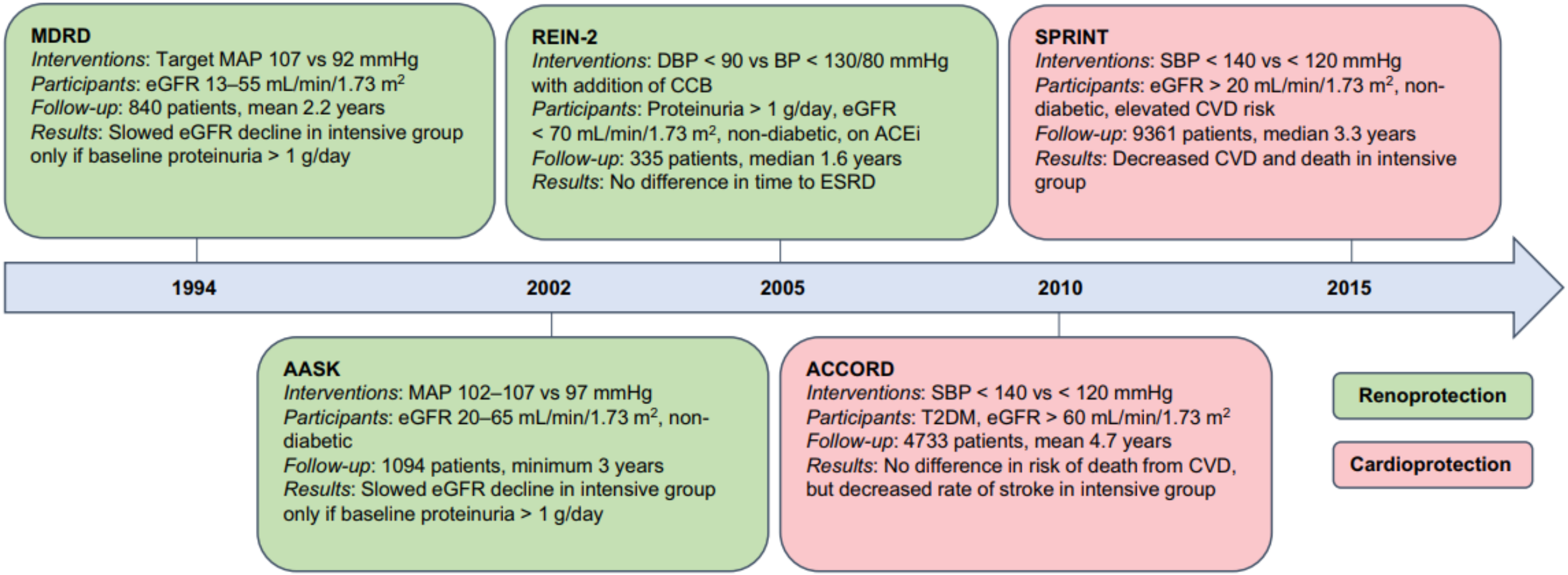
Kalaitzidis RG et al. Curr Hypertens Rep. 2018 ;20(8):64

Blood pressure control

- BP targets should be tailored according to age, tolerability and the level of proteinuria.
- An angiotensin receptor blocker (ARB) or angiotensin converting enzyme (ACE)-I is suggested for both diabetic and non-diabetic patients with CKD and urine albumin excretion >300 mg/24 h (or equivalent)
- RAAS inhibitors are not used if there is intractable hyperkalaemia.
- For diabetic and non-diabetic patients with AER less than 30 mg/24 h (or equivalent), the suggested BP target is ≤140/90 mmHg.
- For diabetic and non-diabetic patients with UAE ≥30 mg/24 h (or equivalent), the suggested BP target is ≤130/80 mmHg.

Tang SC et al. Nephrology (Carlton).2019 ;24 (1):9

Timeline of landmark randomised trials comparing standard with intensive blood pressure control



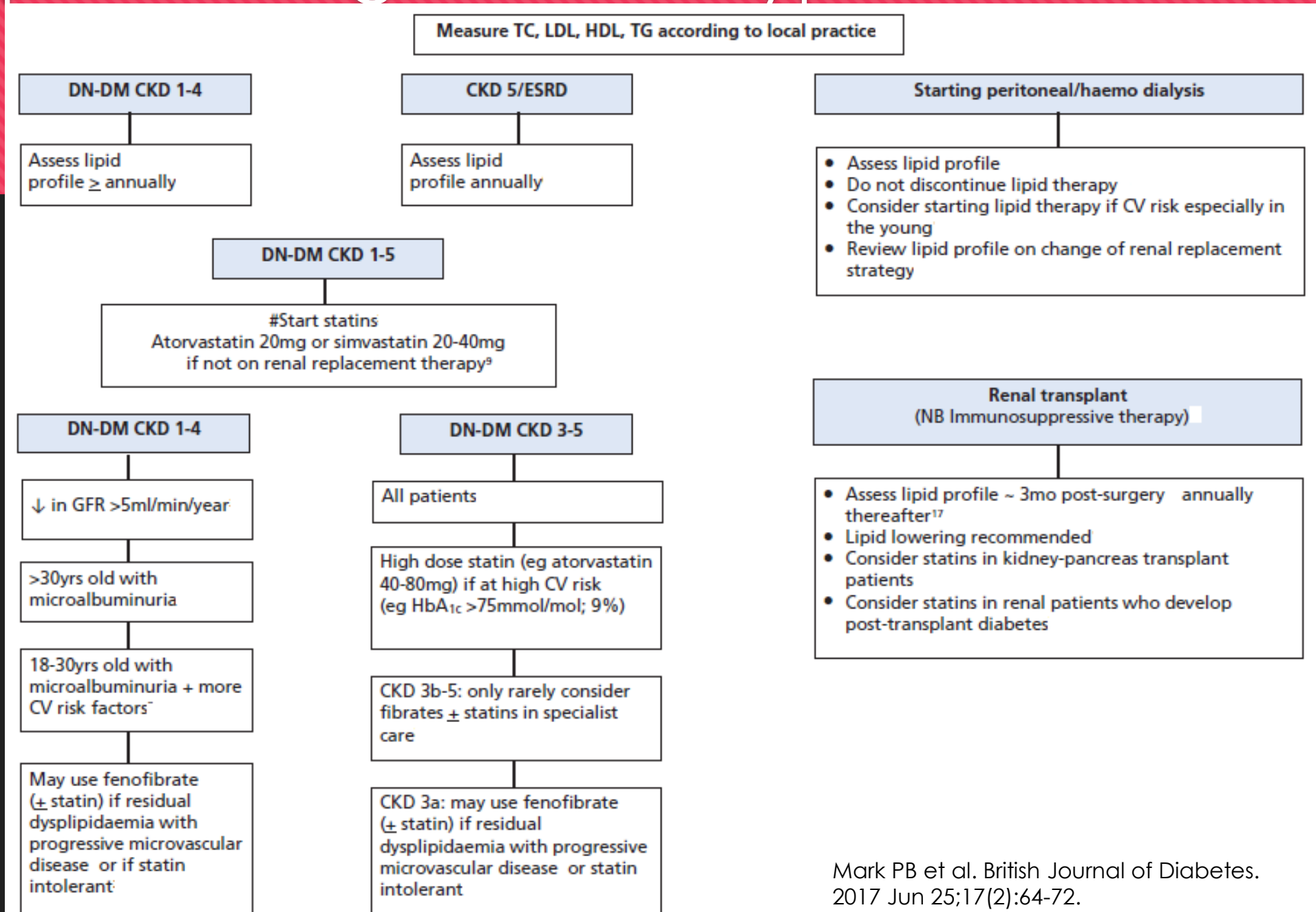
Pugh D et al. Drugs 2019; 79(4): 365–379

Anti proteinuric measures

- The level of proteinuria has been shown to correlate with renal prognosis in both diabetic and non-diabetic CKD.
- Every attempt should be made to lower proteinuria.
- Treatment with a RAS blocker (ACEi or ARB) appears to be the only proven therapeutic option.
- Combination of ACEi/ARB, ARB/mineralocorticoid receptor blocker or ARB/direct renin inhibitor is in general not recommended due to potential adverse events, mainly AKI, hyperkalaemia or hypotension

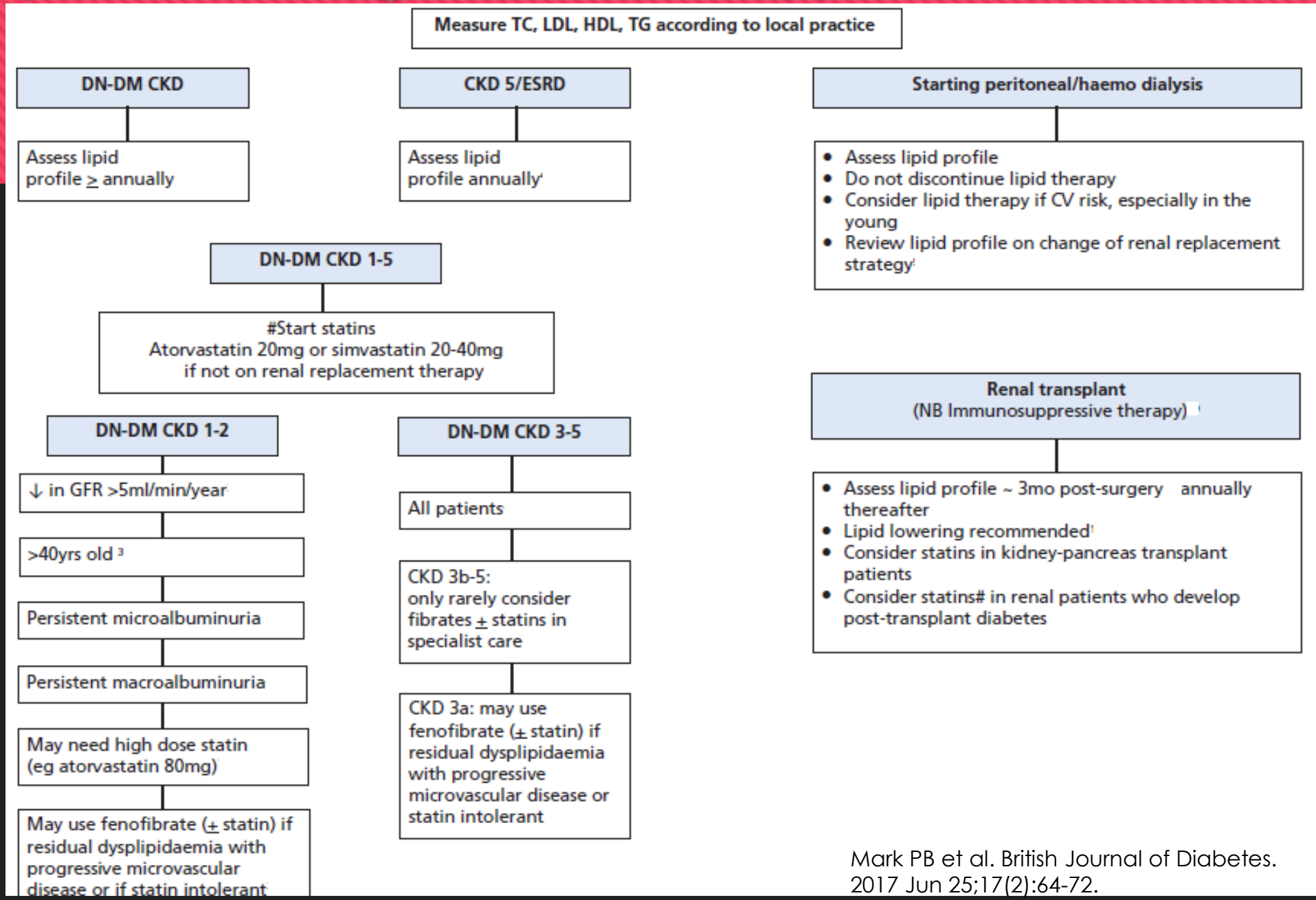
Tang SC et al. Nephrology (Carlton).2019 ;24 (1):9-26

Lipid management in type 1 diabetes



Mark PB et al. British Journal of Diabetes. 2017 Jun 25;17(2):64-72.

Lipid management in type II diabetes



Mark PB et al. British Journal of Diabetes. 2017 Jun 25;17(2):64-72.

Key Recommendations for anaemia treatment

Group	Title	Key recommendations
National Institute for Health and Care Excellence	Anaemia Management in Chronic Kidney Disease: Partial Update 2015	Initiation of IV iron therapy: • Serum ferritin should not exceed 800 ng/mL. Review dose of iron when ferritin reaches 500 ng/mL Evaluation of iron status: • Do not use TSAT or serum ferritin measurement alone to assess iron deficiency status in people with anaemia of CKD
European Renal Best Practices (ERBP)	Kidney Disease: Improving Global Outcomes guidelines on anaemia management in chronic kidney disease: a European Renal Best Practice position statement	Initiation of IV iron therapy in patients not on ESA: • Initiate a trial of IV iron if there is absolute iron deficiency (TSAT <20%, ferritin <100 ng/mL) or if TSAT <25%, ferritin <200 ng/mL in CKD-ND patients, or TSAT<25%, ferritin <300 ng/mL in patients on dialysis • TSAT 30% ferritin 500 ng/mL should not be intentionally exceeded • Initiate ESA and IV iron together in patients with ferritin >300 ng/mL Initiation of IV iron therapy in patients on ESA: • Use oral iron as a first step if tolerated • Initiate IV iron if TSAT <30%, ferritin <300 ng/mL • Do not exceed ferritin 500 ng/mL, especially if TSAT >30%
Kidney Disease Outcomes Quality Initiative (KDOQI)	KDOQI US commentary on the 2012 KDIGO Clinical Practice Guideline for Anaemia in CKD	Initiation of IV iron therapy in patients on ESA: • Initiate a trial of IV iron if TSAT <30%, even if ferritin is > 500 ng/mL Cautions regarding iron therapy: • High molecular weight iron dextran should be avoided • Have resuscitative facilities and personnel available when administering IV iron IV iron and systemic infections: • No evidence that IV iron exacerbates infection; iron deficiency may worsen ability to respond to infection

Berns JS et al. Clin Kidney J. 2017

Key Recommendations for anaemia treatment

Group	Title	Key recommendations
Canadian Society of Nephrology	Canadian Society of Nephrology Commentary on the 2012 KDIGO Clinical Practice Guideline for Anaemia in CKD	Initiation of IV iron therapy: • Increase in Hb is less likely when TSAT >30% and ferritin >500 ng/mL Iron status evaluation: • Be mindful of the half-life of iron products administered; time testing of iron status accordingly Cautions regarding iron therapy: • 30 min of monitoring postadministration is probably sufficient • Important to distinguish between allergic reactions and reactions to high amounts of free iron
KDIGO Controversies Conference	Iron management in chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference	Initiation of IV iron therapy: • Doses >3 g/year are more likely to cause positive iron balance; if high doses seem necessary, look for causes of increased iron loss Iron status evaluation: • Current methods to assess iron status are insufficient • Elevated ferritin does not always correlate with high liver iron Cautions regarding iron therapy: • Important to distinguish between allergic reactions and reactions to large amounts of free iron • High molecular weight iron dextran should be avoided, lower molecular weight formulations should be used IV iron and systemic infections: • RCT evidence is lacking • Observational studies may be confounded

Berns JS et al. Clin Kidney J. 2017 ;10(1):i3-i8

Managing Hyperphosphatemia

	DIET	PHOSPHATE BINDERS AND OTHER MEDICATIONS	DIALYTIC PHOSPHATE REMOVAL
CKD stages 3-5 and kidney transplant recipients (KTRs) with hyperphosphatemia	Suggest limiting dietary phosphate intake alone or in combination with other treatments ***G 4.1.7 (2D)***	Suggest using phosphate binders ***G 4.1.4 (2D)***, taking into account (NG): • CKD stage • Presence of other components of CKD-MBD • Concomitant therapies • Side effect profile	N.A.
CKD stages 3-5 and KTRs with hyperphosphatemia and persistent or recurrent hypercalcemia		Recommend restricting dose of: ***G 4.1.5 (1B)*** • Calcium-based phosphate binders and/or • Calcitriol or vitamin D analogue	
CKD stages 3-5 and KTRs with hyperphosphatemia and arterial calcification and/or adynamic bone disease and/or persistently low PTH levels		Suggest restricting the dose of calcium-based phosphate binders ***G 4.1.5 (2C)***	
CKD stage 5D		Suggest using phosphate binding agents. ***G 4.1.4 (2B)*** Suggest the choice of agent should take into account: ***G 4.1.4 (NG)***: • CKD stage • Presence of other components of CKD-MBD • Concomitant therapies • Side effect profile	Suggest increasing dialytic phosphate removal in the treatment of hyperphosphatemia ***G 4.1.8 (2C)***.

Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group
Kidney Int Suppl (2011). 2017;7(1):1-

urate-lowering agents with recommendations for urate-lowering management in patients with normal and reduced kidney function

Urate-lowering agents	Doses	Recommendations for CKD 3–5	Recommendations for CKD 5D (dialysis)
		Xanthine oxidase inhibitors (XOI)	
Allopurinol	Starting: 50–100 mg daily; maximal approved: 800 mg/day (900 mg/day in the UK)	CrCl ≥30 mL/min: start with ≤100 mg/day CrCl <30 mL/min: start with 50 mg/day	Intermittent HD: should be administered post-dialysis[28,29], start with 100 mg alternate days post-dialysis; daily HD: additional 50% of dose may be required post-dialysis; daily PD: start with 50 mg/day; all types of RRT: up-titrate dose with 50 mg-increments every 2–5 weeks, measure serum urate pre-dialysis
Febuxostat	Starting: 40 mg daily; maximal approved: 80 mg/day (120 mg in Europe)	Insufficient data for CrCl <30 mL/min	Despite some successful reports of dialysis patients using febuxostat up to 80 mg/day, this agent is not FDA-approved for use in dialysis due to a lack of trials in this population[30–34]
		Uricosuric Agents	
Benzbromarone	Starting: 25–50 mg daily; maximal approved: 200 mg/day	Contraindicated if CrCl <20 mL/min	Contraindicated
Lesinurad	Starting: 200 mg daily together with XOI; maximal approved: 200 mg/day	Contraindicated if CrCl <45 mL/min	Contraindicated
Probenecid	Starting: 250 mg twice daily; maximal approved: 2000 mg/day	Not effective if CrCl ≤30 mL/min	Contraindicated
Sulfinpyrazone	Starting: 50 mg twice daily; maximal approved: 800 mg/day	Not effective if CrCl ≤30 mL/min	Contraindicated

CKD: chronic kidney disease; CrCl: creatinine clearance; HD: hemodialysis; IV: intravenous; PD, peritoneal dialysis; RRT, renal replacement therapy

Vargas Santos AB et al. Am J Kidney Dis. 2017;70(3):422-439

Treatment for a gout flare in patients with normal and decreased kidney function

	Normal kidney function	CKD 3–5	CKD 5D (Dialysis)
Colchicine	1.2 mg at the first sign of a gout flare followed by 0.6 mg one hour later; then, 0.6 mg every 12 hours or followed by other gout flare therapy	Not recommended in patients already receiving colchicine for prophylaxis; **CrCl ≥30 mL/min:** dosage adjustment not required; **CrCl <30 mL/min:** consider dosage reduction; treatment course should not be repeated more frequently than every 14 days per FDA label	0.6 mg as a single dose; FDA approved label states that treatment course should not be repeated more frequently than every 14 days; not removed by dialysis
NSAID	Any NSAID in its full daily dose	**CrCl 30 to 59 mL/min:** avoid or use with caution depending on the kidney disease; **CrCl <30 mL/min:** relatively contraindicated	May be used
Steroid	0.5 mg/kg/day, followed by progressive weaning; for example, start prednisone at 30 mg/day, then reduce by 5 mg every 2 days	Dosage adjustment for CKD not required	Dosage adjustment for CKD not required
ACTH	Subcutaneous or intramuscular; treatment option for patients with restrictions to oral drugs; initial dose of 25–40 IU; doses repeated as clinically indicated	Dosage adjustment for CKD not required	Dosage adjustment for CKD not required
Interleukin-1 inhibitors	The off-label use of anakinra to treat gout flares in patients with multiple comorbidities and contraindications to the above-mentioned options has become more frequent in the US; canakinumab is approved for gout flare management by the EMA; dose: Anakinra 100 mg/day subcutaneously; Canakinumab 150 mg SC single dose, to be repeated no sooner than at least 12 weeks in patients who respond and require retreatment	CrCl <30 mL/min: For anakinra, mean plasma clearance of anakinra declined by 70–75%; consider dose reduction, as 100 mg every other day; for canakinumab, no dose reduction is needed, though clinical experience is limited	For anakinra: <2.5% of the administered dose of anakinra is removed by hemodialysis or continuous ambulatory peritoneal dialysis; consider dose reduction, as 100 mg every other day; for canakinumab, no dose reduction is needed, though clinical experience is limited

CKD: chronic kidney disease; CrCl: creatinine clearance; NSAID: nonsteroidal anti-inflammatory drug; ACTH: adrenocorticotropic hormone; IU: international units; SC: subcutaneous; FDA, US Food and Drug Administration; EMA, European Medicines Agency.

Vargas Santos AB et al. Am J Kidney Dis. 2017;70(3):422-439

Prognosis of chronic kidney disease by estimated glomerular filtration rate and albuminuria

Prognosis of CKD according to eGFR and albuminuria: 2012 KDIGO

				Categories for albuminuria, description and interval		
				A1	A2	A3
				Normal or slight increase	Moderate increase	Severe increase
				<30mg/g < 3mg/mmol	30-299mg/g 3-29mg/mmol	≥ 300mg/g ≥ 30mg/mmol
Categories for eGFR, description and range (ml/min/1.73 m²)	G1	Normal or high	> 90			
	G2	Slight decrease	60-89			
	G3a	Slight-moderate decrease	45-59			
	G3b	Moderate-severe decrease	30-44			
	G4	Severe decrease	15-29			
	G5	Renal failure	< 15			

CKD: chronic kidney disease, eGFR: estimated glomerular filtration rate, KDIGO: Kidney Disease Improving Global Outcomes.
Note: The colours show the relative risk adjusted for five events (overall mortality, cardiovascular mortality, renal failure treated with dialysis or transplantation, acute renal failure and progression of kidney disease) from a meta-analysis of general population cohorts. Green corresponds to the lowest risk ("low risk category"; if there are no renal lesion data, it cannot be classified as CKD), followed by yellow ("moderately high" risk), orange ("high risk") and red ("very high risk"), which express increasing risk for the events mentioned. Reproduced with the permission of KDIGO.[6]
Albumin/creatinine ratio: 1mg/g = 0.113mg/mmol. 30mg/g (3.4mg/mmol).

KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl 2013;3:S6-308

Summary

- Chronic kidney disease affects 8%to 16%of the populationworldwide
- and is a leading cause of death.
- Optimal management of CKD includes cardiovascular risk reduction, treatment of albuminuria, avoidance of potential nephrotoxins, and adjustments to drug dosing.
- Patients also require monitoring for complications of CKD, such as hyperkalemia, metabolic acidosis, anemia, and other metabolicabnormalities.
- Diagnosis, staging, and appropriate treatment of CKD is important in reducing the burden of CKD