



Patient management in CKD stage 3-5

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KDIGO: Prognosis of CKD by GFR and albuminuria categories				Persistent albuminuria categories		
				Description and range		
				A1	A2	A3
				Normal to mildly increased <30 mg/g <3 mg/mmol	Moderately increased 30–300 mg/g 3–30 mg/mmol	Severely increased >300 mg/g >30 mg/mmol
GFR categories (ml/min/1.73 m ²) 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			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red: very high risk. GFR, glomerular filtration rate.

Table 1 | Criteria for chronic kidney disease (either of the following present for a minimum of 3 months)

Markers of kidney damage (1 or more)	Albuminuria (ACR ≥ 30 mg/g [≥ 3 mg/mmol]) Urine sediment abnormalities Persistent hematuria Electrolyte and other abnormalities due to tubular disorders Abnormalities detected by histology Structural abnormalities detected by imaging History of kidney transplantation
Decreased GFR	GFR < 60 ml/min per 1.73 m^2 (GFR categories G3a–G5)

ACR, albumin-to-creatinine ratio; GFR, glomerular filtration rate.

CKD evaluation

CKD evaluation

- Consider initiation of treatments for CKD at first presentation.
- Evaluation of cause.
- Evaluation of albuminuria and proteinuria.
- For people with CKD, a change in eGFR of $>20\%$ on a subsequent test exceeds the expected variability and warrants evaluation.
- Among people with CKD who initiate hemodynamically active therapies, GFR reductions of $>30\%$ on subsequent testing exceed the expected variability and warrant evaluation.
- For albuminuria monitoring of people with CKD, a doubling of the ACR on a subsequent test exceeds laboratory variability and warrants evaluation.

Monitoring for progression of CKD

- ✓ Assess albuminuria and GFR at least **annually** in people with CKD. Assess albuminuria and GFR more often for individuals at higher risk of CKD progression.
- ✓ All patients with type 2 diabetes should have **annual** spot measurement of UACR and eGFR.
- ✓ Patients with type 2 diabetes and $\text{UACR} \geq 300 \text{ mg/g}$ and/or eGFR of 30-60 should be monitored **twice** annually.

Table 54.2 Overview of Chronic Kidney Disease Management by Stage

Features	Stages 1 and 2	Stage 3a	Stage 3b	Stage 4	Stage 5
Estimated GFR	≥ 60 mL/min/1.73 m ² + albuminuria or hematuria or structural kidney damage	45-59 mL/ min/1.73 m ²	30-44 mL/ min/1.73 m ²	15-29 mL/ min/1.73 m ²	<15 mL/min/1.73 m ²
Frequency of monitoring	Annual	6-12 months	3-6 months	3-4 months	1-3 months
Laboratory testing	Annual electrolytes and estimated GFR Annual urine ACR (or other estimate of proteinuria) Baseline anemia and mineral and bone profiles Glucose, lipids, and HbA _{1c} See Table 54.3 for causes of AKI after initiation of ACE inhibitor or ARB therapy.				Check electrolytes and estimated GFR 1 week after new use or higher doses of ACE inhibitors or ARBs; otherwise, assess electrolytes/estimated GFR, mineral and bone, and anemia profiles every 3-6 months, depending on GFR decline.

CKD evaluation :When to refer a patient

In people with CKD G3–G5:

- ✓ A 5-year kidney failure risk of 3%–5% can be used to determine need for nephrology referral .
- ✓ A 2-year kidney failure risk of >10% can be used to determine the timing of multidisciplinary care.
- ✓ A 2-year kidney failure risk threshold of >40% can be used to determine the modality education, timing of preparation for kidney replacement therapy (KRT) including vascular access planning or referral for transplantation.

7:19
67

Kidney Failure Risk...

Answer all questions...

Sex?
Unanswered

Age?
Unanswered

eGFR?
Unanswered

Urine Albumin Creatinine Ratio? (Note units carefully)
Unanswered

Patient location?
Unanswered

Results

Please answer all questions

Try 8-Variable Kidney Failure Risk Equation
Estimate risk of progression to end-stage renal disease in CKD patients with more precision using 8 variables.

7:19
67

Kidney Failure Risk...

Answer all questions...

Sex?
Unanswered

Age?
Unanswered

eGFR?
Unanswered

Urine Albumin Creatinine Ratio?
Unanswered

Serum Calcium?
Unanswered

Serum Phosphorous?
Unanswered

Serum Bicarbonate?
Unanswered

Serum Albumin?
Unanswered

Patient location?
Unanswered

Results

Please answer all questions

CKD evaluation :When to refer a patient

- ✓ Once a patient has reached CKD stage 4, they should be under a nephrologist care.
- ✓ Patients with an eGFR less than 20 ml/min should be educated about all modalities of KRT .
- ✓ Evaluation the need for dialysis should begin at a eGFR around 10-12 ml/min (earlier in patients with heart failure or refractory fluid retention).
- ✓ Best time for creating AVF/AVG is when GFR falls below 20 ml/min/1.73.

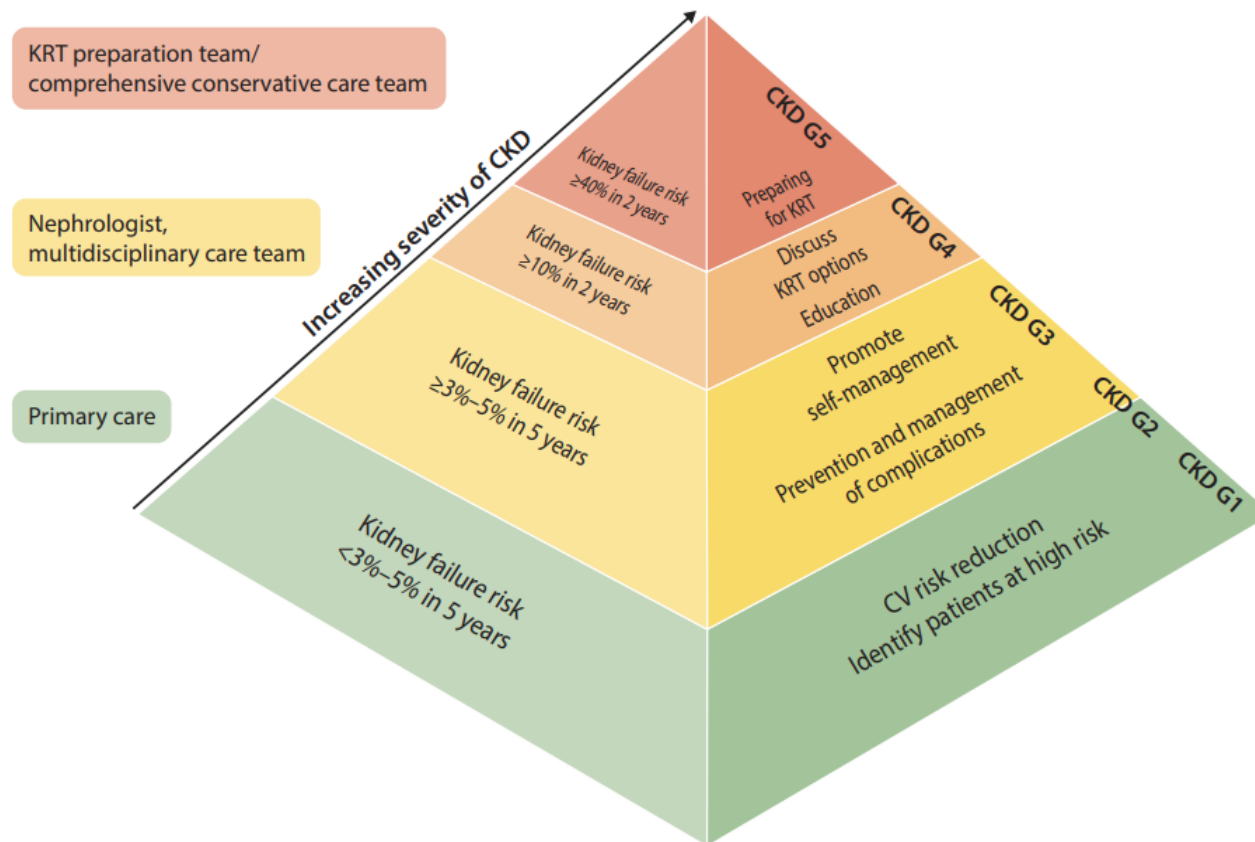


Figure 3 | Optimal care model by increasing severity of chronic kidney disease (CKD). CV, cardiovascular; KRT, kidney replacement therapy.

Table 54.2 Overview of Chronic Kidney Disease Management by Stage (Continued)

Features	Stages 1 and 2	Stage 3a	Stage 3b	Stage 4	Stage 5
Referral guidance from primary care physician to nephrologist	Progressive or abrupt fall in estimated GFR Proteinuria (urine protein levels >0.5 g/day; ACR >300 mg/g or >30 mg/mmol)			Refer unless patient is terminally ill	Refer unless patient is terminally ill.

ACE, Angiotensin-converting enzyme; ACR, albumin-to-creatinine ratio; AKI, acute kidney injury; ARB, angiotensin receptor blocker; ARVD, atherosclerotic renovascular disease; AVF, arteriovenous fistula; BMI, body mass index; BP, blood pressure; CHF, congestive heart failure; CKD, chronic kidney disease; CVD, cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; ESA, erythropoietin-stimulating agent; GFR, glomerular filtration rate; GLP1RA, glucagon-like peptide 1 receptor agonists; HbA_{1c}, hemoglobin A_{1c}; PD, peritoneal dialysis; nsMRA, nonsteroidal Mineralocorticoid Receptor Antagonist; PTH, parathyroid hormone; RAAS, renin-angiotensin-aldosterone system; RRT, renal replacement therapy; SGLT2, sodium-glucose cotransporter-2.

CKD evaluation: Evaluation of GFR

- ✓ Serum Cr level must always be interpreted in the context of patients muscle mass.
- ✓ Cockcroft-Gault equation estimates GFR based on age, body size, gender, race.
- ✓ Best way of calculating eGFR is with equations with least effect of race: EPI-CKD.
- ✓ Exception: High muscle mass, Cachexia, Limb amputation, Spinal cord injury, Advanced liver cirrhosis, pregnancy
- ✓ In these people you should calculate eGFR for drug dosing with 24 hour urine Cr clearance.

1. Cockcroft-Gault Equation (mL/min)	$CCr = \frac{(140 - \text{age}) \times \text{LBW [kg]}}{\text{Cr [mg/dL]} \times 72}$ <i>For women Multiply by 0.85</i>
2. MDRD study equation (mL/min/1.73 m ²)	$GFR = 186.3 \times (SCr)^{-1.154} \times (\text{Age})^{-0.203}$ <i>Multiply by 0.742 for women</i> <i>Multiply by 1.21 for African ancestry</i>
3. CKD-EPI equation	$GFR = 141 \times \min(SCr/\kappa)^{\alpha} \times \max(SCr/\kappa)^{-1.209} \times 0.993^{\text{age}}$ <i>Multiply by 1.018 for women</i> <i>Multiply by 1.159 for African ancestry</i> κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of SCr/κ or 1, & max indicates the maximum of SCr/κ or 1

CKD evaluation: Evaluation of GFR

- eGFR in amputated patient:

IBW adjusted=IBW×(1−%amputation)

Amputation	% Body Weight
Entire arm	5%
Forearm + hand	2.3%
Hand	0.7%
Entire leg	16%
Below-knee	6%
Above-knee	11%
Foot	1.5%

- 24hour urine Cr clearance:

$$\text{CrCl (mL/min)} = \frac{U_{Cr} \times V}{P_{Cr} \times t}$$

$$\text{CrCl} = \frac{U_{Cr} \times \text{Urine Volume (mL)}}{P_{Cr} \times 1440}$$

CKD evaluation

- Delaying CKD progress

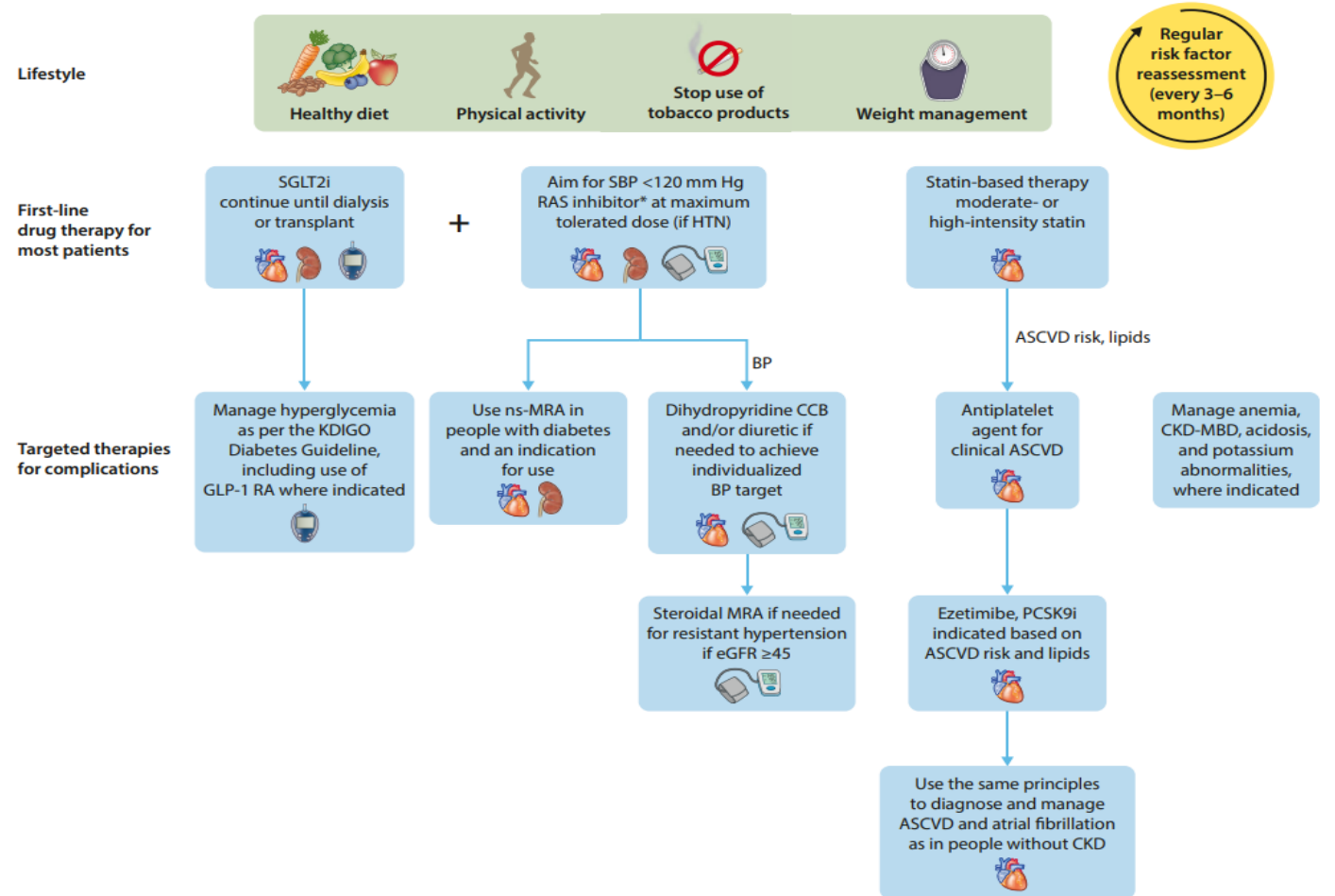


Figure 18 | Holistic approach to chronic kidney disease (CKD) treatment and risk modification. *Angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker should be first-line therapy for blood pressure (BP) control when albuminuria is present; otherwise dihydropyridine calcium channel blocker (CCB) or diuretic can also be considered. All 3 classes are often needed to attain BP targets. Icons presented indicate the following benefits: blood pressure cuff = blood pressure-lowering; glucometer = glucose-lowering; heart = heart protection; kidney = kidney protection; scale = weight management. ASCVD, atherosclerotic cardiovascular disease; CKD-MBD, chronic kidney disease-mineral and bone disorder; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HTN, hypertension; KDIGO, Kidney Disease: Improving Global Outcomes; MRA, mineralocorticoid receptor antagonist; ns-MRA, nonsteroidal mineralocorticoid receptor antagonist; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; RAS, renin-angiotensin system; SBP, systolic blood pressure; SGLT2i, sodium-glucose cotransporter-2 inhibitor. Modified from Kidney Disease: Improving Global Outcomes Diabetes Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int.* 2022;102:S1–S127.²³ Copyright © 2022, KDIGO: Kidney Disease Improving Global Outcomes. Published by Elsevier Inc. on behalf of the International Society of Nephrology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

CKD evaluation: Delaying CKD progress

- Diet: higher consumption of plant-based foods compared to animal-based foods and a lower consumption of ultra-processed foods.
- in adults with CKD G3–G5, protein intake of 0.8 g/kg /d.
- Avoid high protein intake (>1.3 g/kg body weight/d) in adults with CKD at risk of progression.
- Do not restrict protein below 0.8 gr/kg/day
- In older adults with underlying conditions such as frailty and sarcopenia, consider higher protein and calorie dietary targets.
- Sodium intake: sodium intake be <2 g of sodium per day (or <5 gr of sodium chloride per day).

CKD evaluation: Delaying CKD progress

- Physical activity : people with CKD be advised to undertake moderate-intensity physical activity for a cumulative duration of at least 150 minutes per week, or to a level compatible with their cardiovascular and physical tolerance
- Recommendations for physical activity should consider age, ethnic background, presence of other comorbidities
- advised to avoid sedentary behavior
- Weight management: achieve an optimal body mass index (BMI < 25)

CKD evaluation

- Delaying CKD progress

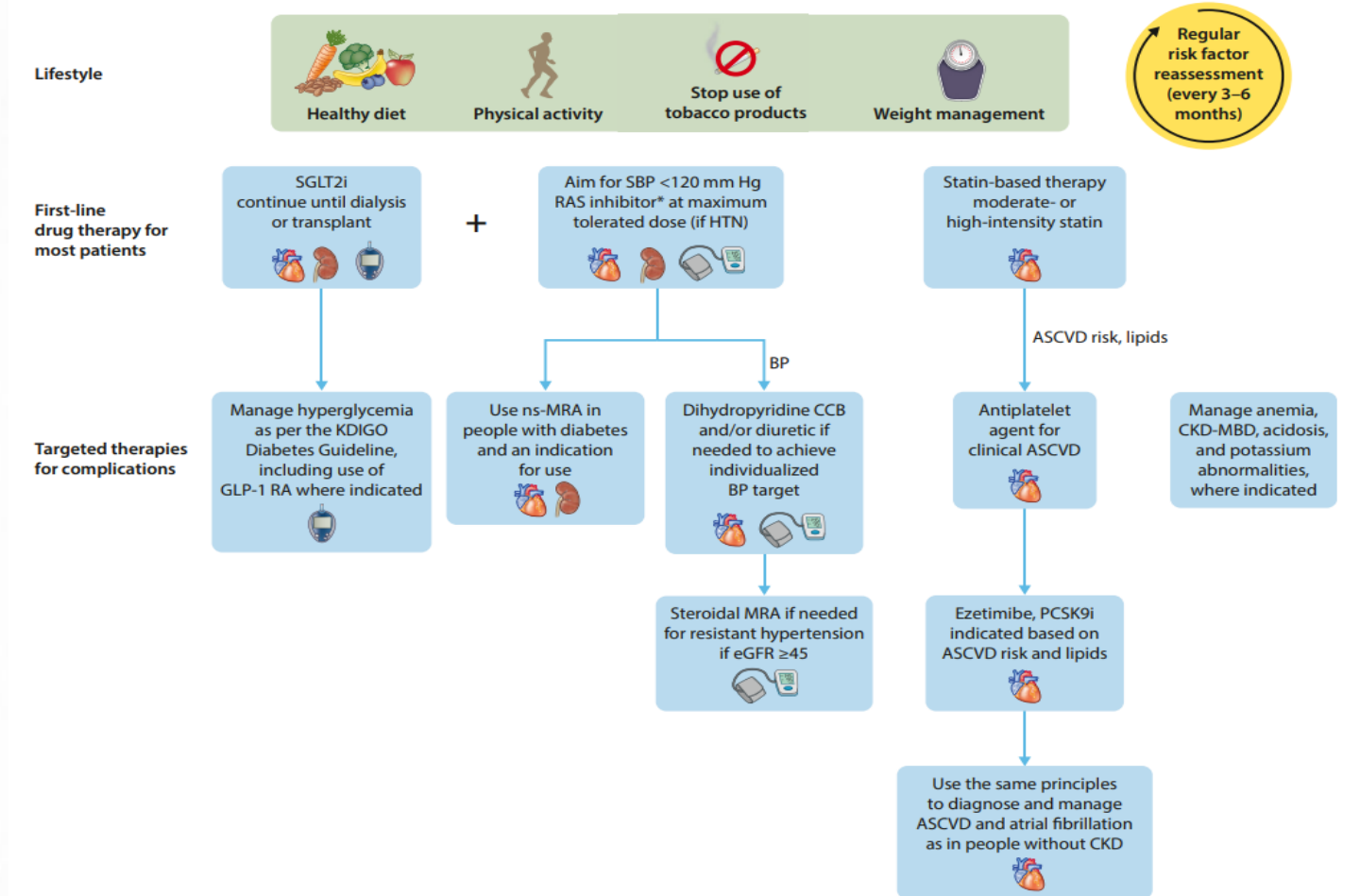


Figure 18 | Holistic approach to chronic kidney disease (CKD) treatment and risk modification. *Angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker should be first-line therapy for blood pressure (BP) control when albuminuria is present; otherwise dihydropyridine calcium channel blocker (CCB) or diuretic can also be considered. All 3 classes are often needed to attain BP targets. Icons presented indicate the following benefits: blood pressure cuff = blood pressure-lowering; glucometer = glucose-lowering; heart = heart protection; kidney = kidney protection; scale = weight management. ASCVD, atherosclerotic cardiovascular disease; CKD-MBD, chronic kidney disease-mineral and bone disorder; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HTN, hypertension; KDIGO, Kidney Disease: Improving Global Outcomes; MRA, mineralocorticoid receptor antagonist; ns-MRA, nonsteroidal mineralocorticoid receptor antagonist; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; RAS, renin-angiotensin system; SBP, systolic blood pressure; SGLT2i, sodium-glucose cotransporter-2 inhibitor. Modified from Kidney Disease: Improving Global Outcomes Diabetes Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int.* 2022;102:S1–S127.²³ Copyright © 2022, KDIGO: Kidney Disease Improving Global Outcomes. Published by Elsevier Inc. on behalf of the International Society of Nephrology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

CKD evaluation: Delaying CKD progress

- Blood pressure control

Features	Stages 1 and 2	Stage 3a	Stage 3b	Stage 4	Stage 5
Blood pressure targets	BP target <130/80 mm Hg with proteinuria BP target <140/90 mm Hg without proteinuria if no clinical or radiologic evidence of ARVD or previous episodes of AKI				Risk of AKI is increased in elderly persons (>75 years), those with CHF, and those with ARVD; 140/90 mm Hg may be more appropriate for these groups.

- Consider less intensive BP-lowering therapy in people with frailty, high risk of falls and fractures, very limited life expectancy, or symptomatic postural hypotension.

CKD evaluation: Delaying CKD progress

Renin-angiotensin system inhibitors:

- Indication:
 - ✓ CKD and moderately-to-severely increased albuminuria (G1–G4, >30 mg/g albuminuria) without diabetes
 - ✓ CKD and moderately-to-severely increased albuminuria (G1–G4, >30 mg/g albuminuria) with diabetes
 - ✓ CKD with hypertension
- RASi (ACEi or ARB) should be administered using the highest approved dose that is tolerated to achieve the benefits
- Changes in BP, serum creatinine, and serum potassium should be checked within 2–4 weeks of initiation or increase in the dose
- Continue ACEi or ARB therapy unless serum creatinine rises by more than 30% within 4 weeks following initiation of treatment or an increase in dose.
- Continue ACEi or ARB in people with CKD even when the eGFR falls below 30 ml/min per 1.73 m²

CKD evaluation: Delaying CKD progress

Sodium-glucose cotransporter-2 inhibitors (SGLT2i)

- Indication
 - ✓ CKD with an eGFR ≥ 20 with type 2 diabetes
 - ✓ CKD with an eGFR ≥ 20 with UACR > 200 mg/g (even without diabetes)
 - ✓ CKD with an eGFR ≥ 20 with heart failure (even without diabetes and irrespective of level of albuminuria)
- Once an SGLT2i is initiated, it is reasonable to continue an SGLT2i even if the eGFR falls below 20 ml/min per 1.73 m², unless it is not tolerated or KRT is initiated.
- withhold SGLT2i during times of prolonged fasting, surgery, or critical medical illness (when people may be at greater risk for ketosis).
- the reversible decrease in eGFR on initiation is generally not an indication to discontinue therapy.

CKD evaluation: Delaying CKD progress

Mineralocorticoid receptor antagonists (MRA)

- Indication of nonsteroidal mineralocorticoid receptor antagonist for adults with T2D, an eGFR >25 ml/min per 1.73 m², normal serum potassium concentration, and albuminuria >30 mg/g despite maximum tolerated dose of RAS inhibitor.
- A nonsteroidal MRA may be added to a RASi and an SGLT2i for treatment of T2D and CKD in adults.
- Continue nsMRA as tolerated in GFR <15 ml/min/ 1.73 .
- A steroidal MRA may be used for treatment of heart failure, hyperaldosteronism, or refractory hypertension.
- monitor serum potassium regularly.

CKD evaluation: Statin therapy

Statin indication

- ✓ Adults aged ≥ 50 years with eGFR < 60 but not treated with chronic dialysis or kidney transplantation (GFR categories G3a–G5) : statin or statin/ezetimibe combination
- ✓ Adults aged ≥ 50 years with CKD and eGFR ≥ 60 ml/min per 1.73 m² (GFR categories G1–G2) : statin
- ✓ Adults aged 18–49 years with CKD but not treated with chronic dialysis or kidney transplantation, we suggest statin treatment in people with one or more of the following :
 1. Known coronary disease (myocardial infarction or coronary revascularization)
 2. Diabetes mellitus
 3. Prior ischemic stroke
 4. 10-year ASCVD score $> 10\%$

CKD evaluation: Aspirin therapy

Aspirin indication:

- Use only as secondary prevention
- Little benefit of primary intervention and increased risk of GIB

CKD evaluation: CKD complication management

- **Metabolic acidosis:** pharmacological treatment with or without dietary intervention (fruit and vegetables) in serum bicarbonate < 18 mmol/l (clinical goal : $\text{HCO}_3^- > 22$)
- Monitor treatment for metabolic acidosis to ensure it does not result in serum bicarbonate concentrations exceeding the upper limit of normal

CKD evaluation: CKD complication management

CKD complication management

- **Hyperuricemia:** people with CKD and symptomatic hyperuricemia should be offered uric acid–lowering intervention.
- Consider initiating uric acid–lowering therapy for people with CKD after their first episode of gout (particularly where there is no avoidable precipitant or serum uric acid concentration is >9 mg/dl).
- For symptomatic treatment of acute gout in CKD, low-dose colchicine or intra-articular/oral glucocorticoids are preferable to nonsteroidal anti-inflammatory drugs (NSAIDs).
- We suggest not using agents to lower serum uric acid in people with CKD and asymptomatic hyperuricemia to delay CKD progression .

Table 38 | Management strategies for common symptoms in CKD

Symptom	Comment	Management strategies		
		Lifestyle	Pharmacological	Other
Pain	Management should be determined by etiology and severity	Physiotherapy, exercise and massage therapy, and heat for musculoskeletal pain. Consider complementary therapies such as acupuncture.^{838,840,849}	Use of an adapted World Health Organization (WHO) Analgesic Ladder that takes into account pharmacokinetic data of analgesics in CKD.⁸⁵⁰ Before starting opioids, healthcare providers should assess risk of substance abuse and obtain informed consent after a discussion around goals, expectations, risks, and alternatives. Topical analgesics may be effective but used with caution to avoid adverse events due to systemic absorption. There are no studies on long-term use of any analgesics in people with CKD; therefore, attention should be paid to issues of efficacy and safety.	Referral to a specialist pain clinic or palliative/supportive care clinic may be beneficial for those at risk of aberrant behaviors, adverse outcomes, or in special circumstances such as end of life. ⁸⁴⁹
Sleep disorders	Associated with fatigue, poor HRQoL. ⁸³⁸ May be related to pruritus, pain, anemia, anxiety/depression, and shortness of breath. ⁸⁴⁰	Management of basic sleep hygiene, exercise, optimal positioning when sleeping, and removal of dietary or other stimulants ⁸³⁸	Melatonin ⁸⁵¹ and simple sedatives ^{852,853}	Cognitive behavioral therapy, ⁸⁵⁴ addressing contributing factors such as anemia, fluid retention, mood disorders, pain, and pruritus
Restless leg syndrome	Associated with impaired sleep and HRQoL	Management of basic sleep hygiene, exercise, optimal positioning when sleeping, and removal of dietary or other stimulants ⁸³⁸	Cessation of medications that interfere with the dopamine pathway, or trials with levodopa, nonergot dopamine antagonists, or low-dose gabapentinoids ⁸⁵⁵⁻⁸⁵⁷	Correction of contributing factors such as hyperphosphatemia and iron deficiency/anemia
Uremic pruritus	Associated with decreased HRQoL and contributes to other symptoms, such as poor sleep, fatigue, and depression ⁸³⁸	Acupuncture ⁸⁵⁸	Gabapentinoids with continued assessment of symptom experience and titration by a medical provider⁸⁵⁹⁻⁸⁶¹ Topical agents (capsicum, rehydrating emollients if concurrent dry skin)⁸⁶¹	Ultraviolet B therapy⁸⁶² Topical cannabis can be considered⁸⁶³

Symptom	Comment	Lifestyle	Pharmacological	Other
Depression	May be related to CKD burden and perception, loss of control, and medication effects. Associated with increased morbidity, hospitalization, and mortality, and is integral to the assessment of HRQoL⁸³⁸	Exercise ⁸⁶⁴ and acupuncture ⁸⁶⁵	Before commencing pharmacological treatment for depression, healthcare providers should be aware of the potential necessity to adjust dosage, and follow-up with the patient, due to altered pharmacokinetics in CKD.⁸⁴⁰ In some circumstances this may need to be done in conjunction with specialist psychiatric services. Options may include: • Serotonin reuptake inhibitors (e.g., citalopram, escitalopram, fluoxetine, paroxetine, and sertraline) • Serotonin-norepinephrine reuptake inhibitors (e.g., venlafaxine, duloxetine, and mirtazapine) • Atypical antidepressants (e.g., bupropion, trazodone, and nefazodone) • Tricyclic antidepressants (e.g., amitriptyline)⁸⁶⁶⁻⁸⁶⁹	Cognitive behavioral therapy⁸⁷⁰ Social support⁸⁶⁹ Address contributing factors (e.g., pain, pruritus and mood disorders)
Poor appetite and anorexia	Associated with depression, malnutrition, poor HRQoL, increased hospitalization, and mortality rates ⁸³⁸	Increased physical activity may increase appetite ⁸⁷¹	No data to support the use of appetite stimulants in people with CKD not on KRT. Management has not been studied systematically in CKD.⁸³⁸	Address contributing factors (pain, heartburn, mood disorders, any dental issues/mouth ulceration, constipation, social and economic factors, and lack of physical activity) Dietary assessment by a dietitian
Nausea and vomiting	Impact has not been assessed systematically in CKD. ⁸³⁸		Pharmacological management has not been systematically studied in CKD. ⁸³⁸	Address contributing factors (pain, heartburn, mood disorders, any dental issues/mouth ulceration, constipation, social and economic factors, and lack of physical activity) Dietary assessment by a dietitian

CKD evaluation: Timing the initiation of dialysis

Identification and assessment of symptoms:

- Assess uremic symptoms (e.g., reduced appetite, nausea, level of fatigue/lethargy, involuntary weight loss, fragility, fatigue, feeling cold, personality change, bleeding tendency) at each consultation.
- Screen people with CKD G4–G5 for malnutrition, **twice** annually.

TABLE

2.3

Complications That May Prompt Initiation of Kidney Replacement Therapy

Intractable extracellular volume overload and/or hypertension

Hyperkalemia refractory to dietary restriction and pharmacologic treatment

Metabolic acidosis refractory to bicarbonate treatment

Hyperphosphatemia refractory to dietary counseling and to treatment with phosphate binders

Anemia refractory to erythropoietin and iron treatment

Otherwise unexplained decline in functioning or well-being

Recent weight loss or deterioration of nutritional status, especially if accompanied by nausea, vomiting, or other evidence of gastroduodenitis

Urgent Indications

Neurologic dysfunction (eg, neuropathy, encephalopathy, psychiatric disturbance)

Pleuritis or pericarditis without other explanation

Bleeding diathesis manifested by prolonged bleeding time

Data from the National Kidney Foundation's 2006 Kidney Disease Outcomes Quality Initiative (KDOQI) hemodialysis adequacy guidelines.

CKD-MBD

CKD-MBD

In patients with CKD G3a–G5D

- With evidence of CKD-MBD and/or risk factors for osteoporosis, we suggest BMD testing with DXA to assess fracture risk if results will impact treatment decisions.
- Treatments of CKD-MBD should be based on serial assessments of phosphate, calcium, and PTH levels, considered together.
- Avoid hypercalcemia.
- Mild and asymptomatic hypocalcemia (e.g., in the context of calcimimetic treatment) can be tolerated in order to avoid inappropriate calcium loading in adults.

CKD-MBD

- In patients with CKD G3a–G5 not on dialysis, the optimal PTH level is not known. However, patients with levels of intact PTH progressively rising or persistently above the upper normal limit, be evaluated for modifiable factors, including hyperphosphatemia, hypocalcemia, high phosphate intake, and vitamin D deficiency .
- Modest increases in PTH may represent an appropriate adaptive response to declining kidney function (secondary hyperparathyroidism)
- Treatment should not be based on a single elevated value.
- In adult patients with CKD G3a–G5 not on dialysis, calcitriol and vitamin D analogs better not be routinely used .It is reasonable to reserve the use of calcitriol and vitamin D analogs for patients with CKD G4–G5 with severe and progressive hyperparathyroidism

CKD-MBD: Monitoring interval

- Monitor serum levels of calcium, phosphate, PTH, and alkaline phosphatase activity **beginning** in CKD **G3a**.
- In patients with CKD G3a–G5D, it is reasonable to base the frequency of monitoring serum calcium, phosphate, and PTH on the presence and magnitude of abnormalities, and the rate of progression of CKD.
- 25(OH)D (Calcidiol): Measure if indicated; repeat testing based on baseline levels and therapy. Treat vitamin D deficiency/insufficiency according to general population guidelines (goal > 30)

CKD-MBD

CKD Stage	Serum Calcium & Phosphate	Parathyroid Hormone (PTH)	Alkaline Phosphatase (ALP)
CKD G3a–G3b	Every 6–12 months	Based on baseline PTH level and CKD progression	-
CKD G4	Every 3–6 months	Every 6–12 months	Every 12 months*
CKD G5 (including G5D)	Every 1–3 months	Every 3–6 months	Every 12 months*

* For CKD G4–G5D, measure alkaline phosphatase (ALP) at least annually, or more frequently if PTH levels are elevated.

CKD-MBD: hyperphosphatemia

In patients with CKD G3a–G5D

- Lower elevated phosphate levels toward the normal range.
- Limit dietary phosphate intake in the treatment of hyperphosphatemia alone or in combination with other treatments.
- Receiving phosphate-lowering treatment, we suggest restricting the dose of calcium-based phosphate binders .
- phosphate-lowering therapies may only be indicated in the event of “progressive or persistent hyperphosphatemia,” and not to prevent hyperphosphatemia.
- Avoid the long-term use of aluminum containing phosphate binders.

TABLE	
34.1	Foods Especially High in Phosphate
Dairy products (milk, yogurt, cheese)	
Organ and processed meat	
Beans/peas	
Nuts/seeds	
Whole-grain breads, bran, and cereals	
Many soft drinks (particularly colas)	

CKD-MBD

Phosphate lowering drugs

Product	Trade Names	Dose (mg) per Tablet	Elemental Calcium	Maximum Dose per Day	Comments
Calcium carbonate	(Generic, multiple names)	Multiple doses	40% elemental calcium	1.5 g of elemental calcium/d	Administered with meals as a binder; on an empty stomach as a supplement
	TUMS	500 mg	200 mg/tab	As above (7 tablets)	
	TUMS EX	750 mg	300 mg/tab	As above (5 tablets)	
	TUMS Ultra	1,000 mg	400 mg/tab	As above (3 tablets)	
	TUMS 500	1,250 mg	500 mg/tab	As above (3 tablets)	
	Os-Cal 500	1,250 mg	500 mg/tab	As above (3 tablets)	
	Os-Cal + D	1,250 mg	500 mg/tab	As above (3 tablets)	
	Caltrate	600 mg	240 mg/tab	As above (6 tablets)	
Calcium acetate	PhosLo	667 mg	169 mg of elemental calcium/tab	As above (9 tablets)	200 IU of vitamin D/tab
Magnesium carbonate with calcium carbonate	MagneBind	200:200 mg MgCO ₃ with 400 mg CaCO ₃	160 mg/tab	Dose limited by serum Mg levels and diarrhea	More expensive than calcium carbonate. Prescription medication
Magnesium carbonate with calcium carbonate	MagneBind	300:300 mg MgCO ₃ with 250 mg CaCO ₃	100 mg/tab	Dose limited by serum Mg levels and diarrhea	85 mg of elemental magnesium/tab. Dialysate magnesium concentrations should be adjusted.
Magnesium carbonate + calcium acetate	OsvaRen	435 mg of MgCO ₃ and 235 mg of Ca acetate	60 mg/tab		85 mg of elemental magnesium/tab. Dialysate magnesium concentrations should be adjusted. Reduction of calcium load; Mg may have anticalcification properties; not available in the United States
Lanthanum carbonate	Fosrenol	250- and 500-mg tablets	0	1,250 mg t.i.d. Higher doses have not been tested long term.	Significantly more expensive than other products. Must be chewed
Sevelamer carbonate	Renvela	400- and 800-mg tablets and powder	0	Has been tested to 14 g/d in normal individuals. Dose may be limited by side effects of GI discomfort.	Significantly more expensive than other products
Sucroferric oxyhydroxide (PA21)	Velphoro	500 mg	0	3 g/d	Designed to minimize iron absorption from this iron-containing binder
Ferric citrate (JTT-751)	Not yet assigned	210-mg ferric iron	0	2.5 g/d ferric iron	210 mg elemental iron per tablet as 1 g ferric citrate. Associated with a significant increase in serum iron markers

Reference: KDIGO CKD-Mineral and Bone Disorder guideline, Handbook of dialysis

CKD-MBD

Phosphate lowering drugs in Iran

Drug	composition	dose	Starting dose	Maximum Dose	Side effects	Important note
Calcium carbonate	40% elemental calcium by weight	Tab 500 mg (200 mg ca)	1–2 tablets with each meal	1.5 g elemental calcium/day	Hypercalcaemia/ nausea/ constipation	PPIs reduce efficacy
Sevelamer carbonate	Non-calcium phosphate binder	Tab 800 mg	800–1600 mg TDS (with each meal)	14 g/day	Dyspepsia/ constipation / diarrhea	give other drugs 1 hour before and 3 hour after sevelamer

Anemia in CKD

Anemia in CKD

- Anemia is defined as Hb <12 for women and <13 for men
- Anemia is impacting more than half of people with CKD G4 and G5.
- Potential causes for anemia:

Potential causes (can be multiple)



- EPO deficiency/hyporesponsiveness
- Iron deficiency
- Blood loss (GI [malignancy, parasites], dialysis)
- Shortened RBC survival
- Hyperparathyroid or thyroid dysfunction
- Bone marrow suppression by inflammation; drugs (ACEi, ARBs, proliferation signal inhibitors in KTRs); or malignancy (MDS, myelofibrosis)
- Other nutritional deficiency (folate, vitamin B₁₂)
- Chronic inflammation (CHF, obesity, autoimmune diseases)
- Inherited anemia (thalassemia, sickle cell anemia)
- Anti-ESA antibody-mediated pure red cell aplasia (PRCA)

Anemia in CKD

- People with CKD should be tested for anemia and iron deficiency at **referral**, when anemia is suspected based on symptoms, and regularly during follow-up
- Testing intervals are at least **annually** for CKD G3, **twice a year** for CKD G4, and **every 3 months** for CKD G5 or G5 receiving dialysis (G5D)
- Anemia should be evaluated with complete blood count, reticulocytes, ferritin, and TSAT.
- If initial tests do not reveal the cause, check blood smear review, haptoglobin, lactate dehydrogenase, C-reactive protein, vitamin B12, folate, liver function tests, serum protein electrophoresis with immunofixation, serum free light chains, urinary Bence-Jones protein, thyroid-stimulating hormone, and fecal occult blood test and Parathyroid hormone.

Anemia in CKD

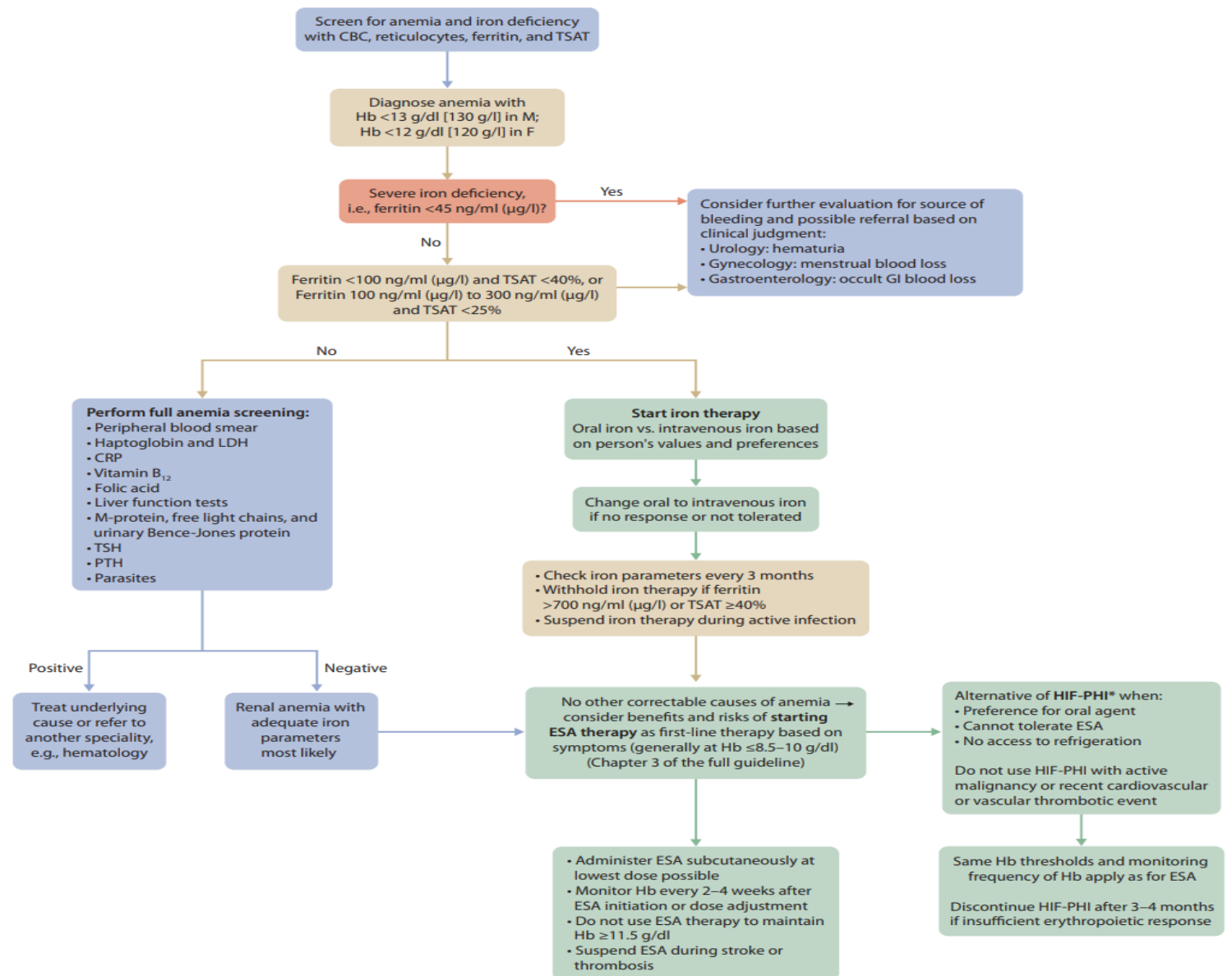


Figure 5 | Management of anemia in chronic kidney disease not receiving dialysis. CBC, complete blood count; CRP, C-reactive protein; ESA, erythropoiesis-stimulating agent; F, female; GI, gastrointestinal; Hb, hemoglobin; HIF-PHI, hypoxia-inducible factor–prolyl hydroxylase inhibitor; LDH, lactate dehydrogenase; M, male; PTH, parathyroid hormone; TSAT, transferrin saturation; TSH, thyroid-stimulating hormone. *While not U.S. Food and Drug Administration approved for this patient population, HIF-PHIs have been approved by other regulatory agencies.

Anemia in CKD

- Iron initiation indication:
 - ✓ Ferritin <100 mg/ml and TSAT $\leq 40\%$
 - ✓ Ferritin is between 100 and 300 mg/l with TSAT $<25\%$
 - ✓ people with CKD and profound iron deficiency (ferritin <30 ng/ml and TSAT $<20\%$) in the absence of anemia, especially in the presence of symptoms
- For all people with CKD treated with iron, it is reasonable to withhold routine iron if ferritin >700 ng/ml (>700 mg/l) or TSAT $>40\%$

Anemia in CKD

- In people with anemia and CKD not receiving HD, either oral iron or i.v. iron is suggested based on the person's values and preferences, the degree of anemia and iron deficiency, and the relative efficacy, tolerability, availability, and cost of each.
- In people with CKD not receiving HD treated with iron, it is reasonable to monitor TSAT, ferritin, and Hb at least **every 3 month**
- In people who are treated with oral iron, if there is insufficient effect after **1–3 months** or if tolerability is poor, switching to i.v. iron is advised.
- Iron may worsen outcomes in certain infections. Temporarily holding iron therapy should be considered during systemic infections

Anemia in CKD

- ESAs improve anemia-related fatigue and reduce the risk of RBC transfusions, although they do not reduce the risk of adverse cardiovascular outcomes or have a major effect on QoL in people.
- Before initiating ESA treatment, healthcare providers should ensure that patients are iron replete and that other reversible causes of anemia have been investigated.
- people with certain cancers show that using ESAs to treat anemia may lead to increased risk of cancer progression and death.

Anemia in CKD

- Target Hb ≤ 11.5 g/dl and typically between 10 -11.5
- a Hb of $\leq 9-10$ g/dl is a reasonable threshold for initiation among people receiving maintenance dialysis.
- CKD not receiving dialysis, the Hb threshold for the initiation of ESAs should be individualized based on the presence of symptoms attributable to anemia, the potential benefits of higher Hb concentration, and the potential harms of RBC transfusion or ESA therapy. For most people, the Hb threshold for initiation should be 8.5–10.0 g/dl . However, a lower Hb threshold could be considered in people with cardiovascular disease, thromboembolic disease, and malignancy.

Anemia in CKD

- Avoid rapid increases of more than about 1 g/dl (10 g/l) every 2 weeks.
- If rapid rises of this magnitude occur, the dose should be reduced by 25%–50%.
- If Hb exceeds 11.5 g/dl (115 g/l), reducing the dose of ESA may be preferable or temporary discontinuation.
- Using ESAs to target higher Hb levels (e.g., >13 g/dl) increases the risk of cardiovascular events, such as stroke and vascular access loss.
- Excess risk of hypertension at Hb targets >11.5 g/dl and the risks of vascular events at even higher targets.

Anemia in CKD

ESA	Initial dose	Dose adjustment ^a
Epoetin alfa and beta	CKD not receiving dialysis: ~50 U/kg once or twice weekly (some use up to 100 U/kg once every 2 wk) (may also round to a convenient dose in units, such as 4000 or 10,000 U, using the lower dose range once or twice weekly and a higher dose range every 2 wk) CKD G5D: 50–100 U/kg 3 times weekly (may round to a convenient dose in units)	CKD not receiving dialysis: Increase or decrease the dose and/or dosing frequency as needed (generally not given more than once weekly) CKD G5D: Increase the dose by 25 U/kg/dose if Hb rise is <1.0 g/dl (<10 g/l) after 4 wk. Decrease the dose by 10–25 U/kg/dose if Hb rise is >2 g/dl (>20 g/l) in 4 wk

Anemia in CKD

Table 9 | Causes of hyporesponsiveness to erythropoiesis-stimulating agents

- | |
|--|
| • Iron deficiency |
| • Inflammation (infections, dialysis catheter use, and autoimmune disease) |
| • Hyperparathyroidism |
| • Blood loss (GI tract, dialysis procedure, and menses) |
| • Inadequate dialysis |
| • Malignancy |
| • Hematologic disorders (hemoglobinopathies, multiple myeloma, hemolysis, and antibody-mediated pure red cell aplasia) |
| • Nutritional deficiencies (copper, zinc, folate, vitamin B ₁₂ , carnitine, and vitamin E) |
| • Medications (RAS inhibition) |
| • Unexplained (~ 30%) |

Anemia in CKD

- Transfusions indication:
 - ✓ Hb level <7 g/dl for asymptomatic and hemodynamically stable adult inpatients
 - ✓ Hb level <7.5 g/dl for people undergoing cardiac surgery
 - ✓ Hb level <8 gr/dl for those undergoing orthopedic surgery or those with clinically significant cardiovascular disease.

Vaccination in CKD

Vaccination in CKD

Vaccine	Indication for CKD	Indication After Transplant	Dose and Schedule
Influenza	All patients, annually	All patients, annually, starting 4 wk after transplant; no live vaccine	Age <60 y, single-injection standard vaccine; ≥60 y, single-injection high-dose vaccine
Pneumococcus	All patients aged ≥19 years	All patients aged ≥19 y, starting 6 mo after transplant	Never vaccinated: one PCV injection; has received PPSV23: one PCV booster >1 y after PPSV23
RSV	All patients aged ≥75 y, CKD 3+ and dialysis aged ≥60 y	All patients aged ≥60 y, starting 6 mo after transplant	Single dose, no vaccine type preference
SARS-CoV-2	All patients, annual revaccination	All patients, annual revaccination, consider 6-mo interval	Single-dose mRNA vaccine, most recent virus variant;
Hepatitis B	All patients with CKD 3b–5 (d)	No specific recommendation	3-4 injections of regular or double-dose vaccines (according to product label), serological monitoring and boosting (see Fig 3)
Herpes zoster	Patients aged ≥50 (ACIP), 60 (RKI), or 65 y (NHS), patients aged ≥19 y with therapeutic immunosuppression	All aged ≥19 y (except RKI: ≥50 y)	Two injections of recombinant vaccine 2-6 mo apart
Meningococcus	Only patients with particular risk, eg, asplenia, complement inhibition, travel to endemic areas	Only patients with particular risk, eg, asplenia, complement inhibition, travel to endemic areas	MenB or MenACWY depending on epidemiological situation; single dose; evaluate need for additional antibiotic prophylaxis
Human papillomavirus	Children aged 9-14 y, catch-up until 26 y	Children aged 9-14 y, catch-up until 26 y	Enhanced vaccination schedule (3 injections, months 0, 2, 6)
Tetanus, diphtheria, pertussis	All patients, every 5-10 y	All patients, every 5-10 y	Single-injection combination vaccine

Vaccination in CKD

- Hepatitis B vaccination is recommended for pre-end-stage renal disease patients before they become dialysis dependent.
- Assess antibody titer to hepB surface antigen(anti-HBs). First titer should be done 1–2 months after the primary course is completed and annually thereafter.
- Booster dose should be given if anti-HBs titer falls below 10 mU/ml
- Revaccination with full doses is recommended for persons who do not develop protective antibody titer after primary course.
- Higher vaccine dosages or an increased number of doses are recommended for subjects with CKD (eGFR < 30).
- If an adult patient begins the vaccine series with a standard dose before beginning hemodialysis treatment, then moves to hemodialysis treatment before completing the series, complete the series using the higher dose recommended for hemodialysis patients.

CKD and Diabetes

CKD and Diabetes

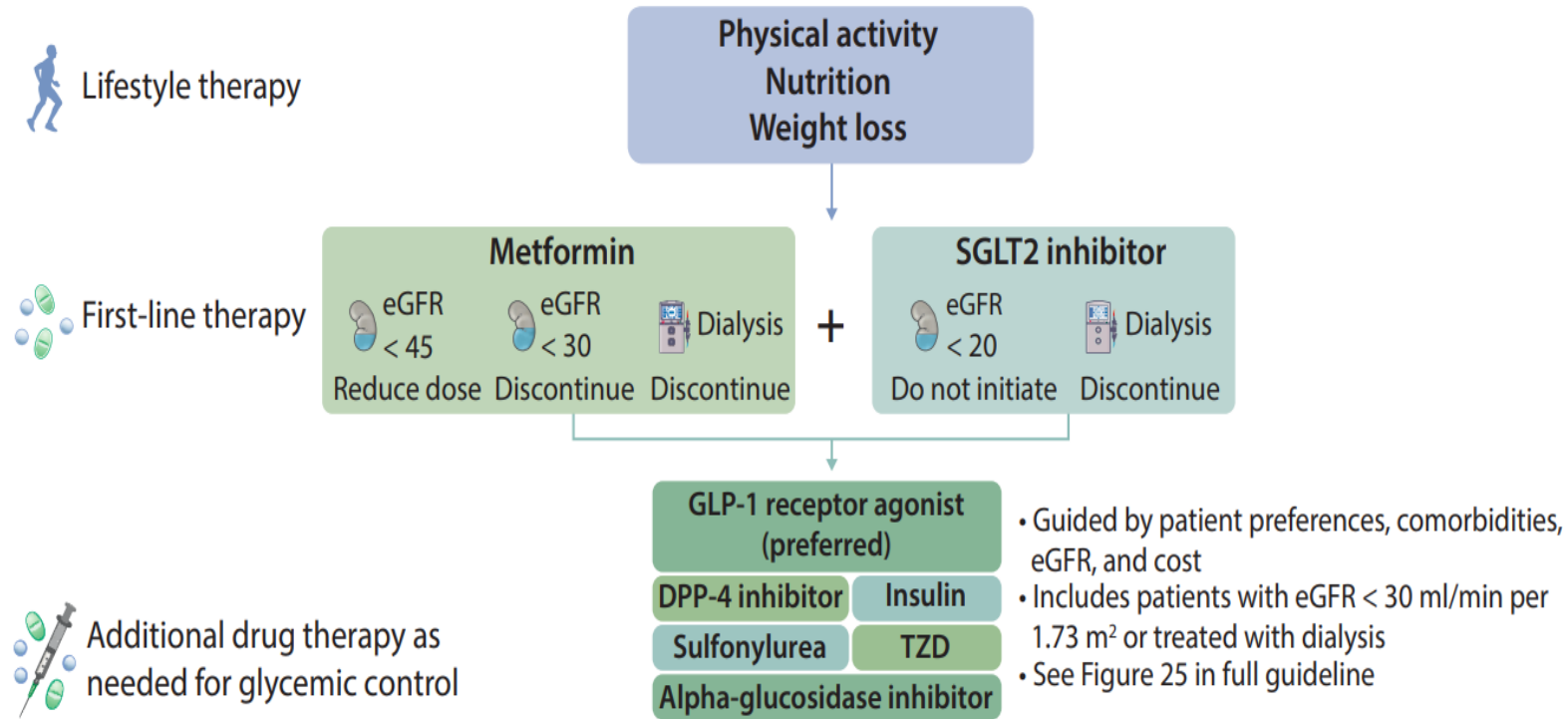


Figure 2 | Treatment algorithm for selecting glucose-lowering drugs for patients with type 2 diabetes (T2D) and chronic kidney disease (CKD). Kidney icon indicates estimated glomerular filtration rate (eGFR; ml/min per 1.73 m²); dialysis machine icon indicates dialysis. DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; SGLT2, sodium-glucose cotransporter-2; TZD, thiazolidinedione.

CKD and Diabetes

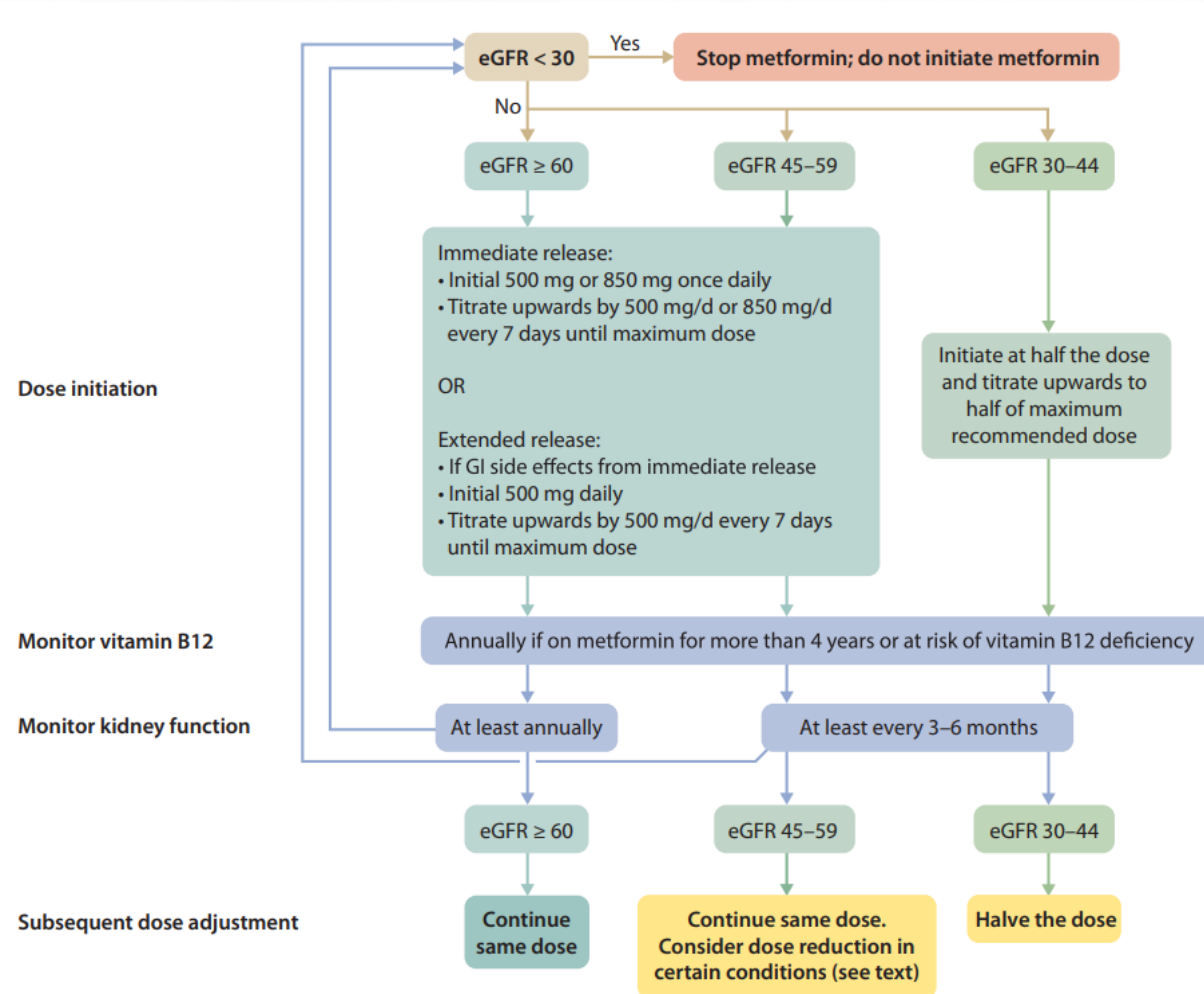


Figure 27 | Suggested approach in dosing metformin based on the level of kidney function. eGFR, estimated glomerular filtration rate (in ml/min per 1.73 m²); GI, gastrointestinal.

CKD and Diabetes

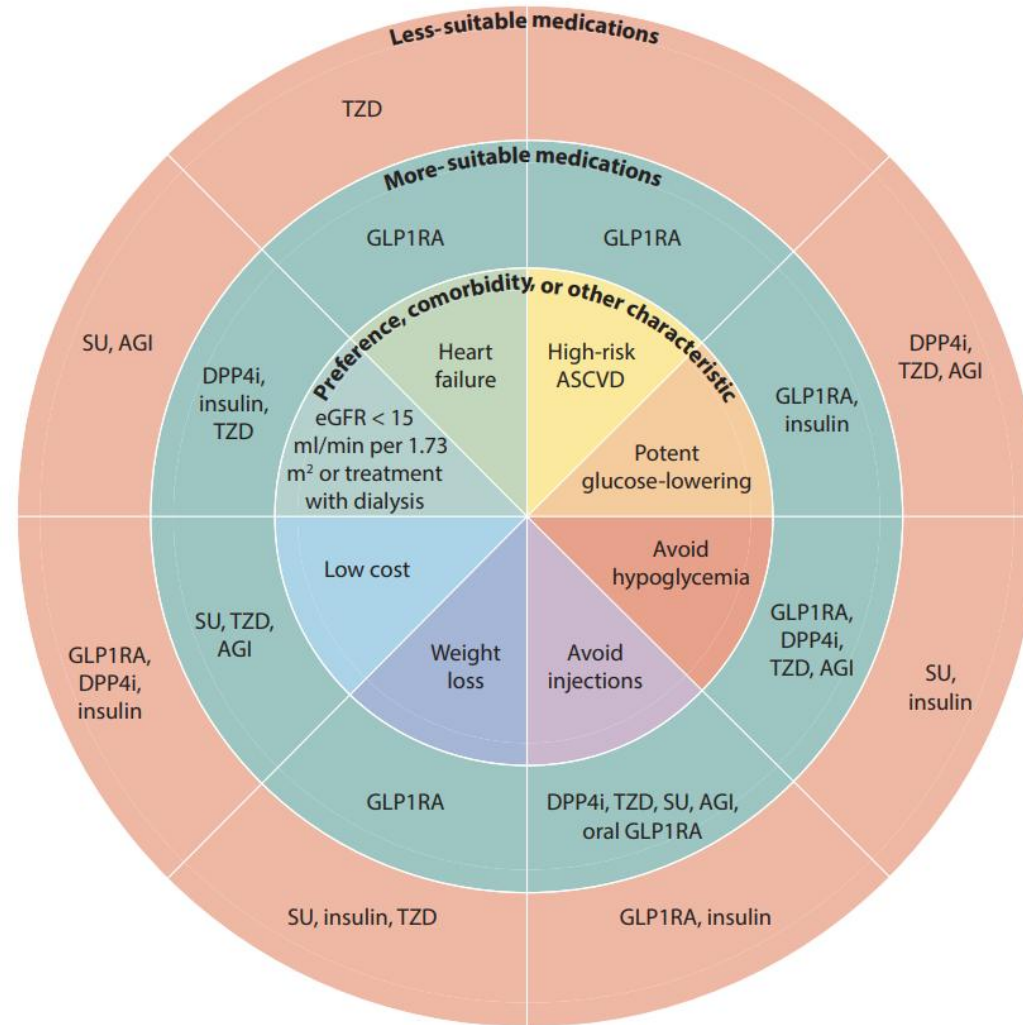


Figure 25 | Patient factors influencing the selection of glucose-lowering drugs other than sodium-glucose cotransporter-2 inhibitor (SGLT2i) and metformin in type 2 diabetes (T2D) and chronic kidney disease (CKD). AGI, alpha-glucosidase inhibitor; ASCVD, atherosclerotic cardiovascular disease; DPP4i, dipeptidyl peptidase-4 inhibitor; eGFR, estimated glomerular filtration rate; GLP1RA, glucagon-like peptide-1 receptor agonist; SU, sulfonylurea; TZD, thiazolidinedione.

CKD and Diabetes

Drug Class	Drug	eGFR ≥60	45–59	30–44	15–29	<15 or Dialysis
Biguanide	Metformin	Full dose (≤2000 mg/day)	Continue; monitor renal function	Max 1000 mg/day; do not initiate if eGFR <45	Contraindicated / discontinue	Contraindicated
Sulfonylurea	Glipizide	No adjustment	No adjustment	No adjustment	Start low (2.5 mg/day)	Preferred SU in dialysis (low dose)
	Gliclazide (MR)	No adjustment	No adjustment	Use lower dose	Avoid if eGFR <15	Avoid
	Glimepiride	No adjustment	Reduce dose	Low starting dose	Avoid if possible	Avoid
	Glyburide (Glibenclamide)	Avoid in CKD	Avoid	Avoid	Contraindicated	Contraindicated
Meglitinide	Repaglinide	No adjustment	No adjustment	Start 0.5 mg before meals	Low-dose acceptable	Can be used cautiously
	Nateglinide	No adjustment	Caution	Reduce dose	Avoid	Avoid

CKD and Diabetes

Drug Class	Drug	eGFR ≥60	45–59	30–44	15–29	<15 or Dialysis
TZD	Pioglitazone	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment
DPP-4 inhibitor	Sitagliptin	100 mg/day	100 mg/day	50 mg/day	25 mg/day	25 mg/day
	Linagliptin	5 mg/day	No adjustment	No adjustment	No adjustment	No adjustment
SGLT2 inhibitor	Empagliflozin	10–25 mg/day	Continue	Continue	Continue if already indicated for CKD/HF	Not recommended on dialysis
	Dapagliflozin	10 mg/day	Continue	Continue	Continue	Not recommended in dialysis
	Canagliflozin	100–300 mg/day	Usually 100 mg/day	100 mg/day	May continue for CKD indication	Not recommended
α-Glucosidase inhibitor	Acarbose	No adjustment	No adjustment	Avoid if Cr >2 mg/dL / eGFR <25	Contraindicated	Contraindicated
	Miglitol	No adjustment	No adjustment	Contraindicated	Contraindicated	Contraindicated

CKD and Diabetes

Drug	eGFR ≥60	45–59	30–44	15–29	<15 / Dialysis
Semaglutide (Ozempic® SC)	No adjustment	No adjustment	No adjustment	No adjustment	Limited data; generally not recommended in dialysis
Liraglutide (Victoza®)	No adjustment	No adjustment	No adjustment	No adjustment	Limited experience in ESRD
Tirzepatide (Mounjaro®)	No adjustment	No adjustment	No adjustment	No adjustment	Limited data in dialysis

ممنون از توجه شما

