

BMJ Best Practice

Chronic kidney disease

Straight to the point of care



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Summary

Chronic kidney disease (CKD) is a common condition that is often unrecognised until the most advanced stages.

Diagnosis is determined only by laboratory studies: proteinuria or haematuria, and/or a reduction in the glomerular filtration rate, for more than 3 months' duration.

The most common causes are diabetes mellitus and hypertension.

Glycaemic control for diabetic kidney disease and optimisation of blood pressures are key in slowing the progression of the disease. Use of agents that block the renin-angiotensin system and sodium-glucose co-transporter-2 (SGLT2) inhibitors have kidney function preserving benefits that are independent of blood pressure and glucose control.

CKD is a risk factor for cardiovascular disease, independent of comorbidities such as diabetes, hypertension, and dyslipidaemia.

Definition

Chronic kidney disease (CKD), also known as chronic renal failure, is defined as abnormalities of kidney structure or function, present for ≥ 3 months, with implications for health.^[1] This means a glomerular filtration rate less than 60 mL/minute/1.73 m², or the presence of one or more of the following markers of kidney damage: albuminuria/proteinuria, urine sediment abnormalities (e.g., haematuria), electrolyte abnormalities due to tubular disorders, abnormalities detected by histology, structural abnormalities detected by imaging, or history of kidney transplantation.^[1]

[BMJ talk medicine: chronic kidney disease] (<https://soundcloud.com/bmjpodcasts/chronic-kidney-disease?in=bmjpodcasts/sets/bmj-best-practice-clinical>)

Epidemiology

Chronic kidney disease (CKD) is a common condition that is often unrecognised until the most advanced stages. It is estimated that 9% to 13% of the adult population worldwide has CKD.[3] [4] [5] In 2017, the estimated worldwide prevalence of CKD stages 1 to 2 accounted for 5%, stage 3 for 3.9%, stage 4 for 0.16%, stage 5 for 0.07%, dialysis for 0.041%, and kidney transplantation for 0.011%.[5] The global prevalence of CKD is rising and is thought to be due to an ageing population; a higher incidence of diseases such as diabetes and hypertension, which are the most common causes in the adult population; and an increased incidence of glomerular disorders such as focal segmental glomerulosclerosis.[4] [6] [7] Black people, Hispanic people, and those with a family member who has a diagnosis of kidney disease have a higher prevalence than the general population.[8] [9] Additionally, individuals with an episode of acute kidney injury are most likely to be at risk for chronic kidney injury and end-stage kidney disease in the future.[10]

CKD is a condition associated with high racial and socioeconomic disparities. In 2016, the age-standardised incidence of end-stage renal disease was almost threefold higher among black people compared with white people in the US, whereas data from the ACCORD study revealed that race was not associated with accelerated development and progression of CKD in participants who received standardised medical care.[11] The results suggest that equitable health care delivery for patients with diabetes may reduce racial disparities in diabetes-associated CKD.

Aetiology

The most common cause in the adult population is diabetes.[6] It is estimated that one third of patients with diabetes will develop kidney disease, as defined by albuminuria and/or a reduction in the glomerular filtration rate within 15 years after the diagnosis of diabetes.[12] [13]

Hypertension is the second most common cause.[6] The interaction between hypertension and CKD is complex, with hypertension a cause and a consequence of CKD.[14]

Often people are given the diagnosis of hypertensive renal disease if no other identifiable aetiology is evident.

Less frequent causes include cystic disorders of the kidney (polycystic kidney disease), obstructive uropathy, glomerular nephrotic and nephritic syndromes such as focal segmental glomerulosclerosis, membranous nephropathy, lupus nephritis, amyloidosis, and rapidly progressive glomerulonephritis.[1]

Around one third of adults with CKD have a positive family history of CKD, which suggests genetic causation.[15]

Climate also plays a significant role in some CKD presentations.[16] Heat stress nephropathy may represent one of the first epidemics due to global warming. Various presentations in different parts of the world, such as Mesoamerican nephropathy, Sri Lankan nephropathy, and CKD of unknown origin (CKDu), may all be related to the climate.[17] The mechanisms implicated are hyperthermia, dehydration, and toxin and heavy metal concentration in drinking water and soil, in addition to worsening poverty with climate change leading to poor harvests.[16] [17]

Pathophysiology

The pathophysiology is complex. Regardless of the method of renal injury (i.e., diabetes, hypertension, or glomerular disorders), once renal damage has occurred, a cascade of events ensues.[18] [19]

- In response to renal injury, there is thought to be an increase in intra-glomerular pressure with glomerular hypertrophy, as the kidney attempts to adapt to nephron loss to maintain constant glomerular filtration.
- An increase in glomerular permeability to macro-molecules such as transforming growth factor-beta (TGF-beta), fatty acids, pro-inflammatory markers of oxidant stress, and protein may result in toxicity to the mesangial matrix, causing mesangial cell expansion, inflammation, fibrosis, and glomerular scarring.
- Additionally, renal injury results in an increase in angiotensin II production, causing an upregulation of TGF-beta, contributing to collagen synthesis and renal scarring within the glomerulus.
- Both the structural alterations and accompanying biochemical, cellular, and molecular changes seem to account for progressive renal scarring and loss of kidney function.
- All forms of CKD are also associated with tubulo-interstitial diseases; the exact mechanism of injury is not known, but is thought to be secondary to a reduction in blood supply in addition to an infiltration of lymphocytes and inflammatory mediators that result in interstitial fibrosis and tubular atrophy.

Classification

Kidney Disease: Improving Global Outcomes (KDIGO) classification[1]

KDIGO classifies CKD based on cause (C), glomerular filtration rate category (G), and albuminuria category (A).

- Cause is ascertained from history (e.g., diabetic kidney disease, hypertensive nephrosclerosis).
- Glomerular filtration rate (GFR) category is based on GFR (mL/minute/1.73 m²):
 - G1 GFR ≥90: normal or high
 - G2 GFR 60 to 89: mildly decreased
 - G3a GFR 45 to 59: mildly to moderately decreased
 - G3b GFR 30 to 44: moderately to severely decreased
 - G4 GFR 15 to 29: severely decreased
 - G5 GFR <15: kidney failure.
- Albuminuria category is based on albumin excretion rate (AER) or albumin to creatinine ratio (ACR):
 - A1 AER <30 mg albumin/24 hours or ACR <3 mg/mmol (<30 mg/g): normal to mildly increased
 - A2 AER 30 to 300 mg albumin/24 hours or ACR of 3 to 30 mg/mmol (30 to 300 mg/g): moderately increased
 - A3 AER >300 mg albumin/24 hours or ACR >30 mg/mmol (>300 mg/g): severely increased.

There is substantial existing literature using the term microalbuminuria; however, the KDIGO work group encourages the adoption of the term 'albuminuria', with subsequent quantification of the level or amount.[1]

A urine ACR >220 mg/mmol (>2200 mg/g) may be accompanied by signs and symptoms of nephrotic syndrome (e.g., low serum albumin, oedema, and high serum cholesterol).[1]

However, nephrotic level proteinuria is conventionally defined as >3.5 g proteinuria per 24 hours.[2]

Case history

Case history #1

A 54-year-old man with a 10-year history of diabetes and hypertension, with complications of diabetic retinopathy and peripheral neuropathy, presents to his primary care physician with complaints of fatigue and weight gain of 4.5 kg over the past 3 months. He denies any changes in his diet or glycaemic control but does state that he has some intermittent nausea and anorexia. He states that he has noticed that his legs are more swollen at the end of the day but improve with elevation and rest. Physical examination reveals an obese man with a sitting blood pressure of 158/92 mmHg. The only pertinent physical examination findings are cotton wool patches and micro-aneurysms bilaterally on fundoscopic examination and pitting, bilateral lower-extremity oedema.

Other presentations

Chronic kidney disease presents insidiously over months with vague complaints of fatigue, mild reduction in appetite, and, at more advanced stages, nausea and anorexia. Oedema is a common presentation - as the glomerular filtration rate declines, there is an inability to effectively excrete salt and water to remain in metabolic balance with dietary intake. Additionally, proteinuria with a decrease in serum albumin may contribute to the development of peripheral oedema.^[3]

Approach

It is important to note that a significant proportion of people are asymptomatic, and the diagnosis relies on pathological evidence of kidney damage such as haematuria and/or proteinuria, or laboratory evidence of a reduction in the glomerular filtration rate (GFR) with an elevated serum creatinine.

History

Signs and symptoms are often vague, including fatigue (which may be related to uraemia or the anaemia associated with CKD), nausea, and possibly the development of oedema. Uraemic illness is due largely to the accumulation of organic waste products that are normally cleared by the kidneys, and symptoms may be present to some degree in the early stages of kidney failure.[44] As kidney failure progresses to the more advanced stages of uraemia, patients will often describe anorexia, nausea, vomiting, restless legs, pruritus, and overall not feeling well.[45] If patients begin to have a lack of urine production, then the resulting fluid overload may be present with dyspnoea and orthopnoea due to pulmonary oedema. Cognition may be affected in all stages of CKD.[3] In the most advanced stages of uraemia, patients may present with seizures or coma.[46]

Examination

Signs as a consequence of CKD are hypertension, peripheral oedema (due to sodium retention and exacerbated by hypoalbuminaemia), and pallor due to anaemia.[3] Physical examination findings are also directed towards the discovery of end-organ damage associated with causative disease states such as diabetes or hypertension, which cause CKD. A fundoscopic eye examination is critical for the diagnosis of diabetic or hypertensive retinopathy as evidence of microvascular damage that has probably occurred in the kidney, resulting in CKD. In men, a rectal examination for prostatic enlargement or for the diagnosis of prostate nodules can be helpful in determining a diagnosis of obstructive uropathy. In glomerular nephrotic and nephritic syndromes, the signs and symptoms of CKD may present more acutely with accelerated hypertension, peri-orbital and peripheral oedema, rashes, or arthritis on musculoskeletal examination for patients with autoimmune disorders.[47] Patients may describe their urine as foamy if significant proteinuria is present, or tea- or cola-coloured in the setting of haematuria.

Initial investigations

Most people are unaware that they have CKD and are informed only after abnormalities are discovered by blood and/or urine tests.[3] The first diagnostic tests to order are a serum creatinine (as part of renal chemistry), estimated GFR (with consideration of serum cystatin-C in people with extremes of muscle mass), and urinalysis to assess for haematuria and proteinuria.[1] [3] Laboratories should estimate GFR using an equation without a race variable.[48] [49] [50] [National Kidney Foundation: eGFR calculator] (https://www.kidney.org/professionals/gfr_calculator)

For the diagnosis of CKD, urinary albumin assessment is usually preferred to that of total urine protein with calculation of the albumin excretion rate (AER) or the albumin to creatinine ratio (ACR).[1] [50] However, nephrotic level proteinuria is conventionally defined as >3.5 g proteinuria per 24 hours.[2]

Proteinuria is both a diagnostic and a prognostic variable in the evaluation of patients with CKD.[3] [51]

Renal ultrasound is required to evaluate kidney size, mass lesions, urinary tract obstruction, and, with a duplex examination, renal arterial flow.[3] [52]

Additional investigations

Kidney biopsies are performed in a minority of patients with CKD.[1] A kidney biopsy to determine a pathological diagnosis is indicated if a glomerular nephrotic or nephritic syndrome is suspected, or in people with diabetes with atypical presentations such as rapidly progressive kidney failure. Nephrotic syndrome may be suggested by proteinuria, and both nephritic and nephrotic syndromes may be suggested by severe presenting symptoms (accelerated hypertension, periorbital and peripheral oedema) or with symptoms of underlying autoimmune diseases (rashes or arthritis). Certain infections, such as hepatitis B and C, syphilis, and streptococcal pharyngitis are associated with glomerular disorders. A kidney biopsy is critical in these cases to determine the correct diagnosis.[2]

Imaging of the genitourinary tract may be helpful in the evaluation of a patient with CKD. Plain abdominal x-ray is a non-specific test that may aid in the detection of calcium-containing kidney stones. Other radiological tests, such as an abdominal computed tomography, are reserved for evaluation of stone disease and further characterisation of renal cystic or mass lesions. Magnetic resonance imaging is reserved for renal mass lesions such as renal cell carcinoma.

History and exam

Key diagnostic factors

presence of risk factors (common)

- Risk factors include age >50 years, male sex, black or Hispanic ethnicity, family history, smoking, obesity, long-term analgesic use, diabetes, hypertension, and autoimmune disorders.

fatigue (common)

- Signs and symptoms of CKD are often vague and commonly include fatigue, which may be due to uraemia or anaemia.[44] Anaemia is associated with CKD due to the lack of erythropoietin produced by the kidney, usually once the glomerular filtration rate declines to <50 mL/minute/1.73 m². [3] There can also be other deficiency anaemias (e.g., iron) that manifest during the assessment of CKD.

oedema (common)

- Periorbital and peripheral oedema develop as a result of salt and water retention as the glomerular filtration rate declines, and may be exacerbated by hypoalbuminaemia.[3]

nausea with/without vomiting (common)

- Thought to be due to an accumulation of toxic waste products in the circulation, such as urea that is not excreted by the kidney. As kidney failure progresses to the more advanced stages of uraemia, patients may report vomiting. They may also report a metallic taste in the mouth further worsening the nausea.

pruritus (common)

- Thought to be due to an accumulation of toxic waste products in the circulation and under the skin, such as urea that is not excreted by the kidney.[44]

restless legs (common)

- A symptom of uraemia.^[44] Present in all stages of CKD.^[54]

anorexia (common)

- Thought to be due to an accumulation of toxic waste products in the circulation, such as urea that is not excreted by the kidney.

infection-related glomerular disease (uncommon)

- Infections such as hepatitis B and C, syphilis, and streptococcal pharyngitis are associated with glomerular disorders.
- A kidney biopsy is critical in these cases to determine the correct diagnosis.^[2]

Other diagnostic factors**arthralgia (common)**

- If the patient has concomitant autoimmune disorder.

enlarged prostate gland (common)

- Prostate examination in men should be performed to exclude obstructive uropathy.

foamy-appearing urine (uncommon)

- Indicative of proteinuria.

cola-coloured urine (uncommon)

- Indicative of haematuria.

rashes (uncommon)

- Ecchymosis and purpura are signs of haematological consequences of CKD.
- The patient may have a concomitant autoimmune disorder: for example, systemic lupus erythematosus and butterfly rash.

dyspnoea (uncommon)

- Associated with pulmonary oedema due to reduced urine output in worsening disease.

orthopnoea (uncommon)

- Associated with pulmonary oedema due to reduced urine output in worsening disease.

seizures (uncommon)

- Occurs in advanced-stage disease.^[46]
- Thought to be due to an increase in neurotoxins that are not excreted by the kidney.

retinopathy (uncommon)

- Fundoscopy is a key examination in determining the presence of diabetic or hypertensive retinopathy, as evidence of microvascular damage, which occurs in uncontrolled diabetes/hypertension. Diabetic and hypertensive patients should be screened for such changes.

Risk factors

Strong

diabetes mellitus

- This is the most common cause.[\[6\]](#)
- It is estimated that approximately 20% to 40% of people with diabetes will have CKD, as documented by albuminuria and/or a reduction in the glomerular filtration rate, within 15 years of diagnosis.[\[12\]](#) [\[13\]](#) CKD rarely develops in patients with type 1 diabetes before 10 years following diagnosis, whereas CKD is present at time of diagnosis in around 3% of patients with type 2 diabetes.[\[13\]](#)
- Glycaemic control directly correlates with the development of diabetic kidney disease and the rapidity of progression to end-stage renal disease.[\[12\]](#)
- Hyperglycaemia results in formation of advanced glycated end products.[\[20\]](#) This leads to mesangial oxidative stress, which results in matrix expansion and increased vascular permeability, which in turn attracts inflammatory mediators.[\[21\]](#) These promote collagen production, leading to glomerular sclerosis.

hypertension

- This is the second most common cause of CKD.[\[6\]](#)
- Hypertension is also a consequence of CKD (including from other causes such as diabetic kidney disease, and glomerular nephrotic and nephritic syndrome), and contributes to its progression to end-stage renal disease.[\[14\]](#)
- Hypertension is thought to affect both the vasculature and tubulo-interstitial components of the kidney, resulting in ischaemic damage from arterial narrowing. The end result is loss of nephron mass, and atrophy and fibrosis of the tubules and interstitium.

age >50 years

- Older age is a key predictor of CKD. Healthy ageing is associated with structural changes in the kidney and a decrease in glomerular filtration rate (GFR).[\[22\]](#) Typically the GFR declines by 0.75 mL/minute/1.73 m² per year in healthy ageing, but urine albumin excretion does not change, thus, the increase in the prevalence of criteria-defined CKD in healthy older adults is due more to a GFR decline than to increasing albuminuria and has a much lower risk of progression to end-stage renal disease.[\[22\]](#) However, increasing age is associated with an increased likelihood of comorbid conditions that are risk factors for CKD, such as diabetes, hypertension, and cardiovascular disease.[\[23\]](#)

childhood kidney disease

- A history of childhood kidney disease is a risk factor for adult CKD and end-stage renal disease (ESRD). Children with a medical history of congenital anomalies, glomerular disease, or pyelonephritis with normal kidney function and blood pressure have a four-fold increased risk for ESRD as compared to children without kidney disease.[\[24\]](#)

Weak

smoking

- Smoking has been associated as a risk factor for the development and progression of the disease, probably because of accelerated atherosclerosis and vascular disease, as well as exacerbating underlying hypertension.[\[25\]](#) [\[26\]](#)

obesity

- Obesity is an associated risk factor.[27] It may contribute to the development of diabetes, exacerbate poor control of hypertension, contribute to renal ischaemia and hypertension with associated sleep apnoea, and cause glomerular strain with hypertrophy and glomerulosclerosis.[28]

black or Hispanic ethnicity

- Black or Hispanic people are at higher risk than white people.[29] [30] The mechanism is not known, but is thought to be due in part to a higher incidence of diseases such as diabetes and hypertension in these populations. Additionally, in black and Hispanic populations, genetic factors such as apolipoprotein L1 risk variants increase the risk for non-diabetic kidney disease.[31]

family history of CKD

- People with a close family member with the disease are at a higher risk themselves of developing CKD.[9] [15] The mechanism is thought to be due in part to genetic susceptibility to certain disease states, such as diabetes, hypertension, polycystic kidney disease, Alport syndrome, and possibly glomerular syndromes, such as IgA nephropathy and focal segmental glomerulosclerosis.

autoimmune disorders

- Autoimmune disorders such as systemic lupus erythematosus, rheumatoid arthritis, sarcoidosis, and Sjogren syndrome may cause glomerular or tubulo-interstitial CKD.[32] [33]

male sex

- Men are at a higher risk of CKD progression than women.[34]
- The mechanism of renal injury is not known but is thought to be related to differences in sex hormones and the differential effect of sex on lifestyle and traditional risk factors.[34]

long-term use of non-steroidal anti-inflammatory drugs

- Long-term use of anti-inflammatory analgesics for rheumatological disorders and pain control have been associated with the development of CKD.[35] [36] Non-steroidal anti-inflammatory drugs, and previously phenacetin, have been described as causing analgesic nephropathy.

high uric acid levels

- There is an expected increase in uric acid levels with advancing CKD. Literature also discusses uric acid as a contributory factor to CKD worsening.[37] [38] [39] However, trials of urate-lowering treatment did not result in clinically meaningful benefits to kidney outcomes.[40] [41]

Investigations

1st test to order

Test	Result
renal chemistry - Includes sodium, potassium, chloride, bicarbonate, urea, creatinine, and glucose. - Serum creatinine alone is insufficient to determine CKD and may be falsely low in conditions of low muscle mass, as in older or malnourished people, or patients with liver failure. - Normal creatinine in men is 70 to 120 micromol/L (0.8 to 1.4 mg/dL), and in women 50 to 97 micromol/L (0.6 to 1.1 mg/dL). However, there is significant variation due to calibration methods between laboratories.[3] - Electrolyte abnormalities may indicate an underlying cause of CKD, such as tubular disorders.[1] Adaptations in acid excretion by the kidneys initially prevent a fall in serum bicarbonate concentration, but as GFR declines, metabolic acidosis develops.[1]	elevated serum creatinine; electrolyte abnormalities
estimation of GFR - A GFR estimating equation using serum creatinine is recommended for initial assessment. - Determines more accurately, by mathematical equations such as the CKD EPI equation, the GFR and the severity and stage of CKD.[55] - Laboratories should estimate GFR using an equation without a race variable.[48] [49] [50] [National Kidney Foundation: eGFR calculator] (https://www.kidney.org/professionals/gfr_calculator) - Formulas have not been proven to be reliable estimators in patients with a GFR >59 mL/minute/1.73 m². [1]	<60 mL/minute/1.73 m²
serum cystatin C and cystatin C-based estimation of GFR - Warranted in specific circumstances when GFR estimates based on serum creatinine are thought to be inaccurate, such as in people with extremes of muscle mass (e.g., bodybuilders, people with muscle-wasting disorders, older or malnourished people).[1] - Laboratories should estimate GFR using an equation without a race variable.[48] [49] [50] [National Kidney Foundation: eGFR calculator] (https://www.kidney.org/professionals/gfr_calculator)	reduced muscle mass will lead to overestimation; increased muscle mass to underestimation of the GFR
urinalysis Screening test to determine for pathological markers of kidney damage excreted in the urine.	haematuria and/or proteinuria
urinary albumin Classification of CKD requires quantification of urinary albumin as based on albumin excretion rate (AER) or albumin to creatinine ratio (ACR).[1] [50] Moderately increased albuminuria is a risk factor for the development of progressive CKD and coronary artery disease associated with diabetes and hypertension. Indicated in patients with diabetes and CKD if there was no evidence of proteinuria on urine dipstick.[56]	moderately increased (AER 30-300 mg/day; ACR 30-300 mg/g)

Test	Result
renal ultrasound - Helps to diagnose CKD if kidney atrophy is present. - Can help to diagnose obstruction with hydronephrosis or bladder retention.^[3] ^[52]	small kidney size; presence of obstruction/hydronephrosis; kidney stones

Other tests to consider

Test	Result
kidney biopsy Helps to determine pathological diagnosis of CKD in glomerular nephrotic and nephritic syndromes, and in people with diabetes with atypical presentations such as rapidly progressive kidney failure. Also essential in determining whether pathological lesions are due to infection (e.g., hepatitis B and C, syphilis, and streptococcal pharyngitis). Provides insight into treatment options based on severity or chronicity of scarring of glomeruli and interstitium.	variable depending on aetiology
plain abdominal radiograph Non-specific test that may aid in the detection of calcium-containing kidney stones, as medicine and urate stones are not apparent on plain radiography.	may reveal calcium-containing kidney stones
abdominal CT Imaging test that is helpful to determine the presence or absence of kidney stones and confirms obstructive component. It is also helpful to further evaluate cystic lesions or mass lesions in the kidney. Intravenous contrast is used with caution in high-risk patients, such as those with CKD with a reduction in the estimated GFR <60 mL/minute, as it can cause acute kidney injury. Prophylaxis with intravenous normal saline may be indicated or considered in some patients.^[57]	may reveal kidney stones, renal masses, or cysts
abdominal MRI - Imaging test that further characterises mass lesions in the kidney, such as renal cell carcinoma. - Gadolinium-based MRI examinations have been associated with nephrogenic systemic fibrosis in patients with kidney disease. However, not all gadolinium-containing contrast agents have the same risk of nephrogenic systemic fibrosis, and the benefits of gadolinium-based MRI use may exceed its risk.^[58]	may reveal mass lesions in the kidney

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Diabetic kidney disease	History of poorly controlled diabetes for about 10 years. Often with co-existing diabetic retinopathy and other stigmata of diabetic microvascular disease.	- HbA1c is typically >53 mmol/mol (>7%). - Diagnostic tests include urinalysis for albuminuria and a serum creatinine for GFR assessment. - The quantification of proteinuria is variable over time and will decrease as the GFR declines. - Urine albumin is key for the diagnosis of early diabetic kidney disease. - Kidney ultrasound will typically show small, atrophic kidneys only in late stages of the disease, once substantial renal injury occurs.
Hypertensive nephrosclerosis	History of poorly controlled hypertension for years. More common in black people than white people.	- Diagnostic tests include urinalysis for microalbumin or protein and a serum creatinine for GFR assessment. - The urine sediment is described as bland without formed elements or haematuria. Quantification of proteinuria is <2 g/24 hours. - Kidney ultrasound typically reveals small, atrophic kidneys.
Ischaemic nephropathy	- History of long-standing essential hypertension that is suddenly uncontrolled. More common in white people and older people. - Often will have a history of atherosclerotic disease such as coronary artery disease or peripheral vascular disease. There is also a history of tobacco abuse and hyperlipidaemia.	- The urine sediment is described as bland, without formed elements or haematuria. Quantification of proteinuria is <2 g/24 hours. - Kidney ultrasound reveals asymmetrical kidney size of ≥ 2.5 cm with unilateral disease, and duplex scan demonstrates an increase in the resistive index, suggesting obstruction. - ACE inhibitor renogram, CT angiogram, magnetic resonance angiogram, or renal arteriogram (test of choice) demonstrates luminal narrowing of the renal artery.

Condition	Differentiating signs / symptoms	Differentiating tests
Obstructive uropathy	• More common in men and older people. Often due to prostatic enlargement or cancer. • Typical symptoms include urinary frequency, hesitancy, inability to empty the bladder completely, and decrease in urinary stream. • Urinary tract infections may develop. • Rectal examination may reveal prostatic enlargement or nodules.	• Kidney ultrasound is the diagnostic test of choice to document kidney obstruction. It would show hydronephrosis, and there may also be post-void residual volume in those cases when there is obstruction to bladder outflow.
Nephrotic syndrome	• Often associated with a more sudden onset of hypertension, or acceleration of essential hypertension and development of periorbital and peripheral oedema.	• Laboratory evidence may reveal hypoalbuminaemia, hyperlipidaemia and an increase in serum creatinine. Urinalysis has proteinuria as defined at >3.5 g/24 hours. • A kidney biopsy is required to determine the pathological lesion for nephrotic syndrome. • Serological tests for secondary causes of nephrotic syndrome such as anti-nuclear antibody in systemic lupus erythematosus, HIV in focal segmental glomerulosclerosis, and hepatitis B and C in membranous nephropathy, and serum protein electrophoresis for amyloidosis, are often helpful in confirming the diagnosis of the nephrotic syndrome.
Glomerulonephritis	• Often associated with a sudden onset of hypertension or acceleration of essential hypertension. • Patients with autoimmune disorders may have a skin rash or arthritis; post-infectious glomerulonephritis has a recent history of a pharyngeal or cutaneous infection; bloody diarrhoea is associated with haemolytic uraemic syndrome.	• Laboratory evidence reveals an increased serum creatinine, and urinalysis is significant for haematuria and proteinuria. • Urine sediment is evaluated for the presence of dysmorphic red blood cells (RBC) and RBC casts, which are diagnostic of glomerulonephritis. • Serological tests such as antinuclear antibody, complement levels, hepatitis

Condition	Differentiating signs / symptoms	Differentiating tests
		B and C antibodies, anti-neutrophil cytoplasmic antibody, anti-glomerular basement antibody, and anti-streptolysin O titre are often helpful in confirming the diagnosis of glomerulonephritis. A kidney biopsy is required to confirm the pathological lesion of glomerulonephritis.

Criteria

Diagnostic classification^[1]

CKD is divided into 6 distinct categories based on glomerular filtration rate (GFR). The GFR category (G1-G5) has the same GFR thresholds as the CKD stages 1 to 5 recommended previously, as follows:^[1]

- G1: GFR >90 mL/minute/1.73 m², and evidence of kidney damage based on pathological diagnosis, abnormalities of radiographic imaging, or laboratory findings such as haematuria and/or proteinuria
- G2 GFR 60 to 89: mL/minute/1.73 m²
- G3a GFR 45 to 59: mL/minute/1.73 m²
- G3b GFR 30 to 44: mL/minute/1.73 m²
- G4 GFR 15 to 29: mL/minute/1.73 m²
- G5 GFR <15 : mL/minute/1.73 m².

The albumin category is also documented based on albumin excretion rate (AER) or albumin to creatinine ratio (ACR):

- A1 AER <30 mg albumin/24 hours or ACR <3 mg/mmol (<30 mg/g): normal to mildly increased
- A2 AER 30 to 300 mg albumin/24 hours or ACR of 3 to 30 mg/mmol (30 to 300 mg/g): moderately increased
- A3 AER >300 mg albumin/24 hours or ACR >30 mg/mmol (>300 mg/g): severely increased.

Screening

There are no established screening guidelines for the general population for CKD; screening for CKD is controversial. However, early identification of CKD in people at risk is likely to be beneficial if it is combined with risk stratification and treatment to delay progression and reduce cardiovascular risk.^{[59] [60]}

Based on expert consensus emerging from a Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference, the following recommendations were developed for CKD screening and risk stratification for people considered high-risk:^[59]

- Screening is recommended in people with hypertension, diabetes, or cardiovascular disease.
- Screening should be considered for people with other risk factors (e.g., older age, high-risk race/ethnicity, systemic diseases that impact kidneys, family history of kidney disease, genetic risk factors,

poor access to health care or low socioeconomic status, high-risk occupations and environmental exposures, prior acute kidney injury, preeclampsia, exposure to nephrotoxins, and obesity).

- Decisions about starting and frequency of CKD screening should be individualised based on kidney and cardiovascular risk profiles and individual preferences.
- Screening should include estimated glomerular filtration rate (eGFR; creatinine and cystatin C, if available) and measurement of albuminuria (urine albumin-to-creatinine ratio).

The American Diabetes Association recommends assessing eGFR and albuminuria at least annually in people with type 1 diabetes of ≥ 5 years duration and all people with type 2 diabetes regardless of treatment.^[61]

The UK National Institute for Health and Care Excellence (NICE) recommends annual monitoring for patients taking drugs that can adversely affect kidney function (e.g., calcineurin inhibitors, lithium, chronic use of nonsteroidal anti-inflammatory drugs [NSAIDs]).^[50]

Approach

All aetiologies of CKD are progressive. The main goal of treatment is to slow the progressive loss of kidney function and prevent the need for renal replacement therapy or kidney transplantation.

It is important to identify patients early in the course of their disease and classify the stage of CKD (GFR category G1-G5) so that risk factor modification can ensue and identification of comorbidities such as anaemia and secondary hyperparathyroidism may be treated.

CKD is divided into 6 distinct categories based on glomerular filtration rate (GFR). The GFR category (G1-G5) has the same GFR thresholds as the CKD stages 1 to 5 recommended previously:[1]

- G1: GFR >90 mL/minute/1.73 m², and evidence of kidney damage based on pathological diagnosis, abnormalities of radiographic imaging, or laboratory findings such as haematuria and/or proteinuria
- G2: GFR of 60 to 89 mL/minute/1.73 m²
- G3a: GFR of 45 to 59 mL/minute/1.73 m²
- G3b: GFR of 30 to 44 mL/minute/1.73 m²
- G4: GFR of 15 to 29 mL/minute/1.73 m²
- G5: GFR <15 mL/minute/1.73 m²

GFR category G1 to G4 first-line therapy

Several classes of agents have been shown to slow CKD progression. Renin-angiotensin system blockade (e.g., with an ACE inhibitor or an angiotensin-II receptor antagonist) and sodium-glucose co-transporter-2 (SGLT2) inhibitors (e.g., empagliflozin, canagliflozin, dapagliflozin) can preserve kidney function by reducing intra-glomerular pressure independently of blood pressure (BP) and glucose control. [62] [63] [64]

SGLT2 inhibitors are recommended for the treatment of CKD, particularly in adults at risk of progression, in combination with an ACE inhibitor or an angiotensin-II receptor antagonist. [BMJ Rapid Recommendation: SGLT2-inhibitors for adults with CKD] (<https://www.bmj.com/content/387/bmj-2024-080257>)

The major cause of death for patients with CKD is cardiovascular disease. Therefore, treatment of cardiovascular risk factors, such as optimising glycaemic control, optimising BP with an ACE inhibitor or an angiotensin-II receptor antagonist, introducing lipid-lowering agents (e.g., statins, ezetimibe), and reducing proteinuria is recommended.[61] [65] [66] [67]

Diabetes

- Glycaemic goals should be individualised. Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend a HbA1c target ranging from $<6.5\%$ to $<8.0\%$ for patients with diabetes and chronic kidney disease not receiving dialysis. A lower target (e.g., $<6.5\%$ or $<7.0\%$) may be appropriate for individuals in whom preventing complications is the key goal, whereas a higher target (e.g., $<7.5\%$ or $<8.0\%$) may be preferred in those with multimorbidity or increased burden of hypoglycaemia.[20] In patients with diabetes and CKD, there is a risk for hypoglycaemia because of impaired kidney clearance of drugs (such as insulin or sulfonylureas) and impaired kidney gluconeogenesis.
- Patients with type 1 diabetes require treatment with insulin, regardless of whether they are on dialysis or not.

- In patients with type 2 diabetes, some specific anti-hyperglycaemic drugs significantly reduce all-cause or cardiovascular mortality, or major cardiovascular events or renal complications in some patient subgroups, and should be considered independently of HbA1c targets.[68] [69] [70] [71] [72]
- There is evidence that the use of SGLT2 inhibitors prevents major kidney outcomes (e.g., dialysis, transplantation, or death due to kidney disease) in people with type 2 diabetes.[64] [73][74] SGLT2 inhibitors, in addition to reducing hyperglycaemia, have renal benefits through independent effects on renal tubular glucose reabsorption, weight, BP, intra-glomerular pressure, albuminuria, and slowed GFR loss.[75] [76]
- KDIGO guidelines advise that most patients with type 2 diabetes and CKD would benefit from treatment with metformin (if eGFR ≥ 30 mL/minute/1.73 m²) and an SGLT2 inhibitor (if eGFR ≥ 20 mL/minute/1.73 m²).[20] The American Diabetes Association recommends the use of SGLT2 inhibitors in patients with CKD and type 2 diabetes (if eGFR ≥ 20 mL/minute/1.73 m²), regardless of urinary albuminuria.[61] Use of SGLT2 inhibitors is not recommended in patients with end-stage renal disease (ESRD) who are on dialysis.[77]
- If additional glycaemic control is required for patients receiving metformin and an SGLT2 inhibitor, a drug from a different class should be selected. A glucagon-like peptide-1 (GLP-1) is the preferred option. If required, other agents (e.g., a dipeptidyl peptidase-4 [DPP-4] inhibitor, a sulfonyleurea, insulin, a thiazolidinedione, or an alpha-glucosidase inhibitor) may be considered based on eGFR, comorbidities, and patient preference.[20]
- As a class of drugs, GLP-1 agonists have beneficial effects on cardiovascular, mortality, and kidney outcomes in patients with type 2 diabetes.[78] [79] GLP-1 agonists may be considered for cardiovascular risk reduction.[61] Liraglutide, dulaglutide, and semaglutide are not renally excreted and are the preferred agents in this class.
- Studies report that DPP-4 inhibitors are renoprotective but do not have a cardiovascular benefit.[80] [81] Some DPP-4 inhibitors require dose adjustment in renal impairment.
- Finerenone, a non-steroidal mineralocorticoid receptor antagonist, reduces the progression of kidney disease in patients with type 2 diabetes mellitus and known CKD.[82] Finerenone is approved by the US Food and Drug Administration (FDA) to reduce the risk of kidney function decline, kidney failure, cardiovascular death, non-fatal heart attacks, and hospitalisation for heart failure in adults with CKD associated with type 2 diabetes. Guidelines recommend finerenone for patients with type 2 diabetes and albuminuria, despite maximum tolerated dose of an ACE inhibitor or an angiotensin-II receptor antagonist (if eGFR is ≥ 25 mL/minute/1.73 m² and serum potassium level is normal).[20] [61] Finerenone can be added to an SGLT2 inhibitor and an ACE inhibitor or an angiotensin-II receptor antagonist.

Hypertension

- Hypertension is one of the greatest risk factors for the progression of CKD, regardless of aetiology. Most patients with CKD will require at least two or three different types of antihypertensive agent to achieve the optimal BP control.
- There is ongoing debate on the optimal BP target for patients with CKD. The 2014 Joint National Committee 8 redefined the target BP goal for patients with CKD as $<140/90$ mmHg.[83] However, the 2017 American College of Cardiology/American Heart Association guideline recommends adults with hypertension and CKD should be treated to a BP goal of less than $130/80$ mmHg.[84] There may be benefit in strict BP control to reduce the relative risk of death, and delay the onset of ESRD in some subgroups of patients with CKD (age ≥ 40 years, BMI ≥ 30 kg/m²).[85] [86] The 2021 Kidney Disease: Improving Global Outcomes (KDIGO) guideline recommends a target systolic

BP of less than 120 mmHg, if tolerated, in patients with CKD, with and without diabetes, and not receiving dialysis.[62]

- A combination of antihypertensive agents should be used to meet the target BP goal. ACE inhibitors and angiotensin-II receptor antagonists should not be combined within the same regimen.[62]
- ACE inhibitors and angiotensin-II receptor antagonists have been shown in numerous clinical trials to slow the progression of CKD and delay the need for renal replacement therapy in both diabetic and non-diabetic CKD.[87] [88] [89] In one meta-analysis of patients with CKD, blockade of the renin angiotensin system with either ACE inhibitors or angiotensin-II receptor antagonists reduced the risk for kidney failure and cardiovascular events.[90] ACE inhibitors are also more likely to reduce the risk of death in people with CKD.[90]
- Other classes of antihypertensive agents (e.g., thiazide or thiazide-like diuretics, beta-blockers, dihydropyridine calcium-channel blockers, aldosterone antagonists, vasodilators, alpha-2 adrenergic agonists) should be added when the target BP is not achieved with the use of an ACE inhibitor or an angiotensin-II receptor antagonist, or if there are other specific clinical indications, such as beta-blockers for angina pectoris.[62]

Dyslipidaemia

- Common in patients with CKD.
- KDIGO guidelines recommend that CKD patients not on dialysis should start treatment with a statin without the need for routine follow-up to check lipid values, or to change dose regimen based on set targets (i.e., a 'treat and forget' approach).[65] For patients aged ≥ 50 years with CKD GFR category G3 or G4, ezetimibe can be combined with the statin simvastatin.[66]
- Statin therapy has been shown to have cardioprotective effects in patients with CKD.[91] [92] [93] [94] In those individuals not on dialysis, the use of statins in a large meta-analysis resulted in the reduction of all-cause mortality by 21% (relative risk [RR] 0.79, 95% CI 0.69 to 0.91) and cardiovascular mortality by 23% (RR 0.77, 95% CI 0.69 to 0.87).[95]
- One meta-analysis found that statin use in patients undergoing dialysis did not improve all-cause mortality or cardiovascular-related deaths.[96]

GFR category G1 to G4 intolerant to first-line therapy

If a patient is unable to tolerate either an ACE inhibitor or angiotensin-II receptor antagonist due to adverse effects, then an alternative is warranted. Non-dihydropyridine calcium-channel blockers have been demonstrated to have more proteinuric-lowering effects than other antihypertensive agents. Clinical trials in both diabetic and non-diabetic CKD have demonstrated greater protein-lowering effects than other classes of antihypertensive agents.[97]

GFR category G2

The directed therapy is to continue to modify cardiovascular risk factors, but also estimate the rate of loss of kidney function to determine the eventual need for renal replacement therapy (i.e., dialysis, transplant).

GFR category G3a/G3b

Education can play a significant role in delaying progression of CKD, as well as helping the patient understand his/her options if CKD progresses.[98] [99] [100] Most CKD-related complications occur during this stage of transition (GFR category G3a/G3b). Identification of comorbidities such as anaemia and secondary hyperparathyroidism is recommended, and treatment commenced if required.

Treatment of anaemia with the use of erythropoietin-stimulating agents is recommended for patients with CKD after other causes of anaemia such as iron, vitamin B12, folate, or blood loss have been excluded.^[101] Patients with CKD frequently have iron deficiency, and iron replacement should be considered as a goal of treatment.

Erythropoietin stimulating therapy may be initiated if the haemoglobin (Hb) falls to <100 g/L (<10 g/dL) and the patient has symptoms and signs of anaemia. The target Hb for patients with CKD on erythropoietin therapy is 10-11 g/dL, as normalisation of Hb has resulted in increased risk for death and cardiovascular disease in this population.^{[102] [103]} In the TREAT study of patients with diabetes with CKD and anaemia, treatment with the erythropoietin-stimulating agent darbepoetin failed to show a beneficial effect of active treatment on cardiovascular events, death, or ESRD compared with those receiving placebo (individuals would receive a rescue dose of darbepoetin if the haemoglobin fell to <90g/L [<9 g/dL]).^[104] Interestingly, as in other studies of anaemia treatment in CKD, the TREAT investigators demonstrated that individuals in the active treatment arm had an increased risk of stroke (RR 1.92, 95% CI 1.38 to 2.68).^[105] In their opinion, the risks of treatment may outweigh the benefits, and discussion between the patient and physician should ensue prior to treatment initiation.^{[101] [104] [106] [107]}

All patients should have an assessment of iron stores if erythropoietin therapy is planned. The goal ferritin for those not on haemodialysis is >100 nanograms/mL, while for those on haemodialysis it is <200 nanograms/mL. All patients should have a transferrin saturation >20%. Iron replacement can be given orally or parenterally.^[108]

For secondary hyperparathyroidism, calcium, phosphorus, and intact parathyroid hormone (PTH) levels should be measured every 6 to 12 months. The calcium and phosphorus levels should be maintained in the normal range with dietary restriction and/or phosphate-binding drugs. The optimal PTH level is currently not known.

25-OH vitamin D deficiency should be excluded. If the serum level of 25-OH vitamin D is <75 nanomol/L (<30 nanograms/mL), vitamin D supplementation with ergocalciferol should be initiated.^{[109] [110]} For those with GFR category G3 to G5 CKD not on dialysis, it is not routinely recommended to use active vitamin D analogues due to the risk of hypercalcaemia and lack of improvement in clinically relevant outcomes.^[111] Use of active vitamin D analogue therapy in patients with CKD not requiring dialysis is indicated if hyperparathyroidism is progressive or severe.^{[111] [112]} There is evidence that the use of non-calcium-based phosphate binders has a survival advantage over calcium-based phosphate binders in patients with CKD.^{[111] [113] [Evidence B]}

GFR category G4

Educate patients about renal replacement therapy such as haemodialysis, peritoneal dialysis, and kidney transplantation.^{[99] [114]}

Patient preference, family support, underlying comorbid conditions, and proximity to a dialysis facility should be addressed when choosing a modality or consideration for palliative care. All patients should undergo CKD education for modality choice.^[99]

Patients should be referred to surgery for dialysis access and/or evaluated for kidney transplantation, based on patient preference for renal replacement modality at GFR category G4.

All patients who are proceeding with haemodialysis should be educated about vein preservation with limiting venipuncture and intravenous access in the access arm.^[115]

Kidney transplantation is indicated once the eGFR is <20 mL/minute and the patient has been evaluated and undergone the required testing process by a transplant team.

Treatment of anaemia and secondary hyperparathyroidism should be continued. It is recommended to check serum calcium and phosphate every 3 to 6 months, and intact PTH every 6 to 12 months.^[111] [\[Evidence C\]](#) Additionally, for those patients who develop metabolic acidosis, supplementation with oral sodium bicarbonate has been shown to slow progression of CKD.^[116] Oral sodium bicarbonate is well tolerated in this group.

GFR category G5 and uraemia

Renal replacement therapy may be initiated once patients have G5 disease or signs of uraemia such as weight loss, lack of appetite, nausea, vomiting, acidosis, hyperkalaemia, or fluid overload.^[1] Treatment of anaemia and secondary hyperparathyroidism should be continued. Those with G5 CKD on dialysis, calcium, phosphorus, and intact PTH should be managed with phosphate binding agents, calcimimetics, active vitamin D analogues, or a combination of these therapies, based on serial laboratory assessments of calcium and phosphate every 1 to 3 months, and PTH every 3 to 6 months.^[111] [\[Evidence C\]](#) Calcimimetics (e.g., cinacalcet, etelcalcetide) negatively feedback on the parathyroid glands and do not have the consequences of calcium augmentation.^[117] Cinacalcet lowers PTH levels in patients with CKD and secondary hyperparathyroidism both prior to and after the initiation of dialysis, but it is associated with hypocalcaemia, and long-term benefits are not known.^[118] ^[119]

There is no other medical therapy to keep patients alive once they have reached the need for dialysis, other than kidney transplantation. Of note, patients aged over 80 years and those with significant comorbidities, such as advanced congestive heart failure, may do poorly with dialysis and frequently are not considered transplant candidates. For these patients, and for all patients approaching ESRD for that matter, the treating nephrologist should have a discussion with the patient regarding end of life care and palliative care as an additional option.^[120]

For those who are considered transplant candidates, transplant confers a significant survival advantage over maintenance dialysis therapy, predominantly due to a decrease in the risk of cardiovascular death. All patients who are on dialysis therapy are potentially eligible for kidney transplantation. A transplant centre including a nephrologist and transplant surgeon will determine the final eligibility and status of the patient for kidney transplantation, after a complete medical history and evaluation.^[121] ^[122]

Other measures

Although data are more limited in the CKD population than in the general population, tobacco cessation and weight loss are recommended.

People with CKD ($\geq$ G3) and diabetes who are not on dialysis should target protein intake of 0.8 g/kg body weight per day.^[20] ^[61] Severe protein restriction should not be recommended until late GFR category G4 or G5 disease as a management strategy to delay the initiation of dialysis.^[123] Severe protein restriction may result in malnourishment and poorer outcomes.^[124]

Aspirin use has also been beneficial for cardioprotection in those with CKD, although there is a higher risk for minor bleeding than in the general population.

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

Acute (summary)		
GFR category G1 to G2 without uraemia		
	1st	ACE inhibitor or angiotensin-II receptor antagonist
	adjunct	sodium-glucose co-transporter-2 (SGLT2) inhibitor
	plus	statin
	adjunct	additional antihypertensive therapy
	adjunct	glycaemic control
	adjunct	finerenone
	2nd	non-dihydropyridine calcium-channel blocker
	adjunct	sodium-glucose co-transporter-2 (SGLT2) inhibitor
	plus	statin
	adjunct	additional antihypertensive therapy
	adjunct	glycaemic control
	adjunct	finerenone
GFR category G3 to G4 without uraemia		
	1st	ACE inhibitor or angiotensin-II receptor antagonist
	adjunct	sodium-glucose co-transporter-2 (SGLT2) inhibitor
	plus	statin ± ezetimibe
	adjunct	additional antihypertensive therapy
	adjunct	glycaemic control
	adjunct	finerenone
	adjunct	education about renal replacement therapy
	2nd	non-dihydropyridine calcium-channel blocker
	adjunct	sodium-glucose co-transporter-2 (SGLT2) inhibitor

Acute		(summary)	
		plus	statin ± ezetimibe
		adjunct	additional antihypertensive therapy
		adjunct	glycaemic control
		adjunct	finerenone
		adjunct	education about renal replacement therapy
■	with anaemia	adjunct	erythropoietin-stimulating agent
		adjunct	iron
■	with secondary hyperparathyroidism	plus	dietary modification ± phosphate-binding drug
		adjunct	ergocalciferol
		adjunct	active vitamin D analogue
■	with metabolic acidosis	adjunct	oral sodium bicarbonate
GFR category G5 or with uraemia			
		1st	dialysis
■	with anaemia	adjunct	erythropoietin-stimulating agent
		adjunct	iron
■	with secondary hyperparathyroidism	plus	dietary modification ± phosphate-binding drug
		adjunct	calcimimetic ± active vitamin D analogue
		adjunct	ergocalciferol
		2nd	kidney transplant

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

Acute

GFR category G1 to G2 without uraemia

1st ACE inhibitor or angiotensin-II receptor antagonist

Primary options

» **lisinopril**: 2.5 to 5 mg orally once daily initially, adjust dose gradually according to response, maximum dose depends on level of impairment

OR

» **ramipril**: 1.25 mg orally once daily initially, adjust dose gradually according to response, maximum dose depends on level of impairment

OR

» **enalapril**: 2.5 mg orally once daily initially, adjust dose gradually according to response, maximum dose depends on level of impairment

OR

» **perindopril**: 2 mg orally once daily initially, adjust dose gradually according to response, maximum dose depends on level of impairment

OR

» **trandolapril**: 0.5 mg orally once daily initially, adjust dose gradually according to response, maximum dose depends on level of impairment

OR

» **captopril**: 12.5 to 25 mg orally two to three times daily initially, adjust dose gradually according to response, maximum dose depends on level of impairment

OR

Acute

» **losartan**: 50 mg orally once daily initially, adjust dose gradually according to response, maximum 100 mg/day

OR

» **irbesartan**: 75 mg orally once daily initially, adjust dose gradually according to response, maximum 300 mg/day

OR

» **telmisartan**: 20 mg orally once daily initially, adjust dose gradually according to response, maximum 80 mg/day

» Several classes of agents have been shown to slow CKD progression. Renin-angiotensin system blockade (e.g., with an ACE inhibitor or an angiotensin-II receptor antagonist) can preserve kidney function by reducing intra-glomerular pressure independently of blood pressure (BP) and glucose control.[62] [63]

» ACE inhibitors and angiotensin-II receptor antagonists have been shown in numerous clinical trials to slow the progression of CKD and delay the need for renal replacement therapy in both diabetic and non-diabetic CKD.[87] [88] [89]

» The 2014 Joint National Committee 8 redefined the target BP goal for patients with CKD as <140/90 mmHg, given the evidence from clinical trials that this is associated with the lowest risk of cardiovascular outcomes and mortality.[83] However, the 2017 American College of Cardiology/American Heart Association guideline recommends adults with hypertension and CKD should be treated to a BP goal of less than 130/80 mmHg.[84] The Kidney Disease: Improving Global Outcomes guideline recommends a target systolic BP of less than 120 mmHg, if tolerated, in patients with CKD, with and without diabetes, and not receiving dialysis.[62]

» ACE inhibitors and angiotensin-II receptor antagonists may be associated with hyperkalaemia and acute kidney injury, more commonly in older people, those with an estimated glomerular filtration rate (eGFR) <30 mL/minute/1.73 m², and with use of longer-acting agents. These complications are usually reversible with discontinuation of the drug and appropriate treatment.

Acute

adjunct

» Doses should be low initially and adjusted gradually according to clinical response.

sodium-glucose co-transporter-2 (SGLT2) inhibitor

Treatment recommended for SOME patients in selected patient group

Primary options

» dapagliflozin: 10 mg orally once daily

OR

» empagliflozin: 10 mg orally once daily

OR

» canagliflozin: 100-300 mg orally once daily

» SGLT2 inhibitors (e.g., empagliflozin, canagliflozin, dapagliflozin) can preserve kidney function by reducing intra-glomerular pressure independently of blood pressure (BP) and glucose control.[63] [64] [68]

» There is evidence that the use of SGLT2 inhibitors prevents major kidney outcomes (e.g., dialysis, transplantation, or death due to kidney disease) in people with type 2 diabetes.[64] [73] [74] SGLT2 inhibitors, in addition to reducing hyperglycaemia, have renal benefits through independent effects on renal tubular glucose reabsorption, weight, BP, intra-glomerular pressure, albuminuria, and slowed GFR loss.[75] [76]

» SGLT2 inhibitors are recommended for the treatment of CKD, particularly in adults at risk of progression, in combination with an ACE inhibitor or an angiotensin-II receptor antagonist. [BMJ Rapid Recommendation: SGLT2-inhibitors for adults with CKD] (<https://www.bmj.com/content/387/bmj-2024-080257>)

» Recommendations for the use of SGLT2 inhibitors in patients with different degrees of kidney disease may vary; consult your local drug information source for more information.

» Use of SGLT2 inhibitors is not recommended in patients with end-stage renal disease who are on dialysis.[77]

plus

statin

Treatment recommended for ALL patients in selected patient group

Acute

Primary options

» [simvastatin](#): 20-40 mg orally once daily

OR

» [pravastatin](#): 40 mg orally once daily

OR

» [rosuvastatin](#): 5-10 mg orally once daily

OR

» [atorvastatin](#): 10-20 mg orally once daily

» Statin therapy has been shown to have cardioprotective effects in patients with CKD.[91] [92] [93] [94] In those individuals not on dialysis therapy, the use of statins in a large meta-analysis resulted in the reduction of all-cause mortality by 21% (relative risk [RR] 0.79, 95% CI 0.69 to 0.91) and cardiovascular mortality by 23% (RR 0.77, 95% CI 0.69 to 0.87).[95]

» Kidney Disease: Improving Global Outcomes guidelines recommend that CKD patients ≥ 50 years or those with a high risk of cardiovascular mortality (not on dialysis) should be treated with a statin without the need for routine follow-up to check lipid values, or to change dose regimen based on set targets (i.e., a 'treat and forget' approach).[65]

» Statin therapy has been associated with liver dysfunction and myopathy and should be monitored in patients with CKD.

adjunct **additional antihypertensive therapy**

Treatment recommended for SOME patients in selected patient group

Primary options

» [chlortalidone](#): 12.5 to 25 mg orally once daily initially, adjust dose gradually according to response, maximum 50 mg/day

OR

» [hydrochlorothiazide](#): 12.5 mg orally once daily initially, adjust dose gradually according to response, maximum 50 mg/day

OR

Acute

» **atenolol**: 25 mg orally once daily initially, adjust dose gradually according to response, maximum 25-50 mg/day

OR

» **metoprolol**: 25 mg orally (extended-release) once daily initially, adjust dose gradually according to response, maximum 100 mg/day

OR

» **nifedipine**: 30-60 mg orally (extended-release) once daily initially, adjust dose gradually according to response, maximum 90 mg/day (120 mg/day for some brands)

OR

» **amlodipine**: 5 mg orally once daily initially, adjust dose gradually according to response, maximum 10 mg/day

OR

» **felodipine**: 2.5 mg orally once daily initially, adjust dose gradually according to response, maximum 20 mg/day

OR

» **spironolactone**: 12.5 mg orally once daily initially, adjust dose gradually according to response, maximum 200 mg/day given in 2-4 divided doses

Secondary options

» **hydralazine**: 10 mg orally three to four times daily initially, adjust dose gradually according to response, maximum 300 mg/day

OR

» **minoxidil**: 5 mg orally once daily initially, adjust dose gradually according to response, maximum 40 mg/day

OR

» **clonidine**: 0.1 mg orally (immediate-release) twice daily initially, adjust dose gradually according to response, maximum 0.6 mg/day

Acute

» Hypertension is one of the greatest risk factors for the progression of CKD, regardless of the underlying aetiology of CKD. Most patients with CKD will require at least two or three different types of antihypertensive agent to achieve the optimal BP control. A combination of antihypertensive agents should be used. ACE inhibitors and angiotensin-II receptor antagonists should not be combined within the same regimen.[62]

» Other classes of antihypertensive agents (e.g., thiazide, or thiazide-like diuretics, beta-blockers, dihydropyridine calcium-channel blockers, aldosterone antagonists, vasodilators, alpha-2 adrenergic agonists) should be added when the target blood pressure is not achieved with the use of an ACE inhibitor or an angiotensin-II receptor antagonist, or if there are other specific clinical indications, such as beta-blockers for angina pectoris.[62]

adjunct glycaemic control

Treatment recommended for SOME patients in selected patient group

» In patients with diabetes, glycaemic goals should be individualised. Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend a HbA1c target ranging from <6.5% to <8.0% for patients with diabetes and chronic kidney disease not receiving dialysis. A lower target (e.g., <6.5% or <7.0%) may be appropriate for individuals in whom preventing complications is the key goal, whereas a higher target (e.g., <7.5% or <8.0%) may be preferred in those with multimorbidity or increased burden of hypoglycaemia.[20] [125] In patients with diabetes and CKD, there is a risk for hypoglycaemia because of impaired kidney clearance of drugs (such as insulin or sulfonylureas) and impaired kidney gluconeogenesis.

» Patients with type 1 diabetes require treatment with insulin, regardless of whether they are on dialysis or not.

» Some specific anti-hyperglycaemic drugs used by patients with type 2 diabetes significantly reduce all-cause or cardiovascular mortality, or major cardiovascular events or renal complications in some patient subgroups, and should be considered independently of HbA1c targets.[68] [69] [70] [71] [72]

» There is evidence that the use of sodium-glucose co-transporter-2 (SGLT2) inhibitors

Acute

prevents major kidney outcomes (e.g., dialysis, transplantation, or death due to kidney disease) in people with type 2 diabetes.[64] [73] [74]

SGLT2 inhibitors, in addition to reducing hyperglycaemia, have renal benefits through independent effects on renal tubular glucose reabsorption, weight, blood pressure, intra-glomerular pressure, albuminuria, and slowed glomerular filtration rate (GFR) loss.[75] [76]

» KDIGO guidelines advise that most patients with type 2 diabetes and CKD would benefit from treatment with metformin (if eGFR ≥ 30 mL/minute/1.73 m²) and an SGLT2 inhibitor (if eGFR ≥ 20 mL/minute/1.73 m²).[20] The American Diabetes Association recommends the use of SGLT2 inhibitors in patients with CKD and type 2 diabetes (if eGFR ≥ 20 mL/minute/1.73 m²) regardless of urinary albuminuria.[61] Use of SGLT2 inhibitors is not recommended in patients with end-stage renal disease who are on dialysis.[77]

» If additional glycaemic control is required for patients receiving metformin and an SGLT2 inhibitor, a drug from a different class should be selected. A glucagon-like peptide-1 (GLP-1) is the preferred option. If required, other agents (e.g., a dipeptidyl peptidase-4 [DPP-4] inhibitor, a sulfonylurea, insulin, a thiazolidinedione, or an alpha-glucosidase inhibitor) may be considered based on eGFR, comorbidities, and patient preference.[20]

» As a class of drugs, GLP-1 agonists have beneficial effects on cardiovascular, mortality, and kidney outcomes in patients with type 2 diabetes.[78] [79] GLP-1 agonists may be considered for cardiovascular risk reduction.[61]

» Liraglutide, dulaglutide, and semaglutide are not renally excreted and are the preferred agents in this class.

» Studies report that DPP-4 inhibitors are renoprotective, but do not have a cardiovascular benefit.[80] [81] Some DPP-4 inhibitors require dose adjustment in renal impairment.

adjunct

finerenone

Treatment recommended for SOME patients in selected patient group

Primary options

» finerenone: 20 mg orally once daily

Acute

» Finerenone, a non-steroidal mineralocorticoid receptor antagonist, reduces the progression of kidney disease in patients with type 2 diabetes mellitus and known CKD.^[82] Finerenone is approved by the US Food and Drug Administration (FDA) to reduce the risk of kidney function decline, kidney failure, cardiovascular death, non-fatal heart attacks, and hospitalisation for heart failure in adults with CKD associated with type 2 diabetes.

» Guidelines recommend finerenone for patients with type 2 diabetes and albuminuria, despite maximum tolerated dose of an ACE inhibitor or an angiotensin-II receptor antagonist (if eGFR is ≥ 25 mL/minute/1.73 m² and serum potassium level is normal).^{[20] [61]} Finerenone can be added to an sodium-glucose co-transporter-2 (SGLT2) inhibitor and an ACE inhibitor or an angiotensin-II receptor antagonist.

» Monitor serum potassium levels during treatment, and use caution when administering with other drugs that increase serum potassium levels.

2nd non-dihydropyridine calcium-channel blocker

Primary options

» **diltiazem**: 120 mg orally (extended-release) once daily initially, adjust dose gradually according to response, maximum 360 mg/day

OR

» **verapamil**: 120 mg orally (extended-release) once daily initially, adjust dose gradually according to response, maximum 360 mg/day

» If an ACE inhibitor or an angiotensin-II receptor antagonist needs to be discontinued due to adverse effects (such as cough, angio-oedema, haemodynamic decline in renal function, and/or hyperkalaemia), then non-dihydropyridine calcium-channel blockers have been demonstrated to have more proteinuric-lowering effects than other antihypertensive agents.^[126]

adjunct sodium-glucose co-transporter-2 (SGLT2) inhibitor

Treatment recommended for SOME patients in selected patient group

Primary options

Acute

» dapagliflozin: 10 mg orally once daily

OR

» empagliflozin: 10 mg orally once daily

OR

» canagliflozin: 100-300 mg orally once daily

» SGLT2 inhibitors (e.g., empagliflozin, canagliflozin, dapagliflozin) can preserve kidney function by reducing intra-glomerular pressure independently of blood pressure (BP) and glucose control.[63] [64] [68]

» There is evidence that the use of SGLT2 inhibitors prevents major kidney outcomes (e.g., dialysis, transplantation, or death due to kidney disease) in people with type 2 diabetes.[64] [73] [74] SGLT2 inhibitors, in addition to reducing hyperglycaemia, have renal benefits through independent effects on renal tubular glucose reabsorption, weight, BP, intra-glomerular pressure, albuminuria, and slowed GFR loss.[75] [76]

» SGLT2 inhibitors are recommended for the treatment of CKD, particularly in adults at risk of progression, in combination with an ACE inhibitor or an angiotensin-II receptor antagonist. [BMJ Rapid Recommendation: SGLT2-inhibitors for adults with CKD] (<https://www.bmj.com/content/387/bmj-2024-080257>)

» Recommendations for the use of SGLT2 inhibitors in patients with different degrees of kidney disease may vary; consult your local drug information source for more information.

» Use of SGLT2 inhibitors is not recommended in patients with end-stage renal disease who are on dialysis.[77]

plus

statin

Treatment recommended for ALL patients in selected patient group

Primary options

» simvastatin: 20-40 mg orally once daily

OR

» pravastatin: 40 mg orally once daily

OR

Acute

» [rosuvastatin](#): 5-10 mg orally once daily

OR

» [atorvastatin](#): 10-20 mg orally once daily

» Statin therapy has been shown to have cardioprotective effects in patients with CKD.[91] [92] [93] [94] In those individuals not on dialysis therapy, the use of statins in a large meta-analysis resulted in the reduction of all-cause mortality by 21% (relative risk [RR] 0.79, 95% CI 0.69 to 0.91) and cardiovascular mortality by 23% (RR 0.77, 95% CI 0.69 to 0.87).[95]

» KDIGO guidelines recommend that CKD patients not on dialysis should be treated with a statin without the need for routine follow-up to check lipid values, or to change dose regimen based on set targets (i.e., a 'treat and forget' approach).[65]

» Statin therapy has been associated with liver dysfunction and myopathy and should be monitored in patients with CKD.

adjunct additional antihypertensive therapy

Treatment recommended for SOME patients in selected patient group

Primary options

» [chlortalidone](#): 12.5 to 25 mg orally once daily initially, adjust dose gradually according to response, maximum 50 mg/day

OR

» [hydrochlorothiazide](#): 12.5 mg orally once daily initially, adjust dose gradually according to response, maximum 50 mg/day

OR

» [atenolol](#): 25 mg orally once daily initially, adjust dose gradually according to response, maximum 25-50 mg/day

OR

» [metoprolol](#): 25 mg orally (extended-release) once daily initially, adjust dose gradually according to response, maximum 100 mg/day

OR

Acute

» **nifedipine**: 30-60 mg orally (extended-release) once daily initially, adjust dose gradually according to response, maximum 90 mg/day (120 mg/day for some brands)

OR

» **amlodipine**: 5 mg orally once daily initially, adjust dose gradually according to response, maximum 10 mg/day

OR

» **felodipine**: 2.5 mg orally once daily initially, adjust dose gradually according to response, maximum 20 mg/day

OR

» **spironolactone**: 12.5 mg orally once daily initially, adjust dose gradually according to response, maximum 200 mg/day given in 2-4 divided doses

OR

» **aliskiren**: 150 mg orally once daily initially, adjust dose gradually according to response, maximum 300 mg/day

Secondary options

» **hydralazine**: 10 mg orally three to four times daily initially, adjust dose gradually according to response, maximum 300 mg/day

OR

» **minoxidil**: 5 mg orally once daily initially, adjust dose gradually according to response, maximum 40 mg/day

OR

» **clonidine**: 0.1 mg orally (immediate-release) twice daily initially, adjust dose gradually according to response, maximum 0.6 mg/day

» Hypertension is one of the greatest risk factors for the progression of CKD, regardless of the underlying aetiology of CKD. Most patients with CKD will require at least two or three different types of antihypertensive agent to achieve the optimal BP control. A combination

Acute

of antihypertensive agents should be used. ACE inhibitors and angiotensin-II receptor antagonists should not be combined within the same regimen.[62]

» Other classes of antihypertensive agents (e.g., thiazide or thiazide-like diuretics, beta-blockers, dihydropyridine calcium-channel blockers, aldosterone antagonists, vasodilators, alpha-2 adrenergic agonists) should be added when the target blood pressure is not achieved with the use of a non-dihydropyridine calcium-channel blocker, or if there are other specific clinical indications, such as beta-blockers for angina pectoris.[62]

adjunct glycaemic control

Treatment recommended for SOME patients in selected patient group

» In patients with diabetes, glycaemic goals should be individualised. Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend a HbA1c target ranging from <6.5% to <8.0% for patients with diabetes and chronic kidney disease not receiving dialysis. A lower target (e.g., <6.5% or <7.0%) may be appropriate for individuals in whom preventing complications is the key goal, whereas a higher target (e.g., <7.5% or <8.0%) may be preferred in those with multimorbidity or increased burden of hypoglycaemia.[20] [125] In patients with diabetes and CKD, there is a risk for hypoglycaemia because of impaired kidney clearance of drugs (such as insulin or sulfonylureas) and impaired kidney gluconeogenesis.

» Patients with type 1 diabetes require treatment with insulin, regardless of whether they are on dialysis or not.

» Some specific anti-hyperglycaemic drugs significantly reduce all-cause or cardiovascular mortality, or major cardiovascular events or renal complications in some patient subgroups, and should be considered independently of HbA1c targets.[68] [69] [70] [71] [72]

» There is evidence that the use of sodium-glucose co-transporter-2 (SGLT2) inhibitors prevents major kidney outcomes (e.g., dialysis, transplantation, or death due to kidney disease) in people with type 2 diabetes.[64] [73] [74] SGLT2 inhibitors, in addition to reducing hyperglycaemia, have renal benefits through independent effects on renal tubular glucose reabsorption, weight, blood pressure, intra-

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glomerular pressure, albuminuria, and slowed glomerular filtration rate (GFR) loss.[75] [76]

» KDIGO guidelines advise that most patients with type 2 diabetes and CKD would benefit from treatment with metformin (if eGFR ≥ 30 mL/minute/1.73 m²) and an SGLT2 inhibitor (if eGFR ≥ 20 mL/minute/1.73 m²).[20] The American Diabetes Association recommends the use of SGLT2 inhibitors in patients with CKD and type 2 diabetes (if eGFR ≥ 20 mL/minute/1.73 m²) regardless of urinary albuminuria.[61] Use of SGLT2 inhibitors is not recommended in patients with end-stage renal disease who are on dialysis.[77]

» If additional glycaemic control is required for patients receiving metformin and an SGLT2 inhibitor, a drug from a different class should be selected. A glucagon-like peptide-1 (GLP-1) is the preferred option. If required, other agents (e.g., a dipeptidyl peptidase-4 [DPP-4] inhibitor, a sulfonylurea, insulin, a thiazolidinedione, or an alpha-glucosidase inhibitor) may be considered based on eGFR, comorbidities, and patient preference.[20]

» As a class of drugs, GLP-1 agonists have beneficial effects on cardiovascular, mortality, and kidney outcomes in patients with type 2 diabetes.[78] [79] GLP-1 agonists may be considered for cardiovascular risk reduction.[61]

» Liraglutide, dulaglutide, and semaglutide are not renally excreted and are the preferred agents in this class.

» Studies report that DPP-4 inhibitors are renoprotective, but do not have a cardiovascular benefit.[80] [81] Some DPP-4 inhibitors require dose adjustment in renal impairment.

adjunct finerenone

Treatment recommended for SOME patients in selected patient group

Primary options

» **finerenone**: 20 mg orally once daily

» Finerenone, a non-steroidal selective mineralocorticoid receptor antagonist, reduces the progression of kidney disease in patients with type 2 diabetes mellitus and known CKD.[82] Finerenone is approved by the US Food and Drug Administration to reduce the risk of kidney function decline, kidney failure, cardiovascular death, non-fatal heart attacks,

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and hospitalisation for heart failure in adults with CKD associated with type 2 diabetes.

» Guidelines recommend finerenone for patients with type 2 diabetes and albuminuria (if eGFR is ≥ 25 mL/minute/1.73 m² and serum potassium level is normal).[20] [61]

» Monitor serum potassium levels during treatment, and use caution when administering with other drugs that increase serum potassium levels.

GFR category G3 to G4 without uraemia

1st **ACE inhibitor or angiotensin-II receptor antagonist**

Primary options

» **lisinopril**: 2.5 to 5 mg orally once daily initially, adjust dose gradually according to response, maximum dose depends on level of impairment

OR

» **ramipril**: 1.25 mg orally once daily initially, adjust dose gradually according to response, maximum dose depends on level of impairment

OR

» **enalapril**: 2.5 mg orally once daily initially, adjust dose gradually according to response, maximum dose depends on level of impairment

OR

» **perindopril**: 2 mg orally once daily initially, adjust dose gradually according to response, maximum dose depends on level of impairment

OR

» **trandolapril**: 0.5 mg orally once daily initially, adjust dose gradually according to response, maximum dose depends on level of impairment

OR

Acute

» **captopril**: 12.5 to 25 mg orally two to three times daily initially, adjust dose gradually according to response, maximum dose depends on level of impairment

OR

» **losartan**: 50 mg orally once daily initially, adjust dose gradually according to response, maximum 100 mg/day

OR

» **irbesartan**: 75 mg orally once daily initially, adjust dose gradually according to response, maximum 300 mg/day

OR

» **telmisartan**: 20 mg orally once daily initially, adjust dose gradually according to response, maximum 80 mg/day

» Several classes of agents have been shown to slow CKD progression. Renin-angiotensin system blockade (e.g., with an ACE inhibitor or an angiotensin-II receptor antagonist) can preserve kidney function by reducing intra-glomerular pressure independently of blood pressure (BP) and glucose control.[62] [63]

» ACE inhibitors and angiotensin-II receptor antagonists have been shown in numerous clinical trials to slow the progression of CKD and delay the need for renal replacement therapy in both diabetic and nondiabetic CKD.[87] [88] [89]

» The Joint National Committee 8 redefined the target BP goal for patients with CKD as <140/90 mmHg, given the evidence from clinical trials that this is associated with the lowest risk of cardiovascular outcomes and mortality.[83] However, the 2017 American College of Cardiology/American Heart Association guideline recommends adults with hypertension and CKD should be treated to a BP goal of less than 130/80 mmHg.[84] The Kidney Disease: Improving Global Outcomes guideline recommend a target systolic BP of less than 120 mmHg, if tolerated, in patients with CKD, with and without diabetes, and not receiving dialysis.[62]

» ACE inhibitors and angiotensin-II receptor antagonists may be associated with hyperkalaemia and acute renal failure, more commonly in older people, those with an

Acute

adjunct

estimated GFR <30 mL/minute/1.73 m², and with use of longer-acting agents. These complications are usually reversible with discontinuation of the drug and appropriate treatment.

sodium-glucose co-transporter-2 (SGLT2) inhibitor

Treatment recommended for SOME patients in selected patient group

Primary options

» **dapagliflozin**: 10 mg orally once daily

OR

» **empagliflozin**: 10 mg orally once daily

OR

» **canagliflozin**: 100-300 mg orally once daily

» SGLT2 inhibitors (e.g., empagliflozin, canagliflozin, dapagliflozin) can preserve kidney function by reducing intra-glomerular pressure independently of blood pressure (BP) and glucose control.[63] [64] [68]

» There is evidence that the use of SGLT2 inhibitors prevents major kidney outcomes (e.g., dialysis, transplantation, or death due to kidney disease) in people with type 2 diabetes.[64] [73] [74] SGLT2 inhibitors, in addition to reducing hyperglycaemia, have renal benefits through independent effects on renal tubular glucose reabsorption, weight, BP, intra-glomerular pressure, albuminuria, and slowed GFR loss.[75] [76]

» SGLT2 inhibitors are recommended for the treatment of CKD, particularly in adults at risk of progression, in combination with an ACE inhibitor or an angiotensin-II receptor antagonist. [BMJ Rapid Recommendation: SGLT2-inhibitors for adults with CKD] (<https://www.bmj.com/content/387/bmj-2024-080257>)

» Recommendations for the use of SGLT2 inhibitors in patients with different degrees of kidney disease may vary; consult your local drug information source for more information.

» Use of SGLT2 inhibitors is not recommended in patients with end-stage renal disease who are on dialysis.[77]

plus

statin ± ezetimibe

Acute

Treatment recommended for ALL patients in selected patient group

Primary options

» [simvastatin](#): 20-40 mg orally once daily

OR

» [pravastatin](#): 40 mg orally once daily

OR

» [rosuvastatin](#): 5-10 mg orally once daily

OR

» [atorvastatin](#): 10-20 mg orally once daily

OR

» [ezetimibe/simvastatin](#): 10 mg (ezetimibe)/20 mg (simvastatin) orally once daily

» Statin therapy has been shown to have cardioprotective effects in patients with CKD.[91] [92] [93] [94] In those individuals not on dialysis therapy, the use of statins in a large meta-analysis resulted in the reduction of all-cause mortality by 21% (relative risk [RR] 0.79, 95% CI 0.69 to 0.91) and cardiovascular mortality by 23% (RR 0.77, 95% CI 0.69 to 0.87).[95]

» Kidney Disease: Improving Global Outcomes guidelines recommend that GFR category G3 or G4 CKD patients not on dialysis should be treated with a statin without the need for routine follow-up to check lipid values, or to change dose regimen based on set targets (i.e., a 'treat and forget' approach).[65] For patients aged ≥50 years with CKD category G3 or G4, ezetimibe can be added to simvastatin.[66]

» Statin therapy has been associated with liver dysfunction and myopathy and should be monitored in patients with CKD.

adjunct additional antihypertensive therapy

Treatment recommended for SOME patients in selected patient group

Primary options

» [chlortalidone](#): 12.5 to 25 mg orally once daily initially, adjust dose gradually according to response, maximum 50 mg/day

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OR

» **hydrochlorothiazide**: 12.5 mg orally once daily initially, adjust dose gradually according to response, maximum 50 mg/day

OR

» **atenolol**: 25 mg orally once daily initially, adjust dose gradually according to response, maximum 25-50 mg/day

OR

» **metoprolol**: 25 mg orally (extended-release) once daily initially, adjust dose gradually according to response, maximum 100 mg/day

OR

» **nifedipine**: 30-60 mg orally (extended-release) once daily initially, adjust dose gradually according to response, maximum 90 mg/day (120 mg/day for some brands)

OR

» **amlodipine**: 5 mg orally once daily initially, adjust dose gradually according to response, maximum 10 mg/day

OR

» **felodipine**: 2.5 mg orally once daily initially, adjust dose gradually according to response, maximum 20 mg/day

OR

» **spironolactone**: 12.5 mg orally once daily initially, adjust dose gradually according to response, maximum 200 mg/day given in 2-4 divided doses

Secondary options

» **hydralazine**: 10 mg orally three to four times daily initially, adjust dose gradually according to response, maximum 300 mg/day

OR

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» **minoxidil**: 5 mg orally once daily initially, adjust dose gradually according to response, maximum 40 mg/day

OR

» **clonidine**: 0.1 mg orally (immediate-release) twice daily initially, adjust dose gradually according to response, maximum 0.6 mg/day

» Hypertension is one of the greatest risk factors for the progression of CKD, regardless of the underlying aetiology of CKD. Most patients with CKD will require at least two or three different types of antihypertensive agent to achieve the optimal BP control. A combination of antihypertensive agents should be used. ACE inhibitors and angiotensin-II receptor antagonists should not be combined within the same regimen.[62]

» Other classes of antihypertensive agents (e.g., thiazide or thiazide-like diuretics, beta-blockers, dihydropyridine calcium-channel blockers, aldosterone antagonists, vasodilators, alpha-2 adrenergic agonists) should be added when the target blood pressure is not achieved with the use of an ACE inhibitor or an angiotensin-II receptor antagonist, or if there are other specific clinical indications, such as beta-blockers for angina pectoris.[62]

adjunct glycaemic control

Treatment recommended for SOME patients in selected patient group

» In patients with diabetes, glycaemic goals should be individualised. Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend a HbA1c target ranging from <6.5% to <8.0% for patients with diabetes and chronic kidney disease not receiving dialysis. A lower target (e.g., <6.5% or <7.0%) may be appropriate for individuals in whom preventing complications is the key goal, whereas a higher target (e.g., <7.5% or <8.0%) may be preferred in those with multimorbidity or increased burden of hypoglycaemia.[20] [125] In patients with diabetes and CKD, there is a risk for hypoglycaemia because of impaired kidney clearance of drugs (such as insulin or sulfonylureas) and impaired kidney gluconeogenesis.

» Patients with type 1 diabetes require treatment with insulin, regardless of whether they are on dialysis or not.

Acute

» Some specific anti-hyperglycaemic drugs significantly reduce all-cause or cardiovascular mortality, or major cardiovascular events or renal complications in some patient subgroups, and should be considered independently of HbA1c targets.[68] [69] [70] [71] [72]

» There is evidence that the use of sodium-glucose co-transporter-2 (SGLT2) inhibitors prevents major kidney outcomes (e.g., dialysis, transplantation, or death due to kidney disease) in people with type 2 diabetes.[64] [73] [74]

SGLT2 inhibitors, in addition to reducing hyperglycaemia, have renal benefits through independent effects on renal tubular glucose reabsorption, weight, blood pressure, intra-glomerular pressure, albuminuria, and slowed glomerular filtration rate (GFR) loss.[75] [76]

» KDIGO guidelines advise that most patients with type 2 diabetes and CKD would benefit from treatment with metformin (if eGFR ≥ 30 mL/minute/1.73 m²) and an SGLT2 inhibitor (if eGFR ≥ 20 mL/minute/1.73 m²).[20] The American Diabetes Association recommends the use of SGLT2 inhibitors in patients with CKD and type 2 diabetes (if eGFR ≥ 20 mL/minute/1.73 m²) regardless of urinary albuminuria.[61] Use of SGLT2 inhibitors is not recommended in patients with end-stage renal disease who are on dialysis.[77]

» If additional glycaemic control is required for patients receiving metformin and an SGLT2 inhibitor, a drug from a different class should be selected. A glucagon-like peptide-1 (GLP-1) is the preferred option. If required, other agents (e.g., a dipeptidyl peptidase-4 [DPP-4] inhibitor, a sulfonylurea, insulin, a thiazolidinedione, or an alpha-glucosidase inhibitor) may be considered based on eGFR, comorbidities, and patient preference.[20]

» As a class of drugs, GLP-1 agonists have beneficial effects on cardiovascular, mortality, and kidney outcomes in patients with type 2 diabetes.[78] [79] GLP-1 agonists may be considered to achieve glycaemic targets and for cardiovascular risk reduction.[61]

» Liraglutide, dulaglutide, and semaglutide are not renally excreted and are the preferred agents in this class.

» Studies report that DPP-4 inhibitors are renoprotective, but do not have a cardiovascular benefit.[80] [81] Some DPP-4 inhibitors require dose adjustment in renal impairment.

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adjunct finerenone

Treatment recommended for SOME patients in selected patient group

Primary options

» **finerenone**: 20 mg orally once daily

» Finerenone, a non-steroidal selective mineralocorticoid receptor antagonist, reduces the progression of kidney disease in patients with type 2 diabetes mellitus and known CKD.[82] Finerenone is approved by the US Food and Drug Administration to reduce the risk of kidney function decline, kidney failure, cardiovascular death, non-fatal heart attacks, and hospitalisation for heart failure in adults with CKD associated with type 2 diabetes.

» Guidelines recommend finerenone for patients with type 2 diabetes and albuminuria, despite maximum tolerated dose of an ACE inhibitor or an angiotensin-II receptor antagonist (if eGFR is ≥ 25 mL/minute/1.73 m² and serum potassium level is normal).[20] [61] Finerenone can be added to a sodium-glucose cotransporter-2 (SGLT2) inhibitor and an ACE inhibitor or an angiotensin-II receptor antagonist.

» Monitor serum potassium levels during treatment, and use caution when administering with other drugs that increase serum potassium levels.

adjunct education about renal replacement therapy

Treatment recommended for SOME patients in selected patient group

» Educate patients about renal replacement therapy such as haemodialysis, peritoneal dialysis, and kidney transplantation.[99] [114]

Patient preference, family support, underlying comorbid conditions, and proximity to a dialysis facility should be addressed when choosing a modality or consideration for palliative care. All patients should undergo CKD education for modality choice.[99]

» Patients should be referred to surgery for dialysis access and/or evaluated for kidney transplantation, based on patient preference for renal replacement modality at glomerular filtration rate (GFR) category G4.

» All patients who are proceeding with haemodialysis should be educated about vein

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preservation with limiting venipuncture and intravenous access in the access arm.[115]

» Kidney transplantation is indicated once the estimated GFR is <20 mL/minute and the patient has been evaluated and undergone the required testing process by a transplant team.

2nd non-dihydropyridine calcium-channel blocker

Primary options

» **diltiazem**: 120 mg orally (extended-release) once daily initially, adjust dose gradually according to response, maximum 360 mg/day

OR

» **verapamil**: 120 mg orally (extended-release) once daily initially, adjust dose gradually according to response, maximum 360 mg/day

» If an ACE inhibitor or an angiotensin-II receptor antagonist needs to be discontinued due to adverse effects (such as cough, angio-oedema, haemodynamic decline in renal function, and/or hyperkalaemia), then non-dihydropyridine calcium-channel blockers have been demonstrated to have more proteinuric-lowering effects than other antihypertensive agents.[126]

adjunct sodium-glucose co-transporter-2 (SGLT2) inhibitor

Treatment recommended for SOME patients in selected patient group

Primary options

» **dapagliflozin**: 10 mg orally once daily

OR

» **empagliflozin**: 10 mg orally once daily

OR

» **canagliflozin**: 100-300 mg orally once daily

» SGLT2 inhibitors (e.g., empagliflozin, canagliflozin, dapagliflozin) can preserve kidney function by reducing intra-glomerular pressure independently of blood pressure (BP) and glucose control.[62] [63] [64][68]

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» There is evidence that the use of SGLT2 inhibitors prevents major kidney outcomes (e.g., dialysis, transplantation, or death due to kidney disease) in people with type 2 diabetes.[64] [73] [74] SGLT2 inhibitors, in addition to reducing hyperglycaemia, have renal benefits through independent effects on renal tubular glucose reabsorption, weight, BP, intra-glomerular pressure, albuminuria, and slowed GFR loss.[75] [76]

» SGLT2 inhibitors are recommended for the treatment of CKD, particularly in adults at risk of progression, in combination with an ACE inhibitor or an angiotensin-II receptor antagonist. [BMJ Rapid Recommendation: SGLT2-inhibitors for adults with CKD] (<https://www.bmj.com/content/387/bmj-2024-080257>)

» Recommendations for the use of SGLT2 inhibitors in patients with different degrees of kidney disease may vary; consult your local drug information source for more information.

» Use of SGLT2 inhibitors is not recommended in patients with end-stage renal disease who are on dialysis.[77]

plus

statin ± ezetimibe

Treatment recommended for ALL patients in selected patient group

Primary options

» [simvastatin](#): 20-40 mg orally once daily

OR

» [pravastatin](#): 40 mg orally once daily

OR

» [rosuvastatin](#): 5-10 mg orally once daily

OR

» [atorvastatin](#): 10-20 mg orally once daily

OR

» [ezetimibe/simvastatin](#): 10 mg (ezetimibe)/20 mg (simvastatin) orally once daily

» Statin therapy has been shown to have cardioprotective effects in patients with CKD.[91] [92] [93] [94] In those individuals not on dialysis therapy, the use of statins in a large meta-

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analysis resulted in the reduction of all-cause mortality by 21% (relative risk [RR] 0.79, 95% CI 0.69 to 0.91) and cardiovascular mortality by 23% (RR 0.77, 95% CI 0.69 to 0.87).^[95]

» Kidney Disease: Improving Global Outcomes guidelines recommend that GFR category G3 or G4 CKD patients not on dialysis should be treated with a statin without the need for routine follow-up to check lipid values, or to change dose regimen based on set targets (i.e., a 'treat and forget' approach).^[65] For patients aged ≥ 50 years with CKD GFR category G3 or G4, ezetimibe can be added to simvastatin.^[66]

» Statin therapy has been associated with liver dysfunction and myopathy and should be monitored in patients with CKD.

adjunct additional antihypertensive therapy

Treatment recommended for SOME patients in selected patient group

Primary options

» **chlortalidone**: 12.5 to 25 mg orally once daily initially, adjust dose gradually according to response, maximum 50 mg/day

OR

» **hydrochlorothiazide**: 12.5 mg orally once daily initially, adjust dose gradually according to response, maximum 50 mg/day

OR

» **atenolol**: 25 mg orally once daily initially, adjust dose gradually according to response, maximum 25-50 mg/day

OR

» **metoprolol**: 25 mg orally (extended-release) once daily initially, adjust dose gradually according to response, maximum 100 mg/day

OR

» **nifedipine**: 30-60 mg orally (extended-release) once daily initially, adjust dose gradually according to response, maximum 90 mg/day (120 mg/day for some brands)

OR

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» **amlodipine**: 5 mg orally once daily initially, adjust dose gradually according to response, maximum 10 mg/day

OR

» **felodipine**: 2.5 mg orally once daily initially, adjust dose gradually according to response, maximum 20 mg/day

OR

» **spironolactone**: 12.5 mg orally once daily initially, adjust dose gradually according to response, maximum 200 mg/day given in 2-4 divided doses

OR

» **aliskiren**: 150 mg orally once daily initially, adjust dose gradually according to response, maximum 300 mg/day

Secondary options

» **hydralazine**: 10 mg orally three to four times daily initially, adjust dose gradually according to response, maximum 300 mg/day

OR

» **minoxidil**: 5 mg orally once daily initially, adjust dose gradually according to response, maximum 40 mg/day

OR

» **clonidine**: 0.1 mg orally (immediate-release) twice daily initially, adjust dose gradually according to response, maximum 0.6 mg/day

» Hypertension is one of the greatest risk factors for the progression of CKD, regardless of the underlying aetiology of CKD. Most patients with CKD will require at least two or three different types of antihypertensive agent to achieve the optimal BP control. A combination of antihypertensive agents should be used. ACE inhibitors and angiotensin-II receptor antagonists should not be combined within the same regimen.^[62]

» Other classes of antihypertensive agents (e.g., thiazide, or thiazide-like diuretics, beta-blockers, dihydropyridine calcium-channel blockers, aldosterone antagonists, vasodilators, alpha-2

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adrenergic agonists) should be added when the target blood pressure is not achieved with the use of a non-dihydropyridine calcium-channel blocker, or if there are other specific clinical indications, such as beta-blockers for angina pectoris.[62]

adjunct glycaemic control

Treatment recommended for SOME patients in selected patient group

» In patients with diabetes, glycaemic goals should be individualised. Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend a HbA1c target ranging from <6.5% to <8.0% for patients with diabetes and chronic kidney disease not receiving dialysis. A lower target (e.g., <6.5% or <7.0%) may be appropriate for individuals in whom preventing complications is the key goal, whereas a higher target (e.g., <7.5% or <8.0%) may be preferred in those with multimorbidity or increased burden of hypoglycaemia.[20] [125] In patients with diabetes and CKD, there is a risk for hypoglycaemia because of impaired kidney clearance of drugs (such as insulin or sulfonylureas) and impaired kidney gluconeogenesis.

» Patients with type 1 diabetes require treatment with insulin, regardless of whether they are on dialysis or not.

» Some specific anti-hyperglycaemic drugs significantly reduce all-cause or cardiovascular mortality, or major cardiovascular events or renal complications in some patient subgroups, and may should be considered independently of HbA1c targets.[68] [69] [70] [71] [72]

» There is evidence that the use of sodium-glucose co-transporter-2 (SGLT2) inhibitors prevents major kidney outcomes (e.g., dialysis, transplantation, or death due to kidney disease) in people with type 2 diabetes.[64] [73] [74] SGLT2 inhibitors, in addition to reducing hyperglycaemia, have renal benefits through independent effects on renal tubular glucose reabsorption, weight, blood pressure, intra-glomerular pressure, albuminuria, and slowed glomerular filtration rate (GFR) loss.[75] [76]

» KDIGO guidelines advise that most patients with type 2 diabetes and CKD would benefit from treatment with metformin (if eGFR ≥ 30 mL/minute/1.73 m²) and an SGLT2 inhibitor (if eGFR ≥ 20 mL/minute/1.73 m²).[20] The American Diabetes Association recommends the use

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of SGLT2 inhibitors in patients with CKD and type 2 diabetes (if eGFR ≥ 20 mL/minute/1.73 m²) regardless of urinary albuminuria.[61] Use of SGLT2 inhibitors is not recommended in patients with end-stage renal disease who are on dialysis.[77]

» If additional glycaemic control is required for patients receiving metformin and an SGLT2 inhibitor, a drug from a different class should be selected. A glucagon-like peptide-1 (GLP-1) is the preferred option. If required, other agents (e.g., a dipeptidyl peptidase-4 [DPP-4] inhibitor, a sulfonylurea, insulin, a thiazolidinedione, or an alpha-glucosidase inhibitor) may be considered based on eGFR, comorbidities, and patient preference.[20]

» As a class of drugs, GLP-1 agonists have beneficial effects on cardiovascular, mortality, and kidney outcomes in patients with type 2 diabetes.[78] [79] GLP-1 agonists may be considered for cardiovascular risk reduction.[61]

» Liraglutide, dulaglutide, and semaglutide are not renally excreted and are the preferred agents in this class.

» Studies report that DPP-4 inhibitors are renoprotective, but do not have a cardiovascular benefit.[80] [81] Some DPP-4 inhibitors require dose adjustment in renal impairment.

adjunct finerenone

Treatment recommended for SOME patients in selected patient group

Primary options

» **finerenone**: 20 mg orally once daily

» Finerenone, a non-steroidal selective mineralocorticoid receptor antagonist, reduces the progression of kidney disease in patients with type 2 diabetes mellitus and known CKD.[82] Finerenone is approved by the US Food and Drug Administration to reduce the risk of kidney function decline, kidney failure, cardiovascular death, non-fatal heart attacks, and hospitalisation for heart failure in adults with CKD associated with type 2 diabetes.

» Guidelines recommend finerenone for patients with type 2 diabetes and albuminuria (if eGFR is ≥ 25 mL/minute/1.73 m² and serum potassium level is normal).[20] [61]

» Monitor serum potassium levels during treatment, and use caution when administering

Acute

■ with anaemia

adjunct

with other drugs that increase serum potassium levels.

education about renal replacement therapy

Treatment recommended for SOME patients in selected patient group

» Educate patients about renal replacement therapy such as haemodialysis, peritoneal dialysis, and kidney transplantation.^[99] ^[114] Patient preference, family support, underlying comorbid conditions, and proximity to a dialysis facility should be addressed when choosing a modality or consideration for palliative care. All patients should undergo CKD education for modality choice.^[99]

» Patients should be referred to surgery for dialysis access and/or evaluated for kidney transplantation, based on patient preference for renal replacement modality at GFR category G4.

» All patients who are proceeding with haemodialysis should be educated about vein preservation with limiting venipuncture and intravenous access in the access arm.^[115]

» Kidney transplantation is indicated once the estimated GFR is <20 mL/minute and the patient has been evaluated and undergone the required testing process by a transplant team.

adjunct

erythropoietin-stimulating agent

Treatment recommended for SOME patients in selected patient group

Primary options

» **epoetin alfa**: consult specialist for guidance on dose

OR

» **darbepoetin alfa**: consult specialist for guidance on dose

» When GFR category G3a/G3b has been reached, identification of comorbidities such as anaemia is recommended and treatment begun if required.

» Treatment of anaemia with the use of erythropoietin-stimulating agents is recommended for patients with CKD after other causes of anaemia such as iron, vitamin B12, folate, or blood loss have been excluded.^[101]

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- » Due to the possibility of an increased risk of stroke in those on erythropoietin-stimulating agents, discussion between the patient and physician should ensue prior to treatment initiation.^{[101] [104] [106] [107]}
- » Erythropoietin-stimulating agents are initiated once the haemoglobin (Hb) falls to <10 g/dL and the patient has signs and symptoms of anaemia.
- » The target Hb for patients with CKD on erythropoietin therapy is 10 to 11 g/dL, as normalisation of Hb has resulted in increased risk for death and cardiovascular disease in this population.^{[102] [103]}

adjunct iron

Treatment recommended for SOME patients in selected patient group

Primary options

- » **ferrous sulfate**: 60 mg orally once to three times daily
Dose refers to elemental iron.

OR

- » **ferrous gluconate**: 60 mg orally once to three times daily
Dose refers to elemental iron.

Secondary options

- » **sodium ferric gluconate complex**: consult specialist for guidance on dose

OR

- » **iron sucrose**: consult specialist for guidance on dose

OR

- » **ferumoxytol**: consult specialist for guidance on dose

OR

- » **ferric carboxymaltose**: consult specialist for guidance on dose

- » All patients should have an assessment of iron stores if erythropoietin therapy is planned. The goal ferritin for those not on haemodialysis is >100 nanograms/mL, while for those on

Acute

■ with secondary hyperparathyroidism

plus

haemodialysis is >200 nanograms/mL. All patients should have a transferrin saturation >20%. Iron replacement can be given orally or parenterally.[108] [127]

dietary modification ± phosphate-binding drug

Treatment recommended for ALL patients in selected patient group

Primary options

» **sevelamer hydrochloride**: 800-1600 mg orally three times daily, titrate according to serum phosphate level

OR

» **calcium acetate**: 1334 mg orally with each meal, titrate according to serum phosphate level

OR

» **calcium carbonate**: 1-2 g/day orally given in 3-4 divided doses

OR

» **lanthanum**: 500-1000 mg orally three times daily, titrate according to serum phosphate level

OR

» **sucroferric oxyhydroxide**: 500 mg orally three times daily initially, titrate according to serum phosphate level, maximum 3000 mg/day

OR

» **colestilan**: 2-3 g orally three times daily initially, titrate according to serum phosphate level, maximum 15 g/day

» When GFR category G3a/G3b has been reached, identification of comorbidities such as secondary hyperparathyroidism is recommended and treatment begun if required. The calcium and phosphorus levels should be maintained in the normal range with dietary restriction and/or phosphate-binding drugs.

» Phosphate binders should be initiated to normalise phosphorus levels if patients are

Acute

unable to sufficiently restrict phosphorus in the diet.^[111] Calcium-based phosphate binders should be restricted if there is associated hypercalcaemia, arterial calcification, suppressed parathyroid hormone (PTH), or adynamic bone disease.^[111]

» Calcium, phosphorus, and PTH testing should be performed every 6 to 12 months for patients with GFR category G3a/G3b CKD and secondary hyperparathyroidism. For patients with GFR category G4 CKD and secondary hyperparathyroidism, calcium and phosphate should be checked every 3 to 6 months, and PTH every 6 to 12 months.^[111] [Evidence C]

» There is limited evidence that dietary restriction in calcium and phosphorus affects renal osteodystrophy.^[128]

» There is emerging evidence that the use of non-calcium-based phosphate binders has a survival advantage over calcium-based phosphate binders in patients with CKD.^[111] [113] [Evidence B]

adjunct ergocalciferol

Treatment recommended for SOME patients in selected patient group

Primary options

» **ergocalciferol**: dose depends on serum 25-OH vitamin D level; consult specialist for guidance on dose

» 25-OH vitamin D deficiency should be excluded. If the serum level of 25-OH vitamin D is <75 nanomol/L (<30 nanograms/mL), vitamin D supplementation with ergocalciferol should be initiated.^[109]^[110]

adjunct active vitamin D analogue

Treatment recommended for SOME patients in selected patient group

Primary options

» **calcitriol**: consult specialist for guidance on dose

OR

» **paricalcitol**: consult specialist for guidance on dose

OR

Acute

■ with metabolic acidosis

adjunct

» [doxercalciferol](#): consult specialist for guidance on dose

» It is not routinely recommended to use active vitamin D analogues for CKD not requiring dialysis unless hyperparathyroidism is progressive or severe.^[111]

» The optimal parathyroid hormone level is currently not known.

oral sodium bicarbonate

Treatment recommended for SOME patients in selected patient group

Primary options

» [sodium bicarbonate](#): consult specialist for guidance on dose

» For patients who develop metabolic acidosis, supplementation with oral sodium bicarbonate has been shown to slow progression of CKD.^[116] Oral sodium bicarbonate is well tolerated in this group.

GFR category G5 or with uraemia

GFR category G5 or with uraemia

1st

dialysis

» Renal replacement therapy is initiated once patients have GFR category G5 disease and/or signs of uraemia such as weight loss, lack of appetite, nausea, vomiting, acidosis, hyperkalaemia, or fluid overload.^[1]

» Renal replacement therapy in the form of dialysis is designed to remove toxic waste products from the blood, such as urea, and normalise potassium and serum bicarbonate levels, as well as to remove fluid that will accumulate once the kidneys have failed.

» All patients should undergo CKD education for modality choice.^[99]

» Peritoneal dialysis is performed at home and is available to all patients. A peritoneal dialysis catheter is inserted into the abdomen and dialysis fluid is instilled in order to allow for toxic waste products and fluid to be removed and drained from the body on a daily basis.

» Continuous cycling peritoneal dialysis is done with a machine at night on a daily basis.

» Continuous ambulatory peritoneal dialysis is done on a daily basis. Patients manually exchange the peritoneal fluid.

Acute

■ with anaemia

adjunct

» Haemodialysis is usually prescribed in a treatment centre 3 times a week for approximately 4 hours each session. Haemodialysis can also be carried out at home, usually 4 to 5 days a week, 3 to 4 hours a day. The patient's blood is removed from the body through an arteriovenous fistula, an arteriovenous graft, or a dialysis catheter, and then returned after traversing a dialysis membrane and dialysis solution. Other dialysis options include short daily dialysis and nocturnal dialysis, which are available at some treatment centres.

erythropoietin-stimulating agent

Treatment recommended for SOME patients in selected patient group

Primary options

» **epoetin alfa**: consult specialist for guidance on dose

OR

» **darbepoetin alfa**: consult specialist for guidance on dose

» Treatment of anaemia with the use of erythropoietin-stimulating agents is recommended for patients with CKD after other causes of anaemia such as iron, vitamin B12, folate, or blood loss have been excluded.^[101] Due to the possibility of an increased risk of stroke in those on erythropoietin-stimulating agents, discussion between the patient and physician should ensue prior to treatment initiation.^{[101] [104] [106] [107]}

» Erythropoietin-stimulating agents are initiated once the haemoglobin (Hb) falls to <10 g/dL and the patient has signs and symptoms of anaemia.

» The target Hb for patients with CKD on erythropoietin therapy is 10 to 11 g/dL, as normalisation of Hb has resulted in increased risk for death and cardiovascular disease in this population.^{[102] [103]}

adjunct

iron

Treatment recommended for SOME patients in selected patient group

Primary options

» **ferrous sulfate**: 60 mg orally once to three times daily

Dose refers to elemental iron.

Acute

OR

» **ferrous gluconate**: 60 mg orally once to three times daily
Dose refers to elemental iron.

OR

» **sodium ferric gluconate complex**: consult specialist for guidance on dose

OR

» **iron sucrose**: consult specialist for guidance on dose

OR

» **ferumoxytol**: consult specialist for guidance on dose

OR

» **ferric carboxymaltose**: consult specialist for guidance on dose

OR

» **ferric pyrophosphate citrate**: consult specialist for guidance on dose

» All patients should have an assessment of iron stores if erythropoietin therapy is planned. The goal ferritin for those not on haemodialysis is >100 nanograms/mL, while for those on haemodialysis it is >200 nanograms/mL. All patients should have a transferrin saturation >20%. Iron replacement can be given orally or parenterally.[108] [127] Oral iron will be sufficient to maintain and attain the Hb within targets in erythropoietin-stimulating agent-treated CKD patients on peritoneal dialysis; however, most patients on haemodialysis will require intravenous iron.[129]

■ with secondary hyperparathyroidism

plus

dietary modification ± phosphate-binding drug

Treatment recommended for ALL patients in selected patient group

Primary options

» **sevelamer hydrochloride**: 800-1600 mg orally three times daily initially, titrate according to serum phosphate level

Acute

OR

» **calcium acetate**: 1334 mg orally with each meal initially, titrate according to serum phosphate level

OR

» **calcium carbonate**: 1-2 g/day orally given in 3-4 divided doses

OR

» **lanthanum**: 500-1000 mg orally three times daily initially, titrate according to serum phosphate level

OR

» **sucroferric oxyhydroxide**: 500 mg orally three times daily initially, titrate according to serum phosphate level, maximum 3000 mg/day

» For patients with GFR category G5 CKD on dialysis, calcium, phosphorus, and intact parathyroid hormone (PTH) levels should be managed with phosphate binding agents, calcimimetics, active vitamin D analogues, or a combination of these based on serial laboratory assessments.

» Phosphate binders such as calcium, lanthanum, and sevelamer should be initiated to normalise phosphorus levels if patients are unable to sufficiently restrict phosphorus in the diet.^[111] Calcium-based phosphate binders should be restricted if there is associated hypercalcaemia, arterial calcification, suppressed PTH, or adynamic bone disease.^[111]

» Increasing dialytic phosphate removal may be required in cases of persistent hyperphosphataemia.

» Calcium and phosphorus testing every 1 to 3 months and PTH testing every 3 to 6 months should be performed for patients with GFR category G5 CKD and secondary hyperparathyroidism.^[111] [\[Evidence C\]](#)

adjunct

calcimimetic ± active vitamin D analogue

Treatment recommended for SOME patients in selected patient group

Acute

Primary options

» **cinacalcet**: 30 mg orally once daily initially, increase dose according to serum PTH level, maximum 180 mg/day

--AND/OR--

» **calcitriol**: consult specialist for guidance on dose

-or-

» **paricalcitol**: consult specialist for guidance on dose

-or-

» **doxercalciferol**: consult specialist for guidance on dose

Secondary options

» **etelcalcetide**: adults: 5 mg intravenously three times weekly at the end of haemodialysis treatment, adjust dose according to PTH level and corrected serum calcium response, maintenance dose ranges from 2.5 to 15 mg three times weekly

--AND/OR--

» **calcitriol**: consult specialist for guidance on dose

-or-

» **paricalcitol**: consult specialist for guidance on dose

-or-

» **doxercalciferol**: consult specialist for guidance on dose

» For those requiring parathyroid hormone (PTH)-lowering therapy, calcimimetics (e.g., cinacalcet, etelcalcetide), active vitamin D analogues (e.g., calcitriol, paricalcitol, doxercalciferol), or a combination of a calcimimetic with an active vitamin D analogue should be given.^[111]

» Etelcalcetide is a second-generation, type II calcimimetic that may be used when treatment with a calcimimetic is indicated but cinacalcet is not a suitable option. It is given intravenously (rather than orally like cinacalcet) and has a longer half-life than cinacalcet.

adjunct ergocalciferol

Treatment recommended for SOME patients in selected patient group

Primary options

Acute

» **ergocalciferol**: dose depends on serum 25-OH vitamin D level; consult specialist for guidance on dose

» 25-OH vitamin D deficiency should be excluded. If the serum level of 25-OH vitamin D is <75 nanomol/L (<30 nanograms/mL), vitamin D supplementation with ergocalciferol should be initiated.^{[109][110]}

2nd kidney transplant

» Kidney transplant confers a significant survival advantage over maintenance dialysis therapy, predominantly due to a decrease in the risk of cardiovascular death. All patients who are on dialysis therapy are potentially eligible for kidney transplantation. A transplant centre including a nephrologist and transplant surgeon will determine the final eligibility and status of the patient for kidney transplantation, after a complete medical history and evaluation. Kidneys may be transplanted from deceased or living donors.

Emerging

Roxadustat

Roxadustat is an oral inhibitor of hypoxia-inducible factor (HIF) prolyl hydroxylase that stimulates erythropoiesis and regulates iron metabolism. It shows promise as an alternative to epoetin alfa as a therapy for anaemia in patients with CKD. It is currently in phase 3 clinical trials.^{[130] [131]} One meta-analysis of existing phase 2 and phase 3 trials concluded that haemoglobin levels increased in patients with CKD who were not on dialysis and haemoglobin levels were maintained in those patients requiring dialysis.^[132] The European Medicines Agency has approved the use of roxadustat for the treatment of adults with symptomatic anaemia associated with CKD. The US Food and Drug Administration has requested further trials on the safety of roxadustat in both non-dialysis-dependent and dialysis-dependent patient populations.

Daprodustat

Daprodustat is an oral inhibitor of HIF prolyl-hydroxylase. In phase 3 trials of patients with CKD (not undergoing dialysis and undergoing dialysis) and anaemia, it was shown to be non-inferior to erythropoiesis-stimulating agents for change in the haemoglobin level from baseline and major cardiovascular adverse events.^{[133] [134]} Daprodustat is currently approved for use in Japan.

Veverimer

Veverimer is a non-absorbed polymer which selectively binds and removes hydrochloric acid from the gastrointestinal lumen and is being investigated for the treatment of metabolic acidosis in patients with CKD. It has been shown to significantly increase serum bicarbonate concentration, with minimal adverse effects. The US Food and Drug Administration is currently reviewing an application for approval.^{[135] [136]}

Primary prevention

The evidence for the prevention of CKD is lacking as compared with large-scale randomised trials for cardiovascular disease. Most trials have focused on modifiable diseases and risk factors that have been associated with CKD, namely diabetes and hypertension. Clinical evidence supports the recommendation for a goal HbA1c <7%, blood pressure target of <140/90 mmHg, tobacco cessation, and ideal body weight with BMI <27 to prevent the development of CKD.^{[26] [29][42]} Due to the lack of widespread screening guidelines with serum creatinine or urinary albumin, often patients are diagnosed after CKD has developed.^[43]

Secondary prevention

Prevention of further kidney function loss is the primary goal in conservative management of people with CKD.^[63] Kidney-preserving care includes non-pharmacological (e.g., dietary and lifestyle adjustments) and pharmacological strategies.^[63] Underlying risk factors associated with disease states should be treated, including optimisation of glycaemic control in diabetes and achievement of the goal blood pressure of <140/90 mmHg with ACE inhibitors or angiotensin-II receptor antagonists. Consideration can be given to a lower blood pressure goal in those with proteinuria of >500 mg per 24 hours.^{[83] [84] [90]} Although data are limited in the CKD population as compared with the general population, tobacco cessation, weight loss, salt restriction, and optimal lipid management with statin therapy are indicated. Protein restriction is recommended in late-stage (GFR category G4 or G5) disease, as a management strategy to delay the initiation of dialysis; however, severe protein restriction may result in malnourishment and impact on quality of life.^[123] Aspirin use has also been beneficial for cardioprotection in those with CKD, although there is a higher risk for minor bleeding than in the general population.

Patient discussions

Patients with CKD need to take an active role in managing their disease and monitoring their progression to more advanced stages such as glomerular filtration rate (GFR) category G4 to G5. Dietary therapy

such as restriction of potassium, phosphorus and salt, protein, and fluids is typically advocated for GFR category G3 to G5. Adherence to drug therapy, optimisation of glycaemic control, and blood pressure control are the leading factors that delay progression of CKD and the need for renal replacement therapy.

As patients progress to GFR category G4 CKD, it is recommended that they attend educational classes at a CKD clinic where different dialysis modalities such as haemodialysis and peritoneal dialysis are discussed, to determine their option of choice. Patients may be evaluated for kidney transplantation and referred to a transplant centre at this time. Once a patient has attended educational classes and made an informed decision about dialysis modality, referral for surgery may be done for dialysis access placement.

Monitoring

Monitoring

Patients with risk factors for CKD, such as diabetes, hypertension, or cardiovascular disease, should be evaluated with estimated glomerular filtration rate (GFR; based on creatinine and, if available, cystatin C) and measurement of albuminuria (urine albumin-to-creatinine ratio). See Screening .

CKD progression

For those with established CKD, the rate of progression of CKD should be serially assessed starting in GFR category G3a/G3b disease.

For patients with diabetes and CKD, the American Diabetes Association recommends monitoring with urinary albumin and eGFR 1-4 times per year, depending on the stage of disease (e.g., 1-2 times a year if G1 to G3a and normal or moderately increased albuminuria; 3-4 times a year if severely increased albuminuria or G4 or G5).^[61]

Patients should be screened for anaemia and bone mineral disorders at least every 6-12 months, with a haemoglobin, calcium, phosphorus, and intact parathyroid hormone (PTH). For those in GFR category G4 disease, haemoglobin, calcium, phosphorus should be monitored every 3-6 months and intact PTH every 6-12 months. For patients in GFR category G5 CKD, anaemia should be evaluated with a monthly haemoglobin, and bone mineral disease with a calcium and phosphorus every 1-3 months and an intact PTH every 3-6 months. Lipids should be checked annually for all patients with CKD.

Complications

Complications	Timeframe	Likelihood
anaemia	long term	high
Anaemia of chronic kidney disease is due to a deficiency of erythropoietin as the glomerular filtration rate (GFR) declines. Anaemia is typically identified in GFR category G3a/G3b CKD. Patients should be screened with a full blood count at least every 6 to 12 months, and an erythropoietin-stimulating agent may be considered once the haemoglobin (Hb) falls to <100 g/L (<10 g/dL) and there are symptoms of anaemia. The target Hb is 100 to 110 g/L (10 to 11 g/dL).^{[101] [104] [137]} If the patient is iron-deficient, oral or intravenous supplementation may also be prescribed.^[108] Patients with CKD on erythropoietin-stimulating agents for the treatment of anaemia have a higher risk of death and cardiovascular complications if the Hb is normalised >130 g/L (>13 g/dL).^{[102] [103][138] [139] [140]}		
renal osteodystrophy	long term	high
May be caused by an elevation in parathyroid hormone (PTH) as a result of phosphorus retention and hypocalcaemia from 1,25 vitamin D deficiency as the glomerular filtration rate (GFR) declines. Severe hyperparathyroidism and hyperphosphataemia are risk factors for death, cardiovascular disease, and vascular calcification in patients with CKD.^{[111] [Evidence C]} Patients with GFR category G3 to G5 CKD should be routinely monitored for hyperparathyroidism and treatments based on serial assessments of phosphorus, calcium, and PTH levels, considered together.^[111] 25-OH vitamin D should be monitored and treatment initiated if the serum level of 25-OH vitamin D is <75 nanomol/L (<30 nanograms/mL).^{[109][110]}		
cardiovascular disease	long term	high
CKD is a risk factor for cardiovascular disease independent of comorbidities such as diabetes, hypertension, and dyslipidaemia. Cardiovascular disease is the leading cause of death for these patients, and the overwhelming majority of patients with CKD will die prior to reaching the need for renal replacement therapy. The goal in treatment of cardiovascular disease in patients with CKD is early recognition and risk factor modification, including lipid therapy, optimisation of blood pressure and glycaemic control, tobacco cessation, and aspirin use.^{[142] [143]}		
protein malnutrition	variable	medium
As the glomerular filtration rate falls, patients develop anorexia, nausea, vomiting, and lack of protein intake. Previously, patients with advanced CKD were placed on very-low- to low-protein diets to reduce the risk for end-stage kidney disease, but this recommendation has limitations due to its worsening of malnutrition. It is recommended for patients with CKD stages 3 to 5 who are metabolically stable to have 0.6 g/kg body weight protein intake daily and those with diabetes (not on dialysis) to have 0.6 to 0.8 g/kg body weight protein intake daily.^[141] In patients on dialysis, a dietary protein intake of 1.0 to 1.2 g/kg body weight daily is recommended to maintain a stable nutritional status.^[141]		

Complications	Timeframe	Likelihood
metabolic acidosis	variable	medium
Metabolic acidosis is common in patients with CKD, due to the inability of the kidney to excrete acid once the estimated glomerular filtration rate is <50 mL/minute. The anion gap is typically normal, but may be increased in uraemia with retention of phosphate anions. Rarely does the serum bicarbonate level fall below 12 mmol/L (12 mEq/L). Metabolic acidosis may worsen renal osteodystrophy and cause malnutrition, hypercatabolism, and growth retardation. Treatment involves the administration of sodium bicarbonate 0.5 to 1.0 mmol/kg/day (0.5 to 1.0 mEq/kg/day) for a target serum bicarbonate level >20 mmol/L (>20 mEq/L). Sodium citrate as a bicarbonate source is generally avoided in patients with CKD, as it increases the absorption of aluminium and may contribute to bone disease and dementia.^{[144] [145]}		
hyperkalaemia	variable	medium
Hyperkalaemia is common in patients with CKD, due to the kidney's inability to excrete potassium from the diet as the estimated glomerular filtration rate declines. Hyperkalaemia is more common in patients with oliguria, resistant or deficient aldosterone state, or co-existing metabolic acidosis. Most patients with hyperkalaemia are asymptomatic, but some may present with muscle weakness. The hallmark for the severity of hyperkalaemia is identification of cardiac disturbances on an ECG with peaked T waves, prolongation of the conduction system, sine wave, or asystole. Hyperkalaemia associated with cardiac conduction disturbances is a medical emergency and is treated with intravenous calcium; drugs to shift potassium into the cells, such as insulin and dextrose; beta-agonists and the focused removal of potassium from the body with loop diuretics, if kidney function is intact; oral potassium binders (e.g., sodium polystyrene sulfonate, patiomer, sodium zirconium cyclosilicate); and, in severe cases, haemodialysis.		
pulmonary oedema	variable	medium
Fluid overload occurs in patients with CKD, especially those with concomitant congestive heart failure. Treatment of fluid overload with loop diuretics is often used to prevent episodes of pulmonary oedema and manage peripheral oedema. In some instances, a combination diuretic regimen (e.g., a loop and a thiazide diuretic) provides a more effective diuresis in patients. Failure to maintain fluid balance in those with advanced glomerular filtration rate category G4 and G5 CKD is an indication to start renal replacement therapy.		

Prognosis

CKD is mostly progressive and leads to end-stage renal disease (ESRD) and the need for renal replacement therapy (i.e., dialysis, transplant). Though it cannot be cured, it can be controlled and managed to a large extent. CKD is a strong cardiovascular risk factor, and the majority of patients with CKD will die prior to reaching ESRD. As kidney function declines, complications such as anaemia and hyperparathyroidism develop that may contribute to worsening cardiovascular disease and renal osteodystrophy, respectively. Glycaemic control directly correlates with the development of diabetic kidney disease and the rapidity of progression to end-stage renal disease.^[12] There is evidence that the use of sodium-glucose co-

transporter-2 (SGLT2) inhibitors prevents major kidney outcomes (e.g., dialysis, transplantation, or death due to kidney disease) in people with type 2 diabetes.[73] Optimisation of blood pressure control with the use of ACE inhibitors or angiotensin-II receptor antagonist agents and reduction in proteinuria may slow the rate of progression to ESRD and the eventual need for renal replacement therapy.

Diagnostic guidelines

United Kingdom

Chronic kidney disease: assessment and management (<https://www.nice.org.uk/guidance/ng203>)

Published by: National Institute for Health and Care Excellence

Last published: 2021

International

KDIGO clinical practice guideline for the evaluation and management of chronic kidney disease (<https://kdigo.org/guidelines>)

Published by: Kidney Disease: Improving Global Outcomes

Last published: 2012

North America

ACR appropriateness criteria: renal failure (<https://www.acr.org/Clinical-Resources/ACR-Appropriateness-Criteria>)

Published by: American College of Radiology

Last published: 2020

Treatment guidelines

United Kingdom

Management of adults with diabetes on dialysis (<https://abcd.care/joint-british-diabetes-societies-jbds-inpatient-care-group>)

Published by: Joint British Diabetes Societies

Last published: 2022

Chronic kidney disease: assessment and management (<https://www.nice.org.uk/guidance/ng203>)

Published by: National Institute for Health and Care Excellence

Last published: 2021

Clinical practice guideline: exercise and lifestyle in chronic kidney disease (<https://ukkidney.org/health-professionals/guidelines/guidelines-commentaries>)

Published by: Renal Association

Last published: 2021

Anaemia of chronic kidney disease (<https://renal.org/health-professionals/guidelines/guidelines-commentaries>)

Published by: Renal Association

Last published: 2020

Haemodialysis (<https://renal.org/health-professionals/guidelines/guidelines-commentaries>)

Published by: Renal Association

Last published: 2019

Undernutrition in chronic kidney disease (<https://renal.org/health-professionals/guidelines/guidelines-commentaries>)

Published by: Renal Association

Last published: 2019

Renal replacement therapy and conservative management (<https://www.nice.org.uk/guidance/ng107>)

Published by: National Institute for Health and Care Excellence

Last published: 2018

International

KDIGO clinical practice guideline for diabetes management in chronic kidney disease (<https://kdigo.org/guidelines>)

Published by: Kidney Disease: Improving Global Outcomes

Last published: 2022

KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease (<https://kdigo.org/guidelines>)

Published by: Kidney Disease: Improving Global Outcomes

Last published: 2021

KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD) (<https://kdigo.org/guidelines>)

Published by: Kidney Disease: Improving Global Outcomes

Last published: 2017

KDIGO clinical practice guideline for lipid management in chronic kidney disease (<https://kdigo.org/guidelines>)

Published by: Kidney Disease: Improving Global Outcomes

Last published: 2013

KDIGO clinical practice guideline for the evaluation and management of chronic kidney disease (<https://kdigo.org/guidelines>)

Published by: Kidney Disease: Improving Global Outcomes

Last published: 2012

KDIGO clinical practice guideline for anemia in chronic kidney disease (<https://kdigo.org/guidelines>)

Published by: Kidney Disease: Improving Global Outcomes

Last published: 2012

North America

Standards of care in diabetes - 2024: chronic kidney disease and risk management (https://diabetesjournals.org/care/issue/47/Supplement_1)

Published by: American Diabetes Association

Last published: 2023

Clinical practice guideline for nutrition in CKD: 2020 update (<https://www.kidney.org/professionals/guidelines>)

Published by: National Kidney Foundation Kidney Disease Outcomes Quality Initiative

Last published: 2020

Preservation of peripheral veins in patients with chronic kidney disease (<https://www.avainfo.org/page/PositionPapers>)

Published by: Association for Vascular Access

Last published: 2011

Online resources

1. [BMJ talk medicine: chronic kidney disease \(https://soundcloud.com/bmjpodcasts/chronic-kidney-disease?in=bmjpodcasts/sets/bmj-best-practice-clinical\)](https://soundcloud.com/bmjpodcasts/chronic-kidney-disease?in=bmjpodcasts/sets/bmj-best-practice-clinical) (*external link*)
2. [National Kidney Foundation: eGFR calculator \(https://www.kidney.org/professionals/gfr_calculator\)](https://www.kidney.org/professionals/gfr_calculator) (*external link*)
3. [BMJ Rapid Recommendation: SGLT2-inhibitors for adults with CKD \(https://www.bmj.com/content/387/bmj-2024-080257\)](https://www.bmj.com/content/387/bmj-2024-080257) (*external link*)

Evidence tables

What are the effects of calcium-containing phosphate binders versus calcium-free phosphate binders in people with chronic kidney disease-mineral and bone disorder (CKD-MBD)?^[111]



This table is a summary of the analysis reported in a guideline (underpinned by a systematic review) that focuses on the above important clinical question.

View the full source guideline (<https://kdigo.org/guidelines/ckd-mbd>)

Evidence B ^{*}

Confidence in the evidence is moderate or low to moderate where GRADE has been performed and the intervention may be less effective or likely to be more harmful than the comparison for key outcomes.

Population: Pre-dialysis or dialysis adults with hyperphosphatemic CKD ^a

Intervention: Calcium-containing phosphate binders

Comparison: Calcium-free phosphate binders

Outcome	Effectiveness (BMJ rating) [†]	Confidence in evidence (GRADE) [‡]
Mortality	Favours comparison	Moderate
Cardiovascular and cerebrovascular events	See note ^b	Low

Recommendations as stated in the source guideline

The 2017 Kidney Disease Improving Global Outcomes (KDIGO) guideline on CKD-MBD makes the following recommendation:

In adult patients with CKD (GFR category) G3a–G5D receiving phosphate-lowering treatment, we suggest restricting the dose of calcium-based phosphate binders (weak recommendation; moderate-quality evidence).

Note

^a Population as reported by the guideline.

^b The guideline reported results for this outcome narratively due to inconsistent results across studies. See guideline for more information.

What are the effects of lower versus higher levels of serum phosphate or calcium in people with chronic kidney disease (CKD) G3a-G5 or G5D?[111]

 This table is a summary of the analysis reported in a guideline (underpinned by a systematic review) that focuses on the above important clinical question.

[View the full source guideline \(https://kdigo.org/guidelines/ckd-mbd\)](https://kdigo.org/guidelines/ckd-mbd)

Evidence C * Confidence in the evidence is very low or low where GRADE has been performed and the intervention may be more effective/beneficial than the comparison for key outcomes. However, this is uncertain and new evidence could change this in the future.

Population: People with CKD G3a-G5 or G5D

Intervention: Lower concentrations of serum phosphate or calcium

Comparison: Higher concentrations of serum phosphate or calcium

Outcome	Effectiveness (BMJ rating) [†]	Confidence in evidence (GRADE) [‡]
Serum phosphate		
Mortality	Favours intervention	Low
Glomerular Filtration Rate (GFR) decline	See note ^a	Very Low
Cardiovascular and cerebrovascular events	See note ^b	Very Low
Serum calcium		
Mortality	Favours intervention	Low
Cardiovascular and cerebrovascular events	Favours intervention	Low

Recommendations as stated in the source guideline

The 2017 Kidney Disease Improving Global Outcomes (KDIGO) guideline on CKD-MBD makes the following recommendations:

- In patients with CKD (GFR category) G3a–G5D, treatments of CKD-MBD should be based on serial assessments of phosphate, calcium, and parathyroid hormone (PTH) levels, considered together (not graded).
- In people with CKD G3a-G5D, we suggest lowering elevated phosphate levels toward the normal range (weak recommendation; low-quality evidence).
- In adult patients with CKD G3a–G5D, we suggest avoiding hypercalcaemia (weak recommendation; low-quality evidence).

- 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 (not graded).^c

Note

The guideline only identified evidence from observational studies to answer this clinical question.

- ^a Reported as inconclusive based on indirect evidence from 8 observational studies (N=3755).
- ^b Reported as inconclusive based on direct evidence from 7 observational studies (N=34231).
- ^c The guideline group also recommended reasonable monitoring intervals (not graded). See guideline for more information.

* Evidence levels

The Evidence level is an internal rating applied by BMJ Best Practice. See the [EBM Toolkit \(https://bestpractice.bmj.com/info/evidence-tables/\)](https://bestpractice.bmj.com/info/evidence-tables/) for details.

Confidence in evidence

- A** - High or moderate to high
- B** - Moderate or low to moderate
- C** - Very low or low

† Effectiveness (BMJ rating)

Based on statistical significance, which demonstrates that the results are unlikely to be due to chance, but which does not necessarily translate to a clinical significance.

‡ Grade certainty ratings

High	The authors are very confident that the true effect is similar to the estimated effect.
Moderate	The authors are moderately confident that the true effect is likely to be close to the estimated effect.
Low	The authors have limited confidence in the effect estimate and the true effect may be substantially different.
Very Low	The authors have very little confidence in the effect estimate and the true effect is likely to be substantially different.

BMJ Best Practice EBM Toolkit: What is GRADE? (<https://bestpractice.bmj.com/info/toolkit/learn-ebm/what-is-grade/>)

Key articles

- Kidney Disease: Improving Global Outcomes (KDIGO). KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl.* 2013 Jan;3(1):1-150. [Full text \(https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf\)](https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf)
- National Institute for Health and Care Excellence. Chronic kidney disease: assessment and management. 2021 [internet publication]. [Full text \(https://www.nice.org.uk/guidance/ng203\)](https://www.nice.org.uk/guidance/ng203)
- Expert Panel on Urologic Imaging., Wong-You-Cheong JJ, Nikolaidis P, et al. ACR Appropriateness Criteria® Renal Failure. *J Am Coll Radiol.* 2021 May;18(5s):S174-S188. [Full text \(https://www.doi.org/10.1016/j.jacr.2021.02.019\)](https://www.doi.org/10.1016/j.jacr.2021.02.019) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33958111?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33958111?tool=bestpractice.bmj.com)

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2. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 clinical practice guideline for the management of glomerular diseases. *Kidney Int.* 2021 Oct;100(4s):S1-276. [Full text \(https://kdigo.org/guidelines/gd\)](https://kdigo.org/guidelines/gd) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34556256?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34556256?tool=bestpractice.bmj.com)
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This approach is in line with the guidance of the [International Bureau of Weights and Measures Service](#).

Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

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