

# Managing chronic kidney disease

**Chronic kidney disease (CKD) is a major public health issue affecting one in seven Australians. GPs play a vital role in the identification and early management of renal disease and their interventions can prevent affected patients progressing to kidney failure and dying from cardiovascular disease.**

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The first national kidney disease prevalence study, the 2003 AusDiab Kidney Study, established that one in three Australians is at risk of developing chronic kidney disease (CKD).<sup>1</sup> In addition, it found that one in seven adults aged over 25 years already has at least one indicator of CKD – proteinuria, haematuria or a reduced glomerular filtration rate (GFR).<sup>1</sup> In the same year, 2003, CKD ranked as the seventh most common cause of death in Australia.<sup>2</sup> Worldwide, the economic and healthcare burden associated with kidney disease continues to climb. In Australia, the population has grown by less than 40% over the last 25 years while the number of Australians being treated with dialysis or kidney transplantation has increased by more than 400%.

A major difficulty with early identification of patients with CKD is that in 80 to 90% of cases the

disease goes unrecognised because many people lack symptoms. Early detection is, however, crucial because CKD is a major risk factor for cardiovascular disease. Individuals with CKD have up to a 10- to 20-fold increased risk of cardiac death than age- and sex-matched controls without CKD. For example, a 25-year-old woman with advanced CKD has approximately the same risk of cardiovascular death as a 75-year-old man without kidney disease.

Patients with CKD are at least 20 times more likely to die from cardiovascular disease than survive to the point of needing dialysis or kidney transplantation. Early identification and management of CKD in at-risk patients has been shown to be cost-effective and can reduce the risk of kidney failure progression and cardiovascular disease by 20 to 50%.

## IN SUMMARY

- Over two million Australians have chronic kidney disease (CKD).
- The major risk factors for CKD are diabetes, hypertension, smoking, obesity, age over 50 years, a family history of CKD, and Aboriginal and Torres Strait Islander origin.
- 'Kidney checks', which include measurement of blood pressure, serum creatinine and estimated glomerular filtration rate and urine dipstick testing for protein, should be carried out annually for patients with one or more CKD risk factors.
- Patients with CKD are at increased risk of developing cardiovascular disease and more likely to die from this than end up on dialysis.
- Lifestyle modification, treatment of blood pressure to target and the reduction of proteinuria are the key tasks for managing CKD.
- Only a small proportion of patients with CKD require referral to a nephrologist.

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**Table 1. CKD management: the GP's role**

- Identification and screening of patients with risk factors for CKD
- Early detection of CKD
- Reduction of cardiovascular risk and progression of kidney failure in patients with CKD
- Timely management of CKD complications
- Avoidance of nephrotoxic medications
- Evaluation of medications to ensure dosages are appropriate for patients' level of kidney function
- Counselling and support of patients with CKD
- Timely referral of patients to a nephrologist (only required by a few patients with CKD)

This article describes the crucial role general practitioners play in screening, identifying and managing patients with CKD and provides practical advice in relation to this role (Table 1).

**Definition and staging of CKD**

**Definition**

CKD is defined as a moderate to severe reduction in kidney function measured by a GFR of less than 60 mL/min/1.73 m<sup>2</sup> and/or evidence of kidney damage for at



Figure. Urine dipstick testing for proteinuria should be carried out as part of an annual kidney check for patients with one or more risk factors for CKD.

least three months. Evidence of kidney damage (with or without a decrease in GFR) is indicated by any of the following:

- microalbuminuria – a urinary albumin excretion rate of 30 to 300 mg/day
- macroalbuminuria – a urinary albumin excretion rate of greater than 300 mg/day
- persistent haematuria – where other causes, such as urological causes, have been excluded
- pathological abnormalities – such as abnormal renal biopsy
- radiological abnormalities – such as scarring or polycystic kidneys on renal ultrasound.

**Staging**

CKD is classified into five stages according to the severity of the GFR reduction and the presence of kidney damage (Table 2). In Australia, it is estimated that 400,000 people have stage 1 CKD, 500,000 have stage 2, and 1.4 million Australians have stage 3 CKD. As many as 40,000 Australians have stage 4 CKD and 15,000 have stage 5 (end-stage disease), where their GFR is less than 15 mL/min/1.73 m<sup>2</sup> or dialysis is required.

**Screening for CKD**

Seven risk factors for CKD have been identified and classified into modifiable or nonmodifiable factors (Table 3). Screening patients with CKD risk factors is recommended under the RACGP *Guidelines for Preventive Activities in General Practice* (the Red Book).<sup>4</sup> Patients considered 'at risk' should receive an annual 'Kidney Check'. This should include measurement of:

- blood pressure
- serum creatinine
- estimated GFR (eGFR) and
- measurement of proteinuria using urine dipstick testing.

It is essential that all the 'kidney check' tests be performed to maximise the likelihood of detecting CKD because there

**Table 2. Stages of chronic kidney disease\***

Stage	GFR (mL/min/1.73 m <sup>2</sup> )
<b>Stage 1.</b> Kidney damage with normal or increased GFR	≥90
<b>Stage 2.</b> Kidney damage with mildly decreased GFR	60–89
<b>Stage 3.</b> Moderately decreased GFR with or without kidney damage	30–59
<b>Stage 4.</b> Severely decreased GFR with or without kidney damage	15–29
<b>Stage 5.</b> End-stage kidney failure	<15 or on dialysis

\* Based on the Caring for Australasians with Renal Impairment (CARI) guidelines, 2005.<sup>3</sup>

**Table 3. Risk factors for CKD****Modifiable risk factors**

Diabetes mellitus  
Hypertension  
Smoking  
Obesity

**Nonmodifiable risk factors**

Age greater than 50 years  
Family history of CKD  
Aboriginal or Torres Strait Islander origin

**Table 4. Patients in whom eGFR should be interpreted cautiously**

- Patients with rapidly changing kidney function – e.g. acute kidney failure
- Dialysis-dependent patients
- Patients with exceptional dietary intake – e.g. those who have a vegetarian or high protein diet, or take creatine supplements
- Patients who have ingested cooked meat within three hours prior to blood sampling
- Patients with extremes of body size
- Patients with diseases of skeletal muscle, paraplegia or high muscle mass, and amputees
- Patients with severe liver disease
- Children aged under 18 years
- Patients with eGFR values above 60 mL/min/1.73 m<sup>2</sup>
- Aboriginal and Torres Strait Islander peoples
- Asian populations (including Japanese, Chinese and Vietnamese)
- Maori and Pacific Islander peoples

is variable overlap with the four individual indicators of kidney damage. For example, in the AusDiab study<sup>1</sup>, 92% of patients with an eGFR of less than 60 mL/min/1.73 m<sup>2</sup> did not have proteinuria and 57% of subjects with proteinuria did not have an eGFR of less than 60 mL/min/1.73 m<sup>2</sup>. Most Australian laboratories now automatically report eGFR with every serum creatinine ordered for adult patients. At

levels below 60 mL/min/1.73 m<sup>2</sup> eGFR has acceptable accuracy, although there are clinical situations in which the eGFR result should be interpreted cautiously (Table 4). If there is any doubt in these situations, it is wise to measure GFR formally, generally using a timed urine collection for

creatinine clearance test.

For patients who do not have diabetes, the presence of urinary protein should be initially evaluated using urine dipstick testing. Dipstick proteinuria of 1+ or greater should prompt quantitation of proteinuria. Either a timed urine collection

**Table 5. Strategies to reduce CKD progression and cardiovascular risk<sup>5,7</sup>**

Parameter	Goal	Intervention
Smoking	Smoking cessation	Lifestyle counselling
Nutrition	At least 5% weight loss if overweight or obese (ideal waist circumference is <94 cm for men and <80 cm for women; ideal BMI is 18.5–24.9 kg/m <sup>2</sup> ) Healthy diet (low in saturated and total fat, low in cholesterol and high in fibre, fruit and vegetables) Dietary salt intake <100 mmol/day	Lifestyle counselling
Alcohol	No more than two standard glasses of alcohol per day	Lifestyle counselling
Physical activity	At least 30 minutes per day of moderate physical activity	Lifestyle counselling
Blood pressure	130/80 mmHg (125/75 mmHg if proteinuria >1g/day)	ACE inhibitor and/or ARB as first-line therapy Lifestyle modification
Proteinuria	At least a 50% reduction in baseline proteinuria value	ACE inhibitor and/or ARB as first-line therapy
Cholesterol	Total cholesterol <4.0 mmol/L LDL cholesterol <2.5 mmol/L	Dietary advice Statin therapy
Blood glucose (patients with diabetes)	Preprandial BGL 4.4–6.7 mmol/L HbA <sub>1c</sub> ≥7.0%	Lifestyle modification Oral hypoglycaemic agents Insulin therapy
Dietary protein	0.75–1.0 g/kg bodyweight/day (normal)	Dietary advice

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**Table 6. CKD complications and their treatments**

Complication	Goal	Treatment
Anaemia	Haemoglobin 110–120 g/L	Correct iron deficiency Consider erythropoietin (Eprex, NeoRecormon) or darbepoetin (Aranesp) in consultation with a nephrologist
Acidosis	Serum bicarbonate >22 mmol/L	Sodium bicarbonate tablets, typically 1–2 tablets twice or three times daily
Hyperkalaemia	Serum potassium ≤6.0 mmol/L	Dietary advice Loop diuretics Sodium polystyrene sulfonate (Resonium A), 15 g daily or twice daily Cease ACE inhibitors and/or ARBs if potassium is persistently increased
Hyperparathyroidism or osteodystrophy	Serum phosphate 1.65 mmol/L 1,25-vitamin D levels >30 mg/mL Parathyroid hormone 2–5 times upper limit of normal	Calcitriol (0.25 µg daily) Phosphate binders: calcium carbonate, aluminium hydroxide,* magnesium trisilicate, sevelamer (Renagel),* lanthanum carbonate (Fosrenol)* Cinacalcet (Sensipar)*
Malnutrition	Albumin ≥35 g/L	Dietary advice
Restless legs	Control symptoms	Correct iron deficiency Consider dopaminergic agents
Sleep apnoea	Prevent apnoeic episodes	Weight reduction Avoid CNS depressants CPAP therapy (if sleep apnoea has an obstructive pattern) <sup>†</sup>
Infection	Minimise infection risk	Annual influenza vaccination 5-yearly pneumococcal vaccination

\* Must only be prescribed by nephrologists experienced in their use. <sup>†</sup> CPAP = continuous positive airway pressure.

or a protein to creatinine ratio using a random (spot) urine test should be performed. In patients with diabetes, annual measurement of the albumin to creatinine ratio on a first-voided urine sample is a simple and convenient tool for detecting diabetic CKD.

**Reducing CKD progression and cardiovascular risk**

Even a moderately severe reduction in GFR (below 60 mL/min/1.73 m<sup>2</sup>) is associated with an exponential increase in the risk of cardiovascular death. The strategies outlined in Table 5 will slow the decline in kidney function and decrease cardiovascular risk but monitoring at least every three months is essential. Treating blood pressure to target levels is the single most

important treatment step in CKD because blood pressure accounts for half of the variance in kidney failure progression. Each 10 mmHg reduction in blood pressure is associated with a slowing of decline in GFR by 2.2 mL/min/year. Patients with CKD often require three or four anti-hypertensive medications to reach blood pressure targets.<sup>5</sup> Unless an aggressive approach to control of blood pressure is taken the majority of patients with CKD will not reach target.

ACE inhibitors and/or angiotensin II receptor blockers (ARBs) are the preferred initial antihypertensive agents for lowering blood pressure in CKD, followed by loop diuretics. It is prudent to measure serum creatinine and eGFR at one week and then four weeks after initiating ACE

inhibitor or ARB therapy. An acute rise in serum creatinine concentration of less than 30% of the baseline level that stabilises within the first month is expected. This change in creatinine concentration is associated with a beneficial long term response compared with that seen in patients who have no change in their serum creatinine or eGFR following initiation of ACE inhibitor and/or ARB treatment.<sup>6</sup> If the creatinine concentration rises higher than 30% above the baseline value, ACE inhibitor and/or ARB therapy should be stopped. ACE inhibitor treatment should also be withdrawn if a patient's serum potassium concentration exceeds 6 mmol/L, despite dose reduction, dietary potassium restriction and concomitant diuretic therapy.

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**Table 7. Foods with a high potassium content**

Fruit	Vegetables	Dairy and beverages	Others
Apricots	Artichoke	Coconut milk and cream	Bread (heavy grains, dark rye)
Avocado	Baked beans	Evaporated and condensed milk	Cereal (All Bran, Bran Plus, muesli)
Banana	Brussel sprouts	Milk and soy milk (patients should have less than 1 cup [250 mL] each day)	Cocoa, chocolate
Coconut	Cauliflower	Percolated coffee	Golden syrup
Custard apple	Chickpeas	Red wine	Molasses
Dried fruit	Kidney beans	Vegetable juices	Nuts
Dried fruit/nut mixes	Hot chips	Yoghurt	Peanut butter
Fruit cake	Parsnip		Potato crisps
Mulberry	Potato		Salt substitutes
Rockmelon	Pumpkin		Seeds (sunflower, pumpkin)
Tomato (including soup, sauces, paste, juice)	Spinach		Treacle
Tropical fruit salad	Vegetable soups (thick and homemade)		

The aspect of CKD management that often receives inadequate attention is lifestyle modification, which can substantially reduce the risks of hypertension, obesity, diabetes mellitus, cardiovascular disease and kidney failure progression. For example, each 10 kg of weight loss is associated with a 5 to 10 mmHg reduction in blood pressure and manifest reductions in the risks of both diabetes mellitus and cardiovascular disease.

**Timely management of CKD complications**

Many of the known complications of CKD are often already evident in patients with stage 3 of the disease (Table 6). Regular monitoring for all potential complications, at least three monthly for patients with stage 3 CKD and monthly for those with stage 4 CKD, is necessary. Timely treatment is also essential.

For patients with moderate to severe CKD, hyperkalaemia is a particularly common complication encountered in the primary care setting. Hyperkalemia can also be seen in patients with stage 3 CKD. Patients should be advised to avoid all fruits (including dried fruits) and vegetables that have high potassium contents and to eat no more than two serves of

other fruit and four small serves of other vegetables each day (Table 7). All fruit and vegetables should be peeled and boiled. Microwave cooking, steaming and stir-frying of foods should also be avoided.

Loop diuretics are often useful for controlling hyperkalaemia but higher doses can be required to ensure their effectiveness when a patient’s GFR is low. For example, the dosage of frusemide increases from 40 mg daily for patients with a GFR of 60 mL/min/1.73 m<sup>2</sup> to approximately 250 mg daily for those with a GFR of less than 10 mL/min/1.73 m<sup>2</sup>.

Sodium polystyrene sulfonate (Resonium A) is also effective at controlling serum potassium levels, although the preparation is often unpalatable and is expensive for patients because it is not available on the PBS. Treatment with ACE inhibitors and ARBs should be ceased if the patient’s potassium level remains persistently above 6 mmol/L.

**Avoidance of nephrotoxic medications**

Commonly prescribed drugs that can further reduce GFR in patients with CKD include NSAIDs, COX-2 inhibitors, some antibiotics (such as aminoglycosides) and radiographic contrast.

It is important to be aware there is a significant risk of precipitating acute renal failure arising from the ‘triple whammy’ effect of combinations involving either an ACE inhibitor or an ARB in combination with a NSAID and a diuretic. A recent survey conducted by Kidney Health Australia revealed that nearly 10% of patients taking blood pressure medications were at risk of renal failure because they were taking this ‘triple whammy’. It is important to note that low dose aspirin has not been implicated in the ‘triple whammy’ and should not be stopped in patients prescribed an ACE inhibitor or ARB with a diuretic.

**Dose adjustment of renally cleared medications**

Dosage reduction or cessation of renally excreted medications is generally required once a patient’s GFR falls below about 50 mL/min/1.73 m<sup>2</sup>. A list of commonly prescribed renally excreted medications that should be reviewed in patients with CKD is provided (Table 8).

One of the most important medications in this respect is metformin because in the setting of CKD it can result in life-threatening lactic acidosis. Metformin is contraindicated if a patient has stage 4

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**Table 8. Examples of renally excreted medications**

**Analgesics:** codeine, gabapentin, morphine, pethidine

**Anticoagulants:** low molecular weight heparin

**Antibiotics:** aminoglycosides, vancomycin

**Antifungals:** fluconazole

**Antivirals:** aciclovir, famciclovir, valaciclovir, valganciclovir

**Cardiac drugs:** digoxin, sotalol

**Diabetic drugs:** insulin, metformin, sulfonylureas

**Glaucoma drugs:** acetazolamide

**Gout drugs:** allopurinol, colchicine

**Table 9. When to refer patients to nephrologists**

- eGFR is  $<30$  mL/min/1.73 m<sup>2</sup>
- Unexplained decline in kidney function ( $>15\%$  drop in GFR over three months)
- Proteinuria  $>1$ g/24 h
- Glomerular haematuria (particularly if proteinuria is present)
- Target blood pressure difficult to reach
- Presence of diabetes with an eGFR  $<60$  mL/min/1.73 m<sup>2</sup>
- Unexplained anaemia (Hb  $<100$  g/L) with an eGFR  $<60$  mL/min/1.73 m<sup>2</sup>

or 5 CKD, i.e. with a GFR below 30 mL/min/1.73 m<sup>2</sup>. Metformin should also be used with caution in patients with stage 3 CKD who need to cease medication

temporarily during intercurrent illnesses or 24 hours before having surgery, radiological procedures involving contrast media or other invasive procedures.

**Referral to a nephrologist**

With the exception of patients at the severe end of the CKD spectrum, general practitioners manage most of the two million Australian adults affected by the disease. The Kidney Check Australia Taskforce's recommended indications for referring a patient with CKD to nephrologists are outlined in Table 9. These indications seek to identify patients who are at significant risk of progressing to end stage renal failure or those who may have a potentially treatable underlying renal condition. These include: primary glomerulonephritis, a connective tissue disease, plasma cell dyscrasia and renal artery stenosis.

When referring patients to a nephrologist, it is important to ensure that they

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have had a recent kidney ultrasound and current blood chemistry and quantitation of their proteinuria. Referral is usually unnecessary for patients who have the following:

- stage 2 or 3 CKD
- a stable GFR
- minor proteinuria (less than 0.5 g/day or protein to creatinine ratio of 50 mg/mmol) and
- controlled blood pressure (especially if the patient does not have diabetes).

### Conclusion

CKD is a common, eminently treatable but largely under-recognised condition affecting one in seven Australian adults. General practitioners have important roles in identifying and screening patients with CKD risk factors, modifying the risk of cardiovascular disease and preventing progression of kidney failure in these patients. Equally important are

their roles in identifying, detecting and treating CKD complications as they arise and ensuring prescribed medications and dosages are appropriate for the level of kidney function. Only a small number of patients with CKD need specialist referral.

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