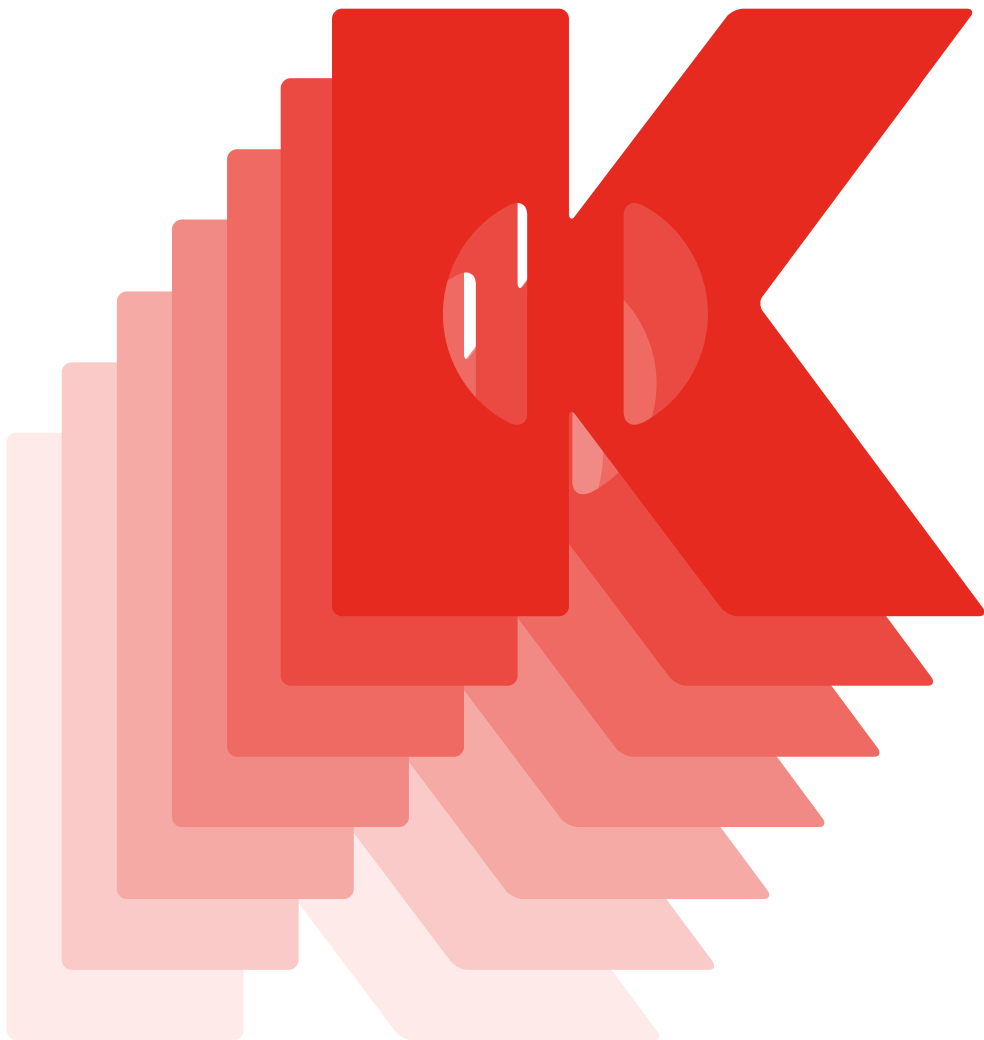


Guidance and clinical
tips to help identify,
manage and refer
CKD in your practice

CHRONIC KIDNEY DISEASE (CKD) MANAGEMENT IN GENERAL PRACTICE



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- CKD is a silent condition, but can be readily detected with tests for proteinuria, haematuria, and eGFR
- CKD is becoming increasingly common due to our ageing population and a rising incidence of Type 2 diabetes
- CKD is a potent independent risk factor for cardiovascular disease
- Optimal management of the risk factors for cardiovascular disease also slows the progression of CKD
- The majority of people with CKD will be managed in general practice, not by specialists

What is Chronic Kidney Disease (CKD)?

CKD is defined as¹:

Glomerular filtration rate (GFR)

< 60mL/min/1.73m² that is present for ≥ 3 months with or without evidence of kidney damage,

or

Evidence of kidney damage with or without decreased GFR that is present for ≥ 3 months as evidenced by any of the following:

- microalbuminuria
- proteinuria
- glomerular haematuria
- pathological abnormalities (e.g. abnormal renal biopsy)
- anatomical abnormalities (e.g. scarring seen on imaging or polycystic kidneys)

Clinical Tip

If the eGFR is ≥ 60 mL/min/1.73m², and there is no evidence of kidney damage, then CKD is not present.

Common causes of CKD

The most common reasons why people start dialysis or kidney transplantation in Australia are²:

- diabetic nephropathy (32% of all new patients)
- glomerulonephritis (24%)
- hypertension (14%)
- reflux nephropathy (3%)

While the causes of end stage kidney disease are well known, the causes of CKD are not established. Irrespective of the underlying cause of CKD the treatment follows the principles outlined in this booklet.

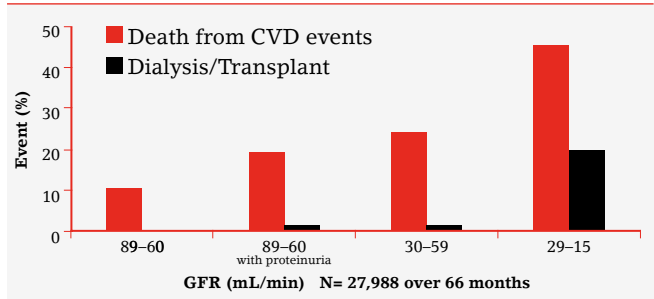
Why should I worry about CKD?

Australian population surveys have revealed that CKD is more common than you may think.

- 1 in 3 adults are at increased risk of developing CKD
- 1 in 7 adults have some sign of CKD

Symptoms of CKD may not appear until kidney function is severely and irreversibly impaired.

Outcomes in patients with CKD

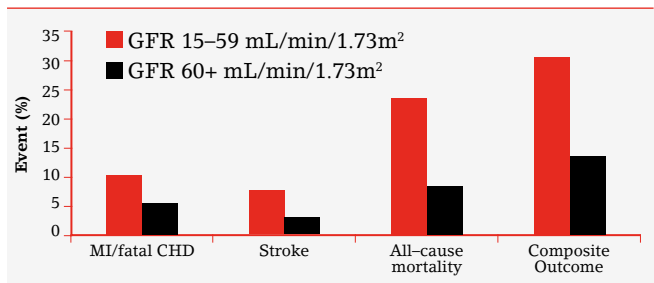


Source: Keith et al. Arch Intern Med 2004;164:659-63.

CKD is a potent risk factor for cardiovascular disease

- Individuals with CKD have a 10 to 20-fold greater risk of cardiac death than individuals without CKD^{3,4}
- Recent studies have confirmed that even early CKD constitutes a significant risk factor for cardiovascular events and death⁴⁻⁶
- For people with CKD, the risk of dying from cardiovascular events is 20 times greater than requiring dialysis or transplantation⁷

Outcomes by level of kidney function



Source: Weiner et al. J Am Soc Nephrol 2004;15:1307-15.

Who is at risk of CKD?

Modifiable risk factors:

- smoking
- diabetes
- high blood pressure
- obesity

Non-modifiable risk factors:

- age over 50 years
 - family history of kidney disease
 - Aboriginal or Torres Strait Islander heritage
-

Importance of early detection

- Increasing amounts of protein in the urine correlate directly with an increased rate of progression into end-stage kidney disease
 - The amount of proteinuria/albuminuria in the urine can be reduced significantly by the use of an ACE inhibitor or ARB agent singly or in combination
 - Reduction in the amount of proteinuria is associated with improved outcomes
 - Early intervention can reduce CKD progression and cardiovascular risk by 50%⁸, and improves quality of life
-

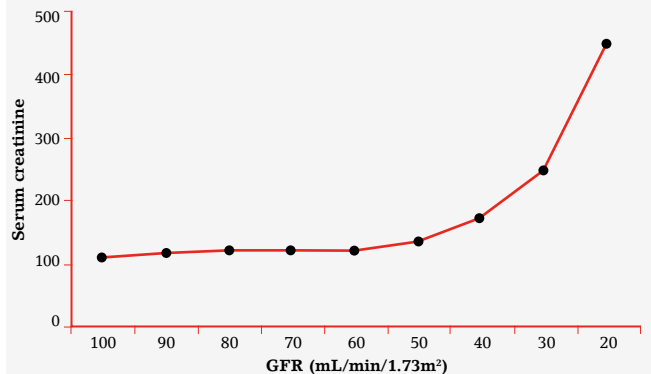
Screening for CKD

- Certain factors are associated with an increased risk of developing CKD
- All people attending their general practitioner should be assessed for CKD risk factors as part of routine primary health encounters
- Evidence supports a targeted opportunistic screening program among high-risk individuals to identify those with CKD

Using eGFR to detect CKD

- Estimated Glomerular Filtration Rate (eGFR) using the MDRD formula is the recommended method of measuring kidney function
- eGFR may be markedly reduced while the serum creatinine is still in the normal range
- An eGFR is automatically provided with every laboratory request for a serum creatinine (in people aged ≥ 18 years)
- eGFR values are automatically reported up to 90 mL/min/1.73m². Values greater than this are reported as > 90 mL/min/1.73m²
- Knowledge of eGFR between 60–90mL/min/1.73m² may be of assistance in providing an earlier warning of eGFR reduction and allowing monitoring of trends over time
- Further investigation of eGFR is only required if the eGFR is < 60 mL/min/1.73m²

Serum creatinine does not increase beyond normal limits until more than 50% of GFR has been lost



Clinical presentation of CKD

CKD is generally asymptomatic.

- Patients do not normally present with symptoms of CKD, so annual checking of those at risk is essential
- People with CKD may not notice any symptoms until they reach end stage kidney disease requiring dialysis or transplant (eGFR < 15 mL/min/1.73m²)

Symptoms of end stage kidney disease include:

- nocturia
- malaise
- anorexia/nausea/vomiting
- pruritus
- restless legs
- dyspnoea

Early detection of CKD using kidney health check

Who is at higher risk of kidney disease?	What should be done?	How often?
Age > 50 years Diabetes High blood pressure Smoking Obesity Family history of kidney disease Aboriginal or Torres Strait Islander	blood pressure urine dipstick (microalbuminuria if diabetes present) eGFR	Every 12 months

Source: Adapted from Guidelines for preventive activities in general practice (The Red Book) 6th edition. 2005. The Royal Australian College of General Practitioners, South Melbourne, Victoria, Australia.

Tests used to investigate CKD

URINE TESTS: PROTEINURIA

- Proteinuria is a key marker of kidney damage
- Increasing amounts of protein in the urine correlate directly with an increased rate of progression to end-stage kidney disease
- Microalbuminuria (albumin excretion above the normal range but below the level of detection by tests for total protein) is a sensitive indicator of CKD in people with diabetes, and indicates an increased risk of micro and macro vascular disease that requires aggressive intervention

Clinical Tip

Screen annually for proteinuria among people at risk of CKD, except for those with diabetes who should be screened for microalbuminuria.

- The amount of proteinuria/albuminuria can be reduced significantly by the use of an ACE inhibitor or ARB agent singly or in combination
- Reduction in the amount of proteinuria is associated with improved clinical outcomes
- Once protein in the urine has been detected, quantitative measurements are necessary to precisely determine the protein excretion for prognostic purposes

HOW TO DETECT AND QUANTIFY PROTEINURIA

- Urine dipsticks are quick, cheap and readily accessible
- Should be performed at least annually for any person at increased risk of CKD
- Proteinuria present if the dipstick is 1+ or more⁹
- Protein/creatinine ratio on a random spot urine sample is recommended to further quantify proteinuria¹⁰
- Where this is abnormal a repeat specimen a few weeks later is recommended to determine if it is persistent
- People with diabetes should have tests for microalbuminuria performed at least annually by albumin/creatinine ratio (using early morning spot urine sample)
- If test positive for microalbuminuria, two further samples should be sent for albumin/creatinine ratio within two months

Clinical tip

The daily protein excretion (g/24hrs) can be estimated from the protein:creatinine ratio (measured in mg/mmol) by multiplying by a factor of 10.

Example:

- Urine protein = 900 mg/L,
urine creatinine = 6 mmol/L
- Urine protein:creatinine
ratio = $900/6 = 150$ mg/mmol
- daily protein excretion \approx
 $150 \times 10 = 1500$ mg = 1.5 g/24 hrs

DEFINITIONS OF ALBUMINURIA AND PROTEINURIA

	Microalbuminuria	Macroalbuminuria	Proteinuria
Albumin/creatinine ratio	Females: 3.6–35 mg/mmol Males: 2.6–25 mg/mmol	Females: > 35 mg/mmol Males: > 25 mg/mmol	–
Dipstick	> 3 mg/dL (albumin specific dipstick)	> 20 mg/dL (albumin specific dipstick)	Dipstick = 1 + or more
Protein/creatinine ratio	–	–	> 30 mg/mmol
24 hour protein	–	–	> 0.3 g/24 hrs

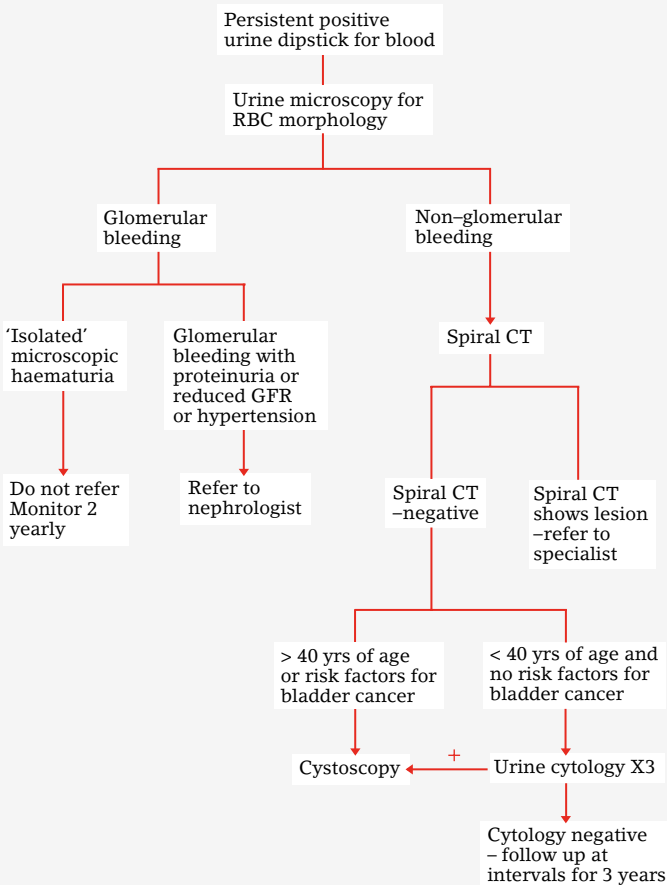
URINE TESTS: HAEMATURIA

- In many people, haematuria is related to menstruation or urinary tract infection (UTI)
- Persistent haematuria, or haematuria found in conjunction with other indicators of kidney damage necessitates investigation
- 'Isolated microscopic haematuria' refers to when haematuria is the only abnormality, and there is no albuminuria, blood pressure is normal, and $eGFR > 60$ mL/min/1.73m²
- Glomerular haematuria is due to kidney disease
- Non-glomerular haematuria may be due to urological conditions (UTI, renal calculi, prostatic disease, urinary tract tumours) or menstrual contamination

HOW TO DETECT HAEMATURIA

- Urine dipsticks are very sensitive and can identify all significant bleeding
- A positive dipstick for blood should be repeated (between menstrual periods) and then confirmed with urine microscopy
- A culture should be performed to exclude infection
- Urine phase contrast microscopy can be used to differentiate between glomerular and non-glomerular haematuria (fresh specimen required)

ALGORITHM FOR MANAGEMENT OF PERSISTENT MICROSCOPIC HAEMATURIA¹¹



BLOOD TESTS: SERUM CREATININE

- Unreliable and insensitive marker for mild to moderate chronic kidney disease
 - Affected by many factors other than kidney function and varies with age, gender and muscle mass
 - **Patients may lose 50% or more of their kidney function before the serum creatinine value rises above the upper limit of normal**
 - Serum creatinine concentration is useful for following the trend of kidney function, in an individual over time
-

BLOOD TESTS: ESTIMATED GLOMERULAR FILTRATION RATE (eGFR)

- GFR is widely accepted as the best measure of kidney function
- GFR can be estimated (eGFR) from serum creatinine using predictive equations
- eGFR is recommended to be automatically reported (using Modification of Diet in Renal Disease (MDRD) equation) with every request for serum creatinine in adults aged > 18 years¹²
- MDRD is more accurate than the Cockcroft-Gault equation among elderly and obese people, and is also more accurate as kidney function declines
- eGFR values are automatically reported up to 90 mL/min/1.73m². Values greater than this are reported as > 90 mL/min/1.73m²
- Knowledge of eGFR between 60–90mL/min/1.73m² may be of assistance in providing an earlier warning of eGFR reduction and allowing monitoring of trends over time
- Further investigation of eGFR is only required if the eGFR is < 60mL/min/1.73m²
- In healthy adults the eGFR falls by up to 10 mL/min/1.73m² per decade beyond the age of 40 – BUT reduced eGFR is associated with cardiovascular risk for all ages
- In people aged over 70 years of age, eGFR values between 45 and 59 mL/min/1.73m² should be interpreted with caution. If other signs of kidney damage (e.g. proteinuria, haematuria etc) are not present, a stable eGFR in this range may be consistent with normal GFR for this age and an absence of CKD related complications

INTERPRETING eGFR IN SPECIAL SITUATIONS

Clinical situations where eGFR results may be unreliable and/or misleading include:

- acute changes in kidney function (e.g. acute kidney failure)
 - dialysis-dependent patients
 - exceptional dietary intake (e.g. vegetarian diet, high protein diet, recent consumption of cooked meat, creatine supplements)
 - extremes of body size
 - diseases of skeletal muscle, paraplegia, or amputees (may underestimate) or high muscle mass (may overestimate)
 - children under the age of 18 years
 - severe liver disease present
-

USE OF eGFR IN DIFFERENT ETHNIC POPULATIONS

- The original MDRD formula contains a factor to be applied to African-American subjects raising the possibility that other variations in the formula may be required for optimal performance in different racial groups
 - Pending publication of validation studies it is recommended Australasian laboratories continue to automatically report eGFR in Aboriginal and Torres Strait Islander peoples and other ethnic groups
-

eGFR AND DRUG DOSING

- Where an eGFR (using MDRD) is on hand it is clinically appropriate to use this to assist drug dosing decision making
- For critical dose drugs, particularly in the hospital setting, it remains important to adhere to the published recommendations
- Published recommendations usually involve the use of the Cockcroft-Gault equation to estimate eGFR, or to measure creatinine clearance in order to amend dosing for renal function

FURTHER EVALUATION

If the eGFR is $< 60\text{mL}/\text{min}/1.73\text{m}^2$ further assessment is recommended:

- blood pressure
- dipstick for haematuria and proteinuria
 - random spot urine protein/creatinine ratio if dipstick positive for protein
- random spot urine albumin/creatinine ratio for people with diabetes even if dipstick negative for protein
 - confirmatory urea/electrolytes/creatinine
- fasting lipids
- fasting glucose
- full blood count

If the abnormal eGFR is confirmed on repeat testing, kidney ultrasound should be considered.

Depending on the age of the patient and the severity of CKD, consideration may also be given to iron studies, serum calcium, phosphate and parathyroid hormone.

eGFR clinical action plan

* imaging or biopsy abnormalities, or proteinuria/haematuria
 ** hypertension, diabetes, smoker, age > 50 yrs, obesity, family history of kidney disease, Aboriginal and Torres Strait Islander people

eGFR mL/min/1.73m ²	Description	Clinical Action Plan
90	Stage 1 CKD – kidney damage* with normal kidney function	Further investigation for CKD may be indicated in those at increased risk**: – blood pressure – assessment of proteinuria – urinalysis
60–89	Stage 2 CKD – kidney damage* with mild ↓ kidney function	Cardiovascular risk reduction: – blood pressure – lipids – blood glucose – lifestyle modification (smoking, weight, physical activity, nutrition, alcohol)
30–59	Stage 3 CKD – moderate ↓ kidney function	As above, + : – monitor eGFR three monthly – avoid nephrotoxic drugs – prescribe antiproteinuric drugs (ACE inhibitors and/or ARBs) if appropriate – address common complications – ensure drug dosages appropriate for level of kidney function Consider indications for referral to a nephrologist
15–29	Stage 4 CKD – severe ↓ kidney function	As above + referral to nephrologist is usually indicated for physical and psychosocial preparation for renal replacement therapy (dialysis, pre-emptive transplantation, transplantation) or conservative medical management
<15	Stage 5 CKD – end-stage kidney disease	As above + referral to a nephrologist

Indications for referral to a Nephrologist

Appropriate referral is associated with:

- reduced rates of progression to end stage kidney disease
- decreased need for and duration of hospitalisation
- increased likelihood of permanent dialysis access created prior to dialysis onset
- reduced initial costs of care following the commencement of dialysis
- increased likelihood of kidney transplantation
- decreased patient morbidity and mortality

WHO MAY BE CONSIDERED FOR REFERRAL TO A NEPHROLOGIST?

Anyone with:

- eGFR < 30mL/min/1.73m²
- Unexplained decline in kidney function (> 15% drop in eGFR over three months)
- Proteinuria > 1g/24hrs (see clinical tip)
- Glomerular haematuria (particularly if proteinuria present)
- CKD and hypertension that is hard to get to target
- Diabetes with eGFR < 60mL/min/1.73m²
- Unexplained anaemia (Hb < 100 g/L) with eGFR < 60mL/min/1.73m²

Anyone with an acute presentation and signs of acute nephritis should be regarded as a medical emergency and referred without delay.

Clinical tip

Urine protein:creatinine ratio of 100 mg/mmol ≈ daily protein excretion of 1g/24hrs.

WHO DOES NOT USUALLY NEED TO BE REFERRED TO A NEPHROLOGIST?

CKD Stage 2 and 3

- Stable eGFR 30–89 mL/min/1.73m²
- Minor proteinuria (<0.5 g/24hrs with no haematuria)
- Controlled blood pressure

The decision to refer or not must always be individualised, and particularly in younger patients the indications for referral may be less stringent (e.g. minor proteinuria).

In CKD Stages 2 and 3

- Don't refer to nephrologist if targets of therapy are achieved
- Pay attention to CVD risk reduction
- Use ACE inhibitors/ARBs
- Monitor three to six monthly

Clinical tip

When referring to a nephrologist, ensure patient has had a recent kidney ultrasound, current blood chemistry, and quantification of proteinuria.

CKD Management: Stage 1 and 2 (eGFR \geq 60 mL/min/1.73m²)

GOALS OF STAGE 1–2 CKD MANAGEMENT

- investigations to exclude treatable kidney disease
 - reduce progression of kidney disease
 - reduce cardiovascular risk
-

MONITORING IN STAGE 1–2 CKD

When monitoring patients with Stage 1–2 CKD consider:

- 3–6 monthly clinical review
 - clinical assessment
 - blood pressure
 - weight
 - urine dipstick
 - laboratory assessment
 - biochemical profile including urea, creatinine and electrolytes
 - eGFR
 - fasting glucose
 - fasting lipids
-

CARDIOVASCULAR RISK REDUCTION

The presence of CKD is one of the most potent known risk factors for cardiovascular disease^{6,13}.

All people with CKD should undergo cardiovascular and kidney disease risk factor modification^{1,14}.

Individuals with CKD have a 10–20 fold greater risk of cardiac death than age and sex matched controls without CKD⁴.

People with CKD are at least 20 times more likely to die from cardiovascular disease than survive to need dialysis or a transplant⁷.

Lifestyle modification

- Lifestyle modification: cessation of smoking, weight reduction, low-salt diet, physical activity, and moderate alcohol consumption are successful in reducing overall cardiovascular risk
- Refer to SNAP guide for detection and management of lifestyle risk factors¹⁵

Blood pressure reduction

- CKD can cause and aggravate hypertension, and hypertension can contribute to the progression of CKD
- Reducing blood pressure to target levels is one of the most important goals in management of CKD¹⁶
- ACE inhibitors are recommended as first line therapy. ARBs may provide similar kidney protection¹⁷
- Maximal tolerable doses of ACE inhibitors and/or ARBs are recommended
- Hypertension may be difficult to control and multiple (three to four) medications are frequently required⁸

Clinical Tip

- **ACE inhibitors and ARBs can cause an increase in serum creatinine when treatment is initiated**
- **If the increase in creatinine is less than 30% and stabilises within two months of starting therapy, medication should be continued¹⁸**
- **If the rise in creatinine level exceeds 30% above the baseline value, medication should be ceased and consideration given to investigating for bilateral renal artery stenosis¹⁸**

Lipid-lowering treatments

- Statin therapy produces a modest reduction in proteinuria and results in a small reduction in the rate of kidney function loss, especially in people with cardiovascular disease¹⁹

Glycaemic control

- For people with diabetes, intensive blood glucose control significantly reduces the risk of developing CKD²⁰⁻²³, and in those with CKD reduces the rate of progression

CKD GOALS OF STAGE 3 CKD MANAGEMENT

Management:
Stage 3
(eGFR 30–59
mL/min/
1.73m²)

- reduce progression of kidney disease
- reduce cardiovascular risk
- early detection and management of complications
- avoidance of renally-excreted and nephrotoxic medications
- adjustment of medication doses to levels appropriate for kidney function
- appropriate referral when indicated

MONITORING IN STAGE 3 CKD

When monitoring patients with Stage 3 CKD consider:

- One to three monthly clinical review
- clinical assessment
 - blood pressure
 - weight
 - urine dipstick
- laboratory assessment
 - biochemical profile including urea, creatinine and electrolytes
 - eGFR
 - fasting glucose
 - fasting lipids
 - full blood count
 - iron stores
 - calcium and phosphate
 - parathyroid hormone (quarterly)

MEDICATIONS REVIEW

Dosage reduction or cessation of renally excreted medications is generally required once the GFR falls below 60 mL/min/1.73m².

It is important to review renally excreted medications, as well as avoid nephrotoxic medications in people with CKD.

Commonly prescribed drugs that need to be reduced in dose or ceased in people with CKD:

- Colchicine
- Digoxin
- Famciclovir
- Gabapentin
- Glibenclamide
- Glimepiride
- Lithium
- Metformin (significantly increased risk of lactic acidosis when GFR < 50 mL/min/1.73m²)
- Sotalol
- Valaciclovir

Commonly prescribed drugs that can adversely affect kidney function in people with CKD:

- NSAIDs and COX-2 inhibitors
- Beware the 'triple whammy' of NSAID/COX-2 inhibitor, ACE inhibitor and diuretic (low dose aspirin is okay)
- Radiographic contrast agents
- Aminoglycosides
- Lithium

Clinical Tip

- **The combination of ACE inhibitor (or ARB), diuretic and NSAID (except low-dose aspirin) can result in a potentially fatal interaction, the 'triple whammy'**
- **Ensure your patients on blood pressure medication are aware of the need to discuss pain relief medication with a general practitioner or pharmacist**

EFFECT OF ACE INHIBITORS AND ARBS ON KIDNEY FUNCTION

- When treatment with an ACE inhibitor or ARB is initiated, the creatinine levels can rise.
- Refer Clinical Tip in CKD Management Stage 1 and 2

CKD GOALS OF STAGE 4 CKD MANAGEMENT

**Management:
Stage 4
(eGFR 15–
29 mL/
min/1.73m²)**

- referral to a nephrologist for physical and psychosocial preparation for renal replacement therapy (dialysis, pre-emptive transplantation, transplantation) or conservative management
- reduce progression of kidney disease
- reduce cardiovascular risk
- early detection and management of complications
- avoidance of renally-excreted and nephrotoxic medications
- adjustment of medication doses to levels appropriate for kidney function

MONITORING IN STAGE 4 CKD

When monitoring patients with Stage 4 CKD consider:

- monthly clinical review
- clinical assessment
 - blood pressure
 - weight
 - oedema
 - urine dipstick
- laboratory assessment
 - biochemical profile including urea, creatinine and electrolytes
 - eGFR
 - fasting glucose
 - fasting lipids
 - full blood count
 - iron stores
 - calcium and phosphate
 - parathyroid hormone (quarterly)

REFERRAL TO A NEPHROLOGIST

The CARI guidelines recommend that patients should be referred to a nephrologist at least 12 months prior to the anticipated commencement of dialysis and/or kidney transplantation (i.e. referral when eGFR < 30 mL/min/1.73 m²)¹⁶.

Appropriate referral is associated with:

- reduced rates of progression to end stage kidney disease
- decreased need for and duration of hospitalisation
- increased likelihood of permanent dialysis access created prior to dialysis onset
- reduced initial costs of care following the commencement of dialysis
- increased likelihood of kidney transplantation
- decreased patient morbidity and mortality

Clinical tip

When referring to a nephrologist ensure patient has had a recent kidney ultrasound, current blood chemistry, and quantification of proteinuria.

PRE-EMPTIVE TRANSPLANTATION

Pre-emptive transplantation means receiving a kidney transplant from a live donor prior to initiation of dialysis. The option of pre-emptive transplantation (transplantation prior to the initiation of dialysis) is associated with^{24,25}:

- reduced rates of death
- longer duration of functioning of the transplanted kidney
- psychosocial benefits
- economic benefits

A pre-emptive transplant can only be performed when the individual's kidney function has deteriorated to a level that justifies the risks and complications of transplantation (eGFR usually 8–15 mL/min/1.73m²), but before they are so unwell that dialysis is essential.

CKD GOALS OF STAGE 5 CKD MANAGEMENT

**Management:
Stage 5
(eGFR < 15 mL/
min/1.73m²)**

- referral to a nephrologist for physical and psychosocial preparation for renal replacement therapy (dialysis, pre-emptive transplantation, transplantation) or conservative management
- reduction in cardiovascular and kidney risk
- early detection and management of complications
- avoidance of renally-excreted and nephrotoxic medications
- adjustment of medication doses to levels appropriate for kidney function

MONITORING IN STAGE 5 CKD

When monitoring patients with Stage 5 CKD consider:

- monthly clinical review (shared with renal unit)
- clinical assessment
 - blood pressure
 - weight
 - oedema
 - urine dipstick
- laboratory assessment
 - biochemical profile including urea, creatinine and electrolytes
 - eGFR
 - fasting glucose
 - fasting lipids
 - full blood count
 - iron stores
 - calcium and phosphate
 - parathyroid hormone (quarterly)

Clinical tip

While the renal unit undertakes most of the CKD management during this stage, it is still important that the patient maintains contact with their regular general practitioner to ensure coordination of whole-patient care, routine screening and health promotion, and psychosocial support.

ADVANCED CARE DIRECTIVES

During this stage it may be necessary to consider end of life decisions including advanced care directives to outline wishes for future health and personal care, including conservative treatment (no dialysis or transplantation), and palliative care arrangements.

The process varies between states, and more information is available from the Australian General Practice Network (www.agpn.com.au).

Treatment targets for people with CKD¹⁷

Golden Rules

- Blood pressure targets in CKD are < 130/80 mmHg or < 125/75 if proteinuria > 1 g/24hrs or diabetes is present
- Urine protein:creatinine ratio of 100 mg/mmol ≈ daily protein excretion of 1g/24hrs
- Achieving adequate BP targets will often require the use of more than one agent
- As eGFR declines more drugs will typically be required to achieve target blood pressure

Parameter	Target	Treatment & effects on systolic BP
Lifestyle Factors		
Smoking	Cease smoking	Lifestyle modification – refer to SNAP guide ²⁶
Weight	BMI ≤ 25 kg/m ² WC males ≤ 94 cm ²⁷ (≤ 90 cm in Asian populations) ²⁸ WC females ≤ 80 cm ²⁷	Lifestyle modification – refer to SNAP guide SBP reduction = 5–20 mmHg/10 kg loss
Physical activity	>30 mins physical activity/day	Lifestyle modification – refer to SNAP guide SBP reduction = 4–9 mmHg
Nutrition	Dietary salt intake 40–100 mmol/day ²⁹	Lifestyle modification – refer to SNAP guide SBP reduction = 2–8 mmHg
Alcohol	Moderate alcohol consumption only (1–2 standard drinks/day)	Lifestyle modification – refer to SNAP guide SBP reduction = 2–4 mmHg
Clinical Factors		
Blood pressure	< 130/80 mmHg < 125/75 mmHg if proteinuria > 1g/24hrs or diabetes present	Lifestyle modification ACE inhibitor and/or ARB first-line
Proteinuria	> 50% reduction of baseline value	ACE inhibitor and/or ARB first-line
Cholesterol	Total < 4.0 mmol/L LDL < 2.5 mmol/L	Dietary advice Statins
Blood glucose (for people with diabetes)	Pre-prandial BSL 4.4–6.7 mmol/L HbA1c < 7.0%	Lifestyle modification Oral hypoglycaemics Insulin

The NHMRC also recommends immunisation against influenza and invasive pneumococcal disease for people with diabetes and/or end stage kidney disease.

Common CKD complications

Early detection and intervention has been shown to reduce the progression of CKD and its complications. It is essential to regularly check for the known complications of CKD and to monitor treatment targets.

Hypertension

Target:

< 130/80 mmHg
or

< 125/75 mmHg
if proteinuria
> 1g/24hrs
or if diabetes
present

Urine protein:
creatinine ratio
of 100 mg/mmol
≈ daily protein
excretion of
1g/24 hrs

Hypertension is both a cause of CKD and a complication of CKD and can be difficult to control. The risks of uncontrolled hypertension include progression of kidney disease and increased risk of coronary heart disease^{17,30,31}.

Management

- Lifestyle: weight management, physical activity, limit alcohol intake to no more than two standard drinks per day (men), one standard drink per day (women), cease smoking, low salt diet
- Multiple medications (often three or more drugs) will be needed to control hypertension adequately in most patients with CKD⁸
- People with diabetes or proteinuria should be treated with an ACE inhibitor or ARB as first line therapy³²
- When treatment with an ACE inhibitor or ARB is initiated, the creatinine and potassium levels can rise
 - If the acute rise in creatinine is less than 30% above the baseline level and stabilises within two months, the medication should be continued. People whose creatinine rises are most likely to achieve the greatest benefit in terms of kidney protection
 - If the rise in creatinine is greater than 30% above baseline value, the medication should be stopped and the person investigated for bilateral renal artery stenosis
 - If the serum potassium concentration is greater than 6 mmol/L despite dose reduction, diuretic therapy and dietary potassium restriction, then the medication (including spironolactone) should also be stopped¹⁷
- Diuretics should be used in most patients³¹. Both non loop diuretics (e.g. thiazides) and loop diuretics (e.g. frusemides) are effective as adjunct antihypertensive therapy. Additional agents can be chosen based on cardiovascular indications³¹
- Beta-blockers may be useful in people with coronary heart disease, tachyarrhythmias and heart failure, but are contraindicated in asthma, chronic obstructive pulmonary disease and heart block
- Calcium channel blockers may be used for people with angina, the elderly and those with systolic hypertension

Principles of management of hypertension in people with CKD

Manage lifestyle risk factors continuously

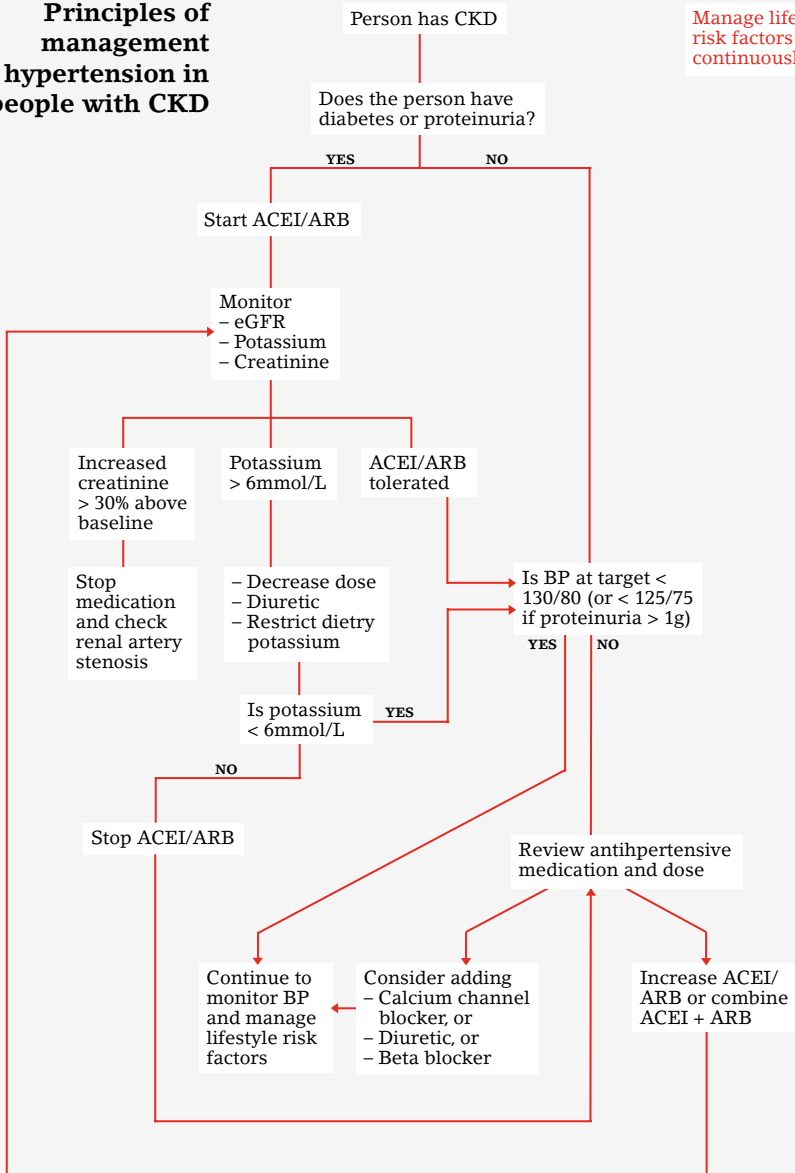


Figure reproduced with permission from Med-E-Serv Pty Ltd, Chronic Kidney Disease (CKD) Update (<http://www.kidneyprimed.com.au/>)

<p>Lipids</p> <p>Target:^{33,34}</p> <p>Total <4.0 mmol/L</p> <p>LDL <2.5 mmol/L</p>	<p>CKD is associated commonly with substantial abnormalities of lipid metabolism, including increased low-density lipoproteins, triglycerides, very-low-density lipoproteins, and lipoprotein (a), and reduced levels of high-density lipoprotein cholesterol. Dyslipidaemia is more severe in patients with proteinuria, particularly those with nephrotic syndrome. Dyslipidaemia should be treated as per cardiovascular disease recommendations and targets³⁴.</p> <p>Management</p> <ul style="list-style-type: none"> - Dietary advice - Statins (dose reduction not necessary)
<p>Glycaemic Control</p> <p>Target:¹⁶</p> <p>Pre-prandial BSL 4.4-6.7 mmol/L</p> <p>HbA1c <7.0%</p>	<p>Intensive blood glucose control significantly reduces the risk of developing microalbuminuria, macroalbuminuria and/or overt nephropathy in people with Type 1^{20,21} and Type 2 diabetes^{22,23}.</p> <p>Management</p> <ul style="list-style-type: none"> - Lifestyle modification - Oral hypoglycaemics - Insulin
<p>Proteinuria</p> <p>Target</p> <p>Proteinuria >50% reduction of baseline value after two to three months</p>	<p>Proteinuria is an important prognostic feature of CKD. The degree of proteinuria relates to the severity of the kidney disease and with a greater likelihood of progression to end-stages of CKD. The amount of proteinuria can be reduced significantly by the use of an ACE inhibitor or ARB agent singly or in combination. Reduction in the amount of proteinuria is associated with improved outcomes.</p> <p>Management</p> <ul style="list-style-type: none"> - ACE inhibitor and/or ARB as first-line therapy - Reduction in salt output through reducing oral salt intake - Spironolactone (use with caution)
<p>Sleep Apnoea</p>	<p>Sleep apnoea can affect up to 50% of people with Stage 5 CKD⁴³.</p> <p>Management</p> <ul style="list-style-type: none"> - weight reduction - avoid central nervous system depressants - CPAP therapy (if obstructive pattern)

Mineral and Bone Disorder

Target:^{35,36}

$\text{PO}_4 < 1.8 \text{ mmol/L}$
PTH 2–4 x upper
limit of normal

Changes in the metabolism of calcium, phosphate, parathyroid hormone and Vitamin D typically start to occur once $\text{GFR} \leq 60 \text{ mL/min/1.73m}^2$. As kidney function decreases the renal clearance of phosphate is diminished, leading to higher serum phosphate levels. Calcium resorption by the kidney also decreases, leading to lower serum calcium levels. These two changes in turn stimulate parathyroid hormone excretion, which increases bone resorption.

In addition, as kidney function decrease the kidney produces less activated Vitamin D leading to increased prevalence of Vitamin D deficiency with declining renal function. These changes are associated with abnormal bone metabolism and increased risk of fracture and also increased cardiovascular mortality, perhaps mediated by accelerated vascular calcification.

Management

- Phosphate
 - Dietary restriction of phosphate. This is best managed with advice from a renal dietician
 - Use of phosphate binders. These are typically either calcium or non-calcium tablets taken with meals. These bind dietary phosphate to prevent absorption. The most common binder is Caltrate, available on PBS Authority for the indication of kidney disease and hyperphosphataemia
- Calcium
 - If phosphate is controlled, calcium will typically remain in normal range. If the level is low with normal phosphate level consider Vitamin D supplementation
- Vitamin D
 - Vitamin D may be used in CKD for two indications – Vitamin D deficiency and/or suppression of secondary hyperparathyroidism
 - Two agents are available for Vitamin D deficiency, either ergocalciferol or calcitriol. Ergocalciferol (Vitamin D2) is not the activated (Vitamin D3) form of the hormone, but can be used in early stage of CKD with Vitamin D deficiency
 - In later stages of CKD and/or for suppression of hyperparathyroidism, calcitriol is preferred. Calcitriol is available on PBS Authority for ‘the indication of hypocalcaemia due to renal disease’
- Treatment to maintain PTH in desired range is via intervention above
- The major side effect of therapy is hypercalcaemia

<p>Anaemia</p> <p>Target:³⁷</p> <p>Hb 110 – 120 g/L</p>	<p>Anaemia in CKD is related to both a reduction in erythropoietin production by the kidney and resistance to the action of erythropoietin. Anaemia related to CKD may occur at GFR of ≤ 60 mL/min/1.73m². The prevalence of anaemia increases with decreasing GFR.</p> <p>Management</p> <ul style="list-style-type: none"> – Other forms of anaemia should be excluded – B12, folate and iron levels should be checked and corrected if deficient – Thyroid stimulating hormone should be assessed and hypothyroidism treated if present – Significant hyperparathyroidism or systemic inflammation may contribute to anaemia and also may cause refractoriness to erythropoietin therapy – Treatment with erythropoietin is available for patients with anaemia related to CKD with GFR < 60 mL/min/1.73m² – Treatment must be commenced by or in consultation with a nephrologist. There are three drugs currently available for this indication in Australia. All three are pre-filled syringes and are usually administered subcutaneously – These drugs are available either through hospital pharmacies or on Authority prescription under section 100 of the PBS for ‘treatment of anaemia requiring transfusion, defined as a haemoglobin level of less than 100 g/L, where intrinsic renal disease as assessed by a nephrologist, is the primary cause of the anaemia’³⁸. A Private Hospital provider number is required to access the drug on Authority prescription – Treatment can be divided into two phases: <ul style="list-style-type: none"> – Correction – treatment commenced with the aim of achieving target Hb. Monitor Hb two to four weekly and iron stores monthly. The aim is a rise of Hb at a rate of approximately 1 g/L/month. Rapid correction of anaemia has been associated with hypertension and seizures – Maintenance – target Hb is not fully defined in CKD, but the range is between 110 – 120 g/L. There is evidence of harm when Hb exceeds 130 g/L³⁹. Monitoring of Hb and iron studies is generally at three monthly intervals – Iron supplementation is typically required. This can be given either as oral iron or not uncommonly as intravenous supplementation
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<p>Dietary protein</p> <p>Target:⁴⁰</p> <p>No lower than 0.75 g/kg body weight/day</p>	<p>Dietary protein restriction has been shown to result in modest slowing of CKD progression⁴¹. However, the beneficial effect of protein restriction is typically outweighed by the deleterious effects of nutritional restriction.</p> <p>Management</p> <ul style="list-style-type: none"> - dietary advice
<p>Malnutrition</p> <p>Target:</p> <p>Serum albumin ≥ 35 g/L</p>	<p>Poor food intake due to the symptoms of CKD can lead to malnutrition and low serum albumin.</p> <p>Management</p> <ul style="list-style-type: none"> - dietary advice
<p>Uraemia</p>	<p>Uraemia is a syndrome caused by the accumulation of the breakdown products of protein metabolism. The symptoms include anorexia, nausea, vomiting, lethargy, confusion, muscle twitching, convulsions and coma. Although urea and creatinine levels are high, the symptoms are most likely due to the accumulation of other toxic end products. These symptoms can lead to poor food intake and malnutrition. By the time uraemia becomes symptomatic dialysis is typically indicated.</p> <p>Management</p> <ul style="list-style-type: none"> - Dialysis should be commenced as soon as uraemic symptoms develop - If dialysis is not planned: <ul style="list-style-type: none"> - A low protein diet will help control gastrointestinal symptoms - Fluid control should be strict to avoid pulmonary oedema - Avoid unnecessary medications - Anti-emetics are of limited value
<p>Acidosis</p> <p>Target:</p> <p>HCO₃ > 20mmol/L</p>	<p>People with stage 4–5 CKD are at increased risk of metabolic acidosis. The main factor is decreased renal acid excretion compounded by a reduction in bicarbonate production. Acidosis contributes to demineralization of bone and increased protein degradation, which may be associated with increased morbidity.</p> <p>Management</p> <ul style="list-style-type: none"> - Supplementation with sodium bicarbonate (SodiBic) tablets to meet target - Increased sodium load may worsen blood pressure control

<p>Hyperkalaemia</p> <p>Target:</p> <p>$K^+ \leq 6.0$ mmol/L</p>	<p>In CKD, excretion of potassium (K^+) in the urine is impaired. Levels may also rise with ACE inhibitors and ARBs used to treat hypertension or with use of spironolactone. Levels consistently above 6.0 mmol/L are of concern and should be managed. Hyperkalaemia, especially levels > 6.5 mmol/L, predisposes to cardiac arrhythmias.</p> <p>Management</p> <ul style="list-style-type: none"> – Low K^+ diet – diuretics – resonium – cease ACE inhibitor/ARB if K^+ persistently > 6.0 mmol/L, and not responsive to above therapies
<p>Restless Legs</p>	<p>Restless Legs Syndrome (RLS) is common in CKD. As many as eight in ten people with Stage 5 CKD have RLS or a related movement disorder called periodic limb movements in sleep (PLMS)⁴².</p> <p>Management</p> <ul style="list-style-type: none"> – iron replacement therapy – Dopaminergic agents or dopamine agonists (e.g. Levodopa, Ropinirole) – Benzodiazepines
<p>Sleep Apnoea</p>	<p>Sleep apnoea can affect up to 50% of people with Stage 5 CKD⁴³</p> <p>Management</p> <ul style="list-style-type: none"> – weight reduction – avoid central nervous system depressants – CPAP therapy (if obstructive pattern)
<p>Depression</p>	<p>Mental health problems, particularly depression, often occur with CKD. Depression is the most common mental health problem in people undergoing dialysis, affecting at least one-quarter to one-third of people on dialysis⁴⁴. Depression in people with CKD has detrimental effects on mortality, rates of hospitalisation, medication and treatment adherence, nutrition, and overall quality of life⁴⁵.</p> <p>Management</p> <ul style="list-style-type: none"> – Treatment of depressive symptoms in patients with chronic kidney disease has the potential to improve health outcomes^{46,47} – Psychosocial interventions such as cognitive behavioural therapy, structured problem solving, interpersonal therapy and social work support can play a valuable role – There is good evidence for the use of antidepressants in treating depression in the context of chronic medical illness⁴⁸ – The medication should generally be introduced at a low dose which is then slowly increased⁴⁶

Multi-disciplinary care

The management of CKD is always a collaborative effort, involving at least the patient and their general practitioner. As kidney function declines, and as complications and co-morbidities increase, it becomes increasingly likely that the contribution of others will be needed for optimal care.

These may include:

- Family members or other lay carers
- Practice nurse
- Nephrologist
- Renal nurse/nurse practitioner
- Pharmacist
- Endocrinologist and other professionals specialising in diabetes
- Cardiologist
- Dietician
- Vascular and transplant surgeons
- Mental health professionals
- Community health professionals
- Social worker

The efficient integration of their various contributions becomes more challenging as the numbers of professionals involved in the patient's care increases. The general practitioner plays a crucial role, sustaining an ongoing relationship with the patient and their family, coordinating the care provided by others and ensuring that this care remains focused on the patient's own goals and priorities.

At times the general practitioner may be required to advocate for the patient with other professionals. In addition, he or she has continuing responsibility for primary care of the patient, including:

- Supporting and assisting the patient in the management of their kidney disease and other chronic health problems
- Responding appropriately to new symptoms
- Screening for developing problems and co-morbidities
- Provision of health promotion and disease prevention advice and interventions
- Assistance with addressing psychosocial issues

Even if the patient progresses to end stage kidney disease and has regular contact with the dialysis or transplant team, the general practitioner, practice staff and other health professionals remain vital to optimal care.

In Australia, a number of Medicare items are designed to support proactive, integrated, multidisciplinary care of patients with chronic disease.

USEFUL MBS ITEMS FOR CKD AND ITS COMPLICATIONS

For general practitioners

721	Preparation of a general practitioner management plan
723	Coordination of team care arrangements
725, 727, 729, 731	Contribution to or review of multidisciplinary care plans
734, 736, 738, 740, 742, 744, 746, 749, 757	Organisation and coordination of case conferences
759, 762, 765, 768, 771, 773, 775, 778, 779	Participation in case conferences
900, 903	Medication management review

For nephrologists

820, 822, 823, 830, 832, 834	Organisation and coordination of case conferences
825, 826, 828, 835, 837, 838	Participation in case conferences

For other health professionals

10950, 10951, 10954, 10956, 10958, 10968	Allied health services
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Further information about these items is available at: www.health.gov.au/epc or contact your local Division of General Practice found at www.agpn.com.au

Resources

For a full list of references contained in this document, please go to www.kidney.org.au

Kidney Specific Resources

<p>Kidney Health Australia www.kidney.org.au (03) 9674 4300 1800 682 531 Kidney Health Information Service (KHIS) line</p>	<p>Kidney Health Australia has a range of programs and services to assist general practitioners in their efforts to prevent, detect, and appropriately manage CKD:</p> <ul style="list-style-type: none">– Health professional education programs– eGFR resources– Access to reports and publications– Patient fact sheets
<p>Kidney Check Australia Taskforce (KCAT) www.kidney.org.au (go to KCAT from the Health Professionals link)</p>	<p>KCAT is Kidney Health Australia’s early detection and intervention program for health professionals. Initiatives include:</p> <ul style="list-style-type: none">– Interactive workshops coordinated by Divisions of General Practice– Online learning programs– eGFR resources
<p>On-line learning programs www.kidney.primed.com.au www.thinkgp.com.au</p>	<p>KCAT have worked with PriMed and Genesis Ed to develop a series of on-line CKD learning activities.</p> <ul style="list-style-type: none">– The PriMed program includes a range of individual modules around early detection of CKD using eGFR automatic reporting, assessment of kidney function and chronic disease management strategies– The Genesis Ed ‘The assessment and management of CKD’ program consists of a series of three one-hour e-chats which are now available to access online at www.omnus.com.au <p>30 Category One, RACGP QA&CPD points can be earned by completing six hours of KCAT on-line education.</p>
<p>Caring for Australasians with Renal Impairment (CARI) www.cari.org.au</p>	<p>Online evidence-based clinical practice guidelines for the management of adult and paediatric patients with chronic kidney disease.</p>

<p>Renal Drug Reference Guide www.renaldrugreference.com.au</p>	<p>First Australian resource focusing on drug dosing in people with kidney disease. Virtual tours and copies available to order online.</p>
<p>General Practice Resources</p>	
<p>Royal Australian College of General Practitioners www.racgp.org.au</p>	<p>Professional guides available to download online including:</p> <ul style="list-style-type: none"> – Smoking, Nutrition, Alcohol and Physical Activity (SNAP) Guide – Red Book: Guidelines for preventive activities in general practice – Green Book: Putting prevention into practice – National guide to a preventive assessment in Aboriginal and Torres Strait Islander peoples
<p>Australian General Practice Network www.agpn.com.au</p>	<p>The peak national body representing divisions of general practice and their state-based organisations across Australia. Online resources include:</p> <ul style="list-style-type: none"> – Chronic Disease Management – Lifescripts – Enhanced Divisional Quality Use of Medicines
<p>Type 2 Diabetes from the GP's perspective www.servier.com.au</p>	<p>NEFRON study data coupled with pragmatic advice for general practitioners</p>

Abbreviations

ACE inhibitor	Angiotensin-Converting Enzyme inhibitor
ARB	Angiotensin II Receptor Blocker
CARI	Caring for Australasians with Renal Impairment
BMI	body mass index
CKD	chronic kidney disease
CVD	cardiovascular disease
eGFR	estimated glomerular filtration rate
FBC	full blood count
GFR	glomerular filtration rate
MDRD	Modification of Diet in Renal Disease
NSAIDS	non-steroidal anti-inflammatory drugs
PBS	Pharmaceutical Benefits Scheme
PTH	parathyroid hormone
WC	waist circumference

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Disclaimer

This guide is based upon the best information available at the time of publication. It is designed to provide information and assist decision-making. It is not intended to indicate an exclusive course of action, or serve as a standard of medical care. Variations, taking individual circumstances into account, may be appropriate. Every health-care professional making use of this guide is responsible for evaluating the appropriateness of applying it in the setting of any particular clinical situation. The authors assume no responsibility for personal or other injury, loss or damage that may result from the information in this publication.

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CKD management according to stage

CKD Stage	1	2	3	4	5
Description	Kidney damage + normal or ↑ eGFR	Kidney damage + mild ↓ eGFR	Moderate ↓ eGFR	Severe ↓ eGFR	End stage kidney disease
eGFR (mL/min/1.73m²)	≥ 90	60–89	30–59	15–29	<15 or on dialysis
Common Signs and Symptoms	Nil		Nil or nocturia, mild malaise, anorexia	As for stage 3 + nausea, pruritis, restless legs, dyspnoea	As for stage 4
Common Complications	Hypertension		As for stage 1–2 + Mineral and Bone Disorder Anaemia Sleep Apnoea Restless legs CVD Malnutrition Depression	As for stage 3 + Hyperphosphataemia Acidosis Hyperkalaemia	As for stage 4 + Pericarditis GIT bleeding Encephalopathy Neuropathy
Clinic Assessment	BP Weight Urine dipstick		As for stage 1–2	As for stage 1–2 + Oedema	As for stage 4
Lab Assessment	General chemistry, eGFR Glucose Lipids		As for stage 1–2 + FBC Iron stores Ca/PO ₄ PTH (quarterly)	As for stage 3	As per monthly blood schedule specified by Renal Unit
Management	Diagnosis Cardiac and kidney risk factor modification Treat BP to target <130/80 mmHg or <125/75 mmHg if proteinuria >1g/24hrs or diabetes present (urine protein: creatinine ratio of 100 mg/mmol ≈ daily protein excretion of 1g/24hrs)		As for stage 1–2 + Treat complications Medication review	As for stage 3 + Dialysis education Dialysis access surgery	As for stage 4 + Dialysis or transplantation (or conservative medical management)
Frequency of clinical review	4–6 monthly		1–3 monthly	Monthly	Monthly (shared with renal unit)
Nephrologist Referral	Consider referral if indication is present		Consider referral if indication is present	All patients should be referred to a nephrologist	All patients should be referred to a nephrologist