B-QuiCK: Chronic kidney disease (CKD)

Overview of the diagnosis and classification of patients with CKD in primary care

Patient at risk of CKD, e.g.:

- **Diabetes or hypertension**
- Established CVD
- Family history of kidney disease
- History of acute kidney injury
- Age ≥ 60 years
- Nephrotoxic medicine use
- Urological disease or prostatic syndrome
- Māori, Pacific or South/Indo Asian ethnicity
- Obesity (BMI > 30 kg/m²)
- Smoker/vaper

Note: nephrology discussion or referral is generally recommended for patients with:

- eGFR < 30 mL/min/1.73 m² or < 45 mL/min/1.73 m², with co-morbid diabetes and persistent urine ACR > 30 mg/mmol
- Sustained decrease in eGFR of 10 – 15 mL/min/1.73 m² or ≥ 25% and a change in eGFR category within 12 months, or change in eGFR of ≥ 20% between measurements
- Persistent macroalbuminuria (i.e. urine ACR > 30 mg/mmol) with haematuria, or urine ACR > 70 mg/mmol
- Uncertain or unclear cause of CKD
- Hereditary kidney disease
- Recurrent extensive nephrolithiasis
- Suspected intrinsic kidney damage (e.g. glomerulonephritis) or renal artery stenosis
- Five-year risk of kidney replacement > 3 – 5%

Patient with either of the following incidental laboratory findings

Assess blood pressure and request:

- Serum creatinine (for eGFR)
- Urine ACR

eGFR and urine ACR normal → **Repeat assessments every 1 – 2 years** (annually if patient has diabetes, hypertension or history of acute kidney injury)

eGFR < 60 mL/min/1.73 m²

Repeat serum creatinine (for eGFR) within two weeks

Consider possibility of acute kidney injury if eGFR has reduced ≥ 20%; discuss with, or refer to, a nephrologist

Urine ACR ≥ 3 mg/mmol

Repeat in three months

At least two reduced eGFRs OR elevated urine ACRs over ≥ 3 months?

Yes

No → Consider need for other investigations or referral

		Description	eGFR (mL/min/1.73 m²)	Persistent albuminuria category (based on urine ACR) A1 (normal) < 3 mg/mmol	A2 (microalbuminuria) 3 – 30 mg/mmol	A3 (macroalbuminuria) > 30 mg/mmol
eGFR category	G1	Normal or high	≥ 90		Monitor	Refer
	G2	Mildly decreased	60 – 89			
	G3a	Mildly to moderately decreased	45 – 59	Monitor	Monitor	Refer
	G3b	Moderately to severely decreased	30 – 44	Monitor	Monitor	
	G4	Severely decreased	15 – 29			
	G5	Kidney failure	< 15 or dialysis			

Prognostic risk: Low | Moderate | High | Very high

Determine the underlying cause; request additional tests/investigations as needed (see main text)

Combine the underlying cause + eGFR category + persistent albuminuria category (CGA) to fully classify CKD, e.g. CKD G3a with microalbuminuria (A2) due to diabetes

Management of patients with CKD in primary care

Lifestyle management

Weight	■ Target BMI < 25 kg/m^2; but any reduction in weight is beneficial ■ Target waist circumference < 94 cm for males, < 80 cm for females N.B. Aim for lower values for people of Asian ethnicity.
Exercise	■ Aim for at least 150 minutes/week of moderate-intensity physical activity (or to a level that is tolerable) ■ Strength/resistance training on at least two days/week
Nutrition	■ Recommend a balanced diet emphasising vegetables, fruits, nuts, low-fat dairy products, whole grains and fish (e.g. DASH diet); reduce sodium intake, avoid trans fats, processed meats, refined carbohydrates, sweetened beverages. Water should be the main fluid but avoid over-consumption. ■ Avoid high levels of protein intake but do not advise a protein-restricted diet unless under dietitian or nephrologist supervision
Alcohol	■ No specific recommendation for people with CKD (other than standard advice), but the less alcohol consumed, the lower the risk of harm
Smoking	■ Encourage smoking and vaping cessation, if applicable

Provide "sick day" advice. Advise patients to temporarily withhold sulfonylureas, ACE inhibitors, diuretics, metformin, ARBs, NSAIDs and SGLT-2 inhibitors during an acute illness (SADMANS).

Pharmacological management

Main goals:

1. Slow progressive loss of kidney function
2. Reduce CVD risk

The "four pillars" approach is becoming the new standard of care, particularly for those with diabetes and at high risk of progression to advanced CKD:

- An ACE inhibitor or ARB; ***and***
- A SGLT-2 inhibitor; ***and/or***
- A GLP-1 receptor agonist; ***and/or***
- A non-steroidal mineralocorticoid receptor antagonist (not routinely available in New Zealand)

Initiate an ACE inhibitor/ARB in all patients with CKD

- Aim for BP < 120 – 130/80 mmHg for most patients
- Up-titrate the ACE inhibitor/ARB to the maximum (approved) tolerated dose
- Monitor for acute reductions in eGFR and hyperkalaemia - ideally two to four weeks after initiation or dose increase
  - Serum creatinine increase up to 30% or eGFR reduction up to 25% is acceptable; reduce dose or discontinue medicine if changes above these values occur
  - Serum potassium up to 6.0 mmol/L is acceptable. Manage hyperkalaemia with dietary and pharmacological measures (diuretic) before withholding or reducing the dose. Discuss or refer patients with persistent hyperkalaemia to a nephrologist.
- If antihypertensive treatment escalation is required, add a calcium channel blocker or diuretic (thiazide or loop)

Initiate empagliflozin (SGLT-2 inhibitor), where possible

- Prescribe empagliflozin 10 mg, daily (Special Authority criteria apply) for patients with an eGFR ≥ 20 mL/min/1.73 m^2 who have:

  - Type 2 diabetes
  - Moderately increased albuminuria (urine ACR ≥ 20 mg/mmol)*
  - Heart failure
- Do not initiate empagliflozin if eGFR is < 20 mL/min/1.73 m^2, however, it can be continued if eGFR drops below this value during treatment (if tolerated)
- Expect a transient reduction in eGFR when initiating empagliflozin; this is not a reason for discontinuation
- Possible adverse effects include ketoacidosis, genital mycotic infections, Fournier's gangrene (rare), osmotic diuresis

* If urine ACR is < 20 mg/mmol in a patient with an eGFR 20 – 45 mL/min/1.73 m^2, a SGLT-2 inhibitor is *suggested* in KDIGO guidelines

Best Practice Tip: For patients who are self-funding empagliflozin, consider ways to reduce cost for them, e.g. use of a disability allowance if applicable, checking costs of tablets of different strengths and between pharmacies.

Prescribe a GLP-1 receptor agonist to patients with co-morbid diabetes

- Aim for a target HbA_{1C} of ≤ 53 mmol/mol for most patients; ensure metformin is dosed according to eGFR (see **Table 3** for dosing)
- Prescribe GLP-1 receptor agonist (dulaglutide and liraglutide are funded with; Special Authority approval) if HbA_{1c} not adequately controlled with metformin and/or empagliflozin (or if not tolerated)
- Initiate GLP-1 receptor agonist at a low dose and up-titrate slowly to reduce the risk of gastrointestinal effects

Best Practice Tip: For patients with co-morbid CKD, type 2 diabetes and heart failure, apply for funded empagliflozin under the Special Authority for heart failure and funded dulaglutide/liraglutide under the Special Authority for diabetes if the patient's HbA_{1c} remains above target.

N.B. More studies are needed to determine the role of GLP-1 receptor agonists in CKD management for people without diabetes; emerging evidence suggests benefit with semaglutide in those who are overweight/obese. Click here for approved indications for GLP-1 receptor agonists in New Zealand.

Non-steroidal mineralocorticoid receptor antagonists (MRAs): not routinely available

- Non-steroidal MRAs are not approved nor readily available in New Zealand, therefore, are not part of routine management
  - Internationally, they are recommended for people with CKD (with an eGFR > 25 mL/min/1.73 m^2) and diabetes who have persistent albuminuria (> 3 mg/mmol) despite taking the maximum tolerated dose of an ACE inhibitor/ARB
- Steroidal MRAs (e.g. spironolactone, eplerenone) are not a suitable substitute for patients in whom a non-steroidal MRA is recommended. They may be prescribed to patients with CKD and co-morbid heart failure, hyperaldosteronism or resistant hypertension; caution is required due to risk of hyperkalaemia and reversible decline in glomerular filtration.

Consider other pharmacological treatments

- Initiate a statin (atorvastatin or rosuvastatin if Special Authority criteria are met), with or without ezetimibe, in patients with an eGFR ≥ 15 mL/min/1.73 m^2 and CVD risk ≥ 10% (or ≥ 5% in Māori)
  - Consider a statin after discussing benefits and risks in patients with a CVD risk of 5 – 10%
  - Statin treatment may benefit any patient with CKD regardless of their calculated CVD risk, e.g. those with persistent albuminuria
- Consider long-term use of low-dose aspirin for secondary prevention if established CVD
- Potentially nephrotoxic medicines (e.g. NSAIDs, lithium) may need to be switched or discontinued

Ongoing monitoring of treatment

See **Table 4** for suggested monitoring and investigation schedule.

- Review eGFR, urine ACR and blood pressure at least annually, in addition to other relevant laboratory investigations, e.g. serum electrolytes, full blood count.
- Ensure vaccinations are up to date, e.g. influenza, COVID-19, pneumococcal and meningococcal, herpes zoster (Shingrix), hepatitis A and B, *Haemophilus influenzae* type b
- Discuss with or refer to a nephrologist as needed, e.g. if complications of advanced CKD (e.g. metabolic acidosis) are identified

Table 3. Maximum daily dose of metformin based on eGFR.

eGFR (mL/min/1.73 m²)*	Maximum metformin dose per day
60 – 120	2 g
30 – 60	1 g N.B. KDIGO guidelines for diabetes management in CKD (2022) recommend that a metformin dose of up to **2 g, daily, is safe when eGFR is > 45 mL/min/1.73 m².**The New Zealand Society for the Study of Diabetes advises that best practice is now to only reduce the dose of metformin when the eGFR is < 45 mL/min/1.73 m² (this recommendation is off-label, but widely adopted).
15 – 30	0.5 g
< 15	Contraindicated

* While in many cases eGFR will be sufficient to estimate kidney function in patients taking metformin, the Manufacturer advises using creatinine clearance, calculated from the Cockcroft and Gault equation, to estimate kidney function

Table 4. Suggested monitoring and investigation schedule for patients with CKD.

CKD parameters	Frequency of review	Laboratory investigations	Clinical assessment
■ eGFR ≥ 60 mL/min/1.73 m² with microalbuminuria (A2) **or** ■ eGFR 45 – 59 mL/min/1.73 m² with normal albumin (A1)	Annually	Recommended: ■ Creatinine (eGFR) ■ Urine ACR ■ Urea ■ Electrolytes ■ Full blood count N.B. Urea is not often tested in a primary care setting, but if disproportionately elevated compared to creatinine, it may suggest causes such as corticosteroid use, increased protein breakdown or gastrointestinal bleeding, rather than true kidney function decline. Consider: ■ HbA_{1c} ■ Lipid panel ■ Iron studies ■ Dipstick urinalysis for haematuria	■ Blood pressure ■ Weight and waist circumference ■ Smoking/vaping status ■ Medicine use; avoid nephrotoxic options and adjust doses depending on kidney function ■ Check for oedema (if macroalbuminuria irrespective of eGFR or eGFR < 30 mL/min/1.73 m² irrespective of albuminuria)
■ eGFR 30 – 59 mL/min/1.73 m² with microalbuminuria (A2) **or** ■ eGFR 30 – 44 mL/min/1.73 m² with normal albumin (A1)	Every three to six months	In addition to above, consider: ■ Calcium and phosphate ■ Parathyroid hormone ■ Albumin N.B. Albumin can be requested alone or as part of a LFT panel. Low serum albumin can occur with nephrotic range proteinuria (ACR > 300 mg/mmol) and nephrotic syndrome (oedema, ACR < 300 mg/mmol).	
■ Macroalbuminuria irrespective of eGFR **or** ■ eGFR < 30 mL/min/1.73 m² irrespective of albuminuria	Every one to three months		

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