CKM Guidance

Cardiovascular-Kidney-Metabolic Disease

Preventing Adverse Outcomes in Cardiovascular Kidney Metabolic Conditions

Last content update date: 1st February 2026
File date: 13th June 2026
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Instructions:

The guidance is separated into the multiple sections.

Clicking on the yellow highlighted text will take you to the relevant section of the guidance on the guidance web site.

Clicking on a pink highlighted abbreviation will take you to the relevant abbreviation within the abbreviations section of this document.

Clicking on a blue link will open relevant external guidance in a new window for more detailed information.

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9. Management of chronic kidney disease

Definition of chronic kidney disease (CKD)

- CKD is defined as renal impairment (eGFR <60mL/min) AND/OR persistent albuminuria (2 out of 3 UACR >3 mg/mmol) for more than 3 months.
    - Albuminuria indicates endothelial inflammation.
    - Renal impairment indicates renal damage or scarring.
    - Both are independent risk factors for CV disease irrespective of each other with and without diabetes.

Overview of management of CKD

- This guidance focusses on the management of albuminuria and renal impairment relevant to CKM conditions. Detailed guidance on the staging, investigation and management of chronic kidney disease (CKD) can be found here. This is important in identifying the cause of the CKD, which is critical in best management.

- All people diagnosed with CKD should have a CKM risk assessment to help guide management. Best management of CKD includes 7 key areas to reduce progression of CKD and adverse sequelae:
    1. Healthy living interventions
    2. Renin-Angiotensin system (RAS) inhibitors and blood pressure (BP) lowering therapy
    3. SGLT2 inhibitors
    4. GLP1 receptor agonists
    5. Mineralocorticoid receptor antagonists
    6. Lipid lowering therapy and antiplatelet therapy
    7. Other key practice points in managing CKD

NB: Starting this standard of care management as soon as possible in CKD is important because it achieves at least 7 more years of health free of significant kidney disease.

Healthy living interventions in CKD

- Healthy living interventions in CKD are similar to those for all CKM conditions , particularly in reducing hyperglycaemia and BP to slow progression of CKD. Important specific advice to CKD includes:
    - Low sodium intake (< 2 g of sodium or < 5 g of salt per day) especially if high BP.
        - Avoiding processed foods and adding salt to food important.
    - A low potassium diet should not be recommended routinely unless persistent hyperkalaemia (K^+ > 6 mmol/L).
    - Specialist renal dietitian advice is recommended if eGFR < 45 mL/min/1.73m^2 if ANY of the following:
        - Persistent hyperkalaemia despite addressing other causes e.g. medications, constipation etc.
        - Consideration of very low calorie or low carbohydrate diets
        - Very high protein intake can be harmful and may lead to kidney hyperfiltration and glomerular injury
        - Concerns over malnutrition or electrolyte disturbances

Renin - Angiotensin system (RAS) inhibitors and blood pressure (BP) lowering therapy

- Treatment regimen with either an ACE inhibitor (ACEi) or angiotensin receptor blocker (ARB) is dependent on whether albuminuria is present (UACR > 3 mg/mmol). Calcium channel blockers (CCB) and thiazide diuretics (TD) may also be required if the BP is above target. The target BP for most with CKD is a systolic BP < 120 mmHg.

- **Relaxed BP targets to the lowest reasonably and safely achievable BP are appropriate if any of the following:**
    - Frailty and/or limited life expectancy
    - Age ≥ 85 years
    - Symptomatic postural hypotension → treat to standing BP if > 10 mmHg postural drop.
    - Intolerant of BP lowering medications
- **Albuminuria present**:
    - Start ACEi OR ARB if no concerns over hypotension → titrate to maximal tolerated dose
        - Add a CCB or TD if BP > target
        - If BP still above target add other e.g. TD if CCB used previously
- **No albuminuria but BP above target**
    - Start low dose ACEi OR ARB with CCB in combination → if BP above target increase dose of combination agents
    - If BP remains above target then add TD

- When starting or changing the dose of ACEi or ARB it is important to:
    - Ensure up to date sick day management advice and contraception if applicable
    - Measure creatinine and serum potassium 1-2 weeks after dose change
        - K^+ < 6 mmol/L and < 30% decrease in eGFR requires no change
        - If K^+ ≥ 6 mmol/L urgently review
            - Exclude spurious hyperkalaemia due to dietary intake, haemolysis and/or delayed processing, or medication effect e.g. trimethoprim.
            - K^+ ≥ 6.5 mmol/L is a potential medical emergency
            - If K^+ is 6 - 6.5 mmol/L and K^+ rise is < 30% aim to reduce K^+ by:
                - Decreasing other K^+ increasing medications, especially NSAIDs, trimethoprim and β-blockers if appropriate

        - β-blockers have greater K+ retention effects than RAS inhibition but should not generally be stopped abruptly

    - Reducing dietary potassium intake
    - Consider frusemide if volume overload or refractory hypertension
    - Consider oral sodium bicarbonate if metabolic acidosis

- If K^+ is 6 - 6.5 mmol/L but K^+ rise is ≥ 30% withhold ACEi or ARB and other K^+ elevating medications
    - Recheck K^+ in 1-2 days and reintroduce ACEi or ARB as soon as K^+ normalises
    - Titrate ACEi or ARB to maximal dose based on K^+ levels

- If > 30% decrease in eGFR withhold ACEi or ARB and review
    - Assess for other causes of acute kidney injury particularly medications e.g. diuretics, NSAIDs
    - Correct volume depletion
    - Recheck eGFR and ensure person is well hydrated before the test. Restart ACEi or ARB if eGFR close to baseline
    - If appears ACEi or ARB-induced then discuss with renal team whether restart ACEi/ARB and consider renal artery stenosis

NB: ACEi, ARB, CCB, and TD are discussed in detail in management of elevated blood pressure and hypertension

SGLT2 inhibitors in chronic kidney disease

- Start SGLT2 inhibitor, e.g. empagliflozin 10 mg daily if ANY of the below AND eGFR > 20 mL/min:
    - Type 2 diabetes with UACR > 3 mg/mmol
    - Heart failure
    - UACR > 20 mg/mmol
    - eGFR 20 – 44 mL/min at any level of albuminuria
    - **NB:** Empagliflozin is only funded at present under special authority if type 2 diabetes and/or reduced ejection heart failure is present. Although currently expensive at ~$85 per month, self-funding should be offered including tips to increase access
        - Utilising the disability allowance to cover the cost of empagliflozin if able

        - Prescribing half the 25 mg tablet of empagliflozin or 1 tablet of empagliflozin 12.5 mg with metformin (Jardiamet) if type 2 diabetes to halve the cost to approximately $43 per month – please note this is off-label.
        - Checking the cost between pharmacies because there continues to be wide variation

- The dose of empagliflozin can be increased to 25 mg daily if type 2 diabetes AND the HbA1c remains above target
    - Beware glucose-lowering effects of empagliflozin are eGFR < 30 mL/min

- Empagliflozin should only be stopped if adverse effects occur or dialysis is started.
    - A transient decrease in eGFR is normal when starting empagliflozin

- Sick day advice AND tips to reduce adverse effects should be provided for all on empagliflozin:
    - Withhold empagliflozin in acute illness and 3 days before (including day of) major surgery, bowel prep or low carb diet. Restart when well and eating and drinking normal.
    - Doses of sulfonylureas may need to be reduced by 50% and doses of insulin by approximately 20% to avoid hypoglycaemia when starting empagliflozin → typically only required when baseline HbA1c < 64 mmol/mol.
    - Discuss importance of genital hygiene particularly for individuals who may have difficulty accessing the genital area (e.g., due to body habitus or limited mobility). Warn people to stop if there is any hint of pain or redness.
    - Do not use in pregnancy, breastfeeding or children < 10 years of age
    - Do not use in type 1 diabetes, significant alcohol intake, previous diabetic ketoacidosis (DKA) or low carbohydrate diets without specialist advice
    - If symptoms of DKA (e.g. nausea, vomiting, abdominal pain etc.) need to present to GP practice or A+E urgently to ensure blood ketones are < 1.5 mmol/L. DKA needs to be excluded if ketones > 1.5 mmol/L.
    - Beware glucose levels may be normal or only mildly elevated in DKA with empagliflozin

GLP1 receptor agonists (GLP1Ra) in chronic kidney disease

- GLP1Ra should be considered in CKD if weight loss is desirable (i.e. if overweight or obese) and/or if type 2 diabetes and the HbA1c is above target despite metformin and empagliflozin. GLP1Ra are not currently recommended if the eGFR is < 15 mL/min/1.73m^2
    - Please click here for more information on using GLP1Ra in type 2 diabetes (dulaglutide and liraglutide currently funded but would need to self-fund empagliflozin)
    - Please click here for more information on using GLP1Ra for weight loss (no GLP1Ra are currently funded without diabetes)

- Post hoc analyses suggest that semaglutide may reduce the progression of kidney and cardiovascular disease in those with a BMI < 27 kg/m^2 and without diabetes. Further dedicated studies are underway to confirm safety and efficacy in this population. At present semaglutide (Wegovy) is only registered for those with a BMI > 27 kg/m^2 in Aotearoa New Zealand.

Mineralocorticoid receptor antagonists (MRAs)

- Non-steroidal MRAs such as finerenone are a pillar of management CKD internationally, but are currently not available in Aotearoa New Zealand.
- Older MRAs such as spironolactone or eplerenone may still be used to treat concomitant heart failure or refractory hypertension despite ACEi or ARB, CCB and TD. However, the use of spironolactone or eplerenone in CKD should only be with specialist input due to the risk of hyperkalaemia.

Lipid lowering therapy and antiplatelet therapy in CKD

- Start lipid lowering therapy if eGFR > 15 mL/min aiming for LDLc < 1.4 mmol/L and > 50% reduction in LDLc from baseline if ANY of the below:
    - UACR ≥ 30 mg/mmol
    - eGFR < 45 mL/min
    - UACR 3 – 29 mg/mmol AND eGFR 45 – 59 mL/min
    - LDLc ≥ 4.9 mmol/L and/or known familial hypercholesterolaemia
    - CV disease including asymptomatic coronary or carotid disease (includes CT calcium score > 300)
    - Diabetes with any microvascular or macrovascular complication(s) → includes diabetic kidney disease
    - 5 year CV risk ≥ 10%
- Lipid lowering therapy is also recommended if none of the above and 5 year CV risk 5 – 9.9% aiming for target LDLc < 1.8 mmol/L and > 50% reduction in LDLc from baseline.
- Lipid lowering therapy should be considered if none of the above and 5 year CV risk 3 – 4.9% and additional risk factors for CVD. Target LDLc is < 1.8 mmol/L.
    - Risk factors to consider lipid lowering therapy include:
        - < 50 years of age
        - Direct family history of CV disease at < 50 years of age
        - Cardiac calcium score 100 - 300
        - Previous gestational diabetes and/or preeclampsia
        - MASLD
- Lipid lowering therapy is discussed in detail in management of dyslipidaemia

- Aspirin is important for secondary prevention of CV events in CKD. However, the balance of benefits and risks for aspirin for primary prevention in CKD is unknown.

Other key practice points in managing chronic kidney disease

- Addressing inequities are important in CKD
    - Incidence of CKD is 1.3 to 3 times higher in Māori, Pacific peoples, and people from Indo-Asia. Advanced CKD incidence is 3 to 5 times higher in these populations.
    - Consider cultural supports early to address any barriers to diagnosis and management.
    - Aim for whānau-based care if possible and integrate care with Rongoā Māori practitioners if whānau wish

- Ensuring adequate coding of CKD to enable best care
    - Coding of CKD is missing in 60 – 95% of cases internationally and is associated with:
        - Faster rates of CKD progression and reduced access to best care
        - Increased end stage kidney disease and major adverse CV events

- Optimising management of hyperglycaemia and gout in CKD is important to reduce the progression of CKD and CV risk
    - Healthy living interventions, metformin AND empagliflozin +/- GLP1Ra are best management of all people with CKD and T2D
    - Please click here for more information on these interventions and other treatment options if the HbA1c remains above target

- Medication adjustment is often required in CKD
    - Please click here for more information on medications that require dose adjustment or cessation in CKD

- Provide vaccinations as per the Immunisation Advisory Centre guidance in pre-dialysis, dialysis and pre- and post-kidney transplant

- People with CKD are at high risk of an acute kidney injury so it is important to:
    - Avoid nephrotoxic medications if possible e.g. NSAIDs
    - Ensure adequate hydration and sick day management plan

- Strongly consider renal advice if ANY of the following:
    - eGFR < 30 mL/min/1.73m^2

        - Formal review may not be required if eGFR stable, UACR < 30 mg/mmol or if the individual is frail.

    - eGFR 30 - 45 mL/min/1.73m^2 and UACR > 30 mg/mmol if known diabetes
        - Formal review may not be required if eGFR stable, UACR < 30 mg/mmol or if the individual is frail.

    - eGFR < 60 mL/min/1.73m^2 and declining by > 10mL/min/1.73m^2 in the last 12 months AND/OR UACR > 70 mg/mmol on ≥ 2 occasions as at high risk of progressive CKD.
    - If family history of, or known intrinsic kidney disease e.g. Polycystic Kidney Disease
    - **NB:** It may be prudent to recheck/confirm eGFR before referral if the decrease in eGFR may be an anomaly, ensuring adequate hydration before the repeat test.

- Depression is common in CKD and should be screened for and treated as required
    - The PHQ-2 score can be a useful screening tool

- People with advanced kidney disease (eGFR < 15 mL/min) usually have symptoms that significantly impact quality of life.
    - Treatment involves consideration of kidney replacement therapy (dialysis or kidney transplantation) and symptom management.
    - Consider advanced care plan (ACP) and palliative care input.
    - Examine feet and consider podiatry input as high risk of active foot disease

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Abbreviations:

CKM
Cardiovascular-Kidney-Metabolic

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