CKM Guidance

Cardiovascular-Kidney-Metabolic Disease

Preventing Adverse Outcomes in Cardiovascular Kidney Metabolic Conditions

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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.

Contents:

6. Management of elevated blood pressure and hypertension

Definition of elevated BP and hypertension and how to measure BP

- Treatment of high blood pressure (BP) is likely the most easily modifiable risk factor in preventing CV and renal sequelae in CKM disease so BP should be measured at every practical opportunity
- An individualised approach is recommended taking into account competing risks and preferences and explored through shared decision making
- **Recommended thresholds for treatment of BP depend whether other CKM disease features are present:**

- **BP ≥ 140/90 mmHg → prompt confirmation and treat with lifestyle advice + pharmacotherapy in all if appropriate**
    - Ideally elevated BP should be confirmed as soon as possible on validated home or ambulatory BP monitoring. Home monitoring is best done in a structured approach e.g. morning and evening BP measurements at rest for 1 week. If home or ambulatory BP monitoring not available then recommend measurement of BP in clinic with the following:
        - Measure BP after 5 mins seated comfortably in a quiet environment with a validated device with an appropriate cuff size with the cuff at the level of the heart.
        - Measure BP 3 times 1-2 mins apart and average the last 2 readings
        - Often useful to measure BP at both arms and to assess whether postural drop at 1st visit to aid monitoring at future visits.

- **BP 130 – 139/80 - 89 mmHg → prompt confirmation and treat with lifestyle advice + pharmacotherapy if 5 year CV risk ≥ 10% OR ANY of the following:**
    - Ideally elevated BP should be confirmed as soon as possible on validated home or ambulatory BP monitoring. Home monitoring is best done in a structured approach e.g. morning and evening BP measurements at rest for 1 week. If home or ambulatory BP monitoring not available then recommend measurement of BP in clinic with the following:
        - Measure BP after 5 mins seated comfortably in a quiet environment with a validated device with an appropriate cuff size with the cuff at the level of the heart.
        - Measure BP 3 times 1-2 mins apart and average the last 2 readings
        - Often useful to measure BP at both arms and to assess whether postural drop at 1st visit to aid monitoring at future visits.
    - CVD including ischaemic heart disease, cerebrovascular disease, peripheral arterial disease, atrial fibrillation and heart failure
    - Diabetes with any microvascular or macrovascular complication
    - Familial hypercholesterolaemia
    - Chronic kidney disease (eGFR <60mL/min and/or UACR >3 mg/mmol)
    - NB: Gout, MASLD and OSA all independently increase CV risk and events, but are not currently included in the PREDICT CV risk calculator. Therefore, CV risk is likely underestimated in these conditions and treatment of BP 130-139/80-89 mmHg should still be considered in these conditions if no other indications, particularly if 5 year CV risk 4-5%.

- **BP 130 - 138/80 - 89 mmHg and 5 year CV risk 5 - < 10% → lifestyle advice + treat underlying condition + consider pharmacotherapy IF ANY of the following:**

        - Gout or auto-immune inflammatory disease
        - MASLD
        - OSA
        - Severe mental illness particularly with antipsychotic use
        - Previous gestational diabetes and/or preeclampsia
        - Direct family history of CVD < 40 years of age
        - Cardiac calcium score ≥ 100

    - **BP 130 - 138/80 - 89 mmHg and 5 year CV risk < 5% → lifestyle advice alone**

- **Target systolic BP is 120 – 129 mmHg in most individuals**
    - A systolic BP < 120 mmHg is not concerning if well tolerated and likely preferable if young or heart failure
    - **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
            - Measure lying/standing or sitting/standing BP if high risk of postural hypotension and treat to standing BP if > 10 mmHg postural drop.
        - Intolerant of antihypertensives
    - Unlike other features of CKM, treating BP has no 'metabolic memory or legacy effect'. Therefore, BP targets and treatment should only be relaxed when clinically appropriate
    - Diastolic BP targets are now no longer first-line BP targets due to evidence for the greater benefit of controlling systolic BP. Although it is desirable to have a diastolic BP < 80 mmHg, a systolic BP 120 – 129 mmHg is the primary target.

- Treatment consists of both non-pharmacological and pharmacological management and should ideally be based on several 'out of office' or home BP monitoring at rest as BP levels in clinic are typically ≥ 5 mmHg higher. Home monitoring is best done in a structured approach e.g. morning and evening BP measurements at rest for 1 week.
    - If out of office BP monitoring not available then measure BP after 5 mins seated comfortably in a quiet environment with a validated device with an appropriate cuff size with the cuff at the level of the heart. Ideally BP should be measured 3 times 1-2 mins apart with the average of the last 2 readings

used.

- Non-pharmacological management is always important and is discussed in detail in lifestyle management. Key points include:
    - Smoking and alcohol cessation
        - Increasing evidence that vaping cessation is also beneficial
    - A low-salt diet with fruit and leafy vegetables to ensure adequate potassium intake
    - Increased physical activity and movement
    - Aiming for > 5% total body weight loss if overweight
- First line pharmacotherapy for lowering BP are ACE inhibitors (ACEi) or angiotensin receptor blockers (ARB), calcium channel blockers (CCB) and thiazide diuretics (TD). Typically, these medications are more effective and better tolerated in low doses in combination, but may be used alone. Cardioselective beta blockers (β-blocker) may be used if ischaemic heart disease, heart failure or atrial fibrillation. Guidance on likely best agents in each to use based on efficacy and tolerance is below.
- Best choice of ACEi, ARB, CCB or TD is dependent on whether renal disease predominates and presence of other comorbidities:
    - Chronic kidney disease is present (eGFR <60 mLmin and/or UACR > 3 mg/mmol):
        - Strongly consider ACEi or ARB if no hypotension and check BP in 1 month
        - Titrate ACEi or ARB to maximal tolerated dose
        - Check BP monthly until to target – if BP remains above target add CCB or TD
        - If BP still above target then add other (e.g. TD if CCB previously added)
    - No renal or CV disease:
        - Strongly consider low dose ACEi or ARB and CCB in combination
        - Check BP in 1 month → if above target increase dose of combination agents
        - Check BP monthly until to target - if BP remains above target then add TD
    - Gout:
        - Consider ACEi or ARB as first-line options. (Note that losartan and dihydropyridine CCBs may serve as helpful adjuncts due to their small uricosuric effect, but they should not replace urate-lowering therapy and the focus should be on the most effective anti-hypertensive)
        - Beware TD typically increase uric acid levels

- Ischaemic heart disease, heart failure or atrial fibrillation:
    - β-blockers may be added at any stage. May need to decrease CCB and/or TD if hypotension
    - In heart failure Entresto (Sacubitril/Valsartan) is preferred renin-angiotensin system inhibitor (rather than ACEi or ARB) but need to meet special authority criteria for funding. Use spironolactone or eplerenone and empagliflozin rather than TD or CCB if risk of hypotension.
        - Current special authority criteria for Entresto requires the following:
            - NHYA/WHO functional II-IV AND
            - LVEF ≤ 35% OR echocardiogram is not reasonably practical AND
            - Other standard treatments of heart failure are optimised
        - Maximise doses of Entresto, β-blocker and spironolactone before addition of other agents.
            - Remember to monitor potassium when using Entresto or spironolactone as per ACEi/ARB below

- Causes of secondary hypertension should be considered if young and/or persistent hypertension despite adherence to ≥ 3 antihypertensive agents
    - Obstructive sleep apnoea is likely the most common cause of secondary hypertension in CKM and is often missed
    - Consider other investigations as appropriate to exclude renal disease, pregnancy, and endocrine conditions such as primary hyperaldosteronism, Cushing's syndrome, thyrotoxicosis and acromegaly.
    - Consider referral to secondary care to discuss addition of other antihypertensives as required
        - Spironolactone likely preferable if heart failure
            - Caution advised if low eGFR and/or baseline hyperkalaemia
        - Alpha blockers likely preferable if prostatic disease

- Likely preferred agents in each of blood pressure lowering medications available in Aotearoa NZ:
    - ACEi and ARB:
        - Ramipril typically preferred ACEi but perindopril useful alternative. Quinapril also useful alternative if combination with TD desirable but often requires twice daily dosing.

        - Usual dose range of ramipril is 2.5 mg – 10 mg daily but may start 1.25 mg daily if elderly and/or risk of hypotension
        - Usual dose range of perindopril is 2 mg - 8 mg daily
        - Usual dose range of quinapril is 2.5 mg – 20 mg once or twice daily. Combination with hydrochlorothiazide available at 10 mg and 20 mg doses of quinapril.
    - Candesartan typically preferred ARB but losartan useful alternative if combination with TD desirable.
        - Usual dose range of candesartan is 8 mg – 32 mg daily but may start at 4 mg daily if elderly and/or risk of hypotension
        - Usual dose range of losartan is 50 mg – 100 mg daily but may start at 12.5 mg - 25 mg daily if elderly and/or risk of hypotension. Combination with hydrochlorothiazide available at 50 mg losartan dose.
    - Check creatinine + electrolytes 2-4 weeks after starting or dose change to ensure no hyperkalaemia or deterioration of renal function
        - K+ < 5.5 mmol/L and up to 30% decrease in creatinine requires no dose change
        - Hyperkalaemia is often spurious due to haemolysis during the delay from collection until analysis in the lab - consider repeating to ensure real.
- CCB:
    - Amlodipine and felodipine preferred with usual dose range for both 2.5 mg – 5 mg daily
    - 10 mg daily doses associated with greater risk of adverse effects for often little benefit
    - Useful if elevated diastolic BP as vasodilators
- TD:
    - Chlorthalidone is typically preferred TD but bendroflumethazide useful alternative.
    - Usual dose of chlorthalidone: is 12.5 mg – 25 mg daily and usual dose of bendroflumethazide is 2.5 mg - 5 mg daily. Higher doses typically lead to little additional BP lowering but greatly increase adverse effects.
    - Hydrochlorothiazide is a weak BP lowering agent but may be useful if combination tablets preferable
    - Check eGFR + electrolytes 1-2 weeks after starting to ensure no adverse effects
- β-blockers – Metoprolol controlled release (CR) or bisoprolol preferred for ischaemic heart disease and rate control

        - Carvedilol likely preferable if congestive heart failure

- ***The guidance in this section is predominantly based on the 2024 European Society of Cardiology Guidelines for the management of elevated blood pressure and hypertension, which can be accessed at www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Elevated-Blood-Pressure-and-Hypertension***

Treatment approach to elevated BP and hypertension

Treatment approach to elevated BP and hypertension

- All with a confirmed BP ≥ 130/80 mmHg should have a CKM risk assessment and causes of secondary hypertension considered particularly if young without risk factors or family history of hypertension. Interventions to optimise healthy living should also be offered to all with specific advice including:
    - Smoking and alcohol cessation. Complete cessation of vaping also likely beneficial
        - There is no safe alcohol limit for cardiovascular health
    - Low-salt intake (< 2 g of sodium or < 5 g of salt per day) and ideally 5-7 serves of vegetables and 2 fruit per day to ensure adequate potassium intake
        - Avoiding processed foods and adding salt to food important
        - Mediterranean diet and Dietary Approaches to Stop Hypertension (DASH) are eating patterns with best long-term evidence for reducing BP and CV risk.
            - These eating patterns emphasise fruits, vegetables, whole grains, low-fat dairy and lean proteins.
    - Avoiding medications that increase BP e.g. NSAIDs.
    - Increased physical activity and movement
    - Interventions for weight loss if overweight or obese aiming for > 5% total body weight loss
- BP lowering therapy is recommended in addition to healthy living interventions:
    - Immediately if BP ≥ 160/100 mmHg
    - If BP persistently ≥ 140/90 mmHg
    - If BP persistently 130 – 139/80 – 89 mmHg and ANY of the following:
        - 5 year CV risk ≥ 10%

        - CV disease including asymptomatic coronary or carotid disease (includes CT calcium score > 300)
        - CKD (UACR > 3 mg/mmol and/or eGFR < 60 mL/min/1.73m^2)
        - Diabetes with microvascular and/or macrovascular complications
        - LDLc ≥ 4.9 mmol/L and/or known familial hypercholesterolaemia

- BP lowering therapy should still be strongly considered if BP persistently 130 – 139/80 – 89 mmHg and 5 year CV risk 5 – 9.9% → particularly if additional risk factors for CVD
    - Additional risk factors for CVD 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

- BP lowering therapy is typically not required if BP 130 – 139/80 – 89 mmHg and 5 year CV risk < 5%, but healthy living interventions remain important.

Treatment targets

- A systolic BP < 130 mmHg is the treatment target for most
    - **NB:** A systolic BP < 120 mmHg should be considered if hypertension-induced organ effects including left ventricular hypertrophy, aortic root dilatation and/or CKD.

- **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

Secondary hypertension

Secondary hypertension

- Most people with hypertension have primary or essential hypertension where there is no identifiable cause for their high blood pressure. However, 5 - 10% of adults with hypertension have secondary hypertension where there is an underlying and potentially correctable cause of their high blood pressure.
- Secondary hypertension should be considered at the outset of confirmed hypertension, particularly if young without risk factors or a family history of hypertension. Secondary hypertension should also be considered if persistent hypertension despite adherence to ≥ 3 blood pressure lowering therapies
- Causes of secondary hypertension include:
    - Obstructive sleep apnoea
    - Renovascular disease and renal parenchymal disease
    - Medications e.g. oral contraceptive pill, NSAIDs, steroids, cyclosporin etc.
    - Recreational drug use e.g. amphetamine, cocaine, excess alcohol intake
    - Endocrine disorders e.g. primary hyperaldosteronism, Cushing's disease, thyroid disease and acromegaly
    - Pregnancy
    - Coarctation of the aorta
- History and examination often provide guide to which investigations should be performed to confirm or exclude causes of secondary hypertension.

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* Primary hyperaldosteronism is a common cause of secondary hypertension in adults and plasma renin activity and aldosterone levels are best performed before starting BP lowering medications.

Choice of BP lowering therapy

Choice of blood pressure lowering therapy

- First line BP lowering medications are ACE inhibitors (ACEi) or angiotensin receptor blockers (ARB), calcium channel blockers (CCB) and thiazide diuretics (TD).
    - **Typically these medications are more effective and better tolerated in low doses in combination**.
    - Cardioselective beta blockers (β-blocker) may be used if ischaemic heart disease, heart failure or atrial fibrillation.
- Best choice of ACEi, ARB, CCB or TD is dependent on whether albuminuria (UACR > 3 mg/mmol) or other comorbidities are present:
    - Albuminuria (UACR > 3 mg/mmol):

        - Start ACEi or ARB if no hypotension and titrate to maximal tolerated dose
        - If BP remains above target add CCB or TD
        - If BP still above target then add other (e.g. TD if CCB previously added)

    - No albuminuria present (UACR < 3 mg/mmol):
        - Strongly consider low dose ACEi or ARB and CCB in combination
        - If BP above target increase dose of combination agents
        - If BP remains above target then add TD

    - Gout:
        - Losartan and CCBs may be helpful due to their small uricosuric effect, but they should not replace urate-lowering therapy and the focus should be on the best BP-lowering agent
        - Beware TD typically increase uric acid levels
        - Serum urate will rise with heart, kidney and respiratory failure

    - Ischaemic heart disease, heart failure or atrial fibrillation:
        - Cardioselective β-blockers may be added at any stage. May need to decrease CCB and/or TD if risk of hypotension
        - Entresto (Sacubitril/Valsartan) is the preferred neprilysin/renin-angiotensin system inhibitor in heart failure rather than other ARB or ACEi, but requires special authority funding.
            - Current special authority criteria for Entresto requires the following:
                - NHYA/WHO functional II-IV AND
                - LVEF ≤ 35% OR echocardiogram is not reasonably practical AND
                - Other standard treatments of heart failure are optimised
        - Empagliflozin and spironolactone or eplerenone are also preferred in heart failure rather than TD or CCB if risk of hypotension.

- When starting BP lowering therapy ensure up date sick day management advice and contraception if applicable e.g. for ACEi/ARB
- Check serum creatinine 1-2 weeks after a dose change for either ACEi/ARB or TD to ensure no significant derangement
    - If K^+ < 6 mmol/L and < 30% decrease in eGFR then no change required

- 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

- Consider causes of secondary hypertension if BP still above target despite adherence to ≥ 3 BP lowering therapies

Recommended agents in each class of BP lowering therapy

Choice of agent in each of BP lowering medications

The likely preferred agents in each of blood pressure lowering medications based on efficacy, tolerance and availability in Aotearoa NZ are:

- ACEi and ARB:

- Ramipril typically preferred ACEi but perindopril useful alternative. Quinapril also useful alternative if combination with TD desirable but often requires twice daily dosing.
    - Usual dose range of ramipril is 2.5 mg – 10 mg daily but may start 1.25 mg daily if elderly and/or risk of hypotension
    - Usual dose range of perindopril is 2 mg - 8 mg daily
    - Usual dose range of quinapril is 2.5 mg – 20 mg once or twice daily.
    - Combination with hydrochlorothiazide available at 10 mg and 20 mg doses of quinapril.
- Candesartan typically preferred ARB
    - Usual dose range of candesartan is 8 mg – 32 mg daily but may start at 4 mg daily if elderly and/or risk of hypotension
    - Usual dose range of losartan is 50 mg – 100 mg daily but may start at 12.5 mg - 25 mg daily if elderly and/or risk of hypotension.
    - Combination with hydrochlorothiazide available at 16 and 32 mg doses of candesartan and 50 mg dose of losartan

- CCB:
    - Amlodipine and felodipine preferred with usual dose range for both 2.5 mg – 5 mg daily
    - 10 mg daily doses are associated with greater risk of adverse effects for often little additional benefit
    - Useful if elevated diastolic BP due to vasodilatory effect

- TD:
    - Usual dose of chlorthalidone: is 12.5 mg – 25 mg daily and usual dose of bendroflumethazide is 2.5 mg - 5 mg daily. Higher doses typically lead to little additional BP lowering but greatly increase adverse effects.
    - Chlorthalidone has a significantly longer half-life (lasting up to 72 hours) compared to other TDs. This may be helpful and more efficacious, but the prolonged duration of action also means a sustained effect on renal sodium and water excretion, and should be balanced against the increased likelihood of cumulative electrolyte disturbances over time.
    - Hydrochlorothiazide is a weak BP lowering agent but may be useful if combination tablets preferable

- β-blockers:
    - Metoprolol controlled release (CR) or bisoprolol preferred for ischaemic heart disease and rate control
    - Carvedilol likely preferable if congestive heart failure

Other key practice points in managing elevated BP and hypertension

Other key practice points in managing elevated BP and hypertension

- Management of high blood pressure should not occur in isolation. Ensure up to date CKM risk assessment with smoking cessation and management of other CKM conditions as required.
- Measure BP at least 6 – 12 monthly once treatment optimised to ensure targets are still met
- Consider urgent referral if BP ≥ 180/110 mmHg AND pregnant OR signs of malignant hypertension
    - Signs of malignant hypertension include:
        - Severe headache
        - Altered vision
        - Papillioedema, retinal haemorrhages and exudates
        - Altered mental state
        - Acute kidney injury with proteinuria and haematuria
- Consider non-urgent referral if BP above target despite adherence to ≥ 3 BP lowering therapies and/or any concerns over potential secondary hypertension.

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Abbreviations:

ACE
Angiotensin-Converting Enzyme

ACEi
Angiotensin Converting Enzyme Inhibitors

ARB
Angiotensin Receptor Blocker

β-Blocker
Beta Blocker

BP
Blood Pressure

CCB
Calcium Channel Blocker

CKM
Cardiovascular-Kidney-Metabolic

CV
Cardiovascular

eGFR
Estimated Glomerular Filtration Rate

LVEF
Left Ventricular Ejection Fraction

NHYA
New York Heart Association

TD
Thiazide Diuretic

UACR
Urinary Albumin:Creatinine Ratio

WHO
World Health Organisation

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