Heart Foundation™

Guide to management of hypertension 2008

Assessing and managing raised blood pressure in adults

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Guideline development process

The Heart Foundation convened an expert committee in 2006 to review the 2004 edition of *Hypertension management guide for doctors* and other current international guidelines for the management of hypertension, including those published by the US Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure, the UK National Institute of Clinical Excellence, and the European Society of Hypertension/European Society of Cardiology.[1–4] The committee conducted literature searches in key topic areas to identify relevant clinical studies published since 2003, and met regularly between late 2006 and mid-2007 to analyse the literature and reach consensus recommendations. These guidelines were developed in accordance with the principles and aims of the National Strategy for Quality Use of Medicines.[5]

Visit www.heartfoundation.org.au/Professional_Information/Clinical_Practice/Hypertension for:

- a list of relevant stakeholders involved in the review of the draft guidelines
- a list of committee members and their declarations of interest
- full references.

These guidelines have been endorsed by:

The Royal Australian College of General Practitioners

National Prescribing Service Limited

Internal Medicine Society of Australia & New Zealand

Kidney Health Australia

strokefoundation

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A Quick Reference Guide is also available from www.heartfoundation.org.au.

Summary of recommendations

Measuring blood pressure (BP)

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Use the recommended technique at every BP reading to ensure accurate measurements and avoid common errors. Pay particular attention to the following: • Measure BP with a regularly serviced mercury sphygmomanometer, or regularly validate your instrument against a mercury sphygmomanometer. • At the patient's first BP assessment, measure BP on both arms. Thereafter, use the arm with the higher reading. • In patients who may have orthostatic hypotension (e.g. the elderly, those with diabetes), measure BP in sitting position, and repeat after the patient has been standing for at least 2 minutes.	5
If possible, obtain BP measurements outside the clinic (by ambulatory BP monitoring or self-measurement), particularly for patients with any of the following: • unusual variation between BP readings in the clinic • suspected 'white coat hypertension' (e.g. clinic hypertension in a person without known cardiovascular risk factors) • hypertension that is resistant to drug treatment • suspected hypotensive episodes (e.g. in those who are elderly or have diabetes). Interpret ambulatory BP profiles using standard reference values for daytime (awake), night-time (asleep) and 24-hour means.	6

Diagnosis and classification of hypertension

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Recheck BP regularly, at intervals determined by both BP category and absolute cardiovascular risk.	8

Evaluation in patients with confirmed hypertension

In all patients with hypertension, perform a clinical assessment (including a careful history, physical examination, initial investigations and further investigations as required) in order to: • identify all cardiovascular risk factors • detect end-organ damage and related or comorbid clinical conditions • identify causes of secondary hypertension.	9
If secondary hypertension is suspected, consider specialist referral.	11
Assess absolute cardiovascular risk in all patients with hypertension in order to determine the optimal management plan.	11
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When to intervene in patients with confirmed hypertension

The decision to intervene and the development of a comprehensive management plan (including lifestyle advice and drug treatment) should be based on a thorough clinical investigation to identify associated clinical conditions and/or end-organ damage and assessment of absolute cardiovascular risk.	**12**
Advise lifestyle risk reduction for all patients, especially those with high-normal BP or hypertension.	**12**
Initiate antihypertensive drug treatment immediately in patients with any of the following: • grade 3 hypertension or isolated systolic hypertension with widened pulse pressure (SBP ≥ 160 mmHg and DBP ≤ 70 mmHg) • associated conditions or evidence of end-organ damage (regardless of BP) • high absolute risk of cardiovascular disease, based on the presence of markers of high risk or as estimated using a risk calculator.	**12**
Also consider drug therapy for: • patients with moderate risk of cardiovascular disease as estimated using a risk calculator • Aboriginal and Torres Strait Islander adults.	**12**
Explain the health implications of current risk and the potential benefits of the recommended treatment.	**12**

Lifestyle modification

Manage identified lifestyle risk factors in all patients, whether or not BP is elevated.	**13**
Advise patients to aim for healthy targets: • At least 30 minutes of moderate-intensity physical activity on most, if not all, days of the week (daily total can be accumulated e.g. three 10-minute sessions). Advise patients of all ages to become more active. • Smoking cessation. Refer patients to Quitline. Consider recommending nicotine replacement therapy and/or prescribing oral therapy (bupropion or varenicline) in patients who smoke more than 10 cigarettes per day and have no contraindications. • Waist measurement < 94 cm for men and < 80 cm for women, body mass index (BMI) < 25 kg/m^2. When recommending weight loss, advise patients on reducing kilojoule intake as well as increasing physical activity. • Dietary salt restriction: ≤ 4 g/day (65 mmol/day sodium). Recommend low-salt and reduced-salt foods as part of a healthy eating pattern. • Limited alcohol intake: ≤ two standard drinks per day for men or ≤ one standard drink per day for women.	**13**

Drug treatment

Initiating drug therapy	**18**
For patients with uncomplicated hypertension, begin antihypertensive monotherapy with any of these agents: • angiotensin-converting enzyme (ACE) inhibitors (or angiotensin II receptor antagonists) • calcium channel blockers • thiazide diuretics (consider for patients 65 years or older only).	**18**
For patients with comorbid or associated conditions, consider: • the benefits, contraindications and cautions associated with specific agents • potential drug–drug interactions.	**19**
Begin antihypertensive therapy with the lowest recommended dose.	**18**
Attaining targets	**18**
For all patients, arrange regular follow-up to reassess drug treatment and adjust the management plan to achieve targets for BP (Table 6) and other modifiable risk factors.	**18**
If the initial agent is not tolerated, change to a drug of a different class.	**18**
If target BP is not achieved, add a second low-dose agent from a different pharmacological class (see recommended combinations, page 23) before increasing doses. If target is not achieved and both drugs are well tolerated, increase dose/s.	**18**
Use up to four antihypertensive drugs in combination, if necessary to achieve target.	**23**
Avoid these combinations: • ACE inhibitor (or angiotensin II receptor antagonist) plus potassium-sparing diuretic • beta-blocker plus verapamil.	**23**
Trial each regimen change for at least 6 weeks.	**24**
Non-responsive hypertension	**27**
If BP remains elevated despite maximal doses of at least two appropriate agents, reassess for: • non-adherence • undiagnosed secondary hypertension • hypertensive effects of other drugs • treatment resistance due to sleep apnoea • undisclosed use of alcohol or recreational drugs • unrecognised high salt intake (particularly in patients taking ACE inhibitors or angiotensin II receptor antagonists) • 'white coat' hypertension • technical factors affecting measurement • volume overload, especially with chronic kidney disease (CKD).	**27**

Blood pressure and health

Higher levels of blood pressure (BP) are strongly associated with increasing rates of cardiovascular disease, cardiovascular events and death. Observational studies show that the lower the BP, the lower the risk of stroke, coronary heart disease, chronic kidney disease (CKD), heart failure and death. This relationship applies across whole range of BP levels usually encountered in clinical practice. Systolic BP is a stronger and more consistent predictor of cardiovascular events such as stroke than diastolic BP. Among patients with hypertension, lowering BP reduces cardiovascular risk.[3]

Hypertension is responsible for more deaths and disease than any other biomedical risk factor worldwide.[6] It is the major risk factor for stroke and coronary heart disease, and is a major contributor to chronic heart failure (CHF), CKD, and their progression.[7] The total burden of cardiovascular disease, particularly CHF, is expected to increase over the next few decades due to population ageing.[8,9]

The dividing line between normotension and hypertension is arbitrary, and the decision to intervene depends on the individual's overall cardiovascular risk profile and the presence or absence of end-organ damage. Antihypertensive drug treatment and lower targets are recommended for all patients with BP-sensitive conditions (e.g. stroke,* diabetes[10] or CKD[11]) even if initial BP is within the 'normal' range. Optimal BP control has been shown to:

- prevent or delay the development of end-stage kidney failure[11]
- prevent the development of CHF and help manage symptoms of existing CHF[12]
- prevent strokes and their recurrence.[13]

For most patients, hypertension can be attributed to a combination of genetic and lifestyle factors. In a minority, it is secondary to other disease processes.

Aboriginal and Torres Strait Islander peoples have a high prevalence of risk factors for cardiovascular disease. Rates of death due to cardiovascular disease are markedly higher for Indigenous Australians than for other Australians and have not shown the downward trend seen in the rest of the Australian community during the past 40 years. Age-standardised rates of death remain 10 times higher among those aged 25–44 years and 2–3 times higher overall.[8] Cross-sectional population survey data for adults aged 25–54 years suggest that the age-standardised prevalence of hypertension (defined as BP ≥ 140/90 mmHg or on antihypertensive medication) is approximately three times higher in Aboriginal and Torres Strait Islander people living in isolated communities in northern and central Australia, compared with non-Indigenous Australians living in Queensland and the Northern Territory.[14]

Similar observations have been reported for Maori and Pacific Islander peoples. New Zealand population studies suggest that age-adjusted and sex-matched hypertension prevalences among Maori and Pacific Islanders are 1.5 to 2 times higher, compared with New Zealanders of European or other origin.[15,16]

* See page 25 for further information.

Measuring blood pressure

Mercury sphygmomanometers give the most accurate non-invasive BP readings. Accuracy varies widely between other available devices. If a non-mercury (e.g. digital) sphygmomanometer is used, it should be checked and validated every 6 months to maintain accuracy. Where possible, validation against a mercury sphygmomanometer should be conducted by measuring BP simultaneously with both devices on a single arm using a simple Y-piece connection (for instructions on validation, see www.heartfoundation.org.au/Professional_Information/Clinical_Practice/Hypertension). All sphygmomanometers require servicing at least once each year.

In future, mercury sphygmomanometers may be phased out due to environmental concerns about heavy metal contamination, but at present there is no agreement on an optimal replacement (for a list of validated meters published by the British Hypertension Society, see www.bhsoc.org/blood_pressure_list.stm).

Ideally, patients should not consume caffeine or smoke for at least 2 hours before BP is measured, because these may produce short-term BP increases, particularly in combination.

At the patient's first BP assessment, measure BP on both arms. This is particularly important if there is evidence of peripheral arterial disease. Variation of up to 5 mmHg in BP between arms can be acceptable, but if BP varies by more than 5 mmHg (e.g. in the presence of chronic aortic dissection or subclavian artery stenosis), use the arm with the higher reading for all subsequent BP measurements.

In patients in whom orthostatic hypotension might be suspected (e.g. elderly patients, those with diabetes), measure both sitting and standing BP. Repeat the measurement after the patient has been standing for at least 2 minutes.

The possibility of raised BP in response to the assessment itself ('white coat' hypertension) should be considered and ruled out (see *Ambulatory blood pressure monitoring*, page 6).

How to measure BP accurately in the clinic

- The patient should be seated and relaxed, preferably after several minutes of sitting in a quiet room prior to the measurement.
- The selected arm should be free of constricting clothing so that the cuff can be wrapped around the upper arm without impediment.
- Select the appropriate cuff size. The bladder length should be at least 80% and width at least 40% of the circumference of the mid-upper arm. The use of 'standard'-sized cuffs in people with large arms can result in artificially high BP readings. If an oversized cuff cannot be satisfactorily fitted on a large arm, consider using an appropriately sized cuff on the forearm and auscultating the radial artery instead.
- Wrap the cuff snugly around the upper arm, with the centre of the cuff bladder positioned over the brachial artery and the lower border of the cuff about 2 cm above the bend of the elbow.
- Ensure that the cuff is at heart level by supporting the arm.
- Palpate the radial pulse while inflating the cuff and note the pressure at which the radial pulse ceases to be palpable. Continue to inflate the cuff a further 30 mmHg above this pressure.
- Deflate the cuff at a rate of 2–3 mmHg/beat or less while palpating and note the pressure at which the radial pulse reappears.
- Fully deflate the cuff, wait approximately 30 seconds, then inflate the cuff to at least 30 mmHg above that at which the radial pulse reappeared.
- While deflating the cuff at a rate of 2–3 mmHg/beat or less, auscultate over the brachial artery in the antecubital fossa.
- Record the result for systolic and diastolic BP to the nearest 2 mmHg. For the systolic reading, record the level at which the beats (at least two consecutive beats) are heard, even if they then disappear transiently with progressive deflation (the 'auscultatory gap'). For the diastolic reading, use disappearance of sound (phase V Korotkoff). Use muffling of sound (phase IV Korotkoff) **only** if sound continues to zero.
- Wait 30 seconds before repeating the procedure in the same arm.
- Average the readings. If the first two readings differ by more than 10 mmHg systolic or 6 mmHg diastolic, or if initial readings are high, have the patient rest quietly for 5 minutes then take several readings until consecutive readings do not vary by greater than these amounts.

Common errors in BP measurement

The following errors can contribute to under-treatment of hypertension:

- cuff placed over clothing
- incorrect cuff size
- worn cuff
- inaccurate sphygmomanometer (e.g. not serviced regularly, not validated correctly)
- arm elevated above heart
- failure to check that both arms give comparable readings (e.g. at initial visit)
- patient not rested before measurement
- patient talking during measurement
- failure to palpate radial pulse before auscultatory measurements (results in failure to detect auscultatory gap)
- deflating the cuff too quickly (> 2–3 mmHg/beat, whether using a mercury or digital sphygmomanometer)
- re-inflating the cuff to repeat measurement before it has fully deflated
- rounding off actual reading by more than 2 mmHg when recording measurement
- taking a single measurement.

BP measurements outside the clinic

Additional readings may be obtained by 24-hour ambulatory BP monitoring or by self-measurement of BP. It is useful to obtain BP readings outside the clinic, because approximately 15% of the general population show elevated BP when measured in the clinic but not in other settings ('isolated clinic' or 'white coat' hypertension).[3] In a similar proportion of people, ambulatory BP may be high while clinic BP is normal ('isolated ambulatory', 'masked' or 'reverse white-coat' hypertension).[3]

Ambulatory BP monitoring

Ambulatory BP monitoring provides detailed information over a 24-hour period, and is useful if the diagnosis of hypertension is in doubt. It requires specialised equipment and is not generally used for long-term follow up, but may be indicated in patients with 'white-coat' hypertension.[17]

Treatment decisions should be based on ambulatory BP, where available, because end-organ disease and cardiovascular event rates correlate more closely with ambulatory BP than clinic measurements.[17] Available data suggest that clinical outcomes in patients with isolated clinic hypertension or isolated ambulatory hypertension correlate more closely with ambulatory BP than with clinic BP readings.[17] Night-time (asleep) BP may be a stronger predictor of cardiovascular events than daytime (awake) BP.[17]

Compare the recorded profile with standard ambulatory BP values (**Table 1**). Note that normal values for ambulatory BP differ from clinic-measured BP normal values. Take into account any patient diary information and time of drug treatment, where relevant.

The diagnosis of hypertension is supported if the patient's average ambulatory BP reading exceeds standard values for daytime BP or night-time BP **or** if ambulatory BP load (area under the BP–time curve) is reported and exceeds the reference range by more than 20%.

Mean night-time ambulatory BP level should be at least 10% lower than the daytime level.[17] Patients who do not show a night-time lowering of BP ('non-dippers') are at increased cardiovascular risk.[18]

Table 1. Standard ambulatory BP values

'Normal' ambulatory BP values for non-pregnant adults (95th centile of BP distributions in larger Caucasian populations)	
Daytime (awake)	< 135/85 mmHg
Night-time (asleep)	< 120/70 mmHg
Over 24 hours	< 130/80 mmHg

Adapted from reference 17

Self-measurement of BP

BP measurements taken by the patient can complement clinic measurements to give an accurate BP profile on which to base therapeutic decisions. Self-measurement provides multiple measurements over longer periods and may be particularly useful during long-term follow up.

Self-measurement of BP helps patients understand their hypertension and the effects of treatment, promotes involvement in self-management and improves adherence to treatments. The effect of changes in antihypertensive medications can be assessed more fully using self-measured BP than clinic BP monitoring, and changing trends in BP levels can be detected sooner. Self-measurement also provides the opportunity to confirm or exclude any suspected relationship between episodic symptoms and periods of high or low BP (e.g. light-headedness due to medication-induced hypotension).

Accurate self-measurement of BP requires:

- an accurate, validated device that is serviced regularly and re-calibrated every 6 months
- practical instruction of the patient in good technique by a trained health professional
- written instructions for reference at home
- follow-up reassessment to ensure correct technique.

As BP varies from moment to moment, multiple readings at various times and during various activities (e.g. lying, standing, morning before getting out of bed, 2–4 hours after morning antihypertensive medication, just before bedtime) over several weeks are needed to provide an accurate picture of a patient's overall BP control. Once BP levels are stable and target levels have been achieved, the frequency of readings can be decreased.

When interpreting self-measured BP readings, remember that:

- An individual's self-measured BP readings are usually lower than clinic BP readings.
- The upper limit of 'normal' mean self-measured BP is 135/85 mmHg, as for daytime (awake) ambulatory BP.
- A diurnal pattern or postural effect may be evident from average readings for each time of day.
- The patient's drug regimen and diary information should be correlated with BP readings.

Measuring BP – Recommendations

Use the recommended technique at every BP reading to ensure accurate measurements and avoid common errors. Pay particular attention to the following:

- Measure BP with a regularly serviced mercury sphygmomanometer, or regularly validate your instrument against a mercury sphygmomanometer.
- At the patient's first BP assessment, measure BP on both arms. Thereafter, use the arm with the higher reading.
- In patients who may have orthostatic hypotension (e.g. the elderly, those with diabetes), measure BP in sitting position, and repeat after the patient has been standing for at least 2 minutes.

If possible, obtain BP measurements outside the clinic (by ambulatory BP monitoring or self-measurement), particularly for patients with any of the following:

- unusual variation between BP readings in the clinic
- suspected 'white coat hypertension' (e.g. clinic hypertension in a person without known cardiovascular risk factors)
- hypertension that is resistant to drug treatment
- suspected hypotensive episodes (e.g. in those who are elderly or have diabetes).

Interpret ambulatory BP profiles using standard reference values for daytime (awake), night-time (asleep) and 24-hour means.

Diagnosis and classification of hypertension

The diagnosis of hypertension should be based on multiple BP measurements taken on several separate occasions, e.g. at least twice, one or more weeks apart (sooner if hypertension is severe).

International definitions of hypertension vary. The suggested classification system used in this guideline was developed following an assessment of the systems used in the United States and in Europe. Although the term 'hypertension' is potentially misleading because BP-related risk is a continuum with no defined lower cut-point, it has been retained in this guideline for practical reasons, on the understanding that individual cardiovascular risk assessment determines appropriate management in each patient.

Reassess BP regularly, at intervals determined by both BP category (**Table 2 – see fold out**) and the patient's absolute cardiovascular risk (page 14).

Diagnosis and classification of hypertension – Recommendations

The diagnosis of hypertension should be based on multiple BP measurements taken on separate occasions.

Recheck BP regularly, at intervals determined by both BP category and absolute cardiovascular risk (see **Table 2 – see fold out**).

Evaluation in patients with confirmed hypertension

The diagnostic process (history, physical examination and investigations) aims to:

- identify all risk factors
- detect end-organ damage and related or comorbid clinical conditions (**Table 3 – see fold out**)
- identify causes of secondary hypertension.

History

Take a full history with particular attention to the following:

- known duration of raised BP and previous levels
- ambulatory or self-measured BP levels (if known)
- previous antihypertensive therapy, efficacy and adverse effects
- past history or current symptoms of ischaemic heart disease, heart failure, cerebrovascular disease or peripheral arterial disease
- past history or current symptoms that suggest CKD, e.g. nocturia, dark urine (suggesting haematuria)
- symptoms suggestive of a condition that may cause secondary hypertension, e.g. phaeochromocytoma (paroxysmal headache, sweating, palpitations), sleep apnoea (obesity, snoring)
- the presence of asthma, chronic obstructive pulmonary disease, diabetes, dyslipidaemia, gout, erectile dysfunction, sleep apnoea or other significant illnesses
- family history of hypertension, diabetes, dyslipidaemia, stroke, CKD or premature (before age 60 years) coronary heart disease
- modifiable lifestyle risk factors: obesity, physical inactivity, smoking, excessive intake of alcohol, salt or saturated fats, recreational drug use (amphetamines, cocaine)
- medications (including complementary medicines) that raise BP (**Table 4**, **Table 5**)
- personal, psychosocial and environmental factors that could influence the course and outcome of antihypertensive care e.g. educational background, family situation, work environment and associated psychological stress (assess for depression, social isolation and quality of social support).
- history of hypokalaemia or suggestive symptoms (e.g. muscle weakness, hypotonia, muscle tetany, cramps, cardiac arrhythmias).

Table 4. Medications that may increase BP

- Clozapine
- Corticosteroids
- Haemopoietic agents (darbepoetin, epoetin)
- Immunomodifiers (cyclosporin, tacrolimus)
- Leflunomide
- Monoamine oxidase inhibitors: reversible (moclobemide), irreversible (phenelzine, tranylcypromine)*
- Non-steroidal anti-inflammatory drugs (conventional and cyclooxygenase-2 selective)
- Oral contraceptives
- Oral decongestants (e.g. pseudoephedrine)
- Sibutramine
- Stimulants (dexamphetamine sulfate, methylphenidate hydrochloride)
- Sympathomimetic agents
- Venlafaxine (dose-related)

Rebound hypertension may occur following abrupt withdrawal of the following:

- bromocriptine
- clonidine.

*The use of monoamine oxidase inhibitors in combination with tyramine-rich foods (e.g. matured or out-of-date cheese, fermented or matured meats, yeast and soy bean extracts, and others) can lead to hypertensive crisis.

Adapted with permission from reference 19

Table 5. Complementary medicines that may increase BP

- American mistletoe
- Angel's trumpet
- Butcher's broom
- Caffeine-containing products (e.g. guarana, black tea, cola nut, green tea, maté)
- Ephedra (ma huang)
- Gentian
- Ginger preparations
- Ginseng preparations
- Liquorice
- Melatonin
- Peyote
- Phenylalanine
- Sage
- St John's wort

Adapted with permission from reference 19

Physical examination

Perform a physical examination with particular attention to the cardiovascular system, including the following:

- pulse rate, rhythm and character
- jugular venous pulse and pressure
- evidence of cardiac enlargement (displaced apex, extra heart sounds), or evidence of decompensation (basal crackles or wheeze on lung auscultation, peripheral oedema, abdominal signs, e.g. pulsatile liver)
- evidence of arterial disease (e.g. carotid, renal or abdominal bruits, abdominal aortic aneurysm, absent femoral pulses, radiofemoral delay)
- abnormalities of the optic fundi (e.g. tortuosity, thickening or arteriovenous nipping of retinal arteries, retinal haemorrhages, exudates, diabetic retinopathy, papilloedema)
- evidence of CKD (e.g. palpable kidneys)
- focal neurological signs
- evidence of abnormalities of the endocrine system (e.g. Cushing's syndrome, thyroid disease)
- waist circumference (cm) and/or body mass index (BMI): weight (kg) in light clothing, divided by the square of height (m) without shoes.

Initial investigations

Undertake the following investigations to assess for end-organ disease or associated clinical conditions:

- Dip stick testing of urine for blood and protein
  - If abnormal, proceed to urine microscopy.
  - If proteinuria detected (≥ 1+ on dip stick), measure 24-hour urinary protein excretion.
- Assessment of microalbuminuria (highly recommended for all patients and mandatory for those with diabetes). Microalbuminuria status correlates with cardiovascular risk and its presence indicates end-organ damage.
  - The most accurate screening test is urinary albumin/creatinine ratio on a spot urine sample. Use this method where available.
  - If albumin/creatinine ratio ≥ 2.0 mg/mmol (males) or ≥ 2.5 mg/mmol (females) is detected, repeat the test to confirm.
  - If confirmed, obtain a 24-hour urine collection for accurate measurement.
- Blood analysis (sodium, potassium, chloride, bicarbonate, urea, creatinine, uric acid, haemoglobin, fasting glucose, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, liver function tests).
- Electrocardiogram (ECG) to detect conduction disturbances, arrhythmias, coronary heart disease or left ventricular hypertrophy. The presence of strain pattern (ST depression and T-wave inversion) is associated with increased cardiovascular risk in patients with hypertension.

Further investigations

Further investigations should be undertaken as indicated on the basis of clinical suspicion following the history, physical examination and routine investigations. These may include the following:

- Echocardiogram (if available), where the result will affect treatment decisions. Echocardiography is the most accurate widely available method of detecting left ventricular hypertrophy.
- Ankle-brachial index (ABI) in those with risk factors for peripheral arterial disease (e.g. smoking, diabetes, vascular bruits, older age). A finding of < 0.9 is diagnostic for peripheral arterial disease. For more information on ABI, see the position statement by Society of Interventional Radiology.[20]
- Carotid Doppler as indicated (e.g. if bruits detected).
- Plasma aldosterone/renin ratio. Primary aldosteronism occurs in 5–10% of patients with hypertension and is not excluded by normal serum potassium.[21] It should be considered in all patients with hypertension, especially those with moderate-to-severe or treatment-resistant hypertension and those with hypokalaemia. For information on testing procedure, including medications that affect the result, see www.heartfoundation.org.au/Professional_Information/Clinical_Practice/Hypertension. Referral to a specialist for investigation is recommended when primary aldosteronism is suspected.
- 24-hour urinary catecholamine, metanephrine and normetanephrine excretion (with creatinine) and/or plasma catecholamine, metanephrine* and normetanephrine* concentration. These tests are indicated by symptoms of episodic catecholamine excess and/or episodic hypertension (suggestive of phaeochromocytoma).
- Renal artery duplex ultrasound, renal nuclear medicine imaging, and/or CT angiography–indicated in young females with hypertension, older patients who might have atherosclerotic renal artery disease, and patients with a renal bruit.

*Medicare rebate not available

Absolute cardiovascular risk

The management plan for a person with hypertension should take into consideration the individual's absolute risk of cardiovascular disease (see *When to intervene*, page 12).

Absolute cardiovascular risk is the probability (expressed as a percentage) of an individual experiencing a cardiovascular event (e.g. myocardial infarction or stroke) during a predefined period of time (e.g. the next 5 years). Blood pressure is a major determinant of absolute cardiovascular risk. Patients at highest absolute risk include those with existing cardiovascular disease or those with multiple risk factors (e.g. diabetes, older age, overweight/obesity and dyslipidaemia).

The purposes of assessing absolute cardiovascular risk are:

- to identify other modifiable risk factors that require management
- to predict who will benefit most from intervention and determine the appropriate management plan to reduce BP
- to enable the patient to understand the degree of urgency for reducing BP and correcting other risk factors.

Several tools for estimating an individual's absolute cardiovascular risk are available, most of which are based on data from the Framingham Heart Study. The New Zealand cardiovascular risk calculator [22] (**Figure 1 – see centrefold**) has been validated for use in the Australian population. However, available absolute risk calculators may significantly underestimate cardiovascular risk in some groups, including people with diabetes or CKD, Aboriginal and Torres Strait Islander peoples, and Maori and Pacific Islanders. The National Aboriginal Community Controlled Health Organisation has developed specific recommendations for the assessment of cardiovascular risk in Aboriginal and Torres Strait Islander adults.[23]

Evaluation in patients with confirmed hypertension – Recommendations

In all patients with hypertension, perform a clinical assessment (including a careful history, physical examination, initial investigations and further investigations as required) in order to identify all cardiovascular risk factors, detect end-organ damage and related or comorbid clinical conditions, and identify causes of secondary hypertension.

If secondary hypertension is suspected, consider specialist referral.

Assess absolute cardiovascular risk in all patients with hypertension (**Figure 1 – see centrefold**) in order to determine the optimal management plan.

Available absolute risk calculators may significantly underestimate cardiovascular risk in Aboriginal, Torres Strait Islander, Maori, and Pacific Islander peoples.

When to intervene in patients with confirmed hypertension

The appropriate timing, type and intensity of interventions – including lifestyle changes and drug treatment – depends on absolute cardiovascular risk (**Figure 1** – **see centrefold**) and the presence of associated clinical conditions and/or end-organ damage.

Hypertension should be managed within a comprehensive management plan to reduce BP, reduce overall cardiovascular risk and minimise end-organ damage (**Figure 2 – see fold out**).

Advise lifestyle risk reduction for **all** patients, especially those with high-normal BP or hypertension (see *Lifestyle modification*, page 13).

Identify patients who need drug treatment

Initiate antihypertensive drug treatment (page 18) immediately in patients with:

- grade 3 hypertension (SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg)
- isolated systolic hypertension and widened pulse pressure (SBP ≥ 160 mmHg and DBP ≤ 70 mmHg)
- one or more associated conditions or evidence of end-organ damage (**Table 3 – see fold out**), even if BP is within the high-normal range
- high absolute risk for cardiovascular disease assessed according to clinical indicators or the risk calculator (**Figure 1 – see centrefold**).

Early initiation of antihypertensive drug therapy and intensive management of all identified cardiovascular risk factors is recommended in Aboriginal and Torres Strait Islander adults with hypertension.

Treatment targets (**Table 6 – see fold out**) are now generally lower than previously recommended, particularly in patients with high risk for cardiovascular disease, because:

- lower BP targets have been associated with lower achieved BP levels and better outcomes in clinical trials
- clinical outcomes were insufficiently improved under previous recommendations.

When to intervene in patients with confirmed hypertension – Recommendations

The decision to intervene and the development of a comprehensive management plan (including lifestyle advice and drug treatment) should be based on a thorough clinical investigation to identify associated clinical conditions and/or end-organ damage and assessment of absolute cardiovascular risk.

Initiate antihypertensive drug treatment immediately in hypertensive patients with any of the following:

- grade 3 hypertension or isolated systolic hypertension with widened pulse pressure (SBP ≥ 160 mmHg and DBP ≤ 70 mmHg)
- associated conditions or evidence of end-organ damage (regardless of BP)
- high absolute risk of cardiovascular disease, based on the presence of markers of high risk or as estimated using a risk calculator.

Advise lifestyle risk reduction for all patients, especially those with high-normal BP or hypertension (see *Lifestyle modification*, page 13).

Also consider drug therapy for:

- patients with moderate risk of a cardiovascular event (10–15% probability within the next 5 years) as estimated using a risk calculator
- Aboriginal and Torres Strait Islander adults.

Explain the health implications of current risk and the potential benefits of the recommended treatment.

Lifestyle modification

Lifestyle modification is indicated for all patients with hypertension, regardless of drug therapy. It may reduce, or even abolish, the need for antihypertensive drugs.

Regular physical activity

- There is strong evidence that regular physical activity has an independent cardioprotective effect.[24]
- Regular aerobic exercise can lower systolic BP by an average of 4 mmHg and diastolic BP by an average of 2.5 mmHg.[25]

People with any the following should defer physical activity until medical review:

- grade 3 hypertension (systolic BP ≥ 180 mmHg or diastolic BP ≥ 110 mmHg)
- unstable angina, uncontrolled heart failure, severe aortic stenosis, resting tachycardia or arrhythmias
- symptoms (e.g. chest discomfort, shortness of breath) on low activity
- diabetes with poor glycaemic control
- other acute illness.

Advise all patients to become physically active, as part of a comprehensive plan to control hypertension, regardless of drug treatment. Aim for 30 minutes of moderate-intensity physical activity on most, if not all, days of the week.

See *National Heart Foundation of Australia physical activity recommendations for people with cardiovascular disease* (available at www.heartfoundation.org.au).[26]

Notes

The daily dose can be accumulated in shorter bouts (e.g. three 10-minute walks).

Moderate-intensity physical activity (e.g. brisk walking, lawn mowing, low-paced swimming, cycling, gentle aerobics) will cause a slight increase in breathing and heart rate, and may cause light sweating.

Advise against isometric exercise routines that may raise BP (e.g. weight lifting), except within professionally supervised programs.

Smoking cessation

- Smoking cessation may not directly reduce BP, but markedly reduces overall cardiovascular risk. The risk of myocardial infarction is 2–6 times higher [27,28] and the risk of stroke is 3 times higher in people who smoke than in non-smokers.[29,30]
- Advice from health professionals is effective in increasing quit rates. Even 3–5 minutes taken to encourage smokers to attempt to quit can increase success rates.[31]
- Pharmacotherapy (nicotine replacement therapy, bupropion, varenicline) is effective. The risk of adverse effects is small and is generally outweighed by the significant risk of continuing to smoke.

Give all patients clear, unambiguous advice to stop smoking. Assess each person's readiness to quit and provide appropriate counselling.

Refer to Quitline (13 QUIT). Consider referral to a smoking cessation program.

Consider pharmacotherapy for those who smoke more than 10 cigarettes per day and have no contraindications.

Continued on page 16.

Assessing absolute cardiovascular risk in hypertension management

Numerical absolute cardiovascular risk assessment is now recommended for all Australians aged 45–74 who are not already known to be at high risk, whether or not they have hypertension.

The management of hypertension should be based on a thorough clinical assessment that includes an estimate of the patient's absolute risk for cardiovascular disease, as well as BP levels and other clinical investigations (see *When to intervene,* page 12). Assessment of absolute cardiovascular risk helps both doctor and patient understand the individual's overall risk profile and the potential benefit of preventive interventions.

Patients who need immediate antihypertensive drug treatment include (but are not restricted to) those at high absolute cardiovascular risk (> 15% probability of a cardiovascular event within the next 5 years).

High cardiovascular risk can be assumed for the following groups of patients without using a risk calculator:

Group A. Patients aged 75 years and over

For almost all individuals aged ≥ 75 years, the absolute risk of a cardiovascular event in the next 5 years is > 15%.

Group B. Patients with existing cardiovascular disease

Assume risk of a cardiovascular event > 20% in the next 5 years if either of the following present:

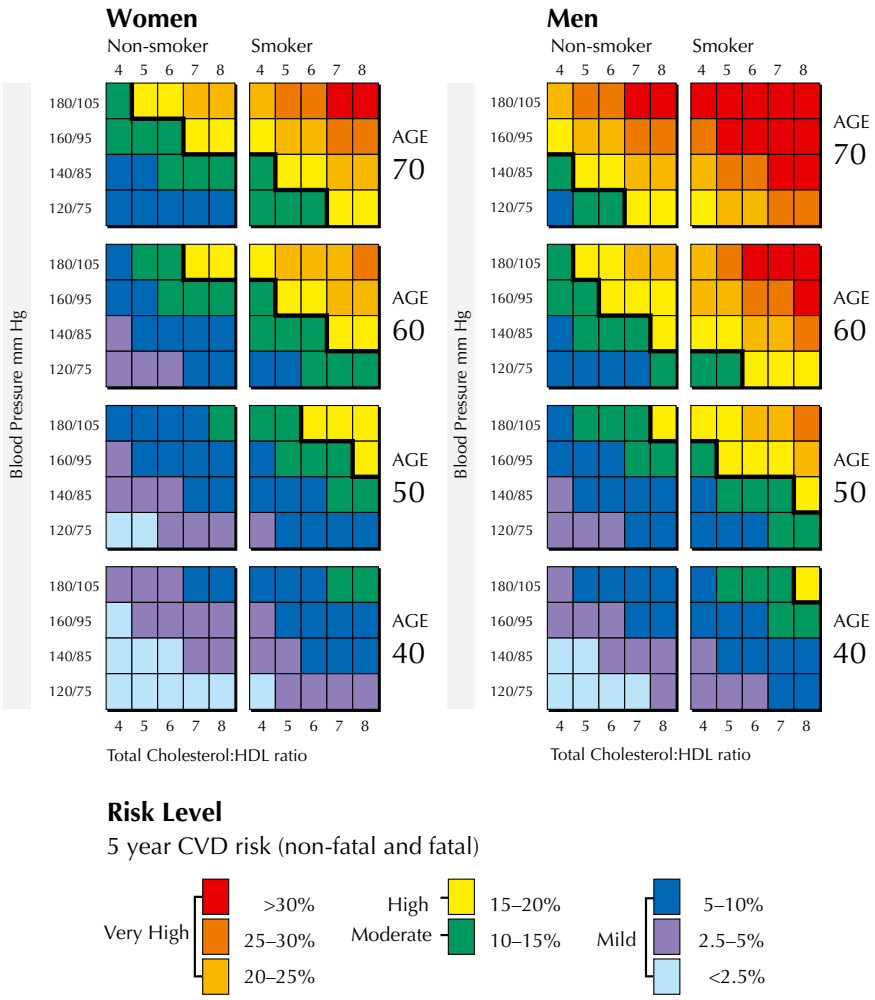
- symptomatic cardiovascular disease (e.g. angina, myocardial infarction, chronic heart failure, stroke, transient ischaemic attack, peripheral arterial disease)
- left ventricular hypertrophy diagnosed with electrocardiography or echocardiography.

Group C. Patients with associated clinical conditions and end-organ disease (see Table 3 – see fold out)

For this group, assume risk of a cardiovascular event > 15% in the next 5 years. Antihypertensive drug treatment is required (e.g. to preserve renal function).

For all other patients, estimate absolute risk using the chart (**Figure 1 – see centrefold**).

Figure 1. Modified New Zealand cardiovascular risk calculator



Adapted with permission: New Zealand Guidelines Group. New Zealand cardiovascular guidelines handbook: developed for primary care practitioners. Wellington, NZ: 2005(www.nzgg.org.nz).[22]

How to use the charts

The estimated risk of cardiovascular events is not precise and is presented as a range with interpolation required between categories.

Step 1. Identify the table relating to the person's sex, smoking history and age. 'Smoker' is defined as either current daily cigarette smoker or former smoker who has quit within the previous 12 months.

Step 2. Within the appropriate square, choose the cell nearest to the person's BP and TC:HDL ratio.

- BP (mean of two readings on two occasions). When the systolic and diastolic values fall in different risk levels, the higher category applies.
- Total cholesterol/high-density lipoprotein cholesterol (HDL-C) ratio (ensure correct ratio is used).
- For people who fall exactly on a threshold between cells, use the cell corresponding to higher risk.

Step 3. Revise clinical assessment of risk.

The risk calculator is likely to underestimate cardiovascular risk in these groups:

- Aboriginal and Torres Strait Islander adults*
- adults with diabetes
- adults who are overweight or obese
- socioeconomically deprived groups.

*While routine absolute cardiovascular risk assessment is recommended for all adults aged 45–74 who are not already known to have cardiovascular disease, a thorough cardiovascular assessment should be made earlier for Aboriginal and Torres Strait Islander adults due to their increased risk at each age bracket, compared with the general population. For more information refer to *National guide to a preventive health assessment in Aboriginal and Torres Strait Islander peoples* (available at www.racgp.org.au).[23]

Dietary modification

- There is strong evidence that salt restriction can reduce systolic BP by approximately 4–5 mmHg in hypertensive individuals and 2 mmHg in normotensive individuals.[32] Responses vary between individuals–generally greatest among the elderly and those with severe hypertension.
- (Suitable for patients with **normal renal function only**): Increasing dietary potassium can reduce systolic BP by 4–8 mmHg in hypertensive individuals and 2 mmHg in normotensive individuals.[32]
- A healthy eating pattern includes mainly plant-based foods e.g. fruits, vegetables, pulses and a wide selection of wholegrain foods, moderate amounts of low-fat or reduced-fat dairy products, moderate amounts of lean unprocessed meats, poultry and fish, moderate amounts of polyunsaturated and monounsaturated fats (e.g. olive oil, canola oil, reduced-salt margarines).

Limit salt intake to ≤ 4 g/day (65 mmol/day sodium) by:

- choosing foods processed without salt, foods labelled 'no added salt' or 'low salt' (or 'reduced salt' products when other options are unavailable)
- avoiding high-salt processed foods, salty snacks, takeaway foods high in salt, salt added during cooking or at the table.

Patients with normal renal function only: increase potassium intake by eating a wide variety of fruits and vegetables, plain unsalted nuts (limit quantity and frequency to avoid excess kilojoules), and legumes (e.g. beans, lentils, dried peas).

Patients taking potassium-sparing diuretics must limit potassium intake to avoid severe hyperkalaemia.

Notes

Refer to a dietitian for initial review and follow up, where appropriate.

Dietary sodium intake can be monitored by periodical measurement of 24-hour urinary sodium excretion rate, which closely approximates intake. The results can be discussed with the patient.

Weight reduction

- Every 1% reduction in body weight lowers systolic BP by an average of 1 mmHg.[33,34]
- Weight reduction by as little as 4.5 kg reduces BP and/or prevents hypertension in a large proportion of overweight people.[1] Weight loss of 10 kg can reduce systolic BP by 6–10 mmHg.[33,35,36]
- Sibutramine may increase BP in some patients, particularly those who are both obese and hypertensive – monitor BP regularly.

Assess waist circumference (preferable) and BMI. Targets are:

- waist circumference < 94 cm (males); < 80 cm (females)
- BMI < 25 kg/m^2 (see notes below).

Set achievable intermediate goals in consultation with patients and assess progress regularly.

Advise patients on how to reduce kilojoule intake as well as increase physical activity. Explain that energy input (kilojoules) from food and drinks must be less than the kilojoules expended in daily activities and planned regular physical activity in order to lose weight. To lose weight, most people will need to do more physical activity than the 30 minutes of moderate-intensity physical activity per day recommended for general health benefits.

Emphasise that there is no quick solution; lifestyle changes must be practical and able to be maintained for a lifetime.

Notes

Stated targets are based on data from European populations and may not be appropriate for all ages and ethnocultural groups. Compared with Europeans, the BMI cut-point associated with increased risk of type 2 diabetes and cardiovascular disease is typically *higher* for Polynesian populations and *lower* for Aboriginal and Torres Straight Islander populations and some Asian populations (e.g. Hong Kong Chinese, Indonesians and Singaporeans).[8,33,34,37] A World Health Organization expert consultation has identified the cut-point of 23 kg/m^2 as an additional trigger for public health action in Asian countries.[37]

Limiting alcohol

- Moderate drinking may increase BP[38–40] and binge drinking may increase the risk of hypertension.[38,41]
- Reducing alcohol consumption can substantially lower BP in some patients.[42]

Advise patients with hypertension to limit their intake to:

- a maximum of two standard drinks per day for men
- a maximum of one standard drink per day for women.

Advise at least two alcohol-free days per week.

Supporting long-term lifestyle changes

- Tailor advice to individual patient's needs and set realistic goals.
- Give regular encouragement. Respond positively to any incremental success, even if targets have not been achieved (e.g. reduction in smoking or weight).
- Provide specific written instructions.
- Review progress regularly.
- Refer to other health professionals (e.g. accredited practising dietitians or exercise professionals) for ongoing support and follow-up where appropriate.

More information

The Heart Foundation's heart health information service: 1300 36 27 87 or www.heartfoundation.org.au.

Lifescripts tools for assessing and managing lifestyle risk factors in Australian general practice are available from the Australian General Practice Network (www.adgp.com.au).

Lifestyle – Recommendations

Manage identified lifestyle risk factors in all patients, whether or not BP is elevated.

Advise patients to aim for healthy targets:

- At least 30 minutes of moderate-intensity physical activity on most, if not all, days of the week (daily total can be accumulated e.g. three 10-minute sessions). Advise patients of all ages to become more active.
- Smoking cessation. Refer patients to Quitline. Consider recommending nicotine replacement therapy and/or prescribing oral therapy (bupropion or varenicline) in patients who smoke more than 10 cigarettes per day and have no contraindications.
- Waist measurement < 94 cm for men and < 80 cm for women, body mass index (BMI) < 25 kg/m^2. When recommending weight loss, advise patients on reducing kilojoule intake as well as increasing physical activity.
- Dietary salt restriction: ≤ 4 g/day (65 mmol/day sodium). Recommend low-salt and reduced-salt foods as part of a healthy eating pattern.
- Limited alcohol intake: maximum of two standard drinks per day for men or one standard drink per day for women.

Drug treatment

Selecting an antihypertensive agent

For all major antihypertensive drug classes, the beneficial effect is mainly due to BP lowering, irrespective of their mechanism of action.

In uncomplicated hypertension, the following classes of antihypertensive agents are equally effective for first-line use, both in initial and maintenance therapy (**Figure 3 – see fold out**):

- ACE inhibitors (or angiotensin II receptor antagonists)*
- dihydropyridine calcium channel blockers
- low-dose thiazide diuretics (for patients aged 65 years and older).

Thiazide diuretics have been associated with increased risk of new-onset diabetes and should be used with caution in patients with glucose intolerance and/or metabolic syndrome.[46] The use of thiazide diuretics as first-line therapy should be limited to older patients, in whom the benefits of managing isolated systolic hypertension and preventing stroke with these agents are likely to outweigh the risk of diabetes onset.

Beta-blockers are no longer recommended as first-line therapy in uncomplicated hypertension because of the increased risk of developing diabetes and the recently described trend towards worse outcomes in patients treated with beta-blockers (mainly atenolol) compared with those treated with other classes of antihypertensive drugs.[47]

For patients with stable, well-controlled hypertension who are already taking a beta-blocker, it is reasonable to continue the regimen unchanged.

The initial drug choice should be based on:

- the patient's age (**Figure 3 – see fold out**)
- the presence of associated clinical conditions or end-organ damage (**Table 3 – see fold out**)
- the presence of other co-existing conditions that either favour or limit the use of particular drug classes (**Table 7**)
- potential interactions with other drugs
- implications for adherence (**Table 8**)
- cost.

Most classes of antihypertensive agents used as monotherapy lower BP by a similar average amount. However, the individual response to each agent is unpredictable.

*ACE inhibitors and angiotensin II receptor antagonists have been shown to be equally efficacious in prevention of cardiovascular end points and in lowering BP.[43,44,45]

General principles of drug treatment

Attempt to reach recommended targets (**Table 6 – see fold out**). There is a direct linear relationship between BP and cardiovascular risk across the continuum of BP levels normally seen in clinical practice; lower BP levels have been associated with the strongest benefits.

Combination drug therapy will often be required to reach targets. Even if targets are not met, patients are likely to benefit from any BP reduction achieved.

How to achieve target BP

- Start with the lowest recommended dose of selected first-line agent (**Table 9**).
- If the initial drug is not well tolerated, change to a drug of a different class, starting with the lowest recommended dose.
- If target BP (**Table 6 – see fold out**) not reached or there is no significant reduction with initial monotherapy, add a second agent from a different pharmacological class at a low dose, rather than increasing the dose of the first agent (see *Combination therapy*, page 23). This approach maximises antihypertensive efficacy while minimising adverse effects, and is recommended pending further evidence clarifying the role of fixed-combination regimens.
- If BP is still above target and both antihypertensive agents have been well tolerated, increase the dose of one agent (other than a thiazide diuretic) incrementally to maximal recommended dose before increasing the dose of the other agent.

- Trial each dose regimen for at least 6 weeks before altering doses, because a stable response to a particular dose takes at least 3–4 weeks.
- Choose long-acting drugs to provide 24-hour efficacy with once daily administration.
- Once a combination regimen is established as long-term therapy, it may be more convenient for the patient to use a combined preparation (e.g. ACE inhibitors/thiazide diuretics, angiotensin II receptor antagonists/thiazide diuretics, ACE inhibitors/calcium channel blockers).
- Encourage full adherence to medications (**Table 8**) and assess adherence regularly.
- Targets may be difficult to achieve or may not be tolerated in some patients (e.g. the very elderly, those with a superimposed 'white-coat' effect or those with critical carotid stenosis).

Table 7. Choice of antihypertensive agent in patients with comorbid and associated conditions

Condition	Potentially beneficial	Potentially harmful	
		Caution	Contraindicated
Angina	Beta-blockers (except oxprenolol, pindolol), calcium channel blockers, ACE inhibitors	Calcium channel blockers (on initiation or withdrawal)	
Atrial fibrillation	Remodelling: ACE inhibitors, angiotensin II receptor antagonists[†] Rate control: nondihydropyridine calcium channel blockers, beta-blockers		
Asthma/COPD		Cardioselective beta-blockers, (e.g. atenolol, metoprolol controlled release): use cautiously in mild/moderate disease only	Beta-blockers (except cardioselective agents)
Bradycardia, second- or third-degree atrioventricular block			Beta-blockers, verapamil, diltiazem
Depression		Beta-blockers, clonidine, methyldopa, moxonidine	
Gout	Angiotensin II receptor antagonists (telmisartan, olmesartan, losartan)	Thiazide diuretics	
Heart failure	ACE inhibitors, angiotensin II receptor antagonists,[†] thiazide diuretics, beta-blockers[*] (bisoprolol, carvedilol, metoprolol controlled release), spironolactone	Calcium channel blockers (especially verapamil, diltiazem)	Alpha blockers in aortic stenosis Beta-blockers in uncontrolled heart failure
Post myocardial infarction	Beta-blockers (except oxprenolol, pindolol), ACE inhibitors, eplerenone		

Continued on next page.

Table 7. Choice of antihypertensive agent in patients with comorbid and associated conditions (continued)

Condition	Potentially beneficial	Potentially harmful	
		Caution	Contraindicated
Pregnancy	Beta-blockers (oxprenolol, labetolol)		ACE inhibitors, angiotensin II receptor antagonists, diuretics, calcium channel blockers (before 22 weeks' gestation), atenolol
Chronic kidney disease	ACE inhibitors, angiotensin II receptor antagonists†		
Tight bilateral renal artery stenosis (unilateral in patient with solitary kidney)		ACE inhibitors, angiotensin II receptor antagonists	
Post stroke	Low-dose thiazide diuretics ± ACE inhibitors, eprosartan		
Type 1 or type 2 diabetes with proteinuria or microalbuminuria	ACE inhibitors, angiotensin II receptor antagonists†	Beta-blockers, thiazide diuretics‡	

Adapted from references 19 and 48

*Particular beta-blockers are now indicated in the treatment of heart failure. See the Heart Foundation *Guidelines for the prevention, detection and management of chronic heart failure in Australia, 2006*[11] (available at www.heartfoundation.org.au).

†Careful monitoring of kidney function is required if a combination of ACE inhibitors and angiotensin II receptor antagonists are used.[43]

‡When used in combination with an ACE inhibitor, may be beneficial in type 2 diabetes.[10]

Table 8. Strategies for maximising adherence to the management plan

Communication	
• Express empathy to earn the patient's trust and establish good communication. • Treat the patient as a partner in management decisions. • Assess the patient's expectations of treatment.	• At each visit, ask the patient "How are you managing with your medicines?" • Discuss consequences of non-adherence to medicines.
Tailoring advice	
• Discuss treatment options and agree on an initial treatment plan, including how to reach target BP. • Provide specific written instructions and patient education materials. • Involve the patient's family in the therapeutic plan. • Discuss the use of compliance aids (e.g. dosette boxes, Webster packaging).	• Use self-measurement of BP for monitoring, where appropriate. • Consider referral for a Home Medicines Review. • Evaluate the social and economic barriers that may affect medication supply and storage.
Maintaining motivation	
• Explain the risks and benefits of treatment, and the risks of not treating. • Clearly explain that drug treatment will be life-long. • Reassure the patient about prognosis and ability to lead a normal life.	• Address quality-of-life issues including any new symptoms or side effects of treatment. • Address psychosocial factors that may limit adherence (e.g. manage depression, if present). • Reinforce lifestyle modifications at follow-up visits.

Table 9. Recommended doses for antihypertensive drugs

ACE inhibitors	
Captopril	12.5–50 mg twice daily
Enalapril	5–40 mg once daily or in two equally divided doses
Fosinopril	10–40 mg once daily
Lisinopril	5–40 mg once daily
Perindopril erbumine	4–8 mg once daily
Perindopril arginine	5–10 mg once daily
Quinapril	5–40 mg once daily or in two equally divided doses
Ramipril	2.5–10 mg once daily or in two equally divided doses
Trandolapril	1–4 mg once daily

Note
Commence at the lowest dose in elderly patients and those taking diuretics.

Calcium channel blockers – dihydropyridine	
Amlodipine	2.5–10 mg once daily
Felodipine	5–20 mg once daily (controlled release)
Lercanidipine	10–20 mg once daily
Nifedipine	10–40 mg twice daily (conventional) 20–120 mg once daily (controlled release)

Notes
Amlodipine and felodipine: lowest doses are recommended, particularly in the elderly.
Nifedipine: long-acting formulations are preferable.

Calcium channel blockers – nondihydropyridine	
Diltiazem	180–360 mg once daily (controlled release)
Verapamil	120–240 mg once daily (controlled release)

Angiotensin II receptor antagonists	
Candesartan	8–16 mg once daily
Eprosartan	600–800 mg once daily
Irbesartan	150–300 mg once daily
Losartan	50–100 mg once daily
Telmisartan	20–80 mg once daily
Olmesartan	20–40 mg once daily

Notes
Commence at the lowest dose in elderly patients and those taking diuretics.
Use with caution in those who have experienced angioedema with ACE inhibitors.

Table 9. Recommended doses for antihypertensive drugs (continued)

Thiazide diuretics	
Chlorthalidone	12.5–25 mg once daily
Hydrochlorothiazide	12.5–25 mg once daily
Indapamide	1.25– 2.5 mg once daily

Notes
It is usually unnecessary to exceed the doses shown.

If plasma potassium concentration drops below the laboratory reference range during thiazide diuretic therapy, a potassium-sparing diuretic (e.g. amiloride 2.5–5 mg orally daily or triamterene 50 mg orally) may be prescribed in combination with the thiazide. This may not be necessary if the patient is also taking an ACE inhibitor or angiotensin II receptor antagonist.

Loop diuretics (e.g. frusemide) are not recommended as antihypertensive agents unless volume overload is present.

Beta-blockers	
Bisoprolol	1.25–10 mg daily
Atenolol	25–100 mg once daily
Carvedilol	12.5–50 mg daily
Labetalol	100–400 mg twice daily
Metoprolol tartrate	50–100 mg twice daily
Metoprolol succinate (controlled release)	12–190 mg daily
Oxprenolol	40–160 mg twice daily

Note
Atenolol: recommended only in combination with other agents. For patients on current atenolol monotherapy, consider replacing with another beta-blocker or another drug class (due to adverse outcomes in meta-analyses of monotherapy clinical trials).

Metoprolol succinate (controlled release): see approved product information for titration schedule.

Bisoprolol: see approved product information for titration schedule. Reimbursement on PBS available only for people with stable moderate-to-severe heart failure.

Other	
Clonidine	50–300 µg twice daily
Hydralazine	12.5–100 mg twice daily
Methyldopa	125–500 mg twice daily
Moxonidine	200–600 µg daily
Prazosin	0.5–10 mg twice daily

Notes
Clonidine: rebound hypertension may occur on sudden cessation

Hydralazine: generally used only in combination with a beta-blocker or verapamil, which prevent reflex tachycardia. Maintenance doses above 100 mg daily are associated with increased risk of lupus-like syndrome and should not be given without determining patient's acetylator status.

Prazosin: to avoid postural hypotension, commence at night and with low dose.

Combination therapy

An estimated 50–75% of patients with hypertension will not achieve BP targets with monotherapy.[49] For most patients, a combination of antihypertensive drugs from two or more pharmacological classes is needed.

Occasionally a combination of more than three antihypertensive drugs may be required to achieve adequate BP control.

Based on the best available evidence, the most effective combination is:			
ACE inhibitor or angiotensin II receptor antagonist*	**plus**	calcium channel blocker	*(particular role in the presence of diabetes or lipid abnormalities)*[50]

Other effective combinations include:			
ACE inhibitor or angiotensin II receptor antagonist*	**plus**	thiazide diuretic	*(particular role in the presence of heart failure or post stroke)*
ACE inhibitoror or angiotensin II receptor antagonist*	**plus**	beta-blocker	*(recommended post myocardial infarction or in people with heart failure)*
beta-blocker	**plus**	dihydropyridine calcium channel blocker	*(particular role in the presence of coronary heart disease)*
thiazide diuretic	**plus**	calcium channel blocker	
thiazide diuretic	**plus**	beta-blocker	*(not recommended in people with glucose intolerance, metabolic syndrome, or established diabetes)*

Avoid the following combinations:			
ACE inhibitor or angiotensin II receptor antagonist	**plus**	potassium-sparing diuretic	*(due to risk of hyperkalaemia)*
verapamil	**plus**	beta-blocker	*(due to risk of heart block)*

* ACE inhibitors and angiotensin II receptor antagonists have been shown to be equally efficacious in prevention of combined end points of cardiovascular disease death, myocardial infarction, stroke and heart failure admissions in patients at high risk due to past cardiovascular events.[43]

Monitoring response to drug treatment

During stabilisation, reassess response every 6 weeks or as indicated; appropriate intervals vary between a few days and 2 months. Consider adverse effects of medications (**Table 10**).

Once stabilised, the interval between visits can be lengthened, e.g. review every 3 months for the next 12 months and 6-monthly thereafter while BP remains stable (**Figure 4 – see fold out**).

Table 10. Potential adverse effects

Common adverse effects	ACE inhibitors*	Angiotensin II receptor antagonists*†	Calcium channel blockers	Thiazide diuretics	Beta-blockers
Constipation	–	–	+ Especially verapamil	–	–
Cough, angioedema	+	±	–	–	–
Dyspnoea	–	–	–	–	+
Gout	–	–	–	+	–
Headache, flushing	–	–	+	–	–
Hyperglycaemia	–	–	–	+	–
Hyperkalaemia	+	+	–	–	–
Hypokalaemia	–	–	–	+	–
Hyponatraemia	+	–	–	+	–
Erectile dysfunction	–	–	–	+	+
Lethargy	–	–	–	–	+
Oedema	–	–	+	–	–
Postural hypotension	+	+	+	+	– [‡]

+ predictable adverse effect; – clinically significant rates not reported; ±: rare reports

Adapted from reference 51

*An initial rise in serum creatinine is commonly observed after initiation of ACE inhibitors or angiotensin II receptor agonists. An increase of 30% or less is acceptable. If creatinine increases by more than 30% from baseline, consider possible contributory factors (e.g. hypovolaemia, renal artery stenosis, NSAIDs). If none present, consider ceasing treatment. Do not commence these agents if serum potassium is > 5.0 mmol/L.

ACE inhibitors and angiotensin II receptor antagonists are not nephrotoxic, but they reduce the kidney's ability to respond to an acute reduction in renal perfusion. Their use should be temporarily suspended during any episode which may lower renal perfusion (e.g. shock or sepsis).

†Caution should be exercised in introducing angiotensin II receptor antagonists in those who have experienced angioedema with ACE inhibitors.

‡Beta-blockers do not appear to induce or worsen postural hypotension.[52]

Treatment considerations in patients with other cardiovascular conditions

Stroke

There is well established evidence that BP-lowering therapy is effective in preventing recurrent stroke and other major vascular events (and possibly also cognitive decline and dementia) in people with an established history of stroke or transient ischaemic attack.

Even those with BP initially less than 140/90 mmHg benefit from antihypertensive therapy.[53] The benefits appear to be greater in those with a history of intracerebral haemorrhage than other stroke subtypes.[54]

The most direct available evidence for effective secondary prevention of stroke comes from studies using diuretics or combination of ACE inhibitors and diuretics.[13] However, all five major classes of antihypertensive agents are effective in preventing first ever stroke and can be considered, depending on cost, adverse effect profiles and comorbidities.

Acute stroke

There is no evidence for benefits of intensive early BP reduction in patients with acute ischaemic or haemorrhagic stroke. However, it appears safe and effective to commence oral antihypertensive therapy 1–2 weeks after the acute event, when the patient is clinically stable.[55]

Antihypertensive therapy should be initiated with caution in the very old or frail, in patients with severe carotid stenosis, and in those with initial BP levels less than 120 mmHg systolic.

Chronic heart failure

Management of hypertension reduces the risk of CHF. In patients with hypertension who are at risk of CHF, calcium channel blockers are not the preferred agent because ACE inhibitors or the combination of beta-blocker plus diuretic appear to be more effective than calcium channel blockers in preventing or delaying the onset of CHF.[56]

Other clinical trial data suggest that chlorthalidone is more effective in the prevention of CHF than either lisinopril or amlodipine during the first year of treatment, although lisinopril appears equally effective over longer-term treatment.[57]

There is strong clinical trial evidence to support the use of ACE inhibitors and beta-blockers in all patients with established systolic heart failure who do not have contraindications. Angiotensin II receptor antagonists may be considered as an alternative to ACE inhibitors.[58]

Spironolactone is beneficial in patients with severe (New York Heart Association functional class 3 or 4) CHF.[59] Eplerenone has been shown to reduce mortality in the period immediately post myocardial infarction (3–14 days).[60]

Diuretics are used to alleviate salt and water retention, despite the lack of formal clinical trial evidence.

In patients with heart failure with preserved systolic function (diastolic heart failure), candesartan has been investigated and its safety demonstrated,[61] but its efficacy is not well established.

For more information on the management of CHF, see Heart Foundation *Guidelines for the prevention, detection and management of chronic heart failure in Australia, 2006* (available at www.heartfoundation.org.au).[12]

Hypertension in pregnancy

For women with hypertension who are planning a pregnancy, suitable first-line agents include beta-blockers (labetalol, oxprenolol), methyldopa and clonidine. Hydralazine is a suitable second-line agent.

ACE inhibitors, angiotensin II receptor antagonists and diuretics are contraindicated at all stages of pregnancy. Calcium channel blockers are contraindicated in early pregnancy but have been shown safe and effective in the late second and third trimesters. Specialist referral is recommended for all pregnant women with hypertension.

Refer to the Australasian Society for the Study of Hypertension in Pregnancy consensus statement on the management of hypertension in pregnancy.[62]

Managing other cardiovascular risk factors

Monitor other cardiovascular risk factors and treat to targets.

Antiplatelet therapy

Low-dose aspirin is recommended for all patients with existing coronary heart disease. It is also reasonable to prescribe low-dose aspirin in patients with hypertension with all of the following:

- well-controlled BP
- high to very high risk of coronary heart disease, history of ischaemic cerebrovascular event or presence of significant carotid artery disease
- absence of known contraindications (e.g. elevated risk of gastrointestinal or other bleeding, allergy).

For more information on the prevention of further cardiovascular events in people with coronary heart disease, see the Heart Foundation and CSANZ guide *Reducing risk in heart disease 2007* (available at www.heartfoundation.org.au).[63]

Lipid abnormalities

The addition of lipid-lowering therapy to BP-lowering therapy in patients with lipid abnormalities has been shown to reduce both total cardiovascular events and stroke. Low dietary intake of saturated fats should be advised to reduce total cardiovascular risk. If target lipid levels are not achieved, treatment with HMG-CoA reductase inhibitors (statins) and/or ezetimibe should be considered. Foods supplemented with plant sterols may also be useful. For guidelines on lipid management, see the current *Position statement on lipid management–2005* by the Heart Foundation and the Cardiac Society of Australia and New Zealand (available at www.heartfoundation.org.au).[64]

Managing inadequate response to treatment

Failure of response to initial therapy or loss of initial BP control occurs due to a wide range of prescriber-related, patient-related and drug-related factors.

First, check that treatment has followed recommended prescribing guidelines for achieving BP targets (see *Drug treatment*, page 18).

If BP remains above target despite maximal doses of at least two appropriate agents after a reasonable period, consider the following potential explanations:

- non-adherence to therapy, including recommended lifestyle modifications
- secondary hypertension due to an undiagnosed underlying condition
- use of medications that may increase BP (**Table 4**, **Table 5**)
- treatment resistance due to sleep apnoea
- undisclosed alcohol or recreational drug use (including tobacco)
- unrecognised high salt intake (particularly in patients taking ACE inhibitors or angiotensin II receptor antagonists)
- 'white coat' hypertension
- BP measurement artefacts e.g. inadequate cuff size
- volume overload, especially with CKD.

In some patients (e.g. the very elderly), recommended target levels may not be tolerable or achievable. In this case, comorbidities and individual cardiovascular risks should be considered when planning management.

Long-term management

Arrange recall and annual review for people with hypertension to ensure early detection of end-organ damage.

Once initiated, antihypertensive drug therapy is usually considered life-long unless the diagnosis is in doubt or the patient requests a trial cessation of treatment.

Withdrawal of antihypertensive drug therapy should not be attempted in patients at high absolute risk for a cardiovascular event, e.g. those with associated clinical conditions (stroke, diabetes or CKD), end-organ disease or other cardiovascular disease risk factors. Withdrawal of antihypertensive drugs may be appropriate in patients who have achieved BP targets with low doses and agree to:

- continue behaviours to reduce lifestyle risk factors
- undergo regular BP monitoring
- restart drug therapy if BP increases.

A practice register is recommended to assist in the monitoring of patients with hypertension.

Factors associated with successful maintenance of normotension after ceasing antihypertensive medication include younger age, single antihypertensive drug therapy, lower pre-treatment BP, and a willingness to accept or maintain lifestyle modifications such as salt restriction and loss of weight (where indicated).

Long-term management – Recommendations

Initiating drug therapy

For patients with uncomplicated hypertension, begin antihypertensive monotherapy with any of these agents:

- ACE inhibitors (or angiotensin II receptor antagonists)
- calcium channel blockers
- thiazide diuretics (consider for patients 65 years or older only).

For patients with comorbid or associated conditions, consider:

- the benefits, contraindications and cautions associated with specific agents (**Table 7**)
- potential drug–drug interactions.

Begin antihypertensive therapy with the lowest recommended dose.

Attaining targets

For all patients, arrange regular follow-up to reassess drug treatment and adjust the management plan to achieve targets for BP (**Table 6 – see fold out**) and other modifiable risk factors.

If the initial agent is not tolerated, change to a drug of a different class.

If target BP is not achieved, add a second low-dose agent from a different pharmacological class (see recommended combinations) before increasing doses. If target is not achieved and both drugs are well tolerated, increase dose/s.

Use up to four antihypertensive drugs in combination, if necessary to achieve target.

Avoid these combinations:

- ACE inhibitor (or angiotensin II receptor antagonist) plus potassium-sparing diuretic
- beta-blocker plus verapamil.

Trial each regimen change for at least 6 weeks.

Non-responsive BP

If BP remains elevated despite maximal doses of at least two appropriate agents, reassess for:

- non-adherence
- undiagnosed secondary hypertension
- hypertensive effects of other drugs
- treatment resistance due to sleep apnoea
- undisclosed use of alcohol or recreational drugs
- unrecognised high salt intake (particularly in patients taking angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists)
- 'white coat' hypertension
- technical factors affecting measurement
- volume overload, especially with CKD.

Table 2. Classification and follow-up of blood pressure levels in adults

Diagnostic category*	Systolic (mmHg)	Diastolic (mmHg)	Follow up
Normal	< 120	< 80	**Recheck in 2 years** (or earlier as guided by patient's absolute cardiovascular risk).†
High-normal	120–139	80–89	**Recheck in 1 year** (or earlier as guided by patient's absolute cardiovascular risk).†
Grade 1 (mild) hypertension	140–159	90–99	**Confirm within 2 months.** See *When to intervene* (page 12)
Grade 2 (moderate) hypertension	160–179	100–109	**Reassess or refer within 1 month.** See *When to intervene* (page 12)
Grade 3 (severe) hypertension	≥ 180	≥ 110	**Reassess or refer within 1–7 days as necessary.** See *When to intervene* (page 12)
Isolated systolic hypertension	≥ 140	< 90	**As for category corresponding to systolic BP.**
Isolated systolic hypertension with widened pulse pressure	≥ 160	≤ 70	**As for grade 3 hypertension.‡**

* When a patient's systolic and diastolic BP levels fall into different categories, the higher diagnostic category and recommended action/s apply.

† See *Assessing absolute cardiovascular risk* (page 14)

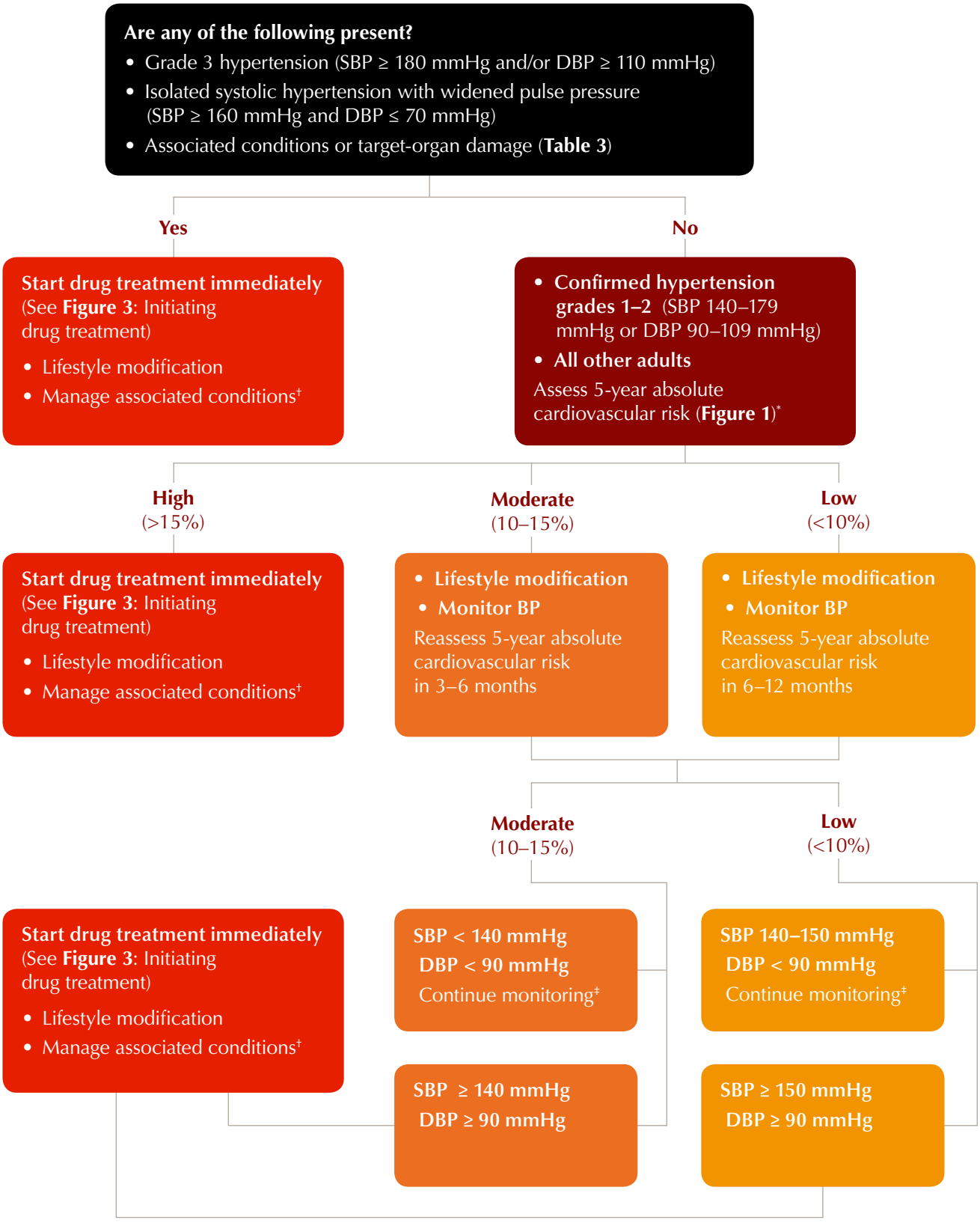
‡ In middle-aged and elderly patients with cardiovascular risk factors or associated clinical conditions, isolated systolic hypertension with large pulse pressure indicates high absolute risk for cardiovascular disease.[3]

Table 6. Treatment targets in adults

Patient group	Target (mmHg)
People with proteinuria >1 g/day (with or without diabetes)	< 125/75
People with associated condition/s or end-organ damage:* • Coronary heart disease • Diabetes • Chronic kidney disease • Proteinuria (> 300 mg/day) • Stroke/TIA	< 130/80
People with none of the following: • Coronary heart disease • Diabetes • Chronic kidney disease • Proteinuria (> 300 mg/day) • Stroke/TIA	< 140/90 or lower if tolerated

* Specific lower BP targets have not been established for other high-risk groups (e.g. those with peripheral arterial disease, those with familial hypercholesterolaemia or those at high absolute risk of cardiovascular disease) due to the current lack of evidence from clinical trials. Targets will be set when evidence becomes available.

Figure 2. When to initiate blood pressure-lowering drug treatment



BP: blood pressure; SBP: systolic BP, DBP: diastolic BP

* For Aboriginal and Torres Strait Islander adults, consider managing as though at a higher risk level.

† e.g. diabetes (strict glycaemic control lowers cardiovascular risk); lipid disorders (cholesterol-lowering therapy reduces the risk of primary and secondary coronary events – Refer to National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand. Position statement on lipid management—2005 (available at www.heartfoundation.org.au).

‡ Continue lifestyle modification, monitor BP and reassess absolute cardiovascular risk regularly. Note that patients with mild hypertension will require antihypertensive drug treatment if their absolute risk of cardiovascular disease is elevated due to changes in other risk factors.

Table 3. Associated clinical conditions and end-organ disease*

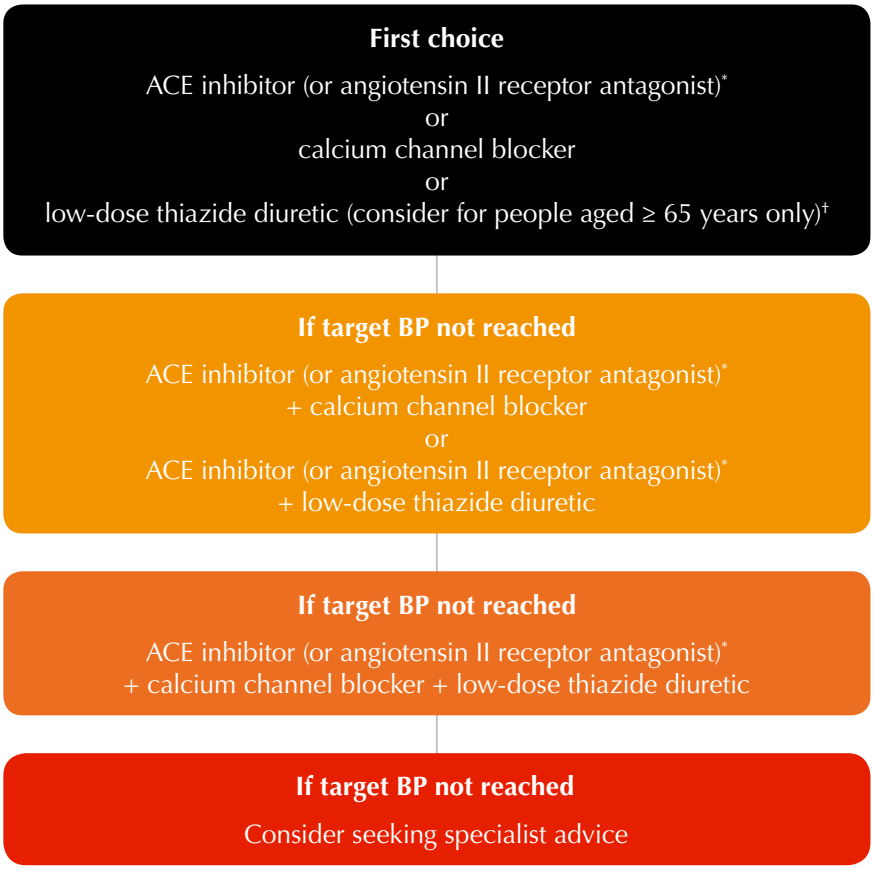
Associated clinical conditions	
Diabetes	
Cerebrovascular disease	• Ischaemic stroke • Cerebral haemorrhage • Transient ischaemic attack
Coronary heart disease	• Myocardial infarction • Angina • Coronary revascularisation
Chronic heart failure	
Chronic kidney disease	• Diabetic nephropathy • Glomerulonephritis • Hypertensive kidney disease
Aortic disease	• Dissecting aneurysm • Fusiform aortic aneurysm
Peripheral arterial disease	(clinical diagnosis or ABI < 0.9)
Hypercholesterolaemia	(total cholesterol > 7.5 mmol/L)
Family history of:	• premature cardiovascular disease • familial hypercholesterolaemia
End-organ disease	
Left ventricular hypertrophy	(diagnosed by electrocardiogram, echocardiogram)
Microalbuminuria	Defined as either of following: • albumin/creatinine ratio ≥ 2.0 mg/mmol (males) or ≥ 2.5 mg/mmol (females) on spot urine screening test† • 24-hour urinary albumin excretion rate ≥ 20 µg/minute
Chronic kidney disease	Presence of either of the following: • Proteinuria defined as either protein/creatinine ratio ≥ 30 mg/mmol† on spot urine test or urine protein > 300 mg/day on timed urine sample • Glomerular filtration rate (eGFR)‡ < 60 mL/minute/1.73m^2
Vascular disease	• Atherosclerotic plaque (aorta, carotid, coronary, femoral and iliac arteries) evident on ultrasound or radiology • Hypertensive retinopathy (grade II or greater)

* Conditions that warrant immediate treatment with antihypertensive drugs, regardless of BP or overall cardiovascular risk profile

† Value for ratio where albumin or total protein is measured in milligrams per litre and creatinine is measured in millimoles per litre. Reference range will differ where laboratories report creatinine level expressed in micromoles per litre.

‡ Estimated glomerular filtration rate obtained using the Modification of Diet in Renal Disease (MDRD) study GFR equation (used by most pathology laboratories and routinely reported with serum creatinine in adults). This method is generally accurate for GFR below 60 mL/min/1.73m^2. Studies are underway to validate this in Aboriginal and Torres Strait Islander populations.

Figure 3. Initiating drug treatment for newly diagnosed hypertension



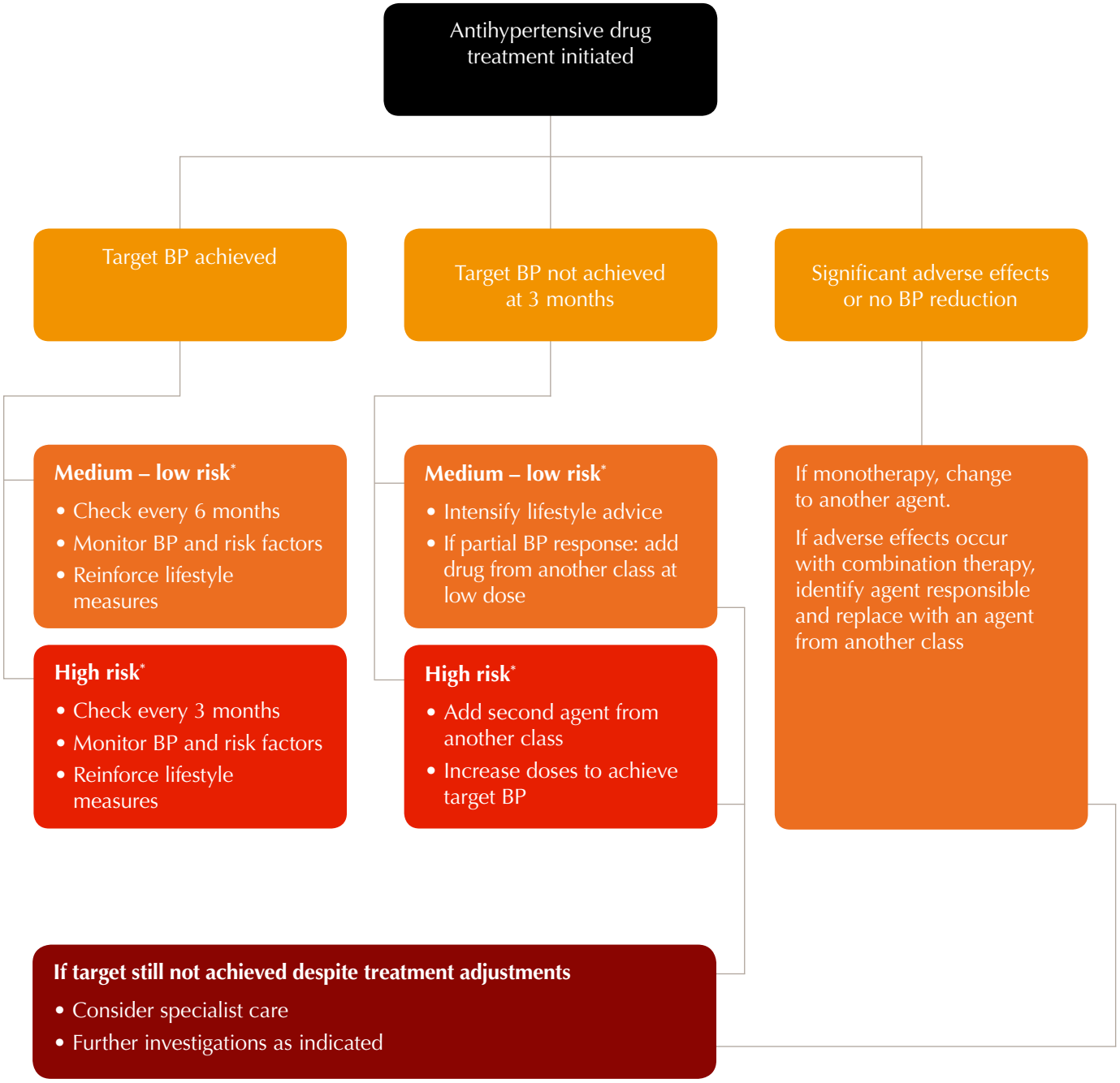
* ACE inhibitors and angiotensin II receptor antagonists have been shown to be equally efficacious in prevention of cardiovascular end points and in lowering BP.[43,44,45]

† Thiazide diuretics are not recommended for younger patients due to risk of diabetes associated with long-term use.[46]

See **Table 7** for information regarding choice of antihypertensive agent in patients with comorbid and associated conditions.

See page 23 for information on combination therapy.

Figure 4. Stabilisation, maintenance and follow-up after initiation of antihypertensive drug therapy



* Absolute cardiovascular risk assessed clinically and/or numerically (**Figure 1**)

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Guide to management of hypertension 2008

The following tables and figures are located on the back cover of this guide:

- Figure 2. When to initiate blood pressure-lowering drug treatment – page iii
- Figure 3. Initiating drug treatment for newly diagnosed hypertension – page iv
- Figure 4. Stabilisation, maintenance and follow-up after initiation of antihypertensive drug therapy – page vii
- Table 2. Classification and follow-up of blood pressure levels in adults – page iii
- Table 3. Associated clinical conditions and end-organ disease – page v
- Table 6. Treatment targets in adults – page iii

The Modified New Zealand cardiovascular risk calculator (Figure 1) can be found in the centrefold on page 15.

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