

Managing hypertension as a cardiovascular risk factor

Key Messages

Assess absolute cardiovascular risk and manage hypertension along with other modifiable risk factors

- use a cardiovascular risk calculator in primary prevention

When selecting antihypertensive drugs, consider potentially favourable effects on coexisting conditions

- low-dose thiazides have strong clinical outcome evidence for most populations
- use beta blockers in people with cardiac disease (heart failure, post-MI, angina)
- use ACE inhibitors or angiotensin II-receptor antagonists in diabetic nephropathy

If using a fixed-dose combination product, choose according to the drug components and the dose range available

- most people require two or more antihypertensive drugs

Assess adherence with medication and lifestyle changes at every opportunity and intervene if necessary

Assess absolute cardiovascular risk and manage hypertension along with other modifiable risk factors

Assess absolute risk of a cardiovascular event

High blood pressure is one aspect of cardiovascular risk. Base the decision to start antihypertensive drug therapy on an assessment of total cardiovascular risk as well as the blood pressure level.

Those with highest absolute risk will benefit most from intervention

The absolute benefit of antihypertensive drug therapy is greatest in those at highest risk. Address modifiable risk factors and consider the need for other medications (e.g. lipid-modifying therapy).

Use a cardiovascular risk calculator in primary prevention

To assess absolute cardiovascular risk in primary prevention, use a tool such as the New Zealand Cardiovascular Risk Calculator (available on the NPS website: www.nps.org.au). Some patients are automatically at high risk of a cardiovascular event and using a calculator for them is not appropriate — for example, people who have had a previous cardiovascular event or have symptomatic coronary heart disease (including previous myocardial infarction, stroke or transient ischaemic attack); Aboriginal and Torres Strait Islander, Maori or Pacific Islander peoples; people with diabetes; or those with existing target organ damage.

NPS is an independent, non-profit organisation for Quality Use of Medicines, funded by the Australian Government Department of Health and Ageing.

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Educate patients about the relationship between blood pressure and cardiovascular risk

As well as being a useful prognostic tool, cardiovascular risk calculators can help your patients understand the importance of blood pressure for their overall cardiovascular risk by demonstrating how much modifying blood pressure or other risk factors can reduce absolute cardiovascular risk.

Encourage lifestyle change to reduce cardiovascular risk

Lifestyle modifications can allow some patients to avoid or delay the need for antihypertensive drugs. Encourage lifestyle changes to reduce absolute cardiovascular risk, even if blood pressure cannot be managed with lifestyle changes alone.

Combining a weight-loss diet with exercise in overweight individuals can reduce blood pressure by up to 10 mmHg without drug therapy. In trials of up to 1 year, weight loss alone resulted in a reduction in blood pressure of 2–6 mmHg, but 25% to 40% of patients reduced their blood pressure by around 10 mmHg. The reason for the variation is unclear.¹

Similarly, reducing alcohol consumption¹ and salt restriction² have modest effects on blood pressure, while smoking cessation is important for reducing cardiovascular risk.¹

Guidelines for lifestyle interventions to reduce blood pressure and cardiovascular risk are available from the National Heart Foundation (www.heartfoundation.com.au).

When selecting antihypertensive drugs, consider potentially favourable effects on coexisting conditions

Reducing blood pressure is the most important aspect of antihypertensive therapy

All major antihypertensive drug classes reduce blood pressure, and this determines their effectiveness in preventing cardiovascular events.^{3–5} Effects on mortality beyond blood pressure lowering have not been consistently demonstrated.

Low-dose thiazides have strong clinical outcome evidence for most populations

All major antihypertensive drug classes reduce blood pressure, and this determines their effectiveness in preventing cardiovascular events.^{3–5} Effects on mortality beyond these effects have not been consistently demonstrated.

Low-dose thiazide diuretics have consistent and substantive cardiovascular outcome evidence and are a good first choice for most patients with uncomplicated hypertension.^{6–8} If a patient has an increased risk of diabetes^{1,9}, thiazides may not be appropriate, as this class has been associated with a small increased risk of incident diabetes in clinical trials compared with other antihypertensives (up to 3.6% absolute difference).¹⁰

For patients with comorbid conditions, choose an antihypertensive that has evidence of benefit for the coexisting condition. Potential adverse effects should also influence choice and may limit adherence. (See insert: *Specific considerations for patients with coexisting conditions*.)

Regardless of the therapy chosen or the rationale, monitor blood pressure regularly — benefits of medication are unlikely if blood pressure is not reduced.

Beta blockers are first choice in cardiac disease

Beta blockers are indicated in angina and post myocardial infarction (except oxprenolol, pindolol).⁵ In heart failure, ACE inhibitors and beta blockers have additive effects in reducing mortality. Choose a heart failure-specific beta blocker (bisoprolol, carvedilol or metoprolol succinate extended release). (See *NPS News* 36.)

Diabetic nephropathy — use ACE inhibitors or angiotensin II-receptor antagonists

Both ACE inhibitors and angiotensin II-receptor antagonists slow the progression of renal disease in patients with diabetic nephropathy*, demonstrating a reduced risk of both end-stage renal disease (ESRD) and of doubling serum creatinine, compared with placebo.¹¹

Guidelines suggest they can be used interchangeably, except when cost considerations are important.^{1,5,13} Neither drug class has a clear mortality benefit in diabetic nephropathy — a recent Cochrane review found a mortality benefit for ACE inhibitors at maximum tolerated doses but not at the lower doses used in renal impairment; there was no benefit for angiotensin II-receptor antagonists compared with placebo.¹¹

There are insufficient data to compare angiotensin II-receptor antagonists with ACE inhibitors for preventing the progression of diabetic renal disease.¹¹

* Patients with diabetes and microalbuminuria (albumin excretion 30–300 mg/day) or macroalbuminuria (albumin excretion >300 mg/day).¹¹ ACE inhibitors are contraindicated in bilateral renal artery stenosis, or unilateral artery stenosis with one kidney.¹²

When selecting fixed-dose combination products, choose the drug components and be aware of the doses available

Most people need more than one antihypertensive to achieve blood pressure goals

Many people with hypertension (especially those with diabetes) will need two or more antihypertensive drugs to achieve good control. In clinical trials, fewer than 50% of people achieve satisfactory blood pressure with a single antihypertensive drug.⁵ The common benefit of all combination therapy is the ability to reduce blood pressure to a greater extent than monotherapy.¹⁴

Choose combination therapy based on favourable effects on comorbidity

Start with a single antihypertensive drug chosen according to favourable effects on the patient's comorbidity or risk profile. Use lower doses (i.e. usual recommended doses) of two drugs from different classes in preference to maximum doses of a single agent.

When adding a second antihypertensive, choose the drug and dose being added using a similar rationale — take potential adverse effects into consideration. A regimen with minimal adverse effects should aid adherence.⁵ A thiazide will be an appropriate choice in combination with most other antihypertensives (see Table 1).

There are some data showing that combination therapy with two antihypertensives approximately doubles blood pressure-lowering effects (about 10–20 mmHg). Adverse effects increased with two drugs but did not double, compared with single drug therapy (from 5.2% to 7.5%).¹⁴ The quality of adverse-effect reporting in the trials varied and this rate may not accurately reflect adverse effects in the real world. Nonetheless, many guidelines advocate low-dose combination therapy, recognising that monotherapy will be inadequate for many people.^{1,8}

There is little evidence to guide drug choice when more than two drugs are required.¹ Use a combination of first-line choices and seek specialist advice.

Note: always consider secondary causes of hypertension in treatment failure, including use of drugs with pro-hypertensive effects, such as some antidepressants (e.g. venlafaxine, reboxetine), NSAIDs, sibutramine, steroids and amphetamines.⁵

Choose fixed-dose combination products according to their components and dosing flexibility

Be aware of the drugs and their doses present in fixed-dose combination preparations.

While fixed-dose combination preparations may be cost-saving for patients and once-daily administration may aid adherence, dosing may be problematic.

- Check the components and doses of combination preparations and the implications for dose adjustments. Some combinations are only available at higher doses than would normally be prescribed. For example, candesartan 8 mg is the usual dose but only a 16 mg strength is available in combination with hydrochlorothiazide. Avoid preparations that involve an increased dose of either component if this has not been proven necessary.
- Avoid starting treatment using fixed-dose combination preparations — titration is problematic, and the source of adverse events may be difficult to identify. If monotherapy does not achieve sufficient blood pressure reduction, trial the second agent as a separate drug before prescribing a combination preparation.
- Using fixed-dose combination preparations for initiation is outside PBS restrictions, which require inadequate control with one antihypertensive before a second is added.

Table 1: Combinations of antihypertensive drug classes

Some useful combinations	Potential benefits (and harms)
ACE inhibitor with calcium-channel blocker	Useful in diabetes or lipid abnormalities ⁵
Beta blocker with dihydropyridine calcium-channel blocker*	Useful in coronary heart disease ⁵
Beta blocker with ACE inhibitor	Useful in heart failure Useful post myocardial infarction
Low-dose thiazide [†] with beta blocker	Evidence of mortality and cardiovascular benefits BUT May impair glucose tolerance and increase glucose levels in diabetes ⁵
Low-dose thiazide [†] with ACE inhibitor (or angiotensin II-receptor antagonist)	Useful in heart failure Useful in secondary stroke prevention ¹⁵ Potassium retention caused by ACE inhibitor/ angiotensin II-receptor antagonist is balanced by potassium-depleting effects of thiazide ¹² BUT Adding an NSAID to combined ACE inhibitor, or angiotensin II-receptor antagonist, and diuretic therapy increases the risk of renal failure ('triple whammy') ¹⁶
Combinations to avoid or use with caution	
<ul style="list-style-type: none"> • Beta blocker with verapamil or diltiazem (risk of severe bradycardia) • ACE or angiotensin II-receptor antagonist with potassium-sparing diuretic (increases risk of hyperkalaemia)⁵ • ACE inhibitor with angiotensin II-receptor antagonist (may adversely affect renal function)¹⁷ — reserve for use in diabetic nephropathy or diabetes with proteinuria on specialist advice 	

* Dihydropyridine calcium-channel blockers are amlodipine, felodipine, lercanidipine, nifedipine.

† Includes thiazide-like diuretics.

Optimise adherence with medication and lifestyle management at every opportunity

Treat every visit as an opportunity to optimise adherence

Encouraging adherence with long-term treatment in a largely asymptomatic condition is challenging but important.

No single strategy consistently improves adherence, but reducing the number of doses or using reminder systems may help some patients.^{18–20}

Assess adherence and the need to intervene

Always consider poor adherence as a possible cause of treatment failure. Explore the reasons for non-adherence in a non-threatening way; this may assist in finding solutions and engaging your patient as an active partner in managing their condition.

Asking specific, structured questions (see Box 1) may identify patients who warrant more intensive efforts to improve adherence²¹ (for example, a Home Medicines Review). The questions are intended to elicit appropriate and accurate information from the patient and have been validated for assessing adherence.²²

An Australian study found that patients who adhered to their medication regimen were less likely to experience cardiovascular events or death. Conversely, those who answered 'yes' to the question 'Do you ever forget to take your medicines?' (Box 1) were more likely to have a cardiovascular event.²¹

Acknowledge and discuss adverse effects

Adverse effects may be unpalatable for a relatively asymptomatic condition like hypertension. Discuss adverse effects and their expected duration and, when possible, use drugs and doses that minimise these. Provide a consumer medicine information leaflet to help inform consumers about adverse effects and how to manage these.

Treat the patient as an active partner and agree on treatment goals

Agree on blood pressure goals in partnership with the patient and discuss:

- how they will try to reach the goal blood pressure (drug therapy, lifestyle changes)
- the time frame — arrange follow-up visits accordingly.¹

Misunderstanding the seriousness of their condition (that is, the direct relationship between blood pressure and cardiovascular risk) and the goals of treatment may contribute to non-adherence.

Monitor progress towards target

Home blood pressure measurement may help people monitor their progress towards target and maintain motivation. One randomised controlled trial found self-measurement in the clinic reduced blood pressure in the short term and was acceptable to patients. However, improvements were not sustained after 1 year.²³

Specific guidance for health professionals about blood-pressure self-monitoring is available from the National Heart Foundation (see www.heartfoundation.com.au/downloads/SelfMeasurement_BP_HP.pdf).

Treatment withdrawal may be possible for some

Most people with hypertension require lifelong treatment and patients need to acknowledge and understand this.

Candidates for treatment withdrawal include:

- those who are willing to maintain lifestyle changes (when this is sufficient to reduce blood pressure)
- younger patients
- those who do not have a high risk of a cardiovascular event
- those without specific comorbidity requiring antihypertensive therapy
- those in the goal range for blood pressure while on drug treatment.¹

Continue to monitor blood pressure, as hypertension may revert at any time.

Box 1: Questions to ask about adherence*²²

1. Do you ever forget to take your medication?
2. Are you careless at times about taking your medication?
3. When you feel better, do you sometimes stop taking your medication?
4. Sometimes, if you feel worse when you take your medicine, do you stop taking it?

* These questions are validated for identifying people who are not adhering to treatment.

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Online citations available at www.nps.org.au/healthpro

The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decisions based on this information should be made in the context of the clinical circumstances of each patient.



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Specific considerations for patients with coexisting conditions

Coexisting conditions/ characteristics	Potentially favourable effects	Potentially unfavourable effects	
		Contraindications	Precautions
Angina	Beta blockers, calcium-channel blockers		Calcium-channel blockers (on initiation or withdrawal)
Asthma/COPD		Beta blockers (except cardioselective agents, e.g. atenolol, metoprolol)	Cardioselective beta blockers, e.g. atenolol, metoprolol (use cautiously in mild/moderate disease)
Benign prostatic hypertrophy	Alpha blockers		
Bilateral renal artery stenosis (or unilateral with 1 kidney)		ACE inhibitors, angiotensin II-receptor antagonists	
Bradycardia (severe), grade 2 or 3 atrioventricular block		Beta blockers, calcium-channel blockers	
Diabetes mellitus – without renal disease	ACE inhibitors, angiotensin II-receptor antagonists*, beta blockers, low-dose thiazides or thiazide-like diuretics		
– with microalbuminuria/proteinuria	ACE inhibitors, angiotensin II-receptor antagonists		
Elderly	Calcium-channel blockers, low-dose thiazides or thiazide-like diuretics		Beta blockers (generally less effective), calcium-channel blockers (start with a low dose), thiazides or thiazide-like diuretics (increased risk of electrolyte imbalance)
Gout			Thiazides or thiazide-like diuretics
Heart failure	ACE inhibitors, angiotensin II-receptor antagonists*, beta blockers (i.e. bisoprolol, carvedilol, metoprolol CR), low-dose thiazides or thiazide-like diuretics	Alpha blockers in heart failure due to mechanical obstruction, e.g. aortic stenosis; beta blockers in uncontrolled heart failure	Calcium-channel blockers (especially verapamil, diltiazem)
Hyperkalaemia		ACE inhibitors, angiotensin II-receptor antagonists	
Isolated systolic hypertension	Calcium-channel blockers, low-dose thiazides or thiazide-like diuretics		
Myocardial infarction (post)	ACE inhibitors, beta blockers		
Non-diabetic nephropathy	ACE inhibitors		
Orthostatic hypotension			Alpha blockers (in volume depletion and the elderly), thiazides or thiazide-like diuretics (when symptomatic)
Peripheral vascular disease			Beta blockers
Pregnancy	Refer to <i>Australian Medicines Handbook</i> , approved product information and <i>Therapeutic Guidelines: Cardiovascular</i>		
Renal impairment	Refer to <i>Australian Medicines Handbook</i>		
Secondary stroke prevention	Low-dose thiazides or thiazide-like diuretics ± ACE inhibitors		
Tachyarrhythmias	Beta blockers		

* Consider using an angiotensin II-receptor antagonist when there is a documented ACE inhibitor intolerance.

For more detailed information about the above drugs, refer to *Australian Medicines Handbook* 2007 and the approved product information for the drug. Further information can be obtained from TAIS on 1300 138 677.

Developed from:

- Australian Medicines Handbook, 2007.
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