



# Drug treatment of elevated blood pressure

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## Summary

**The decision on when to start drugs for the treatment of elevated blood pressure should be determined by an individual's absolute risk of having an adverse cardiovascular event. The choice of drug depends on its safety and effectiveness and its indications and contraindications for individual patients. Most patients will require two or more drugs to reach their target blood pressure. The main classes of antihypertensive drugs are equally effective at reducing blood pressure, but beta blockers are no longer recommended as first-line treatment for most patients.**

Key words: antihypertensives, cardiovascular disease, hypertension.

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## Introduction

All patients with elevated blood pressure should be encouraged to have a healthy lifestyle.<sup>1</sup> Although there are benefits from weight loss, salt and alcohol reduction and exercise, these lifestyle changes may be insufficient to control a patient's blood pressure. This leaves them at risk of coronary heart disease, stroke and renal failure. If the high blood pressure is confirmed by accurate measurements on several occasions, drug treatment should be considered.

## Who should receive drug therapy?

Drug treatment for elevated blood pressure should not be based solely on accurate blood pressure readings. It should also consider an individual's absolute cardiovascular risk – their risk of having a stroke or myocardial infarction over a specified period of time, usually five years.<sup>2</sup> An absolute risk calculator can be used to identify who is most likely to benefit from treatment.<sup>3</sup> The previous underestimation of risk in Aboriginal and Torres Strait Islander people by such calculators has been addressed in the recently published Australian risk calculator.<sup>4–6</sup>

Immediate treatment to lower blood pressure is recommended for patients with confirmed hypertension (multiple measures on at least two separate occasions):

- systolic blood pressure 180 mmHg or greater
- diastolic blood pressure 110 mmHg or greater
- systolic blood pressure 160 mmHg or greater and diastolic blood pressure 70 mmHg or less.

Patients with associated conditions (for example, stroke or myocardial infarction) or evidence of end-organ damage (for example, microalbuminuria, left ventricular hypertrophy) also need urgent treatment (Fig. 1).

## Starting drug therapy

Once the decision has been made to start drug therapy, the choice of antihypertensive drug should be based on the patient's age and the presence of associated clinical conditions or end-organ damage. The presence of other diseases may favour or limit the use of particular drug classes and there may be potential interactions with other drugs (Table 1). Cost and the ease of adhering to treatment should also be considered. Antihypertensive drugs in different classes have similar efficacy. In uncomplicated cases the recommendation is to start with an angiotensin-converting enzyme (ACE) inhibitor, angiotensin receptor antagonist, calcium channel blocker or diuretic (in the aged).<sup>2</sup> Beta blockers are no longer recommended as first-line treatment for uncomplicated high blood pressure as meta-analyses show they have an adverse relative risk of stroke and new onset diabetes compared to other drugs.<sup>7,8</sup>

## Target blood pressure

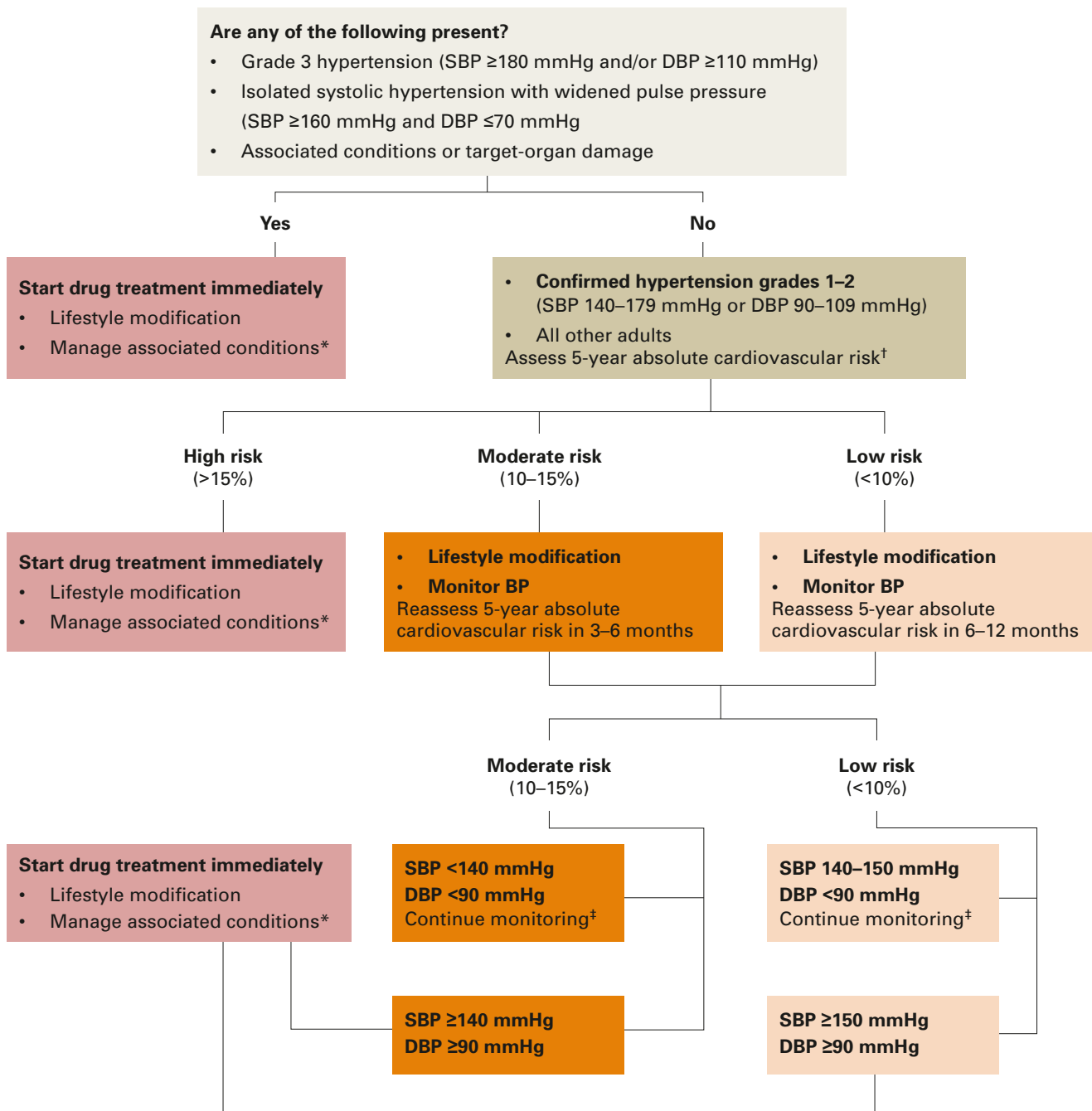
A patient's comorbidity helps to determine which blood pressure to aim for. In uncomplicated hypertension the target should be 140/90 mmHg or lower if tolerated. The target is under 130/80 mmHg in patients with end-organ damage or conditions such as diabetes, and under 125/75 mmHg in patients with proteinuria (>1 g/day).

It is important that patients be treated to reach their recommended blood pressure. Failure to do so leaves patients at significant residual adverse risk.

Start with the lowest recommended dose of the selected drug and review the patient after six weeks. If the drug is not well tolerated or is ineffective, change to a drug of a different class. If the target blood pressure is still not reached, add a further drug from a different pharmacological class at a low dose, rather than increasing to the maximum dose of the first drug.

Fig. 1

When to start drug treatment for hypertension <sup>2</sup>



BP blood pressure SBP systolic blood pressure DBP diastolic blood pressure

\* For example, diabetes (strict glycaemic control lowers cardiovascular risk), lipid disorders (cholesterol-lowering therapy reduces the risk of primary and secondary coronary events). See National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand: Position statement on lipid management 2005 ([www.heartfoundation.org.au](http://www.heartfoundation.org.au)).

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

‡ Continue lifestyle modification, monitor blood pressure 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.

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Table 1

Choice of antihypertensive drug in patients with comorbid and associated conditions <sup>2</sup>

Condition	Potentially beneficial	Potentially harmful	
		Caution	Contraindicated
Angina	Beta blockers (except oxprenolol, pindolol), calcium channel blockers, ACE inhibitors		
Atrial fibrillation	Remodelling: ACE inhibitors, angiotensin receptor antagonists* Rate control: verapamil, diltiazem, beta blockers		
Asthma/COPD		Cardioselective beta blockers (e.g. atenolol, metoprolol): use cautiously in mild–moderate asthma/COPD only	Beta blockers (except cardioselective drugs)
Bradycardia, second- or third-degree atrioventricular block			Beta blockers, verapamil, diltiazem
Depression		Beta blockers, clonidine, methyl dopa, moxonidine	
Gout	Losartan	Thiazide diuretics	
Heart failure	ACE inhibitors, angiotensin 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		
Pregnancy <sup>§</sup>			ACE inhibitors, angiotensin receptor antagonists, diuretics, calcium channel blockers (before 22 weeks gestation), atenolol
Chronic kidney disease	ACE inhibitors, angiotensin receptor antagonists*		
Tight bilateral renal artery stenosis (unilateral in patient with solitary kidney)		ACE inhibitors, angiotensin receptor antagonists	
Post stroke	ACE inhibitors, angiotensin receptor antagonists, low-dose thiazide-like diuretics		
Type 1 or type 2 diabetes with proteinuria or microalbuminuria	ACE inhibitors, angiotensin receptor antagonists*	Beta blockers, thiazide diuretics‡	

ACE angiotensin-converting enzyme COPD chronic obstructive pulmonary disease

\* Careful monitoring of kidney function is required if a combination of ACE inhibitors and angiotensin receptor antagonists is used

† 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 (available at [www.heartfoundation.org.au](http://www.heartfoundation.org.au)).

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

§ Currently under review by the Heart Foundation

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This treatment approach maximises efficacy while minimising adverse effects. Titrate the dose of one drug then the other until the target blood pressure is reached. Additional drugs may be required.

Attaining and maintaining the target blood pressure may be assisted by:

- choice of long-acting drugs to provide once-daily administration
- regular assessment and encouragement of drug adherence
- treating the patient as a partner in management decisions and involving the patient's family when appropriate
- providing specific written instructions and patient education materials
- discussing the use of dose administration aids (e.g. dosette boxes, blister packs) and home medicines review
- use of self-measurement of blood pressure for monitoring, if appropriate
- evaluating the social and economic barriers that may affect medication supply and storage
- using effective combinations (Table 2) when more than one drug is required.

### Combination therapy

Approximately 60% of patients with elevated blood pressure will not achieve their blood pressure targets with monotherapy. Most patients will require a combination of two

or more drugs to achieve adequate blood pressure control.

There are several effective combinations (Table 2). In the ACCOMPLISH trial an ACE inhibitor and calcium channel blocker combination reduced cardiovascular events more than a combination of the ACE inhibitor with a diuretic.<sup>9</sup>

### Long-term drug treatment

Drug treatment is usually lifelong, as age is the most important determinant of adverse risk, unless the blood pressure is well controlled by profound lifestyle changes.<sup>10</sup> If blood pressure is normal and stable, the interval between visits can be lengthened, for example, review every three months for the next 12 months and six-monthly thereafter.

If treatment is stopped, the patient's blood pressure should be checked regularly. Patients should continue the lifestyle changes and agree to resume drug treatment if their blood pressure rises again.

### Resistant blood pressure

Failure to control blood pressure can be due to a wide range of prescriber, patient, healthcare system and drug related factors. If blood pressure remains above the target despite maximal doses of at least two appropriate drugs after a reasonable period, consider the following potential explanations:

- non-adherence to drug therapy and lifestyle modifications
- secondary hypertension (e.g. sleep apnoea, chronic kidney disease)

Table 2

#### Recommended and discouraged drug combinations for hypertension<sup>2</sup>

Recommended combinations			Recommendation
ACE inhibitor or angiotensin receptor antagonist	plus	calcium channel blocker	Diabetes or dyslipidaemia
	plus	thiazide diuretic	Heart failure or post stroke
	plus	beta blocker	Post myocardial infarction or heart failure
Beta blocker	plus	dihydropyridine calcium channel blocker	Coronary heart disease
Thiazide diuretic	plus	calcium channel blocker	
	plus	beta blocker	<b>Not</b> with glucose intolerance, metabolic syndrome or diabetes
Combinations to avoid			Recommendation
ACE inhibitor or angiotensin receptor antagonist	plus	potassium-sparing diuretic	Avoid because of risk of hyperkalaemia
Verapamil	plus	beta blocker	Avoid because of risk of heart block
ACE inhibitor	plus	angiotensin receptor antagonist	In a large trial, combination therapy did not reduce cardiovascular death or morbidity in patients with vascular disease or diabetes while increasing the risk of hypotensive symptoms, syncope and renal dysfunction

ACE = angiotensin-converting enzyme

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- use of drugs that may increase blood pressure (e.g. non-steroidal anti-inflammatory drugs, prednisolone)
- alcohol or recreational drug use
- high salt intake (particularly in patients taking ACE inhibitors or angiotensin II receptor antagonists)
- 'white coat' hypertension
- blood pressure measurement artefact
- volume overload (especially with chronic kidney disease).

## Drug treatment in older people

In the elderly, isolated elevated systolic blood pressure is more prevalent due to large vessel stiffness associated with ageing. Calcium channel blocker- or diuretic-based drug treatment is recommended.

In the very elderly, the recommended blood pressure targets may be difficult to achieve due to comorbidity, reduced physiological function and polypharmacy. However, the elderly are most at risk of adverse cardiovascular events and trials have shown that drug therapy is just as effective in advanced age. The Hypertension in the Very Elderly Trial (HYVET) studied patients aged 80 years or more (mean age 83.6 years). It showed a 39% relative reduction in the rate of death from stroke, a 21% reduction in the rate of death from any cause, a 23% reduction in the rate of death from cardiovascular causes and a 64% reduction in the rate of heart failure for those on active treatment versus placebo. Fewer serious adverse events were reported in the active treatment group so concerns about causing more harm than good are allayed.<sup>11</sup>

## Conclusion

Drug therapy is warranted in individuals with a high risk of adverse cardiovascular events. It does not obviate the need for behavioural modification. All classes of antihypertensive drugs have similar efficacy, but specific recommendations are made according to the patient's characteristics. Whichever drug is started, it is important to treat until the target blood pressure is reached. Usually more than one drug is required to reach the target.

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## Self-test questions

*The following statements are either true or false (answers on page 131)*

3. Isolated systolic hypertension does not require treatment if the diastolic blood pressure is under 70 mmHg.
4. When there is no response to the initial dose of an antihypertensive drug, it should be titrated to its maximum dose before switching to another drug.