## MOH CLINICAL PRACTICE GUIDELINES 1/2017 HYPERTENSION EXECUTIVE SUMMARY



Chapter of Family Medicine Physicians Academy of Medicine, Singapore







College of Family Physicians Singapore



Singapore Hypertension Society

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#### EXECUTIVE SUMMARY OF RECOMMENDATIONS

#### Introduction

This is the executive summary of the MOH Clinical Practice Guidelines (CPG) on Hypertension. It is intended to be used with reference to the full version of the CPG which is freely available on the MOH website at this link:

https://www.moh.gov.sg/content/moh\_web/healthprofessionalsportal/doctors/guidelines/cpg\_medical.html

Hypertension is the leading associated risk factor for cardiovascular disease. It is prevalent and increasing in many developing and developed countries. The Singapore National Health Survey (NHS) 2010 showed that the crude prevalence of hypertension (defined as BP of  $\geq$  140/90 mmHg) among Singapore residents aged 30 to 69 years was 23.5%, compared to 24.9% in 2004 and 27.3% in 1998. However, the age-specific prevalence for hypertension rises markedly from age 40 years onwards and, with our ageing population, we continue to face challenges in the prevention and control of hypertension.

#### Target audience

These guidelines are developed for all healthcare professionals in Singapore, as an evidence-based resource to provide up-to date information and guidance on diagnosis, classification, treatment, outcomes, and follow-up.

#### How to use this document

All recommendations made in the CPG are summarised in this document.

Please note the following:

- Each recommendation has a corresponding Grade of Recommendation and Level of Evidence (refer to back cover page for details)
- b. The details/explanations of each recommendation can be found in the full CPG document using the page numbers provided.

Key recommendations are highlighted in light brown.

## Commonly used abbreviations

The following is a list of abbreviations commonly used in this set of guidelines (arranged in alphabetical order), and a description of what they represent:

- ABPM ambulatory blood pressure monitoring
- ACE angiotensin-converting enzyme
- ACR albumin:creatinine ratio
- ARB angiotensin II receptor blocker
- BMI body mass index
- BP blood pressure
- CAD coronary artery disease
- ECG electrocardiography
- eGFR estimated glomerular filtration rate
- HBPM home blood pressure monitoring
- LVH left ventricular hypertrophy
- NHS National Health Survey
- PCR protein:creatinine ratio
- RAAS renin-angiotensin-aldosterone system
- RCT randomised controlled trial

## Classification of hypertension

D Classify hypertension according to systolic BP and diastolic BP levels. When the systolic BP and the diastolic BP fall into different categories, the higher category applies. (Grade D, Level 4, CPG pg. 18)

Definitions are given in Table 1 for subjects who are not on antihypertensive medication and not acutely ill.

Table 1 Definitions and classification of BP levels for adults aged 18 years

and older (CPG pg. 18)

Category	Systolic BP	Diastolic BP
Normal BP	< 130 mmHg	< 85 mmHg
High-normal BP	130 to 139 mmHg	85 to 89 mmHg
Grade 1 hypertension	140 to 159 mmHg*	90 to 99 mmHg
Grade 2 hypertension	160 to179 mmHg*	100 to 109 mmHg
Grade 3 hypertension	≥ 180 mmHg*	≥ 110 mmHg
Isolated systolic hypertension	≥ 140 mmHg*	< 90 mmHg

<sup>\*</sup> Isolated systolic hypertension is graded according to the same level of systolic BP.

As BP is characterised by large spontaneous variations, the diagnosis of hypertension should be based on multiple BP measurements taken on several separate occasions.

## How should BP be measured?

For clinic or office BP measurement, the BP is measured at rest several times on several occasions, with the patient in a supine or sitting position.

- D Use the following procedures when recording BP:
- 1. Allow the patient to sit or lie down for at least 3 minutes before measuring the BP.
- 2. The patient should refrain from smoking or taking caffeinated drinks during the 30 minutes before measurement.
- 3. Use a cuff with a bladder 12-13 cm x 35 cm in size. A cuff with a larger bladder should be used for large upper arms; where a thigh cuff should be used for extremely large arms.
- 4. When using the auscultatory method, use the disappearance of phase V Korotkoff sounds to measure the diastolic BP.
- 5. Measure the BP in both arms at the first visit; subsequently re-measure BP on the arm with the higher reading, if applicable.
- 6. Take 2 or more readings separated by 2 minutes. Average these two values. If the first two readings differ by 5 mmHg or more, further readings should be obtained and averaged.
- 7. In elderly subjects and diabetic patients, measure the BP in the supine (or sitting) position, and within 2 minutes after standing, to record any postural fall in BP.
- 8. Place the manometer cuff at the level of the heart, regardless of the position of the patient.

(Grade D, Level 4, CPG pg. 19)

When measuring BP in clinic or office, the alerting response can result in exaggerated BP, leading to the diagnosis of isolated clinic ("white-coat") hypertension. Compared to clinic or office measurement, BP values obtained by HBPM or by 24-hour ABPM are usually several mmHg lower. Both HBPM and ABPM methods are valid.

Wherever practicable, HBPM or ABPM (in that order) should be offered to younger patients, and to those whom target organ damage is found without a raised BP. (Grade D, Level 4, CPG pg. 20)

The preferred manometer is an automated oscillometric device, with or without memory. (Grade C, Level 2+, CPG pg. 21)

D To ensure reliable values, the patient or carer needs training in device use, and a BP log-book (for basic devices without memory). (Grade D, Level 4, CPG pg. 21)

GPP ABPM is recommended whenever in doubt about the diagnosis, e.g. to confirm borderline hypertension or abnormal results from HBPM. (CPG pg. 21)

GPP ABPM is also indicated for older, cognitively impaired, anxious or obsessive patients, in whom HBPM might be unreliable or inappropriate. (CPG pg. 21)

The definitions of hypertension based on HBPM and ABPM are listed in Table 2.

Table 2 Definitions of hypertension in HBPM and ABPM (CPG pg. 22)

	Systolic BP	Diastolic BP
HBPM	≥ 135 mmHg	≥ 85 mmHg
ABPM		
<ul> <li>Daytime</li> </ul>	≥ 135 mmHg	≥ 85 mmHg
• 24-hour	≥ 130 mmHg	≥ 80 mmHg
Night-time	≥ 120 mmHg	≥ 70 mmHg

D Patients with an average BP  $\geq$ 135/85 mmHg measured repeatedly at rest at home may be regarded as hypertensive. (Grade D, Level 3, CPG pg. 22)

D Patients with a 24-hour ABPM average BP  $\geq$ 130/80 mmHg, or a daytime average BP  $\geq$ 135/85 mmHg, or a night-time average BP  $\geq$ 120/70 mmHg, are regarded as hypertensive. (**Grade D, Level 4, CPG pg. 22**)

## How should hypertension be evaluated?

- D Routine clinical evaluation of a patient with elevated BP includes the following:
- 1. Clinical and family history
- 2. Full standard physical examination
- 3. Laboratory investigations, including:
  - a) Urine analysis: Dipstick for haematuria/albumin, microscopic examination, and test for albuminuria
  - b) Measurement of serum concentrations of electrolytes, creatinine, urea, fasting glucose and fasting lipids
  - c) Computation of eGFR
- 4. 12-lead ECG

(Grade D, Level 4, CPG pg. 24)

The identifiable secondary causes of hypertension are listed in Table 3 below.

Table 3 Identifiable secondary causes of hypertension (CPG pg. 25)

#### **Identifiable secondary causes of hypertension**

- 1. Drug-related and substance-related\* causes
- 2. Chronic kidney disease
- 3. Renal artery stenosis
- 4. Primary hyperaldosteronism
- 5. Hypercortisolism (Cushing's syndrome)
- 6. Phaeochromocytoma
- 7. Thyroid or parathyroid disease
- 8. Coarctation of the aorta
- 9. Obstructive sleep apnoea syndrome
- 10. Nephropathy from Type 1 diabetes mellitus
- 11. Rare monogenic ion transport disorders

## Stratifying risk and approach to hypertension management

- GPP Assess the overall cardiovascular risk and the patient's BP to guide the management of high BP. (CPG pg. 26)
- D Refer to the locally adapted Framingham Risk Score to estimate cardiovascular risk. (Grade D, Level 4, CPG pg. 26)
- **GPP** Offer to start drug treatment immediately in patients with hypertension and existing high cardiovascular risk. (**CPG pg. 26**)
- D Take the BP and other prognostic factors into account when deciding on the management of hypertensive patients. (Grade D, Level 4, CPG pg. 26)

Patients' risk level for cardiovascular disease depends on BP and prognostic factors (see Table 4).

<sup>\*</sup> Several non-prescribed and illicit substances causes hypertension, e.g. liquorice, cocaine, amphetamine, crystal methamphetamine, and 3,4-methylenedioxy-methamphetamine (MDMA, 'Ecstasy')

Table 4 Risk stratification (CPG pg. 28)

BP Category	Prognostic factors			S
	0-2 risk factors	≥ 3 risk factors	Established	Symptomatic cardiovascular
			cardiovascular or renal disease	disease, chronic kidney disease stage >4 or diabetes with organ
			Tenar disease	damage or risk factors
Grade 1 HT SBP 140-159 mmHg/ DBP 90-99 mmHg	Lov	v risk		
Grade 2 HT SBP 160-179 mmHg/ DBP 100-109 mmHg		Med	lium risk	
<u>Grade 3 HT</u> SBP≥180 mmHg/ DBP≥110 mmHg			High or	very high risk

HT: Hypertension

A For high or very high risk individuals, begin immediate drug treatment for hypertension when other risk factors or conditions are present. (Grade A, Level 1<sup>++</sup>, CPG pg. 28)

B For medium risk individuals, monitor the BP and other risk factors for several weeks, and obtain further information, before deciding whether to begin drug treatment. (Grade B, Level 1<sup>+</sup>, CPG pg. 28)

B For low risk individuals, observe the patient over a significant period of time before deciding whether or not to begin drug treatment. (Grade B, Level 1<sup>+</sup>, CPG pg. 28)

## Treating high blood pressure

⚠ Wherever possible, use a team-based approach to manage a patient with hypertension, involving trained nurses and pharmacists with medical practitioners. (Grade A, Level 1<sup>+</sup>, CPG pg. 30)

#### Lifestyle modifications

- A Recommend lifestyle changes to all hypertensive patients, and in patients with high normal BP. However, drug treatment should not be delayed without reason beyond 3 to 6 months if indicated. (Grade A, Level 1<sup>+</sup>, CPG pg. 31)
- Advise patient to restrict salt intake to 5 to 6 g per day. (Grade A, Level 1<sup>+</sup>, CPG pg. 31)
- A Moderate alcohol consumption to no more than 2 standard drinks per day for men, and to no more than 1 standard drink per day for women. (Grade A, Level 1<sup>+</sup>, CPG pg. 31)
- ▲ Increase the consumption of vegetables, fruits, low-fat dairy products, and decrease the intake of saturated and total fats. (Grade A, Level 1<sup>+</sup>, CPG pg. 31)
- B Unless contraindicated, advise patients to reduce weight to a BMI below 23 kg/m<sup>2</sup> and to a waist circumference below 90cm in men, and below 80cm in women (for Asians). (Grade B, Level 2<sup>+</sup>, CPG pg. 31)
- Advise patients to do at least 30 minutes of moderate dynamic exercise 5 to 7 days per week. Any physical exercise above the basal level, up to about 150 minutes a week, confers incremental cardiovascular and metabolic benefits, including BP reduction. (Grade A, Level 1<sup>+</sup>, CPG pg. 32)
- Advise and offer assistance to all smokers to quit smoking. (Grade A, Level 1+, CPG pg. 32)

# Pharmacological treatment

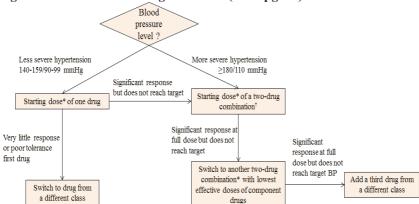


Figure 1 Flowchart for drug treatment (CPG pg. 32)

Begin appropriate combination treatment in patients whose pretreatment BP is raised (i.e. ≥ 140/90 mmHg), and specifically in patients whose BP is severely raised (≥ 180/110 mmHg), as they will require two or more drugs for adequate BP control. (Grade B, Level 2<sup>+</sup>, CPG pg. 33)

D Initiate treatment at low doses, either singly or as a two-drug combination, to minimise side effects. (Grade D, Level 4, CPG pg. 33)

▲ If an adequate dose of the first drug used demonstrated limited response or was poorly-tolerated, change to a different drug class instead of increasing the dose of the first drug. (Grade A, Level 1+, CPG pg. 33)

B Add a second drug when a single drug fails to achieve target BP. (Grade B, Level 1<sup>+</sup>, CPG pg. 34)

B Use long-acting drugs which provide 24-hour efficacy daily. (Grade B, Level 2<sup>+</sup>, CPG pg. 34)

<sup>\*</sup>Start with the lowest effective dose

<sup>&</sup>lt;sup>†</sup>Two-drug combinations may be either 2 separate drugs, or a fixed two-drug combination tablet.

## Choice of antihypertensive drugs

The choice of antihypertensive drug should be tailored to the individual patient, taking into account the following factors, in addition to risk profile and cost:

- 1. Side effects
- 2. Drug-drug interactions
- 3. Patient preference

Begin first-line antihypertensive treatment with any one, or an appropriate combination, of the five major drug classes available in Singapore, namely:

- 1. Angiotensin-converting enzyme inhibitor (ACE inhibitor)
- 2. Angiotensin II receptor blocker (ARB)
- 3. Calcium-channel blocker (CCB)
- 4. Diuretic (thiazide, thiazide-like, or loop)
- 5. Beta-blocker

Other classes of antihypertensive drugs, such as methyldopa, hydralazine, and alpha-adrenergic receptor blockers (peripheral alpha-1 blockers such as terazosin; central alpha-2 blockers like clonidine) may be used in combination treatment as third or fourth-line agents.

**B** In hypertensive patients without compelling indications or contraindications for any particular drug, consider any one, or any appropriate combination, of the five major pharmacological classes of antihypertensive drugs as the initial treatment. (Grade B, Level 2<sup>++</sup>, CPG pg. 34)

A Take compelling indications and contraindications into account when prescribing an antihypertensive drug. (Grade A, Level 1<sup>+</sup>, CPG pg. 34)

The guidelines for selecting drug(s) for antihypertensive treatment is in Table 5.

Table 5 Guidelines for selectii	ng drug(s) for antil	Table 5 Guidelines for selecting drug(s) for antihypertensive treatment (CPG pgs. 35-36)	
Concomitant conditions	Status	Drugs	Grade and level
Heart failure	Recommended	Diuretic, ACE inhibitor, ARB, aldosterone antagonist (spironolactone, eplerenone), or beta-blocker (bisoprolol, carvedilol)	Grade A, Level 1 <sup>++</sup>
	Supplementary treatment	Dihydropyridine calcium-channel blocker (amlodipine, felodipine)	Grade C, Level 2 <sup>+</sup>
	Contraindicated	Non-dihydropyridine calcium-channel blocker (verapamil, diltiazem)	Grade D, Level 4
Angina pectoris	Recommended	Beta-blocker or dihydropyridine calcium-channel blocker	Grade A, Level 1+
Previous myocardial infarction	Recommended	Beta-blocker, ACE inhibitor, or ARB	Grade A, Level 1 <sup>++</sup>
Atrial fibrillation, prevention	Recommended	Beta-blocker, ACE inhibitor, or ARB	Grade B, Level 1+
Atrial fibrillation, ventricular	Recommended	Beta-blocker	Grade A, Level 1+
rate control	Recommended	Non-dihydropyridine calcium-channel blocker	Grade B, Level 2 <sup>++</sup>
Heart block	Contraindicated <sup>†</sup>	Beta-blocker, or non-dihydropyridine calcium-channel blocker	Grade B, Level 2**
Peripheral artery disease	Recommended	ACE inhibitor or dihydropyridine calcium-channel blocker	Grade C, Level 2+
Aortic aneurysm	Recommended	Beta-blocker	Grade C, Level 2+

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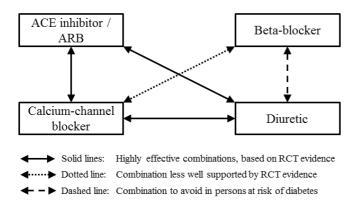
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Concomitant conditions	Status	Drugs	Grade and level
Isolated systolic hypertension	Recommended	Diuretic, or dihydropyridine calcium-channel blocker	Grade A, Level 1+
Diabetes mellitus	Recommended	ACE inhibitor or ARB	Grade A, Level 1+
	Recommended	Dihydropyridine calcium-channel blocker	Grade B, Level 2 <sup>++</sup>
	Supplementary treatment	Diuretic or beta-blocker	Grade B, Level 1+
Diabetes mellitus with albuminuria (moderately- or	Recommended	ACE inhibitor or ARB	Grade A, Level 1+
severely- increased albuminuria)	Contraindicated	Any combination of ACE inhibitor with ARB	Grade A, Level 1+
Previous stroke	Recommended	Any drug which effectively lowers the BP	Grade A, Level 1 <sup>++</sup>
Asthma & chronic obstructive pulmonary disease	Contraindicated <sup>†</sup>	Beta-blocker	Grade B, Level 2**
Gout	Contraindicated <sup>†</sup>	Diuretic	Grade C, Level 2+
Bilateral renal artery stenosis	Contraindicated <sup>†</sup>	ACE inhibitor or ARB	Grade B, Level 2 <sup>++</sup>
Chronic kidney disease stage 5 (end-stage renal failure)	Recommended	ACE inhibitor or ARB*	Grade A, Level 1+
	Contraindicated	Aldosterone antagonist	Grade C, Level 2+

\*An ACE inhibitor should not be combined with an ARB in chronic kidney disease  ${}^*\mathsf{Consider}$  use of other first-line antihypertensive drug classes on page 11.

- D Be aware of the cost of treatment in selecting antihypertensive drugs. (Grade D, Level 4, CPG pg. 37)
- D Generic formulations, which usually cost less than newer non-generic (i.e. proprietary) drugs, are acceptable for use. (Grade D, Level 4, CPG pg. 37)
- Do not offer aldosterone (mineralocorticoid) antagonists (e.g. spironolactone) to patients with chronic kidney disease, in particular when combined with an ACE inhibitor or ARB. This is because of the risks of further renal function impairment, and of hyperkalaemia. An aldosterone antagonist might be considered in patients with resistant hypertension after a full work-up has excluded secondary hypertension (Table 3, pg. 7). (Grade C, Level 2<sup>+</sup>, CPG pg. 38)
- Prescribe a diuretic with caution as initial treatment in patients with uncomplicated hypertension, who are at risk for diabetes, because it might cause hyperglycaemia. (Grade B, Level 2+, CPG pg. 38)
- A Use beta-blockers with caution in patients at risk of developing diabetes, as it raises blood glucose concentrations. (Grade A, Level 1<sup>+</sup>, CPG pg. 38)

## **Combination therapy**

Figure 2 Pairing the major drug classes (CPG pg. 38)



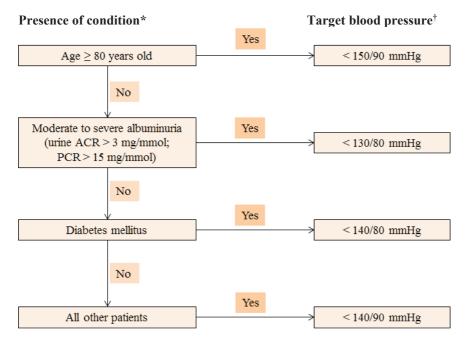
- B Use the following drug combinations to treat hypertension:
- Calcium-channel blocker (dihydropyridine type) plus ACE inhibitor or ARB
- 2. Calcium-channel blocker plus diuretic
- 3. Diuretic plus ACE inhibitor or ARB
- 4. Beta-blocker plus calcium-channel blocker (see caveat in Figure 2 above)
- 5. Beta-blocker plus diuretic (see caveat in Figure 2 above) (Grade B, Level 2<sup>++</sup>, CPG pg. 39)
- B Avoid treating patients with an ACE inhibitor plus ARB combination, particularly patients who have chronic kidney disease. (Grade B, Level 1<sup>+</sup>, CPG pg. 39)
- Beware of an increased risk of diabetes mellitus when offering a betablocker plus diuretic combination to patients with risk factors such as obesity or metabolic syndrome. (Grade B, Level 2<sup>++</sup>, CPG pg. 39)
- A Do not offer renal sympathetic denervation for routine treatment of resistant hypertension. (Grade A, Level 1<sup>+</sup>, CPG pg. 40)
- B Do not offer carotid-sinus baroreceptor reflex activation for routine treatment of resistant hypertension. (Grade B, Level 2<sup>++</sup>, CPG pg. 40)

## Treatment goals and follow up

#### **Treatment goals**

- A The recommended target BP treatment levels are:
- 1. BP < 140/90 mmHg in patients aged under 80 years
- 2. BP < 150/90 mmHg in patients aged 80 years or older In fragile elderly individuals, the systolic BP goals should be adapted to individual tolerability. (Grade A, Level 1<sup>+</sup>, CPG pg. 41)

Figure 3 Flowchart for clinic blood pressure targets (CPG pg. 42)



<sup>\*</sup>If 2 conditions exist in the same patient, the condition that is mentioned first will determine the blood pressure level.

Home blood pressure target will be the lower of either 135 / 85 mmHg, or the clinic target as determined above.

<sup>†</sup>Blood pressure control should be optimised for individual patients to achieve the blood pressure targets without worsening the eGFR and cardiovascular outcomes.

#### Follow-up

Follow-up during evaluation and stabilisation of treatment should be sufficiently frequent to monitor the BP and other cardiovascular risk factors (Table 6).

# C Table 6 Frequency of recommended tests/actions

Recommended test/action	Recommended frequency
BP monitoring	
Risk level*	
- Low added risk	6-monthly to annually
- Medium to very high risk	3- to 6-monthly
BMI	Annually or more frequently, as per
Fasting glucose	individual risk profile
Fasting lipid profile	
Serum electrolytes, urea, creatinine	
Urine-albumin measurement	
ECG	As per individual risk and cardiac profile
Patient education	At each visit
Lifestyle modification and	
Medication adherence	

<sup>\*</sup> Goal BP achieved.

(Grade C, Level 2<sup>+</sup>, CPG pg. 43)

- **D** Patients with the following problems should be referred to a hypertension specialist or clinic:
- 1. Conditions needing emergency or urgent treatment, e.g. malignant hypertension, hypertensive heart failure, or other impending complications
- Hypertension that is difficult to manage, e.g. unusually labile BP, or hypertension refractory to multiple drugs in different pharmacological classes
- 3. Secondary hypertension, i.e. hypertension due to an underlying cause, such as hyperaldosteronism
- 4. Hypertension in special circumstances, e.g. pregnancy, and young children. (Grade D, Level 4, CPG pg. 43

## Treating high blood pressure in special conditions

## Type 2 diabetes mellitus

- **B** For patients with type 2 diabetes mellitus who have hypertension, an acceptable treatment target BP is below 140/80 mmHg. (Grade B, Level 2<sup>+</sup>, CPG pg. 44)
- △ Use ACE inhibitor, ARB, or calcium-channel blocker as first-line treatment in patients with diabetes without chronic kidney disease or proteinuria. (**Grade** A, Level 1<sup>+</sup>, CPG pg. 44)
- A Optimised BP control is recommended to reduce the risk, or slow the progression, of diabetic nephropathy. (Grade A, Level 1<sup>+</sup>, CPG pg. 46)
- A Treat patients with diabetic nephropathy to a target below 140 mmHg systolic BP. (Grade A, Level 1<sup>+</sup>, CPG pg. 46)
- **B** If a diabetic nephropathy patient has severe albuminuria (equivalent to urinary albumin:creatinine ratio (ACR) more than 30 mg/mmol, or urinary PCR more than 50 mg/mmol), consider target below 130 mmHg systolic BP provided GFR changes are monitored carefully. (Grade B, Level 2+, CPG pg. 47)
- D Treat diabetic chronic kidney disease patients with moderate albuminuria (urinary ACR 3-30 mg/mmol, or urinary PCR between 15-50 mg/mmol) to a target BP equal to or below 130/80 mmHg. (Grade D, Level 4, CPG pg. 47)
- △ Use an ACE inhibitor or ARB as first-line treatment, whenever treatment with BP-lowering drugs is indicated in diabetic nephropathy. (Grade A, Level 1+, CPG pg. 48)
- D In diabetic nephropathy, if one class of RAAS blocker (either ACE inhibitor or ARB) is not tolerated, replace it with the other class. (Grade D, Level 4, CPG pg. 48)
- A Combination treatment with both an ACE inhibitor and an ARB should not be routine in diabetic nephropathy. (Grade A, Level 1<sup>+</sup>, CPG pg. 48)

- D When ACE inhibitors, ARBs, or diuretics are used in diabetic nephropathy, it is recommended to monitor the serum creatinine and potassium levels for the possible development of acute kidney injury and hyperkalemia. (Grade D, Level 4, CPG pg. 48)
- A Beta-blockers, calcium-channel blockers, and thiazides are all appropriate second-line therapy in diabetic nephropathy. (Grade A, Level 1<sup>+</sup>, CPG pg. 49)

## Non-diabetic chronic kidney disease

- A Treat non-diabetic, non-proteinuric chronic kidney disease patients to a target BP below 140/90 mmHg. (Grade A, Level 1<sup>+</sup>, CPG pg. 50)
- A Treat non-diabetic chronic kidney disease patient with severe albuminuria to a target BP equal to or below 130/80 mmHg. (Grade A, Level 1<sup>+</sup>, CPG pg. 50)
- D Treat non-diabetic chronic kidney disease patients with moderate albuminuria to a target BP below 130/80 mmHg. (Grade D, Level 4, CPG pg. 0)
- △ Use either an ACE inhibitor or an ARB as the first-line drug whenever treatment with BP-lowering drugs is indicated in non-diabetic chronic kidney disease patients. (Grade A, Level 1<sup>+</sup>, CPG pg. 50)
- A Combination treatment with both an ACE inhibitor and an ARB should not be routinely prescribed in non-diabetic chronic kidney disease patients. (Grade A, Level 1<sup>+</sup>, CPG pg. 50)

#### Stroke

⚠ Where systolic BP is above 140 mmHg but below 220 mmHg within the first two weeks of onset of acute ischaemic stroke, lowering of high BP should be based on individual clinical judgment after careful consideration of all the contraindications. (Grade A, Level 1<sup>++</sup>, CPG pg. 51)

- D It is reasonable to lower, with care, a markedly elevated BP (systolic BP above 220 mmHg or diastolic BP above 120 mmHg, or both) by 10% to 15% during the first 24 hours after the onset of acute ischaemic stroke. (Grade D, Level 4, CPG pg. 52)
- D After the acute phase of stroke, begin antihypertensive treatment in hypertensive patients if the systolic BP is more than 140 mmHg and diastolic BP is more than 90 mmHg. (Grade D, Level 4, CPG pg. 52)
- ⚠ Use any of the five major pharmacological classes of antihypertensive drugs for stroke prevention in patients after the acute phase of stroke, provided that the BP is effectively lowered. (Grade A, Level 1<sup>++</sup>, CPG pg. 53)
- GPP The target BP level in patients after transient ischemic attack and after acute phase stroke should be individualised, with careful consideration of medical comorbidities. A lower systolic BP target might benefit a patient who has small vessel disease, but might harm a patient with severe cerebrovascular stenosis. (CPG pg. 53)

#### **Pregnancy**

- D Even though the classification of mild, moderate and severe hypertension by BP level is different in pregnancy, pharmacological treatment is recommended in pregnant women with chronic hypertension who have a persistently elevated systolic BP of 150 mmHg or greater, or a diastolic BP of 100 mmHg or greater. (Grade D, Level 4, CPG pg. 54)
- GPP Avoid aggressive rates of lowering of BP in pregnant women with chronic hypertension, because of the potential risk of compromising the uteroplacental blood flow. (CPG pg. 54)
- D In pregnant women with no target organ damage, and uncomplicated chronic hypertension, aim to keep the BP below 150/100 mmHg. (Grade D, Level 4, CPG pg. 54)
- D In pregnant women with target organ damage secondary to chronic hypertension, aim to keep the BP below 140/90 mmHg. (Grade D, Level 4, CPG pg. 54)

- D In pregnant women with uncomplicated chronic hypertension, do not use drug treatment to decrease the diastolic BP to below 80 mmHg. (Grade D, Level 4, CPG pg. 54)
- D Treat pregnant women with chronic hypertension using methyldopa, labetalol, nifedipine, or a combination thereof. (Grade D, Level 4, CPG pg. 54)
- **GPP** Methyldopa, labetolol, and nifedipine are also considered safe for use during breastfeeding postpartum. (**CPG** pg. 54)
- D ACE inhibitors, ARBs, direct renin inhibitors (e.g. aliskiren), and aldosterone antagonists should be avoided during pregnancy. (Grade D, Level 4, CPG pg. 55)

#### **Elderly**

- ▲ In elderly hypertensive patients whose systolic BP is 160 mmHg or higher, the BP should be reduced to below 150/90 mmHg. (Grade A, Level 1<sup>+</sup>, CPG pg. 55)
- **B** In patients under the age of 80 years with good physical and mental status, systolic BP can be lowered to below 140 mmHg if treatment is well tolerated. (**Grade B, Level 2**<sup>++</sup>, **CPG pg. 55**)
- ▲ The management of hypertension in the elderly follows the same general guidelines, but begin drug treatment gradually, especially in the frail elderly. On starting drug treatment, carefully consider the patients' associated clinical conditions. (Grade A, Level 1<sup>+</sup>, CPG pg. 56)
- In elderly patients with isolated systolic hypertension, consider using calcium-channel blockers and diuretics. (Grade B, Level 2<sup>+</sup>, CPG pg. 56)
- GPP In the elderly, measure BP often in the supine (or sitting) position and standing position to detect a postural drop in the BP. Take care to avoid fluid depletion and electrolyte imbalance in the elderly. (CPG pg. 56)

#### Treatment of associated risk factors

#### Cholesterol lowering and antiplatelet therapy

There are benefits of decreasing cardiovascular risk in patients with high serum cholesterol levels by using lipid regulating drugs, and in patients with a history of CAD or cerebrovascular disease by using antiplatelet drugs.

▲ Take into account the use of other drugs that decrease cardiovascular risk, such as lipid regulating drugs and antiplatelet drugs, in hypertensive patients with concomitant risk factors and increased cardiovascular risk. (Grade A, Level 1<sup>++</sup>, CPG pg. 57)

### Clinical quality improvement

The recommended target BP levels in antihypertensive treatment are

- Below 140/90 mmHg in patients aged under 80 years\*
- Below 150/90 mmHg in patients aged 80 years or more

\*In elderly patients aged under 80 years with good physical and mental status, if treatment is well tolerated.

The objective of managing hypertension is ultimately to decrease the patients' overall risks of morbidity and mortality. The greater the total cardiovascular disease risk, the more rigorously the BP should be controlled.

However, the BP level attainable with antihypertensive treatment is influenced by medication side effects and other comorbidities, such as diabetes, chronic kidney disease, CAD, and cerebrovascular disease. Good clinical judgment should therefore be exercised in every patient.

The schedules shown in Table 6 (pg. 17) are recommended to allow patients and healthcare providers to optimise the quality of care.

# Levels of evidence and grades of recommendation

## Levels of evidence

Level	Type of Evidence
1++	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

#### Grades of recommendation

Grade	Recommendation
A	At least one meta-analysis, systematic review of RCTs, or RCT rated as 1 <sup>++</sup> and directly applicable to the target population; or
	A body of evidence consisting principally of studies rated as 1 <sup>+</sup> , directly applicable to the target population, and demonstrating overall consistency of results
В	A body of evidence including studies rated as 2 <sup>++</sup> , directly applicable to the target population, and demonstrating overall consistency of results; or
C	Extrapolated evidence from studies rated as 1 <sup>++</sup> or 1 <sup>+</sup> A body of evidence including studies rated as 2 <sup>+</sup> , directly applicable to the target population and demonstrating overall consistency of results; or
D	Extrapolated evidence from studies rated as 2 <sup>++</sup> Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2 <sup>+</sup>
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group.