CLINICAL PRACTICE GUIDELINES

Hypertension

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1. Significance of high blood pressure

Blood Pressure (BP) levels are continuously related to the risk of cardiovascular disease (CVD). The definition of hypertension or raised BP is therefore arbitrary.

Even within the normotensive range, people with the lowest levels of BP have the lowest rates of CVD

Epidemiology

More than a quarter of the world adult population is already hypertensive and this number is projected to increase to 29%, 1.·56 billion, by 2025. Almost three quarters of the worldwide population with hypertension will be in developing countries. In 1990, 5.8% of deaths worldwide were attributed to high blood pressure and, by 2000, this had increased to 7.2%. By 2020, hypertension will be the most common risk factor for death and disability globally. In Sri Lanka, about 15 % of deaths are due to cardiovascular diseases and ranks the main cause of death. In addition, hypertensive heart disease accounts for approximately 10 % of cardiovascular deaths. Studies have shown that lowering the systolic blood pressure by 10–12mmHg and diastolic blood pressure by 5-6mmHg can reduce the relative risk of stroke by about 40% and coronary disease by about 15%.

In Sri Lanka, a recent survey in four provinces shows the prevalence of hypertension to be 18.8% in males and 19.3% in females. Furthermore, only 22% of diagnosed hypertensives in Sri Lanka are adequately controlled and the percentage of patients who are adequately evaluated for risk factors for cardiovascular disease and target organ damage is only 6 to 15 %.

2. Definition of high blood pressure

Blood Pressure (BP) is characterised by large spontaneous variations. Hence, the diagnosis of hypertension should be based on multiple BP measurements taken on several separate occasions.

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

C Grade hypertension according to systolic and diastolic BP levels.

Table 1: New definition and classification of blood pressure levels (mmHg).

Category	Systolic	Diastolic
Normal	<120	<80
Pre-hypertension	120 - 139	80 - 89
Grade 1 hypertension (mild).	140 - 159	90 - 99
Grade 2 hypertension (moderate)	160 - 179	100 - 109
Grade 3 hypertension (severe)	≥180	≥110
Isolated systolic hypertension	≥140	<90

When the systolic and diastolic BP fall into different categories, the higher category should apply. For example, a BP of 162/92 mmHg should be Grade 2 Hypertension.

In some patients, office (or clinic) BP is persistently elevated whereas daytime BP outside the clinic environment is normal. There is continuing debate as to whether "isolated" office hypertension ("white coat hypertension") is an innocent phenomenon or whether it carries an increased burden of cardiovascular risk.

Prehypertension

Prehypertension is not a disease category. It is a designation chosen to identify individuals at high risk of developing hypertension and cardiovascular complications so that both patients and clinicians are alerted to this risk and encouraged to intervene and prevent or delay the disease from developing. In the National Prevalence Survey, more men than women had prehypertension. One quarter of the males and a fifth of the females are in the prehypertension range. Based on these estimates, there would be 630,000 male prehypertensives and 590,000 female prehypertensives in the age range 30-65 years.

For prehypertensives with diabetes or kidney disease, drug therapy is indicated if a trial of lifestyle modification fails to reduce their blood pressure to 130/80 mmHg or less.

3. Evaluation of high blood pressure

3.1 Aims of evaluation

The clinical and laboratory evaluation of the hypertensive patient should be conducted with the following four aims:

- to confirm the presence of chronic elevation of BP and determine the BP level
- to exclude or identify secondary causes of hypertension
- to determine the presence of target organ damage and quantify its extent
- to search for other cardiovascular risk factors and clinical conditions that may influence the prognosis and treatment

3.2 Clinical blood pressure measurement

BP should be measured several times on several occasions with the patient in a supine or sitting position using a mercury sphygmomanometer or other non-invasive device. Ensure that non-mercury devices are accurate by periodic calibration with values obtained simultaneously from a mercury sphygmomanometer.

C **Use the following procedures when recording BP**

- Allow the patient to sit or lie down for several minutes before measuring the BP.
- The patient should refrain from smoking or ingesting caffeine during the 30 minutes preceding the measurement
- Use a cuff with a bladder that is 12-13 cm x 35 cm in size, with a larger bladder for fat arms.
  The bladder within the cuff should encircle at least 80% of the arm.
- Place the cuff at heart level, whatever the position of the patient.
- Use the disappearance of Phase V Korotkoff sounds to measure the diastolic BP
- Measure the BP in both arms at the first visit and take 2 or more readings separated by 1 minute. Average these 2 values. If the first 2 readings differ by more than 5 mmHg,

additional readings should be obtained and averaged
- Measure the BP in both the standing and supine position for elderly subjects and diabetic patients
- In pregnant women, supine blood pressure should be measured in the left lateral position.

Table 2 Recommendations for follow-up based on initial blood pressure measurements for adults without acute end organ damage

Initial blood pressure	Follow up recommended
Normal	Re-check in 2 years*
Pre-hypertension	Re-check in 1 year#
Grade 1	Confirm within 2 months‡
Grade 2	Evaluate within one month
Grade 3	Evaluate and treat immediately or within one week depending on clinical situation and complications

** If systolic and diastolic categories are different, follow recommendations for shorter time follow-up (e.g., 160/86 mmHg should be evaluated or referred to source of care within 1 month).#Modify the scheduling of follow-up according to reliable information about past BP measurements, other cardiovascular risk factors, or target organ disease.*

3.3 Home and ambulatory BP measurement

BP values obtained by home measurement or by ambulatory monitoring are usually several mmHg lower than those obtained by office measurement.

C **Persons with an average BP of more than 135/85 mmHg measured at home may be considered to be hypertensive.**

Reliable information about the long-term prognostic value of ambulatory and home BP monitoring is awaited.

Situations in which ambulatory BP monitoring should be considered:
- Unusual variability of BP over the same or different visits
- Office ("white coat") hypertension in subjects with low cardiovascular risk
- Symptoms suggesting hypotensive episodes
- Hypertension apparently resistant to drug treatment

3.4 Clinical evaluation

C **Routine clinical evaluation includes:**

- clinical and family history
- full standard physical examination
- laboratory investigations
- electrocardiography (ECG)

Routine investigations recommended on all patients with persistent hypertension with no clinical evidence of secondary hypertension

Table 3

	Secondary causes	TOD	Risk Factor
Urinanalysis(ailbumin, glucose,deposits)	✓	✓	
Serum creatinine or blood urea	✓	✓	
Serum electrolytes	✓		
Fasting blood glucose	✓		✓
Lipid profile(Serum total cholesterol,HDL cholesterol and triglyceride)			✓
12 lead electrocardiogram		✓	✓

Table 7: Additional and special investigations

Further investigations should be guided by the history, examination and results of routine investigations. These investigations aim to seek secondary causes of hypertension or to obtain results that may significantly influence the management of the patient. Such investigations include tests for creatinine clearance, microalbuminuria, 24-hour urine protein and catecholamines, blood uric acid, calcium, thyroid function indices, plasma renin and aldosterone.

A limited echocardiography may be performed to determine the presence of left ventricular hypertrophy and vascular ultrasonography to detect aortic, carotid and peripheral arterial disease.

Table 4

Additional investigations for target organ disease
· Chest radiography
· Creatinine clearance · Echocardiography · Ultrasound scan of abdomen · Serum uric acid · 24 hour urinary proteins · Microalbuminuria
· Vascular-ultrasonography
Investigations for secondary hypertension
· Investigations for hypercortisism · Plasma renin levels and aldosterone levels · Catecholamines and metabolites · Thyroid function tests · Intravenous urography · Aortography · Renal angiography · DTPA renal scan · Computer assisted tomography of adrenals
These tests should be done in specific instances and further tests can be done depending on the facilities available and based on individual needs.

When to suspect secondary hypertension.

- <20 years and > 50 years
- Clues from history and examination
- Abnormal laboratory investigations
  hypokalaemia
  urine deposits
- Difficult to control blood pressure
- Sudden loss of control of blood pressure
- Sudden onset of hypertension

4. Prognostic factors of hypertension and risk assessment

B Decisions about the management of patients with hypertension should not be made based on their BP levels alone, but also on the presence of other risk factors, target organ damage, concomitant disease such as diabetes and cardiovascular or renal disease, as well as other aspects of the patient's individual and medical circumstances

Risk assessment

Besides the level of BP, it is also important to assess the overall cardiovascular risk of a patient prior to definitive therapy in order to optimize risk-benefit ratio. Adding the numbers of traditional, documented risk factors in a person is one such way. The use of well tested and accepted risk tables, charts or formulae to estimate a patient's absolute risk is encouraged. The risk factors included in current scoring systems are drawn from those used in the original Framingham score. As these may not be applicable to all the populations, WHO has recently developed cardiovascular risk prediction charts for each WHO subregion (and country), which will be made available in the near future. These charts are intended to allow the introduction of the total risk stratification approach for management of cardiovascular disease, particularly where cohort data and resources are not readily available for development of population-specific charts. The charts have been generated from the best available data, using a modelling approach, with age, sex, smoking, blood pressure, blood cholesterol, and presence of diabetes as clinical entry points for overall management of cardiovascular risk.

When is grading cardiovascular risk using charts unnecessary for making treatment decisions?

Some individuals are at very high cardiovascular risk because they have already experienced a cardiovascular event, or have very high levels of individual risk factors. Risk stratification is not necessary for making treatment decisions for these individuals as they belong to the high risk category (individuals with Target organ Damage [TOD] and/or Associate Clinical Conditions [ACC]; all of them need intensive lifestyle interventions and appropriate drug therapy. Risk prediction charts may tend to underestimate cardiovascular risk in such individuals, who include the following:

- patients with established angina pectoris, coronary heart disease, myocardial infarction, transient ischaemic attacks, stroke, or peripheral vascular disease, or who have had coronary revascularization or carotid endarterectomy;

- those with left ventricular hypertrophy (shown on electrocardiograph) or hypertensive retinopathy (grade III or IV);

- individuals without established CVD who have a total cholesterol ≥ 8 mmol/l (320 mg/dl) or low-density lipoprotein (LDL) cholesterol ≥ 6 mmol/l (240 mg/dl) or TC/HDL-C ratio >8;

- individuals without established CVD who have persistent raised blood pressure (>160–170/100–105 mmHg) (38–41, 43, 83);

- patients with type 1 or 2 diabetes, with overt nephropathy or other significant renal disease;

- patients with known renal failure or renal impairment.

A family history of premature vascular disease by itself does not place a person in the very high risk category, unless they also have a familial dyslipidaemia, in which case the lipid levels will be elevated.

Table 5

BLOOD PRESSURE (mmHg)	Other Risk Factors & Disease History		
Level	I. no other risk factors	II. 1-2 risk factors	III. 3 or more risk factors or TOD or diabetes or ACC
Grade 1 SBP 140-159 or DBP 90-99	LOW RISK	MED RISK	HIGH RISK
Grade 2 SBP 160-179 or DBP 100-109	MED RISK	MED RISK	HIGH RISK
Grade 3 SBP 180 or DBP 110	HIGH RISK	HIGH RISK	HIGH RISK

Risk strata (typical 10 year risk of stroke or myocardial infarction): Low Risk = less than 15%; Medium Risk = about 15-20% risk ; High Risk = over 20%

1. TOD – Target Organ Damage (Table 6)
2. ACC – Associated Clinical Conditions, including clinical cardiovascular disease or renal disease (Table 6)

Table 6

Risk Factors For Cardiovascular Diseases	Target Organ Damage(TOD)	Associated Clinical Conditions(ACC)
1. Levels of systolic and diastolic blood pressure (Grades 1-3) 2. Men >55 years 3. Women >65 years 4. Smoking 5. Total cholesterol >6.1 mmol/L (240 mg/dl)	1. Left ventricular hypertrophy · electrocardiogram, · echocardiogram	1.Cerebrovascular disease ·Ischaemic stroke, ·haemorrhage, ·TIA 2.Heart disease ·MI, ·angina, ·coronary revascularization, ·CHF
6. LDL cholesterol > 4.0 mmol/L (160 mg/dl) 7. HDL cholesterol M < 1.0, F < 1.2 mmol/L (<40, <45 mg/dL)	2. Microalbuminuria (20-30 mg / day) 3. Ultrasound or radiological evidence of atherosclerotic plaque (aorta,carotid, coronary, iliac, and femoral arteries)	3.Renal disease ·Plasma creatinine F>1.4, M>1.5 mg/dL ·Albuminuria >300 mg/day
8. Obesity, inactivity 9. History of cardiovascular disease in first degree relatives < 50 years	4. Hypertensive retinopathy grade III or IV	4.Peripheral vascular disease

5. Management of hypertension

5.1 Overall strategy

A Assess the overall risk profile as a guide to management.

Refer to Table (page) to assess if the patient is at low, medium or high risk.

- **If high risk**

A Institute immediate drug treatment for hypertension and other risk factors and conditions present

- **If medium risk**

A Monitor BP and other risk factors for several weeks and obtain further information before deciding whether to institute drug treatment.

- **If low risk**

A Observe the patient over a significant period of time before deciding whether to institute drug treatment.

5.2 Lifestyle modifications/Non-pharmacological therapy

B Lifestyle modifications and non-pharmacological measures should be instituted wherever appropriate in all hypertensive patients, including those who require drug treatment or those within the high normal BP range.

These modifications include:

- Smoking cessation
- Weight reduction
- Moderation of alcohol consumption
- Reduction of intake of salt
- Reduction of intake of cholesterol and saturated fats
- Maintenance of adequate intake of dietary potassium
- Increased physical activity

5.3 Treatment plan according to the risk

Table 7

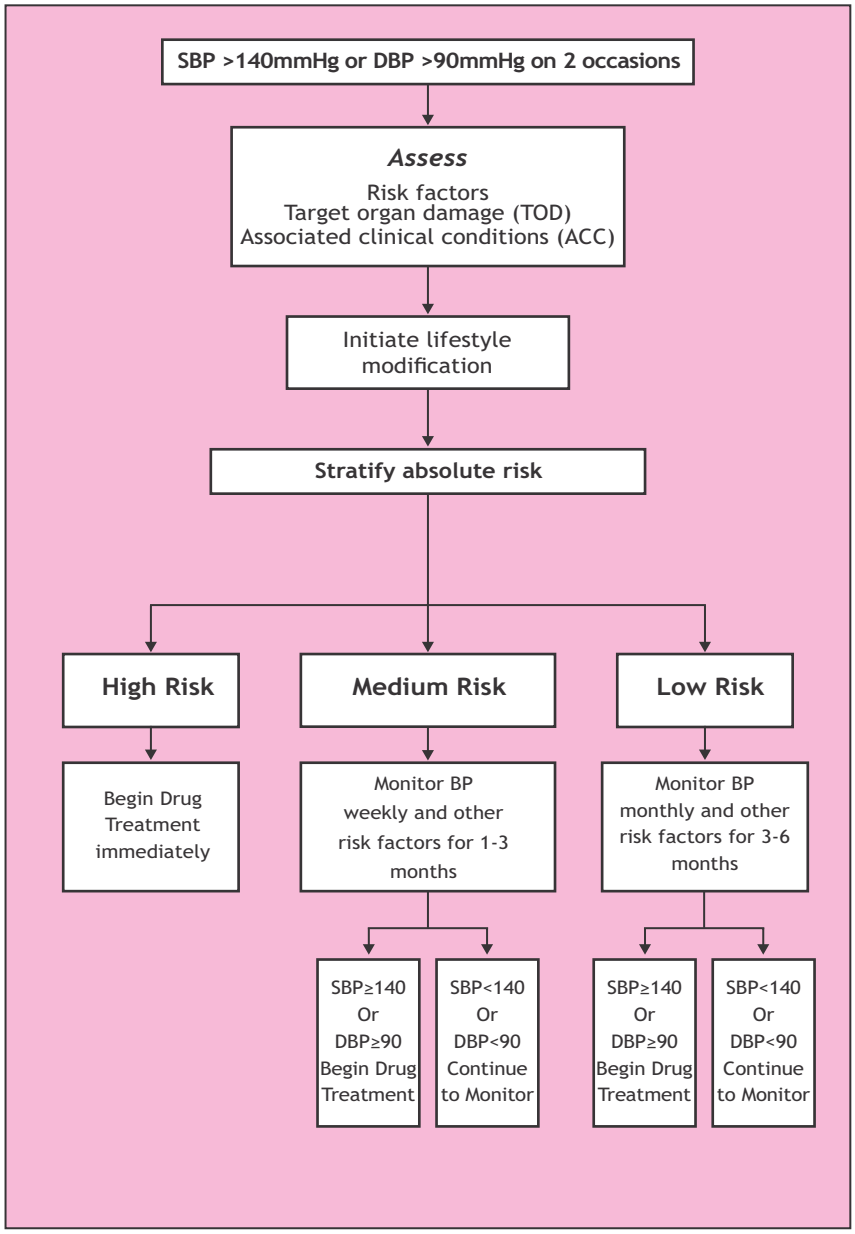
BLOOD PRESSURE (mmHg)	Other Risk Factors & Disease History		
Level	I. no other risk factors	II. 1-2 risk factors	III. 3 or more risk factors or TOD or diabetes or ACC
Grade1 SBP140-159 or DBP 90-99	**LOW RISK** Life style modifications 3-6 months	**MED RISK** Life style modifications 1-3 months	**HIGH RISK** Life style modifications Immediate drug therapy
Grade 2 SBP 160-179 or DBP 100-109	**MED RISK** Life style modifications 1-3 months	**MED RISK** Life style modifications 1-3 months	**HIGH RISK** Life style modifications Immediate drug therapy
Grade 3 SBP 180 or DBP 110	**HIGH RISK** Life style modifications Immediate drug therapy	**HIGH RISK** Life style modifications Immediate drug therapy	**HIGH RISK** Life style modifications Immediate drug therapy

Risk strata (typical 10 year risk of stroke or myocardial infarction):

Low Risk = less than 15%;
Medium Risk = about 15-20% risk ;
High Risk = over 20%

1. **TOD** - Target Organ Damage (Table 6)
2. **ACC** - Associated Clinical Conditions, including clinical cardiovascular disease or renal disease (Table 6)

Based on this risk stratification, recommendations on initiation of treatment are outlined in the algorithm in Figure 1



6. Treatment goals and follow up

6.1 Treatment goals

The primary treatment goal of a patient with hypertension is to achieve the maximum reduction in the total risk of CVD. This requires identification and treatment of all reversible risk factors, such as smoking, raised cholesterol and diabetes, management of associated clinical conditions and treatment of the raised BP per se.

Since the relationship between cardiovascular risk and BP is a continuous one, the goal of antihypertensive therapy should be to reduce BP to <140/90 mmHg.

Effective blood pressure control is especially important for patients with diabetes mellitus as well as for those with chronic renal disease.

A **Low and Medium risk** - < 140/90 mmHg.

There is no clinical trial evidence for thresholds < 160/90 mmHg but observational data support the lowering of the systolic threshold < 140/90 mmHg.

A **High risk** - <130/80 mmHg

There is evidence for lowering both systolic & diastolic thresholds significantly below 160 / 90 mmHg: <130/80 mmHg

In Grade I hypertension, it would seem desirable in young patients to achieve a systolic blood pressure of at least 120 -130 mm Hg and a diastolic blood pressure of 80 mmHg. In elderly patients it would seem desirable to lower blood pressure to below 140 mmHg for systolic blood pressure and 90 mm Hg for diastolic blood pressure, while in patients with isolated systolic hypertension the goal should be systolic blood pressure of at least 140 mm Hg if this is tolerated. However in the elderly the blood pressure should be reduced gradually.

A In elderly patients, the target BP should be at least <140/90 mmHg, provided no orthostatic hypotension occurs.

6.2 Follow-up

Follow-up during evaluation and stabilization of treatment should be sufficiently frequent to monitor BP and other risk factors.

Patients with the following problems should be referred to a hypertension specialist or clinic:

- Emergency or urgent treatment indicated e.g. malignant hypertension, hypertensive cardiac failure or other impending complications
- Hypertension difficult to manage e.g. unusually labile BP, hypertension refractory to multiple drug regimens
- Secondary hypertension i.e. hypertension due to an underlying cause, such as hyperaldosteronism
- Hypertension in special circumstances e.g. pregnancy, young children.

6.3 Patient education

Good communication between the physician and the patient lies at the core of the successful management of hypertension. Since the treatment of hypertension is for life, it is essential that the physician establishes a good professional relationship with the patient, provides the patient with information (both verbal and written forms) and answers any questions the patient may have.

Adequate information on the following is essential for satisfactory life-long control of hypertension:

BP and hypertension,
risks involved and prognosis,
target BP level,
expected benefits as well as the risks and side effects of treatment, and lifestyle modification.

B Lifestyle modifications should be applied to all patients regardless of whether the patient is on medical treatment. Non-pharmacological measures may sometimes be sufficiently effective to reduce the need for antihypertensive drugs. These include smoking cessation, weight reduction, moderation of alcohol consumption, increased physical activity, reduction of salt intake and maintenance of adequate intake of dietary potassium.

7. Principles of drug treatment

Recent studies have shown that the most important issue in the treatment of hypertension is achieving goal BP levels expeditiously.

There is a general agreement on the principles governing the use of antihypertensive drugs to lower BP that is independent of the choice of any particular drug. These principles include:

Use low doses of drugs to initiate therapy, beginning with the lowest available dose of the particular drug, with the aim of reducing adverse effects. If there is a significant response to a low dose of a single drug but the BP is still above target level, we could either increase the dose of the same drug, provided that this is well tolerated, or add a low dose of a second drug from a different class.

There are advantages of adding a low dose of a second drug rather than increasing the dose of the original drug. This allows both the first and the second drug to be used in the low dose range that is more likely to be free of

A Use appropriate drug combinations to achieve target BP levels if this cannot be achieved by one single antihypertensive agent.

A Use of appropriate drug combinations enables BP lowering efficacy to be maximized while minimizing side effects. In most patients, appropriate combination therapy produces BP reductions that are twice as great as those obtained with monotherapy (e.g. reductions in BP increasing from 12 to 22 mmHg systolic BP and from 7 to 14 mmHg diastolic BP in patients with an initial BP of 160/100 mmHg).

A In patients whose pretreatment BP is moderately elevated (e.g.BP ≥160/100 mmHg) or especially if it is severely elevated (e.g. BP ≥ 180/110 mmHg), it may be appropriate to begin with combination therapy, because many such patients will require 2 or even 3 drugs for adequate BP control.

- Change to a different drug class altogether if there is very little response or poor tolerability to the first drug, before prescribing a higher dose of the first drug or adding a second one.
- The advantages of long-acting drugs include improvement in adherence to therapy and minimization of BP variability as a consequence of smoother and more consistent BP control. This may provide greater protection against the risk of major cardiovascular events and the development of target organ damage.

C Use long-acting drugs providing 24-hour efficacy on a once daily basis.

8. Choice of antihypertensive drugs and cost effectiveness

8.1 Choice of antihypertensive drugs

There are five main classes of antihypertensive agents available. They are:

(a) diuretics (D)
(b) beta-blockers (BB)
(c) calcium channel blockers (CCB)
(d) angiotensin converting enzyme inhibitors (ACEI)
(e) angiotensin II receptor blockers (ARB)

There are other classes of drugs which are uncommonly used, such as the alpha-blockers, hydralazine and methyldopa.

The effectiveness of drug therapy for hypertension in reducing cardiovascular complications and death has been shown in a number of randomized controlled studies. All five major classes of drugs have been shown to be effective in lowering blood pressure and reducing cardiovascular outcome.

More recently concerns have been expressed on the efficacy of beta-blockers and the adverse effects of beta-blockers and diuretics. For nearly three decades, beta-blockers have been recommended as an acceptable first-line therapy for uncomplicated hypertension (JNC 6, JNC 7, WHO/ISH Guidelines, ESH/ESC Guidelines, BHS Guidelines). These recommendations were based partially on results from trials that compared these agents with placebo and partially on their proven effectiveness in preventing recurrent MI. However, a recent meta-analysis and the Guideline Development Group of the recently updated NICE clinical guideline on management of hypertension in adults in primary care noted that in head to-head trials, beta-blockers were usually less effective than the comparator drug at reducing major cardiovascular events, in particular stroke. Therefore, in the absence of other compelling indications for beta-blockade (for example, angina), beta-blockers should not be a preferred initial treatment for hypertension. However, beta-blockers

may be considered in younger people, particularly: those with an intolerance or contraindication to ACE inhibitors and angiotensin-II receptor antagonists or women of child-bearing potential or patients with evidence of increased sympathetic drive. Although BBs can cause adverse effects on glucose homeostasis in diabetics, including worsening of insulin sensitivity and potential masking of the epinephrine-mediated symptoms of hypoglycemia, these problems are usually easily managed and are not absolute contraindications for BB use.

JNC7 and a recent clinical trial (ALLHAT) have supported the use of thiazide diuretics as the preferred initial pharmacological treatment for hypertension. Thiazide-type diuretics are beneficial in diabetics, either alone or as part of a combined regimen. Of potential concern is the tendency for thiazide-type diuretics to worsen hyperglycemia, but this effect tends to be small and does not produce more cardiovascular events compared to the other drug classes.

However, there is an increased incidence of new onset diabetes among those patients receiving thiazide diuretics and beta-blockers. Therefore, the combination of a beta-blocker with a thiazide-type diuretic is best avoided. This recommendation is of particular importance to Sri Lanka as nearly 14% have diabetes and a similar proportion have impaired fasting glucose.

A Consider any compelling indications and contraindications for an antihypertensive agent when prescribing its use. (Table 8)

Table 8

		Contraindications	
Class	Conditions favouring the use	Compelling	Possible
Diuretics (thiazides)	Congestive heart failure; elderly hypertensives; isolated systolic hypertension; hypertensives of African origin	Gout	Pregnancy
Diuretics (loop)	Renal insufficiency; congestive heart failure		
Diuretics (anti-aldosterone)	Congestive heart failure; post-myocardial infarction	Renal failure; hyperkalaemia	
β-Blockers	Angina pectoris; post-myocardial infarction; congestive heart failure (up-titration); pregnancy; tachyarrhythmias	Asthma; chronic obstructive pulmonary disease; A-V block (grade 2 or 3)	Peripheral vascular disease; glucose intolerance; athletes and physically active patients
Calcium antagonists (dihydropyridines)	Elderly patients; isolated systolic hypertension; angina pectoris; peripheral vascular disease; carotid atherosclerosis; pregnancy		Tachyarrhythmias congestive heart failure
Calcium antagonists (verapamil, diltiazem)	Angina pectoris; carotid atherosclerosis; supraventricular tachycardia	A-V block (grade 2 or 3); congestive heart failure	
Angiotensin-converting enzyme (ACE) inhibitors	Congestive heart failure; LV dysfunction; post-myocardial infarction; non-diabetic nephropathy; type 1 diabetic nephropathy; proteinuria	Pregnancy; hyperkalaemia; bilateral renal artery stenosis	
Angiotensin II receptor antagonists (AT_1-blockers)	Type 2 diabetic nephropathy; diabetic microalbuminuria; proteinuria; left ventricular hypertrophy; ACE-inhibitor cough	Pregnancy; hyperkalaemia; bilateral renal artery stenosis	
α-Blockers	Prostatic hyperplasia (BPH); hyperlipidaemia	Orthostatic hypotension	Congestive heart failure

A Most guidelines recommend thiazide type diuretic as a first-line choice and a CCB as an alternative.

A In hypertensive patients aged 55 or over, the first choice for initial therapy should be either a thiazide-type diuretic or a calcium-channel blocker.

C In hypertensive patients younger than 55, the first choice for initial therapy could be an ACE inhibitor**.

B If initial therapy was with a calcium-channel blocker or a thiazide-type diuretic and a second drug is required, add an ACE inhibitor*. If initial therapy was with an ACE inhibitor*, add a calcium-channel blocker or a thiazide-type diuretic.

B If treatment with three drugs is required, the combination of ACE inhibitor**, calciumchannel blocker and thiazide-type diuretic should be used.

C If blood pressure remains uncontrolled on adequate doses of three drugs, consider adding a fourth and/or seeking expert advice.

C If a fourth drug is required, one of the following should be considered:

- a higher dose of a thiazide-type diuretic or the addition of another diuretic (careful monitoring is recommended) or
- beta-blockers or
- selective alpha-blockers.

C If blood pressure remains uncontrolled on adequate doses of four drugs and expert advice has not yet been obtained, this should now be sought.

B Beta-blockers are not a preferred initial therapy for hypertension. However, beta-blockers may be considered in younger people, particularly:

- those with an intolerance or contraindication to ACE inhibitors and angiotensin-II receptor antagonists or
- women of child-bearing potential or
- patients with evidence of increased sympathetic drive.

C In these circumstances, if therapy is initiated with a beta-blocker and a second drug is required, add a calcium-channel blocker rather than a thiazide-type diuretic to reduce the patient's risk of developing diabetes.

C In patients whose blood pressure is not controlled (ie over 140/90 mmHg) despite a treatment regimen including a beta-blocker, treatment should be revised.

C In patients whose blood pressure is well-controlled (ie 140/90 mmHg or lower) with a regimen which includes a beta-blocker, long-term management should be considered as part of their routine review. In these patients, there is no absolute need to replace the beta-blocker with an alternative agent.

C When a beta-blocker is withdrawn, the dose should be stepped down gradually. Beta-blockers should not be withdrawn in patients with compelling indications for beta-blockade, for example those who have symptomatic angina or who have had a myocardial infarction.

C Provide appropriate guidance and materials about the benefits of drugs and the unwanted side effects sometimes experienced in order to help patients make informed choices.

A Offer patients with isolated systolic hypertension (systolic BP >160 mmHg) the same treatment as patients with both raised systolic and diastolic blood pressure.

A Offer patients over 80 years of age the same treatment as other patients over 55, taking account of any comorbidity and their existing burden of drug use.

A Where possible, recommend treatment with drugs taken only once a day.

B Prescribe non-proprietary drugs where these are appropriate and minimize cost. Generic formulations usually cost less than nongeneric newer drugs and are acceptable if they meet prescribed standards of quality.
Some combination preparations may also cost less than the total cost of their separate components.
Differences in cost and dosing frequencies among drugs in the same class should also be taken into consideration.
The choice of antihypertensive drug should be tailored to the individual patient, taking the following factors into consideration, in addition to risk profile and cost:

- Side effects
- Drug interactions
- Patient preference

8.2 Effective drug combinations

A Effective drug combinations to treat hypertension are:

- Diuretic and angiotensin converting enzyme (ACE) inhibitor or angiotensin II receptor blocker
- Diuretic and calcium channel blocker (non dihydropridines)
- Calcium channel blocker (dihydropyridines only) and beta-blocker
- Calcium channel blocker and ACE inhibitor or angiotensin II receptor blocker

The combination of beta-blocker and ACE inhibitor or angiotensin II receptor blocker has not been shown to have synergistic effects.

A Although effective for lowering BP, the combination of a diuretic and a beta-blocker may increase the risk of developing diabetes mellitus. Therefore, it should be used with caution in patients who already have risk factors for diabetes mellitus, such as obesity or the metabolic syndrome.

Table 9

Class	Drug	Usual dose range In mg/day	Usual daily frequency
Thiazide diuretics	chlorothiazide hydrochlorothiazide indapamide metolazone	125 -500 12.5-50 1.25-2.5 0.5-1.0	1-2 1 1 1
Loop diuretics	bumetanide frusemide	0.5-2 20-80	2 2
Potassium-sparing diuretics	amiloride triamterene	5-10 50-100	1-2 1-2
Aldosterone receptor blockers	spironolactone	25-50	1
Beta-blockers	atenolol bisoprolol metoprolol metoprolol extended release propranolol	25-100 2.5-10 50-100 50-100 40-160	1 1 1-2 1 2
Combined alpha- and Beta-blockers	carvedilol labetalol	12.5-50 200-800	2 2
ACE inhibitors	captopril enalapril fosinopril lisinopril perindopril ramipril trandolapril	25-100 5-40 10-40 10-40 4-8 2.5-20 1-4	2 1-2 1 1 1 1 1
Angiotensin II antagonists	candesartan irbesartan losartan valsartan	8-32 150-300 25-100 80-320	1 1 1-2 1-2
Calcium Channel Blockers—nondihydropyridines	diltiazem extended release diltiazem immediate release verapamil immediate release	180-420 180-360 80-320	1 2 2
Calcium Channel Blockers—dihydropyridines	amlodipine felodipinen ifedipine long-acting	2.5-10 2.5-20 30-60	1 1 1
Alpha-1 blockers	doxazosin prazosin terazosin	1-16 2-20 1-20	1 2-3 1-2
Central alpha-2 agonists and other centrally acting drugs	clonidine methyldopa reserpine	0.1-0.8 250-1,000 0.1-0.25	2 2 1
Direct vasodilators	hydralazine minoxidil	25-100 2.5-80	2 1-2

8.3 Cholesterol lowering therapy

A Consider the use of other drugs that reduce cardiovascular risk, such as lipid lowering agents and antiplatelet agents, in patients with concomitant risk factors and increased cardiovascular risk.

In patients with high cholesterol, the benefits of cholesterol lowering therapy appear to be similar in those with or without high BP. Therefore, the use of cholesterol lowering therapy can be recommended for hypertensive patients who have elevated cholesterol levels, according to National Lipid Guidelines.

8.4 Antiplatelet therapy

A In patients with a history of CHD or cerebrovascular disease, there is evidence that aspirin and some other antiplatelet agents (ticlopidine, clopidogrel) can reduce cardiovascular risks. Antiplatelet therapy should also be considered in some patients in the high risk categories who have satisfactory blood pressure control (i.e. <140/<90 mmHg).

9. Quality indicators for hypertension management

The target BP treatment levels are
BP <140/<90 mmHg in all patients, except
BP <130/<80 mmHg in patients with diabetes or chronic renal disease

C Process indicators and recommended frequency

Table 10

Performance Parameter	**Recommended review frequency after stabilization of blood pressure
Risk level* -Low and medium risk -High risk	 6 monthly 3 monthly
Weight Fasting blood glucose Fasting lipid profile Serum electrolyte, urea and Creatinine Urinalysis	Annually or more frequently according to individual risk factor profile
Patient education* -Low and medium risk -High risk	At diagnosis and regular intervals according to risk level 6 monthly 3 monthly

* Goal blood pressure achieved.

It should be emphasized that the ultimate objective of treatment of hypertension is not to lower BP per se but to reduce overall morbidity and mortality risk, which is also influenced by other concomitant risk factors. The greater the risk profile, the more rigorous should the BP control be.

However, BP level attainable with treatment may also be influenced by medication side effects and other co-morbidities, such as cerebrovascular disease. Good clinical judgement should be exercised in every individual situation.

10. Treatment of hypertension in Type 2 diabetes

Hypertension is a common co-morbidity in people with disorders of glucose metabolism. Individuals with type 2 diabetes mellitus (which is more common than type 1 diabetes mellitus by about 20-fold) often have the metabolic syndrome of which hypertension is one of the defining features. Prevalence of hypertension in patients with type 2 diabetes increases further with the development of nephropathy. In patients with type 1 diabetes, hypertension is often associated with the onset of nephropathy. The presence of hypertension in individuals with diabetes is associated with higher rates of cardiovascular complications as well as microvascular complications (such as nephropathy and retinopathy). Intensive hypertension treatment has been shown to reduce adverse cardiovascular outcomes (similar to those without diabetes) as well as adverse microvascular outcomes.

The target for BP control in individuals with diabetes has been recommended by several guidelines to be 130/80 mmHg. The rationale for this target is the improvement in outcomes in clinical trials with more intensive BP lowering.

In addition, a systolic BP goal of even <130 mmHg should be considered in patients with urine total protein of >0.5g/24 hours but systolic BP levels of <110 mmHg should be avoided.

There is inadequate evidence for recommendation of any specific initial pharmacological agent in the treatment of hypertension in diabetic patients. In any case it has been shown in many recent clinical trials that multiple agents from different classes of antihypertensive agents are required to achieve target BP control. However in patients with diabetes and microalbuminuria as well as more advanced degrees of nephropathy, blockade of the renin-angiotensin-

aldosterone axis has been shown to retard progression of renal disease. In such patients with hypertension, there is reason to choose an agent which inhibits the renin-angiotensin-aldosterone axis such as an ACE inhibitor or an angiotensin receptor blocker as the initial agent.

A People with diabetes who are hypertensive should be treated to target BP of <130/<80 mmHg.

A There is inadequate evidence to recommend a specific initial antihypertensive agent for the treatment of hypertension in patients with diabetes. However, in those patients with incipient or overt nephropathy, the use of an agent, which inhibits the renin-angiotensin-aldosterone axis, should be considered.

11. Treatment of hypertension during pregnancy

Hypertension in pregnancy is usually defined by an absolute level of BP (e.g. ≥140/90 mmHg). Hypertension in pregnancy is typically classified as:

- Pre-existing chronic hypertension
- Preeclampsia-eclampsia
- Gestational hypertension
  Transient hypertension of pregnancy, if there is no preeclampsia at delivery, and BP becomes normal by 3 months post-partum Chronic hypertension if elevation of BP persists beyond 3 months post- partum
- Preeclampsia superimposed on chronic hypertension.

C BP levels of >160/100 mmHg should be lowered to protect the mother against the risk of stroke or to permit possible prolongation of the pregnancy and thereby improve fetal maturity. Opinion is divided on the need for drug treatment for BP readings below this level.

Chronic hypertension

Use of antihypertensive drugs in pregnant women with chronic hypertension varies greatly among centers. Some clinicians prefer to stop antihypertensive medications while maintaining close observation, including use of home BP monitoring.

Women with grade 1 hypertension are at low risk for cardiovascular complications during pregnancy and are candidates for lifestyle modification therapy only, as there is no evidence that pharmacologic treatment improves neonatal outcomes.

C However, for pregnant women with target organ damage or a prior requirement for multiple antihypertensive agents for BP control, antihypertensive medication should be continued as needed to control BP. In all cases, treatment should be re-instituted once BP reaches 160 mmHg systolic or 100 mmHg diastolic, in order to prevent increases in BP to very high levels during pregnancy.

C Aggressive treatment of severe chronic hypertension in the first trimester is critical, since fetal loss rates of 50 percent and significant maternal mortality have been reported in these patients.

Preeclampsia

Antihypertensive therapy should be prescribed only for maternal safety; it does not improve perinatal outcomes and may adversely affect uteroplacental blood flow. Selection of antihypertensive agents and route of administration depends on anticipated timing of delivery. If delivery is likely more than 48 hours away, oral methyldopa is preferred due to its safety record. Oral labetalol is an alternative, and other BBs and calcium antagonists are also acceptable. If delivery is imminent, parenteral agents are practical and effective. Antihypertensives are administered before induction of labor for persistent DBPs of 105–110 mmHg or higher, aiming for levels of 95–105 mmHg.

Drugs most widely used to lower BP **acutely** in pregnancy include:

labetalol , nifedipine , hydralazine

Drugs most widely used for chronic treatment of raised BP in pregnancy include:

methyldopa ,
beta-blockers, in particular labetalol, pindolol, acebutolol and oxprendol.
However, atenolol is associated with foetal growth retardation when used long- term throughout pregnancy.
prazosin, hydralazine, nifedipine and isradipine

B Drugs that should be **avoided** during pregnancy include: ACE inhibitors (associated with possible adverse foetal effects) and angiotensin receptor blockers, the effects of which may be similar to those of ACE inhibitors. Diuretics are also used infrequently due to concern about reduction of the already compromised plasma volume.

Lowering BP is only one of the aspects of the management of preeclampsia that ideally involves a multidisciplinary team approach, including an early and timely delivery.

B Antihypertensive medications considered compatible with breastfeeding include methyldopa, labetalol, propranolol, nifedipine, verapamil and hydralazine. Drugs which should be used with caution include atenolol, nadolol, sotalol and diltiazem (due to significant accumulation in breast milk).

12. Treatment of hypertension in the elderly

Elevated systolic hypertension is a common finding in the elderly and is termed isolated systolic hypertension. As age advances, arterial compliance decreases, and this results in a gradual rise in systolic pressure and a fall in diastolic pressure. A wide pulse pressure correlates well with increased cardiovascular and cerebro-vascular events as well as congestive heart failure.

Randomised trials have clearly shown the benefits of treating systolic hypertension across a wide age range.

A In general the treatment of hypertension in the elderly should follow the same general guidelines but drug therapy should be instituted gradually especially in the frail elderly. On initiating drug therapy the patients' associated clinical conditions should be taken into consideration.

B All 5 classes of drugs (diuretics, beta-blockers, calcium channel blockers, ACE inhibitors and angiotensin II receptor blockers) have been shown in trials to be efficacious and beneficial in the elderly. In isolated systolic hypertension, diuretics, calcium channel blockers, ACE inhibitors and angiotensin II receptor blockers, are all useful, and may be used. However, the first choice for initial therapy should be either a diuretic or a calcium channel blocker as they have been shown to be the most likely drugs to confer benefit as the first line treatment for most patients.

As in other patients, many elderly patients also require two or more anti-hypertensive drugs to achieve good BP control. Control of the diastolic pressure is difficult to regulate and the optimum range of the diastolic pressure needs further clarification. The current impression is that the diastolic pressure should not be allowed to fall below 60 mmHg especially in those with known coronary artery disease as this may increase the risk of coronary events.

Monitoring of BP in the elderly should include frequent measurements in the erect position to assess postural drop. Care should also be taken to avoid fluid depletion and electrolyte imbalance in the elderly.

13. Hypertensive crises

Emergencies and urgencies

Hypertensive crises are clinical circumstances that require rapid reduction of the blood pressure Different terms characterise these clinical situations. Hypertensive urgency, is referred to severe hypertension without any end-organ damage while hypertensive emergencies are referred to a sudden increase in systolic and diastolic associated with 'acute end-organ damage' (i.e. cardiovascular, renal, central nervous system) that requires immediate management. Situations that qualify as hypertensive emergencies are listed in **Table11**.

Patients with hypertensive urgencies can be generally managed without hospitalization. Those with hypertensive emergencies require hospitalization for immediate reduction of blood pressure (within 1 hour).

A persistent diastolic blood pressure >130mmHg is often associated with acute vascular damage. (The rapidity of the rise of blood pressure may be more important than the absolute level in producing the acute vascular damage). Therefore all patients with diastolic blood pressures >130mmHg should be treated with an aim of reducing the blood pressure within a few hours.

The term accelerated-malignant hypertension is used when the rise in blood pressure results in acute damage to retinal vessels. When only retinal haemorrhages and exudates are present, the term accelerated hypertension is used whereas when there is papilloedema, the term malignant hypertension is given. This separation is not useful as clinical features and survival rates are similar in the two groups.

Hypertensive encephalopathy is characterised by headache, irritability, and alterations in consciousness, focal neurological deficits and seizures with sudden and marked elevations in blood pressure.

Clinical characteristics of hypertensive crises

Symptoms and signs are usually dramatic. However, some patients are relatively asymptomatic despite markedly elevated pressures and extensive target organ damage.

The following features are generally seen.

1. **Blood pressure**; usually >130 mmHg diastolic
2. **Funduscopic findings**: Haemorrhages, exudates, papilloedema
3. **Neurological status**:Headache, confusion, somnolence, stupor, visual loss, focal deficits, seizures, coma
4. **Cardiac findings**: Prominent apical impulse, cardiac enlargement, congestive cardiac failure
5. **Renal**: Oliguria, azotaemia, protein and red cells in the urine
6. **Blood**: disseminated intravascular coagulation and microangiopathic haemolytic anaemia
7. **Gastrointestinal**: Nausea and vomiting
8. **Hypokalaemia** due to secondary hyperaldosteronism

Hypertensive emergencies are those rare situations that require immediate (within 1 hour) blood pressure reduction (not necessarily to normal ranges) to avoid the risk of serious morbidity (to prevent or limit target organ damage) such as hypertensive encephalopathy, intracranial hemorrhage, unstable angina pectoris, acute myocardial infarction, acute left ventricular failure with pulmonary edema, dissecting aortic aneurysm and eclampsia or death.

Parenteral drugs for hypertensive emergencies are listed in ***Table 12*** *.*

A Most hypertensive emergencies are treated initially with parenteral administration of an appropriate agent.

B The initial goal of therapy in hypertensive emergencies is to reduce mean arterial blood pressure by no more than 25 percent (within minutes to 2 hours), then toward 160/100 mmHg within 2 to 6 hours, avoiding excessive falls in pressure that may precipitate renal, cerebral, or coronary ischaemia.

Although sublingual administration of fast-acting nifedipine has been widely used for this purpose, several serious adverse effects have been reported with its use and the inability to control the rate or degree of fall in blood pressure makes this agent unacceptable. **Hypertensive urgencies** are those situations in which it is desirable to reduce blood pressure within a few hours. Examples include upper levels of Grade 3 hypertension, hypertension with optic disc edema, progressive target organ complications, and severe peri-operative hypertension. Elevated blood pressure alone, in the absence of symptoms or new or progressive target organ damage, rarely requires emergency therapy.

B Hypertensive emergencies can be managed with oral doses of drugs with relatively fast onset of action. A partial reduction of blood pressure to relieve the symptoms is the goal. The choices include loop diuretics, beta-blockers, ACE inhibitors, alpha 2 - agonists, or calcium channel blocker.

The routine use of sublingual nifedipine whenever blood pressure rises beyond a predetermined level in post-operative and indoor patients is not appropriate. Rather the proximate causes of elevated blood pressure, such as pain or a distended urinary bladder, should be addressed.

B 180/120 mmHg, one of the previously mentioned oral Blood pressure should be monitored over 15-30 minute intervals; if it remains greater than agents may be given. If such high levels of blood pressure are frequent, adequate doses of long-acting agents should be provided.

Table 11

Hypertensive emergencies
***Accelerated-malignant hypertension**
***Cerebrovascular**
Hypertensive encephalopathy
Intracranial haemorrhage
Subarachnoid haemorrhage
***Cardiac**
Acute aortic dissection
Acute left ventricular failure
Acute coronary syndromes
After coronary bypass surgery
***Renal**
Acute glomerulonephritis
Renal crises from collagen vascular diseases
Severe hypertension following renal transplantation
***Excessive circulating catecholamines**
Pheochromocytoma crisis
Food or drug interactions with MAO inhibitors
Sympathomimetic drug use (cocaine)
Rebound hypertension following sudden cessation of antihypertensive drugs
***Eclampsia**
***Surgical**
Severe hypertension in patients requiring immediate surgery
Postoperative hypertension
Postoperative bleeding from vascular suture lines
***Severe body burns**
***Severe epistaxis**

Table 12
PARENTERAL DRUGS FOR TREATMENT OF HYPERTENSIVE EMERGENCIES

Drug	Dose	Onset of Action	Duration of action	Adverse Effects	Special Indications
Vasodilators					
Glyceryl trinitrate	5-100mcg /min as IV infusion	2-5 min	3-5 min	Headache, vomiting, methaemoglobinaemia, tolerance with prolonged use	Coronary ischaemia:
Sodium nitroprusside	0.2510mcg kg/min as IV infusions (max. dose for 10mins only)	Immediate	1-2 min	Nausea, Vomiting, muscle twitching, sweating, thyocyanate and cyanide intoxication	Most hypertensive emergencies, caution with increased intracranial pressure and azotaemia
Hydralazine hydrochloride	10-20mg IV 10-50mg IM	10-20 min 20-30 min	3-8 h	Tachycardia, flushing, headache, vomiting, aggravation of angina	Eclampsia
Adrenergic inhibitors					
Labetalol hydrochloride	20-80mg IV bolus every 10min 0.5-2.0 mg/min IV infusion	5-10 min	3-6 h	Vomiting, scalp tingling, burning in throat, dizziness, nausea, heart block, orthostatic hypotension	Most hypertensive emergencies except acute heart failure
Esmolol	250-500mcg /kg/min for 1 min, then 50-100 mcg/kg/min for 4 min; may repeat sequence	1-2 min	10-20 min	Hypotension, nausea	Aortic dissection, perioperative
Phentolamine	5-15mg IV	1-2 min	3-10 min	Tachycardia, flushing, headache	Catecholamine excess

14. Treatment of hypertension in stroke

Stroke is a heterogeneous clinical syndrome characterized by rapidly developing clinical signs of focal or global disturbance in the cerebral function, with the deficit lasting 24 hrs or more or resulting in death, with no apparent cause other than of vascular origin.

Strokes are classified according to the vascular pathology in to

1. ischaemic stroke (cerebral infarction)
2. intracerebral haemorrhage.
3. subarachnoid haemorrhage.

Hypertension is an important risk factor in each of these. Management of hypertension is important in relation to stroke in

1. primary prevention of stroke
2. the acute phase of the stroke
3. secondary prevention of stroke

Blood pressure is the most consistent and powerful predictor of stroke. A strong linear relationship without a threshold is seen between blood pressure and stroke mortality starting at systolic blood pressure 115 mmHg and diastolic 75 mmHg between the ages 50-89. At ages 40 to 69 years, each difference in blood pressure of 20 mmHg systolic or 10 mmHg diastolic was associated with a >2-fold difference in stroke mortality. More recently, the Asian Pacific Cohort Studies Collaboration reported that in both sexes systolic blood pressure tended to be more predictive than diastolic blood pressure in all age groups with the exception of men less than 50 years.

Primary prevention of stroke

A 5-6 mmHg reduction in DBP, accompanied by a two-fold greater reduction in SBP, confers a 38% reduction in the incidence of stroke. Significant benefits are seen for younger and older patients and for patients with mild, moderate and severe hypertension.

A No specific agent has been proven to be clearly superior to all others for stroke protection but beta-blockers are inferior to other classes.

Secondary prevention of stroke

A metanalysis of seven trials of secondary prevention of stroke showed a 24% reduction of recurrent stroke and 21% reduction of vascular events (44, 45) However, different classes of drugs produced different effects with ACEI reducing myocardial infraction but not stroke, diuretics reducing stroke but not myocardial infarction and beta-adrenergic blockers reducing neither.

Combination of two drugs was most effective in reducing all the end points. Lowering of blood pressure by an effective combination of drugs is the best way of reducing the risk of subsequent stroke. However, a substantial proportion of stroke patients blood pressure remains poorly controlled, partly due the use of a single drug.

A A combination of a thiazide type diuretic and an ACE inhibitor should be given to all patients following a stroke for secondary prevention. This combination is recommended for normotensive patients as well based on the PROGRESS trial.

Hypertension in the acute phase of the stroke

A transient rise in blood pressure is common after a stroke and this usually resolves spontaneously by 7-10 days. Antihypertensive therapy immediately after cerebral infarction or primary intracerebral haemorrhage may optimize blood flow in to the area but on the other hand a precipitous fall in the blood pressure may jeopardize perfusion.

C There still are no large clinical studies upon which to base definitive recommendations. Nevertheless, the American Stroke Association has provided the following guidelines: in patients with recent ischemic stroke whose SBP is >220 mmHg or DBP 120–140 mmHg, cautious reduction of BP by about 10–15 percent is suggested, while carefully monitoring the patient for neurologic deterioration related to the lower pressure. If the DBP is >140 mmHg, carefully monitored infusion of sodium nitroprusside or glyceryl trinitrate should be used to reduce the BP by 10–15 percent.

Subarachnoid haemorrhage

Transient elevation of intracranial pressure produced at the time of the rupture of intracerebral saccular aneurysms, and the mass effect and obstructive hydrocephalus produced by the SAH may impair blood flow.

A Delayed ischaemia due to cerebral "vasospasm" is a significant cause of morbidity and mortality. The calcium antagonist nimodipine is given (60 mg 4 hourly) to prevent vasospasm.

Indications for antihypertensive therapy are the same as in other causes of stroke.