

STANDARD TREATMENT GUIDELINES

Hypertension

Screening, Diagnosis, Assessment, and Management of
Primary Hypertension in Adults in India

Quick Reference Guide

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सत्यमेव जयते

**Ministry of Health & Family Welfare
Government of India**

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1.INTRODUCTION:

Hypertension is the number one health related risk factor in India, with the largest contribution to burden of disease and mortality^(3, 4). It contributes to an estimated 1.6 million deaths, due to ischemic heart disease and stroke, out of a total of about 10 million deaths annually in India. Fifty seven percent of deaths related to stroke and 24% of deaths related to coronary heart disease are related to hypertension⁽⁷⁾. Hypertension is one of the commonest non-communicable diseases in India, with an overall prevalence of 29.8% among the adult population, and a higher prevalence in urban areas (33.8% vs. 27.6%) according to recent estimates.

Awareness of hypertension in India is low while appropriate treatment and control among those with hypertension is even lower: Hypertension is a chronic, persistent, largely asymptomatic disease. A majority of the patients with hypertension in India are unaware of their condition. This is because of low levels of awareness and the lack of screening for hypertension in adults—either as a systematic programme or as an opportunistic exercise during visits to healthcare providers.

The contexts for the screening, diagnosis, evaluation and management of hypertension in India are different from countries where awareness of hypertension in the general population is high and screening for hypertension is a routine part of primary care, practitioners are trained in delivering lifestyle interventions and medical management of hypertension, and patients are aware of the need and have the means to adhere to therapy. This is why a standard treatment guideline is being developed for the management of hypertension in the Indian context. **The guideline has a primary care focus and a public health approach.**

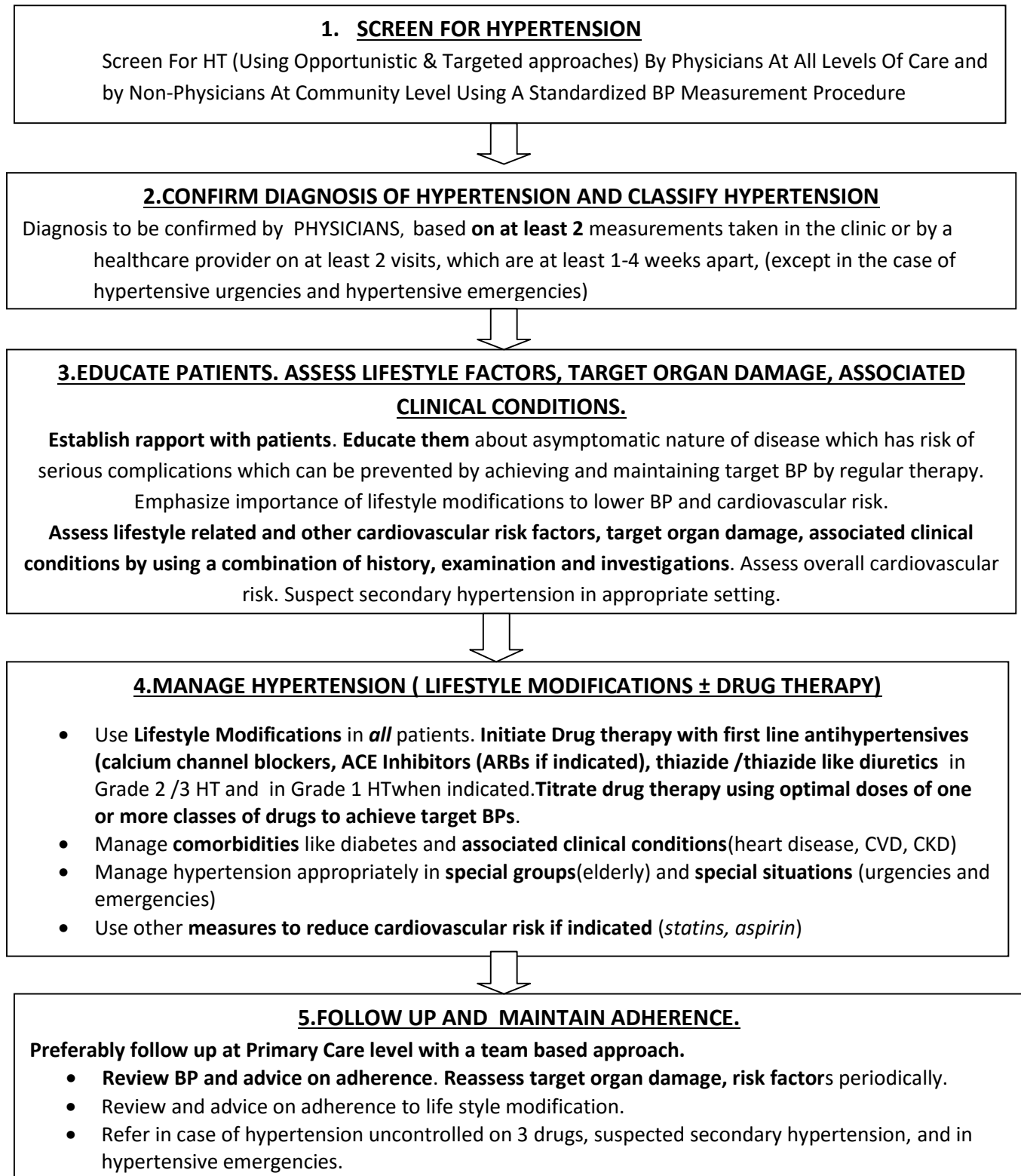
A public health approach to hypertension in India would involve the five components stated below:

- a. Prevention:** Promotion of a five point population wide interventions on weight reduction in the obese, increasing exercise levels in the sedentary, decrease in salt, sugar and fat intake, cessation of tobacco use, moderation of alcohol use. Increased intake of fruits and vegetables in addition to decreased salt intake has the potential to lower blood pressure significantly.
- b. Screening:** Screening for hypertension in all adults will involve **opportunistic** screening of people > 18 years of age at every point of contact with health professionals or allied health staff. Since healthcare facilities may not be accessed by all potential hypertensives, the guideline also suggests a targeted screening initiative at the community level aimed at detection of hypertension in high risk population. Screening will involve BP measurement using a standardized procedure and persons will receive advice and/or referral appropriate to the BP level.
- c. Diagnosis:** Diagnosis and evaluation of hypertension will be made at the PHC level which will also serve as the point of follow up for patients diagnosed at higher level facilities. Diagnosis and evaluation of hypertension can also occur at all other levels of care. Assessment will focus on target organ damage related to hypertension, co morbidities like diabetes, and correctable risk factors.
- d. Management including lifestyle changes:** Ensure availability of representative drugs from a core list of 5 groups of medications – thiazide diuretics, long acting calcium channel blockers,

low cost ACE inhibitors, (low cost Angiotensin Receptor blockers in case patients develop side effects to ACE inhibitors) , and beta-blockers. Lifestyle changes are a vital component of management of hypertension, and may be sufficient for control of mild hypertension.

- e. Follow-up, Monitoring Adherence:** Enable a hypertension registry accessible to all healthcare providers in the local public health system, promote adherence to therapy by simplified regimens, and monitoring by allied health staff.

Figure 1: Clinical pathway for hypertension care



KEY RECOMMENDATIONS:

1. SCREENING:

- 1.1 An ongoing initiative to increase awareness of hypertension as a widely prevalent but asymptomatic disease associated with many adverse outcomes like heart attacks, strokes, heart failure, kidney failure. Early diagnosis and effective control of BP can save people from much morbidity, mortality and disability.
- 1.2 All adults above the age of 18 years should undergo opportunistic screening by healthcare providers at all points of care in India, either during the course of their visits to the health facilities, or separately as a screening examination if requested by the person. Targeted screening at the community level of high-risk groups like adults above 50 years of age, persons with diabetes, obese, smokers, those with existing cardiovascular diseases, family history of hypertension, can be undertaken by trained non-physician staff. a physician or trained non physician staff, using an automated BP instrument or any other validated device, and following a standardized BP measurement procedure, mentioned in table 1 below.

TABLE 1- STANDARDIZED BP MEASUREMENT PROCEDURE –

STANDARD PROCEDURE FOR BP MEASUREMENT	
1.Patient preparation and position	Patient should be in a relaxed state for 5 minutes before measurement of BP. Patient should not have had caffeine in the past 1 hour or smoked in the past 30 minutes. Patient should be seated comfortably with back supported, with arm at heart level, and legs in an uncrossed position.
2.Choice of BP device	Mercury sphygmomanometer or any other device (including electronic digital oscillometric devices) which has been validated using a standard protocol, and has been calibrated regularly.
3.Cuff size and placement	The cuff size should be appropriate for the patient. Length of bladder should be 80% of arm circumference and width should be 40% of arm circumference, and a large adult cuff should be used for an obese patient. Patient should not wear any constrictive clothing. Place the midline of the cuff over the pulsations of the brachial artery, at a distance of 2-3 cm above the cubital fossa.
4. Procedure to measure systolic and diastolic blood pressure(applicable in case of auscultation based BP measurement)	Palpate the radial pulse and then inflate the cuff to 30 mm beyond the disappearance of the radial pulse. Deflate the cuff at 2-3 mm per second and record by auscultation with the stethoscope over the brachial artery, the first and the last sounds as the systolic and diastolic blood pressure respectively. In oscillometric devices, follow the instructions of the manufacturer, the systolic and diastolic BP will be displayed automatically. If the patient is diabetic or above 65 years measure the BP in supine position, and 2 minutes after assuming the standing position to check for postural hypotension.
5.No. of measurements and recording the result	At least 2 readings should be taken at an interval of 1 minute. If the readings differ by more than 5 mm Hg takes a third reading. The lower of the readings should be taken as the representative SBP and DBP.

1.3 The diagnosis of hypertension should be done by a physician or trained non physician staff, using an automated BP instrument or any other validated device, and following a standardized BP measurement procedure.

1.4. The sources of error during measurement of blood pressure are given in the table below.

TABLE 2 : SOURCES OF ERROR DURING MEASUREMENT OF BLOOD PRESSURE.

Source of measurement error (2)	Comment (2)
Back is not supported	Diastolic BP may increase by 6 mm
Arm is not at level of heart	Dangling the hand unsupported increases BP by 10-12 mm Hg.
Legs are crossed	Systolic BP increases by 2-8 mm Hg
Caffeine in the last 1 hour	Transient increase in BP
Smoking in the previous 30 mins. s	Transient increase in BP
Cuff size not appropriate	May overestimate systolic BP by 10-50 mm in obese persons in whom a smaller cuff has been used
Rapid deflation greater than 3 mm/sec	May underestimate systolic BP and overestimate diastolic BP
Patient's anxiety/ conditional response to an unusual situation in the presence of a physician	This may result in elevated BP readings, which may be normal when recorded by a nurse or when recorded at home. This "white coat hypertension" or "isolated office hypertension" amounted to 32% of hypertensive subjects in population based surveys, and is more prevalent in those with Grade 1 HT. If the facility is available, then ambulatory or home based BP monitoring, can be used to differentiate white coat hypertension from true hypertension.

1.5 Patients who are screened for hypertension should be advised lifestyle measures including restriction of salt intake , advice on diet and exercise in case the person is obese, stopping use of tobacco and moderating consumption of alcohol to reduce their blood pressure and to reduce their overall risk of cardiovascular complications.

Suggested response to BP readings:

TABLE 3: SUGGESTED RESPONSE TO INITIAL BP READINGS

Initial BP reading on screening		Advice and Recommendations for Follow up
SBP mm Hg	DBP mm Hg	
<130	<85	Advise lifestyle modifications esp. smoking, weight reduction if possible : Recheck in 2 years

130-139	85-89	Advise lifestyle modifications: Recheck in 1 year
140-159	90-99	Recheck BP within 1-2 weeks. Advise lifestyle modifications. Refer to nearest health facility within 1 month for diagnosis, assessment.
160-179	100-109	Recheck BP within 1 week. Advise lifestyle modifications. Refer to nearest health facility for confirmation of diagnosis and initiation of treatment.
>180	>110	Check for any symptoms/signs of any acute target organ damage (assess symptoms and signs referred to in the mnemonic 'ABCDEFG' ¹ mentioned in pathway on assessment and management of hypertensive crisis). In cases of acute target organ damage, treat as hypertensive emergency. Refer to PHC/CHC for evaluation and treatment immediately after confirming elevated readings in this range. Initiate therapy before referral, if seen at PHC.

2. CONFIRMATION OF DIAGNOSIS AND CLASSIFICATION OF HYPERTENSION

2.1 Diagnosis of hypertension should be made at primary health centres and facilities above that level using validated and calibrated BP measurement devices and following the standardised BP measurement procedure.

2.2 Diagnosis of hypertension should be based **on at least 2** measurements taken in the clinic or by a healthcare provider on at least 2 visits, which are at least 1-4 weeks apart, except in the case of hypertensive urgencies and hypertensive emergencies, where hypertension is diagnosed during the first visit itself. Ambulatory blood pressure monitoring and home based BP monitoring is not feasible for diagnosis for most patients with hypertension in India and is therefore not generally recommended. They may be considered where indicated e.g. in patients with suspected white coat hypertension, when the expertise and the facility is available.

2.3 Hypertension should be diagnosed when BP is persistently above a systolic of 140 mm and/or diastolic of 90 mm.

2.4. Patients with hypertension should be classified in the manner given in the table below:

¹ Abbreviation explained -A: Altered consciousness B: Breathlessness C: Chest pain(Ischemic) D: Deficit (weakness of limbs) or Decreased Urine output E: Edema F: Fundus if feasible which is showing hemorrhages, exudates, papilledema G: Generalised seizures

TABLE 4: CLASSIFICATION OF HYPERTENSION

Category	SBP(mm Hg)	DBP(mm Hg)
Optimal	<120	and <80
Normal	120 – 129	and/or 80 – 84
High Normal	130 – 139	and/or 85 – 89
Grade 1 Hypertension	140 – 159	and/or 90 – 99
Grade 2 Hypertension	160 – 179	and/or 100 – 109
Grade 3 Hypertension	≥ 180	and/or ≥110
Isolated Systolic Hypertension	≥ 140	and < 90
Hypertensive urgency	>180	and/or >110 Severe asymptomatic hypertension with no evidence of acute target organ damage
Hypertensive emergency	>180	and /or >110-120 Severe hypertension associated with cardiovascular (e.g. left ventricular failure, cerebral (e.g. hypertensive encephalopathy, stroke), renal (acute renal failure), Grade III-IV retinopathy

3. PATIENT EDUCATION AND ASSESSMENT

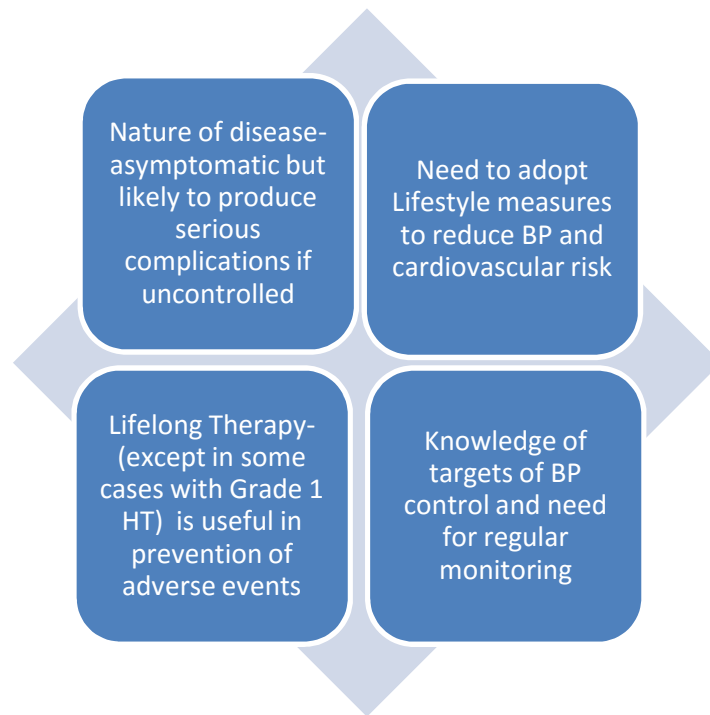


Figure 2:Patient Education matrix

3.1 Patient education will consist of awareness on:

- a. Nature of disease: Hypertension is an asymptomatic condition which can lead to disabling and life-threatening complications like stroke, heart attack and renal failure
- b. Therapy: Emphasise need for long-term therapy with regularity of drug intake to prevent damage to target organs and prevent adverse events.
- c. BP control: Educate about the targets for BP control, and encourage patients to monitor efficacy of therapy through regular check-ups which can include home based monitoring of BP.
- d. Lifestyle measures: It is important to highlight the important role of lifestyle measures in reducing hypertension and reducing risks of cardiovascular disease. (see annexure for details of lifestyle modifications)

3.2 Assessment of patients with hypertension:

3.2.1 Assessment of a patient with hypertension has the following 5 components

- a. Assessing the **lifestyle related and other cardiovascular risk factors** in patients with hypertension and the capability each patient’s capacity or willingness to change these factors.

Assess lifestyle factors and other cardiovascular risk factors	
History:	Smoking history Dietary consumption of salt, saturated fats Exercise pattern Alcohol consumption Family history of premature coronary artery disease
Examination:	Weight & Height and calculation of BMI, abdominal circumference
Laboratory evaluation:	Blood glucose, Lipids

- b. Assessing the **target organ damage** related to hypertension viz. heart failure, left ventricular hypertrophy, proteinuria, retinopathy.

Assess target organ damage: Heart (heart failure), Kidney, and Retina	
History	Breathlessness on effort Swelling on feet
Examination	Raised Jugular venous pressure, edema, gallops on auscultation (heart failure)
Funduscopy evidence	of hypertensive retinopathy-hemorrhages, exudates, papilledema
Laboratory evaluation	ECG: SV1 +RV6 > 3.5 Mv (LVH) Urine protein, Serum creatinine

- c. Assessing the presence of **associated clinical conditions** like diabetes, kidney disease or symptomatic cardiovascular disease with angina, myocardial infarction, cerebrovascular disease (stroke, TIA) or peripheral arterial disease.

Assess associated clinical conditions: Myocardial infarction, Stroke, Chronic Kidney disease	
History:	Episode of chest pain at rest (Myocardial infarction) in past Weakness on one half of body (Stroke) in the past
Examination:	Significant pallor in the presence of HT– chronic kidney disease
Laboratory:	S. Creatinine
ECG:	Ischemia, infarction, conduction disturbances, arrhythmias (atrial fibrillation)

- d. Assessing the clues to a **secondary cause of hypertension**- see table below:

Assess clues to presence of secondary hypertension
History: Abrupt onset of hypertension below the age of 30 years and above the age of 60 years (renovascular hypertension) Paroxysms of palpitations, pain(headache), perspiration (pheochromocytoma) ⁽¹⁾ Snoring at night, breathing pauses reported by partner, daytime sleepiness (sleep apnoea) Drug intake: NSAIDs, Steroids, Oral contraceptive pill
Examination: mooning of facies, striae: Cushing syndrome Unequal pulses: diminished/absent radial pulses- Takayasu's arteritis Diminished & delayed femoral pulse in lower limb: Coarctation of aorta. Tachycardia and postural hypotension (pheochromocytoma) Bruit over renal arteries: renal artery stenosis (renovascular hypertension)
Laboratory investigations: Abnormal urinalysis (proteinuria, haematuria), elevated creatinine. Abnormal kidneys on USG- renal parenchymal disease, renal artery Doppler for renal artery stenosis.

- e. Assessment of overall cardiovascular risk of a patient. As seen in the table below the overall cardiovascular risk increases with the grade of HT, number of risk factors, presence of organ damage, diabetes, symptomatic cardiovascular disease or chronic kidney disease.

	Grade 1 HT	Grade 2 HT	Grade 3 HT
No risk factor	Low risk	Moderate risk [#]	High [§] risk
1-2 risk factor*	Moderate risk	Moderate to high	High risk
>3 risk factor*	Moderate to High risk	High	High risk
Target Organ damage, DM, CKD stage 3	High risk	High risk	Very high risk
Symptomatic CVD(stroke, coronary artery disease), diabetes with organ damage, CKD>stage 4	Very high risk	Very high risk	Very high risk

20-30% risk of CV event over 10 years § >30% risk of CV event over 10 years *Risk factors(apart from hypertension) : age (> 55 years in men, 65 years in women), male gender, diabetes mellitus,smoking,obesity(including abdominal obesity), dyslipidemia(High LDL, Low HDL,High TG), impaired fasting glucose(FPG 100-125 mg/dl), family history of premature coronary artery disease.

3.2.2 Pragmatic approach to assessment of hypertensives in India: In the context of the Indian public health system, we suggest an approach which balances the needs of patients and the resources available at various levels and outline a pragmatic approaches to assessment – **essential** assessment in all patients with Grade 1 HT, **desirable assessment** in those with grade 2 HT or those with diabetes and/or proteinuria, and **comprehensive assessment** in those with Grade 3 HT, or those with diabetic complications, CKD, heart failure, or with a suspicion of secondary hypertension are suggested. This approach also takes into account the fact that some investigations like ECG for left ventricular hypertrophy have poor sensitivity , while there is insufficient evidence that a routine ophthalmoscopic examination is required for all patients with hypertension. On the other hand, patients with diabetes, symptomatic cardiovascular disease, smokers, obese, and those with proteinuria, which are all associated with greater cardiovascular risk can be identified even at the level of a primary health centre using a combination of clinical features (history and clinical examination) and investigations. Assessment of lipids is desirable in patients with hypertension, with a higher yield in those who are diabetics, obese and have cardiovascular disease. Patients can be referred to the community health centre for evaluation of lipids, but the need is not urgent.

Essential assessment

Should be done in all patients attending primary care facilities, also in patients with Grade 1 hypertension
History and physical examination for risk factors (smoking, obesity, diet and exercise patterns, family history of premature CVD), clinical cardiovascular disease (angina, heart failure, stroke)
Fasting capillary blood (FCG) or fasting plasma glucose (FPG). FCG > 126 mg/dl or FPG >126 mg/dl is abnormal and suggestive of diabetes. Abnormal fasting capillary glucose needs to be checked against a fasting plasma glucose obtained in the laboratory

Urinalysis for proteinuria: Presence of proteinuria doubles the risk of morbidity and mortality for a certain BP and is an independent predictor of all-cause mortality in hypertension.

Desirable assessment

Desirable in patients with Grade 2 hypertension and above, with family history of premature cardiovascular disease, in patients with diabetes and in patients with proteinuria

Essential assessment plus

Serumcreatinine: Abnormality more often seen in patients with severe hypertension, diabetic nephropathy, chronic kidney disease or occasionally in patients on ACE inhibitors.

Lipids: more often abnormal in patients who are obese, in diabetics, in patients with cardiovascular disease. Commonest abnormality in India is low HDL, increased triglycerides

ECG: Low sensitivity for detection of LVH. LVH if present however indicates increased cardiovascular risk. LVH with strain strong predictor of heart failure. May yield evidence of ischemic heart disease, conduction system disturbance or arrhythmias.

Comprehensive evaluation: In patients with Grade 3 hypertension, patients with CKD, heart failure

Desirable evaluation plus

History and physical examination: exclude signs of secondary hypertension

Serum sodium and potassium: hypokalemia clue to secondary hypertension (renovascular, primary hyperaldosteronism)

Ultrasound kidney: for evidence of CKD

Echocardiography: in case of suspected heart failure (on basis of history, physical examination)

3.3 Screening for diabetes (which is to be available at all health facilities under the free diagnostics initiative) is an integral part of evaluation of hypertension because of the common association of hypertension and diabetes. The care of diabetes should be integrated with management of hypertension.

3.4 All patients should be asked about tobacco use and advised to stop it.

4. MANAGEMENT OF HYPERTENSION: THERAPEUTIC RECOMMENDATIONS

4.1. Overall aim: The overall aim of the management of hypertension is not only reduction of BP to target levels but also to lower the cardiovascular risk of the patient. Management of hypertension should be tailored to the individual and his or her circumstances.

4.2. Lifestyle modifications

4.2.1 Lifestyle measures including adopting a heart-healthy diet with reduced salt and saturated fat intake, stopping use of tobacco products , regular exercise and reduction of body weight in those who are obese, are part of management of all patients with hypertension.

4.2.1.1. These lifestyle measures may be sufficient for treatment of Grade 1 hypertension, may reduce the doses required for control of hypertension, and will also reduce the cardiovascular risk in all grades of hypertension.

4.2.1.2 A trial of lifestyle measures should be monitored for 1-3 months following diagnosis of Grade 1 hypertension. The lower range of durations should be considered in the presence of other risk factors like age, obesity, lipid levels, and smoking status.

4.3 Initiation of drug therapy

4.3.1 Drug therapy is indicated in patients with Grade 1 hypertension with

- Any sign of target organ damage (LVH on ECG, proteinuria on urinalysis, hypertensive retinopathy on fundus examination).
- Any evidence of coronary artery disease, congestive heart failure, cerebrovascular disease, peripheral arterial disease (clinical cardiovascular disease)
- Diabetes
- Presence of chronic kidney disease
- Patients with 3 or more risk factors² (including age, gender, smoking, obesity, dyslipidemia, diabetes, impaired fasting glucose, family history of premature coronary artery disease).

4.3.2. Drug therapy in patients with grade I hypertension uncomplicated by any organ damage, without coexisting diabetes mellitus, clinical cardiovascular disease, or multiple cardiovascular risk factors should be initiated after a trial of 1-3 months of lifestyle modifications.

4.3.3. Drug therapy is indicated in all patients with Grade 2 and Grade 3 hypertension and should be combined with lifestyle measures.

² Age > 55 in men, >65 in women; Male gender; smoking; diabetes; obesity including abdominal obesity; impaired fasting glucose (FBS 100-125 mg/dl); dyslipidaemia (high LDL, high TG, low HDL); family history of premature coronary artery disease

4.3.3.2. Drug therapy is initiated in patients with Grade 2 hypertension on confirmation of the diagnosis on repeat BP measurements in the visits *subsequent* to the initial visit when Grade 2 HT was first detected.

4.3.3.3. Drug therapy in patients with Grade 3 hypertension is initiated after repeat measurements in the initial visit confirm the severe elevation of the blood pressure.

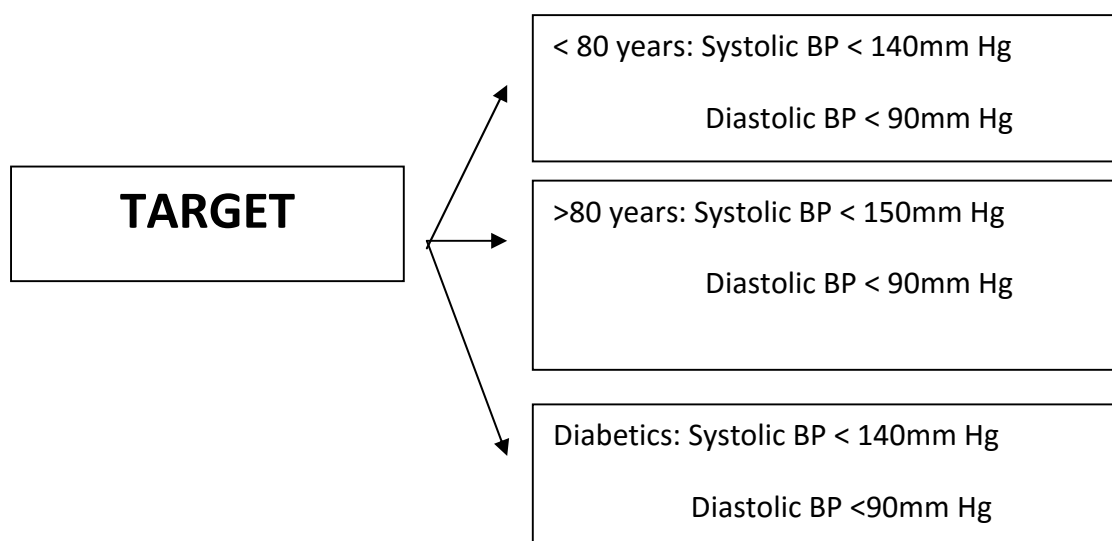
4.4. Treatment goals for management of hypertension:

4.4.1 The current target for control of BP for patients under 80 years of age should be less than systolic blood pressure less than 140 mm and diastolic blood pressure less than 90 mm.

4.4.2 The current target for control of BP for patients 80 years or older should be less than 150 mm systolic and less than 90 mm diastolic.

4.4.3 A recent trial (SPRINT trial) in **non-diabetic** population at high cardiovascular risk has shown a reduction in cardiovascular mortality in patients in the intensive treatment group where the goal BP was less than 120 mm systolic and 80 mm diastolic. However this was accompanied by more than 2 fold increased frequency of serious adverse events and increase in serum creatinine. Based on the currently available evidence we do not recommend this lower target generally for physicians and patients in India, except for individual patients and physicians in situations who have agreed upon these targets and where close monitoring for adverse effects is feasible.

4.4.4 Current evidence based on trials of BP targets of <130 mm and < 85 mm diastolic in **patients with diabetes** have failed to show significant overall benefit on cardiovascular disease outcomes, and have been accompanied by increased frequency of serious adverse events. Therefore we currently recommend the standard BP target of <140 mm systolic and <90 mm in patients with diabetes in India.



4.5 Key recommendation: Classes of antihypertensive drugs & preferred choices

- 4.5.1 The primary issue in treatment of hypertension is reduction of cardiovascular risk by effective control of blood pressure. Overall the benefits of antihypertensive treatment are due to lowering of blood pressure rather than choice of therapy. Many patients will require more than one drug for control of hypertension.
- 4.5.2 All classes of drugs- calcium channel blockers, ACE inhibitors/ARBs, diuretics; beta-blockers have approximately the same efficacy on lowering of blood pressure, and on outcomes, although beta-blockers have been associated with lesser protection against strokes. All combinations of drugs are not however similarly efficacious, and some are preferred.
- 4.5.3 The different classes of drugs have differing side effect profiles and requirements for monitoring, which may influence their use and prescription in the health system.
- 4.5.4 In the absence of any associated clinical conditions (noted below) providing a compelling indication for the use of a particular drug , a long acting calcium channel blocker, a low dose thiazide diuretic, or a low cost ACE inhibitor may be used as the initial antihypertensive drug.
- 4.5.5 The presence of associated clinical conditions (diabetes, clinical cardiovascular disease, chronic kidney disease) in a patient may provide compelling indication for the use of specific classes of drugs.
- 4.5.5.1 Preferred drugs for treatment of patients with diabetes and hypertension are ACE inhibitors, especially in those with proteinuria. Calcium channel blockers /low dose diuretics may be used in addition if required to achieve control.
- 4.5.5.2 Preferred drugs for patients with heart failure and hypertension are ACE inhibitors, diuretics (including loop diuretics) and beta-blockers.
- 4.5.5.3 Preferred drugs for patients with coronary artery disease and hypertension are beta-blockers, ACE Inhibitors or calcium channel blockers.
- 4.5.6 The specific drugs within these classes recommended on the basis of availability and affordability include amlodipine, (a long acting calcium channel blocker); enalapril or lisinopril, (ACE inhibitor); low dose hydrochlorothiazide, (thiazide) or chlorthalidone (thiazide like diuretic) and if required, losartan, (a low cost angiotensin II receptor blocker).
- 4.5.7 Angiotensin receptor blockers have a mode of action, efficacy and indications similar to ACE inhibitors, but are currently more expensive than them. They should therefore be used in the place of ACE inhibitors, *in case there are side effects with ACE inhibitors* like cough, angioedema.

Clinical condition	Drug to be preferred as first drugs	Second drug if needed to achieve BP control	Third drug if needed to achieve BP control
Isolated systolic hypertension (elderly)	CCB/Thiazide Diuretic	ACE Inhibitor*	Thiazide diuretic + ACE Inhibitor*+ CCB
Hypertension and diabetes	ACE inhibitor*	CCB or thiazide diuretic	ACE inhibitor* + CCB+ thiazide diuretic
Hypertension and chronic kidney disease(defined as albuminuria or an eGFR< 60 ml/min/1.73 m ² for > 3 months)	ACE inhibitor*where close clinical and biochemical monitoring is possible. Otherwise CCB may be preferable	CCB or thiazide diuretic (loop diuretic if eGFR is below 30 ml/min)	ACE inhibitor* +CCB+ thiazide diuretic
Hypertension and previous myocardial infarction	BB, ACE Inhibitor*	CCB or diuretic	
Hypertension associated with heart failure	Thiazide/ loop diuretic+ ACE Inhibitor*+BB [#] + Spironolactone		
Hypertension associated with previous stroke	ACE inhibitor*	Diuretic or CCB	ACE Inhibitor* +CCB+ diuretic

Table 9: Clinical conditions which may be associated in a patient with hypertension and the drugs to be preferred

*Angiotensin receptor blockers (ARBs) may be used for this indication if there is intolerance to ACE inhibitors (cough, angioedema)Abbreviations: ACE inhibitor: angiotensin converting enzyme inhibitor; CCB, calcium channel blocker; BB, beta-blocker.Notes: Examples of representative drugs: ACE inhibitors - Enalapril, Calcium channel blockers-Amlodipine, Thiazide diuretic- Hydrochlorothiazide, Beta-blocker- Atenolol.[#] In patients with heart failure the preferred beta-blockers are metoprolol, carvedilol, bisoprolol.

§ Source: adapted from ref.⁽²¹⁾

Table 10: Compelling and possible **contraindications** to the use of antihypertensive drugs[#]

Drug	Compelling contraindication	Possible contraindication
Diuretics	Gout	Metabolic syndrome, glucose intolerance, hypokalemia, hypercalcemia
Beta-blockers	Asthma, AV block (grade 2 or 3)	Metabolic syndrome, glucose intolerance, chronic obstructive pulmonary disease
Calcium channel blockers(dihydropyridines)		Tachyarrhythmia, heart failure
Calcium channel blockers(non-dihydropyridines)	AV block (Grade 2 or 3),severe left ventricular dysfunction, heart failure	
ACE inhibitors	Pregnancy Hyperkalemia Bilateral renal artery stenosis	Women with childbearing potential
Angiotensin receptor blockers	Pregnancy Hyperkalemia Bilateral renal artery stenosis	Women with childbearing potential
Mineralocorticoid receptor antagonists (e.g. spironolactone)	Acute or severe renal failure (eGFR<30 ml/min)	

Abbreviations: AV, atrioventricular; eGFR, estimated glomerular filtration rate

KEY RECOMMENDATIONS

4.6 The treatment regimen and the use of combinations:

- 4.6.1 In patients with Grade 1 or Grade 2 hypertension, therapy can be initiated with **one** drug (CCBs, ACE inhibitors, thiazide diuretics) in combination with lifestyle modifications (**Step 1** in table 13). Average initial doses can be 5 mg of amlodipine, 5 mg of enalapril and 12.5 mg of hydrochlorothiazide.
- 4.6.2 In patients with Grade 3 hypertension, the therapy should be initiated with **two** drugs, in combination with lifestyle modifications (**Step 2** in table 13). The combinations can be calcium channel blocker (amlodipine) + ACE inhibitor (enalapril) or calcium channel blocker (amlodipine) + thiazide diuretic (hydrochlorothiazide) or ACE inhibitor (enalapril) + thiazide diuretic (hydrochlorothiazide).
- 4.6.3 The dose of drugs can be increased or a new drug added at approximately 2- to 4-week intervals. This frequency can be faster or slower depending on the clinical circumstances of the patient and the judgment of the practitioner.
- 4.6.4 The addition of a new drug in patients with Grade 1 or Grade 2 hypertension may be preferable to maximising the dose of the initial drug. In case a calcium channel blocker (amlodipine) has been used as initial therapy, the add-on drug can be ACE inhibitor (enalapril) or a thiazide diuretic. Similarly if ACE inhibitors have been used as initial therapy, a calcium channel blocker or a diuretic can be used as add on therapy. When amlodipine is used as an add-on therapy, the initial dose used should be 2.5 mg. Similarly if an ACE inhibitor like enalapril is added to a diuretic, the initial dose used may be 2.5 mg to avoid hypotension.
- 4.6.5. If the second drug in a usual dose also fails to reduce BP to target levels then the third class of drug previously unutilised should be added (**Step3** in table 13). An optimal 3 drug combination in case it is required is a calcium channel blocker with a low dose thiazide diuretic and an ACE inhibitor (e.g. amlodipine+ enalapril+ hydrochlorothiazide).
- 4.6.6. The preferred 2 drug combinations are combination of calcium channel blockers with ACE inhibitors, ACE inhibitors with low dose diuretics, and calcium channel blockers with low dose diuretics.
- 4.6.7. Prescription of a single pill combination of antihypertensive drugs in a defined proportion may be considered if available, *after BP has been stabilised* with a dose of two drugs given singly in the same proportion.

- 4.6.8. The practitioner should aim for patients to reach target BP levels with an effective treatment regimen, whether 1, 2, or 3 drugs, within 6 to 8 weeks.
- 4.6.9. Add-on drugs for control of BP drugs should be added at intervals of 2-4 weeks.
- 4.6.10. Negative recommendation: ACE Inhibitors should not be combined with Angiotensin receptor blockers.
- 4.6.11. Avoid prescribing a combination of beta-blockers and diuretics as they can increase the risk of diabetes mellitus in those at risk, e.g. persons with impaired glucose tolerance or obesity and metabolic syndrome.
- 4.6.12. If the BP is not controlled despite use of 3 anti-hypertensives, then the hypertension should be termed resistant and the patient should be referred to a specialist at the medical college for further evaluation and management.

The management of hypertension is shown in text form in the box below and the doses of the drugs to be used are mentioned in table 12.

Review and respond to possible causes of poor response to BP medications

4.7. Key Recommendations:

When a patient does not respond to two drugs given in full doses, the physician should review the underlying issues -related to

- BP measurements,
- poor adherence to drug and lifestyle modifications, including stoppage of medicines due to belief in other systems of medicine
- suboptimal treatment regimens,
- presence of associated conditions,
- use of non-antihypertensive drugs which can interfere with the action of anti-hypertensives, and
- Consider the possibility of secondary hypertension.

MANAGEMENT OF HYPERTENSION - target BP <140/90 mmHg in those < 80 years, 150/90 in those over 80 years.

ALL PATIENTS REQUIRE LIFE-LONG LIFESTYLE MODIFICATION

Dietary change to Heart-healthy diet– salt 5 g/day, low-fat diet
Regular exercise

Maintain weight – target BMI 18.5-22.9 kg/m²

Stop smoking

Patients with Grade 1 hypertension may require only lifestyle modification, which should be tried for 3 months.

GRADE 1 HYPERTENSION (SBP 140-159 mm, DBP 90-99mm) with

Inadequate control after 3 months of lifestyle modification **OR** more than 3 risk factors:

Male, Age: men >55 years, women >65 years, smoking, obesity, including abdominal obesity

Dyslipidaemia, impaired fasting glucose, family history of early coronary artery disease

Drug therapy – A or C¹ or D

Add second drug - A+C or C+D or A+D if response not adequate within 2-4 weeks

Add third drug – A+C+D if response not adequate within 2-4 weeks

GRADE 2 HYPERTENSION (SBP 160-179, DBP 100-109)

Drug therapy – A or C or D

Add second drug - A+C or C+D or A+D if response not adequate within 2-4 weeks

Add third drug – A+C+D if response not adequate within 2-4 weeks

GRADE 3 HYPERTENSION (SBP ≥180, DBP ≥110)

Use two drugs - A+C or C+D or A+D

Add third drug – A+C+D if response not adequate within 2-4 weeks

ALL GRADES OF HYPERTENSION WITH ASSOCIATED CLINICAL CONDITIONS

CAD: coronary artery disease - B+A², C

CHF: congestive heart failure - D+A+B, MRA

CKD: chronic kidney disease – A or C or D³

DM: diabetes mellitus – A or C, D

Drugs are added only if they are required to achieve the target BP of <140/90 mm Hg (in patients <80 years old) or <150/90 mm Hg (in patients >80 years of age)

Abbreviations: **CAD:** coronary artery disease, **CHF:** congestive heart failure, **CKD:** chronic kidney disease, **DBP:** diastolic blood pressure, **DM:** diabetes mellitus, **SBP:** systolic blood pressure, **TOD:** target organ damage.

Drug classes: **A:** Angiotensin converting enzyme (ACE) inhibitors, (e.g. enalapril) or Angiotensin II receptor blockers (ARBs) (e.g. losartan) if intolerance to ACE inhibitors, **B:** Beta-blockers (e.g. atenolol), **C:** Calcium channel blockers (e.g. amlodipine), **D:** thiazide diuretics (e.g. hydrochlorothiazide), **MRA:** mineralocorticoid receptor antagonist (e.g. spironolactone).

Drug doses: Doses for initiation of therapy : A : enalapril 5 mg; B: Atenolol 50 mg; C: Amlodipine 5 mg (2.5 mg in elderly); D: Hydrochlorothiazide/Chlorthalidone 12.5 mg.

Add-on doses: A : enalapril 5 mg (reduce in elderly or in those on diuretics), C: amlodipine 2.5 mg, D: hydrochlorothiazide 12.5 mg

Maximal doses: A : enalapril 20-40 mg; B: Atenolol 100 mg C: Amlodipine 10 mg; D: Hydrochlorothiazide: 25 mg

Footnotes :

¹ Calcium channel blockers are antihypertensives of choice in the elderly (> 60 years).

² Patients with CAD and history of myocardial infarction should receive both beta-blockers and ACE inhibitors

³ Patients with CKD may require loop diuretics if the glomerular filtration rate is low. Patients on ACE inhibitors will require monitoring of serum creatinine and potassium.

Based on references: Hypertension: Clinical management of primary hypertension in adults NICE guidelines [CG127].

National Institute for HealthCare Excellence; 2011 Weber MA, Schiffrin EL, White WB, et al. The Journal of Clinical

Hypertension. 2014;16(1):14-26.

Table 12: Initial and maximal doses for initiation and titration of therapy for Indian patients with hypertension: (source: adapted from ref ^{(24), (70)} and product monographs listed at health Canada www.health-sc.gc.ca)

Drug class	Low dose in certain situations	Usual Initial dose suggested for Indian patients with hypertension		Maximal dosage suggested for Indian patients with hypertension	Doses per day
Calcium channel blockers					
Dihydropyridines					
Amlodipine	2.5 mg*	5 mg		10 mg	1
Angiotensin converting enzyme inhibitors					
Enalapril	2.5 mg [§]	5 mg		10-20 mg	1-2
Lisinopril		5 mg		10 mg	1
Angiotensin receptor blockers					
Losartan	25 mg [#]	50 mg		100 mg	1-2
Telmisartan		40 mg		80 mg	1
Diuretics					
Thiazides					
Hydrochlorothiazide		12.5 mg		25 mg	1
Thiazide-like					
Chlorthalidone		12.5 mg		25 mg	1
Beta-blockers					
Atenolol	25 mg	50 mg		100 mg	1
Metoprolol succinate		50 mg		100 mg	2

*Reduce dose of amlodipine to 2.5 mg once a day when it is started in low body weight elderly patients, and when amlodipine is added to another antihypertensive medication.

§ Reduce dose to enalapril 2.5 mg when it is used in elderly (>65 years) and when the patient has been on diuretic therapy.

Use dose of 25 mg in patients less than 50 kg (Canadian labelling)

Initiation with single drug Step 1	Initiation with 2 drugs or titration of drugs in a patient not controlled on a single drug : Step 2			Use of three drugs in a patient not controlled with 2 drugs Step 3
	CCB (amlodipine)	Diuretic (hydrochlorothiazide)	ACE inhibitor (enalapril)	
ACE inhibitor Enalapril 5 mg Or	Enalapril 5 mg+ Amlodipine 2.5 mg , later raise to 5 mg	Enalapril 5 mg + Hydrochlorothiazide 12.5mg	Enalapril 10 mg (less preferred strategy)	ACE inhibitor (Enalapril 5/10mg) + CCB Amlodipine 5/10 mg) + Thiazide Hydrochlorot hiazide 12.5mg/25 mg)
CCB Amlodipine 5 mg Or	Amlodipine 10 mg (less preferred strategy)	Amlodipine 5 mg + Thiazide 12.5 mg	Amlodipine 5 mg +Enalapril 5 mg	
Thiazide diuretic Hydrochlorothiazide 12.5 mg	Diuretic + CCB (Amlodipine 2.5 mg, later 5 mg)	Hydrochlorothiazide 25 mg (less preferred strategy)	Hydrochlorothiazide 12.5 mg Enalapril 2.5 mg , later 5 mg	

Table 13: Medication pathway in this guideline evolving from Step 1 (single drug) to Step 2 (two drugs) to Step 3

When a patient is not responding to BP medications, as determined by persistently high BP readings on repeat visits, the physician should pay attention to the following factors:

1. Issues related to BP measurement in the clinic: This may include “white coat effect” because of which the clinic based BP measurements by a doctor may be higher than those obtained at home or by another healthcare provider. Improper size of cuff and improper technique may also give falsely elevated BP readings.
2. Adherence to medications: In a chronic disease, which are asymptomatic, patients often miss doses or even discontinue medications, and the regularity of drug intake should be enquired about from the patient and their relatives. The reasons for non-adherence should also be explored which may include doubts about the diagnosis, belief in lifestyle modifications being sufficient, cost of therapy, or side effects related to medicines. Belief in other systems of medicine may also lead to stoppage of medicines
3. Adherence to lifestyle modifications: Excessive salt intake, excessive alcohol consumption, tobacco use, obesity all can contribute to poor control of hypertension.
4. Suboptimal treatment regimens: This can be the result of low doses, or use of inappropriate combinations. Drug dosages should be optimized. The combinations should be of medicines which are complementary in action. Addition of diuretics in patients not responding to a combination of drugs, usually results in good control.
5. Presence of associated conditions: Presence of sleep apnea, chronic pain can all impair control of BP.
6. Drug interactions: Some commonly used drugs like non-steroidal anti-inflammatory drugs (NSAIDs), oral contraceptives, corticosteroids and anabolic steroids, and common cold remedies which contain sympathomimetics can all result in higher BP. NSAIDs (including cyclooxygenase-2 inhibitors) can cause salt retention and interfere with the action of all antihypertensives except calcium channel blockers. Addition of a diuretic may mitigate their effect.
7. Secondary hypertension: The most frequent cause of secondary hypertension is chronic kidney disease, which can be diagnosed on the abnormal urinalysis& blood chemistries, at the level of the CHC. The other causes of secondary hypertension would include endocrine causes (pheochromocytoma, Cushing’s’ syndrome), vascular causes (renovascular hypertension, contraction of aorta, Takayasu’s arteritis); which will require evaluation by a specialist at a medical college level.

4.8. Therapy of hypertension, comorbidities and associated conditions:

A large proportion of patients with hypertension have co-morbidities such as diabetes mellitus, which need to be managed.

4.8.1 Diabetes mellitus:

4.8.1.1 Patients with diabetes mellitus should be initiated on drug treatment when the SBP is greater than 140 mm Hg, and the target for control should be a SBP of less than 140 mm Hg, and a diastolic BP of less than 90 mm Hg.

4.8.1.2 ACE inhibitors are preferred as initial therapy and calcium channel blockers and diuretics may be used as add on therapy. Thiazide diuretics can be associated with glucose intolerance.

4.8.1.3 Drugs which inhibit the renin angiotensin systems- ACE inhibitors and ARBs should be used if the patients have proteinuria (or microalbuminuria).

4.8.2 Heart disease:

4.8.2.1 Beta-blockers should be prescribed in patients with hypertension and a recent myocardial infarction. These patients should also receive an ACE inhibitor.

4.8.2.2 In patients with angina, beta-blockers and calcium channel blockers, should be considered among the antihypertensive drugs for their effect on symptoms.

4.8.2.3 In patients with heart failure and hypertension, ACE inhibitors, thiazide diuretics, and beta-blockers, and mineralocorticoid receptor antagonists are recommended for reduction in mortality and hospitalization.

4.8.3 Kidney disease (diabetic or non-diabetic):

4.8.3.1 The target for BP reduction should be a SBP of less than 140 mm Hg, but a SBP of less than 130 mm Hg should be considered for those with overt proteinuria.

4.8.3.2 ACE inhibitors /ARBs are effective in reducing albuminuria and should be used in patients with hypertension and overt proteinuria (or microalbuminuria). *Monitoring serum creatinine and potassium in the first week of therapy is advisable after initiation of therapy or any increase in the dose of ACE inhibitors.*

4.8.3.4 Use of ACE inhibitors and Thiazide or thiazide like diuretics should be used as other antihypertensive agents, and in the presence of volume overload, loop diuretics like frusemide may be used.

4.8.4 Cerebrovascular disease:

4.8.4.1 Prevention of stroke can occur with all classes of antihypertensive drugs if BP is effectively controlled.

4.8.4.2 In patients with a history of stroke or TIA, initiation of drug treatment should be considered even with Grade 1 hypertension, and a systolic BP of less than 140 mm Hg should be targeted. An ACE inhibitor/ARB is considered an initial drug.

4.8.4.3 In the first 72 hours of an ischemic stroke, do not administer antihypertensive treatment, since excessive lowering of BP can exacerbate the existing ischemia.

4.8.4.4 In patients who are not undergoing thrombolytic therapy for ischemic stroke, extreme values of BP, e.g. systolic BP > 220 mm Hg or diastolic BP > 120 mm Hg should be treated by agents to reduce mean arterial pressure by about 15% in the first hour and no more than 25% in the first 24 hours and with gradual reduction thereafter. In patients who are candidates for thrombolytic therapy, BP above systolic of 185 mm Hg and diastolic of 110 mm Hg should be treated cautiously and maintained below these levels.

4.8.4.5 In patients with intracerebral haemorrhage, with SBP > 200 mm Hg or MAP³>150 mm Hg, aggressive reduction of blood pressure with intravenous infusion of antihypertensives is indicated and the patient should be examined every 5 minutes.

4.8.4.6 In patients with intracerebral haemorrhage, with SBP >180 mm Hg or MAP > 130 mm Hg, modest reduction of BP to 160/90 is indicated using an intermittent or continuous IV infusion with frequent re-examination is indicated.

4.8.4.7 In patients presenting with intracerebral haemorrhage and a SBP of 150-220 mm Hg, BP can probably be lowered to a SBP of 140 mm Hg safely.

4.8.5 Hypertension in the elderly:

4.8.5.1 Postural hypotension is more common in elderly people. Assess patients for postural hypotension at diagnosis and on follow up by checking BP in sitting and in standing position after 2 minutes.

³ MAP = Mean arterial pressure which is calculated as follows $MAP = \frac{SBP + 2(DBP)}{3}$ where SBP is systolic blood pressure and DBP is diastolic blood pressure

- 4.8.5.2 Postural fall of >20 mm in systolic and >10 mm diastolic indicates postural hypotension is a risk factor for falls.
- 4.8.5.3 In a patient with postural hypotension titrate target according to standing BP.
- 4.8.5.4 Start therapy with lower doses of drugs and change doses or add drugs at a slower rate in elderly patients.
- 4.8.5.5 In elderly patients less than 80 years of age, the blood pressure target for control may be <140 mm systolic and <90 mm diastolic if the patient is fit and the treatment is well tolerated.
- 4.8.5.6 In elderly patients more than 80 years (the very elderly), the blood pressure target for control is <150 mm systolic and <90 mm diastolic.
- 4.8.5.7 The drug of choice for initiation of therapy in the elderly is a long acting calcium channel blocker, or a low dose thiazide diuretic in the absence of compelling indications.
- 4.8.5.8 There is a higher likelihood of certain side effects in the elderly- e.g. hyponatremia in the case of thiazides, and hyperkalemia in the case of ACE inhibitors.
- 4.8.5.9 There is a likelihood of drug –drug interactions in the elderly who often receive other drugs; e.g. .NSAIDs for arthritis interferes with action of ACE inhibitors, and diuretics.

4.9 **Hypertensive emergencies:**

- 4.9.1 Hypertensive emergencies are those in which severe hypertension (elevations of systolic >180 mm Hg) and/ or diastolic (> 120 mm Hg) is associated with symptoms and signs of acute ongoing organ damage. Such elevations of blood pressure may be associated with neurologic emergencies (hypertensive encephalopathy, cerebral infarction, and cerebral haemorrhage), cardiac emergencies (acute left ventricular failure, acute coronary syndrome), renal emergencies like acute renal failure, and obstetric emergencies like eclampsia (symptoms and signs of such dysfunction are referred to under the mnemonic of 'ABCDEFGH' in pathway on assessment and management on hypertensive crisis). Eclampsia can occur even at levels of BP less than 180 mm systolic and/or 120 mm diastolic.
- 4.9.2 The magnitude and rate of reduction of BP varies according to the organ involvement in the hypertensive emergency. In many hypertensive emergencies including hypertensive encephalopathy reduction of *mean* arterial pressure of ≤ 25 percent in the first hour, with a gradual reduction to 160 mm systolic and diastolic of 110-120 mm Hg over 2-6 hours, and gradual normalization of blood pressure

over 24-48 hours is recommended. Parenteral agents like IV labetalol, nicardipine may be used initially with a change to oral agents later.

- 4.9.3 In patients with ischemic stroke as noted earlier, reduction of systolic BP below 220 mm Hg and 120 mm Hg are not treated, unless the patient is being considered for thrombolytic therapy.
- 4.9.4 Negative recommendation: Oral or sublingual nifedipine may cause excessive, abrupt fall of blood pressure which may result in cardiac, cerebral or renal ischemic complications. It is not recommended in the treatment of any hypertensive emergency.
- 4.9.5 In the case of acute left ventricular failure reduction of the elevated BP is indicated with a parenteral loop diuretic like furosemide in addition to vasodilators like nitroglycerine. In patients with acute coronary syndrome with severe hypertension, intravenous nitroglycerine may be used in association with intravenous beta-blockers like esmolol or labetalol.
- 4.9.6 Patients with a hypertensive emergency should be examined for any clinical clues to the presence of secondary hypertension and be evaluated for the same.

4.10 Hypertensive urgencies:

4.10.1 This refers to situations when severe hypertension (SBP > 180 mm, DBP > 110 mm) is not associated with any signs of acute or ongoing organ damage (cerebral, cardiac, renal, visual), and the patient is relatively asymptomatic except for a mild headache (none of the symptoms, signs referred to in the mnemonic 'ABCDEFGH' in pathway on hypertensive crisis). Patients with severe hypertension should be assessed clinically and by laboratory investigations, and target organ damage should be excluded before hypertensive urgency is diagnosed.

4.10.2 Hypertensive urgencies may occur in patients with chronic hypertension in a number of situations. This includes non-adherence to therapy, after sudden withdrawal of beta-blocker or clonidine therapy, after ingestion of large quantity of salt, or due to anxiety.

4.10.3 There is no benefit from rapid reduction of BP in patients with severe but asymptomatic hypertension and the BP should be reduced over a period of hours and days.

4.10.4 Nursing the patient in a quiet room and relief of anxiety may reduce BP to a certain extent.

4.10.5 Negative recommendation: Do not attempt excessive, rapid and uncontrolled reduction of blood pressure in hypertensive urgencies, with intravenous drugs or oral or

sublingual nifedipine. This aggressive reduction of BP in a patient with severe asymptomatic hypertension may cause fall of BP below the threshold of autoregulation in vascular beds, and cause serious cerebral and cardiac complications related to ischemia.

4.10.6 Re-institution of therapy or intensification of therapy by increasing the dose of drugs or adding a diuretic may suffice for gradual reduction of blood pressure in a patient who has developed severe asymptomatic hypertension on the background of chronic hypertension.

4.10.7 If BP reduction over few hours is required in view of imminent cardiovascular events, then oral frusemide, oral clonidine can be used. These can be followed by long term therapy with CCBs, ACE inhibitors or diuretics.

Hypertensive emergencies	
Cardiac conditions	Acute left ventricular failure
	Acute myocardial infarction
Renal conditions	Acute glomerulonephritis
	Renovascular hypertension
Cerebrovascular conditions	Hypertensive encephalopathy
	Cerebral infarction
	Intracerebral hemorrhage
	Subarachnoid hemorrhage
Head injury	
Accelerated hypertension with exudates and/or papilledema	
Obstetric conditions	Eclampsia
Surgical conditions	Postoperative hypertension
	Severe burns
Excess catecholamines	Pheochromocytoma
	Abrupt withdrawal of clonidine, beta-blockers

Table 14: Conditions presenting as hypertensive emergencies

Drug	Dose	Onset of action	Adverse effects	Comments
IV Frusemide	20-40 mg in 1-2 min	5-15 min	Hypovolemia, hypokalemia	May be used in combination with other drugs to maintain their efficacy. Indicated in acute left ventricular failure

IV labetalol	20-80 mg IV	5-10 min	Scalp tingling, dizziness, nausea, heart block	Can be used in many hypertensive emergencies. Avoid in acute heart failure
IV nicardipine	5-15 mg per hour as IV	5-10 min	Tachycardia, headache, nausea, tachycardia	Can be used in many hypertensive emergencies. Avoid in acute heart failure
IV nitroglycerine	5-100 µg/min	2-5 min	Headache, vomiting, methemoglobinemia, tolerance	Useful in myocardial ischemia with hypertension

Table 15: Selected intravenous drugs useful in management of hypertensive emergencies

4.11 Integration with other interventions to reduce cardiovascular risks

4.11.1 The treatment of hypertension should be integrated with treatment of associated risk factors like lipid lowering therapy and antiplatelet therapy, apart from lifestyle interventions already mentioned.

4.11.2 Antiplatelet therapy with low-dose aspirin (75 mg/day) is recommended in patients *with controlled hypertension* who have previous history of cardiovascular event (previous MI, stroke, angina, bypass surgery or coronary angioplasty), because of a favourable benefit –harm ratio.

4.11.3 Low dose aspirin may be considered for those hypertensives who are well controlled and have a high cardiovascular risk (Grade 3 hypertension, 3 or more risk factors, target organ damage).

4.11.4 Negative recommendation: Do not use low-dose aspirin in hypertensive patients without cardiovascular disease and who are at low-moderate risk as the risk of major bleeds (intracranial and gastrointestinal) outweighs the potential benefit.

4.11.5 The use of low dose aspirin in patients with diabetes without cardiovascular or cerebrovascular disease is not recommended in view of the uncertain risk-benefit ratio.

4.11.6 Prescribe statins for use in hypertensive patients with overt atherosclerotic cardiovascular disease [coronary artery disease including acute coronary syndromes, history of myocardial infarction, stable angina), cerebrovascular disease (stroke or transient ischemic attack), and peripheral arterial disease], regardless of age.

4.11.7 Prescribe statins in hypertensive patients

- aged more than 40 years, with LDL –cholesterol more than 190 mg/dl, where secondary causes have been ruled out
- in hypertensive patients who are diabetic and in the age group of 40-79 years,
- in hypertensive patients aged more than 40 years with high cardiovascular risk (3 or more out of list of 11 cardiovascular risk factors)

4.11.8 Hypertensive patients who smoke or chew tobacco should be provided advice to stop smoking and chewing tobacco.

5. FOLLOW UP, MONITORING AND IMPROVING ADHERENCE TO THERAPY

Key Recommendations:

5.1 A simplified regime using long acting drugs which can be used once a day may improve adherence.

5.2 The patients should be monitored for efficacy of the regimen, both at the clinic and community level. In patients who are yet to achieve target BP, follow-up visits at 1-2 weeks can be scheduled till target BP is achieved. Thereafter the patient can be seen by a physician at a frequency determined by the severity of the hypertension, presence of comorbidities, target organ damage. Streamlined methods to collect drugs should be allowed to enable compliance by the patient.

5.3. The patients should be monitored for side effects of drugs.

5.4. The common side effect of calcium channel blockers is peripheral edema, which is dose dependent and may subside with reduction of dose or combination with ACE inhibitor.

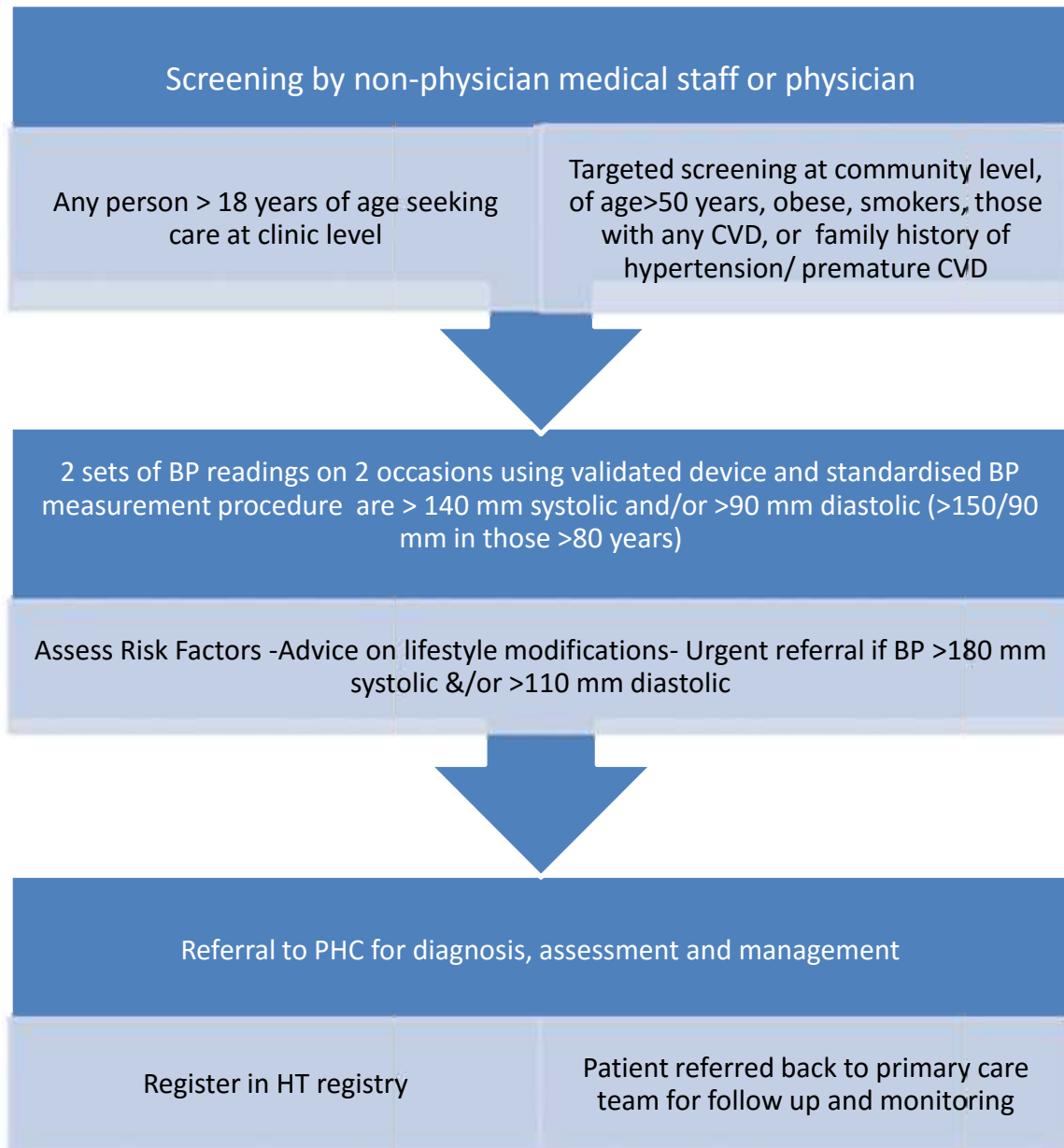
5.4.1. The common side effects of diuretics are metabolic side effects like hypokalemia, hyperglycemia but which are less frequent when these are used in doses of 12.5 mg and when they are combined with ACE inhibitors.. A particular concern is of thiazide induced hyponatremia which is commoner in the elderly, those with a low body weight. This can develop rapidly and manifest as altered consciousness, and even seizures, and may require hospitalisation and administration of normal or hypertonic saline.

5.4.2. The common side effect of ACE inhibitors is dry cough, which may necessitate withdrawal of therapy. There is a risk of hypotension when ACE inhibitors are started on

patients who are on diuretics, or are on very low salt diet. A small rise in serum creatinine can occur on ACE inhibitors, which is reversible. Hyperkalemia can develop with high doses of ACE inhibitors, but also more commonly in patients with renal insufficiency, diabetes, concurrent use of potassium sparing diuretics, and the elderly.

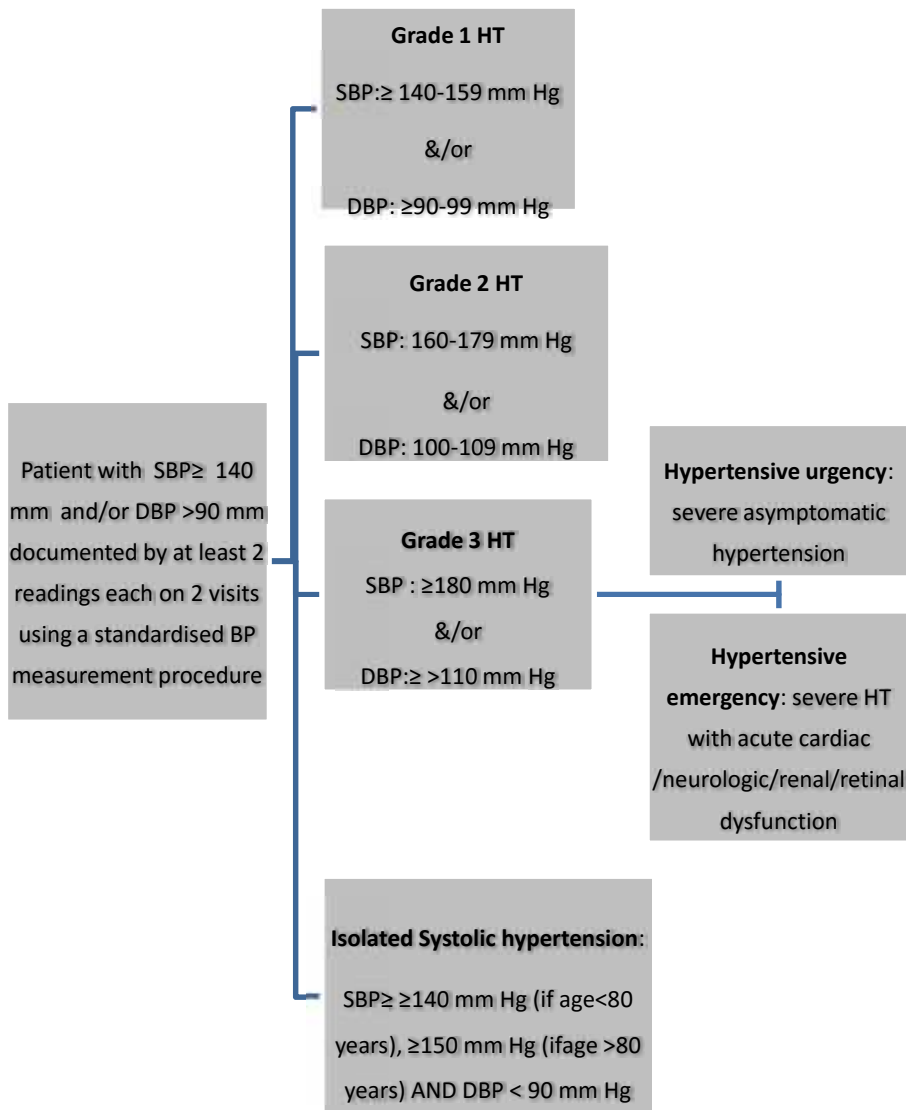
- 5.5. Consider the use of pill counts, participation of a family member in supervision of drug intake, periodic counselling and provision of patient information leaflets to improve adherence and control.
- 5.6 Diagnosis and management of hypertension in India, needs to be embedded in the system of primary care. A team approach to management of hypertension needs to be evolved which involves the physicians, allied staff and community based health workers.
- 5.7 Community based health workers can be trained to play a critical role in meeting the challenge of undetected, untreated and uncontrolled hypertension in India. They can improve detection, promote lifestyle modifications, monitor response and ensure adherence to therapy. They can also help prevent hypertension by advising appropriate lifestyle modifications in those who have a high normal BP (130-139 mm Hg systolic and 85-89 mm Hg diastolic)
- 5.8 We strongly recommend creation of a hypertension registry at the PHC & CHC level to ensure tracking of patients and create a system of recall which can involve the community based health workers.
- 5.9. Patients with hypertension should be encouraged to consider home blood pressure monitoring using an automated device which has been validated with a clinic based device.
- 5.10. All patients with hypertension, should undergo an annual review of control of BP, implementation of lifestyle modifications (e.g. maintenance of body weight), target organ damage (proteinuria), review of treatment including side effects of drugs.
- 5.11 All patients with high normal BP should also be encouraged to undergo an annual review, and advised appropriate lifestyle modifications e.g. dietary changes, weight maintenance, and abstinence from tobacco

ANNEXURE 1: PATHWAYS : CLASSIFICATION, ASSESSMENT, MANAGEMENT

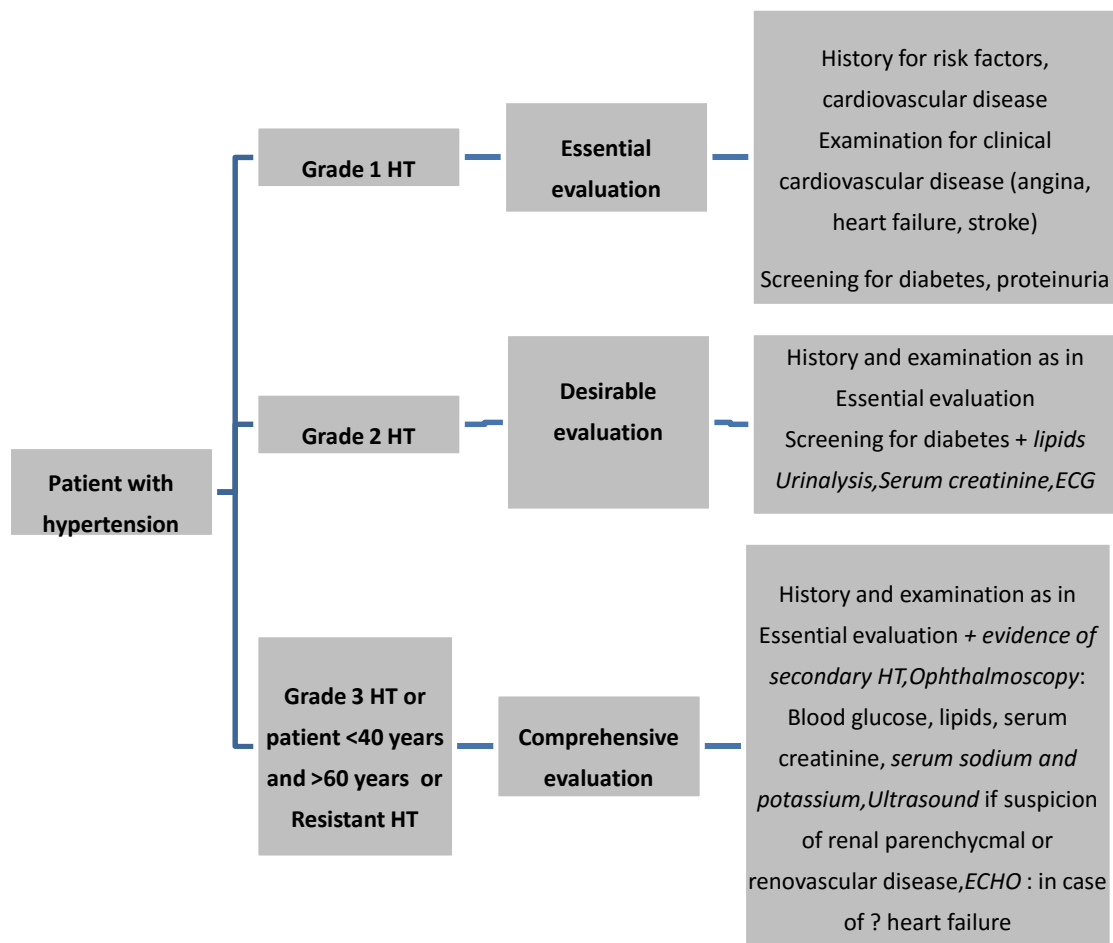


Pathway 1: Screening Pathway

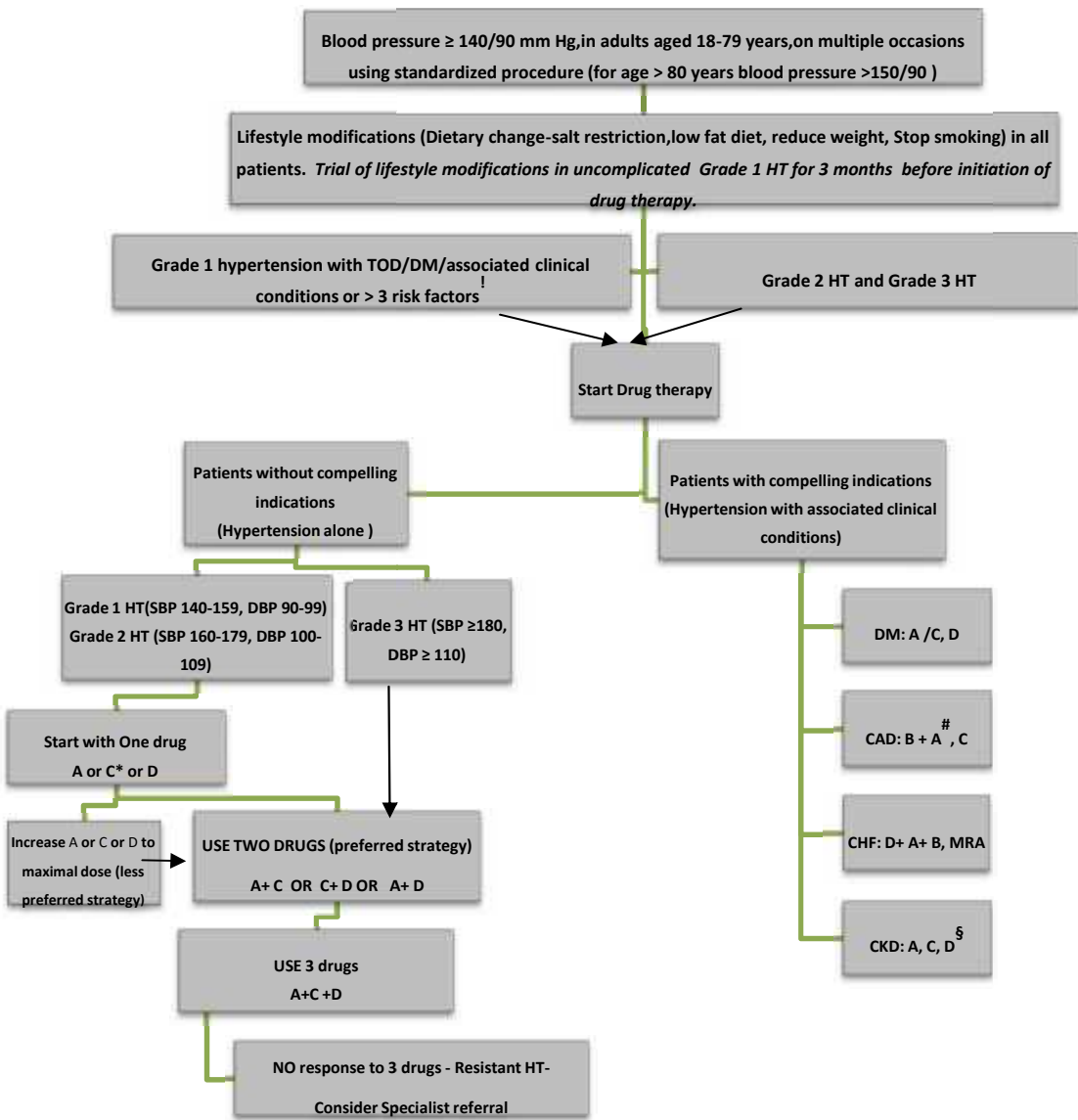
Standard Procedure for BP measurement	
1. Patient preparation and position	Patient should be in a relaxed state for 5 minutes before measurement of BP. Patient should not have had caffeine in the past 1 hour or smoked in the past 30 minutes. Patient should be seated comfortably with back supported, with arm at heart level, and legs in an uncrossed position.
2. Choice of BP device	Mercury sphygmomanometer or any other device (including electronic digital oscillometric devices) which has been validated using a standard protocol, and has been calibrated regularly.
3. Cuff size and placement	The cuff size should be appropriate for the patient. Length of bladder should be 80% of arm circumference and width should be 40% of arm circumference, and a large adult cuff should be used for an obese patient. Patient should not wear any constrictive clothing. Place the midline of the cuff over the pulsations of the brachial artery, at a distance of 2-3 cm above the cubital fossa.
4. Procedure to measure systolic and diastolic blood pressure(applicable in case of auscultation based BP measurement)	<p>Palpate the radial pulse and then inflate the cuff to 30 mm beyond the disappearance of the radial pulse. Deflate the cuff at 2-3 mm per second and record the first and the last sounds as the systolic and diastolic blood pressure respectively.</p> <p>In oscillometric devices the systolic and diastolic BP will be displayed automatically.</p> <p>If the patient is diabetic or above 65 years measure the BP in supine and 2 minutes after assuming the standing position to check for postural hypotension.</p>
5. No. of measurements and recording the result	<p>1.1. At least 2 readings should be taken at an interval of 1 minute. If the readings differ by more than 5 mm Hg takes a third reading. The lower of the two readings should be taken as the representative SBP and DBP.</p>



Pathway 3: Classification pathway



Pathway 4: Assessment pathway



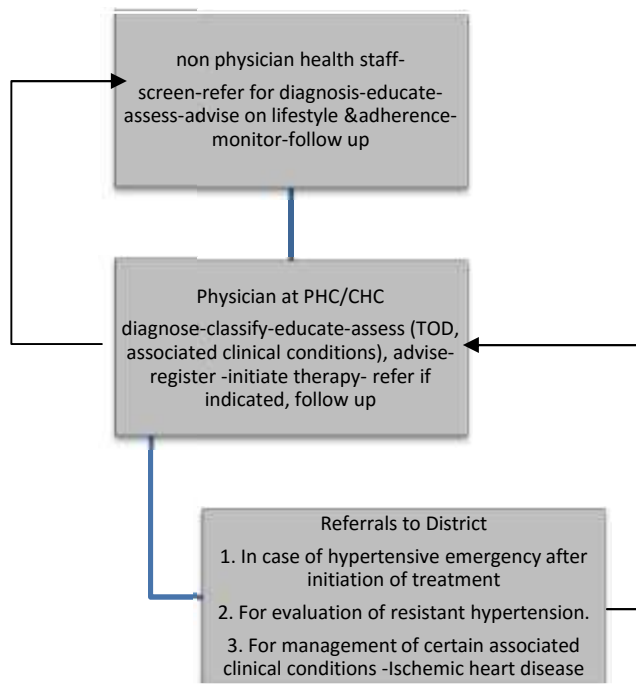
Pathway 5 A.: Management pathway (algorithm form)

Drugs are added only if they are required to achieve the target BP of <140/90 mm Hg (in patients <80 years old) or BP <150/90 mm Hg (in patients >80 years of age)

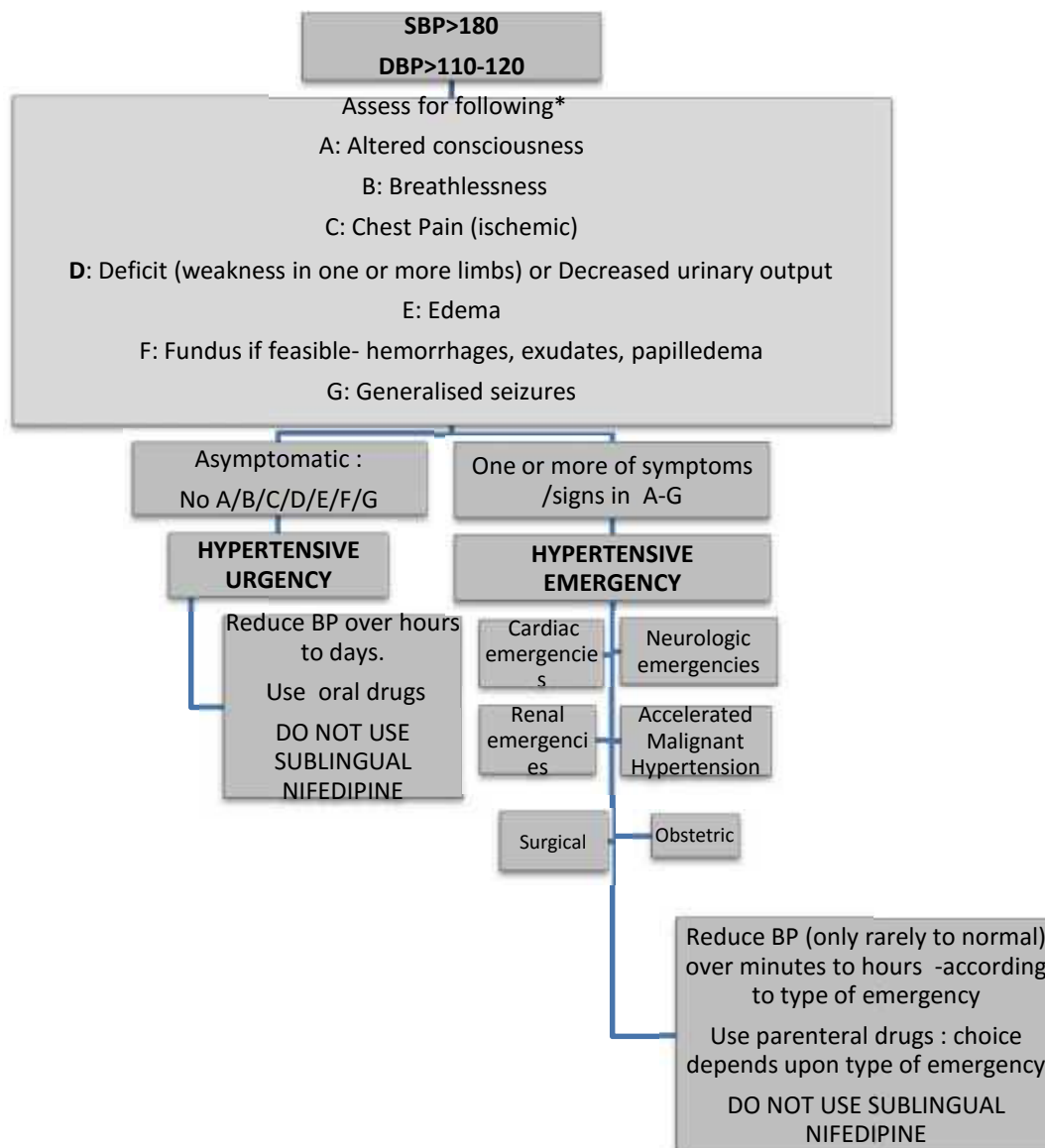
Abbreviations: SBP : Systolic blood pressure, DBP: Diastolic blood pressure, TOD :target organ damage, DM: diabetes mellitus, CAD: coronary artery disease, CHF: Congestive heart failure, CKD: Chronic kidney disease. **Drug abbreviations:** **A** : Angiotensin converting enzyme(ACE) inhibitors (e.g. enalapril) or Angiotensin II receptor blockers(ARBs)(e.g. losartan) *only if intolerance to ACE inhibitors*, **C**: Calcium channel blocker(e.g. amlodipine), **D**: Thiazide diuretics(e.g. hydrochlorothiazide), **B**: Beta-blockers(e.g. atenolol), **MRA** : Mineralocorticoid receptor antagonist (e.g. spironolactone).

Footnotes :! Other Risk factors(apart from hypertension) : age (> 55 years in men, 65 years in women), male gender, diabetes mellitus, smoking, obesity(including abdominal obesity), dyslipidemia, impaired glucose tolerance, family history of premature coronary artery disease.

* calcium channel blockers are antihypertensives of choice in the elderly (> 60 years).# Patients with CAD and history of myocardial infarction should receive both beta-blockers and ACE inhibitors.§ Patients with CKD may require loop diuretics if the Glomerular filtration rate is low. Those patients who are started on ACE inhibitors will require monitoring of serum creatinine and potassium after initiation of treatment. Based on references^(24, 49)



Pathway 6:Patient flow pathway



Pathway 7: Assessment and management pathway in a patient with hypertensive crisis (> 180 mm systolic, >110-120 mm diastolic)

*Also investigate as appropriate: Serum creatinine (in all), X-ray chest, ECG, CT scan if indicated.

Cardiac emergencies: Acute left ventricular failure, Myocardial infarction, unstable angina; Neurologic emergencies: Hypertensive encephalopathy, Ischemic stroke, Intracerebral haemorrhage, subarachnoid haemorrhage, Head injury ;Renal emergencies: Acute glomerulonephritis[#], renovascular hypertension; Surgical emergencies: Post-operative hypertension, severe burns ;Obstetric: Eclampsia[#]

[#]: Hypertensive emergency may occur even at BP levels lower than 180 mm systolic and 110 mm diastolic

ANNEXURE 2: LIFE STYLE CHANGES RECOMMENDED FOR PATIENTS DIAGNOSED TO HAVE HYPERTENSION AND FOR THOSE AT RISK OF DEVELOPING HYPERTENSION

Background:

Lifestyle modifications are an integral part of the management of persons with hypertension, regardless of severity of hypertension. Reduction of BP following lifestyle modifications may suffice for the control of grade I hypertension, while they may aid the control of hypertension and reduce the dosages of drugs required for control of other grades of hypertension. Lifestyle modifications also help to reduce the overall cardiovascular risk in a person with hypertension.

Lifestyle modifications are also an integral part of the prevention of hypertension at both an individual and the population level, and may help prevent progression of high normal BP to hypertensive levels.

1. Physical Activity (adapted from ref. ⁽⁸⁴⁾)

- Physical activity includes daily activity like walking and cycling, household work, work related activity, and leisure activity. Moderate intensity physical activity of 30 minutes per day or at least 2.5 hours (150 mins) per week, which can be performed in bouts of 10 minutes or more in 4-7 sessions per week, should be advised to all individuals for its cardio-protective effect . Moderate intensity physical activity includes any activity which can increase the heart rate, make the breathing rapid and make the body warmer such as brisk walking (at 3-4 mph), stair-climbing, light swimming, walking the treadmill at 3-4 mph, or . 45 minutes (accumulated) exercise per day is recommended for cardiovascular fitness, while 60 minutes (accumulated) per day is recommended for weight reduction. The specific form of physical activity chosen by or for the patient should be enjoyable and sustainable.

- Alternatively persons can indulge in 75 minutes of vigorous physical activity like running (at 6-8 mph), cycling at 12-14 mph. This kind of activity makes the breathing

very hard, the heartbeat rapid and makes it difficult to carry on a conversation comfortably.

- All adults should include physical activities to improve muscle strength at least twice a week.
- Regular aerobic exercises can reduce the systolic blood pressure average of 4 mmHg and diastolic BP by an average of 2.5 mmHg.⁽²⁹⁾
- Epidemiologic evidence suggests that physical activity reduces cardiovascular morbidity and mortality. There is strong evidence that regular physical activity has an independent cardio protective effect. Physical activity improves cardiorespiratory fitness, lowers SBP and DBP, improves insulin sensitivity and glycemic control, helps reduce and control weight, and lowers markers of inflammation.⁽⁵³⁾
- Chronically sedentary individuals should not start a program of vigorous activity suddenly, but should gradually increase the duration and intensity of physical activity, starting for example with 10 minutes of moderate activity per session.⁽⁸⁵⁾ This is done to minimise the risk of a sudden cardiac event and musculoskeletal injuries. Any patient experiencing chest discomfort, jaw pain, palpitations, syncope or dyspnea, should undergo evaluation before continuing with exercise. Patients with decompensated heart failure and acute coronary syndromes should not embark on an exercise program.

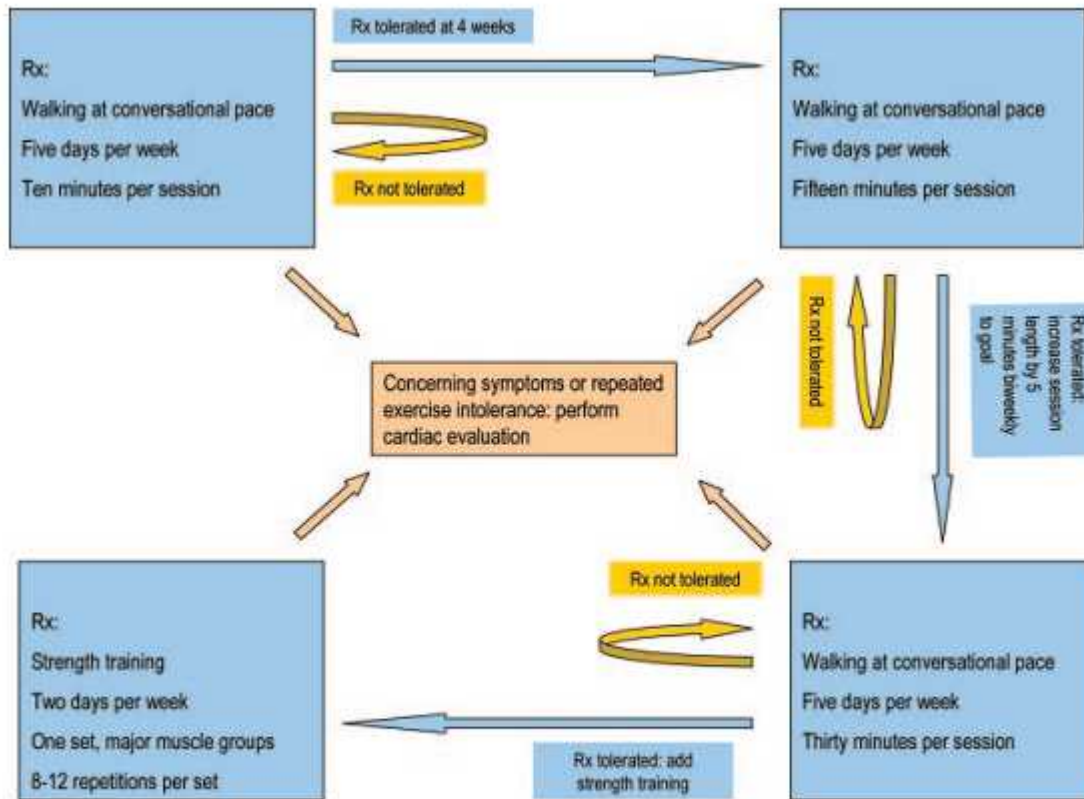


Figure. An approach to staged exercise prescriptions: Any enjoyable, moderate-intensity activity such as those listed in Table 2 may be substituted for walking. Specific strength training exercises are also listed in Table 2. Rx indicates prescription.

Source: Ref⁽⁸⁵⁾

Table 2. Recommended Exercise Routines in Addition to Activities of Daily Living^{5,12,17}

Type of Exercise	Frequency	Intensity	Length
Aerobic: Walking, stair-climbing, elliptical machine, dancing, light swimming, cycling on flat ground	At least 5 days per week	Moderate	30 min total in segments of no less than 10 min
Aerobic: Running, singles tennis, swimming	At least 3 days per week	Vigorous	20 min
Resistance training: Biceps curls, military presses, shoulder shrugs, 1-arm bent rowing, bent-knee pushups, quarter squats, toe raises, and bent-knee abdominal crunches	At least 2 days per week	Moderate, allowing for completion of set without straining	8–12 repetitions per set starting at a single set twice per week

Moderate and vigorous activities can be combined toward the goal amount of activity.

Source : ref⁽⁸⁵⁾

2. **Weight Reduction:** achieve and maintain desirable body weight.

All individuals who are overweight or obese should be encouraged to lose weight through a combination of a reduced calorie diet, increased physical activity and behaviour modification. Dietary changes and recommendations for physical activity are mentioned in other sections.

Overweight or obesity is assessed by measuring body mass index (BMI), which is calculated as weight in kg/height in meter². For Indian population 18.5 to 22.9 BMI is normal, 23 to 24.9 is considered as overweight and BMI of ≥ 25 kg/m² is considered as obesity in Indians.⁴ Apart from BMI which is a measure of general adiposity, it is also important to measure the abdominal adiposity, which is also associated with a higher cardiovascular risk. Abdominal adiposity can be measured by measurement of the waist circumference and the waist-hip ratio. The waist circumference is measured at the end of several consecutive natural breaths, midpoint between the top of the iliac crest and the lower margin of the last palpable rib in the mid axillary line. Waist circumference should be <90 cm for men and <80 cm for women. Another measure of central obesity is Waist Hip Ratio (WHR), which is the waist circumference divided by the hip circumference. The hip circumference is measured at the maximum circumference of the buttocks. Normal WHR is <0.85 for women and <0.90 for men.

⁴Misra A, Chowbey P, Makkar B, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. *JAPI*. 2009;57(2):163-170.

3. Alcohol Consumption

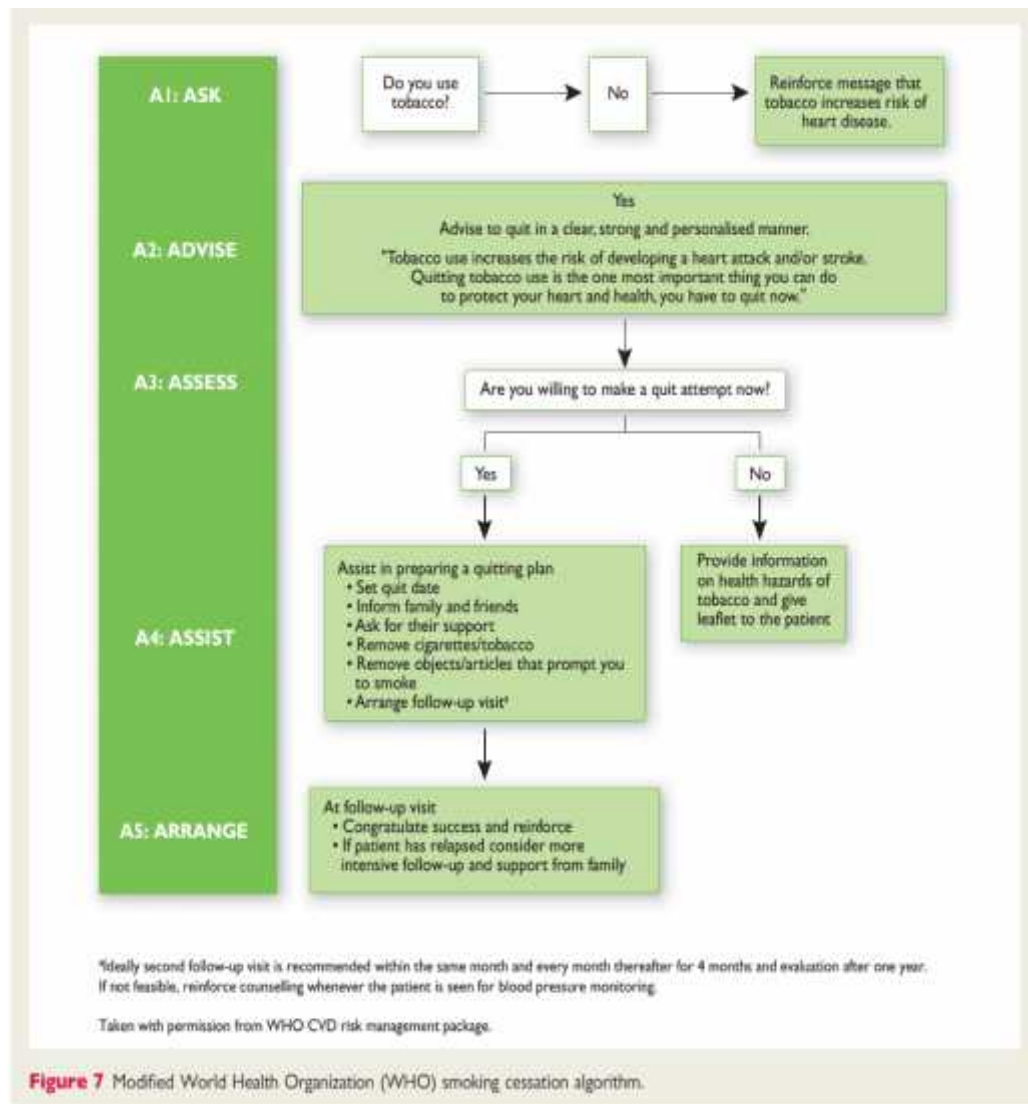
- Reducing alcohol intake can lower the blood pressure substantially. On other hand moderate drinking and binge drinking increases the blood pressure and risk of developing hypertension.
- Zero alcohol consumption is recommended for women who are pregnant or planning to have pregnancy and also for those hypertensives who had already suffering from a complication due to hypertension like stroke, heart disease or renal disease.
- Alcohol consumption is measured in terms of units of alcohol (UK) or standard drinks (e.g. Australia, USA). 1 unit of alcohol is 10 ml ethanol (around 8 gms ethanol), while 1 standard drink contains 10 g ethanol (Australia) or 14 g ethanol (USA).
- The no. of units consumed per day can be calculated using the drink volume and the Alcohol by (ABV), which is mentioned as a percentage on the container. E.g. Beer may be around 5% ABV, wine is around 12.5%, while whisky and vodka are around 40% ABV.
- The number of units of alcohol = Drink volume x ABV /1000. Therefore 100 ml of whisky will be $100 \times 40/1000 = 4$ units.
- Healthy adults should not regularly drink more than 3-4 units per day in the case of men and 2-3 units in the case of women. If there has been heavy alcohol consumption, there should be no alcohol intake for 48 hours.
- Tips on cutting down should be offered to patients and should be employed in an incremental fashion(86) : These include keeping track of alcohol intake (including counting and measuring) and keeping intake within recommended limits, setting goals for consumption, drinking slowly and preferably with some food in the stomach. In patients who have decided to quit, avoiding triggers, dealing with urges, and refusing offers of drinks politely are of vital importance. Talking and enlisting the support of spouses, non-drinking friends, and mutual support groups like alcoholics anonymous are also very helpful.

4. Tobacco cessation

Non-smokers should be encouraged not to start smoking.⁽⁸⁷⁾ All smokers should be encouraged to quit smoking, and should be supported by the health professional in their efforts to do so.⁽⁸⁷⁾

Patients who use other forms of tobacco should be motivated to stop doing so.

- Smoking cessation may not reduce the blood pressure directly but markedly reduces overall cardiovascular risk. The risk of myocardial infarction is 2–6 times higher and the risk of stroke is 3 times higher in people who smoke than in non-smokers. Smokers who quit reduce their risk of coronary heart disease.
- Brief advice from health professionals is effective in helping persons to quit smoking, increasing quit rates. Even 3–5 minutes taken to encourage smokers to attempt to quit can increase success rates.
- The WHO has recommended a 5 **A**s approach to aid in smoking cessation in routine practice- The patient should be asked about smoking status at every opportunity. Then the patient should be advised about to quit smoking, and assessed about his degree of addiction and readiness to quit. The health professional should assist in formulating a smoking cessation strategy including setting a quit date, counseling and other measures, and finally arrange a follow up visit.
- Pharmacotherapy to stop smoking with nicotine replacement therapy, bupropion, nortryptiline and varenicline are effective and should be offered to motivated smokers who fail to quit with counseling. The risk of adverse effects is small and is generally outweighed by the significant risk of continuing to smoke.



Ref: (23)

5. Dietary Recommendations

All patients should be encouraged to adopt a heart healthy diet.

Fat: All individuals should be strongly encouraged to reduce total fat and saturated fat intake. Total fat intake should be reduced to about 30% of calories, saturated fat to less than 10% of calories, trans-fatty acids (present in margarine and bakery products) intake should be reduced as much as possible or eliminated and most dietary fat should be polyunsaturated (up to 10% of calories) or monounsaturated (10–15% of calories).

Salt: All individuals should be strongly encouraged to reduce daily salt intake by at least one third and, if possible, to <5g or <90mmol per day.

Fruits, vegetables, fibre: All individuals should be encouraged to eat at least 400 g a day of a range of fruits and vegetables as well as whole grains and pulses.

6. Salt Intake

All patients should be strongly encouraged to limit their salt intake to < 5 g salt(or 90 mmol) per day as per WHO recommendations.⁽⁸⁷⁾ There is lack of representative data on salt intake in India, although in a study in urban India, the mean intake was found to be 8.5 g salt per day.⁽⁸⁸⁾

Reduction of salt intake can be accomplished by not adding additional salt in diet, choosing foods processed without salt, avoiding high-salt processed foods, salty snacks, takeaway foods high in salt and salt added during cooking or at the table.

Preparations which are high in salt and need to be moderated are: Pickles, chutneys, sauces and ketchups, papads, chips and salted biscuits, cheese and salted butter, bakery products and dried salted fish.

The above recommendation for dietary salt restriction may have to be individualised in the case of certain occupational exposures. Acclimation to heat occurs rapidly; thus, within a few days of exposure to hot and humid conditions, individuals lose only small amounts of sodium through sweat. But in the case of workers performing intense physical activity under conditions of heat stress, may lose significant amounts of fluid and salt in sweat. In a study it

was estimated that a 10 hour shift of working in moderately hot climatic conditions(35⁰C) can result in loss of 10-15 g salt.⁽⁸⁹⁾

7. Stress management

- In hypertensive patients in whom stress may be contributing to blood pressure elevation, stress management should be considered as an intervention.
- A recent systematic review and meta-analysis of Yoga concluded that there were clinically important effects on cardiovascular disease risk factors and that Yoga could be considered an ancillary intervention to reduce cardiovascular risk.⁽⁹⁰⁾With regard to its role in hypertension management, another systematic review concluded that there was emerging but low-quality evidence for Yoga as an adjunct to medical therapy, but larger confirmatory studies were required.⁽⁹¹⁾

ANNEXURE 3: FORMULARY

Calcium channel blockers (CCBs) with focus on amlodipine

Pharmacology of CCBs: These drugs interfere with the inward movement of calcium ions through the slow channels of cell membranes in the heart and the vascular smooth muscle. They are divided into 2 major classes, the dihydropyridines CCBs which includes amlodipine, nifedipine, felodipine) which do not have a major negative inotropic effect and no antiarrhythmic activity, and the non-dihydropyridines like verapamil, and diltiazem, which have both significant negative inotropic and anti-arrhythmic activity.

Amlodipine: Amlodipine has a very long elimination half-life (35 to 48 hours) and can be given once daily. It has a good safety profile, very few drug interactions, and no adverse effect on glucose, lipid levels. Other agents in this class like cilnidipine, nifedipine, lercanidipine, have no major advantage over amlodipine whose outcome benefits have been established in large trials. An isomer of amlodipine, S-Amlodipine is also marketed in India, along with the amlodipine in its racemic form. The limited high quality data available suggests that there is no difference in therapeutic efficacy as well as adverse effects between the two forms(92). The S-Amlodipine form is more expensive. The racemic amlodipine is available in various forms – amlodipine besilate, amlodipine mesilate, and amlodipine maleate, but these are interchangeable.

Indications for amlodipine:

Used alone or in combination for hypertension, chronic stable angina, coronary artery disease without heart failure or an ejection fraction <40%

Dose, titration, and use in combinations

Initial dose: 5 mg once daily. In elderly, small patients, and patients with hepatic impairment, the initial dose may be 2.5 mg once daily. The dose of 2.5 mg may also be used when adding amlodipine to other antihypertensive agents. Dose may be increased at intervals of 7-14 days to achieve BP goals. Doses may be increased up to a maximum of 10 mg once daily.

Amlodipine can be used in combination with ACE inhibitors/ARBs, and low dose diuretics for treatment of hypertension. Use in combination with beta-blockers is of benefit in patients with chronic stable angina.

Contraindications:

Cardiogenic shock, unstable angina, significant aortic stenosis. Worsening angina or increased risk of myocardial infarction may be seen

Cautions:

Drug interactions: Beta-blockers enhance hypotensive effect of amlodipine. Amlodipine increases exposure to simvastatin (dose of simvastatin should not exceed 20 mg per day). Amlodipine also increases exposure to ciclosporin and tacrolimus.

Side effects:

Generally well tolerated. Side effects are dose related and commoner in women. Pedal edema is the chief side effect, seen in around 10% of people on 10 mg daily, and may be decreased in patients receiving angiotensin converting enzyme inhibitors or angiotensin receptor blockers. Headache and flushing related to vasodilation may disappear after a few days.

Use in Pregnancy and breast feeding

Pregnancy Class C. Use if potential benefits outweigh risk. Avoid in lactation.

Hepatic impairment: may need dose reduction

Renal impairment: No modification of drug dose is required.

Angiotensin converting enzyme inhibitors with focus on enalapril and its use in hypertension

Pharmacology: Angiotensin converting enzyme (ACE) inhibitors are drugs which inhibit the conversion of angiotensin I to angiotensin II (a potent vasoconstrictor) and the degradation of bradykinin. They represent a real advance in cardiovascular therapy and have broad spectrum of proven beneficial effects in heart failure, hypertension, renal disease and cardio-protection after myocardial infarction. They are generally well tolerated with no effect on blood glucose or lipids, with adverse effects which are occasional (e.g. cough), or quite rare (e.g. Angioedema). These adverse effects are not dose related. Some adverse effects are seen when administered in patients with heart failure on high dose diuretics (first dose hypotension), or pre-existing renal parenchymal and vascular disease (rise in creatinine, hyperkalaemia), which may be dose related. ***Use of all ACE inhibitors is contraindicated in pregnancy.***

Indications for enalapril:

Hypertension, heart failure (all stages), nephropathy (non-diabetic and diabetic), cardio-protection in early phase acute MI and post-MI LV dysfunction.

Dose, titration, and use in combinations:Initial dose in hypertension: 5 mg in one or two divided doses daily. In patients who have received diuretics, those who were elderly, the initial dose may be 2.5 mg⁵. The dose may be usually increased to 10 mg above which the additional benefit may be minimal⁶, although the maximum dose mentioned for hypertension is 20 mg per day.

Enalapril can be used in combination with low dose diuretics, calcium channel blockers for treatment of hypertension. ACE inhibitors should not be combined with ARBs.

Contraindications: Pregnancy is a contraindication for use of ACE inhibitors. Bilateral renal artery stenosis, History of hypersensitivity (including angioedema).

Cautions:

Renal function may be assessed before starting therapy. In patients receiving diuretics especially high dose diuretics, there is a risk of first dose hypotension, which may be minimised by using a low dose of enalapril, close medical supervision. Up to 30% increase in serum creatinine may occur on starting ACE inhibitors, which is reversible. Hyperkalemia can occur if there is renal impairment, or patient is on potassium containing salt substitutes.

Side effects:

⁵70. Opie L.H, Gersh B.J, editors. Drugs for the Heart. 8th ed: Saunders; 2013.

⁶70. Ibid.

Generally well tolerated. Cough is the most common side effect; angioedema is rare and may be potentially serious.

Breast feeding: Limited information. Do not use enalapril for the first few weeks of life, especially in the case of preterm infants because of risk of neonatal hypotension

Pregnancy Class D Use in second and third trimesters confers risk of oligohydramnios, and birth malformations.

Hepatic impairment: may need dose reduction, and close monitoring.

Renal impairment: may need dose reduction when creatinine clearance is less than <30 ml/min (approximate serum creatinine 3 mg/dl), when dose should be 2.5 mg once a day.⁷

⁷ US FDA full prescribing information for enalapril.

Thiazide diuretics for use in hypertension with special focus on low dose hydrochlorothiazide:

They act by increasing sodium excretion. Thiazide diuretics are useful agents in the therapy of hypertension as first line drugs and as add on therapy when initial therapy with calcium channel blockers, ACE inhibitors does not achieve target for BP control. Benefits on cardiovascular outcomes have been proven for hydrochlorothiazide, chlorthalidone and indapamide. They are long acting agents effective as once a day therapy. In high doses(25 mg and above) thiazides have metabolic side effects like glucose intolerance, worsening of lipids, hypokalaemia, but given in low doses (12.5 mg) they exert near maximal lowering of BP without producing biochemical changes as noted above. Thiazide like agents like chlorthalidone, indapamide are also available, which are longer acting than hydrochlorothiazide, and have beneficial outcomes on cardiovascular mortality documented in clinical trials.

Indications for thiazides:

Hypertension, Heart failure

Dose, titration, and use in combinations in hypertension

Dose in hypertension: 12.5 mg once daily. Increasing the dose to 25 mg daily may not increase antihypertensive effect but can increase risk of hyperglycemia.

Low dose hydrochlorothiazide can be used in combination with calcium channel blockers, and ACE inhibitors for treatment of hypertension. **The combination of thiazide diuretics with beta-blockers is not preferred as it increases the risk of new onset diabetes as well has an adverse effect on lipids.**

Contraindications: severe hypokalemia, hyponatremia, hypercalcemia.

Cautions

Thiazides can worsen glycemic control and gout.

Side effects: Gastro-intestinal disturbances, orthostatic hypotension, altered plasma lipid concentration, metabolic and electrolyte disturbances (including hypokalaemia, hyponatraemia, hypomagnesaemia, hypercalcaemia, hyperglycaemia). Occasional thrombocytopenia, impotence.

Pregnancy: Not used to treat hypertension in pregnancy. Administration in third trimester carries risk of neonatal thrombocytopenia.

Hepatic impairment: Avoid in severe liver disease; hypokalemia may precipitate hepatic encephalopathy

Renal impairment: Avoid if creatinine clearance is less than <30 ml/min (approximate serum creatinine 3 mg/dl), when they may be ineffective.

Drug group	Compelling indications	Compelling contraindications	Usual dose (reduce in elderly)	Side effects
Thiazide diuretics Hydrochlorothiazide	Isolated systolic hypertension (in elderly)	Gout	12.5-25 mg	Metabolic – hypokalemia, hyperglycemia, hyperuricemia Low dose minimizes metabolic effects
ACE inhibitors Enalapril	Diabetes (especially with proteinuria or cardiac disease) History of stroke, MI, hypertension with heart failure CKD where close biochemical monitoring possible	Pregnancy Hyperkalemia Bilateral renal artery stenosis	5 -20 mg (enalapril)	Dry irritating cough Angioedema Hyperkalemia and reversible decline in renal function in some
Calcium channel blockers Amlodipine	Isolated systolic hypertension (in elderly) CKD where close biochemical monitoring NOT feasible	No compelling contraindication. Heart failure, tachyarrhythmia are possible contraindications	5-10 mg	Pedal edema at higher doses Headache Tachycardia
Beta-blockers Atenolol	Previous MI Heart failure (use metoprolol, bisoprolol, carvedilol)	Asthma AV block	25-100 mg (atenolol)	Fatigue, reduced exercise tolerance Hyperglycemia especially when combined with diuretics
Angiotensin receptor blockers Losartan	As in ACE inhibitors Use if ACE inhibitors have side effects like cough	Pregnancy Hyperkalemia Bilateral renal artery stenosis	50-100 mg (losartan)	Cough (rare) Hyperkalemia and reversible decline in renal function in some

Adjunctive therapy

Low dose aspirin may be given to patients with hypertension and cardiovascular disease, or well controlled hypertensives with high cardiovascular risk (>3 risk factors).

Statins are indicated in hypertensives with cardiovascular disease, LDL-C >190 mg/dl, coexisting diabetes, or multiple cardiovascular risk factors.

HYPERTENSIVE URGENCIES AND EMERGENCIES

SBP>180, DBP>110-120

Assess for following and **investigate as appropriate**: creatinine (all), x-ray chest, ECG, CT scan

- A** Altered consciousness
- B** Breathlessness
- C** Chest pain (ischemic)
- D** Deficit (weakness in one or more limbs) or decreased urinary output
- E** Edema
- F** Fundus if feasible- hemorrhages, exudates, papilledema
- G** Generalized seizures

HYPERTENSIVE URGENCY - none of the above

Use **oral** drugs

Reduce BP over hours to days

HYPERTENSIVE EMERGENCY – one or more of the above

Reduce BP (only rarely to normal) over minutes to hours, according to type of emergency

Use **parenteral** drugs, choice depends upon type of emergency (see list below)

DO NOT USE SUBLINGUAL NIFEDIPINE

Types of hypertensive emergencies

Accelerated Malignant Hypertension

Cardiac – acute left ventricular failure, myocardial infarction, unstable angina

Neurologic – hypertensive encephalopathy, ischemic stroke, intracranial hemorrhage, head injury

Renal – acute glomerulonephritis#, renovascular hypertension

Surgical – post-operative hypertension, severe burns

Obstetric – eclampsia#

Hypertensive emergency may occur even at BP levels lower SBP 180 and DBP 110 mmHg

FOLLOW UP, MONITORING AND IMPROVING ADHERENCE

Team approach involving physicians, allied staff and community based health workers.

Hypertension registry at PHC and CHC level to ensure tracking of patients.

Monitor **every 1-2 weeks till target BP achieved**. Thereafter frequency determined by severity of hypertension, co-morbidities, and target organ damage.

Annual review of control of BP, implementation of lifestyle modifications, target organ damage, review of treatment including side effects of drugs.

People with high normal BP should also be advised appropriate lifestyle modifications and encouraged to undergo an annual review.

Improve adherence by

- a **simplified regime** using long acting drugs once a day
- **streamlined methods of dispensing drugs and pill counts**
- supervision by a **family member**
- **periodic counselling** and patient information leaflets
- **home blood pressure monitoring** using a validated automated device

Monitor side effects of drugs

- **Calcium channel blockers** – **peripheral edema**. Dose-dependent, may subside with reduction of dose or combination with ACE inhibitor.
- **Diuretics** – **hypokalemia**, hyperglycemia. Less frequent at lower doses and when combined with ACE inhibitors. **Thiazide induced hyponatremia commoner in elderly**. Can develop rapidly – altered consciousness or seizures.
- **ACE inhibitors** – **dry cough**. May necessitate withdrawal. Risk of hypotension with ACE inhibitors in patients already on diuretics, or on a very low salt diet. **Hyperkalemia** can develop with **high doses of ACE inhibitors**, more commonly in those with renal insufficiency, diabetes, concurrent use of potassium sparing diuretics, and the elderly. A small reversible rise in serum creatinine can occur.

PREVENTION

Promotion of a five point population-wide intervention

- **Weight reduction** in the obese
- **Regular exercise** in the sedentary
- **Decrease salt, sugar and fat** intake
- **Quit tobacco use**
- **Moderation of alcohol** intake

Increased intake of **fruits and vegetables** in addition to decreased salt intake has the potential to lower blood pressure significantly.

This prescription for healthy living along with avoidance of tobacco use can also prevent **obesity, diabetes, cardiovascular disease** and many **common types of cancer**.

FURTHER READING

- 1 STG for Screening, Diagnosis, Assessment, Management of Primary Hypertension in Adults in India – Quick Reference Guide. MoHFW, GOI 2016
Contains key recommendations, clinical pathways and a formulary for healthcare providers.
- 2 STG for Screening, Diagnosis, Assessment, Management of Primary Hypertension in Adults in India – Full Guideline. MoHFW, GOI 2016
Contains details of recommendations with evidence base and methodology followed in developing the guidelines and implementation issues for healthcare providers and programme managers.

This guideline has been developed by the Medicine Sub-group of the Task Force for the Development of Standard Treatment Guidelines for the National Health Mission of the Ministry of Health and Family Welfare, Government of India.

HYPERTENSION

Screening, diagnosis, assessment, and management of primary hypertension in adults in india

Standard Treatment Guidelines - Ready Reckoner

OVERVIEW

Cardiovascular disease is the leading cause of death (including premature death) in India.

Hypertension is the leading risk factor for cardiovascular disease.

Its **prevalence is rising** and approaches **a third of all adults** in urban India.

It is **symptomatic only** when the BP is **extremely high** or when **complications** occur.

Uncontrolled hypertension is a ‘silent killer’. It can cause **serious complications** like stroke (paralysis), heart attack, heart failure, kidney failure and vision loss.

Only a quarter of adults in India are aware of their BP status, **only a quarter of hypertensives are on treatment**, and **only 10-20% of hypertensives have their BP under control**.

Prevention, detection, and effective management of hypertension can prevent deaths and serious disability in lakhs of people, and save hundreds of crores in healthcare costs every year.

This standard treatment guideline has been developed for the **management of hypertension in the Indian context** and has a **primary care focus** and a **public health approach**.



May 2016

Ministry of Health and Family Welfare

Government of India

SCREENING – Zero Cost-No Pain-High Gain Procedure

Opportunistic screening for hypertension should occur **at every encounter with the health system** including with community based health workers.

Targeted screening for hypertension should be community based and target **those at risk of developing hypertension** – age **over 50** years, **overweight** and obese persons, those with **diabetes**, existing **cardiovascular disease**, those with **family history** of hypertension and **smokers**.

Measuring blood pressure

1 Choice of BP device

Mercury sphygmomanometer or any other device (including electronic digital oscillometric devices) **validated** using a standard protocol, and **calibrated** regularly.

2 Patient preparation and position

Patient should **relax for 5 minutes** before measurement. Should **not have had caffeine** in the past hour **or smoked** in the past 30 minutes. Should be seated comfortably with **back supported, arm at heart level**, and legs uncrossed.

3 Cuff size and placement

Appropriate cuff size – length of bladder 80% of arm circumference, width 40% of arm circumference. Use a large adult cuff for an obese patient. Patient should not wear any constrictive clothing. Place **midline of cuff over pulsation of the brachial artery**, 2-3 cm above the cubital fossa.

4 Procedure

For **auscultation based BP measurement**, inflate cuff to 30 mm beyond the disappearance of the radial pulse. Deflate cuff at 2-3 mm per second and record the first and the last sounds by auscultation over the brachial artery as the systolic and diastolic blood pressure respectively.

For **oscillometric devices** follow the manufacturer's instructions and the BP will be displayed automatically.

5 Number of measurements and recording the result

At least 2 readings at an interval of 2 minutes. If readings differ by more than 5 mmHg take a third reading. The lower of the readings should be taken as the representative SBP and DBP.

Recommended action on BP readings (in mmHg) for persons screened by health workers

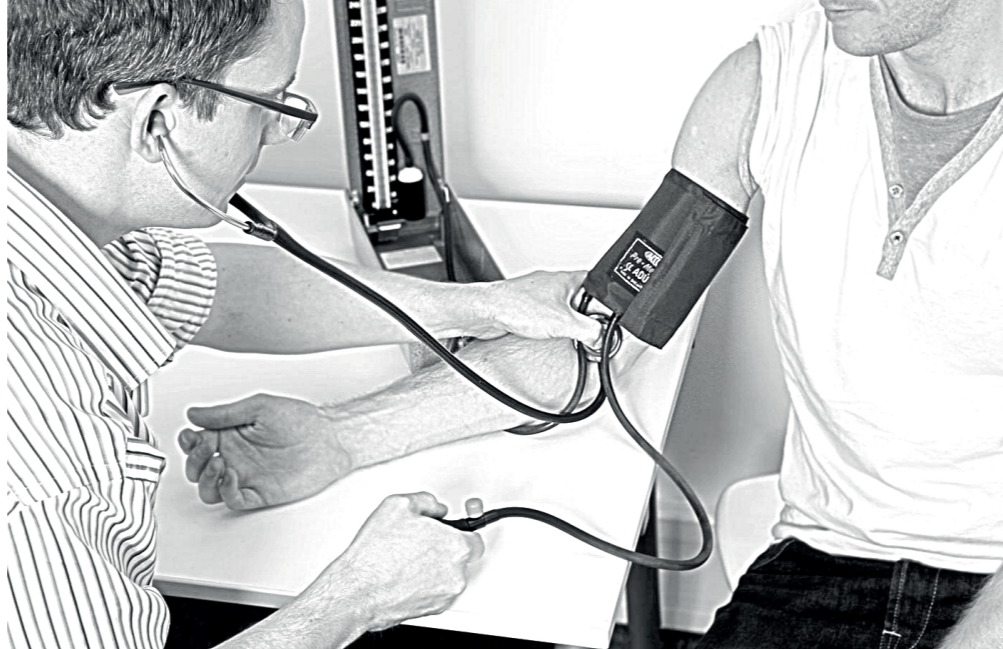
SBP ≥180 and/or DBP ≥110 with or without complications **REFER IMMEDIATELY** to PHC/CHC

SBP 160-179 and/or DBP 100-109 refer to PHC **within 1 week**

SBP 140-159 and/or DBP 90-99 refer to PHC **within 1 month**

SBP 130-139 and/or DBP 85-89 recheck in **1 year**

SBP < 120 and DBP <80 recheck in **2 years**



DIAGNOSIS, CLASSIFICATION

Hypertension is **systolic BP 140 mmHg or higher** and **diastolic BP 90 mmHg or higher**.

TWO readings on at least **TWO occasions**.

Valid device and **standardised BP measurement procedure**.

Category	Systolic BP mmHg		Diastolic BP mmHg
Optimal	<120	and	<80
Normal	120 – 129	and/or	80 – 84
High Normal	130 – 139	and/or	85 – 89
Grade 1 Hypertension	140 – 159	and/or	90 – 99
Grade 2 Hypertension	160 – 179	and/or	100-109
Grade 3 Hypertension	≥180	and/or	≥110
Isolated Systolic Hypertension	≥ 140	and	< 90
Hypertensive urgency ¹	≥180	and/or	≥110
Hypertensive emergency ²	≥180	and/or	≥110

1 Severe asymptomatic hypertension with **no evidence of acute target organ damage**

2 Severe hypertension associated with **ongoing target organ damage** – cardiovascular (e.g. left ventricular failure), cerebral (e.g. hypertensive encephalopathy or stroke), renal (acute renal failure), Grade III-IV retinopathy

EVALUATION

Assess the presence of

- other **cardiovascular risk factors**
- **target organ damage** (LVH or heart failure, proteinuria, renal failure, retinopathy)
- **associated clinical conditions** (diabetes, ischemic heart disease, cerebrovascular disease, CKD)

Essential evaluation

- **History** – **cardiovascular risk factors** (diet and exercise patterns, smoking, alcohol consumption, family history of premature CAD) **symptoms of target organ damage** or **associated clinical conditions** (breathlessness, angina, history of transient ischemic attack or stroke)
- **Examination** – weight, height, BMI, unequal pulses, raised jugular venous pulsations, S3 gallop, and pedal edema
- **Investigation** – fasting capillary/blood sugar, proteinuria

Desirable evaluation in patients with Grade 2 hypertension, diabetes or proteinuria

- History, examination – as above
- Investigations – as above **PLUS** serum creatinine, fasting lipid profile, ECG

Comprehensive evaluation in patients with Grade 3 hypertension, CKD, heart failure

- History and examination – as above **PLUS** fundus examination **PLUS** examine for **clues for secondary hypertension** (moon facies, unequal pulses, postural hypotension, renal artery bruit, palpable kidneys)
- Investigations – as above **PLUS** serum electrolytes, USG abdomen, 2-D Echo

MANAGEMENT - target BP <140/90 mmHg, <150/90 in patients over 80.

The overall aim is to reduce BP to target levels within 6-8 weeks and to reduce cardiovascular risk.

PATIENT EDUCATION discuss the following points

Nature of disease – hypertension is asymptomatic but can produce damage to heart, brain, and kidney if uncontrolled.

Lifestyle measures – can reduce BP, reduce the doses of medicines, and reduce risk of damage to the heart.

Therapy – medicines should be taken every day without a break. The patient should inform the doctor if he notices any side effects.

BP targets and monitoring – inform patients about target BP- which is generally < 140 mm systolic and <90 mm diastolic. Encourage patient to monitor BP at home, if possible.

ALL PATIENTS REQUIRE LIFE-LONG LIFESTYLE MODIFICATION

Dietary change – salt restricted (<5g/day), low-fat diet

Reduce weight – target BMI 18.5-22.9 kg/m²

Regular exercise – moderate intensity, 30 minutes, 5 days a week

STOP SMOKING

GRADE 1 HYPERTENSION (SBP 140-159, DBP 90-99) with

Diabetes **OR** TOD (proteinuria, LVH, retinopathy) **OR** associated clinical conditions

OR more than 3 risk factors – male
men aged >55 years, women aged >65 years
smoking
obesity, including abdominal obesity
dyslipidemia
impaired glucose tolerance
family history of early coronary artery disease

OR inadequate control after 3 months of lifestyle modification

Drug therapy – A or C¹ or D

Add second drug - A+C or C+D or A+D if response not adequate within 2-4 weeks

Add third drug – A+C+D if response not adequate within 2-4 weeks

GRADE 2 HYPERTENSION (SBP 160-179, DBP 100-109)

Drug therapy – A or C or D

Add second drug - A+C or C+D or A+D if response not adequate within 2-4 weeks

Add third drug – A+C+D if response not adequate within 2-4 weeks

GRADE 3 HYPERTENSION (SBP ≥180, DBP ≥110)

Use two drugs - A+C or C+D or A+D

Add third drug – A+C+D if response not adequate within 2-4 weeks

ALL GRADES OF HYPERTENSION WITH ASSOCIATED CLINICAL CONDITIONS

CAD: coronary artery disease - B+A², C

CHF: congestive heart failure - D+A+B, MRA

CKD: chronic kidney disease - A, C, D³

DM: diabetes mellitus - A/C, D

Abbreviations: CAD: coronary artery disease, CHF: congestive heart failure, CKD: chronic kidney disease, DBP: diastolic blood pressure, DM: diabetes mellitus, LVH: left ventricular hypertrophy, SBP: systolic blood pressure, TOD: target organ damage.

Drug classes: **A:** Angiotensin converting enzyme (ACE) inhibitors, (e.g. enalapril) or Angiotensin II receptor blockers (ARBs, e.g. losartan) only if intolerance to ACE inhibitors, **B:** beta-blockers (e.g. atenolol), **C:** calcium channel blockers (e.g. amlodipine), **D:** thiazide diuretics (e.g. hydrochlorothiazide), **MRA:** mineralocorticoid receptor antagonist (e.g. spironolactone).

Footnotes:

¹ Calcium channel blockers are antihypertensives of choice in the elderly (> 60 years).

² Patients with CAD and history of myocardial infarction should receive both beta-blockers and ACE inhibitors.

³ Patients with CKD may need loop diuretics if GFR is low. Those on ACE inhibitors need regular monitoring of creatinine and potassium.