Background Document

Hypertension

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

March 2016

सत्यमेव जयते

Ministry of Health & Family Welfare
Government of India

Section -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 annually in India, due to ischemic heart disease and stroke[6] . 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% (95% CI: 26.7, 33.0) and a higher prevalence in urban areas (33.8% vs. 27.6%, p=0.05), according to recent estimates[8].India's demographic transition with an increasing proportion of elderly people and a sedentary lifestyle and obesity associated with increasing urbanisation, and other lifestyle factors like high levels of salt intake, alcohol and tobacco consumption, are contributing to this burden of hypertension.

Hypertension is a major modifiable risk factor for cardiovascular and renal disease in India, and improved detection and treatment of hypertension in India would reduce a preventable burden of cardiac (congestive heart failure, coronary artery disease), cerebrovascular (ischemic and haemorrhagic stroke) and renal (chronic kidney disease) disease related to hypertension. It has been estimated that a 2 mm population wide decrease in systolic blood pressure in India, would prevent 151,000 deaths due to coronary artery disease and 153,000 deaths due to stroke would be prevented.[7]

Awareness of hypertension in India is low while appropriate treatment and control are 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 prevalence of awareness of hypertension is only in a quarter of rural and two-fifths of urban Indians, and only a quarter and a third of those identified in rural and urban India receive treatment for it. Those who are identified as hypertensive often receive inappropriate care or fail to adhere to therapy, and remain uncontrolled [8]. The prevalence of controlled hypertension is only in around 10% and 20% of rural and urban patients with hypertension respectively.(8) Apart from undiagnosed, uncontrolled hypertension, there is also the challenge of misdiagnosis of hypertension in India. This is because of poorly standardized techniques of BP measurement, poorly calibrated measurement devices, reliance on single readings taken on a single visit for diagnosis rather than multiple readings confirmed by elevated readings on follow up.

The need for a standard guideline for hypertension in India. The published literature consists of guidelines on diagnosis and management of hypertension, some of which are based on a rigorous review of the evidence, while others in addition, have also incorporated consensus based recommendations to address areas of uncertainty. Most guidelines are national in scope (NICE, JNC 8, Canadian Hypertension Education Program, Australian), while others are focused on a wider regional or international audience (European Society of Hypertension guidelines, American Society of Hypertension/International Society of

Hypertension). 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, 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. In view of the above stated reasons a standard guideline was developed for the management of hypertension in the Indian context.

The purpose and approach of the guideline: The National Health Mission has commissioned this guideline to enable a systematic cost-effective approach to the screening, detection, evaluation and management of hypertension in India. This guideline and its accompanying implementation tools in the form of a quick reference guide, algorithms, patient information leaflet and quality standards are intended for use by the healthcare providers, patients and administrators. **The guideline has a primary care focus and a public health approach.** The focus on primary care is crucial since our biggest challenge is that the majority of hypertensives are undiagnosed because of the asymptomatic nature of the disease, and increased detection can only be accomplished by a sustained effort to measure BP in adults at a clinic or by a healthcare provider closest to them. **Hypertension is a primary care problem which is therefore best detected, managed and followed up at a primary care level by a primary care team led by a physician.** The involvement of the community level health workers including the 2.3 million village health workers in India who are trained, supervised, provided logistical support, and suitably compensated, is crucial if we wish to improve detection, assessment, therapy and control of hypertension in India. *The evidence of the potential of community health workers to effectively contribute to control and management of non-communicable diseases is emerging from a number of low and middle income countries* [(9-14)].

Overall this guideline emphasises a public health approach to hypertension, which envisages population based strategies which could decrease the burden of hypertension, increased detection of hypertension by non-physician staff, education of the patient to improve outcomes of treatment, use of cost-effective diagnostic tools and a core list of 5 efficacious, safe and economical anti-hypertensives, and suggests systemic mechanism to maintain adherence. It is a tool to empower healthcare providers, especially those in primary care, to manage hypertension. It builds on the technical and operational platform suggested by the guidelines of the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular diseases and Stroke[(15).] It also incorporates elements of the Indian Public Health Standards as they relate to the assessment and management at public health facilities in India[(16)]**.Improved detection of hypertension is a public health imperative in India, and management of hypertension is one of the most important and cost-effective interventions in primary care.**

A public health approach to hypertension in India would involve the five components detailed below. This includes 5 population level interventions for prevention of hypertension of which reduction of obesity, salt intake and cessation of tobacco use are the most important; screening of the adult population at 5 points of care for hypertension by trained staff using standardised BP measurement with validated devices, and management

of hypertension with lifestyle modifications combined with therapy using representative drugs from five classes of anti-hypertensives, which should be made available in the public health system:

1. **Prevention**: Promotion of a five point population wide intervention on weight reduction in the obese, increasing exercise levels in the sedentary, decrease in salt intake, cessation of tobacco use, moderation of alcohol use.
2. **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. This will include all points and levels of care – the village/multipurpose health worker, trained non-physician staff at sub-centres, primary health centre, community health centre, and referral hospital (District hospital, Medical College). This screening will also enable people with high normal BP to be identified, so that they can be prevented from developing hypertension by use of appropriate lifestyle modifications.

   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 those in which hypertension is most prevalent and poses the maximum risk. This includes people with age > 50 years, those who are obese, diabetic, current smokers, those who have history of any cardiovascular disease (coronary artery diseases, stroke etc.), or a history of hypertension or premature cardiovascular disease in the family. We recommend that one validated electronic BP device and at least 1 trained person per village should be made a reality, so that these high risk group can be screened for hypertension at least once every 2 years. Screening will involve BP measurement using a standardised procedure and persons will receive advice and/or referral appropriate to the BP level.
3. **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. Assessment will focus on target organ damage related to hypertension, co morbidities like diabetes, and correctable risk factors. Initiation of treatment whenever required, should take precedence over referral for detailed laboratory evaluation. The guideline envisages integration of care of hypertension with care of other non-communicable diseases.
4. **Management**: Ensure availability of representative drugs from a core list of 5 medications – diuretics, calcium channel blockers, ACE inhibitors, Angiotensin Receptor blockers, and beta-blockers.
5. **Monitoring and 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.

Hypertension can be easily diagnosed using inexpensive technologies, and easily treated with medications which are effective and safe.[17] Management of hypertension can be of the one most cost-effective public health interventions. The current cost of provision of antihypertensive therapy with 2 drugs viz. a calcium channel blocker and an ACE inhibitor,

along with aspirin and a statin in a pooled public procurement based system is as low as under a rupee a day.

This guideline while emphasising a primary care led approach also recommends creation of a continuum of care for this chronic disease, with referrals proceeding in both directions in the health system. The suggested model for the screening, diagnosis and management of hypertension offers scope for integration of initiatives for other chronic diseases e.g. diabetes mellitus, while lifestyle interventions suggested in this guideline would also have a salutary effect on incidence of other chronic diseases. The accompanying patient information material for patients with hypertension will be of value to patients with hypertension as well as the general population, to increase awareness of this common disease which can be easily diagnosed and treated.

SECTION 2.1 EXECUTIVE SUMMARY OF ISSUES FOR PROVIDERS AND PROGRAMME

Key issues for the Providers:

1. Most people with hypertension in India are unaware of their condition. To improve rates of detection of hypertension, all adults over the age of 18 should undergo opportunistic screening for hypertension during visits to non-physician health staff as well as health facilities. In addition, community based health workers should also do targeted screening of high risk groups under their care – elderly > 60 years, diabetic, obese, those with any cardiovascular disease, family history of premature cardiovascular disease.

2. Screening for hypertension should involve measurement of blood pressure using a validated device (mercury or digital) with an appropriate sized cuff, following a standardised procedure on a relaxed patient, seated with arm supported at the heart level with the legs uncrossed. Diagnosis of hypertension should be based on a minimum of 2 sets of readings on 2 different occasions, which are at least 1-4 weeks apart, except in the case of hypertensive emergencies and urgencies. Hypertension in persons <80 years of age is diagnosed on documentation of persistent elevation of systolic BP of > 140 mm and/or 90 mm diastolic.

3. Patients should be educated about the nature of the disease and its therapy, about lifestyle modifications that can reduce BP and cardiovascular risk. Patients should undergo assessment for cardiovascular risk factors, target organ damage related to hypertension, associated clinical conditions like diabetes, chronic kidney disease, and cardiovascular disease (e.g. coronary artery disease, stroke). Most of these assessments which involve history, clinical examination, and examination for proteinuria, diabetes, serum creatinine, lipids and ECG will be possible to complete at the PHC and CHC levels with the advent of the free diagnostics initiative.

4. Hypertension is a primary care issue and best managed at the primary care level with a team approach involving physicians, and allied staff. .Hypertension should be managed using a combination of lifestyle modifications and use of drug therapy with ACE inhibitors, Calcium channel blockers and thiazide diuretics, either alone or in combination. The benefit of treatment is related to reduction of BP rather than the use of a particular drug. All drug classes have equivalent effects but some are preferred in the presence of compelling indication. Both Calcium channel blockers and ACE inhibitors are effective, have few side effects, and have no adverse metabolic consequences or high requirements for monitoring.

5. The target BP should be less than < 140 mm systolic in persons < 80 year old and < 150 mm systolic in those over 80 years old, while the target diastolic BP is < 90 mm Hg. To achieve the target BP especially in those with Grade 2 and Grade 3 Hypertension may require the use of 2 or even drugs. Grade 1 HT which is uncomplicated, may be given a trial of lifestyle modifications alone for 3 months,

6. Efforts should be made to promote follow up and adherence to long term therapy to antihypertensive. In selected patients especially those with associated cardiovascular disease, both statin and aspirin may be given along with antihypertensive to reduce risk of CV event. In patients with diabetes, statins may be indicated.

Key issues for the programme:

1. Hypertension is a major modifiable health related risk factor in India, contributing to the top causes of death in the country. Detection and proper management of hypertension could lead to substantial decrease in the burden of coronary artery disease, heart failure, stroke, and renal failure in the country. Hypertension can be prevented by minimising risk factors like obesity, physical inactivity, and high salt intake, moderate to high alcohol consumption at the population level.

2. Hypertension is a non-communicable disease whose diagnosis can be accomplished non-invasively, which does not require frequent laboratory assessment, and which can be managed using a core list of 3-4 safe, efficacious and cost-effective drugs.

3. The improved detection, assessment, and management of hypertension will require availability of a trained community health worker and a BP measurement device – preferably a digital device which will obviate the need for auscultation. Such personnel can also receive training in the education of patients with hypertension. We recommend that the Bureau of Indian Standards validates the digital BP devices available in the market using international validation protocols.

4. The assessment of patients with hypertension will require upgradation of diagnostic services at the primary and community health centres. The key investigations required will be screening tests for diabetes and proteinuria and an ECG machine at the PHC level, and facilities for lipid profiles and renal function tests at CHC level.

5. The programme should ensure adequate quantities of a list of first line antihypertensives – amlodipine, enalapril, hydrochlorothiazide, at all times in the public health system. Some other drugs like atenolol, losartan, may sometimes be required for individual patients. To deal with hypertensive emergencies, the public health system will require availability of intravenous frusemide, oral clonidine, and intravenous labetalol. Adjunctive drugs like statin, and aspirin will also be required. The entire package of antihypertensive and adjunctive drugs is available to quality assured public procurement programme at less than a rupee a day. Detection and management of hypertension can be a truly cost-effective intervention in public health.

6. We recommend the creation of a hypertension registry at the PHC level which will generate data on burden of hypertension in the community, facilitate follow up of patients especially those with severe hypertension, and allow analysis of outcomes. It will also create a template which can be used for other non-communicable diseases.

Section 2.2- KEY RECOMMENDATIONS

KEY RECOMMENDATION: SCREENING

1: Target population, and operational procedure of screening

1.1. We recommend an ongoing initiative to increase awareness of hypertension as a widely prevalent but asymptomatic disease associated with many adverse outcomes like heart attacks, strokes, kidney failure. Most patients with hypertension in India are unaware of their status and remain undetected. 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 the elderly (>60 years), obese, current smokers, those with diabetes, those with existing cardiovascular disease, and those with a strong family history of heart disease or stroke can be undertaken by trained non-physician staff.

2: Standardised BP measurement procedure

1.3. The screening 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 standardised BP measurement procedure.

1.4. Blood pressure should be measured a few (5) minutes after the patient is in a relaxed state, is seated with the arm at the level of the heart, with legs uncrossed. The cuff should have a bladder whose length is about 80% and whose breadth is about 40% of the arm circumference. If the auscultation based method is being used, the then the cuff should initially be inflated to at least 30 mm Hg beyond the point of disappearance of the radial pulse. It should then be deflated at a rate of 2-3 mm per second. The first and the last audible Korotkoff sounds should be taken at the systolic BP and diastolic BP respectively. The column should be read to the nearest 2 mm Hg.

1.5. At least 2 readings should be taken at each visit with an interval of at least 1 minute between the measurements. If the two readings are substantially different a third reading should be taken. The lower of the two readings should be taken as the representative SBP and DBP.

3. Rescreening, reassessment, and referral of individuals found to be normal or elevated BP on screening by allied health staff

1.6. Depending on the BP readings, the person may be advised review up on an annual or 2 yearly basis, or referral (immediate or deferred) for diagnosis or treatment of hypertension.

1.6.1 Persons with normal BP (<130/80) should be advised a recheck in 2 years.

1.6.2 Persons with high normal BP: systolic BP of 130-139 mm Hg and diastolic of 80-89 mm Hg should be advised a recheck in 1 year, or sooner if indicated due to other risk factors or diseases.

1.6.3 Persons with BP > 140 mm Hg systolic and/or greater than 90 mm Hg diastolic should be rechecked within 1-2 weeks and then classified as hypertensive or high normal.

1.6.4 Persons with BP of >160 mm Hg systolic and/or greater than 100 mm Hg diastolic should be advised early referral to the primary health centre if measurements have been made at a peripheral health facility below the level of a primary health centre, for confirmation of the diagnosis of hypertension.

1.6.5 Persons with BP of >180 mm Hg systolic and/or greater than 110 mm diastolic if documented by a non-physician staff, should be immediately referred to the primary health centre or community health centre (whichever is nearer to the residence) for further investigation to exclude any acute target organ damage, and for initiation of treatment, which is required on an immediate basis. Patients documented with this level of BP in a health facility would require assessment for target organ damage, and gradual reduction of BP over hours and days if there is no acute target organ damage.

1.6.6 Hypertensive emergencies are potentially life-threatening situations where hypertension (usually severe and > 180 mm systolic and >120 mm diastolic associated with the presence of recent onset and progressive target organ damage resulting in cardiovascular, neurologic, renal and visual dysfunction. These situations may include severe hypertension associated with acute coronary syndrome (chest pain), acute left ventricular dysfunction (shortness of breath), and hypertensive encephalopathy (altered sensorium), stroke (focal weakness), and renal failure. It is most often associated with severe hypertension, except in children and pregnant women where hypertensive emergencies can occur with lower elevations of BP.

1.7 All persons who are screened for hypertension should be advised lifestyle measures including maintaining a daily salt intake appropriate to their occupation, 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.

KEY RECOMMENDATION: 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 recommended.

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

2.4 Patients with hypertension should be classified in the following manner:

- **Grade 1 Hypertension**: systolic 140-159 mm and/or diastolic 90-99 mm
- **Grade 2 Hypertension** : systolic 160-179 mm and/or diastolic 100-109 mm
- **Grade 3 Hypertension** : systolic 180 or above and/or diastolic 110 or above
- **Isolated systolic hypertension**: systolic > 140 mm but diastolic <90 mm.
- **Hypertensive urgency**: Severe asymptomatic hypertension (usually Systolic > 180 mm , Diastolic >120 mm)
- **Hypertensive emergency**: Severe hypertension accompanied by cardiac (e.g. acute left ventricular failure), neurological (e.g. hypertensive encephalopathy), or renal dysfunction.

KEY RECOMMENDATIONS: PATIENT EDUCATION AND ASSESSMENT

3.1 Patients should be counselled about the nature of the disease, and the management of hypertension, before being subjected to laboratory evaluation and drug treatment. The education and assessment of the patients should be tailored to their understanding, preferences and social circumstances.

3.1.1 Patients should be counselled about hypertension being an asymptomatic condition which can lead to disabling and life-threatening complications like stroke, heart attack and renal failure. Patient should be counselled about need for long-term therapy, need for regularity of drug intake, informed about the targets for BP control, and encouraged to monitor efficacy of therapy through regular check-ups which can include home based monitoring of BP.

3.1.2 The patient should be counselled about the important role of lifestyle measures in reducing hypertension and reducing risks of cardiovascular disease.

3.2 The effective control of blood pressure by initiation of therapy, if required, should not be delayed if laboratory evaluation is delayed or cannot be done.

3.3 The assessment of a patient with hypertension is aimed at assessing **overall cardiovascular risk for cardiovascular events like stroke, ischemic heart disease, heart failure, peripheral artery disease**.

3.3.1 The risk of clinical events in a patient with hypertension depends on

- the level of blood pressure
- risk factors (diabetes or impaired glucose tolerance, smoking, dyslipidemia, obesity, male gender, age >55 years in male,) ,
- target organ damage(heart, kidney, retina),
- Presence of associated clinical conditions [clinical cardiovascular disease (coronary artery disease, cerebrovascular disease, PAD), kidney disease].

3.4 The risk factors, target organ damage and associated clinical conditions can be detected on history, physical examination (including ophthalmoscopy), and investigations like blood glucose, lipids, serum creatinine, urinalysis, and ECG.

3.4.1 Physicians and allied health staff should assess and evaluate patients for cardiovascular risk factors like smoking, obesity, diabetes. Reduction of risk by adoption of healthy living habits-(dietary changes, exercise, smoking cessation) is to be reinforced by all cadres of health workers. Screening for hyperlipidemia can be suggested and carried out in patients at PHC/CHC especially in those who are obese, or have family history of premature coronary artery disease, or have existing cardiovascular disease.

3.4.2 Physicians and allied staff can detect target organ damage by eliciting symptoms of shortness of breath, decreased urine output, and noting signs of heart failure like swelling of feet, and other signs of heart failure. Target organ damage can also been detected by testing urine for proteinuria, noting evidence of left ventricular hypertrophy on ECG, and features of hypertensive retinopathy on ophthalmoscopy. These signs of target organ damage can all be detected at PHC/CHCs.

3.4.3 Physicians and allied staff can detect associated clinical conditions like clinical cardiovascular disease and chronic kidney disease by eliciting history of chest pain suggestive of angina and/or pain in the lower limbs on walking suggestive of claudication, and/or history of stroke with weakness of limbs. CKD can be detected by persistently abnormal serum creatinine measured at the CHC level.

3.5 The overall risk of cardiovascular events can be assessed from these assessments as follows:

Level of blood pressure: Grade 2 Hypertension even in isolation confers moderate risk (20-30% risk of CV event over 10 years), while Grade 3 hypertension confers high risk (Over 30% risk of CV event over 10 years).

Risk factors: Presence of 3 or more risk factors confers moderate to high risk even in a patient with Grade 1 hypertension, while even fewer risk factors increase risk in Grade 2 hypertension.

TOD/Diabetes/CKD/Clinical cardiovascular disease: Presence of any target organ damage, diabetes, chronic kidney disease or clinical cardiovascular disease confers high to very high risk on patients.

3.6 The level of BP and results of the assessment will influence the following:

- when to start antihypertensive therapy,
- Which antihypertensive to use.
- whether statins and/or aspirin are indicated, to reduce cardiovascular risk
- Which other associated conditions will need management (diabetes, clinical cardiovascular disease, chronic kidney disease).

3.7 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.

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

KEY RECOMMENDATIONS: THERAPEUTIC RECOMMENDATIONS

Lifestyle modifications and initiation of drug therapy

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 measures** including reduction of salt intake, stopping tobacco intake, and reduction of body weight in those who are obese, are part of management of all patients with hypertension.

4.2.1 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.

4.2.2. 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.

4.3.1 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 (clinical cardiovascular disease), PAD
- Diabetes
- Presence of chronic kidney disease
- Patients with 3 or more risk factors[1] (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

[1] 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

disease 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.

4.3.4. 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. If the initial screening by the non-physician medical staff revealed Grade 2 hypertension, then therapy can be initiated on the first visit of the patient to the primary health centre/community health centre.

4.3.5. 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 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 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) and if required and 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.

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. 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. 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 used as an add on therapy, the initial dose of amlodipine 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. 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.

4.6.10 Negative recommendation: 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.

4.6.11. 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.

4.7. Recommendation: Review and respond to possible causes of poor response to BP medications

4.7.1 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.

4.8 Therapy of hypertension and associated conditions:

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 (4.5.2.1) 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.*

4.8.3.3 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 MAP[2]>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 Hypertension in the elderly:

[2] 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

4.9.1Postural 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.

Postural fall of >20 mm in systolic and >10 mm diastolic indicates postural hypotension is a risk factor for falls.

4.9.2 In a patient with postural hypotension titrate target according to standing BP.

4.9.3 Start therapy with lower doses of drugs and change doses or add drugs at a slower rate in elderly patients.

4.9.4 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.

4.9.5. In elderly patients more than 80 years (the very elderly), the blood pressure target for control is <150 mm systolic and <90 mm diastolic.

4.9.6. 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.

4.9.7 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.

4.9.8 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. 10. **Hypertensive emergencies:**

4.10.1 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 'ABCDEFG' 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.

4.10.2 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.

4.10.3 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.

4.10.4 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.

4.10.5 In the case of acute left ventricular failure reduction of the elevated BP is indicated with a parenteral loop diuretic like frusemide 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.

4.10.6 Patients with a hypertensive emergency should be examined for any clinical clues to the presence of secondary hypertension and be evaluated for the same.

4.11. Hypertensive urgencies

4.11.1 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 (patient has none of the symptoms or signs referred in the mnemonic ‘ABCDEFG’ in the pathway on assessment and management of 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.

4.11.2. 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.

4.11.3. 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.

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

4.11.5 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 auto regulation in vascular beds, and cause serious cerebral and cardiac complications related to ischemia.

4.11.6 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.

4.11.7 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.

4.12 Integration with other interventions to reduce cardiovascular risks

4.12.1 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.

4.12.2 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.

4.12.3 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).

4.12.4 **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.

4.12.5 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.

4.12.6 **Statins are recommended, regardless of presence/absence of hypertension** in the following patient groups[3]

- Patients with overt atherosclerotic cardiovascular disease (coronary artery disease, cerebrovascular disease, and peripheral arterial disease), regardless of age.

- Patients with age with≥ 21 years, where LDL –cholesterol is more than 190 mg/dl, and where secondary cause of hyperlipidemia has been excluded.

- In patients who are diabetic and in the age group of 40-75 years, and LDL cholesterol is between 70-189 mg/dl

4.12.7. Statins are indicated in **hypertensive patients** aged more than 40 years with high cardiovascular risk (3 or more of a list of 11 cardiovascular risk factors)[4]

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

KEY RECOMMENDATION: MONITORING, FOLLOW UP AND IMPROVING ADHERENCE TO THERAPY

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

[3]Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology.* 2014; 63(25_PA):2889-2934.

[4]Daskalopoulou SS, Rabi DM, Zarnke KB, et al. The 2015 Canadian Hypertension Education Program recommendations for blood pressure measurement, diagnosis, and assessment of risk, prevention, and treatment of hypertension. *Canadian Journal of Cardiology.* 2015; 31(5):549-568.

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 co morbidities, 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.

5.3.1. 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.

5.3.2. 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.

5.3.3. 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. Angiotensin receptor blockers have a lower rate of drug-induced cough but higher rate of hypotension.

5.4 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.

5.5 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.

5.6 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)

5.7 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.

5.8 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.

5.9 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.

5.10 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.

SECTION 3: METHODOLOGY OF DEVELOPMENT OF GUIDELINE

A Task Force was constituted in December 2014 to guide the development of Standard Treatment Guidelines (STG) in India for application in the National Health Mission. The Task Force subsequently approved the draft STG development manual of India (Part 1) for development of adapted guidelines. In addition, it approved a list of 14 topics recommended by a subgroup of the task force appointed to select prioritized topics for STG development. These 14 topics are from 10 clinical specialties for which the first set of STGs will be developed. The topic of Detection, Assessment, Management of Essential Hypertension was included in this first list and was the dealt with by the Internal Medicine clinical subgroup.

1. Formation of the STG group:

A multidisciplinary group composed of a mix of primary care practitioners, family medicine practitioners, teaching faculty, practising and academic cardiologists, nurse practitioners, voluntary sector representatives, and a patient representative was formed by June 2015. The composition of the subgroup is mentioned in the table below.

Scoping the STG: The scope of the STG was discussed at the first clinical subgroup meeting in Delhi in July 2015 and was finally subsequently in an online consultation held with all members of the subgroup, since some were unable to attend the meeting in Delhi.

Facilitator	Anurag Bhargava, Professor, Dept. of Medicine, Yenepoya Medical College, Mangalore, Karnataka
Writing team	Anurag Bhargava, RajkumarRamasamy, Ambuj Roy, KartikKalyanram, Rakesh Biswas, Reginald Alex
Expert	Ambuj Roy, Additional Professor, Department of Cardiology, All India Institute of Medical Sciences, New Delhi
Primary Care practitioners	RajkumarRamasamy, (KC Patty Primary Health Care Centre, KC Patty, Kodaikanal Taluk, Tamil Nadu),KartikKalyanram, Rishi Valley Rural Health Centre,Venkatesh , Department of Family Medicine, Christian Medical College, Vellore
Physician	Rakesh Biswas,Professor, L.N.Medical College, Bhopal Reginald Alex, Professor, Department of Emergency Medicine

Private Practitioner	Prashant Jagtap, Wockhardt Hospital, Nagpur
Nursing Practitioner	Mercy Oomen, Department of Nursing, Christian Fellowship Hospital, Bissamcuttack,Orissa
Patient representative	SouravDutta,Bhopal
Public health specialist	John Oomen, Department of Community Medicine, Christian Fellowship Hospital,Bissamcuttack, Orissa
NGOs	KartikKalyanram, RajkumarRamasamy (affiliations as mentioned above)
Others	SurajitNundy (Physician, and Expert on Health Information systems, New Delhi)

The induction and orientation session was held on 21st July 2015 in which the facilitator (Chair) welcomed all the members of the subgroup, and set up the rules of operation based on the STG development manual, on the consistent use of terminology and definitions, using the structured power-point presentation provided by NHSRC/NICE. None of the members report any conflict of interest in the development of this guideline and have all signed their declarations

2. **Search and selection of evidence based guidelines:**

In view of the paucity of time available to develop this guideline, a decision was taken by the Task Force for the Development of STGs for the National Health Mission that these STGs would be adopted and/or adapted from existing evidence based guidelines to make them relevant to our context, resource settings and priorities.

A search was conducted for evidence based guidelines on primary hypertension, which had been published within the past 5 years and which had been framed using evidence based methodology and using international guideline development criteria. The National Guidelines Clearinghouse (NGC) website was used since the guidelines have already gone through a rigorous 'quality' sifts based on international standards (http://www.guideline.gov/). The criteria for Inclusion of Clinical Practice Guidelines in NGC are based on the Institute of Medicine (IOM) Clinical Guidelines Standards 2011 and IOM systematic review standards 2014. The guidelines available on the database have

been developed, reviewed, or revised within the past five years. The NGC entry criteria are similar to the AGREE II Instrument criteria[5].

Three of these guidelines were listed on the National Guidelines Clearinghouse , viz: Hypertension: Clinical management of primary hypertension in adults NICE guidelines [CG127]: National Institute for HealthCare Excellence; 2011 from the UK([18]), The 2015 Canadian Hypertension Education Program recommendations for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension([19]); the 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8),from USA.([20]) An additional guideline selected was the 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC).([21]) This guideline was evaluated by a methodology expert from NICE UK, who opined that its methodology was evidence based and its formulation was in concordance with the AGREE 2 instrument. There were some other guidelines e.g. Indian Guidelines on Hypertension-3, and the National Heart Foundation of Australia (National Blood Pressure and Vascular Disease Advisory Committee).Guide to management of hypertension 2008. Updated December 2010, which were not evidence based and did not follow the criteria for development of guidelines; which were therefore not followed. We also referred to the WHO /International Society of Hypertension guidelines of 2003 and the seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report.

The scope of our guideline was broad and to address the evidence base for certain sections e.g. screening and cardiovascular risk prevention, we searched other evidence based guidelines like the US Preventive Services Task Force guideline for screening for high blood pressure,([22]) and the European guidelines on cardiovascular disease prevention in clinical practice.([23]) We also utilised the Cochrane database of Systematic Reviews for certain issues like the use of aspirin for primary and secondary prevention of cardiovascular diseases.

Some of the issues in the management of patients of hypertension are a matter of judgement since there is no supporting data from randomised controlled trials. For example, whether the best strategy for optimisation of BP control is to add drugs sequentially, or to maximise the dosage of the first. We therefore also utilised some recommendations from a consensus based guideline developed for international use by the American Society of Hypertension and the International Society for Hypertension. ([24])

3. Search and select recommendations:

Each of the guidelines referred to above was searched for recommendations relevant to the scope of our guidelines, and there were significant areas of consensus between evidence based guidelines. It was found that there was no single guideline which could

[5] AGREE II Instrument http://www.agreetrust.org/

be adopted fully to suit our requirements. For example, the NICE guideline had many recommendations applicable to our setting but considered ambulatory blood pressure monitoring as the gold standard for diagnosis. The assessments recommended for hypertensives varied between guidelines and different cardiovascular risk estimation tools were in use which were based on data on cohorts of the local population e.g. QRISK2 in UK, SCORE in Europe, pooled cohort equation based tool in USA. Therefore for each issue mentioned in the scope document we searched all the evidence based guidelines for recommendations and selected them on the basis of the suitability to our settings in terms of contexts, resources and our priorities.

4. Adaptation and adoption of recommendations:

The clinical sub-group decided in the meeting to adapt recommendations in existing evidence based guidelines by paraphrasing them & paying close attention to the integrity of the recommendation, rather than quote verbatim. This decision was taken for a number of reasons explained here. As mentioned in the preceding paragraph we selected recommendations from a number of guidelines for the purpose of our STG. The different guidelines had differing purpose, different target audiences, and differing presentation and linguistic styles. While NICE guidelines used a user-friendly format in terms of language, other guidelines made recommendations with mention of strength of evidence.

Also the population, the healthcare setting and the resources available, the assessment tools and therapies available are different in the Indian context. For these reasons and in order to harmonise these different formats and linguistic styles, and have a uniformity of presentation in our STG, we decided to adapt existing evidence based guidelines. The quotation of recommendations verbatim would have also involved intellectual property related issues.

The table below outlines some key recommendations in these guidelines, their source and some comments related to their adaptation.

Key recommendation	Source guideline(s)	Comment
All adults above the age of 18 years should undergo opportunistic screening for hypertension by healthcare providers at every point of contact with health services.	US Preventive Services Task Force. Screening for high blood pressure: US Preventive Services Task Force recommendation statement.	Adapted. We added the component of opportunistic screening and screening by both physicians as well as non-physician staff.
Screening of hypertension should be done using an automated BP instrument or any other validated device, using a standardised BP measurement procedure.	NICE, European society of Cardiology guidelines	Adopted.
Depending upon the readings	Joint National Committee	Adapted.

the person may be advised review on an annual or 2 yearly basis or referral within a few for diagnosis or treatment of hypertension	on Prevention, Detection, Evaluation and Treatment of High Blood Pressure – Seventh Report	We have used the term "high normal" for SBP of 130-139 mm Hg and DBP of 85-89 mm Hg used in WHO/ISH guideline and the ESC/ESH Guideline, instead of the term "pre-hypertension" used in JNC 7
Diagnostic standard for hypertension	ESC/ESH guidelines	Adapted. Reworded. It is based on clinic based measurement using a standardised BP measurement procedure.
Recording the measured BP : average measurement vs. lower measurement	NICE guidelines 2011	Adapted. Original recommendation." If blood pressure measured in the clinic is 140/90 mmHg or higher: Take a second measurement during the consultation. If the second measurement is substantially different from the first, take a third measurement. Record the lower of the last two measurements as the clinic blood pressure." In the Indian setting, with the proposed BP measurement by non-physician health workers , taking the lower instead of the average reading is more feasible and will avoid calculation errors.
Classification of hypertension	ESC/ESH 2013 guideline. WHO/ISH guideline 2003	Adopted. We retained the Grade 3 hypertension category (SBP >180 mm Hg &/or DBP >110 mm Hg). This category is mentioned

		in the ESC/ESH guidelines and was part of the WHO/ISH guidelines. Even in guidelines like NICE which do not mention this grade, this level of SBP and DBP is classified as severe in these guidelines. This category has both prognostic and therapeutic importance. Prognostically, grade 3 hypertension is associated with high cardiovascular risk. Therapeutically it is important as it indicates need for immediate referral and initiation of therapy.
The assessment of a patient with hypertension should include assessment for risk factors, target organ damage, and associated clinical conditions (diabetes, cardiovascular disease, cerebrovascular disease, chronic kidney disease, peripheral arterial disease)	ESC/ESH, WHO/ISH	Adopted. We used the same framework of assessment of risk factor, target organ damage, which along with the presence of associated clinical conditions, determine the overall cardiovascular risk.
Management of hypertension : Lifestyle measures	ESC/ESH guidelines NICE guidelines	Adapted. ESC/ESH recommend reduction of salt intake, moderation of alcohol consumption, reduction of BMI to <25 kg/m^2 , eating a diet with plenty of vegetables, moderate intensity exercise, advice on smoking cessation as Class I recommendations. We have used an optimal BMI cut-off of less than 23 kg/m^2, in view of the lower cut-offsfor defining obesity in

		Indians(defined as BMI>25 kg/m^2)compared to the cut off for obesity of BMI>30 kg/m^2 in western population.
Indications for drug therapy in Grade I hypertension	NICE guidelines	Adapted. We followed the NICE recommendation of initiating therapy except the one which recommended initiation in those with a 10 year cardiovascular risk equivalent of 20% or greater. This is because there is no formal cardiovascular risk estimation tool which has been validated in an Indian population, and the variables required for these estimates are not available at the primary care level.
BP targets General population : <140/90 mm Hg in people under 80 years <150/90 mm Hg in people 80 years and over	NICE guidelines	Adapted. Reworded. The original recommendation is "aim for a target clinic BP below 140/90 in people aged less than 80 years with treated hypertension." And "Aim for a target clinic BP below 150/90 in people aged 80 years and over, with treated hypertension."
BP targets Diabetes	JNC 8 guidelines Cochrane database of Systematic reviews (Arguedas JA, Leiva V, and Wright JM. Blood pressure targets for hypertension in people with diabetes mellitus. *Cochrane*	Adapted Original JNC8 recommendation: "In the population aged ≥18 years with diabetes, initiate pharmacologic treatment to lower BP at SBP

	Database Syst Rev. 2013; 10:CD008277).	≥140 mm Hg or DBP ≥90 mm Hg and treat to a goal SBP <140 mm Hg and goal DBP <90 mm Hg. (Expert Opinion – Grade E)" The Cochrane review noted some reduction of stroke mortality in the lower SBP target group, (RR:0.58, absolute risk reduction -1%), there was an increase in risk of serious adverse with a RR of 2.58, and an increase of absolute risk of 2%.The Cochrane review on the subject concluded" At the present time, evidence from randomized trials does not support blood pressure targets lower than the standard targets in people with elevated blood pressure and diabetes. More randomized controlled trials are needed, with future trials reporting total mortality, total serious adverse events as well as cardiovascular and renal events".
Choice of drugs General population without compelling indications:	JNC 8 guidelines ESC/ESH guidelines	Adapted. JNC 8 recommendation: "In the general nonblack population, including those with diabetes, initial antihypertensive treatment should include a thiazide type diuretic, calcium channel blocker (CCB), angiotensin converting enzyme

		inhibitor (ACEI), or angiotensin receptor blocker (ARB). (Moderate Recommendation – Grade B) ESC/ESH: "Diuretics (thiazides, chlorthalidone and indapamide), beta-blockers, calcium antagonists, ACE inhibitors, and angiotensin receptor blockers are all suitable and recommended for the initiation and maintenance of antihypertensive treatment, either as monotherapy or in some combinations with each other." (Class I Level A)
Choice of drugs : Compelling indications	ESC/ESH guidelines	Adapted. Original recommendation. "Some agents should be considered as the preferential choice in specific conditions because used in trials in those conditions or because of greater effectiveness in specific types of OD.(Class II a Level C)"
Treatment strategy for achieving control	ESC/ESH guidelines	Adapted. Reworded. A combination of 2 drugs is recommended with very marked elevation of BP. We have recommended initiation of therapy with 2 drugs

		in patients with Grade 3 hypertension.
Treatment of Hypertension with associated clinical conditions	CHEP guidelines for treatment of hypertension with stroke, chronic kidney disease, heart disease	Adapted reworded
Review poor response to BP medications	CHEP guidelines	Adapted. Supplemental table 10 describes factors that underlie poor response to therapy.

The scope of the guideline, an illustrative format of the guideline developed by the Medicine sub-group was presented in a Task Force meeting on 26.8.2015. This scope was developed after extensive online consultation on an ongoing basis.

5. Submission of the draft STG for peer review:

We submitted the draft STG inclusive of annexure to the Task Force in November 2015.

6. Peer review:

We received general and specific comments In January 2016, which helped improve the clarity of our draft. Some of the comments were of a substantive nature and are discussed in the following table. Many others were pointed in the text of the guidelines and included requests for references etc.

S.No	Comment	Response
INTRODUCTION		
NICE	What population is recommended for targeted screening? If high risk population, request to define it and also document the evidence on which recommendation is based	The population groups at high risk are older adults (>50 - 60 years), persons with diabetes, obesity especially those with a higher abdominal circumference, current smokers, those with any cardiovascular disease, and those with family history of premature cardiovascular disease. Predictors for the presence of hypertension have been developed in Indian cohort studies and these risk scores are again based on age, current smoking, presence of abdominal obesity

IHG	Salt intake recommendation to be corrected and uniform throughout the document.	We have mentioned a dietary intake of 6 gm. salt per day for the general population, and have added a qualifier that this limit may be reconsidered in some patients who are engaged in heavy manual labour under hot climatic conditions, where substantial loss of salt in sweat may occur, as seen in some studies.
IHG	The age cut off for screening should be 30 years, rather than 18 years.	This lower cut-off is based on the US Preventive Services Task Force recommendations. A cut off above 30 years conveys an impression that younger adults (including pregnant women) cannot have hypertension. This is not so as explained below: 1. Hypertension including essential hypertension may present earlier than 30 years. Studies have shown that hypertension was prevalent in 15% of children in the 5-16 year age group (NMJI 2007 Raj et al). 2. Patients with secondary hypertension including chronic renal disease may present before thirty years 3. Pregnancy induced hypertension: We envisage that this guideline will be followed by a guideline on pregnancy induced hypertension. This is a major cause of maternal morbidity and mortality, and all pregnant women in India (most of them less than 30 years) need to be screened for hypertension as part of antenatal care. This guideline will create the platform for screening of antenatal women. A large number of persons with high normal BP may be identified by screening who can progress to hypertension. IF the recommendations of this guideline on weight reduction, tobacco cessation, and salt reduction are implemented, we might prevent their progression to essential hypertension with them.
SCOPE OF HT GUIDELINE		
IHG	The choice of BP measuring device should be discussed with Health Technology Assessment and finalized.	India is committed to phasing out mercury and alternatives have to be considered. Electronic digital oscillometric devices are emerging as the clinical standard for BP measurement worldwide, and have proved to be

		accurate and robust. Aneroid sphygmomanometers need frequent calibration. Both mercury and aneroid sphygmo3manometers need an auscultation based measurement which may be less feasible for non-physician health staff.
LIST OF RECOMMENDATIONS		
NICE	Ambulatory BP/ HBP are the gold standard and may be possible in urban areas. Perhaps both recommendations can be put along with clearly stating that in the absence of ambulatory BP, clinic BP is recommended as an alternative.	Addressed
IHG	Definition of Obesity	The Indian cut off for BMI defining obesity is ≥ 25.0 kg/m^2 and is mentioned
	Age for BP cut-off for 80 years and above the group opines that 80 years is too high a cut-off for Indian population. may consider 65 years as per JNC guidelines	The cut off of elderly as per the JNC guidelines was in fact 60 years, and not 65 years as the reviewers have indicated. The cut off of 80 years for defining elderly is purely for the purpose of the target BP level. In JNC 8 guidelines a higher target of <150 mm systolic was considered for people over 60 years of age. This was one recommendation on which the committee failed to reach consensus. The findings of the recently published SPRINT trial included a high proportion of those over 60 years, and presents evidence in favour of an even lower target BP of <120/80. The higher target of 150/90 for a patient for example aged 62 years, will be even more problematic in this light.
THERAPEUTIC RECOMMENDATIONS		
IHG	The Group commented on a table of commonly used antihypertensive drugs including their doses. Western guidelines tend to mention high doses of drugs e.g. enalapril dose is 5-40 mg. The group also wanted atenolol, thiazide like diuretic and losartan to be removed from the list.	In the introduction of the guideline itself we had indicated our requirement for only 1 representative drug from each class, and our choice of these drugs are reflected in the formulary – amlodipine, enalapril/Lisinopril , thiazide, low cost ARB (losartan), and atenolol. Losartan needs to be retained as a possible low cost ARB option in case of cough due to ACE inhibitors. We have now indicated lower doses of enalapril

IHG	Re look at recommendation for FDC, the group feels should not include it here in the national guidelines	We have mentioned fixed dose combinations mainly because many guidelines now refer to them. We have clarified in the guideline that FDCs are to be considered for use only after stabilisation of blood pressure. In fact their use as initial therapy creates problems of titration of drug dosages. FDC use in the National Health Mission will also create problems of a logistical nature in terms of ensuring stocks of multiple combinations.
IHG	Add interval for monitoring and dose increase or decision to add another drug	These have been added
IHG	The guideline may clearly mention that aspirin is not indicated for primary prevention, instead of " it is of uncertain value"	Phrasing has been changed
IHG	Criteria for starting statins in patients with more than 3 risk factors is difficult to apply in the absence of hyperlipidemia	This criterion is mentioned in the CHEP guidelines. Also the ESC/ESH mentions that presence of 3 risk factor confers high risk of cardiovascular disease
IHG	Suggested only atorvastatin as a statin	We agreed
IHG	Suggested chronic review feedback in tabular form	We agree
IHG	We're not sure about whether a formulary is required in a guideline	We strongly feel that a guideline to be a stand –alone document useful in all settings in India, needs to have information on indications, contraindications, side effects of a drug, so that drugs are used rationally and safely.
IHG	Also include foods to be encouraged. Elaborate on salt intake	We agree.

FULL GUIDELINE

Hypertension:
Screening, Diagnosis, Assessment and Management of Primary Hypertension in Adult Men and Women in India.

SECTION 4: SCOPE AND OBJECTIVE OF THE GUIDELINE.

a) **To increase detection of hypertension in adults in India using a systematic, primary care led approach based on standardised measurements of BP and their follow up.**
b) **To provide guidance on assessment of persons with hypertension appropriate to different levels of care in India.**
c) **To provide a structured , simplified and standardised treatment guideline for hypertension in adults in India, along with implementation tools(quick reference guide, quality standards, patient information leaflets)**
d) **To provide guidance on availability of a core list of medications in the public health system for treatment of hypertension.**
e) **To outline research issues related to hypertension in India.**

1. Population

Groups that will be covered

a) Adults at risk of hypertension (18 years and older)

b) Adults with hypertension (18 years and older) with or without cardiovascular disease.

c) People with diabetes

d) People with severe hypertension or high blood pressure in emergency care settings.

Groups that will not be covered

a) Children and young people (younger than 18 years).

b) Pregnant women

c) Secondary causes of hypertension: For example, chronic kidney disease, endocrine causes of hypertension [Cushing's syndrome, pheochromocytoma] and renovascular hypertension. However clues to suspect of secondary causes of hypertension will be mentioned.

2. Healthcare setting

a) Community settings: These would be involved in promoting awareness of cardiovascular risk factors and their modification by a healthy lifestyle. Screening of hypertension at this level so through trained non-physician staff is a major point of emphasis in this guideline

b) Sub-centres: These would be involved in screening for hypertension, patient education and assessment, and follow up of diagnosed patients.

c) Primary health centres. These would be involved in diagnosis, patient education, assessment with simple laboratory tests, management and follow up of patients.

d) Community Health Centres: These would be involved in diagnosis, patient education, assessment by physician and biochemical investigations (including renal function and lipid profile), and management and follow up of patients.

e) District Hospitals, Medical Colleges: These would be involved in diagnosis, assessment,

Key clinical issues that will be covered in the guideline

A. **Screening for hypertension in adults in India:**

a) Age at screening
b) Health care settings for screening and role of non-physician staff.
c) BP devices for measurement: sphygmomanometers or oscillometric devices or aneroid devices
d) Standardised BP measurement procedure and sources of error.

B. Diagnosis of hypertension in India:

a) Number of measurements required for diagnosis
b) Classification of hypertension in India according to BP levels.
c) Time frame for recheck and review of elevated BP readings in case of grade 1 and Grade 2 hypertension.

C. Patient education and assessment of persons with hypertension in India:

a) Education of the patient regarding nature of disease, its treatment, and the importance of adherence to treatment.
b) Assessment for target organ damage at different levels of care.
c) Assessment of associated clinical conditions at different levels of care
d) Assessment of cardiovascular risk at different levels of care.
e) Patient assessment to rule out secondary hypertension.

D. Management of hypertension

1. Initiation of treatment in different grades of hypertension.
2. Targets for BP control.
3. Classes of antihypertensive drugs and preferred choices.
4. Treatment regimens and strategies to achieve effective control of BP including optimisation of drug dosages and addition of other medications.
5. Treatment of hypertension associated with other conditions like diabetes, heart disease, cerebrovascular disease.
6. Reasons for poor response to therapy.

7. Integration of interventions to reduce global cardiovascular risk including cessation of tobacco use, antiplatelet therapy and lipid lowering therapy.
8. Improving adherence to therapy and systems for long term follow up of patients.

Specialist management of secondary hypertension (that is, hypertension arising from other medical conditions).

1. Outcome and quality indicators

Outcomes:

The evidence based guidelines sourced by this guideline for its preparation have relied on the following clinical cardiovascular outcomes occurring in hypertensive individuals to frame recommendations-

1. Fatal or non-fatal stroke.
2. Myocardial infarction
3. Heart failure and other cardiovascular deaths.

Annexure:

I. Lifestyle intervention for exercise: brief description

II. Lifestyle intervention for weight control: brief description.

III. Lifestyle intervention for reducing salt intake (recommendations for intake in summer?): brief description.

IV. Lifestyle intervention for reducing alcohol and tobacco consumption.

V. Lifestyle intervention for stress management. Relaxation techniques including Yoga.

VI. Formulary pages: 2 pages for each class of drugs with indications, cautions, contraindications, use in hepatic, renal impairment, pregnancy and breast-feeding, side-effects, dosages (initial and increments) of representative drugs of that class.

1. Screening:

Detailed recommendations:

1: Target population, and operational procedure of screening

1.1. We recommend an ongoing initiative to increase awareness of hypertension as a widely prevalent but asymptomatic disease associated with many adverse outcomes like heart attacks, strokes, kidney failure. Most patients with hypertension in India are unaware of their status and remain undetected. 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 the elderly (>60 years), obese, current smokers, those with diabetes, those with existing cardiovascular disease, and those with a strong family history of heart disease or stroke can be undertaken by trained non-physician staff.

Background:

Hypertension is a commonly prevalent disease in adults in India, affecting more than a 65 million persons, most of whom are unaware of their hypertension status.[8] The prevalence of hypertension increases with increasing age and more than half of people over the age of 60 years may be affected[25]. It is asymptomatic in most of its course and symptoms are present only in the stage of complications. Patients with lower grades/stages of hypertension are also likely to progress to more severe forms of hypertension. Detection of people with hypertension helps in identification of people at higher cardiovascular risk and effective treatment can provide significant protection from stroke, heart attacks, congestive heart failure and kidney disease, without causing significant harm.

The availability of automated (oscillometric) BP measurements and their acceptance as a clinical standard[26] has created opportunities for measurement of BP by non-physician aides, since these do not require training on auscultation.

Implementation:

The implementation of the screening programme on hypertension will require that **opportunistic screening** for hypertension is offered to all adults during the course of their visits to health facilities or healthcare providers – i.e. the health care providers should use the opportunity provided by the visit to screen for hypertension, and record

the measurement in a patient card. Systematic and sustainable practical methods need to be developed to screen the asymptomatic population for hypertension and can be integrated with screening of other non-communicable diseases. Allied health staff should be trained to check hypertension using automated validated BP apparatus and follow the referral guidelines on screening measurements.

The high risk groups which may be focused on are those with age >50 years years)([25], [27]) as well as those with diabetes[28] where prevalence of hypertension has been noted to be more than 30-50%, and yet often remains undetected[27, 29]. Studies in India have also shown that the risk of hypertension is higher in those who have general or abdominal obesity and those who consume tobacco or alcohol.[30]There is a need to spread awareness of these risk factors for hypertension and cardiovascular disease, through the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke. The major risk factors for hypertension and cardiovascular disease can be summarised as ABCDE as shown below-

The **ABCDE**s of risk of hypertension and cardiovascular disease in India

A: Age e.g. > 50 years

B: Body mass index – Obesity (BMI >25 kg/m^2) which is related to diet and activity levels, and especially abdominal obesity(waist circumference >90 cm in men,>80 cm in women)

C: Consumption of tobacco and alcohol

D: Diabetes, Dyslipidemia

Implementation of the screening program will require training of the non-physician aides in the measurement of blood pressure, the availability of an automated (oscillometric) BP measurement device, and preferably cuffs of 2 sizes to enable measurement of BP in obese patients too. Implementation will also require that the Bureau of Indian Standards develop a quality standard for the digital (oscillometric) devices in the market, on the lines of the standards and validation procedures in UK, USA and Europe. This will ensure that validated devices are available in the Indian market. At present the Bureau of Indian Standards has quality standards only for mercury and aneroid sphygmomanometers.

Rationale:

Benefit outweighs harm: The evidence of the benefits and the harms of screening for hypertension have been systematically reviewed (U.S. Preventive Services Task Force. Screening for high blood pressure: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2007:147-783-786) and found to have a net benefit. The USPTF therefore recommended “screening for high blood pressure in adults 18 and over”.

Screening by non-physician health workers: The operational guidelines of the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular diseases and Stroke envisages that screening for hypertension is to be done at sub-centre by non-physician health workers like ANM or male health worker.[31] There is emerging evidence from India and other low-income Asian countries that community based interventions to assess cardiovascular risk factors,[13] task shifting to non-physician health workers should be considered,[32] and finally that delivery of a package of interventions for non-communicable diseases including screening by non-physician health workers is both feasible and effective.[11].

Groups at high risk of hypertension are easily identifiable: Cohort studies in south India have identified risk factors which can be helpful in identifying groups at particular risk of developing hypertension. These include persons with age≥ 35 years, current smokers, persons with central obesity (measured by waist circumference), persons with previous record of high normal BP.[33, 34]. All these risk factors can be identified by non-physician healthcare workers and can help prioritise groups who require targeted screening.

The age threshold for screening: The age related threshold for screening has been previously suggested to be 30 years in India under the operational guidelines of the National Programme for Prevention and control of cancer, diabetes, cardiovascular diseases and stroke.[31] However systematic reviews of the evidence have suggested a lower threshold and the US Preventive Services Task Force "recommends screening for high blood pressure in adults in adult 18 and over". The lower threshold suggested may also be considered in light of other factors. Patients with essential hypertension can present even at an age less than 30 years, especially in those with a family history of hypertension or increased body mass index. In a study of apparently normal 10-16 year old school children in south India ,a prevalence of 6.6% of essential hypertension which was associated with high BMI was noted[35]. Patients with secondary forms of hypertension including chronic kidney disease can also present below 30 years of age. There are special populations like pregnant women who may be below 30 years of age, but should also be screened for hypertension to prevent maternal and foetal complications. Indians have a lower age of presentation of cardiovascular events like coronary artery disease than their western counterparts.[36] Persons even below the age of 30 years may have prevalence of other risk factors like obesity in which prevalence of hypertension is higher, or smoking or alcohol consumption which will increase their risk for future cardiovascular disease. Measurement of BP in persons aged 18 years and above offers opportunities for prevention of hypertension by identifying persons with high normal BP in whom progression to hypertension may be prevented by lifestyle modifications.

Use of digital (oscillometric) devices: Guidelines like NICE,[18] ASH/ISH[24], ESC[21], now suggest the use of electronic BP measurement instruments based on the oscillometric approach to record BP in both clinic as well as home based settings. Protocols for the validation, and a list of instruments validated by organisations like the British Hypertension Society, European Society of Hypertension, and Association for Advancement of Medical Instrumentation are also available.[37, 38]In evidence based systematic review, oscillometric devices were considered appropriate for use in adults

(Level A recommendation) including for those with trauma and shock, and were given a Level B recommendation for use in adults with hypertension, because of discrepancies accruing from increased arterial stiffness. Oscillometric However other studies have cited concerns about their accuracy.[39] In a study of validated digital devices in practice settings, 88% of digital devices had measurement within 3 mm Hg of the reference standard compared to 95% of mercury sphygmomanometers, suggesting that digital devices can have accuracy equivalent to mercury sphygmomanometers.[40]. *The World Health Organisation recommends the use of electronicdevices, which are affordable and reliable and which have the capacity for manual settings.*[41]

Key Recommendation: Standardised BP measurement procedure

1.3 The screening 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 standardised BP measurement procedure.

1.4 Blood pressure should be measured a few (5) minutes after the patient is in a relaxed state, is seated with the arm at the level of the heart, with legs uncrossed. The cuff should have a bladder whose length is about 80% and whose breadth is about 40% of the arm circumference. If the auscultation based method is being used, the then the cuff should initially be inflated to at least 30 mm Hg beyond the point of disappearance of the radial pulse. It should then be deflated at a rate of 2-3 mm per second. The first and the last audible Korotkoff sounds should be taken at the systolic BP and diastolic BP respectively. The column should be read to the nearest 2 mm Hg.

1.5 At least 2 readings should be taken at each visit with an interval of at least 1 minute between the measurements. If the two readings are substantially different a third reading should be taken. The lower of the two readings should be taken as the representative SBP and DBP.

Background

Hypertension is a condition which requires life-long monitoring and management. This diagnosis is based on measurement of blood pressure in the clinic setting and it is essential that this measurement be made as reliable as possible. A number of factors- the level of training of the observer, the setting for the measurement of BP (home or clinic), timing of the day, preceding caffeine intake or smoking, the position of the patient during the procedure, the accuracy of the BP measuring instrument, the size and placement of the cuff, the number of readings taken, all affect the readings and thereby the reliability of this measurement.[2]It is important that the provider is trained, the BP measurement device is accurate and validated, the patient conditions for measurement of BP are met, and the procedure of recording the BP is standardised. We recommend the use of both existing mercury BP sphygmomanometers and digital oscillometric BP devices.

Implementation

We suggest that for expanding the access to screening, diagnosis and monitoring of blood pressure, digital BP devices be made available, especially at levels of care delivered by non-physicians. A WHO expert committee meeting on measurement of blood pressure in low resource settings concluded that "Given the serious inherent inaccuracy of the auscultatory technique, validated and affordable electronic devices, that have the option to select manual readings, seem to be a suitable solution for low resource settings."[41]. The technical specifications recommended were "high accuracy, adoption of electronic transducers and solar batteries for power supply, standard rates of cuff inflation and deflation, adequate cuff size, digital display powered by solar batteries, facilities for adequate calibration, environmental requirements, no need of memory function, resistance to shock and temperature changes, and low cost".[37]We recommend that the Bureau of Indian Standards undertakes a validation of the devices being marketed in India according to internationally accepted protocols.[37]. The accuracy can be re-checked periodically against a reference mercury sphygmomanometer in the PHC/CHC retained for this purpose. We recommend that the healthcare providers be trained in the use of these devices and the standardised conditions and procedure for measuring BP. The chosen device for BP measurement should also undergo periodic calibration.

BP measurement procedure: (ref: (2))

Auscultation based procedure:

Patient preparation and position: Allow the patient to be seated 5 minutes before taking the BP measurement. BP should be measured with the patient in a relaxed state, sitting with the back supported, *the arm at the level of the heart*, and with the legs uncrossed. There should not have been caffeine intake in the preceding 1 hour and smoking in the preceding 30 minutes. The patient should remove all clothing which may interfere with the placement of the cuff and have a constrictive effect.

BP device: The device should be a validated device with an appropriate cuff size.

Cuff size and placement: The cuff should have a bladder whose length is at least 80% of the arm circumference, and a width that is at least 40% of the arm circumference. The cuff should be placed with its midline over the pulsations of the brachial artery, identified by palpation above the antecubital fossa. If the patient is obese then a large adult size cuff will be preferable. If an auscultation based method is being used for measurement of BP, a 2-3 cm space should be available between the lower end of the cuff and the antecubital fossa.

Procedure: If the BP measurement involves auscultation, then the cuff should initially be inflated to at least 30 mm Hg beyond the point of disappearance of the radial pulse. It should then be deflated at a rate of 2- 3 mm per second. The first and the last audible Korotkoff sounds should be taken at the systolic BP and diastolic BP respectively. The column should be read to the nearest 2 mm Hg.

No. of measurements:

At least 2 readings should be taken at each visit with an interval of at least 1 minute between the measurements. We suggest, in line with the new recommendation in the

NICE guidelines (2011), that the physician or non-physician measuring the BP records the lower of the 2 measurements as the representative systolic and diastolic BP. This will also avoid the calculation error involved in averaging the 2 measurements. Because of the variability of BP measurements, the diagnosis of hypertension should be only made after multiple readings over at least a week confirm the diagnosis of hypertension, except in the case of hypertensive emergencies and urgencies where the diagnosis may be established with another BP recording in the same visit.

If the patient is above 65 years of age, or a diabetic then the patient should have the BP checked in supine and 2 minutes after assuming the standing position. A fall in systolic

Recommended cuff sizes for accurate measurement of Blood Pressure(source: Ref(2))

Patient (by arm circumference)	**recommended cuff size**
22 to 26 cm	12 x 22 cm (small adult)
27 to 34 cm	16 x 30 cm (normal adult)
35 to 44 cm	16 x 36 cm (large adult)

BP more than 20 mm Hg and 10 mm or more in the diastolic pressure suggests the presence of postural hypotension.[(2)]

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 half an hour	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" may constitute 32% of hypertensive subjects in 4 population based surveys.[42]

White coat effect and white coat hypertension:

The white coat effect can occur in all patients with hypertension and can result in higher BP readings in clinic settings than outside it.[43] It may result in misclassification of severity of hypertension. The effect varies from minimal to marked increases in clinic BP readings compared to ambulatory or home recording with an overall mean increase of 27 mm Hg in the systolic BP observed in one study.[44] White coat hypertension or isolated clinic hypertension occurs in persons who are normotensives on out of clinic measurements. The white coat effect is due to an alerting reaction and reflex activation of the sympathetic nervous system.[43]

Rationale

Use of oscillometric devices and the involvement of non-physician community health workers:

Measurement of BP with a mercury sphygmomanometer is considered a gold standard, but India is a signatory to the Minamata convention and has committed to the phasing out of mercury in healthcare, because of environmental concerns. Mercury based sphygmomanometers are also prone to breakages. Aneroid BP instruments are an alternative but they require frequent calibration. Both mercury and aneroid devices require an auscultation based procedure, which has its inaccuracies and more intensive requirements for training. Digital BP devices based on oscillometric approach are now considered the "clinical standard" and are being widely used in both clinic and home settings in developed countries.[26]They have the advantages of lower training requirements facilitating use by non-physicians, portability. In a large study measurements with these oscillometric devices had a mean underestimation of less than 2 mm Hg,[45] and in a clinic based observational study, the accuracy was found to be acceptable.[40] Preliminary studies support the use of electronic devices by community health workers.[46]A mercury sphygmomanometer will still need to be retained at each facility to check the accuracy of these devices.[2]

A number of studies have shown that with proper training, supervision, and community based workers can measure blood pressure and assess cardiovascular risk factors accurately.

Rescreening, reassessment, and referral of individuals found to have normal or elevated BP on screening by allied health staff

1.6. Depending on the BP readings, the person may be advised review up on an annual or 2 yearly basis, or referral (immediate or deferred) for diagnosis or treatment of hypertension.

1.6.1 Persons with normal BP (<130/80) should be advised a recheck in 2 years.

1.6.2 Persons with high normal BP: systolic BP of 130-139 mm Hg and diastolic of 80-89 mm Hg should be advised a recheck in 1 year, or sooner if indicated due to other risk factors or diseases.

1.6.3 Persons with BP > 140 mm Hg systolic and/or greater than 90 mm Hg diastolic should be rechecked within 1-2 weeks and then classified as hypertensive or high normal.

1.6.4 Persons with BP of >160 mm Hg systolic and/or greater than 100 mm Hg diastolic should be advised early referral to the primary health centre if measurements have been made at a peripheral health facility below the level of a primary health centre, for confirmation of the diagnosis of hypertension.

1.6.5 Persons with BP of >180 mm Hg systolic and/or greater than 110 mm diastolic if documented by a non-physician staff, should be immediately referred to the primary health centre or community health centre (whichever is nearer to the residence) for further investigation to exclude any acute target organ damage, and for initiation of treatment,which is required on an immediate basis. Patients documented with this level of BP in a health facility would require assessment for target organ damage, and gradual reduction of BP over hours and days if there is no acute target organ damage.

1.6.6 Hypertensive emergencies are potentially life-threatening situations where hypertension (usually severe and > 180 mm systolic and >120 mm diastolic associated with the presence of recent onset and progressive target organ damage resulting in cardiovascular, neurologic, renal and visual dysfunction. These situations may include severe hypertension associated with acute coronary syndrome (chest pain), acute left ventricular dysfunction (shortness of breath), and hypertensive encephalopathy (altered sensorium), stroke (focal weakness), and renal failure. It is most often associated with severe hypertension, except in children and pregnant women where hypertensive emergencies can occur with lower elevations of BP.

1.7 All persons who are screened for hypertension should be advised lifestyle measures including maintaining a daily salt intake appropriate to their occupation, 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.

Implementation:

The health care staff will need to be trained not only in the measurement of BP using a standardised procedure, but also to interpret the measurements of normal or elevated BP readings and take appropriate actions. This will be facilitated by the availability of key messages for the detection, assessment and management of hypertension in a flyer and quick reference guide.

Suggested response to 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' 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.

TABLE 3: SUGGESTED RESPONSE TO INITIAL BP READINGS : Adapted from references (29, 47)

Rationale:

There is no evidence from randomised controlled trials regarding the appropriate rescreening intervals for people screened for hypertension.[47] Recently the US Preventive Services Task Force published recommendations regarding rescreening intervals. The weighted mean incidence of hypertension over rescreening intervals varying between 1 and 5 years was found to range between 2.5% and 13.8%

respectively. In studies persons with even a single risk factor like high normal BP (SBP 130-139 mm and DBP 85-89mm), persons who are obese or overweight , and those with age >40 years are at greater than 20% risk of developing hypertension within the next 3-5 years, and therefore such persons should be screened annually for hypertension.

The intervals suggested for confirmation and evaluation at a source of care have been adapted from the recommendations of the JNC 7.[29]

KEY RECOMMENDATION: 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 recommended.

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

2.4 Patients with hypertension should be classified in the following manner:

- **Grade 1 Hypertension**: systolic 140-159 mm and/or diastolic 90-99 mm
- **Grade 2 Hypertension** : systolic 160-179 mm and/or diastolic 100-109 mm
- **Grade 3 Hypertension** : systolic 180 or above and/or diastolic 110 or above
- **Isolated systolic hypertension**: systolic > 140 mm but diastolic <90 mm.
- **Hypertensive urgency**: Severe asymptomatic hypertension (usually Systolic > 180 mm , Diastolic >120 mm)

- **Hypertensive emergency**: Severe hypertension accompanied by cardiac (e.g. acute left ventricular failure), neurological (e.g. hypertensive encephalopathy), or renal dysfunction.

Background

The diagnosis of hypertension depends on multiple BP measurements taken in the office setting over a period of time. 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, when the diagnosis of hypertension is made during the first visit itself. Classification of hypertension is important for therapy and prognosis as the level of cardiovascular risk and the risk of target organ damage increases with the severity of hypertension.

Implementation:

Diagnosis of hypertension will be made at primary health centres and facilities above that level using validated and calibrated BP measurement devices and following a standardised BP measurement procedure. Hypertension should be diagnosed when BP is persistently above a systolic of 140 mm and/or diastolic of 90 mm. The classification of patients into those with optimal BP, Normal BP and different grades of hypertension is made as per the table below.

In India, for the diagnosis of most patients with hypertension, ambulatory blood pressure monitoring and home based BP monitoring is not feasible and is therefore not recommended.

Rationale:

All guidelines define hypertension for the general population as persistent elevation of SBP higher than 140 mm and/or DBP higher than 90 mm Hg. However the classification of hypertension varies across guidelines. While the WHO/ISH guidelines(48) and the ESH/ESC guidelines (21)mention the grades of hypertension referred in the table, the JNC 7(29) and JNC 8 and NICE guidelines define only 2 stages of hypertension, collapsing the Stage 3 hypertension category into Stage 2,considering them to be therapeutically similar. The nomenclature of BP levels below 140 mm and 90 mm also differ. The ESC/ESH guidelines define normal as <130 mm systolic and/or <85 mm diastolic, the JNC7 guidelines define normal as <120 and or 80 mm and categorise all persons with BP of 120-139 mm SBP and 80-89 mm diastolic as having “pre-hypertension”.

We adopted the ESC/ESH guidelines for the classification of hypertension because of a consensus that Category 3 mentioned in these guidelines is retained and the category of pre-hypertension mentioned in JNC is avoided. Category 3 mentioned in the ESC/ESH guidelines was part of the WHO/ISH guidelines.[48] Even in guidelines like NICE which do not mention this grade, this level of SBP and DBP is classified as severe in these guidelines. This category has both prognostic and therapeutic importance. Prognostically, grade 3 hypertension is associated with high cardiovascular risk. Therapeutically it is important as it indicates need for immediate referral and initiation of therapy. We

agreed that life-style modifications be advised to all persons with persons above 120 mm Hg systolic and/or 80 mm Hg diastolic but felt that the label of “pre-hypertension” may become a source of anxiety.

Category	SBP(mm Hg)		DBP(mm Hg)
Optimal	**<120**	**and/or**	**<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 dysfunction (e.g. Left ventricular failure, cerebral dysfunction (e.g. Hypertensive encephalopathy, stroke),renal dysfunction (acute renal failure), or Grade III-IV hypertensive retinopathy(haemorrhages, exudates, papilledema)**

KEY RECOMMENDATIONS: PATIENT EDUCATION AND ASSESSMENT

3.1 Patients should be counselled about the nature of the disease, and the management of hypertension, before being subjected to laboratory evaluation and drug treatment. The education and assessment of the patients should be tailored to their understanding, preferences and social circumstances.

3.1.1 Patients should be counselled about hypertension being an asymptomatic condition which can lead to disabling and life-threatening complications like stroke, heart attack and renal failure. Patient should be counselled about need for long-term therapy, need for regularity of drug intake, informed about the targets for BP control, and encouraged to monitor efficacy of therapy through regular check-ups which can include home based monitoring of BP.

3.1.2 The patient should be counselled about the important role of lifestyle measures in reducing hypertension and reducing risks of cardiovascular disease.

3.2 The effective control of blood pressure by initiation of therapy, if required, should not be delayed if laboratory evaluation is delayed or cannot be done.

3.3 The assessment of a patient with hypertension is aimed at assessing **overall cardiovascular risk for cardiovascular events like stroke, ischemic heart disease, heart failure, peripheral artery disease**.

3.3.1 The risk of clinical events in a patient with hypertension depends on

- the level of blood pressure
- risk factors (diabetes or impaired glucose tolerance, smoking, dyslipidemia, obesity, male gender, age >55 years in male,) ,
- target organ damage(heart, kidney, retina),
- Presence of associated clinical conditions [clinical cardiovascular disease (coronary artery disease, cerebrovascular disease, PAD), kidney disease].

3.4 The risk factors, target organ damage and associated clinical conditions can be detected on history, physical examination (including ophthalmoscopy), and investigations like blood glucose, lipids, serum creatinine, urinalysis, and ECG.

3.4.1 Physicians and allied health staff should assess and evaluate patients for cardiovascular risk factors like smoking, obesity, diabetes. Reduction of risk by adoption of healthy living habits-(dietary changes, exercise,

smoking cessation) is to be reinforced by all cadres of health workers. Screening for hyperlipidemia can be suggested and carried out in patients at PHC/CHC especially in those who are obese, or have family history of premature coronary artery disease, or have existing cardiovascular disease.

3.4.2 Physicians and allied staff can detect target organ damage by eliciting symptoms of shortness of breath, decreased urine output, and noting signs of heart failure like swelling of feet, and other signs of heart failure. Target organ damage can also been detected by testing urine for proteinuria, noting evidence of left ventricular hypertrophy on ECG, and features of hypertensive retinopathy on ophthalmoscopy. These signs of target organ damage can all be detected at PHC/CHCs.

3.4.3 Physicians and allied staff can detect associated clinical conditions like clinical cardiovascular disease and chronic kidney disease by eliciting history of chest pain suggestive of angina and/or pain in the lower limbs on walking suggestive of claudication, and/or history of stroke with weakness of limbs. CKD can be detected by persistently abnormal serum creatinine measured at the CHC level.

3.5 The overall risk of cardiovascular events can be assessed from these assessments as follows:

Level of blood pressure: Grade 2 Hypertension even in isolation confers moderate risk (20-30% risk of CV event over 10 years), while Grade 3 hypertension confers high risk (Over 30% risk of CV event over 10 years).

Risk factors: Presence of 3 or more risk factors confers moderate to high risk even in a patient with Grade 1 hypertension, while even fewer risk factors increase risk in Grade 2 hypertension.

TOD/Diabetes/CKD/Clinical cardiovascular disease: Presence of any target organ damage, diabetes, chronic kidney disease or clinical cardiovascular disease confers high to very high risk on patients.

3.6 The level of BP and results of the assessment will influence the following:

- when to start antihypertensive therapy,
- Which antihypertensive to use.
- whether statins and/or aspirin are indicated, to reduce cardiovascular risk

- Which other associated conditions will need management (diabetes, clinical cardiovascular disease, chronic kidney disease).

3.7. 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.

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

Key recommendations:

Background:

Hypertension is most often asymptomatic and the benefits of treatment are not immediately apparent to a patient. The therapy of hypertension involves costs (indirect as well as direct), and occasional experience of adverse effects, and is often lifelong which may create barriers to adherence to therapy. Improving adherence to long-term treatment is a key part of management. The patient is more likely to adhere to medications, lifestyle modifications if he/she understands the nature of the condition and its management.

The assessment of cardiovascular risk factors, target organ damage due to hypertension, associated clinical conditions all help in assessment of cardiovascular risk and guide therapy of hypertension. These can be assessed by a relevant history, examination and appropriate investigations, many of which can be evaluated even by non-physician staff. It may also indicate the need for other therapies like low-dose aspirin and statin to reduce cardiovascular risk. Decisions on initiation of therapy, choice of medications, BP targets for control are dependent on these factors as much as the severity of hypertension. Grade 1 hypertension may be managed with lifestyle modifications alone in the absence of other risk factors.

Implementation of patient education and assessment

Patient education related to hypertension is a part of the initial care and should be reinforced during the continuing care of patients with hypertension, e.g. during annual reviews. It can be delivered by both physician and non-physician staff and can be supported by aids like patient information leaflets (attached). Non-physician staff at the community level can reinforce messages related to healthy living, monitoring of BP and adhering to treatment.

Patient education: Patient education will facilitate the patient's participation and cooperation in the management of a life-long disease. They should understand the following features of the disease and its management:

- The disease is asymptomatic but is a risk factor for serious consequences like heart attacks, strokes, heart and kidney failure, which can be prevented by controlling hypertension to a target BP which is usually less than 140 mm systolic

and 90 mm diastolic. The disease is persistent and although it cannot be cured it can be controlled.

- Healthy living habits (lifestyle modification) like stopping smoking, eating a healthy diet lower in salt and saturated fat, exercising losing weight has many benefits with no cost. It can reduce blood pressure, may suffice for the management of grade 1 hypertension, reduce the dosage of medicines required for control of grade 2 and 3 hypertension, and help reduce the overall risk of heart attacks and stroke.
- The assessment of damage to the heart, kidney, vessels in the eye, and to detect the presence of associated conditions like diabetes are needed to determine the overall risk of cardiovascular and to frame an effective treatment regime.
- Medications may have to be taken lifelong, and monitoring with regular checks of blood pressure is required to note their efficacy. Taking medications regularly without BP checks is suboptimal, as is checking BP regularly without regular intake of medications. Most drugs can be given only once a day and can control BP with minimal side effects.

Patient education should be given in an empathic and culturally appropriate manner. It should elicit their views of the disease, and their expectations from treatment. It can be given by both physicians and non-physician staff.

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; e.g.
b. Assessing the target organ damage related to hypertension.
c. Assessing the presence of associated clinical conditions like diabetes, kidney disease or symptomatic cardiovascular disease.
d. Assessing the clues to a secondary cause of hypertension.
e. Assessment of overall cardiovascular risk of a patient

To assess patients for each of the above components the healthcare provider should ask relevant questions, look for relevant features on physical examination, and carry out appropriate laboratory investigations, which may be available at that level of care or may require referral .Some of these assessments can be done at any level of care, while others are only possible at a community health centre level. *The tables below have been made keeping in mind the resources and level of training of healthcare providers in India and are not exhaustive.*

a. **Assessment of lifestyle and other cardiovascular risk factors**: This is mentioned in table 1.

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.
Laboratory evaluation:	Blood glucose, Lipids

Table 1: **Assessment of lifestyle and other cardiovascular risk factors**

Table 2: Risk factors for cardiovascular disease

Risk factors for cardiovascular disease[5] (Apart from hypertension):

1. Male sex
2. Age (men >55 years, women>65 years).
3. Smoking.
4. Dyslipidemia (LDL > 115 mg/dl and/or Total cholesterol >190 mg/dl and/or HDL < 40 mg/dl and/or Triglycerides > 150 mg/dl).
5. Diabetes
6. Obesity (BMI> 25 kg/m^2), abdominal obesity with waist circumference >90 cm in men and >80cm in women.
7. Fasting plasma glucose 100-125 mg/dl or abnormal glucose tolerance test

A comprehensive list of risk factors is given in table 2. It is vital to ask every hypertensive patient about their smoking history, confirm it with a relative, since it is often underreported, and advise on cessation of tobacco use. Tobacco use is an independent and powerful predictor of cardiovascular diseases. The diet with regard to fat and salt content and exercise pattern should be enquired. On examination, body weight and height should be measured and the body mass index [weight in kg/ (height in metre) ^{2}]calculated. In laboratory evaluation, the blood glucose should be checked to rule out undetected diabetes (currently available at CHCs), and the lipid profile should be carried out whenever feasible. Detection of associated diabetes should be an integral part of evaluation of hypertension and diabetes care should be integrated with the care of hypertension.

b. Assessment of target organ damage related to hypertension is described in table 2.

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)
Funduscopic evidence of hypertensive retinopathy-hemorrhages, exudates, papilledema	
Laboratory evaluation	ECG: SV1 +RV6 > 3.5 Mv (LVH)
	Urine protein, Serum creatinine

Table3: **Assess target organ damage**

The target organs affected by hypertension are the brain, heart, kidney, and eye.

- A history of breathlessness on walking briskly or climbing stairs may indicate its effect on the heart, as does the complaints of swelling over both feet.
- On examination the presence of pulsatile elevation of jugular venous pressure, presence of edema on the feet, and presence of changes of hypertensive retinopathy (Grade II or higher) indicate target organ damage.
- ECG if feasible may show changes suggestive of left ventricular hypertrophy. Microalbuminuria with an increased urine protein/creatinine ratio on spot urine is an early marker of renal damage, but is not widely available. However macroalbuminuria detected by a dipstix or serum creatinine estimation must be done whenever possible.

  Referral for assessment of TOD: Patients with Grade 2 hypertension and above, and those with diabetes, should be *referred early* to the community health centre to enable evaluation by ophthalmoscopy, ECG, urinalysis and creatinine estimation, *after initiation of treatment.* Patients with Grade 3 hypertension should be referred on an *urgent* basis *after initiation of treatment*. Those who have Grade 3 hypertension and clinical features of hypertensive emergencies (papilledema with proteinuria) should be referred to an emergency department of a **secondary level centre**, after initiation of treatment.

b. Assessment of associated clinical conditions/clinical cardiovascular disease: Hypertension often occurs in association with other clinical conditions e.g. coronary artery disease (myocardial infarction or angina pectoris), cerebrovascular disease (history of ischemic or haemorrhagic stroke), and chronic kidney disease (diabetic or non-diabetic). A patient with hypertension may have been already been diagnosed with these conditions. Thepresence of these conditions determine choice of therapy and may favour particular classes of drugs. . For example, although beta-blockers are no longer considered the first choice drugs in hypertension, but they are preferred drugs in the presence of angina or past history of infarction.

These associated conditions can be assessed by eliciting history as shown in table. On examination, significant pallor in the presence of hypertension may indicate presence of chronic kidney disease. ECG may show signs of ischemia, infarction, and conduction system disturbances. Urinalysis may be abnormal and creatinine may be elevated in kidney 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)

Table 4: **Assessment of associated clinical conditions**

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 in lower limb: Coarctation of aorta.
Tachycardia and postural hypotension (pheochromocytoma)
Bruit over renal arteries: renal artery stenosis (renovascularhypertension)
Laboratory investigations: Abnormal urinalysis (proteinuria, haematuria), elevated creatinine. Abnormal kidneys on USG- renal parenchymal disease

Table 5: Assessment of clues to presence of secondary hypertension

c. Assessment of clues to secondary hypertension:

There are clues to the presence of secondary causes of hypertension which may be noticed during the evaluation of the patient. These are important to recognise because an underlying secondary cause may result in difficult to control hypertension. Sometimes addressing the underlying cause e.g. renal artery stenosis may result in cure of hypertension. Long term therapy with oral steroids, often given inappropriately for asthma, arthritis and skin disorders, is common in India and may result in Cushing's syndrome. Takayasu arteritis is also seen in India and should be suspected in the presence of diminished or absent pulses in the upper limb.

	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
Organ damage, diabetes, 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

Table 6: **Overall Assessment of cardiovascular risk** [5]:

Using this table the overall risk in a patient with Grade 1 hypertension can vary from low to very high depending upon the above factors. E.g. a non-smoking, non-obese 50 year old man with grade 1 hypertension may be low risk, a smoking male aged 60 years is at moderately to high risk while a diabetic irrespective of other factors is at high risk.

Framework for assessment of patients with hypertension in the health system in India:

It is clear that patients with hypertension require a continuum of care with participation of healthcare providers at all levels. The non-physician staff with some training can play an important role in detection, assessment, management and long term care of patients with hypertension. Their role in monitoring of blood pressure, adherence to healthy living habits and use of medications is crucial. We also feel that hypertension and many other chronic diseases are best managed at the primary care level and re-training of primary care providers in the prevention, screening, diagnosis and management of these conditions will provide a foundation for programs for these diseases. The health system will also need strengthening in terms of availability of diagnostic tests. In this context, t*he proposed free diagnostics initiative of the Government will make the basic evaluation of the patient with hypertension possible at the sub-centre, PHC and CHC level.*

The table below details the role that the different cadres of health workers can play in the assessment of patients. Much information on cardiovascular risk factors, target organ damage, detection of associated clinical conditions, and suspecting secondary causes of hypertension, can be obtained from the history, and general examination.

	Village(Village health worker)	Sub centre(Trained auxiliaries)	PHC(Primary health care physician)	CHC(Specialist)
History of cardiovascular risk factors: smoking, diet, exercise, diabetes.	√	√	√	√
History suggestive of target organ damage(heart)	√	√	√	√
History of associated clinical conditions, coronary artery disease, stroke	√	√	√	√
History of secondary causes of hypertension	Suspect in case of hypertension not responding to medicines. Refer.	Suspect in case of hypertension not responding to medicines. Refer.	√ [may also refer in case of hypertension non-response]	√
Examination for risk factors	Obesity : Weight, Height	Obesity : Weight, height	Obesity : Weight, height, waist circumference Fasting capillary blood glucose	Obese: Weight, height Diabetes: fasting plasma glucose Hyperlipidemia: lipid profile
Examination for end organ damage/secondary causes of hypertension	Edema(heart, kidney)	Edema(heart, kidney)	Clinical signs of heart failure Clinical clues to secondary hypertension	Clinical signs + Investigations for selected causes like kidney disease. Refer to medical college for evaluation of other causes.
Investigations	Motivate patient to undergo evaluation	Motivate patient to undergo evaluation	Urinalysis : proteinuria, abnormal sediment Fasting capillary blood glucose	Fasting plasma glucose Serum creatinine Lipid profile

Table 7 : Role of different cadres of health workers in patient assessment

Guidelines for assessment of patients with hypertension in developed countries recommend performance of a panel of diagnostic tests (biochemical investigations, urinalysis, ECG, ophthalmoscopy) in all patients, even though this recommendation is based on weak evidence. In our context, this is not currently feasible or cost-effective because of low yields of certain tests (e.g. serum creatinine, serum electrolytes), and we suggest a graded pragmatic approach to assessment.

Three approaches to assessment – **essential** in all patients with Grade 1 HT, **desirable** in those with grade 2 HT or those with diabetes and/or proteinuria, and **optimal** in those with Grade 3 HT, or those with diabetic complications,CKD,heart failure, or with a suspicion of secondary hypertension are suggested.

Essential evaluation: **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 or plasma glucose. 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.

Table 8: Essential and desirable steps in evaluation

Rationale/Evidence:

A comprehensive history and physical examination have been considered useful in assessing risk factors, target organ damage, associated clinical conditions, providing potential clues to secondary hypertension and determination of overall cardiovascular risk, across guidelines.[5, 29] This is therefore being recommended as an essential part of the evaluation of a patient with hypertension in India. Evaluation for diabetes has similarly been

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
History and physical examination:
Serum creatinine: 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.

recommended based on substantial evidence from randomised trials, in most guidelines. [5, 19, 49] The performance of ECG, and serum creatinine, lipids is recommended in all patients in most guidelines, although the evidence on which this is based is largely on consensus of experts and observational studies. [5, 19] Even the performance of some of these tests is suboptimal , e.g. the sensitivity of ECG for detection of left ventricular hypertrophy is low.[5])Some tests like albumin-creatinine ratio on morning spot urine, which can give clue to the presence of microalbuminuria are not available in the public health system.

The graded pragmatic approach to assessment outlined above is based on the importance and utility of the test, its current availability and feasibility in the Indian public health system, and the clinical circumstances of the patient. Detection of diabetes is important and is emphasised. A patient with diabetes is also directly a candidate for statin therapy according to current recommendations.[50] Proteinuria is an independent risk factor which doubles the risk of a cardiovascular event can be done at all levels of the healthcare system.[51] Patients with Grade 2 HT and above, those who are obese, who are diabetic and proteinuric will need estimation of serum creatinine, and lipids, while in the case of patients with grade 3 HT, CKD, or heart failure, there is a need for ophthalmoscopy, estimation of serum electrolytes.

The overall cardiovascular risk can be estimated in absolute terms, using different risk

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)

calculators viz. the Framingham risk score, the **S**ystematic **C**erebrovascular and Coronary **R**isk **E**valuation (SCORE), QRISK2 etc. In this guideline we avoided the calculation of absolute risk over a period of time-e.g.20% over 10 years for the following reasons. These calculations have not been developed using Indian data, including data on prevalence and mortality risk. In a study on patients presenting with a first myocardial infarction, it was seen that the international scoring systems like WHO/ISH, Framingham risk score, ACC/AHA had insufficient accuracy in predicting cardiovascular risk in Indian patients.[52]

Calculations of this risk scores may not be possible in clinic settings in India because of a variety of reasons including lack of laboratory resources for estimating lipid levels. Therefore a semi-quantitative approach based on presence of risk factors, target organ damage, presence of associated clinical conditions, mentioned in the European Society of Cardiology/European Society of Hypertension guidelines.[5]

4. 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 reduction of salt intake, stopping tobacco intake, 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

4.3.1Drug 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 (clinical cardiovascular disease), PAD
- Diabetes
- Presence of chronic kidney disease
- Patients with 3 or more risk factors[6] (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

[6] 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

cardiovascular disease 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.

4.3.3.1 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. If the initial screening by the non-physician medical staff.

4.3.3.2. 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.

Background:

The management of elevated BP involves lifestyle modifications and drug therapy when indicated. Hypertension is a major modifiable risk factor for mortality due to stroke, myocardial infarction.[53] In India for example the incidence of stroke is 119-145 per 100,000 population with a case fatality which varies between 27-42%.[54]There is evidence from multiple randomised controlled trials and meta-analysis that BP reduction leads to reduction in CAD, stroke and total mortality. The meta-analysis suggested a linear relationship with increasing reduction in SBP and DBP resulting in greater CHD and stroke reduction.[5, 55]

Implementation:

Advice on lifestyle modification can be given by both physician and trained non-physician staff, and brief descriptions of this advice are given in the annexure of this guideline. Initiation of drug therapy can be done at any facility starting at the PHC level and above after confirming the diagnosis of hypertension and severity of hypertension (grade 1 or grade 2 or grade 3).

Before initiation of therapy the patient will be educated about hypertension, and assessed for other cardiovascular risk factors (e.g. diabetes), presence of target organ damage, and associated clinical conditions (coronary artery disease, stroke or TIA, and renal disease) as discussed in the section on assessment.

The drug therapy to be initiated will depend on the presence of compelling indications related to these associated clinical conditions, and in case there are no compelling indications for the use of a specific class of drugs, any drug from the first line classes of antihypertensives like calcium channel blockers, ACE inhibitors/Angiotensin receptor blockers, and low dose thiazide diuretics may be used. The availability of a core list of 4 drugs representative of the main groups of anti-hypertensive drugs need to be ensured at all health facilities. These include a long acting calcium channel blocker(amlodipine), ACE inhibitor (enalapril), low dose thiazide diuretic (hydrochlorothiazide), and a cardioselective beta-blocker(atenolol) all of which are listed in the National List of Essential Medicines

2015[56]. In addition a representative drug of the class of Angiotensin receptor blockers like Losartan should be available in case the patient develops adverse effects like cough due to ACE inhibitors. The National List of Essential Medicines (NLEM) 2011 had losartan on its list, but in the NLEM 2015 this has been replaced by telmisartan, while generic lower cost versions of losartan are being procured by state procurement agencies, is therapeutically similar but currently more expensive in India compared to losartan.

Rationale:

Lifestyle interventions have efficacy in lowering BP to a varying extent with the most significant decreases occurring with weight loss - 0.5-2 mm reduction of systolic BP per kg of weight loss, and 6-15 mm reduction in systolic BP with dietary sodium restriction[29]. In patients with grade 1 hypertension, therefore lifestyle modifications with weight reduction and dietary sodium restriction, alone may be efficacious in lowering BP below target levels over a period of time. There is agreement among guidelines about the initiation of drug therapy in those with Grade 1 hypertension and those with target organ damage, cardiovascular disease, and other CV risk factors[19, 49]. There is variation in the duration of the trial of lifestyle modification in those with Grade 1 hypertension with no target organ damage, no associated clinical conditions, no diabetes or CKD. While some guidelines mention a trial of up to 6-12 months of lifestyle modification in Grade 1 hypertension[5], other do not specify any time period. In view of the difficulties in accessing the health system, the higher cardiovascular risk in Indians, and likelihood of loss of follow up in patients in India, we felt it reasonable to advise a 3 month trial of lifestyle modification in patients with Grade 1 hypertension who are low risk, without diabetes, target organ damage and clinical cardiovascular disease. A similar recommendation has been made in an advisory issued by the American Heart Association/American College of Cardiology and Center for Disease Control (AHA/ACC/CDC).[57]. At any level of blood pressure, Indians are considered to be at a higher cardiovascular risk.

Profile of patient	Advice	Rationale
50 year with multiple BP records in the range of 170/100	Drug therapy + Life style modification	Patient has Grade 2 HT and rx is indicated.
60 year old with BP readings in the range of 180-190 systolic & 110-120 diastolic	Immediate drug therapy with 2 drugs at half maximal dosages + lifestyle modification	Patient has Grade 3 HT and rx is indicated
45 year non-smoking female with BP of 150/96 , obese, with normal fasting glucose	Lifestyle modification for 3 months	Grade 1 HT with obesity, no diabetes and multiple risk

		factors
66 year old smoker, obese, male with BP of 154/96	Drug therapy+ Lifestyle modifications	Grade 1 HT with multiple risk factors (male, age > 65,smoker, obesity)
60 year old non-smoker with diabetes with BP of ~ 150/90 mm Hg on multiple readings	Drug therapy + lifestyle modifications	Grade I HT with diabetes
50 year old female with Grade 1 HT. Fundus shows Grade 2 hypertensive retinopathy, and urine shows 1+ proteinuria	Drug therapy +lifestyle modifications	Grade 1 HT with target organ damage(eye, kidney)
75 year old female with recent history of stroke with Grade 1 HT	Drug therapy +lifestyle modifications	Grade 1 HT with clinical cardiovascular disease (stroke)

Table 9: Translation of recommendation into practice

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.

Background:

Healthcare providers and patients alike need to know the target BP to be achieved as part of control of hypertension. This has been an evolving area of debate and investigations, and this issue has been addressed by recent guidelines like the JNC 8 which have systematically reviewed the evidence. The interim results of a recent study – the Systolic Blood Pressure Intervention Trial (SPRINT) which involved intensive reduction of BP < 120 mm are provocative in terms of potential for reduction of mortality, which have to be weighed against increased incidence of serious adverse events noted.[58]

Implementation:

The target BP may be achieved at 6-8 weeks, for which the patient can be assessed at 2-4 weekly intervals for achievement of target BP. At each visit lifestyle interventions can be emphasised, adherence may be assessed and reinforced. If the BP does not show a downward trend on the follow up, medicines from other classes may be added to achieve the target BP.

Rationale:

Target BP: There is agreement among all evidence based guidelines for the targets of Systolic BP ≤ 140 and diastolic BP ≤ 90 mm Hg in the general adult population. (18-21) We have therefore adopted the same targets. A recent study the Systolic Blood Pressure Intervention trial (SPRINT) has examined the effect of reduction of systolic blood pressure below 120 mm on cardiovascular outcomes in non-diabetic patients who were considered at high risk for cardiovascular outcomes.[58]) There was a 25% relative risk reduction in the primary outcome, but this was achieved with a mean of 3 antihypertensive drugs, and there was a significantly increased frequency of serious adverse events including hypotension, syncope, electrolyte abnormalities. Also there was a three-fold higher risk of more than 30% decline in GFR in the intensive treatment group.[58] Since the trial excluded diabetics, the generalisation of these results to diabetics is questionable, especially with the lack of benefit on outcomes in the ACCORD trial which examined the role of intensive BP reduction in diabetics.[59]We feel that these results deserve a nuanced discussion about their generalisability in the context of our health system, where intensive monitoring and access to care is particularly challenging for a large part of our population. Therefore we continue to propose the targets of <140 mm systolic for the general.

Targets for elderly: The definition of elderly differs across guidelines, as JNC 8 guidelines categorised as elderly as those over 60 years [20], while all other guidelines have defined the elderly as people above 80 years of age. [18, 19, 21] . There is agreement among all guidelines, based on data from the HYVET study,[60] that the target for BP of systolic BP of ≤150 mm and diastolic BP ≤90 mm Hg should be considered for patients above 80 years of age.

Targets for patients with diabetes: Earlier guidelines like the JNC 7[29] recommended target BP of <130 mm Hg systolic and <80 mm Hg diastolic for patient populations e.g. diabetics, but recent evidence based guidelines like JNC 8 revised these targets to <140 mm systolic and <90 mm diastolic, based on appraisal of evidence from randomised controlled trials [20]. A large randomised controlled trial – the ACCORD (Action to Control Cardiovascular Risk in Diabetes) found that there was no significant cardiovascular benefit in the intensive BP reduction group where BP was lowered less than 120 mm Hg except a reduction in stroke. [59] In the intensive treatment group there was a more than 2 fold higher risk of serious adverse effects (hypotension, hyperkalemia, angioedema) and elevation of serum creatinine. The most recent Cochrane review on this subject has recommended the standard BP target of <140 mm Hg and <90 mm Hg since "evidence from randomized trials does not support blood pressure targets lower than the standard targets in people with elevated blood pressure and diabetes."[61].

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) and if required and 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.

Background:

Current guidelines suggest that all the 4 drug classes of antihypertensive drugs–thiazide diuretics, calcium channel blockers, ACE inhibitors, Angiotensin receptors blockers for

initiation as well as add-on agents to control BP.[20] Beta-blockers are not considered first line drugs in most guidelines, but may be used in patients with hypertension and associated coronary artery disease or heart failure. Many patients will require combination of drugs for control of hypertension.

Implementation:

In a general patient where hypertension is the only or main condition, any of the 4 classes of drugs can be used as initial therapy, except in the case of elderly patients with isolated systolic hypertension, where a calcium channel blocker or diuretic would be preferred. In case hypertension is associated with other clinical conditions detected during assessment of a patient with hypertension– diabetes, hypertension associated with previous myocardial infarction or stroke, heart failure, angina, and then some drugs would be preferred as mentioned in *table 9*. Consideration should also be given to the compelling and possible contraindications to the use of each class of these drugs before initiation of therapy, mentioned in *table 10*.

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 CCB	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 10: 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

§ Source: adapted from ref.[21]

Angiotensin converting enzyme inhibitors (ACE inhibitors) and Angiotensin receptor blockers (ARBs) both act by targeting the renin-angiotensin system. Both are generally well tolerated, have similar indications and contraindications for their use, although ACE inhibitors have a

more robust evidence base with regard to reduction of cardiovascular mortality.[62] ARBs are preferred if patients develop cough, or angioedema with the use of ACE inhibitors. Many individual ACE inhibitors and ARBs are available. The choice should be guided by considerations of cost, and lower cost ACE inhibitors like enalapril/lisinopril and lower cost ARBs like losartan, may be used.

Beta-blockers are not preferred as first line drugs in isolated cases of hypertension as recent meta-analysis have stated that the benefits of CVD protection especially stroke reduction are lower with it than other class of drugs, and their use may be associated with fatigue, sexual dysfunction, and increased incidence of new onset diabetes.[63]

Patients occasionally may require the use of other drug classes for control of severe hypertension. These include vasodilators (minoxidil), central alpha-agonists (clonidine), and alpha blockers (prazosin)

Table 11: 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

Source: ref.[21]

Rationale:

All major guidelines recommend the four main classes of antihypertensive drugs for the treatment of hypertension.[18-21] As the benefits of antihypertensive treatment is related to reduction of BP and is independent of the drug being used, there is no need to distinguish between drugs within a particular class.[21] In the NICE guidelines thiazide like diuretics viz. chlorthalidone, and indapamide have been preferred over thiazide diuretics like hydrochlorothiazide,[18] in view of greater evidence for the clinical outcome benefits (like reduction of strokes and major cardiovascular events) with these drugs, but other guidelines

like the ESH/ESC do not consider this evidence substantial enough to prefer them over thiazides.[21] All guidelines recommend calcium channel blockers or a diuretic for initiation of therapy in blacks' [18-21] but whether a similar differential response to these agents exists with regard to Indians is not clear.

The recommendations for the use of specific drugs for use in associated clinical conditions are broadly similar in all major guidelines.[18-21]

4.6 Key recommendation: 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 (**Step 3** 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. **Negative recommendation**: 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 in optimal doses, 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.

Implementation:

The initiation of drug therapy will be with monotherapy with any of the 3 classes of drugs (CCBs, low dose thiazides, ACE Inhibitors) or with two drugs representing 2 different drug classes.

Choice of initial drugs in primary care:

Long acting Calcium channel blockers can be used in general population (especially the elderly) as well as patients with diabetes, cardiovascular disease and CKD. They can be used as a once a day drug, have no serious side effects, do not affect the glucose and lipids, and have no need for laboratory based monitoring. The common side effects like pedal edema and tachycardia are not of a serious nature.

ACE inhibitors can similarly be used in general population (except in pregnant women), as well as in patient groups with diabetes, (especially those with proteinuria) cardiovascular disease and CKD, and do not affect glucose and lipids. In general population, they do not require laboratory monitoring. However in patients with diabetic nephropathy and CKD they may require monitoring of potassium and creatinine as these levels can show a rise after initiation of therapy. They can be used on a once daily basis.

Thiazide diuretics can be used in the general population (including elderly), as well as patients with diabetes, CKD. However they can because metabolic side effects which include modest increases in glucose, total cholesterol, hypokalaemia. These side effects are dose related and are seen in doses exceeding 25 mg. The increase in antihypertensive effect between the doses of 12.5 mg and 25 mg are marginal,[64] and therefore the preferred dose is 12.5 mg once a day. Hyponatremia is a potentially life threatening complication associated with thiazide use[65, 66] and is more common in elderly patients, and those with low body weight.[67] Thiazide diuretics potentiate the effect of ACE inhibitors, calcium channel blockers and some of the side effects like hypokalemia are also minimised when they are used in combination. In patients with metabolic syndrome, the risk of new onset of type 2 diabetes is increased with the use of thiazides, especially in combination with beta-blockers.[68]

Calcium channel blockers are efficacious agents which can used once daily, have no effect on glucose, lipids, electrolytes, and can be used in both general populations and patients

with diabetes. If patients have diabetes with proteinuria, or CKD, ACE inhibitors are indicated but may require monitoring of serum creatinine and potassium after initiation of therapy.

	Once a day dosing	**Requirement for laboratory monitoring: effect on glucose, lipids, electrolytes**	**Drug-drug interactions**	**Cost**
Calcium channel blockers	Yes	Nil: no effect on lipids, glucose, electrolytes	Nil	Low in public procurement system
ACE inhibitors	Yes (may require BD dosing)	No effect on lipid, glucose. Potassium, serum creatinine may rise in some patients	Effect decreased by NSAIDS	Low in public procurement system
Thiazide diuretics	Yes	Small rise in glucose, cholesterol, hypokalemia in higher doses	Effect decreased by NSAIDs.	Low in public procurement system

Table 12 : Comparison of 3 first line anti-hypertensive drugs

Table 13 mentions the 3 initial drugs and their 6 combinations, which can be prescribed. In general the therapy can be started at half the maximal dose-e.g. 5 mg of amlodipine, 12.5 mg of hydrochlorothiazide, and 5 mg of Enalapril or 50 mg of Losartan. On review after 2-4 weeks if BP control has not been achieved, then a second drug from one of the classes that has not been used (CCB, diuretic, ACE inhibitor, ARB), and the patient reviewed again for BP control. The doses of drugs to be used as initial or add-on therapy is mentioned in *table 5*

Certain combinations e.g. of CCB with ARBs/ACE inhibitors or diuretics with ARBs/ACE inhibitors are preferred, while combinations of ACE inhibitors with ARBs, and diuretics with beta-blockers are avoidable. The combination of ACE inhibitors with ARBs has an increased risk of end-stage renal failure and stroke as documented in trial settings, [(69)] and is advised against by all guidelines.[(18-21)] The combination of thiazide and beta-blockers is also effective but since both these drugs can elevate blood glucose concentration, the combination should be used with caution in those with a higher risk of developing diabetes (obese, positive family history, glucose intolerance).[(24, 68)]

If the BP is not at goal even after optimal doses of 2 drugs and with regular adherence, then a 3rd drug may be added. According to most guidelines the preferred 3 drug combination is

of a calcium channel blocker along with ACE inhibitor and a diuretic. (CCB+ ACE Inhibitor +diuretic).

Table 13: Initial drug therapy, preferred drug combinations and combinations to be avoided

Initial drug	Preferred combination (as initial or add on therapy)	Combinations for use in Limited settings	Combinations to be avoided
CCB	CCB + ACE Inhibitor*	CCB (dihydropyridines)+ beta-blocker [use in patients with HT and coronary artery disease]	CCB (verapamil/diltiazem) + beta-blocker
	CCB + thiazide diuretic		
Diuretic	Thiazide diuretic +ACE Inhibitor*		Diuretic + beta-blocker
	Thiazide Diuretic +CCB		
ACE inhibitor	ACE Inhibitor* + diuretic	ACE Inhibitor + mineralocorticoid antagonist(potential for hyperkalemia)	ACE Inhibitor* +ARB
	ACE Inhibitor* + CCB		

*Angiotensin Receptor blockers (ARBs) can be used if there is intolerance to ACE inhibitors (cough, angioedema)

Abbreviations: CCB, calcium channel blocker; ACE Inhibitor, Angiotensin converting enzyme inhibitor; ARB, Angiotensin receptor blocker.

In patients who qualify for initiation of drug therapy, 2-4 weekly follow up would be needed to be advised to monitor response to therapy and achievement of BP target. The doctor at the PHC/CHC can record the initial BP in the patient record, and the patient can be monitored for response at the field level by health auxiliaries, or again at the health facility, according to the circumstances. If the patient achieves reduction of BP to target levels, then they would continue the same therapy and be monitored every 2-3 monthly at the PHC level. In case the target BP is not achieved, then increasing the dose or addition of a new drug would be considered.

The administration of two drugs in patients in grade 3 hypertension should initially be as two separate pills. Once target BP has been achieved, then a combination pill with the individual drugs in the same proportion, i.e. a single pill combination (SPC), if available, may be considered.

A single pill combination should be considered for use in patients with hypertension, if it is available and after the patient has been stabilised on the individual components in the same proportions.

Sc

Table 14: 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					1
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)

Rationale:

Use of initial monotherapy: Most of the evidence based guidelines like CHEP, ESC/ESH recommend therapy with a single drug in the case of grade 1 hypertension[19, 21], and with a combination of 2 drugs in patients with grade 2 hypertension. NICE however recommends treatment of grade 2 patients with a single drug initially [18], while JNC 8 recommends that the physician may at his/her discretion, initiate treatment of both grade 1 and grade 2 hypertension with one or two drugs.[20] We decided on the basis of consensus, to recommend a single drug therapy in grade 1 & 2 and with 2 drugs in the case of grade 3 hypertension, in India.

Therapeutic strategy to achieve control of BP: There is no RCT based evidence on the best therapeutic strategy to achieve the target BP. The JNC 8 report has suggested the following strategies for achievement of target BP. These are as follows

1. Select a drug from one of the following classes: calcium channel blocker, ACE inhibitors or ARBs, or thiazide diuretics.
2. Select one of the following strategies to achieve control
    i. Start one drug, titrate to maximal dose, and then add drug from another class.
    ii. Start one drug, add drug from another class if not controlled. Finally titrate to maximal dose of initial drug.
    iii. Start with 2 drugs initially as individual drugs or as a single pill combination.
3. Add a drug from a third class. Maximise doses till control of BP is achieved.

We suggest the following strategy based on the above recommendation in this guideline:

Step 1 therapy: In patients with Grade 1 and Grade 2 hypertension, we suggest initiation with the usual doses of ACE inhibitors/Calcium channel blockers/Thiazide diuretics mentioned in table.

Step 2 therapy: This involves either use of 2 drugs or using maximal doses of the initial drug. Maximising drug doses of the initial drug is less preferable because of the dose plateau relationship in antihypertensive drugs, and because of the likelihood of appearance of adverse effects at high doses. We recommend Step 2 therapy for control of BP in either failure of Step 1 therapy in Grade 1 HT or Grade 2 HT or as initial treatment of patients with Grade 3 HT.

Step 3 therapy: This involves addition of a drug from a third class of drugs

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 Hydrochlorothiazide 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 Hydrochloro-thiazide 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 15: Medication pathway in this guideline evolving from Step 1 (single drug) to Step 2

Single pill combinations: The use of single pill combinations has been suggested as they reduce the number of pills to be taken and have been associated with modest improvements in compliance, and non-significant improvement in persistence of therapy and efficacy.[71].If SPCs are used as initial therapy then titration of dose is difficult since increased dose of one is not possible without increasing the dose of the other. Other factors which need to be considered are availability of 3 combinations in the public health system, the often higher cost of these combinations compared to their constituent drugs in India, and the logistics of maintaining stocks of both single ingredient and combinations of certain drugs. At the moment there is uncertain availability of even single ingredient antihypertensives in public health facilities in India.[72] We therefore recommend the imp

Doses of drugs: The doses recommended need some explanation. In the case of some drugs like thiazide diuretics, it has been seen that the antihypertensive efficacy does not increase at a dose beyond 25 mg while the metabolic side effects escalate with increase in dose.[70] In the case of ACE inhibitors little added antihypertensive efficacy has been noted for example with enalapril above the dose of 10 mg, [73] although doses of up to 40 mg for hypertension have been mentioned in guidelines.[24]A lower dose of some drugs has been

mentioned for elderly (> 65 years) in the case of enalapril and amlodipine (especially if the patient has low body weight and is frail).

Time period to achieve BP target: Control of BP to target BP without causing adverse effects can improve adherence to treatment by gaining the patient's confidence. The evidence based guidelines do not address the question of the time period over which target BP should be reached specifically. However the ASH/ISH guidelines, on the basis of consensus, mentions that an effective treatment regime should be established within 6-8 weeks,[24]and we have adopted this recommendation. Drug doses may be increased or additional drugs introduced at 2 weekly intervals.

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.

When a patient does not respond to two drugs, the physician should review the underlying issues -related to BP measurements, poor adherence to drug and lifestyle modifications, suboptimal treatment regimens, presence of associated conditions, drug interactions, and consider the possibility of secondary hypertension.

Background:

Although the means to control BP effectively now exist, only a minority of patients are well controlled on therapy. In India BP reduction to target levels was achieved in only 11% of rural Indians and 20% of urban Indians who are hypertensive.[8].This is undesirable as control of BP is a highly cost-effective intervention for the prevention of cardiovascular mortality, heart attack and stroke.

Most patients can be controlled with 1 or 2 antihypertensives, especially combinations of ACE inhibitors with calcium channel blockers or diuretics. Some patients have resistant hypertension which may even require more than 3 antihypertensive drugs to control. However more commonly we may have “pseudo resistant” hypertension as a result of measurement, patient, and drug therapy related factors mentioned above. Once these factors have been excluded, there may be secondary causes of hypertension underlying the difficult to control hypertension.

Implementation:

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 optimised. 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, coarctation of aorta, Takayasu's arteritis); which will require evaluation at a medical college level.

Rationale/Evidence:

The factors underlying poor response to antihypertensives have been enumerated in the CHEP guidelines, and have been adapted from this source. [19]

4.8. Therapy of hypertension and associated conditions:

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.

4.8.2.3. 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.

4.8.3.3 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 MAP[7]>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.

[7] 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

Background:

Patients with hypertension often have associated conditions like diabetes, clinical cardiovascular disease with ischemic heart disease or cerebrovascular disease, or chronic kidney disease. Some classes of antihypertensive drugs have special roles in the presence of such conditions, some drugs are best avoided in the presence of conditions like chronic kidney disease, while in other conditions like acute stroke, reduction of elevated BP in general by any class of drugs, should be cautious.

Implementation:

The evaluation of these clinical conditions would be best done at the CHC level, where in addition to the history and physical examination, the patient could be subjected to

Investigations like X-ray chest (cardiomegaly in case of heart failure), ECG (reveal changes suggestive of ischemic heart disease), renal function tests (abnormal in patients with chronic kidney disease) and urinalysis. Patients with chronic kidney disease and heart disease may require monitoring and follow up at the CHC level, while patients with diabetes and previous cerebrovascular disease may be followed up at the PHC level with periodic review at the CHC. The group recommends that the doctors at the PHC level need to be empowered to deal with hypertension and diabetes, and the patients should get access to investigations like serum creatinine, lipids and ECG through a referral arrangement with the CHC.

Rationale:

The issue of treatment of associated conditions is addressed by guidelines like ESC/ESH, JNC 8 and CHEP, though not specifically by NICE. There is broad consensus between these guidelines on the choice of drugs for the treatment of hypertension in the presence of associated conditions.

Diabetes: However there is some variation in the targets for BP control across guidelines. CHEP guidelines for example recommend lower systolic and diastolic BP targets for patients with diabetes (systolic BP < 130 mm Hg and diastolic BP < 80 mm Hg)[(19)] while the European guidelines recommend a diastolic BP target of less than 85 mm Hg while recommending the same systolic BP target of 140 mm Hg. The JNC 8 guideline specifically reviewed the evidence from randomised controlled trials in favour of lower targets for systolic and diastolic BP in diabetics and concluded that there was insufficient evidence supporting them, and suggested similar targets as for the general population.[(20)] We decided to adopt the JNC 8 recommendation in light of the evidence presented in them and the conclusions of a recent Cochrane review which were similar to the JNC 8 recommendations.[(61)] Also a similar target for BP control in diabetics as well as the general population would favour guideline implementation.

Cerebrovascular diseases: The recommendations regarding antihypertensive treatment in patients with ischemic stroke has been adopted from the CHEP guidelines,[(19)]the ESC/ESH guidelines and the Seventh Report of the JNC. The recommendations related to blood

pressure management in patients with spontaneous intracerebral haemorrhage has been adapted from a recent guideline from the American Heart Association/American Stroke Association.[74] Recent studies have demonstrated the lack of an ischemic penumbra in hemorrhagic strokes, and the reduction of BP in the acute phase of stroke can be safely undertaken.

4.9 Hypertension in the elderly:

4.9.1 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.

4.9.2 Postural fall of >20 mm in systolic and >10 mm diastolic indicates postural hypotension is a risk factor for falls.

4.9.3 In a patient with postural hypotension titrate target according to standing BP.

4.9.4 Start therapy with lower doses of drugs and change doses or add drugs at a slower rate in elderly patients.

4.9.5 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.

4.9.6 In elderly patients more than 80 years (the very elderly), the blood pressure target for control is <150 mm systolic and <90 mm diastolic.

4.9.7 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.

4.9.8 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.

4.9.9 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.

4.10 Hypertensive emergencies:

4.10.1 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 'ABCDEFG" 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.

4.10.2 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.

4.10.3 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.

4.10.4 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.

4.10.5 In the case of acute left ventricular failure reduction of the elevated BP is indicated with a parenteral loop diuretic like frusemide 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.

4.10.6 Patients with a hypertensive emergency should be examined for any clinical clues to the presence of secondary hypertension and be evaluated for the same.

4.11 Hypertensive urgencies:

4.11.1 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 or signs referred in the mnemonic 'ABCDEFG' in the pathway on assessment and management of 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.

4.11.2. 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.

4.11.3 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.

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

4.11.5. 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.

4.11.6 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.

4.11.7 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.

Background:

Severe elevations of BP can be asymptomatic and can occur in those with undiagnosed, uncontrolled hypertension or in hypertensive patients who were on therapy but were non-adherent or have stopped some agents like beta-blockers or clonidine suddenly. Such asymptomatic severe elevation of BP termed “hypertensive urgencies” demand reduction of BP over hours and days. Severe hypertension may be associated with life-threatening events involving cardiac, cerebral or renal systems, in which case the term “hypertensive emergency” is used and BP is reduced appropriately over minutes to hours. Appropriate management of hypertension in these situations can prevent morbidity and mortality, while inappropriate management which includes sudden excessive reduction of BP may result in serious complications.

Implementation:

Physicians will need to be trained in the clinical and laboratory assessment of severe hypertension and to distinguish between hypertensive urgency and an emergency

Patients with hypertensive emergencies have symptoms, signs, and laboratory abnormalities suggestive of cardiac, cerebral, renal complications, listed in the table below, and will need care at a secondary/tertiary care facility. *However treatment should not be delayed and the patient should be referred after an initial reduction of BP.*

The healthcare facility will need to keep stock of certain essential medicines for the management of hypertensive urgencies and emergencies. These are indicated in the table below. A minimum list would contain IV frusemide, IV labetalol, and IV nitroglycerine.

Rationale: There is no good quality evidence from randomised controlled trials to guide the management of patients with acute severe hypertension with/without complications, and current recommendations The and are based on the Seventh Report.[29]

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 catecholamine	Pheochromocytoma
	Abrupt withdrawal of clonidine, beta-blockers

Table 16: 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 17: Selected intravenous drugs useful in management of hypertensive emergencies

4.12 Integration with other interventions to reduce cardiovascular risks

4.12.1 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.

4.12.2 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.

4.12.7 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).

4.12.8 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.

4.12.9 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.

4.12.10 **Regardless of presence/absence of hypertension** statins are recommended in the following patient groups[8]

[8]Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology.* 2014;63(25_PA):2889-2934.

- Patients with overt atherosclerotic cardiovascular disease (coronary artery disease, cerebrovascular disease, and peripheral arterial disease), regardless of age.

- Patients with age with ≥ 21 years, where LDL –cholesterol is more than 190 mg/dl, and where secondary cause of hyperlipidemia has been excluded.

- In patients who are diabetic and in the age group of 40-75 years, and LDL cholesterol is between 70-189 mg/dl

4.12.7. Statins are indicated in **hypertensive patients** aged more than 40 years with high cardiovascular risk (3 or more cardiovascular risk factors)[9]

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

Background

Aspirin is used for its antiplatelet effect in patients for prevention of cardiovascular outcomes including myocardial infarction (MI) and stroke, and cardiovascular disease (CVD) death. Aspirin use however also carries a risk of increase in incidence of major bleeds – gastrointestinal or intracranial.

Lowering lipid levels to target levels lowers cardiovascular risks in those with moderate to high cardiovascular risk. The relative benefits of lowering statins are greatest in those who are also diabetic. However they contribute the highest additional costs to antihypertensive treatment. Where the cost factor may be a major cause for default from treatment, the costs benefits of adding statins should be carefully considered and discussed with the patient.

Implementation:

Aspirin: Aspirin in a dose of 75 mg should be available in the public health system for use in well controlled hypertensives that have had a previous cardiovascular event like previous MI or angina, bypass surgery or angioplasty, or stroke. In patients without cardiovascular disease , aspirin should be considered in *those with a high cardiovascular risk* – as discussed in the section on assessment, these would be patients with controlled Grade 2 /Grade 3 hypertension, with 3 or more risk factors, or with organ damage.

Statins: Some statins e.g. atorvastatin are off-patent and available in quality assured public pooled procurements for as low as Rs. 0.22 for a 10 mg

[9]Daskalopoulou SS, Rabi DM, Zarnke KB, et al. The 2015 Canadian Hypertension Education Program recommendations for blood pressure measurement, diagnosis, and assessment of risk, prevention, and treatment of hypertension. *Canadian Journal of Cardiology.* 2015; 31(5):549-568.

tablet(seehttp://www.tnmsc.com/tnmsc/new/user_pages/drugtender.php?drugcat=drug2015). The indications for statin use are fairly clear cut for three categories of patients – Those with existing cardiovascular disease, those with diabetes in the age group of 40-79 years, and those with a LDL-C of > 190 mg/dl. Physicians at the PHC and CHC level can be trained in the use of statins and recognise these indications for statin therapy. With the availability of statins of generic origin and trained health personnel, risk reduction with statins in terms of all-cause mortality, nonfatal MI and stroke, for patients with hypertension with cardiovascular disease in India is feasible in the public health system.

Rationale:

Use of Aspirin: Aspirin due to its antiplatelet effect has the potential to reduce cardiovascular outcomes including myocardial infarction, stroke and other such complications. However its use is also associated with higher risk of gastrointestinal and extracranial bleeds. It should be used therefore when the benefit outweighs the possible harm. Evidence based guidelines like the ESH/ESC, after reviewing the data from recent large meta-analysis[(75),] have indicated the situations where the potential benefit outweighs the harms, and recommended aspirin in the *secondary* prevention of cardiovascular disease.[(21)] We have adopted these recommendations. When aspirin is used for primary prevention, it does reduce the risk of MI, but its effect on reducing risk of stroke and CVD death is inconclusive, whereas the possibility of harm remain.[(76)] The prescription of aspirin for primary prevention of cardiovascular disease is based on judgement of the healthcare provider who must weight possible benefit against the risk of major bleeding.[(76)] In patients with diabetes, the existing data suggests that aspirin use is associated with a modest but not statistically significant reduction in stroke and myocardial infarction.[(77)]

Aspirin should only be given for risk reduction after the BP has been well controlled

Statin therapy: Statin therapy has been recommended as part of global vascular protection or treatment of associated risk factors in some of the guidelines e.g. CHEP and the ESC/ESH guidelines. There is consensus that these are effective in lowering mortality, risk of myocardial infarction and stroke in patients with cardiovascular disease.[(19, 21)]*In such patients statins are an adjunct to diet, exercise, effective control of hypertension and smoking cessation.[(19)]*The use of statins may increase the absolute risk of diabetes by 1%, especially in those with features of the metabolic syndrome, and are associated with a risk of muscle damage.[(78)] Myositis occurs in about 5-10% of recipients. The use of statins in patients without cardiovascular disease requires discussion of the possible adverse effects of statins with the patients. Use of statins in such individuals has been recommended for example if the 10 year risk of cardiovascular disease exceeds a threshold determined by risk assessment tools. The caveats with this calculation based approach are that the pooled cohort equation and the data, on which these risk assessment tools are modelled, are not based on the Indian population. The CHEP guidelines have however defined a high risk individual as someone with 3 or more cardiovascular risk factors out of a list of 11 factors.[(19)] This is an approach that might be feasible to implement in a public health programme in India.

Cardiovascular risk factors for consideration of statin therapy in patients with hypertension: Consider if 3 or more risk factors are present

1. Male sex
2. Smoking
3. Family history of premature cardiovascular disease
4. Diabetes mellitus
5. Left ventricular hypertrophy
6. Family history of premature cardiovascular disease
7. Total cholesterol to high-density lipoprotein ratio ≥ 6
8. Other ECG abnormalities: Left bundle branch block, left ventricular strain, pattern, abnormal Q-waves or ST-T changes, compatible with ischemic heart disease
9. Microalbuminuria or proteinuria
10. Previous stroke or transient ischemic attack
11. Peripheral arterial disease

Table 18: Cardiovascular risk factors for consideration of statin therapy in patients with hypertension

Cessation of tobacco use:

Key recommendations:

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

Background: Tobacco use which includes smoking and chewing tobacco is a major avoidable and modifiable risk factor for cardiovascular disease.[79] In the INTERHEART study which examined the risk of myocardial infarction with tobacco use in 52 countries, the odds ratio for myocardial infarction associated with current smoking cigarettes, smoking beedies, and chewing tobacco were 2.95, 2.89, and 2.23 respectively. The highest risk was associated with current smokers who also chewed tobacco (OR: 4.09).[79] Studies suggest smoking causes up to 60% of cardiovascular disease in urban men in India which is higher than in richer countries.[80] Cessation of tobacco use is therefore an integral component of global vascular protection for patients with hypertension.

I**mplementation:**Assess history of tobacco use as smoking or chewing, and consider appropriate brief interventions as an integral part of hypertension management, which have been well described in the operational guidelines of the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular diseases and Stroke.[15] This part of treatment can be done by non- medical staff if they are provided information and skills in this area.

Rationale:

Systematic reviews of a large number of randomized controlled trials have established that brief physician advice to stop smoking can lead to significant increases in smoking cessation.[81] Brief interventions using non-judgemental and evidence based methods are effective, feasible, cost nothing and carry large benefits to those with hypertension. Also combining advice on tobacco cessation with pharmacotherapy (nicotine replacement therapy, administration of bupropion, and varenicline) also resulted in a higher likelihood of sustained quitting.

5. Monitoring, follow up 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.

Background: Screening and initiation of therapy for hypertension is worthwhile only if it can be sustained. Many patients commenced on treatment remain with uncontrolled hypertension because of poor treatment adherence. Since adherence is a multi-dimensional phenomenon, poverty, poor access to care, patient's perceptions about the need and benefit of lifelong therapy, availability of medications in the public health system, the quality of interactions and communication between healthcare providers and patients, concerns about costs and side effects of therapy all demand careful consideration in the management of patients with hypertension Monitoring of ongoing treatment compliance and recalls are necessary to help treatment compliance. Community based health workers can assist in recalls.

Implementation:

Patient education about the need and benefits of therapy in preventing life-threatening complications is essential for adherence and healthcare providers would need to be trained in providing guidance to patients with hypertension. In patients where this is possible, home BP monitoring may aid adherence to the regime.

The patient may be asked to tailor his intake of pills to fit his daily habits. A simplified regime using long acting drugs which can be used once a day may improve adherence. When multiple anti-hypertensives are being given, a single pill combination can be considered. The use of pill counts, participation of a family member in supervision of drug

intake, periodic counselling and provision of patient information leaflets may be considered to improve adherence and control. A sample patient information leaflet is provided.

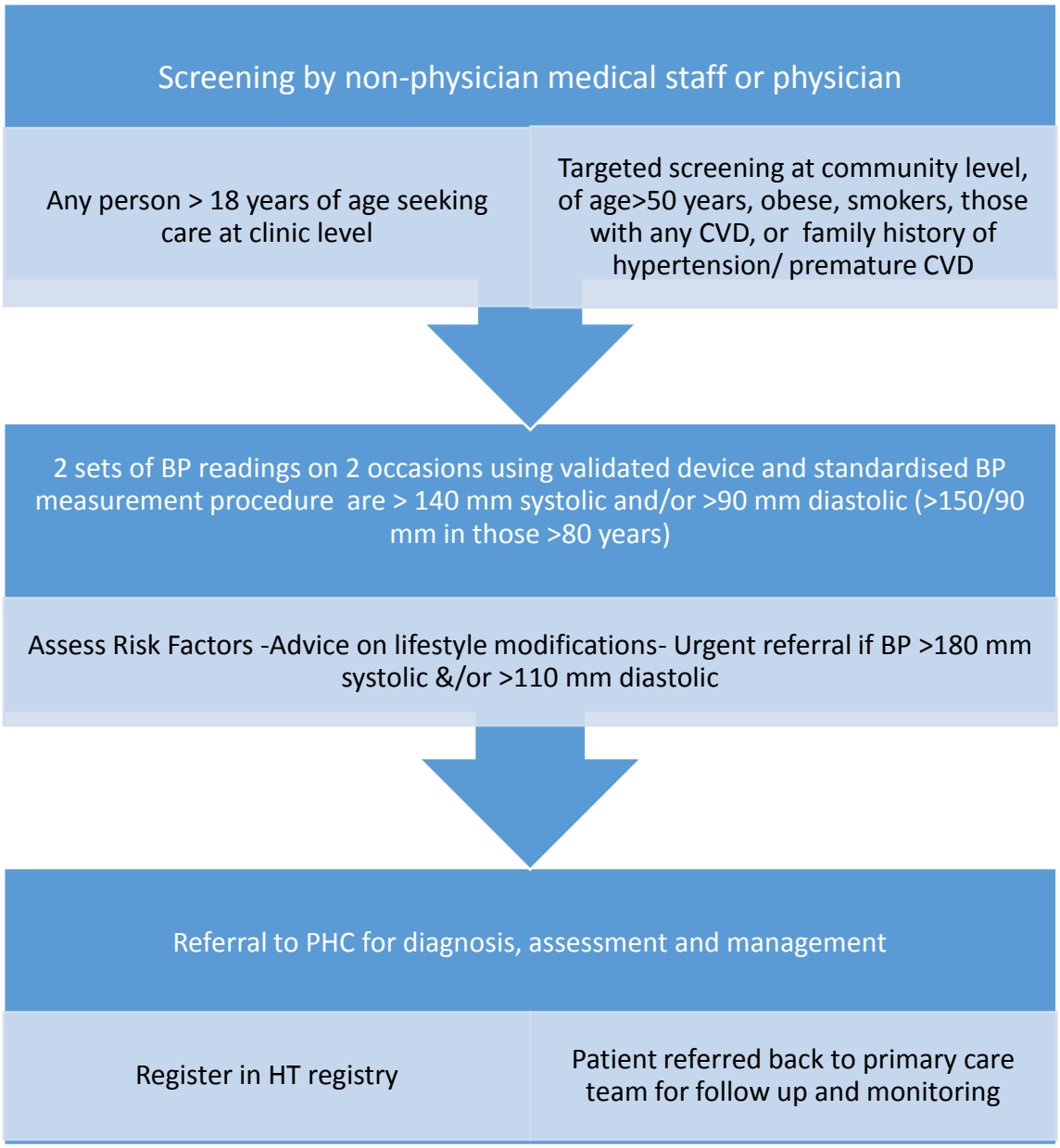
The patients should be monitored for efficacy as well as safety of the regimes used. They should be aware of the common side effects of the drugs being used.

A paper or computer based monitoring system for chronic diseases should be maintained for the target population of a primary health care provider which recognises failure to adhere to treatment. There should be an organised system of interventions when a patient defaults, so that default is not due to lack of knowledge, financial resources or lack of access to health services. Recall systems are effective if they are non-judgemental and respectful of patient choices.

Rationale:

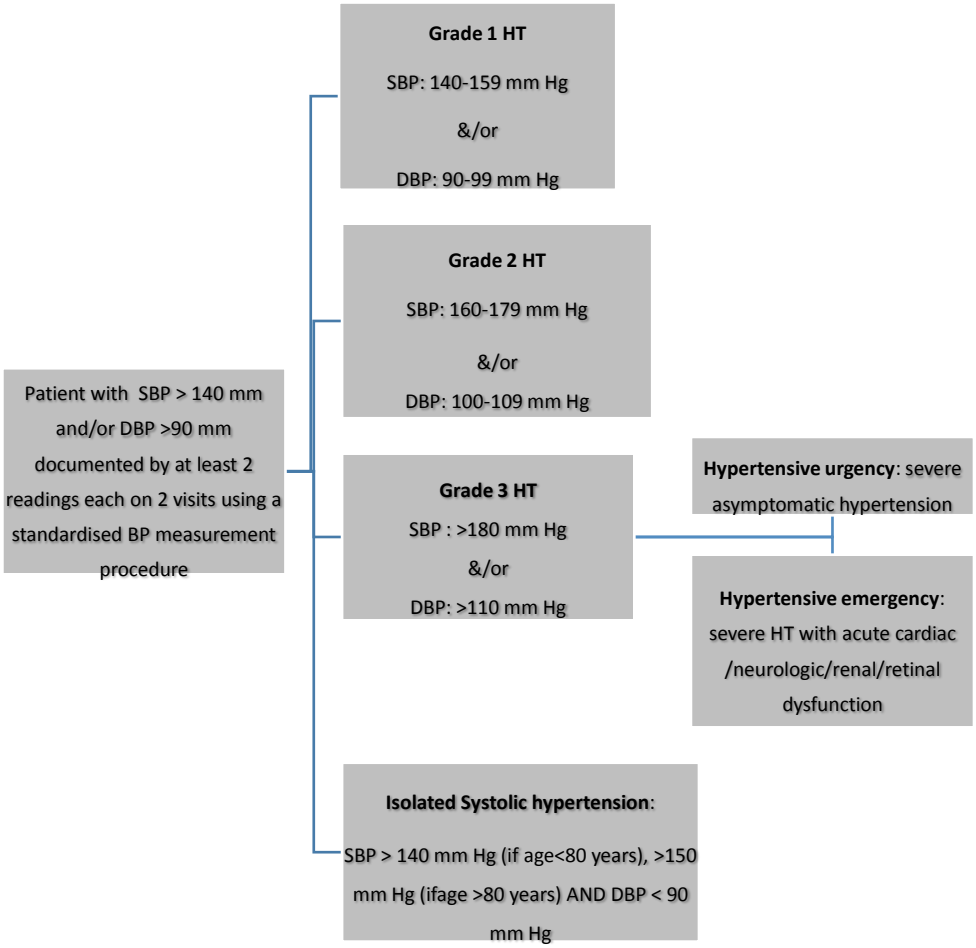
The framework for adherence and the evidence for action have been developed in a WHO document which this guideline draws upon. [82] Among the hypertension related guidelines the CHEP and ESC/ESH guidelines have recommended the multipronged and team approach for management of hypertension, although the evidence base is weak. The above points for action are adapted from these guidelines. According to a systematic review , the involvement of community health workers can improve the control of blood pressure, appointment keeping and adherence to medications, healthcare utilisation and even cardiovascular outcomes.[83]

PATHWAYS IN SCREENING, DIAGNOSIS, CLASSIFICATION, ASSESSMENT AND MANAGEMENT OF HYPERTENSION:

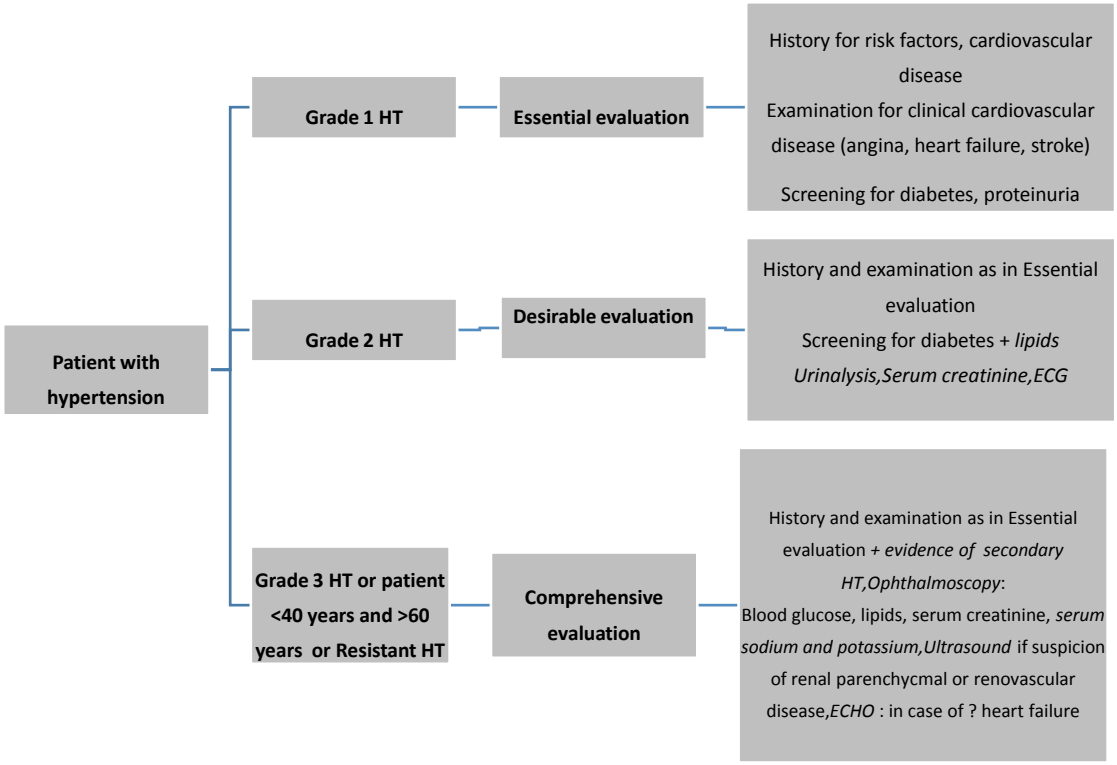


1. **Screening pathway**

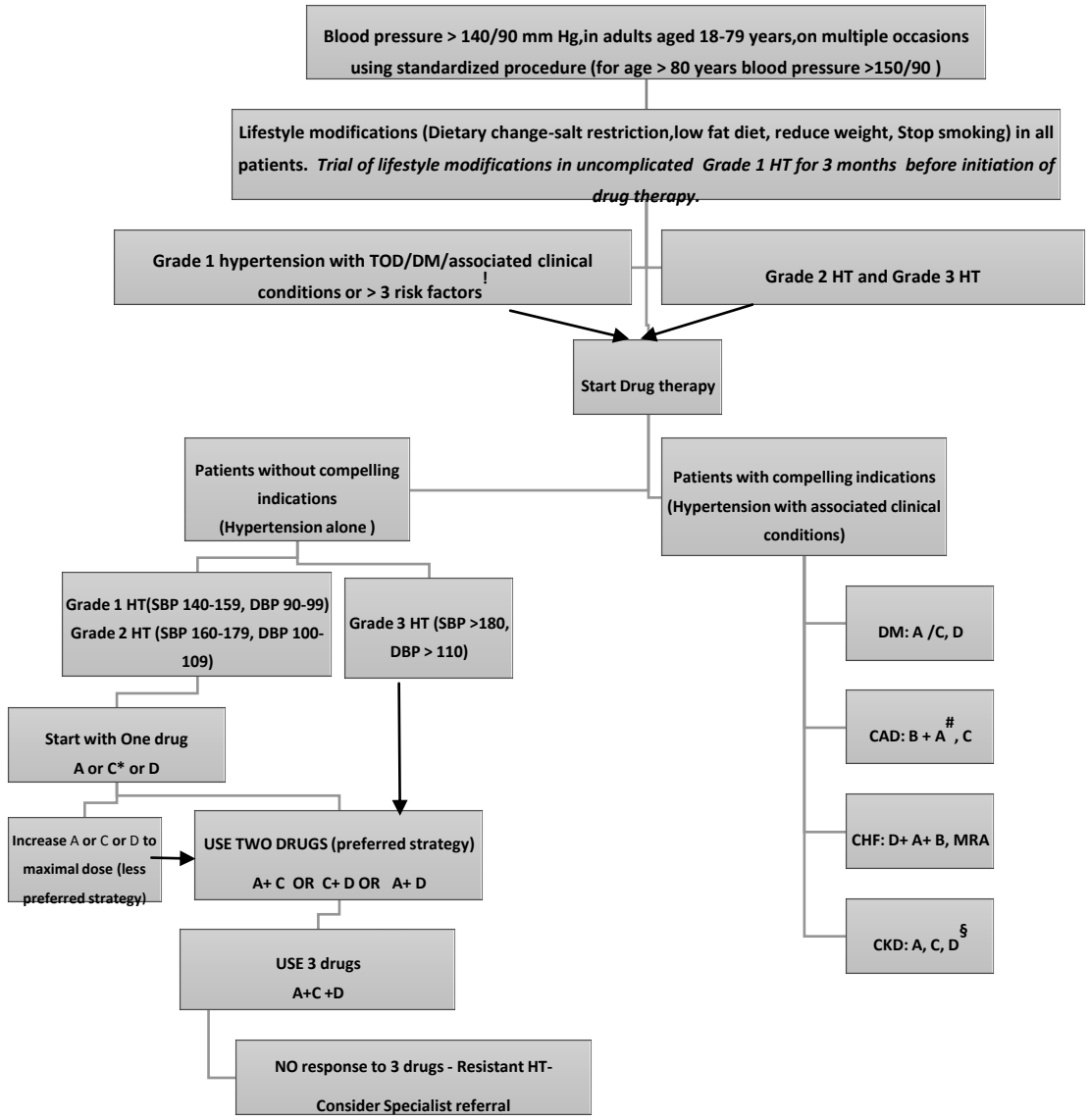
Standard Procedure for BP measurement	
1.Patient preparation and position	Patient should be in a relaxed state for 5 minutes before measurement of BP. Patient should not have had caffeine in the past 1 hour or smoked in the past 30 minutes. Patient should be seated comfortably with back supported, with 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)	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. In oscillometric devices the systolic and diastolic BP will be displayed automatically. 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.
5.No. of measurements and recording the result	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.



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** : **A**ngiotensin converting enzyme(ACE) inhibitors (e.g. enalapril) or **A**ngiotensin II receptor blockers(ARBs)(e.g. losartan) *onlyif intolerance to ACE inhibitors*, **C**: **C**alcium channel blocker(e.g. amlodipine), **D**: Thiazide diuretics(e.g. hydrochorothiazide), **B**: **B**eta-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 inhibitorswill require monitoring of serum creatinine and potassium after initiation of treatment.Based on references[24, 49]

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/m^2 Stop smoking

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

GRADE 1 HYPERTENSION (SBP 141-159 mm, DBP 91-99mm) 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 glucose tolerance

family history of early coronary artery disease

Drug therapy – A or C[1] 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 141-159, DBP 91-99)

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+A[2], C

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

CKD: chronic kidney disease – A or C or D[3]

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: **A**ngiotensin converting enzyme (ACE) inhibitors, (e.g. enalapril) or Angiotensin II receptor blockers (ARBs) (e.g. losartan) only if intolerance to ACEinhibitors, **B**: **B**eta-blockers (e.g. atenolol), **C**: **C**alcium channel blockers (e.g. amlodipine), **D**: thiazide **d**iuretics (e.g. hydrochorothiazide), **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: Hydrochlorthiazide 12. 5 mg.

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

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

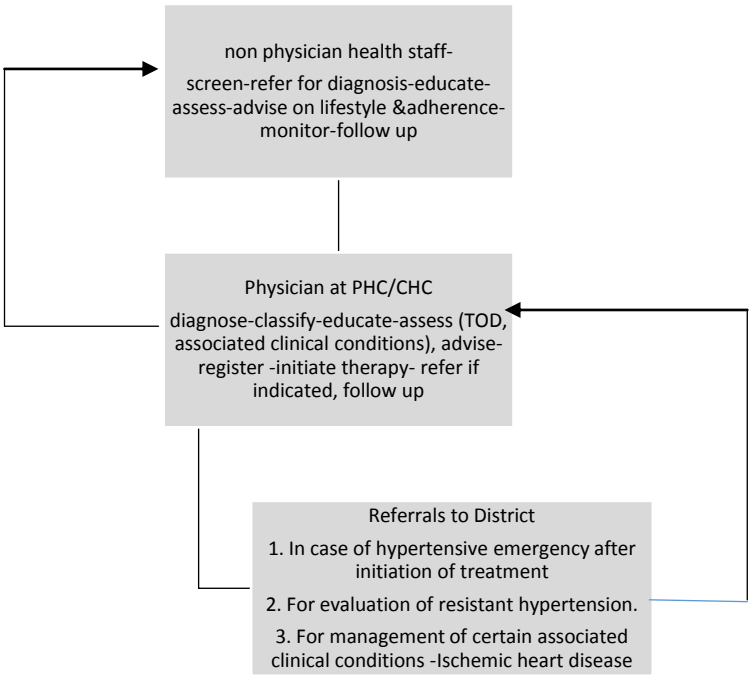
Footnotes :

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

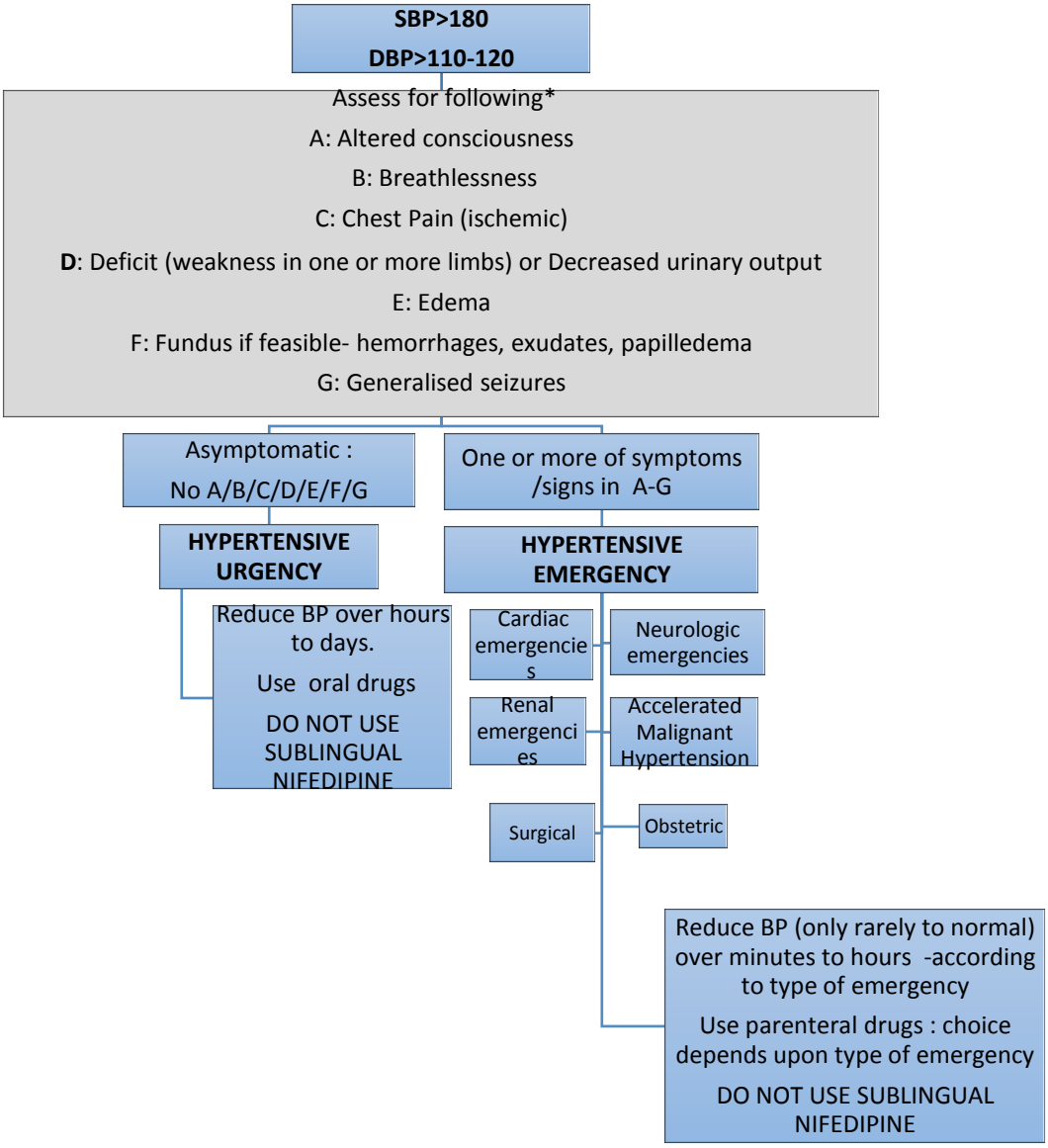
[2] Patients with CAD and history of myocardial infarction should receive both beta-blockers and ACE inhibitors

[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 {, 2011 #138;Weber, 2014 #85}



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

ANNEXURES

Annexure 1: Glossary and Abbreviations

Abdominal obesity	Abdominal obesity, also known as central obesity, is when excessiveabdominal fat around the stomach and abdomen has built up to the extent that it is likely to have a negative impact on health. It is assessed by measuring the waist circumference or calculating the ratio of the circumference at the waist to that at the hip (waist-hip ratio). Abdominal obesity has been strongly linked to risk of cardiovascular disease.
ACC/AHA	American College of Cardiology/American Heart Association
ACE Inhibitor	Angiotensin-Converting Enzyme Inhibitor. These slow down the effect of the angiotensin converting enzyme (ACE) and reduce the levels of angiotensin II. These are used in treatment of hypertension and heart failure. Examples include enalapril, lisinopril.
ARB	Angiotensin II Receptor Blocker. They are used in treatment of hypertension, kidney disease and heart failure and act by blocking the effect of angiotensin II on the receptors in the blood vessels. Examples include losartan, and telmisartan.
BMI	Body mass index is the weight in kilograms divided by the square of the height in metres. Cut offs exist to define thinness, normal weight, overweight, obesity.
CCB	Calcium channel blocker. A group of drugs used in treatment of hypertension and angina. Examples include amlodipine,nifedipine, diltiazem and verapamil.
CHC	community health centre
CHEP	Canadian Hypertension Education Program
CKD	Chronic kidney disease: disease in which kidneys start failing in their function of filtering waste, removing water and salt. It can result from a variety of causes, among which hypertension and diabetes are common.
CVD	Cardiovascular disease. It is a class of disease affecting the heart or vessels. It may manifest as angina or myocardial infarction (heart attack), heart failure, stroke or disease of the arteries in the limbs.
DBP	Diastolic blood pressure-the pressure in the arteries during the relaxation of the heart, between beats.
Diuretic	A class of drugs which promotes the production of urine. They are used in treatment of hypertension, heart failure and kidney disease.
DM	Diabetes mellitus - a disease in which there is abnormal handling of the sugar in the body.
Dyslipidemia	Abnormal amount of lipids (fats) in the blood, usually cholesterol, triglycerides.
ECG	Electrocardiogram
ESH/ESC	European Society of Hypertension/European Society of Cardiology
Hyperlipidemia	excess of cholesterol and other fats in the blood
Hypertension	High blood pressure
Hypertensive emergency	Hypertensive emergency is a situation where the blood pressure is severely elevated [systolic blood pressure 180 or higher, or diastolic

	pressure 110 or higher), along with symptoms , signs and other evidence of associated organ damage which may manifest as altered consciousness, stroke, breathlessness, chest pain, kidney failure, visual disturbance.
Hypertensive urgency	Hypertensive urgency is a situation where the blood pressure is severely elevated [systolic blood pressure 180 or higher or diastolic pressure 110 or higher), but there is no associated organ damage
IHG	Internal Harmonisation Group- a group of experts constituted by the National Health Systems Resource Centre, New Delhi to harmonise guideline development
ISH	Internal Society of Hypertension
JNC	Joint National Committee is a group of experts in the United States which has provided periodically, guidelines on prevention, detection, evaluation and treatment of hypertension
Lifestyle modifications	Changes in lifestyle which are healthier
LVH	left ventricular hypertrophy -an enlargement of the left side of the heart due to high blood pressure
NICE	The National Institute for Health and Care Excellence is an executive non-departmental public body under the Department of Health in the United Kingdom, reputed for its formulation of guidelines for clinical practice.
Obesity	Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have a negative effect on health. The international cut-off is a BMI of 30 kg/m2 or higher, but a lower cut off of 25 kg/m2 for Indians has been suggested.
Oscillometric device	This is a BP measuring device which uses electronic pressure sensors and an algorithm to estimate the systolic and diastolic blood pressures which are available as a numerical readout.
PHC	primary health centre
Primary(essential) hypertension	It is the usual form of hypertension that by definition has no identifiable cause. It is linked to genetics, dietary factors, inactivity and obesity
Proteinuria	the presence of abnormal quantities of protein in the urine, which may indicate damage to the kidneys
Retinopathy	damage to the retina and the circulation of the retina due to high blood pressure
SBP	Systolic Blood pressure- the pressure produced in the arteries during the contraction of the heart
Screening	Screening, in medicine, is a strategy used in a population to identify the possible presence of an as-yet-undiagnosed disease in individuals without signs or symptoms.
Secondary hypertension	It is the less common form of hypertension where the hypertension is associated with an underlying medical condition of the kidneys, arteries, or endocrine system.
Stroke	A medical emergency when either clogging of arteries or bleeding in the brain may result in death of brain cells and appearance of

	weakness or numbness of the body, trouble with speech, vision. Hypertension is a major risk factor for strokes, which can result in death or disability.
Target organ damage	Target organ damage usually refers to damage occurring in major organs fed by the circulatory system (heart, kidneys, brain, eyes) which can sustain damage due to uncontrolled hypertension.
White coat effect	The white coat refers to the coats traditionally worn by doctors. This effect is present when the blood pressure readings recorded in a visit to the clinic are consistently higher than those recorded at home. This effect may be seen in both treated and untreated forms of hypertension.
White coat hypertension	This is a situation where people with normal BP outside the clinic setting have hypertension during measurement of BP by doctors and nurses.
WHO	World Health Organisation

ANNEXURE 2: LIFE STYLE MODIFICATIONS IN HYPERTENSION

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.

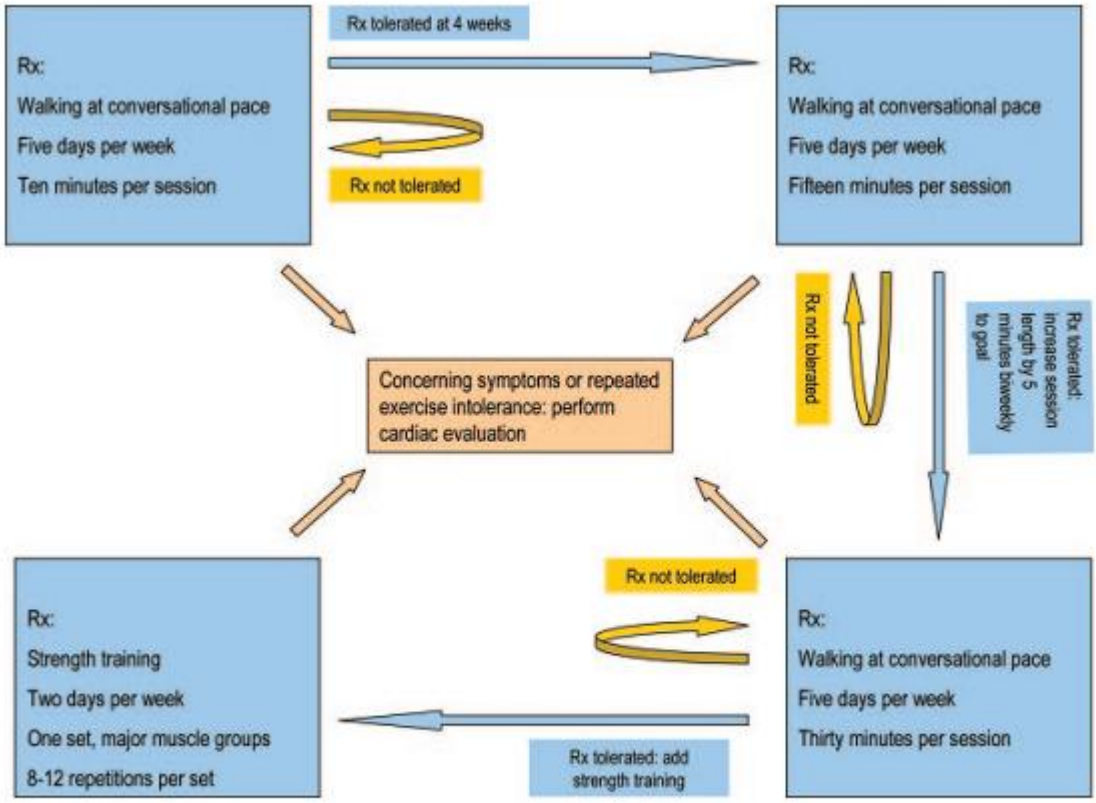


Figure. An approach to staged exercise prescriptions: Any enjoyable, moderate-intensity activity such as those listed in Table 2 may be substituted for walking. Specific strength training exercises are also listed in Table 2. Rx indicates prescription.

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 meter^2. For Indian population 18.5 to 22.9 BMI is normal, 23 to 24.9 is considered as overweight and BMI of ≥25 kg/m^2 is considered as obesity in Indians.[10] 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.

[10]Misra 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 that 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 volume 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 x 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 **a**sked about smoking status at every opportunity. Then the patient should be**a**dvised about to quit smoking, and **a**ssessed about his degree of addiction and readiness to quit. The health professional should **a**ssist in formulating a smoking cessation strategy including setting a quit date, counselling and other measures, and finally **a**rrange 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 counselling. The risk of adverse effects is small and is generally outweighed by the significant risk of continuing to smoke.

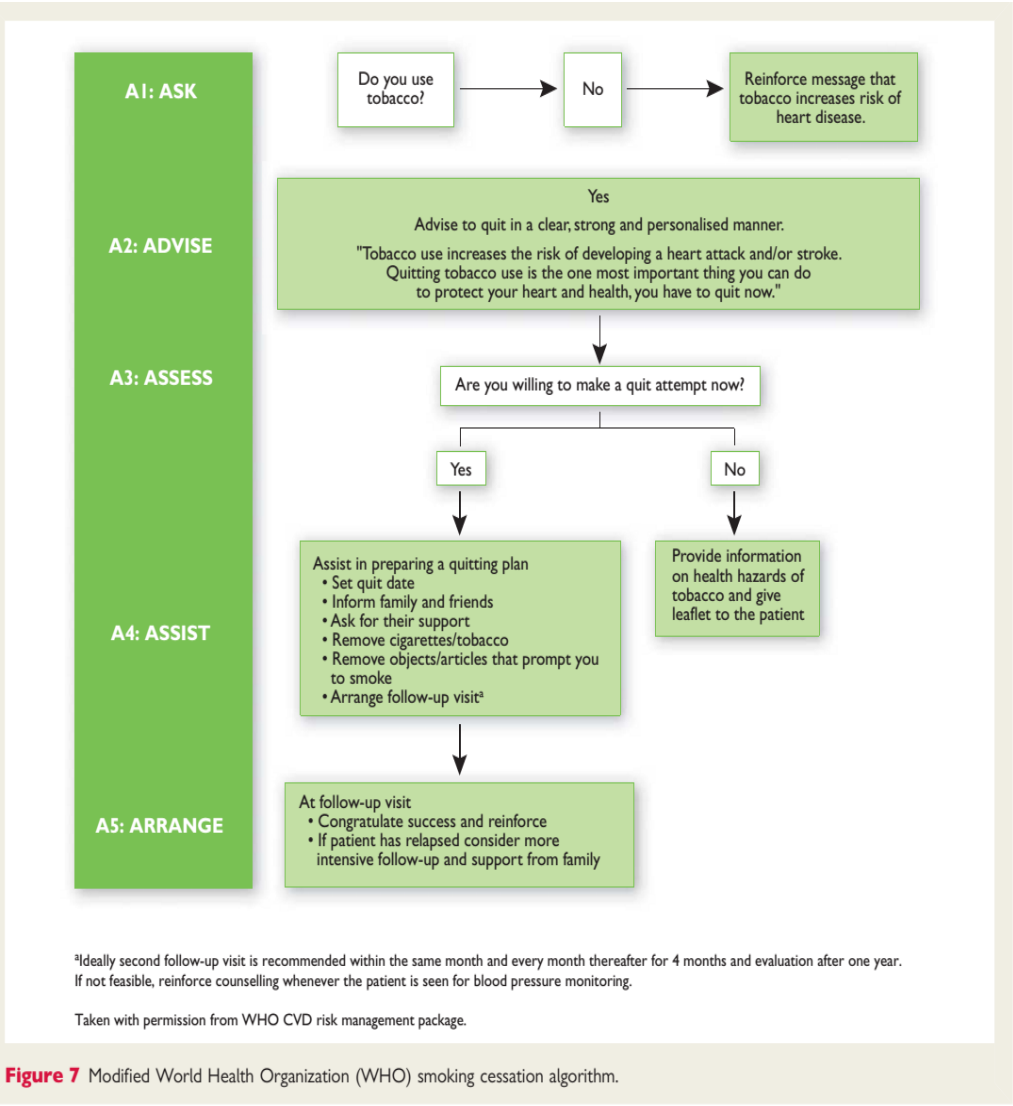


Figure 7 Modified World Health Organization (WHO) smoking cessation algorithm.

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(35^0C) 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, nicardipine, 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 does may be 2.5 mg[11]. The dose may be usually increased to 10 mg above which the additional benefit may be minimal[12], 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, is on potassium containing salt substitutes.

Side effects:

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

[11]70. Opie L.H, Gersh B.J, editors. Drugs for the Heart. 8th ed: Saunders; 2013.
[12]70. Ibid.

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.[13]

[13] 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 glycemiccontrol 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.

ANNEXURE 4: BIBLIOGRAPHY

1. Atkins G, Rahman M, Wright Jr JT. Diagnosis and Treatment of Hypertension. In: Fuster V, Walsh RA, Harrington RA, editors. Hurst's The Heart. 13th ed: McGraw Hill Medical 2011. p. 1587.
2. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, et al. Recommendations for blood pressure measurement in humans and experimental animals part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Hypertension. 2005;45(1):142-61.
3. Forouzanfar MH, Alexander L, Anderson HR, Bachman VF, Biryukov S, Brauer M, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015 Dec 5;386(10010):2287-323.
4. Travasso C. High blood pressure is the leading health risk factor in India, finds study. BMJ. 2015;351:h5034.
5. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, et al. 2013 ESH/ESC Practice Guidelines for the Management of Arterial Hypertension. Blood Press. 2014 Feb;23(1):3-16.
6. India high blood pressure [database on the Internet]2014. Available from: Available from: http://www. healthmetricsandevaluation.org/search-gbd-data.
7. Deedwania P, Gupta R. Hypertension in South Asians. In: Black HR, Elliott WJ, editors. Hypertension : A companion to Braunwald's Heart Disease. Second ed: Elsevier Saunders; 2012.
8. Anchala R, Kannuri NK, Pant H, Khan H, Franco OH, Di Angelantonio E, et al. Hypertension in India: a systematic review and meta-analysis of prevalence, awareness, and control of hypertension. J Hypertens. 2014 Jun;32(6):1170-7.
9. Jafar TH, Hatcher J, Poulter N, Islam M, Hashmi S, Qadri Z, et al. Community-based interventions to promote blood pressure control in a developing country: a cluster randomized trial. Ann Intern Med. 2009 Nov 3;151(9):593-601.
10. Farzadfar F, Murray CJ, Gakidou E, Bossert T, Namdaritabar H, Alikhani S, et al. Effectiveness of diabetes and hypertension management by rural primary health-care workers (Behvarz workers) in Iran: a nationally representative observational study. Lancet. 2012 Jan 7;379(9810):47-54.
11. Dukpa Wangchuk, Navkiran Kaur Virdi, Renu Garg, Shanthi Mendis, Nani Nair, Dorji Wangchuk, et al. Package of essential noncommunicable disease (PEN) interventions in primary health-care settings of Bhutan: a performance assessment study. WHO South-East Asia Journal of Public Helath 2014;3(2):154-60.
12. Gaziano TA, Bertram M, Tollman SM, Hofman KJ. Hypertension education and adherence in South Africa: a cost-effectiveness analysis of community health workers. BMC Public Health. 2014;14:240.
13. Menon J, Joseph J, Thachil A, Attacheril TV, Banerjee A. Surveillance of noncommunicable diseases by community health workers in Kerala: the epidemiology of noncommunicable diseases in rural areas (ENDIRA) study. Glob Heart. 2014 Dec;9(4):409-17.
14. Liang X, Chen J, Liu Y, He C, Li T. The effect of hypertension and diabetes management in Southwest China: a before- and after-intervention study. PLoS ONE. 2014;9(3):e91801.
15. National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular diseases and Stroke (NPCDCS). Operational Guidelines.: Directorate General of Health Services, Ministry of Health and Family Welfare. Government of India.; 2008.
16. Bonita R, Beaglehole R, Kjellstrom T, editors. Basic Epidemiology. second ed. Geneva: World Health Organisation, ; 2006.
17. World Health Organization. Package of essential noncommunicable (PEN) disease interventions for primary health care in low-resource settings. 2010.
18. Hypertension: Clinical management of primary hypertension in adults NICE guidelines [CG127]. National Institute for HealthCare Excellence; 2011.
19. Daskalopoulou SS, Rabi DM, Zarnke KB, Dasgupta K, Nerenberg K, Cloutier L, et al. The 2015 Canadian Hypertension Education Program recommendations for blood pressure measurement,

diagnosis, assessment of risk, prevention, and treatment of hypertension. Canadian Journal of Cardiology. 2015;31(5):549-68.
20. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). Jama. 2014;311(5):507-20.
21. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Blood pressure. 2013;22(4):193-278.
22. US Preventive Services Task Force. Screening for high blood pressure: recommendations and rationale. American journal of preventive medicine. 2003;25(2):159-64.
23. European guidelines on cardiovascular disease prevention in clinical practice (version 2012). Rockville MD: Agency for Healthcare Research and Quality (AHRQ); 2012 [10/7/2015]; Available from: http://www.guideline.gov/content.aspx?id=39354&search=smoking+cessation.
24. Weber MA, Schiffrin EL, White WB, Mann S, Lindholm LH, Kenerson JG, et al. Clinical Practice Guidelines for the Management of Hypertension in the Community. The Journal of Clinical Hypertension. 2014;16(1):14-26.
25. Kalavathy MC, Thankappan KR, Sarma PS, Vasan RS. Prevalence, awareness, treatment and control of hypertension in an elderly community-based sample in Kerala, India. Natl Med J India. 2000 Jan-Feb;13(1):9-15.
26. Alpert BS, Quinn D, Gallick D. Oscillometric blood pressure: a review for clinicians. J Am Soc Hypertens. 2014 Dec;8(12):930-8.
27. John J, Muliyil J, Balraj V. Screening for hypertension among older adults: a primary care "high risk" approach. Indian J Community Med. 2010 Jan;35(1):67-9.
28. Joshi SR, Saboo B, Vadivale M, Dani SI, Mithal A, Kaul U, et al. Prevalence of diagnosed and undiagnosed diabetes and hypertension in India—results from the Screening India's Twin Epidemic (SITE) study. Diabetes technology & therapeutics. 2012;14(1):8-15.
29. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo Jr JL, et al. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. JAMA. 2003;289(19):2560-71.
30. Laxmaiah A, Meshram, II, Arlappa N, Balakrishna N, Rao KM, Reddy Ch G, et al. Socio-economic & demographic determinants of hypertension & knowledge, practices & risk behaviour of tribals in India. Indian J Med Res. 2015 May;141(5):697-708.
31. National Programme for Prevention and Control of Diabetes, Cardiovascular diseases and Stroke: Operational Guidelines. Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India; 2008.
32. Joshi R, Alim M, Kengne AP, Jan S, Maulik PK, Peiris D, et al. Task Shifting for Non-Communicable Disease Management in Low and Middle Income Countries – A Systematic Review. PLoS ONE. 2014;9(8):e103754.
33. Sathish T, Kannan S, Sarma PS, Razum O, Thankappan KR. Incidence of hypertension and its risk factors in rural Kerala, India: a community-based cohort study. Public Health. 2012 Jan;126(1):25-32.
34. Midha T, Krishna V, Nath B, Kumari R, Rao YK, Pandey U, et al. Cut-off of body mass index and waist circumference to predict hypertension in Indian adults. World J Clin Cases. 2014 Jul 16;2(7):272-8.
35. Savitha MR, Krishnamurthy B, Fatthepur S, Yashwanth Kumar AM, Khan M. Essential hypertension in early and mid-adolescence. Indian J Pediatr. 2007 2007/11/01;74(11):1007-11.
36. Sharma M, Ganguly NK. Premature Coronary Artery Disease in Indians and its Associated Risk Factors. Vasc Health Risk Manag. 2005 Sep;1(3):217-25.

37. O'Brien E, Atkins N, Stergiou G, Karpettas N, Parati G, Asmar R, et al. European Society of Hypertension International Protocol revision 2010 for the validation of blood pressure measuring devices in adults. Blood Press Monit. 2010 Feb;15(1):23-38.
38. O'Brien E, Petrie J, Littler W, de Swiet M, Padfield PL, Altman DG, et al. An outline of the revised British Hypertension Society protocol for the evaluation of blood pressure measuring devices. J Hypertens. 1993 Jun;11(6):677-9.
39. Skirton H, Chamberlain W, Lawson C, Ryan H, Young E. A systematic review of variability and reliability of manual and automated blood pressure readings. J Clin Nurs. 2011 Mar;20(5-6):602-14.
40. A'Court C, Stevens R, Sanders S, Ward A, McManus R, Heneghan C. Type and accuracy of sphygmomanometers in primary care: a cross-sectional observational study. Br J Gen Pract. 2011 Sep;61(590):e598-603.
41. Parati G, Mendis S, Abegunde D, Asmar R, Mieke S, Murray A, et al. Recommendations for blood pressure measuring devices for office/clinic use in low resource settings. Blood Press Monit. 2005 Feb;10(1):3-10.
42. Fagard RH, Cornelissen VA. Incidence of cardiovascular events in white-coat, masked and sustained hypertension versus true normotension: a meta-analysis. Journal of hypertension. 2007;25(11):2193-8.
43. Franklin SS, Thijs L, Hansen TW, O'Brien E, Staessen JA. White-Coat Hypertension: New Insights From Recent Studies. Hypertension. 2013 December 1, 2013;62(6):982-7.
44. Mancia G, Bertinieri G, Grassi G, Parati G, Pomidossi G, Ferrari A, et al. Effects of blood-pressure measurement by the doctor on patient's blood pressure and heart rate. Lancet. 1983 Sep 24;2(8352):695-8.
45. Ostchega Y, Zhang G, Sorlie P, Hughes JP, Reed-Gillette DS, Nwankwo T, et al.: Blood pressure randomized methodology study comparing automatic oscillometric and mercury sphygmomanometer devices: National health and nutrition examination survey, 2009-2010.
46. Reidpath DD, Ling ML, Yasin S, Rajagobal K, Allotey P. Community-based blood pressure measurement by non-health workers using electronic devices: a validation study. Glob Health Action. 2012;5:14876.
47. U.S. Preventive Services Task Force. Final Recommendation Statement: High Blood Pressure in Adults: Screening.

. 2015 [cited 2015 23rd October]; Available from: http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/high-blood-pressure-in-adults-screening.
48. World Health Organization, International Society of Hypertension Writing Group. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. Journal of hypertension. 2003;21(11):1983-92.
49. Hypertension: Clinical management of primary hypertension in adults.NICE Guidelines[CG 127]: National Institute for Health and Care Excellence 2011.
50. National Guideline C. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Rockville MD: Agency for Healthcare Research and Quality (AHRQ); [1/24/2016]; Available from: https://www.guideline.gov/content.aspx?id=48337&search=cholesterol+guidelines.
51. Beevers G, Lip GY, O'Brien E. ABC of Hypertension: John Wiley & Sons; 2014.
52. Bansal M, Kasliwal RR, Trehan N. Comparative accuracy of different risk scores in assessing cardiovascular risk in Indians: A study in patients with first myocardial infarction. Indian Heart J. 2014 Nov-Dec;66(6):580-6.
53. Ridker P, Libby P, Buring J. Risk markers and the primary prevention of cardiovascular disease. In: Mann D, Zipes D, Libby P, Bonow R, editors. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine Tenth ed: Elsevier Saunders; 2015. p. 891-933.

54. Pandian JD, Sudhan P. Stroke Epidemiology and Stroke Care Services in India. Journal of Stroke. 2013;15(3):128-34.
55. Law M, Morris J, Wald N. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ. 2009;338.
56. National List of Essential Medicines 2015. In: Welfare MoHaF, editor. New Delhi: Government of India; 2015.
57. Go AS, Bauman MA, Coleman King SM, Fonarow GC, Lawrence W, Williams KA, et al. An effective approach to high blood pressure control: a science advisory from the American Heart Association, the American College of Cardiology, and the Centers for Disease Control and Prevention. Hypertension. 2014 Apr;63(4):878-85.
58. Wright JT, Williamson JD, Whelton PK, Snyder JK, Sink KM, Rocco MV, et al. A randomized trial of intensive versus standard blood-pressure control. New England Journal of Medicine. 2015;373(22):2103-16.
59. Cushman WC, Evans GW, Byington RP, Goff DC, Jr., Grimm RH, Jr., Cutler JA, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med. 2010 Apr 29;362(17):1575-85.
60. Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, et al. Treatment of hypertension in patients 80 years of age or older. N Engl J Med. 2008 May 1;358(18):1887-98.
61. Arguedas JA, Leiva V, Wright JM. Blood pressure targets for hypertension in people with diabetes mellitus. Cochrane Database Syst Rev. 2013;10:CD008277.
62. Li EC, Heran BS, Wright JM. Angiotensin converting enzyme (ACE) inhibitors versus angiotensin receptor blockers for primary hypertension. Cochrane Database Syst Rev. 2014;8:CD009096.
63. Wiysonge CS, Bradley HA, Volmink J, Mayosi BM, Mbewu A, Opie LH. Beta-blockers for hypertension. Cochrane Database Syst Rev. 2012;11.
64. Lacourciere Y, Poirier L. Antihypertensive effects of two fixed-dose combinations of losartan and hydrochlorothiazide versus hydrochlorothiazide monotherapy in subjects with ambulatory systolic hypertension. Am J Hypertens. 2003 Dec;16(12):1036-42.
65. Rodenburg EM, Hoorn EJ, Ruiter R, Lous JJ, Hofman A, Uitterlinden AG, et al. Thiazide-associated hyponatremia: a population-based study. Am J Kidney Dis. 2013 Jul;62(1):67-72.
66. Rao MY, Sudhir U, Anil Kumar T, Saravanan S, Mahesh E, Punith K. Hospital-based descriptive study of symptomatic hyponatremia in elderly patients. J Assoc Physicians India. 2010 Nov;58:667-9.
67. Chow KM, Szeto CC, Wong TY, Leung CB, Li PK. Risk factors for thiazide-induced hyponatraemia. QJM. 2003 Dec;96(12):911-7.
68. Mason JM, Dickinson HO, Nicolson DJ, Campbell F, Ford GA, Williams B. The diabetogenic potential of thiazide-type diuretic and beta-blocker combinations in patients with hypertension. J Hypertens. 2005 Oct;23(10):1777-81.
69. Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, Schumacher H, et al. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl J Med. 2008 Apr 10;358(15):1547-59.
70. Opie L.H, Gersh B.J, editors. Drugs for the Heart. 8th ed: Saunders; 2013.
71. Gupta AK, Arshad S, Poulter NR. Compliance, safety, and effectiveness of fixed-dose combinations of antihypertensive agents: a meta-analysis. Hypertension. 2010 Feb;55(2):399-407.
72. Prinja S, Bahuguna P, Tripathy JP, Kumar R. Availability of medicines in public sector health facilities of two North Indian States. BMC Pharmacology and Toxicology. 2015;16(1):1-11.
73. Opie L.H, Pfeffer MA. Inhibitors of the Renin-Angiotensin-Aldosterone System. In: Opie L.H, Gersh B.J, editors. Drugs for the Heart. 8th ed: Elsevier Saunders; 2013. p. 142.
74. Morgenstern LB, Hemphill JC, 3rd, Anderson C, Becker K, Broderick JP, Connolly ES, Jr., et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2010 Sep;41(9):2108-29.

75. Baigent C, Blackwell L, Collins R, Emberson J, Godwin J, Peto R, et al. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. Lancet. 2009 May 30;373(9678):1849-60.
76. Hennekens CH, Dalen JE. Aspirin in the primary prevention of cardiovascular disease: current knowledge and future research needs. Trends Cardiovasc Med. 2014 Nov;24(8):360-6.
77. Bartolucci AA, Tendera M, Howard G. Meta-analysis of multiple primary prevention trials of cardiovascular events using aspirin. Am J Cardiol. 2011 Jun 15;107(12):1796-801.
78. Desai CS, Martin SS, Blumenthal RS. Non-cardiovascular effects associated with statins. BMJ. 2014;349:g3743.
79. Teo KK, Ounpuu S, Hawken S, Pandey MR, Valentin V, Hunt D, et al. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. Lancet. 2006 Aug 19;368(9536):647-58.
80. Rastogi T, Jha P, Reddy KS, Prabhakaran D, Spiegelman D, Stampfer MJ, et al. Bidi and cigarette smoking and risk of acute myocardial infarction among males in urban India. Tob Control. 2005 Oct;14(5):356-8.
81. Stead LF, Buitrago D, Preciado N, Sanchez G, Hartmann-Boyce J, Lancaster T. Physician advice for smoking cessation. Cochrane Database Syst Rev. 2013;5:CD000165.
82. World Health Organization. Adherence to long-term therapies: evidence for action. . Geneva: WHO; 2003.
83. Brownstein JN, Chowdhury FM, Norris SL, Horsley T, Jack L, Jr., Zhang X, et al. Effectiveness of community health workers in the care of people with hypertension. Am J Prev Med. 2007 May;32(5):435-47.
84. National Institute for Health and Care Excellence. Physical activity: brief advice for adults in primary care. London: National Institute for Health and Care Excellence2013 Contract No.: ph44.
85. Metkus TS, Baughman KL, Thompson PD. Exercise Prescription and Primary Prevention of Cardiovascular Disease. Circulation. 2010 June 15, 2010;121(23):2601-4.
86. Tips for cutting down on drinking. In: U.S. Department of Health and Human Services, editor.: National Institutes of Health

National Institute of Alcohol Abuse and Alcoholism,; 2008.
87. World Health Organization. Prevention of cardiovascular disease: pocket guidelines for assessment and management of cardiovascular risk:(WHO). 2007.
88. Radhika G, Sathya RM, Sudha V, Ganesan A, Mohan V. Dietary salt intake and hypertension in an urban south Indian population--[CURES - 53]. J Assoc Physicians India. 2007 Jun;55:405-11.
89. Bates GP, Miller VS. Sweat rate and sodium loss during work in the heat. J Occup Med Toxicol. 2008;3(4).
90. Cramer H, Lauche R, Haller H, Steckhan N, Michalsen A, Dobos G. Effects of yoga on cardiovascular disease risk factors: a systematic review and meta-analysis. Int J Cardiol. 2014 May 1;173(2):170-83.
91. Cramer H, Haller H, Lauche R, Steckhan N, Michalsen A, Dobos G. A systematic review and meta-analysis of yoga for hypertension. Am J Hypertens. 2014 Sep;27(9):1146-51.
92. Liu F, Qiu M, Zhai SD. Tolerability and effectiveness of (S)-amlodipine compared with racemic amlodipine in hypertension: a systematic review and meta-analysis. Curr Ther Res Clin Exp. 2010 Feb;71(1):1-29.

ANNEXURE 5: PATIENT INFORMATION LEAFLET

HYPERTENSION OR HIGH BLOOD PRESSURE (BP)- patient information leaflet

Why is high blood pressure called a silent killer? In the past most illnesses made us feel unwell. We know we are ill because we get symptoms like diarrhoea or fever or cough. We see the doctor to get help. But when we have high blood pressure there are no symptoms for many years. It's like a silent killer who comes quietly behind you and stabs you. High BP slowly damages the important blood vessels in our body without us knowing it. Later wecan become suddenly very sick. Only then we know we had hypertension but it may be too late to treat it by then.

What is hypertension? The pressure of air in a bus tyre must not be too high or too low. If it is too high it may burst without warning. If the pressure of water in a hose is too high it may suddenly burst. In the same way our blood flows to different parts of the body in blood vessels. If the pressure in the blood vessels is too high the blood vessels will become damaged over time. We do not always know why some people get high blood pressure. In a few people there are reasons like kidney disease and alcohol overuse.

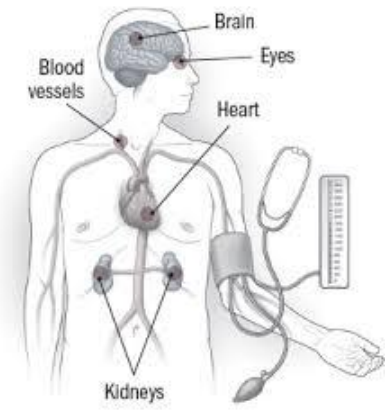
If hypertension causes no symptoms of disease at the start, how can we find hypertension early?

The only way to check blood pressure is through blood pressure machines.

What is the normal blood pressure? Our heart is a pump that first fills with blood and then pumps it to the blood vessels. It then fills again and then pumps again. So blood pressure readings have 2 numbers. The first number or systolic BP is when the heart is pumping blood. The second number or diastolic BP is when it is filling. The normal blood pressure is 130 systolic and 80 diastolic and we write that as 130/80. Readings lower than 130/80 can be normal. However the blood pressure of every person can vary from time to time. When we are exercising or worried it can increase. When we are resting it can be lower. So your blood pressure may need to be repeated s few times when you are resting if it was found to be high. Anyone who keeps having readings over 140/90 has high blood pressure.

What are the effects of high blood pressure on the body? If untreated high blood pressure damages the blood vessels to different parts of the body causing

- Strokes- we get sudden paralysis or numbness of one side of the body or speech which may not get better
- Heart attacks- sudden blockage of blood vessel in the heart can cause severe chest pain and sudden death
- Kidney failure
- Damage to vision and many other problems
- **Sadly these problems may happen very suddenly without warning.**



When should I have my blood pressure checked? You should check your blood pressure even if you feel well because in the early stages it causes no symptoms. All those over 18 years should have the blood pressure checked every 2 years. If you are overweight, have diabetes, do little exercise, smoke, drink alcohol, or have family members with high blood pressure you should have it checked once a year. Your health centre nurse or health worker can check your BP. You do not need to see a doctor to check BP.

If I have high blood pressure what can I do to help it myself? There are several things you can do

- Stop smoking: smoking markedly increases the damage caused by high blood pressure.
- If you already do not do hard work, do some exercise you enjoy doing that makes you a little short of breath for at least 30 minutes each day.

- If you are overweight reducing your weight by even 5 kg over 6 months can lower blood pressure.
- If you work hard and sweat a lot just avoid salty food. Otherwise reduce the salt you add in cooking by half.
- Avoid fatty food like oils or oily fried food, fatty meat (take off the fat before you cook goat or take the skin off chicken). Eat more vegetables and fish.

- Do not take excessive alcohol.
- Don't drink more than 2 glasses of coffee each day.

Do I need to take tablets? How long will I need to take these tablets? People with high blood pressure of 160/100 or higher and those for whom changing lifestyle does not work need tablets to lower blood pressure. Disease like pneumonia, typhoid can be cured by taking tablets for only a limited time. But blood pressure tablets do not cure the disease but control it only as long as you take them. It's like dying your hair which has turned grey as you get older. It will become black only as long as you keep dying it black! You must keep taking the tablets regularly and not stop them without asking your doctor. Most tablets can be taken once a day either in the morning or night. It should become a routine like brushing your teeth. Make sure you get more tablets before your last lot run out. **Remember that treating high BP will be one of the best things you can do to protect your health in the future. Treatment of hypertension may not help always make you feel better straight away.**

Will the tablets cause harm? Blood pressure tablets are usually very safe. If you do get side effects there are many different medications to choose from and the doctor will find one that suits you. The doctor may ask you take other medicines like aspirin and some tablets to lower your blood cholesterol which is a chemical in blood that can worsen the effects of high blood pressure.

How often do I need to see the doctor? Till your blood pressure is controlled the doctor may see you once a month. Once the blood pressure is controlled you only need to see the doctor once in 6 months. Continue your medications and you can see the doctor at any time if you have any worries over your treatment. **Remember- take your medications regularly. TOGETHER WE CAN STOP THE SILENT KILLER AND PREVENT UNNECESSARY SUDDEN DEATHS AND DISABILITY.**