# Indian Guidelines on Hypertension-IV (2019)

**Running Title :** Indian Guidelines on Hypertension-IV

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**Word count : 5098** **References : 79**

**Preamble**

Hypertension is a major contributor to cardiovascular morbidity and mortality worldwide and in India. In view of the unique geographical and climatic conditions, ethnic background, dietary habits, literacy levels and socio- economic variables in India, the Association of Physicians of India (API), Cardiological Society of India (CSI), Indian College of Physicians (ICP), and Hypertension Society of India (HSI) developed the "FIRST INDIAN GUIDELINES FOR THE MANAGEMENT OF HYPERTENSION - 2001."[1] The second and third versions of the guidelines were published in 2007[2] and 2013.[3]

We now present the fourth edition of the Indian Guidelines on Hypertension (IGH-IV). This update incorporates recent changes in the diagnosis and management of hypertension, including change in definition of hypertension by the American college of cardiology/ American heart association (ACC/AHA), changes in target BP[4], greater use of home blood pressure monitoring (HBPM) and ambulatory blood pressure monitoring (ABPM), reduced interest in renal angioplasty and renal denervation therapy and use of spironolactone for resistant hypertension. New epidemiological data on hypertension and hypertension mediated organ damage (HMOD) have also been included. The guideline has been harmonized with guidelines from

other organizations released recently.[5-8]

The primary aim of these guidelines is to offer balanced information to guide clinicians, rather than rigid rules that would constrain their judgment about the management of a patient. Individual patients can differ in their personal, medical, social, economic, ethnic and clinical characteristics. We recognize that the responsible physician's judgment and decision remains paramount for clinical decision making for individual patient. These guidelines do not include recommendations for treatment of hypertension in children and adolescents.

This document has been reviewed and endorsed by the CSI, HSI, ICP, Indian Society of Nephrology (ISN), Research Society for Study of Diabetes in India (RSSDI) and Indian Academy of Diabetes (IAD) and has been published in full text in the Journal of Physicians of India.[9]

**What is New in Indian Guidelines on Hypertension – IV**

- The diagnosis of hypertension should be based on office blood pressure reading of >140/90.
- HBPM and ABPM readings are lower than office readings. The threshold for diagnosis by HBPM mean and daytime ABPM is >135/85 mm of Hg and a 24

hour mean ABPM of >130/80.

- For clinic (office) use, the mercury sphygmomanometers are being replaced by aneroid and digital oscillometric devices. Indian physicians should start using these.
- HBPM should be encouraged for better patient involvement and compliance. Reliable oscillometric devices should be used. HBPM correlates better with HMOD than the office recordings.
- Like the white coat hypertension, masked hypertension should also be recognized.
- According to current data, the prevalence of hypertension in Indian adults is 29.8% (urban areas 33.8%, rural areas 27.6%). With increasing longevity, the prevalence of hypertension is increasing in India.
- The levels of control of blood pressure are low, at 20% in urban and 11% in rural population. Public health measures are urgently required to improve these dismal rates.
- Special features of hypertension in India have been included and discussed for the first time (Table 1).
- Drugs that block the angiotensin pathway (angiotensin converting enzyme inhibitors ACEIs and angiotensin receptor blockers ARBs) are the preferred

agents for treatment of hypertension in those under the age of 60 years. Calcium channel blockers and diuretics are the preferred agents in those over this age.

- A majority of patients need more than one agent for control of blood pressure. Combination therapy in single pill is encouraged for better compliance.
- Treatment should be started with a two-drug combination, preferably in a single pill, for stage 2 hypertension.
- Beta-blockers are no longer considered as first line agents for treatment of hypertension, and are reserved for use in specific indications.
- Some combinations are preferred. ACEIs/ARBs in combination with CCB's is considered a first line combination. Diuretics may be used as the third agent in combination.
- Treatment of hypertension even in octogenarians (more than 80 years) has been showed to be beneficial (newer data) and is recommended.
- After the recent SPRINT study and the HOPE III study the threshold for starting antihypertensive therapy and the target blood pressure has been lowered as compared to the IGH III guidelines.[10-11] The threshold for starting antihypertensive drugs should be 140/90 in most patients.

- In patients of Coronary Artery Disease (CAD) and Heart Failure (HF), antihypertensive therapy may be started beyond 130/80.
- The target blood pressure should be <130/80 mm Hg in those under the age of 60 years. The target should be individualized in the elderly.
- All patients with hypertension should be screened for the presence of kidney disease at the time of initial diagnosis. Kidney functions should be monitored in all patients with hypertension.
- The guidelines describe the clinical implications of obstructive sleep apnea (OSA).
- Patients with HFnEF derive significant benefit with good blood pressure control and target of <130/80 should be achieved, just as in HFrEF.
- Statins are beneficial in hypertensive individuals with dyslipidemia and should be used based on the findings of the HOPE III study.
- Aspirin has no role as a prophylactic agent in hypertension.

## Definition and Classification

### Definition

There is a continuous relationship between the level of blood pressure and the risk of complications. Starting at 115/75 mmHg, CVD risk doubles with each increment

of 20/10 mm Hg throughout the blood pressure range. Risk of CV death increases two-fold if BP rises to 135/85, fourfold if BP rises to 155/95 and eightfold at 175/105.[12,13] Recently, the ACC/ AHA guidelines have changed the definition of hypertension to 130/80.[7] However, the European guidelines and many others maintain the earlier definition of 140/90.[8] The Indian guidelines IV will continue with the previous definition of 140/90 and also the staging that we followed in the IGH III guidelines.

**We recommend that hypertension in adults, age 18 years and older, be defined as systolic blood pressure (SBP) of ≥140 mm Hg and/or diastolic blood pressure (DBP) of ≥ 90 mm Hg or any level of blood pressure in patients taking antihypertensive medication.[12,13]**

**Classification**

Classification of adult blood pressure, although arbitrary, is useful for clinicians to make treatment decisions based on a constellation of factors along with the actual level of blood pressure. Table 2 provides a classification of blood pressure for adults .[1,14]

This classification is for individuals who are not taking antihypertensive medication and who have no acute illness. It is based on the average of two or more blood

pressure readings taken at least on two separate occasions, one to three weeks apart. In addition to classifying stages of hypertension on the basis of blood pressure levels, clinicians should specify presence or absence of target organ disease and additional risk factors.

The current definition and classification of hypertension is based on office readings taken by healthcare providers. HBPM may also be taken in account for staging and therapy of the patient. More recently, the SPRINT study used automatic office blood pressure (AOBP) recording which is not always feasible and so not recommended routinely by us.[10] AOBP readings are 10-15 / 5-7 mm Hg lower than the office BP readings that we routinely use for definition of hypertension.[15]

We encourage the use of HBPM for follow up and making management decisions for patients with hypertension. White coat hypertension is diagnosed when office blood pressure (OBP) readings are high and home BP is normal. Masked hypertension indicates normal office BP and high home BP. Incidence of white coat hypertension is 10-15% and that of masked hypertension is 5-10%. Recording of OBP and HBP both are important for recognizing these entities. (Table 3).[16] The cut off levels for defining hypertension for the OBP, HBPM and ABPM are shown in Table 4.

**Epidemiology of Hypertension**

**Global**

Cardiovascular disorders (CVD) are the leading cause of morbidity and mortality worldwide.[17] CVD accounts for an estimated 17.5 million deaths annually, more than 75% of which occur in lower middle-income countries (LMIC).[18] While the death rates due to CVD have declined in several high- income countries (HIC), the trend has not been the same in LMIC.[19,20] South Asia (India, Pakistan, Bangladesh, Nepal, Sri Lanka), that represents one of the most densely populated regions in the world, experienced an increase of 73% in healthy life-years lost due to ischemic heart disease between 1990 and 2010, compared to a global increase of 30%.[21] Moreover, South Asians have been shown to experience their first myocardial infarction (MI) almost 10 years earlier compared to people from other countries.[22-24] This increase is largely due to high prevalence of risk factors like hypertension, diabetes and dyslipidemia.

The Global Burden of Diseases (GBD) Chronic Disease Risk Factors Collaborating Group reported 25-year (1980-2005) trends of mean levels of body mass index (BMI), systolic BP and cholesterol in 199 high-income, middle-income and low-income countries. Mean SBP declined in high and middle-income countries but increased in low-income countries and is now more than in high-income countries.

The India specific data was similar to the overall trends in low- income countries.

**National**

India is experiencing an increase in CV diseases, mainly due to uncontrolled hypertension.[29] A recent meta-analysis reported that prevalence rates of CAD and stroke have more than trebled in the Indian population. In the INTERHEART and INTERSTROKE study, hypertension accounted for 17.9% and 34.6% of population attributable risk for CAD and stroke respectively.[30]

The reported prevalence of hypertension from India in the late nineties and early twentieth century ranged from 2-15% in urban and 2-8% in rural areas. Presently the prevalence of hypertension in urban areas is 33.8% and in rural areas it is 27.6%, with an overall prevalence of 29.8%.[25,26] The studies in the 1970's and 1980's had used a threshold of 160/90 mm Hg for diagnosis of hypertension, whereas the more recent studies had 140/90 mm Hg as the cut-off (Figure 1). The prevalence increases with age, from 13.7% in the 3rd decade to 64% in the 6th decade.

The reasons for the recent rural-urban convergence in hypertension are not well-understood, but could be due to the recent rapid changes in the lifestyle of those living in rural areas including increase in salt intake.[27,28]

A few special features of hypertension in Indians are; onset relatively early in life, a rural-urban divide in prevalence, clustering of multiple cardiovascular risk factors and a significant seasonal variation of BP (Table 1). Recent studies have shown a progressive rise in average BP in general population over the last two decades as against a decrease seen in some western countries. The rates of awareness, treatment and control of hypertension in India remain low. (awareness 42% and 25%, treatment rates 38% and 25% and control 20% and 11% in urban and rural areas respectively). These figures are lower than the figures in other nations like in the US where awareness, treatment and control are 81, 74 and 53%, respectively.[28]

There are large regional differences in cardiovascular mortality in India. South Indian states, north eastern states and Punjab have a high mortality whereas central and eastern Indian states of Rajasthan, Uttar Pradesh and Bihar have lower rates.

The Global Burden of Disease Study shows that there is an increasing trend in deaths and DALYs due to high blood pressure in India over the last 26 years as shown by data from the GBD study (Table 5).[30]

According to 2016 data, IHD is responsible for largest number of deaths in India followed by COPD, diarrheal diseases and cerebrovascular disease (CVA) in that order. In 1990 diarrheal diseases, lower respiratory infections, neonatal preterm

296 birth, tuberculosis and measles were the five leading causes of DALY (Figure 2).

297

298 The prevalence of hypertension varies in different regions of the country. This
299 variation is due to social, economic, dietary differences in different parts of the
300 country. The socio-economic factors are depicted by the human development
301 index and the urbanization index. Also, the epidemiological transition has been
302 variable in different parts of our country. Table 6 shows state wise distribution of
303 parameters of human development index from Government of India,
304 Epidemiological Transition Index from the GBD study (2016), prevalence of
305 hypertension from the national family health survey 4 (NFHS-4) and the District
306 Level Household Survey 4 (2012-2014) (DLHS-4).

307 The GBD study was done over 1990-2016 and it reflects the epidemiological
308 transition index over this period in various states. The socio economic and cultural
309 factors which are different in various states effect the prevalence of hypertension
310 and partly explain the variation in the prevalence across our vast country. The
311 national family health survey 4 (2015-16) (NFHS-4) looked at 6,01,509 households
312 which included 6,99,686 women and 1,03,525 men from 28,583 primary sampling
313 units in 640 districts of the country. The NFHS-4 data shows significant difference
314 in hypertension prevalence across states.[31] A major shortcoming of this study is

315 exclusion of older age adults (>50 years) who have a higher prevalence of
316 hypertension. In the DLHS-4 study the Government of India with registrar general
317 of India has estimated CV risk factors in all states of the country.[32] In this, data on
318 BP measurement and hypertension prevalence are available since 2012 and so
319 reflects the latest trends in prevalence across India. The DLHS-4 survey was
320 undertaken in 2012-2014 and thus provides the state wise recent data. There is a
321 significant association of state--level hypertension prevalence among NFHS-4 and
322 DLHS-4 studies in both men and women suggesting that the high prevalence of
323 hypertension in younger population of NFHS-4 survey has tracked into the older
324 age population of DLHS-4 survey.
325 An important consideration is the requirement of long-term therapy and the
326 associated costs. About 70% patients in our country meet treatment expenses "out
327 of pocket" since they have no insurance cover. Treatment cost has important
328 bearing on drug compliance in India. The proposed Health and Wellness Clinics
329 currently being set up under the National
330 Health Policy and Pradhan Mantri Jan Arogya Yojana (PM-JAY) will focus on
331 prevention of non-communicable diseases by providing effective treatment for risk
332 factors such as hypertension.
333

## Measurement of Blood Pressure

### Clinic (Office) Blood Pressure Measurement

- Blood pressure is characterized by large spontaneous variations, therefore the diagnosis of hypertension should be based on multiple BP measurements taken on several occasions.
- The aneroid, large dial apparatus is the best for use in the office. It needs calibration every six months since the spring can loosen. Proper maintenance and calibration of the sphygmomanometer should be ensured.
- The blood pressure cuff should have a bladder that encircles and covers 80% of the length of the upper arm. A standard cuff with a bladder that is 12 cm X 35 cm is appropriate for most adults. A larger bladder will be needed for individuals with fat arms.

### Home Blood Pressure Measurement

Measurement of blood pressure outside the clinic provides valuable information for the initial evaluation of patients with hypertension and for monitoring the response to treatment. Home measurement has the advantage that it distinguishes sustained hypertension from "white coat hypertension". It is important to emphasize the need for validated of the automated (oscillometric) machines that

use the brachial artery (arm) for measurement. Of the devices currently available in the market, less than 15% have been validated.

Finger and wrist monitors are inaccurate and are not recommended. Home Blood pressure should be used complimentary to the clinic readings for diagnosis and follow up. Patients are to be encouraged to make morning and evening recordings for 3-5 days. A mean of these multiple readings reflects the true home blood pressure. Besides providing real life readings, it also encourages patient compliance and participation in the management. Oscillometric devices may not work well in patients who have atrial fibrillation or other arrhythmias.

Technique:

- Caffeine, smoking, alcohol, bathing and exercise should be avoided for at least 30 minutes before the reading is taken.
- The patient should sit calmly with back support, feet flat on floor for 5 minutes before taking a reading. Upper arm should be bare. When taking a reading the arm with cuff should be supported on a firm surface (table or arm-rest) at heart level. The cuff should fit snugly on the arm, about V-1 inch above the elbow crease.
- Readings should be taken in the morning before medication and at night. Each time, two readings should be taken, separated by one to two minutes

between readings. Take readings twice a day for 7 consecutive days. Discard the readings of the first day. The average of the remaining 12 readings is the Home blood pressure measurement.

**Ambulatory Blood Pressure Measurement**

Ambulatory blood pressure monitoring (ABPM) is useful to identify white-coat hypertension, masked hypertension, nocturnal hypertension (non-dippers), resistant hypertension, episodic hypertension; in evaluating the effect of antihypertensive drugs and in individuals with hypotensive episodes while on antihypertensive medication. ABPM also identifies patterns of blood pressure variation such as; dipping, non-dipping, extreme dipping and reverse dipping.

For ambulatory blood pressure measurement, a portable monitor is worn on a belt connected to a standard cuff on the upper arm. BP measurements are taken over a 24-48 hour period every 15-20 minutes during the daytime (8 am to 10 pm) and every 60 minutes during night time.[36] BP has a reproducible circadian profile with higher values while awake and mentally and physically active and much lower values during rest and sleep.

Early morning surge in BP for 3 or more hours during transition from sleep to wakefulness, can be an independent risk factor for complications and needs to be managed effectively[37] by addition of a second dose in the evening. Nocturnal

dipping of blood pressure is a normal phenomenon. Non-dipping and extreme dipping are associated with increase cardiovascular and cerebrovascular event rates. In the case of reverse dipping, a diagnosis of obstructive sleep apnea should be considered.

## Management of Hypertension

### Goals of Therapy

The primary goal of therapy of hypertension should be to prevent, reverse or delay complications and thus reduce the overall risk without adversely affecting the quality of life. Patients should be explained that the lifestyle modifications and drug treatment are generally lifelong and compliance to both is important.

### Initiation of therapy

Management of hypertension should be determined by the overall risk profile of the individual.

- In patients with stage I hypertension repeat readings should be taken within 2-3 weeks following institution of lifestyle modification. Pharmacotherapy, if needed, should be initiated after 1 month.
- BP should be recorded in both arms and in lying and standing before initiation of pharmacotherapy.

- In patients with stage II or III hypertension, a shorter waiting period (in stage III repeat readings after few hours only) is desirable.
- In those who have evidence of HMOD and target organ damage, pharmacotherapy should be started early.

**Treatment targets**

The target blood pressure should be 130/80 mm Hg amongst those <60 years and 130-140/80-90 mm Hg in those >60 years. This needs to be individualized according to age, activity level, other concomitant diseases and therapies. The target should take into account the balance of benefits and harms for the individual. A higher target BP may be acceptable in frail elderly individuals and those with postural hypotension and at risk of falls. The target BP should not be <120/70, since at pressures lower than this the risk is increased. Recognizing the wide variation of BP readings in any given individual, one should aim at having most readings in this range, fully recognizing that some would be beyond it in both directions.

**Management Strategy**

- The Systolic BP determines the HMOD and target organ damage more than the diastolic BP. [38-45] The rise in SBP continues throughout life. In contrast, the DBP rises until approximately 50 years of age beyond which the rise tends to level off and may even fall later in life. DBP is a more potent cardiovascular

risk factor than SBP until age 50; thereafter, SBP is more important.[13]

- Trials describe population averages for the purpose of developing guidelines, whereas physicians must focus on the individual patient's clinical responses.[46]
- BP control should be considered in the context of individualized care in which the patient profile (race, age, risk factors, associated diseases, HMOD) will affect the need of treatment, choice of antihypertensive medications and treatment targets.

**Non-pharmacologic Therapy**

Life-style measures should be instituted in all patients, including those who require immediate drug treatment. These include:

- Patient education: Patients need to be educated about the risks of high blood pressure, benefits to be gained by lifestyle changes, need for long-term adherence to treatment and need for regular monitoring and therapy.
- Weight reduction: Weight reduction of as little as 4.5 kg has been found to reduce blood pressure in a large proportion of overweight persons with hypertension.[47]
- Physical activity: Regular aerobic physical activity promotes weight loss,

increases functional status and decreases the risk of cardiovascular disease and all-cause mortality. A program of 30-45 minutes of brisk walking or swimming 3-4 times a week can lower SBP by 7-8 mm Hg.

- Alcohol intake: Excess alcohol intake causes a rise in blood pressure, induces resistance to antihypertensive therapy and increases the risk of stroke. [48,49] Alcohol consumption should be limited to no more than 2 drinks per day (24 oz beer, 10 oz wine, 3 oz of 80-proof whiskey) for most men and no more than 1 drink per day for women and lighter weight people.[13]
- Salt intake: Epidemiological evidence suggests an association between dietary salt intake and elevated BP. Indian cooking involves a high usage of salt. An ICMR task force study conducted in 13 states documented daily salt intake of 13.8 g per day.[50] The SCRIPT study conducted across 4 regions of India showed that a region wise mean daily salt intake in north, east, west and south was 14.1, 9.8, 10.1 and 9.4 g per day respectively. These are much higher than the WHO recommendation of <5 g per day which is also our IGH guideline recommendation.[51]

Patients should be advised to avoid added salt, processed foods, and salt-containing foods such as pickles, papads, chips, chutneys and preparations containing baking powder. Most breads, cereals, packaged namkeen,

readymade soups, canned food, pizzas and chinese takeaway are also high in salt content. The salt content of some commonly used food items is given in Table 8.

- Smoking: Consumption of tobacco in any form is the single most powerful modifiable lifestyle factor for prevention of CVD in hypertensives.[52-54] Cardiovascular benefits of cessation of smoking can be seen within one year in all age groups.[47] E-cigarettes, are also harmful and their use needs to be strongly discouraged.
- Yoga and Meditation: Yoga, meditation and biofeedback have been shown to reduce blood pressure in randomized controlled studies, including from India. The fall in SBP after yoga therapy has been between 2-6 mm Hg. A recent study shows mean SBP reduction by 4 and 6 mm Hg with lifestyle modification (LSM) and LSM + yoga respectively. Yoga also resulted in reduction of heart rate, waist circumference and lipid levels, all of which reduce CVD prevalence and mortality.[55-59]

**Diet:**

- Vegetarians have a lower BP compared to meat-eaters.[60] This is due to higher intake of fruit, vegetables and fibers, coupled with a low intake of saturated fats and not due to an absence of intake of meat protein.[61]

- Intake of saturated fats should be reduced since concomitant hyperlipidemia is often present in hypertensives.
- Regular fish consumption may enhance blood pressure reduction in obese hypertensives.[62]
- Adequate potassium intake from fresh fruits and vegetables may improve blood pressure control in hypertensives. Food items with high potassium content are shown in Table 9.[63]
- Caffeine intake increases BP acutely but there is rapid development of tolerance to its pressor effect. Epidemiological studies have not demonstrated a direct link between caffeine intake and high BP.[64]
- Indians consume higher level of carbohydrates than others. Recent data from the PURE study shows that high carbohydrate intake (> 60% of energy) was associated with adverse impact on total mortality. In this study high fat intake was not associated with a higher risk of total mortality and stroke. [65]
- The diet should be rich in whole grains, fruits, vegetables and low-fat dairy products and avoid saturated fat and cholesterol. This eating plan is known as the Dietary Approaches to Stop Hypertension (DASH) diet.
- Bakery Products (Bread, Biscuits, cakes) contain baking powder (Sod. bicarb). Instead of bread, sandwiches made with thick crisp chapati or bhakri

should be preferred. A thick crisp crust of bhakri can be a good alternative to pizza crust. Low salt paneer can be used instead of cheese.

- The food items to be avoided in hypertensives are shown in Table 10.[66]

**Pharmacologic Therapy**

**Principles of drug treatment**

- Over the past decade, the goals of treatment have shifted from blood pressure lowering to patient's overall wellbeing, control of associated risk factors and protection from future HMOD.[67]
- The reduction in blood pressure should be gradual. Use low doses of antihypertensive drugs to initiate therapy.
- Five classes of drugs can be recommended as first line treatment for stage 1-2 hypertension. These include: 1) ACE inhibitors, 2) Angiotensin receptor blockers, 3) Calcium channel blockers, 4) Diuretics and 5) Newer β-blockers.
- The Blood Pressure Lowering Treatment Trialists' Collaboration concluded that treatment with any commonly used regimen reduces the risk of total major cardiovascular events and larger reductions in blood pressure produce larger reductions in risk.[68]
- Choice of an antihypertensive agent is influenced by age, concomitant risk factors, presence of HMOD, other co-existing diseases, socioeconomic

considerations, availability of the drug and experience of the physician.

- Combining low doses of two or more drugs having synergistic effect is likely to produce lesser side effects. In 70 % of patients, goal blood pressure will be achieved with two or more agents only.
- Use fixed dose formulations to improve compliance. Drugs with synergistic effects should be combined.
- Use of long acting drugs that provide 24-hour efficacy with once daily administration ensures smooth and sustained control of blood pressure, which in turn provides greater protection against the risk of major cardiovascular events and HMOD. Once daily administration also improves patient compliance.
- Although antihypertensive therapy is generally lifelong, an effort to decrease the dosage and number of antihypertensive drugs should be considered after effective control of hypertension (step-down therapy).
- Due to a greater seasonal variation of temperatures in India, marginal alterations in dosages of drugs may be needed from time to time.[69,70]

**Antihypertensive Drug Combinations**

Combination therapy is required since a majority of patients will require two or

more drugs for sustained and effective control of blood pressure.[13,14] Combination therapy with different classes of drugs with different mechanism of action can achieve effective control of blood pressure with minimal side effects. For stage 2 hypertension, therapy can be initiated either with two drugs or as a fixed dose combination. The ACCOMPLISH trial has shown that combination of ACEIs with CCBs is better than a combination of ACEIs with diuretic and this should be the preferred combination.[71]

Younger individuals have high renin hypertension, hence ACEIs/ARBs or newer β-blockers are preferred; while older individuals have low renin hypertension and hence diuretics or CCBs are preferred as first line agents. In combination, one out of the two groups A [ACE inhibitor/ ARB] or B [β- blocker] is combined with C [calcium channel blocker] or D [thiazide diuretic] (step 2). In refractory patients, when 3 agents are to be used, A+C+D is a good choice (step 3).[14] The stepped care approach suggested in the IGH IV guidelines is shown in Figure 3.

Certain drug combinations have synergistic effect and increase the effectiveness of the other agent. However, some combinations are not effective and thus undesirable. These are shown in Table 11.

**Drug Interactions**

Since multiple drugs are used in hypertensive patients and often these patients have other co-existing conditions, common drug interactions should be kept in mind, as shown in Table 12.[72] The sequence of drug therapy after choosing an initial agent depends on the response to the first. In case target BP is not achieved, combination should be used in a manner shown in Figure 4.

**Maintenance Therapy and Follow-up**

Once therapy has been initiated, patients need to be seen at frequent intervals in order to monitor changes in blood pressure and see whether non-pharmacologic measures are being followed. At least once in a fortnight, blood pressure should be measured at the clinic or at home. Other CHD risk factors as well as coexisting diseases/conditions should be monitored. The overall risk category of a patient and the level of blood pressure decide the frequency of follow up visits to a large extent. The frequency can be reduced once BP is stabilized and other risk factors are controlled. Tobacco avoidance and alcohol moderations must be promoted vigorously.

**Associated Therapies**

In order to reduce the overall risk, patients with hypertension need therapies for

control of other risk factors. Low dose aspirin should be prescribed to all hypertensives with cardiovascular disease and stroke (secondary prevention). All Hypertensive patients with coronary, peripheral, or cerebrovascular disease with LDL levels >100 mg/dL should receive statins as secondary prevention strategies. Hypertensive patients without CV diseases but those in high-risk group should also receive statins for primary prevention as shown in the recently published HOPE III trial. Rosuvastatin 10 mg/day resulted in greater benefit than even antihypertensive drugs in a high risk hypertensive population.[11,73,74]

Aspirin should not be used in patients of hypertension without evidence of ASCVD. Recently, three primary prevention trials the ASCEND, ARRIVE and the ASPREE trial looked at role of aspirin for primary prevention in elderly (ARRIVE and ASPREE) and diabetic (ASCEND) individuals. All three trials were negative for any benefit. [75,76,77]

**Newer Modalities**

A novel baroreflex activation therapy has been evaluated recently. It stimulates baroreceptors through an implanted device and has been shown to reduce significant change in BP in patients with resistant hypertension. This therapy is still experimental and has no clinical application yet.

Renal sympathetic denervation therapy has also been evaluated. In this

radiofrequency ablation of sympathetic plexus around renal arteries is performed. In the SYMPLICITY hypertension -2 trial,[78] it was shown to reduce BP significantly over and above the pharmacological therapy. However, the more recent and meticulously conducted SIMPLICITY III trial has not shown any effect on BP reduction with renal denervation compared to sham-controlled placebo therapy.[79] Thus, renal denervation therapy is presently still under evaluation and is not advocated for routine clinical use.

## References


1. Indian Guidelines Management of Hypertension 2001. Hypertension India 2001; 15:1-34.
2. http://www.apiindia.org/hsi_guideline_ii.html.
3. Association of Physicians of India. Indian guidelines on hypertension (I.G.H.) - III 2013. J Assoc Physicians India 2013; 61:6-36.
4. Swedberg K, Komajda M, Bohm M, Borer JS, Ford I, Dubost- Brama A, SHIFT investigators. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study. The Lancet 2010; 376:875-85.
5. Genevieve M Gabb, Arduino A Mangoni, Craig S Anderson, Diane Cowley, John S Dowden, Jonathan Golledge, et al. Guideline for the diagnosis and management of hypertension in adults — 2016. Med J Aust 2016; 205:85-89.
6. Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults. Can J Cardiol 2017; 33:557-576. doi: 10.1016/j. cjca.2017.03.005.
7. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/ AAPA/ABS/ ACPM/AGS/APhA/ASH /ASPC/NMA/PCNA guideline for the prevention, detection, evaluation and management of high blood pressure in adults: executive summary. J Am Coll

Cardiol 2018; 71:2199-269.

8. Williams B, Mancia G, Spiering W, Rosei EA, Azizi M, Burnier M, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. Eur Heart J 2018; 39:3021-104.
9. Indian Guidelines on Hypertension-IV (2019). Supplement to J Assoc Physicians India 2019; 67:8-46. (http://www.japi.org/october_2019_spl/contents.html)
10. SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. New England Journal of Medicine 2015; 373:2103-16.
11. Yusuf S, Bosch J, Dagenais G, Zhu J, Xavier D, Liu L, et al. Cholesterol lowering in intermediate-risk persons without cardiovascular disease. New England Journal of Medicine 2016; 374:2021-31.
12. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age- specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. Prospective Studies Collaboration. Lancet 2002; 360:1903-1913.
13. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. Seventh Report of the Joint National Committee on Prevention, Detection,

645 Evaluation and Treatment of High Blood Pressure. Hypertension 2003;
646 42:1206-52.
647 14. Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF, Sever PS,
648 Thom SM. Guidelines for management of hypertension: report of the fourth
649 working party of the British Hypertension Society, 2004—BHS IV. Journal of
650 human hypertension. 2004 Mar;18(3):139-85.
651 15. Myers MG, Godwin M, Dawes M, Kiss A, Tobe SW, Kaczorowski J.
652 Measurement of blood pressure in the office: recognizing the problem and
653 proposing the solution. Hypertension 2010; 55:195-200.
654 16. Banegas JR, Ruilope LM, de la Sierra A, Vinyoles E, Gorostidi M, de la Cruz JJ,
655 et al. Relationship between clinic and ambulatory blood-pressure
656 measurements and mortality. New England Journal of Medicine 2018;
657 378:1509-20.
658 17. Roth GA, Huffman MD, Moran AE, Feigin V, Mensah GA, Naghavi M, Murray
659 CJ. Global and regional patterns in cardiovascular mortality from 1990 to
660 2013. Circulation. 2015 Oct 27;132(17):1667-78.
661 18. World Health Organization. Global status report on noncommunicable
662 diseases 2014. World Health Organization; 2014.
663 19. Roth GA, Forouzanfar MH, Moran AE, Barber R, Nguyen G, Feigin VL, et al.

664 Demographic and epidemiologic drivers of global cardiovascular mortality.
665 New England Journal of Medicine 2015; 372:133341.
666 20. O'Flaherty M, Buchan I, Capewell S. Contributions of treatment and lifestyle
667 to declining CVD mortality: why have CVD mortality rates declined so much
668 since the 1960s?. Heart 2013; 99:159-62.
669 21. Institute for Health Metrics and Evaluation. The Global Burden of Disease:
670 Generating Evidence, Guiding Policy— South Asia Regional Edition.
671 22. Joshi P, Islam S, Pais P, Reddy S, Dorairaj P, Kazmi K, et al. Risk factors for
672 early myocardial infarction in South Asians compared with individuals in
673 other countries. JAMA 2007; 297:286-94.
674 23. Rehman H, Samad Z, Mishra SR, Merchant AT, Narula JP, Mishra S, et al.
675 Epidemiologic studies targeting primary cardiovascular disease prevention in
676 South Asia. Indian Heart Journal 2018; 70:721-30.
677 24. https://www.who.int/gho/ncd/risk_factors/blood_pressure_prevalence/en
678 /.
679 25. Anand SS, Yusuf S. Stemming the global tsunami of cardiovascular disease.
680 Lancet 2011; 377:529-532.
681 26. Gupta R. Trends in hypertension epidemiology in India. Journal of human
682 hypertension. 2004 Feb;18(2):73-8.

27. Gupta R, Gaur K, Ram CV. Emerging trends in hypertension epidemiology in India. Journal of Human Hypertension 2018:1.
28. Wander GS, Ram CV. Blood pressure-Methods to record & numbers that are significant: Lets make a tailored suit to suit us. The Indian Journal of Medical Research 2018; 147:435.
29. Wander GS, Ram CV. Global impact of 2017 American Heart Association/American College of Cardiology hypertension guidelines: a perspective from India. Circulation 2018; 137:549-50.
30. Dandona L, Dandona R, Kumar GA, Shukla DK, Paul VK, Balakrishnan K, et al. Nations within a nation: variations in epidemiological transition across the states of India, 1990-2016 in the Global Burden of Disease Study. The Lancet 2017; 390:2437-60.
31. National Family Health Survey. http://rchiips.org/nfhs/abt. html. Accessed April 2, 2018.
32. District Level Household and Facility Survey. https://data. gov.in/resources/hypertension-age-18-years-and-above- dlhs-iv. Accessed 7 May 2018.
33. Wander GS, Ram CV. Optimal Blood Pressure Goals Recommended by the Latest Hypertension Guidelines: India may benefit the most. European

HeartJournal Volume 2018; 39:3012-3016.

34. https://www.icmr.nic.in/sites/default/files/press_realease_files/Hypertension.pdf.

35. Gupta R. Trends in hypertension epidemiology in India. J Hum Hypertens 2004; 18:73-78.

36. Krause T, Lovibond K, Caulfield M, McCormack T, Williams B. New NICE guidelines for hypertension. BMJ 2011; 343:d4891.

37. Gupta R, Guptha S, Gupta VP, Agrawal A, Gaur K, Deedwania PC. Twenty-year trends in cardiovascular risk factors in India and influence of educational status. European journal of preventive cardiology. 2012 Dec;19(6):1258-71.

38. Izzo JL, Levy D, Black HR. Importance of systolic blood pressure in older Americans. Hypertension 2000; 35:1021-24.

39. The Heart outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin converting enzyme inhibitor, ramipril on cardiovasucler events in high risk patients. New England Journal of Medicine 2000; 342:145-53.

40. The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensinconverting enzyme inhibitor or calcium channel blocker vs diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent

721 Heart Attack Trial (ALLHAT). JAMA 2002; 288:2981-2997.
722 41. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research
723 Group Diuretic Versus -Blocker as First-Step Antihypertensive Therapy Final
724 Results From the Antihypertensive and Lipid-Lowering Treatment to Prevent
725 Heart Attack Trial (ALLHAT). Hypertension 2003; 42:239-46.
726 42. Staessen JA, Fagard R, Thijs L, Celis H, Arabidze GG, Birkenhager WH, et al.
727 Randomised double-blind comparison of placebo and active treatment for
728 older patients with isolated systolic hypertension. The Systolic Hypertension
729 in Europe (Syst-Eur) Trial Investigators. Lancet 1997; 350:757-764.
730 43. Wang J, Staessen JA, Gong L, Liu L for the Systolic Hypertension in China (Syst-
731 China) Collaborative Group. Chinese Trial on Isolated Systolic Hypertension
732 in the Elderly. Arch Intern Med 2000; 160:211-220.
733 44. SHEP Cooperative Research Group. Prevention of Stroke by antinypertensive
734 drug treatment in older persons with isolated Systolic hypertension. Final
735 results of the Systolic hypertension in the Elderly Program (SHEP). JAMA
736 1991; 265:3255- 64.
737 45. Dahlof B, Sever PS, Poulter NR, Wedel H, Beevers DG, Caulfield M, et al for
738 the ASCOT investigators. Prevention of cardiovascular events with an
739 antihypertensive regimen of amlodipine adding perindopril as required

versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. Lancet 2005; 366:895-906.

46. Frohlich ED.Treating Hypertension -What Are We to Believe? N Engl J Med 2003; 348:639-641.

47. Whelton PK, Appel LJ, Espeland MA, Applegate WB, Ettinger Jr WH, Kostis JB, et al. For the TONE collaborative research group. Sodium reduction and weight reduction in treatment of hypertension in older patients. A randomised controlled Trial Of Non-pharmacological interventions in the Elderly (TONE). JAMA 1998; 279:839-846.

48. Stamier I, Cagguila AW, Grandito GA. Relation of body mass and alcohol, nutrient, fibre and caffeine intake to blood pressure in the special intervention and usual care groups in the Multiple Risk Factor Intervention Trial. Am J Clin Nutr 1997; 65(suppl l):338S-365S.

49. Puddey IB, Parker M, Beiten LJ, Vandongen R, Maseree JRL. Effects of alcohol and calorie restriction on blood pressure and serum lipids in overweight men. Hypertension 1992; 20:533-541.

50. Mittal RDJ, Mukherjee A, Saxena BN. Salt Consumption Pattern in India: an ICMR Task Force Study. New Delhi: Indian Council of Medical Research; 1996.

759 51. Kumbla D, Dharmalingam M, Dalvi K, Ray S, Shah MK, Gupta S, et al. A Study
760 of salt and fat Consumption pattern in Regional Indian diet among
761 hypertensive and dyslipidemic Patients- SCRIPT study. J Assoc Physicians
762 India 2016; 64:47-54.
763 52. Greenberg G. Thompson SG, Brennan PJ. The relationship between smoking
764 and the response to antihypertensive treatment in mild hypertensives in the
765 Medical Research Council's trial of treatment. Int J Epidemiol 1987; 16:225-
766 230 F.
767 53. Gupta R, Gurm H, Bartholomew JR. Smokeless Tobacco and Cardiovascular
768 Risk. Arch Intern Med 2004; 164:1845-1849.
769 54. US Department of Health and Human Services. The Health Benefits of
770 Smoking Cessation A Report of the Surgeon General Rockville. MD: Centers
771 for Disease Control. Center for Chronic Disease Prevention and Health
772 Promotion. Office on Smoking and Health; DHHS publication no. (CDC)
773 90:8416: 1990 Pr.
774 55. Patel C. 12-month follow-up of yoga and bio-feedback in the management of
775 hypertension. Lancet 1975; 1:62-64.
776 56. Sunder S, Agrawal SK, Singh VP, Bhattacharya SK, Udupa KN, Vaish SK. Role
777 of yoga in management of essential hypertension. Acta Cardiol 1984; 39:203-

208.

57. Datey KK. Role of biofeedback training in hypertension and stress. J Postgrad Med 1980; 26:68-73.
58. Damodaran A, Malathi A, Patil N ,Shah N, Suryavanshi, Marathe S. Therapeutic potential of yoga practices in modifying cardiovascular risk profile in middle aged men and women. J Assoc Physicians India 2002; 50:633-40.
59. Thiyagarajan R, Pal P, Pal GK, Subramanian SK, Trakroo M, Bobby Z, et al. Additional benefit of yoga to standard lifestyle modification on blood pressure in prehypertensive subjects: a randomized controlled study. Hypertension Research 2015; 38:48.
60. Rouse IL, Armstrong BD, Beilin LJ. The relationship of blood pressure to diet and lifestyle in two religious populations. J Hypertens 1983; 1:65-71.
61. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM. et al. A clinical trial of the effects of dietary patterns on blood pressure. New England Journal of Medicine 1997; 336:1117-24.
62. Bao DG, Mori TA, Burke V, Puddey IB, Beilin LJ. Effects of dietary fish and weight reduction on ambulatory blood pressure in overweight hypertensives. Hypertension 1998; 32:710-717.

797 63. Whelton PK, He J, Cutler JA, Brancati FL, Appel LJ, Follmann D, et al. Effects
798 of oral potassium on blood pressure: Meta analysis of randomized controlled
799 trials. JAMA 1999; 277:1624-1632.
800 64. Stamier I, Cagguila AW, Grandito GA. Relation of body mass and alcohol,
801 nutrient, fibre and caffeine intake to blood pressure in the special
802 intervention and usual care groups in the Multiple Risk Factor Intervention
803 Trial. Am J Clin Nutr 1997; 65(suppl l):338S-365S.
804 65. Dehghan M, Mente A, Zhang X, Swaminathan S, Li W, Mohan V, et al.
805 Associations of fats and carbohydrate intake with cardiovascular disease and
806 mortality in 18 countries from five continents (PURE): a prospective cohort
807 study. The Lancet 2017; 390(10107):2050-62.
808 66. Srilakshmi B. Diet in diseases of cardiovascular system. In: Srilakshmi B
809 editor. Dietetics. Revised. 5th ed. New Delhi: New Age International (P)Ltd
810 2005;189-213.
811 67. Gavras H, Gavras I. On the JNC V report. A different point of view. Am J
812 Hypertens 1994; 7:288-293.
813 68. Blood Pressure Lowering Treatment Trialists'Collaboration. Effects of
814 different blood-pressure-lowering regimens on major cardiovascular events:
815 results of prospectively designed overviews of randomised trials. Lancet

2003; 362:1527-1535.

69. Goyal A, Aslam N, Kaur S, Soni RK, Midha V, Chaudhary A, et al. Factors affecting seasonal changes in blood pressure in North India: A population based four-seasons study. Indian Heart Journal 2018; 70:360-7.
70. Goyal A, Narang K, Ahluwalia G, Sohal PM, Singh B, Chhabra ST, et al. Seasonal variation in 24 h blood pressure profile in healthy adults-A prospective observational study. Journal of Human Hypertension 2019:1.
71. Jamerson K, Weber MA et al for the ACCOMPLISH Trial Investigators. Benazepril plus Amlodipine or Hydrochlorothiazide for Hypertension in High-Risk Patients. New England Journal of Medicine 2008; 359:2417-28.
72. Opie LH. Drug interactions of antihypertensive agents. S Afr Fam Pract 2012; 54(Suppl 1):S23-S25.
73. The Heart Outcomes Prevention Evaluation Study Investigators. Vitamin E supplementation and cardiovascular events in high-risk patients. New England Journal of Medicine 2000; 342:154-60.
74. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomized placebo controlled trial. Lancet 2002; 360:7-22.
75. ASCEND Study Collaborative Group. Effects of aspirin for primary prevention

in persons with diabetes mellitus. New England Journal of Medicine 2018; 379:1529-39.

76. McNeil JJ, Nelson MR, Woods RL, Lockery JE, Wolfe R, Reid CM, et al. Effect of aspirin on all-cause mortality in the healthy elderly. New England Journal of Medicine 2018; 379:1519-28.

77. Gaziano JM, Brotons C, Coppolecchia R, Cricelli C, Darius H, Gorelick PB, et al. Use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease (ARRIVE): a randomised, double-blind, placebo-controlled trial. The Lancet 2018; 392:1036-46.

78. Symplicity HTN-2 Investigators. Renal sympathetic denervation in patients with treatment-resistant hypertension (The Symplicity HTN-2 Trial): a randomised controlled trial. The Lancet 2010; 376:1903-1909.

79. Bhatt DL, Kandzari DE, O'Neill WW, D'Agostino R, Flack JM, Katzen BT, Leon MB, Liu M, Mauri L, Negoita M, Cohen SA. A controlled trial of renal denervation for resistant hypertension. New England Journal of Medicine. 2014 Apr 10;370(15):1393-401.

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853 **Legends to Tables**

854 Table 1 : Hypertension in India - Special features

855 Table 2 : Classification of blood pressure for adults age 18 and older

856 Table 3 : Patterns of Blood Pressure

857 Table 4 : Blood pressure values for diagnosis of Hypertension by different methods

858 Table 5 : Increasing trends in deaths and disability adjusted life years (DALYs) due

859 to high systolic blood pressure in India (Global Burden of Diseases Study 2016)

860 Table 6: Correlation of parameters of HDI, UI and ETI by GBD Study with the

861 prevalence of hypertension by the NFHS-4 and the DLHS-4 surveys

862 Table 7: Ambulatory blood pressure measurement (Values for diagnosis of

863 hypertension)

864 Table 8: Sodium content of foods per 100 gms – Common Indian diets

865 Table 9 : Foods with high potassium

866 Table 10: Food items to be avoided in hypertensives

867 Table 11 : Undesirable drug combinations

868 Table 12 : Drug interactions.

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**Legends to Figures**

Fig. 1: Increasing trend in hypertension prevalence in India in urban (top panel) and rural (bottom panel) populations according to cross sectional regional studies from 1990's to date.

Fig. 2: Leading causes of DALY in 1990 and 2016 show an epidemiological shift from communicable to non communicable diseases36 (Modified from Global Burden of Diseases (GBD) Study)

Fig. 3: Algorithm for recommended drug combination

Fig. 4: Algorithm for treatment

Conflicts of Interest : None