Hypertension: An Overview of Risk Factors, Pathophysiology, Diagnosis, and Management

Dr. Pradeep Balu[1], Dr. Rohith Venkatesha[2]

Abstract

Hypertension is a major global health concern, affecting over a billion people and significantly contributing to cardiovascular disease, kidney failure, and stroke. This review briefly discusses its risk factors, pathophysiology, diagnostic criteria, and management strategies. Lifestyle changes and pharmacological interventions are essential for prevention and control.

Epidemiology

Hypertension affects one-third of adults worldwide, with its prevalence projected to reach 1.56 billion by 2025. It accounts for 10.8 million deaths annually and is more common among older adults.

Risk Factors

- **Modifiable**: High salt intake, obesity, physical inactivity, tobacco use, alcohol consumption, and stress.
- **Non-Modifiable**: Age, genetic predisposition, and comorbidities such as diabetes.

Pathophysiology

Hypertension involves overactivation of the sympathetic nervous system (SNS), dysregulation of the renin-angiotensin-aldosterone system (RAAS), endothelial dysfunction, and blood pressure variability. These factors increase vascular resistance and contribute to organ damage.

Diagnosis

Hypertension is defined as systolic blood pressure (BP) ≥130 mmHg or diastolic BP ≥80 mmHg, confirmed through repeated measurements in-office or via home/ambulatory monitoring.

Management

- **Lifestyle Modifications**: DASH diet, regular exercise, weight management, stress reduction, and smoking cessation.**Medications**: ACE inhibitors, angiotensin receptor blockers (ARBs), calcium channel blockers, and diuretics, often used in combination.

Organ Damage

Chronic hypertension impacts the brain (stroke), heart (left ventricular hypertrophy), kidneys (CKD), and eyes (retinopathy). Early detection prevents severe outcomes.

Conclusion

Addressing hypertension requires a proactive approach, including prevention, early diagnosis, and tailored treatment strategies. Public health initiatives and innovative research are vital to reducing its global impact.

Key words: Hypertension, Angiotensin, Diagnosis, Risk factors, Treatment.

Hypertension: A Comprehensive Overview of Risk Factors, Pathophysiology, Diagnosis, and Management.

Dr. Pradeep Balu[1], Dr. Rohith Venkatesha[2]

Hypertension, also known as high or raised blood pressure, is a condition in which the blood vessels have persistently raised pressure. High blood pressure continues to be a major preventable cause of illness and mortality. Hypertension is major risk factor for stroke, retinopathy, ischemia heart diseases, kidney disease. It is a major cause of premature death worldwide, with upwards of 1 in 4 men and 1 in 5 women – over a billion people – having the condition (world health organization).

It has estimated that 31.1% of adults worldwide, equating to 1.39 billion people, had hypertension in 2010. It has seen more in low- and middle-income countries about 31.5% compared to high-income countries 28.5%. Prevalence of hypertension varies significantly across different regions, highest in Poland. In India lowest reported prevalence in rural India (3.4% in men and 6.8% in women) . According to 2017 ACC/AHA guidelines it has shown higher prevalence of among Indians aged 15-49 years is about (40.6%), compared to based on the older JNC7 guidelines, In rural areas, 14.5% in the north to 21.1%, in the south, while in urban areas, it ranges from 28.8% in the north to 35.8% the west[(1,2)]

History of hypertension

De motu cordis who describe the circulation of blood in the body, William Harvey who understand the cardiovascular system. In 1733 English clergyman Stephen Hales made first measurement of blood pressure. In 1808-1836 Thomas Young especially Richard Bright described of hypertension came. The term essential hypertension was introduced in 1925 by physiologist otto frank. In 1928, the term malignant hypertension was coined by Mayo clinic.[(3,4,5)]In 1937 Paul Dudley White us cardiologist who suggest that “hypertension may be an important compensatory mechanism which should not be tampered with even where it certain that we could control it”. In 1949 Charles Friedberg’s wrote a classic book “Disease of the heart”, stated that “people with mild hypertension need not to be treated.[(3,4,5)]

Definition of hypertension:

Persistent elevation of systolic blood pressure above130 mmHg systolic blood pressure 90 mmHg diastolic Blood Pressure. [5]

Table 1. Classification of hypertension based on office blood pressure (BP) Measurement[6,16]

Classification	Systolic (mmHg)	Diastolic (mmHg)
Normal	<120	<80
Prehypertension	120-139	80-89
Stage 1	140-159	90-99
Stage 2	>160	>100

Types of Hypertension

Office Blood Pressure Measurement (OBPM)

- Auscultatory OBP in Clinical Practice: Traditional method using a stethoscope and sphygmomanometer.
- Automated Attended OBP in Clinical Practice: Uses automated devices with a healthcare provider present.
- Research Setting OBP: Standardized for research purposes.
- Unattended Automated OBP: Automated devices used without a healthcare provider present.[10]

Ambulatory Blood Pressure Monitoring (ABPM)

- 24-Hour ABPM: Measures BP continuously over 24 hours, providing insights into daily BP variations.
- Daytime ABPM: Focuses on BP during waking hours.
- Nighttime ABPM: Measures BP during sleep, often lower than daytime readings[8]

Home Blood Pressure Monitoring (HBPM)

- Casual HBPM: BP measurements taken at home, typically lower than OBPM readings.[8]

Secondary hypertension:

Sustained Hypertension[7]

- Elevated BP in both clinic and ambulatory settings.
- More common in elderly, men, and those with cardiovascular comorbidities.

White-Coat Hypertension (WCH)[7]

- Elevated BP in the clinic but normal BP in ambulatory settings.
- More common in elderly, obese women.

Masked Hypertension

- Normal BP in the clinic but elevated BP in ambulatory settings.
- More common in men with diabetes and in Asian populations[7]

Isolated Systolic Hypertension (ISH)

- Elevated systolic BP with normal diastolic BP.
- Strongly associated with cardiovascular disease (CVD) mortality[9]

Isolated Diastolic Hypertension (IDH)

- Elevated diastolic BP with normal systolic BP.
- Also associated with increased CVD risk [9]

Systolic-Diastolic Hypertension (SDH)

- Both systolic and diastolic BP are elevated.
- Highest risk for CVD mortality among hypertension types. [9]

Blood Pressure Variability (BPV)

Types of BPV

- Very-Short-Term (Beat-to-Beat): Variations between individual heartbeats.
- Short-Term (Within 24 Hours): Daily fluctuations.
- Medium-Term (Within Days): Variations over several days.
- Long-Term (Over Months and Years): Changes over extended periods.[11,9]

Clinical Significance

- Increased BPV is linked to higher risks of cardiovascular events, chronic kidney disease, cognitive decline, and mental illness. [11,13]

Genetic Factors in Blood Pressure Regulation

- Genetic variations play a significant role in BP regulation.
- Specific genes, such as those encoding the type 1A angiotensin II receptor, are crucial for vascular responses and BP control.[12]

- Recent studies have identified multiple genetic loci associated with BP, providing potential targets for therapeutic intervention.(14)

- Risk factors:
- Hypertension (HTN) is a multifactorial disease influenced by both modifiable and non-modifiable risk factors.
- Modifiable Risk Factors(15-23)

- Age more than 60: Risk of developing hypertension in a individuals age, due to altered in the cardiovascular system, particularly in the blood vessel which leading to stiffening of blood vessels causing systolic hypertension, commonly seen in older age.
- Overweight and Obesity: Body weight is a major contributor to hypertension. Obesity which causes increase in the blood pressure by increased sympathetic activity, leading to activation of RAAS and inflammation.
- Hyperuricemia: Increased in the uric acid levels can leads to hypertension by promoting vascular damage and increasing vascular resistance .
- Hyperglycemia : High blood sugar, when uncontrolled hyperglycemia, leads to increased blood pressure. Common in type 2 diabetes, which plays a role in raising blood pressure by affecting vascular health.
- Hypercholesterolemia: Increased in the cholesterol levels (LDL,VLDL,TG),reduced in good cholesterol(HDL) can lead to the development of atherosclerosis, which narrows and stiffens arteries, raising blood pressure. Combination of high cholesterol and high blood pressure significantly increases cardiovascular risk.
- Salt Consumption: High intake of salt leading to water retention, increasing blood volume and consequently raising blood pressure.
- Reduced in the Physical activity: Regular activity helps in reducing blood pressure by improving heart function, enhancing vascular health, and reducing arterial stiffness.
- Tobacco and Alcohol : Smoking and alcohol consumption causes increase in the blood pressure by activating the sympathetic nervous system, contributing to vascular damage, and increasing fluid retention.
- Environmental Stress: Chronic stress, which included work-related stress, shift works, and occupational toxic exposure (e.g., lead, mercury, arsenic), has been shown to increased in the blood pressure. This contribute to the sustained activation of the body's stress response systems, leading to hypertension.

- Non-Modifiable Risk Factors[15-23]
- Family History: Genetics history play an important role in the development of hypertension. People with a history of hypertension are set to have a higher risk of developing hypertension.
- Age: As the age, increases the elasticity of their blood vessels decreases, and blood pressure also increases, seen in systolic blood pressure. Above 65 years of age Hypertension is more common in individuals.
- Co-morbidity Diseases: Diabetes and kidney disease increase the risk of hypertension by affecting kidney function and fluid balance. Diabetic nephropathy, for example, is closely linked to hypertension due to renal damage.

Pathophysiology of Hypertension[24-27]

Hypertension (HTN) is classified into two types: primary (essential) and secondary hypertension. 95% of cases are Primary hypertension and has no clear cause. Secondary hypertension, results from underlying health issues like renal artery stenosis, chronic kidney disease, sleep apnea, or adrenal gland disorders.

Progression of hypertension involves several physiological mechanisms, such as the sympathetic nervous system (SNS), renin-angiotensin-aldosterone system (RAAS), endothelial dysfunction, and fluid retention. These systems impact on blood pressure by affecting cardiac output, peripheral vascular resistance (PVR), and vascular tone.

1. Cardiac Output and Peripheral Vascular Resistance (PVR)

Blood pressure depends on cardiac output (CO) and PVR. In hypertension, an overexcited sympathetic nervous system leading to increases cardiac output by raising heart rate and heart muscle contractility. Same time, PVR increases to maintain balance, which leads to high blood pressure.

2. Sympathetic Nervous System (SNS)

The SNS plays an important role in heart rate, vascular tone, and kidney function. When there is an increase in activity, leading to raises blood pressure by increasing heart rate, tightening blood vessels, and causing fluid retention. Some research, such as the cardiac study, shows that sharp sympathetic activity is often paired with reduced parasympathetic activity, worsening hypertension. Renal sympathetic system also contributes through two pathways:

- Efferent pathway: Increases renin release and fluid retention.
- Afferent pathway: Boosts overall sympathetic activity.

3. Renin-Angiotensin-Aldosterone System (RAAS)

The RAAS helps regulate blood pressure, particularly during reduced kidney perfusion , SNS activation. Renin, released by the kidneys, converts angiotensinogen into angiotensin I, which is transformed into angiotensin II by the angiotensin-converting enzyme (ACE). Angiotensin II raises blood pressure by constricting blood vessels and triggering aldosterone release, leading to sodium and water retention.

4. Endothelial Dysfunction:

Endothelium, which ranks on the blood vessels, which helps in regulation of vascular tone through substances like nitric oxide (NO), a vasodilator. In hypertension, oxidative stress is reduces the NO availability, leading to endothelial dysfunction. Causing blood vessels to constrict, increasing vascular resistance and blood pressure.

5. Vasoactive Substances

Vasoactive substances regulate vascular tone and blood pressure. For example:

- Endothelin: It is a strong vasoconstrictor that counteracts with the NO. Increased in the endothelin levels may play a role in hypertension.
- Bradykinin: It is a vasodilator that augments NO and prostaglandin production. Which helps in the sodium and water excretion, lowering blood pressure. ACE inhibitors, which prevent bradykinin breakdown, are effective in treating hypertension but can cause side effects like coughing.

6. Atrial Natriuretic Peptide (ANP)

ANP is a hormone released by the atria due to increased blood pressure or volume. It lowers blood pressure by promoting sodium and water excretion, reducing PVR, and counteracting the effects of the RAAS and SNS.

These mechanisms highlight how hypertension develops and is maintained, offering insights into potential treatment strategies.

Screening for Secondary Hypertension[6,28,29]

- General Approach:
  - Laboratory and imaging investigations should be done based on the patient's clinical presentation and appropriate screening tests should be done .
  - If screening shows positive results for secondary hypertension should undergo confirmatory testing. Referral to specialists.

- Renal Parenchymal Disease:
    - Serum creatinine, serum urea with estimated glomerular filtration rate (eGFR), urine analysis, urinary protein/protein-to-creatinine ratio, and renal ultrasound.
    - Renal biopsy: It is considered as the gold standard for confirming renal parenchymal disease.
- Endocrine Disorders

  Primary Aldosteronism:
    - It is a key factor for hypertension with hypokalemia, often seen in individuals with a family history of early-onset hypertension or cerebrovascular events.
    - Screening Test: Plasma aldosterone or renin ratio, performed after correcting hypokalemia and discontinuing aldosterone antagonists for at least four weeks.
    - Confirmatory Tests:
        - 24-hour urinary aldosterone measurement after oral sodium loading.
        - Plasma aldosterone measurement following intravenous saline infusion.
    - Further Evaluation: Adrenal imaging (CT/MRI) is used to locate the lesion.

  Pheochromocytoma:
    - It is an episodic hypertension, palpitations, headache, postural hypotension, some features of neurofibromatosis.
    - Screening Test: Plasma or urinary metanephrines. CT or MRI is recommended to localize the tumor.
    - Additional Tests: Midnight salivary cortisol and 24-hour urinary free cortisol.

  Thyroid Disorders:
    - Diagnosed through measurements of TSH and free T4/T3 levels.
- Renovascular Hypertension
    - Suspected in cases of resistant hypertension, renal bruit, or worsening renal function after ACE inhibitor use.
    - Screening and Diagnostic Test: Ultrasound renal Doppler.

2. Vascular Causes
    - Coarctation of the Aorta:

- A significant cause of secondary hypertension, particularly in younger patients. Echocardiography also used.
- Confirmatory Imaging: Computed tomographic aortogram (CTA) or magnetic resonance angiography (MRA).

3. Obstructive Sleep Apnea (OSA)
    - Diagnostic Test: Polysomnography, preferably performed in a sleep laboratory, is the gold standard for OSA diagnosis.
4. Other Causes
    - Scleroderma: Laboratory findings may include thrombotic microangiopathy, autoantibodies against RNA polymerase III, and a positive antinuclear antibody (ANA) test.

Diagnosis of hypertension [6,28,29]

1) Diagnosed is made based on persistently high blood pressure.
2) It requires three separate sphygmomanometer measurements at one monthly interval. Assessment of the hypertensive people should include a complete history and physical examination. With the availability of 24-hour ambulatory blood pressure monitors and home blood pressure machines.

Table no 2 Measuring blood pressure.

Conditions	Quiet room with comfortable temperature, before measurements avoid smoking, caffeine and exercise for 30 min, empty bladder, remain seated and relaxed for 3–5 min neither patient nor staff should talk before, during and between measurements.
Positions	Sitting arm resting on table with mid-arm at heart level, back supported on chair, legs uncrossed and feet flat on floor .
Device	Validated electronic (oscillometric) upper-arm cuff device. lists of accurate electronic devices for office, home and ambulatory BP measurement in adults, children and pregnant women are available. Alternatively use a calibrated auscultatory device, (aneroid, or hybrid as mercury sphygmomanometers are banned in most countries) with 1st Korotkoff sound for systolic blood pressure and 5th for diastolic with a low deflation rate.

Cuff	Size according to the individual's arm circumference. For manual auscultatory devices the inflatable bladder of the cuff must cover 75%–100% of the individual's arm circumference. For electronic devices use cuffs according to device instructions.
Protocol	At each visit take 3 measurements with 1 min between them. Calculate the average of the last 2 measurements. If BP of first reading is required.
Interpretation	Blood pressure of 2–3 office visits ≥140/90 mmHg indicates hypertension.

Office Blood Pressure (BP) Measurement[6,10,28,29]

- Blood pressure measurement in a clinical setting is the most commonly used method for diagnosing and monitoring hypertension.
- A single office visit is generally insufficient for diagnosis; 2–3 visits over 1–4 weeks are typically required to confirm hypertension.
- An exception is made if BP is ≥180/110 mmHg with signs of cardiovascular disease (CVD), where the diagnosis can be made during a single visit.
- Management recommendations based on office BP levels are outlined in Table 2.

Confirmation of Hypertension

- When feasible, hypertension diagnosis should be validated with out-of-office BP measurements.
- Measurement Techniques and Special Considerations
- Initial Evaluation:
- Measure BP in both arms, ideally simultaneously.
- If a consistent inter-arm difference >10 mmHg is observed, use the arm with the higher reading for subsequent measurements.
- Differences >20 mmHg warrant further investigation.
- Standing BP:
- In patients receiving treatment, BP should be measured while standing at 1 and 3 minutes to evaluate for postural hypotension, particularly in elderly individuals and those with diabetes.
- Automated Office BP:

- Multiple automated BP readings taken while the patient is alone in the room offer a more standardized assessment, often yielding lower readings than traditional office measurements. However, these thresholds for diagnosing hypertension are less clear.
- Out-of-Office BP Confirmation:
- Most treatment decisions should be based on confirmation using out-of-office BP measurements.
- Out-of-Office BP Measurements
- BP readings taken at home or via 24-hour ambulatory blood pressure monitoring (ABPM) are more reliable than office measurements. They are more strongly associated with hypertension-related organ damage and cardiovascular risk.
- Out-of-office measurements also help identify:
- White Coat Hypertension: Elevated BP in the office but normal readings outside.
- Masked Hypertension: Normal BP in the office but elevated readings outside.
- When Out-of-Office Measurements Are Recommended
- Out-of-office monitoring is crucial for confirming hypertension and guiding treatment decisions, especially in patients with borderline office BP readings (systolic 130–159 mmHg or diastolic 85–99 mmHg).
- Proper techniques and protocols for home and ambulatory BP monitoring should be followed for accuracy.

Table no 3 Clinical uses of home and ambulatory blood pressure (BP) monitoring[6,32,33].

	Home Blood Pressure Monitoring	**24-Hour Ambulatory Blood Pressure Monitoring**
Position	As for the office blood pressure, as for the office BP	Routine working day. Avoid strenuous activity, arm still and relaxed during each measurement.
Device cuff	Validated electronic (oscillometric) upper-arm cuff device.Size according to the individual's arm circumference.	
Measurement protocol	Before each visit to the health professional: • 3–7-day monitoring in the morning (before drug intake if treated) and the evening. • Two measurements on each occasion	• 24-hour monitoring at 15–30 min intervals during daytime and nighttime. • At least 20 valid daytime and 7 nighttime BP readings are required. If

	after 5 min sitting rest and 1 min between measurements. • Long-term follow-up of treated hypertension: 1–2 measurements per week or month.	less, the test should be repeated.
Interpretation	• Average home blood pressure after excluding readings of the first day ≥135 or 85 mm Hg indicates hypertension.	• 24-hour ambulatory blood pressure ≥130/80 mm Hg indicates hypertension (primary criterion). • Daytime (awake) ambulatory blood pressure ≥135/85 mm Hg and nighttime (asleep) ≥120/70 mm Hg indicates hypertension

Hypertension-Mediated Organ Damage (HMOD)[6,28]

Hypertension-mediated organ damage (HMOD) : It refers to structural and functional changes in the arteries or organs they supply, caused by high blood pressure. Target organs include the brain, heart, kidneys, arteries, and eyes. While HMOD assessment is less impactful in patients already at high cardiovascular risk (e.g., those with CVD, stroke, diabetes, CKD, or familial hypercholesterolemia), it is valuable for reclassifying risk in low- or moderate-risk patients. This helps guide treatment and tailor therapies to address specific organ damage.

Brain

- Common manifestations include transient ischemic attacks (TIA) and strokes.
- MRI is the most sensitive tool for detecting early subclinical changes, such as white matter lesions, microinfarcts, microbleeds, and atrophy, but is not recommended for routine use due to cost and limited availability.
- MRI is advised in cases of neurological symptoms, cognitive decline, or memory loss.

Heart

- A 12-lead ECG is routinely used to detect left ventricular hypertrophy (LVH) using criteria like the Sokolow-Lyon index or Cornell index.
- ECG has low sensitivity; a transthoracic echocardiogram (TTE) is preferred for accurate assessment, including left ventricular mass index (LVMI), left atrial volume, and LV systolic/diastolic function.

Kidneys

- Hypertension can both cause and result from kidney damage.
- Routine evaluation includes measuring serum creatinine, estimating glomerular filtration rate (eGFR), and checking for albuminuria using dipstick tests or the urinary albumin-to-creatinine ratio (UACR).

Arteries

- Three arterial assessments are used for HMOD:
    1. Carotid ultrasound for plaques and intima-media thickness (IMT).
    2. Pulse wave velocity (PWV) to assess aortic stiffness.
    3. Ankle-brachial index (ABI) for peripheral artery disease.
- Routine use is not recommended unless clinically indicated (e.g., neurological symptoms, isolated systolic hypertension, or suspected peripheral artery disease).

Eyes

- Fundoscopy is used to detect hypertensive retinopathy, including hemorrhages, microaneurysms, and papilledema, especially in hypertensive emergencies.
- It is recommended for patients with grade 2 hypertension, ideally by experienced practitioners or with digital fundus imaging when available.

Drug or Substance Exacerbators and Inducers of Hypertension.[6,28]

- Nonsteroidal Anti-inflammatory Drugs (NSAIDs): Celecoxib may cause increase of up to 1-3mm Hg in blood pressure, while nonselective NSAIDs can lead to a 1-3mm Hg increase. Aspirin does not raise blood pressure. NSAIDs directly effects on RAAS inhibitors and beta-blockers.
- Combined Oral Contraceptives: High-dose estrogen-containing pills (>50 mcg estrogen with 1–4 mcg progestin) can increase blood pressure by approximately 3-6 mm Hg.
- Antidepressants: SNRIs (selective norepinephrine and serotonin reuptake inhibitors) may increase blood pressure by 2 mm Hg. Tricyclic antidepressants are associated with a higher risk of hypertension. SSRIs (selective serotonin reuptake inhibitors) generally do not elevate blood pressure.
- Acetaminophen: Regular, near-daily use is linked to a 1.5 times increased risk of developing hypertension.

- Other Medications:
    - Steroids.
    - Antiretroviral Therapy: Findings on its effect on blood pressure are inconsistent.
    - Sympathomimetics: Drugs like pseudoephedrine, cocaine, and amphetamines can raise blood pressure.
    - Antimigraine Medications: Serotonergic agents may also elevate blood pressure.
    - Recombinant Human Erythropoietin and Calcineurin Inhibitors: These are associated with potential blood pressure increases.

Management of hypertension:

- Life Style Modification [6,28]

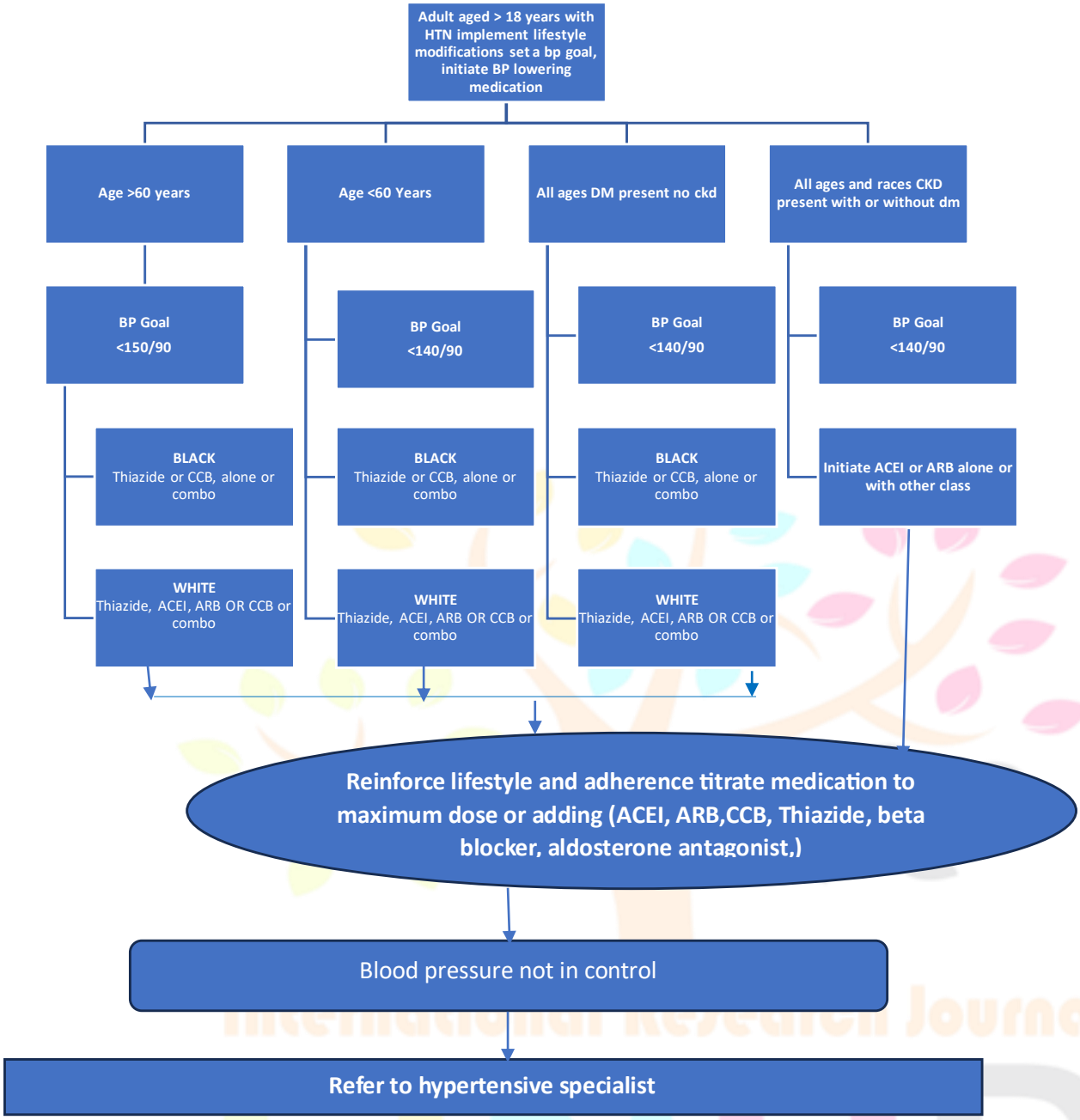
Good lifestyle can prevent the onset of high BP, which reduce the cardiovascular events. Lifestyle modification is the first line of antihypertensive treatment.

Table 4 showing Lifestyle modifications

Salt reduction	There is a relationship between salt intake and increased blood pressure. Reduce in salt consumption during preparing foods, and at the table.Limit consumption of high salt foods such as soy sauce, fast foods and processed food including breads and cereals high in salt.
Healthy diet	Eating a healthy diet such as whole grains, fruits, vegetables, polyunsaturated fats and dairy products, increase intake of vegetables which has high in nitrates known to reduce BP example leafy vegetables and beetroot. Other beneficial foods and nutrients include those high in magnesium, calcium and potassium such as avocados, nuts, seeds, legumes and tofu. Reduces intake of high sugar food, saturated fat and trans fats, such as the DASH diet.
Healthy drinks	Reasonable consumption of coffee, green and black tea. Other beverages that can be beneficial include karkadé (hibiscus) tea, pomegranate juice, beetroot juice and cocoa.
Moderation of alcohol consumption	Recommended daily limit for alcohol consumptions is 2 standard drinks for men and 1.5 for women (10 g alcohol/standard drink). Avoid binge drinking.
Weight reduction	Weight reduction is indicated to prevent obesity. Mostly abdominal obesity should be managed. Ethnic-specific cut-offs for BMI and waist circumference should be used. Alternatively, a waist-to-height ratio<0.5 is recommended for all population.

Smoking cessation	Smoking is a major risk factor for CVD, COPD, MI and cancer. Smoking cessation and referral to smoking cessation programs are advised
Regular physical activity	Regular aerobic and resistance exercise helpful for both the prevention and treatment of hypertension. Moderate intensity aerobic exercise (walking, jogging, cycling, yoga, or swimming) for 30 minutes on 5–7 days per week or HIIT (high intensity interval training) which involves alternating short bursts of intense activity with subsequent recovery periods of lighter activity.
Reduce stress-meditation	Chronic stress has been associated to high blood pressure later in life. Stress can be reduced by meditation which should be introduced into the daily routine. More research should be conducted to determine the effects of chronic stress on blood pressure, randomized clinical trials examining the effects of transcendental meditation on blood pressure suggest that this practice lowers blood pressure.
Complementary, alternative medicines	Large proportions of hypertensive patients use complementary, alternative medicines which is seen in Africa and China. Clinical trials are required to evaluate the efficacy and safety of these medicines.
Reduce exposure to air pollution and cold temperature	Evidence from studies support a negative effect of air pollution on blood pressure in the long-term.

Management of hypertension :According JNC8 guidance



Compelling indication[30]

Indication	Treatment choice
Heart Failure	ACEI/ARB +BB +Diuretic+ Spironolactone
Post MI/ Clinical CAD	ACEI/ARB and BB
CAD	ACEI,BB, diuretic, CCB
Diabetes	ACEI/ARB, CCB, Diuretic
CKD	ACEI/ARB
Recurrent stroke prevention	ACEI, Diuretic
Pregnancy	Labetalol, nifedipine, methyldopa

Recommendation for general principle of drug therapy: Hypertensive[6,31]

1. Thiazide :

- **Chlorthalidone**: Dose- 12.5–25 mg/day, once daily
  - Preferred due to prolonged half-life and proven cardiovascular disease (CVD) risk reduction.
  - Monitor for hyponatremia, hypokalemia, uric acid, and calcium levels.
  - Use with caution in patients with a history of acute gout unless on uric acid–lowering therapy.
- **Hydrochlorothiazide**: Dose- 25–50 mg/day, once daily
- **Indapamide**: Dose- 1.25–2.5 mg/day, once daily
- **Metolazone**: Dose- 2.5–5 mg/day, once daily

2. ACE Inhibitors

- **Captopril**: Dose- 12.5–150 mg/day, 2–3 times daily
- **Enalapril**: Dose- 5–40 mg/day, once or twice daily
- **Lisinopril**: Dose- 10–40 mg/day, once daily
- **Ramipril**: Dose- 2.5–20 mg/day, once or twice daily
  - Do not combine with ARBs.
  - Increased risk of hyperkalemia, especially in chronic kidney disease (CKD) and those on potassium supplements, potassium-sparing drugs.
  - Risk of acute renal failure in severe bilateral renal artery stenosis.
  - Contraindication in pregnancy and patients with a history of angioedema due to ACE inhibitors.

3. ARBs (Angiotensin Receptor Blockers)

- **Losartan**: Dose- 50–100 mg/day, once or twice daily
  - Avoid combining with ACE inhibitors.
  - Risk of hyperkalemia in CKD or potassium supplementation.
  - Contraindicated in pregnancy.

- Other drugs are:
    - **Valsartan**: Dose - 80–320 mg/day.
    - **Olmesartan**: Dose- 20–40 mg/day.
    - **Telmisartan**: Dose- 20-40 mg/day.

4. Calcium Channel Blockers (CCBs)

- **Dihydropyridines**:
    - **Amlodipine**: 2.5–10 mg/day, once daily
        - Associated with dose-dependent pedal edema.
    - **Nifedipine** : 30–90 mg/day, once daily
    - Other drugs are also used.
- **Non-dihydropyridines**:
    - **Diltiazem ER**: 120–360 mg/day, once daily
        - Avoid use with beta-blockers due to risk of bradycardia and heart block.
        - Avoid in heart failure with reduced ejection fraction .

Secondary Agents

1. Loop Diuretics

- **Furosemide**: Dose- 20–80 mg/day.
    - Preferred in symptomatic heart failure or moderate-to-severe CKD (GFR < 30 mL/min).

2. Potassium-Sparing Diuretics

- **Spironolactone**: Dose- 25–100 mg/day.
    - Common add-on therapy in resistant hypertension.
    - Avoid in renal dysfunction

3. Beta-Blockers

- **Cardioselective**:
    - **Metoprolol**: Dose- 50–200 mg/day
        - Preferred in heart failure with reduced ejection fraction.

- **Atenolol**: 25–100 mg/day.

- **Non-cardioselective**:
  - **Propranolol IR**: 80–160 mg/day.
- **Combined Alpha and Beta-Blockers**:
  - **Carvedilol**: 12.5–50 mg/day.

4. Central Alpha-2 Agonists

- **Clonidine** : 0.1–0.8 mg/day.
  - Reserved for last-line therapy due to significant CNS side effects.

5. Direct Vasodilators

- **Hydralazine**: 100–200 mg/day.
  - It is combined with diuretic and beta-blocker to prevent reflex tachycardia and fluid retention.

Conclusion

Hypertension is a significant global health concern, and its prevalence is increasing due to the aging population. Preventive strategies, such as maintaining a healthy diet and engaging in regular physical activity, should be implemented early in life to reduce the risk of developing hypertension. For individuals already diagnosed, early detection and timely treatment are essential to prevent complications. Effective management of hypertension often requires the use of combination therapy, as single medications may not provide adequate blood pressure control for many patients. The selection of drug combinations should be rational and evidence-based, taking into account the patient's overall health, coexisting conditions, and the pharmacological properties of the medications. This individualized approach ensures optimal blood pressure control, minimizes adverse effects, and improves long-term health outcomes.

Reference

1). Abariga, S., Khachan, H., & Kibria, G. (2019). Prevalence and Determinants of hypertension in India based on the 2017 ACC/AHA Guideline: Evidence from the India National Family Health Survey.. *American journal of hypertension*. https://doi.org/10.1093/ajh/hpz181.

2). Tabrizi, J. S., Sadeghi-Bazargani, H., Farahbakhsh, M., Nikniaz, L., & Nikniaz, Z. (2016). Prevalence and associated factors of prehypertension and hypertension in Iranian population: The Lifestyle Promotion Project (LPP). *PLoS ONE*, *11*(10), e0165264. https://doi.org/10.1371/journal.pone.0165264.

3) Mahmood, S., Levy, D., Vasan, R., & Wang, T. (2014). The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective. *The Lancet*, 383, 999-1008. https://doi.org/10.1016/S0140-6736(13)61752-3.

4) Mills, K., Stefanescu, A., & He, J. (2020). The global epidemiology of hypertension. *Nature Reviews Nephrology*, 16, 223-237. https://doi.org/10.1038/s41581-019-0244-2.

5) Sadeeqa, S. (2019). Hypertension: A Case Study. *Virology & Immunology Journal*. https://doi.org/10.23880/vij-16000211.

6) Unger, T., Borghi, C., Charchar, F., Khan, N. A., Poulter, N. R., Prabhakaran, D., Ramirez, A., Schlaich, M., Stergiou, G. S., Tomaszewski, M., Wainford, R. D., Williams, B., & Schutte, A. E. (2020). 2020 International Society of Hypertension Global Hypertension Practice Guidelines. *Hypertension*, *75*(6), 1334–1357. https://doi.org/10.1161/hypertensionaha.120.15026

7) Omboni, S., Aristizábal, D., De La Sierra, A., Dolan, E., Head, G., Kahan, T., Kantola, I., Kario, K., Kawecka-Jaszcz, K., Malan, L., Narkiewicz, K., Octavio, J., Ohkubo, T., Palatini, P., Siègelovà, J., Silva, E., Stergiou, G., Zhang, Y., Mancia, G., & Parati, G. (2016). Hypertension types defined by clinic and ambulatory blood pressure in 14143 patients referred to hypertension clinics worldwide. Data from the ARTEMIS study. *Journal of Hypertension*, 34, 2187–2198. https://doi.org/10.1097/HJH.0000000000001074.

8) Little, P. (2002). Comparison of agreement between different measures of blood pressure in primary care and daytime ambulatory blood pressure. *BMJ*, *325*(7358), 254. https://doi.org/10.1136/bmj.325.7358.254

9) Guo, J., Lv, J., Guo, Y., Bian, Z., Zheng, B., Wu, M., Yang, L., Chen, Y., Su, J., Zhang, J., Yao, J., Chen, J., Chen, Z., Yu, C., & Li, L. (2021). Association between blood pressure categories and cardiovascular disease mortality in China. *PLoS ONE*, *16*(7), e0255373. https://doi.org/10.1371/journal.pone.0255373

10) Stergiou, G. S., Kyriakoulis, K. G., & Kollias, A. (2018). Office blood pressure measurement types: Different methodology—Different clinical conclusions. *Journal of Clinical Hypertension*, *20*(12), 1683–1685. https://doi.org/10.1111/jch.13420

11) Yeh, J., Lee, C., Chen, Y., Huang, S., Wang, W., Huang, C., Chiu, T., Chen, C., Chiang, C., & Cheng, H. (2022). AGREEMENT BETWEEN DIFFERENT TYPES OF BLOOD PRESSURE MONITORING: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS. *Journal of Hypertension*, 40, e87 - e88. https://doi.org/10.1097/01.hjh.0000836064.12341.81.

12) Stergiou, G. S., Kyriakoulis, K. G., & Kollias, A. (2018). Office blood pressure measurement types: different methodology—Different clinical conclusions. *Journal of Clinical Hypertension*, *20*(12), 1683–1685. https://doi.org/10.1111/jch.13420

13) Parati, G., Torlasco, C., Pengo, M., Bilo, G., & Ochoa, J. (2020). Blood pressure variability: its relevance for cardiovascular homeostasis and cardiovascular diseases. *Hypertension Research*, 43, 609-620. https://doi.org/10.1038/s41440-020-0421-5.

14) Tragante, V., Barnes, M. R., Ganesh, S. K., Lanktree, M. B., Guo, W., Franceschini, N., Smith, E. N., Johnson, T., Holmes, M., V., Padmanabhan, S., Karczewski, K. J., Almoguera, B., Barnard, J., Baumert, J., Chang, Y. C., Elbers, C. C., Farrall, M., Fischer, M. E., Gaunt, T. R., . . . Pankratz, N. (2014). Gene-centric meta-analysis in 87,736 individuals of European ancestry identifies multiple Blood-Pressure-Related Loci. *Carolina Digital Repository (University of North Carolina at Chapel Hill)*. https://doi.org/10.17615/me3a-0836

15) Sesso, H. D., Cook, N. R., Buring, J. E., Manson, J. E., & Gaziano, J. M. (2008). Alcohol consumption and the risk of hypertension in women and men. *Hypertension*, *51*(4), 1080–1087. https://doi.org/10.1161/hypertensionaha.107.104968

16) Fraser-Bell, S., Symes, R., & Vaze, A. (2017). Hypertensive eye disease: a review. *Clinical & Experimental Ophthalmology*, 45, 45 - 53. https://doi.org/10.1111/ceo.12905.

17) Debora, C., Tolimba, C., Palunggi, S., Siregar, D., & Harefa, L. (2023). Risk factors for hypertension among adults living in a rural area, Minahasa. *Deleted Journal*, *26*(1), 36–45. https://doi.org/10.7454/jki.v26i1.2527

18) Burnier, M., & Damianaki, A. (2023). Hypertension as Cardiovascular Risk Factor in Chronic Kidney Disease. *Circulation Research*, 132, 1050 - 1063. https://doi.org/10.1161/CIRCRESAHA.122.321762.

19) Leung, A. A., Bushnik, T., Hennessy, D., McAlister, F. A., & Manuel, D. G. (2019). Risk factors for hypertension in Canada. *PubMed*, *30*(2), 3–13. https://pubmed.ncbi.nlm.nih.gov/30785634

20) Huang, Z. (1998). Body weight, weight change, and risk for hypertension in women. *Annals of Internal Medicine*, *128*(2), 81. https://doi.org/10.7326/0003-4819-128-2-199801150-00001

21) Tsao, C. W., Aday, A. W., Almarzooq, Z. I., Anderson, C. A., Arora, P., Avery, C. L., Baker-Smith, C. M., Beaton, A. Z., Boehme, A. K., Buxton, A. E., Commodore-Mensah, Y., Elkind, M. S., Evenson, K. R., Eze-Nliam, C., Fugar, S., Generoso, G., Heard, D. G., Hiremath, S., Ho, J. E., . . . Martin, S. S. (2023). Heart disease and stroke statistics—2023 Update: A report from the American Heart Association. *Circulation*, *147*(8). https://doi.org/10.1161/cir.0000000000001123

22) Cohen, L., Curhan, G. C., & Forman, J. P. (2012). Influence of age on the association between lifestyle factors and risk of hypertension. *Journal of the American Society of Hypertension*, *6*(4), 284–290. https://doi.org/10.1016/j.jash.2012.06.002

23) Boutouyrie, P., Chowienczyk, P., Humphrey, J., & Mitchell, G. (2021). Arterial Stiffness and Cardiovascular Risk in Hypertension.. *Circulation research*, 128 7, 864-886 . https://doi.org/10.1161/CIRCRESAHA.121.318061.

24) Delacroix, S., & Chokka, R. G. (2014). Hypertension: Pathophysiology and treatment. *Journal of Neurology & Neurophysiology*, *05*(06). https://doi.org/10.4172/2155-9562.1000250

25) Harrison.D , Thomas M. Coffman, Christopher S. Wilcox. Pathophysiology of Hypertension *Journal of the American Society of Hypertension*, 2021;128:847–863. DOI: 10.1161/CIRCRESAHA.121.318082.

26) Kobori H, Nangaku M, Navar LG, Nishiyama A (2007) Theintrarenal renin-angiotensin system: from physiology to the pathobiology of hypertension and kidney disease. See comment in PubMed Commons below Pharmacology Rev 59: 251-287.

27) Guzik, T. J., Mohiddin, S. A., Dimarco, A., Patel, V., Savvatis, K., Marelli-Berg, F. M., Madhur, M. S., Tomaszewski, M., Maffia, P., D'Acquisto, F., Nicklin, S. A., Marian, A. J., Nosalski, R., Murray, E. C., Guzik, B., Berry, C., Touyz, R. M., Kreutz, R., Wang, D. W., . . . McInnes, I. B. (2020). COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. *Cardiovascular Research*, *116*(10), 1666–1687. https://doi.org/10.1093/cvr/cvaa106

28) Wilkins, L. (2018). Correction to: 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guid. *Hypertension*. https://doi.org/10.1161/HYP.0000000000000075.

29) James PA, Oparil S, Carter BL, 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):507–520. doi:10.1001/jama.2013.284427

30) JNC 8 Hypertension Guideline .

31) Goodman & Gilman's: The Pharmacological Basis of Therapeutics, Thirteenth Edition