

**A Practical Guide
To
Hypertension
Management**

Definition

Hypertension is defined as a sustained increase in systolic blood pressure (SBP) of 140 mmHg or greater and/or diastolic blood pressure (DBP) of 90 mmHg or greater.

Types of hypertension

- Primary or essential hypertension (no underlying cause)
- Secondary hypertension (hypertension due to other disorders like kidney disease, vascular or endocrine disorders)

Classification of blood pressure

Joint National Committee - 7 (JNC - 7) guidelines

Category	Systolic BP		Diastolic BP
Normal	< 120	and	< 80
Prehypertension	120 – 139	or	80 - 89
Stage 1 hypertension	140 – 159	or	90 - 99
Stage 2 hypertension	≥ 160	or	≥ 100

European Society of Hypertension - European Society of Cardiology (ESH-ESC 2007) guidelines

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

* Isolated systolic hypertension (ISH) should be graded (grades 1, 2 & 3) according to the systolic BP values indicated, provided that diastolic values are < 90 mmHg.

Cardiovascular risk stratification for management of hypertension

The real threshold of hypertension must be considered as flexible, being higher or lower based on total cardiovascular (CV) risk of each individual. Hence, the therapeutic approach should be guided by the 10-year cardiovascular risk of the individual as shown below:

Blood pressure (mmHg)					
Other risk factors, OD or Disease	Normal SBP 120–129 or DBP 80–84	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥ 180 or DBP ≥ 110
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1–2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
3 or more risk factors, MS, OD or Diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
Established CV or renal disease	Very high added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

Risk factors affecting prognosis: systolic & diastolic BP levels; age (male > 55 years; female > 65 years); pulse pressure level (in elderly); smoking; high intake of alcohol; co-existing disorders such as dyslipidemia, renal dysfunction or abdominal obesity or metabolic syndrome; family history of premature cardiovascular disease (male < 55 years; female < 65 years); less active lifestyle

OD (Subclinical organ damage): LVH; slight increase in plasma creatinine (male: 1.3-1.5 mg/dl; female: 1.2-1.4 mg/dl); low estimated glomerular filtration rate (< 60 ml/min/1.73 m²) or creatinine clearance (< 60 ml/min); microalbuminuria

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Major complications of untreated hypertension

- Myocardial infarction
- Stroke
- Renal failure
- Retinopathy

Management of Hypertension

The decision to start antihypertensive treatment should be based on two criteria, i.e. the level of systolic and diastolic BP and the level of cardiovascular risk.

Other risk factors OD or disease	Blood pressure (mmHg)				
	Normal SBP 120–129 or DBP 80–84	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other risk factors	No BP intervention	No BP intervention	Lifestyle changes for several months then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + Immediate drug treatment
1–2 risk factors	Lifestyle changes	Lifestyle changes	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + Immediate drug treatment
≥3 risk factors, MS or OD	Lifestyle changes	Lifestyle changes and consider drug treatment	Lifestyle changes + Drug treatment	Lifestyle changes + Drug treatment	Lifestyle changes + Immediate drug treatment
Diabetes	Lifestyle changes	Lifestyle changes + Drug treatment	Lifestyle changes + Drug treatment	Lifestyle changes + Drug treatment	Lifestyle changes + Immediate drug treatment
Established CV or renal disease	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment

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Lifestyle modification

- Stop smoking
- Reduce weight if overweight & stabilize the weight
- Limit alcohol intake
- Increase physical activity
- Reduce salt intake
- Increase fruit and vegetable intake
- Decrease saturated and total fat intakes

Drug therapy for hypertension

When initiating drug therapy

- Monotherapy could be the initial treatment for a mild BP elevation with a low or moderate total cardiovascular risk. Initiation of the treatment should be with a low dose of a single drug. If BP is not controlled, either a full dose of the initial agent can be given or the patient can be switched to an agent of a different class.
- A combination of two drugs at low doses should be preferred as first-step treatment when initial BP is in grade 2 or 3 range or total cardiovascular risk is high or very high.
- In uncomplicated hypertensives and in the elderly, antihypertensive therapy should normally be initiated gradually. In higher risk hypertensives, goal BP should be achieved more promptly, with quicker adjustment of doses.
- Drugs providing longer duration of action, i.e. 24 hrs (once daily), should be preferred to provide:
 - Smooth and consistent BP control
 - Enhanced patient compliance (less likelihood of patients missing out on dose)

Available drug options

Class of drug	Example	Initiating dose	Usual maintenance dose
Diuretics	Hydrochlorothiazide	12.5 mg/day	12.5-25 mg/day
β-blockers	Metoprolol extended release	25-50 mg/day	50-100 mg/day
	Nebivolol	2.5-5 mg/day	2.5-5 mg/day
Calcium channel blockers	Amlodipine	2.5-5 mg/day	5-10 mg/day
Angiotensin converting enzyme inhibitors	Ramipril	1.25-2.5 mg/day	2.5-10 mg/day
	Lisinopril	2.5-5 mg/day	5-20 mg/day
Angiotensin receptor blocker	Telmisartan	40 mg/day	40-80 mg/day
	Losartan	25-50 mg/day	50-100 mg/day
α-blockers	Doxazoxin	1 mg/day	1-16 mg/day
Aldosterone antagonist	Eplerenone	25-50 mg/day	50-100 mg/day

Choosing the appropriate antihypertensive

- Hypertension not associated with any co-existing condition

Preferably a drug from any of the five classes may be selected: diuretics, beta-blockers, calcium channel blockers, angiotensin converting enzyme inhibitors and angiotensin receptor blockers.

ESH-ESC 2007 guidelines & JNC-7 guidelines

- Hypertension associated with co-existing conditions

Condition	Preferred drug	Other drugs that can be used	Drugs to be avoided
Diabetes mellitus	ACEIs, ARBs. If needed add thiazide diuretic (GFR > 50 ml/min/1.73m ²) & loop diuretic (GFR < 50 ml/min/1.73m ²)	CCBs	Beta blockers
Diabetic nephropathy	ACEIs, ARBs. If needed add CCBs, beta blockers or diuretics	CCBs, beta blockers or diuretics can be used as alternate therapy when ACEIs/ARBs are contraindicated	
Nephropathy	ACEIs, ARBs, ACEI-ARB	CCBs, Beta	

(non-diabetic)	combination	blockers, Diuretics	
ESRD/proteinuria	ACEIs, ARBs, loop diuretics	Beta blockers, CCBs	
Asthma, Chronic obstructive pulmonary disease	CCBs	ARBs, ACEIs, Diuretics	Beta blockers
Previous stroke	ARBs, ACEIs, diuretic, CCBs	Beta blockers	
Angina pectoris	ACEIs, Beta blockers, long acting CCBs	ARBs, Diuretics	
Previous myocardial infarction	Beta blockers, ACEIs, ARBs, Aldosterone antagonist	Diuretics, CCBs	
Left ventricular hypertrophy	ACEIs, ARBs, CCBs	Diuretics, Beta blockers	
Left ventricular dysfunction	ACEIs	Beta blockers, diuretics, ARBs, CCBs	
Congestive heart failure	Diuretics, ACEIs, ARBs, Beta blockers, aldosterone antagonists		CCBs
Atrial fibrillation A) Recurrent B) Permanent	ARBs, ACEIs Beta blockers, non-dihydropyridine CCBs (verapamil, diltiazem)	Diuretics	
Peripheral arterial disease	ACEIs, CCBs	Diuretics, ARBs, α -blockers	Beta blockers,
Metabolic syndrome	ACEIs, ARBs, followed with its combination with CCBs or low-dose thiazide diuretics (if needed)	Vasodilating beta blockers (carvedilol, nebivolol)	Non-vasodilating beta blockers and their combination with thiazide diuretics
High cholesterol level	α -blockers, ACEIs, ARBs, CCBs		Beta blockers, diuretics
Pregnancy	Dihydropyridine CCBs, Methyldopa, Labetalol, Beta blockers		ACEIs, ARBs, diuretics
Isolated systolic hypertension	Thiazide diuretics, CCBs	ARBs, ACEIs, Beta blockers	
Elderly	Thiazide diuretics, CCBs, ARBs, ACEIs, Beta blockers		

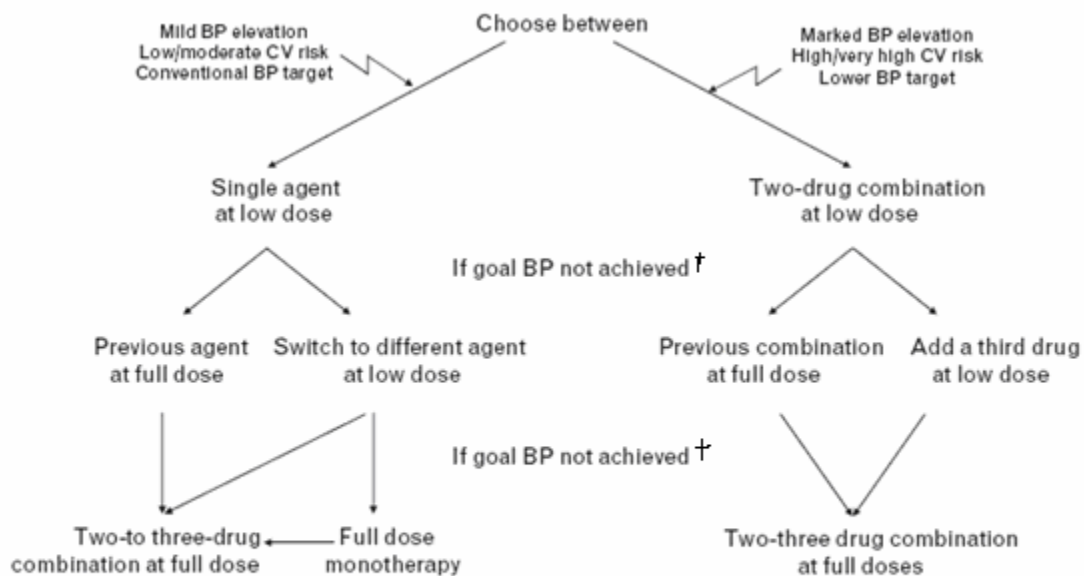
Benign Prostatic Hyperplasia	α -blockers	Beta blockers, ACEIs, ARBs, diuretics, CCBs	
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ACEI - Angiotensin Converting Enzyme Inhibitor, ARB - Angiotensin Receptor Blocker, CCB - Calcium Channel Blocker

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Combination therapy

- More than two-third of hypertensives cannot be controlled on one drug and will require two or more antihypertensives selected from different classes of drugs.
- In high-risk hypertensives, 9 out of 10 patients require two or more antihypertensives to reduce their BP to < 140/90 mmHg.
- When BP is more than 20/10 mmHg above the goal, consideration should be given to initiate therapy with two drugs, either as separate prescriptions or in fixed-dose combination.
- Starting treatment with two-drug combination may allow BP targets to be reached earlier than monotherapy.



+ BP goal: Hypertension without concomitant disease: < 140/90 mm Hg
 Hypertension with concomitant disease or risk factor: < 130/80 mm Hg

- **Advantages of fixed-dose combination:**
 - Better BP control
 - Lesser incidence of individual drug's side effects
 - Neutralization of side effects
 - Increased patient compliance

- Lesser cost of therapy
- *Recommended fixed-dose combinations by JNC-7 & ESH-ESC 2007 guidelines*
 - Calcium channel blocker & Beta blocker (e.g. Amlodipine & Nebivolol)
 - Calcium channel blocker & Angiotensin converting enzyme inhibitor (e.g. Amlodipine & Lisinopril)
 - Calcium channel blocker & Angiotensin receptor blocker (e.g. Amlodipine & Telmisartan)
 - Calcium channel blocker & Thiazide diuretic (e.g. Amlodipine & hydrochlorothiazide)
 - Angiotensin converting enzyme inhibitor & Thiazide diuretic (e.g. Ramipril & hydrochlorothiazide)
 - Angiotensin receptor blocker & Thiazide diuretic (e.g. Telmisartan & hydrochlorothiazide)
 - Angiotensin converting enzyme inhibitor & Angiotensin receptor blocker (e.g. Ramipril & Telmisartan)
 - Beta blocker & diuretic* (e.g. Nebivolol & Hydrochlorothiazide)
 - Thiazide diuretic & potassium-sparing diuretic (e.g. Frusemide & Amiloride)

*The combination should be avoided in hypertensives with metabolic syndrome and when there is high risk of incident diabetes. However this may not be applicable to vasodilating beta-blockers like nebivolol and carvedilol.

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Improving compliance to treatment

- Inform the patient on the risk of hypertension and the benefit of effective treatment
- Provide clear written and oral instructions about treatment
- Tailor the treatment regimen to the patient's lifestyle and needs
- Simplify treatment by reducing, if possible, the number of daily medicaments
- Involve the patient's partner or family in information on disease and treatment plans
- Make use of behavioural strategies such as reminder systems.
- Pay great attention to side effects (even if subtle) and be prepared to timely change drug doses or types if needed
- Dialogue with patient regarding adherence and be informed of his/her problems

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Antihypertensive therapy: Side effects & Contraindications

Class of drugs	Contraindications		Side effects
	Compelling	Possible	
Thiazide diuretics (eg. Hydrochlorothiazide)	Anuria, Gout, Hypersensitivity	Metabolic syndrome, Glucose intolerance, Pregnancy	Electrolyte & fluid imbalance, hyperglycemia, hyperuricemia

<p>Selective beta-blockers</p> <p>(eg. Metoprolol extended release)</p>	<p>Severe bradycardia, Heart block (grade 2 or 3), Cardiogenic shock, Decompensated cardiac failure, Sick sinus syndrome, Hypersensitivity</p>		<p>Tiredness, dizziness, depression, headache, somnolence, insomnia, diarrhoea, pruritus, bradycardia, cold extremities, wheezing, dyspnea, nausea, dry mouth, constipation, flatulence and palpitations.</p>
<p>Non-selective beta blockers</p> <p>(eg. Carvedilol)</p>	<p>Bronchial asthma or related bronchospastic conditions, Atrioventricular block (grade 2 & 3), Sick sinus syndrome or severe bradycardia, Cardiogenic shock or who have decompensated heart failure requiring the use of intravenous inotropic therapy.</p>	<p>Peripheral artery disease, Metabolic syndrome, Glucose intolerance, Athletes and physically active patients, Chronic obstructive pulmonary disease</p>	<p>Asthenia, bradycardia, hypotension, diarrhea, hyperglycemia, dizziness, insomnia, postural hypotension, edema</p>
<p>Calcium antagonists (dihydropyridines)</p> <p>(eg. Amlodipine)</p>	<p>Hypersensitivity</p>	<p>Tachyarrhythmias, Heart failure</p>	<p>Headache, edema, fatigue, flushing, palpitations, dizziness</p>
<p>Calcium antagonists (non-dihydropyridines)</p> <p>(eg. Verapamil, Diltiazem)</p>	<p>Sick Sinus Syndrome, Atrioventricular block (grade 2 or 3), Heart failure, Hypotension, Severe left ventricular dysfunction, Acute myocardial infarction & pulmonary</p>		<p>Headache, edema, dizziness, asthenia, first degree atrioventricular block, constipation, nausea</p>

	congestion, Atrial flutter or atrial fibrillation & an accessory bypass tract, Hypersensitivity		
ACE inhibitors (eg. Ramipril)	Pregnancy, Angioneurotic edema, Hyperkalemia, Bilateral renal artery stenosis, Hypersensitivity		Cough, headache, dizziness, hypotension, angioedema, hyperkalemia
Angiotensin receptor antagonists (eg. Telmisartan)	Pregnancy, Hyperkalemia, Bilateral renal artery stenosis, Hypersensitivity		Headache, dizziness, back pain, fatigue and nausea
Diuretics (antialdosterone) (eg. Eplerenone)	Type 2 diabetes with microalbuminuria, Serum creatinine >2 mg/dl in males or >1.8 mg/dl in females, Creatinine clearance <50ml/min, Concomitant use of potassium supplements or potassium sparing diuretics (amiloride, spironolactone, or triamterene)		Headache, dizziness, diarrhea, coughing, fatigue, influenza-like symptoms and hyperkalemia
α -blockers (eg. Doxazosin)	Hypersensitivity		Postural hypotension, dizziness, dyspnea, headache, asthenia, hypotension and somnolence

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Suggested references:

- The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and treatment of High Blood Pressure. *JAMA* 2003;289:2560-72
- ESH-ESC 2007 Guidelines for the Management of Arterial Hypertension. *J Hypertens* 2007;25:1105-87