



# Hypertension

KAIS AL BALBISSI, MD, FACC, FSCAI

ASSOCIATE PROFESSOR OF INTERNAL MEDICINE

*CARDIOLOGY DIVISION, INTERNAL MEDICINE DEPARTMENT,  
COLLEGE OF MEDICINE, UNIVERSITY OF JORDAN*

# Hypertension

- Brief History of Hypertension Guidelines
- Burden of Hypertension
- Diagnosis of Hypertension
  - White Coat Hypertension & Masked Hypertension
- Secondary Hypertension
- Management of Hypertension
  - Non Pharmacological
  - Pharamcological
- Hypertension & Co- Morbidities
- Hypertensive Crises
- Resistant Hypertension

The background of the slide is a dark blue gradient. It features a series of curved, concentric lines that create a tunnel-like effect, leading towards a central vanishing point. On the left side, there is a faint, grid-like pattern of small squares, suggesting a digital or data theme. The overall aesthetic is modern and professional.

# Brief history of Hypertension Guidelines

# Hypertension Guidelines Brief History

**JNC 1**  
**1976**

**JNC 6**  
**1997**

**JNC 7**  
**2003**

**JNC 8**  
**2014**

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Panel: Experts in	
HTN	14
PCP	6
Geriatricians	2
Cardiology	2
Nephrology	3
Nursing	1
Pharmacology	2
Clinical Trials	6
EBM	3
Epidemiology	1
Informatics	4
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JNC 6 CATEGORY	
	SBP/DBP
<b>OPTIMAL</b>	<120/80
<b>NORMAL</b>	120-129/80-84
<b>BORDERLINE</b>	130-139/85-89
<b>HYPERTENSION</b>	≥140/90
STAGE 1	140-159/90-99
STAGE 2	160-179/100-109
STAGE 3	≥180/110

CLASSIFICATION OF BLOOD PRESSURE (BP)*			
CATEGORY	SBP mmHg	and	DBP mmHg
Normal	<120	and	<80
Prehypertension	120-139	or	80-89
Hypertension, Stage 1	140-159	or	90-99
Hypertension, Stage 2	≥160	or	≥100

\* See Blood Pressure Measurement Techniques (reverse side)  
Key: SBP = systolic blood pressure; DBP = diastolic blood pressure

	Goal BP
Age ≤ 60 yrs	<140/90
Age ≥ 60 yrs	<150/90
DM	<140/90
CKD	<140/90

# Hypertension Guidelines History

# JNC 7 2003

## EVALUATION

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\* See Blood Pressure Measurement Techniques (Series 440).  
 \* May: SBP = systolic blood pressure; DBP = diastolic blood pressure.

### DIAGNOSTIC WORKUP OF HYPERTENSION

- Assess risk factors and comorbidities.
- Reveal identifiable causes of hypertension.
- Assess presence of target organ damage.
- Conduct history and physical examination.
- Obtain laboratory tests: urinalysis, blood glucose, hematocrit and lipid panel, serum potassium, creatinine, and calcium. Optional: urinary albumin/creatinine ratio.
- Obtain electrocardiogram.

### ASSESS FOR MAJOR CARDIOVASCULAR DISEASE (CVD) RISK FACTORS

- Hypertension
- Obesity (body mass index ≥30 kg/m<sup>2</sup>)
- Dyslipidemia
- Diabetes mellitus
- Cigarette smoking
- Physical inactivity
- Microalbuminuria, estimated glomerular filtration rate <60 mL/min
- Age (≥55 for men, ≥65 for women)
- Family history of premature CVD (men age <55, women age <65)

### ASSESS FOR IDENTIFIABLE CAUSES OF HYPERTENSION

- Sleep apnea
- Drug induced (related)
- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Cushing's syndrome or steroid therapy
- Pheochromocytoma
- Coarctation of aorta
- Thyroid/parathyroid disease

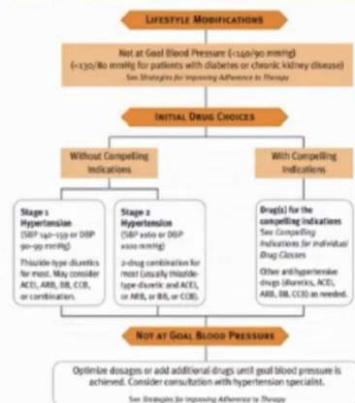
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 NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

## TREATMENT

### PRINCIPLES OF HYPERTENSION TREATMENT

- Treat to BP <140/90 mmHg or BP <130/90 mmHg in patients with diabetes or chronic kidney disease.
- Majority of patients will require two medications to reach goal.

### ALGORITHM FOR TREATMENT OF HYPERTENSION



### NONPHARMACEUTICAL CATEGORIES

Method	Notes
In-office	Two readings, 5 minutes apart, sitting in chair. Confirms elevated reading in contralateral arm.
Automated BP monitoring	Indicated for evaluation of "white coat hypertension." Absence of 10-20 percent BP decrease during sleep may indicate increased CVD risk.
Patient self-check	Provides information on response to therapy. May help improve adherence to therapy and is useful for evaluating "white coat hypertension."

### CHOICES OF HYPERTENSION TREATMENT

- Improve BP measurement
- Reduce sodium intake
- Inadequate therapy
- Medication
  - Inadequate doses
  - Drug actions and interactions (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs], diuretic drugs, sympathomimetics, oral contraceptives)
  - Over-the-counter (OTC) drugs and herbal supplements
  - Excess alcohol intake
  - Identifiable causes of hypertension (see reverse side)

### COMPELLING INDICATIONS FOR INDIVIDUAL DRUG CLASSES

Compelling Indication	Initial Therapy Options
Heart failure	THIAZ, BB, ACEI, ARB, ALDO ANT
Post myocardial infarction	BB, ACEI, ALDO ANT
High CVD risk	THIAZ, BB, ACEI, CCB
Diabetes	THIAZ, BB, ACEI, ARB, CCB
Chronic kidney disease	ACEI, ARB
Recurrent stroke prevention	THIAZ, ACEI

See THIAZ = thiazide diuretic; BB = beta-blocker; CCB = calcium channel blocker; ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; ALDO ANT = aldosterone antagonist.

### STRATEGIES FOR IMPROVING ADHERENCE TO THERAPY

- Clinicians empathically increase patient trust, motivation, and adherence to therapy.
- Physicians should consider their patients' cultural beliefs and individual attitudes in formulating therapy.

The National High Blood Pressure Education Program is coordinated by the National Heart, Lung, and Blood Institute (NHLBI) at the National Institutes of Health. Copies of the JNC 7 Report are available on the NHLBI Web site at <http://www.nhlbi.nih.gov> or from the NHLBI Health Information Center, 310, Res. Bldg., Bethesda, MD 20894-6101, Phone: 301-495-6173 or 1-800-829-3243 (TTY), Fax: 301-495-8453.

### RECOMMENDATIONS FOR PATIENTS

- Encourage healthy lifestyles for all individuals.
- Prescribe lifestyle modifications for all patients with prehypertension and hypertension.
- Components of lifestyle modification include weight reduction, DASH eating plan, dietary sodium reduction, aerobic physical activity, and moderation of alcohol consumption.

### DIETARY MODIFICATION RECOMMENDATIONS

Modification	Recommendation	Avg. SBP Reduction Range*
Weight reduction	Maintains normal body weight (body mass index: 18.5-24.9 kg/m <sup>2</sup> ).	5-20 mmHg/10 kg
DASH eating plan	Adopt a diet rich in fruits, vegetables, and low-fat dairy products with reduced content of saturated and total fat.	8-14 mmHg
Dietary sodium reduction	Reduce dietary sodium intake to ≤100 mmol per day (2.4 g sodium or 6 g sodium chloride).	2-8 mmHg
Aerobic physical activity	Regular aerobic physical activity (e.g., brisk walking) at least 30 minutes per day, most days of the week.	4-9 mmHg
Moderation of alcohol consumption	Men limit to ≤2 drinks* per day. Women and lighter weight persons limit to ≤1 drink* per day.	2-4 mmHg

\* 1 drink = 12 oz beer or 5 oz ethanol, or 1 oz wine, or 1.5 oz 40 percent alcohol spirits. See also <http://www.nhlbi.nih.gov> for more information.



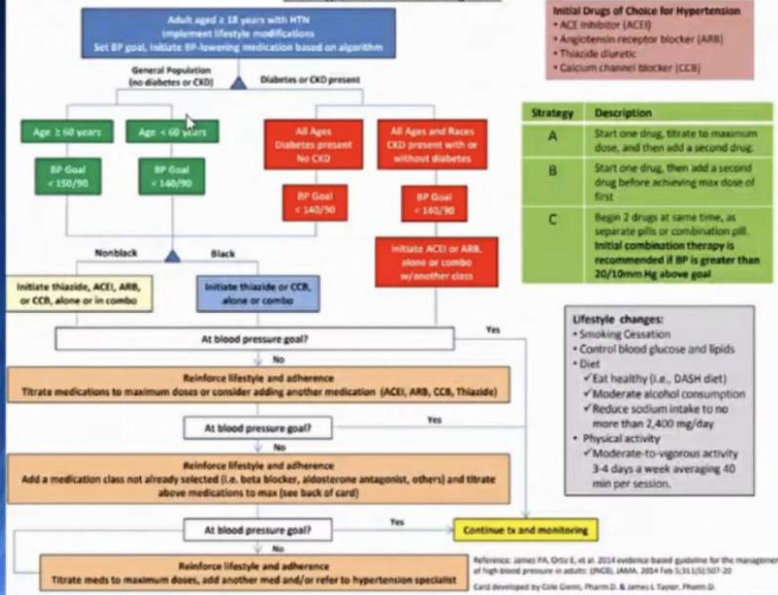
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 NATIONAL HIGH BLOOD PRESSURE EDUCATION PROGRAM

NIH Publication No. 03-5221  
 May 2003

# Hypertension Guidelines History

# JNC 8 2014

JNC 8 Hypertension Guideline Algorithm



Indication	Treatment Choice
Heart Failure	ACEi/ARB + BB + diuretic + spironolactone
Post-MI/Coronary CAD	ACEi/ARB AND BB
CAD	ACEi, BB, diuretic, CCB
Diabetics	ACEi/ARB, CCB, diuretic
CKD	ACEi/ARB
Recurrent stroke prevention	ACEi, diuretic
Pregnancy	labetalol (first line), nifedipine, methyldopa

## Hypertension Treatment

**Beta-1 Selective Beta-blockers** – possibly safer in patients with COPD, asthma, diabetes, and peripheral vascular disease:

- metoprolol
- bisoprolol
- betaxolol
- acebutolol

Drug Class	Agents of Choice	Comments
Diuretics	HCTZ 12.5-50mg, chlorthalidone 12.5-25mg, indapamide 1.25-2.5mg furosemide 100mg 40 mg spironolactone 25-50mg, amiloride 5-10mg, triamterene 100mg	Monitor for hypokalemia Most SE are metabolic in nature Most effective when combined w/ ACEi Stronger clinical evidence w/ thiazolidione Spironolactone - gynecomastia and hyperkalemia Loop diuretics may be needed when GFR < 40ml/min
ACEi/ARB	ACEi: lisinopril, benazepril, fosinopril and quinopril 10-40mg, ramipril 5-10mg, trandolapril 2-8mg ARB: candesartan 8-32mg, valsartan 80-320mg, losartan 50-100mg, olmesartan 20-40mg, telmisartan 20-80mg	SE: Cough (ACEi only), angioedema (more with ACEi), hyperkalemia Losartan lowers uric acid levels, candesartan may prevent migraine headaches
Beta Blockers	metoprolol succinate 50-100mg and tartrate 50-100mg twice daily, nebivolol 5-10mg, propranolol 40-120mg twice daily, carvedilol 6.25-25mg twice daily, bisoprolol 5-10mg, labetalol 100-300mg twice daily.	Not first line agents – reserve for post-MI/CHF Cause fatigue and decreased heart rate Adversely affect glucose, mask hypoglycemia awareness
Calcium channel blockers	dihydropyridines: amlodipine 5-10mg, nifedipine ER 30-90mg Non-dihydropyridines: diltiazem ER 180-360 mg, verapamil 80-120mg 3 times daily or ER 240-480mg	Cause edema; dihydropyridines may be safely combined w/ beta blocker Non-dihydropyridines reduce heart rate and proarrhythmia
Vasodilators	hydralazine 25-100mg twice daily, minoxidil 5-10mg	Hydralazine and minoxidil may cause reflex tachycardia and fluid retention – usually require diuretic + beta blocker
Centrally-acting Agents	clonidine 0.1-0.2mg twice daily, methyldopa 250-500mg twice daily guanfacine 1-3mg	Clonidine available in weekly patch formulation for resistant hypertension

# Hypertension Guidelines History

	JNC 8 <sup>1</sup>	NICE <sup>2</sup>	JSH <sup>3</sup>	ESH/ESC <sup>4</sup>	CCS <sup>5</sup>
<b>General</b>	<140/90 (<60 years old)	<140/90	<130/85	<140/90	<140/90
<b>Diabetes</b>	<140/90	NR	<130/80	<140/85	<130/80
<b>CKD</b>	<140/90	<130/80	<130/80	<140/90	<140/90
<b>MI</b>	NR	NR	<130/80	<140/90	<140/90
<b>Stroke</b>	NR	<130/80	<140/90	<140/90	<140/90
<b>Elderly</b>	<150/90 (≥60 years old)	<150/90 (≥80 years old)	<140/90	<140/90 (<80 years old)	<150/90 (≥80 years old)

CKD=chronic kidney disease; CCS=Canadian Cardiovascular Society; ESC=European Society of Cardiology; ESH=European Society of Hypertension; JNC 8=Eighth report of the Joint National Committee; JSH=Japanese Society of Hypertension; MI=myocardial infarction; NICE=National Institute for Health and Care Excellence; NR=not reported

# Hypertension Guidelines History



BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 - 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 - 139	or	80 - 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120



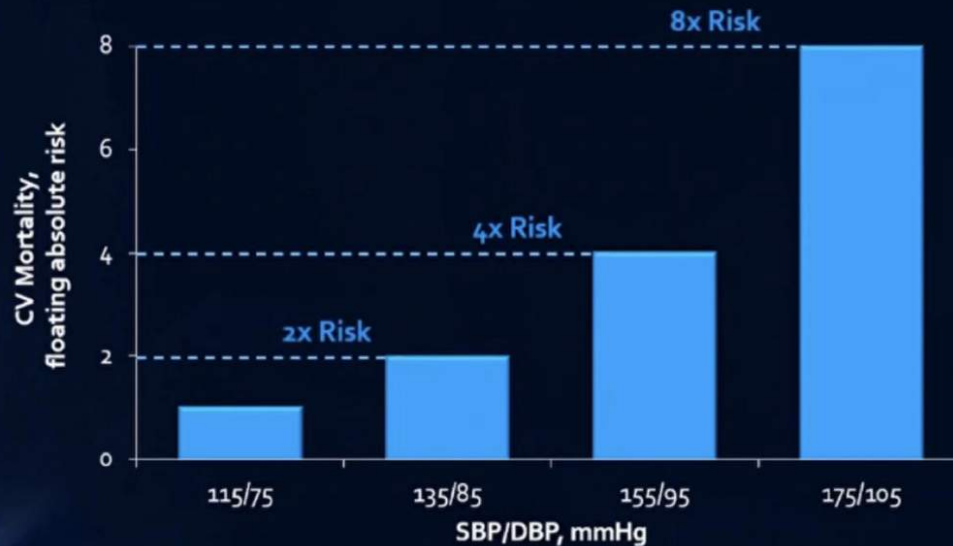
Hypertension disease staging	Other risk factors, HMDD, or disease	BP (mmHg) grading			
		High normal SBP 130-139 DBP 85-89	Grade 1 SBP 140-159 DBP 90-99	Grade 2 SBP 160-179 DBP 100-109	Grade 3 SBP ≥180 or DBP ≥110
Stage 1 (uncomplicated)	No other risk factors	Low risk	Low risk	Moderate risk	High risk
	1 or 2 risk factors	Low risk	Moderate risk	Moderate to high risk	High risk
	≥3 risk factors	Low to Moderate risk	Moderate to high risk	High Risk	High risk
Stage 2 (asymptomatic disease)	HMDD, CKD grade 3, or diabetes mellitus without organ damage	Moderate to high risk	High risk	High risk	High to very high risk
Stage 3 (established disease)	Established CVD, CKD grade ≥4, or diabetes mellitus with organ damage	Very high risk	Very high risk	Very high risk	Very high risk



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# Burden of Hypertension

## Effect of Hypertension on Risk of Cardiovascular Death



\*Based on observational studies, risk was present in all age groups 40–89 years  
BP=blood pressure; CV=cardiovascular; DBP=diastolic blood pressure; IHD=ischemic heart disease; SBP=systolic blood pressure  
Chobanian AV, et al. *Hypertension*. 2003;42:1206-1252.

# What is the big deal about BP Control?

Analysis of 5 major observational studies demonstrated that small differences in SBP resulted in significant risk difference in developing complications:<sup>1</sup>



A meta-analysis of 61 prospective randomized studies involving 12.7 million person-years demonstrated that modest SBP reduction was associated with significant risk reduction in developing complications:<sup>2</sup>



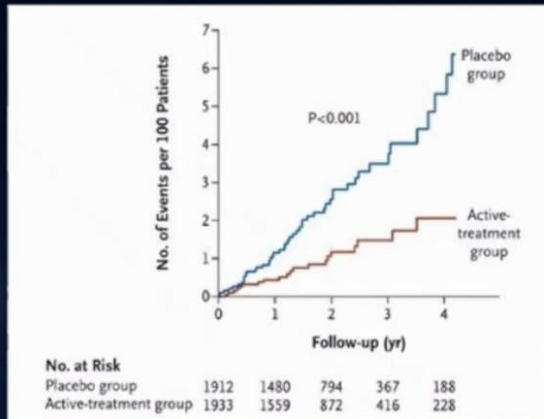
CHD=coronary heart disease; IHD=ischemic heart disease; SBP=systolic blood pressure

1. Stalmer R. *Hypertension*. 1991;17(Suppl1):116-120.

2. Lewington S, et al. *Lancet*. 2002;360:1903-1913.

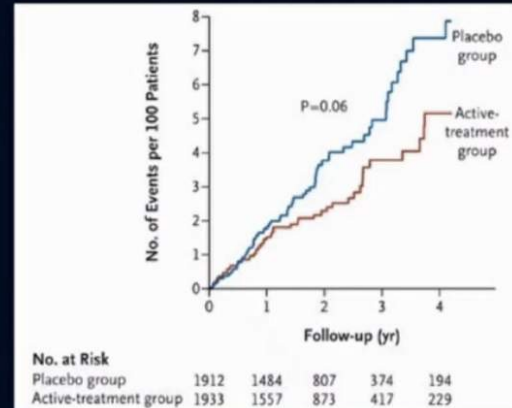
# Treatment works !!

## HF



1. Kostis et al. SHEP Cooperative Research Group. *JAMA* 1991;270: 222-6.

## CVA



2. Beckett et al. HYVET. *N Engl J Med* 2008;358:187-98.

## Among Adults with Hypertension: Awareness, Treatment, and At Target



## Number of Medications Needed to Achieve Goal Systolic Blood Pressure

### Patients Without Chronic Kidney Disease (achieved SBP)

HOT (138 mmHg)  
UKPDS (144 mmHg)  
ALLHAT (138 mmHg)  
INVEST (136 mmHg)



### Patients With Chronic Kidney Disease (achieved SBP)

MDRD (132 mmHg)  
ABCD (132 mmHg)  
AASK (128 mmHg)  
IDNT (138 mmHg)  
RENAAL (141 mmHg)



Antihypertensive Medications, n

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# Diagnosis of Hypertension

# Diagnosis of Hypertension

## • Guidelines for Proper Technique for measurement of BP

### Posture

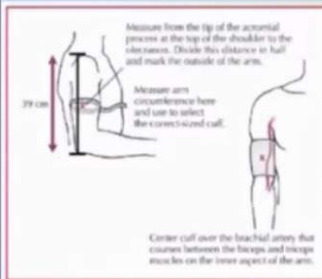
- Patient sit quietly for 3-5 minutes before taking the measurement
- Support the arm at heart level during measurement
- BP should be measured in both arms, with the arm with the higher pressure being used to make future measurements
- Initially, check for postural changes by taking readings after five minutes supine, then immediately and two minutes after standing; this is particularly important in patients over age 65 years, diabetics, or those taking antihypertensive drugs
- Sitting pressures are recommended for routine follow-up; the patient should sit quietly with the back supported for five minutes and the arm supported at the level of the heart

### Circumstances

- No caffeine during the hour preceding the reading, and no smoking during the preceding 30 minutes
- No exogenous adrenergic stimulants, such as phenylephrine in decongestants or eye drops for pupillary dilatation
- A quiet, warm setting
- Home readings should be taken upon varying circumstances

### Equipment

- Cuff size
  - The length of the bladder should be 80%, and the width of the bladder should be at least 40% of the circumference of the upper arm
- Manometer
  - Aneroid gauges should be calibrated every six months against a mercury manometer



### Technique

- Number of readings
  - Take at least two readings on each visit, separated by as much time as possible; if readings vary by more than 5 mmHg, take additional readings until two consecutive readings are close
- If the arm pressure is elevated, take the pressure in one leg, particularly in patients under age 30 years
- Performance
  - Inflate the bladder quickly to 20 mmHg above the systolic pressure as estimated from loss of radial pulse
  - Deflate the bladder by 3 mmHg per second
  - Record the Korotkoff phase V (disappearance) as the diastolic pressure except in children in whom use of phase IV (muffling) may be preferable
  - If the Korotkoff sounds are weak, have the patient raise the arm, open and close the hand 5 to 10 times, and then inflate the bladder quickly
- Note the pressure, patient position, arm, and cuff size: eg, 140/90, seated, right arm, large adult cuff



# Diagnosis of Hypertension

## • Guidelines for Proper Technique for measurement of BP

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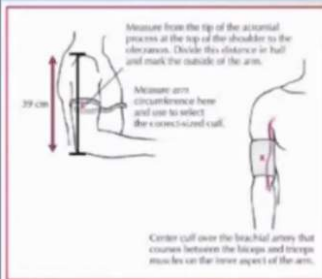
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For the diagnosis of hypertension, take three readings at least one week apart

## Diagnosis of Hypertension

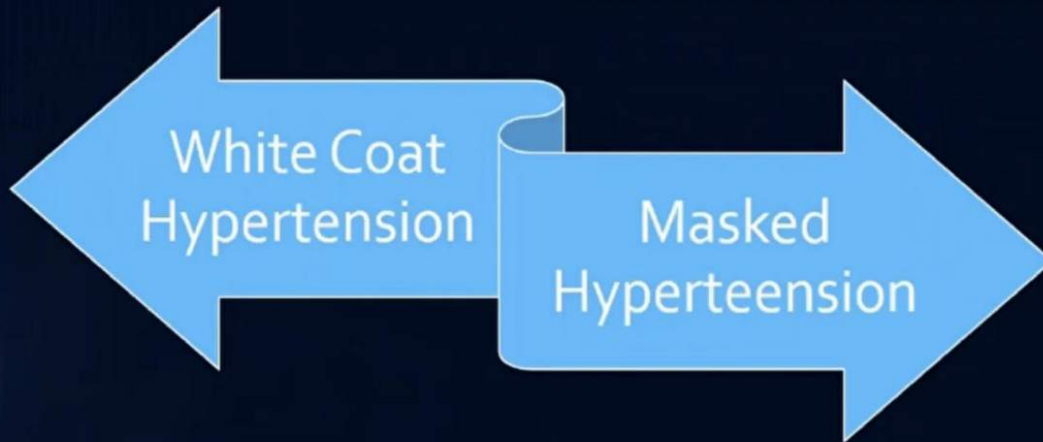
- **Ambulatory (ABPM) and Home BP Monitoring (HBPM)**
  - Very useful for patients with white coat hypertension
  - Ideally be attained in all patients with resistant hypertension
  - If out-of-office readings are at or below the desired target, while office readings remain elevated, home or office readings may be used to guide medication adjustments.
  - Ambulatory monitoring is also a better predictor than office blood pressure measurements of cardiovascular morbidity (ie, end-organ damage) and mortality in patients with resistant hypertension
  - Goal is an average of Systolic BP < 135 mmHg and Diastolic BP < 85 mmHg

## Diagnosis of Hypertension:

**Corresponding Values of Systolic BP/Diastolic BP for Clinic, Home (HBPM), Daytime, Nighttime, and 24-Hour Ambulatory (ABPM) Measurements.**

Clinic	HBPM	Daytime ABPM	Nighttime ABPM	24-Hour ABPM
120/80	120/80	120/80	100/65	115/75
130/80	130/80	130/80	110/65	125/75
140/90	135/85	135/85	120/70	130/80
160/100	145/90	145/90	140/85	145/90

## Diagnosis of Hypertension

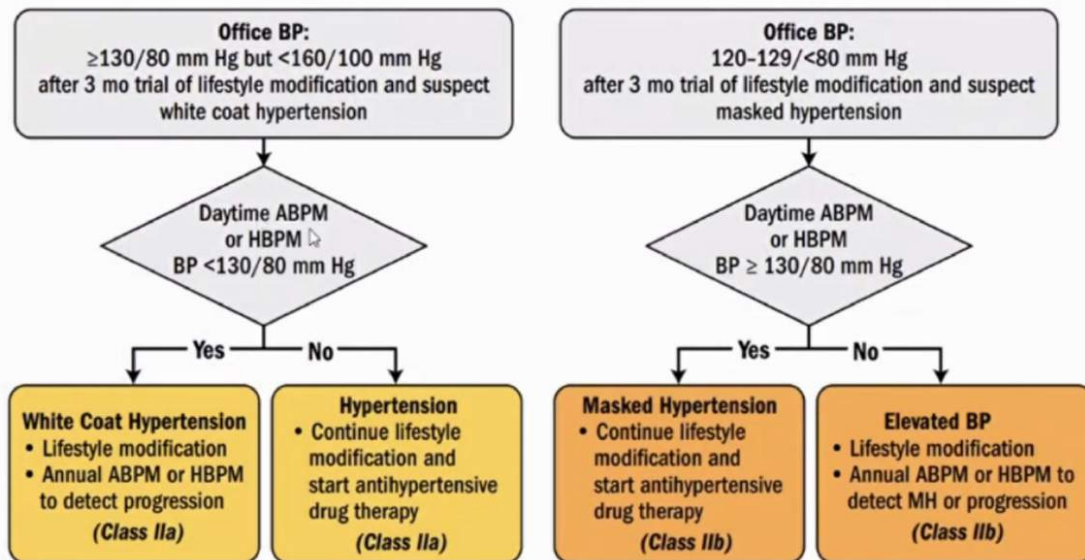


## Diagnosis of Hypertension:

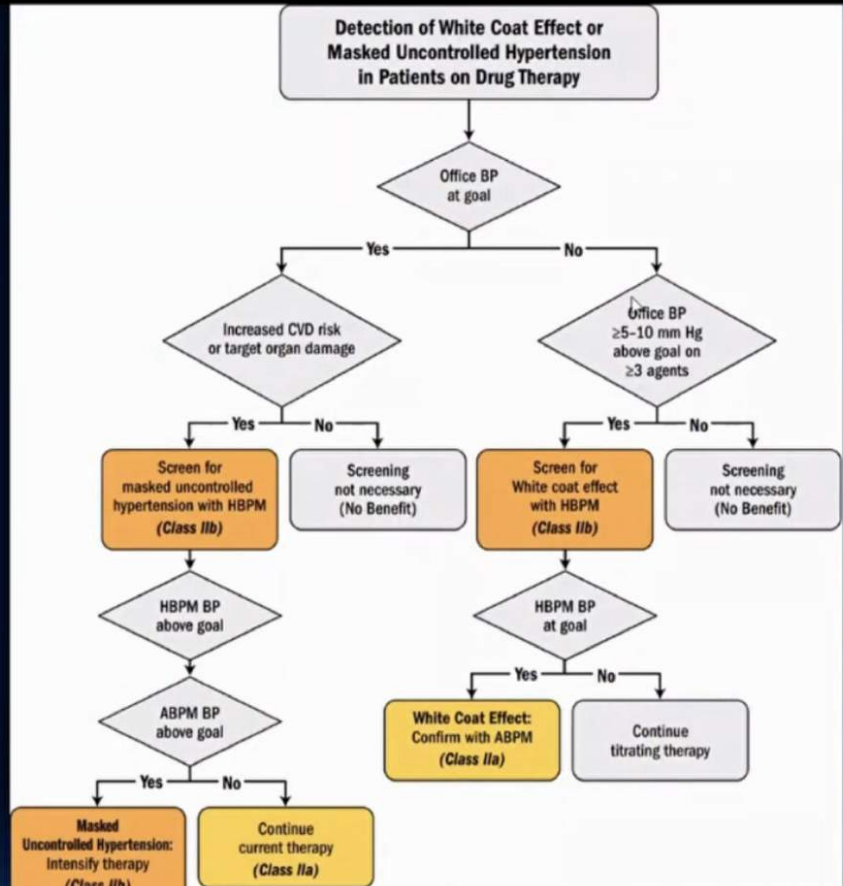
	Office/Clinic/Healthcare Setting	Home/Nonhealthcare/A BPM Setting
Normotensive	No hypertension	No hypertension
Sustained hypertension	Hypertension	Hypertension
Masked hypertension	No hypertension	Hypertension
White coat hypertension	Hypertension	No hypertension

# Diagnosis of Hypertension:

## Detection of White Coat Hypertension or Masked Hypertension in Patients Not on Drug Therapy



# Diagnosis of Hypertension:



# Diagnosis of Hypertension:

## Primary Work up

BP check is advised routinely  
every 5 years

<b>Basic Testing</b>	Fasting blood glucose*
	Complete blood count
	Lipid profile
	Serum creatinine with eGFR*
	Serum sodium, potassium, calcium*
	Thyroid-stimulating hormone
	Urinalysis
<b>Optional Testing</b>	Electrocardiogram
	Echocardiogram
	Uric acid
	Urinary albumin to creatinine ratio

\*May be included in a comprehensive metabolic panel



# Diagnosis of Hypertension:

## Primary Work up

### End organ damage in arterial hypertension

#### Vasculopathy

- Endothelial dysfunction
- Remodeling
- Generalized atherosclerosis
- Arteriosclerotic stenosis
- Aortic aneurysm

#### Cerebrovascular damage

- Acute hypertensive encephalopathy
- Stroke
- Intracerebral hemorrhage
- Lacunar infarction
- Vascular dementia
- Retinopathy

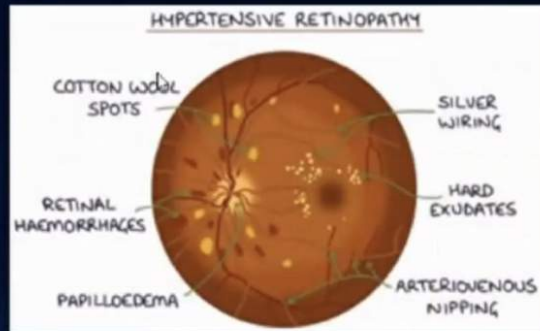
#### Heart disease

- Left ventricular hypertrophy
- Atrial fibrillation
- Coronary microangiopathy
- CHD, myocardial infarction
- Heart failure

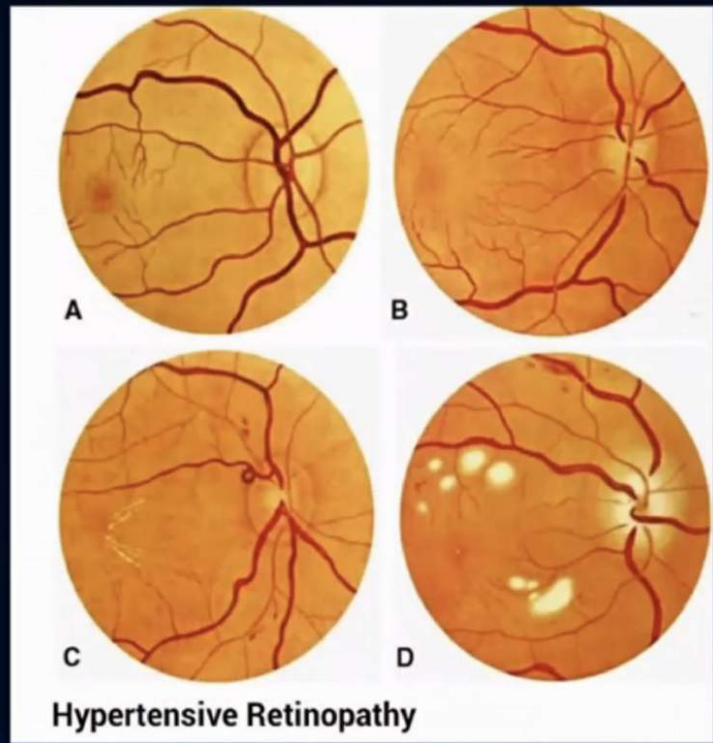
#### Nephropathy

- Albuminuria
- Proteinuria
- Chronic renal insufficiency
- Renal failure

# Diagnosis of Hypertension:



Grade	Classification
Grade I	Mild generalized retinal arteriolar narrowing or sclerosis
Grade II	Definite focal narrowing and arteriovenous crossings Moderate to marked sclerosis of the retinal arterioles Exaggerated arterial light reflex
Grade III	Retinal hemorrhages, exudates and cotton wool spots Sclerosis and spastic lesions of retinal arterioles
Grade IV	Severe grade III and papilledema



# Diagnosis of Hypertension:

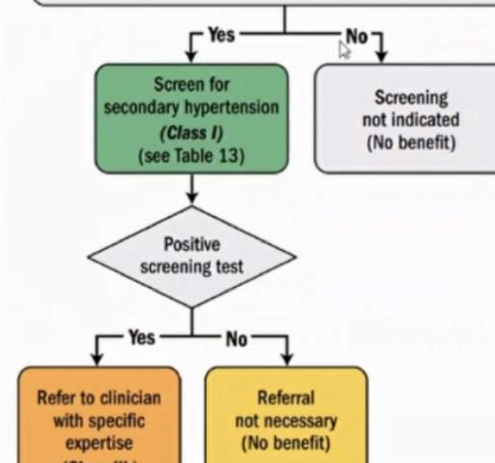
## Secondary Work up

### Screening for Secondary Hypertension

#### New Onset or Uncontrolled Hypertension in Adults

##### Conditions

- Drug-resistant/induced hypertension;
- Abrupt onset of hypertension;
- Onset of hypertension at <30 y;
- Exacerbation of previously controlled hypertension;
- Disproportionate TOD for degree of hypertension;
- Accelerated/malignant hypertension
- Onset of diastolic hypertension in older adults ( $\geq 65$  y)
- Unprovoked or excessive hypokalemia



K, et al.  
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# Secondary Hypertension

# Secondary Hypertension

Common causes
Renal parenchymal disease
Renovascular disease
Primary aldosteronism
Obstructive sleep apnea
Drug or alcohol induced
Uncommon causes
Pheochromocytoma/paraganglioma
Cushing's syndrome
Hypothyroidism
Hyperthyroidism
Aortic coarctation (undiagnosed or repaired)
Primary hyperparathyroidism
Congenital adrenal hyperplasia
Mineralocorticoid excess syndromes other than primary aldosteronism
Acromegaly

Whelton PK, et al. *Hypertension*. Nov. 2017.

# Secondary Hypertension

Whelton PK, et al. Hypertension. Nov. 2017.

	Prevalence	Clinical Indications	Physical Exam	Screening Tests	Additional/Confirmatory Tests
<b>Common Causes</b>					
Renal parenchymal disease	1%-2%	Urinary tract infections; obstruction, hematuria; urinary frequency and nocturia; analgesic abuse; family history of polycystic kidney disease; elevated serum creatinine; abnormal urinalysis	Abdominal mass (polycystic kidney disease); skin pallor	Renal ultrasound	Tests to evaluate cause of renal disease
Renovascular disease	5%-34%*	Resistant hypertension; hypertension of abrupt onset or worsening or increasingly difficult to control; flash pulmonary edema (atherosclerotic); early onset hypertension, especially in women (fibromuscular hyperplasia)	Abdominal systolic-diastolic bruit; bruits over other arteries (carotid - atherosclerotic or fibromuscular dysplasia), femoral	Renal Duplex Doppler ultrasound; MRA; abdominal CT	Bilateral selective renal intraarterial angiography
Primary aldosteronism	8%-20%†	Resistant hypertension; hypertension with hypokalemia (spontaneous or diuretic-induced); hypertension and muscle cramps or weakness; hypertension and incidentally discovered adrenal mass; hypertension and obstructive sleep apnea; hypertension and family history of early onset hypertension or stroke	Arrhythmias (with hypokalemia); especially atrial fibrillation	Plasma aldosterone/renin ratio under standardized conditions (correction of hypokalemia and withdrawal of aldosterone antagonists for 4-6 wk)	Oral sodium loading test (prior to 24 h urine aldosterone) or IV saline infusion test with plasma aldosterone at 4 h of infusion. Adrenal CT scan, Adrenal vein sampling, trial of mineralocorticoid receptor blockers‡
Obstructive sleep apnea‡	25%-50%	Resistant hypertension; snoring; fitful sleep; breathing pauses during sleep; daytime sleepiness	Obesity, Mallampati class III-IV; loss of normal nocturnal BP fall	Berlin Questionnaire (8); Epworth Sleepiness Score (9); overnight oximetry	Polysomnography
Drug- or alcohol-induced§	2%-4%	Sodium-containing antacids; caffeine; nicotine (smoking); alcohol; NSAIDs; oral contraceptives; cyclosporine or tacrolimus; sympathomimetics (decongestants, anorectics); cocaine, amphetamines and other illicit drugs; neuro psychiatric agents; erythropoiesis stimulating agents; clonidine withdrawal; herbal	Fine tremor, tachycardia, sweating (cocaine, ephedrine, MAO inhibitors); acute abdominal pain (cocaine)	Urinary drug screen (illicit drugs)	Response to withdrawal of suspected agent

# Secondary Hypertension

Whelton PK, et al. Hypertension. Nov. 2017.

	Prevalence	Clinical Indications	Physical Exam	Screening Tests	Additional/Confirmatory Tests
<b>Uncommon Causes</b>					
Pheochromocytoma/paraganglioma	0.1%-0.6%	Resistant hypertension; paroxysmal hypertension or crisis superimposed on sustained hypertension; "spells", BP lability, headache, sweating, palpitations, pallor; positive family history of pheochromocytoma/paraganglioma; adrenal incidentaloma	Skin stigmata of neurofibromatosis (café-au-lait spots; neurofibromas); orthostatic hypotension	24-h urinary fractionated metanephrines or plasma metanephrines under standard conditions (30' supine position with indwelling IV cannula)	CT or MRI scan of abdomen/pelvis
Cushing's syndrome	<0.1%	Rapid weight gain, especially with central distribution; proximal muscle weakness; depression; hyperglycemia	Central obesity, "moon" face, dorsal and supraclavicular fat pads, wide (1 cm) violaceous striae, hirsutism	Overnight 1 mg dexamethasone suppression test	24-h urinary free cortisol excretion (preferably multiple); midnight salivary cortisol
Hypothyroidism	<1%	Dry skin; cold intolerance; constipation; hoarseness; weight gain	Delayed ankle reflex; periorbital puffiness; coarse skin; cold skin; slow movement; goiter	Thyroid stimulating hormone; free thyroxine	None
Hyperthyroidism	<1%	Warm, moist skin; heat intolerance; nervousness; tremulousness; insomnia; weight loss; diarrhea; proximal muscle weakness	Lid lag; fine tremor of the outstretched hands; warm, moist skin	Thyroid stimulating hormone, free thyroxine	Radioactive iodine uptake and scan
Aortic coarctation (undiagnosed or repaired)	0.1%	Young patient with hypertension (<30 y of age)	BP higher in upper extremities compared to lower extremities; absent femoral pulses; continuous murmur over patient's back, chest, or abdominal bruit; left thoracotomy scar (postoperative)	Echocardiogram	Thoracic and abdominal CT or MRA
Primary hyperparathyroidism	Rare	Hypercalcemia	Usually none	Serum calcium	Serum parathyroid hormone

# Secondary Hypertension

	Prevalence	Clinical Indications	Physical Exam	Screening Tests	Additional/Confirmatory Tests
<b>Uncommon Causes</b> (continued from previous page)					
Congenital adrenal hyperplasia	Rare	Hypertension and hypokalemia; virilization (11-beta-hydroxylase deficiency [11-beta-OH]) incomplete masculinization in males and primary amenorrhea in females (17-alpha-hydroxylase deficiency [17-alpha-OH])	Signs of virilization (11-beta-OH) or incomplete masculinization (17-alpha-OH)	Hypertension and hypokalemia with low or normal aldosterone and renin	11-beta-OH: elevated deoxycorticosterone (DOC), 11-deoxycortisol and androgens 17-alpha-OH: decreased androgens and estrogen; elevated deoxycorticosterone and corticosterone
Mineralo-corticoid excess syndromes other than primary aldosteronism	Rare	Early onset hypertension; resistant hypertension; hypokalemia or hyperkalemia	Arrhythmias (with hypokalemia)	Low aldosterone and renin	Urinary cortisol metabolites; genetic testing
Acromegaly	Rare	Acral features, enlarging shoe, glove or hat size; headache, visual disturbances; diabetes mellitus	Acral features; large hands and feet; frontal bossing	Serum growth hormone $\geq 1$ ng/mL during oral glucose load	Elevated age- and sex-matched IGF-1 level; MRI scan of the pituitary

\* Depending on the clinical situation (hypertension alone, 5%; hypertension starting dialysis, 22%; hypertension and peripheral vascular disease, 28%; hypertension in the elderly with congestive heart failure, 34%).

† 8% in general population with hypertension; up to 20% in patients with resistant hypertension.

‡ Although obstructive sleep apnea is listed as a cause of secondary hypertension, RCTs on the effects of continuous positive airway pressure on lowering BP in patients with hypertension have produced mixed results

§ May treat patients with resistant hypertension with a MRA whether or not primary aldosteronism is present.



# Secondary Hypertension

Whelton PK, et al. Hypertension. Nov. 2017.


Agent	Possible Management Strategy
Alcohol	<ul style="list-style-type: none"> <li>Limit alcohol to <math>\leq 1</math> drink daily for women and <math>\leq 2</math> drinks for men</li> </ul>
Amphetamines (e.g., amphetamine, methylphenidate, dextroamphetamine)	<ul style="list-style-type: none"> <li>Discontinue or decrease dose</li> <li>Consider behavioral therapies for ADHD</li> </ul>
Antidepressants (e.g., MAOIs, SNRIs, TCAs)	<ul style="list-style-type: none"> <li>Consider alternative agents (e.g., SSRIs,) depending on indication</li> <li>Avoid tyramine containing foods with MAOIs</li> </ul>
Atypical antipsychotics (e.g., clozapine, olanzapine)	<ul style="list-style-type: none"> <li>Discontinue or limit use when possible</li> <li>Consider behavior therapy where appropriate</li> <li>Lifestyle modification (Section 6.2)</li> <li>Consider alternative agents associated with lower risk of weight gain, diabetes mellitus, and dyslipidemia (e.g., aripiprazole, ziprasidone).</li> </ul>
Caffeine	<ul style="list-style-type: none"> <li>Generally limit caffeine intake to <math>&lt;300</math> mg/d</li> <li>Avoid use in patients with uncontrolled hypertension</li> <li>Coffee use in patients with hypertension associated with acute increases in BP; long-term use not associated with increased BP or CVD</li> </ul>
Decongestants (e.g., phenylephrine, pseudoephedrine)	<ul style="list-style-type: none"> <li>Use for shortest duration possible and avoid in severe or uncontrolled hypertension</li> <li>Consider alternative therapies (e.g., nasal saline, intranasal corticosteroids, antihistamines) as appropriate</li> </ul>
Herbal supplements (e.g., Ma Huang [ephedra], St. John's wort [with MAO inhibitors, yohimbine])	<ul style="list-style-type: none"> <li>Avoid use</li> </ul>
Immunosuppressants (e.g., cyclosporine)	<ul style="list-style-type: none"> <li>Consider converting to tacrolimus, which may be associated with less effects on BP</li> </ul>
Oral contraceptives	<ul style="list-style-type: none"> <li>Use low-dose (e.g., 20-30 mcg ethinyl estradiol) agents or a progestin-only form of contraception and/or consider alternative forms of birth control where appropriate (e.g., barrier, abstinence, IUD)</li> <li>Avoid use in women with uncontrolled hypertension</li> </ul>
NSAIDs	<ul style="list-style-type: none"> <li>Avoid systemic NSAIDs when possible</li> <li>Consider alternative analgesics (e.g., acetaminophen, tramadol, topical NSAIDs,) depending on indication and risk</li> </ul>
Recreational drugs (e.g., "bath salts" [MDPV], cocaine, methamphetamine, etc.)	<ul style="list-style-type: none"> <li>Discontinue and/or avoid use</li> </ul>
Systemic corticosteroids (e.g., dexamethasone, fludrocortisone, methylprednisolone, prednisone, prednisolone)	<ul style="list-style-type: none"> <li>Avoid or limit use when possible</li> <li>Consider alternative modes of administration (e.g., inhaled, topical) when feasible</li> </ul>
Angiogenesis inhibitor (eg. bevacizumab) and tyrosine kinase inhibitors (eg. sunitinib, sorafenib)	<ul style="list-style-type: none"> <li>Initiate or intensify antihypertensive therapy</li> </ul>



# Management of Hypertension

# Management of Hypertension:

Know your Goal



## ACC/AHA Guidelines

BP Category	Systolic	Diastolic	10 yrs CVD Risk	Rx	Goal BP
Normal	< 120	<80		Lifestyle Modification	√
Elevated	120-129	<80		Non Pharm. Rx	√
Stage 1	130-139	80-89	<10%	Non Pharm. Rx	
			>10% T2DM CRI	+ BP Medications	< 130/80
Stage 2	>140	>90		+ BP Medications	< 130/80

# Management of Hypertension:

Know your Goal

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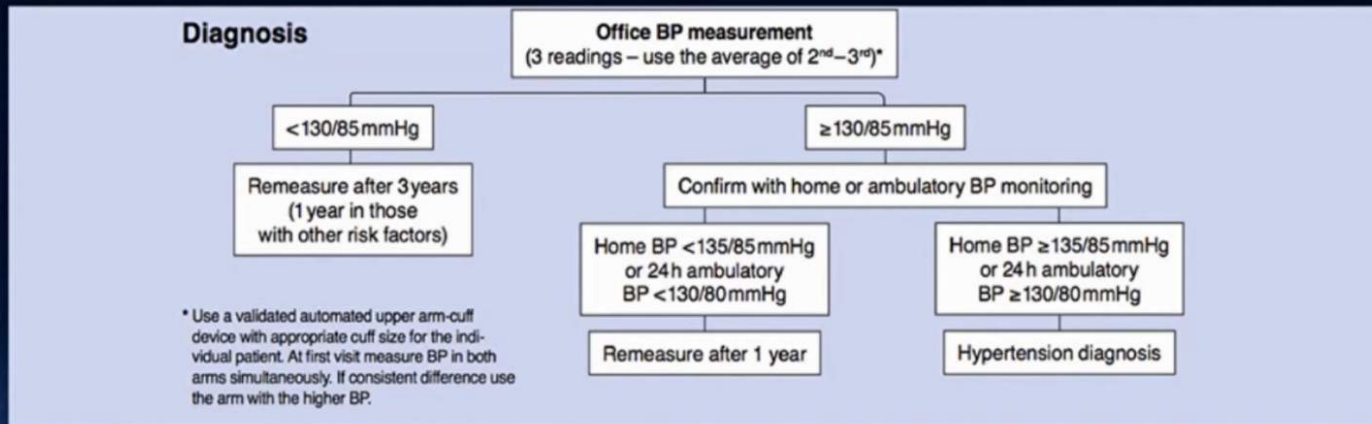


# Management of Hypertension:



# Management of Hypertension

## ISH 2020 Recommendations



# Management of Hypertension

## ISH 2020 Recommendations

### Evaluation

#### History & Physical Exam

- Exclude drug-induced hypertension
- Evaluate for organ damage
- Consider additional CV risk factors
- Assess total cardiovascular risk
- Search for symptoms/signs of secondary hypertension
- Check adherence

#### Lab Tests

- Serum sodium, potassium & creatinine, uric acid
- Lipid profile & glucose
- Urine dipstick
- 12 lead ECG

#### Additional Tests

- If necessary for suspected organ damage or secondary hypertension

# Management of Hypertension

## ISH 2020 Recommendations

### Treatment

#### Grade 1 Hypertension:

140–159/90–99 mmHg

1. Start lifestyle interventions
2. Start drug treatment:

- **Immediately:** In high-risk patients (CVD, CKD, diabetes or organ damage)

- **After 3–6 months of lifestyle intervention:** In low-moderate risk patients with persistent BP elevation

#### Grade 2 Hypertension:

≥160/100 mmHg

1. Start drug treatment immediately
2. Start lifestyle intervention

#### Lifestyle Interventions

- Stop smoking
- Regular exercise
- Lose weight
- Salt reduction
- Healthy diet and drinks
- Lower alcohol intake
- Lower stress
- Reduce exposure to air pollution

#### Drug Therapy Steps

Simplify regimen with once daily dosing and single pill combinations.  
Consider monotherapy in low-risk grade 1 hypertension and in patients aged >80 years or frail

#### Non-Black Patients

1. Low dose ACEI/ARB\* + DHP-CCB
2. Increase to full dose
3. Add thiazide-like diuretic
4. Add spironolactone or, if not tolerated or contraindicated, amiloride, doxazosin, eplerenone, clonidine or beta-blocker

#### Black Patients

1. Low dose ARB\* + DHP-CCB or DHP-CCB + thiazide-like diuretic
2. Increase to full dose
3. Add diuretic or ACEI/ARB
4. Add spironolactone or, if not tolerated or contraindicated, amiloride, doxazosin, eplerenone, clonidine or beta-blocker

\* No ACEI/ARB in women with or planning pregnancy



# Management of Hypertension

## ISH 2020 Recommendations

### Monitoring

#### Target

- BP <130/80 mmHg
- Individualise for elderly based on frailty

#### Monitor

- BP control (achieve target within 3 months)
- Adverse effects
- Long-term adherence

#### Referral

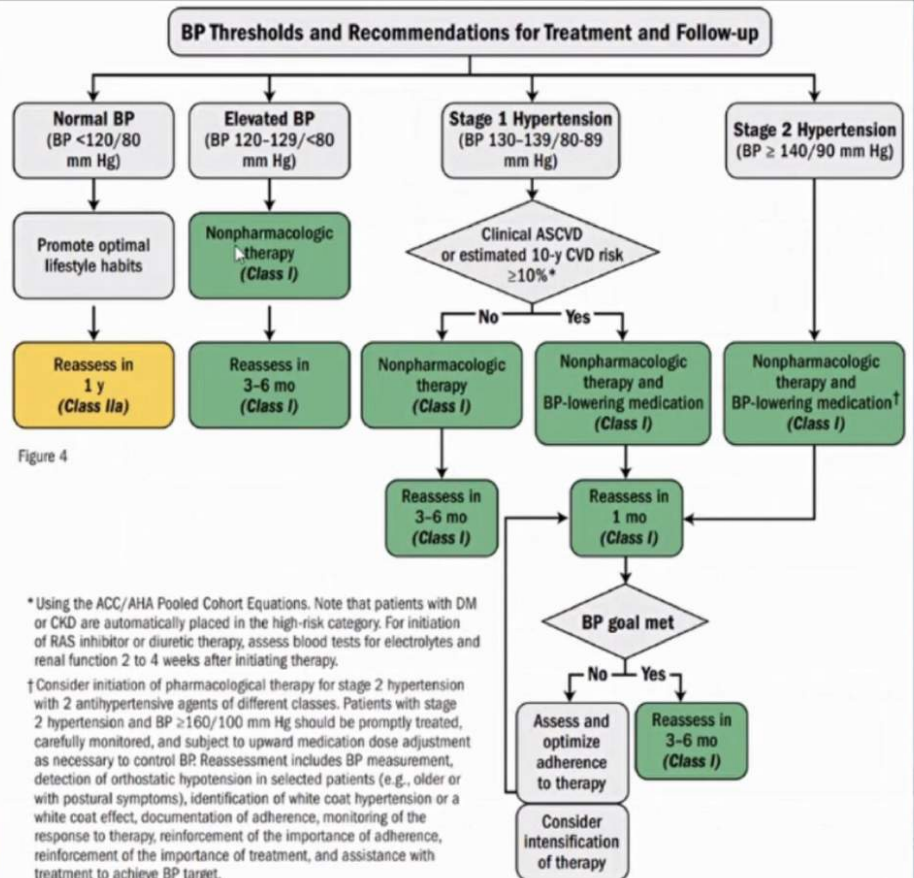
- If BP still uncontrolled, or other issue, refer to care provider with hypertension expertise

# Management of Hypertension

## Non Pharmacological Interventions

	Nonpharmacologic Intervention	Dose	Approximate Impact on SBP	
			Hypertension	Normotension
<b>Weight loss</b>	Weight/body fat	Ideal body weight is best goal but at least 1 kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1 kg reduction in body weight.	-5 mm Hg	-2/3 mm Hg
<b>Healthy diet</b>	DASH dietary pattern	Diet rich in fruits, vegetables, whole grains, and low-fat dairy products with reduced content of saturated and trans fat	-11 mm Hg	-3 mm Hg
<b>Reduced intake of dietary sodium</b>	Dietary sodium	<1,500 mg/d is optimal goal but at least 1,000 mg/d reduction in most adults	-5/6 mm Hg	-2/3 mm Hg
<b>Enhanced intake of dietary potassium</b>	Dietary potassium	3,500-5,000 mg/d, preferably by consumption of a diet rich in potassium	-4/5 mm Hg	-2 mm Hg
<b>Physical activity</b>	Aerobic	<ul style="list-style-type: none"> <li>• 120-150 min/wk</li> <li>• 65%-75% heart rate reserve</li> </ul>	-5/8 mm Hg	-2/4 mm Hg
	Dynamic Resistance	<ul style="list-style-type: none"> <li>• 90-150 min/wk</li> <li>• 50%-80% 1 rep maximum</li> <li>• 6 exercises, 3 sets/exercise, 10 repetitions/set</li> </ul>	-4 mm Hg	-2 mm Hg
	Isometric Resistance	<ul style="list-style-type: none"> <li>• 4 x 2 min (hand grip), 1 min rest between exercises, 30%-40% maximum voluntary contraction, 3 sessions/wk</li> <li>• 8-10 wk</li> </ul>	-5 mm Hg	-4 mm Hg
<b>Moderation in alcohol intake</b>	Alcohol consumption	In individuals who drink alcohol, reduce alcohol to: <ul style="list-style-type: none"> <li>• Men: ≤2 drinks daily</li> </ul>	-4 mm Hg	-3 mm Hg

# Management of Hypertension Pharmacological Interventions



## Management of Hypertension:

- Choice of Initial Medication:

- Thiazide diuretics
- CCBs
- ACE inhibitors or ARBs

- Use two 1<sup>st</sup> line agents in patients with:

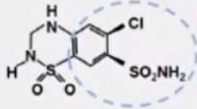
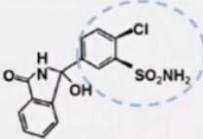
- Stage 2 hypertension
- Average BP >20/10 mm Hg above their BP target

# Anti-Hypertensive Medications

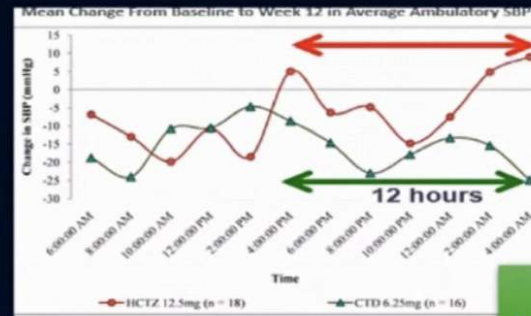
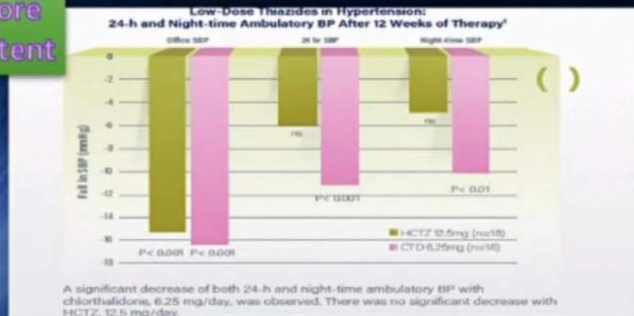
Class	Drug	Usual Dose, Range (mg per day)*	Daily Frequency	Comments
<b>Primary Agents</b>				
Thiazide or thiazide-type diuretics	<b>Chlorthalidone</b>	12.5-25	1	<ul style="list-style-type: none"> <li>• Chlorthalidone preferred based on prolonged half-life and proven trial reduction of CVD</li> <li>• Monitor for hyponatremia and hypokalemia, uric acid and calcium levels.</li> <li>• Use with caution in patients with history of acute gout unless patient is on uric acid-lowering therapy</li> </ul>
	<b>Hydrochlorothiazide</b>	25-50	1	
	<b>Indapamide</b>	1.25-2.5	1	
	<b>Metolazone</b>	2.5-10	1	
ACE Inhibitors	<b>Benazepril</b>	10-40	1 or 2	<ul style="list-style-type: none"> <li>• Do not use in combination with ARBs or direct renin inhibitor</li> <li>• Increased risk of hyperkalemia, especially in patients with CKD or in those on K<sup>+</sup> supplements or K<sup>+</sup>-sparing drugs.</li> <li>• May cause acute renal failure in patients with severe bilateral renal artery stenosis</li> <li>• Do not use if history of angioedema with ACE inhibitors.</li> <li>• Avoid in pregnancy</li> </ul>
	<b>Captopril</b>	12.5-150	2 or 3	
	<b>Enalapril</b>	5-40	1 or 2	
	<b>Fosinopril</b>	10-40	1	
	<b>Lisinopril</b>	10-40	1	
	<b>Moexipril</b>	7.5-30	1 or 2	
	<b>Perindopril</b>	4-16	1	
	<b>Quinapril</b>	10-80	1 or 2	
	<b>Ramipril</b>	2.5-10	1 or 2	
<b>Trandolapril</b>	1-4	1		
ARBs	<b>Azilsartan</b>	40-80	1	<ul style="list-style-type: none"> <li>• Do not use in combination with ACE inhibitors or direct renin inhibitor</li> <li>• Increased risk of hyperkalemia in CKD or in those on K<sup>+</sup> supplements or K<sup>+</sup>-sparing drugs</li> <li>• May cause acute renal failure in patients with severe bilateral renal artery stenosis</li> <li>• Do not use if history of angioedema with ARBs. Patients with a history of angioedema with an ACEI can receive an ARB beginning 6 weeks after ACEI discontinued.</li> <li>• Avoid in pregnancy</li> </ul>
	<b>Candesartan</b>	8-32	1	
	<b>Eprosartan</b>	600-800	1 or 2	
	<b>Irbesartan</b>	150-300	1	
	<b>Losartan</b>	50-100	1 or 2	
	<b>Oltmesartan</b>	20-40	1	
	<b>Telmisartan</b>	20-80	1	
	<b>Valsartan</b>	80-320	1	
CCB—dihydropyridines	<b>Amlodipine</b>	2.5-10	1	<ul style="list-style-type: none"> <li>• Avoid use in patients with HF/EF; amlodipine or felodipine may be used if required</li> <li>• Associated with dose-related pedal edema, which is more common in women than men</li> </ul>
	<b>Felodipine</b>	5-10	1	
	<b>Isradipine</b>	5-10	2	
	<b>Nicardipine SR</b>	5-20	1	
	<b>Nifedipine LA</b>	60-120	1	
	<b>Nisoldipine</b>	30-90	1	
CCB—non-dihydropyridines	<b>Diltiazem SR</b>	180-360	2	<ul style="list-style-type: none"> <li>• Avoid routine use with beta blockers due to increased risk of bradycardia and heart block</li> <li>• Do not use in patients with HF/EF</li> <li>• Drug interactions with diltiazem and verapamil (CYP3A4 major substrate and moderate inhibitor)</li> </ul>
	<b>Diltiazem ER</b>	120-480	1	
	<b>Verapamil IR</b>	40-80	3	
	<b>Verapamil SR</b>	120-480	1 or 2	
	<b>Verapamil-delayed onset ER (various)</b>	100-480	1 (in the evening)	

Table is continued in the next two pages

## Why Chlorthalidone (CLD) as Thiazide like diuretic?

Properties	Hydrochlorothiazide (HCTZ)	Chlorthalidone (CLD)
Classification	Benzothiadiazine (thiazide) diuretic	Thiazide-like diuretic
Chemical Structure*		
Half-Life	6-9 hours	40 hours
Inhibition of Carbonic Anhydrase		1-3 orders of magnitude stronger on several carbonic anhydrase isozymes

More Potent



More Consistent

Carter BL, et al. Hypertension. 2004;43:4-9.  
Kurtz TW. Hypertension. 2010;56:335-337.

# Anti-Hypertensive Medications

Class	Drug	Usual Dose, Range (mg per day)*	Daily Frequency	Comments
<b>Secondary Agents</b>				
Diuretics—loop	<b>Bumetanide</b>	0.5-4	2	<ul style="list-style-type: none"> <li>• Preferred diuretics in patients with symptomatic HE. Preferred over thiazides in patients with moderate-to-severe CKD (e.g., GFR &lt;30 mL/min)</li> </ul>
	<b>Furosemide</b>	20-80	2	
	<b>Torsemide</b>	5-10	1	
Diuretics—potassium sparing	<b>Amiloride</b>	5-10	1 or 2	<ul style="list-style-type: none"> <li>• Monotherapy agents minimally effective antihypertensives</li> <li>• Combination therapy of potassium sparing diuretic with a thiazide can be considered in patients with hypokalemia on thiazide monotherapy</li> <li>• Avoid in patients with significant CKD (e.g., GFR &lt;45 mL/min)</li> </ul>
	<b>Triamterene</b>	50-100	1 or 2	
Diuretics—aldosterone antagonists	<b>Eplerenone</b>	50-100	12	<ul style="list-style-type: none"> <li>• Preferred agents in primary aldosteronism and resistant hypertension</li> <li>• Spironolactone associated with greater risk of gynecomastia and impotence compared to eplerenone</li> <li>• Common add-on therapy in resistant hypertension</li> <li>• Avoid use with K<sup>+</sup> supplements, other K<sup>+</sup>-sparing diuretics or significant renal dysfunction</li> <li>• Eplerenone often requires twice daily dosing for adequate BP lowering</li> </ul>
	<b>Spironolactone</b>	25-100	1	
Beta blockers—cardioselective	<b>Atenolol</b>	25-100	12	<ul style="list-style-type: none"> <li>• Beta blockers are not recommended as first-line agents unless the patient has IHD or HF</li> <li>• Preferred in patients with bronchospastic airway disease requiring a beta blocker</li> <li>• Bisoprolol and metoprolol succinate preferred in patients with HFrEF</li> <li>• Avoid abrupt cessation</li> </ul>
	<b>Betaxolol</b>	5-20	1	
	<b>Bisoprolol</b>	2.5-10	1	
	<b>Metoprolol tartrate</b>	100-400	2	
	<b>Metoprolol succinate</b>	50-200	1	
Beta blockers—cardioselective and vasodilatory	<b>Nebivolol</b>	5-40	1	<ul style="list-style-type: none"> <li>• Induces nitric oxide-induced vasodilation</li> <li>• Avoid abrupt cessation</li> </ul>
Beta blockers—noncardioselective	<b>Nadolol</b>	40-120	1	<ul style="list-style-type: none"> <li>• Avoid in patients with reactive airways disease</li> <li>• Avoid abrupt cessation</li> </ul>
	<b>Propranolol IR</b>	160-480	2	
	<b>Propranolol LA</b>	80-320	1	
Beta blockers—intrinsic sympathomimetic activity	<b>Acebutolol</b>	200-800	2	<ul style="list-style-type: none"> <li>• Generally avoid, especially in patients with IHD or HF</li> <li>• Avoid abrupt cessation</li> </ul>
	<b>Carteolol</b>	2.5-10	1	
	<b>Penbutolol</b>	10-40	1	
	<b>Pindolol</b>	10-60	2	

Table is continued in the next page

# Anti-Hypertensive Medications

Class	Drug	Usual Dose, Range (mg per day)*	Daily Frequency	Comments
<b>Secondary Agents</b> (continued from previous page)				
Beta blockers—combined alpha- and beta-receptor	<b>Carvedilol</b>	12.5-50	2	<ul style="list-style-type: none"> <li>• Carvedilol preferred in patients with HF/EF</li> <li>• Avoid abrupt cessation</li> </ul>
	<b>Carvedilol phosphate</b>	20-80	1	
	<b>Labetalol</b>	200-800	2	
Direct renin inhibitor	<b>Aliskiren</b>	150-300	1	<ul style="list-style-type: none"> <li>• Do not use in combination with ACE inhibitors or ARBs</li> <li>• Aliskiren is very long acting</li> <li>• Increased risk of hyperkalemia in CKD or in those on K+ supplements or K+ sparing drugs</li> <li>• May cause acute renal failure in patients with severe bilateral renal artery stenosis</li> <li>• Avoid in pregnancy</li> </ul>
Alpha-1 blockers	<b>Doxazosin</b>	1-8	1	<ul style="list-style-type: none"> <li>• Associated with orthostatic hypotension, especially in older adults</li> <li>• May consider as second-line agent in patients with concomitant BPH</li> </ul>
	<b>Prazosin</b>	2-20	2 or 3	
	<b>Terazosin</b>	1-20	1 or 2	
Central alpha1-agonist and other centrally acting drugs	<b>Clonidine oral</b>	0.1-0.8	2	<ul style="list-style-type: none"> <li>• Generally reserved as last-line due to significant CNS adverse effects, especially in older adults</li> <li>• Avoid abrupt discontinuation of clonidine, which may induce hypertensive crisis; clonidine must be tapered to avoid rebound hypertension</li> </ul>
	<b>Clonidine patch</b>	0.1-0.3	1 weekly	
	<b>Methyldopa</b>	250-1000	2	
	<b>Guanfacine</b>	0.5-2	1	
Direct vasodilators	<b>Hydralazine</b>	250-200	2 or 3	<ul style="list-style-type: none"> <li>• Associated with sodium and water retention and reflex tachycardia; use with a diuretic and bet a blocker</li> <li>• Hydralazine associated with drug-induced lupus-like syndrome at higher doses</li> <li>• Minoxidil associated with hirsutism and requires a loop diuretic. Can induce pericardial effusion</li> </ul>
	<b>Minoxidil</b>	5-100	1-3	

\*Dosages may vary from those listed in the FDA approved labeling (available at <http://dailymed.nlm.nih.gov/dailymed/index.cfm>).

Adapted with permission from Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Preventing, Detecting, Evaluating, and Treating High Blood Pressure. The JAMA. 2003; 289: 2560-72.





# Hypertension & Co-Morbidities

# Hypertension & Co- morbidities

## Heart Failure with Reduced Ejection Fraction (HFrEF)

### Recommendations for Treatment of Hypertension in Patients with Heart Failure with Reduced Ejection Fraction (HFrEF)

Referenced studies that support recommendations are summarized in  
online Data Supplement 34

COR	LOE	Recommendations
I	C-EO	1. Adults with HFrEF and hypertension should be prescribed GDMT* titrated to attain a BP less than 130/80 mm Hg.
III: No Benefit	B-R	2. Nondihydropyridine CCBs are not recommended in the treatment of hypertension in adults with HFrEF.

# Hypertension & Co- morbidities

## Heart Failure with Preserved Ejection Fraction (HFpEF)

### Recommendations for Treatment of Hypertension in Patients with Heart Failure with Preserved Ejection Fraction (HFpEF)

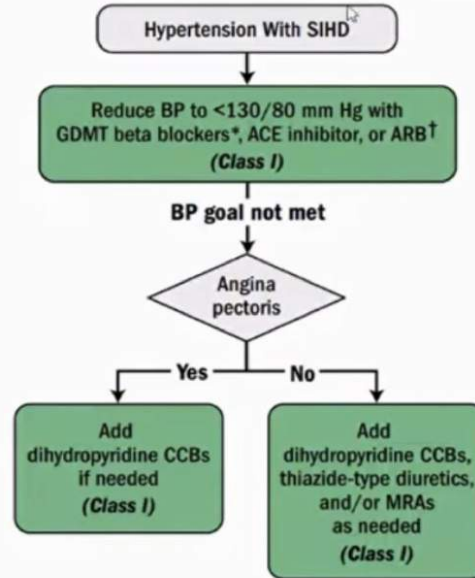
Referenced studies that support recommendations are summarized in  
online Data Supplement 35, 36

COR	LOE	Recommendations
I	C-EO	1. In adults with HFpEF who present with symptoms of volume overload, diuretics should be prescribed to control hypertension.
I	C-LD	2. Adults with HFpEF and persistent hypertension after management of volume overload should be prescribed ACE inhibitors or ARB and beta blockers titrated to attain systolic BP less than 130 mm Hg.

# Hypertension & Co-morbidities

Whelton PK, et al. Hypertension. Nov. 2017.

## Management of Hypertension in Patients with Stable Ischemic Heart Disease (SIHD)



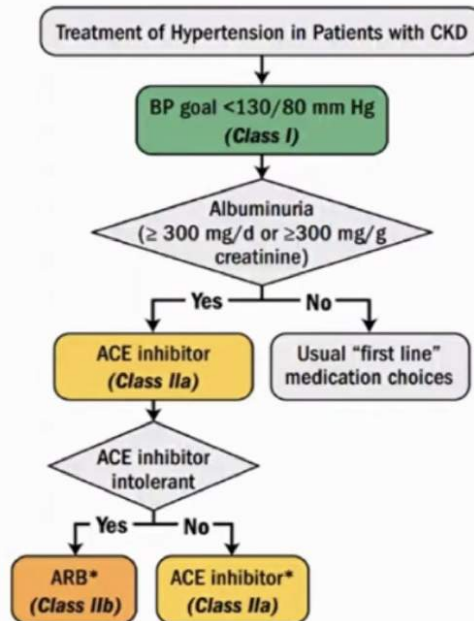
\* GDMT beta blockers for BP control or relief of angina include carvedilol, metoprolol tartrate, metoprolol succinate, nadolol, bisoprolol, propranolol, and timolol. Avoid beta blockers with intrinsic sympathomimetic activity. The beta blocker atenolol should not be used because it is less effective than placebo in reducing cardiovascular events.

† If needed for BP control.

# Hypertension & Co-morbidities

Whelton PK, et al. Hypertension. Nov. 2017.

## Management of Hypertension in Patients with Chronic Kidney Disease

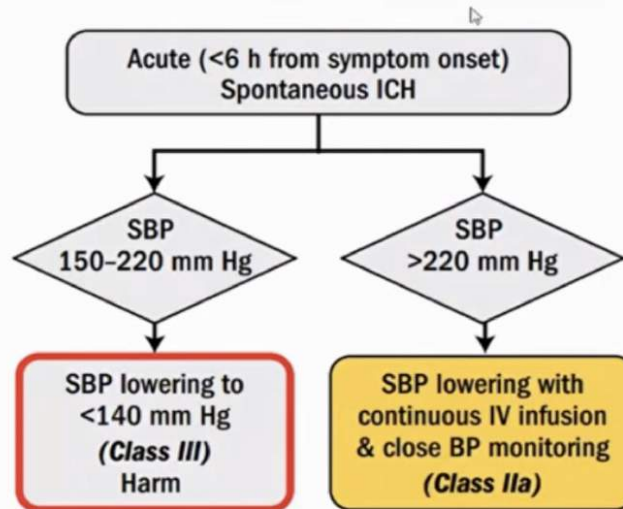


\*CKD stage 3 or higher or stage 1 or 2 with albuminuria ≥300 mg/d or ≥300 mg/g creatinine.



## Hypertension & Co-morbidities

### Management of Hypertension in Patients with Acute Intercerebral Hemorrhage



# Hypertension & Co-morbidities

## Management of Hypertension in Patients with Acute ischemic Stroke

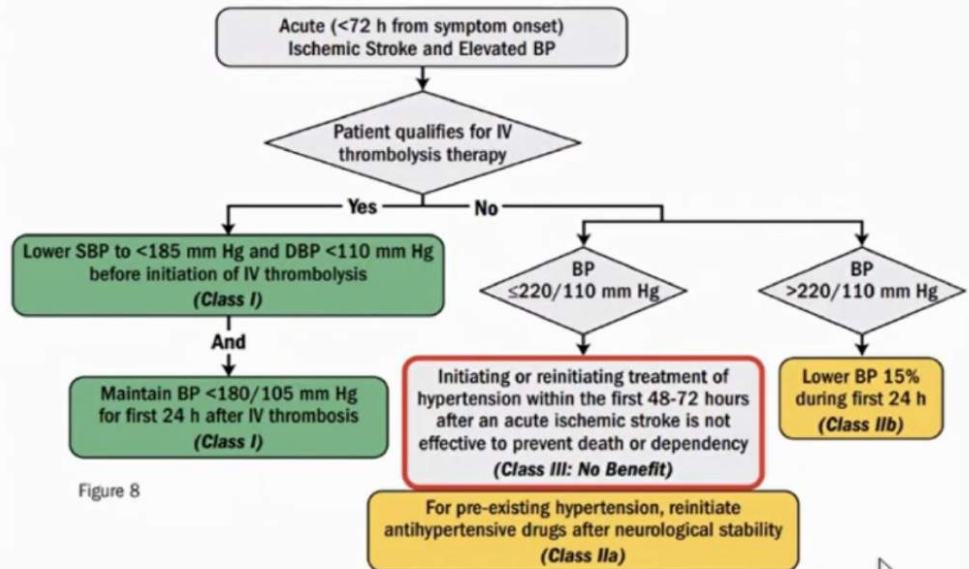
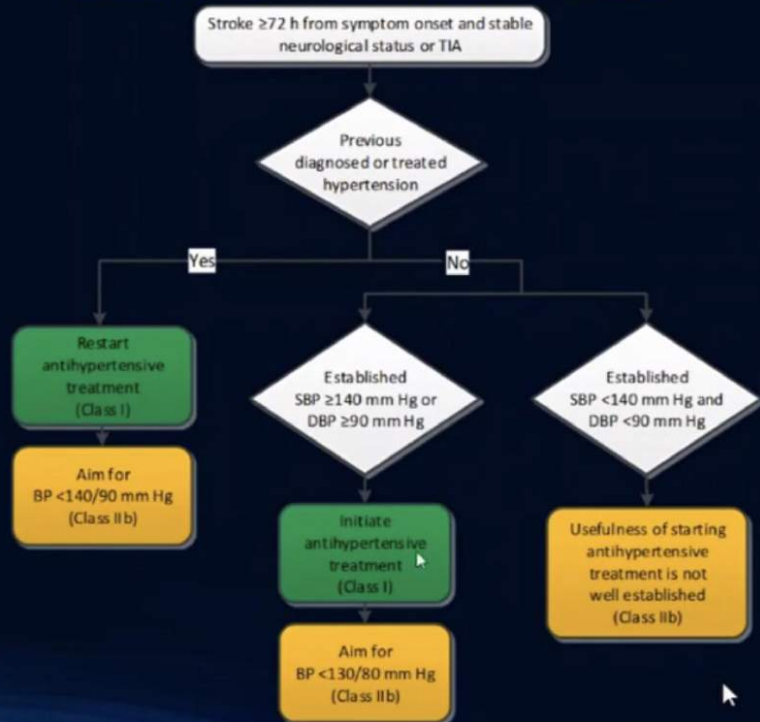


Figure 8

# Hypertension & Co-morbidities

Whelton PK, et al. Hypertension. Nov. 2017.

## MANAGEMENT OF HYPERTENSION IN PATIENTS WITH A PREVIOUS HISTORY OF STROKE (SECONDARY STROKE PREVENTION)





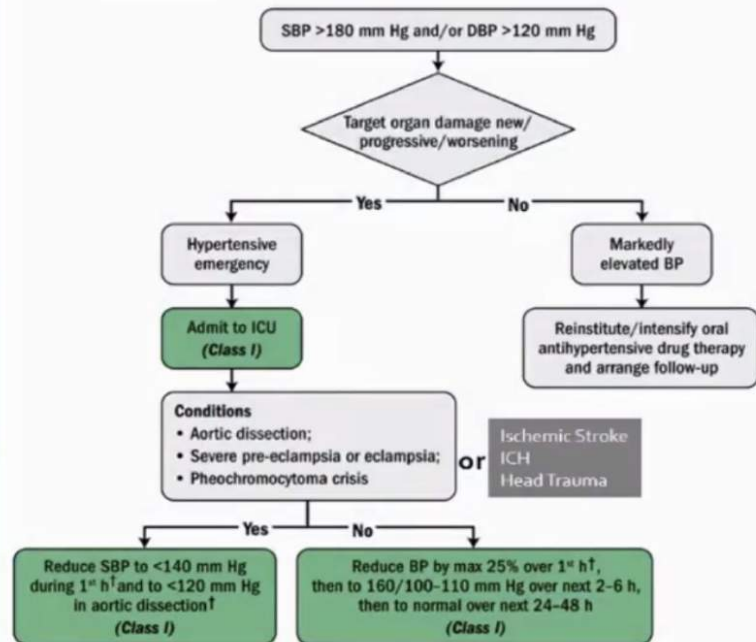
# Hypertension & Co- morbidities

- Diabetes Mellitus
  - All first-line classes of antihypertensive agents (i.e., diuretics, ACE inhibitors, ARBs, and CCBs) are useful and effective.
  - ACE inhibitors or ARBs may be considered in the presence of albuminuria
- Atrial Fibrillation
  - ARB can be useful for prevention of recurrence of AF
- Aortic Regurgitation
  - Avoid Bradycardia
- Aortic Disease
  - Beta blockers

# Hypertensive Crises

# Hypertensive Crises

## Diagnosis and Management of a Hypertensive Crisis



Use drug(s) specified in Table 19.

†If other comorbidities are present, select a drug specified in Table 20.

# Hypertensive Crises Medications

Agent	Drugs	Usual Dose Range	Comments
CCB-dihydropyridines	<b>Nicardipine</b>	Initial 5 mg/h, increasing every 5 min by 2.5 mg/h to maximum 15 mg/h.	Contraindicated in advanced aortic stenosis; no dose adjustment needed for elderly.
	<b>Clevidipine</b>	Initial 1-2 mg/h, doubling every 90 s until BP approaches target, then increasing by < double every 5-10 min; maximum dose 32 mg/h; maximum duration 72 h.	Contraindicated in pts with soybean, soy product, egg, and egg product allergy and in pts with defective lipid metabolism (e.g., pathological hyperlipidemia, lipid nephrosis or acute pancreatitis). Use low-end dose range for elderly pts.
Vasodilators-mitric oxide dependent	<b>Sodium nitroprusside</b>	Initial 0.3-0.5 mcg/kg/min; increase in increments of 0.5 mcg/kg/min to achieve BP target; maximum dose 10 mcg/kg/min; duration of treatment as short as possible. For infusion rates $\geq 4-10$ mcg/kg/min or duration $>30$ min, thiosulfate can be coadministered to prevent cyanide toxicity.	Intra-arterial BP monitoring recommended to prevent "overshoot". Lower dosing adjustment required for elderly. Tachyphylaxis common with extended use. Cyanide toxicity with prolonged use can result in irreversible neurologic changes and cardiac arrest.
	<b>Nitroglycerin</b>	Initial 5 mcg/min; increase in increments of 5 mcg/min every 3-5 min to a maximum of 20 mcg/min.	Use only in pts with acute coronary syndrome and/or acute pulmonary edema. Do not use in volume-depleted pts.
Vasodilators-direct	<b>Hydralazine</b>	Initial 10 mg via slow IV infusion (maximum initial dose 20 mg); repeat every 4-6 h as needed.	BP begins to decrease within 10-30 min and the fall lasts 2-4 h. Unpredictability of response and prolonged duration of action do not make hydralazine a desirable first-line agent for acute treatment in most pts.
Adrenergic blockers beta1 receptor selective antagonist	<b>Esmolol</b>	Loading dose 500-1,000 mcg/kg/min over 1 min followed by a 50 mcg/kg/min infusion. For additional dosing, the bolus dose is repeated and the infusion increased in 50 mcg/kg/min increments as needed to a maximum of 200 mcg/kg/min.	Contraindicated in pts with concurrent beta-blocker therapy, bradycardia and/or decompensated HF. Monitor for bradycardia. May worsen HF. Higher doses may block beta2 receptors and impact lung function in reactive airway disease.

Agent	Drugs	Usual Dose Range	Comments
Adrenergic blockers-combined alpha1 and nonselective beta receptor antagonist	<b>Labetalol</b>	Initial 0.3-1.0 mg/kg dose (maximum 20 mg) slow IV injection every 10 min or 0.4-1.0 mg/kg/h IV infusion up to 3 mg/kg/h. Adjust rate up to total cumulative dose of 300 mg. This dose can be repeated every 4-6 h.	Contraindicated in reactive airways disease or chronic obstructive pulmonary disease. Especially useful in hyperadrenergic syndromes. May worsen HF and should not be given in pts with 2nd or 3rd degree heart block or bradycardia.
Adrenergic blockers-non-selective alpha receptor antagonist	<b>Phentolamine</b>	IV bolus dose 5 mg. Additional bolus doses every 10 min as needed to lower BP to target.	Used in hypertensive emergencies induced by catecholamine excess (pheochromocytoma, interactions between monoamine oxidase inhibitors and other drugs or food, cocaine toxicity, amphetamine overdose or clonidine withdrawal).
Dopamine1-receptor selective agonist	<b>Fenoldopam</b>	Initial 0.1-0.3 mcg/kg/min; may be increased in increments of 0.05-0.1 mcg/kg/min every 15 min until target BP is reached. Maximum infusion rate 1.6 mcg/kg/min.	Contraindicated in pts at risk for increased intraocular pressure (glaucoma) or intracranial pressure and those with sulfite allergy.
Angiotensin converting enzyme inhibitor	<b>Enalaprilat</b>	Initial 1.25 mg over a 5 min period. Doses can be increased up to 5 mg every 6 h as needed to achieve BP target.	Contraindicated in pregnancy and should not be used in acute MI or bilateral renal artery stenosis. Mainly useful in hypertensive emergencies associated with high plasma renin activity. Dose not easily adjusted. Relatively slow onset of action (15 min) and unpredictability of BP response.

The background of the slide is a dark blue gradient with a subtle, abstract pattern of curved lines and a grid-like structure, creating a sense of depth and movement. The text is centered in the lower half of the slide.

# Resistant Hypertension

## Definitions

- Uncontrolled HTN
- Resistant HTN
- Refractory HTN
- Apparent Resistant HTN
- True Resistant HTN
- Pseudo-Resistant HTN

## Definitions

- Uncontrolled Hypertension:
- BP not meeting goal BP

## Definitions

- Resistant Hypertension:
- Blood pressure that remains above goal in spite of concurrent use of three antihypertensive agents of different classes
- If tolerated, one of the three agents should be a diuretic
- All agents should be prescribed at optimal doses
  - 50 % or more of the maximum recommended antihypertensive dose
- Resistant hypertension may be in both systolic and diastolic but *isolated systolic hypertension is common*



## Definitions

- Refractory Hypertension:
- ***Resistant hypertension*** that cannot be controlled, even with ***maximal*** medical therapy with  **$\geq 4$  drugs** with complementary mechanisms given at maximal level under the ***care of a hypertension specialist***.
- Refractory hypertension patients also have significantly higher heart rates despite more beta blocker use
- Diminished responses to spironolactone therapy
- Treatment failure may be due to neurologic mechanisms (? sympathetic overactivity)

## Definitions

- Apparent Resistant Hypertension:
- Uncontrolled BP despite being prescribed  $\geq 3$  HTN meds
- Controlled BP on  $\geq 4$  HTN meds
  
- This could be:
  - True Resistant Hypertension
  - Pseudo-Resistant Hypertension

## Definitions

- True Resistant Hypertension:
- Uncontrolled BP despite
  - Being **compliant** with an antihypertensive regimen
  - Regimen includes three or more drugs including a diuretic and each at optimal doses
  - Uncontrolled blood pressure confirmed by 24-hour ambulatory blood pressure monitoring

## Definitions

- Pseudo-Resistant Hypertension:
- Uncontrolled hypertension that appears resistant but is actually attributable to other factors
  
- 5 most common causes:
  - Inaccurate measurement of blood pressure
  - Poor adherence to antihypertensive therapy
  - Suboptimal antihypertensive therapy
    - Diuretic and two or more additional drugs each at 50 percent or more of the maximal recommended antihypertensive dose
  - Poor adherence to lifestyle and dietary approaches to lower blood pressure such as a reduced sodium intake
  - White coat hypertension

# Definitions

- White Coat Hypertension:
  - AKA: Isolated clinic or office hypertension
  - **Office** readings that averages to be uncontrolled and **reliable out-of-office** readings that averages to be controlled.
  
- Prevalence:
  - 20-30% of patients
  - 37-44% in Apparent Resistant HTN patients
  
- Tend to have less severe target organ damage and appear to be at less CV Risk
  
- Having the BP in the office taken by a nurse or technician, rather than the clinician, may minimize the white coat effect

# Epidemiology

- Prevalence:
  - 8.9% among Hypertensive patients
  - Number of resistant HTN is increasing. Possible reasons include:
    - Increases in the average age
    - Increases in the average weight

# Risk Factors

## PATIENT RELATED

- Higher baseline BP (particularly systolic)
- Presence of LVH
- Older age
- Obesity
- African-American race
- Chronic kidney disease
- Diabetes

## POTENTIALLY REVERSIBLE

- Suboptimal therapy
- Lifestyle and diet
- Medications
- Extracellular volume expansion
- Secondary causes of hypertension
- OSA

# Risk Factors

- Suboptimal therapy
- Lifestyle and diet
  - Obesity
  - High-salt diet
  - Physical inactivity
  - Heavy alcohol intake
- Extracellular volume expansion
  - Renal insufficiency
  - Sodium retention due to therapy with vasodilators
  - Ingestion of a high-salt diet (which can be assessed by measuring sodium excretion in a 24-hour urine collection)



# Risk Factors

- Medications

- Can raise BP or reduce the response to antihypertensive drugs
- Most commonly implicated agents are:
  - NSAIDs
    - NSAIDs can interfere with the antihypertensive effect of virtually any agent, except calcium channel blockers
  - Sympathomimetics
    - Diet pills
    - Decongestants
    - Amphetamine-like stimulants
    - Cocaine
  - Alcohol
  - Glucocorticoids
  - Estrogen-containing contraceptives
  - Erythropoietin
  - Herbal preparations (ephedra or ma huang)
  - Natural Licorice
  - Calcineurin inhibitors (cyclosporine and tacrolimus)
  - Antidepressants

# Risk Factors

- Secondary causes of hypertension
  - Should be considered in all patients with resistant HTN
  - More common:
    - Primary aldosteronism
    - Renal artery stenosis
    - Chronic kidney disease
    - Obstructive sleep apnea
  - Less common:
    - Pheochromocytoma
    - Cushing's syndrome
    - Hyperparathyroidism
    - Aortic coarctation

# Risk Factors

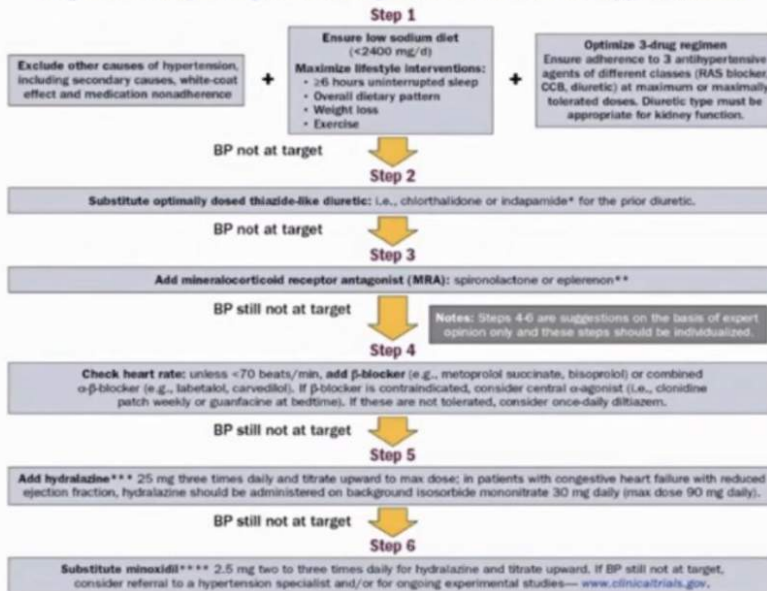
- Primary Aldosteronism
  - 10-20% of patients with resistant hypertension
  - Unexplained hypokalemia is the major clue (>50% of patients with proven primary hyperaldosteronism are normokalemic)
- Renal Artery Stenosis
  - common cause
  - 2 forms:
    - Atherosclerotic disease
    - Fibromuscular dysplasia
- Chronic kidney disease
  - As renal function declines, there is an increasing need for additional antihypertensive medications
  - Diuretics play a central role
  - "Dry weight" defined as the weight at which further fluid loss leads to either symptoms (fatigue, orthostatic hypotension) or decreased tissue perfusion as evidenced by an otherwise unexplained elevation in the blood urea nitrogen and/or serum creatinine concentration

# Risk Factors

- Obstructive sleep apnea
  - Severity of sleep apnea correlates with the severity of hypertension
  - Screen for OSA in Resistant HTN with following risk factors:
    - Obesity
    - Loud snoring
    - Daytime sleepiness
  - Treatment of OSA with positive airway pressure provides a usually modest antihypertensive benefit among patients with hypertension.

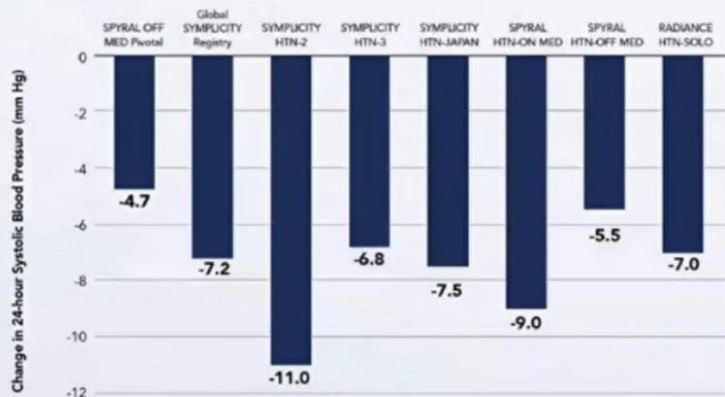
# Management of Resistant Hypertension

## Algorithm Depicting the Management of Resistant Hypertension



# Renal Denervation

Blood pressure reductions (mm Hg) among patients treated with renal denervation in randomized trials and the Global SYMPPLICITY Registry.



Note: Global SYMPPLICITY Registry, SYMPPLICITY HTN-2, 3 and JAPAN trials involve treatment with SYMPPLICITY Flex catheter (Medtronic CardioVascular, Santa Rosa, CA); SPYRAL ON and OFF MED and SPYRAL OFF-MED Pivotal Trial, SYMPPLICITY Spyrax catheter (Medtronic CardioVascular); RADIANCE HTN-SOLO, Paradise RDN system (ReCor Medical, Palo Alto, CA).

## Renal Denervation



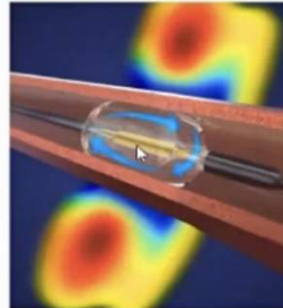
**RADIANCE HTN  
TRIO**

# Renal Denervation

## RADIANCE HTN TRIO

- Ring of ablative energy (depth of 1-6 mm) to interrupt renal nerve traffic
- Arterial wall protected by water circulating through balloon
- 2-3 sonications lasting 7 seconds each are delivered to each main renal artery

**Thermal Profile**  
Ultrasonic Heating + Water Cooling



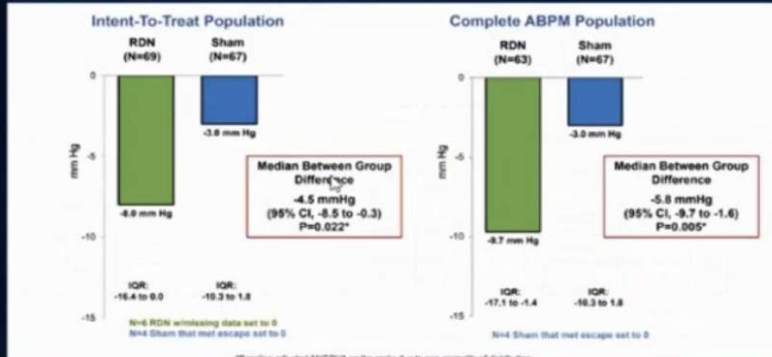
Source: ACC.21 Presentation Slides for RADIANCE-HTN TRIO: Endovascular Ultrasound Renal Denervation to Treat



# Renal Denervation

## RADIANCE HTN TRIO

Primary Efficacy Endpoint:  
Change in Daytime Ambulatory SBP at 2 Months



Source: ACC.21 Presentation Slides for RADIANCE-HTN TRIO: Endovascular Ultrasound Renal Denervation to Treat

**Thank You**