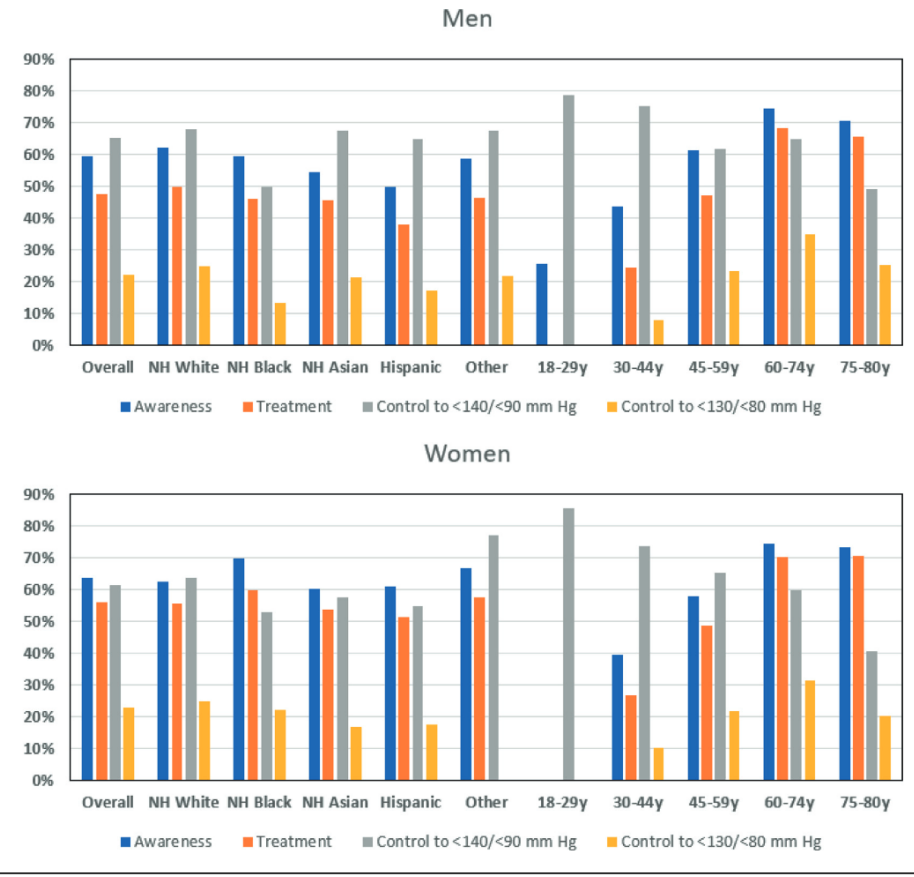
Hypertension

Amir Kazerouninia, MD PhD

How are we doing?

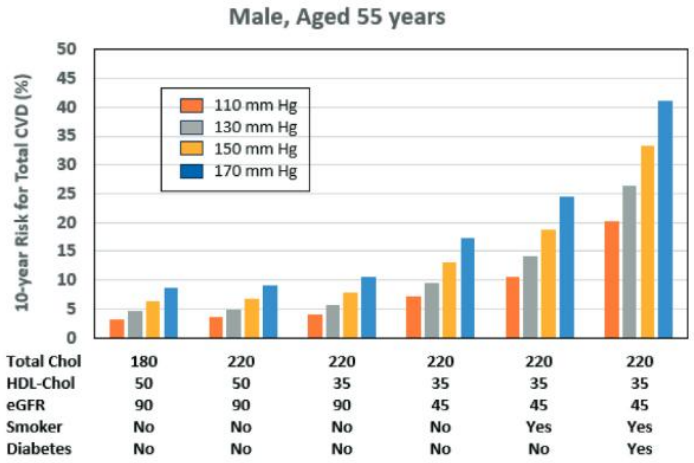
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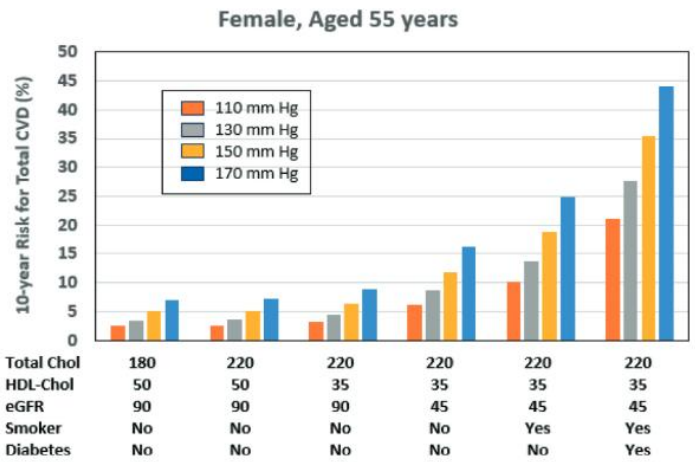
FIGURE 1 Rates of Awareness, Treatment, and Control of Hypertension Among U.S. Adults Aged 18 to 80 Years, 2017 to 2020*



Who cares?

FIGURE 2 Estimated 10-Year Risks for Total Cardiovascular Disease Using the PREVENT™ CVD Risk Equations, Stratified by Blood Pressure Levels With Selected Combinations of Risk Factors





CVD indicates cardiovascular disease; eGFR, estimated glomerular filtration rate; and HDL, high-density lipoprotein. Derived from Khan et al[19,20] via PREVENT.

What about secondary causes of hypertension?

TABLE 10 Causes of Secondary Hypertension With Indications for Additional Testing and Diagnostic Screening Tests

	Prevalence	Indications for Additional Testing	Physical Examination Findings	Screening Tests	Confirmatory Tests
Common causes					
OSA[5-7]	25%-50%	Snoring, choking, gasping during sleep; daytime sleepiness; resistant hypertension	Obesity, large neck size (eg, >17 inches [men]; >16 inches [women], Mallampati class 3-4; loss of normal nocturnal BP fall	STOP-Bang Questionnaire[15]; Berlin Questionnaire[16]; overnight oximetry	Referral for polysomnography or home sleep apnea testing if no suspicion of nonrespiratory sleep disorders (eg, narcolepsy)
CKD[17,18]	14%	Diabetes, obstruction, hematuria; urinary frequency and nocturia; urinary incontinence, analgesic abuse; family history of polycystic kidney disease; elevated serum creatinine; abnormal urinalysis	Abdominal mass or large palpable kidneys (polycystic kidney disease); skin pallor	Electrolytes, including sodium, potassium, chloride, and bicarbonate, serum creatinine, urinalysis, urine microalbumin, serum cystatin C, renal ultrasound	Tests to evaluate cause of CKD
Primary aldosteronism[1-3,9,19]	5%-25%	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 AF	Electrolytes, including sodium and potassium, plasma aldosterone/renin activity ratio (correction of hypokalemia and withdrawal of MRA for 4-6 wks)	Oral sodium loading test (with 24-h urine aldosterone) or IV saline infusion test with plasma aldosterone at 4 h of infusion or captopril suppression test (in patients not on ACEi or ARB treatment), adrenal CT scan, adrenal vein sampling

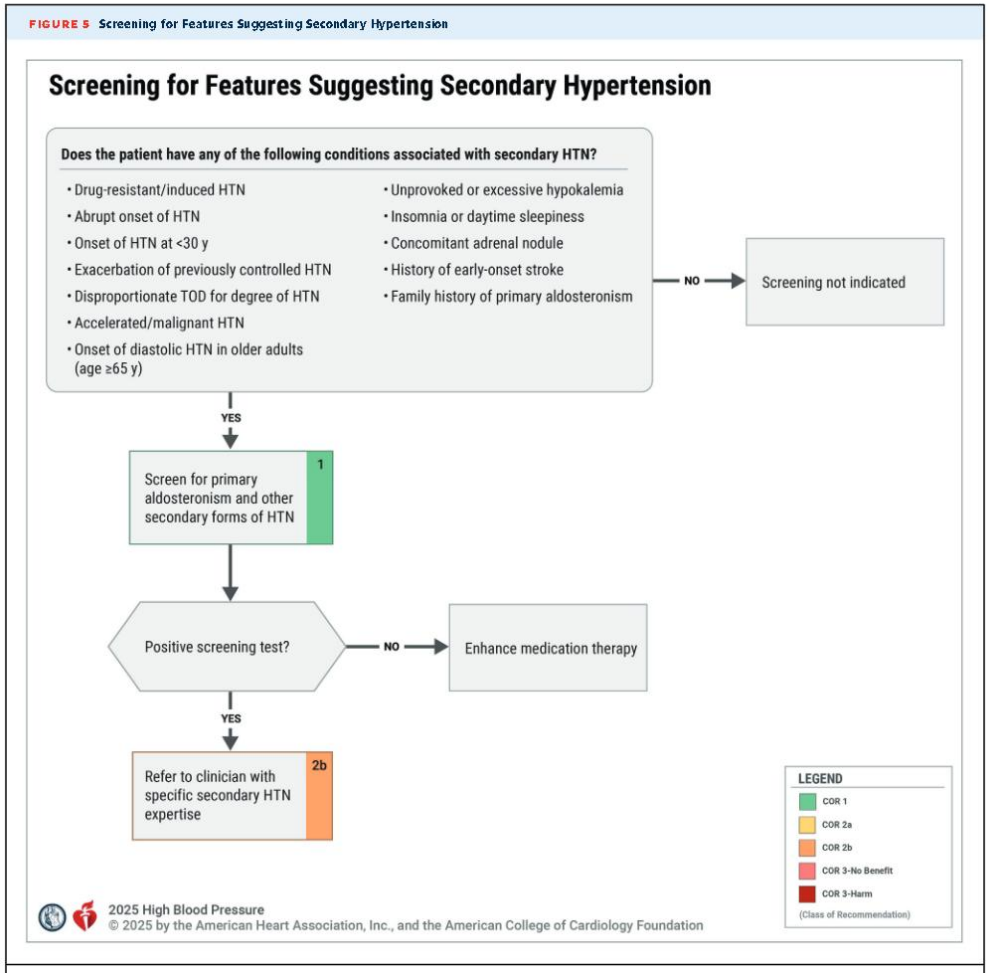
But my patient has a pheo!

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TABLE 10 Continued

	Prevalence	Indications for Additional Testing	Physical Examination Findings	Screening Tests	Confirmatory Tests
Pheochromocytoma/paraganglioma[21,22]	<0.6%	Resistant hypertension; paroxysmal hypertension or crisis superimposed on sustained hypertension; "spells," BP lability, headache, sweating, palpitations, piloerection; 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 (supine position with indwelling IV cannula)	CT or MRI scan of abdomen/pelvis, Ga-DOTATATE PET/CT scan

Screening for secondary hypertension



Lifestyle modifications

- Weight loss of at least 5% of body weight
- DASH eating plan
- Sodium reduction (<1,500 mg/day)
- Alcohol abstinence (< 1 drink/day for women, <2 drinks/day for men)
- Structured exercise program

Impacts of lifestyle modification

TABLE 12 Lifestyle and Stress Reduction Interventions to Lower Blood Pressure

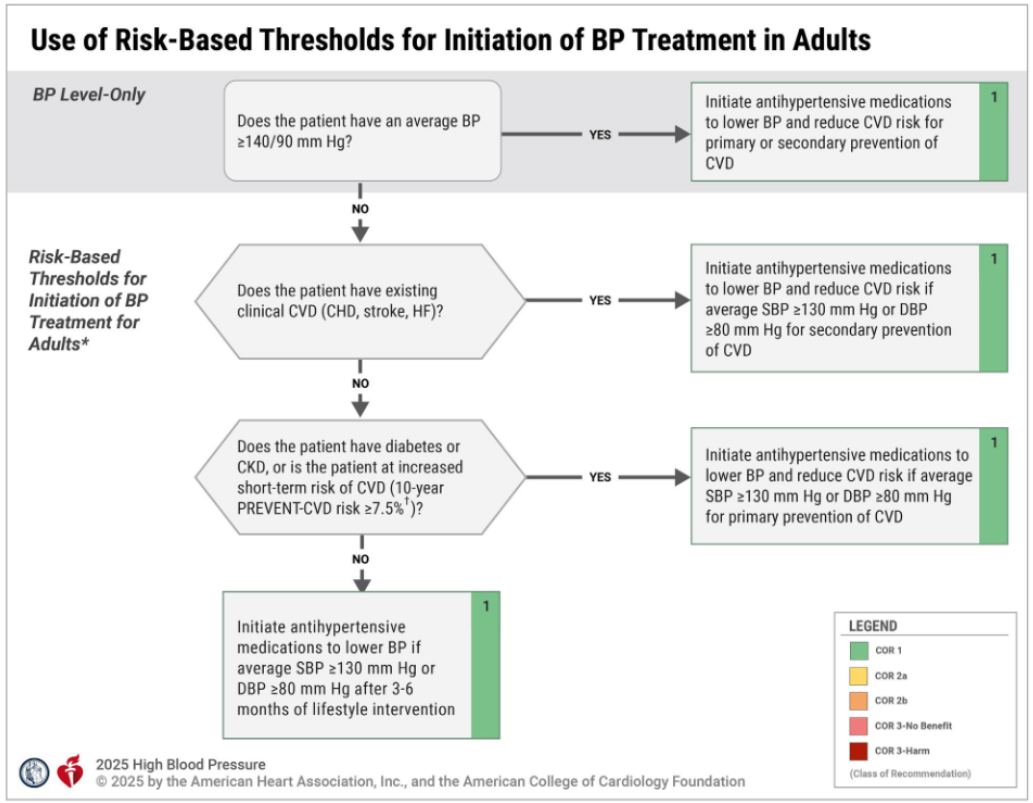
Intervention	Target/Biomarker	Evidence-Based Goals	Approximate Mean Change in SBP (mm Hg)*		References
			With Hypertension	Without Hypertension	
Weight loss	Body weight or BMI	Aim for sustained >5% reduction in body weight or >3 kg/m^2 reduction in BMI; expect about 1 mm Hg reduction for every 1-kg reduction in body weight	6 to 8	3 to 5	2,6,14,52
Heart-healthy diet	DASH eating pattern	Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat	5 to 8	3 to 7	13-15,64,120
Reduced intake of sodium	Dietary sodium intake; 24-h urinary sodium	Optimal goal is <2,300 mg/d, but aim for an ideal limit of <1,500 mg/d	6 to 8	1 to 4	16-18,79,120,121
Use of salt substitute	Replace cooking/table salt (100% sodium chloride) with salt substitute (25%-30% potassium chloride, 65%-75% sodium chloride, and 0%-10% flavoring agents); 24-h urinary sodium and potassium	Reduce dietary sodium intake as above	5 to 7	5	20-22,93
Enhanced intake of potassium	Dietary potassium intake; 24-h urinary potassium	Aim for 3,500-5,000 mg/d, ideally by consumption of a diet rich in potassium; or alternative use of moderate-dose pharmacological potassium supplementation (<80 mmol)	6	3 to 6	25-27
Reduced alcohol intake	Alcohol consumption	Optimal goal is abstinence for all adults for best health outcomes; in patients who consume alcohol, aim for >50% reduction in daily intake to no more than 2 drinks/d in men or 1 drink/d in women	4 to 6	3	29
Exercise	Aerobic exercise	90-150 min/wk 65%-75% heart rate reserve	4 to 8	2 to 7	14,33,36,120,122
	Dynamic resistance	90-150 min/wk 50%-80% 1 rep maximum 6 exercises, 3 sets/exercise, 10 repetitions/set	2 to 7	2 to 5	33,36,106,107
	Isometric resistance	4 × 2 min (hand grip), 1 min rest between exercises, 30%-40% maximum voluntary contraction, 3 sessions/wk	5 to 10	4 to 6	14,32,33,36,109,110
Meditation	Transcendental meditation	Training by a professional, followed by 2 × 20 min sessions/d while seated comfortably with eyes closed	5 to 7	5	14,119
Breathing control	Slowing respiration	Device-guided session to decrease respiration to <10 breaths/min for 15 min/d	5	5	14

*Because inclusion/exclusion criteria and comparator groups vary across interventions, these values should not be compared directly to indicate comparative effectiveness. Modified with permission from Whelton et al.[123] Copyright 2018 American College of Cardiology Foundation and American Heart Association, Inc.

BMI indicates body mass index; DASH, Dietary Approaches to Stop Hypertension; and SBP, systolic blood pressure.

How to start:

FIGURE 6 Use of Risk-Based Thresholds for Initiation of BP Treatment in Adults



*In older adults who may be frail or have a limited life expectancy, a clinician-patient assessment of potential benefits and harms of BP lowering should be pursued to align care with patient goals. †Increased short-term or 10-year risk is defined as a 10-year predicted risk for CVD events of ≥7.5% using PREVENT. BP indicates blood pressure; CHD, coronary heart disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; HF, heart failure; PREVENT, Predicting Risk of cardiovascular EVENTs; and SBP, systolic blood pressure.

What are the first line medications?

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TABLE 13 FDA-Approved Drugs for Treatment of Hypertension

Class	Drug	Usual Dose, Range (mg/d)*	Daily Frequency	Comments
Agents recommended for initial therapy				
Thiazide-type diuretics	Chlorthalidone	12.5-25	1	Chlorthalidone has a longer half-life and is more potent than hydrochlorothiazide on a mg-to-mg basis. Monitor for hyponatremia and hypokalemia, increased glucose, uric acid, and calcium levels. Monitor patients with history of acute gout unless patient is on uric acid-lowering therapy.
	Hydrochlorothiazide	25-50	1	
	Indapamide	1.25-2.5	1	
ACEi	Benazepril	10-40	1 or 2	Do not use in combination with ARB or direct renin inhibitor. There is an increased risk of hyperkalemia, especially in patients with CKD or in those on K+ supplements or K+-sparing drugs. There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis. Do not use if patient has history of angioedema with ACEi. Avoid use in pregnancy.
	Captopril	12.5-150	2 or 3	
	Enalapril	5-40	1 or 2	
	Fosinopril	10-40	1	
	Lisinopril	10-40	1	
	Moexipril	7.5-30	1 or 2	
	Perindopril	4-16	1	
	Quinapril	10-80	1 or 2	
	Ramipril	2.5-20	1 or 2	
	Trandolapril	1-4	1	
ARBs	Azilsartan	40-80	1	Do not use in combination with ACEi or direct renin inhibitor. There is an increased risk of hyperkalemia in CKD or in those on K+ supplements or K+-sparing drugs. There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis. Do not use if patient has history of angioedema with ARBs. Patients with a history of angioedema with an ACE inhibitor can receive an ARB beginning 6 weeks after ACE inhibitor is discontinued. Avoid use in pregnancy.
	Candesartan	8-32	1	
	Eprosartan	600-800	1 or 2	
	Irbesartan	150-300	1	
	Losartan	50-100	1 or 2	
	Olmesartan	20-40	1	
	Telmisartan	20-80	1	
	Valsartan	80-320	1	
CCB—dihydropyridines	Amlodipine	2.5-10	1	Associated with dose-related lower extremity edema, which is more common in women than men.
	Felodipine	2.5-10	1	
	Isradipine	5-10	2	
	Nicardipine SR	60-120	2	
	Nifedipine LA	30-90	1	
	Nisoldipine	17-34	1	

What if blood pressure is still high?

- Did you check for OSA?
  - And other causes of secondary hypertension
    - Order an aldosterone/renin activity ratio
- Have you done a medication reconciliation including supplements?



What next?

Diuretics—aldosterone antagonists	Eplerenone	50-100	1 or 2	These are preferred agents in primary aldosteronism and resistant hypertension. Spironolactone is associated with greater risk of gynecomastia and impotence compared with eplerenone. Demonstrated efficacy as fourth-agent add-on therapy for resistant hypertension. Avoid use with K+ supplements, other K+-sparing diuretics, or significant renal dysfunction (eg, GFR <45 mL/min). Eplerenone often requires twice-daily dosing for adequate BP lowering. Avoid use in pregnancy.
	Spironolactone	25-100	1	

The back shelf

CCB—nondihydropyridines	Diltiazem ER	120-360	1	Avoid routine use with beta blockers because of increased risk of bradycardia and heart block. Do not use in patients with HFrEF. There are drug interactions with diltiazem and verapamil (CYP3A4 major substrate and moderate inhibitor).
	Verapamil IR	120-360	3	
	Verapamil SR	120-360	1 or 2	
	Verapamil-delayed onset ER	100-300	1 (in the evening)	

The back shelf

Diuretics—loop	Bumetanide	0.5-2	2	These are preferred diuretics in patients with symptomatic HF. They are preferred over thiazide-type diuretics in patients with moderate-to-severe CKD (eg, GFR <30 mL/min). The longer-acting choice of torsemide is preferred for treatment of hypertension. A loop diuretic is an option for patients who develop thiazide-type diuretic associated hyponatremia.
	Furosemide	20-80	2	
	Torsemide	5-10	1	

The back shelf

Beta blockers—cardioselective	Atenolol	25-100	2	Beta blockers are not recommended as first-line agents unless the patient has CHD or HF. These are preferred in patients with bronchospastic airway disease requiring a beta blocker. Bisoprolol and metoprolol succinate are preferred in patients with HFrEF. Avoid abrupt cessation.
	Betaxolol	5-20	1	
	Bisoprolol	2.5-10	1	
	Metoprolol tartrate	100-200	2	
	Metoprolol succinate	50-200	1	
Beta blockers—cardioselective and vasodilatory	Nebivolol	5-40	1	Nebivolol induces nitric oxide-induced vasodilation. Avoid abrupt cessation.
Beta blockers—noncardioselective	Nadolol	40-120	1	Avoid use in patients with reactive airways disease. Avoid abrupt cessation.
	Propranolol IR	80-160	2	
	Propranolol LA	80-160	1	
Beta blockers—intrinsic sympathomimetic activity	Acebutolol	200-800	2	Generally avoid, especially in patients with CHD or HF. Avoid abrupt cessation.
	Penbutolol	10-40	1	
	Pindolol	10-60	2	
Combined alpha and beta blockers	Carvedilol	12.5-50	2	Use of carvedilol is preferred in patients with HFrEF. Avoid abrupt cessation.
	Carvedilol phosphate	20-80	1	
	Labetalol	200-1,200	2	

The back shelf

Alpha-1 blockers	Doxazosin	1-16	1	These are associated with orthostatic hypotension, especially in older adults with a greater BP drop with first dose effect. These may be considered a second-line agent in patients with symptomatic benign prostatic hypertrophy.
	Prazosin	2-20	2 or 3	
	Terazosin	1-20	1 or 2	

The back shelf

Direct vasodilators	Hydralazine	100-200	2 or 3	These are associated with sodium and water retention and reflex tachycardia and should be used with a diuretic and beta blocker. Hydralazine is associated with a drug-induced lupus-like syndrome at higher doses. Minoxidil is associated with hirsutism and requires a loop diuretic. Minoxidil can induce pericardial effusion.
	Minoxidil	5-40	1-2	

The back shelf

Central alpha-2-agonist and other centrally acting drugs	Clonidine oral	0.1-0.8	2	These are generally reserved as last-line choices because of significant CNS adverse effects, especially in older adults. Avoid abrupt discontinuation of clonidine, which may induce hypertensive crisis. Clonidine must be tapered to avoid rebound hypertension.
	Clonidine patch	0.1-0.3	1 weekly	
	Methyldopa	250-1,000	2	
	Guanfacine	0.5-2	1	

Common interactions

TABLE 16 Pharmacokinetic Drug-Drug Interactions With Antihypertensive Medications

Blood Pressure Drug	Potential Interacting Drug	Clinical Effect
Absorption		
Thiazide-type diuretics	Cholestyramine	Decreased absorption leading to reduced BP lowering
Amlodipine, furosemide, metoprolol, carvedilol, bisoprolol, nebivolol, telmisartan	Potassium binder (patiromer)	Decreased absorption of antihypertensives leading to reduced BP-lowering effects. To mitigate this, administer the antihypertensives at least 3 h before or after taking the potassium binder
Furosemide	Potassium binder (sodium zirconium cyclosilicate)	Increased absorption of furosemide due to increased gastric pH leading to increased clinical effects (eg, diuresis or risk of hypokalemia); effect diminished with separation of administration by 2 h
Methyldopa	Iron salts	Decreased absorption of methyldopa leading to reduced BP lowering
Metabolism		
Bisoprolol, carvedilol, metoprolol	CYP2D6 inhibitors (eg, amiodarone, cimetidine, diphenhydramine, fluoxetine, paroxetine, terbinafine)	Increased BB concentration leading to enhanced clinical effects (eg, hypotension and bradycardia)
Diltiazem, verapamil	CYP3A4 inhibitors (eg, clarithromycin, erythromycin itraconazole, ketoconazole)	Increased nondihydropyridine concentration leading to enhanced clinical effects (eg, hypotension and bradycardia)
Diltiazem, verapamil	CYP3A4 inducers (eg, carbamazepine, phenobarbital, phenytoin, St. John's Wort, rifampin)	Decreased nondihydropyridine CCB concentration leading to reduced clinical effects (eg, minimization of blood pressure and pulse lowering)
CYP3A4 inhibition via amlodipine, verapamil, or diltiazem or other CYP3A4 inhibitors	Tacrolimus, cyclosporine	Increased calcineurin inhibitor concentration leading to increased risk for side effects (eg, renal impairment)
	Dabigatran, rivaroxaban	Increased concentration leading to increased risk for bleeding
	Atorvastatin, simvastatin	Increased statin concentration leading to increased risk for side effects (eg, myopathy)
	Colchicine	Increased colchicine concentration leading to increased risk for adverse effects (eg, neuromuscular toxicity)
	Eplerenone	Increased risk of hypotension and hyperkalemia Using a lower dose of eplerenone when combined with diltiazem could be considered a productive interaction, as the inhibition of eplerenone's metabolism might allow for lower doses to be effective, reducing the risk of adverse effects while maintaining efficacy
Elimination		
Thiazide-type diuretics, RAS blockers	Lithium	Reduced lithium clearance leading to increased lithium toxicity risk
P-glycoprotein (P-gp)		
Verapamil via P-gp inhibition	Dabigatran	Reduced P-gp efflux of dabigatran leading to increased dabigatran levels, which results in a higher risk of bleeding
Verapamil and carvedilol via P-gp inhibition	Digoxin	Reduced P-gp efflux of digoxin leading to increased digoxin levels, resulting in a higher risk of digoxin toxicity

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BB indicates beta blocker; BP, blood pressure; CCB, calcium channel blocker; h, hour; and P-gp, P-glycoprotein.

Important interactions

TABLE 17 Pharmacodynamic Drug–Drug Interactions With Antihypertensive Medications

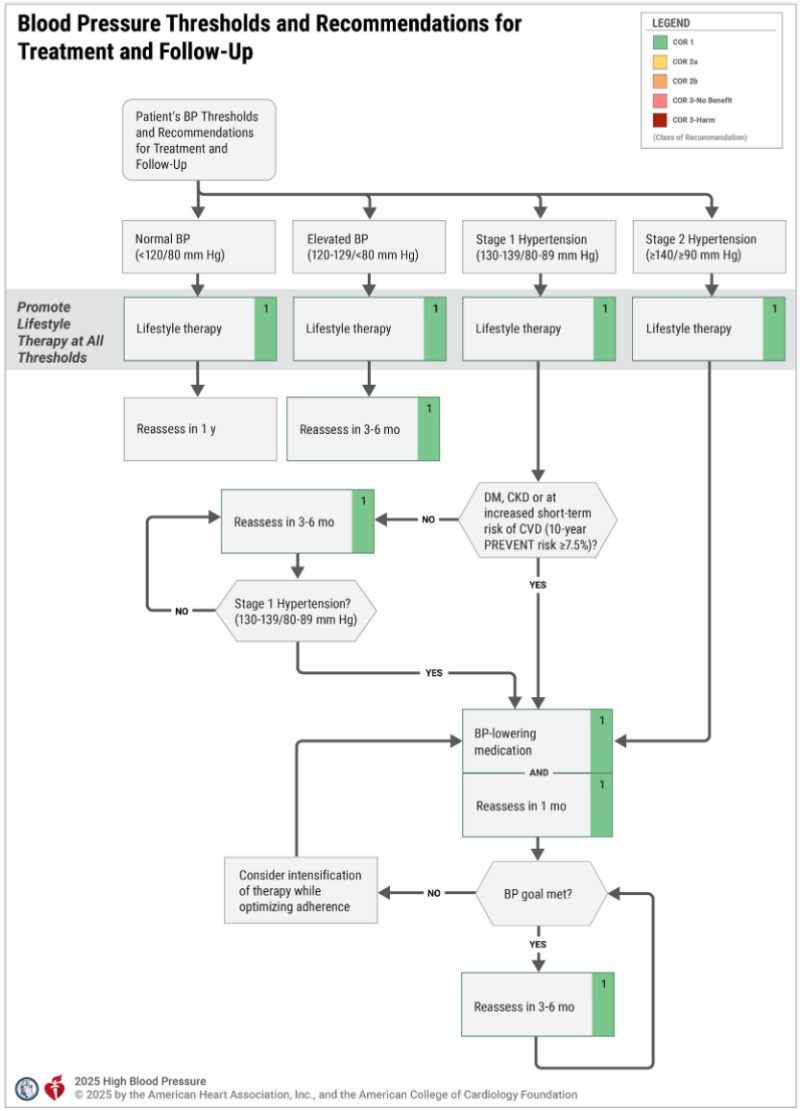
Drug Combinations		Clinical Effect
Cautionary interactions		
Any antihypertensive medication	NSAIDs	Reduced BP lowering via sodium retention
	Sympathomimetic (eg, pseudoephedrine, dextroamphetamine)	Reduced BP lowering
	Venlafaxine	Reduced BP lowering
Nondihydropyridine CCB	Beta blockers	Bradycardia or atrioventricular block
ACEi	ARBs	AKI, hyperkalemia
	Potassium-sparing diuretics (Spironolactone, eplerenone, triamterene, amiloride)	Hyperkalemia
	Sulfamethoxazole/trimethoprim	Hyperkalemia
	Potassium supplements	Hyperkalemia
	NSAIDs (eg, ibuprofen, naproxen)	AKI
Clonidine, methyldopa, guanfacine	CNS depressants (eg, zolpidem, alprazolam)	Sedation
Clonidine	Noncardioselective BB (eg, nadolol or propranolol)	Unopposed alpha agonism upon BB withdrawal leading to hypertensive crisis

Is there a good side?

Advantageous interactions		
Dihydropyridine CCB	RAS inhibitor	Reduced risk of dihydropyridine CCB-induced lower leg swelling
RAS inhibitors	Diuretics	Balanced effects on serum potassium levels with diminished possibility for hypokalemia (with diuretic) or hyperkalemia (with RAASi)
RAS inhibitors	Potassium binder	Lowers risk of hyperkalemia from the RAS inhibitor
Diuretic	Potassium supplement	Lowers risk of hypokalemia from the diuretic

Follow-up

FIGURE 7 BP Thresholds and Recommendations for Treatment and Follow-Up



Citations

- Jones, D, Ferdinand, K, Taler, S. et al. 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. JACC. 2025 Nov, 86 (18) 1567–1678. https://doi.org/10.1016/j.jacc.2025.05.007