

VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE DIAGNOSIS AND MANAGEMENT OF HYPERTENSION IN THE PRIMARY CARE SETTING

GUIDELINE SUMMARY

EXECUTIVE SUMMARY

- The primary objective in hypertension (HTN) management treatment is to decrease blood pressure (BP) to less than 140/90 mm Hg. The blood pressure goal may be lower in patients with diabetes mellitus (DM) or renal disease with proteinuria.
- Clinical management should begin by prescribing lifestyle modifications in all patients with HTN. Non-pharmacologic measures can control BP or decrease the amount of required medication in most patients.
- If lifestyle modification alone is used as initial therapy, the trial should be relatively short (no longer than 6 to 12 months), with frequent monitoring. Drug therapy should be instituted if blood pressure goals are not attained.
- Once effective control has been achieved, follow-up can be scheduled at three to six month intervals. Periodic follow up is important for management of the hypertensive patient and to assess the long-term response to therapy, monitor the development of target organ damage, and reinforce lifestyle modifications.

KEY POINTS (REFER TO BOXES IN ALGORITHMS)

- Manage severe HTN immediately (>210 and/or >120 mm Hg) (Box 3, 4)
- Identify and manage secondary causes of HTN (Box 8, 9, 10, 11)
- Initiate appropriate management including lifestyle modification and drug therapy (Box 12, 13, 14, 16, 17)
- Emphasize adherence to the medication regimen (Box 14, 16, 19)
- If control not achieved, continue a once a day regimen by increasing drug dose as tolerated OR substituting another drug OR adding an agent from a different class (Box 21, 22, 23, 25)
- Multi-drug regimens should include a thiazide diuretic for synergy, unless contraindicated (Box 22, 25)
- If BP control is not achieved with three drugs in compliant patients, further evaluation or referral should be considered (Box 25)
- Ensure achievement of HTN goal (Box 19, 24)
- Schedule adequate follow-up (Box 19, 24)

RECOMMENDATIONS FOR FOLLOW-UP BASED ON INITIAL BLOOD PRESSURE MEASUREMENTS FOR ADULTS^A (ANNOTATION C)

Systolic	Diastolic	Recommended Follow-up
< 130	< 85	Recheck in 2 years
130-139	85-89	Recheck in 1 year ^b
140-159	90-99	Confirm within 2 months ^c
160-179	100-109	Evaluate or refer to source of care within 1 month
> 180	> 110	Evaluate or refer to source of care immediately or within 1 week, depending on clinical situation

If systolic and diastolic categories are different, follow recommendations for shorter follow-up (e.g. 160/86 mm Hg should be evaluated or referred to source of care within 1 month).

Modify the scheduling of follow-up according to reliable information about past blood pressure measurements, other cardiovascular risk factors, or target organ disease.

Provide advice about lifestyle modifications

LIFESTYLE MODIFICATIONS (ANNOTATION K)

- Weight reduction for patients greater than 110% IBW (reduction of even 5 to 10 pounds can be helpful in controlling HTN)
- Limit alcohol intake to no more than one ounce (24 ounces of beer, or 10 ounces of wine, or 2 ounces of 100 proof whiskey) per day for men and 0.5 ounces per day for women and lighter weight men
- Sodium intake limited to not more than 2.4g/day (6 grams of sodium chloride)
- Aerobic exercise (target of 30-45 minutes 3-5 times/week)
- Diet modifications, i.e., diet high in fruits, vegetables, low-fat dairy products, fiber, potassium, calcium, and magnesium; low in saturated and total fat and cholesterol; and moderately high in protein (e.g., DASH diet)
- Smoking cessation (refer to VA/DoD Clinical Practice Guideline to Promote Tobacco Use Cessation in the Primary Care Setting)

EVALUATION: HISTORY, PHYSICAL EXAM, LABORATORY AND OTHER DIAGNOSTIC TESTS (ANNOTATION E, G, H)

Recommended tests include urinalysis, CBC, serum chemistries including serum creatinine and BUN, lipid profile, ECG.

RECOMMENDED TESTING FOR PATIENTS SUSPECTED OF HAVING SECONDARY HYPERTENSION (ANNOTATION I)

Disease	Recommended Test/Referrals
Renovascular disease	There are a variety of screening tests for renovascular HTN, depending on equipment and expertise in institutions. There is no single best test for renovascular HTN. Therefore, consult experts in your institution for current recommendations. Note: Intravenous pyelography (IVP) is not commonly used, and is relatively contraindicated in diabetics.
Thyroid disease	Thyroid-stimulating hormone (thyrotropin) (TSH)
Pheochromocytoma	24-hour urine for metanephrines or urinary catecholamines. Consider specialty referral
Cushing's syndrome	24-hour urine for free cortisol
Hyperaldosteronism	Serum potassium
Hyperparathyroidism	Serum calcium and parathyroid hormone (PTH) level
Renal parenchymal disease	Urinalysis, urine sediment, serum creatinine, 24-hour urine for protein and creatinine clearance. Consider referral to nephrology
Sleep apnea	Referral for sleep study

RISK STRATIFICATION AND TREATMENT (ANNOTATION J)

Assess patient for target organ damage and clinical cardiovascular disease

- Heart diseases: Left ventricular (LV) hypertrophy, angina or prior myocardial infarction (MI), prior coronary revascularization, heart failure
- History of transient ischemic attack or stroke
- Peripheral arterial disease
- Renal disease
- Retinopathy

Assess patient for major risk factors for cardiovascular disease and treat as indicated

- Smoking
- Dyslipidemia
- DM
- Age >60 yr
- Gender: Men, postmenopausal women
- Family history of CVD: Men <55 yr, women <65 yr

GENERAL GUIDELINES FOR MANAGEMENT^a (ANNOTATION J)

BP STAGE	RISK GROUP A ^b	RISK GROUP B ^c	RISK GROUP C ^d
High-normal 130-139/85-89	Advise about lifestyle modifications for reducing BP	Advise about lifestyle modifications for reducing BP	Consider drug therapy for patients with heart failure, renal insufficiency, or DM
Stage 1 140-159/90-99	Advise about lifestyle modifications for controlling BP (up to 12 months)	Advise about lifestyle modifications for controlling BP (up to 6 months)	Begin drug therapy and advise about lifestyle modifications
Stages 2 & 3 > 160/ > 100	Begin drug therapy and advise about lifestyle modifications ^e	Begin drug therapy and advise about lifestyle modifications	Begin drug therapy and advise about lifestyle modifications

^a Acute target organ damage (e.g., papilledema) associated with HTN requires immediate management

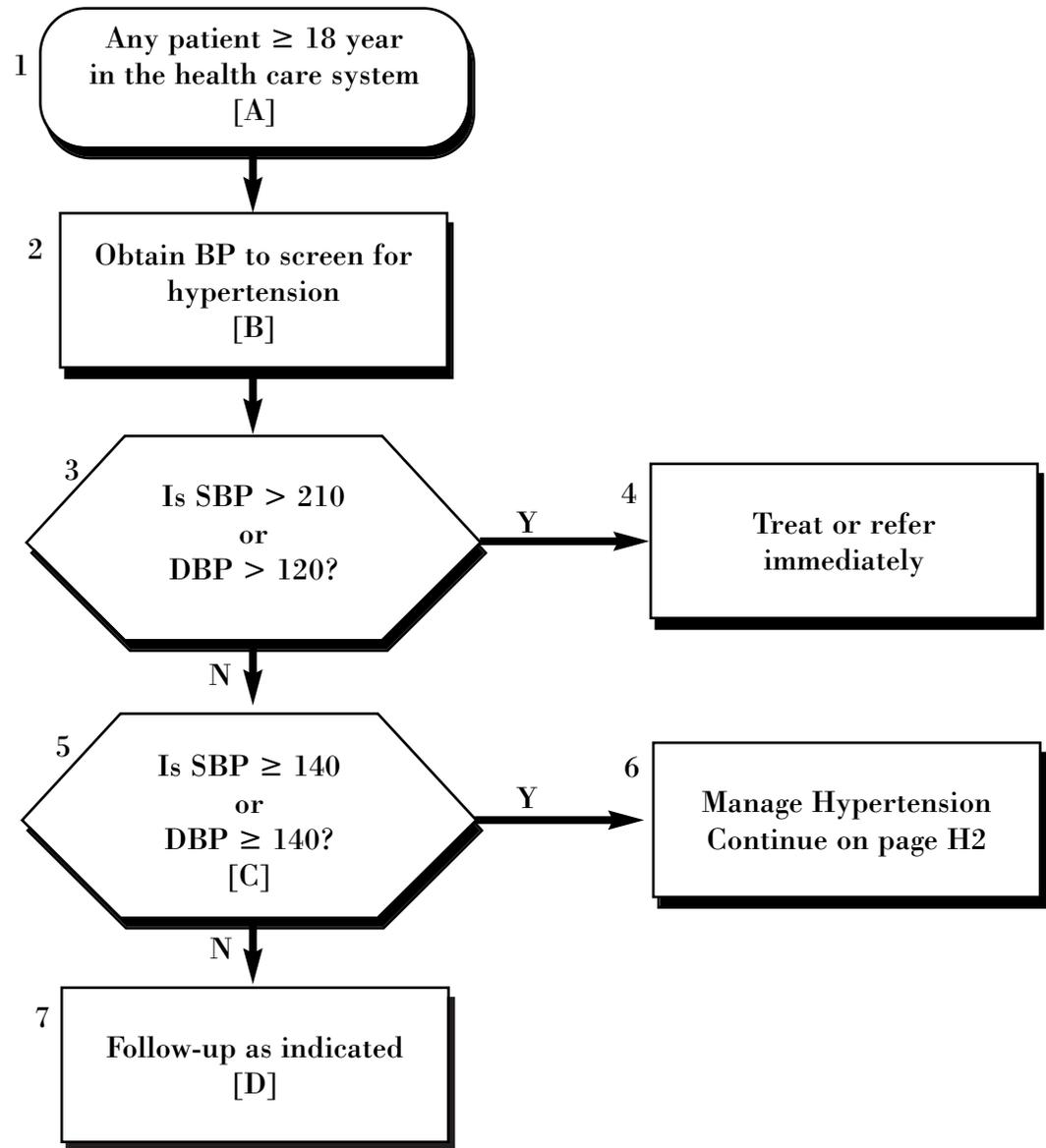
^b Risk Group A=no CVD risk factors; no target organ damage or clinical CVD

^c Risk Group B=at least 1 risk factor for CVD (not including DM); no evidence of target organ disease or clinical CVD

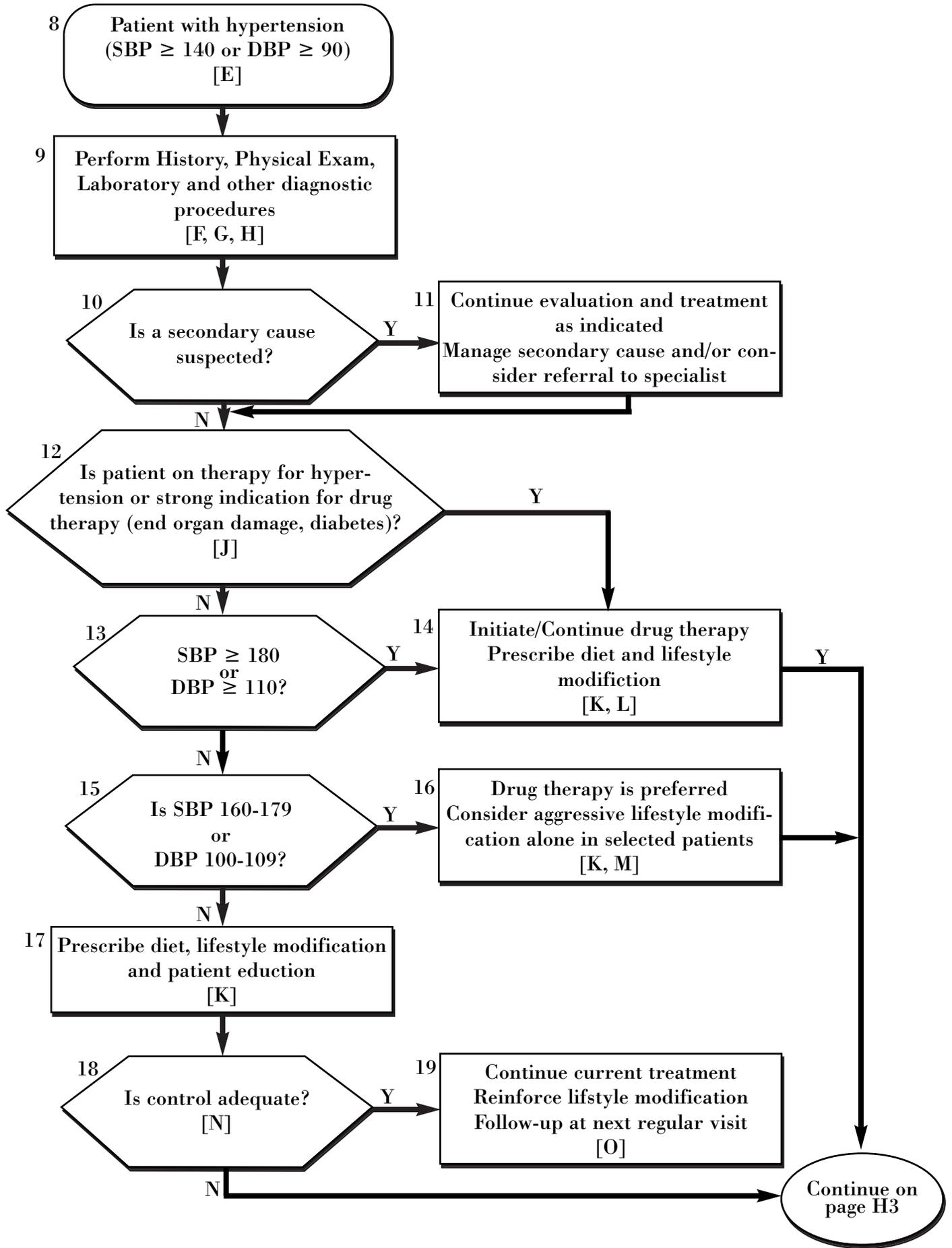
^d Risk Group C=evidence of target organ disease or clinical CVD and/or DM with or without other CVD risk factors

^e Consider aggressive lifestyle modification alone in selected patients with Stage 2 HTN in Risk Group A

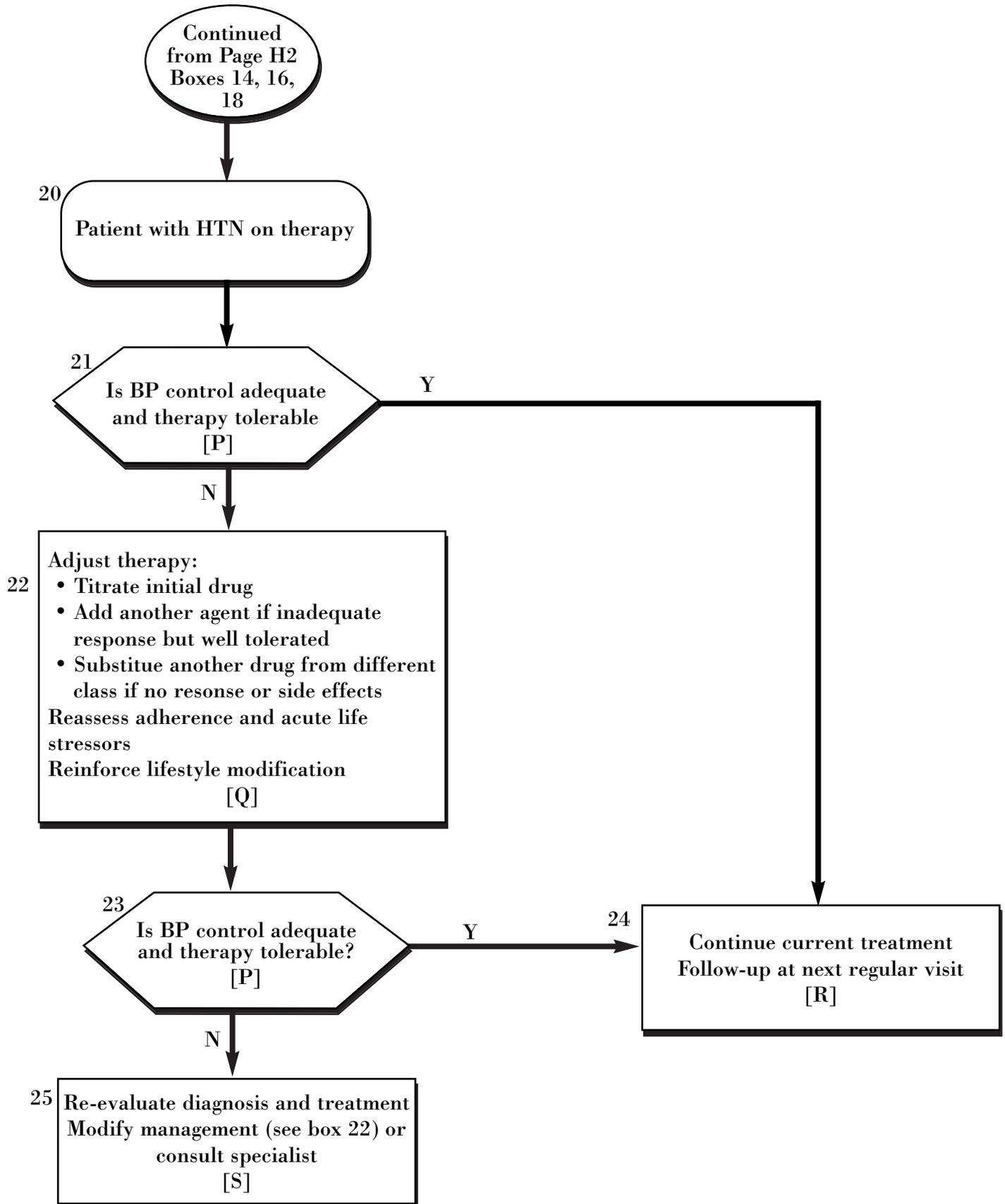
Screening Algorithm (H1)



Treatment Algorithm (H2)



Treatment Algorithm (H3)



SPECIAL POPULATIONS, COMORBIDITIES, AND PREFERRED AGENTS^{4b} (ANNOTATION D)

	PREFERRED AGENTS	ALTERNATE AGENTS	OTHER SELECTED AGENTS	COMMENTS
Uncomplicated	thiazide diuretic, β-blocker	ACEI, CCB	α-blocker, clonidine, reserpine	Short-acting nifedipine should not be used for long-term management of HTN
African-American Race	thiazide diuretic	CCB, β-blocker, ACEI	α-β-blocker, clonidine, α-blocker	Differences in efficacy among patient populations are not as apparent when diuretics are added to ACEIs and β-blockers
Asthma/COPD	thiazide diuretic	ACEI, CCB	clonidine, α-blocker	β-blockers generally contraindicated in patients with bronchospastic disease
BPH – Symptomatic	α-blocker ^a	β-blocker, ACEI, thiazide diuretic (low dose), CCB	clonidine	Diuretics may influence symptoms of polyuria and frequency
Coronary artery disease	β-blocker (non-ISA post-MI)	verapamil, diltiazem	DHP SR, ACEI, thiazide diuretic	Non-ISA β-blockers are the drugs of choice post-MI; ACEIs are also indicated post-MI in patients with systolic dysfunction
LVD – Diastolic	β-blocker, diuretic	verapamil, diltiazem	ACEI, α-blocker	Diuretics are first-line agents if symptoms of volume overload exist
LVD – Systolic	ACEI, diuretic ^d	angiotensin II antagonist, hydralazine/ nitrates	amlodipine, felodipine	ACEIs are preferred for their potential improvement in morbidity and mortality in this patient population; diuretics should be used if symptoms of volume overload exist; angiotensin II antagonists may be used where an ACEI is not tolerated; other selected agents may be used in conjunction with an ACEI in stable CHF patients; β-blockers ^d and CCBs should be used with caution
CRI (CrCl < 25ml/min or S _{cr} >2.5 mg/dL)	furosemide, ACEI	β-blocker, CCB, α-blocker, indapamide, metolazone	clonidine, minoxidil, hydralazine	Potassium (K ⁺)-sparing diuretics, K ⁺ supplements, and/or ACEI may cause ↑ K ⁺ ; ACEI with caution in patients S _{cr} >3.0 mg/dL; metoprolol is the preferred β-blocker due to hepatic excretion
Depression	thiazide diuretic	ACEI, CCB, α-blocker	angiotensin II antagonist	Clonidine, reserpine, methyldopa, β-blockers may exacerbate depression
DM	ACEI ^e (types 1 & 2 DM with proteinuria)	thiazide diuretic (low dose), CCB, β-blocker, α-blocker		High-dose thiazide diuretics and β-blockers may worsen glucose control; β-blockers may mask hypoglycemia; use of DHP SR in patients with HTN and type 2 DM remains controversial
Elderly (age >65 yrs)	thiazide diuretic	β-blocker, CCB, ACEI	α-blocker	Use caution with α-blockers in elderly due to first-dose syncope or dizziness
Gout	β-blocker	ACEI, CCB, thiazide diuretic (low dose)	α-blocker	Diuretic-induced hyperuricemia does not require treatment in the absence of gout or kidney stones
Dyslipidemia	thiazide diuretic (low dose), β-blocker	ACEI, CCB, α-blocker		Thiazide diuretics may ↑ TC and ↓ TG and non-ISA β-blockers may ↓ HDL and ↑ TG, although these effects may be transient
Isolated systolic hypertension	thiazide diuretic	DHP SR, β-blocker, ACEI	α-blocker	The use of DHP SR as first-line therapy remains controversial, although studies are available to indicate benefit
Left ventricular hypertrophy	ACEI, thiazide diuretic, β-blocker	CCB	α-blocker, clonidine	Direct-acting vasodilators do not reduce left ventricular hypertrophy
Peripheral vascular disease	thiazide diuretic, ACEI	CCB, β-blocker	α-blocker	Nonselective β-blockers without α-blockade may worsen resting ischemia or severe claudication symptoms
Pituits	thiazide diuretic, lisinopril			
Pregnancy (chronic HTN)	methyldopa	labetalol	hydralazine (generally used for pre-eclampsia)	Except for ACEI and angiotensin II antagonists that are contraindicated during pregnancy, any antihypertensive drug may be continued if taken prior to pregnancy; β-blockers may cause growth retardation in 1st trimester

^aAdapted from JNC VI. **Bold**=compelling indication per outcome data (unless contraindicated); *Italics*=may have favorable effect on comorbid conditions

^bACEI=angiotensin-converting enzyme inhibitor; BUN=blood urea nitrogen; CCB=calcium channel blocker; DHP SR=long-acting diltiazem; COPD=chronic obstructive pulmonary disease; BPH=benign prostatic hyperplasia; ISA=intrinsic sympathomimetic activity; MI=myocardial infarction; LVD=left ventricular dysfunction; CHF=chronic heart failure; CRI=chronic renal insufficiency; DM=diabetes mellitus; TC=total cholesterol; TG=triglyceride; HDL=high-density-lipoprotein cholesterol

^cGenerally recommended for use as adjunct therapy to other antihypertensive agents

^dThere is compelling evidence to use β-blockers as adjunct therapy in patients with NYHA II to III CHF who are stable on an ACEI with or without a diuretic; refer to PBM-MAP The Pharmacologic Management of Chronic Heart Failure at www.vapbm.org or <http://vapbm.med.va.gov>

^eCompelling indication in type 1 DM with proteinuria; preferred agent in types 1 and 2 DM with proteinuria

Recommended Dosage for Selected Hypertension Drug Therapy (Adapted from PBM-MAP The Pharmacologic Management of HTN, Supplement to the VA/DoD Clinical Practice Guideline on HTN)

Drug ^a	Dosage Range ^{d,e}	Comments
THIAZIDE DIURETICS Hydrochlorothiazide ^b HCTZ/Triamterene ^b	12.5-25 mg/day (max=50mg/day) 25/37.5-50 mg/75 mg/day	Use HCTZ/Triamterene with caution with ACEI and other K+ retaining drugs or supplements
β-BLOCKERS <i>Noncardioselective</i> Propranololb <i>Cardioselective</i> Atenololb Metoprolol	IR: 40-480 mg/day in divided doses SR: 80-160 mg/day 25-100 mg/day (adjust dose in CRI) IR: 50-300 mg/day (once daily or divided doses)	β-blockers are contraindicated in asthma patients Discontinue with slow taper over 1 week As doses increase, cardioselectivity decreases
CCBs Verapamil IR ^b Verapamil SR ^c Diltiazem IR ^b Diltiazem SR (Tiaza ^{cb}) <i>Dihydropyridines</i> Felodipine Nifedipine SR (Adalat“CCb)	120-360 mg/day (in 2-3 divided doses) 120-480 mg/day (once daily or 2 divided doses) 90-360 mg/day (in 3-4 divided doses) 120-540 mg/day heart block 2.5-10 mg/day 30-120mg/day (manufacturer max=90 mg/d)	Verapamil is contraindicated in AV node dysfunction (2nd or 3rd degree heart block), systolic CHF and decreased LV function Diltiazem may decrease sinus rate and cause Monitor adverse effects (DHPs may cause ankle edema, dizziness, flushing, headache) Use CCBs with caution in patients with liver or renal dysfunction
ACEIs Captopril ^b Fosinopril Lisinopril ^b	25-150 ^f mg/day (in 2-3 divided doses) 10-40 mg/day 5-40 mg/day	Avoid in 2nd and 3rd trimesters of pregnancy due to possible fetal and neonatal morbidity and death Monitor K+ and renal function
α-BLOCKERS Prazosin ^b Terazosin ^b	1-15 mg/day (in 2-3 divided doses) (max=20mg/d) 1-5 mg/day (max=20 mg/d)	Initiate at low doses (1mg) with 1st dose given at bedtime to avoid syncope
ANGIOTENSIN II ANTAGONIST Candesartan due Irbesartan Losartan Telmisartan Valsartan	8-32 mg/day (once daily or 2 divided doses) 150-300 mg/day 25-100 mg/day (once daily or 2 divided doses) 20-80 mg/day 80-320 mg/day	Contraindicated in 2nd and 3rd trimesters pregnancy to potential for fetal and neonatal morbidity and death
CENTRALLY ACTING Clonidine Tablet ^b Clonidine Patch Methyldopa	0.1-0.8 mg/day (in 2-3 divided doses) (max can be up to 2.4 mg/d) 0.1-0.6 mg patch weekly 500 mg-3g/day (in 2-4 divided doses)	Taper dose to discontinue Clonidine patches are costly but may be useful in selected patients
PERIPHERALLY ACTING Reserpine	0.05-0.25 mg/day	Monitor for sedation, nightmares, tremors, nasal congestion, activation of peptic ulcer
VASODILATING AGENTS Minoxidil Hydralazine ^b	5-40 mg/day (once daily or 2 divided doses) (max=100 mg/day) 30-200 mg/day (in 2-3 divided doses)	Should be used with a diuretic and β-blockers to reduce edema and reflex tachycardia Monitor for hypertrichosis, pericardial effusions with minoxidil Monitor for headache and SLE (dose-related) with hydralazine

^a Partial list

^b DoD BCF item; all BCF items are available through the DoD NMOP

^c Calan, SR, Ioptin, SR, and generic equivalents are on the DoD BCF

^d Once daily dosing unless specified otherwise

^e IR=immediate release; SR=sustained release

^f Patients should take 1 hour prior to food ingestion (empty stomach)

MODIFICATION OF DRUG THERAPY TO HELP ACHIEVE BP CONTROL (ANNOTATION Q)

Agents from all of the five major classes of antihypertensive medications are shown to decrease BP. Diuretics and β -blockers have consistently been shown to decrease morbidity and mortality in the treatment of HTN and should be considered first-line therapy. Diuretics should be used in low to moderate doses. Alternatively, clinicians may consider alpha-blockers, ACEIs, and CCBs as well as other medications as therapy for selected pre-existing conditions. Clinicians should consider cost where therapeutic effect is equal, and to maximize compliance, should choose medications that keep regimens simple.

If the blood pressure continues to be elevated, clinicians may consider choosing one of the strategies that have proven effective in the treatment of HTN:

- 1. Increase the dose of the original medication:** Approximately 50 percent of patients can be controlled with a single agent. Single-agent therapy is simpler and decreases the risk of interaction with other drugs. Note that cost may not be an issue: in many facilities within the VA and DoD, the higher doses are the same price as the lower doses.
- 2. Discontinue the first medication and start a new agent:** Discontinuing the original medication and starting a new agent has also been studied in clinical trials, again with approximately 50 percent of patients controlled. This regimen offers similar advantages to the first, and may avoid side effects seen with higher-dose titration. If side effects occur, clinicians should consider discontinuing the agent and switching to a medication from a different class. Since side effects tend to be similar across classes, a medication from a different class is usually preferred.
- 3. Add another agent:** Adding a second medication to the regimen, sometimes called step therapy, is also a well-studied procedure and was recommended by the Joint National Committee. The addition of a second agent has theoretical advantages in that the antihypertensive effects of different agents are often additive, resulting in better control of BP. Disadvantages include a potential for drug-drug interactions; additive therapy may require a complicated regimen with which the patient must comply. Furthermore, adding another drug can increase cost. If a diuretic is not chosen as the initial drug, it is usually indicated as a second-step agent because its addition frequently enhances the effects of the initial agents.

PATIENT FOLLOW-UP (ANNOTATION R)

Once an effective and well-tolerated regimen has been obtained, follow-up can be scheduled at 3- to 6- month intervals. Periodic follow-up is important to the management of the hypertensive patient and should help to:

- Assess the long-term response to therapy
- Reassess for side effects that might complicate therapy or limit efficacy
- Monitor the development of target organ damage
- Reinforce lifestyle modification

CAUSES OF INADEQUATE RESPONSE TO THERAPY (ANNOTATION S)

Non-adherence to therapy	Evaluate causes of non-adherence with patient
Pseudo-resistance	"White Coat" hypertension or office elevation, Pseudohypertension in older patients, Use of regular cuff on very obese arm
Volume overload	Excess salt intake, Progressive renal damage (nephrosclerosis), Fluid retention from reduction of blood pressure, Inadequate diuretic therapy
Drug-related causes	Nonsteroidal anti-inflammatory drugs, Dose(s) too low, Wrong type of diuretic, Inappropriate combinations, Drug actions and interactions, Sympathomimetics, Nasal decongestants, Appetite suppressants, Cocaine and other illicit drugs, Caffeine, Oral contraceptives, Adrenal steroids, Licorice (as may be found in chewing tobacco), Cyclosporine, tacrolimus, Erythropoietin, Antidepressants
Associated conditions	Smoking, Obesity, Sleep apnea, Hyperinsulinemia, Ethanol intake more than 3 oz. (90 ml) per day, Anxiety-induced hyperventilation or panic attacks, Chronic pain, Intense vasoconstriction (arteritis), Organic brain syndrome (e.g., memory deficit)
Identifiable secondary causes of HTN	See Table 2, Recommended Testing for Patients Suspected of Having Secondary Hypertension