VA/DoD Clinical Practice Guideline

Diagnosis and Management of Hypertension in Primary Care Setting

Version 3.0

GUIDELINE SUMMARY 2014

VA/DoD Evidence Based Practice

Department of Veterans Affairs

Department of Defense

VA/DoD Clinical Practice Guideline

for

The Diagnosis and management of Hypertension in Primary Care Setting

Guideline Summary

Prepared by:

The Hypertension

Working Group

With support from:

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and

Quality Performance Assurance Directorate, United States Army MEDCOM

Full guideline available at:

http://www.healthquality.va.gov *or* https://www.qmo.amedd.army.mil

QUALIFYING STATEMENTS

The Department of Veterans Affairs (VA) and The Department of Defense (DoD) guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision-making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

Variations in practice will inevitably and appropriately occur when providers take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every health care professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

Version 3.0 – 2014

DISCLAIMER

This Clinical Practice Guideline is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendations.

These guidelines are not intended to represent TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care. Additional information on current TRICARE benefits may be found at www.tricare.mil or by contacting your regional TRICARE Managed Care Support Contractor.

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SUMMARY

In the United States (US), about 77.9 million adults (one out of every three) have hypertension. Of those only 81.5% are aware of their condition, 74.9% are undergoing treatment, and just over half (52.5%) have their hypertension controlled. [1] Uncontrolled hypertension has been shown to be higher in older Americans, non-Hispanic blacks and individuals with certain co-morbid conditions, including diabetes and chronic kidney disease (CKD). [2]

In a 2008 study, it was found that 13% of active duty Service Members had hypertension, the majority of which were <40 years of age. [3] It was reported that, as in the civilian population, increased age, increased body mass index (BMI), male sex, black race/ethnicity, and senior rank were all independently associated with hypertension. Over 37% of Veterans have hypertension, making it the most common chronic medical condition among Veterans. [4] The control of hypertension, however, has significantly improved among Veterans. While only 45.7% of Veterans had their blood pressure controlled in 2000, by 2010, the rate had improved to 76.3%. [5]

Hypertension is clinically defined as a systolic blood pressure (SBP) ≥140 mmHg or a diastolic blood pressure (DBP) of ≥90 mmHg. Prehypertension is classified as SBP 120-139 or DBP 80-89. Hypertension is usually asymptomatic; therefore, routine screening is important in order to diagnosis the condition. Also, because patients will mostly not feel sick, the asymptomatic nature of hypertension can lead to challenges with adherence to treatment.

Complications of hypertension include damage to the large arteries (macrovascular complications) that can lead to stroke, myocardial infarction (MI), or peripheral arterial diseases, as well as damage to the smaller arteries (microvascular complications) that can lead to CKD or retinopathy. In addition to these arterial complications, hypertension by itself can lead to left ventricular hypertrophy (LVH) and congestive heart failure (CHF), another frequent cause of death in the US.

The Department of Veterans Affairs (VA) and the Department of Defense (DoD) Clinical Practice Guideline (CPG) for the Diagnosis and Management of Hypertension in the Primary Care Setting is intended to assist healthcare providers in all aspects of outpatient care for patients with hypertension. The system-wide goal of evidence-based guidelines is to improve the patient's health and wellbeing. The overall expected outcome of successful implementation of this guideline is to:

- Formulate an efficient and effective assessment of the patient's condition
- Optimize the use of therapy to reduce symptoms and enhance functionality
- Minimize preventable complications and morbidity
- Emphasize the use of personalized, proactive, patient-driven care

This CPG addresses various management strategies for patients with hypertension (HTN). This includes assessing the benefits and harms associated with antihypertensive pharmacologic therapies as well as the blood pressure thresholds to initiate therapy and appropriate blood pressure targets. In addition to primary care provider pharmacological management strategies, the CPG discusses the impact of non- pharmacologic therapies (e.g., weight reduction, sodium reduction, physical activity) on improving hypertension management. The CPG also reviews what measurement techniques are the best indicators to initiate hypertension therapy.

STRENGTH OF RECOMMENDATIONS

This CPG uses the GRADE methodology to assess the quality of the evidence base and assign a grade for the strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation: [6]

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence
- Values and preferences
- Other implications, as appropriate, e.g.,:
  - Resource Use
  - Equity
  - Acceptability
  - Feasibility
  - Subgroup considerations

The framework below was used by the VA/DoD HTN Work Group to guide discussions on each domain.
Table 1. Evidence to Recommendation Framework

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Decision Domain	Judgment
Balance of desirable and undesirable outcomes	
Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa? Are the desirable anticipated effects large? Are the undesirable anticipated effects small? Are the desirable effects large relative to undesirable effects?	Benefits outweigh harms/burden Benefits slightly outweigh harms/burden Benefits and harms/burden are balanced Harms/burden slightly outweigh benefits Harms/burden outweigh benefits
Confidence in the quality of the evidence	
Is there high or moderate quality evidence that answers this question? What is the overall certainty of this evidence?	High Moderate Low Very low
Values and preferences	
Are you confident about the typical values and preferences and are they similar across the target population? What are the patient's values and preferences? Are the assumed or identified relative values similar across the target population?	Similar values Some variation Large variation
Other implications (e.g., resource use, equity, acceptability, feasibility, subgroup considerations):	
Are the resources worth the expected net benefit from the recommendation? What are the costs per resource unit? Is this intervention generally available? Is this intervention and its effects worth withdrawing or not allocating resources from other interventions? Is there lots of variability in resource requirements across settings?	Various considerations

The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects, and is based on the framework above, which combines the four domains. [6]

The GRADE of a recommendation is based on the following elements:

- Four decision domains used to determine the strength and direction (described above)
- Relative strength (Strong or Weak)
- Direction (For or Against)

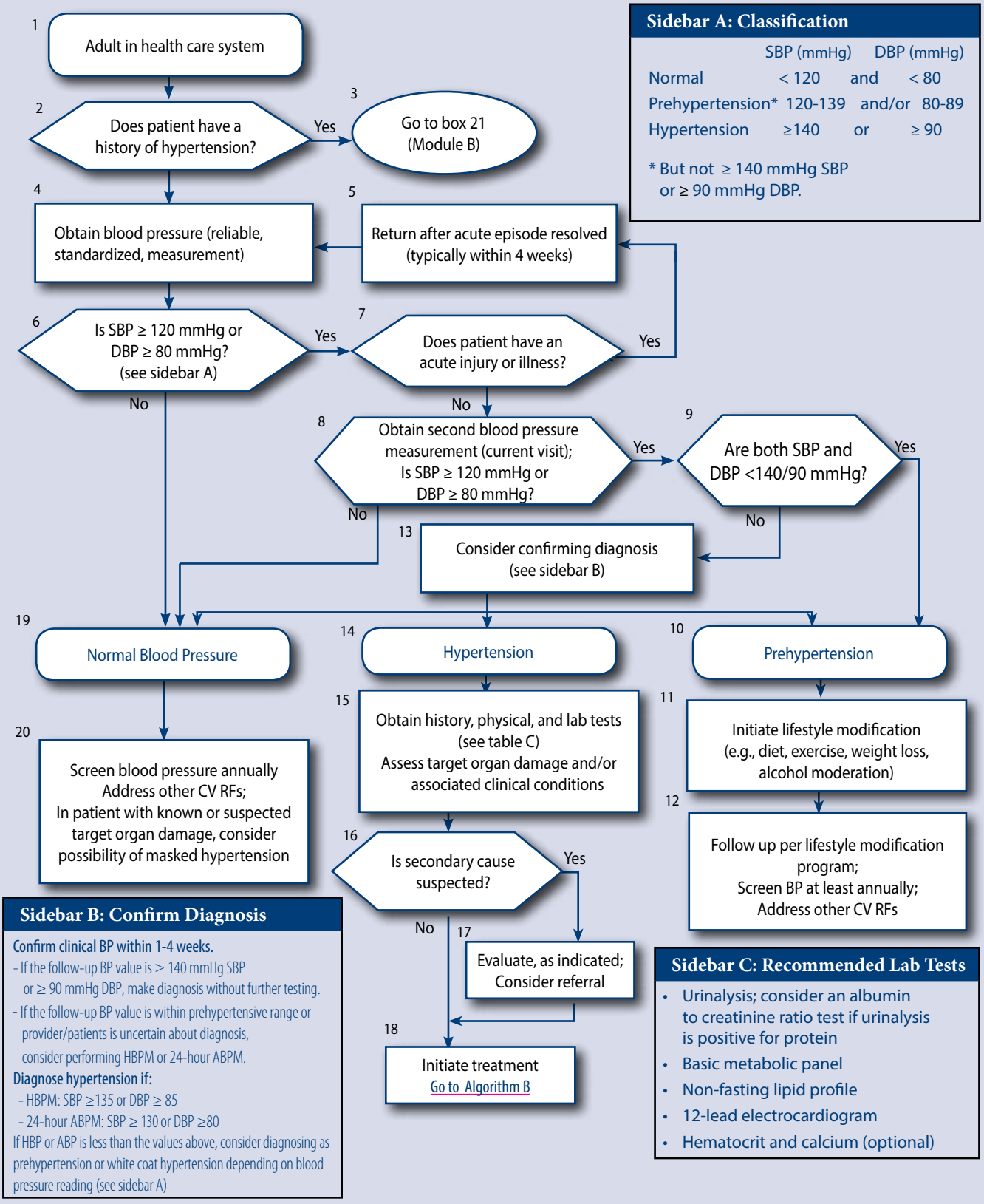
The relative strength of the recommendation is based on a binary scale, "Strong" or "Weak." A strong recommendation indicates that the Work Group is highly confident that desirable outcomes outweigh undesirable outcomes. If the Work Group is less confident of the balance between desirable and undesirable outcomes, they present a weak recommendation.

Similarly, a recommendation for a therapy or preventive measure indicates that the desirable consequences outweigh the undesirable consequences. A recommendation against a therapy or preventive measure indicates that the undesirable consequences outweigh the desirable consequences.

Using these elements, the grade of each recommendation is presented as part of a continuum:

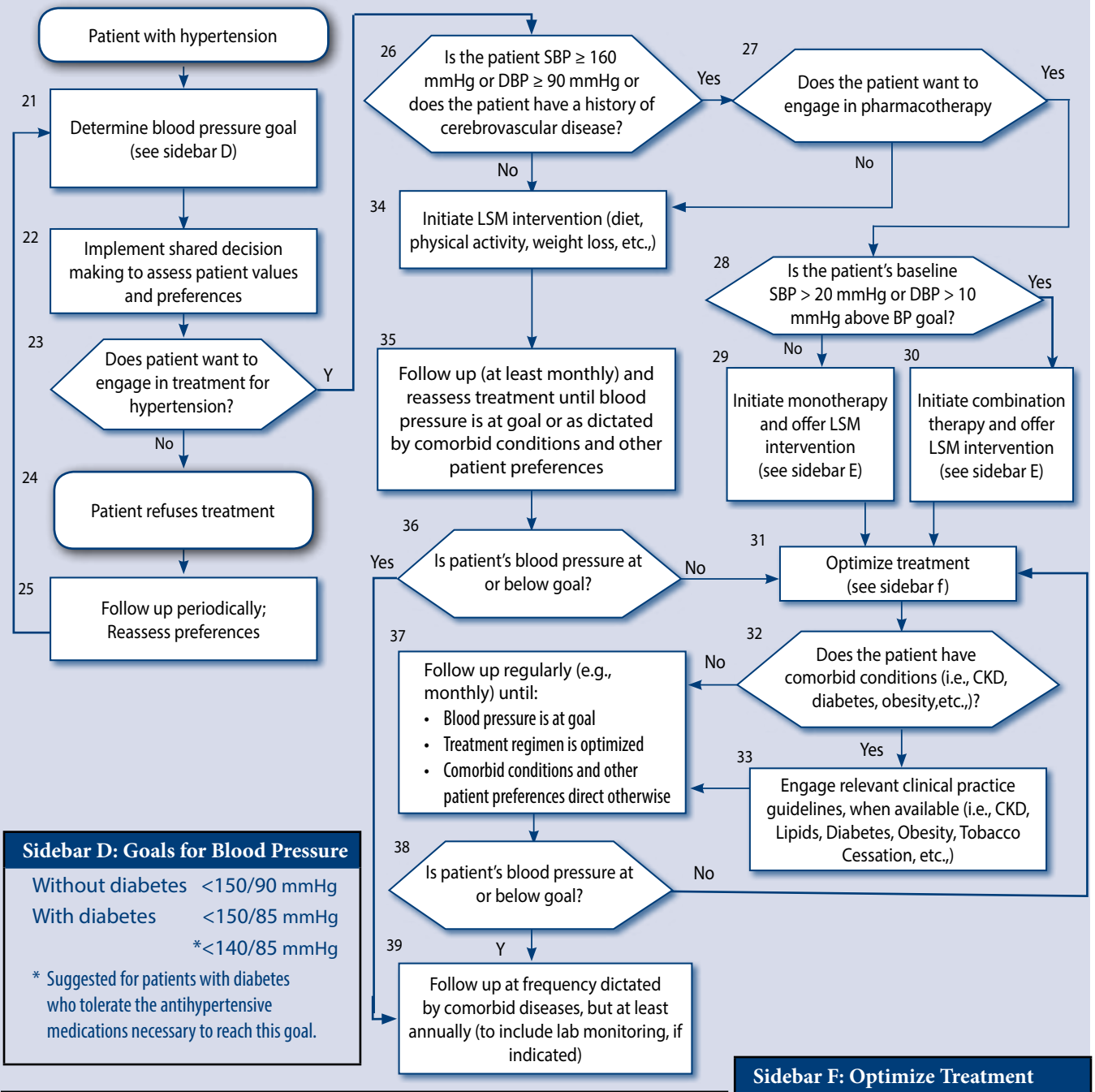
- **Strong For** (or "We recommend offering this option …")
- **Weak For** (or "We suggest offering this option …")
- **Weak Against** (or "We suggest not offering this option …")
- **Strong Against** (or "We recommend against offering this option …")

Algorithm A — Screening and Diagnosis



ABPM= Ambulatory Blood Pressure Monitoring; HBPM =Home Blood Pressure Monitoring; ACEI=Angiotensin-converting Enzyme Inhibitor; ARB=Angiotensin II Receptor Blocker; CKD=Chronic Kidney Disease; DBP=Diastolic Blood Pressure ; DHP CCB=Dihydropyridine Calcium Channel Blocker; TOD=Target Organ Damage; SBP=Systolic Blood Pressure;

Algorithm B — Management of Hypertension



Sidebar D: Goals for Blood Pressure

Without diabetes	<150/90 mmHg
With diabetes	<150/85 mmHg
	*<140/85 mmHg

* Suggested for patients with diabetes who tolerate the antihypertensive medications necessary to reach this goal.

Sidebar E: Initiate drug Therapy

General population (including patients with coronary diseas, prior MI, or diabetes)

1st Line Thiazide type diuretics

2nd Line ACEIs, ARBs, or long acting DHP CCBs

Additional drug classes may be added as needed to reach BP goal. ((See Table 3)

Specific Populations:

For patients with CKD, recommend ACEIs or ARBs as 1st line therapy

For African American patients, recommend not using ACEIs or ARBs as monotherapy.

For African American patients with CKD, suggest combining a thiazide type diuretics with an ACEI or ARB.

Sidebar F: Optimize Treatment

- Optimize treatment (see Table 3)
  - Titrate initial drug
  - Add another agent from a different class
- Assess adherence
- Reevaluate diagnosis (resistant HTN)
- Consider evaluation for interfering substances or contributing secondary causes of hypertension
- Consider specialty consultation for patients with resistant hypertension

Recommendations

A Screening

1. We recommend screening adults for elevated blood pressure occur periodically, preferably annually. [**Strong For**]
   (Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)
2. We suggest that screening occur at the time of routine preventive care or routine health assessment. [**Weak For**]
   (Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)

B. Diagnosis

3. We recommend the diagnosis of hypertension be determined based on at least two blood pressure readings on two separate patient visits **[Strong For]**

   (Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)

C. Measurement Techniques

4. We recommend that blood pressure be measured with a technique recommended for the measurement of blood pressure in adults using a properly calibrated and validated sphygmomanometer. **[Strong For**]

   (Modified from the 2004 CPG without an updated systematic review of the evidence.)
5. For patients whose diagnosis of hypertension remains uncertain, we recommend offering home blood pressure monitoring to confirm diagnosis prior to beginning pharmacologic treatment. (Two to three times a day for seven consecutive days, disregard the first day and take the average of measurements.) [**Strong For**]
6. For patients whose diagnosis of hypertension remains uncertain, we suggest offering 24 hour ambulatory blood pressure monitoring as an alternative to home blood pressure monitoring to confirm diagnosis prior to beginning pharmacologic treatment. [**Weak For**]

D. Adherence to Therapy

7. We suggest offering a multi-modal approach to adherence interventions, which could include tele-monitoring, multi-disciplinary group medical appointments, (e.g., shared medical appointments), case management (by pharmacists, nurses, social workers), patient and provider education, behavioral therapy, etc.. [**Weak For**]

E. Lifestyle Modification

8. We recommend offering lifestyle modification interventions for patients with prehypertension or hypertension based on patient indications and preferences as well as assessment of available local resources. [**Strong For**]
   (Modified from 2004 VA/DoD HTN CPG)

Weight Reduction

9. We recommend discussing healthy weight range and advising overweight or obese hypertensive patients to reduce their body mass index to below 25. [**Strong For**]
   (Modified from 2004 VA/DoD HTN CPG)
10. If a normal body mass index (<25) cannot be achieved, we suggest advising patients that a weight reduction of at least 10 pounds can achieve a decrease in blood pressure. [**Weak For**]

Exercise/Physical Activity

11. We recommend a target for aerobic exercise of 30 to 45 minutes per session, at least four times per week. [**Strong For**]
    (Modified from 2004 VA/DoD HTN CPG)
12. We suggest the use of a self-monitoring device (e.g., pedometer, mobile apps, etc.) to increase adherence to physical activity. [**Weak For**]

Mind-body/Alternative Therapies

13. For patients interested in complementary and alternative medicine, we suggest considering mind-body therapies such as transcendental meditation or yoga. [**Weak For**]
14. We **suggest not** offering Tai Chi for the treatment of hypertension as there is a moderate body of evidence that shows this intervention does not reduce blood pressure. [**Weak Against**]

Dietary Modification

15. We recommend a dietician-led Dietary Approaches to Stop Hypertension (DASH) Diet for the treatment and/or prevention of hypertension for patients with hypertension and/or interested patients with prehypertension and other cardiovascular risk factors. [**Strong For**]
    (Modified from 2004 VA/DoD HTN CPG)
16. In patients with additional cardiovascular risk factors, such as dyslipidemia, we suggest considering a dietician-led Mediterranean Diet as an alternative to the DASH Diet. [**Weak For**]
17. We recommend **against** the use of soy protein supplements for the treatment of hypertension. [**Strong Against**]

Sodium Reduction

18. In patients with hypertension or prehypertension, we recommend that sodium intake be limited to no more than 2300 mg/day (100 mmol/day), with referral to a dietician or other support as appropriate. [**Strong For**]
    (Modified from 2004 VA/DoD HTN CPG).

Alcohol Reduction

19. We recommend advising hypertensive and prehypertensive patients to limit alcohol intake to no more than 1 oz per day for men or 0.5 oz of alcohol per day for women. (This is approximately 2 drinks/day in men and 1 drink/day in women, where a drink is 1.5 oz 80-proof liquor, 12 oz beer, or 5 oz wine [all 14g]). [**Strong For]**
    (Modified from 2004 VA/DoD HTN CPG).

H. Initiation of Pharmacotherapy

20. We recommend offering pharmacologic treatment for hypertensive patients 60 years and older with a systolic blood pressure ≥ 160mmHg. [**Strong For]**
21. We suggest considering pharmacologic treatment using a shared decision- making model for hypertensive patients 60 years and older with systolic blood pressure <160mmHg. [**Weak For**]
22. We suggest offering pharmacologic treatment to patients with a history of cerebrovascular disease (stroke, transient ischemic attack, or asymptomatic carotid artery disease) and a systolic blood pressure ≥140mmHg. [**Weak For**]
23. We suggest pharmacologic treatment for hypertensive patients younger than 60 with a systolic blood pressure ≥160mmHg, regardless of diastolic blood pressure. [**Weak For**]
24. We recommend offering pharmacologic treatment for patients 30 years and older with a diastolic blood pressure ≥90mmHg. [**Strong For]**
25. We suggest offering pharmacologic treatment for patients age 18 to 29 with a diastolic blood pressure ≥90mmHg. [**Weak For**]

G. Blood Pressure Goals

26. For patients 60 years and over, we recommend treating to a systolic blood pressure goal of <150mmHg. [**Strong For]**
27. For patients below 60 years of age, we suggest treating to a systolic blood pressure goal of <150mmHg. [**Weak For**]
28. We recommend treating to a diastolic blood pressure goal <90mmHg in patients 30 years and older. [**Strong For]**
29. We suggest treating to a diastolic blood pressure goal <90mmHg in patients age 18 to 29. [**Weak For**]
30. For patients with diabetes (all age groups), we recommend treating to a systolic blood pressure goal of <150mmHg. [**Strong For]**
31. For patients with diabetes (all age groups) who tolerate antihypertensive drugs, we suggest treating to a systolic blood pressure goal of <140mmHg. **[Weak For]**
32. For patients with diabetes, we recommend treating to a diastolic blood pressure goal <85mmHg. [**Strong For]**

H. Hypertension Control and Follow-up

33. We suggest that patients be seen within one month of initiation of lifestyle or pharmacological therapy to determine adequacy of hypertension control, degree of patient adherence, and presence of adverse effects. **[Weak For]**

    (Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)

34. Once the patient's blood pressure is controlled, we suggest follow-up at least annually or more frequently as indicated, depending on patient preference. **[Weak For]**

    (Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)

I Monotherapy or Combination Therapy

35. We suggest taking into consideration the patient's baseline blood pressure and presence of comorbidities, when deciding on either monotherapy or combination therapy (two drugs) when initiating drug therapy. **[Weak For]**
    (Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)

36. We suggest initiating combination therapy for patients with a baseline systolic blood pressure of >20mmHg or diastolic blood pressure of >10mmHg above the patient's goal. **[Weak For]**
    (Modified from 2004 VA/DoD HTN CPG without an updated systematic review of the evidence.)

J. First Line Therapy

37. We recommend the use of thiazide-type diuretics for the treatment of hypertension. **[Strong For]**
38. We suggest the use of thiazide-type diuretics at recommended treatment doses as first line therapy for drug treatment of hypertension either as monotherapy or in combination with other agents. **[Weak For]**
    (Modified from 2004 VA/DoD HTN CPG)
39. To initiate treatment of hypertension with a thiazide-type diuretic, we suggest the use of chlorthalidone or indapamide over hydrochlorothiazide. **[Weak For]**
40. We **do not suggest** switching from hydrochlorothiazide to chlorthalidone or indapamide if the patient is adequately controlled on and tolerating hydrochlorothiazide. **[Weak Against]**
41. We suggest considering a switch from hydrochlorothiazide to chlorthalidone for patients whose hypertension is inadequately controlled on 50mg/day of hydrochlorothiazide. **[Weak For]**
42. We recommend a dosage of 12.5-25mg/day of chlorthalidone, 25-50mg/day of hydrochlorothiazide, or a dosage of 2.5mg/day immediate-release or 1.5- 2.5mg/day sustained-release (not currently available in the US) of indapamide. **[Strong For]**

K. Alternative or Supplementary Therapies

43. We recommend using the following as alternative therapies for patients who cannot tolerate thiazide-type diuretics, as supplementary therapies for patients who do not reach their hypertensive goals, or for those starting on combination therapy: **[Strong For]**
    a. Angiotensin-converting-enzyme inhibitors or angiotensin II receptor blockers (but not together)
    b. Long-acting dihydropyridine calcium channel blockers.

    (Modified from 2004 VA/DoD HTN CPG)

44. We recommend **against** the use of more than one of the following three drug classes together in the same patient: angiotensin-converting-enzyme inhibitors, angiotensin II receptor blockers, or direct renin inhibitors. **[Strong Against]**
45. We recommend additional therapy in refractory hypertension (for those who do not tolerate or are not adequately controlled with triple therapy [i.e., thiazide- type diuretics, ACEI or ARB, and CCBs] described in Recommendation 43) or as supplementary therapy in some clinical indications. Drug classes for consideration can include (not in priority order): **[Strong For]**
    a. Aldosterone/mineralocorticoid receptor antagonists (e.g., spironolactone, eplerenone)
    b. Other potassium-sparing diuretic (i.e., amiloride)

c. Alpha adrenergic blockers

d. Beta adrenergic blockers

e. Non-dihydropyridine calcium channel blockers

f. Combined alpha-beta adrenergic blockers

g. Peripherally acting antiadrenergic agents (reserpine, pending availability)

h. Direct acting vasodilators (e.g., hydralazine, minoxidil)

i. Centrally acting antiadrenergic drugs (e.g., clonidine, methyldopa).

46. We recommend **against** the use of alpha-adrenergic blockers as monotherapy, but this class of agents may be used as supplemental therapy or if warranted by comorbid conditions (e.g., symptomatic prostatic hypertrophy). **[Strong Against]**
    (Modified from 2004 VA/DoD HTN CPG)

L. Specific Populations

47. In patients with hypertension and chronic kidney disease (reduced kidney function with albuminuria), we recommend treatment with an angiotensin- converting-enzyme inhibitor, or angiotensin II receptor blocker for improving kidney outcomes. **[Strong For]**
    (Modified from 2004 VA/DoD HTN CPG)

48. In African American patients with hypertension, we recommend **against** using an angiotensin-converting-enzyme inhibitor or angiotensin II receptor blocker as monotherapy. **[Strong Against]**

49. In African American patients with hypertension and stage 1-3 chronic kidney disease, we suggest a combination of a thiazide-type diuretic (for cardiovascular protection) with either an angiotensin-converting-enzyme inhibitor or angiotensin II receptor blocker (for renal protection). **[Weak For]**

Table 2. Blood Pressure Thresholds to Initiate Pharmacologic Treatment and Treatment Goals by Patient Category and Age

			Category of Patient		
Patient Age		Blood Pressure (mmHg)[a]	General Population	Diabetic Population	History of cerebrovascular disease
18-29 years	Initiate	SBP	≥160 (Suggested)	≥160 (Suggested)[b]	≥140 (Suggested)
		DBP	≥90 (Suggested)	≥90 (Suggested)[b]	≥90 (Suggested)[b]
	Goals	SBP	<150 (Suggested)	<150 (Recommended) <140 (Suggested for those who tolerate medication)	<150 (Suggested)[b]
		DBP	<90 (Suggested)	<85 (Recommended)	<90 (Suggested)[b]
30-59 years	Initiate	SBP	≥160 (Suggested)	≥160 (Suggested)[b]	≥140 (Suggested)
		DBP	≥90 (Recommended)	≥90 (Recommended)[b]	≥90 (Recommended)[b]
	Goals	SBP	<150 (Suggested)	<150 (Recommended) <140 (Suggested for those who tolerate medication)	<150 (Suggested)[b]
		DBP	<90 (Recommended)	<85 (Recommended)	<90 (Recommended)[b]
>60 years	Initiate	SBP	≥160 (Recommended) 160 > SBP ≥ 140 (Suggested; using shared decision making)	≥160 (Recommended)[b] 160 > SBP ≥ 140 (Suggested; using shared decision making)[b]	≥140 (Suggested)
		DBP	≥90 (Recommended)	≥90 (Recommended)[b]	≥90 (Recommended)[b]
	Goals	SBP	<150 (Recommended)	<150 (Recommended) <140 (Suggested for those who tolerate medication)	<150 (Recommended)[b]
		DBP	<90 (Recommended)	<85 (Recommended)	<90 (Recommended)[b]

a Initiate pharmacologic treatment at SBP OR DBP threshold; once pharmacologic treatment is initiated, treat to SBP AND DBP goals.

b Evidence was not reviewed which indicated the blood pressure value should be different from the general population.

Table 3. Recommended Dosage for Selected Hypertension Drug Therapy

Drug [a]	Usual Dose Range	Comments [h]
Thiazide-type Diuretics		
Chlorthalidone[b]	12.5-25 mg daily	• May cause hyperuricemia/gout. • Monitor K+ levels. • May cause photosensitivity (rare).
HCTZ[b]	12.5-50 mg daily [f]	
Indapamide	IR: 2.5 mg daily SR: 1.25 – 2.5 mg daily	• SR not currently available in the US. • For complete drug information, review the manufacturer's prescribing information.
Angiotensin-Converting Enzyme Inhibitors		
Benazepril	10-40 mg/day (daily or divided bid)	• When pregnancy is detected, discontinue as soon as possible, due to potential for fetal and neonatal morbidity and death. Patients of childbearing potential should also be educated about the risks. • Do not use if history of angioedema. • Avoid concomitant use of ACEI with ARB or direct renin inhibitor due to increased risk of hypotension, syncope, increased K+, and changes in renal function (See recommendation #44). • Monitor K+ and kidney function; use caution if combined with, K+ sparing diuretic, or K+ supplement. • Consider interruption or discontinuation in patients who develop clinically significant decline in kidney function after initiation of therapy, until further work-up, as indicated (e.g., renal artery stenosis).
Enalapril	5-40 mg/day (daily or divided bid)	
Fosinopril	10-40 mg daily	
Lisinoprilb	10-40 mg daily	
Ramipril [b,c]	2.5-20 mg/day (daily or divided bid) (10 mg daily for CV risk prevention)	
Angiotensin II Receptor Blockers		
Azilsartan[c]	40-80 mg daily	• When pregnancy is detected, discontinue as soon as possible. Drugs that act directly on the renin angiotensin system can cause injury and death to the developing fetus. Patients of childbearing potential should also be educated about the risks. • Avoid concomitant use of ACEI with angiotensin II receptor blocker or direct renin inhibitor due to increased risk of hypotension, syncope, increased K+, and changes in renal function (See recommendation #44). • Monitor K+ and kidney function; use caution if combined with, K+ sparing diuretic, or K+ supplement. • Consider interruption or discontinuation in patients who develop clinically significant decline in kidney function after initiation of therapy, until further work-up, as indicated (e.g., renal artery stenosis).
Candesartan[c]	8-32 mg daily	
Eprosartan[c]	400-800 mg/daily (daily or divided bid)	
Irbesartan[c]	150-300 mg daily	
Losartan[b]	25-100 mg/day (daily or divided bid)	
Olmesartan[c]	20-40 mg daily	
Telmisartan[c]	20-80 mg daily	
Valsartan[b,d]	80-320 mg daily	
Long-Acting Dihydropyridine Calcium Channel Blockers		
Amlodipine[b]	2.5-10 mg daily	• Monitor adverse effects (DHP CCBs may cause ankle edema, dizziness, flushing, headache). • Use with caution in patients with hepatic or kidney dysfunction.
Felodipine	2.5-10 mg daily	
Nifedipine SR[b]	30-120 mg daily	
Aldosterone/mineralocorticoid Receptor Antagonists		
Eplerenone[c]	50-100 mg/day (daily or divided bid)	• Avoid use if hyperkalemia or severe kidney dysfunction. • Monitor K+ and kidney function; consider risk vs. benefit if combined with ACEI, ARB, K+ sparing diuretic, or K+ supplement. • Higher risk of gynecomastia with spironolactone than eplerenone.
Spironolactone[b]	25-50 mg/daily	

Drug [a]	Usual Dose Range	Comments [h]
Other Potassium-Sparing Diuretics		
Amiloride[c]	5-10 mg daily	• Avoid use if hyperkalemia or severe kidney dysfunction. • Helpful in reducing hypokalemia caused by thiazide diuretics.
Alpha-Adrenergic Blockers		
Doxazosin	1-16 mg daily	• Initiate at low doses (1 mg) • Administer 1st dose at bedtime to avoid syncope. • Avoid as monotherapy (See recommendation #46 in the CPG).
Prazosin	2-20 mg/day (Divided bid or tid)	
Terazosin[b]	1-20 mg daily	
Beta-Adrenergic Blockers		
Noncardioselective:		• Discontinue with slow taper over one week. • Avoid combination with non-DHP CCB due to increased risk of bradycardia. • As doses increase, cardioselectivity decreases. • Beta-blockers should be used cautiously in asthma
Propranolol	IR: 80-160 mg/day (divided bid)	
	SR: 80-160 mg daily	
Cardioselective:		
Atenolol[b]	25-100 mg daily (adjust dose in CKD)	
Metoprolol tartrate[b]	IR: 50-300 mg/day (daily or divided bid)	
Metoprolol succinate (XL) [b,d]	SR: 25-200 mg/day	
Long-Acting Non-Dihydropyridine Calcium Channel Blockers		
Verapamil SR[b]	120-480 mg divided daily-bid	• Verapamil may cause constipation; verapamil is contraindicated in AV node dysfunction (2nd or 3rd degree heart block), systolic HF and lower LV function.
Diltiazem SR[b]	120-540 mg daily	• Diltiazem may reduce sinus rate and cause heart block. • Use CCBs with caution in patients with liver or kidney dysfunction
Combined Alpha-beta adrenergic blockers		
Carvedilol	IR[b]: 12.5-50 mg/day (divided bid)	• Precautions for beta-blockers apply.
	SR[c]: 20-80 mg/day	
Labetalol[c]	200-800 mg/day (divided bid)	
Peripherally Acting Adrenergic Agents		
Reserpine	0.1-0.25 mg daily	• Monitor for sedation, and nasal congestion. • Reserpine not currently available in the U.S. due to changes in requirements for raw materials (re-verified 10/15/2014). Refer to FDA Drug Shortages for current information.
Direct Acting Vasodilators		
Minoxidil	2.5-100 mg/day (daily or divided bid)	• Direct acting vasodilators often need concomitant use of diuretic and beta-blocker to reduce edema and reflex tachycardia. • Monitor for hypertrichosis and pericardial effusions with minoxidil. • Monitor for headache and SLE (dose-related) with hydralazine.
Hydralazine[b]	50-200 mg/day (divided bid)	
Centrally Acting Antiadrenergic Drugs		
Clonidine Tablet[b]	0.1-0.8 mg/day (divided bid)	• Monitor for somnolence and dry mouth. Taper dose to discontinue. • Clonidine patches may be useful in selected Patients.
Clonidine patch	0.1-0.3 mg patch weekly	
Methyldopa	500-2,000 mg/day (divided bid)	

ACEI=angiotensin-converting enzyme inhibitor; ARB=angiotensin II receptor blocker; AV=atrioventricular; bid=twice daily; CCB=calcium channel blockers; CKD=chronic kidney disease; CV=cardiovascular; HCTZ=hydrochlorothiazide; HF=heart failure; IR=immediate-release; K+=potassium; LV=left ventricular; SLE=systemic lupus erythematosus; SR=sustained-release

a. Partial list; refer to http://www.pbm.va.gov/nationalformulary.asp for items available on the VA National Formulary (VANF) and refer to http://pec.ha.osd.mil/formulary_search.php?submenuheader=1 for items available on the DoD Uniform Formulary. All drugs listed are on the DoD Uniform Formulary.

b. DoD Basic Core Formulary (BCF) item.

c. Item not on VANF

d. Restricted to patients with chronic heart failure in VA.

e . Reserpine not currently available in the U.S. due to changes in requirements for raw materials (re-verified 10/15/2014; next available supply estimated March 2015). Refer to FDA Drug Shortages for current information.

f. 12.5 mg may be considered as an initial dose with titration recommended to 25 to 50mg daily; refer to Recommendation 42 and associated discussion for further information.

g. Indapamide SR not currently available in the US.

h. For complete drug information, review the manufacturer's prescribing information.

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