

# The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

## The JNC 7 Report

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FOR MORE THAN 3 DECADES, THE National Heart, Lung, and Blood Institute (NHLBI) has administered the National High Blood Pressure Education Program (NHBPEP) Coordinating Committee, a coalition of 39 major professional, public, and voluntary organizations and 7 federal agencies. One important function is to issue guidelines and advisories designed to increase awareness, prevention, treatment, and control of hypertension (high blood pressure [BP]). Since the publication of "The Sixth Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure"

See also pp 2534 and 2573.

"The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure" provides a new guideline for hypertension prevention and management. The following are the key messages: (1) In persons older than 50 years, systolic blood pressure (BP) of more than 140 mm Hg is a much more important cardiovascular disease (CVD) risk factor than diastolic BP; (2) The risk of CVD, beginning at 115/75 mm Hg, doubles with each increment of 20/10 mm Hg; individuals who are normotensive at 55 years of age have a 90% lifetime risk for developing hypertension; (3) Individuals with a systolic BP of 120 to 139 mm Hg or a diastolic BP of 80 to 89 mm Hg should be considered as prehypertensive and require health-promoting lifestyle modifications to prevent CVD; (4) Thiazide-type diuretics should be used in drug treatment for most patients with uncomplicated hypertension, either alone or combined with drugs from other classes. Certain high-risk conditions are compelling indications for the initial use of other antihypertensive drug classes (angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers,  $\beta$ -blockers, calcium channel blockers); (5) Most patients with hypertension will require 2 or more antihypertensive medications to achieve goal BP (<140/90 mm Hg, or <130/80 mm Hg for patients with diabetes or chronic kidney disease); (6) If BP is more than 20/10 mm Hg above goal BP, consideration should be given to initiating therapy with 2 agents, 1 of which usually should be a thiazide-type diuretic; and (7) The most effective therapy prescribed by the most careful clinician will control hypertension only if patients are motivated. Motivation improves when patients have positive experiences with and trust in the clinician. Empathy builds trust and is a potent motivator. Finally, in presenting these guidelines, the committee recognizes that the responsible physician's judgment remains paramount.

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(JNC VI) released in 1997,<sup>1</sup> many large-scale clinical trials have been published.

The decision to appoint a committee for "The Seventh Report of the Joint

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National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure" (JNC 7) was based on 4 factors: publication of many new hypertension observational studies and clinical trials; need for a new clear and concise guideline that would be useful for clinicians; need to simplify the classification of BP; and a clear recognition that the JNC reports were not being used to their maximum benefit. This JNC report is presented in 2 separate publications: this current succinct practical guide and a more comprehensive report to be published separately, which will provide a broader discussion and justification for the current recommendations. In presenting these guidelines, the committee recognizes that the responsible physician's judgment is paramount in managing his or her patients.

## METHODS

Since publication of the JNC VI report, the NHBPEP Coordinating Committee, chaired by the director of the NHLBI, has regularly reviewed and discussed the hypertension clinical trials at their biannual meetings. In many instances, the principal investigator of the larger studies has presented the information directly to the Coordinating Committee. The Committee's presentations and reviews are summarized and posted on the

NHLBI Web site.<sup>2</sup> In agreeing to commission a new report, the director requested that the Coordinating Committee members provide in writing a detailed rationale explaining the necessity to update the guidelines and to describe the critical issues and concepts to be considered for a new report. The JNC 7 chair was selected in addition to a 9-member executive committee appointed entirely from the NHBPEP Coordinating Committee membership. The NHBPEP Coordinating Committee served as members of 5 writing teams, each of which were co-chaired by 2 executive committee members.

The concepts identified by the NHBPEP Coordinating Committee membership were used to develop the report outline. A timeline was developed to complete and publish the work in 5 months. Based on the identified critical issues and concepts, the executive committee identified relevant Medical Subject Headings (MeSH) terms and keywords to further review the scientific literature. These MeSH terms were used to generate MEDLINE searches that focused on English-language, peer-reviewed scientific literature from January 1997 through April 2003. Various systems of grading the evidence were considered and the classification scheme used in JNC VI and other NHBPEP clinical guidelines was se-

lected,<sup>3,4</sup> which classifies studies in a process adapted from Last and Abramson.<sup>5</sup>

The executive committee met on 6 occasions, 2 of which included meetings with the entire Coordinating Committee. The writing teams also met by teleconference and used electronic communications to develop the report. Twenty-four drafts were created and reviewed in a reiterative fashion. At its meetings, the executive committee used a modified nominal group process to identify and resolve issues. The NHBPEP Coordinating Committee reviewed the penultimate draft and provided written comments to the executive committee. In addition, 33 national hypertension leaders reviewed and commented on the document. The NHBPEP Coordinating Committee approved the JNC 7 report.

## RESULTS

### Classification of BP

TABLE 1 provides a classification of BP for adults aged 18 years or older. The classification is based on the mean of 2 or more properly measured seated BP readings on each of 2 or more office visits. In contrast with the classification provided in the JNC VI report, a new category designated prehypertension has been added, and stages 2 and 3 hypertension have been combined.

**Table 1.** Classification and Management of Blood Pressure for Adults Aged 18 Years or Older

BP Classification	Systolic BP, mm Hg*		Diastolic BP, mm Hg*		Lifestyle Modification	Management*	
						Initial Drug Therapy	
						Without Compelling Indication	With Compelling Indications†
Normal	<120	and	<80	Encourage			
Prehypertension	120-139	or	80-89	Yes	No antihypertensive drug indicated	Drug(s) for the compelling indications‡	
Stage 1 hypertension	140-159	or	90-99	Yes	Thiazide-type diuretics for most; may consider ACE inhibitor, ARB, $\beta$ -blocker, CCB, or combination	Drug(s) for the compelling indications Other antihypertensive drugs (diuretics, ACE inhibitor, ARB, $\beta$ -blocker, CCB) as needed	
Stage 2 hypertension	$\geq$ 160	or	$\geq$ 100	Yes	2-Drug combination for most (usually thiazide-type diuretic and ACE inhibitor or ARB or $\beta$ -blocker or CCB)§	Drug(s) for the compelling indications Other antihypertensive drugs (diuretics, ACE inhibitor, ARB, $\beta$ -blocker, CCB) as needed	

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; BP, blood pressure; CCB, calcium channel blocker.

\*Treatment determined by highest BP category.

†See Table 6.

‡Treat patients with chronic kidney disease or diabetes to BP goal of less than 130/80 mm Hg.

§Initial combined therapy should be used cautiously in those at risk for orthostatic hypotension.

**Table 2.** Trends in Awareness, Treatment, and Control of High Blood Pressure in Adults With Hypertension Aged 18 to 74 Years\*

	National Health and Nutrition Examination Surveys, Weighted %			
	II (1976-1980)	III (Phase 1, 1988-1991)	III (Phase 2, 1991-1994)	1999-2000
Awareness	51	73	68	70
Treatment	31	55	54	59
Control†	10	29	27	34

\*Data for 1999-2000 were computed (M. Wolz, unpublished data, 2003) from the National Heart, Lung, and Blood Institute and data for National Health and Nutrition Examination Surveys II and III (phases 1 and 2) are from "The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure."<sup>11</sup> High blood pressure is systolic blood pressure of at least 140 mm Hg or diastolic blood pressure of at least 90 mm Hg or taking antihypertensive medication.

†Systolic blood pressure of less than 140 mm Hg and diastolic blood pressure of less than 90 mm Hg.

Patients with prehypertension are at increased risk for progression to hypertension; those in the 130/80 to 139/89 mm Hg BP range are at twice the risk to develop hypertension as those with lower values.<sup>6</sup>

### Cardiovascular Disease Risk

Hypertension affects approximately 50 million individuals in the United States and approximately 1 billion individuals worldwide. As the population ages, the prevalence of hypertension will increase even further unless broad and effective preventive measures are implemented. Recent data from the Framingham Heart Study<sup>7</sup> suggest that individuals who are normotensive at 55 years of age have a 90% lifetime risk for developing hypertension.

The relationship between BP and risk of cardiovascular disease (CVD) events is continuous, consistent, and independent of other risk factors. The higher the BP, the greater the chance of myocardial infarction, heart failure (HF), stroke, and kidney disease. For individuals aged 40 to 70 years, each increment of 20 mm Hg in systolic BP or 10 mm Hg in diastolic BP doubles the risk of CVD across the entire BP range from 115/75 to 185/115 mm Hg.<sup>8</sup>

The classification prehypertension, introduced in this report (Table 1), recognizes this relationship and signals the need for increased education of health care professionals and the public to decrease BP levels and prevent the development of hypertension in the general population.<sup>9</sup> Hypertension prevention strategies are available to achieve

this goal (see "Lifestyle Modifications" section).

### Benefits of Lowering BP

In clinical trials, antihypertensive therapy has been associated with 35% to 40% mean reductions in stroke incidence; 20% to 25% in myocardial infarction; and more than 50% in HF.<sup>10</sup> It is estimated that in patients with stage 1 hypertension (systolic BP, 140-159 mm Hg and/or diastolic BP, 90-99 mm Hg) and additional cardiovascular risk factors, achieving a sustained 12-mm Hg decrease in systolic BP for 10 years will prevent 1 death for every 11 patients treated. In the presence of CVD or target-organ damage, only 9 patients would require this BP reduction to prevent a death.<sup>11</sup>

### BP Control Rates

Hypertension is the most common primary diagnosis in the United States with 35 million office visits as the primary diagnosis.<sup>12</sup> Current control rates (systolic BP <140 mm Hg and diastolic BP <90 mm Hg), although improved, are still far below the Healthy People 2010 goal of 50%; 30% are still unaware they have hypertension (TABLE 2). In the majority of patients, controlling systolic hypertension, which is a more important CVD risk factor than diastolic BP except in patients younger than 50 years<sup>13</sup> and occurs much more commonly in older persons, has been considerably more difficult than controlling diastolic hypertension. Recent clinical trials have demonstrated that effective BP control can be achieved in most patients

with hypertension, but the majority will require 2 or more antihypertensive drugs.<sup>14,15</sup> When physicians fail to prescribe lifestyle modifications, adequate antihypertensive drug doses, or appropriate drug combinations, inadequate BP control may result.

### Accurate BP Measurement in the Office

The auscultatory method of BP measurement with a properly calibrated and validated instrument should be used.<sup>16</sup> Patients should be seated quietly for at least 5 minutes in a chair rather than on an examination table, with feet on the floor and arm supported at heart level. Measurement of BP in the standing position is indicated periodically, especially in those at risk for postural hypotension. An appropriate-sized cuff (cuff bladder encircling at least 80% of the arm) should be used to ensure accuracy. At least 2 measurements should be made. Systolic BP is the point at which the first of 2 or more sounds is heard (phase 1) and diastolic BP is the point before the disappearance of sounds (phase 5). Physicians should provide to patients, verbally and in writing, their specific BP numbers and BP goals.

### Ambulatory BP Monitoring

Ambulatory BP monitoring<sup>17</sup> provides information about BP during daily activities and sleep. Ambulatory BP monitoring is warranted for evaluation of (white-coat) hypertension in the absence of target-organ injury. It is also helpful to assess patients with apparent drug resistance, hypotensive symptoms with antihypertensive medications, episodic hypertension, and autonomic dysfunction. The ambulatory BP values are usually lower than clinic readings. Awake hypertensive individuals have a mean BP of more than 135/85 mm Hg and during sleep, more than 120/75 mm Hg. The level of BP using ambulatory BP monitoring correlates better than office measurements with target-organ injury.<sup>18</sup> Ambulatory BP monitoring also provides a measure of the percentage of BP readings that are elevated, the overall BP load, and the extent of BP reduction dur-

ing sleep. In most individuals, BP decreases by 10% to 20% during the night; those in whom such decreases are not present are at increased risk for cardiovascular events.

### Self-measurement of BP

Blood pressure self-measurements may benefit patients by providing information on response to antihypertensive medication, improving patient adherence with therapy,<sup>19</sup> and in evaluating white-coat hypertension. Individuals with a mean BP of more than 135/85 mm Hg measured at home are generally considered to be hypertensive. Home measurement devices should be checked regularly for accuracy.

### Patient Evaluation

Evaluation of patients with documented hypertension has 3 objectives: (1) to assess lifestyle and identify other cardiovascular risk factors or concomitant disorders that may affect prognosis and guide treatment (BOX 1); (2) to reveal identifiable causes of high BP (BOX 2); and (3) to assess the presence or absence of target-organ damage and CVD. The data needed are acquired through medical history, physical examination, routine laboratory tests, and other diagnostic procedures.

The physical examination should include an appropriate measurement of BP, with verification in the contralateral arm; examination of the optic fundi; body mass index calculated as weight in kilograms divided by the square of height in meters (measurement of waist circumference also may be useful); auscultation for carotid, abdominal, and femoral bruits; palpation of the thyroid gland; thorough examination of the heart and lungs; examination of the abdomen for enlarged kidneys, masses, and abnormal aortic pulsation; palpation of the lower extremities for edema and pulses; and neurological assessment.

### Laboratory Tests and Other Diagnostic Procedures

Routine laboratory tests recommended before initiating therapy include an electrocardiogram; urinary-

#### Box 1. Cardiovascular Risk Factors\*

##### Major Risk Factors

- Hypertension†
- Cigarette smoking
- Obesity (BMI  $\geq 30$ )†
- Physical inactivity
- Dyslipidemia†
- Diabetes mellitus†
- Microalbuminuria or estimated GFR  $< 60$  mL/min
- Age ( $> 55$  years for men,  $> 65$  years for women)
- Family history of premature cardiovascular disease (men  $< 55$  years or women 65 years)

##### Target-Organ Damage

- Heart
  - Left ventricular hypertrophy
  - Angina or prior myocardial infarction
  - Prior coronary revascularization
  - Heart failure
- Brain
  - Stroke or transient ischemic attack
- Chronic kidney disease
- Peripheral arterial disease
- Retinopathy

\*BMI indicates body mass index calculated as weight in kilograms divided by the square of height in meters; GFR, glomerular filtration rate.

†Components of the metabolic syndrome.

sis; blood glucose and hematocrit; serum potassium, creatinine (or the corresponding estimated glomerular filtration rate), and calcium<sup>20</sup>; and a lipid profile (after a 9- to 12-hour fast) that includes high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides. Optional tests include measurement of urinary albumin excretion or albumin/creatinine ratio. More extensive testing for identifiable causes is not indicated generally unless BP control is not achieved.

### Treatment

**Goals of Therapy.** The ultimate public health goal of antihypertensive therapy is the reduction of cardiovascular and renal morbidity and mortality. Because most patients with hypertension, especially those aged at least 50 years, will reach the diastolic BP goal once systolic BP is at goal, the primary focus should be on achieving the systolic BP goal (FIGURE). Treating systolic BP and diastolic BP to targets that are less than 140/90 mm Hg is associ-

#### Box 2. Identifiable Causes of Hypertension

- Sleep apnea
- Drug-induced or drug-related (see Box 3)
- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Chronic steroid therapy and Cushing syndrome
- Pheochromocytoma
- Coarctation of the aorta
- Thyroid or parathyroid disease

ated with a decrease in CVD complications. In patients with hypertension with diabetes or renal disease, the BP goal is less than 130/80 mm Hg.<sup>21,22</sup>

**Lifestyle Modifications.** Adoption of healthy lifestyles by all individuals is critical for the prevention of high BP and an indispensable part of the management of those with hypertension. Major lifestyle modifications shown to lower BP include weight reduction in

those individuals who are overweight or obese<sup>23,24</sup>; adoption of Dietary Approaches to Stop Hypertension eating plan,<sup>25</sup> which is rich in potassium and calcium<sup>26</sup>; dietary sodium reduction<sup>25-27</sup>; physical activity<sup>28,29</sup>; and moderation of alcohol consumption

(TABLE 3).<sup>30</sup> Lifestyle modifications decrease BP, enhance antihypertensive drug efficacy, and decrease cardiovascular risk. For example, a 1600-mg sodium Dietary Approaches to Stop Hypertension eating plan has effects similar to single drug therapy.<sup>25</sup> Combinations

of 2 or more lifestyle modifications can achieve even better results.

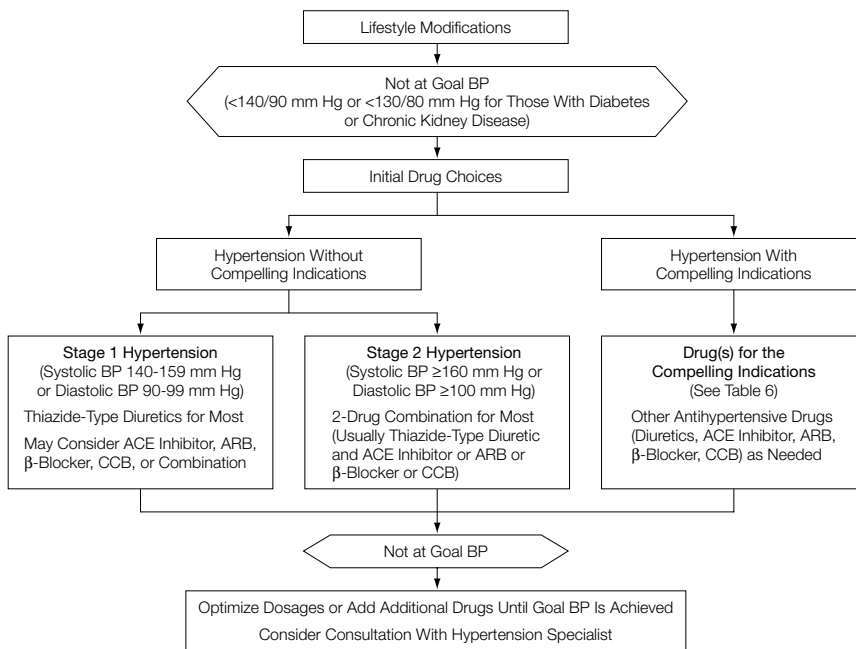
**Pharmacologic Treatment.** Excellent clinical trial outcome data prove that lowering BP with several classes of drugs, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs),  $\beta$ -blockers, calcium channel blockers (CCBs), and thiazide-type diuretics, will all reduce the complications of hypertension.<sup>10,31-37</sup> TABLE 4 and TABLE 5 provide a list of commonly used antihypertensive agents.

Thiazide-type diuretics have been the basis of antihypertensive therapy in most outcome trials.<sup>37</sup> In these trials, including the recently published Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial,<sup>33</sup> diuretics have been virtually unsurpassed in preventing the cardiovascular complications of hypertension. The exception is the Second Australian National Blood Pressure trial<sup>36</sup> that reported slightly better outcomes in white men with a regimen that began with an ACE inhibitor compared with one starting with a diuretic. Diuretics enhance the antihypertensive efficacy of multidrug regimens, can be useful in achieving BP control, and are more affordable than other antihypertensive agents. Despite these findings, diuretics remain underused.<sup>39</sup>

Thiazide-type diuretics should be used as initial therapy for most patients with hypertension, either alone or in combination with 1 of the other classes (ACE inhibitors, ARBs,  $\beta$ -blockers, CCBs) demonstrated to be beneficial in randomized controlled outcome trials. The list of compelling indications requiring the use of other antihypertensive drugs as initial therapy are listed in TABLE 6. If a drug is not tolerated or is contraindicated, then 1 of the other classes proven to reduce cardiovascular events should be used instead.

**Achieving BP Control in Individual Patients.** Most patients with hypertension will require 2 or more antihypertensive medications to achieve their BP goals.<sup>14,15</sup> Addition of a second drug from a different class should be initiated when use of a single drug in ad-

**Figure.** Algorithm for Treatment of Hypertension



BP indicates blood pressure; ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; and CCB, calcium channel blocker.

**Table 3.** Lifestyle Modifications to Manage Hypertension\*

Modification	Recommendation	Approximate Systolic BP Reduction, Range
Weight reduction	Maintain normal body weight (BMI, 18.5-24.9)	5-20 mm Hg/10-kg weight loss <sup>23,24</sup>
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat	8-14 mm Hg <sup>25,26</sup>
Dietary sodium reduction	Reduce dietary sodium intake to no more than 100 mEq/L (2.4 g sodium or 6 g sodium chloride)	2-8 mm Hg <sup>25,27</sup>
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week)	4-9 mm Hg <sup>28,29</sup>
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks per day (1 oz or 30 mL ethanol [eg, 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey]) in most men and no more than 1 drink per day in women and lighter-weight persons	2-4 mm Hg <sup>30</sup>

Abbreviations: BMI, body mass index calculated as weight in kilograms divided by the square of height in meters; BP, blood pressure; DASH, Dietary Approaches to Stop Hypertension.

\*For overall cardiovascular risk reduction, stop smoking. The effects of implementing these modifications are dose and time dependent and could be higher for some individuals.

equate doses fails to achieve the BP goal. When BP is more than 20/10 mm Hg above goal, consideration should be given to initiating therapy with 2 drugs, either as separate prescriptions or in fixed-dose combinations (Figure). The initiation of drug therapy with more than 1 agent may increase the likelihood of achieving the BP goal in a more timely fashion, but particular caution is advised in those at risk for orthostatic hypotension, such as patients with diabetes, autonomic dysfunction, and some older persons. Use of generic drugs or combination drugs should be considered to reduce prescription costs.

**Follow-up and Monitoring.** Once antihypertensive drug therapy is initiated, most patients should return for follow-up and adjustment of medications at approximately monthly intervals until the BP goal is reached. More frequent visits will be necessary for patients with stage 2 hypertension or with complicating comorbid conditions. Serum potassium and creatinine should be monitored at least 1 to 2 times per year.<sup>60</sup> After BP is at goal and stable, follow-up visits can usually be at 3- to 6-month intervals. Comorbidities, such as HF, associated diseases, such as diabetes, and the need for laboratory tests influence the frequency of visits. Other cardiovascular risk factors should be treated to their respective goals, and tobacco avoidance should be promoted vigorously. Low-dose aspirin therapy should be considered only when BP is controlled, because the risk of hemorrhagic stroke is increased in patients with uncontrolled hypertension.<sup>61</sup>

### Special Considerations

The patient with hypertension and certain comorbidities requires special attention and follow-up by the clinician.

**Compelling Indications.** Table 6 describes compelling indications that require certain antihypertensive drug classes for high-risk conditions. The drug selections for these compelling indications are based on favorable outcome data from clinical trials. Combination of agents may be required. Other management considerations include medica-

tions already in use, tolerability, and desired BP targets. In many cases, specialist consultation may be indicated.

**Ischemic Heart Disease.** Ischemic heart disease is the most common form of target-organ damage associated with hypertension. In patients with hypertension and stable angina pectoris, the first drug of choice is usually a  $\beta$ -blocker; alternatively, long-acting

CCBs can be used.<sup>1</sup> In patients with acute coronary syndromes (unstable angina or myocardial infarction), hypertension should be treated initially with  $\beta$ -blockers and ACE inhibitors,<sup>49</sup> with addition of other drugs as needed for BP control. In patients with postmyocardial infarction, ACE inhibitors,  $\beta$ -blockers, and aldosterone antagonists have proven to be most benefi-

**Table 4.** Oral Antihypertensive Drugs\*

Class	Drug (Trade Name)	Usual Dose, Range, mg/d	Daily Frequency
Thiazide diuretics	Chlorothiazide (Diuril)	125-500	1
	Chlorthalidone (generic)	12.5-25	1
	Hydrochlorothiazide (Microzide, HydroDIURIL)†	12.5-50	1
	Polythiazide (Renese)	2-4	1
	Indapamide (Lozol)†	1.25-2.5	1
	Metolazone (Mykrox)	0.5-1.0	1
Loop diuretics	Metolazone (Zaroxolyn)	2.5-5	1
	Bumetanide (Bumex)†	0.5-2	2
	Furosemide (Lasix)†	20-80	2
Potassium-sparing diuretics	Torsemide (Demadex)†	2.5-10	1
	Amiloride (Midamor)†	5-10	1-2
Aldosterone-receptor blockers	Triamterene (Dyrenium)	50-100	1-2
	Eplerenone (Inspra)	50-100	1-2
Aldosterone-receptor blockers	Spironolactone (Aldactone)†	25-50	1-2
	$\beta$ -Blockers	Atenolol (Tenormin)†	50-100
Betaxolol (Kerlone)†		5-20	1
Bisoprolol (Zebeta)†		2.5-10	1
Metoprolol (Lopressor)†		50-100	1-2
Metoprolol extended release (Toprol XL)		50-100	1
Nadolol (Corgard)†		40-120	1
Propranolol (Inderal)†		40-160	2
Propranolol long-acting (Inderal LA)†		60-180	1
Timolol (Blocadren)†		20-40	2
$\beta$ -Blockers with intrinsic sympathomimetic activity		Acebutolol (Sectral)†	200-800
	Penbutolol (Levitol)	10-40	1
	Pindolol (generic)	10-40	2
Combined $\alpha$ - and $\beta$ -blockers	Carvedilol (Coreg)	12.5-50	2
	Labetalol (Normodyne, Trandate)†	200-800	2
ACE inhibitors	Benazepril (Lotensin)†	10-40	1-2
	Captopril (Capoten)†	25-100	2
	Enalapril (Vasotec)†	2.5-40	1-2
	Fosinopril (Monopril)	10-40	1
	Lisinopril (Prinivil, Zestril)†	10-40	1
	Moexipril (Univasc)	7.5-30	1
	Perindopril (Aceon)	4-8	1-2
	Quinapril (Accupril)	10-40	1
	Ramipril (Altace)	2.5-20	1
	Trandolapril (Mavik)	1-4	1

(continued)

cial.<sup>50,52,53,62</sup> Intensive lipid management and aspirin therapy are also indicated.

**Heart Failure.** Heart failure, in the form of systolic or diastolic ventricular dysfunction, results primarily from systolic hypertension and ischemic heart disease. Fastidious BP and cholesterol control are the primary preventive measures for those at high risk for HF.<sup>40</sup> In asymptomatic individuals with demonstrable ventricular dysfunction, ACE inhibitors and  $\beta$ -blockers are recommended.<sup>52,62</sup> For those with

symptomatic ventricular dysfunction or end-stage heart disease, ACE inhibitors,  $\beta$ -blockers, ARBs, and aldosterone blockers are recommended along with loop diuretics.<sup>40,41-48</sup>

**Diabetic Hypertension.** Combinations of 2 or more drugs are usually needed to achieve the target BP goal of less than 130/80 mm Hg.<sup>21,22</sup> Thiazide diuretics,  $\beta$ -blockers, ACE inhibitors, ARBs, and CCBs are beneficial in reducing CVD and stroke incidence in patients with diabetes.<sup>33,54,63</sup> The ACE inhibitor- or ARB-based treatments

favorably affect the progression of diabetic nephropathy and reduce albuminuria,<sup>55,56</sup> and ARBs have been shown to reduce progression to macroalbuminuria.<sup>56,57</sup>

**Chronic Kidney Disease.** In patients with chronic kidney disease, defined by either (1) reduced excretory function with an estimated glomerular filtration rate of less than 60 mL/min per 1.73 m<sup>2</sup> (corresponding approximately to a creatinine of >1.5 mg/dL [ $>132.6$   $\mu$ mol/L] in men or >1.3 mg/dL [ $>114.9$   $\mu$ mol/L] in women)<sup>20</sup> or (2) the presence of albuminuria (>300 mg/d or 200 mg albumin per gram of creatinine), therapeutic goals are to slow deterioration of renal function and prevent CVD. Hypertension appears in the majority of these patients and they should receive aggressive BP management, often with 3 or more drugs to reach target BP values of less than 130/80 mm Hg.<sup>59,64</sup>

The ACE inhibitors and ARBs have demonstrated favorable effects on the progression of diabetic and nondiabetic renal disease.<sup>55-59,64</sup> A limited increase in serum creatinine of as much as 35% above baseline with ACE inhibitors or ARBs is acceptable and not a reason to withhold treatment unless hyperkalemia develops.<sup>65</sup> With advanced renal disease (estimated glomerular filtration rate <30 mL/min per 1.73 m<sup>2</sup>, corresponding to a serum creatinine of 2.5-3.0 mg/dL [221-265  $\mu$ mol/L]), increasing doses of loop diuretics are usually needed in combination with other drug classes.

**Cerebrovascular Disease.** The risks and benefits of acute lowering of BP during an acute stroke are still unclear; control of BP at intermediate levels (approximately 160/100 mm Hg) is appropriate until the condition has stabilized or improved. Recurrent stroke rates are lowered by the combination of an ACE inhibitor and thiazide-type diuretic.<sup>35</sup>

**Other Special Situations.** *Minority Populations.* Blood pressure control rates vary in minority populations and are lowest in Mexican Americans and Native Americans.<sup>1</sup> In general, the treatment of hypertension is similar for all demographic groups, but socioeco-

**Table 4.** Oral Antihypertensive Drugs (cont)\*

Class	Drug (Trade Name)	Usual Dose, Range, mg/d	Daily Frequency
Angiotensin II antagonists	Candesartan (Atacand)	8-32	1
	Eprosartan (Tevetan)	400-800	1-2
	Irbesartan (Avapro)	150-300	1
	Losartan (Cozaar)	25-100	1-2
	Olmesartan (Benicar)	20-40	1
	Telmisartan (Micardis)	20-80	1
	Valsartan (Diovan)	80-320	1
Calcium channel blockers—non-dihydropyridines	Diltiazem extended release (Cardizem CD, Dilacor XR, Tiazac)†	180-420	1
	Diltiazem extended release (Cardizem LA)	120-540	1
	Verapamil immediate release (Calan, Isoptin)†	80-320	2
	Verapamil long-acting (Calan SR, Isoptin SR)†	120-360	1-2
	Verapamil-coer (Covera HS, Verelan PM)	120-360	1
Calcium channel blockers—dihydropyridines	Amlodipine (Norvasc)	2.5-10	1
	Felodipine (Plendil)	2.5-20	1
	Isradipine (Dynacirc CR)	2.5-10	2
	Nicardipine sustained release (Cardene SR)	60-120	2
	Nifedipine long-acting (Adalat CC, Procardia XL)	30-60	1
	Nisoldipine (Sular)	10-40	1
$\alpha_1$ -Blockers	Doxazosin (Cardura)	1-16	1
	Prazosin (Minipress)†	2-20	2-3
	Terazosin (Hytrin)	1-20	1-2
Central $\alpha_2$ -agonists and other centrally acting drugs	Clonidine (Catapres)†	0.1-0.8	2
	Clonidine patch (Catapres TTS)	0.1-0.3	1 weekly
	Methyldopa (Aldomet)†	250-1000	2
	Reserpine (generic)	0.05-0.25	1‡
	Guanfacine (generic)	0.5-2	1
Direct vasodilators	Hydralazine (Apresoline)†	25-100	2
	Minoxidil (Loniten)†	2.5-80	1-2

Abbreviation: ACE, angiotensin-converting enzyme.

\*Dosages may vary from those listed in the *Physicians' Desk Reference*,<sup>38</sup> which may be consulted for additional information.

†Are now or will soon become available in generic preparations.

‡A 0.1-mg dose may be given every other day to achieve this dosage.

nomic factors and lifestyle may be important barriers to BP control in some minority patients. The prevalence, severity, and impact of hypertension are increased in blacks, who also demonstrate somewhat reduced BP responses to monotherapy with  $\beta$ -blockers, ACE inhibitors, or ARBs compared with diuretics or CCBs. These differential responses are largely eliminated by drug combinations that include adequate doses of a diuretic. Angiotensin-converting enzyme inhibitor–induced angioedema occurs 2 to 4 times more frequently in black patients with hypertension than in other groups.<sup>33</sup>

**Obesity and the Metabolic Syndrome.** Obesity (body mass index  $\geq 30$ ) is an increasingly prevalent risk factor for the development of hypertension and CVD. The Adult Treatment Panel III guideline for cholesterol management defines the metabolic syndrome as the presence of 3 or more of the following conditions: abdominal obesity (waist circumference  $>102$  cm [ $>40$  in] in men or  $>89$  cm [ $>35$  in] in women), glucose intolerance (fasting glucose  $\geq 110$  mg/dL [ $\geq 6.1$  mmol/L]), BP of at least 130/85 mm Hg, high triglycerides ( $\geq 150$  mg/dL [ $\geq 1.70$  mmol/L]), or low high-density lipoprotein cholesterol ( $<40$  mg/dL [ $<1.04$  mmol/L] in men or  $<50$  mg/dL [ $<1.30$  mmol/L] in women).<sup>66</sup> Intensive lifestyle modification should be pursued in all individuals with the metabolic syndrome, and appropriate drug therapy should be instituted for each of its components as indicated.

**Left Ventricular Hypertrophy.** Left ventricular hypertrophy is an independent risk factor that increases the risk of subsequent CVD. Regression of left ventricular hypertrophy occurs with aggressive BP management, including weight loss, sodium restriction, and treatment with all classes of antihypertensive agents except the direct vasodilators, hydralazine and minoxidil.<sup>1,67</sup>

**Peripheral Arterial Disease.** Peripheral arterial disease is equivalent in risk to ischemic heart disease. Any class of antihypertensive drugs can be used in most patients with peripheral arterial disease. Other risk factors should be

managed aggressively and aspirin should be used.

**Hypertension in Older Individuals.** Hypertension occurs in more than two thirds of individuals after age 65 years.<sup>1</sup> This is also the population with the low-

est rates of BP control.<sup>68</sup> Treatment recommendations for older individuals with hypertension, including those who have isolated systolic hypertension, should follow the same principles outlined for the general care of hyperten-

**Table 5.** Combination Drugs for Hypertension

Combination Type	Fixed-Dose Combination, mg*	Trade Name
ACE inhibitors and CCBs	Amlodipine/benazepril hydrochloride (2.5/10, 5/10, 5/20, 10/20)	Lotrel
	Enalapril maleate/felodipine (5/5)	Lexxel
	Trandolapril/verapamil (2/180, 1/240, 2/240, 4/240)	Tarka
ACE inhibitors and diuretics	Benazepril/hydrochlorothiazide (5/6.25, 10/12.5, 20/12.5, 20/25)	Lotensin HCT
	Captopril/hydrochlorothiazide (25/15, 25/25, 50/15, 50/25)	Capozide
	Enalapril maleate/hydrochlorothiazide (5/12.5, 10/25)	Vaseretic
	Lisinopril/hydrochlorothiazide (10/12.5, 20/12.5, 20/25)	Prinzide
	Moexipril HCl/hydrochlorothiazide (7.5/12.5, 15/25)	Uniretic
	Quinapril HCl/hydrochlorothiazide (10/12.5, 20/12.5, 20/25)	Accuretic
ARBs and diuretics	Candesartan cilexetil/hydrochlorothiazide (16/12.5, 32/12.5)	Atacand HCT
	Eprosartan mesylate/hydrochlorothiazide (600/12.5, 600/25)	Teveten HCT
	Irbesartan/hydrochlorothiazide (75/12.5, 150/12.5, 300/12.5)	Avalide
	Losartan potassium/hydrochlorothiazide (50/12.5, 100/25)	Hyzaar
	Telmisartan/hydrochlorothiazide (40/12.5, 80/12.5)	Micardis HCT
	Valsartan/hydrochlorothiazide (80/12.5, 160/12.5)	Diovan HCT
$\beta$ -Blockers and diuretics	Atenolol/chlorthalidone (50/25, 100/25)	Tenoretic
	Bisoprolol fumarate/hydrochlorothiazide (2.5/6.25, 5/6.25, 10/6.25)	Ziac
	Propranolol LA/hydrochlorothiazide (40/25, 80/25)	Inderide
	Metoprolol tartrate/hydrochlorothiazide (50/25, 100/25)	Lopressor HCT
	Nadolol/bendroflumethiazide (40/5, 80/5)	Corzide
	Timolol maleate/hydrochlorothiazide (10/25)	Timolide
Centrally acting drug and diuretic	Methyldopa/hydrochlorothiazide (250/15, 250/25, 500/30, 500/50)	Aldoril
	Reserpine/chlorothiazide (0.125/250, 0.25/500)	Diupres
	Reserpine/hydrochlorothiazide (0.125/25, 0.125/50)	Hydropres
Diuretic and diuretic	Amiloride HCl/hydrochlorothiazide (5/50)	Moduretic
	Spironolactone/hydrochlorothiazide (25/25, 50/50)	Aldactone
	Triamterene/hydrochlorothiazide (37.5/25, 50/25, 75/50)	Dyazide, Maxzide

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; CCB, calcium channel blocker; HCl, hydrochloride; HCT, hydrochlorothiazide; LA, long-acting.

\*Some drug combinations are available in multiple fixed doses. Each drug dose is reported in milligrams.

sion. In many individuals, lower initial drug doses may be indicated to avoid symptoms; however, standard doses and multiple drugs are needed in the majority of older individuals to reach appropriate BP targets.

**Postural Hypotension.** A decrease in standing systolic BP of more than 10 mm Hg, when associated with dizziness or fainting, is more frequent in older patients with systolic hypertension, diabetes, and those taking diuretics, venodilators (eg, nitrates,  $\alpha$ -blockers, and sildenafil-like drugs), and some psychotropic drugs. Blood pressure in these individuals should also be monitored in the upright position. Caution should be used to avoid volume depletion and excessively rapid dose titration of antihypertensive drugs.

**Dementia.** Dementia and cognitive impairment occur more commonly in patients with hypertension. Reduced progression of cognitive impairment may occur with effective antihypertensive therapy.<sup>69,70</sup>

**Hypertension in Women.** Oral contraceptives may increase BP and the risk of hypertension increases with duration of use. Women taking oral contraceptives

should have their BP checked regularly. Development of hypertension is a reason to consider other forms of contraception. In contrast, hormone replacement therapy does not raise BP.<sup>71</sup>

Women with hypertension who become pregnant should be followed carefully because of increased risks to mother and fetus. Methyldopa,  $\beta$ -blockers, and vasodilators are preferred medications for the safety of the fetus.<sup>72</sup> Angiotensin-converting enzyme inhibitors and ARBs should not be used during pregnancy because of the potential for fetal defects and should be avoided in women who are likely to become pregnant. Preeclampsia, which occurs after the 20th gestation week of pregnancy, is characterized by new-onset or worsening hypertension, albuminuria, and hyperuricemia, sometimes with coagulation abnormalities. In some patients, preeclampsia may develop into a hypertensive urgency or emergency and may require hospitalization, intensive monitoring, early fetal delivery, and parenteral antihypertensive and anticonvulsant therapy.<sup>72</sup>

**Children and Adolescents.** In children and adolescents, hypertension is

defined as BP that is, on repeated measurement, at the 95th percentile or greater adjusted for age, height, and sex.<sup>73</sup> The fifth Korotkoff sound is used to define diastolic BP. Clinicians should be alert to the possibility of identifiable causes of hypertension in younger children (ie, kidney disease, coarctation of the aorta). Lifestyle interventions are strongly recommended, with pharmacologic therapy instituted for higher levels of BP, or if there is insufficient response to lifestyle modifications.<sup>74</sup> Choices of antihypertensive drugs are similar in children and adults, but effective doses for children are often smaller and should be adjusted carefully. Angiotensin-converting enzyme inhibitors and ARBs should not be used in pregnant or sexually active girls. Uncomplicated hypertension should not be a reason to restrict children from participating in physical activities, particularly because long-term exercise may lower BP. Use of anabolic steroids should be strongly discouraged. Vigorous interventions also should be conducted for other existing modifiable risk factors (eg, smoking).

**Hypertensive Urgencies and Emergencies.** Patients with marked BP eleva-

**Table 6.** Clinical Trial and Guideline Basis for Compelling Indications for Individual Drug Classes

High-Risk Conditions With Compelling Indication*	Recommended Drugs						Clinical Trial Basis†
	Diuretic	$\beta$ -Blocker	ACE Inhibitor	ARB	CCB	Aldosterone Antagonist	
Heart failure	•	•	•	•		•	ACC/AHA Heart Failure Guideline, <sup>40</sup> MERIT-HF, <sup>41</sup> COPERNICUS, <sup>42</sup> CIBIS, <sup>43</sup> SOLVD, <sup>44</sup> AIRE, <sup>45</sup> TRACE, <sup>46</sup> ValHEFT, <sup>47</sup> RALES <sup>48</sup>
Post-myocardial infarction		•	•			•	ACC/AHA Post-MI Guideline, <sup>49</sup> BHAT, <sup>50</sup> SAVE, <sup>51</sup> Capricorn, <sup>52</sup> EPHEUS <sup>53</sup>
High coronary disease risk	•	•	•		•		ALLHAT, <sup>33</sup> HOPE, <sup>34</sup> ANBP2, <sup>36</sup> LIFE, <sup>32</sup> CONVINC <sup>31</sup>
Diabetes	•	•	•	•	•		NKF-ADA Guideline, <sup>21,22</sup> UKPDS, <sup>54</sup> ALLHAT <sup>33</sup>
Chronic kidney disease			•	•			NKF Guideline, <sup>22</sup> Captopril Trial, <sup>55</sup> RENAAL, <sup>56</sup> IDNT, <sup>57</sup> REIN, <sup>58</sup> AASK <sup>59</sup>
Recurrent stroke prevention	•		•				PROGRESS <sup>35</sup>

Abbreviations: AASK, African American Study of Kidney Disease and Hypertension; ACC/AHA, American College of Cardiology/American Heart Association; ACE, angiotensin-converting enzyme; AIRE, Acute Infarction Ramipril Efficacy; ALLHAT, Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; ANBP2, Second Australian National Blood Pressure Study; ARB, angiotensin-receptor blocker; BHAT,  $\beta$ -Blocker Heart Attack Trial; CCB, calcium channel blocker; CIBIS, Cardiac Insufficiency Bisoprolol Study; CONVINC, Controlled Onset Verapamil Investigation of Cardiovascular End Points; COPERNICUS, Carvedilol Prospective Randomized Cumulative Survival Study; EPHEUS, Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study; HOPE, Heart Outcomes Prevention Evaluation Study; IDNT, Irbesartan Diabetic Nephropathy Trial; LIFE, Losartan Intervention For Endpoint Reduction in Hypertension Study; MERIT-HF, Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure; NKF-ADA, National Kidney Foundation–American Diabetes Association; PROGRESS, Perindopril Protection Against Recurrent Stroke Study; RALES, Randomized Aldactone Evaluation Study; REIN, Ramipril Efficacy in Nephropathy Study; RENAAL, Reduction of Endpoints in Non-Insulin-Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan Study; SAVE, Survival and Ventricular Enlargement Study; SOLVD, Studies of Left Ventricular Dysfunction; TRACE, Trandolapril Cardiac Evaluation Study; UKPDS, United Kingdom Prospective Diabetes Study; ValHEFT, Valsartan Heart Failure Trial.

\*Compelling indications for antihypertensive drugs are based on benefits from outcome studies or existing clinical guidelines; the compelling indication is managed in parallel with the blood pressure.

†Conditions for which clinical trials demonstrate benefit of specific classes of antihypertensive drugs.

tions and acute target-organ damage (eg, encephalopathy, myocardial infarction, unstable angina, pulmonary edema, eclampsia, stroke, head trauma, life-threatening arterial bleeding, or aortic dissection) require hospitalization and parenteral drug therapy.<sup>1</sup> Patients with markedly elevated BP but without acute target-organ damage usually do not require hospitalization, but they should receive immediate combination oral antihypertensive therapy. They should be carefully evaluated and monitored for hypertension-induced heart and kidney damage and for identifiable causes of hypertension (Box 2).

**Additional Considerations in Anti-hypertensive Drug Choices.** Antihypertensive drugs can have favorable or unfavorable effects on other comorbidities.

*Potential Favorable Effects.* Thiazide-type diuretics are useful in slowing demineralization in osteoporosis.  $\beta$ -Blockers can be useful in the treatment of atrial tachyarrhythmias/fibrillation, migraine, thyrotoxicosis (short-term), essential tremor, or perioperative hypertension. Calcium channel blockers may be useful in Raynaud syndrome and certain arrhythmias, and  $\alpha$ -blockers may be useful in prostatism.

*Potential Unfavorable Effects.* Thiazide diuretics should be used cautiously in patients who have gout or who have a history of significant hyponatremia.  $\beta$ -Blockers should generally be avoided in individuals who have asthma, reactive airways disease, or second- or third-degree heart block. Angiotensin-converting enzyme inhibitors and ARBs should not be given to women likely to become pregnant and are contraindicated in those who are; ACE inhibitors should not be used in individuals with a history of angioedema. Aldosterone antagonists and potassium-sparing diuretics can cause hyperkalemia and should generally be avoided in patients who have serum potassium values of more than 5.0 mEq/L while not taking medications.

### Improving Hypertension Control

**Adherence to Regimens.** Behavioral models suggest that the most effective

### Box 3. Causes of Resistant Hypertension

- Improper blood pressure measurement
- Volume overload and pseudotolerance
  - Excess sodium intake
  - Volume retention from kidney disease
- Inadequate diuretic therapy
- Drug-induced or other causes
  - Nonadherence
  - Inadequate doses
  - Inappropriate combinations
  - Nonsteroidal anti-inflammatory drugs; cyclooxygenase 2 inhibitors
  - Cocaine, amphetamines, other illicit drugs
  - Sympathomimetics (decongestants, anorectics)
  - Oral contraceptives
  - Adrenal steroids
  - Cyclosporine and tacrolimus
  - Erythropoietin
  - Licorice (including some chewing tobacco)
  - Selected over-the-counter dietary supplements and medicines (eg, ephedra, ma haung, bitter orange)
- Associated conditions
  - Obesity
  - Excess alcohol intake
- Identifiable causes of hypertension (see Box 2)

therapy prescribed by the most careful clinician will control hypertension only if the patient is motivated to take the prescribed medication and to establish and maintain a health-promoting lifestyle. Motivation improves when patients have positive experiences with and trust in their clinicians. Empathy builds trust and is a potent motivator.<sup>75</sup> Patient attitudes are greatly influenced by cultural differences, beliefs, and previous experiences with the health care system.<sup>76</sup> These attitudes must be understood if the clinician is to build trust and increase communication with patients and families.

Failure to titrate or combine medications, despite knowing the patient is not at goal BP, represents clinical inertia and must be overcome.<sup>77</sup> Decision support systems (ie, electronic and paper), flow sheets, feedback reminders, and involvement of nurse clinicians and pharmacists can be helpful.<sup>78</sup>

The patient and clinician must agree on BP goals. A patient-centered strategy to achieve the goal and an estimation of the time needed to reach the goal are important.<sup>79</sup> When BP is above goal,

alterations in the plan should be documented. Blood pressure self-monitoring can also be useful. Patients' nonadherence to therapy is increased by misunderstanding of the condition or treatment, denial of illness because of lack of symptoms or perception of drugs as symbols of ill health, lack of patient involvement in the care plan, or unexpected adverse effects of medications. The patient should be made to feel comfortable in telling the clinician all concerns and fears of unexpected or disturbing drug reactions.

The cost of medications and the complexity of care (ie, transportation, patient difficulty with polypharmacy, difficulty in scheduling appointments, and life's competing demands) are additional barriers that must be overcome to achieve goal BP. All members of the health care team (eg, physicians, nurse case managers, other nurses, physician assistants, pharmacists, dentists, registered dietitians, optometrists, and podiatrists) must work together to influence and reinforce instructions to improve patients' lifestyles and BP control.<sup>80</sup>

**Resistant Hypertension.** Resistant hypertension is the failure to reach goal BP in patients who are adhering to full doses of an appropriate 3-drug regimen that includes a diuretic. After excluding potential identifiable hypertension (Box 2), clinicians should carefully explore reasons why the patient is not at goal BP (Box 3). Particular attention should be paid to diuretic type and dose in relation to renal function (see “Chronic Kidney Disease” section). Consultation with a hypertension specialist should be considered if goal BP cannot be achieved.

### Public Health Challenges and Community Programs

Public health approaches, such as reducing calories, saturated fat, and salt in processed foods and increasing community and school opportunities for physical activity, can achieve a downward shift in the distribution of a population's BP, thus potentially reducing morbidity, mortality, and the lifetime risk of an individual becoming hypertensive. This becomes especially critical as the body mass index of individuals in the United States has increased to epidemic levels. Currently, 122 million adults are overweight or obese, which contributes to the rise in BP and related conditions.<sup>81</sup> The JNC 7 endorses the American Public Health Association resolution that the food manufacturers and restaurants reduce sodium in the food supply by 50% during the next decade. When public health intervention strategies address the diversity of racial, ethnic, cultural, linguistic, religious, and social factors in the delivery of their services, the likelihood of their acceptance by the community increases. These public health approaches can provide an attractive opportunity to interrupt and prevent the continuing costly cycle of managing hypertension and its complications.

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### Scheme Used for Classification of the Evidence

- M** Meta-analysis; use of statistical methods to combine the results from clinical trials
- Ra** Randomized controlled trials; also known as experimental studies
- Re** Retrospective analyses; also known as case-control studies
- F** Prospective study; also known as cohort studies, including historical or prospective follow-up studies
- X** Cross-sectional survey; also known as prevalence studies
- Pr** Previous review or position statements
- C** Clinical interventions (nonrandomized)

These symbols are appended to the citations in the reference list. The studies that provided evidence supporting the recommendations of this report were classified and reviewed by the staff and the executive committee. The classification scheme is from the JNC VI report.<sup>1</sup>

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