Management of High Blood Pressure in African Americans

Consensus Statement of the Hypertension in African Americans Working Group of the International Society on Hypertension in Blacks

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he purpose of this consensus statement is to offer primary care providers (including physicians, nurse practitioners, and physician assistants) a practical, evidence-based clinical tool for achieving blood pressure goals in African American patients. The need for specific recommendations for African Americans is highlighted by compelling evidence of a higher prevalence of hypertension and poorer cardiovascular and renal outcomes in this group than in white Americans. African Americans have disturbingly higher rates of cardiovascular mortality, stroke, hypertension-related heart disease, congestive heart failure, type 2 diabetes mellitus, hypertensive nephropathy, and end-stage renal disease (ESRD).^{1,2}

Large population-based studies have demonstrated that as diastolic blood pressure (DBP) and systolic blood pressure (SBP) increase, the risk of cardiovascular events and renal failure also increases continuously.³⁻⁶ Remarkably, this is true even for individuals with normal blood pressure. Framingham Heart Study investigators7 recently reported that for individuals who had blood pressure lower than 140/90 mm Hg at study entry, only 5% of those with optimal blood pressure (<120/80mm Hg) developed high blood pressure over the next 4 years, compared with 18% of those with normal blood pressure (120-129/80-84 mm Hg) and 37% of those with high-normal blood pressure (130-139/

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The goal of management of high blood pressure is to assist patients to achieve and maintain a blood pressure that will optimally reduce cardiovascular and renal morbidity and mortality. Barriers to normalizing blood pressure in African Americans have been largely attributed to biologic and social factors, with an inadequate focus on the role of medical management. Undiagnosed, untreated, and inadequately treated hypertension results in an enormous burden of disease for African Americans. Simply stated, a key obstacle is the failure of medical providers to treat high blood pressure early and to

continue treating it persistently to reach and maintain an appropriate target blood pressure.¹² This may be related to a common perception that it is medically more difficult to lower blood pressure in African Americans than in other patients. This perception is unjustified. Furthermore, it may lower providers' outcome expectancy for African Americans and thwart their efforts to appropriately manage high blood pressure in these patients.

The recommendations in this article are based on evidence from clinical trials, a synthesis of existing guidelines, current pharmacologic options, and the consensus of the expert opinions of the members of the Hypertension in African Americans Working Group (HAAW Group). In preparation, we evaluated data from clinical trials that have enrolled significant numbers of African Americans, including the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT),¹³ in which 36% of subjects were African American, and the African American Study of Kidney Disease and Hypertension (AASK).14 A listing of guidelines and scientific statements that were reviewed for their relevance to African Americans are given in a box at the end of this article. In particular, we considered the relevance of 2 major hypertension guidelines to the management of high blood pressure in African Americans: the "Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI)"¹ and the "1999 World Health Organization-International Society of Hypertension (WHO-ISH) Guidelines for the Management of Hypertension."15

The recommendations in the present consensus statement differ from these other guidelines in 2 substantial ways. First, we recommend lower blood pressure goals for patients with diabetes or with nondiabetic renal disease accompanied by proteinuria characterized by more than 1 g/d (<130/80 mm Hg). Second, we recommend the use of combination therapy as first-line therapy for patients with an SBP of 15 mm Hg or more or a DBP of

10 mm Hg or more above target blood pressure.

GENERAL APPROACH

This article describes "best practice" strategies for assessing cardiovascular risk; setting, achieving, and maintaining appropriate blood pressure levels; assisting patients to implement therapeutic lifestyle changes; and initiating effective pharmacologic interventions early and persistently in nonpregnant African American adults with high blood pressure. The recommendations in this article represent a consensus of the opinions of members of the HAAW Group and are based on data within the public domain.

Identifying an optimal management plan for each patient is the key element for successful blood pressure reduction. In the past decade, there have been 3 major paradigm shifts in treating high blood pressure that are particularly applicable to the management of hypertension in African Americans: (1) urging and supporting therapeutic lifestyle changes; (2) conducting a thorough cardiovascular risk assessment; and (3) achieving and maintaining a target blood pressure that is determined by the individual's level of risk.^{1,15} In addition, there is presently a more intense emphasis on lowering SBP than previously, particularly in older adults,16 and increased use of low-dose combination therapy to achieve target blood pressure goals.1 Furthermore, there is an increasing amount of data showing that appropriate agent selection is an important factor in providing target-organ protection.^{1,15,17-25}

The importance of treating high blood pressure persistently to reach and maintain an appropriate target pressure in African Americans cannot be overstated. To succeed, primary care providers will need to heighten their awareness of cardiovascular risk, recognize early markers of target-organ disease, and set blood pressure goals that are related to the individual's risk profile. Success is generally the result of appropriate interventions, including therapeutic lifestyle changes and drug treatment, while failure often indicates an approach that was not

sufficiently intense and persistent. Success also depends on creating a therapeutic alliance between provider and patient; to this end, providers must possess the ability to recognize and alleviate patient- and provider-related barriers as well as economic and social barriers to controlling high blood pressure in African American patients.

RISK ASSESSMENT

Cardiovascular risk assessment is used to identify high-risk patients who need immediate, intense medical intervention. Risk factors for developing high blood pressure, coronary heart disease (CHD), and cardiovascular disease should be identified in African Americans across the life span in all primary care settings. High blood pressure is an independent risk factor for adverse cardiovascular and renal outcomes; thus, African Americans of all ages should be educated about prevalent behaviors that increase the risk of developing high blood pressure, including smoking, obesity, inactivity, high dietary fat and sodium, low dietary potassium, and moderate or high alcohol intake. Because increased risk for cardiovascular events begins early in life, clinical markers associated with hypertension that are known to be prevalent in African Americanssuch as low birth weight²⁶ and a strong family history for cardiovascular disease, diabetes, and premature heart disease-should be recognized as an important part of the entire clinical picture.

A cardiovascular risk assessment is conducted by evaluating the patient's medical history, family history, and health-related behaviors, along with clinical information obtained from the physical examination and laboratory studies. Elements of the adult risk assessment are outlined in Table 1. Analysis of data from the Framingham Heart Study²⁷ has made it possible to predict the likelihood of a CHD event occurring in an individual who currently does not have CHD. A simple tool based on data from the Framingham Heart Study can be used to assess the relative importance of CHD risk factors and to estimate a risk

level for these individuals.²⁸ This tool was recently validated for African American men and women.29

The major risk factors for CHD are cigarette smoking, elevated blood pressure (whether treated or untreated), elevated serum total cholesterol and low-density lipoprotein cholesterol levels, low serum high-density lipoprotein cholesterol level, diabetes, and advancing age.^{1,15,28} Obesity and inactivity, which are known to worsen the impact of other major risk factors, have also been designated as major risk factors for CHD by the American Heart Association.^{30,31} African Americans have a high prevalence of obesity and inactivity, both of which should be viewed as major risk factors in this population. It is also relevant to assess the risk for other adverse cardiovascular and renal outcomes in African Americans, particularly stroke and hypertensive nephropathy. Additional risk factors for cardiovascular disease include preexisting cardiovascular or kidney disease, history of a cardiovascular event, central obesity, blood pressure above the appropriate target level, elevated blood glucose level, male sex, postmenopausal status, family history of cardiovascular disease in women younger than 65 years or men younger than 55 years, evidence of target-organ damage, low socioeconomic status, and elevated triglyceride levels^{1,15,32} (Table 2).

Microalbuminuria (urinary albumin excretion of 30-299 mg/d), even in the nondiabetic, nonhypertensive population, has been shown to be an independent risk factor for cardiovascular and renal disease.33-35 Therefore, assessment for microalbuminuria should be conducted in patients with diabetes mellitus (type 1 or type 2), longstanding hypertension (controlled or uncontrolled), or renal insufficiency (hypertensive nephrosclerosis),³⁶ and may also be useful for risk assessment in patients with significant cardiovascular risk factors³³ (Table 2). Screening for microalbuminuria can be performed most efficiently using a random, spotcollection urine sample for measurement of albumin-creatinine ratio.37

Table 1. Elements of an Initial Cardiovascular Risk Assessment in African American Adults

History
Family history of high blood pressure, CHD, CVD, or type 2 diabetes mellitus
Previous diagnosis of high blood pressure, known duration, levels of blood pressure elevation, treatment
Smoking history
Current alcohol consumption
Leisure-time physical activity
Dietary assessment
Environmental assessment (neighborhood, housing, employment, workplace)
Use of street drugs (in particular, cocaine, amphetamines, phencyclidine)
Current medications (including over-the-counter medications, supplements, herbal products, and home remedies)
Medical and psychiatric history (particularly those that may affect choice of antihypertensive agent, eg, COPD, erectile dysfunction, depression)
Physical examination
Measure height and weight (calculate BMI, if indicated)
Observe for central adiposity (measure waist circumference if indicated)
Perform cardiovascular and pulmonary examination
Measure blood pressure using appropriate technique
Perform funduscopic retinal examination
Laboratory studies
Fasting lipid profile (including total cholesterol, LDL-C, HDL-C, and triglycerides) Serum creatinine
Random urinalysis for protein or protein-creatinine ratio
Fasting plasma glucose
Electrocardiogram
Echocardiogram (if suspicion of LVH)
Microalbuminuria (in patients with type 1 or type 2 diabetes mellitus, longstanding treated or untreated high blood pressure, or renal insufficiency [hypertensive nephrosclerosis])

Abbreviations: BMI, body mass index; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVH, left ventricular hypertrophy.

Many individuals have a cluster of major risk factors that are referred to as the metabolic syndrome. The clinical characteristics of this syndrome are listed in **Table 3**. A defining characteristic of the metabolic syndrome is insulin resistance, usually associated with increased insulin levels and dyslipidemia. Epidemiologic data from the Third National Health and Nutrition Examination Survey (NHANES III) and reported by the American Heart Association² show that predisposing factors for the metabolic syndrome and cardiovascular riskincluding type 2 diabetes mellitus, obesity, and inactivity-are more prevalent in African Americans than in whites. Thus, providers should assess patients for clinical signs of the metabolic syndrome when appropriate.

Regardless of the clinical tools used to identify a patient's relative level of cardiovascular risk, labeling a patient as high risk is of no value if appropriate interventions are not immediately initiated and persistently continued. The clinical tasks of the provider that follow cardiovascular risk assessment are to (1) determine the appropriate blood pressure goal; (2) assist the patient to achieve therapeutic lifestyle changes; (3) determine the appropriate intensity of pharmacologic intervention; and (4) select the most appropriate therapeutic regimen. In addition to identifying, achieving, and maintaining an appropriate blood pressure goal, interventions should be initiated for all modifiable risk factors and associated clinical conditions that are identified through risk assessment.

SETTING BLOOD PRESSURE GOALS

The larger the burden of risk, the more imperative it is to reach blood pressure goals. For patients at high risk for cardiovascular events-in particular, those with type 2 diabetes mellitus (with or without nephropathy) or with nondiabetic renal disease with proteinuria

Obesity Inactivity Excessive alcohol intake High dietary intake of fat and sodium Low dietary intake of potassium Clinical markers associated with high blood pressure ^{1,7,26} Low birth weight Family history of CVD, diabetes, or premature heart disease High-normal blood pressure (130-139/85-89 mm Hg) Adult weight gain Major risk factors for CHD ^{28,30,32} Smoking Elevated blood pressure (whether treated or untreated) Elevated blood pressure (whether treated or untreated) Elevated serum total cholesterol or LDL-C levels Low serum HDL-C level Diabetes mellitus Advancing age Obesity Inactivity Additional important risk factors for CVD ^{1,32} History of cardiovascular event (MI, stroke, revascularization) Kidney disease Evidence of target-organ damage (proteinuria, LVH, heart failure, TIA, peripheral arterial disease, atherosclerosis, retinopathy) Male or postmenopausal woman Family history of CVD in women aged <65 y or men aged <55 y Central obesity Elevated blood glucose level Low socioeconomic status Elevated triglyceride levels	Behavioral markers that increase risk for develo	opment of high blood pressure ^{1,7}
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Abbreviations: CHD, coronary heart disease; CVD, cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVH, left ventricular hypertrophy; MI, myocardial infarction; TIA, transient ischemic attack.

Risk Factor	Definition
Abdominal or central obesity	Waist circumference >40 in (>102 cm) for me or >35 in (>89 cm) for women
Atherogenic dyslipidemia	
Elevated triglyceride levels	≥150 mg/dL (≥1.70 mmol/L)
Low HDL-C level	<40 mg/dL (<1.04 mmol/L) for men or <50 mg/dL (<1.30 mmol/L) for women
High blood pressure	≥130/85 mm Hg
Elevated fasting blood glucose level	\geq 110 mg/dL (\geq 6.1 mmol/L)

Abbreviation: HDL-C, high-density lipoprotein cholesterol.

*Diagnosis of the metabolic syndrome is made when the patient exhibits 3 or more risk factors.³²

characterized by more than 1 g/d the blood pressure target should be lower than 130/80 mm Hg.

Because the relationship between increasing blood pressure and cardiovascular events is continuous, the degree of blood pressure elevation (treated or untreated) over the target goal is a critical element of individual risk assessment. While hypertension is currently defined as blood pressure of 140/90 mm Hg or higher for the purpose of epidemiologic investigations, optimal blood pressure is known to be lower than 120/80 mm Hg.^{1,15} Standards for identification of blood pressure stages are outlined in **Table 4**.

Both WHO-ISH¹⁵ and JNC VI¹ guidelines recommend that all individuals with uncomplicated hypertension should at minimum achieve a target SBP of lower than 140 mm Hg and DBP of lower than 90 mm Hg. Patients with uncomplicated hypertension are those who do not have diabetes or evidence of target-organ damage, who have no history of a cardiovascular event, and who are at low or moderate risk for CHD. It is important to lower both SBP and DBP to the target goals. Achieving one component of the blood pressure goal without achieving the other (eg, reducing blood pressure from 180/90 mm Hg to 150/80 mm Hg) does not offer patients adequate protection.

Compelling evidence demonstrates that maintaining lower blood pressure reduces cardiovascular morbidity and mortality and slows the progression of renal disease for patients with diabetes or renal insufficiency.^{17,38-42} While JNC VI¹ recommends a target blood pressure goal of lower than 130/85 mm Hg for all patients with diabetes and patients with nondiabetic renal disease with proteinuria characterized by more than 1 g/d, some data suggest that even lower blood pressure goals may be desirable. A report developed by the National Kidney Foundation Hypertension and Diabetes Executive Committees Working Group⁴³ recommends a target goal of lower than 130/80 mm Hg for all patients with diabetes, renal insufficiency, or both; this report also recommends lower blood pressure levels (<125/75 mm Hg) for individuals who have proteinuria characterized by more than 1 g/d, regardless of etiology.

In January 2002, a position statement issued by the American Diabetes Association⁴⁴ regarding treatment of hypertension in adults with diabetes recommended a target blood pressure of lower than 130/80 mm Hg for all patients with diabetes. The present recommendation of the HAAW Group to lower the DBP goal to lower than 80 mm Hg in African Americans with diabetes was based on an evaluation of randomized clinical trials, including several large trials that have been published subsequent to publication of the JNC VI1 and WHO-ISH¹⁵ guidelines^{13,14,17,45,46} and 2 small studies (N=86) that included African American patients with dia-

betic nephropathy. One of these small studies enrolled solely African American patients,⁴⁷ and the other enrolled 24% African American patients.⁴⁸ Schrier and colleagues⁴² recently reported a lower rate of stroke and less progression of albuminuria and diabetic retinopathy in patients with type 2 diabetes mellitus who achieved and maintained a mean blood pressure of 128/75 mm Hg during a mean follow-up period of 5.3 years.

Blood pressure reduction has been shown to slow the progression of renal disease, which is particularly important for African Americans, who are 3 to 4 times more likely to develop ESRD than white Americans.49 A meta-analysis of longterm clinical trials demonstrated that increasing preservation of renal function is associated with decreasing blood pressure over a continuum of values.50 However, data from AASK,14 which enrolled nearly 1094 nondiabetic African American patients with hypertensive renal disease, showed no significant difference in the progression of renal disease between the group of patients assigned to the usual blood pressure goal (mean achieved blood pressure, 140/85 mm Hg) and the group assigned to a lower blood pressure goal (mean achieved blood pressure, 127/77 mm Hg). Because of this, we recommend a target blood pressure of lower than 140/90 mm Hg for nondiabetic patients with hypertensive renal disease accompanied by proteinuria characterized by less than 1 g/d. There were too few participants in AASK with proteinuria characterized by more than 1 g/d to make a blood pressure recommendation for this group. Therefore, based on current recommendations for patients with nondiabetic renal disease and proteinuria characterized by more than 1 g/d, we recommend a blood pressure target that is lower than 130/80 mm Hg.1,15 A blood pressure target that is set lower than 140/90 mm Hg (eg, <130/80 mm Hg) may also be preferred for patients with a history of a cardiovascular event, stroke, or transient ischemic attacks51; evidence of target-organ damage, including microalbuminuria⁵²⁻⁵⁴; or CHD or high risk for CHD.

Table 4. Classification of Blood Pressure Stages for Adults 18 Years and Older*

Category	Systolic Blood Pressure, mm Hg	Diastolic Blood Pressure, mm Hg
Optimal	<120	<80
Normal	<130	<85
High-normal	130-139	85-89
Stage 1 hypertension	140-159	90-99
Stage 2 hypertension	160-179	100-109
Stage 3 hypertension	≥180	≥110
Isolated systolic hypertension ⁺	≥140	<90

*Classification is based on blood pressure values without antihypertensive therapy. When systolic and diastolic blood pressures fall into different categories, the higher category should be selected to classify blood pressure status. A diagnosis of hypertension should be based on an average of 2 or more measurements taken during each of 3 or more visits.^{1,15}

†Isolated systolic hypertension can be categorized according to stages 1 to 3, based on degree of systolic blood pressure and diastolic blood pressure less than 90 mm Hg.^{1,15}

THERAPEUTIC LIFESTYLE CHANGES

It is vital that providers assume the important responsibility of offering ongoing education and support for individuals and families in their efforts to lead healthier lives in the areas of diet, physical activity, smoking, and alcohol use. Weight maintenance or reduction, increased physical activity, moderation of salt and alcohol intake, and tobacco avoidance are important therapeutic lifestyle changes that can lower blood pressure.^{1,55-57} Changing health behaviors is not an easy task, and patients deserve ongoing education and support from primary care providers in their efforts. Without an adequate understanding of the causes and consequences of elevated blood pressure, patients are less likely to embark on lifelong lifestyle changes or comply with long-term pharmacologic therapy. Patients should be informed that the risks of untreated hypertension include irreparable damage to any or all of the target organs-heart, blood vessels, brain, kidneys, and eyes.

Because obesity, high sodium and low potassium intake, and inadequate physical activity have been identified as particular obstacles to cardiovascular health in African Americans,^{2,58-61} it is appropriate to emphasize their importance. However, a healthy diet is more important than weight loss,⁶² and enjoyable physical activity is beneficial even if it is not strenuous or associated with weight loss.³¹ Plans for diet, exercise, and other needed changes should be initiated in the primary care setting; realistic, appropriate goals should be established. Recommendations should be specific, individually tailored, and well supported with counseling efforts and effective patient education materials (**Table 5**).^{1,15,55,56}

Dietary Goals

There are several potential nutritional variables that may contribute to lowering blood pressure weight loss, reduced dietary fats and sodium, increased potassium intake, increased dietary fiber, and reduction of alcohol intake, among others. However, only those dietary changes that individuals and their families can safely and readily follow over a lifetime will actually produce health benefits.⁵⁶ The emphasis should be on healthy choices, not dietary restrictions.

Dietary Approaches to Stop Hypertension (DASH)62 is a randomized, controlled dietary study that compares the effect on blood pressure of the DASH diet (rich in fruits, vegetables, fiber, and low-fat dairy foods; includes meat and poultry, but with reduced saturated and total fats) with a typical, high-fat, control diet (that was either high or low in fruits and vegetables) in 459 adults with normal or elevated blood pressure. After 8 weeks, the DASH diet reduced SBP and DBP significantly more than the other diets, without any weight loss or sodium restriction. Importantly, the DASH diet was particularly beneficial in African American participants and in all participants

Table 5. Therapeutic Lifestyle Changes **Medical Target Realistic Personal Plan to Achieve Goal** Normal weight for height Lose weight gradually by making permanent changes in daily diet for the entire family. Set a reasonable weight loss goal (even 5-10 lb [2.2-4.5 kg] can make a difference). Eat fewer fast food and fried foods, and eat more fruits and vegetables. Dietary goals: Eat more grains, fresh fruits, and vegetables. Low fat Eat fewer overall fats and use healthier fats, such as olive oil. Low sodium Eat fewer processed foods and fast foods. High potassium Read labels and pay attention to the sodium and fat content of foods. Adequate calcium Identify high-sodium foods (eg, potato chips or hot dogs) that can be comfortably omitted. Identify low-sodium, high-potassium snacks (eg, dried fruits, bananas, orange juice, raw vegetables). Do not salt foods when cooking; instead, taste foods first and add salt at the table if needed. Use vinegar or lemon juice instead of salt for seasoning. Do not season foods with smoked meats, such as bacon or ham hocks. Become more aware of food sources that are rich in calcium. If lactose intolerant, try lactose-free milk or yogurt, or drink calcium-fortified juices or soy milk. Limit alcohol Men: no more than 2 beers, 1 glass of wine, or 1 shot of whiskey (or hard liquor) per day. Women: no more than 1 beer or 1 glass of wine per day (a shot of whiskey exceeds these recommendations). Physical fitness Increase physical activity as part of the daily routine; eg, if currently sedentary, get off the bus 6 blocks from home, or walk in the evening with a spouse or friend.

with hypertension, but it was most effective in African Americans with high blood pressure. Among all participants with hypertension (n=133), the DASH diet reduced SBP and DBP by 11.6 mm Hg and 5.3 mm Hg, respectively, and among African American participants with hypertension (n=88), the DASH diet reduced SBP and DBP by 13.2 mm Hg and 6.1 mm Hg, respectively.62 The DASH diet plus sodium restriction was also studied and was found to be associated with additional lowering of blood pressure, an effect that was also more pronounced in African American patients than in others.⁶³ It is important to note that this diet, which was based on typically available foods, reduced blood pressure in patients with stage 1 hypertension by about as much as a typical antihypertensive agent.

No tobacco use

The DASH diet is a hearthealthy program from which all Americans could benefit. Providers should strongly recommend the lowsodium DASH diet to all African American patients, with or without high blood pressure, and provide educational materials, which are readily available. Patients following the DASH diet, which is based on an intake of 2000 calories a day, maintained a constant body weight; however, the number of calories in the diet can be reduced for overweight individuals. The diet is described in **Table 6**.

Gradually increase time spent at an enjoyable activity to 30-45 min at least 5 times a week.

Be aware that smokeless tobacco products (eg, chewing tobacco) also have associated risks.

For current smokers, attempt smoking cessation, increase tolerance for failure, and be willing to continue the effort until

For nonsmokers, do not start.

success is achieved.

In all populations, including African American populations, there appears to be a positive association between sodium excretion and blood pressure.63-65 Similar to white Americans, salt sensitivity in African Americans has been linked to obesity.66 However, it has been hypothesized that African Americans may be more salt sensitive and consume less potassium than white Americans. Thus, increasing dietary potassium while moderating sodium chloride intake to the recommended less than 2.4-g/d level is likely to be beneficial in African Americans with hypertension (but without renal failure).⁵⁵ For motivated patients who desire greater dietary effects on lowering blood pressure, weight reduction or further sodium reduction is likely to produce further blood pressure lowering. Data from phase 2 of the randomized Trials of Hypertension Prevention (TOHP II)67 demonstrated that clinically significant long-term reductions in blood pressure and reduced risk for hypertension can be achieved with a modest weight loss of about 10 pounds (4.5 kg).

Physical Activity Goals

Regular physical activity helps control weight, reduces the risk of developing high blood pressure or diabetes, reduces the likelihood of dying prematurely from heart disease, and reduces feelings of depression.68 Individualized, realistic plans should be suggested, including taking a walk every day or dancing or moving to music at home. High-intensity and moderate-intensity energy-expending activities such as brisk walking, bicycling, jogging, swimming and sports such as tennis, baseball, and basketball are especially beneficial when performed regularly. Lowintensity activities are possible for almost everyone and also confer longterm health benefits similar to those associated with higher-intensity activities, if the duration of activity is increased. Low-intensity activities include walking, walking a dog, golf, gardening, yard work, housework, yoga, tai chi, stretching, chair exercise, water exercise, and prescribed home exercise adapted to the individual.31

Other "Heart Healthy" Interventions

Smoking cessation should be strongly encouraged and supplemented with support, education, and medical interventions as needed.⁶⁹ Cholesterol-lowering therapy, including dietary modifications and

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Food Group	Daily Servings (Except as Noted)	Serving Sizes	Examples for a Typical African American Diet	Significance of Each Food Group to the DASH Die
Grains and grain products	7-8	1 slice bread 1 c (0.24 L) ready-to-eat cereal† ½ c (0.12 L) cooked rice, pasta, or cereal	Bread, biscuit, cornbread, cereals, oatmeal, grits, rice, pasta, crackers, unsalted pretzels	Major sources of energy and fiber
Vegetables	4-5	1 c raw leafy vegetable 1/2 c cooked vegetable 6 oz (180 mL) vegetable juice	Fresh, canned or frozen vegetables: tomatoes, corn, potatoes, greens (eg, collards, kale, turnip greens, spinach), yams, squash, carrots, okra	Rich sources of potassium, magnesium, and fiber
Fruits	4-5	1 medium-size fruit 1⁄2 c dried fruit 1⁄2 c fresh, frozen, or canned fruit 6 oz fruit juice	Bananas, grapes, apples, oranges, unsweetened fruit juices, grapefruit, mangoes, melons, peaches, dried fruits	Important sources of potassium, magnesium, and fiber
Low-fat or fat-free dairy foods	2-3	8 oz (240 mL) milk 1 c yogurt 1½ oz (42 g) cheese	Fat-free (skim) or low-fat (1%) milk, fat-free cheeses, low-fat yogurt, low-fat ice cream, or frozen yogurt	Major sources of calcium and protein
Lean meats, poultry, and fish	≤2	3 oz (84 g) cooked lean meats, poultry (remove skin), or fish Broil or roast, rather than fry	Chicken, turkey, ground turkey or chicken, chicken sausage, lean pork, or beef Fish and seafood: haddock, halibut, flounder, catfish, salmon, shrimp, crab, ovsters, clams	Rich sources of protein and magnesium
Nuts, seeds, and beans	4-5 per week	1⁄3 c (0.08 L) or 11⁄2 oz (42 g) nuts 1 tbsp (15 mL) or 1⁄2 oz (14 g) seeds 1⁄2 c cooked dry beans	Black beans, kidney beans, navy beans, pigeon peas, pinto beans, split peas, peanuts (roasted or boiled), almonds, pecans, walnuts, hazelnuts	Rich sources of energy, magnesium, potassium, protein, and fiber
Fats and oils‡	2-3	1 tsp (5 mL) soft margarine 1 tbsp low-fat mayonnaise 2 tbsp (30 mL) light salad dressing 1 tsp vegetable oil	Margarine, low-fat mayonnaise, light salad dressing, vegetable oil (olive, corn, canola, or safflower)	Reduced fat from typical diet (>30% of total calories) to 27% of total calories
Sweets	5 per week	1 tbsp sugar 1 tbsp jelly or jam ½ oz jelly beans 8 oz lemonade	Sugar, jelly, jam, honey, molasses, hard candy, fruit ices	Sweets should be those that are low in fat

*The Dietary Approaches to Stop Hypertension (DASH) dietary plan shown here is based on 2000 calories a day. The number of daily servings may vary according to the individual's daily caloric requirements.

+Serving size should be based on the product's nutrition label.

‡Fat content may change serving counts for fats and oils: eg, 1 tbsp of regular salad dressing equals 1 serving; 1 tbsp of a low-fat dressing equals one-half serving; 1 tbsp of a fat-free dressing equals 0 serving.

lipid-lowering therapy, should be prescribed, based on recent guidelines and cholesterol target goals published by the National Cholesterol Education Program³² (**Table 7**).

There is evidence that the rate of bystander-initiated cardiopulmonary resuscitation (CPR), as well as the rate of survival after out-ofhospital sudden cardiac arrest, is significantly lower among African Americans than among whites.⁷⁰ Patients should be encouraged to learn CPR. They should also be educated in the benefits of aspirin therapy for acute myocardial infarction (MI). Daily aspirin therapy inhibits platelet aggregation and can reduce the risks of heart attack and stroke in a wide range of patients with cardiovascular disease. Therefore, unless contraindicated, patients with CHD or at high risk for CHD should be prescribed daily aspirin therapy (75-325 mg/d).⁷¹

PHARMACOLOGIC INTERVENTIONS

To reach appropriate blood pressure goals, most individuals will likely require combination antihypertensive therapy. The rationale for lowering blood pressure to a specified goal is to protect target organs from hypertension-related damage and to reduce cardiovascular morbidity and mortality. As noted, patients at higher clinical risk for cardiovascular events should have lower blood pressure goals than those with lower risk; however, there are no clinical trial data at present to suggest that lower-than-usual blood pressure targets should be set for high-risk demographic groups such as African Americans.

Large, randomized clinical trials^{13,14,40,72-74} have demonstrated that 2 to 4 antihypertensive agents are required to achieve DBP and SBP goals in adults with uncomplicated hypertension. Clinical trial data also

Value, mg/dL (mmol/L)	Classification
Total cholesterol	
<200 (<5.18)	Desirable
200-239 (5.18-6.19)	Borderline high
≥240 (≥6.20)	High
LDL-C	
<100 (<2.59)	Optimal
100-129 (2.59-3.34)	Near or above optimal
130-159 (3.35-4.12)	Borderline high
160-189 (4.13-4.91)	High
≥190 (≥4.92)	Very high
HDL-C	
<40 (<1.04)	Low
>60 (>1 55)	High

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol, NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III.

*Based on the National Cholesterol Education Program, Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III).32

show that patients with diabetes or renal disease will require an average of 2.6 to 4.3 different antihypertensive medications to achieve a blood pressure goal of lower than 130/80 mm Hg.75 Similarly, in AASK,^{14,76-78} 2 to 3 drugs were needed, on average, to reduce mean arterial blood pressure to lower than 92 to 107 mm Hg in African Americans with hypertension and mildto-moderate renal dysfunction.

In a meta-analysis of controlled clinical trials,⁷⁹ the mean change in DBP weighted by sample size for various commonly used antihypertensive agents ranged from 7.2 mm Hg to 12 mm Hg. Thus, it is reasonable to assume that a very large majority of patients with DBP values that are more than 10 mm Hg above the target goal will require additional therapy to achieve their goal.

Until recently, DBP was generally preferred as an outcome measure for efficacy when evaluating the blood pressure-lowering effects of antihypertensive agents. However, large observational epidemiologic studies (eg, the Framingham Heart Study⁸⁰) have consistently indicated that SBP is a better predictor of cardiovascular events than DBP. Randomized, controlled trials have



Clinical algorithm for achieving target blood pressure (BP) in African American patients with high BP. RAS indicates renin-angiotensin system. Asterisk indicates to initiate monotherapy at the recommended starting dose with an agent from any of the following classes: diuretics, β -blockers, calcium channel blockers (CCBs), angiotensin-converting enzyme (ACE) inhibitors, or angiotensin II receptor blockers (ARBs). Dagger indicates to initiate low-dose combination therapy with any of the following combinations: β-blocker/diuretic, ACE inhibitor/diuretic, ACE inhibitor/CCB, or ARB/diuretic.

demonstrated that the association between SBP and the risk of CHD, stroke, increased left ventricular mass, and ESRD is continuous, graded, and independent⁸¹ and is typically stronger than the association of DBP with these same outcomes.82 A meta-analysis of pooled data from randomized controlled trials83 indicated that an average reduction of 12 mm Hg to 13 mm Hg in SBP over 4 years of follow-up was associated with a 21% reduction in CHD, a 37% reduction in stroke, a 25% reduction in total cardiovascular mortality, and a 13% reduction in all-cause mortality. In a metaanalysis of clinical trials in which the SBP-lowering efficacy of various diuretics as monotherapy was reported,84 SBP decreased by 13 and 18 mm Hg during treatment with low-dose and high-dose thiazide diuretics, respectively. Based on the importance of lowering SBP to a target goal and the likelihood that thiazide diuretics have efficacy similar to that of other classes of antihypertensive agents, it seems reasonable to assume that patients with SBP values that are more than 15 mm Hg above the target will require more than 1 agent to achieve their goal.

Therefore, we recommend that patients with an SBP that is 15 mm Hg or more above their target or a DBP that is 10 mm Hg or more above their target be treated with combination antihypertensive therapy. This means that patients whose appropriate blood pressure target is lower than 140/90 mm Hg and who have untreated blood pressure that is higher than 155/100 mm Hg, measured properly on 2 separate occasions, should be prescribed 2 drugs as their initial therapy. Patients whose appropriate blood pressure target is lower than 130/80 mm Hg and who have untreated blood pressure that is higher than 145/90 mm Hg should also be prescribed a regimen of combination therapy that includes at least 2 drugs (**Figure**).

Blood Pressure–Lowering Efficacy

When combination therapy using agents from 2 major drug classes is required to achieve blood pressure goals, based on data from randomized controlled clinical trials, the fol-

lowing combinations may be considered effective: β-blocker/diuretic, angiotensin-converting enzyme (ACE) inhibitor/diuretic, ACE inhibitor/calcium channel blocker (CCB), or angiotensin II receptor blocker (ARB)/diuretic. All antihypertensive drug classes are associated with blood pressure-lowering efficacy in African Americans.^{1,15} Thus, in terms of efficacy, there is no rationale for using race as a reason to avoid certain classes of agents in African American patients with high blood pressure.85,86 Patients whose blood pressure target is lower than 140/90 mm Hg and who have untreated blood pressure that is lower than 155/ 100 mm Hg may receive the recommended starting dose of an antihypertensive agent from any of the following major antihypertensive classes: diuretics, β-blockers, CCBs (dihydropyridine or nondihydropyridine), and ACE inhibitors. The blood pressure-lowering efficacy of either chlorothalidone (a diuretic) or amlodipine (a dyhydropyridine CCB) was recently confirmed to be superior to that of the ACE inhibitor lisinopril in African Americans.13 In many cases, a single drug will not achieve the desired blood pressurelowering effect of 15 mm Hg for SBP and 10 mm Hg for DBP. In these cases, further efforts should be made to help patients reach the target blood pressure (Figure).

Centrally acting agents and direct vasodilators are not well suited for initial monotherapy because they produce annoying adverse effects in many patients.^{1,15} Based on data reported from ALLHAT,²⁴ α -adrenergic blockers should not be used as first-line agents in patients at high risk for hypertension. Potential advantages and disadvantages of antihypertensive drug classes and considerations regarding their use in African American patients with high blood pressure⁸⁷⁻⁹⁶ are outlined in **Table 8**.

It has been well documented that, as monotherapy or in the absence of a diuretic, β -blockers, ACE inhibitors, and ARBs do not lower blood pressure to the same extent in African American patients that they do in white patients with hypertension.^{13,82,97-99} It has also been reported that, as monotherapy, thia-

zide diuretics and CCBs have greater blood pressure-lowering efficacy than do other drug classes in African Americans.99,100 However, studies reporting these types of data have certain common limitations: (1) they generally do not report SBP responses; (2) they generally reported response rates based on a reduction of 10 mm Hg or more from baseline DBP rather than achievement of target blood pressure; (3) individual agents cannot be used as a proxy for class effect; and (4) conclusions cannot be drawn regarding the best course of treatment for patients for whom antihypertensive treatment was not efficacious in these studies. Furthermore, high-dose diuretic therapy, frequently used in the past, is no longer recommended.15

While β -blockers, ACE inhibitors, and ARBs may not bring patients to a target blood pressure when prescribed as low-dose monotherapy,^{94,99,100} the addition of a low dose of a second agent (eg, a diuretic or a CCB) will typically provide sufficient additional blood pressure lowering to help patients reach their blood pressure goals.¹⁰¹⁻¹⁰⁷

African American patients with high blood pressure will frequently require at least 2 drugs to achieve blood pressure goals. Combining low doses of 2 antihypertensive medications yields additional blood pressure reductions of about 4 to 6 mm Hg in DBP and 8 to 11 mm Hg in SBP compared with the highest recommended dose of monotherapy.^{100,105,108,109} Thus, when a patient is unable to achieve the appropriate blood pressure goal with lowdose monotherapy, it is generally preferable to add a low dose of a second drug rather than increase the dose of the first because adding a second drug to the regimen may produce fewer adverse effects than increasing the dose of a single agent.^{1,110} Combination therapy with 2 drugs from the following list may be considered effective in lowering the patient's blood pressure to target: β-blocker/diuretic¹⁰⁴; ACE inhibitor/diuretic¹¹¹; ACE inhibitor/ CCB^{102,103,105}; or ARB/diuretic.^{101,106,112} Fixed-dose combination products are listed in **Table 9**.¹¹⁰

As an alternative, it is also acceptable to increase the dose of the ini-

tial monotherapy agent to achieve a blood pressure target, provided the patient tolerates the increased dose. There is no sound rationale for discontinuing treatment with a medication that has provided insufficient blood pressure-lowering effects with a low dose without causing adverse effects¹; however, if adverse effects are encountered with a low dose of the agent, the patient's treatment can be switched to an agent from another class. When titrating monotherapy, the clinician should give antihypertensive drugs adequate time to manifest their maximum blood pressurelowering effect. Flack and colleagues⁸⁶ showed improved blood pressure control and fewer adverse effects when the ACE inhibitor quinapril was titrated upward every 6 weeks as opposed to every 2 weeks in patients with mild hypertension.

If blood pressure goals are not achieved with combinations of 2 agents, the dosage of 1 agent can be increased or a third agent from a different class may be added to the regimen (Figure). The provider should consider any factors that may be decreasing patient compliance or reducing blood pressure-lowering efficacy. In particular, it is important to determine whether the patient's sodium intake is excessive and to identify whether the patient is using any prescribed or nonprescribed agents, including over-the-counter medications (eg, decongestants or nonsteroidal anti-inflammatory drugs), herbal or supplementary products (eg, licorice), or illicit drugs (eg, cocaine, methamphetamine [speed] or methylenedioxymethamphetamine [Ecstasy]). Secondary causes of hypertension should always be considered in the overall evaluation of adherent patients who do not achieve blood pressure goals. A referral to a hypertension specialist may be considered for a patient whose blood pressure cannot be controlled with intensive efforts in the primary care setting with a combination of 3 agents.

Target-Organ Protection

Where compelling indications have been identified for prescribing reninangiotensin system (RAS) blocking agents (either ACE inhibitors or ARBs) or β -blockers, these compel-

Table 8. Considerations Regarding the Use of Antihypertensive Classes in African American Patients With High Blood Pressure			
Class	Potential Disadvantages	Potential Benefits	Data Regarding Use in African Americans*
Diuretics ^{1,13,15}			
Thiazide diuretics	High doses should be avoided Potential for erectile dysfunction Potential for hypokalemia, particularly if sodium is not restricted Minimal efficacy with decreasing GFR (eg, GFR <45 mL/min per 1.73 m ²)	Inexpensive and well tolerated Efficacy and reduction of stroke and CHD events demonstrated in elderly, African American, ISH, and heart failure patients Low-dose thiazide diuretics (eg, hydrochlorothiazide 12.5-25 mg/d) potentiate the blood pressure-lowering effects of other classes of agents, including ACE inhibitors, ARBs, and B-blockers	Efficacy for use in low-dose combination therapy well established for African Americans Chlorthalidone demonstrated cardiovascular benefits for African Americans in ALLHAT
Potassium-sparing diuretics ⁸⁷	Observe for hyperkalemia	Patients at risk of hypokalemia Potential benefits in heart failure	Recent evidence for blood pressure-lowering efficacy with a selective aldosterone blocker (eplerenone) in African Americans
Loop diuretics	Must be taken 2-3 times a day to control volume Risk of hypovolemia or hypokalemia Should not be used in patients with normal kidney function	Reserved for use in patients with renal insufficiency (serum creatinine >2.0 mg/dL [>177 µmol/L] for men and >1.8 mg/dL [>159 µmol/L for women])	Not available
β-Blockers ^{1,15,18,88,96}	Cautious use in patients with reactive airway diseases or depression	Indicated for post-MI	Evidence of benefits in African American patients post-MI Evidence of less blood pressure-lowering efficacy as monotherapy in African American vs white patients
α -Antagonists ^{1,15,24}	No evidence for CV benefits Risk for postural hypotension	Indicated for benign prostatic hypertrophy	Negative data reported in ALLHAT for doxasozin in African American patients
CCBs ^{1,15,25,47,89-92}	Rapid- or short-acting CCBs contraindicated <i>Dihydropyridine CCBs:</i> potential for pedal edema, particularly at higher doses <i>Non-dihydropyridine CCBs:</i> potential for conduction abnormalities, constipation; consider potential drug-drug interactions	Dihydropyridine CCBs are potent vasodilators possessing high efficacy at reducing blood pressure CCBs reduce stroke and CV events in a wide range of patients	Evidence of efficacy and benefits in African American patients well established Some evidence of renal benefits in African American patients AASK found that a dihydropyridine CCB (amlodipine) was less renoprotective than ACE inhibitors in African American patients with hypertensive renal insufficiency
ACE inhibitors ^{17,53,86,93,119,127,128}	Adverse effect of bothersome dry cough in some patients Angioedema (rare)	High tolerability Indicated for prevention of CV events and for target-organ protection in patients with diabetes, heart failure, post-MI, diabetic nephropathy	Strong evidence of target-organ protection in African American patients (AASK) Some evidence of less blood pressure-lowering efficacy as monotherapy in African American vs white patients Some evidence of more cough and angioedema related to ACE inhibitor therapy in African American patients compared with white patients
ARBs ^{20-23,86,94,95}	Newest class of agents, so fewer data on clinical outcomes	High tolerability Benefits shown for target-organ protection in patients with diabetic nephropathy or early renal insufficiency Evidence of benefits for patients with heart failure	Small studies show blood pressure-lowering efficacy in African Americans, particularly in combination with hydrochlorothiazide

Abbreviations: AASK, African-American Study of Kidney Disease and Hypertension; ACE, angiotensin-converting enzyme; ALLHAT, Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; ARB, angiotensin II receptor blocker; CCB, calcium channel blocker; CHD, coronary heart disease; CV, cardiovascular; GFR, glomerular filtration rate; ISH, isolated systolic hypertension; MI, myocardial infarction; RAS, renin-angiotensin system. *Contrasts in efficacy for African Americans and white Americans should be viewed with caution, as they have not been established in randomized controlled trials.

ling indications should be applied equally to African American patients. Reducing blood pressure with medications has demonstrated protection against stroke, coronary events, heart failure, progression of

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kidney disease, and all-cause mortality.1 While lowering blood pressure to a target goal is the primary clinical approach to reduce the risk of adverse cardiovascular and renal events, some data also indicate greater

benefits with specific classes of agents in high-risk patients. ALLHAT^{13,24} compared 4 antihypertensive agents as initial therapy in approximately 42400 North American patients 55 years or older with hypertension and

Combination	Fixed-Dose Combination
ACE inhibitors and CCBs	Benazepril-amlodipine (Lotrel)
	Enalapril-felodipine (Lexxel)
	Trandolapril-verapamil SR (Tarka)
ACE inhibitors and diuretics	Benazepril-hydrochlorothiazide (Lotensin HCT)
	Captopril-hydrochlorothiazide (Capozide)
	Enalapril-hydrochlorothiazide (Vaseretic)
	Lisinopril-hydrochlorothiazide (Prinzide)
ARBs and diuretics	Candesartan-hydrochlorothiazide (Atacand HCT)
	Eprosartan-hydrochlorothiazide (Teveten-HCT)
	Irbesartan-hydrochlorothiazide (Avalide)
	Losartan-hydrochlorothiazide (Hyzaar)
	Telmisartan-hydrochlorothiazide (Micardis-HCT)
	Valsartan-hydrochlorothiazide (Diovan-HCT)
β-Blockers and diuretics	Atenolol-chlorthalidone (Tenoretic)
	Bisoprolol-hydrochlorothiazide (Ziac)
	Propranolol-hydrochlorothiazide (Inderide)
	Timolol-hydrochlorothiazide (Timolide)
	Nadolol-bendrofluthiazide (Corzide)

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

Table 10. ALLHAT and AASK at a Glance

at least 1 other CHD risk factor; approximately 35% of subjects were African American and approximately 36% had type 2 diabetes mellitus (Table 10). In this trial, patients were randomly assigned to initial therapy with a diuretic (chlorthalidone), an ACE inhibitor (lisinopril), an α -blocker (doxazosin), or a dihydropyridine CCB (amlodipine). An interim review by the data and safety monitoring board and an independent review panel determined that doxazosin-treated patients developed congestive heart failure at a greater rate than did diuretic-treated patients, and thus, the doxazosin arm was discontinued in 2000. Based on these data, it appears that α -adrenergic blockers should not be used as first-line agents in high-risk patients.

Chlorthalidone, lisinopril, and amlodipine did not differ in preventing major coronary events, the primary outcome of the trial, or in their effect on overall survival. However, chlorthalidone was associated with significantly fewer combined cardiovascular disease events,

Design	Population	Drugs	Terminated Arm	Final Results
		ALLHAT*		
Randomized, double-blind, controlled clinical trial Target blood pressure <130/85 mm Hg Primary outcome: composite of fatal and nonfatal cardiac end points Average follow-up, 6 y	N = 42 448 High-risk hypertensives aged ≥55 y 36% African American; 47% women; 36% diabetic	Chlorthalidone vs amlodipine or lisinopril or doxazosin	Doxazosin arm was terminated by the data and safety monitoring board because doxazosin-treated patients developed congestive heart failure at a greater rate than diuretic-treated patients†	Expected trial end data: 2002 Chlorthalidone, lisinopril, and amlodipine did not differ in preventing major coronary events‡ Chlorthalidone was superior to lisinopril in reducing stroke and heart failure and was superior to amlodipine in reducing heart failure
		AASK§		
Randomized, double-blind, controlled clinical trial 2 Levels of target blood pressure Primary outcome: rate of decline of GFR Average follow-up, 4 y	N = 1094 Nondiabetic African Americans with hypertensive renal disease, aged 18-70 y	Amlodipine vs ramipril vs metoprolol	Amlodipine arm was terminated by the data and safety monitoring board because ramipril was determined by have greater renoprotective effects than amlodipine, independent of blood pressure reduction‡	Ramipril reduced clinical events by 46% compared with amlodipine, and reduced decline in kidney function to a significantly greater extent than amlodipine or metoprolo

Abbreviations: AASK, African American Study of Kidney Disease and Hypertension; ALLHAT, Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; GFR, glomerular filtration rate.

*ALLHAT participants with elevated cholesterol levels (n = 10 377) were co-enrolled in a randomized, open-label trial to compare pravastatin therapy with "usual care" in reducing all-cause death.

+ALLHAT trial data suggest that α -adrenergic blockers should not be used as first-line agents in high-risk hypertensive patients.

‡ALLHAT trial data suggest that a thiazide diuretic should be a component of combination therapy in antihypertensive regimens.

\$AASK trial data demonstrated that dihydropyridine calcium channel blockers (CCBs) are less renoprotective than angiotensin-converting enzyme inhibitors in the presence of mild-to-moderate renal insufficiency. This finding may not apply to nondihydropyridine CCBs.

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including fewer strokes and less heart failure, and better blood pressure control as than lisinopril, and the difference was greater in the African American and other black ALLHAT participants. Amlodipine and chlorthalidone had similar results in terms of these secondary outcomes, with the exception of a higher rate of heart failure with amlodipine. By the completion of the trial, after approximately 5 years of treatment, patients received an average of 2 antihypertensive medications to achieve blood pressures lower than 140/90 mm Hg.

Based on these results, ALLHAT has established that thiazide-type diuretics should be a component of nearly all antihypertensive regimens and further confirms the need for combination therapy in high-risk patients with hypertension. Unfortunately, owing to the trial's design, it was not possible to note clinical outcomes for commonly used combination therapies, such as a diuretic in combination with an ACE inhibitor or CCB, or an ACE inhibitor in combination with a CCB. The ALLHAT data do not support a recommendation for the use of an ACE inhibitor as initial therapy in patients with diabetes without nephropathy. More data from this study will be forthcoming. Meanwhile, other clinical trial data and some current guidelines support the use of ACE inhibitor as initial therapy in patients with diabetes without nephropathy as well as in patients with nondiabetic renal disease, post-MI patients, and patients with heart failure.^{1,15,17,25,113-11}

Data also support the use of β-blockers in patients after MI infarction.^{18,19,120} Recent clinical trial data support initial therapy with an ARB for patients with type 2 diabetic nephropathy,^{20,21} heart failure,²³ or high blood pressure and left ventricular hypertrophy (LVH) with or without diabetes.^{121,122} However. until better data are available for clinical outcomes for African Americans with high blood pressure, ACE inhibitors are preferred to ARBs, except in cases where patients exhibit ACE-inhibitor intolerance.

RAS-Blocking Agents. Data now clearly support the use of RASblocking agents in African Americans with renal disease,¹⁴ and there is also a strong rationale for their use in patients with LVH in the presence or absence of diabetes121,122 and in diabetic nephropathy.^{20,21} The AASK trial^{14,25} evaluated the impact of treatment with an ACE inhibitor (ramipril), a β-blocker (metoprolol), and a CCB (amlodipine) on the progression of hypertensive kidney disease in African Americans with mild to moderate renal insufficiency. During the trial, the data and safety monitoring board determined that ramipril had greater renoprotective effects than amlodipine and terminated the amlodipine arm. The final results of AASK¹⁴ showed that ramipril reduced the decline in kidney function to a significantly greater extent than did metoprolol or amlodipine. Furthermore, ramipril reduced clinical events by 46% compared with amlodipine. Differences in blood pressure level did not account for the protective effects on renal function. These data provide strong evidence for including an ACE inhibitor in the antihypertensive regimen for African American patients with renal disease.

Angiotensin II receptor blockers, which inhibit the RAS by blocking the angiotensin II AT₁ receptor site, have demonstrated blood pressure-lowering efficacy in African American patients, particularly when combined with hydrochlorothiazide.^{94,106,123} Recent trial evidence has shown that in patients with diabetic nephropathy, ARBs slow the rate of progression of nephropathy and proteinuria (irbesartan or losartan)^{20,21} and also blunt an increase in microalbuminuria in patients with early diabetic nephropathy (irbesartan).²² Thus, an ARB may be considered at least as effective as an ACE inhibitor in the treatment of all patients with diabetic nephropathy who have higher than goal blood pressure.124 The Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study^{121,122} included 9193 patients with high blood pressure and LVH (6% were African American) who were randomized to receive either the ARB losartan or the B-blocker atenelol for a mean of 4.8 years. Patients with LVH were selected because they had evidence of target-organ damage. There was little

difference between the 2 groups in the degree of blood pressure reduction; however, losartan reduced the incidence of stroke by 25% more than did atenolol, and 25% fewer losartan-treated patients were diagnosed with new-onset diabetes during the course of the study.¹²¹ Losartan was also more effective than atenolol in reducing cardiovascular morbidity and mortality and all-cause mortality in the subpopulation of patients with high blood pressure, LVH, and diabetes.122 However, the benefit found in the above studies may not extend to the very small groups of African Americans included in these trials.

Because of the extensive data demonstrating their benefits in reducing cardiac events in patients with heart failure, ACE inhibitors are recommended for the African American population. Data from a recent trial also demonstrated a benefit for adding an ARB to the regimen of patients with heart failure.23 In this trial, valsartan significantly reduced signs and symptoms of heart failure and hospitalizations for heart failure compared with placebo. These benefits were seen when valsartan was added to an existing regimen except when the existing regimen was a combination of an ACE inhibitor and a β-blocker. Therefore, triple therapy with an ARB, an ACE inhibitor, and a β-blocker cannot be recommended, although this does not preclude the use of any 2 of these 3 drugs in patients with heart failure. When prescribing ACE inhibitors, the clinician should note that compared with whites, African Americans appear to be at increased risk for ACE inhibitor-associated angioedema,125-127 cough,128 or both. All patients should be instructed to report any symptoms suggestive of angioedema promptly. Patients who experience the bothersome adverse effect of dry cough with ACE inhibitors can be allowed a brief trial period to determine if this effect lessens with time. Because prostaglandins have been proposed as a cause of dry cough, some clinicians recommend having the patient take aspirin (500 mg/d) concomitantly, if not contraindicated.129 If the ACE inhibitorassociated cough is intolerable,

an ARB would be a reasonable alternative.

β-Blockers. β-Blockers comprise an integral component of recommended treatment for patients with stable and unstable angina^{130,131}; thus, African American patients with hypertension and evidence of myocardial ischemia or acute coronary syndromes should receive treatment with β-blockers for short- and long-term management. Likewise, an ACE inhibitor plus a β-blocker should be considered in the regimen of patients at high risk for ischemic heart disease, such as those with diabetes or renal failure.¹³²

Studies have confirmed that all post-MI patients (including African Americans) who received β-blockers had a significantly lower mortality than post-MI patients who did not receive β-blockers.¹⁸ Furthermore, in a placebo-controlled study,¹⁹ the β-blocker carvedilol reduced the risk of worsening heart failure to a similar extent (by about 50%) in all groups studied, including African American subjects. Thus, unless otherwise contraindicated, a β -blocker should be considered as an option for post-MI patients or patients with heart failure. B-Blockers may have adverse effects when used in patients with reactive airway disease or depression.

Additional Risk Factors and Blood Pressure Goals. Signs of hypertensive target-organ damage may appear in the heart, blood vessels, kidneys, brain, or eyes, and patients with these signs have a poorer prognosis than patients with hypertension who lack signs of targetorgan damage. Therefore, patients with diabetes, renal disease, heart failure, LVH, diastolic dysfunction, CHD, vascular diseases, microalbuminuria, transient ischemic attacks, or retinopathy (ie, signs of ongoing target-organ damage) should be considered highrisk patients. For example, data from the Framingham Heart Study¹³³ have shown that patients with hypertension and LVH have a 5-fold increase in the risk of sudden death and a 3-fold increase in the risk for coronary artery disease compared with patients with hypertension characterized by similar blood pressure but without LVH. Data are not available to demonstrate that achieving a lower target blood pressure (<130/80 mm Hg) reduces cardiovascular mortality in these high-risk patients. Nonetheless, it is not unreasonable for providers to attempt to achieve lower blood pressure goals in all highrisk patients.

SUMMARY

A new approach is needed to reduce the adverse cardiovascular and re-

nal outcomes associated with high blood pressure in African Americans. More traditional strategies for management of high blood pressure in African Americans-for example, accepting blood pressure levels above target goals, titrating to high-dose monotherapy, abandoning the use of low-dose diuretics, and avoiding RAS-blocking agentshave proven unsuccessful. The "best practice" strategies described in the present consensus statement are intended to achieve efficacy in blood pressure reduction in tandem with protection against target-organ damage (Table 11). These strategies involve assessing cardiovascular risk; setting, achieving, and maintaining an appropriate blood pressure target; assisting patients to implement therapeutic lifestyle changes; and administering effective pharmacologic interventions early and persistently.

The African American population is far from homogeneous, and each African American patient should be treated as an individual. Nonetheless, observational data suggest that African Americans are at higher risk than the general population for the negative consequences of hypertension. Therefore, the importance of treating high blood pressure to achieve the appropriate blood pressure goal can-

Table 11. Treatment Pearls: Management of High Blood Pressure in African Americans

- Compared with white Americans, African Americans are at greater risk for the development of high blood pressure, type 2 diabetes mellitus, coronary heart disease (CHD), heart failure, left ventricular hypertension, stroke, and end-stage renal disease. These facts suggest the need to obtain blood pressure measurements and assess risk for cardiovascular disease in African Americans at regular intervals across the life span in all primary care settings.
- Clinicians should make concerted efforts to increase awareness among African Americans of the links between lifestyle choices and cardiovascular and renal outcomes.
- Both high dietary sodium and low dietary potassium intake may contribute to excess high blood pressure in African Americans. Clinicians should recommend increasing dietary potassium while moderating sodium intake to the recommended <2.4 g/d.
- Obesity and inactivity are particularly prevalent among African American women and should be viewed as major cardiovascular risk factors in all African Americans.
- The Dietary Approaches to Stop Hypertension (DASH) diet was found to be particularly beneficial in lowering blood pressure in African Americans. Information about this diet is readily available and should be provided to patients.
- African Americans have a high prevalence of type 2 diabetes mellitus. Based on current National Cholesterol Education Program guidelines, patients with type 2 diabetes have a CHD risk that is equivalent to the risk for patients with CHD and require intensive interventions to lower low-density lipoprotein cholesterol levels to the goal of <100 mg/dL (<2.59 mmol/L).
- . The perception that it is more medically difficult to lower blood pressure in African Americans than in other patients is unjustified.
- All antihypertensive drug classes are associated with blood pressure-lowering efficacy in African Americans, although combination therapy may
 frequently be required to achieve and maintain target blood pressure.
- As monotherapy, β-blockers and angiotensin-converting enzyme (ACE) inhibitors may produce less blood pressure-lowering effects in African Americans than in whites.
- Thiazide diuretics and calcium channel blockers may have greater blood pressure-lowering efficacy than do other classes in African Americans.
- Where compelling indications have been identified for prescribing specific classes of agents, such as β-blockers or renin-angiotensin system–blocking
 agents (ACE inhibitors or angiotensin II receptor blockers), these compelling indications should be applied equally to African American patients.
- When prescribing ACE inhibitors, it is important to note that compared with whites, African Americans appear to be at increased risk for ACE inhibitor-associated angioedema, cough, or both. All patients should be instructed to report any symptoms related to angioedema promptly.

Recommendations Reviewed by the HAAW Group

1995 Update of the Working Group Reports on Chronic Renal Failure and Renovascular Hypertension. Washington, DC: National Heart, Lung, and Blood Institute, National Institutes of Health; 1995. NIH publication 95-3719.

American Diabetes Association. Clinical practice recommendations 2001. *Diabetes Care*. 2001;24(suppl 1):S1-S133.

American Diabetes Association. Treatment of hypertension in adults with diabetes. *Diabetes Care*. 2002;25:199-201.

Bakris GL, Williams M, Dworkin L, et al. Preserving renal function in adults with hypertension and diabetes: a consensus approach. *Am J Kidney Dis.* 2000; 36:646-661.

Fletcher GF, Balady G, Froelicher VF. Exercise standards: a statement for healthcare professionals from the American Heart Association. *Circulation*. 1995; 91:580-615.

Grundy SM, Pasternack R, Greenland P, et al. Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology (ACC). *Circulation*. 1999;100:1481-1492.

Guidelines Subcommittee of the World Health Organization–International Society of Hypertension (WHO-ISH) Mild Hypertension Liaison Committee. 1999 World Health Organization–International Society of Hypertension guidelines for the management of hypertension. *J Hypertens*. 1999;17:151-183.

Hennekens CH, Dyken ML, Fuster V. Aspirin as a therapeutic agent in cardiovascular disease: a statement for healthcare professionals from the American Heart Association. *Circulation*. 1997;96:2751-2753.

Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI). *Arch Intern Med.* 1997;157:2413-2466.

Kotchen TA, McCaron DA. Dietary electrolytes and blood pressure: a statement for healthcare professionals from the American Heart Association nutrition committee. *Circulation*. 1998;98:613-617.

Krauss RM, Eckel RH, Howard B, et al. AHA dietary guidelines, revision 2000: a statement for healthcare professionals from the nutrition committee of the American Heart Association. *Circulation*. 2000;102:2284-2299.

not be overemphasized. A greater burden of cardiovascular risk requires that providers set lower blood pressure goals and embark on resolute efforts to achieve these goals. For patients with uncomplicated hypertension and nondiabetic renal insufficiency with proteinuria characterized by less than 1 g/d, the target blood pressure goal should be lower than 140/90 mm Hg at the highest. For patients at high risk for cardiovascular events-in particular, those with type 2 diabetes mellitus or renal insufficiency-the target blood pressure goal should be lower than 130/80 mm Hg.

To reach appropriate blood pressure levels, most African Americans will require combination antihypertensive therapy. When combination therapy using agents from 2 major drug classes is required to achieve target blood pressure goals, the following combinations may be considered effective: β-blocker/diuretic, ACE inhibitor/ diuretic, ACE inhibitor/CCB, or ARB/diuretic.

There are now persuasive data to support the use of thiazide diuretics, β -blockers, RAS-blocking agents, and dihydropyridine CCBs in African Americans to reduce the risk of target-organ damage and adverse outcomes. Where compelling indications have been identified for prescribing β -blockers or RASblocking agents (either ACE inhibitors or ARBs) in certain groups of patients with hypertension, these indications should be applied equally to African American patients.

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REFERENCES

- Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI). Arch Intern Med. 1997:157:2413-2466.
- American Heart Association. 2001 Heart and Stroke Statistical Update. Dallas, Tex: American Heart Association; 2000.
- Klag MJ, Whelton PK, Randall BL, et al. Blood pressure and end-stage renal disease in men. *N Engl J Med.* 1996;334:13-18.
- Psaty BM, Furberg CD, Kuller LH, et al. Association between blood pressure level and the risk of myocardial infarction, stroke, and total mortality: the Cardiovascular Health Study. *Arch Intern Med.* 2001;161:1183-1192.
- Sesso HD, Stampfer MJ, Rosner B, et al. Systolic and diastolic blood pressure, pulse pressure, and mean arterial pressure as predictors of cardiovascular disease risk in men. *Hypertension.* 2000;36:801-807.
- Vasan RS, Massaro JM, Wilson PW, et al. Antecedent blood pressure and risk of cardiovascular disease: the Framingham Heart Study. *Circulation*. 2002;105:48-53.
- Vasan RS, Larson MG, Leip EP, Kannel WB, Levy D. Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham Heart Study: a cohort study. *Lancet.* 2001;358:1682-1686.
- Berenson GS, Voors AW, Webber LS, Dalferes ER Jr, Harsha DW. Racial differences of parameters associated with blood pressure levels in chil-

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dren: the Bogalusa Heart Study. *Metabolism.* 1979;28:1218-1228.

- Young-Hyman D, Schlundt DG, Herman L, De Luca F, Counts D. Evaluation of the insulin resistance syndrome in 5- to 10-year-old overweight/obese African American children. *Diabetes Care.* 2001;24:1359-1364.
- Harshfield GA, Treiber FA. Racial differences in ambulatory blood pressure monitoring-derived 24 h patterns of blood pressure in adolescents. *Blood Press Monit.* 1999;4:107-110.
- Levine RS, Foster JE, Fullilove RE, et al. Blackwhite inequalities in mortality and life expectancy, 1933-1999: implications for healthy people 2010. Public Health Rep. 2001;116:474-483.
- Oliveria SA, Lapuerta P, McCarthy BD, L'Italien GJ, Berlowita DR. Physician-related barriers to the effective management of uncontrolled hypertension. *Arch Intern Med.* 2002;162:413-420.
- The ALLHAT Officers and Coordinators, for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting inhibitor or calcium channel blocker vs diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA. 2002; 288:2981-2197.
- Wright JT Jr, Bakris G, Greene T, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney diseasse: results from the AASK trial. JAMA. 2002;288:2421-2431.
- Guidelines Subcommittee of the World Health Organization–International Society of Hypertension (WHO-ISH) Mild Hypertension Liaison Committee. 1999 World Health Organization– International Society of Hypertension guidelines for the management of hypertension. J Hypertens. 1999;17:151-183.
- Izzo JL Jr, Levy D, Black HR. Clinical advisory statement: importance of systolic blood pressure in older Americans. *Hypertension*. 2000; 35:1021-1024.
- Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G, for the Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med.* 2000;342:145-153.
- Gottlieb SS, McCarter RJ, Vogel RA. Effect of beta-blockade on mortality among high-risk and low-risk patients after myocardial infarction. *N Engl J Med.* 1998;339:489-497.
- Yancy CW, Fowler MB, Colucci WS, et al. Race and the response to adrenergic blockade with carvedilol in patients with chronic heart failure. *N Engl J Med.* 2001;344:1358-1365.
- Lewis EJ, Hunsicker LG, Clarke WR, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med.* 2001; 345:851-860.
- Brenner BM, Cooper ME, De Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med. 2001;345:861-869.
- 22. Parving HH, Lehnert H, Bröchner-Mortensen J, Gomis R, Anderson S, Arner P, for the Irbersartan in Patients With Type 2 Diabetes and Microalbuminuria Study Group. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. *N Engl J Med.* 2001;345:870-878.
- 23. Cohn JN, Tognoni G, for the Valsartan Heart Fail-

ure Trial Investigators. A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure. *N Engl J Med.* 2001;345:1667-1675.

- ALLHAT Collaborative Research Group. Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA. 2000;283:1967-1975.
- Agodoa LY, Appel L, Bakris GL, et al. Effect of ramipril vs amlodipine on renal outcomes in hypertensive nephrosclerosis: a randomized controlled trial. JAMA. 2001;285:2719-2728.
- Law CM, Shiell AW. Is blood pressure inversely related to birth weight? the strength of evidence from a systematic review of the literature. J Hypertens. 1996;14:935-941.
- Kannel WB, McGee D, Gordon T. A general cardiovascular risk profile: the Framingham Study. *Am J Cardiol.* 1976;38:46-51.
- Grundy SM, Pasternak R, Greenland P, Smith S Jr, Fuster V. Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation*. 1999;100:1481-1492.
- D'Agostino RB Sr, Grundy S, Sullivan LM, Wilson P. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. *JAMA*. 2001; 286:180-187.
- Eckel RH. Obesity and heart disease: a statement for healthcare professionals from the Nutrition Committee, American Heart Association. *Circulation*. 1997;96:3248-3250.
- Fletcher GF, Balady G, Froelicher VF, Hartley LH, Haskell WL, Pollock ML. Exercise standards: a statement for healthcare professionals from the American Heart Association Writing Group. *Circulation*. 1995;91:580-615.
- 32. National Cholesterol Education Program. Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Bethesda, Md: National Heart, Lung, and Blood Institute of the National Institutes of Health; 2001.
- Hillege HL, Janssen WM, Bak AA, et al. Microalbuminuria is common, also in a nondiabetic, nonhypertensive population, and an independent indicator of cardiovascular risk factors and cardiovascular morbidity. *J Intern Med.* 2001; 249:519-526.
- 34. Jensen JS, Feldt-Rasmussen B, Borch-Johnsen K, Clausen P, Appleyard M, Jensen G. Microalbuminuria and its relation to cardiovascular disease and risk factors: a populationbased study of 1254 hypertensive individuals. *J Hum Hypertens*. 1997;11:727-732.
- Cirillo M, Senigalliesi L, Laurenzi M, et al. Microalbuminuria in nondiabetic adults: relation of blood pressure, body mass index, plasma cholesterol levels, and smoking: the Gubbio Population Study. Arch Intern Med. 1998;158:1933-1939.
- Keane WF, Eknoyan G. Proteinuria, albuminuria, risk, assessment, detection, elimination (PARADE): a position paper of the National Kidney Foundation. *Am J Kidney Dis.* 1999;33:1004-1010.
- American Diabetes Association. Clinical practice recommendations 2001. *Diabetes Care*. 2001; 24(suppl 1):S1-S133.
- 38. Hebert LA, Kusek JW, Greene T, et al, for the

Modification of Diet in Renal Disease Study Group. Effects of blood pressure control on progressive renal disease in blacks and whites. *Hypertension.* 1997;30:428-435.

- Lewis JB, Berl T, Bain RP, Rohde RD, Lewis EJ, for the Collaborative Study Group. Effect of intensive blood pressure control on the course of type 1 diabetic nephropathy. *Am J Kidney Dis.* 1999;34:809-817.
- Hansson L, Zanchetti A, Carruthers SG, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. *Lancet.* 1998; 351:1755-1762.
- United Kingdom Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ*. 1998; 317:703-713.
- Schrier RW, Estacio RO, Esler A, Mehler P. Effects of aggressive blood pressure control in normotensive type 2 diabetic patients on albuminuria, retinopathy and strokes. *Kidney Int.* 2002; 61:1086-1097.
- Bakris GL, Williams M, Dworkin L, et al, for the National Kidney Foundation Hypertension and Diabetes Executive Committees Working Group. Preserving renal function in adults with hypertension and diabetes: a consensus approach. *Am J Kidney Dis.* 2000;36:646-661.
- American Diabetes Association. Treatment of hypertension in adults with diabetes. *Diabetes Care*. 2002;25:199-201.
- Tuomilehto J, Rastenyte D, Birkenhager WH, Thijs L, Antikainen R, Bulpitt CJ, for the Systolic Hypertension in Europe Trial Investigators. Effects of calcium-channel blockade in older patients with diabetes and systolic hypertension. *N Engl J Med.* 1999;340:677-684.
- Estacio RO, Jeffers BW, Gifford N, Schrier RW. Effect of blood pressure control on diabetic microvascular complications in patients with hypertension and type 2 diabetes. *Diabetes Care*. 2000;23(suppl 2):B54-B64.
- Bakris GL, Mangrum A, Copley JB, Vicknair N, Sadler R. Effect of calcium channel or betablockade on the progression of diabetic nephropathy in African Americans. *Hypertension*. 1997;29:744-750.
- Bakris GL, Copley JB, Vicknair N, Sadler R, Leurgans S. Calcium channel blockers versus other antihypertensive therapies on progression of NIDDM-associated nephropathy. *Kidney Int.* 1996;50:1641-1650.
- Powers DR, Wallin JD. End-stage renal disease in specific ethnic and racial groups: risk factors and benefits of antihypertensive therapy. *Arch Intern Med.* 1998;158:793-800.
- Maki DD, Ma JZ, Louis TA, Kasiske BL. Longterm effects of antihypertensive agents on proteinuria and renal function. *Arch Intern Med.* 1995;155:1073-1080.
- PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure– lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet.* 2001;358:1033-1041.
- Redon J. Treatment of patients with essential hypertension and microalbuminuria. *Drugs.* 1997; 54:857-866.
- 53. Gerstein HC, Mann JF, Pogue J, et al, for the HOPE Study Investigators. Prevalence and determinants of microalbuminuria in high-risk diabetic and nondiabetic patients in the Heart Out-

comes Prevention Evaluation Study. *Diabetes Care.* 2000;23(suppl 2):B35-B39.

- Pedrinelli R, Dell'Omo G, Di Bello V, Pontremoli R, Mariani M. Microalbuminuria, an integrated marker of cardiovascular risk in essential hypertension. J Hum Hypertens. 2002;16:79-89.
- Kotchen TA, McCarron DA. Dietary electrolytes and blood pressure: a statement for healthcare professionals from the American Heart Association Nutrition Committee. *Circulation*. 1998;98: 613-617.
- Krauss RM, Eckel RH, Howard B, et al. AHA dietary guidelines revision 2000: a statement for healthcare professionals from the nutrition committee of the American Heart Association. *Circulation*. 2000;102:2284-2299.
- Neaton JD, Grimm RH Jr, Prineas RJ, et al, for the Treatment of Mild Hypertension Study Research Group. Treatment of Mild Hypertension Study: final results. *JAMA*. 1993;270:713-724.
- Weir MR, Haynes DS. Hypertension in African Americans: a paradigm of metabolic disarray. *Semin Nephrol.* 1996;16:102-109.
- Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation*. 1998;97:1837-1847.
- Weir MR. Salt intake and hypertensive renal injury in African Americans: a therapeutic perspective. Am J Hypertens. 1995;8:635-644.
- Morris RC, Sebastian A, Forman A, Tanaka M, Schmidlin O. Normotensive salt sensitivity: effects of race and dietary potassium. *Hypertension*. 1999;33:18-23.
- Appel LJ, Moore TJ, Obarzanek E, et al, for the DASH Collaborative Research Group. A clinical trial of the effects of dietary patterns on blood pressure. N Engl J Med. 1997;336:1117-1124.
- Sacks FM, Svetkey LP, Vollmer WM, et al, for the DASH-Sodium Collaborative Research Group. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. N Engl J Med. 2001; 344:3-10.
- Appel LJ, Espeland MA, Easter L, Wilson AC, Folmar S, Lacy CR. Effects of reduced sodium intake on hypertension control in older individuals: results from the Trial of Nonpharmacologic Interventions in the Elderly (TONE). Arch Intern Med. 2001;161:685-693.
- Intersalt Cooperative Research Group. Intersalt: an international study of electrolyte excretion and blood pressure: results for 24 hour urinary sodium and potassium excretion. *BMJ*. 1988;297:319-328.
- Flack JM, Grimm RH Jr, Staffileno BA, et al. New salt-sensitivity metrics: variability-adjusted blood pressure change and the urinary sodium-tocreatinine ratio. *Ethn Dis.* 2002;12:10-19.
- Stevens VJ, Obarzanek E, Cook N, et al. Longterm weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, phase II. Ann Intern Med. 2001;134: 1-11.
- National Center for Chronic Disease Prevention and Health Promotion. Physical activity and health: a report of the Surgeon General. Available at: http://www.cdc.gov/nccdphp/sgr/ summary.htm. Accessed April 18, 2002.
- 69. US Department of Health and Human Services. Reducing Tobacco Use: A Report of the Surgeon General—Executive Summary. Atlanta, Ga: US Dept of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and

Health Promotion, Office on Smoking and Health; 2000.

- Demirovic J. Public health aspects of out-ofhospital sudden cardiac arrest among elderly African Americans. *Am J Geriatr Cardiol.* 1997;6: 24-30.
- Hennekens CH, Dyken ML, Fuster V. Aspirin as a therapeutic agent in cardiovascular disease: a statement for healthcare professionals from the American Heart Association. *Circulation*. 1997; 96:2751-2753.
- Hansson L, Lindholm LH, Ekbom T, et al. Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity: the Swedish Trial in Old Patients With Hypertension-2 study. *Lancet.* 1999; 354:1751-1756.
- SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension: final results of the Systolic Hypertension in the Elderly Program (SHEP). JAMA. 1991; 265:3255-3264.
- 74. Staessen JA, Fagard R, Thijs L, et al, for the Systolic Hypertension in Europe (SYST-EUR) Trial Investigators. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. *Lancet.* 1997;350:757-764.
- Bakris GL. Maximizing cardiorenal benefit in the management of hypertension: achieve blood pressure goals. J Clin Hypertens (Greenwich). 1999;1:141-147.
- Lee JY, Greene PG, Douglas M, et al. Appointment attendance, pill counts, and achievement of goal blood pressure in the African American Study of Kidney Disease and Hypertension Pilot Study. *Control Clin Trials.* 1996;17(suppl 4): 34S-39S.
- Agodoa LY, Appel L, Bakris GL, et al. Effect of ramipril vs amlodipine on renal outcomes in hypertensive nephrosclerosis: a randomized controlled trial. JAMA. 2001;285:2719-2728.
- Sica DA, Douglas JG. The African American Study of Kidney Disease and Hypertension (AASK): new findings. J Clin Hypertens (Greenwich). 2001; 3:244-251.
- Hilleman DE, Ryschon KL, Mohiuddin SM, Wurdeman RL. Fixed-dose combination vs monotherapy in hypertension: a meta-analysis evaluation. J Hum Hypertens. 1999;13:477-483.
- Kannel WB. Elevated systolic blood pressure as a cardiovascular risk factor. *Am J Cardiol*. 2000; 85:251-255.
- He J, Whelton PK. Elevated systolic blood pressure as a risk factor for cardiovascular and renal disease. *J Hypertens Suppl.* 1999;17:S7-S13.
- He J, Whelton PK. Elevated systolic blood pressure and risk of cardiovascular and renal disease: overview of evidence from observational epidemiologic studies and randomized controlled trials. *Am Heart J.* 1999;138(3, pt 2):211-219.
- Psaty BM, Smith NL, Siscovick DS, et al. Health outcomes associated with antihypertensive therapies used as first-line agents: a systematic review and meta-analysis. *JAMA*. 1997;277:739-745.
- Ames RP. A comparison of blood lipid and blood pressure responses during the treatment of systemic hypertension with indapamide and with thiazides. *Am J Cardiol.* 1996;77:12B-16B.
- Schwartz RS. Racial profiling in medical research. N Engl J Med. 2001;344:1392-1393.

- Flack JM, Mensah GA, Ferrario CM. Using angiotensin converting enzyme inhibitors in African American hypertensives: a new approach to treating hypertension and preventing targetorgan damage. *Curr Med Res Opin.* 2000;16: 66-79.
- Flack JM, Oparil S, Pratt JH, et al. Efficacy and tolerability of epleronone and losartan in hypertensive black patients and white patients. *J Am Coll Surg.* In press.
- Dargie HJ. Effect of carvedilol on outcome after myocardial infarction in patients with leftventricular dysfunction: the CAPRICORN randomized trial. *Lancet*. 2001;357:1385-1390.
- Abernethy DR, Schwartz JB. Calciumantagonist drugs. N Engl J Med. 1999;341:1447-1457.
- Grossman E, Messerli FH, Goldbourt U. High blood pressure and diabetes mellitus: are all antihypertensive drugs created equal? *Arch Intern Med.* 2000;160:2447-2452.
- Laing C, Unwin RJ. Are calcium antagonists effective in preventing complications of hypertension and progression of renal disease? *Curr Opin* Nephrol Hypertens. 2000;9:489-495.
- Neal B, MacMahon S, Chapman N, for the Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. *Lancet.* 2000;356:1955-1964.
- Exner DV, Dries DL, Domanski MJ, Cohn JN. Lesser response to angiotensin-converting enzyme inhibitor therapy in black as compared with white patients with left ventricular dysfunction. *N Engl J Med.* 2001;344:1351-1357.
- Flack JM, Saunders E, Gradman A, et al. Antihypertensive efficacy and safety of losartan alone and in combination with hydrochlorothiazide in adult African Americans with mild to moderate hypertension. *Clin Ther.* 2001;23:1193-1208.
- McGill JB, Reilly PA. Combination treatment with telmisartan and hydrochlorothiazide in black patients with mild-to-moderate hypertension. *Clin Cardiol.* 2001;24:66-72.
- Prisant LM, Mensah GA. Use of betaadrenergic receptor blockers in blacks. *J Clin Pharmacol.* 1996;36:867-873.
- Richardson AD, Piepho RW. Effect of race on hypertension and antihypertensive therapy. *Int J Clin Pharmacol Ther.* 2000;38:75-79.
- Cushman WC, Reda DJ, Perry HM, Williams D, Abdellatif M, Materson BJ, for the Department of Veterans Affairs Cooperative Study Group on Antihypertensive Agents. Regional and racial differences in response to antihypertensive medication use in a randomized controlled trial of men with hypertension in the United States. Arch Intern Med. 2000;160:825-831.
- Saunders E, Weir MR, Kong BW, et al. A comparison of the efficacy and safety of a β-blocker, a calcium channel blocker, and a converting enzyme inhibitor in hypertensive blacks. *Arch Intern Med.* 1990;150:1707-1713.
- 100. Materson BJ, Reda DJ, Williams D, for the Department of Veterans Affairs Cooperative Study Group on Antihypertensive Agents. Lessons from combination therapy in Veterans Affairs Studies. Am J Hypertens. 1996;9:187S-191S.
- 101. Roca-Cusachs A, Torres F, Horas M, et al. Nitrendipine and enalapril combination therapy in mild to moderate hypertension: assessment of dose-response relationship by a clinical trial of factorial design. *J Cardiovasc Pharmacol.* 2001; 38:840-849.

- 102. Messerli FH, Oparil S, Feng Z. Comparison of efficacy and side effects of combination therapy of angiotensin-converting enzyme inhibitor (benazepril) with calcium antagonist (either nifedipine or amlodipine) versus high-dose calcium antagonist monotherapy for systemic hypertension. *Am J Cardiol.* 2000;86:1182-1187.
- 103. Frishman WH, Ram CV, McMahon FG, et al, for the Benazepril/Amlodipine Study Group. Comparison of amlodipine and benazepril monotherapy to amlodipine plus benazepril in patients with systemic hypertension: a randomized, double-blind, placebo-controlled, parallelgroup study. J Clin Pharmacol. 1995;35:1060-1066.
- 104. Frishman WH, Bryzinski BS, Coulson LR, et al. A multifactorial trial design to assess combination therapy in hypertension: treatment with bisoprolol and hydrochlorothiazide. Arch Intern Med. 1994;154:1461-1468.
- 105. Luscher TF, Waeber B. Efficacy and safety of various combination therapies based on a calcium antagonist in essential hypertension: results of a placebo-controlled randomized trial. J Cardiovasc Pharmacol. 1993;21:305-309.
- 106. McGill JB, Reilly PA. Telmisartan plus hydrochlorothiazide versus telmisartan or hydrochlorothiazide monotherapy in patients with mild to moderate hypertension: a multicenter, randomized, double-blind, placebo-controlled, parallelgroup trial. *Clin Ther.* 2001;23:833-850.
- Glasser SP, Chrysant SG, Graves J, Rofman B, Koehn DK. Safety and efficacy of amlodipine added to hydrochlorothiazide therapy in essential hypertension. Am J Hypertens. 1989;2:154-157.
- 108. Mogensen CE, Neldam S, Tikkanen I, et al. Randomised controlled trial of dual blockade of reninangiotensin system in patients with hypertension, microalbuminuria, and non-insulin dependent diabetes: the candesartan and lisinopril microalbuminuria (CALM) study. *BMJ*. 2000;321:1440-1444.
- 109. Fogari R, Corea L, Cardoni O, et al. Combined therapy with benazepril and amlodipine in the treatment of hypertension inadequately controlled by an ACE inhibitor alone. J Cardiovasc Pharmacol. 1997;30:497-503.
- 110. Sica DA. Rationale for fixed-dose combinations in the treatment of hypertension: the cycle repeats. *Drugs*. 2002;62:443-62.
- 111. Pool JL, Cushman WC, Saini RK, Nwachuku CE, Battikha JP. Use of the factorial design and quadratic response surface models to evaluate the fosinopril and hydrochlorothiazide combination therapy in hypertension. Am J Hypertens. 1997;10:117-123.
- 112. Kochar M, Guthrie R, Triscari J, Kassler-Taub K,

Reeves RA. Matrix study of irbesartan with hydrochlorothiazide in mild-to-moderate hypertension. *Am J Hypertens*. 1999;12:797-805.

- 113. SOLVD Investigators. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. *N Engl J Med.* 1992; 327:685-691.
- Lewis EJ, Hunsicker LG, Bain RP, Rohde ED. The effect of angiotensin converting enzyme inhibition on diabetic nephropathy. *N Engl J Med.* 1993; 329:1456-1462.
- 115. Cleland JG, Erhardt L, Murray G, Hall AS, Ball SG. Effect of ramipril on morbidity and mode of death among survivors of acute myocardial infarction with clinical evidence of heart failure: a report from the AIRE Study Investigators. *Eur Heart J.* 1997;18:41-51.
- 116. Tatti P, Pahor M, Byington RP, et al. Outcome results of the Fosinopril Versus Amlodipine Cardiovascular Events Randomized Trial (FACET) in patients with hypertension and NIDDM. *Diabetes Care*. 1998;21:597-603.
- 117. Estacio R, Jeffers BW, Hiatt WR, Biggerstaff SL, Gifford N, Schipher RW. The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin dependent diabetes and hypertension. *N Engl J Med.* 1998;338:645-652.
- 118. Kober L, Torp-Pedersen C, Carlsen JE, et al, for the Trandolapril Cardiac Evaluation (TRACE) Study Group. A clinical trial of the angiotensinconverting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med*. 1995;333:1670-1676.
- 119. Parving HH, Hommel E, Jensen BR, Hansen HP. Long-term beneficial effect of ACE inhibition on diabetic nephropathy in normotensive type 1 diabetic patients. *Kidney Int.* 2001;60:228-234.
- 120. Haywood LJ. Coronary heart disease mortality/ morbidity and risk in blacks, I: clinical manifestations and diagnostic criteria: the experience with the Beta Blocker Heart Attack Trial. Am Heart J. 1984;108:787-793.
- 121. Dahlöf B, Devereux RB, Kjeldsen SE, et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet*. 2002;359:995-1003.
- 122. Lindholm LH, Ibsen H, Dahlöf B, et al. Cardiovascular morbidity and mortality in patients with diabetes in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet.* 2002; 359:1004-1010.
- 123. Weir MR, Smith DHG, Neutel JM, Bedigian MP.

Valsartan alone or with a diuretic or ACE inhibitor as treatment for African American hypertensives: relation to salt intake. *Am J Hypertens*. 2001;14:665-671.

- 124. Sica DA, Bakris GL. Type 2 diabetes: RENAAL and IDNT—the emergence of new treatment options. J Clin Hypertens (Greenwich). 2002;4:52-57.
- Gainer JV, Nadeau JH, Ryder D, et al. Increased sensitivity to bradykinin among African Americans. J Allergy Clin Immunol. 1996;98:283-287.
- Cohen EG, Soliman AM. Changing trends in angioedema. Ann Otol Rhinol Laryngol. 2001;110: 701-706.
- 127. Brown NJ, Ray WA, Snowden M, Griffin MR. Black Americans have an increased rate of angiotensin converting enzyme inhibitorassociated angioedema. *Clin Pharmacol Ther.* 1996;60:8-13.
- Elliott WJ. Higher incidence of discontinuation of angiotensin converting enzyme inhibitors due to cough in black subjects. *Clin Pharmacol Ther.* 1996;60:582-588.
- 129. Tenenbaum A, Grossman E, Shemesh J, Fisman EZ, Nosrati I, Motro M. Intermediate but not low doses of aspirin can suppress angiotensinconverting enzyme inhibitor-induced cough. Am J Hypertens. 2000;13:776-782.
- 130. Braunwald E, Antman EM, Beasley JW, et al. ACC/ AHA guidelines for the management of patients with unstable angina and non–ST-segment elevation myocardial infarction: executive summary and recommendations: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients with Unstable Angina). *Circulation*. 2000;102:1193-1209.
- 131. Gibbons RJ, Chatterjee K, Daley J, et al. ACC/ AHA/ACP-ASIM guidelines for the management of patients with chronic stable angina: executive summary and recommendations: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients with Chronic Stable Angina). *Circulation.* 1999;99:2829-2848.
- 132. Smith SC Jr, Greenland P, Grundy SM, for the American Heart Association. Beyond secondary prevention: identifying the high-risk patient for primary prevention. *Circulation*. 2000;101: 111-116.
- Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Engl J Med.* 1990;322:1561-1566.

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