HIGH-RISK AFRICAN AMERICANS WITH MULTIPLE RISK FACTORS FOR CARDIOVASCULAR DISEASE: CHALLENGES IN PREVENTION, DIAGNOSIS, AND TREATMENT

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Coronary heart disease (CHD) is the second leading cause of death in the United States. Despite previous downward trends, which have not persisted, CHD mortality remains higher in African Americans than in Whites. Among African American and White adolescents and adults are trends of increased physical inactivity, smoking, and obesity. Approximately 47 million Americans have metabolic syndrome, a constellation of obesity, hypertension, dyslipidemia, and insulin resistance leading to diabetes. Despite a lower prevalence of metabolic syndrome, African Americans are more insulin resistant than Whites at similar degrees of adiposity, have higher blood pressures, and among women, have more obesity. Since African Americans tend to be diagnosed later and have more risk factors, which confers greater than additive risks, we propose the term ''African American multiple-risk patient (AAMRP).'' The AAMRP poses clinical and public health challenges for healthcare providers. We provide clinical and public health strategies for early detection and aggressive management of AAMRP. (*Ethn Dis*. 2006;16:633–639)

Key Words: African Americans, Cardiovascular Disease, High-Risk

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INTRODUCTION

Cardiovascular disease (CVD) is the second leading cause of death in the United States and in most developed countries.[1] Downward trends in coronary heart disease (CHD) mortality are less pronounced in African Americans than in Whites despite a similar or lower prevalence of obstructive coronary disease and earlier clinical onset.[2] In African American and White adolescents as well as adults, we find trends of increased obesity and physical inactivity. In addition, adolescents are now smoking more than their parents at comparable ages.[3–6]

The metabolic syndrome, a constellation of risk factors that includes abdominal obesity, insulin resistance with or without glucose intolerance, elevated blood pressure, and atherogenic dyslipidemia (elevated triglyceride and low high-density lipoprotein cholesterol [HDL-C]) is a major clinical and public health challenge. The clinical challenge derives from the fact that patients with multiple risk factors have greater than additive risk. The public health challenge derives from the fact that ≈47 million Americans, nearly one fourth of the United States population, have metabolic syndrome as defined by the Third Adult Treatment Panel (ATP-III) of the National Cholesterol Education Program and therefore are at high risk for cardiovascular disease.[7–11] In those over age 40, the proportion rises to ≈40%, and their average 10-year risk of a first CHD event is ≈16%–18%. Further, patients with metabolic syndrome are more likely to develop diabetes, which is a CHD risk equivalent. The term ''CHD risk equivalent'' implies that diabetics should be treated as aggressively as survivors of a first myocardial infarction (MI) or stroke.

Approximately 47 million Americans, nearly one fourth of the US population, have metabolic syndrome as defined by the Third Adult Treatment Panel (ATP-III) of the National Cholesterol Education Program and therefore are at high risk for cardiovascular disease.[7–11]

The clinical and public health impact of metabolic syndrome in the African American population is likely to be large and compounded by underdiagnosis, especially in women. According to the Third National Health and Nutrition Examination Survey (NHANES III), African American men and women have the highest age-adjusted prevalence of high blood pressure, and African American women have the highest age-adjusted prevalence of abdominal obesity.[3,7,10] Given that African Americans are diagnosed later, have higher individual risk factors as well as more risk factors, and because the presence of multiple risk factors confers greater than additive risk,[12] we have defined the African American multiple-risk patient (AAMRP). The AAMRP poses major clinical and public health

challenges for healthcare providers. We provide herein clinical and public health strategies for early detection and aggressive management of AAMRP.

WHO IS THE AAMRP?

Cardiovascular risk factors include both genetic and environmental factors. Further, familial and ethnic risk factors have genetic and environmental components.[13] Risk factor clustering is common in African Americans. According to new data from NHANES III, African American men and women have a lower age-specific prevalence of metabolic syndrome than White men and women. African Americans, however, have the highest rates of CHD mortality and tend to have more obesity among women, as well as more hypertension and diabetes mellitus or glucose intolerance. Paradoxically, African Americans are less likely to have the "atherogenic dyslipidemic triad" (elevated low-density lipoprotein cholesterol [LDL-C], high triglycerides, and low HDL-C).[10] In one study, African American men with CHD had significantly higher levels of HDL-C than White men with CHD.[14] African Americans also have a higher prevalence of small, dense LDL-C particles and elevated lipoprotein (a).

The AAMRP may be diagnosed as a patient who self-defines as African American and who fulfills the metabolic syndrome criteria. In these high-risk patients, the various modifiable cardiovascular risk factors are often underdiagnosed, frequently uncontrolled, more severe at presentation, and may be associated with a positive family history. Thus, delays in identification lead to greater difficulties in management, and ultimately, to higher morbidity and mortality.

Target Organ Damage

Many AAMRP at the time of presentation have at least some degree of hypertension, dyslipidemia, diabetes mellitus, and even renal insufficiency, which alone and in combination may increase risks of myocardial infarction (MI), stroke, peripheral arterial disease, end-stage renal disease (ESRD), and cardiovascular death.[15] Cardiovascular and cerebrovascular events such as cardiac arrest, acute MI, atherosclerotic heart disease, and arrhythmia are the most common causes of death in patients with ESRD regardless of race.[16] Combined, these events account for more deaths than septicemia or other known causes in patients with ESRD.

Even patients with mild renal insufficiency typically die from cardiovascular disease. Patients with renal insufficiency have concentric left ventricular hypertrophy (LVH). Up to 60% of patients in one series, whose creatinine clearance was so low as to require dialysis, had LVH on echocardiogram.[17] A graded, stepwise increase in percentage of LVH was highly correlated with creatinine clearance. In another study, patients with ESRD whose left ventricular mass was greater than the mean had shorter survival than those whose left ventricular mass was less than the mean.[18]

Patients with renal disease may develop LVH from increased blood pressure, which includes higher overall levels, a blunted fall in nocturnal blood pressure, and vascular stiffness. Volume overload anemia also may occur in patients in late-stage renal failure; such patients probably also have more insulin resistance and increased exposure to growth factors. The association between insulin resistance and LVH may be due to a hypertrophic factor common to both hypertension and insulin resistance. One such factor might be increased sympathetic nervous system (SNS) activity. Hyperinsulinemia is associated with increased norepinephrine levels and increased SNS activity.[19,20] Elevated plasma norepinephrine levels in the absence of hypertension cause LVH in dogs.[21] Significant increases in left ventricular mass occur after several weeks of diet-induced elevated endogenous catecholamine levels in normotensive offspring of hypertensive parents.[22] These observations may be explained by the ability of catecholamines to elevate intracellular calcium, which initiates a calcineurin-dependent transcriptional pathway resulting in cardiac hypertrophy.[23] Insulin resistance is also associated with an elevation of intracellular calcium.[24] Genetic and environmental factors may cause LVH in patients with renal dysfunction. The five-year ongoing phase of the African American Study of Kidney Disease (AASK) will provide relevant data by collecting genetic information, insulin levels, echocardiograms, and ambulatory blood pressure monitors at baseline and followup.

SCREENING AND DIAGNOSTIC GUIDELINES FOR AAMRP

The Framingham Risk Score includes several major independent risk factors for cardiovascular disease in addition to LDL-C: age, sex, cigarette smoking, blood pressure, and HDL-C.[9] Risk estimates are calculated and appropriate primary and secondary interventions outlined. African Americans with any given Framingham Risk Score should be treated more aggressively because their absolute risks are likely to be higher than those of their White counterparts, in whom the risk scores were derived. Nonetheless, the Framingham Risk Score in African Americans is powerfully associated with the dyslipidemia of insulin resistance.[25]

The ATP-III criteria can be used to diagnose metabolic syndrome (Table 1).[9] In African Americans, however, risk factors tend to be clustered and more severe at presentation. For the AAMRP, a broader, two-step screening approach may allow earlier identification of factors that confer high risk for cardiovascular events (Table 2). Initial

Table 1. National Cholesterol Education Program III Criteria that define metabolic syndrome[9]*

- Abdominal obesity (waist circumference >102 cm [men], 88 cm [women])
- Hypertriglyceridemia (≥150 mg/dL)
- Low HDL-C (<40 mg/dL [men], <50 mg/dL [women])
- Hypertension (≥130/85 mm Hg)
- High fasting plasma glucose (≥110† mg/dL)

* Persons having three or more of these risk factors have metabolic syndrome.
† Some have suggested ≥100 for African Americans.
HDL-C=high-density lipoprotein cholesterol.

criteria include lifestyle, ethnic, and medical history elements. The latter are included because while a family history of diabetes or cardiovascular disease and obesity are not considered under ATP-III/Framingham criteria, both are known cardiovascular risk factors[26] and are well described in the African American population. The second step is the patient evaluation; this phase includes clinical laboratory and physical exam components.

Microalbuminuria, an indicator of early renal disease that is predictive of major cardiovascular events even in patients without clinical diabetes mellitus, should be evaluated in the AAMRP. In the Heart Outcomes Prevention Evaluation (HOPE) trial, microalbuminuria was found in nearly 15% of patients without clinical diabetes.[27,28] Patients with any degree of microalbuminuria had significantly higher relative risks of major cardiovascular events, all-cause death, and hospitalization for heart failure. For every .4-mg/mmol increase in the urine albumin/creatinine ratio in the HOPE trial, the risk of major cardiovascular events increased by 5.9%.[27] In the Hypertension Optimal Treatment (HOT) study, elevated serum creatinine and glomerular filtration rate <60 mL/minute was predictive of major cardiovascular events.[29]

Table 2. Checklist to identify AAMRP

Step 1: Screen Patient Profile	
Risk Factor	**Who is at Risk?**
Ethnicity	African American, other minorities
Age	>45 years
Family history	First-degree relatives with diabetes
Medical history	Acanthosis nigricans, polycystic ovary disease
Physical activity	Sedentary lifestyle
Lifestyle	Smoking history
Pregnancy	Birth of infant weighing 9 lbs or gestational diabetes mellitus
Step 2: Patient Evaluation	
Criteria	**Values**
Waist circumference* (WC)	Men: WC >40 in (102 cm) Women: WC >35 in (88 cm)
Blood pressure*	≥130/85 mm Hg
Triglyceride*	≥150 mg/dL
HDL-C*	Men: <40 mg/dL Women: <50 mg/dL
LDL-C	≥100 mg/dL
Fasting plasma glucose*	≥100 mg/dL
Postprandial glucose	≥140 mg/dL
Microalbuminuria	Diabetic men: ACR (albumin/creatinine ratio) >25 mg/g Diabetic women: ACR>35 mg/g

* Risk factors included in the definition of metabolic syndrome.[9]
AAMRP=African American multiple-risk patient; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol.

TREATMENT GOALS AND TARGETS

While evidence-based values have been used to identify appropriate treatment goals, these targets usually have been established in Whites. Their relevance for African Americans is not clear. Since an AAMRP has such higher absolute risks, targets will need to be lower and input more aggressive (Table 3).

Treatment and Prevention Strategies

In the AAMRP, prevention and management strategies must be multifaceted and comprehensive, focusing on all cardiovascular risk factors. Many notable expert professional and governmental groups have issued guidelines outlining various primary and secondary prevention strategies.[9,30–32] Each also recognizes and echoes the difficulties in identifying and treating these high-risk patients.

Therapeutic Lifestyle Changes

Therapeutic lifestyle changes (TLC) are important in reducing cardiovascular risk.[9,33] The emphasis of TLC is on dietary advice, weight control, increased physical activity, and smoking cessation to normalize lipids, blood pressure, body weight, and glucose intolerance.

Weight Control and Physical Activity

Weight control and management are critical in all adults and especially in African American women. Body mass index (BMI) levels in African American women are much higher than in White women.[34,35] Over a 20-year period, African American women gain weight at a faster rate than Whites.[34] The prevalence of class 3 obesity (BMI

Table 3. Metabolic targets for AAMRP

Parameter	Target Value
Fasting plasma glucose	90–110 mg/dL
HbA1C	Goal <7%; optimal <6%
BMI	<25 kg/m^2
Blood pressure	≤130/85 mm Hg
Lipids	
Total cholesterol	<200 mg/dL
LDL-C	<100 mg/dL for moderate-risk patients; <70 mg/dL for high-risk Patients
HDL-C	>45 mg/dL
Triglyceride	<150 mg/dL

AAMRP=African-American multiple-risk patient; BMI=body mass index; HDL-C=high-density lipoprotein cholesterol; HbA1C=glycosylated hemoglobin; LDL-C=low-density lipoprotein cholesterol.

>30 kg/m^2) is growing at a rapid pace in African American men and women.[4] Physical activity (20 minutes of moderate activity several times per week) confers a 35% to 55% decrease in heart disease risk and a reduction in diabetes development.[36] Though not well studied in African Americans, no evidence supports that the benefits of weight loss would be any less.

Smoking Cessation

African Americans generally have higher smoking rates, lower cessation rates, and begin the habit at later ages than do their White counterparts. Using data from the National Health Interview Survey, King and colleagues[5] showed that middle-aged African American men (between 35 and 44 years of age) had the highest rates of cigarette smoking. Smoking cessation reduces the risk of heart disease in secondary and primary prevention. A recent systematic review of 20 prospective cohort studies showed a 36% reduction in crude relative risk of all-cause death among smokers with CHD who quit smoking after the index cardiac event.[37] Therefore, advice on smoking cessation should be provided to all AAMRP who are current smokers.

Lipids

The AAMRP with lipid disorders should receive treatment for elevated LDL-C, high triglycerides, and low HDL-C. In randomized trials of statin drugs and their meta-analyses, lowering cholesterol by 22% over three years significantly reduced risks of MI, stroke, and vascular death, each by 30%, and total cardiovascular death rates by 20%.[38,39] In one trial, statins reduced the risk of diabetes mellitus by 30%.[40]

Blood Pressure

Hypertension is the most common cause of ESRD in African Americans,[16] and in the risk for ESRD increases with increasing severity of hypertension.[41] The risk of ESRD is higher in African Americans than in Native Americans, Whites, or Asians. African Americans have a relative risk for developing ESRD during their lifetime that is 4.45 times greater than in the White population.[16] The mean age at which African American men develop ESRD is 55.6 years, far younger than any other White, Asian, or Native American counterpart.[16]

Lowering blood pressure with thiazide-type diuretics and many other antihypertensive drugs leads to significant reductions in congestive heart failure, MI, and stroke.[31,42] Lowering diastolic blood pressures to 80–85 mm Hg reduces cardiovascular events in hypertensive diabetic patients.[43–45] In the AAMRP, because baseline blood pressures tend to be high, multiple-drug therapy is likely to be needed; inclusion of an angiotensin-converting enzyme (ACE) inhibitor at an appropriate dose may provide simultaneous benefits on diabetes and renal function.[46]

Despite a large number of safe and effective antihypertensive agents, substantial numbers of AAMRP with elevated blood pressure are not receiving treatment. A survey of Midwest primary care physicians showed that those who were not treating hypertension aggressively were satisfied with elevated systolic blood pressure readings (in 93% of visits, systolic blood pressure readings were ≥140 mm Hg, which is above the currently recommended cut point[31] and well above that which we recommend for the AAMRP).[47] In 29% of visits, blood pressure was not addressed because the visit was not initially set up as a blood pressure check or competing medical problems were present.

Glucose

The risk for all-cause mortality and morbidity increases as a continuum with poorer glucose control.[48–51] Clear-cut evidence exists that microvascular and macrovascular complications of type 2 diabetes can be prevented by the attainment of glycemic treatment goals.[49,51] Attractive clinical outcomes have been demonstrated for high-risk groups, such as people with diabetes, in whom use of an ACE inhibitor was associated with a reduction in MI, stroke, cardiovascular deaths, and total deaths.[52] For example, in addition to blood-pressure treatment effects, a reduction of risk developing type 2 diabetes was apparent in the HOPE study with ramipril.[53] Concerns exist about higher doses of ACE inhibitors needed in African Americans, and although emerging data are promising, whether findings are equally applicable across racial and ethnic groups is not year clear.

Pharmacologic Interventions

In the AAMRP, drug therapy should be used aggressively and early to reach treatment goals. At the point when drug

therapy is needed to achieve target values, TLC should be maintained, as they enhance drug-related reductions in blood pressure, cholesterol, and glucose. In the AAMRP, pharmacologic intervention should be started concomitantly with TLC, as recommended for high-risk patients.[9]

Adjunctive Drug Therapy

Aspirin (325 mg) should be considered in all patients who have suffered a prior occlusive event and in primary prevention in those whose 10-year risk of CHD is ≥10%.[54] Aspirin should be used as an adjunct, not an alternative. Sufficient data from randomized trials with clinical endpoints are not yet available to demonstrate benefit from folic acid supplementation. Randomized trial data show no clinical benefit of antioxidant vitamins (β carotene, vitamin E) in reducing risk of cardiovascular disease.

BARRIERS TO IDENTIFICATION AND TREATMENT OF AAMRP

Many barriers exist to successful identification of the AAMRP as well as to implementation of interventions designed to address cardiovascular and metabolic risk factors. These barriers may be financial, socioeconomic, reimbursement-related, as well as patient- or healthcare provider-based.

To realize the behavioral change needed to improve the level of care for AAMRP, healthcare providers and patients must become active participants in health care and create a solid working partnership (Table 4).[55–57] Focused, directed provider-patient efforts can improve biological and functional clinical outcomes in patients with clinical disease. In one study, interventions conducted by ancillary healthcare personnel, who met with diabetic patients for 20 minutes before their appointment and instructed them to be more interactive and more empowered during the physician visit, resulted in better functional status and better glycosylated hemoglobin values than in patients who did not receive this counseling.[58] When a dialogue exists between patients and healthcare providers such that they concur on which of the patient's medical problems require treatment or followup (versus medical problems mentioned by the provider only), patients perceive that these problems are substantially improved or resolved.[59]

Greater investment in the public health infrastructure may help overcome many of the perceived barriers to improving the care of the AAMRP. Successful interventions can be structured through community or religious organizations. One such community church-based program, "*Eat for Life*," was a multicomponent effort designed to increase fruit and vegetable intake by African Americans.[60] Participants who received motivational telephone calls significantly increased fruit and vegetable intake as compared with two other groups receiving none or only one such call. Another community-based program, "*CardioVision 2020*," ongoing in Olmsted County, Minnesota, involves a multifaceted public health approach to improving cardiovascular risk factors.[61]

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Ancillary personnel such as pharmacists can be involved in efforts to enhance the healthcare provider-patient relationship and should participate in a multidisciplinary patient-centered team approach. Changes in office procedures may enhance communication between visits and thus promote better acceptance of medical or TLC interventions. Ambulatory monitoring programs may provide support by making scheduling easier for the patient.

Table 4. Healthcare provider interventions for behavior change[55–57]

- Establish rapport with the patient; develop a partnership
- Know the patient's goals and values before setting the agenda
- Prioritize health behaviors to modify
- Assess patient's readiness for change
- Make change personally relevant
- Empower the patient/provide autonomy
- Be a good role model
- Provide motivational feedback to increase confidence
- Proceed slowly

CONCLUSIONS

Coronary heart disease remains the leading cause of death in African Americans, despite downward trends. Although African Americans have a lower prevalence than Whites of metabolic syndrome, a constellation of obesity, hypertension, dyslipidemia, and insulin resistance leading to diabetes, African Americans are more insulin resistant at similar degrees of adiposity, have higher blood pressures, and among women, more obesity. Because African Americans are diagnosed later, have higher individual risk factor levels as well as more risk factors, and because multiple risk factors confer greater than additive risks, we propose the term AAMRP,

a high-risk patient who poses significant clinical and public health challenges for healthcare providers. We have provided clinical and public health strategies for their early detection and aggressive management.

ACKNOWLEDGMENTS

This manuscript was derived from information presented at the 3rd Advisory Board Symposium on Managing High-Risk African American Patients, October 18–20, 2002, Hallandale, Fla. This symposium was co-organized by the Minority Health Institute, Inc. and TenenbaumReisch, Mt. Kisco, NY, and supported by unrestricted educational grants provided by Aventis, GlaxoSmithKline, Pfizer, and Takeda. For the specific contribution of Anne E. Sumner, MD, a federal employee, this research was supported by the Intramural Research Program of the National Institutes of Health/ National Institute of Diabetes, Digestive and Kidney Disease.

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REFERENCES

1. National Vital Statistics Report. Number of deaths from 113 selected causes by age: United States, 1999 (Table 9). 2001;49(8). Available at: www.cdc.gov. Accessed on: 4/18/02.
2. Jackson SA, Burke GL, Thach C, et al. Incidence and predictors of coronary heart disease among older African Americans: the Cardiovascular Health Study. *J Natl Med Assoc*. 2001;93:423–429.
3. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999–2000. *JAMA*. 2002; 288:1723–1727.
4. Freedman DS, Khan LK, Serdula MK, Galuska DA, Dietz WH. Trends and correlates of class 3 obesity in the United States from 1990 through 2000. *JAMA*. 2002; 288:1758–1761.
5. King G, Bendel R, Delaronde SR. Social heterogeneity in smoking among African Americans. *Am J Public Health*. 1998; 88:1081–1085.
6. Strauss RS, Pollack HA. Epidemic increase in childhood overweight, 1986–1998. *JAMA*. 2001;286:2845–2848.
7. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the Third National Health and Nutrition Examination Survey. *JAMA*. 2002; 287:356–372.
8. Isomaa B, Almgren P, Tuomi T, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care*. 2001;24:683–689.
9. National Cholesterol Education Program. *Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)* [executive summary]. Bethesda, Md: National Heart, Lung, and Blood Institute, National Institutes of Health; May 2001. NIH Publication No. 01-3670.
10. Park Y-W, Zhu S, Palaniappan L, Heshka S, Carnethon MR, Heymsfield SB. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988–1994. *Arch Intern Med*. 2003;163:427–436.
11. Trevisan M, Lium J, Bahsas FB, Menotti A. Syndrome X and mortality: a population-based study. Risk Factor and Life Expectancy Research Group. *Am J Epidemiol*. 1998; 148:958–966.
12. Kannel WB. Contribution of the Framingham Heart Study to preventive cardiology: the Bishop Lecture. *J Am Coll Cardiol*. 1990; 15:206–211.
13. Hennekens CH, Buring JE. *Epidemiology in Medicine*. Boston, Mass: Little Brown & Co; 1987.
14. Rubins HB, Robins SJ, Collins D, et al. Distribution of lipids in 8,500 men with coronary artery disease. Department of Veterans Affairs HDL Intervention Trial Study Group. *Am J Cardiol*. 1995;75:1196–1201.
15. Beckman JA, Creager MA, Libby P. Diabetes and atherosclerosis: epidemiology, pathophysiology, and management. *JAMA*. 2002; 287:2570–2581.
16. United States Renal Data Systems. Annual Data Report. Available at: www.usrds.org. Accessed on: 4/11/03.
17. Levin A, Thompson CR, Ethier J, et al. Left ventricular mass index in early renal disease: impact of decline of hemoglobin. *Am J Kidney Dis*. 1999;34:125–134.
18. Levin A, Foley RN. Cardiovascular disease in chronic renal insufficiency. *Am J Kidney Dis*. 2000;36(6[suppl 3]):S24–S30.
19. Rowe JW, Young JB, Minaker KL, Stevens AL, Palotta J, Landsberg L. Effects of insulin and glucose infusions on sympathetic nervous system activity in normal man. *Diabetes*. 1981;30:219–225.
20. Anderson EA, Balon TW, Hoffman RP, Sinkey CA, Mark AL. Insulin increases sympathetic activity but not blood pressure in borderline hypertensive humans. *Hypertension*. 1992;9:621–627.
21. Laks MM, Morady F, Swan HJC. Myocardial hypertrophy produced by chronic infusion of subhypertensive doses of norepinephrine in the dog. *Chest*. 1973;64:75–78.
22. Trimarco B, Ricciardelli B, De Luca N, et al. Participation of endogenous catecholamines in the regulation of left ventricular mass in progeny of hypertensive parents. *Circulation*. 1985;72:38–46.
23. Molkentin JD, Lu JR, Antos CL, et al. A calcineurin-dependent transcriptional pathway for cardiac hypertrophy. *Cell*. 1998;93: 215–228.
24. Kristal B, Levy R, Farah R, et al. Hypertension and insulin resistance correlate with intracellular ionized calcium of polymorphonuclear leukocytes [abstract]. *Am J Hypertens*. 1998; 11:151A.
25. Foster WAA II, Joshua J, Genovese DJ, et al. The Framingham risk score (FRS) in African Americans is associated with the dyslipidemia of insulin resistance. *Circulation*. 2002; 106(19S):A221.
26. Wilson PWF, D'Agostino RB, Sullivan L, Parise H, Kannel WB. Overweight and obesity as determinants of cardiovascular risk. The Framingham experience. *Arch Intern Med*. 2002;162:1867–1872.

27. Gerstein HC, Mann JF, Yi Q, et al. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. *JAMA*. 2001;286: 421–426.
28. Mann JF, Gerstein HC, Pogue J, Bosch H, Yusuf S. Renal insufficiency as a predictor of cardiovascular outcomes and the impact of ramipril: the HOPE randomized trial. *Ann Intern Med*. 2001;134:629–636.
29. Ruilope LM, Salvetti A, Jamerson K, et al. Renal function and intensive lowering of blood pressure in hypertensive participants of the Hypertension Optimal Treatment (HOT) study. *J Am Soc Nephrol*. 2001;12:218–225.
30. American Diabetes Association. Standards of medical care for patients with diabetes mellitus. *Diabetes Care*. 2002;25(suppl 1):S33–S49.
31. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003;289: 2560–2572.
32. Whelton PK, He J, Appel LJ, et al. Primary prevention of hypertension: clinical and public health advisory from the National High Blood Pressure Education Program. *JAMA*. 2002; 288:1882–1888.
33. Tuomilehto J, Linstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. 2001;344:1343–1350.
34. Ambrosius WT, Newman SA, Pratt JH. Rates of change in measures of body size vary by ethnicity and gender. *Ethn Dis*. 2001;11: 303–310.
35. Dundas R, Morgan M, Redfern L, Lemic-Stojcevic N, Wolfe C. Ethnic differences in behavioral risk factors for stroke: implications for health promotion. *Ethn Health*. 2001;6: 95–103.
36. Hennekens CH. Increasing burden of cardiovascular disease: current knowledge and future directions for research on risk factors. *Circulation*. 1998;97:1095–1102.
37. Critchley JA, Capewell S. Mortality risk reduction associated with smoking cessation in patients with coronary heart disease: a systematic review. *JAMA*. 2003;290:86–97.
38. Hebert PR, Gaziano JM, Chan KS, Hennekens CH. Cholesterol lowering with statin drugs, risk of stroke, and total mortality: an overview of randomized trials. *JAMA*. 1997;278:313–321.
39. Straus SE, Majumdar SR, McAlister FA. New evidence for stroke prevention: scientific review. *JAMA*. 2002;288:1388–1395.
40. Freeman DJ, Norrie J, Sattar N, et al. Pravastatin and the development of diabetes mellitus: evidence for a protective treatment effect in the West of Scotland Coronary Prevention Study. *Circulation*. 2001;103: 357–362.
41. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Stamler J. End-stage renal disease in African American and White men: 16-year MRFIT findings. *JAMA*. 1997; 277:1293–1298.
42. 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.
43. Bakris GL. A practical approach to achieving recommended blood pressure goals in diabetic patients. *Arch Intern Med*. 2001;161: 2661–2667.
44. 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) randomized trial. *Lancet*. 1998;351:1755–1762.
45. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications of type 2 diabetes: UKPDS 38. *BMJ*. 1998;317: 703–713.
46. Wright JT Jr, Bakris G, Greene T, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. *JAMA*. 2002;288:2421–2431.
47. Oliveria SA, Lapuerta P, McCarthy BD, L'Italien GJ, Berlowitz DR, Asch SM. Physician-related barriers to the effective management of uncontrolled hypertension. *Arch Intern Med*. 2002;162:413–420.
48. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329:977–986.
49. Hanefeld M, Fischer S, Julius U, et al. Risk factors for myocardial infarction and death in newly detected NIDDM: the Diabetes Intervention Study, 11-year followup. *Diabetologia*. 1996;39:1577–1583.
50. Khaw K-T, Wareham N, Luben R, et al. Glycated hemoglobin, diabetes, and mortality in men in Norfolk cohort of European Prospective Investigation of Cancer and Nutrition (EPIC-Norfolk). *BMJ*. 2001;322:1–6.
51. UK Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet*. 1998;352:837–853.
52. Heart Outcomes Prevention Evaluation (HOPE) Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. *Lancet*. 2000;355:253–259.
53. Yusuf S, Gerstein H, Hoogwerf B, et al. Ramipril and the development of diabetes. *JAMA*. 2001b;286:1882–1885.
54. Eidelman RS, Hebert PR, Weissman S, Hennekens CH. Update on aspirin in the primary prevention of cardiovascular disease. *Arch Intern Med*. 2003;163:2006–2010.
55. Prochaska JO, DiClemente CC. Stages and processes of self-change of smoking: toward an integrative model of change. *J Consult Clin Psychol*. 1983;51:390–395.
56. Rollnick S, Mason P, Butler C. *Health Behavior Change: A Guide for Practitioners*. New York, NY: Churchill Livingstone; 1999.
57. Stott NC, Rollnick S, Rees MR, Pill RM. Innovation in clinical method: diabetes care and negotiating skills. *Fam Pract*. 1995;12: 413–418.
58. Greenfield S, Kaplan SH, Ware JE Jr, Yano EM, Frank HJ. Patients' participation in medical care: effects on blood sugar control and quality of life in diabetics. *J Gen Intern Med*. 1988;3:448–457.
59. Starfield B, Wray C, Hess K, Gross R, Birk PS, D'Lugoff BC. The influence of patient-practitioner agreement on outcome of care. *Am J Public Health*. 1981;71:127–131.
60. Resnicow K, Jackson A, Wang T, et al. A motivational interviewing intervention to increase fruit and vegetable intake through Black churches: results of the Eat for Life trial. *Am J Public Health*. 2001;91:1686–1693.
61. Thomas RJ, Kottke T, Brekke MJ, et al. Attempts at changing dietary and exercise habits to reduce risk of cardiovascular disease: who's doing what in the community? *Prev Cardiol*. 2002;5:102–108.

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