

Epidemiology and Burden of Cardiovascular Disease

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Summary: Coronary heart disease (CHD) is the leading cause of death in the United States. The rate of CHD and CHD death varies across racial groups, with higher rates among black men and women than among white men and women. The development of CHD is promoted by major CHD risk factors—dyslipidemia, hypertension, and smoking. These risk factors are independently associated with CHD risk and are common among adults in the United States. Diabetes mellitus is also a significant contributor to CHD risk and is associated with risk of a CHD event equivalent to that conferred by the presence of prior CHD. Metabolic syndrome, a related condition, also confers a high risk for CHD as well as for the development of type 2 diabetes. Diabetes and metabolic syndrome are characterized by the presence of central obesity and insulin resistance, which result in dyslipidemia, hypertension, and cardiovascular derangements that promote CHD. Diabetes and metabolic syndrome illustrate the significance of risk factor clustering, which contributes to CHD risk through the additive effect of each risk factor. Diabetes, metabolic syndrome, and risk factor clustering in general are becoming more prevalent, which illustrates the need for better CHD prevention strategies aimed at risk factor control. The pathologic process associated with risk factor clustering also contributes to the higher CHD burden among black men and women, who have a higher prevalence of risk factor clustering and type 2 diabetes. Furthermore, despite having a higher CHD risk, black men and women are less likely to receive adequate treatment or control of risk factors, including dyslipidemia or hypertension. Eliminating disparities among population groups will thus require aggressive efforts focused on risk assessment, guideline adherence, and risk factor control in populations in need.

Introduction

Cardiovascular diseases are the leading cause of death in the United States. In 2001, diseases of the heart accounted for 29.0% of total deaths and cerebrovascular disease for an additional 6.8% (total 35.8% cardiovascular deaths), compared with 22.9% of deaths attributed to malignant neoplasms.¹ Age-adjusted death rates for blacks exceeded those for whites for both diseases of the heart and cerebrovascular diseases, with black-white ratios of 1.3 and 1.4, respectively. Total cardiovascular diseases accounted for 30.8% of deaths in black men, and 36.5% in black women.²

In 2001, the age-adjusted death rates for coronary heart disease (CHD) of black men and women exceeded those of white men and women (262.0 vs. 228.4, and 176.7 vs. 137.4, respectively, per 100,000).^{2,3} Though CHD mortality has declined in all race-sex groups since 1968, the rate of decline has slowed in blacks, especially black women, in recent years.⁴ Attaining the goal proposed by the U.S. Surgeon General of eliminating health care disparities between population groups by 2010⁵ will require more vigorous preventive efforts.

Risk Factors for Coronary Heart Disease

The risk of CHD can be predicted on the basis of a constellation of risk factors, of which three have come to be regarded as major risk factors: dyslipidemia (or elevated blood cholesterol), hypertension, and cigarette smoking.⁶ Diabetes mellitus has come to be recognized as a significant contributor to risk in many populations.⁷ The constellation of risk factors subsumed under the title “metabolic syndrome” frequently precedes diabetes, and insulin resistance, a cardinal feature of the metabolic syndrome, provides a conceptual framework for investigating and understanding how risk factor clustering contributes to CHD risk.^{8,9}

Dyslipidemia and Elevated Blood Cholesterol

The risk of CHD mortality conferred by cholesterol is continuous and graded, and rises more steeply at levels >200 mg/dl than at lower levels. The range 200–239 mg/dl has been designated borderline high risk, and levels \geq 240

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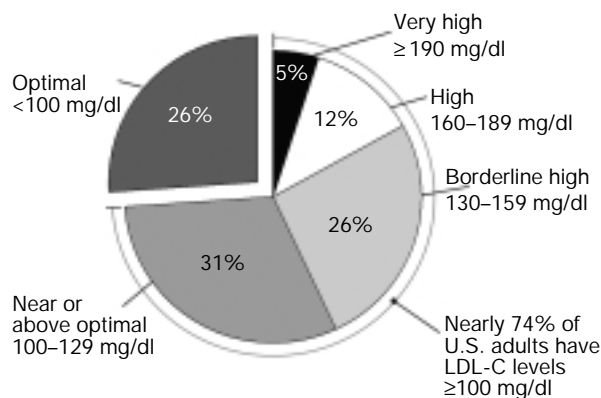


FIG. 1 Low-density lipoprotein cholesterol (LDL-C) levels in the U.S. adult population. Data are from Ref. No. 6.

mg/dl as high risk. About 18 million men (16.7%) and 24 million women (18.7%) in the United States have such levels. Borderline high levels are detected in 33% of men and 32.4% of women.⁶

The risk of CHD is most clearly related to levels of low-density lipoprotein cholesterol (LDL-C). In the Atherosclerosis Risk in Communities (ARIC) study, LDL-C was similarly predictive of CHD events in all race-gender groups.¹⁰ Low-density lipoprotein cholesterol levels regarded as optimal (<100 mg/dl) are present in only 26% of the U.S. adult population (Fig. 1). Levels >130 mg/dl are observed in 43% of the population, with age-adjusted rates of 49.6 and 43.7% for white men and women, respectively, and 46.3 and 41.6% for black men and women, respectively.⁶

There is an inverse relationship between CHD incidence and high-density lipoprotein cholesterol (HDL-C) in epidemiologic studies, most recently in the ARIC study, which showed a similar though slightly less protective effect of HDL in blacks than in white persons.¹⁰ Clinical trials using statin drugs have generally demonstrated reduction in rates of CHD events associated with LDL-C reduction.⁶ In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), a statistically significant (27%) reduction in CHD event rates was observed in black study participants compared with those subjected to usual care in the community.¹¹ In this study, it was evident that black patients with hypertension and elevated LDL-C levels were less likely to be treated with lipid-lowering drugs than were white patients. Earlier studies had revealed that black adults of all ages are less likely to have their blood cholesterol checked than are white adults and had shown disparities in treatment rates between black and white adults.¹²

Hypertension

Hypertension, defined as systolic blood pressure ≥ 140 mmHg, or diastolic blood pressure ≥ 90 mmHg, or taking anti-hypertensive medications, is present in one of four U.S. adults.^{13,14} The age-adjusted prevalence is significantly high-

er in black than in white men aged 20–74 years (36.7 vs. 25.2%, respectively), and the disparity is even greater in black women (36.6 vs. 20.5%). Black Americans develop hypertension earlier in life and have a higher prevalence of more severe (class III) hypertension.¹⁴ Among them, those with the highest pressures are more likely to be middle-aged, less educated, overweight, and less active, and to have diabetes. Data from the ARIC study confirmed that hypertension is a strong predictor of CHD incidence in all race-gender groups, more so in black than in white subjects.¹⁰

Hypertension awareness, treatment, and control rates have improved over the last 25 years, and in the National Health and Nutritional Examination Survey (NHANES) 1999–2000 they were 70, 59, and 34%, respectively.¹⁵ Control rates remain lower in black than in white adults in NHANES 1999–2000 (24 vs. 32%, respectively), despite higher treatment rates (57 vs. 53%, respectively). Evidence from different sources suggests that both physician nonadherence to recommended guidelines¹⁶ and patient noncompliance are contributory.¹⁷

Hypertension appears to contribute to cardiovascular disease mortality in African Americans, both by accelerating the development of coronary atherosclerosis and by inducing more severe left ventricular hypertrophy. The interaction of these two pathologies is the likely cause of the higher sudden death rates in young, black adults.¹⁸

Diabetes

Diabetes has been accorded the status of a coronary risk-equivalent in the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III report.⁶ Compelling evidence for this conclusion is provided by the Finnish East-West Study, in which the 7-year incidence of myocardial infarction was virtually identical in diabetic subjects without myocardial infarction at baseline, and nondiabetic subjects with prior myocardial infarction (18.8 vs. 20.2%, respectively).¹⁹ Other data, from the Multiple Risk Factor Intervention Trial (MRFIT) screenee follow-up, demonstrated a 3- to 4-fold increased risk of cardiovascular death in men with compared with those without diabetes,²⁰ with the greatest population impact at the highest cholesterol levels or in the presence of multiple risk factors.

The prevalence of diabetes has been increasing in the United States in the last half century. Data from NHANES 1999–2000 and NHANES III (1988–1994) indicate that an estimated 29 million (14.4%) of persons aged ≥ 20 years had either diagnosed diabetes, undiagnosed diabetes, or impaired fasting glucose; 29% of diabetes cases were undiagnosed.²¹ The unadjusted prevalence of diagnosed and undiagnosed diabetes in NHANES 1999–2000 was 8.3% (an estimated 16.7 million persons). The age-adjusted prevalence of diabetes, diagnosed and undiagnosed, was higher in black than in white persons (14.9 vs. 7.4%).^{21,22}

The NHANES 1999–2000 detected poor control of risk factors for cardiovascular disease among adults with diagnosed diabetes.²³ Only 35.8% of participants achieved the tar-

get systolic blood pressure (SBP; < 130 mmHg), and diastolic blood pressure (DBP; < 80 mmHg) levels. More than half (51.8%) had cholesterol levels \geq 200 mg/dl. The mean body mass index (BMI) of adults with diagnosed diabetes has increased in the decade between NHANES III (1988–1994) and NHANES 1999–2000, as has the prevalence of obesity (BMI \geq 30), now 54.6% compared with 41.6%. These findings are confirmed in smaller studies in other settings, which reveal a greater likelihood of poor diabetic control and poor blood pressure control in African American than in white patients,²⁴ and a higher prevalence of obesity and poor glycemic control in young adult, urban African Americans.²⁵

Metabolic Syndrome

The NCEP ATP III⁶ recommended a definition of the metabolic syndrome, which is identified as a clustering of cardiovascular risk factors that include central obesity, elevated blood pressure, glucose intolerance, hypertriglyceridemia, and low HDL-C.^{8,9} The syndrome has been linked to elevated insulin levels and resistance to the peripheral effects of insulin¹⁰ and is sometimes referred to as the insulin resistance syndrome. Insulin resistance has been linked to many of the features of the syndrome.

The prevalence of the metabolic syndrome is 24.0% in men and 23.8% in women in the U.S. adult population aged 20–74 years.²⁶ Cross-sectional increases in prevalence are observed in both men and women, with the highest prevalence in individuals aged 60–69 years (43.5% for men and 42% for women). The prevalence in white men (25%) exceeds that in black men (16%), but the prevalence in black women (26%) exceeds that in white women (23%).

The high prevalence of the metabolic syndrome is driven by the increasing prevalence of obesity in the U.S. population.^{27, 28} The age-adjusted prevalence of obesity (BMI \geq 30 kg/m²) in U.S. adults aged 20–74 in NHANES 1999–2000 was similar in white and black men, 27.3 and 28.1%, respectively, but much higher in black than in white women, 49.7 versus 30.1%, respectively. In ARIC, the incidence of diabetes mellitus type 2 was 2.4-fold higher in African-American women than in white women, almost half of that risk being conferred by adiposity.²⁹

The metabolic syndrome confers a high risk for eventual development of diabetes mellitus.³⁰ The metabolic syndrome is associated on a cross-sectional basis with a higher prevalence of CHD.³¹ In analyses that employ a variety of metabolic characteristics, such as fasting glucose levels, postprandial glucose levels, fasting insulin levels, and a number of components of the metabolic syndrome, the metabolic syndrome is associated with an increased risk of cardiovascular disease mortality, CHD incidence, and CHD mortality.^{32,33}

Risk Factor Clustering

The metabolic syndrome also appears to underlie the clustering of risk factors (the occurrence of more than one risk fac-

tor in individuals). Data from the Behavioral Risk Factor Surveillance System (BRFSS) indicate that the percentages of U.S. adults reporting one or more risk factors (high blood cholesterol, high blood pressure, diabetes, cigarette smoking, obesity) increased from 58.2% in 1991 to 64% in 2001, with the greatest relative increases observed for obesity and diabetes (64.7 and 46.5%, respectively).³⁴ In the 2001 data, reports of one or more risk factors were more likely in black adults (71.2%) than white adults (63.5%). The data from the 1999 survey³⁵ reveal that the age-adjusted prevalence of two or more risk factors was 37.8% in African-American adults and 26.7% in white adults (Fig. 2). The most common combination among persons with two risk factors was high blood pressure and high cholesterol, at 23.9%. Among persons with three risk factors, the most common combination was high blood pressure, high cholesterol, and obesity (32.5%). Of those with four risk factors, 43% had the combination of high blood pressure, high cholesterol, obesity, and cigarette smoking, and 40% the combination of high blood pressure, high cholesterol, obesity, and diabetes mellitus. In these data, hypertension and high cholesterol were more than twice as common in individuals with as in those without diabetes. Risk factor clustering of this type was more common in African-Americans than in whites, especially among women. In a similar analysis of NHANES III (1988–1994), black adults had the highest prevalence of three or more risk factors, almost one in five.³⁶

Undertreatment of Minorities: Implications for Disparities

Randomized controlled trials (RCTs) are believed to provide the highest level of evidence for clinical practice, but RCTs frequently do not enroll individuals who are representative of patients seen in the community. Frequently, minority patients as well as women and older subjects are underrepresented in RCTs, and this has implications for the generalization of the data derived from these trials to these patient

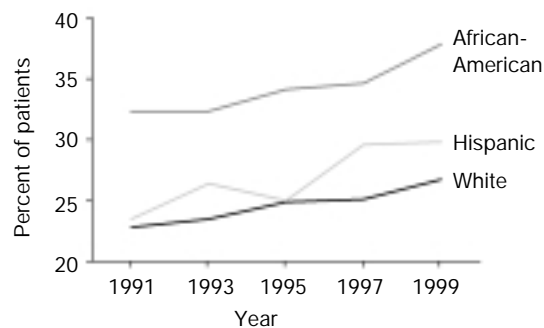


FIG. 2 Individuals reporting two or more risk factors (high blood pressure, high blood cholesterol level, diabetes, obesity, current smoking) by race. Data were collected from the Behavioral Risk Factor Surveillance System and are age-standardized to the 2000 U.S. population. Relative change from 1991 to 1999 was statistically significant ($p < 0.001$) for all 3 groups. Data are from Ref. No. 35.

groups.³⁷ It is unfortunate that there is evidence of undertreatment of black patients in recent cardiovascular RCTs. In ALLHAT, black patients were less likely to attain blood pressure goals than were white patients, with control rates at 5 years of 63.3 and 70.0% for black and white men, respectively, and 58.8 and 65.2% for black and white women, respectively.^{11,38} There was evidence of systematic failure to titrate medications when goal SBP was not attained.³⁸ On the other hand, in the ALLHAT Lipid-Lowering Trial, the black subgroup of statin-treated patients was the only subgroup with a CHD event rate lower than that of the comparison usual-care group in the community.¹¹ Consistent with other observations, black patients in the community had lipid-lowering treatment initiated by their physicians much less frequently than did white patients.¹² In the Heart and Estrogen/Progestin Replacement Study (HERS), black women had higher rates of diabetes, hypertension, and hypercholesterolemia, but were less likely to receive aspirin or statin drugs and were less likely at follow-up to have optimal blood pressure or LDL-C control. The outcomes reflected a two-fold increase in CHD event rates in blacks, and higher cardiovascular mortality.³⁹

Disparities in cardiovascular outcomes between black and white patients persist in part because of the inadequacies of the current health care system and the failure to focus adequate efforts on populations most in need. The global risk management approach recommended by NCEP ATP III and the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure allows health care practitioners to identify high-risk patients and to set strict targets, and offers the potential to exert maximal impact on cardiovascular outcomes. A system-wide response to this challenge would allow the maintenance of a decline in CHD mortality, rather than the leveling or increase the obesity-diabetes epidemic portends.

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