Reduction of Hypertension-associated Heart Disease and Stroke among Black Americans: Past Experience and New Perspectives on Targeting Resources

DANIEL D. SAVAGE, DANIEL L. McGEE, and GERRY OSTER

National Center for Health Statistics;
Centers for Disease Control;
Policy Analysis, Inc.

PAST STRATEGIES AND THE RESULTS OF THOSE strategies for prevention of hypertension-associated morbidity and mortality help to guide assessment of future needs and may serve as prototypes for the development of more efficient efforts for primary and secondary prevention of other chronic diseases. Choices among competing needs and interests and finite resources are becoming increasingly difficult to make: What new efforts are needed and which ones are to be emphasized? What data need to be acquired, and in what ways can these data be used to promote and evaluate preventive programs? Mathematical modeling provides one tool for orderly assessment of such information and for use as an aid in sound decision making. Quantitative information from such modeling does not substitute for the social, ethical, and political dynamics of policy making but helps to clarify the potential impact and cost of specific decisions. It can add precision to the assumptions that are part of policy decisions. It can direct attention to opportunities for more effective use of resources. It can point out subgroups that may need specific strategies that would not be of substantial benefit relative to the cost and other competing needs for the entire population.

The continuing critical role of hypertension in black-white disparities

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in morbidity and mortality (Kumanyika and Savage 1985) makes such analyses particularly important in the assessment of national hypertension-control policies to insure the adequacy of the policy for blacks. Past analyses (Drizd, Dannenberg, and Engel 1986; Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure 1985) have suggested that, in general, the national hypertension-control policies have had as great, if not a greater, positive impact on the black population than on the white population. These analyses appropriately used blood-pressure level as a key indicator of the impact of the policy. Other intermediate measures of the impact of national hypertension-control policies included the percentage of hypertensive persons: (1) aware of their hypertension, (2) taking antihypertensive medications, and (3) having their hypertension under control (i.e., below an agreed-on cut-point). The ultimate measure of success of hypertension-control policies is the degree of reduction in hypertension-associated disease and death. Some evidence (U.S. Public Health Service 1986) points to a similar impact of the national policy on hypertension-associated disease and death (i.e., stroke and death from heart disease) in the black and white populations. Future policy analyses will increasingly focus on strategies to reduce the risk associated with mild elevations of blood pressure, partially because of past successes in reducing the prevalence of moderate and severe hypertension. The greater heterogeneity of risk in black and white populations with mild elevations in blood pressure suggests that, for future gains in efficiency and equity in outcome, past approaches for achieving (and assessing) hypertension control will need to be updated. Blood pressure levels alone may no longer be adequate indicators for such purposes. Tarazi (1985) signaled the potential importance of other factors in hypertension when he stated that the definition of hypertension solely in terms of arterial pressure levels has obscured the other biologic dimensions of the disease. One biologic dimension of hypertension that will become increasingly important in future policy analyses is target organ damage secondary to hypertension. The heart, the brain, the kidneys, and blood vessels throughout the body are major target organs in hypertension. Recently, the use of sound waves (echocardiography) to identify heart changes (such as increased left-ventricular mass) (see appendix) has allowed early identification of target organ damage in the heart before damage is apparent elsewhere (Savage et al. 1979a). There is increasing evidence that such measures may identify individuals at

substantially increased risk of subsequent morbidity and mortality (independent of other standard risk factors, including blood pressure level) (Savage et al. 1985; Casale et al. 1986; Levy et al. 1987a). Framingham data (Savage et al. 1983; Savage et al. 1987; Levy et al. 1987b) suggest that the echocardiographic left-ventricular mass helps to integrate the overall blood pressure experience. This assessment of target organ damage may reflect the risk associated with the overall blood pressure experience better than two or three blood pressure tests taken on one or two occasions (the usual approach for evaluating blood pressure level and risk). The finding by Hammond et al. (1986) and Dunn et al. (1983) of greater echocardiographic evidence of target organ damage in black individuals with mild hypertension—matched by apparent blood pressure level, age, sex, and treatment status to white hypertensive individuals—suggests that analyses of hypertension control and policy decisions based on blood pressure level alone may not have the same meaning in black and white populations and may lead to faulty conclusions on the relative impact of efforts to reduce hypertension-associated morbidity and mortality in black and white populations. The future data requirements for both assessing and planning hypertension-control strategies need to be reexamined.

This article describes the apparently similar impact of national policy on hypertension control in the black and white populations as measured by currently available national indicators. The elements of a type of mathematical modeling previously applied to hypertension-control policy (cost-effectiveness analysis) are briefly described. The suggestion is made that future strategies would be improved by an updating of such analyses, with improved data on stratification of risk in race-specific analyses.

Finally, the article briefly describes a mathematical analysis (based on published Framingham data) that predicts that the stratification of risk associated with echocardiographic assessment of left-ventricular mass as a continuous variable may represent a breakthrough. This stratification of risk in the population could, along with several other benefits, allow much more precise assessment of the adequacy of hypertension control and aid in more efficient targeting of resources to reduce the continuing excess cardiovascular morbidity and mortality in the black as compared to the white population. Future incorporation of such information into assessments of national progress and cost-effectiveness modeling would be severely limited without population-

based data similar to the Framingham data (an almost exclusively white population sample) for the black population. An important step in efficient allocation of resources to reduce the apparent excessive hypertension-associated morbidity and mortality in the black population is a more accurate and sensitive approach to monitoring of target organ damage associated with hypertension. Data presented here suggest that echocardiographic assessment of left-ventricular mass may provide a much-improved assessment of hypertension status. The best data for planning national policy with such profound health and economic implications are national data from representative samples of the black and white populations, because of potential differences between and within racial groups in various areas of the country (Savage et al. 1979b; Gazes et al. 1986; Savage et al. 1987).

Profile of Reduction of Heart Disease and Stroke and Control of Hypertension: Magnitude of the Problem and Progress

Cost-effectiveness modeling in hypertension policy analysis is important partly because of the magnitude of the problem and its associated morbidity and mortality. Small changes in policy could have enormous impact on public health and health care costs. Despite substantial progress in disease prevention and health promotion, as well as the emergence of new important public health concerns, heart disease and stroke remain the number-one cause of death for black and white men and women in the United States. Heart-disease death rates from 1979 to 1981 were 319.4 deaths per 100,000 population for black men, and 274.4 deaths per 100,000 for white men. Heart-disease death rates during this period for black women were 194.4 deaths per 100,000, and for white women were 131.9 deaths per 100,000. Stroke death rates during this period were 76 and 41.2 per 100,000 for black and white men, respectively. Stroke rates during this two-year period were 60.2 and 34.7 for black and white women, respectively (U.S. Department of Health and Human Services 1985, vol. 4, pt. 1; see also Manton, Patrick, and Johnson 1987).

Hypertension-associated cardiovascular disease is a major contributor to this mortality. Based on projections made in the early 1980s from national survey data, 58 million Americans are estimated to be at

increased risk of morbidity and premature mortality because of high blood pressure, warranting some type of systematic monitoring (Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure 1985). This includes 38 percent of the adult black population and 29 percent of the adult white population.

The annual cost of treating cardiovascular disease in the United States (most of which is associated with hypertension) has recently been estimated to be 78.6 billion dollars (Stason 1986). Harlan (1987), citing data from the National Medical Care Utilization Survey indicated that hypertension is the most common chronic disease treated in the medical care system. He has indicated that the per capita cost was about $120 per year in 1980. His analyses indicated that if hypertension is complicated by overt evidence of atherosclerotic disease or associated with other conditions (e.g., renal disease, diabetes, etc.) the per capita costs increased about tenfold. Stason (1986) estimates that nearly eight billion dollars is being spent directly each year on the treatment of hypertension in the United States. The number of individuals with elevated blood pressure taking antihypertensive medications has increased rapidly since the modern era of hypertensive therapy began in the early 1960s.

In one population-based sample of adult men followed for the past 27 years, zero (black men) and 3 percent (white men) of the entire sample of black and white men were taking antihypertensive medications in 1960, whereas 59 percent (black men) and 41 percent (white men) of these subjects were taking such medications two and one-half decades later (Gazes et al. 1986). The estimated prevalence of hypertension in the 1960 sample would have led to an expected finding of roughly 30 percent of the sample taking antihypertensive medications rather than the near-zero percent who actually were. The National Examination Survey of the 1960s and the two National Health and Nutrition Examination Surveys of the 1970s (NHANES I and II) documented the national progress in getting the groups with highest blood pressures on antihypertensive treatment. For example, in the 1970s the definition for "definite hypertension" indicating a need for treatment was a systolic blood pressure equal to or greater than 160 mm Hg and/or a diastolic blood pressure equal to or greater than 95 mm Hg. The 1976 to 1980 national survey data indicated that 73.6 percent of definite hypertensive individuals (i.e., with blood pressures at or above these cut-points or on antihypertensive medications)

had been diagnosed (i.e., had previously been told by a doctor that they had high blood pressure or were hypertensive) (Drizd, Dannenberg, and Engel 1986). Black adult hypertensives found to have definite hypertension during this survey were more likely than their white counterparts to have been previously diagnosed (80.9 percent versus 72.3 percent, respectively). This finding was consistent in the sex-specific comparisons but only reached statistical significance in women. Some 69.1 percent of the black hypertensive men were previously diagnosed, compared to 65.9 percent of the white hypertensive men. Overall, 87.6 percent of black women with definite hypertension had been previously diagnosed, compared to 79.3 percent of their white counterparts. Nearly 90 percent of black women aged 35 years and older with definite hypertension were previously diagnosed as hypertensive (Drizd, Dannenberg, and Engel 1986). This is an extraordinary example of the apparently successful relative impact of preventive action in the black compared to the white population.

Over three-fourths of the diagnosed definite hypertensives reported taking antihypertensive medication "always," "often," or "sometimes" (Drizd, Dannenberg, and Engel 1986). Among hypertensive individuals, the younger groups were less likely than the older age group to be taking medications—40.9 percent for those 18 to 24 years of age versus 85.4 percent of those 65 to 74 years of age. Adult women hypertensives were more likely than hypertensive men to be taking antihypertensive medications (79.3 percent versus 68.9 percent, age-adjusted to the combined population) (Drizd, Dannenberg, and Engel 1986). Among the male hypertensive subjects the percentage taking antihypertensive medications ranged from 37.6 percent for those aged 18 to 24 to 81.8 percent for those aged 65 to 74. For hypertensive women the percentage taking antihypertensive medications ranged from 44 percent for those aged 18 to 24 to 87.2 percent for those aged 65 to 74.

Current data suggest that younger hypertensives with the same level of blood pressure as older hypertensives benefit from treatment with antihypertensive medications as much if not more than the older hypertensives. Of course, older as well as younger hypertensive patients are recommended to have a trial of nonpharmacological therapy when appropriate (e.g., weight reduction if they are overweight, salt reduction if they are salt sensitive, and reduced alcohol intake). If such non-pharmacological therapy is successful in controlling blood pressure

after a few weeks, it may suffice. If not, pharmacological therapy is recommended in addition to the continued attempts at nonpharmacological intervention.

Once diagnosed, black hypertensives were as likely as white hypertensives to be taking antihypertensive medications (72.7 percent versus 75.1 percent, respectively). Women who were previously diagnosed as hypertensive were more likely to be taking medications than men. This was consistent in race-specific comparisons. Thus, 75.9 percent and 66 percent of black diagnosed hypertensive women and men, respectively, and 81 percent and 68.8 percent of white diagnosed hypertensive women and men, respectively, were taking antihypertensive medications. Some 88.9 percent of black women hypertensives aged 65 to 74 were taking antihypertensive medications—the highest rate of all age/sex groups. Thus, 58 percent of all black women aged 65 to 74 in the United States were taking antihypertensive medications (Drizd, Dannenberg, and Engel 1986). The question should be raised as to whether the efforts at nonpharmacologic management in black hypertensive patients are as great as in white hypertensive patients, given the relatively greater prevalence of overweight and possibly salt sensitivity in the black population.

From the early 1960s to the late 1970s the systolic blood pressure declined more in black adults than in white adults. The mean age-adjusted systolic blood pressure declined 4 mm Hg in white men, 6 mm Hg in white women, 8 mm Hg in black men, and 12 mm Hg in black women (Drizd, Dannenberg, and Engel 1986). During this period the decline in mean systolic blood pressure was greatest in the older individuals. For example, the systolic blood pressure declined 12 mm Hg in white men and women aged 65 to 74 compared to a 1 mm drop in those aged 18 to 24.

Repeated cross-sectional blood pressure surveys in several areas—Minnesota (Folsom et al. 1983; Luepker et al. 1984), Baltimore (Apostolides et al. 1978), Chicago (Berkson et al. 1980), Charleston (McClure et al. 1982), Maryland (Entwisle et al. 1983), and Connecticut (Freeman et al. 1985)—have consistently shown the improvement in blood pressure control, supporting the earlier findings of the national surveys (Drizd, Dannenberg, and Engel 1986). Evidence from physician visits (figure 1) continues to show that "large segments of the population are undertaking appropriate measures to control their blood pressure" (Lenfant and Moskowitz 1983). From 1982 to 1985, visits to physicians

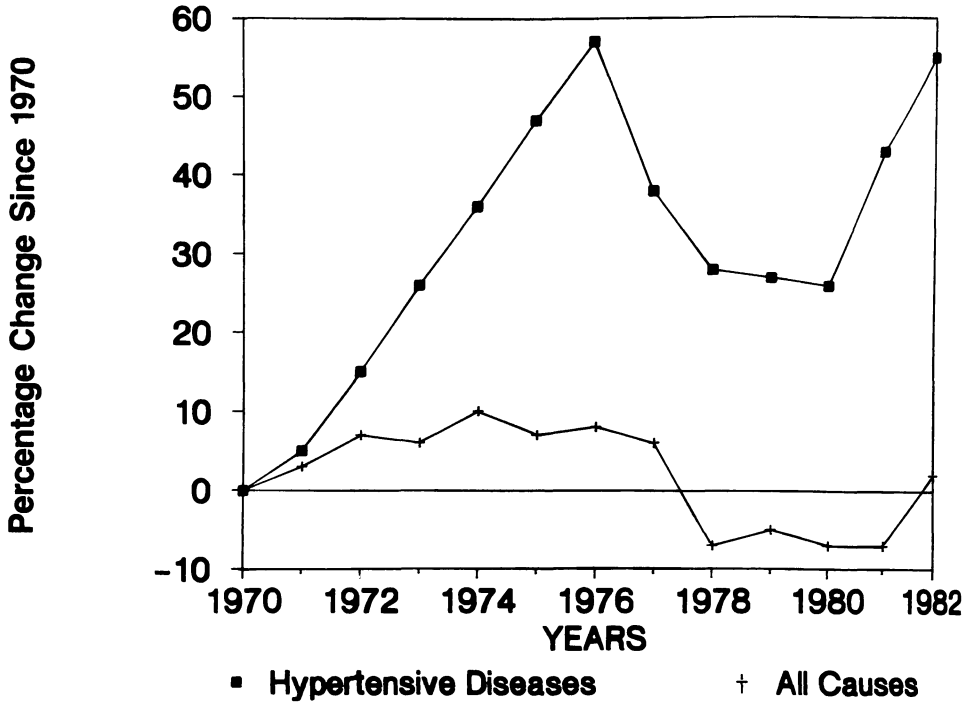

FIG. 1. Percentage change since 1970 in number of physician visits for all causes and for hypertensive disease (hypertensive and hypertensive heart disease). *Source*: National Disease and Therapeutic Index, IMS America (Lenfant and Moskowitz 1983, ref. 13).

for high blood pressure increased 52.7 percent while visits for other reasons increased 4.8 percent (U.S. Public Health Service 1986). The increased visits provide an opportunity for more effective use of non-pharmacological adjunct or primary therapy for elevated blood pressure, which has in some ways lagged behind pharmacological management. For example, the percentage of adult individuals who are overweight (roughly 40 to 45 percent of black women and 20 percent of white men, white women, and black men) has not changed from the early 1960s to the late 1970s (Kumanyika and Helitzer 1985).

Nevertheless, the blood-pressure changes are believed to have made an important contribution to the documented decline in mortality from heart disease and stroke since the 1960s. From 1972 to 1984 the death rate from heart disease, in general, fell 33.9 percent (U.S. Public Health Service 1986). From 1980 to 1986 this death rate fell

at least another 9 percent. Between 1968 and 1976 the annual age-adjusted coronary-heart-disease death rate in all race/sex groups except white women declined by 60 to 70 per 100,000 (U.S. Department of Health and Human Services 1985). For white women the decline was 34 per 100,000. Stroke mortality declined 47.8 percent between 1972 and 1984 and has fallen at least another 17 percent since 1980 (U.S. Public Health Service 1986). Between 1970 and 1980 stroke mortality has shown the greatest decline in black women, falling by 46 to 56 percent in various age decades between 35 and 74 years (U.S. Department of Health and Human Services 1985). The declines in stroke death rates during this time period in the other three race/sex groups were in a similar range, varying from 39 to 48 percent for various age decades between 35 and 74 years.

Public and private efforts have contributed to the progress in hypertension control. In 1972 the National Institutes of Health established the National High Blood Pressure Education Program to bring national attention to hypertension as a major public health problem. A cornerstone of the program, the National High Blood Pressure Education Program Coordinating Committee, was established at that time as well. This committee currently comprises over 30 volunteer health, professional, and public agencies and organizations, and serves as a forum for consensus and action for these groups. It provides direction as well as a national network for the program's education effort. An example of the committee's efforts is the consensus on lowering the level of blood pressure at which pharmacological treatment should begin if nonpharmacological management was not successful from 95 to 90 mm Hg. These recommendations were widely and rapidly disseminated using the network of the coordinating committee. The success of this process is believed to have contributed to the above-noted acceleration in physician visits for hypertension in the early 1980s (figure 1). State and local hypertension control programs have also been an integral part of the program's network. To enhance the effectiveness of the program in minority communities, the Ad Hoc Committee on Hypertension in Minority Populations was formed in 1975. This committee was comprised of Hispanic, Asian, Native American and black health professionals, selected for their strong ties to minority communities throughout the United States. This committee aided in two-way communication between the program and the minority communities. The ad hoc committee continues this function with an expanded role

of aiding in reduction of all of the risk factors for cardiopulmonary disease.

The overall profile of past high blood pressure control efforts and reduction of heart disease morbidity and stroke in the black and white United States populations is positive and suggests a beneficial relative impact on the black population. There are, however, a number of considerations that suggest that these efforts need reassessment and refinement:

1. Despite the overall reduction in heart disease and stroke mortality in all race/sex groups, a five to six year life-expectancy gap (at birth) remains between black women and men compared to white women and men. Expressed in other terms, this gap is responsible for 59,000 deaths annually in black men and women that would not occur if blacks had the same death rates as whites (Manton, Patrick, and Johnson 1987). Forty-one percent of these excess deaths in black women and 24 percent of the excess deaths in black men are attributable to heart disease and stroke (U.S. Department of Health and Human Services 1985). A detailed review of the risk factors for this excess cardiovascular disease identified hypertension as a key contributor (Kumanyika and Savage 1985).

2. Some evidence from the mid-1970s suggests that cardiovascular disease mortality may show a decreased rate of decline in black men and women and white women in contrast to the unchanged rate of decline in white men (Sempos et al. 1986).

3. Clinical trial information suggests that the reduction in heart disease deaths associated with reducing blood pressure with medications is less ("fraction of benefit" equals 40 to 60 percent) than that predicted from observational epidemiologic studies (Russell 1987; Kuller et al. 1986). This is in contrast to the fraction of benefit (nearly 100 percent) in reduction of stroke. Subgroups of subjects with resting electrocardiographic abnormalities (including changes suggesting left-ventricular hypertrophy) at baseline who were treated with diuretics had a significantly greater heart disease mortality than those that had no such resting abnormalities or that were less vigorously treated with diuretics (Kuller et al. 1986).

4. Hypertensive patients with some forms of left-ventricular hypertrophy may be made worse when treated with some classes of

antihypertensive agents (Topol, Traill, and Fortuin 1985; Savage 1987a). Some evidence suggests that black patients may be more likely to have such conditions (Topol, Traill, and Fortuin 1985; Savage 1987b).

5. Some classes of antihypertensive agents (diuretics and beta blockers) have been associated with modest unwanted changes in blood lipid profiles (Wright 1987).

6. New classes of antihypertensive agents are increasingly being used instead of diuretics as first-step therapy for hypertension. These agents are substantially more expensive than diuretics (Gallup and Cotugno 1986; Saunders 1986).

As noted above, policy changes in hypertensive management should be carefully considered because of their potentially large health and economic impact. Groundwork for quantitative considerations of such policy was laid in the mid-1970s by Weinstein and Stason (1976).

Cost-effectiveness Modeling in Hypertension

In 1976 Milton C. Weinstein and William B. Stason published a classic study: *Hypertension: A Policy Perspective*. They examined the cost-effectiveness of the treatment of hypertension. They used data from the long-term prospective epidemiologic study at Framingham to estimate the morbidity and mortality benefits of blood pressure control. They took the social perspective and counted all costs, regardless of who paid them, and all health effects, no matter who experienced them. The cost per year of life gained was calculated using the following formula: cost per year = net costs/net health effects.

As summarized by Russell (1987), net costs are the total costs of treatment, minus the savings in medical costs secondary to heart attacks and strokes prevented, plus the costs of treating side effects of the medications, plus ordinary medical costs during the years of life added by the treatment. The net health effects included years of life added by drug therapy, plus improvements in health because of treatment (valued in an equivalent number of years of life), minus the side effects of drugs (also calculated in an equivalent number of years of life). As noted, the Framingham data gave the risk of heart disease, stroke, and death as a function of blood pressure level. These data fit a logistic curve (i.e., risk of death or disease rose more rapidly

at higher levels of blood pressure). For example, a ten-point rise in blood pressure from 115 mm Hg to 125 mm Hg is associated with a greater increment in risk of disease or death than an increase from 95 mm Hg to 105 mm Hg (Russell 1987). Data were available for white men and women but not for black subjects.

Weinstein and Stason derived their information on effectiveness of treatment from the Veterans Administration clinical trials. Statistical information was not totally adequate for all ages and different lengths of treatment, so they used expert opinions for filling in such gaps in information not available from the trials. They expressed the benefits of antihypertensive therapy in terms of the gain in "quality-adjusted life years." This adjustment allows one to equate a number of years with poor health (e.g., with side effects of medicines) that people would give up in order to have a year of good health (e.g., with no heart disease). They used a number of simplifying assumptions and used national death rates to estimate the remaining parameters. Thus, they estimated that the cost of treatment of hypertension was $4,850 per year of life gained for people with moderate or severe hypertension (Russell 1987). This rose to $7,000 if the cost of screening to identify the individual was included. Age at identification, sex, and initial blood pressure were variables that affected these costs. Adherence to therapy had an important effect since lack of adherence could increase the cost 30 percent to as much as four-fold more (Russell 1987). In a recent update, the cost of screening and treatment for persons with a diastolic pressure of 105 mm Hg was $12,000 per quality-adjusted year of life gained in 1984 dollars (assuming incomplete adherence) (Stason 1986). This increased to more than $60,000 per person per quality-adjusted year of life gained for those with diastolic blood pressure of 90–94 mm Hg.

Hypertensive patients with mild elevations of blood pressure are a heterogeneous group with a lower benefit relative to the cost of pharmacologic treatment. This has increased interest in both nonpharmacologic treatment and in further stratification of this group into high- and low-risk individuals. This could mean that perhaps millions of individuals with mild hypertension could be identified as being at such low risk that they need only be managed with nonpharmacologic therapy. A smaller subgroup (that also had apparently mild hypertension on the basis of their blood pressure level) might be identified who were at much higher risk and might need both pharmacologic and

nonpharmacologic treatment. This could lead to a much more efficient program of reduction in cardiovascular morbidity and mortality. For this reason, interest in assessing cardiac target-organ damage (especially echocardiographically detected increases in left-ventricular mass) for such stratification of risk in individuals with mild to moderate hypertension has grown.

A mathematical model of cardiovascular mortality risk associated with such target-organ damage helps to quantify the potential of the echocardiographic measurements in risk assessment. Such a model is shown in figure 2, in which the gradient of risk associated with increasing echocardiographic left-ventricular mass (from the 50th to 99th percentile) is compared with the gradient of risk between similar percentiles of serum cholesterol or diastolic blood pressure. Details of the construction of this risk model are given in the appendix. The model predicts that a strikingly greater risk of cardiovascular mortality will be associated with increments in left-ventricular mass compared to increments of diastolic blood pressure or total cholesterol. This greater risk is not only striking at very high levels of the risk factors (e.g., the 99th percentile) but, more importantly for potential impact in cost-effectiveness analyses, is also striking at lower percentiles of risk factors. Data derived from our mathematical model predict that echocardiographic left-ventricular mass as a continuous variable may give a much more powerful stratification of risk than the level of blood pressure and, in particular, might help in stratification of risk among mild hypertensive patients.

Data are already available that are consistent with this model. For example, figure 3 records the progressive increase in cardiovascular events in white middle-aged men with mild hypertension associated with an increased left-ventricular mass index. The gradient of risk ranged from 0.8 cardiovascular events per 100 person-years for an echocardiographic left-ventricular mass index of 95 grams/meter squared to 4.3 events per 100 person-years for those with a left-ventricular mass index of 125 grams/meter squared or greater (Casale et al. 1986).

Echocardiograms performed in the Framingham study sample will allow the model to be tested directly in a population-based sample of white adults. As noted earlier, preliminary follow-up data from Framingham have already shown the echocardiographic left-ventricular mass to be a powerful risk marker for two-year all-cause mortality in men and women from the original cohort, independent of the standard

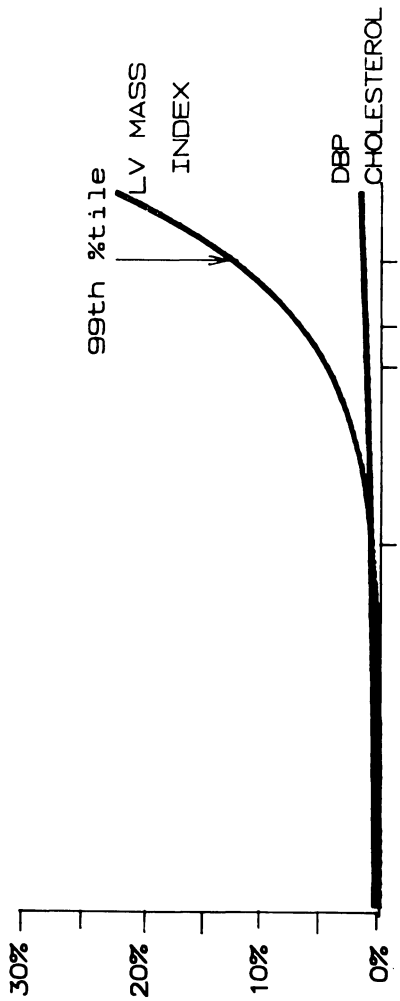

FIG. 2. Incidence of cardiovascular death for two years associated with percentile of echocardiographically determined left-ventricular mass (index), diastolic blood pressure, and total serum cholesterol in men aged 45 to 54. The risk-function curves are derived from interpolation between mean risk for the upper 99th percentile of the distribution of a risk factor and the mean risk for the remainder of the population using published Framingham data. The occurrence of electrocardiographic left-ventricular hypertrophy was conservatively considered the equivalent of the 99th percentile of echocardiographic left-ventricular mass (or mass index). LV = left ventricular, DBP = diastolic blood pressure in mm Hg. Cholesterol in mg/dl. See appendix for details.

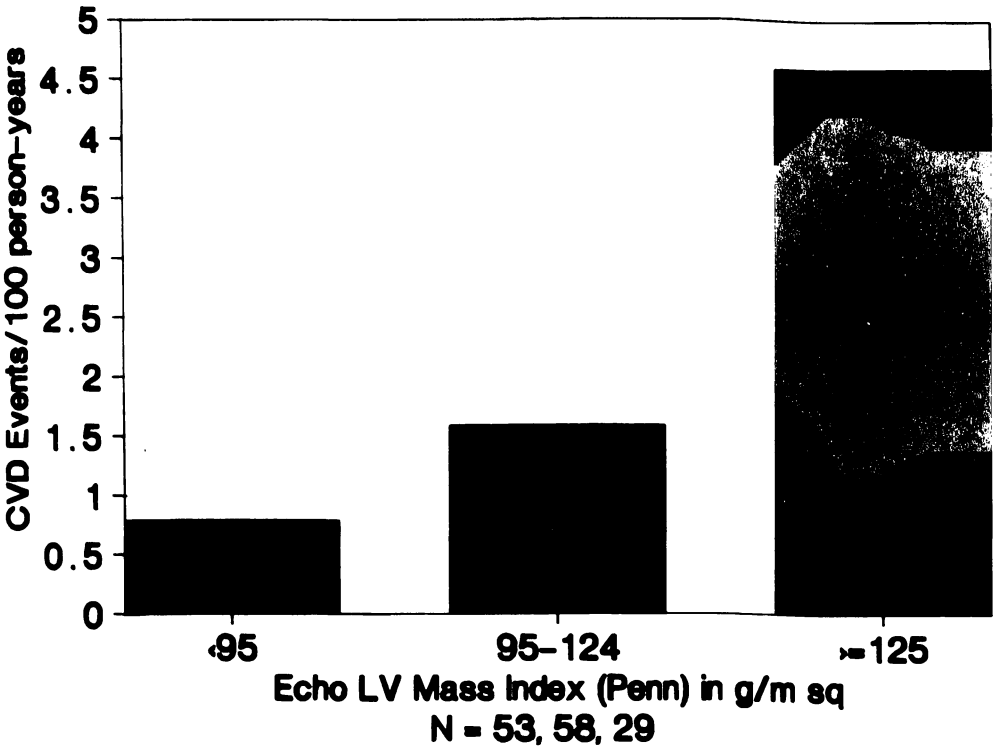

FIG. 3. Risk of development of cardiovascular (CVD) morbid events in middle-aged white men (mean age 48 years) with mild hypertension (and free of overt cardiovascular disease at baseline) as a function of range of echocardiographic left-ventricular mass index. "Penn" criteria LV mass indexed to body surface area was used. *Source:* Savage 1987a (adapted from Casale et al. 1986).

cardiovascular risk factors (Savage et al. 1985). Further analyses will allow more precise coefficients to be developed for the relation of cardiovascular morbidity and mortality to the level of echocardiographic left-ventricular mass. The utility of echocardiographic left-ventricular mass as a tool for stratification of risk will depend partially on the precision of these coefficients. No such data are available for blacks.

Figure 4 records the distribution of left-ventricular mass for a general population sample of Framingham (white) men (Savage et al. 1987) and for a small general population sample of black men aged 60 to 69 (Gazes et al. 1986). The relative shift in left-ventricular mass in black men to higher left-ventricular mass remained after various age-group- and blood-pressure-specific comparisons.

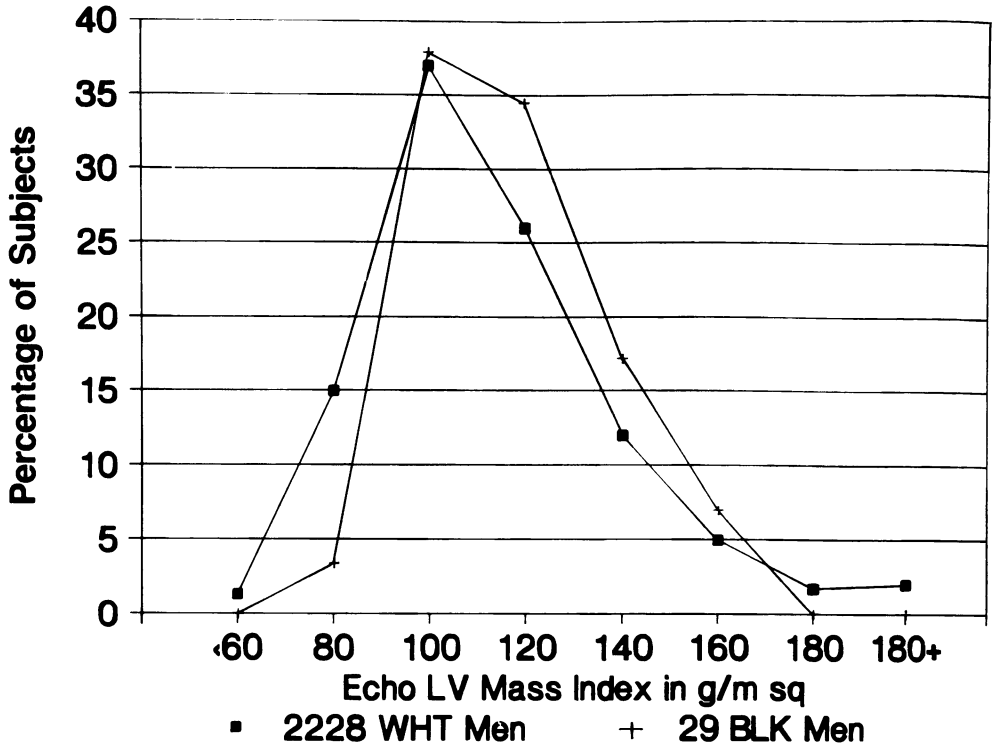

FIG. 4. Distribution of echocardiographic left-ventricular mass index in 2,228 Framingham white (WHT) men and in 29 elderly black (BLK) men. "Penn" criteria LV mass indexed to body surface area was used. *Source:* Savage 1987b.

Conclusions and Implications

These data are of importance for policy decisions regarding hypertensive patients in general but have particular significance for black hypertensive patients. If the above-cited two-fold greater prevalence of echocardiographic left-ventricular hypertrophy in blacks with mild hypertension, as compared with white hypertensives, has generality to the nation, the model would suggest significant differences in the meaning of mild hypertension in black and white hypertensives. This would suggest potentially different strategies for reducing hypertension-associated morbidity and mortality in black and white mild hypertensives. This would be especially important if reversing the increased left-ventricular

mass is shown to be an important independent goal of antihypertension management. More information is needed on the distribution of left-ventricular mass and its prognostic significance in various demographic groups of men and women. Such information may come from the third National Health and Nutrition Examination Survey, which may include echocardiography in the second of two national examination samples. This survey will have long-term follow-up and could be a valuable source of information for investigating the relation of left-ventricular mass to outcome in various demographic groups. Information on the degree of reduction of risk conferred by reducing left-ventricular mass independent of blood pressure reduction in various smaller demographic groups would be needed to complement the national observational data for precise cost-effectiveness analyses.

There are already data that suggest the differing importance of various potential determinants of increased left-ventricular mass in various groups of individuals, such as white and black men (Gazes et al. 1986). Thus, left-ventricular mass increases in one demographic group may have strikingly different implications than those in another group. This suggests that measurement of echocardiographic left-ventricular mass should be a part of clinical trials of antihypertensive agents and surveys assessing cardiovascular risk factors in various demographic groups of subjects. This is important even if the main purpose of a given survey and subsequent analyses is to investigate other risk factors for cardiovascular disease and death, because of the confounding effect that such an apparently important risk factor as left-ventricular mass might have on such analyses (Oster and Epstein 1986). If the prediction of the model developed above is confirmed, these data may have a profound impact on the choice of treatment as well as the therapeutic goal of treatment. The World Health Organization–International Society for Hypertension (1986) joint 1986 memorandum on treatment guidelines has already recommended that echocardiographic left-ventricular hypertrophy, in the absence of another explanation, is an indication for drug therapy in an individual with mild hypertension.

Echocardiographic information from race- sex- age-specific population-based observational studies and clinical trials could be used in refining analyses of the cost-effectiveness of alternative strategies for managing hypertension. Such analyses could lead to a more efficient reduction

of cardiovascular morbidity and mortality for all racial groups, but especially for blacks who appear to be overrepresented in the higher percentiles of echocardiographic left-ventricular mass even after controlling for blood pressure level.

If the assumptions in the model of cardiovascular mortality risk associated with echocardiographic left-ventricular mass prove correct, and the reduction of left-ventricular mass reverses the markedly elevated risk, such reduction of mass may be an essential component of the strategy for reducing the excess cardiovascular mortality in blacks as compared to whites.

Appendix

Mathematical Model Predicting the Prognostic Power of Echocardiographically Determined Left-ventricular Mass (figure 2)

Echocardiography, the use of sound waves to assess the structure and function of the heart, is widely accepted as the most sensitive and specific tool widely available for detecting left-ventricular hypertrophy—increased mass or weight of the left ventricle (Liebson, Devereux, and Horan 1987). The electrocardiogram (EKG) and the chest x ray were used in the past to assess left-ventricular hypertrophy or heart enlargement associated with hypertension. The EKG is still recommended for assessment of cardiac target-organ damage as part of the assessment of all hypertensive patients. It is a highly specific tool for detection of left-ventricular hypertrophy but is not very sensitive. Echocardiography maintains the high specificity of electrocardiography for this diagnosis (Savage et al. 1987, 1979a) while achieving a high sensitivity (correlations with autopsy left-ventricular mass exceed 0.9) (Devereux and Reichek 1977). Thus, only about 10 percent of subjects with echocardiographic left-ventricular hypertrophy are detected by the EKG, while almost all of the subjects with electrocardiographic left-venticular hypertrophy are detected by the echocardiogram (Savage et al. 1987, 1979a). The chest x ray does even less well than the other two tests (Savage et al. 1979a, 1983). Knowledge of the relation between echocardiographic left-ventricular mass and left-ventricular hypertrophy allows exploration

of the prognostic significance of increased left-ventricular mass detected by the echocardiogram.

Two things are now accepted about left-ventricular hypertrophy: first, that it can be treated—that is, it is reversible (Liebson and Savage 1987)—and second, that the simple dichotomization of populations into those with and without left-ventricular hypertrophy is a gross oversimplification of a more complex continuous process (increased left-ventricular mass). Data are beginning to accumulate on many emerging medical technologies including those used to assess left-ventricular hypertrophy. These procedures are often not only technologically complex, but may be expensive to perform. It is important to be able to make rational decisions as to which technologies show the most promise in terms of preventing disease.

One option is "modeling" to compare the impact of numerous risk factors and hypothesize what the decrease in occurrence of disease would be if certain population characteristics were changed. In the current context, the possible relation between a continuous measure of left-ventricular mass and cardiovascular mortality was modelled, based on published data from the Framingham Heart Study and three simple assumptions:

1. Left-ventricular hypertrophy on the electrocardiogram is a marker for a continuous measure of left-ventricular mass.
2. The distribution of this continuous measure may be approximated by a normal distribution.
3. The relation between this continuous measure and disease outcomes can be described by a logistic model.

The assumption that there is a continuous underlying process is reasonable and is supported by most of the recent literature (Savage et al. 1987). The second assumption, that the process has a normal distribution, is made for mathematical simplicity. This assumption is not crucial to the derivation but simplifies the mathematics involved. This assumption could be varied in future analyses. The third assumption, that the relation between the continuous measure and outcome can be described by a logistic equation, is also made for mathematical convenience but the logistic model is the model most generally used in epidemiology to describe the relation between characteristics associated

with risk ("risk factors") and outcome variables. In addition, since the model has two parameters, a two-point estimation procedure can be used.

Having assumed a normal distribution for the underlying characteristic, it was reasoned that the comparison of the upper 2.5 percent of the population with the lower 97.5 percent of the population is approximately equivalent to comparing a person at the mean with a person at the 99th percentile. This assumption was verified by running simulations that indicated that this reasoning was approximately correct, but somewhat conservative. That is, it led to a smaller coefficient than the true one. Nonetheless, this conservative result was used since it was desirable to explore possible relationships and to avoid overestimating the size of these relationships. As indicated, the logistic function involves two parameters. Knowing the value at two points on the X scale, one can derive estimates of the unknown parameters. The simulations involved taking the known relation between a continuous variable, for example diastolic blood pressure, and an outcome—cardiovascular death—and generating populations such that blood pressure was normally distributed and such that the probability of cardiovascular death was described by a logistic function. The diastolic blood pressure in the population was then dichotomized at the 99th percentile and the rate of disease compared in the two groups. The logistic parameters were estimated using the procedure subsequently used for LV mass and these were compared to the known parameters (available from previously published Framingham data, Shurtleff 1974). The results were reasonably close to the underlying logistic function. The simulations were done for populations of several sizes, and were repeated several times for each population of fixed size.

To simplify the problem of parameter estimation and to focus efforts on exploring the relation between left-ventricular mass and cardiovascular sequelae, all analyses, except one, were restricted to males in a ten-year age group, 45 to 54 years. The same procedure was carried out for total cholesterol for comparison. Finally, using the conservative assumption that electrocardiographic left-ventricular hypertrophy represented the 99th percentile of echocardiographic left-ventricular mass (indexed to body size), the relation of echocardiographic left-ventricular mass could be plotted between the 99th percentile and the mean risk of cardiovascular death for men without electrocardiographic left-

ventricular hypertrophy using the logistic function. This resulted in the predicted relation between the percentiles of echocardiographic left-ventricular mass and cardiovascular death shown in figure 2. The relation of diastolic blood pressure and total cholesterol to cardiovascular death is also shown in figure 2.

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Address correspondence to: Daniel D. Savage, M.D., Ph.D., National Center for Health Statistics, Room 1-43, 3700 East-West Highway, Hyattsville, MD 20782.