EDITORIAL COMMENT

Major Risk Factors and Coronary Heart Disease: Much Has Been Achieved but Crucial Challenges Remain*

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Coronary heart disease (CHD) morbidity, disability and mortality remain high in the U.S. and constitute a major challenge to medical science and public health. Annual economic costs (direct and indirect) of cardiovascular diseases (CVD) in this country in 2001 are estimated to exceed $298.2 billion (1).

Over the last half-century, a remarkable pattern has been observed in trends of the CHD epidemic. Between 1940 and 1967, CHD mortality rates rose for all people aged 35 to 74 years. This upward trend was recorded for white men, black men and black women, but not for white women. Since 1968, the trend has reversed i.e., CHD death rates have decreased steadily, with an overall decline of over 50%. This downward trend has involved all age-gender-ethnic groups in the adult population and all regions of the country, but it is less steep for lower socioeconomic strata (SES). It has encompassed both main categories of CHD (i.e., acute myocardial infarction [MI] and chronic ischemic heart disease) but much more so for acute MI than for CHD (2). The U.S. decline in CHD mortality rates is one of the largest—absolutely and relatively—of such trends in industrialized countries (3), but in the 1990s the rate of decline slowed. The drop in CHD mortality rates has been accompanied by an even greater percentage decrease in death rates from stroke, but—again—with a leveling off of the downward trend in the 1990s. During these decades, death rates from the major CVD and all causes also fell substantially, reflecting the declines in CHD and stroke among all strata of the population, in both men and women from ages 35 on, but—again—less so for lower SES strata. In terms of life expectancy, for men particularly an earlier adverse trend was reversed, with prevention of premature death for hundreds of thousands of individuals since 1968.

As experience with control of earlier epidemics has taught us, both prevention and conquest of mass disease require a proper national public policy and its implementation throughout the population. The U.S. was one of the first—if not the first—country to develop public policy in response to adverse CHD–CVD trends in the 1950s and early 1960s. This was done particularly under the leadership of the American Heart Association (AHA), and other professional, voluntary and public organizations (e.g., the American College of Cardiology, the Inter-Society Commission for Heart Disease Resources, the National Heart, Lung and Blood Institute). In 1959, the AHA issued its first statement on smoking and CVD health, and two years later it proposed a landmark dietary intervention against too high serum cholesterol levels (4). Subsequently, statements concerning all the major CHD risk factors were released, including reports on drug treatment of high blood pressure. Corresponding policy was adopted by the federal government, beginning with the historic “Report to the Surgeon General on Smoking and Health” in 1964 (5) and continuing with the White House Conference on Food, Nutrition and Health in 1970 (6), the National High Blood Pressure Education Program in 1972, the Senate Select Committee on Nutrition and Human Needs in 1977 (7) and the National Cholesterol Education Program some years later (8). These were followed in subsequent years by other government policy commitments for CVD–CHD prevention, which have been extended in important ways in the 1980s and 1990s, and have received broad support from major national organizations of physicians and other health professionals (9–13).

In the U.S. and other countries throughout these decades, resources allocated to implement such policies by the national government and by voluntary and private organizations have been modest compared, for example, to expenditures by the big tobacco companies on advertising, lobbying and support for political candidates. Nevertheless, a good deal has been accomplished; the prevention efforts have reached “critical mass.” The concern of the population, its readiness to respond and its positive responses are documented in both “subjective” and “objective” data. For example, in a 1977 nutritional survey by the U.S. Department of Agriculture (14) on a sample of the American population, approximately two-thirds indicated they had made changes in their eating habits in the previous three years for health and nutrition reasons. The reported types of change were related to dietary fats, sugars, salt, calories, blood cholesterol, blood pressure, diabetes and so forth. The two most important reasons given for the changes were advice from a health professional and information from the media. These “subjective” statements find their counterpart in national data indicating improvements in food intake patterns, including declines in dietary cholesterol and saturated fat intake that are substantial, albeit less than national goals. Concordant with the favorable dietary

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trends, declines have occurred in average serum cholesterol of adult population samples, from about 235 mg/dl in the 1950s to about 225 mg/dl in the early 1960s to 205 mg/dl in the late 1980s and early 1990s. Indeed, by the year 2000 the average serum cholesterol of adults is estimated to have reached the national health goal of no more than 200 mg/dl (15). Clearly, this downward trend—all the more remarkable in view of the steady increase in weight of adults—was for a long time unrelated to drugs (i.e., based on improvement in the composition of the diet). Only in the 1990s, with the emergence of the statins, have drugs played an important part in implementing serum cholesterol goals. Data also indicate that population mean blood pressure levels are down (16), in part independent of antihypertensive drug treatment. Moreover, national statistics document impressive rates of smoking cessation and of decline in the proportion of the population currently smoking (17), although recent trends among teenagers and young adults are adverse (15,18), and long-term trends are much less favorable for lower SES (15,17).

Given the dramatic nature of these trends and their importance for public health and for medical care, there has been considerable research interest in their causes and consequences. Investigations have assessed both the efficacy of medical interventions and the economic implications of preventive and therapeutic interventions directed against heart disease and its risk factors.

In this issue of the Journal, Goldman et al. (19) attempt to answer the question “what was the aggregate impact and cost-effectiveness of interventions that were actually implemented in the entire population [ages 35 to 84] between 1981 and 1990?” This is an important query from the point of view of medical care, public health, and of what we get for money invested. The investigators are not projecting what might be accomplished if certain changes or interventions were made; instead, they are modeling what actually happened in terms of changes in blood pressure, blood cholesterol, smoking and the associated costs of screening and interventions to decrease these coronary risk factors. Using data from 1981 to 1990, they quantify the decrease in costs of the disease due to lower incidence, and the increase in costs for intervention to accomplish this decline in disease, and they compute the net cost by subtracting the one from the other. To arrive at a measure of “cost-effectiveness,” they estimate the quality-adjusted additional years of life attributable to the observed reductions in risk-factor levels and disease events, and they divide the net costs by the years of life gained to arrive at a cost at per additional quality-adjusted year of life (QAYL), attributable to reduction in each major risk factor, and overall. Recognizing that the full impact of risk-factor reductions and total costs of intervention does not occur until after the period they modeled, the researchers make projections from 1991 to 2015, assuming that the 1990 levels of risk-factor reduction will be maintained throughout this period.

Based on this computer simulation (20), Goldman et al. (19) come to a very positive bottom line, particularly since projections into 2015 (i.e., over a 35-year period) yield far more favorable cost and cost-effectiveness estimates than for the shorter period of 1981 to 1990. For example, estimated costs for observed reductions in blood pressure per QAYL gained is $95,000 between 1981 and 1990 but only $6,800 for the period 1981 to 2015. For this period, their model predicts reductions in CHD deaths to be 100,000, 1,300,000 and 2,400,000 for risk-factor reductions in smoking, serum cholesterol, and blood pressure, respectively, with an overall reduction of 3,600,000 deaths due to the combined effects of reductions in all three major risk factors. They further predict QAYL gained from these risk-factor reductions to be 6,600,000, 6,500,000 and 22,000,000 for reductions in smoking, serum cholesterol, and blood pressure, respectively; 33,000,000 QAYL gained overall from reductions in all risk factors over the period 1981 to 2015. These dramatic reductions in CHD deaths and resultant substantial increases in years of life gained from reductions in risk factors lead to a prediction of an overall cost-effectiveness ratio of $5,400 per QAYL gained over the 35-year period. Thus, as the investigators (19) state: “Overall we believe our analysis is a strong endorsement of the investment in risk factor reduction in the period 1981 to 1990. Maintenance of these improvements should yield incremental benefit with even more favorable cost-effectiveness ratios.”

Of course, these results are based on assumptions and estimates; therefore, they are subject to criticism related to the soundness of the assumptions, the parameters of the model, and the quality of the data used for making estimates. However, the model employed has been widely utilized in numerous studies, and its predictive capacity has been extensively tested and documented (20,21). Likewise, careful judgment apparently was used in choosing data for estimates of disease rates, costs of disease and costs of risk-factor reductions, and appropriate sensitivity analyses were carried out to gauge the effects of inaccuracies in estimates. Overall, with consideration of such caveats, the results are a strong endorsement for efforts and investments toward risk-factor reduction made in the U.S. over the past 20 years. The investigators (19) provide further significant documentation that reductions in CHD incidence and death and increased years of high-quality life have resulted from reductions in risk factors, and that these accomplishments were achieved with cost-effectiveness acceptable to the health policy community.

Nevertheless, within the context of this impressive “bottom line,” there remains the need to be fully aware of remaining challenges: the flank of the CHD epidemic has been turned, but it continues, and there are no assurances of further favorable downward trends. The estimated costs of treating CHD are enormous ($8730 billion over the period 1981 to 2015 according to Goldman et al. [19]), and the costs of risk-factor reduction—through both population-wide programs and patient-specific interventions—are large.
as well ($350 billion estimated for the same period). Despite reductions in CHD incidence due to lower risk-factor levels, Goldman et al. (19) estimate that the costs of risk-factor reductions still create “about a 15% net increase in the total burden of CHD costs,” compared to no interventions. Moreover, although $5,400 per QAYL gained may be judged “cost-effective” by many, it is a substantial amount, much of which must be borne by society as a whole rather than solely by the individuals who benefit from the added years of life. Therefore, it is reasonable to ask whether further reductions in risk-factor levels can be achieved, whether these reductions can lead to additional decreases in disease, and whether this could be accomplished with better cost-effective measures. These matters were, of course, not encompassed in the goals of the Goldman et al. (19) report. Still, it may be of interest to explore along these lines with the hope both of stimulating additional research with the model and highlighting potential population-wide benefits of crucial strategic emphases related to prevention and control of major risk factors.

One area for exploration relates to the levels chosen to characterize blood pressure and cholesterol in the investigators’ CHD Policy Model. It uses diastolic blood pressure (DBP) levels <95, 95 to 104, >104 mm Hg and serum cholesterol levels <240, 240 to 299, >299 mg/dl. Thus, the lowest category of both these variables includes numerous individuals with elevated levels, placing them at increased risk compared to favorable or optimal levels—for systolic blood pressure (SBP)/DBP, ≤120/≤80 mm Hg; for serum cholesterol, ≤200 mg/dl, per current policy recommendations (13,22,23). Would results with the model be different if these preferred levels chosen were these preferred levels chosen? Also, given recent evidence that SBP is a more sensitive and stable predictor of CHD (24,25), what would be the effect of substituting systolic for diastolic pressure—or including both pressures as a single categoric variable (see the preceding text), as is done in the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC) VI criteria (23)?

Our recent work with individuals who have favorable or optimal levels of all three major CHD risk factors and are without a history of diabetes or myocardial infarction shows that these individuals have a remarkable set of positive outcomes in terms of much lower CHD, stroke, CVD and all-causes mortality, greater longevity, lower CVD and total Medicare expenditures for health care, and higher quality of life (26–28). These results, achieved from long-term observation of large cohorts, confirm statistical estimates from the Framingham and national cooperative Pooling Project studies (29–31). Those smaller studies had to extrapolate for assessment of impact of low risk as there were too few people at low risk (prevalence about 5%) for measurement. Availability of actual data at the end of the twentieth century demonstrate unequivocally that young adults and middle-aged American men and women with favorable levels of all major risk factors are indeed at remarkably low long-term risk of CHD–CVD, and they have considerably longer life expectancy with health. Thus, it would be valuable to learn whether the model is sensitive to the choice of major risk-factor cut-points, yielding significantly different results with projections made relative to individuals at favorable rather than frankly elevated levels of these risk factors.

A similar argument can be advanced regarding the age range (35 to 84 years) used in the projections. By age 35, lifestyles have already been set for decades, all too frequently with resultant adverse risk-factor levels already in place for years. Thus, the model begins at a point where risk-factor levels have already been rising for years. Inevitably, then, the model concentrates on efforts to reverse this trend of increasing risk-factor levels, with no consideration for efforts—crucial to achieve low risk early on—at primary or primordial prevention that could be applied in childhood, youth, and young adulthood at relatively low cost to prevent the rise (rather than just treat the elevation) of these risk factors. The relevance of a focus along these lines is underscored by the fact—evident from repeated national and local surveys—that population median levels of SBP/DBP and serum cholesterol are favorable at ages 18 to 24 years. The challenge is the preservation of these levels with little or no rise. The scientific knowledge is available as to what needs to be done (32–35).

Another area for attention relates to the costs of antihypertensive and cholesterol-lowering interventions, which in this model are largely driven by the costs of medications. In their sensitivity analysis, Goldman et al. (19) demonstrate that changing to lower-cost antihypertensive medications (a 40% savings) reduces the cost-effectiveness ratio from $5,400 to $2,400 per QAYL. This inspires the possibility of even greater cost reductions from substitution of expensive pharmacologic approaches by much lower cost nutritional and lifestyle improvements for lowering risk-factor levels. Goldman et al. (19) offer data showing that population-based educational programs are likely responsible for widespread reductions in risk-factor levels and are at the same time highly cost-effective. This is especially intriguing given that the model incorporated projected increases in mean body mass index (BMI) levels during the simulation period with no mention of costs associated with treatment or prevention. The adverse trend in BMI must be viewed with concern equal to that given to unfavorable trends in blood pressure and serum cholesterol. There is no reason to regard increase in any of these measures as an inevitable consequence of aging.

All these adverse trends of today are societal in origin, either absent or of low order in other societies, and are remediable in ours. Substantially increased national efforts to promote healthy eating patterns and increased physical activity at every age can produce lower mean population levels of BMI and consequent further nonpharmacological
reductions in mean blood pressure and serum cholesterol beyond those already achieved, as well as reduced incidence and prevalence of diabetes. Almost certainly this would further reduce disease and be cost-effective. The investigators (19) state that their data could not be used to separate the epidemiologic benefits of patient-specific compared to population-wide interventions. It would be valuable to extend the model to simulate and explore the matter of comparative cost-effectiveness of long-term population-wide lifestyle interventions versus pharmacological interventions.

Implicit in the good news of the Goldman et al. (19) report is the acceptance of widespread lifelong costly pharmacological interventions to curtail smoking and hold back the tide of increasing blood pressure and cholesterol levels. With this acceptance comes the realization that monies for these endeavors flow largely from the federal government and may not continue to be appropriated. This highlights the key strategic challenge facing the medical and health policy community at the beginning of this century. Do we resign ourselves to a strategy emphasizing treatment of results of disease (secondary prevention) and lowering of already elevated risk factors, or emphasize a strategy focused on prevention of the risk factors themselves? The former approach means endless—decade after decade—efforts to treat risk factors and disease as they come down the road. Only the latter emphasis—namely prevention of the major risk factors in the first place—has the potential to end the CHD epidemic by progressively improving lifestyles in all strata of the population, from conception on, so that people with adverse risk-factor levels become the exception rather than the rule, and people with favorable levels of all major risk factors—low-risk people—become the rule rather than the exception. Key to the successful implementation of this strategy is the recognition of the unsolved problem of improving risk profiles among lower SES strata. Research and policy must address the widening gap between the affluent and the poor in terms of cardiovascular risk, and adequate resources must be allocated to its solution.

Finally, the strong positive message of the Goldman et al. (19) article is that present efforts to combat the epidemic of CHD are cost-effective and represent a worthwhile social investment. With elimination of risk in risk-factor levels with age across all strata of the population irrespective of region, ethnicity, and SES—through concentrated efforts at primary and primordial prevention—further reductions in coronary disease rates and cessation of the epidemic (with better cost-effectiveness) are achievable goals for the next decades.

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