Risk Factor Intervention for Health Maintenance

Lester Breslow

Summary. Risk factors for disease consist of (i) personal habits, such as cigarette smoking and excessive alcohol consumption, and (ii) bodily characteristics, such as hypertension and high serum cholesterol. Progress in identifying and quantifying risk factors is opening the way to the prevention of disease and maintenance of health. Systematic, controlled trials of intervention against risk factors are beginning to produce evidence on the extent of success in reducing both the factors and the mortality from associated diseases.

Nature and Identification of Risk Factors

With the growing prominence on the health scene of certain chronic diseases such as lung cancer, cirrhosis of the liver, and coronary heart disease, various efforts have been undertaken to ascertain and deal with the factors responsible. One direction is to seek discovery of the biologic mechanisms of disease, for example, how an arteriosclerotic plaque develops in the wall of a coronary artery.

Another, and now highly promising, direction is to approach the problem from the epidemiological standpoint. That effort takes the form of trying to identify the characteristics of individuals that are statistically associated with an increased frequency of a disease and mortality from it; and then trying to deal with the characteristics so as to reduce the likelihood of the disease and its effects. One set of factors associated with these diseases includes personal habits, such as cigarette smoking, sedentary life, and excessive alcohol consumption. Another set consists of actual bodily changes not yet sufficient to classify an individual as having a particular disease but recognized as precursors: physiological characteristics, such as hypertension; biochemical characteristics, such as high serum cholesterol; anatomical characteristics, such as cervical dysplasia; and genetic characteristics, such as trisomy 21 (Down's syndrome). Together, these two kinds of characteristics—certain common habits of people and certain bodily changes associated with increased frequency of disease and its consequences—have become known as risk factors.

Knowledge of these risk factors has accumulated rapidly during recent decades. Thoracic surgeons in the late 1930's recognized that their lung cancer patients commonly smoked cigarettes. Subsequently confirmed by many careful epidemiological investigations and summarized in the 1964 Surgeon General's Report (*1*), the association between cigarette smoking and several forms of cancer, coronary heart disease, and chronic lung disease has now been well established.

While cigarette smoking was being identified and gradually accepted as a factor in lung cancer and several other important diseases, investigators noted a comparable relationship between high intake of saturated fat, high blood cholesterol, and coronary heart disease (*2*). Again, these studies began with fairly gross observations of the association, but continued on into prospective epidemiological studies that quantified the relationships (*3*).

More-or-less systematic identification, measurement, and assessment of risk factors for coronary heart disease, the leading cause of mortality in the industrialized nations, has progressed, with attention to hypertension, sedentary living, obesity, electrocardiographic (EKG) abnormalities, personality factors, family history, and diabetes, as well as cigarette smoking and high blood cholesterol (*4*). The most extensive study has been that in Framingham, Massachusetts, from which the probability of having cardiovascular disease according to specified characteristics has been derived (Table 1) (*5*). A 30-fold range exists. Approaching the problem from the standpoint of generic health, rather than individual diseases, investigators at the Human Population Laboratory, Alameda County, California, have identified exercise, no cigarette smoking, 7 to 8 hours of sleep, moderate or no use of alcohol, and regular and moderate eating as positively associated with physical health and negatively associated with mortality from all causes (*6*).

The present situation regarding risk factors, including the potential for intervention, is somewhat analogous to the situation that existed when polluted water became known as a causative factor of enteric infections such as cholera and typhoid, before their etiology and pathogenesis were demonstrated bacteriologically.

Epidemiology of Risk Factors

Before discussing the matter of intervention, however, it may be useful to consider briefly the epidemiology of risk factors themselves—that is, their distribution in the population, their temporal distribution, and what influences their occurrence. Understanding the epidemiology of risk factors per se, as well as the diseases to which they are related, may enhance the possibilities of successful intervention.

For example, the health and nutrition examination survey conducted by the U.S. National Center for Health Statistics between 1971 and 1974 disclosed that 23 million adults, 18.1 percent of the population aged 18 to 74, had hypertension (*7*). The prevalence varied considerably in different segments of the population (Table 2). The survey also disclosed factors associated with that distribution and the extent to which persons were taking antihypertensive medication. Only slightly more than one-third of all hypertensive adults between 18 and 74 had used medication for the condition during the previous 6 months, and 60 percent of these had blood pressures of 160/95 (mm-Hg) or above at the time of examination. The survey also revealed the extent of salt restriction and efforts to control obesity as means of coping with hypertension.

A common notion about cigarette smokers is that they rarely can or will quit the habit. If true, that notion should

The author is the dean of the School of Public Health, University of California, Los Angeles 90024.

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lead those concerned with cigarette-induced health damage to abandon efforts to keep people from smoking cigarettes and to try other means of coping with the problem. In fact, more than 33 million Americans had actually stopped smoking cigarettes by 1976—almost double the number of former smokers in 1964, when the Surgeon General's report (*1*) was issued (*8*).

In 1964, 53 percent of all American men were cigarette smokers; by 1975 the proportion had dropped to 39 percent (*9*). Furthermore, the decline has been greater among younger men with more education. For example, among males up to age 30 years in Alameda County, California (a community fairly typical demographically of the U.S. population), during the period 1965 to 1974, cigarette smoking dropped from 79 percent to 74 percent for those who had not completed high school; 65 percent to 60 percent for those who had completed high school only; and 33 percent to 20 percent for those who had completed college or more education (*10*). There has also been some drop in cigarette smoking among women.

Serum cholesterol concentration is probably the most thoroughly studied and documented risk factor for coronary heart disease. Deliberate efforts to control hypercholesterolemia have included diet, exercise, and drugs. For example, reducing the total calories derived from fat in the typical American male diet from 40 to 45 percent to 20 to 30 percent, altering the ratio of saturated to unsaturated fats from the typical 2:1 or 3:1 to 1:1, reducing daily cholesterol intake, and reducing total caloric intake if the subject is overweight "generally have been successful in lowering serum cholesterol over sustained periods of time" (*4*, p. 519). In The Anticoronary Club study in New York, the serum cholesterol fell an average of 30 milligrams per deciliter in the first year of dieting by free-living middle-aged men and persisted for more than 7 years in subjects maintaining the diet (*11*).

Table 1. (*5*). Probability per 1000 of having cardiovascular disease within 8 years according to specified characteristics in a 45-year-old man. Framingham study: 18-year follow-up.

Glucose intolerance	Cholesterol	Systolic blood pressure (mm-Hg)							
		Does not smoke cigarettes				Smokes cigarettes			
		105	135	165	195	105	135	165	195
No left ventricular hypertrophy by electrocardiogram									
Absent	185	22	35	54	84	38	59	91	138
	235	35	54	84	129	59	91	139	205
	285	55	85	129	192	92	139	206	293
	335	85	130	193	277	140	207	295	401
Present	185	39	61	95	143	67	102	154	226
	235	62	95	144	212	103	155	227	320
	285	96	145	213	303	156	228	321	431
	335	145	214	304	411	229	323	433	550
Left ventricular hypertrophy by electrocardiogram									
Absent	185	60	93	141	208	101	152	223	315
	235	93	142	209	297	153	224	316	425
	285	142	210	298	405	225	317	426	543
	335	211	300	406	523	318	428	545	657
Present	185	105	158	231	324	170	246	344	456
	235	158	232	325	436	247	345	457	574
	285	232	327	437	554	346	459	576	685
	335	328	438	556	667	460	577	686	778

Concept and Methods of Risk Factor Intervention

Important risk factors are thus being identified and data are being accumulated to indicate that it is feasible to control risk factors. One risk factor—for example, cigarette smoking—may be involved in more than one disease entity; one disease—for example, coronary heart disease—may have more than one risk factor.

Until recent years, medicine has focused largely on diseases themselves. Now we are beginning to understand better the natural history of important chronic diseases and the two major possibilities of intervening in their natural history so as to avoid the diseases, reduce their mortality rates, or both.

One possibility is to identify the pathological process early in the affected individual and intervene in some way to stop the process at that point. Thus, screening with the Papanicolaou smear, determining blood pressure, and other means may detect those persons in the population, even without signs or symptoms, who are developing a disease. Intervention at such points, known as secondary prevention (to indicate that while the disease process is under way, its further development can be prevented), is increasingly effective.

Even better, of course, is primary prevention, avoiding those factors that initiate and promote the disease process. Thus, the vast majority of lung cancer and much coronary heart disease can be prevented by avoiding cigarette smoking.

Hence, risk factor intervention as an approach to chronic disease control consists of two elements: (i) identifying and quantifying the relationship of certain personal characteristics—largely habits associated with diet, use of cigarettes, alcohol consumption, exercise, and the like—and dealing with them to avoid the disease process altogether (primary prevention) and (ii) identifying the disease process in its early stages and taking steps to avoid progression of the disease (secondary prevention).

The effectiveness of this strategy depends upon (i) the means available for and the extent of the search for the risk factors in the population and (ii) the means available for controlling the various risk factors and the extent of their proper application. The potential for effective risk factor intervention varies considerably among different diseases and different social situations.

Even though the possibilities seem great, much remains to be learned concerning the extent of the potential and how it may be achieved. In general, three methods of intervention have been tried.

1) The first consists of approaching individual persons (as in a physician's practice or mass screening in a population), identifying their risk factors, and then taking steps to reduce the risk factors found. That is the so-called "medical model."

2) Mass education has been undertaken to change health habits through schools and public media among others. Widespread transmission of information about risk factors and other ways of influencing health-related behavior have apparently already had some impact, as in the case of cigarette smoking.

3) Some efforts have been made to alter the products actually used by people. For example, low-fat milk and soft margarine are now more readily available.

These three means of dealing with the problem are now being intensively explored: personal health services, educational measures, and environmental measures. While these three may be separated for the purposes of analysis, they are in fact often closely related in any particular social situation.

Risk Factor Intervention Trials

So promising did the strategy of risk factor intervention appear by the early 1970's that several investigators in different parts of the world initiated large-scale trials. Three of the major trials were directed at cigarette smoking, high serum cholesterol, and hypertension, the factors most consistently identified as prominent in the risk for coronary heart disease.

Multiple Risk Factor Intervention Trial (MRFIT). The MRFIT responded to the recommendations of the Inter-Society Commission for Heart Disease Resources in 1970 (*12*) and the following year by the National Heart and Lung Institute (NHLI) task force on arteriosclerosis (*13*). The NHLI thereupon initiated a study cooperatively with 20 centers (*14*).

"The primary objective was to determine whether for a group of men at high risk of death from coronary heart disease, a special intervention program which is directed simultaneously toward three risk variables will result in a significant reduction in mortality from coronary heart disease. . . . A second objective is to determine the effect . . . on coronary heart disease incidence (either non-fatal myocardial infarction or coronary heart disease death), cardiovascular mortality, and total mortality (death from any cause). . . . Specific goals [for] risk factor modification [included] (i) a 10 percent reduction from baseline in serum cholesterol; (ii) a 10 percent reduction from baseline in diastolic blood pressure; and (iii) a 20, 30, or 40 percent net reduction in amount of cigarette smoking for heavy, moderate, or light cigarette smokers, respectively" (*15*, p. 12).

The first operational step was to select the individuals at high risk upon whom intervention efforts would be focused. Out of 370,599 persons recruited for initial screening, the participating centers finally selected 12,866 individuals as meeting the criteria for admission to the study: age, 35 to 57 years; increased risk of death from coronary heart disease on the basis of the Framingham risk score, which embraced elevated serum cholesterol, elevated diastolic blood pressure, and cigarette smoking; no pre-existing definite clinical coronary heart disease or other specified causes for exclusion; and willingness to commit themselves to a 6-year intervention program (*16*). Fifty percent were randomly allocated to their usual source of medical care, and the participating centers enrolled the other 50 percent in a special intervention program.

The special intervention program began with a series of ten intensive group sessions emphasizing "factual education, selected principles from the disciplines of behavior modification and group dynamics, and the use of group process to facilitate change in a supportive atmosphere . . . applied to nutrition, smoking and treatment of hypertension" (*15*, p. 14). Those persons who achieve their goals of risk-factor reduction then begin maintenance programs; the unsuccessful ones are referred to more individualized, extended intervention programs.

Table 2. (*7*). Percentage of examinees 18 to 74 years of age with hypertension, by race, sex, and type of hypertension. Data are from the United States, 1971–1974.

Types of hypertension	White		Black	
	Male	Female	Male	Female
Definite	18.5	15.7	27.8	28.6
Severe*	4.9	3.4	11.2	11.1
Borderline†	21.9	15.7	17.6	14.3

*Severe: ≥ 105 mm-Hg diastolic pressure. †Borderline: 140 to 160 mm-Hg systolic or 90 to 95 mm-Hg diastolic pressure.

The only results available from the MRFIT program are the findings from the initial screening: an average serum cholesterol of 257.3 mg/dl, average diastolic blood pressure of 99.2 millimeters of mercury, and an average of 21.62 cigarettes per day with 63.7 percent reporting smoking one or more cigarettes per day. There were essentially no differences between special intervention and usual care groups.

The MRFIT program has been under way too short a time to permit the compiling of findings pertinent to the objectives. From a self-assessment thus far,

"It is clear that a large, complex, multicenter trial such as this can survive phases of planning, controversy and compromise, and enter operations successfully. . . . The response from the mass media and the public has been generally gratifying. . . . The response from the medical profession has also been decidely favorable and helpful; [and] while it is too early even to speculate on the results, it would appear that this expensive undertaking has had an auspicious start" (*14*, pp. 826–827).

The Stanford Heart Disease Prevention Program. A field experiment in three northern California towns, the Stanford heart disease prevention program has focused on the same three risk factors for cardiovascular disease as those in the MRFIT program. It has been mainly a campaign directed toward the total community, with some effort directed toward high-risk individuals (*17, 18*).

The goal was to develop and evaluate methods "to influence the adult population at large to change their living habits in ways that could reduce their risk of premature heart attack and stroke" (*18*, p. 102). Combining biomedical expertise with that of the social sciences, "the family-community model, rather than the medical-center model, was chosen because a community would be able to provide the milieu in which a consensus of support and mutual help could develop and become an essential and integral part of the behavioral change program" (*18*, p. 101).

Three roughly comparable communities in northern California, each with populations of 12,000 to 15,000, were selected for the study. All three communities were surveyed for base-line data. One was then kept as a control. A multimedia campaign in the other two communities extended over a period of 2 years; in one of them certain high-risk subjects identified in the base-line survey received additional face-to-face intensive instruction.

The intitial survey included a behavioral interview and a medical examination of a sample of persons 35 to 59 years of age in all three communities. The survey covered relevant knowledge of and attitudes toward risk-related behavior related to diet, weight, smoking, and exercise. Incorporated into the medical examination were measures included in the Framingham risk score (*19*).

In the two (noncontrol) communities, the Stanford program in 1972 launched a mass-media campaign incorporating materials to teach specific behavioral skills as well as to impart information and affect attitudes regarding risk-related behavior. The campaign included television and radio "spots" and hour-long programming, weekly newspaper columns, newspaper advertisements and stories, billboards, posters, and printed material mailed to participants. In one of the two communities a random sample of individuals in the top quartile of risk were recruited into intensive face-to-face instruction.

Two subsequent annual surveys showed favorable changes both in the physical variables constituting the risk score and in pertinent knowledge and behavior. Improvement in knowledge after two years in the control community was 6 percent; in the two communities where the campaign had been conducted there was 26 to 41 percent improvement, and among those receiving intensive instruction, 54 percent (*18*).

Saturated fat and cholesterol consumption declined 20 to 40 percent over the 2-year period in the campaign communities, a substantially greater drop than in the control community. The drop was especially large among high-risk men

who received intensive instruction. Mean changes in serum cholesterol were highly correlated with the self-reported changes in dietary behavior (*20*).

Cigarette smoking likewise declined to a greater extent among total community participants in the campaign communities, 7 to 24 percent, compared with the control community, where the drop was only 2.5 percent at the end of year 2. Among those who received intensive instruction, the decrease in cigarette smoking was 42 percent (*18*).

In the control community, the risk for coronary heart disease actually increased more than 5 percent during the 2-year period of the study, but the risk in the communities where the campaign had been conducted declined 15 to 20 percent among the total participants. Again the decline was greater in the intensive-instruction high-risk group, 30 percent.

Thus the Stanford heart disease prevention program has demonstrated that a community-focused multimedia campaign over a 2-year period can substantially improve not only knowledge of risk factors for cardiovascular disease but also favorably influence behavior and risk scores. Intensive instruction of individuals identified as having a high risk score augmented the effect in that group.

The North Karelia Project. North Karelia, a county of eastern Finland with a population of approximately 180,000, nearly 70 percent in rural areas where the main occupations are farming and forestry, has an extremely high rate of coronary heart disease—perhaps the highest for any geographic area in the world (*21*).

Reacting to that health situation, local and national governmental representatives of the people petitioned the national government to take action. As a result the North Karelia project, a community program for the control of cardiovascular diseases, was established in 1972. The University of Kuopio assumed responsibility for the project with support from the national government in the amount of approximately $250,000 annually—less than $1.50 per capita per year. That has been essentially the "cost" of the project, the additional resources used beyond those already present in North Karelia.

The main objective was to decrease cardiovascular disease mortality and morbidity among the population of North Karelia—especially among the middle-aged male population. Intermediate objectives were to reduce the same three cardiovascular risk factors as those in the Stanford and MRFIT projects and to promote the early diagnosis, treatment, and rehabilitation of cardiovascular patients. A national objective was to provide tested field methods for nationwide use in connection with the control of cardiovascular disease and other health problems (*22*).

Leaders in the project decided early (i) to mount a comprehensive campaign against risk factors in the entire population of the area, not to "enroll" test subjects; (ii) to focus on just three risk factors: cigarette smoking, serum cholesterol level, and hypertension (since obesity and physical exercise were not problems in the area); (iii) to integrate the project into the existing service structure and social organization of the area; and (iv) to maintain observation of a similar nearby county as a reference (control) population.

A random-sample base-line survey of the North Karelia population 25 to 59 years of age in 1972 revealed that among males 54 percent were currently smoking cigarettes; the mean serum cholesterol was 269 milligrams per 100 milliliters, and 21 percent had a blood pressure of 160/90 (mm-Hg) or above (*24*). Myocardial infarction, hypertension, and stroke registers confirmed the extremely high incidence of these conditions.

The strategy in the comprehensive 6-year phased program was mainly to enlist widespread participation of the people of the region and their organizations and institutions. Activities include (i) providing public health information, through heavy use of television, radio, newspapers and other means; (ii) training personnel in health agencies, schools, and local organizations for community leadership in the project; (iii) organizing health and other public services for maximum participation; (iv) introducing environmental changes, such as restricting smoking cigarettes and encouraging low-fat dairy products; and (v) providing patient information services—for example, hypertension, stroke, and myocardial infarction registries.

Subprograms were aimed at each of the three risk factors. New laws banned cigarette smoking in public buildings and public vehicles; media carried advertisements against it; and special efforts were directed against cigarette smoking among teachers, health personnel, and persons at high risk. Dietary changes to reduce total fat consumption included introducing low-fat milk and margarine, incorporating mushrooms (as a fat replacement) into the popular sausage, and increasing the use of vegetables generally. Persons found to have hypertension in a countywide screening program were placed on therapy and followed by public health nurses. Coronary care units and ambulance services were established or improved.

Findings at the end of 4½ years indicated good cooperation by the people; a decline in cigarette smoking among middle-aged males (from 54 percent of the population smoking to 43 percent); an increase in the use of low-fat milk by from 17 to 50 percent of the population; an increase from 3 to 11 percent of the male population under hypertensive therapy, and among females from 9 to 13 percent; and a decrease in systolic blood pressure of 10 mm-Hg or more among 53 percent of the 1799 persons on the hypertension register, with 40 percent showing a decrease of 10 mm-Hg in diastolic blood pressure. Results have also included a considerable decline in the annual incidence of strokes: from 3.6 per 1000 males in 1972 to 1.9 in 1975 and from 2.8 per 1000 females to 1.8 (*21*). Myocardial infarction rates slightly declined.

> The programme in North Karelia will continue after the initial 5-year period, and a follow-up of [cardiovascular disease (CVD)] and CVD-risk indicators is organized to assess the longer term changes. In the meantime many of the experiences are already being planned for application nationwide [in Finland] (*23*, p. 1).

The three projects described exemplify efforts undertaken during the 1970's to reduce cardiovascular and other major diseases by attacking risk factors. Others include (i) the American Health Foundation's "Know Your Body" program among several thousand 10- to 15-year-old school children in New York City, which screens for and attempts to reduce elevated serum cholesterol, high blood pressure, cigarette smoking, obesity, and other risk factors (*24*); (ii) a program in Switzerland supported by the Swiss National Science Foundation to mobilize community resources to reduce cardiovascular disease risk factors in two communities with 10,000 to 20,000 inhabitants each, compared with two kept as controls (*25*); and (iii) the health hazard appraisal program developed at the Indianapolis Methodist Hospital (*26*).

Discussion

Efforts to cope with the major fatal diseases of the 20th century in the industrially advanced nations, especially the cardiovascular diseases and cancer, have evolved mainly into a two-pronged strategy. One element, primary prevention, is to identify and reduce the

causative factors so as to avoid the occurrence of the diseases, for example, by controlling cigarette smoking. The other element, secondary prevention, is to identify precursor bodily changes or initial stages of disease and avoid the progression of disease by early therapy, for example, by finding and treating asymptomatic hypertension.

At present, several large-scale trials of this strategy, known as risk factor intervention, are under way in the United States and Europe. The general aim is to test the feasibility of reducing (i) the risk factors, an intermediate objective; and (ii) the diseases and mortality from them, the ultimate objective.

Two main tactics are sometimes combined in practice. One approach is to identify those individuals who are at high risk—for example, cigarette smokers with hypertension and high serum cholesterol—and to focus intensive efforts on such persons. This may be called the medical model because it directs medical and related attention to selected individuals, as in medicine generally. The other tactic aims educational and environmental measures toward a whole community, seeking to improve the health-related behavior of a population and thus reduce its risk factors. This may be called the community model because the focus is on the entire community, not just on selected individuals who are at particularly high risk. The MRFIT program clearly follows the medical model, whereas both the Stanford and North Karelia programs are essentially of the community-model type but incorporate the medical as well. None of the projects is designed to evaluate the relative effectiveness of community and medical approaches, although the Stanford project includes that possibility to a limited extent.

Some evidence already indicates that the Stanford and North Karelia projects have been at least partially successful in reducing certain risk factors for cardiovascular disease, although meticulous comparison with the control communities remains to be done. In North Karelia the sharp decline in incidence of strokes is impressive, and the suggestion of decline in death from myocardial infarction is promising; but careful evaluation must await comparison with experience in the reference county.

Interpreting results of the specific programs is confounded by the present general trend toward a decline in risk factors such as cigarette smoking and hypertension in "control" groups or communities, probably due to general public and medical efforts to reduce risk factors apart from the large-scale programs.

The cost-effectiveness of the North Karelia project, funded at about $1.50 per capita target population annually, is likely to be vastly greater than the programs in the United States, for which much larger expenditures are being made. The cost advantage of the North Karelia project may be due both to the deliberate program tactic of comprehensively involving the community infrastructure and to the greater feasibility of that tactic in Finnish than in American society. Individuals, organizations, and community institutions appear more oriented toward the public good in Finland than in the United States.

It must also be noted that in North Karelia the level of risk was higher at the start than in the Stanford or MRFIT original populations (even though North Karelia is not a highly industrialized community) so that improvement there may potentially be more dramatic.

The Stanford project was well designed to test intervention on risk factors themselves but not the ultimate criteria of disease occurrence and mortality. There is, of course, substantial evidence from many studies that reducing certain risk factors, such as cigarette smoking and hypertension, does favorably influence disease incidence and mortality.

The MRFIT program has not yet produced data permitting the evaluation of results. If successful in reaching its objectives, it could have considerable influence on American medical practice. Interpreting data from the project, however, will have to take into account the fact that those identified as at high risk and therefore offered intervention constitute only a minority of the persons in the population who will suffer cardiovascular disease. For example, from the Framingham variables, ten percent of the asymptomatic population can be identified (and the MRFIT program did approximately that) "in whom 25 percent of the coronary heart disease, 40 percent of the occlusive peripheral arterial disease and 50 percent of the strokes and congestive heart failure will evolve" (*5*, p. 269). Thus, 75 percent of the coronary heart disease in the population would not be specifically targeted by the MRFIT program. Interpretation of MRFIT data will also have to include attention to the fact that only a portion of the high-risk eligible individuals actually participated in the intervention program. Evaluation should embrace the entire high-risk group, not just those who accepted the intervention efforts.

From the MRFIT, Stanford, North Karelia, and other current risk factor intervention studies, it seems likely that significant new data on how to control the major diseases of modern times will emerge. The evidence thus far suggests that intervention will prove successful. If it does, efforts to prevent disease and maintain health will probably focus increasingly on risk factors rather than, as now, on diseases themselves. Collaboration between epidemiologists and biomedical scientists concerned with physiological, chemical, anatomical, immunological, behavioral, and genetic aspects of human functioning may point the way to health improvement in the future. That would shift the focus away from the clinical entities that have occupied medicine so largely since the days of Thomas Sydenham (1624–1689) and toward risk factors. It is these factors that now largely predict and apparently determine the extent of chronic disease and premature death; they should receive higher priority in health efforts than the diseases themselves.

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