Review

Declining Mortality in Coronary Heart Disease

Robert I. Levy

Since 1968, there has been a dramatic, unprecedented decline in mortality from cardiovascular disease in the United States, especially from coronary heart disease and stroke. The decline has now been confirmed as real and has been observed in all age, sex, and race groups. Possible causes of the decline in coronary heart disease mortality include the development of the concept of acute coronary care, new drugs, sophisticated surgical techniques such as coronary artery bypass, noninvasive diagnostic methods for earlier disease detection, and the identification of specific cardiovascular risk factors. The decline has been temporally related to risk factor awareness and modification (cigarette smoking cessation, hypertension control, diet change, and reduction in cholesterol). Thus, both primary prevention through lifestyle changes and improved treatment regimes have played a role in the decline.
(Arteriosclerosis 1:312–325, September/October 1981)

It is impossible to overemphasize the magnitude of the health care problem each year caused by coronary heart disease (CHD), which is the leading cause of death in the United States. All forms of cancer combined (the second leading cause of death) were responsible for nearly 400,000 deaths in the United States in 1978. In contrast, CHD alone was responsible for nearly 650,000 deaths in 1978 (figure 1), and over 150,000 of these occurred before age 65.[1] Nearly one-third of the deaths from all causes in persons aged 35–64 years were due to CHD, and nearly 40% of all deaths in white males aged 55 and over were caused by CHD. In 1979 there were 4 million Americans with symptomatic CHD (nearly half below age 65). It is estimated that over 1.25 million Americans suffer a heart attack each year during which time 20% to 25% do not live long enough to receive definitive medical care.

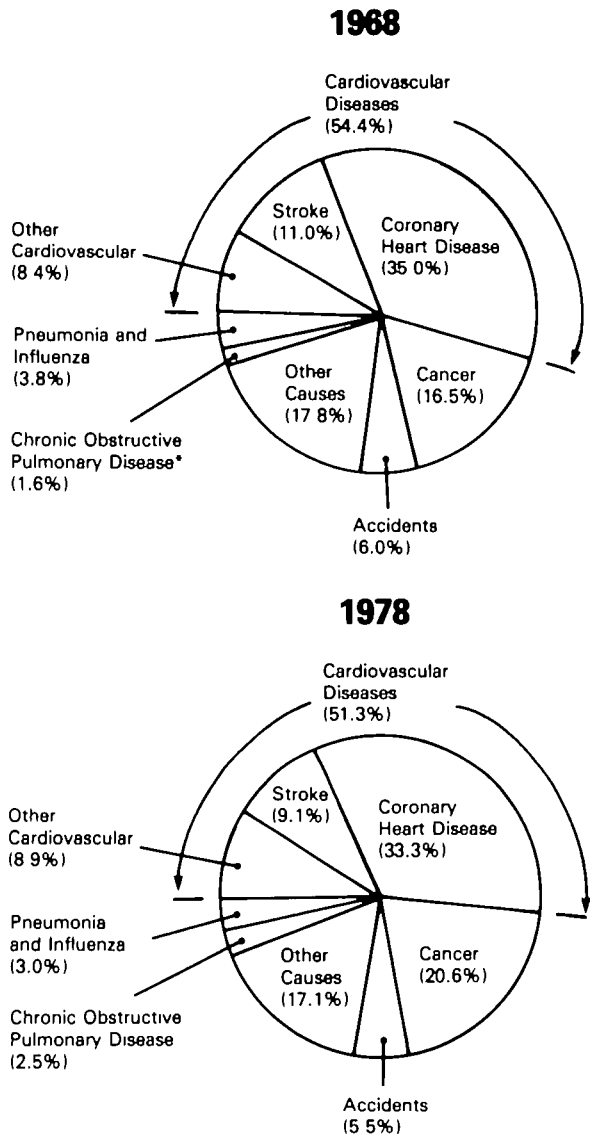
CHD ranks first among all diseases in terms of Social Security disability benefits.[2] It ranks first in terms of acute hospital bed days. It ranks second only to all forms of arthritis in terms of limitation of activity. It ranks second only to all forms of cancer in terms of days confined to bed. It has been conservatively estimated to cost this country each year over $27 billion (considerably more than any other disease), $6 billion of which represents the direct cost of medical care, with the remaining $20+ billion representing indirect costs due to lost productivity from illness and premature death.

Review

Identification of Coronary Heart Disease as a Major Health Problem

It is of interest, however, that CHD has only relatively recently been recognized as a major public health problem. In 1900, infectious diseases reigned supreme as the major killer in the United States. CHD and its major clinical manifestation, myocardial infarction, were rare medi-

From the National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland.
Address for reprints: Dr. Robert I. Levy, Dean, School of Medicine, Tufts University, Boston, Massachusetts 02111.
Received June 30, 1981; revision accepted August 13, 1981.



Cause	Number of Deaths 1968	1978
Cardiovascular Diseases		
Coronary Heart Disease	674,747	642,270
Stroke	211,390	175,629
Other	162,176	170,670
Cardiovascular Subtotal	1,048,313	988,569
Cancer	318,547	398,992
Accidents	114,864	105,561
Pneumonia and Influenza	73,492	58,319
Chronic Obstructive Pulmonary Disease*	30,390	48,616
Other Causes	344,476	329,731
Noncardiovascular Subtotal	881,769	939,219
Total All Causes	1,930,082	1,927,788

*Coded in 1968 as Bronchitis and Emphysema

Sources: National Center for Health Statistics and National Heart, Lung, and Blood Institute Estimates: Percentages Do Not Add to 100% Due to Rounding.

Figure 1. Deaths by cause and percentage of total deaths.

cal entities prior to World War I.[3] This was due in good part to the fact that myocardial infarction was only first described in 1912; in the following decades of the 1920s and 1930s it was recognized with increasing frequency as a common problem among white males in urban areas of North America and Europe, particularly among the more affluent. By 1940, CHD was the leading cause of death in the United States and several other countries, and its frequency continued to increase through the 1950s (table 1).

One must suspect that the major reason why CHD was not recognized earlier (though it clearly occurred even 2000 years ago, as verified by autopsies on Egyptian mummies) is that the process of atherogenesis, the major cause of CHD, is itself so silent and secret. We now realize that almost all CHD is due to atherosclerosis, a specific type of arteriosclerosis that affects large arteries. Although the process of atherogenesis that culminates in atherosclerosis is still not totally understood, it is clear that it is multifocal and multifactorial in nature. In its early stages, in a spotty fashion possibly related to injury, blood pressure, or blood flow, atherogenesis affects the inner layer of an artery with the deposition of fat, particularly cholesterol ester, and an increase in arterial intima cellularity. Some of these deposits of fats and cells enlarge with the appearance of extracellular cholesterol ester crystals, much fibrous tissue, culminating in scarred and thickened plaques. During all this time, a period of decades beginning probably before a person is 15 years old, the process of atherogenesis is totally silent. Ultimately, after periods of time measured in multidecades, clinical signs of CHD suddenly appear, usually because plaques protrude into the lumen of the affected artery so as to interfere with more than two thirds of the normal blood flow, or thrombus occurs on the plaque surface, or the plaque ruptures or hemorrhages, or vasospasm occurs in the diseased vessel impeding or cutting off blood

Table 1. U. S. Death Rates for Coronary Artery Disease, 1940–1978

Year	Death rate*
1940	207.2
1945	208.2
1950	226.4
1955	226.0
1960	238.5
1965	237.7
1970	228.1
1975	196.1
1978	180.9

*Rate per 100,000 population; age adjusted to the U.S. Population, 1940.

Source: National Center for Health Statistics.

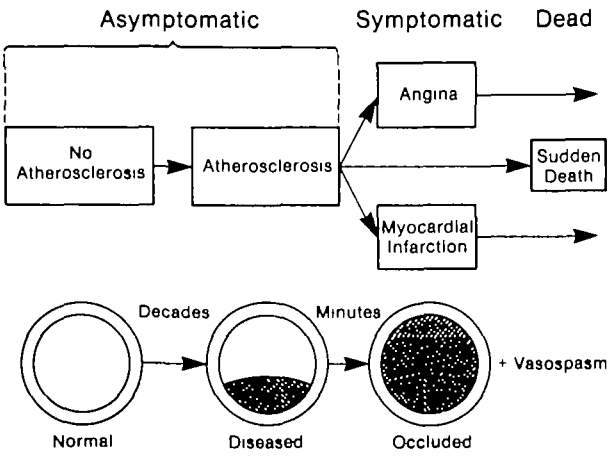


Figure 2. Development of atherosclerosis.

flow (figure 2). Previously silent coronary atherosclerosis then suddenly manifests as angina, myocardial infarction, or sudden death. Because the causative process is so slow, it is not surprising that the clinical symptom complex was missed for so long or that the clinical interest and attention to its diagnosis and treatment took so long to develop.

By the late 1950s and early 1960s, however, the full ramifications of this disease process were appreciated. Concern mounted over what appeared to be a growing epidemic of morbidity and mortality that seemed as devastating (if not more so) as the earlier infectious disease epidemics. Suddenly, however, changes began to occur in CHD mortality (table 1, figure 3). In retrospect, these changes were ignored by most observers for up to 10 years because of delays in mortality reporting and intercurrent flu epidemics, as well as a major change in the International Classification of Diseases code (Code 8) adopted in the United States in 1968. This code change had some dramatic effects. For example, all deaths in which both hypertension and ischemic heart disease (IHD) appeared on the death certificate became codable as an IHD death. Before 1968, if hypertension had been coded first on the certificate, the death would have been attributed to hypertensive heart disease. This one change artificially increased the number of IHD deaths, especially in the hypertensive-prone minority male (table 2). Fortunately, with enough time and information we can correct these dysfunctions in coding. In doing so, it is apparent that the increase in CHD mortality slowed in the late 50s and then began to plateau (table 1, figure 3).

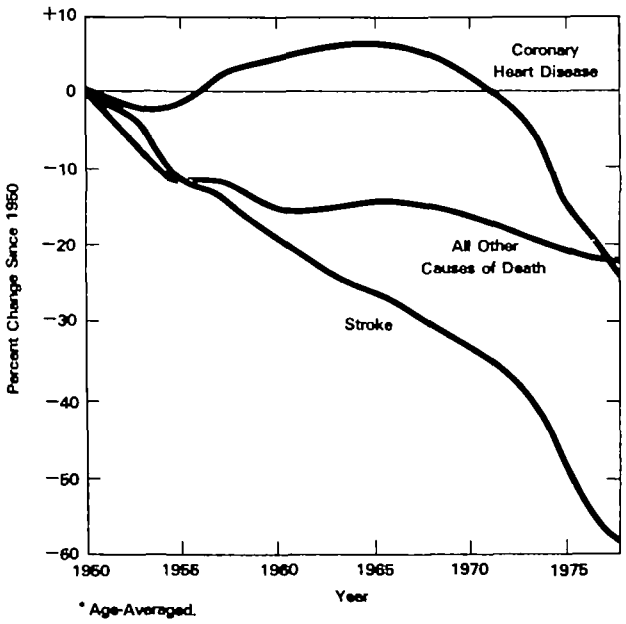


Figure 3. Percent change in death rates since 1950 for coronary heart disease, stroke, and all other causes, ages 35–74, United States, 1950–1978.

Magnitude of Decline in Mortality Rate from Coronary Heart Disease

Examination of the data more closely suggests that a decline in CHD mortality began first in the nonwhite and the female in the early 1960s (about 1963) and that by 1967 the white male as well was experiencing a declining mortality. Moreover, experts examining the causes of the decline have concluded that it is real and not an artifact of age adjustment (using 1940 as a standard so that rates by sex, race, geographic area, or time periods will be comparable in terms of age distribution of the population being compared) or the revision of the International Classification of Diseases code.[4]

The data suggest, as well, that the decline was not and is not homogeneous in the United States. It began first in the Far West and continues to be greater there. Although the decline has now spread to all the United States, both absolute CHD rates and rates of CHD decline have been most heterogeneous, with absolute rates

Table 2. Ischemic Heart Disease Rates Per 100,000 Population by Age for Nonwhite Males: United States, 1950, 1960, 1968, 1976

Age group (yrs)	1950*	1960*	1968†	1976†
35–44	74.3	87.8	134.9	90.3
45–54	254.2	297.0	419.4	326.0
55–64	554.1	723.7	998.1	794.5
65–74	943.1	1,340.2	1,920.2	1,487.9
Age adjusted	164.0	219.5	319.4	249.4

*Seventh revision ICD code 420.
†Eighth revision ICD code 410–413.

highest in the East and Southeast and rates of decline slower in the Appalachian states, especially West Virginia and Kentucky. In the decade ending in 1978, although CHD rates had declined by at least 10% in all states, mortality rates in the five highest states (Kentucky, North Carolina, South Carolina, Louisiana, and West Virginia) of over 427.0 deaths per 100,000 persons aged 35–74 years were nearly twice that in New Mexico and Hawaii (220.4 deaths per 100,000).[5] Looking at the United States in aggregate, we find that CHD mortality rates have now declined by some 29% from their nadir in 1967–1968. The rate of the decline has been almost 3% per year, and for all four sex-race groups, the absolute percent decline was greater for 1973–1978 than for 1968–1973. During this time period, mortality rates from acute myocardial infarction have declined more rapidly than those from chronic CHD.

The CHD death rate decline since 1968 has been dramatic in all age and sex groups in both blacks and whites (table 3). It can be seen in every age and sex group in both our minority and majority populations. In every age decade band from the third to the ninth decade of life, there has been at least a 20% decline in CHD mortality rates during this period. In the age group 25–44 years, primarily because of the decline in CHD deaths, cardiovascular disease deaths declined from first place in 1960 to third place in 1968, now ranking behind accident deaths and all forms of cancer deaths (figure 4). In the age group 45–54 years, while cardiovascular disease still ranks first as a cause of death, CHD deaths are now second to all forms of cancer deaths.[6]

Only one preliminary report has been published on secular trends in the extent and severity of coronary atherosclerotic plaques in the United States during this time period.[7] It reports findings at postmortem examination of New Orleans descendants, white and black, aged 25–44 years, between 1960–1964 and 1968–1972. The comparisons between the earlier and the later series involved blind standardization gradings of coronary atherosclerosis from men dying due to external violence and natural causes other than

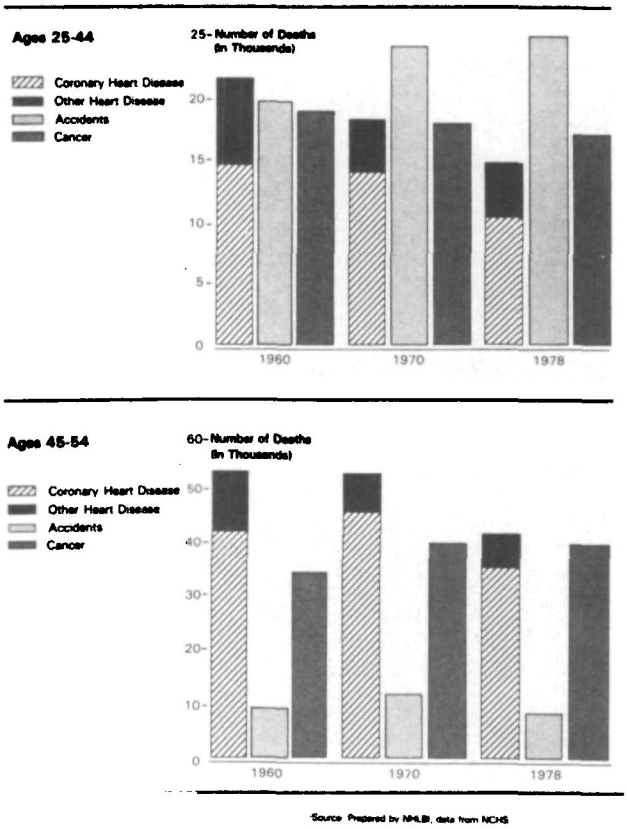


Figure 4. Number of deaths from the three leading causes.

Table 3. Decline in Coronary Artery Disease Death Rates, 1968–1978, by Age, Sex and Race

Age group (yrs)	White decline		Nonwhite decline	
	Male (%)	Female (%)	Male (%)	Female (%)
35–44	36.2	36.2	35.4	53.1
45–54	27.2	24.9	27.3	37.6
55–64	26.2	25.5	22.6	35.8
65–74	24.6	30.6	27.1	34.2

Source: National Center for Health Statistics.

CHD or CHD-related diseases. For white men aged 25–44 years, the percent of coronary internal surface with raised atherosclerotic lesions was lower in 1968–1972 than in 1960–1964. In this report, "raised lesions" was a combined measure of more advanced atherosclerotic lesions comprising fibrous plaques, complicated lesions, and calcified lesions. For black men, mean extent of raised lesions was only slightly less in the second time period. "Fatty streaks" were less extensive in both races in the second study period. Thus, the total coronary intimal surface involvement with atherosclerosis in both black and white males was less in the second study. The authors interpret their data showing an apparent reduction in coronary atherosclerosis as "consistent with recent evidence of diminished CHD mortality in the United States."[7] Obviously, additional studies will be needed to verify and extend these observations. A few of these are underway.

The decline in CHD mortality rates has been accompanied by marked decreases in death rates from the other major atherosclerotic (and hypertensive) diseases, first and foremost in the mortality rates from stroke, the second most important of the adult major cardiovascular diseases.[6] In fact, the percent decline in stroke mor-

tality has been even greater than that from CHD (figure 5).

Conservatively estimated because of the decline in overall mortality rates between 1968–1978, more than 1.2 million lives have been saved; over 55% of this decrease has been in CHD morality and over 80% from a decline in cardiovascular disease. If the age-adjusted death rates that existed in 1968 had continued unchanged through 1978, approximately 220,000 more deaths from CHD would have occurred (because of our ever-enlarging and aging population) for a total of 860,000 deaths from CHD in 1978. In reality, only 641,000 deaths from CHD occurred in 1978.

Thus, the decline is enormous in magnitude. It has often been pointed out that life expectancy has not changed very dramatically since the turn of the century despite the eradication of infectious diseases and the large number of biomedical research advances. In fact, since cardiovascular diseases (especially CHD and cerebrovascular disease) began their precipitous decline, there has been a striking upturn in life expectancy. Both men and women have gained over 2 years during the last decade.[8] The gains have been most striking in black males and females, who have gained more than 3½ years in life expectancy in the last 10 years (figure 6).

Comparison of Mortality Rates in Other Countries

Among the industrialized countries, the United States has experienced the most marked decline in CHD mortality during the 1970s. This is true for both men and women by every criterion — absolute decrease in death rate, percent change, or slope. It is true even in comparison to other countries with CHD mortality rates similar to those of the United States in 1968, such as Australia and Finland.[9] Moreover, in contrast to the decline in rates for the United States and some other countries (table 4, figure 7), the slope of the CHD death rates is positive for men in numerous Eastern, Northern, and Western European countries in the 1970s and sizable for some, such as Bulgaria, Poland, Republic of Ireland, German Federal Republic, USSR,[10] and Sweden. The

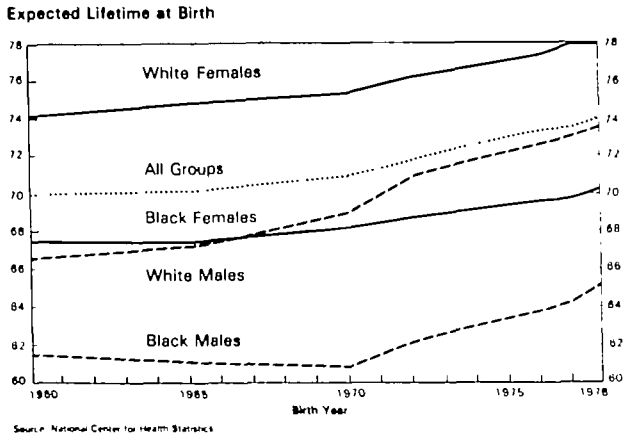


Figure 6. Projected life expectancy at birth by birth year, 1960–1978.

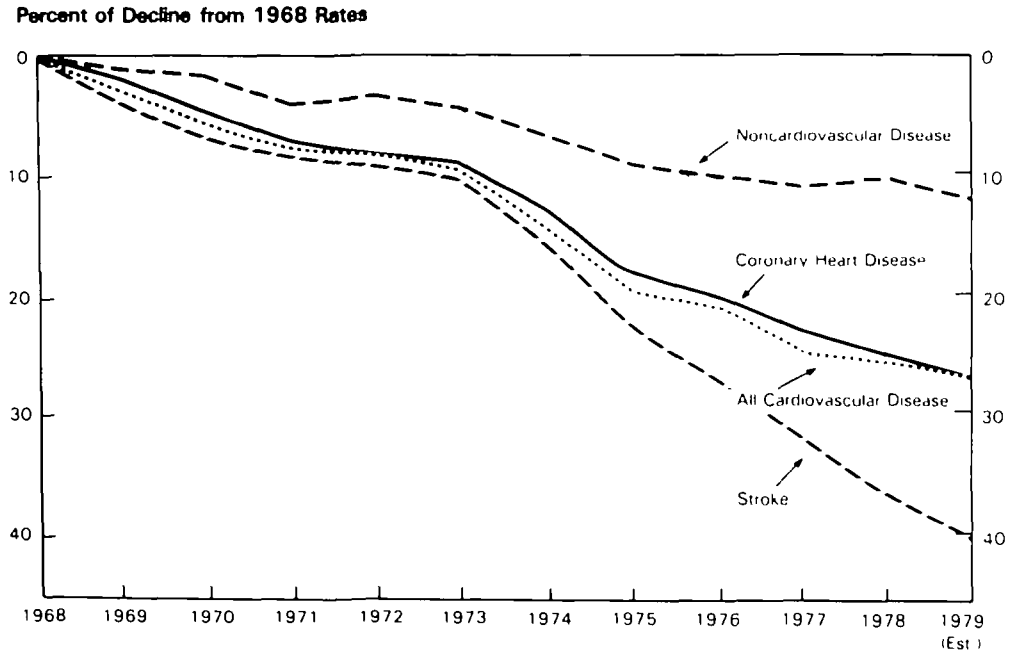


Figure 5. Trends in cardiovascular disease: decline by age-adjusted death rates, 1968–1979.

trend is also upward for women in most of these countries. Whereas in 1969 for American men aged 35–74 years, CHD mortality rates were higher than for any other English-speaking nation and second highest (to Finland) among all countries, by 1978 the United States was lower than for all other English-speaking nations except for Canada, and seventh from the highest among the 27+ countries considered. This latter fact that, despite the sustained sizable decline in CHD mortality, United States CHD death rates are still among the highest in the world for both men and women, makes it clear that we still have a long way to go. The annual toll in sickness, disability, premature death, economic loss, and human misery remains too high.

Causes of the Decline in Mortality

It is difficult to attribute the ebb and flow of CHD mortality to specific events. Many possible factors could be responsible for it: the development of coronary care units, improved emergency medical services, cardiopulmonary resuscitation, advances in surgical and medical treatment, Medicare, Medicaid, and changes in lifestyle (less smoking, blood pressure control, dietary modification, increased leisure time exercise).[11] Environmental factors or even socioeconomic factors could be involved in this nationwide change.

Since the decline in CHD was unexpected, we do not have the mileposts that allow us to quantitatively measure its causes. Moreover, in the United States no formal national or local myocardial infarction registries have existed. Although we know that CHD death has declined precipitously, we do not know what has occurred with CHD morbidity. We do not know if there are fewer heart attacks today than a decade ago. Without such knowledge of new CHD incidence, it is difficult even to attribute the major credit for the decline to either improved medical and surgical *treatment* of existing disease or to the *prevention* of new disease. Two reports were presented at the 1978 Conference on the Decline in CHD Mortality[4] that described CHD trends in local populations. Data from the Kaiser-Permanente Medical Care program in Northern California (largely San Francisco) indicate a steady decline in hospitalizations for acute myocardial infarction from 4.05/1000 in 1971 to 2.96/1000 in 1977, a 27% fall.[12] Middle-aged groups of both men and women showed a decline. Hospitalizations for both first and recurrent infarctions or for any CHD declined over these years. No clear trend occurred, however, in acute heart attack case fatality rate (13% to 16%) over the same period.

In contrast to these findings, the population of Rochester, Minnesota, receiving medical and hospital care almost entirely from the Mayo Clinic, the Olmsted Medical Group, and their affiliated hospitals[13] had a quite different experience. In trends covering the two periods 1960–1969 and 1970–1975, it was stated "there has been no change in the initial manifestation of CHD to parallel the decline in mortality." Age-adjusted mortality rates, given as 3-year moving averages for the period 1968–1975, showed that a 22% decline in CHD mortality observed in Rochester during this time period was due solely to a decline in acute heart attack mortality and that the case fatality rate — based on sudden unexpected deaths and heart attack deaths under 30 days —decreased from 47% in 1950–1955 to 34% between 1970 and 1975. These two apparently conflicting reports emphasize the need to seek more information on morbidity in order to determine whether CHD is being prevented or just being better treated.

A further set of events complicates our attempts to unravel this puzzle. In 1979 the ninth international classification code for diseases went

Table 4. Trends in the Death Rate for Coronary Heart Disease Among Men Aged 35–74 Years in Selected Countries, 1969 and 1977

Country	Change in rate (%)	Rate per 100,000 population* 1969	1977
United States	−22.6	864.7	669.6
Australia	−19.0	843.7	683.1
Japan	−18.8	126.3	102.6
Canada	−11.3	703.3	624.1
Israel	−11.1	653.3	581.0†
Norway	− 7.9	583.0	537.1
Belgium	− 4.3	446.1	426.8†
New Zealand	− 3.4	773.4	747.1
Finland	− 1.7	893.7	878.1†
Italy	− 1.1	313.0	309.6‡
Scotland	− 0.6	813.8	808.6
Czechoslovakia	+ 0.4	587.9	590.4‡
England and Wales	+ 1.4	662.1	671.7
Denmark	+ 1.8	566.1	576.3
Ireland	+ 2.3	662.2	677.7‡
Netherlands	+ 4.6	478.7	500.5
France	+ 6.0	195.2	207.0†
Austria	+ 6.3	428.3	455.3
Sweden	+ 6.9	524.0	560.1
West Germany	+ 7.2	427.3	458.1
Switzerland	+ 7.6	290.4	312.7
Northern Ireland	+10.8	782.4	867.1
Hungary	+13.0	441.6	499.2
Yugoslavia	+23.0	185.0	227.6
Romania	+39.2	170.5	237.4
Bulgaria	+41.4	299.4	423.5
Poland	+65.0	186.5	307.8

*Age-averaged.
†1976.
‡1975.
Source: Unpublished data provided by Dr. Frederic H. Epstein and Dr. Zbynek Pisa.

into effect in the United States. While purporting to change little from the eighth code, it became immediately apparent that the definitional changes under the CHD rubric would require a few years of observation and correction factors to equate CHD events and rates pre- and post-1979.[14] Furthermore, the 1980 U. S. census revealed a population over 4 million larger (2% higher) than projected previously, necessitating a further correction in mortality rates.[15] Thus, although this report is written in 1981, all the data are presented only through 1978. Preliminary analysis suggests that the CHD mortality rate continued to decline in 1979 but rose slightly (approximately 2%) in 1980 (possibly related to the flu epidemic at the beginning and end of 1980), reversing a decade-long trend. Verification and explanation of these recent trends must await the gathering of additional data.

Despite all of these complications, it is possible to define a multitude of changes that may have contributed to the CHD decline from 1968–1978. It should be evident to the reader from the discussion below that we have too many, rather than too few, possible explanations for the decline.

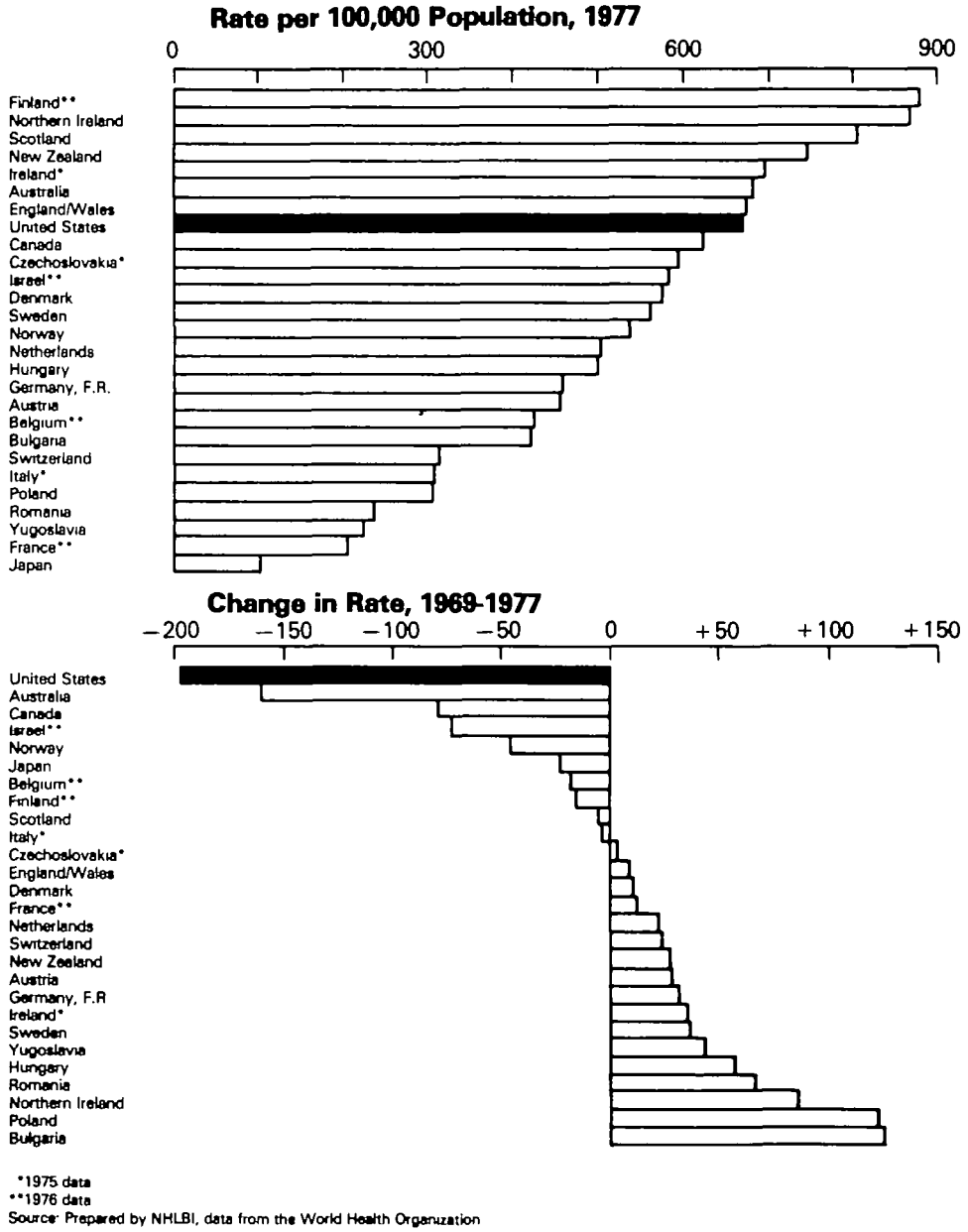


Figure 7. Death rates for coronary heart disease by country: men 35–74 years of age.

The Case for Improved Treatment

Thirty years ago, a patient with an acute heart attack was approached in a very watchful and respectful manner; hospitalization was prolonged. The main concept of management was "not rocking the boat." The patient was put to bed for 3 weeks or longer in the hope that the heart would repair itself and the patient would be restored to function. Today, the current concept of coronary care is based on a much more aggressive approach: the patient is placed in a special unit where his heart rate and rhythm and his state of function are monitored closely. Further, the amount of heart-muscle damage can be measured, and specific forms of therapy are now used to try to decrease the amount of heart-muscle damage that can occur in the first few days after a heart attack.[16] We now have the ability to suspend, restore, and maintain heart rhythm; we have sophisticated cardiopulmonary resuscitative equipment as well as medical and surgical treatments of coronary artery disease that were not even dreamed of in 1950. We can treat and prevent incipient heart failure. There are artificial pacemakers for immediate or long-term control of heart rhythm and better drugs to treat coronary insufficiency.

Are these advances responsible for the decline in cardiovascular mortality? The question is difficult to answer because, although rhythm death has been virtually eliminated as a cause of death in the coronary care units, and deaths within the units have been cut from 30% to 15%, many patients die suddenly before they reach the hospital.[17] Furthermore, there are disturbing data from a recent Johns Hopkins study that suggest that, while in-hospital coronary care death has dropped sharply in the last 30 years, the 1-, 2-, and 3-year survival rates in patients sustaining heart attacks are the same as they were 10 years ago.[18]

What effect has cardiopulmonary resuscitation had?[19] Although those who have experienced or observed CPR in action can see a dramatic saving of life, it cannot really be credited quantitatively with decreasing mortality. For example, in the Seattle Heart Watch program, which involves the total community, there is a saving of only about 100 lives per year in a metropolitan area of over 2 million.[20] Similarly, too many patients who are resuscitated by CPR remain at very high risk for cardiovascular death during the years immediately after resuscitation.

New Drugs, Surgical and Diagnostic Techniques

What role has advanced medical treatment played? Beta-adrenergic blocking drugs such as propranolol, which can relieve angina and decrease heart rate, may have great potential value in preventing life-threatening rhythm problems. Clinical trials undertaken in Sweden and England have suggested that there may be value in using the beta-blocking drugs, alprenolol and practolol.[21, 22] Unfortunately, the studies were not conclusive because of their small size, side effects, and other problems. However, a recently published clinical trial from Norway using another beta-adrenergic blocking agent, timolol, has demonstrated a significant 44.6% decline in heart attack death and total death in patients tested post-heart attack over the 2-year treatment period.[23] In the United States, the Beta-Blocker Heart Attack Trial (BHAT) was initiated in 1978 under the sponsorship of the National Heart, Lung, and Blood Institute. The purpose of this trial is to test the efficacy of the beta-blocking agent, propranolol, in preventing death. Until the results of this trial become available and are widely disseminated to the practicing physician, it will be difficult to credit beta-blocking drugs with a major role in the decline in cardiovascular mortality. Similarly, while the new calcium channel antagonists, verapamil and nifedipine, appear to hold great promise for the treatment of coronary vasospasm and myocardial ischemia[24] in the United States, they have not yet been approved by the Federal Drug Administration (FDA). They remain investigational and are not readily available for physician use.

What role has coronary artery bypass surgery played in reducing mortality? There is no doubt that coronary artery bypass surgery is prominent today.[25] Some 100,000 procedures are now performed in the United States each year at a cost of over $1.5 billion. However, it is difficult to attribute the CHD mortality decline to coronary artery bypass surgery for several reasons. First of all, coronary artery bypass surgery only came into vogue in the 1970s, while the decline in cardiovascular disease and heart attack death in particular began earlier. Second, there is good evidence that coronary artery bypass surgery is only effective in relieving angina.[26] There is growing evidence that it improves left ventricular function but further proof is still being sought. There are no statistically valid data except in patients with left main coronary disease that coronary artery surgery prolongs life.[25] Without that evidence, the decline cannot be clearly traced to coronary bypass surgery. In fact, in view of the magnitude of the CHD decline, it would have been necessary for coronary bypass surgery to save every patient undergoing the procedure in a given year, that is, all 100,000 patients would have died without the bypass. And yet, this could not have explained even 40% of the decline in deaths occurring that year. Clearly, coronary artery bypass surgery has not been the major factor in the decline.

Important advances have been made in developing noninvasive diagnostic instrumentation. The new techniques, including M and B mode echocardiography, radionuclear scanning and cineangiography, high resolution subtraction radiography and computer-assisted tomography, each alone and coupled with improved exercise test techniques, now allow for the diagnosis of ischemic heart disease at a much earlier stage than was previously possible.[27-29] Earlier diagnosis, however, does not guarantee longer survival unless one can prevent future cardiovascular events. In fact, it has been suggested that these noninvasive techniques have just increased the number of patients in whom CHD can be defined. Physicians may be under the impression that patients with CHD are living longer, but in reality they may only be diagnosing them earlier. Noninvasive techniques alone, clearly, are not saving lives. Although there was no definitive evidence and a specific quantitative role for each therapeutic advance could not be given, cardiologists at our meeting in 1978[4] felt it was probable that coronary care, improved medical and surgical treatment of coronary disease, and advances in emergency cardiac care have in aggregate been the major factor responsible for the decrease in mortality from cardiovascular disease.

The Case for Primary Prevention

Cardiovascular epidemiologists, on the other hand, present a contrasting view of the reasons for the decline. They suggest that the major factor responsible for the decline over the last 30 years is the identification through epidemiologic studies of risk factors, traits, or habits which indicate individuals who are at increased risk for CHD.[30] Added to this is the public's and the medical profession's increased attention to altering these risk factors.

The cardiovascular epidemiologists have identified factors that allow physicians to detect highly susceptible individuals long before CHD is manifest. Some risk factors cannot be modified, such as advancing age, male sex, and family history of early heart disease (before age 65); others that can be altered include blood cholesterol level, cigarette smoking, high blood pressure, diabetes, obesity, and Type A personality.[30] These risk factors have different effects on different vascular beds. In the peripheral vascular system, cigarette smoking is by far the most potent risk factor. For cerebrovascular disease, hypertension is the predominant risk factor. For CHD, the three major risk factors are the level of cholesterol, specifically the level of low density lipoprotein (LDL) cholesterol, the level of blood pressure (whether systolic or diastolic), and the number of cigarettes an individual smokes. The higher the cholesterol (LDL), the higher the blood pressure, and the more one smokes, the more likely that individual is to sustain a coronary event. If one has more than one of those risk factors, the risk is more than doubled.

Impact of Risk Factor Modification

Although it is generally agreed that the identification of risk factors is important and that they undoubtedly signal increased risk of heart disease, a major question remains. *Does aggressive treatment of risk factors delay or prevent atherosclerosis and its sequellae?* For some risk factors the answers are available.

Cigarette Smoking

For cigarette smoking, there is a dose/response relationship between the number of cigarettes an individual smokes and the risk. Moreover, anyone can stop smoking although it is sometimes difficult to do so. Although direct clinical trial data do not exist, evidence from prospective and retrospective studies shows that risk decreases rapidly when one stops smoking, so that more than 90% of the increased risk disappears after 1 year of smoking cessation and then declines more rapidly until it is almost completely erased by 10 years.[31, 32] Thus, we aggressively recommend smoking cessation.

Hypertension

With hypertension the issues are a little less clear. There is no doubt that high blood pressure is a risk factor for cerebrovascular disease and CHD. Moreover, there is no doubt that blood pressure could be lowered with the effective medications now available. The Veterans Administration studies done in the 1960s and early 1970s proved conclusively that, by treating moderate and severe blood pressure elevations, one could prevent stroke, renal failure, and heart failure, and so hypertension is treated aggressively.[33] Doubt still exists, however, as to whether treatment of hypertension can prevent heart attack. The recently completed Hypertension Detection and Follow-up Program provides us with some new evidence that treatment of even mild hypertension will reduce stroke and heart attack death.[34] Further confirmation of the effectiveness of blood pressure control in CHD prevention is awaited.

Cholesterol and Diet

The third major risk factor, cholesterol and diet, is still clouded by controversy. There is no doubt that elevated levels of LDL cholesterol are associated with increased risk of heart attack.[35, 36] Nor is there any doubt that LDL can be lowered by diet or drug in almost all patients.[37] In man, however there is still some doubt whether lower-

ing cholesterol will result in a reduced incidence of heart attack. There is a striking amount of epidemiologic evidence, but in man the issue is still presumptive.[38]

Evidence from studies of other risk factors, notably glucose lowering, shows the pitfalls of unproven assumptions. For example, it is known that elevated glucose is associated with increased risk of heart attack, and that glucose levels *can* be lowered with oral drugs. Several drugs were used to lower blood glucose in the University Group Diabetes Program, but the patients in that study had more, not less, heart disease.[39] Although proof is lacking on the cholesterol issue, there is some striking evidence that has been collected in nonhuman primates within the last several years. The data suggest that, if atherosclerosis has been produced by feeding diets high in cholesterol, it *is* possible to stop progression of the atherosclerosis and indeed cause it to regress in these primate models. The most hopeful evidence is from the recent studies by Clarkson et al.[40] A cohort of Rhesus monkeys was placed on high cholesterol diets for 19 months so that cholesterol levels were raised to approximately 800 mg%. One-third of the animals were sacrificed. The other two-thirds were continued on a high cholesterol diet for another 24 months during which time one-half were fed a diet that maintained a cholesterol of 300 mg%, the other group maintained a cholesterol of 200 mg%. All these animals were then sacrificed. Those animals whose cholesterol had been maintained at 300 mg% had not changed very much; there was more stenosis and more fat in the coronary vessels. Those animals whose cholesterol had been lowered to 200 mg% (a level that can be achieved in humans) had significantly less coronary atherosclerosis, less luminal stenosis, less fat in the coronary vessel wall, and less medial elastic lamina damage. Obviously, these studies cannot be reproduced in man.

Testing the "Lipid Hypothesis"

The clinical trials conducted over the past 14 years in humans using diet to lower cholesterol show a reduction in cholesterol levels of 10%.[41] However, in looking at hard endpoints, heart attack and heart attack death, one cannot really see a statistically significant difference in the treated groups. More subjective endpoints do show evidence of change, but only in those studies that were not double-blinded.

Thus, these clinical studies gave no firm evidence that cholesterol lowering is beneficial in man. On the other hand, none of these studies shows that cholesterol lowering does *not* prevent CHD since none of them had a large enough sample size to reject or accept the null hypothesis. The problem was that until 1970 no one appreciated the power requirements and the factors necessary to demonstrate the efficacy of cholesterol-lowering. Two factors, designated as *alpha* and *beta,* must be considered in any clinical trial. *Alpha* factors are involved in insuring that differences will be significant, that an effect will occur once out of 20 or 100 or 1000 times. *Beta* factors are involved in insuring that a clear difference will be observed between treated and control groups. In dealing with heart attack and heart attack deaths even in a population that has heart disease, events will not occur frequently. Of middle-aged men who have had heart attacks, less than 5% will have a fatal heart event in the next year. Therefore, a large number of patients and a long period of time are absolute requirements. If cholesterol can only be lowered by 10%, the difference between the two groups will not be very great.

The dropout rate is another problem. In a trial that must go on for years with a large number of subjects, a dropout rate of 5% to 15% per year can destroy an otherwise exquisitely designed study. The F value is another statistical problem. In an individual whose cholesterol has been lowered from 350 mg% to 250 mg%, does the risk become equal to that of a subject whose cholesterol was always low, or will it take a period of time for the risk to fall? With cigarette smoking, it is known that the risk decreases very rapidly in the first year and then more slowly thereafter, but the F value for cholesterol-lowering is less clear. One can eliminate concern over the F value and the lack of events by increasing the duration of a trial. This, however, will also increase the dropout rate, thus jeopardizing the results.

In the late 1960s the NHLBI considered a National Diet-Heart Study and performed a feasibility trial. The study was conducted in several centers for a short period of time. A total of 1211 men aged 45–53 years (10% of the adult males in the study areas) were followed for 1 year. Specially prepared meats and dairy products were made available to these subjects. The study showed that a double-blind design could be maintained, that cholesterol could be lowered by about 10% by diet, and that the dropout rate during the year could be held to 10%.[42]

When the results were analyzed in terms of the sample size calculations, it became obvious that with a cholesterol-lowering of only 10% and a dropout rate of 10% per year, a national diet heart primary prevention trial would require between 30,000 and 150,000 subjects and 1 to 3 decades. Even before the price of meat went up in the early 1970s in the United States, it was clear that the cost of this study was prohibitive and would have required a major share of the budget of the National Heart, Lung, and Blood Institute. Nonetheless, the issue is being pursued

and trials are underway seeking a definitive answer to the value of cholesterol-lowering.

Clinical Trials of Risk Factor Modification

One study, the Lipid Research Clinics Coronary Primary Prevention Trial (CPPT),[43] has been undertaken to determine whether the reduction of LDL cholesterol in asymptomatic subjects with hypercholesterolemia (cholesterol > 265 mg%) will prevent or lower the incidence of CHD. The power of the study is increased because these patients are at increased risk (their initial cholesterols are elevated). Furthermore, a bile acid sequestrant (cholestyramine) is added to the dietary prescription so that more than a 10% cholesterol-lowering is achieved. This study is underway in 12 clinics and several supporting facilities in the United States and Canada. The Lipid Research Clinics CPPT recruited 3800 patients who are in their fifth year of follow-up.[43] The trial is due to end in 1983.

Another trial focusing on risk factor modification is the Multiple Risk Factor Intervention Trial (MRFIT),[44] which seeks to determine whether aggressive treatment of the upper decile of the population at risk (those with the highest blood pressure, who smoke too much, who have high levels of cholesterol) will delay or prevent CHD. This trial, which is following approximately 12,000 subjects, is underway in 20 clinics around the country; it is due to end in late 1981. Until the results of these trials are available, it is difficult to conclude that altered cholesterol levels have played a role in the decline in cardiovascular mortality.

A further problem is that, even if risk factor alteration proves valuable, it is difficult to achieve and maintain behavioral change in the population. Getting individuals to change lifelong habits such as diet presents a formidable challenge.

Hypertension Detection and Control

What role has modification of the other risk factors played in the decline in CHD mortality? In hypertension and hypertensive cardiovascular disease, major changes have occurred in the last 30 years. Hypertension then was usually only diagnosed when it was symptomatic, when the patient had a clinical sequella — stroke or heart attack. The therapy available then was either a rice diet or drugs that were ineffective or had serious side effects. It was only in the early 1950s that thiazide diuretics were introduced to help the body get rid of salt and water, methyldopa was introduced, and reserpine was found to have a new role.

It was not until the 1960s and early 1970s that the Veterans Administration studies by Freis and his colleagues[33] showed that not only could one safely lower blood pressure but that control of hypertension would prevent stroke, renal failure, and heart failure. In 1972 the federal government examined the issue and found that not only was hypertension extremely prevalent but that the large majority of the American population who had hypertension were not aware of it and that most physicians were not actively treating hypertension despite the availability of safe and effective drugs.

In 1972, the National High Blood Pressure Education Program was begun in an effort to disseminate the information gained in the 1960s to both the public and health professionals. This program has used all dissemination routes, both scientific and public (mass media), to reach its target audience. The message has been a simple one. To the health professional we have emphasized the prevalence of high blood pressure, its symptomless presence, the ease of detection, the availability of therapy, and the importance of effective control. To the public we have emphasized that one in five American adults has the disease, that if you have it you may not know you have it, that it is asymptomatic, that it is easy to detect, that it can be controlled, but that only by controlling it can one prevent the dreadful sequellae — stroke, heart attack, and death. During the time that the program has been in existence, there has been a tremendous change in awareness. Whereas in 1972, 50% of the individuals with high blood pressure did not know they had hypertension, it is estimated now that less than 20% of the hypertensive patients are unaware they have high blood pressure.[2] In 1972 only about one-eighth of the patients — less than 4 million —were on effective therapy. Now the number of Americans who are under effective blood pressure control is estimated to be well above 10 million.

There has been a tremendous increase in the number of patient visits for hypertension. Visits for hypertension have increased by some 50% since 1972, while patient visits for all other causes have increased by only about 5% in that same period.[2] Recent community surveys suggest that the number of hypertensives who are unaware of their condition may now be as small as 10% and that the number on treatment may be as high as 50%. A 1977 survey of 100,000 subjects in Chicago showed that 60% of the subjects with hypertension were under effective control.[45]

The bottom line in a chronic disease prevention program is not awareness or treatment, but change in mortality. Stroke mortality was declining by about 1%/year in the 1950s and 1960s, and by 1.5%/year, a slightly more rapid rate, in the early 1970s. But since 1972, when the National High Blood Pressure Education Program was begun, mortality from stroke has been declining at

a rate of over 5% a year.[2] Thus, in looking at the decline in cardiovascular mortality over the last 10 years, at least the decline of over 37% in stroke mortality can probably be ascribed in major part to the control of hypertension. As for the decline in heart attacks over this time period, the evidence is not as clear but the Hypertension Detection and Follow-up Program and the Australian Mild Hypertension Trial both suggest that blood pressure control may have played a role.[34, 46, 47]

Other Changes in Risk Factors

There have been other changes besides the increased public awareness of and attention to hypertension. The consumption of cigarettes has changed markedly and the number of cigarette smokers has fallen.[48] Since 1963, the per capita consumption of tobacco has declined by over 29%. The consumption of fluid milk and cream is down by over 22%, butter by over 36%, eggs by over 14% in this period.[49] The consumption of saturated fats (fats of animal origin) and oils is down by over 48%, while the consumption of vegetable fats is up 74%. The average American cholesterol intake, which used to be quoted at 600 to 800 mg/day, is now less than 500 mg cholesterol per day.[50] The amount of polyunsaturated fat as compared to the saturated fat in the American diet has changed. The P to S ratio used to be 0.1 to 0.2, but is now closer to 0.4 to 0.5.

Concomitant changes in the average American blood cholesterol level have been observed. By comparing the Health and Nutrition Surveys (Hanes) done in 1960-1962 with those conducted in 1971–1973 and the Lipid Research Clinics surveys done in 1972–1976, it does appear, despite some methodologic differences in these surveys, that a drop in cholesterol levels of 3% to 8% in each age decade has occurred over this time.[51]

A striking parallel observation is a socioeconomic one. Elevated cholesterol used to be considered a problem of affluence, correlating positively with higher levels of education. Now the evidence shows that for every age group the level of cholesterol is *lower* in the most affluent than the least affluent. This is consistent with health learning theory, which predicts that this group would be the first to change its diet by avoiding cholesterol-rich food and saturated fats.

Implications of Risk Factor Changes

Can these changes in risk factors then be responsible for the decline in mortality? It has been pointed out that only in those countries with an aggressive approach to risk factor change is CHD declining. Cardiovascular epidemiologists believe that even if we ignore the real impact of increased leisure exercise activities in America and just evaluate the changes in cholesterol, smoking habits, and blood pressure control, one can calculate that risk factor change alone could explain the entire decline in CHD mortality over the last 10 years. Cardiologists disagree, pointing out that one cannot give credit to primary prevention until better morbidity data are available. It cannot be shown whether we are preventing disease or just treating it better. Thus, it is not at all clear that primary prevention is the major cause of the decline.

Prospects

Although the relative impact of the many changes in our approach to coronary heart disease is unclear, there are many factors that are clear. Mortality from CHD has decreased sizably in the past 10 years. It is clear, however, that we still have a long way to go in our battle to control CHD, for, despite its decline, it is still the leading cause of death in the United States. Furthermore, it is clear that we should not and cannot accept the proposition that coronary atherosclerosis and its clinical sequellae are a natural process of aging. Although our population has aged and increased in the last 10 years, CHD has declined. It is also clear that we have made remarkable strides during the last decade in our approach to the diagnosis and treatment of CHD. Advanced diagnostic screening and monitoring techniques are now available. CHD can be approached surgically. We can replace or repair altered vessels. New forms of chemotherapy exist and allow us to better control blood pressure, cardiac arrhythmias, angina, coronary vasospasm, and congestive heart failure. We have identified and validated additional risk factors. We can even replace irreversibly damaged hearts and through careful selection for heart transplantation achieve a 5-year survival rate of 50%.[52] It is clear today that all CHD complications can ultimately be understood and controlled but the question is: At what price? Palliation and repair are costly. After a heart attack, the amount of cardiac structural and functional damage becomes a much more potent determinant of survival than any of the primary CHD risk factors.[14, 53] Sudden death is responsible for too many deaths for us to be able to wait until CHD becomes manifest.

It is evident that we must focus on prevention of CHD as our long-term goal (figure 8). It is clear from the evidence of the past decade that we can control atherosclerosis or at least its cardiovascular sequellae.[54] Focusing on prevention means much more, however, than merely educating the public and health professionals on lifestyle and behavior change or validating important hypotheses, such as the value of beta-

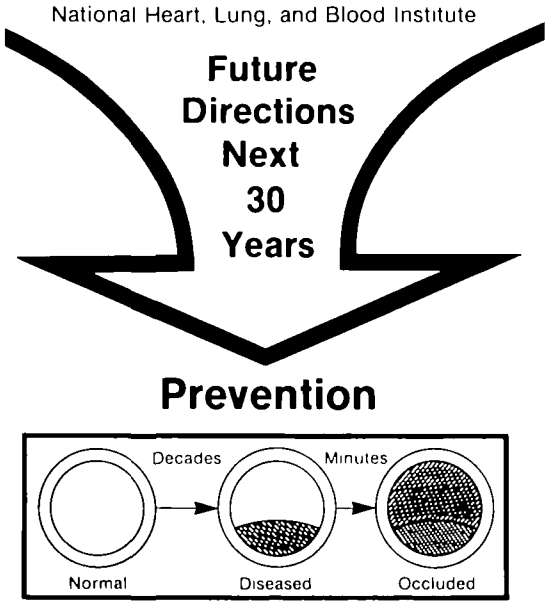


Figure 8. Coronary artery disease: future directions.

adrenergic blockage or cholesterol-lowering. A focus on prevention implies a focus on the basic cause or causes of atherosclerosis, for until we understand this basic process better we cannot hope to control it and thereby prevent its dreadful clinical sequellae. The recently completed report of the 1981 NHLBI Working Group on Atherosclerosis has helped define many areas in need of further inquiry.[35] They include, but are not limited to, further study of the mechanism(s) by which cholesterol accumulates in cells, additional studies of lipoprotein structure and function, further evaluation of the role of diet, platelets and prostaglandins in atherogenesis; the development and exploration of additional experimental models of human atherosclerosis, and study of the relationship between the cells of the arterial wall and atherogenesis. Only when we truly understand atherogenesis will we be able to effectively prevent or retard its occurrence. Seeing how far we have come in the past few decades, however, gives promise of a very bright future. The decline in the CHD epidemic in the 1970s strongly suggests that we can control and eventually eradicate modern civilized man's most serious killer disease.

References

1. **National Heart, Lung, and Blood Institute.** Data from the National Center for Health Statistics, Hyattsville, Maryland and the National Heart, Lung, and Blood Institute, Bethesda, Maryland
2. **National Heart, Lung, and Blood Institute.** Eighth Report of the Director. U.S. Department of Health and Human Services, Public Health Service, National Heart, Lung, and Blood Institute. Washington, DC: US Government Printing Office, 1981
3. **White PD.** Perspectives. Progr Cardiovasc Dis 1971;14: 250–255
4. **Havlik R, Feinleib M, eds.** Proceedings of the Conference on the Decline in Coronary Heart Disease Mortality, Bethesda, October 24–25, 1978. U.S. Department of Health, Education and Welfare. Public Health Service. DHEW Publication No. (NIH) 79-1610, 1979
5. **Leaverton PE, Ingster-Moore LM, Gittelsohn AM.** U.S. geographic patterns in coronary heart disease mortality. In: Proceedings of the 2nd Yves Biraud Symposium. In press
6. **National Heart, Lung, and Blood Institute.** Fact Book for Fiscal Year 1980. U.S. Department of Health and Human Services. Public Health Service. National Institutes of Health. NIH Publication No. 81-2105, 1981
7. **Strong JP, Guzman MA.** Decrease in coronary atherosclerosis in New Orleans. Lab Invest 1980;43:297–301
8. **U.S. Department of Health, Education, and Welfare.** Health United States, 1978. Public Health Service. National Center for Health Statistics. DHEW Publication No. (PHS) 78-1232. Washington DC: US Government Printing Office, 1978
9. **World Health Organization.** World Health Statistics Annual. 1972–1979. Geneva: WHO, 1972–1979
10. **Cooper R.** Rising death rates in the Soviet Union. The impact of coronary heart disease. N Engl J Med 1981; 304:1259–1265
11. **Levy RI.** Progress toward prevention of cardiovascular disease. A 30-year retrospective. Circulation 1979;60: 1555–1559
12. **Friedman GD.** Decline in hospitalizations for coronary heart disease and stroke: The Kaiser-Permanente experience in Northern California, 1971–1977. In: Havlik R, Feinleib, eds. Proceedings of the Conference on the Decline in Coronary Heart Disease Mortality, Bethesda, October 24–25, 1978. US Department of Health, Education, and Welfare. DHEW Report No. (NIH) 79-1610, 1979. pp 109–114
13. **Elveback LR.** Coronary heart disease in Rochester, Minnesota, 1950–1975: Incidence and survivorship In: Havlik R, Feinleib, eds. Proceedings of the Conference on the Decline in Coronary Heart Disease Mortality, Bethesda, October 24–25, 1978. US Department of Health, Education, and Welfare. DHEW Report No. (NIH) 79-1610, 1979. pp. 116–122
14. Monthly Vital Statistics Report. Births, Marriages, Divorces, and Deaths for January, 1981. US Dept. of Health and Human Services, US Public Health Service, National Center for Health Statistics, DHHS No 811-1120, vol 30, no 1, April 20, 1981, pp 1–12
15. Monthly Vital Statistics Report. Births, Marriages, Divorces, and Deaths for 1980. US Dept. of Health and Human Services, US Public Health Service, National Center for Health Statistics, DHHS No. 811-1120, vol 29, no 12, March 18, 1981, pp 1–11
16. **Braunwald E.** Protection of the ischemic myocardium. Harvey Lectures. Series 71, 1975–1976. New York: Academic Press, 1976, pp 247–282
17. **Chapman BL.** Effect of coronary care on myocardial infarct mortality. Br Heart J 1979;42:386–395
18. **Goldberg R, Szklo M, Tonascia JA, Kennedy HL.** Time trends in prognosis of patients with myocardial infarction: A population-based study. Johns Hopkins Med J 1979;144:73–80
19. **Eisenberg MS, Bergner L, Hallstrom A.** Out-of-hospital cardiac arrest: Improved survival with paramedic services. Lancet 1980;1:812–815
20. **Cobb LA, Werner JA, Trobaugh GB.** Sudden cardiac death. I. A decade's experience with out-of-hospital resuscitation Mod Concepts Cardiovasc Dis 1980;49: 31–36
21. **Ahlmark G, Saetre H.** Long-term treatment with β-blockers after myocardial infarction. Eur J Clin Pharmacol 1976;10:77–83
22. Improvements in prognosis of myocardial infarction by

long-term beta-adrenoreceptor blockade using practolol. Multicentre international study. Br Med J 1975;3: 735–740
23. **Norwegian Multicentre Study Group.** Timolol induced reduction in mortality and reinfarction in patients surviving acute myocardial infarction. N Engl J Med 1981;304: 801–807
24. **Antman EM, Stone PH, Muller JE, Braunwald E.** Calcium channel blocking agents in the treatment of cardiovascular disorders. Part 1: Basic and clinical electrophysiologic effects. *Ann Intern Med* 1980;93:875–885
25. **National Heart, Lung, and Blood Institute.** The NHLBI Consensus Development Conference statement on coronary artery bypass surgery; scientific and clinical aspects. N Engl J Med 1981;304:680–684
26. ***McIntosh HD, Garcia JA.*** *The first decade of aorto-coronary* bypass grafting, 1967–1977. A review. Circulation 1978;57:405–451
27. **Shine KI, moderator.** Noninvasive assessment of myocardial infarction. University of California, Los Angeles conference. Ann Intern Med 1980;92:78–90
28. **Bodenheimer MM, Banka VS, Helfant RH.** Nuclear cardiology. I. Radionuclide angiographic assessment of left ventricular contraction: Uses, limitations and future directions. Am J Cardiol 1980;45:661–673
29. ***Bodenheimer MM, Banka VS, Helfant RH.*** *Nuclear cardiology.* II. The role of myocardial perfusion imaging using thallium-201 in diagnosis of coronary heart disease. Am J Cardiol 1980;45:674–684
30. **Levy RI, Feinleib M.** Coronary artery disease: Risk factors and their management. In: Heart disease. Braunwald E, ed. Philadelphia: Saunders, 1980, pp 1246–1278
31. **Gordon T, Kannel WB, McGee D, Dawber TR.** Death and coronary deaths in men after giving up cigarette smoking. A report from the Framingham study. Lancet 1974;2: 1345–1347
32. **Friedman GD, Petitti DB, Bawol RD, Siegelaub AB.** Mortality in cigarette smokers and quitters. Effect of baseline differences. N Engl J Med 1981;304:1407–1410
33. **Veterans Administration Cooperative Study Group on Antihypertensive Agents.** Effects of treatment on morbidity in hypertension. II. Results in patients with diastolic blood pressure averaging 10 through 114 mm Hg. JAMA 1970;213:1143–1152
34. **Cooperative Group: Hypertension Detection and Follow-Up Program.** Five-year findings of the Hypertension Detection and Follow-up Program: I. Reduction in mortality of persons with high blood pressure, including mild hypertension. JAMA 1979;242:2562–2571
35. **National Heart, Lung, and Blood Institute.** Arteriosclerosis 1981. Report of the Working Group. Summary and conclusions. vol 1. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health. NIH Pub No 81-2034
36. **Kannel WB, Castelli WP, Gordon T.** Cholesterol in the prediction of atherosclerotic disease. New perspectives based on the Framingham study. Ann Intern Med 1979; 90:85–91
37. **Levy RI.** Hyperlipoproteinemia and its management. J Cardiovasc Med 1980;5:435–452
38. **Stamler J.** Population studies. In: Levy RI, Rifkind BM, Dennis BH, Ernst ND, eds. Nutrition, lipids and coronary heart disease — a global view. New York: Raven Press, 1979, pp 25–88
39. **Knatterud GL, Klimt CR, Levin ME, Jacobson ME, Goldner MG,** for the University Group Diabetes Program. Effects of hypoglycemic agents on vascular complications in patients with adult-onset diabetes VII. Mortality and selected nonfatal events with insulin treatment. JAMA 1978;240:37–42
40. **Clarkson TB, Lehner DM, Wagner WD, St. Clair RW, Bond MG, Bullock BC.** A study of atherosclerosis regression in *Macaca mulatta* I. Design of experiment and lesion induction. Exp Mol Pathol 1979;30:360–385
41. **Levy RI.** Testing the lipid hypothesis. Practical problems. In Bristol symposium on lipids and heart disease. vol 1, Lipids and heart disease. Wood C, Guyer BM, eds. Bristol, England: Bristol Labs, 1979, pp 16–28
42. **National Diet-Heart Study Research Group.** The National Diet-Heart Study final report. Circulation 1968;37(suppl I):I-1–428
43. **Lipid Research Clinics Program.** The Coronary Primary Prevention Trial: Design and implementation. J Chron Dis 1979;32:609–631
44. **Multiple Risk Factor Intervention Trial Group.** Statistical design considerations in the NHLI Multiple Risk Factor Intervention Trial (MRFIT). J Chron Dis 1977;30:261–275
45. ***Stamler R, Stamler J, Riedlinger WF, Algera G, Roberts RH.*** Weight and blood pressure: Findings in hypertension screening of 1 million Americans. JAMA 1978;240: 1607–1610
46. **Cooperative Group: Hypertension Detection and Follow-Up Program.** Five-year findings of the Hypertension Detection and Follow-up Program. II. Mortality by race-sex and age. JAMA 1979;242:2572–2577
47. **Cooperative Group: Hypertension Detection and Follow-Up Program.** Report of the Management Committee. The Australian therapeutic trial in mild hypertension. Lancet 1980;1:1261–1267
48. **US Dept Health, Education, and Welfare: Office of Smoking and Health.** Smoking and health: a report of the Surgeon General. DHEW Pub No (PHS) 79-50066. Washington DC: US Government Printing Office, 1979
49. **US Department of Agriculture.** Agriculture Statistics 1978. Washington DC: US Government Printing Office, 1978
50. **National Center for Health Statistics.** Fats, cholesterol and sodium intake in the diet of persons 1–74 years: United States 1979. Advance data from Vital and Health Statistics of the National Center for Health Statistics. US Department of Health, Education, and Welfare. Public Health Service. DHEW Pub No (PHS) 80-1250
51. **Lipid Research Clinics Program Epidemiology Committee.** Plasma lipid distributions in selected North American populations: The Lipid Research Clinics Program Prevalence Study. Circulation 1979;60:427–439
52. **Griepp RB.** A decade of human heart transplantation. Transplant Proc 1979;11:285–292
53. **Coronary Drug Project Research Group:** Factors influencing long-term prognosis after recovery from myocardial infarction — three-year findings of the Coronary Drug Project. J Chron Dis 1974;27:267–275
54. **Eleventh Bethesda Conference.** Prevention of coronary heart disease. Am J Cardiol 1981;47:1–64

Index Terms: primary prevention · mortality · coronary heart disease · lifestyle · public health education · stroke · diet · cigarette smoking · bypass surgery · diagnostic techniques · epidemiology