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THE PRIMARY PREVENTION OF THE ATHEROSCLEROTIC DISEASES

Position Paper for the

INTER-SOCIETY COMMISSION FOR HEART DISEASE RESOURCES

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"In view of the fact that atherosclerotic complications cause a majority of the deaths in this country and a substantial proportion of the disability, it is recommended that immediate efforts be made to prevent premature atherosclerotic complications."

Second National Conference on Cardiovascular Diseases, Summary Papers, 1964.

"Coronary Heart Disease has reached enormous proportions, striking more and more at younger subjects. It will result in coming years in the greatest epidemic mankind has faced unless we are able to reverse the trend by concentrated research into its cause and prevention.

"The Board expressed a wish that countries most affected by cardiovascular diseases increase their efforts both to set up efficient services for control and to carry out more extensive research programmes."

Executive Board, World Health Organization, 1969.

Contents

I. THE NEED FOR A NATIONAL COMMITMENT TO PRIMARY PREVENTION AS THE PRINCIPAL MEANS OF CONTROLLING A MAJOR PUBLIC HEALTH PROBLEM -- CORONARY HEART DISEASE AND OTHER ATHEROSCLEROTIC DISEASES.

Atherosclerosis is the major specific type of arteriosclerosis afflicting mankind. Its hallmark is an accumulation of fatty materials (lipids), cholesterol most prominently, in the walls of medium and large arteries. The clinical manifestations of this disease reflect the ischemic complications of severe atherosclerosis. The central problem, therefore, is the prevention of the severe form of this disease, particularly its premature occurrence, e.g., before age 65.

Morbidity, disability and mortality rates from atherosclerotic diseases -- coronary heart disease (CHD), cerebrovascular, aortic, renal vascular and peripheral vascular disease -- remain extremely high in the United States and constitute one of the principal challenges to medical science and public health. This report is based principally on the extensive research data available concerning the critical problem of coronary heart disease. However, its conclusions are probably applicable to atherosclerosis wherever it occurs.

The National Health Examination Survey of 1960-62 estimated that 3.1 million American adults age 18 to 79 had definite coronary heart disease and 2.4 million had suspect CHD, together representing about 5 per cent of this population (Table 1) (1). It was further estimated that of Americans under age 65, almost 1.9 million had definite CHD and 1.6 million had suspect CHD.

Every year about a million persons in the United States experience either a myocardial infarction or sudden CHD death. There are over 600,000 deaths each year due to CHD. (Table 2) (2). Over 200,000

more succumb to atherothrombotic disease of major arterial vessels in other parts of the body (2, 3). Approximately 165,000 of the coronary deaths occur in persons under 65 years of age, with a greater toll (3 to 1) among men than women. For middle-aged men, the United States has one of the highest CHD death rates in the world (Table 3) (4, 5). Analysis of mortality trends give no sign that these high death rates are decreasing (Fig. 1) (3).

A North American man has about one chance in five of developing clinical CHD before age 60, mostly in the form of myocardial infarction (Fig. 2) (6, 6a-k). About 25 per cent of those experiencing a first premature heart attack die within three hours of onset of symptoms, often prior to hospitalization and before medical care can be obtained (Table 4) (6, 6a-k, 7). Another 10 per cent die within the first weeks after their attack. For those middle-aged persons fortunate enough to recover, prognosis for longevity is markedly impaired. They are approximately five times as likely to die within the next five years as those without a history of previous coronary disease (6, 6a-k, 7-9). In most cases death is due to recurrent acute coronary episodes. Clinical atherosclerotic disease in the arteries of other organs is similarly associated with a reduced life expectancy.

These facts strongly indicate that major progress in controlling atherosclerotic diseases is possible only by primary prevention -- reducing first clinical episodes by preventing severe atherosclerosis and its complications. This must be the main strategic thrust of a national effort to control coronary heart disease during the years ahead.

II. THE POSSIBILITY OF ACHIEVING PRIMARY PREVENTION OF ATHEROSCLEROTIC DISEASES.

A. Association of risk factors with atherosclerotic diseases -- major risk factors: Many studies conducted over the past 25 years have demonstrated associations between certain biochemical, physiological and environmental factors and the development of premature coronary heart disease. Numerous risk factors for CHD have been identified such as habitual diet (high in saturated fat-cholesterol-calories), elevated blood lipids+, hypertension, cigarette smoking, hyperglycemia (diabetes mellitus), obesity, sedentary living, psychosocial tensions, and (a positive) family history of premature atherosclerotic disease.

Of central importance in evaluating the association between risk factors and CHD is the finding that arterial lesions cannot generally be produced experimentally in animals without a substantial modification of the diet involving increased intake of cholesterol and fat, leading to elevation of serum lipid levels.* Similarly, with very few exceptions, human populations consuming diets high in saturated fat and cholesterol have high mean serum cholesterol levels and high

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+"Hyperlipidemia" is the generic term for elevation of one or more of the blood (serum) lipids, i.e., cholesterol, triglycerides, phospholipids. The most extensive research on the relationship between the blood lipids and the atherosclerotic diseases has involved serum cholesterol. Recent evidence suggests that elevated serum triglycerides may also be related to increased risk of CHD.

The water-insoluble serum lipids are dissolved in the blood stream by combination with proteins to form several types of serum lipoproteins. The association between lipoprotein patterns and CHD is currently under further study to assess whether any of the types have predictive or diagnostic value over and above that of serum cholesterol and triglyceride levels alone or in combination (38).

*Comprehensive reviews of research (animal, experimental, clinicopathologic and epidemiologic) on the atherosclerotic diseases are available in the recent scientific literature (10-37). This section summarizes evidence considered most pertinent to the matter of achieving primary prevention.

incidence and mortality rates from premature CHD. Human populations consuming diets low in cholesterol and saturated fat have low mean serum cholesterol levels and low incidence and mortality rates from premature CHD. Within any population group, again with few exceptions, the risk of developing premature CHD increases as the serum cholesterol level rises. This fact has been extensively documented for the American male population in several prospective epidemiologic studies (Fig. 3, cf. also Fig. 11 below) (6, 6a-k). The relationship between level of serum cholesterol and disease is continuous. With increasing cholesterol concentration risk is increased. There is no evidence of a critical level of serum cholesterol which separates high from low risk individuals.

Detailed data on relationships among diet, serum lipids and premature CHD are available from many studies. For example, the International Atherosclerosis Project quantitated the degree of atherosclerosis of the aorta and coronary arteries at autopsy in over 31,000 persons age 10 to 69 who died during 1960-65 in 15 cities throughout the world. Marked geographic differences in the extent and severity of atherosclerosis were observed (Fig. 4) (22). Populations in those countries with a high intake of saturated fat and high serum cholesterol levels had more severe atherosclerotic lesions than did populations in countries with low saturated fat intake and low serum cholesterol levels. Decedents from the United States showed the greatest degree of involvement.

Repeated analyses of international mortality statistics have yielded comparable findings. The most recent data deal with mortality rates for 22 developed countries including the British Commonwealth, Europe and North America (Table 3) (4, 5). The sizeable

differences in CHD mortality rates for middle-aged males correlate positively with differences in nutritional factors, e.g., total calories, saturated fat, and cholesterol. The United States is near the top of the list with high per capita levels for all of these indices and for mortality.

Data collected in research on living populations are consistent with those obtained from autopsy studies and mortality statistics. An extensive report from a prospective international study of 18 population samples in seven countries -- Finland, Greece, Italy, Japan, Netherlands, United States and Yugoslavia -- deals with observations on approximately 12,000 men originally age 40-59 who have been studied for about a decade (39, 40). On initial examination, marked differences in prevalence of CHD were recorded among the population samples from the seven countries (Fig. 5) (40). For samples with high prevalence of CHD, including middle-aged American men, the rate was over four times greater than for those from countries with low prevalence.

Data on five year CHD incidence and mortality rates are consistent with the prevalence data (Fig. 5 and Table 5) (40). The highest five year incidence rates were recorded for men from Eastern Finland and the United States -- over 120 and 80 per 1,000 respectively. In contrast, five year incidence rates were about 20 per 1,000 or less for men in Corfu, Crete, Dalmatia and Japan. Differences in CHD mortality rates were frequently paralleled by differences in total mortality rates (Table 5) (40). This finding supports the conclusion that the differences in CHD rates were not due to diagnostic variability. Differences in CHD prevalence, incidence and mortality rates among the populations of these countries were significantly related to saturated fat intake and serum cholesterol level (Figs. 6-8) (40).

Recent clinical studies using angiography to assess narrowing of coronary arteries have further strengthened the evidence on the association between serum lipid levels and CHD. Middle-aged patients with substantial narrowing of the coronary arteries had levels of serum cholesterol, triglycerides or both significantly higher than those of patients without such narrowing (41).

Hypertension also aggravates the atherosclerotic process, particularly in the presence of hyperlipidemia. This conclusion is supported by impressive clinical and experimental data as well as by prospective epidemiologic findings demonstrating significant correlations between blood pressure and the subsequent development of CHD (Fig. 9, 11) (6, 6a-k). This relationship between blood pressure and CHD risk is continuous. At each higher step of the blood pressure scale risk is increased. Hypertension has also been established as a major risk factor for cerebrovascular disease, including atherothrombotic cerebral infarction and cerebral hemorrhage (Fig. 9) (6, 6a-k).

The 1964 Surgeon General's report on cigarette smoking established that on the average cigarette smokers in the United States have a 70 per cent greater chance of developing CHD than non-smokers (42). Recent data from several prospective studies in this country have confirmed this finding and strengthened the association between smoking and atherosclerotic diseases (6, 6a-k, 43-45). The largest of these has involved one million men and women (46). This showed that for each sex and age group CHD mortality increased with increased intensity of cigarette smoking (Table 6) (46). Men age 45-54 smoking two or more packs of cigarettes a day were at highest risk.

The younger the age group, the higher the relative risk

associated with cigarette smoking (Table 7) (6, 6a-k, 47, 48). It has also been demonstrated that the association between cigarette smoking and CHD risk is independent of such other risk factors as serum cholesterol level and blood pressure (Fig.10) (6, 6a-k, 49, 50). In addition, three studies have recently shown that atherosclerosis of aorta and/or coronary arteries is more severe at autopsy in persons who had been habitual cigarette smokers prior to death compared to those who had never smoked (Fig.11) (51, 54).

Finally, as the annual supplements to the Surgeon General's report have noted, research progress has been recorded in elucidating possible mechanisms whereby smoking may exert its deleterious effect on the atherogenic process (43-45).

Morbidity and mortality rates from CHD among Americans living in the same communities differ markedly particularly when classified with respect to all three of the foregoing risk factors — serum cholesterol, blood pressure and cigarette smoking — considered simultaneously. Detailed data are now available from the pooled findings of six major U. S. prospective studies dealing with 7,594 middle-aged American men free of clinical CHD at initial examination (Fig. 12 (6, 6a-k). Those free of the three risk factors — hypercholesterolemia, cigarette smoking and hypertension — experienced much lower CHD morbidity and mortality rates over a ten-year period than did the groups of men with any two or all three of these traits. CHD mortality rate was one-third to one-sixth as high and the suc death rate was one-fourth to one-sixth as high. As a result of the low mortality rate from atherosclerotic diseases, the men free of these major risk factors had less than one-third the ten-year mortality rate from all causes than the men with these traits, and about one-fifth the total mortality rate of those with all three risk factors.

These impressive findings indicate that these three risk factors — hypercholesterolemia, hypertension and cigarette smoking — are properly

designated major risk factors for premature atherosclerotic disease, especially coronary heart disease. This designation is appropriate, first because of the impact of these factors on risk, particularly when present in combination, second because of the consistency of the findings from multiple studies, and third because of the frequency of occurrence of these factors singly and in combination in the American population. All three are potentially amenable to prevention and control.

B. Association of risk factors with atherosclerotic diseases -- other risk factors: Clinical diabetes mellitus has been recognized for years as a serious risk factor for atherosclerotic disease. This relationship has been extensively documented in retrospective studies dealing with coronary, cerebrovascular and peripheral vascular disease (29, 55). These investigations have shown that diabetics have atherosclerotic disease more often, more severely and more prematurely than nondiabetics. A long-term prospective study in industry of persons age 25-64 -- involving an average of more than 73,000 men and women -- has confirmed the role of diabetes as a risk factor, especially when hypertension is also present (Table 8) (56).

Recent retrospective studies also indicate that persons with manifestations of atherosclerotic disease (coronary, peripheral and cerebral) exhibit abnormalities in glucose tolerance more frequently than clinical controls (29, 55).

Finally, long-term prospective studies in U.S. population groups indicate that asymptomatic hyperglycemia — so-called chemical or sub-clinical diabetes — is also an independent risk factor for atherosclerotic disease of major coronary, cerebral and peripheral arteries (Figs. 13 and 14) (29, 55, 57 - 59).

Obesity is another trait implicated as a significant coronary risk factor. For many years, data have been available from life insurance

actuarial studies indicating that overweight persons have an increased risk of dying from coronary and cerebrovascular disease. Risk is a function of degree of overweight (' 60). Although these data indicate an increase in risk, it is smaller than that recorded for such factors as hypercholesterolemia, hypertension and cigarette smoking.

Long-term prospective studies have also noted an increased risk of CHD in overweight men in the United States (6, 6a-k, 29, 61). However, the findings are not entirely consistent. They suggest that the association between overweight and CHD risk may be largely attributable to the increased proneness of overweight men to hypertension, hyperlipidemia and diabetes. Moderate overweight -- in the absence of these risk factors and cigarette smoking -- apparently is associated with only a modest increase in risk.

Epidemiological evidence suggests that sedentary living contributes to the risk of premature atherosclerotic diseases in the economically developed countries (25, 29, 62-67). This evidence is not entirely consistent nor has the role of possible confounding variables been fully clarified. Furthermore, the apparent impact of sedentary living on risk of coronary heart disease observed in some studies is less than that for the major risk factors.

Psycho-social tensions related to personal life situations and/or those inherent in cultural circumstances have long been suspect as factors related to premature CHD. This view has recently received support from several studies. For example, data from investigations on personality-behavior patterns and social incongruities are consistent with this hypothesis. Data have also been obtained indicating a detrimental effect of social and geographic mobility and urbanization (16, 25, 29, 68-71). These various psycho-social influences may be conditioning

or aggravating risk factors in our society, particularly in the presence of other traits enhancing proneness to premature CHD. Clinical experience indicates that emotional crises and unusual fatigue may precipitate acute events (e.g., myocardial infarction, stroke) in persons with pre-existing severe atherosclerotic disease.

Most of the positive findings indicating association between various psycho-social factors and premature CHD have been recorded in single investigations and they require confirmation. This is understandable in view of the complexity of measurement in this area.

Coronary heart disease has long been thought to be related to family history. Evidence exists indicating an increased risk of CHD in close relatives of persons who experience a heart attack early in life, e.g., prior to age 50 (20, 28, 29, 35, 36, 72-75). There are numerous examples of multiple premature attacks within families. In contrast there is little evidence for familial aggregation when the disease first occurs late in life. It is likely that some of this predisposition is mediated by familial resemblances in risk factors, e.g., hypercholesterolemia, hypertension and diabetes. Most of the predisposing influences are under both genetic and environmental control; families share not only genes but also living habits such as eating patterns and smoking.

C. Modification of risk factors: Certain risk factors can be avoided, controlled or corrected by appropriate changes in mode of life. Thus, prevention or control of hyperlipidemia may be effected for most persons by acceptable modification of the diet (17, 19, 24, 25, 28, 29, 33, 34, 38, 64, 76). Weight reduction alone frequently lowers elevated serum triglycerides, blood pressure and plasma glucose levels of obese patients. In addition, well-tested pharmacologic measures are available for the control of hypertension

not responsive to dietary management alone (Fig. 15) (29, 64, 77, 78). Cigarette smoking is also amenable to prevention or correction on a large scale, as shown by recent declines in the proportion of cigarette smokers in the American population (Fig. 16 and Tables 9, 10) (79-82).

Research studies have been done to evaluate long-term effects of modifying diet composition, cigarette smoking and hypertension.

Changes in diet composition: Studies have been conducted in both animals and man to determine whether changes in composition of the diet have an effect on the atheroslcerotic process, and on incidence and mortality from CHD. Change from a high to a low cholesterol diet has resulted in a decrease in size of atherosclerotic plaques in experimental animals (18, 26, 29). Evidence on this matter, available for many years from research with non-primate species, has recently been supplemented by significant confirmatory findings on reversibility of lesions in primates (Table 11 and Fig. 17) (83).

In man, data on the opposite trend -- i.e., effects of increasing saturated fat and cholesterol intake -- have been reported in several epidemiologic studies. For example, migrants (e.g., Japanese, Neapolitans) to the United States from areas with low coronary heart disease death rates have higher serum lipid levels and higher CHD death rates, especially for males, as compared to rates in their native countries (12, 27, 29).

Reports are also available indicating that reduction in calorie, fat and cholesterol intake can lead to regression of lesions in man (29). Data on this matter in the older literature have recently been supplemented by physiologic evidence suggesting partial regression of peripheral atherosclerosis in persons with Type III hyperlipoproteinemia treated by diet and a drug to lower serum lipids (84).

Results of experimental studies of dietary changes in man have recently been reported. Studies in Los Angeles, Helsinki and New York have dealt with primary prevention of CHD (85-87). All three investigations utilized diets reduced in saturated fat and cholesterol. Polyunsaturated fat was added to replace saturated fat removed from the diet. As a consequence the diets -- particularly in the Los Angeles study -- were high in polyunsaturated fat. In the New York Anti-Coronary Club, polyunsaturates were used for partial replacement of saturates. This study also placed obese volunteers on weight reducing diets during their initial months in the project.

The Los Angeles study was a double blind random trial among veterans living in domiciliary facilities. The Helsinki study is a comparison of two mental hospital populations. The New York study compared volunteers placed on a fat modified diet with a somewhat similar group of volunteers on their usual diet. Several hundred men have participated in each study for several years. These three studies reported a sizeable decrease in the incidence of new coronary events in the experimental compared with their respective comparison groups (Figs. 18-20) (85-87). In the Los Angeles study, the effect appeared to be substantially greater in men under age 65 at entry.

Two studies (Los Angeles and Helsinki) also reported mortality findings. Their data indicate that diet change was associated with reductions in CHD mortality rates, although statistical significance was not reached. The Helsinki study also recorded a sizeable reduction in total mortality rate, paralleling the decrease in CHD death rate but again, statistical significance was not reached. The Los Angeles study did not note any decrease in total mortality. The lower death rate from

atherosclerotic disease was offset in the experimental group by a higher death rate from non-cardiovascular causes, including a statistically significant excess of deaths from malignant neoplasms. This last finding has posed a question concerning possible carcinogenic effects of diets very high in polyunsaturated fats.

The results of these three studies are encouraging with regard to the possibility of preventing CHD and other atherosclerotic diseases by dietary fat modification. However, they are not conclusive as to the preventive value of dietary change. Each dealt with a relatively small group and had one or another additional flaws, e.g., high drop-out rates, absence of a suitable control group, lack of double blind design (88,89). Nonetheless, all are consistent in showing a reduction in CHD incidence and indicate the potential for CHD prevention through modification of dietary fat composition.

Control of cigarette smoking: The Surgeon General's reports on "The Health Consequences of Smoking" have concluded that cessation of cigarette smoking is followed by a reduction in CHD risk (42 - 45). This determination was based on evidence obtained from several studies. Two were large prospective studies designed to assess differential mortality among adults classified according to their smoking history. Both reported that CHD mortality rates of former cigarette smokers were well below rates of current smokers, especially among younger groups (Fig. 21) (46 - 48, 54). The differential CHD mortality between former and current smokers was greater when the group of former smokers was restricted to those who stopped smoking for reasons other than doctor's orders. Similar findings were observed in a longitudinal study of mortality among British physicians and in the Western Collaborative Group Study (Table 12) (44, 90, 91). In

the latter it was found that the CHD incidence rate for middle-aged male ex-smokers was intermediate between rates for men who never smoked and men who were heavy cigarette smokers at entry. This finding was recorded after adjusting for several concomitant risk factors (e.g., serum cholesterol, blood pressure, physical activity).

Further, the combined experience of adult males followed prospectively by the [illegible] studies cooperating in the Pooling Project showed that the age-adjusted incidence rate of severe forms of CHD among male ex-smokers was about as low [illegible] as that observed for males who had never smoked, and was much lower than the rate for men smoking a package or more of cigarettes per day at entry (Fig. 11) (6, 6a-k). Again, the findings were independent of serum cholesterol and blood pressure.

The consistent findings of all these studies provide highly suggestive evidence in support of the concept that cessation of cigarette smoking is of value in the effort to prevent CHD.

Drug treatment for hypertension: Drug treatment for patients with diastolic blood pressures averaging from 115 to 129 mm. Hg has produced marked reductions in morbidity from hypertensive complications (Table 13) (77).

Recently an important report was published on the Veterans Administration Cooperative Study of drug therapy for male hypertensive patients with diastolic blood pressures averaging between 90 and 114 mm. Hg (so-called "mild" hypertension) (78). Three hundred eighty such hypertensive men were randomly assigned to either active antihypertensive agents or placebos and followed for periods of one to 5.5 years (average 3.3 years). Fifty-six of the placebo treated patients developed morbid events, as contrasted with 22 of the actively treated patients. Life-table analysis indicated that the estimated risk of developing a mordid event over a five year period was reduced from 55 to 18 per cent by treatment (Fig. 22) (78). Major nonfatal and fatal cardiovascular events (terminating morbid events) occurred in 35 patients of the control group as compared to 9 patients in the treated group. Nineteen deaths related to hyper-

tension or atherosclerosis occurred in the control group and 8 in the actively trea In addition to the morbid events, 20 patients— all in the control group—developed persistent elevation of diastolic blood pressure to 125 mm. Hg or greater. The beneficial effect of treatment was more evident in the patients with higher initial blood pressures than in those with lower levels at entry.

Treatment apparently was most effective in the prevention of congestive heart failure and stroke, and least effective in preventing clinical manifestations of severe coronary atherosclerosis. The limited size of the study precluded a definiti assessment of ability to prevent premature CHD by drug treatment of hypertension. However, the data currently available support the judgment that effective long-term therapy for hypertension may help to prevent CHD and other atherosclerotic diseases.

Control of multiple risk factors: Only one investigation has attempted to explore the possibility of prevention by control of multiple risk factors — hyperlipidemia, obesity, hypertension, cigarette smoking and sedentary living. This Chicago Coronary Prevention Evaluation Program has used diets low in saturated fat and cholesterol, and moderate in calories, total fat, polyunsaturated fat, carbohydrate and salt (29). It has avoided recommending diets high in polyunsaturated fat. It has encouraged cigarette smokers to abandon this habit and urged sedentary men to take up regular, frequent, moderate exercise to enhance cardiopulmonary fitness. Its participants are 519 coronary-prone men originally age 40-59. They are being compared with over 3,200 matched men from the U.S. national cooperative Pooling Project (6, 6a-k).

This study, still in progress, has reported encouraging effects on CHD and total mortality (Fig. 23) (88). Like the other "first generation" field trials described above, the investigation is limited by relatively small sample size, as well as lack of a randomly assigned control group. Therefore, its findings on the possibility of preventing premature death in high risk middle-aged males can be viewed only as suggestive (88, 89).

SUMMARY

Converging lines of epidemiological, clinical and experimental evidence, both animal and human, support the judgment that the relationship between the risk factors, particularly the major risk factors -- i.e., hypercholesterolemia, cigarette smoking, hypertension -- and the development of coronary heart disease is probably causal. This should not be interpreted as implying that the evidence on this matter is conclusive.. Nevertheless, the data strongly indicate that to a considerable degree coronary heart disease in the United States, particularly in the under 60 age group, results principally from the impact of these three widely prevalent risk factors. This critically important conclusion rests on the following foundations: Confirmatory data are available from many sources on the epidemiologic associations; these associations persist when confounding variables are taken into account; the associations are strong and consistent; they are in accord with findings from other research disciplines and are biologically plausible in terms of reasonable pathogenetic mechanisms and concepts of multifactorial etiology relating apparent cause and disease. Alternative hypotheses to account for the associations do not fit the majority of observations to date.

The research findings on risk factors strongly indicate the possibility of effective primary prevention of atherosclerotic disease, particularly premature coronary heart disease (Tables 14-16) (76, 92).

III. RECOMMENDATIONS FOR PRIMARY PREVENTION.

A. The Commission recommends that a strategy of primary prevention of premature atherosclerotic diseases be adopted as long-term national policy for the United States and to implement this strategy that adequate resources of money and manpower be committed to accomplish:

- ....Changes in diet to prevent or control hyperlipidemia, obesity, hypertension and diabetes
- ....Elimination of cigarette smoking
- ....Pharmacologic control of elevated blood pressure.

B. The Commission recommends that a Special Committee be established at a high level of the Federal Government to develop coordinated plans for large-scale, long-term trials to determine the effect of various interventions, particularly diet modification, on the rates of premature atherosclerotic diseases in the United States. The Commission recognizes that differences of opinion exist with regard to the likely beneficial effect of various types of change, particularly fat modification of the diet, on premature CHD in the United States. The public health importance of CHD makes it mandatory to conduct such trials (76, 94, 95).

The Commission further recognizes that even if planning were to start immediately, the American public would probably have to wait at least 10 years for results of these studies. At times urgent public health decisions must be made on the basis of incomplete evidence. Therefore, the Commission recommends that actions with regard to the reasonable and safe changes described below be promptly implemented.

C. The Commission recommends the following modifications of diet for the general public, and particularly for individuals with marked increase

in risk of premature atherosclerotic disease.

1. Caloric intake be adjusted to achieve and maintain optimal weight. Correction of obesity is known to be frequently associated with significant control of certain CHD risk factors, e.g., fall in blood pressure of some hypertensive patients, decrease in blood glucose levels in some patients with maturity-onset diabetes, decline in elevated serum triglyceride levels. It is generally agreed that this measure is a reasonable and safe aspect of any prophylactic regimen.

2. A reduction of dietary cholesterol to less than 300 mg. per day. The average daily diet in the United States contains approximately 600 mg. of cholesterol. Substantial reduction in amount of cholesterol in the diet has been found to lower concentration of cholesterol in the serum of most people. Since cholesterol is present in many protein sources of high biological quality, careful planning is necessary to lower intake of cholesterol without impairing intake of protein.

3. A substantial reduction of dietary saturated fats. This change will lower concentration of cholesterol in the serum of most people. The ideal quantity of fat needed in the diet is not known but moderation in intake is considered desirable, e.g., less than 35 per cent of total calories from all fats. Intake of less than 10 per cent of total calories from saturated fats is of critical importance for attainment of optimal serum cholesterol levels for most people. Unsaturated fats may be used in moderation to replace a portion of the saturated fats, i.e., 10 percent of calories from mono- and up to 10 percent from polyunsaturated fats. With proper control of saturated fat, cholesterol and calorie intake, as recommended

above, ingestion of large amounts of polyunsaturated fats -- i.e., 10 per cent or more of total calories -- is generally not necessary for control of serum lipid levels. International data indicate that populations with low serum lipid levels and low CHD mortality rates habitually consume diets low in saturated fat and cholesterol, and low or moderate in total fat and polyunsaturated fat -- not high in the latter (5, 40).

With these dietary principles, requirements for optimal nutrition can be met for all sectors of the population, including infants, children, adolescents, pregnant and lactating women, and older persons.

Changes in the environment to aid the American people to improve their diet should be a major aspect of this effort at prevention. Recent research has shown that it is entirely possible to prepare foods commercially in ways that will contribute substantially to the control of hyperlipidemia. In the National Diet-Heart Study, many foods were prepared with sizeable reductions in content of total fat, saturated fat, cholesterol and calories (76). This was done with dairy and meat products, baked goods, frozen desserts and other foodstuffs. It was demonstrated that modified foods can be made in forms that are highly acceptable to the consumer.

The Commission therefore recommends that the food industry be encouraged by the medical profession and the government and supported by the general public to make available leaner meats and processed meats, dairy products, frozen desserts and baked goods reduced in saturated fats, cholesterol and calories, and

b. Reduction in saturated fat and cholesterol content of dairy products.

.... Industry and government should review and establish policies (including pricing policies) that will encourage development of low-fat, low-cholesterol milk and milk products, and use of cows producing large amounts of high protein, low fat milk. Wholesale pricing of dairy products is still based on butter fat content, a practice persisting from the days when measurement of butter fat was used to detect skimming or watering of milk.

.... The dairy industry should be helped and encouraged to develop techniques for reducing saturated fat and cholesterol in cheeses of all varieties. Total fluid milk consumption in the United States is decreasing while consumption of cheese is steadily increasing. At current levels of consumption significant control of hyperlipidemia seems unlikely unless composition of cheeses can be altered. The National Diet-Heart Study demonstrated that limited progress has been made in this area, and further progress certainly is possible.

.... Industry should be stimulated to develop creamers low in total fats, saturated fats and cholesterol. Changes in labeling and advertising of cream substitutes are needed, so that their actual fat composition is clear. The so-called non-dairy-fat creamers currently on the market present a special problem. These products are characterized by a high content of coconut oil and/or hydrogenated vegetable oil and therefore of saturated fat (96). Coconut oil is one of the most potent agents for elevating serum cholesterol level. Labels that

read "made with vegetable oil" give an erroneous implication that the product is to be preferred over one containing dairy fat.

c. Reduction of saturated fat, cholesterol and calorie content of baked goods. As the National Diet-Heart Study demonstrated, nutritionally excellent baked goods of all types can be prepared commercially in completely acceptable forms with reduced saturated fat, cholesterol and calorie content. Widespread marketing of these fat modified products should be encouraged.

d. Promotion of fats and oils low in saturated fats and cholesterol for table spreads, shortenings, cooking and salad dressings, etc. In some areas of the country, state and/or local laws prohibit the use of butter substitutes in restaurants and institutions. These laws should be repealed.

e. Reduction of egg yolk consumption. The yolk of the egg is the single highest source of cholesterol in the average American diet, as well as a source of considerable saturated fat. Ingestion of two eggs a day -- in visible and/or invisible form (i.e., in prepared foods) -- will seriously hamper dietary programs aimed at reducing serum cholesterol. Consequently the public should be encouraged to avoid egg yolk consumption, and the food industry should be persuaded to minimize egg yolk content of commercially prepared foods. Food manufacturers have recently developed low cholesterol and low saturated fat egg substitutes which may be used successfully in quantity cookery and for scrambled eggs, omelettes, etc. Such developments should be encouraged.

f. Modernization of regulations on labeling and definition of foods. In December 1959 the Food and Drug Administration introduced into the Federal Register the statement: "The role of cholesterol in heart and artery diseases has not been established" (97). Consequently, it ruled that advertising claiming that the consumption of a food product might protect against diseases of the heart and arteries was false and misleading. The Federal Register in May, 1965 published a proposal favorable to the labeling of edible fats. This was supported by the American Heart Association and the American Diabetes Association. In February 1966 however, the FDA rejected the recommendation to label edible fats and oils, but endorsed a study of this problem to be conducted by the Council on Foods and Nutrition of the American Medical Association. The Council completed its report and transmitted it to the FDA. The report favored such labeling but the FDA took no action.

The FDA's regulation with respect to labeling of foods should be reviewed and updated. A new approach to labeling is needed -- to allow the consumer easily to identify nutrient content (particularly the amount and type of fat and cholesterol) in all foods, including commercially prepared mixed dishes, and to encourage the manufacture of nutritious products low in saturated fats and cholesterol.

Correspondingly rules and regulations of the USDA, state and local agencies on foodstuff definition, adulteration, etc., should be modernized to permit and encourage production, advertising and the sale of products low in saturated fats and cholesterol (e.g.,

processed meats), made with moderate amounts of unsaturated oils instead of large amounts of saturated fats.

g. Improvement in school lunch, food stamp, other supplementary food programs and government administered nutrition practices (e.g., Armed Forces, Veterans Administration facilities). Policies, regulations, practices and educational aspects of these programs should be revised to encourage improved eating habits including consumption of low saturated fat, low cholesterol diets among children, teenagers, young adults and low income groups (98).

h. Development of a comprehensive and sustained public and professional nutrition education program. To effect the required changes in dietary habits, it is essential that the entire community be actively involved through a comprehensive and sustained public and professional education program. This will deepen understanding and appreciation of the need for primary prevention and inform the public and health professions on ways of selecting and preparing foods consistent with sound nutritional practices.

Special emphasis must be directed toward developing effective instructional programs on nutrition in the educational curricula at all levels. For this purpose, particular attention should be given to the institutions training health professionals with expertise in nutrition -- e.g., college and university home economics departments, hospital dietitian instruction programs, schools of medicine, dentistry and nursing, and teachers' colleges. These sources should develop educational programs based on modern concepts of sound nutrition. Succeeding generations should have the advantage of this knowledge beginning in elementary school.

Food manufacturers have an excellent opportunity to provide public education through advertising. They should be encouraged to call attention in their advertising to the type and amount of fat and the cholesterol content of their products.

There is a great need for extensive and continuous dissemination by the news media of information on diet, as well as other risk factors. Public service communications in this area should be substantially strengthened and broadened.

With proper education, information and the availability of fat modified foods, it will be possible for most Americans to make desirable changes in their diets without major dislocation of personal eating habits.

Americans should be encouraged to modify habits with regard to all five major sources of fat in the U.S. diet -- meats, dairy products, baked goods, eggs, table and cooking fats. Specifically a superior pattern of nutrient intake can be achieved by altering habits along the following lines:

.... Use lean cuts of beef, lamb, pork and veal, cooked to dispose of saturated fat and eaten in moderate portion sizes;

.... Use lean meat of poultry and fish;

.... Use fat-modified* processed meat products (frankfurters, sausage, salami, etc.);

..... Use organ meats (e.g., liver) and shellfish in moderation since they are higher in cholesterol than muscle of red meat, chicken and fish;

.... Avoid fat cuts of meat, addition of saturated fat in cooking meat, large meat portions and processed meats high in saturated fat;

*Throughout this set of guidelines fat modified refers to products made with reduced saturated fat and cholesterol content

.... Use low fat and fat modified dairy products;

.... Avoid high saturated fat dairy products;

.... Use fat modified baked goods (pies, cookies, cakes, sweet rolls, doughnuts, crullers);

.... Avoid baked goods high in saturated fat and cholesterol;

.... Use salad and cooking oils, new soft margarines and shortenings low in saturated fat;

.... Avoid butter, margarine and shortenings high in saturated fat;

.... Avoid candies high in saturated fat;

.... Avoid egg yolk, bacon, lard, suet;

.... Use grains, fruits, vegetables, legumes.

D. The Commission recommends that high priority be given to the elimination of cigarette smoking as a national habit.

1. Efforts should be made to reduce smoking among young people by strict restraints on advertising and the sale of cigarettes. All advertising of tobacco in the mass media (including television, radio, newspapers and magazines) should be discontinued. Short of this all advertising should carry an honest, frank, highly visible warning for potential consumers.

2. The mass media education program emphasizing the health hazards of smoking should be continued indefinitely to redress the imbalance created by decades of cigarette advertising.

3. Education programs on the risks of smoking should be strengthened and extended throughout the school system beginning with the early primary grades. Parents, teachers, health professionals

and other adults in positions of responsibility (e.g., television entertainers and sports personalities) should be made aware of the serious adverse influence of their own smoking habit as a poor example for children who may become lifelong cigarette smokers. It is noteworthy that physicians have been particularly successful in giving up cigarette smoking and are in a unique position to exert great influence in helping their patients stop smoking.

4. Cigarette vending machines should be removed from all medical facilities and public buildings or, preferably, banned altogether.

5. The prohibition against smoking in large meetings and mass transit facilities should be vigorously enforced.

6. Revenues from progressive increases in taxes on tobacco should be earmarked for smoking control programs and the care of patients with diseases associated with smoking.

7. Current large subsidies by government for growing and exporting tobacco should be critically reviewed with the objective of making economic supports for agriculture consonant with national health goals.

8. Planning by appropriate social science experts should go forward for the orderly phase out of the tobacco industry without major economic dislocation of those whose livelihood is involved.

E. The Commission recommends a major national effort to detect and control hypertension. Recent studies have shown that the prevalence of elevated blood pressure is generally high in the United States,

especially in the Negro population (Table 17) (99). Many hypertensives have not been identified; many others known to have the disease are not receiving adequate therapy. Programs are urgently needed to identify hypertensives in the community and assure their subsequent treatment. The recently published positive results from the Veterans Administration field trial of drug therapy for so-called "mild" hypertension underscore the potential significance of such programs (78).

F. The Commission recommends that community programs be developed and expanded for the detection and treatment of persons of all ages who are very susceptible to premature atherosclerotic diseases due to combinations of the major risk factors.

This recommendation is premised on extensive experience demonstrating that effective community programs for prevention of disease generally combine measures addressed to the entire population with concerted efforts for the detection and care of high risk individuals. All available evidence indicates that this well-established principle applies to the prevention of the atherosclerotic diseases.

On the basis of recent experience detection programs are likely to identify a very large proportion of the population -- e.g., about 20 or 30 per cent of middle-aged adults -- as being at unusually high risk. For such individuals, community services should be provided to assist their physicians in long-term management.* Such programs will require the training and use of large numbers of allied health professionals, as well as physicians.

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*Detailed proposals concerning these community services will be presented in subsequent reports of the Commission.

G. The Commission presents the following observations on drug treatment of hyperlipidemia and on exercise programs, and their possible role in the preventive effort:

Drugs for the treatment of hyperlipidemia have been developed in recent years. For example, several years of experience with cholestyramine, clofibrate, dextrothyroxine and nicotine acid have demonstrated that they will reduce cholesterol and triglyceride levels in the blood of many patients especially if they are abnormally high. What is yet to be determined is whether the biochemical action of these or similar drugs will exert any favorable effect on the course of the atherosclerotic diseases and whether long term continued use of these substances produces significant deleterious effects. Clinical indications for the prescription of these drugs are now being defined. For example, they are possibly indicated for specific types of patients with marked hyperlipidemia, incapable of being normalized by diet alone. In this situation the risk of progression of atherosclerotic disease may outweigh any as yet unrecognized hazards of long-term medication. There is a need for further development and evaluation of relatively nontoxic drugs for the lowering of elevated blood lipids.

Regular exercise, particularly those forms of endurance exercise which enhance cardiovascular fitness, may have a role to play in the prevention of atheroscletoric diseases. It is important to emphasize, however, that exercise is not free of danger both to the musculoskeletal and the cardiovascular systems. This is particularly true for middle-aged individuals—especially coronary-prone persons—who suddenly take up vigorous exercise after years of minimal physical activity. Physicians and other professionals need aid in guiding a concerned public to avoid these problems. Research on the role and programming of exercise for the prevention of atherosclerotic diseases must be pursued vigorously to obtain more definitive information.

TABLE 1

Prevalence of Definite and Suspect Coronary Heart Disease in Adults, by Age and Sex: United States, 1960-62 -- National Health Examination Survey (1)

Age	Total			Definite			Suspect		
	Both Sexes	Men	Women	Both Sexes	Men	Women	Both Sexes	Men	Women
	Number of Adults in Thousands								
Total-18-79 years---	5,535	3,081	2,454	3,125	1,945	1,180	2,410	1,136	1,274
18-24 years----------	-	-	-	-	-	-	-	-	-
25-34 years----------	77	42	36	60	42	19	17	-	17
35-44 years----------	384	264	119	177	120	57	207	144	63
45-54 years----------	1,126	693	433	517	352	165	609	341	268
55-64 years----------	1,867	1,060	807	1,111	726	384	756	334	422
65-74 years----------	1,723	837	886	1,064	575	489	659	262	397
75-79 years----------	357	185	172	195	130	64	162	55	108
	Rates per 1,000 Adults								
Total-18-79 years---	50	58	42	28	37	20	22	22	22
18-24 years----------	-	-	-	-	-	-	-	-	-
25-34 years----------	4	4	3	3	4	2	1	-	2
35-44 years----------	16	23	10	7	11	5	9	13	5
45-54 years----------	55	69	41	25	35	16	30	34	25
55-64 years----------	119	141	99	71	97	47	48	44	52
65-74 years----------	154	168	143	95	116	79	59	53	64
75-79 years----------	124	130	119	68	91	45	57	38	75

TABLE 2

Number of Deaths and Mortality Rates from Coronary Heart Disease*, by Age, Sex, Color

United States - 1967 (2)

Sex-Color Group	AGE										
	1	1-4	5-14	15-24	25-34	35-44	45-54	55-64	65-74	75-84	85+
	Number of Deaths										
White Male	24	12	27	136	889	9,359	34,865	71,323	99,092	92,377	35,961
White Female	9	8	22	57	252	1,675	7,290	22,490	57,827	89,644	54,761
Non-White Male	10	4	11	52	304	1,432	3,611	6,430	7,937	5,134	1,959
Non-White Female	8	6	5	29	191	752	2,068	4,144	6,332	4,723	2,446
All Males	34	16	38	188	1,193	10,791	38,476	77,753	107,029	97,511	37,920
All Females	17	14	27	86	443	2,427	9,358	26,634	64,159	94,367	57,207
All Whites	33	20	49	193	1,141	11,034	42,155	93,813	156,919	182,021	90,722
All Non-Whites	18	10	16	81	495	2,184	5,679	10,574	14,269	9,857	4,405
All	51	30	65	274	1,636	13,218	47,834	104,387	171,188	191,878	95,127
	Death Rates Per 100,000 Population										
White Male	1.6	0.1	0.2	1.0	8.9	90.1	352.7	937.9	2,072.7	4,083.9	9,081.1
White Female	0.6	0.1	0.2	0.4	2.5	15.5	69.7	268.9	964.6	2,772.8	8,284.5
Non-White Male	3.3	0.3	0.4	2.5	23.8	117.3	343.2	840.5	1,917.1	2,579.9	3,918.0
Non-White Female	2.7	0.5	0.2	1.4	13.1	52.3	174.1	495.7	1,297.6	1,881.6	3,706.0
All Males	1.9	0.2	0.2	1.2	10.6	93.0	351.8	928.9	2,060.7	3,962.3	8,502.3
All Females	1.0	0.2	0.2	0.5	3.8	19.8	80.3	289.5	989.5	2,708.6	7,868.9
All Whites	1.2	0.1	0.2	0.7	5.6	52.1	207.2	587.5	1,456.2	3,312.5	8,583.0
All Non-Whites	3.0	0.4	0.2	2.0	18.2	82.1	253.6	660.1	1,581.9	2,190.5	3,797.4
All	1.4	0.2	0.2	0.8	7.1	55.5	211.8	594.0	1,465.9	3,227.6	8,102.8

* ICD Categories 420-422, Seventh Revision.—

Table 4

Sudden Death and Acute Mortality
with First Major Coronary Episodes
7,594 Men Age 30-59 at Entry
Pooling Project, Ten Year Experience (6, 6a-k)

Event	No. of Events	Proportion per 1,000 Events
All First Major Coronary Episodes, Nonfatal & Fatal	501	1,000.0
Sudden Death (Death within 3 Hours of Onset of Acute Illness)	123	245.5
All Acute Deaths with First Episodes	165	329.3

Table 5

Five Year Age-standardized Mortality Rates, Coronary Heart Disease and All Causes, Eighteen Cohorts from Seven Countries, Men Originally Age 40-59, All Men and Men CHD-Free at Entry -- International Cooperative Study on Cardiovascular Epidemiology (43)

Cohort	All Men							Men CHD-Free at Entry				
	No. of Men	CHD Mortality			Total Mortality			No. of Men	CHD Mortality		Total Mortality	
		No. of Deaths	Death Rate	O/E^{Δ}	No. of Deaths	Death Rate	O/E^{Δ}		No. of Deaths	Death Rate	No. of Deaths	Death Rate
U.S. Railroad--Switchmen	875	13	164	0.73	39	498	0.87	850	13	165	38	483
U.S. Railroad--Sedentary	1,305	37	260	1.08	65	452	0.78	1,235	27	205	51	381
U.S. Railroad--Other	391	12	321	1.26	20	526	0.85	369	6	166	14	372
East Finland	817	29	377	1.58	61	777	1.34	775	16	220	47	641
West Finland	860	9	106	0.43	50	578	0.96	845	4	44	43	504
Zutphen, Netherlands	878	16	177	0.75	50	556	0.95	864	12	133	46	524
Dalmatia, Yugoslavia	672	3	38	0.17	24	311	0.55	671	3	38	24	311
Slavonia, Yugoslavia	699	7	121	0.38	55	716	1.22	694	7	42	54	704
Velika Krsna, Serbia, Yugoslavia	511	1	16	0.08	23	380	0.73	505	1	16	22	370
Zrenjanin, Serbia, Yugoslavia	516	1	25	0.09	15	280	0.52	508	1	27	13	247
Belgrade Faculty, Serbia, Yugoslavia	538	2	46	0.19	5	96	0.18	532	2	47	5	98
Crevalcore, Italy	993	11	116	0.46	60	607	1.00	982	9	94	56	575
Montegiorgio, Italy	719	5	64	0.30	29	412	0.71	713	3	41	27	392
Rome Railroad, Italy	768	2	31	0.12	24	358	0.57	758	2	31	24	362
Crete, Greece	686	1	12	0.06	10	153	0.26	682	1	12	10	153
Corfu, Greece	529	4	80	0.31	11	219	0.35	526	4	80	11	219
Tanushimaru, Japan	509	4	71	0.32	23	427	0.74	-*	-*	-*	-*	-*
Ushibuka, Japan	504	1	20	0.08	24	482	0.82	-*	-*	-*	-*	-*

(Foot notes for Table 5 are attached.)

U.S. Rai[illegible]ad--Other	391	12	321	1.[illegible]	20	526	0.85	369	6	1[illegible]	1[illegible]
East Finland	817	29	377	1	61	777	1.34	775	16	2	47
West Finland	860	9	106	0.43	50	578	0.96	845	4	44	43
Zutphen, Netherlands	878	16	177	0.75	50	556	0.95	864	12	133	46
Dalmatia, Yugoslavia	672	3	38	0.17	24	311	0.55	671	3	38	24
Slavonia, Yugoslavia	699	7	121	0.38	55	716	1.22	694	7	42	54
Velika Krsna, Serbia, Yugoslavia	511	1	16	0.08	23	380	0.73	505	1	16	22
Zrenjanin, Serbia, Yugoslavia	516	1	25	0.09	15	280	0.52	508	1	27	13
Belgrade Faculty, Serbia, Yugoslavia	538	2	46	0.19	5	96	0.18	532	2	47	5
Crevalcore, Italy	993	11	116	0.46	60	607	1.00	982	9	94	56
Montegiorgio, Italy	719	5	64	0.30	29	412	0.71	713	3	41	27
Rome Railroad, Italy	768	2	31	0.12	24	358	0.57	758	2	31	24
Crete, Greece	686	1	12	0.06	10	153	0.26	682	1	12	10
Corfu, Greece	529	4	80	0.31	11	219	0.35	526	4	80	11
Tanushimaru, Japan	509	4	71	0.32	23	427	0.74	-*	-*	-*	-*
Ushibuka, Japan	504	1	20	0.08	24	482	0.82	-*	-*	-*	-*

(Foot notes for Table 5 are attached.)

for five years,

All rates are per 100,000/ age-standardized with equal weight for each of the age ranges 40-44, 45-49, 50-54, and 55-59, i.e. they are the arithmetic averages of the rates for the four five-year age groups.

$\Delta_{O/E}$ = observed deaths/expected deaths, expected from a five-year life table based on 1962 vital statistics for age-matched U.S. White men.

* No data available.

TABLE 6

Coronary Heart Disease Mortality Ratios
among Current Cigarette Smokers Only
by Amount Smoked Daily
-- American Cancer Society Study of One Million Men and Women (49)

Age and Sex	Non-Smokers	Cigarettes Smoked Daily			
		Under 10	10-19	20-39	40+
Men:					
45 to 54	1.0	2.4	3.1	3.1	3.4
55 to 64	1.0	1.5	1.9	2.0	2.1
65 to 74	1.0	1.3	1.6	1.6	*
75 to 84	1.0	1.2	1.4	1.1	------
Women:					
45 to 54	1.0	0.9	2.0	2.7	------
55 to 64	1.0	1.3	1.6	2.0	------
65 to 74	1.0	1.1	1.4	1.9	------
75 to 84	1.0	----------	----------	----------	------

*Expected deaths were less than 10.

Death Rates and Mortality Ratios for Coronary Heart Disease and Stroke
by Amount of Cigarette Smoking, Sex and Age
American Cancer Society Study of One Million Men and Women (50)

Sex and Age	CORONARY HEART DISEASE					CEREBROVASCULAR DISEASE				
	Never Smoked Cigarettes Regularly	Regularly Smoked Cigarettes: Number smoked daily 1-9	10-19	20-39	40 or more	Never Smoked Cigarettes Regularly	Regularly Smoked Cigarettes: Number smoked daily 1-9	10-19	20-39	40 or more
DEATH RATES										
Males:										
40-49 years	68	100	176	256	375	14	39	16Δ	31	23
50-59 years	257	400	548	616	718	40	78	59	81	96
60-69 years	650	961	1,184	1,241	1,166	168	219	242	272	289
70-79 years	1,730	1,970	2,431	2,573	2,548	650	617	598	792	445Δ
Females:										
40-49 years	13	17	27	47	43Δ	10	15	26	29	57Δ
50-59 years	59	68	140	158	220	27	34	73	72	95Δ
60-69 years	268	279	479	558	542Δ	110	139	236	201	--
70-79 years	979	740	963	1,243	---	487	404	276Δ	622	--
MORTALITY RATIOS*										
Males:										
40-49 years	1.00	1.60	2.59	3.76	5.51	1.00	2.79	1.14Δ	2.21	1.64
50-59 years	1.00	1.59	2.13	2.40	2.79	1.00	1.95	1.48	2.03	2.40
60-69 years	1.00	1.48	1.82	1.91	1.79	1.00	1.30	1.44	1.62	1.72
70-79 years	1.00	1.14	1.41	1.49	1.47	1.00	.95	.92	1.22	.68Δ
Females:										
40-49 years	1.00	1.31	2.08	3.62	3.31Δ	1.00	1.50	2.60	2.90	5.70Δ
50-59 years	1.00	1.15	2.37	2.68	3.73	1.00	1.26	2.70	2.67	3.52Δ
60-69 years	1.00	1.04	1.79	2.08	2.02Δ	1.00	1.26	2.15	1.83	----
70-79 years	1.00	.76	.98	1.27	----	1.00	.83	.57Δ	1.28	----

*The mortality ratio is the observed rate divided by the expected rate.
ΔRates based upon only 5 to 9 deaths.

Table 8

Prevalence of Coronary Heart Disease among Diabetics and Controls by Presence or Absence of Hypertension (56)

Diagnostic Status		No. of Persons	Coronary Heart Disease		P Value -- Chi Square Test
Hypertension	Diabetes				
All	Diabetics	662	122*	184△	<0.001
	Controls	662	65	98	
Hypertensive	Diabetics	244	76	311	<0.001
	Controls	158	25	158	
Not hypertensive	Diabetics	418	46	110	>0.10
	Controls	504	40	79	

*Number of persons.

△Rate per 1,000.

TABLE 9

Number and Proportion per 1,000 of Persons 17 Years of Age and Over in Population, by Cigarette Smoking Status According to Sex and Age: United States, Current Population Survey, June 1966, August 1967 and August 1968

Sex and Age	Date	Number of Persons in Thousands	Cigarette Smoking Status -- Rate Per 1,000				
			Total population	Present smoker	Former smoker	Never smoked	Unknown if ever smoked
BOTH SEXES							
Total, 17 years and over	June 1966	124,500	1,000	396	115	464	25
	Aug. 1967	126,579	1,000	391	123	462	25
	Aug. 1968	128,556	1,000	377	132	469	23
17-24 years	June 1966	22,711	1,000	376	44	557	23
	Aug. 1967	23,377	1,000	370	49	558	24
	Aug. 1968	23,962	1,000	348	58	573	21
25-44 years	June 1966	45,132	1,000	496	117	367	20
	Aug. 1967	45,488	1,000	485	126	369	20
	Aug. 1968	45,985	1,000	471	136	375	17
45-64 years	June 1966	38,960	1,000	402	145	424	30
	Aug. 1967	39,649	1,000	400	152	420	28
	Aug. 1968	40,227	1,000	385	161	427	27
65 years and over	June 1966	17,697	1,000	153	138	680	29
	Aug. 1967	18,064	1,000	160	144	665	31
	Aug. 1968	18,381	1,000	159	152	659	29
MALE							
Total, 17 years and over	June 1966	58,469	1,000	486	172	314	28
	Aug. 1967	59,248	1,000	478	182	314	26
	Aug. 1968	60,073	1,000	459	192	326	23
17-24 years	June 1966	10,529	1,000	444	46	483	27
	Aug. 1967	10,739	1,000	438	52	483	27
	Aug. 1968	10,987	1,000	413	65	500	22
25-44 years	June 1966	21,536	1,000	579	160	239	22
	Aug. 1967	21,733	1,000	563	169	249	20
	Aug. 1968	21,987	1,000	547	178	258	17
45-64 years	June 1966	18,688	1,000	501	219	248	33
	Aug. 1967	18,956	1,000	496	231	244	29
	Aug. 1968	19,169	1,000	473	240	260	27
65 years and over	June 1966	7,717	1,000	246	267	454	32
	Aug. 1967	7,821	1,000	255	278	434	33
	Aug. 1968	7,910	1,000	245	288	434	33
FEMALE							
Total, 17 years and over	June 1966	66,031	1,000	316	65	597	22
	Aug. 1967	67,330	1,000	314	70	593	23
	Aug. 1968	68,483	1,000	305	79	594	22
17-24 years	June 1966	12,182	1,000	316	42	622	20
	Aug. 1967	12,638	1,000	312	47	621	20
	Aug. 1968	12,975	1,000	294	53	634	19
25-44 years	June 1966	23,596	1,000	421	79	483	17
	Aug. 1967	23,755	1,000	413	88	480	19
	Aug. 1968	23,998	1,000	402	98	482	17
45-64 years	June 1966	20,272	1,000	311	76	587	26
	Aug. 1967	20,694	1,000	313	79	581	27
	Aug. 1968	21,039	1,000	305	88	579	27
65 years and over	June 1966	9,980	1,000	81	38	855	26
	Aug. 1967	10,243	1,000	87	42	842	29
	Aug. 1968	10,471	1,000	95	49	829	27

NOTE: For official population estimates for more general use, see U.S. Bureau of the Census reports on the civilian population of the United States in Current Population Reports, Series P-20, P-25 and P-60.

TABLE 10

Cigarette Smoking Status, by Age and Sex, Whites

Chicago Heart Association Detection Project

1967 - 1969

Cigarette Smoking Status	Age-Adjusted Rate Per 1,000*			
	3,262 Men Age 25-44	958 Women Age 25-44	2,137 Men Age 45-64	1,249 Women Age 45-64
Never Smoked	261.5	369.6	245.0	511.3
Ex-Smokers	261.2	171.9	340.7	147.2
<10 Per Day	71.8	109.6	63.8	119.6
≥10 Per Day	405.5	348.9	350.5	221.9
$\frac{\text{Ex-Smokers}}{\text{Ever Smoked}} \times 1{,}000$	353.7	272.7	451.3	301.2

*All rates age-adjusted by five year age groups to U.S. white population 1960.

Table 11

Regression of Coronary Atherosclerosis with Cessation of Atherogenic Diet, Male Rhesus Monkeys (83)

Group	Nutritional Regimen	Luminal Narrowing				
		Main Coronary		Left Anterior Descending	Left Circumflex	Distal Continuation, Right Main
		Left	Right			
1	High Egg Yolk Fat, High Cholesterol -- 17 Months	60 ± 8	56 ± 7	53 ± 8	57 ± 9	65 ± 10
2	High Egg Yolk Fat, High Cholesterol -- 17 Weeks; Low Fat, Low Cholesterol -- 40 Months	17 ± 4	14 ± 3	21 ± 4	22 ± 6	15 ± 5
3	High Egg Yolk Fat, High Cholesterol -- 17 Weeks; High Corn Oil Fat, Low Cholesterol -- 40 Months	25 ± 5	26 ± 3	20 ± 5	23 ± 6	18 ± 5

Values are means ± standard errors.

Table 12

Incidence of New Coronary Heart Disease by Smoking Category: Western Collaborative Group Study, Males 30-49 Years of Age at Entry -- 4 1/2 Years Average Observation Data (44,90)

Smoking Category	Number of Men	Rate per 10,000 Population	
		Adjusted for Concomitant Variables	Not Adjusted
Never smoked	540	36	29
Former cigarette smokers	241	67	92
Pipe and cigar only	406	27	16
1-15 cigarettes	212	51	52
16-25 cigarettes	436	89	92
26 cigarettes and over	425	98	104

Table 13

Effects of Treatment on Morbidity and Mortality in Hypertension -- Male Patients with Diastolic Blood Pressures Averaging 115 - 129 mm. Hg at Entry -- Veterans Administration Cooperative Study on Antihypertensive Agents (77)

Type of Event	Number of Events	
	Placebo 70 Men	Hydrochlorothiazide + Reserpine + Hydralazine 73 Men
Deaths	4	0
Class A events	10	0
Subtotal	14	0
Other treatment failures	7	1
Total terminating events	21	1
Class B events (nonterminating)	6	1
Total	27	2

Average period of observation: 15.7 months for the placebo group, 20.7 months for the active-drup group.

Of the four deaths, two were attributed to dissecting aneurysm, one to ruptured abdominal aortic aneurysm and one was a sudden death.

Class A (terminating) morbid events: hypertensive complications as defined in the protocol which required treatment with known active agents and permanent removal from protocol assigned therapy, including: fundoscopic evidence of grade 3 or 4 hypertensive retinopathy; doubling of blood urea nitrogen to levels above 60 mg./dl.; dissecting aortic aneurysm; cerebrovascular hemorrhage (as opposed to thrombosis); subarachnoid hemorrhage; congestive heart failure persisting despite digitalis and mercurial diuretics; elevation of diastolic blood pressure to 140 mm. Hg or higher on three repeated visits and average rehospitalization diastolic pressure to 130 mm. Hg or higher.

Class B (nonterminating) morbid events: as opposed to class A events, were those which did not require permanent discontinuation of protocol treatments. Patients with developing B events could be treated with known antihypertensive agents for as long as six months, after which protocol treatment had to be reinstituted. Class B events included organic complications associated with atherosclerosis, such as cerebrovascular thrombosis (as contrasted to hemorrhage which was considered a class A event) or myocardial infarction. Congestive heart failure which responded to routine therapy with digitalis or mercurials and did not require antihypertensive agents also was classified as a B event.

POTENTIAL IMPACT OF PRIMARY PREVENTION OF CORONARY HEART DISEASE

(TABLES 14,15,16)

Because of the high incidence and mortality from clinical coronary heart disease, the impact of a program of primary prevention may be substantial. Most coronary heart disease deaths occur within the first few hours after the onset of the clinical event, before adequate medical care is available.* In theory, therefore, the majority of these deaths can be prevented only by preventing the occurrence of the initial event. The impact of a program of primary prevention depends upon three variables:

1. The magnitude of the disease in the community as measured by incidence, prevalence, or mortality.
2. The potential effectiveness of the program in reducing the number of events.
3. The percentage of the population at risk that will accept the program.

The estimated incidence of clinical coronary heart disease per year is 4/1,000 at age 35-44, 10/1,000 at age 45-54, and 20/1,000 age 55-64 for white men. Approximately 20 per cent of the new events will result in deaths and about two-thirds of the deaths will be sudden, i.e., occurring within the first few hours after the event. Incidence data for the black population are not available at present but are probably similar to those for whites.

---

*Studies indicate that from 60-70% of coronary heart disease deaths occur outside the hospital. The median time of survival from onset of attack to death for these patients is about 25 minutes.

Based on current United States population estimates, the incidence and number of deaths from an initial coronary event for white males age 35-64 is shown in Table 11.

The estimated impact of a primary prevention program is shown in Table 12. These projections are based on varying percentages of potential efficacy and the percentage of the population that is included.

Note that even if the effectiveness of primary prevention is small (10%) but is available to a large segment of the population, the impact in terms of reduction of mortality and morbidity will be substantial. Thus, the potential for primary prevention of coronary heart disease when based on a community effort as recommended in this report is very great.

Table 14

Estimated Number of New Cases and Deaths from an Initial Coronary Event for White Males (92)

Age	Population	Number of Cases	Number of Deaths*
35-44	10,000,000	40,000	8,000
45-54	10,000,000	100,000	20,000
55-64	8,000,000	160,000	32,000
TOTAL	28,000,000	300,000	60,000

* Deaths following initial event only.

Table 15

Estimation of Number of Events and Deaths that Would be Prevented Based on Effectiveness of the Procedure and Percentage of the Population Included: White Males Age 35-64 (92)

Percentage of Population Accepting Modification	Potential Effectiveness -- and Number of Events Prevented							
	10 Percent Effective		20 Percent Effective		50 Percent Effective		100 Percent Effective	
	Cases Prevented	Deaths Prevented	Cases Prevented	Deaths Prevented	Cases Prevented	Deaths Prevented	Cases Prevented	Deaths Prevented
10 Percent	3,000	600	6,000	1,200	15,000	3,000	30,000	6,000
20 Percent	6,000	1,200	12,000	2,400	30,000	6,000	60,000	12,000
50 Percent	15,000	3,000	30,000	6,000	75,000	15,000	150,000	30,000
00 Percent	30,000	6,000	60,000	12,000	150,000	30,000	300,000	60,000

Table 16

Estimated Relative Reduction in Coronary Heart Disease Incidence (v) Associated with Relative Reduction in Serum Cholesterol (u) (76)

Relative decrease in serum cholesterol (u)	Relative decrease in coronary heart disease incidence (v)	Relative decrease in serum cholesterol (u)	Relative decrease in coronary heart disease incidence (v)
.01	.026	.26	.551
.02	.052	.27	.567
.03	.078	.28	.583
.04	.103	.29	.598
.05	.128	.30	.613
.06	.152	.31	.627
.07	.176	.32	.642
.08	.199	.33	.655
.09	.222	.34	.669
.10	.244	.35	.682
.11	.267	.36	.695
.12	.288	.37	.707
.13	.310	.38	.720
.14	.330	.39	.731
.15	.351	.40	.743
.16	.371	.41	.754
.17	.391	.42	.765
.18	.410	.43	.776
.19	.429	.44	.786
.20	.448	.45	.796
.21	.466	.46	.806
.22	.484	.47	.815
.23	.501	.48	.824
.24	.518	.49	.833
.25	.535	.50	.842

Note: Values of v were obtained from the relationship, $v = 1 - (1-u)^{2.66}$ described in reference (93).

These data illustrate the potential for prevention, and the possibility of achieving declines in CHD morbidity and mortality as projected in the preceding table (Table 15). For example, a ten per cent reduction in serum cholesterol level of the U. S. population (u = .10) is estimated to yield a 24.4 per cent decrease in CHD incidence (v= .244).

Similar estimates can readily be made of the potential for prevention inherent in continuing further decreases in the prevalence of cigarette smoking in the

Table 17

White and Negro Adults with Blood Pressures of at Least 160 Systolic or 95 Diastolic, by Sex and Age: United States, 1960-62 -- U.S. National Health Examination Survey (99)

Sex and Age	Systolic at least 160 mm. Hg		Diastolic at least 95 mm. Hg		Systolic at least 160 mm. Hg or Diastolic 95 mm.	
	White	Negro	White	Negro	White	Negro
	Prevalance Rate per 1,000					
Both sexes-18-79 years	105	188	87	220	147	276
Men						
Total-18-79 years	86	168	91	226	136	276
18-24 years	2	-	17	19	17	19
25-34 years	7	46	34	115	37	125
35-44 years	39	162	109	259	118	265
45-54 years	87	108	138	295	173	308
55-64 years	159	294	119	316	214	446
65-74 years	261	632	123	405	273	660
75-79 years	391	598	133	212	402	598
Women						
Total-18-79 years	123	204	83	215	156	276
18-24 years	-	7	8	34	8	34
25-34 years	7	34	21	85	23	85
35-44 years	23	143	53	241	62	256
45-54 years	107	308	109	343	155	419
55-64 years	253	338	164	367	310	410
65-74 years	454	685	179	321	486	710
75-79 years	427	694	120	263	449	694

U. S. population (cf. Tables 6, 7, 9, 12 and Figs. 11, 16, 21). Similar resonable estimates are also possible in relation to the potential impact of control of hypertension, and of multiple risk factors for the substantial number very high risk persons in the U. S. population (cf. Tables 8, 13, 17 and Figs. 9-11, 13, 15, 22, 23).

Legends

Figure 1 -- Death rates for Arteriosclerotic Heart Disease and Myocardial Degeneration by age, color, and sex: United States, 1940-60 (3).

Figure 4 -- International Atherosclerosis Project; extent of aorta and coronary atherosclerosis at autopsy, per cent surface involved, men and women in 19 populations from five continents (22).

Figure 5 -- International cooperative study on Epidemiology of Cardiovascular Disease / men originally age 40-59 in seven countries; age-standardized prevalence rate of CHD and age-standardized 5-year incidence rate of CHD among the men CHD-free at entry. E = East Finland; U = U.S. railroad; W = West Finland; N = Zutphen, The Netherlands; C = Crevalcore, Italy; R = Rome railroad, Italy; M = Montegiorgio, Italy; S = Slavonia, Yugoslavia; B = Belgrade, Yugoslavia; Z = Zrenjanin, Yugoslavia; G = Corfu, Greece; K = Crete, Greece (40).

Figure 6 -- International cooperative study on Epidemiology of Cardiovascular Disease / men originally age 40-59 in seven countries; average per cent of total calories from saturated fatty acids in the diets, plotted against the median serum cholesterol values of the cohorts; for identification of the cohorts, see legend for Figure 5 (40).

Figure 7 -- International cooperative study on Epidemiology of Cardiovascular Disease / men originally age 40-59 in seven countries; age-standardized 5-year incidence rates for fatal CHD (upper figure) and for all myocardial infarctions (nonfatal + fatal) (lower figure) among men CHD-free at entry, plotted against percentage of total calories provided by saturated fatty acids in the diet; for identification of the cohorts, see legend for Figure 5 (40).

Figure 8 -- International cooperative study on Epidemiology of Cardiovascular Disease / men originally age 40-59 in seven countries; age-standardized 5-year incidence rates for fatal CHD (upper figure) and and for all myocardial infarctions (nonfatal + fatal) (lower figure) among men CHD-free at entry, plotted against median serum cholesterol concentrations; for identification of the cohorts, see legend for Figure 5 (40).

Figure 11 -- East Orange, New Jersey Veterans Administration Hospital study; degree of coronary atherosclerosis at autopsy, men age 45-59 at death, men who had never smoked regularly and those who had been current cigarette smokers prior to death (51,54).

Figure 13 -- Tecumseh, Michigan study; blood glucose level one hour after 100 gm. oral load, blood pressure, serum cholesterol and relative prevalence of coronary heart disease in men (upper graph) and women (lower graph) (57,58).

Figure 14 -- The Framingham study; casual blood sugar and risk of major manifestations of atherosclerosis, men and women age 30-62 at entry; 12 year follow-up data (59).

Figure 15 -- Veterans Administration Cooperative Study on Antihypertensive Agents; changes in systolic (graph on left) and diastolic (graph on right) blood pressure in control group of patients given placebos and experimental group of patients treated with hydrochlorothiazide plus reserpine plus hydralazine (active drugs); men with average diastolic pressure at entry in the range 115-139 mm. Hg (upper graph), and 90-114 mm. Hg (lower graph) (77,78).

Figure 16 -- Percent distribution of the population age 18 years and over, by cigarette smoking status according to sex, 1955 and 1966 (79).

Figure 18 -- Los Angeles Veterans Administration Domiciliary study; graph on left -- cumulative incidence curves for all "hard" end points (definite myocardial infarction, sudden death due to CHD, definite cerebral infarction, ruptured aneurysm, amputation). Points are computed by the life table method and plotted as cumulative incidence rates ± the standard error; where overlap would otherwise occur, standard error is plotted in one direction only, and at some points it is omitted for clarity. "Free of existing complications" refers to any definite or possible manifestation of atherosclerosis, at any site, recognized at the initial examination. Stratification by age was into two groups of equal size; the cut point was 65.5 years. The P values refer to comparisons of entire curves. CON. = control; EXP. = experimental. The graph on the right presents cumulative combined incidence of sudden death due to CHD, definite myocardial infarction (silent or overt), and definite cerebral infarction, after factorial stratification by age at entry and baseline serum cholesterol concentration (85).

Figure 19 -- Finnish mental hospital study; incidence of ECG patterns attributable to CHD, men age 34-64 at entry, 1959-65 (86).

Figure 20 -- The New York Anti-Coronary Club study; CHD incidence in the active experimental, inactive experimental and comparison groups, men age 40-59 at entry, free of clinical CHD (87).

Figure 21 -- U.S. veterans study; coronary heart disease mortality rates of non-smokers, current smokers of 20-39 cigarettes per day, and ex-smokers of 20-39 cigarettes per day, age 35-44 and 45-54; ex-smokers stopped for reasons other than doctors' orders; rates are per hundred thousand per year (48,54).

Figure 22 -- Veterans Administration Cooperative Study on Antihypertensive Agents; estimated cumulative incidence of morbidity over a 5-year period as calculated by life table method; terminating morbid events (upper graph) and all morbid events (lower graph); men with average diastolic blood pressures 90-114 mm. Hg at entry (78).

Figure 23 -- Chicago Coronary Prevention Evaluation Program (CPEP); 7-year cumulative age-adjusted mortality rates of high-risk disease-free men age 40-59 at entry, Pooling Project and CPEP cohorts; all CPEP data as of March 31, 1970; of the total cohort of 519 men in the CPEP study, 377 were continuing active participants (non-dropouts), 142 were dropouts as of March 31, 1970; of the men in the Pooling Project, 2,916 met CPEP age, medical and risk factor criteria; all rates age-adjusted by 5-year age groups to U.S. male population.

Legends

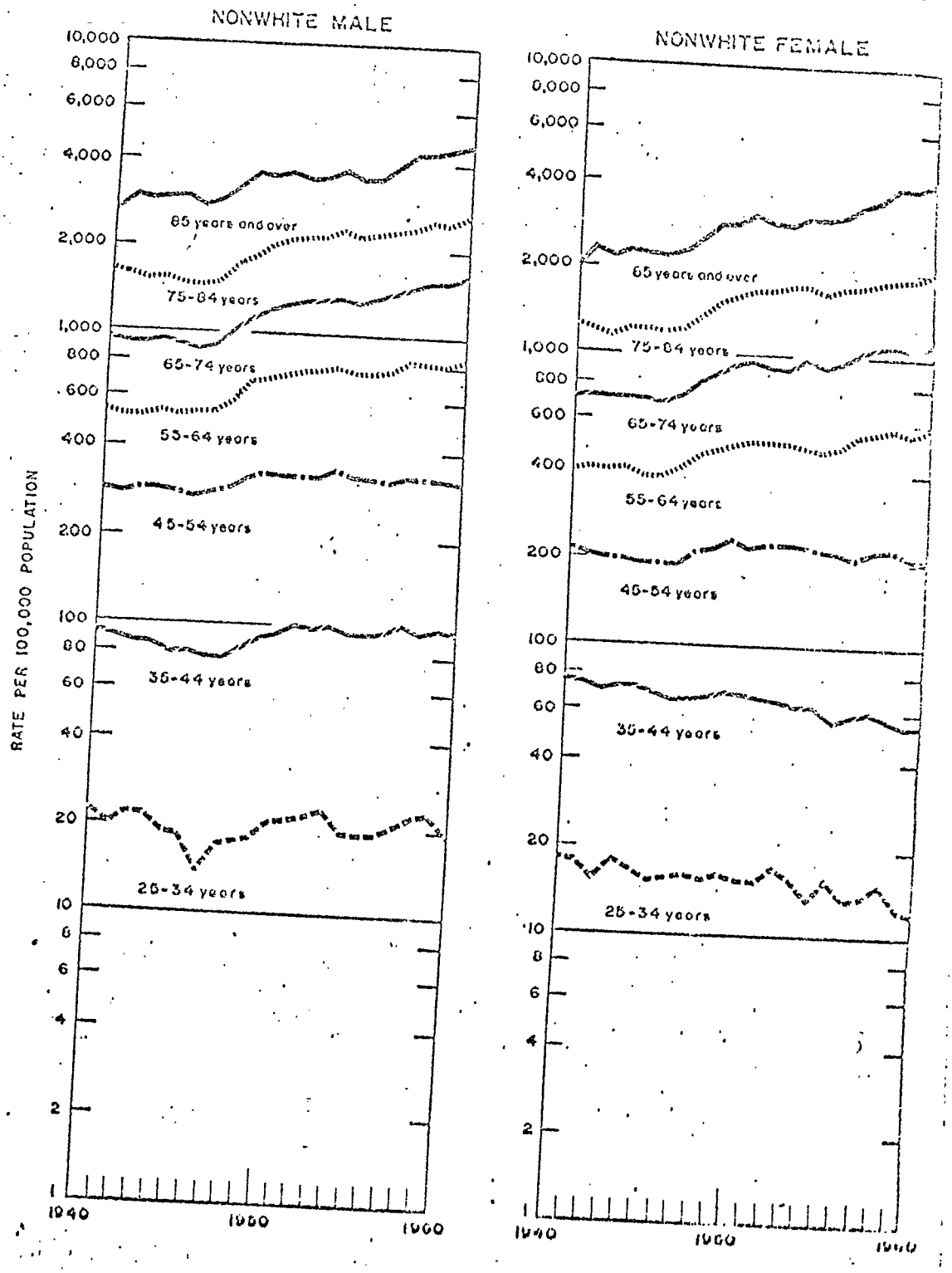
Fig. 2 -- National cooperative Pooling Project; risk of experiencing sudden death, any coronary death, any major coronary event before age 60; U.S. white males age 30-59 at entry; 10-year findings (6, 6a-k).

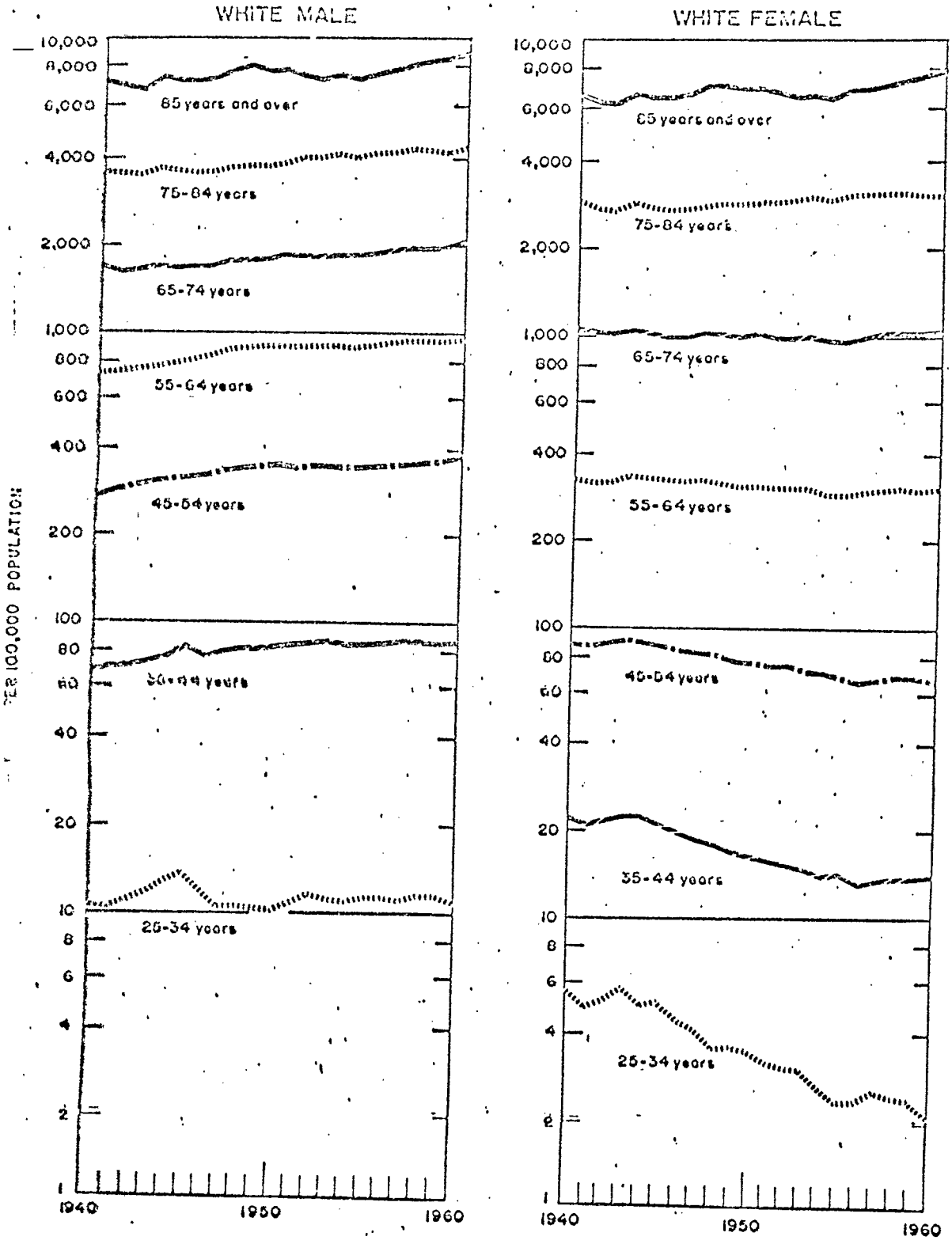
Fig. 3 -- National cooperative Pooling Project; serum cholesterol level at entry and 10-year age-adjusted rates per 1,000 men for: any major coronary event, sudden death, any coronary death, death from all causes; any major coronary event includes nonfatal MI, fatal MI, sudden death due to CHD; U.S. white males age 30-59 at entry; all rates age-adjusted by 10-year age groups to the U.S. white male population, 1960 (6,6a-k).

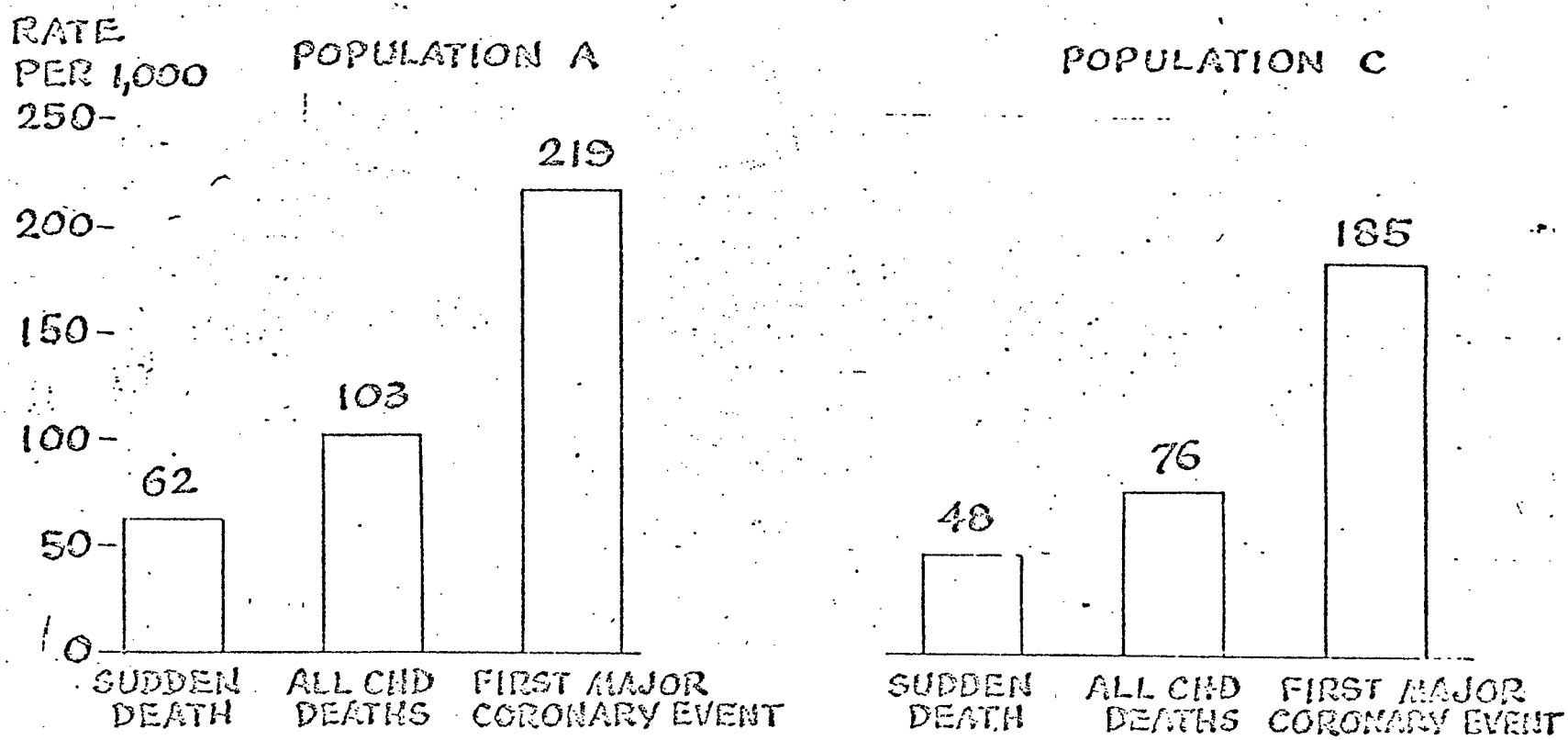
Fig. 9 -- National cooperative Pooling Project; diastolic blood pressure level at entry and 10-year age-adjusted rates per 1,000 men for: any major coronary event, sudden death, any coronary death (upper graph), stroke death, death from all causes (lower graph); any major coronary event includes nonfatal MI, fatal MI, sudden death due to CHD; U.S. white males age 30-59 at entry; all rates age-adjusted by 10-year age groups to the U.S. white male population, 1960 (6, 6a-k).

Fig. 10 -- National cooperative Pooling Project; smoking status at entry and 10-year age-adjusted rates per 1,000 men for: any major coronary event, sudden death, any coronary death, death from all causes; any major coronary event includes nonfatal MI, fatal MI, sudden death due to CHD; U.S. white males age 30-59 at entry; all rates age-adjusted by 10-year age groups to the U.S. white male population 1960; the upper two graphs present the data on smoking status at entry and the 10-year age-adjusted rates per 1,000 irrespective of other risk factors; the lower two graphs present these rates for non-cigarette smokers vs. cigarette smokers at entry with simultaneous control of blood pressure and serum cholesterol level; for the latter analysis, the following cutting points were used: cigarette smoking (S) -- any use at entry, serum cholesterol (C) -- $\geq$ 250 mg./dl., diastolic blood pressure (H) -- $\geq$ 90 mm.Hg.

Fig. 12 -- National cooperative Pooling Project; hypercholesterolemia, hypertension, cigarette smoking and 10-year age-adjusted rates per 1,000 men for: any major coronary event, sudden death, any coronary death, death from all causes; any major coronary event includes nonfatal MI, fatal MI, sudden death due to CHD; U.S. white males, age 30-59 at entry; all rates age-adjusted by 10-year age groups to the U.S. white male population, 1960 (6, 6a-k).

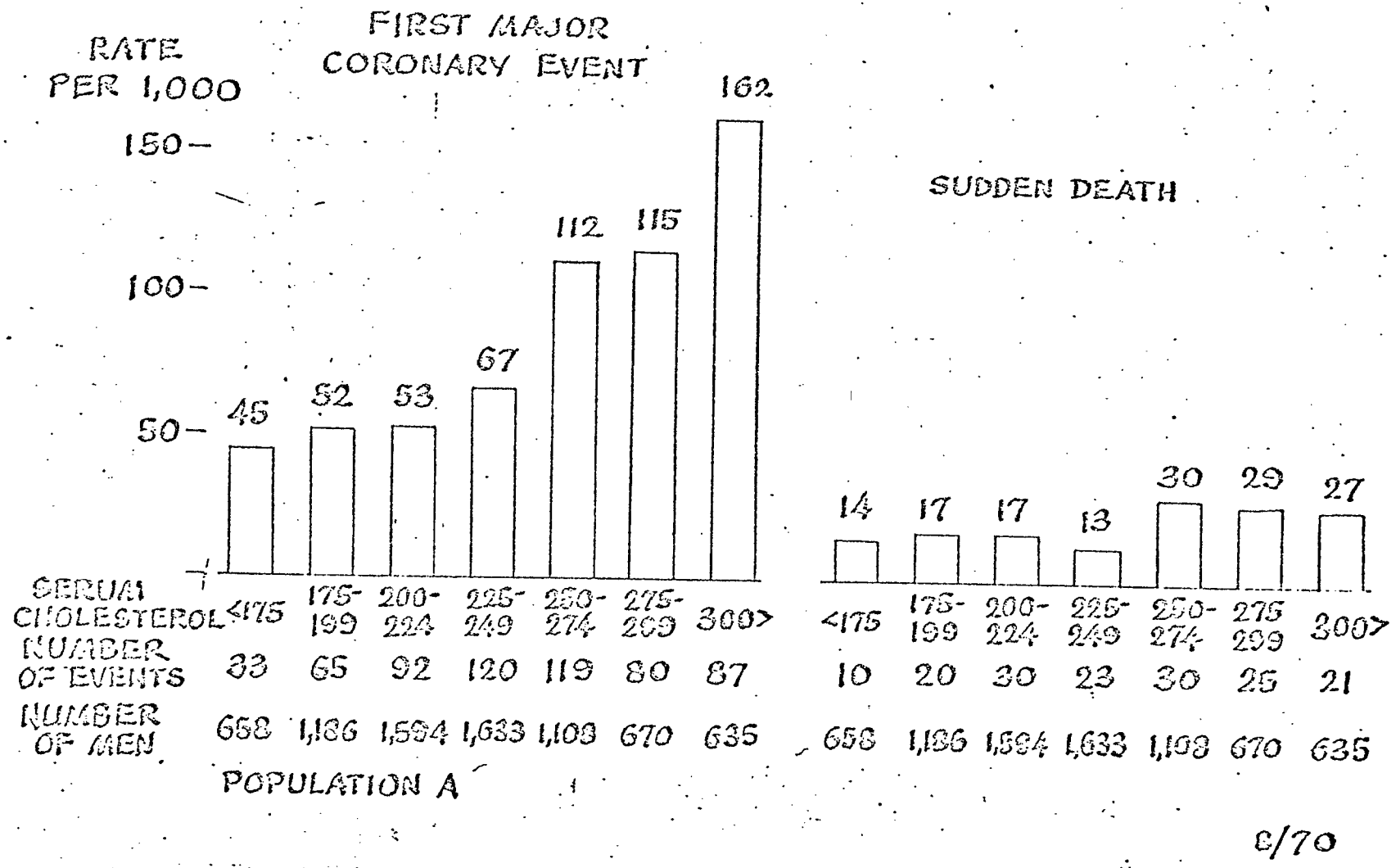

NONWHITE MALE
NONWHITE FEMALE
RATE PER 100,000 POPULATION
10,000
8,000
6,000
4,000
2,000
1,000
800
600
400
200
100
80
60
40
20
10
8
6
4
2
1
65 years and over
75-84 years
65-74 years
55-64 years
45-54 years
35-44 years
25-34 years
1940
1950
1960


WHITE MALE
WHITE FEMALE
PER 100,000 POPULATION
10,000
8,000
6,000
4,000
2,000
1,000
800
600
400
200
100
80
60
40
20
10
8
6
4
2
1
65 years and over
75-84 years
65-74 years
55-64 years
45-54 years
35-44 years
25-34 years
1940
1950
1960



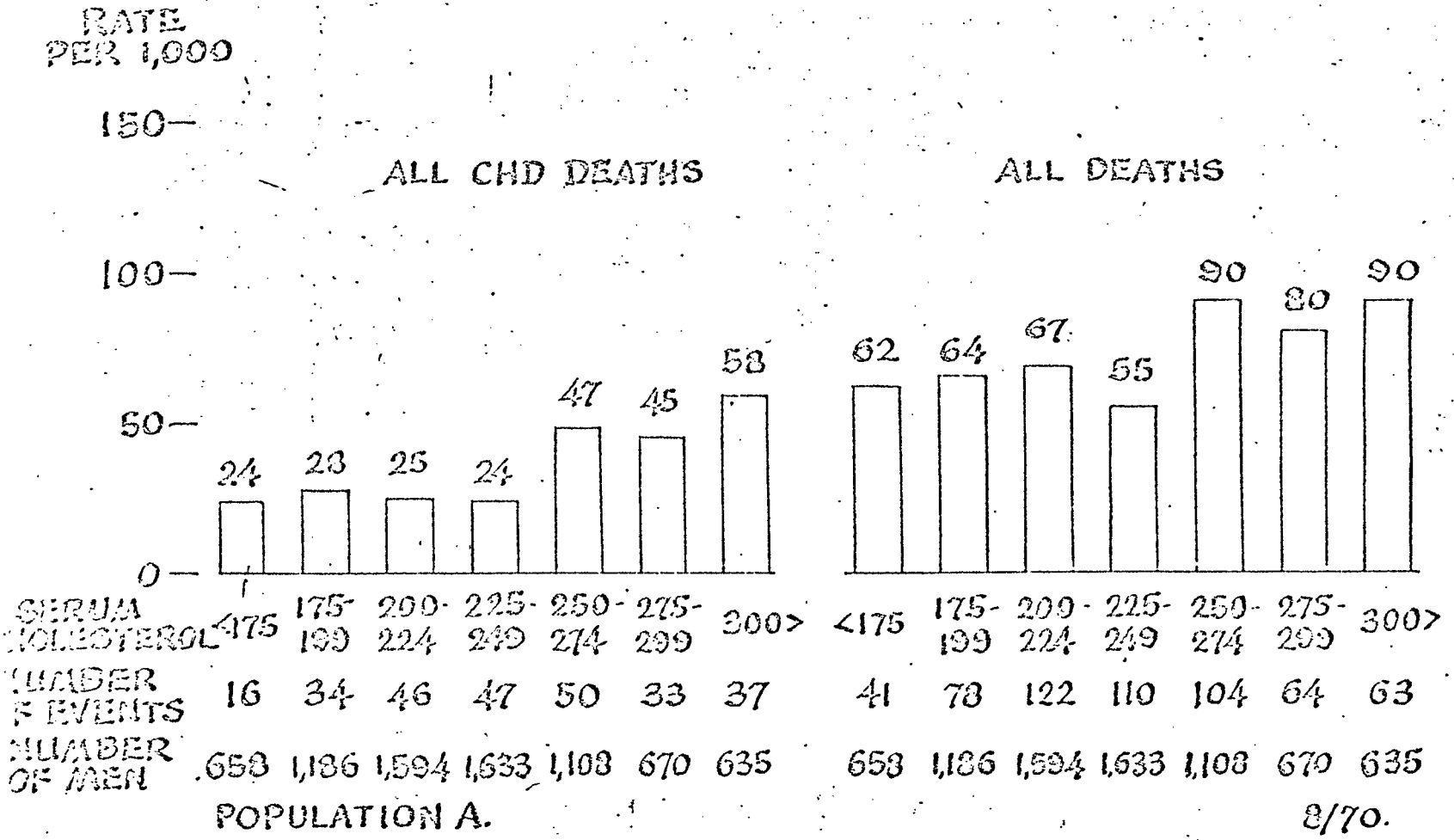
POPULATION A: 7,594 MEN FREE OF DEFINITE CHD AT ENTRY.
POPULATION C: 6,355 MEN FREE OF ANY MAJOR LIFE-LIMITING DISEASE, INCLUDING CV DISEASE, AND WITH NORMAL ECG AT ENTRY.

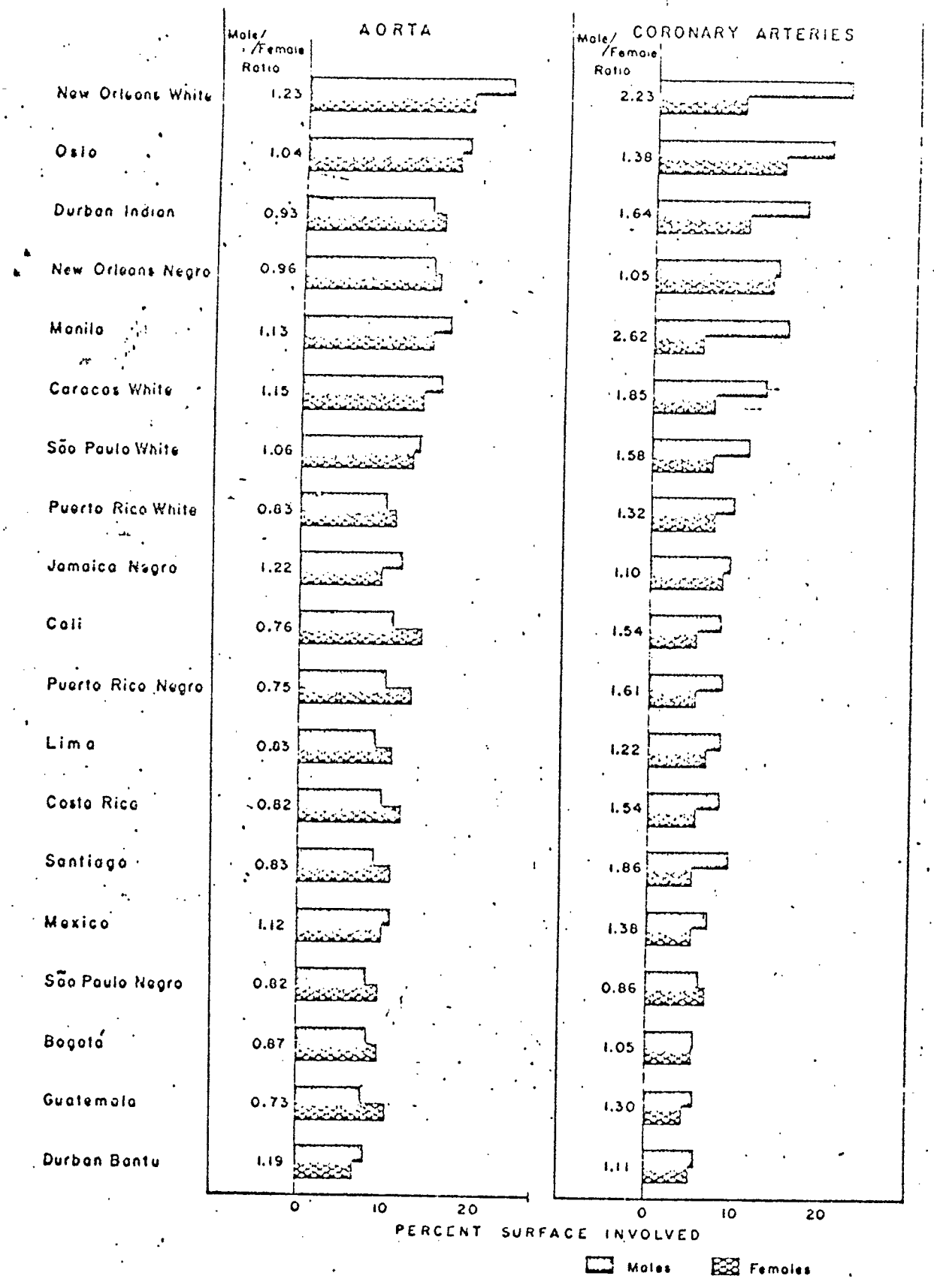
8/70



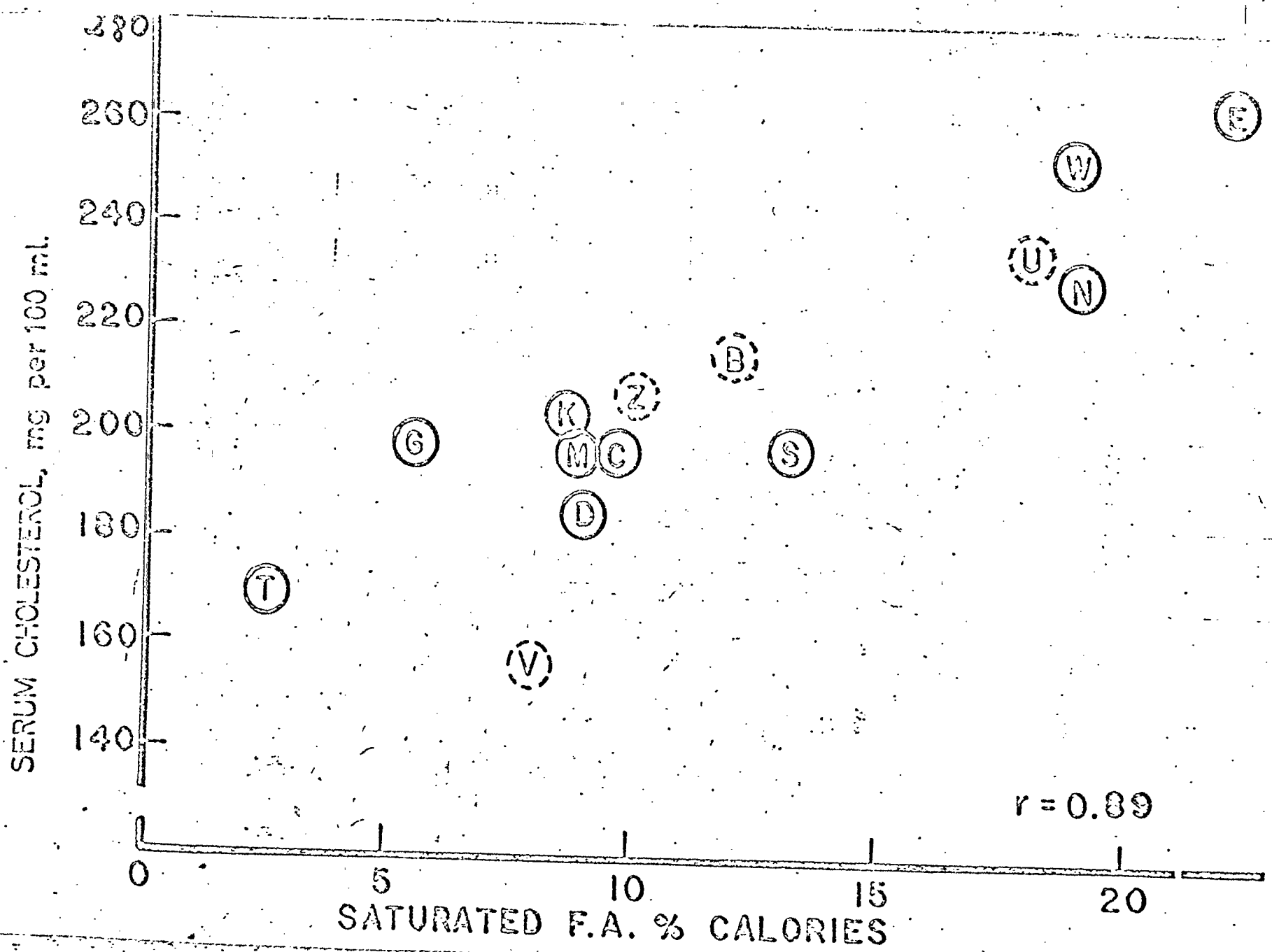
POPULATION A

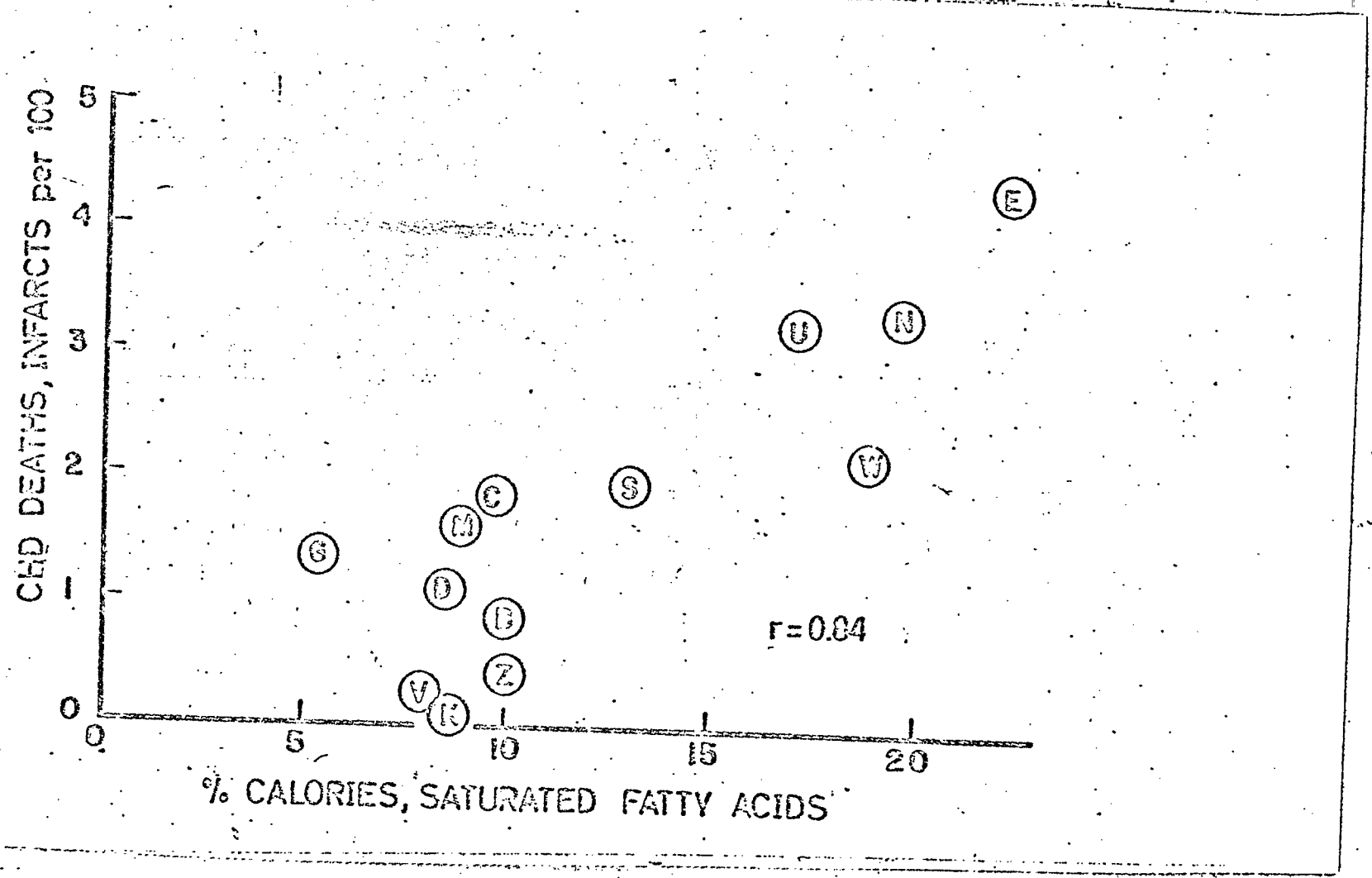
C/70

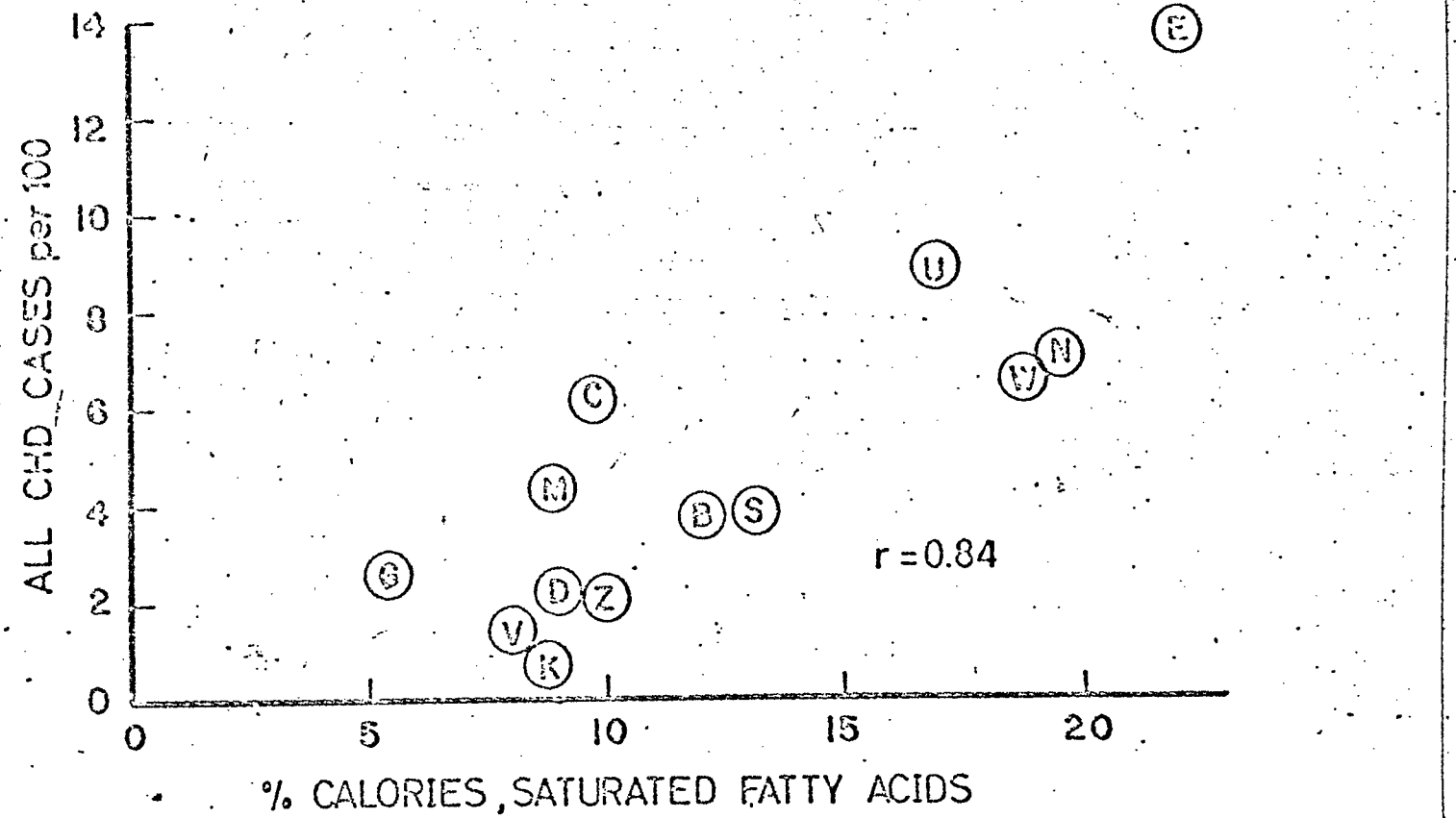

RATE PER 1,000
150
100
50
0
ALL CHD DEATHS
ALL DEATHS
24
23
25
24
47
45
58
62
64
67
55
90
80
90
SERUM CHOLESTEROL
<175
175-199
200-224
225-249
250-274
275-299
300>
NUMBER OF EVENTS
16
34
46
47
50
33
37
41
78
122
110
104
64
63
NUMBER OF MEN
658
1,186
1,594
1,633
1,108
670
635
POPULATION A.
8/70.

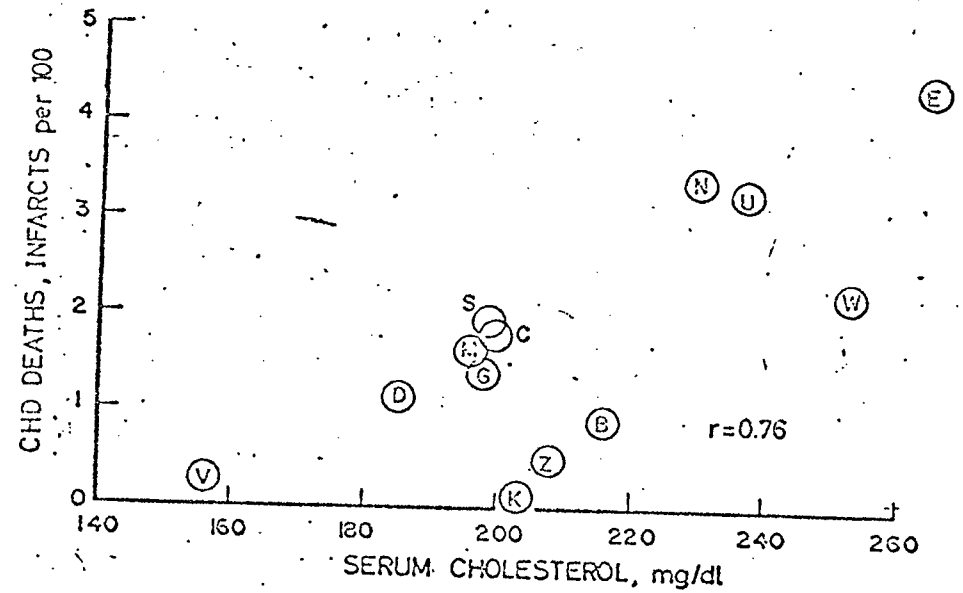

AORTA
CORONARY ARTERIES
Male/Female Ratio
Male/Female Ratio
New Orleans White
Oslo
Durban Indian
New Orleans Negro
Manila
Caracas White
São Paulo White
Puerto Rico White
Jamaica Negro
Cali
Puerto Rico Negro
Lima
Costa Rica
Santiago
Mexico
São Paulo Negro
Bogotá
Guatemala
Durban Bantu
1.23
1.04
0.93
0.96
1.13
1.15
1.06
0.83
1.22
0.76
0.75
0.83
0.82
0.83
1.12
0.82
0.87
0.73
1.19
2.23
1.38
1.64
1.05
2.62
1.85
1.58
1.32
1.10
1.54
1.61
1.22
1.54
1.86
1.38
0.86
1.05
1.30
1.11
0
10
20
0
10
20
PERCENT SURFACE INVOLVED
Males
Females

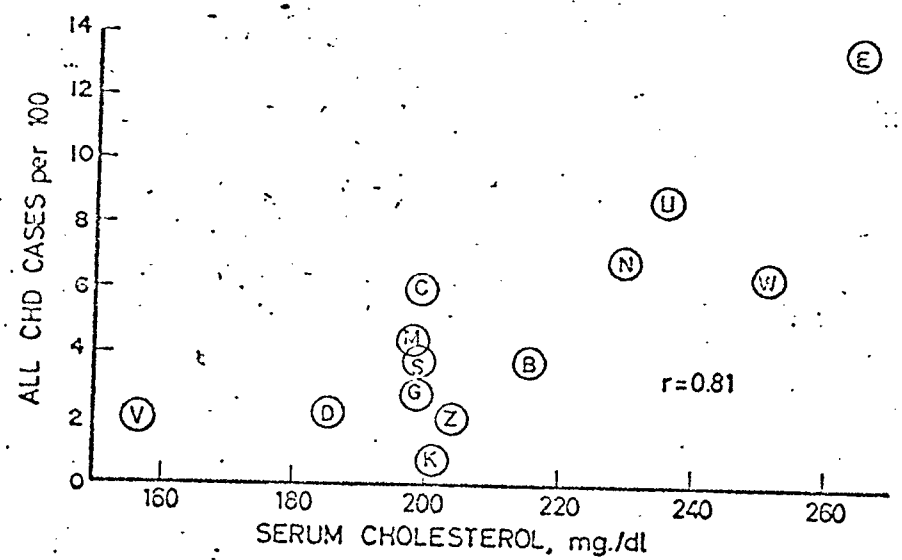
5-YEAR INCIDENCE %
0
2
4
6
8
10
12
14
0
1
2
3
4
5
6
E
U
W
N
C
R
M
S
B
D
Z
V
r = 0.84

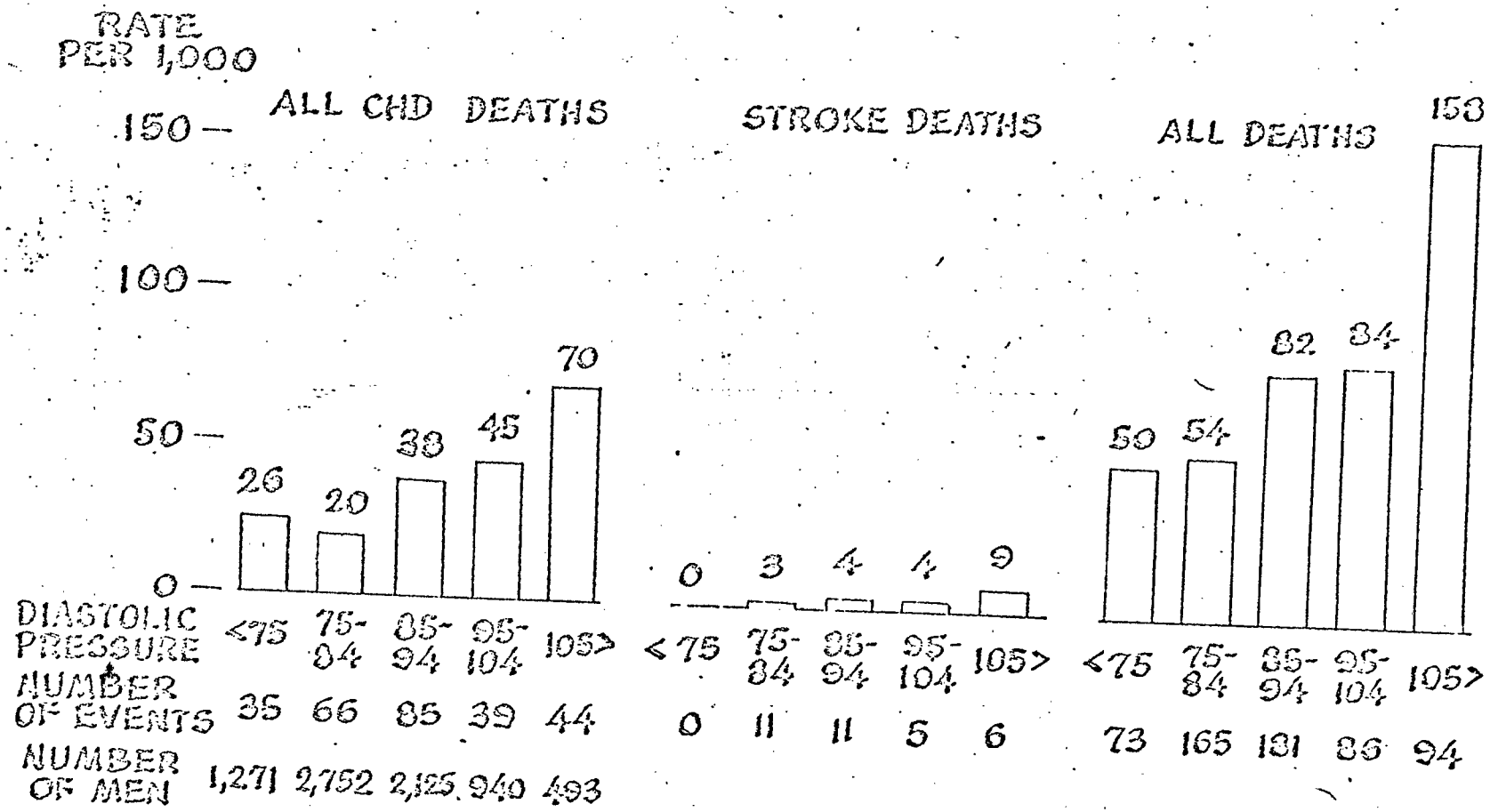

280
260
240
220
200
180
160
140
SERUM CHOLESTEROL, mg per 100 ml.
E
W
U
N
B
Z
K
G
M
C
S
D
T
V
r = 0.89
0
5
10
15
20
SATURATED F.A. % CALORIES

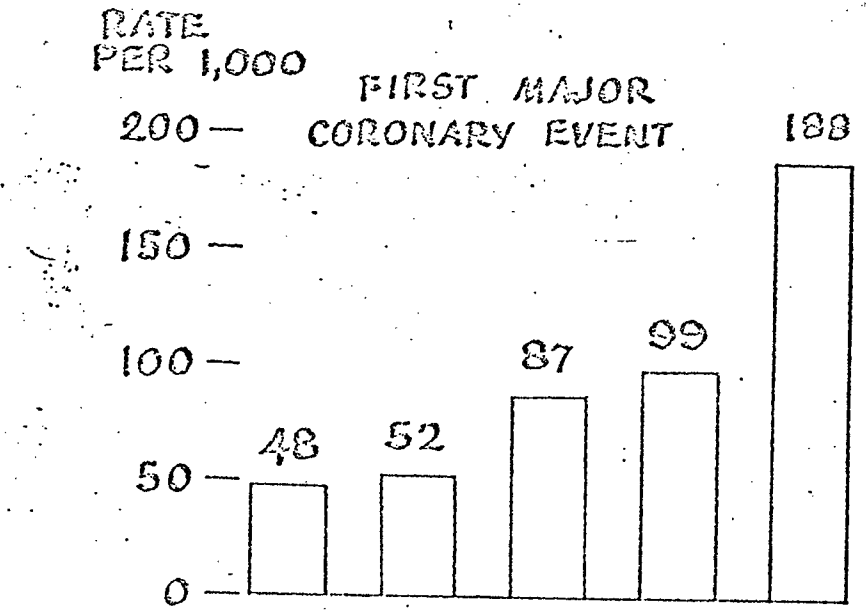

CHD DEATHS, INFARCTS per 100
5
4
3
2
1
0
0
5
10
15
20
% CALORIES, SATURATED FATTY ACIDS
r=0.84
E
U
N
W
S
C
M
G
D
B
Z
V
K


ALL CHD CASES per 100
14
12
10
8
6
4
2
0
0
5
10
15
20
% CALORIES, SATURATED FATTY ACIDS
r = 0.84
E
U
W
N
C
M
B
S
G
D
Z
V
K


CHD DEATHS, INFARCTS per 100
0
1
2
3
4
5
140
160
180
200
220
240
260
SERUM CHOLESTEROL, mg/dl
r=0.76
E
N
U
W
S
C
M
G
D
B
Z
V
K

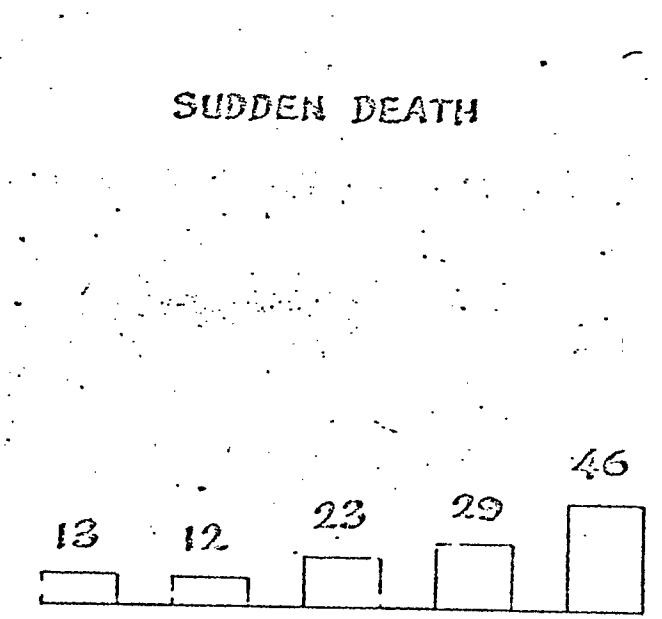

ALL CHD CASES per 100
0
2
4
6
8
10
12
14
160
180
200
220
240
260
SERUM CHOLESTEROL, mg./dl
r=0.81
E
U
N
W
C
M
S
G
B
D
Z
V
K


RATE PER 1,000
ALL CHD DEATHS
STROKE DEATHS
ALL DEATHS
150
100
50
0
26
20
38
45
70
0
3
4
4
9
50
54
82
84
153
DIASTOLIC PRESSURE
<75
75-84
85-94
95-104
105>
NUMBER OF EVENTS
35 66 85 39 44
0 11 11 5 6
73 165 131 86 94
NUMBER OF MEN
1,271 2,752 2,125 940 493
POPULATION A
8/70



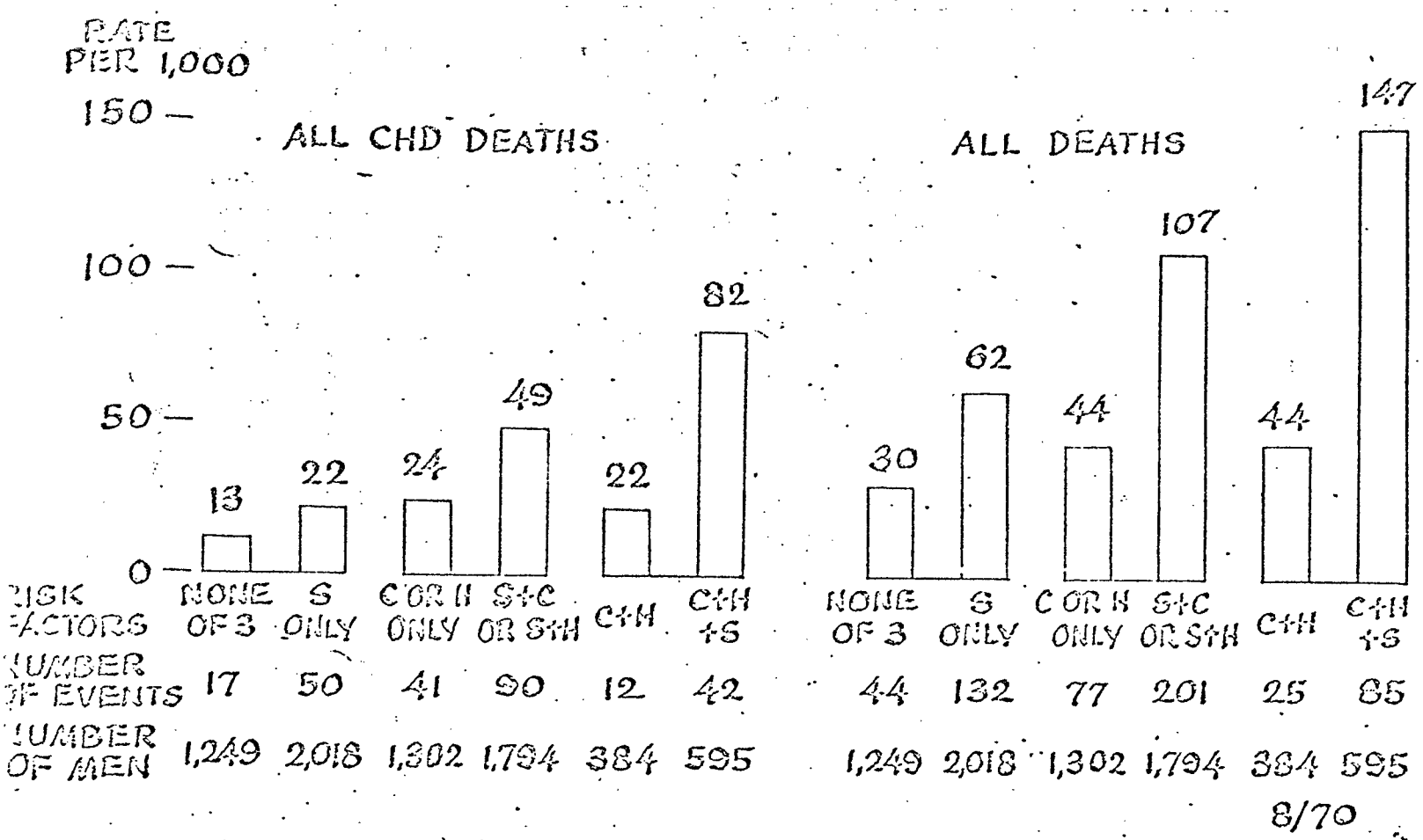
DIASTOLIC PRESSURE	<75	75-85	85-94	95-104	105>
NUMBER OF EVENTS	70	170	186	89	90
NUMBER OF MEN	1,271	2,752	2,125	940	493

POPULATION A

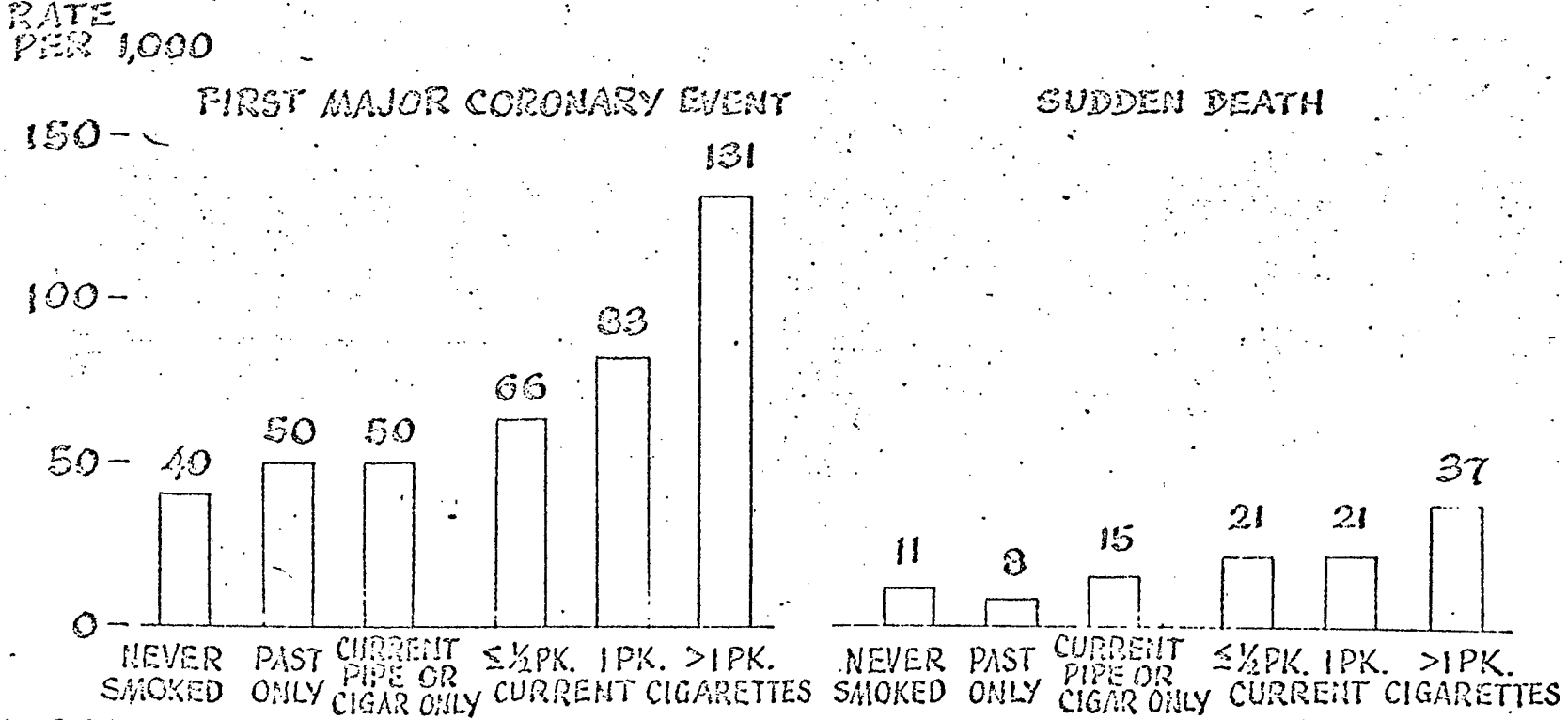


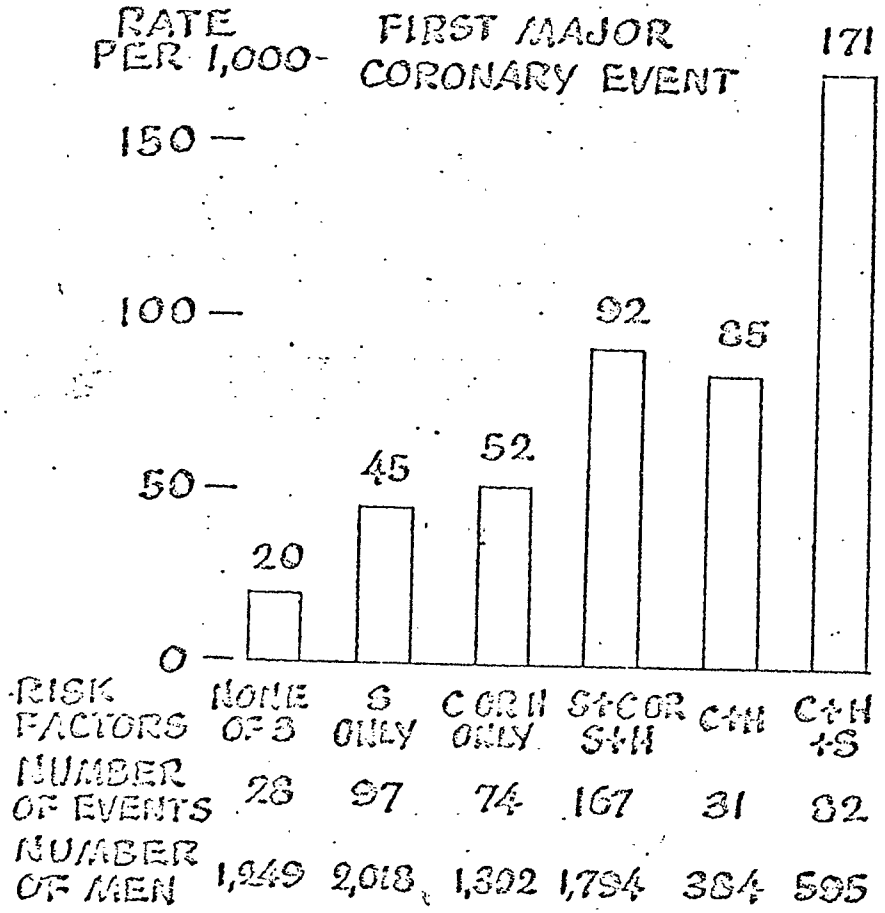
	<75	75-84	85-94	95 104	105>
	16	41	50	28	28
	1,271	2,752	2,125	940	493

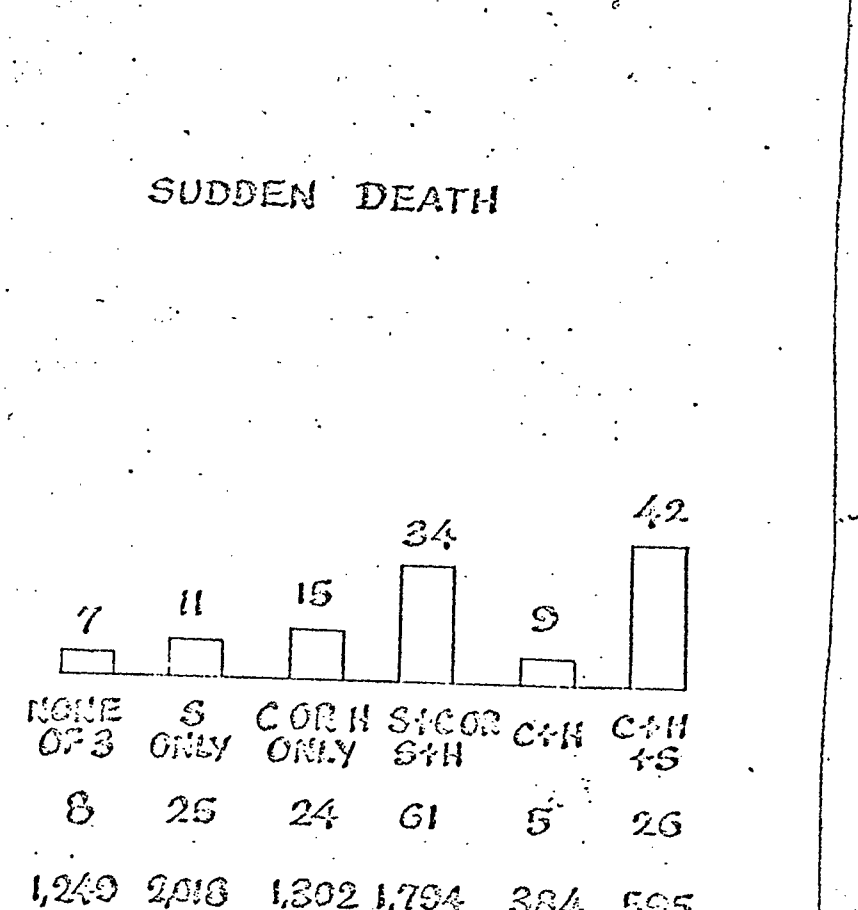
8/70


RATE PER 1,000
150
100
50
0
ALL CHD DEATHS
13
22
24
49
22
82
ALL DEATHS
30
62
44
107
44
147
RISK FACTORS
NONE OF 3
S ONLY
C OR H ONLY
S+C OR S+H
C+H
C+H +S
NUMBER OF EVENTS
17
50
41
90
12
42
44
132
77
201
25
85
NUMBER OF MEN
1,249
2,018
1,302
1,794
384
595
1,249
2,018
1,302
1,794
384
595

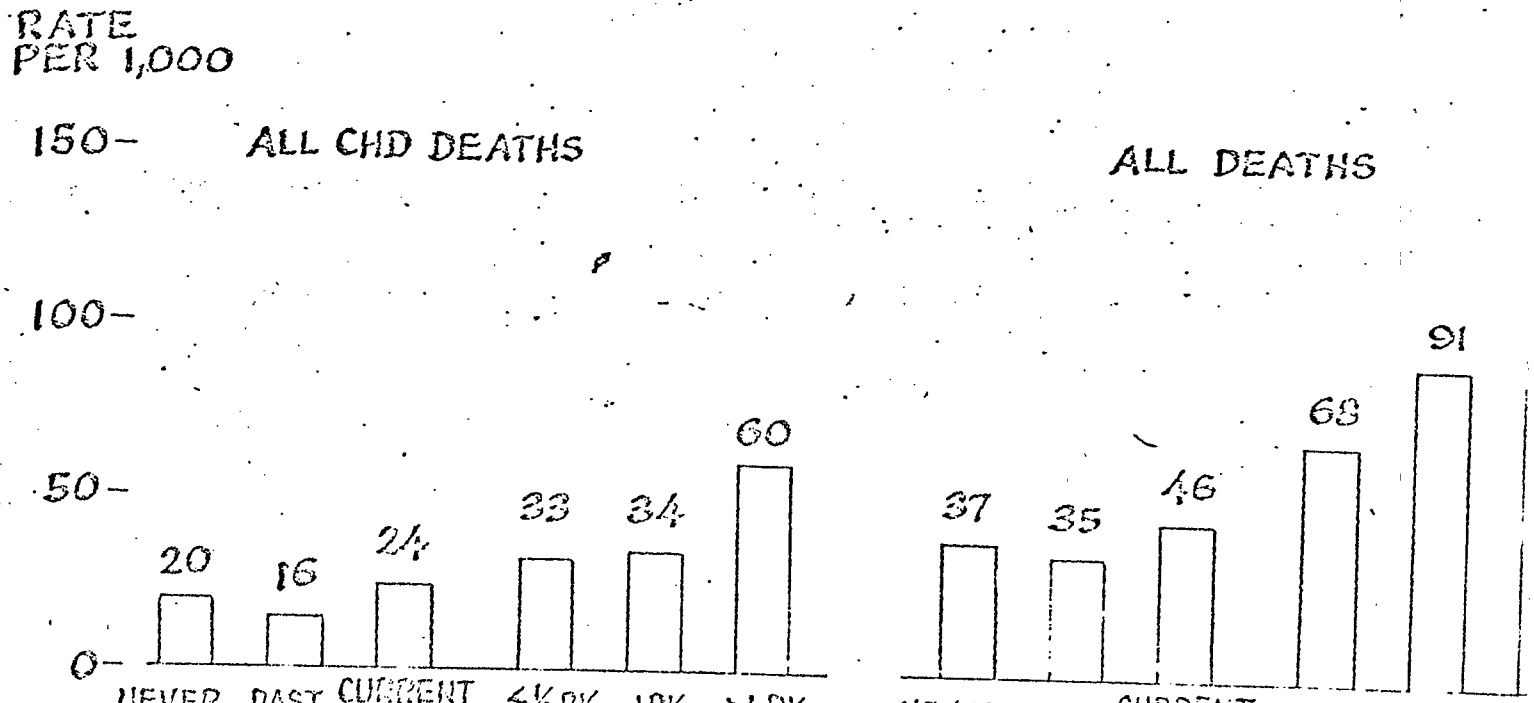
8/70


RATE PER 1,000
FIRST MAJOR CORONARY EVENT
SUDDEN DEATH
150
100
50
0
40
50
50
66
83
131
11
8
15
21
21
37
NEVER SMOKED
PAST ONLY
CURRENT PIPE OR CIGAR ONLY
≤½PK. CURRENT
1PK.
>1PK. CIGARETTES
NUMBER OF EVENTS
53 51 54 72 205 154
15 9 13 23 50 44
NUMBER OF MEN
1,188 804 878 981 2,330 1,146
POPULATION A
8/70

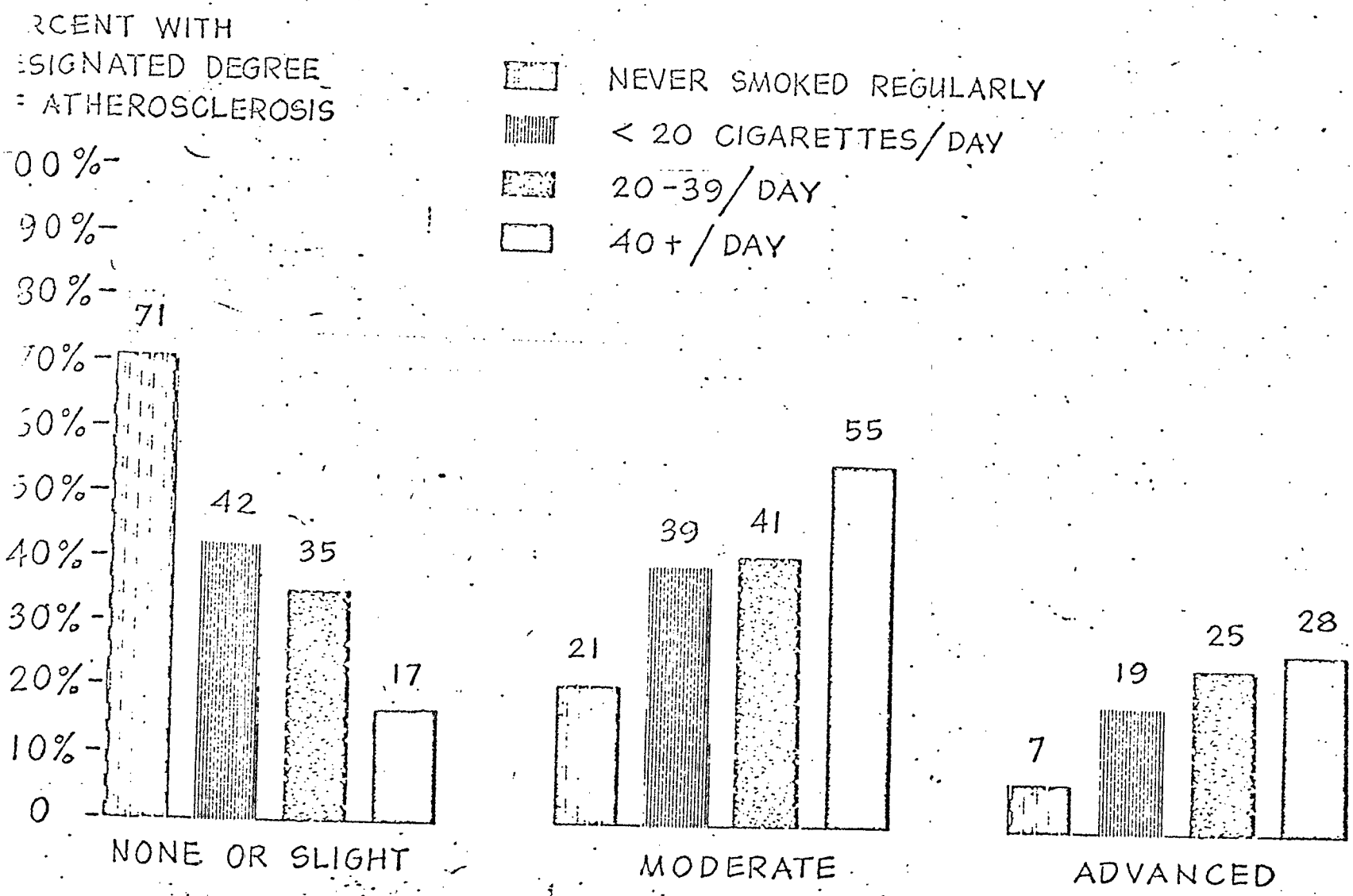

RATE PER 1,000-
FIRST MAJOR CORONARY EVENT
150
100
50
0
20
45
52
92
85
171
RISK FACTORS
NONE OF 3
S ONLY
C OR H ONLY
S+C OR S+H
C+H
C+H +S
NUMBER OF EVENTS
28
97
74
167
31
82
NUMBER OF MEN
1,249
2,018
1,302
1,794
384
595

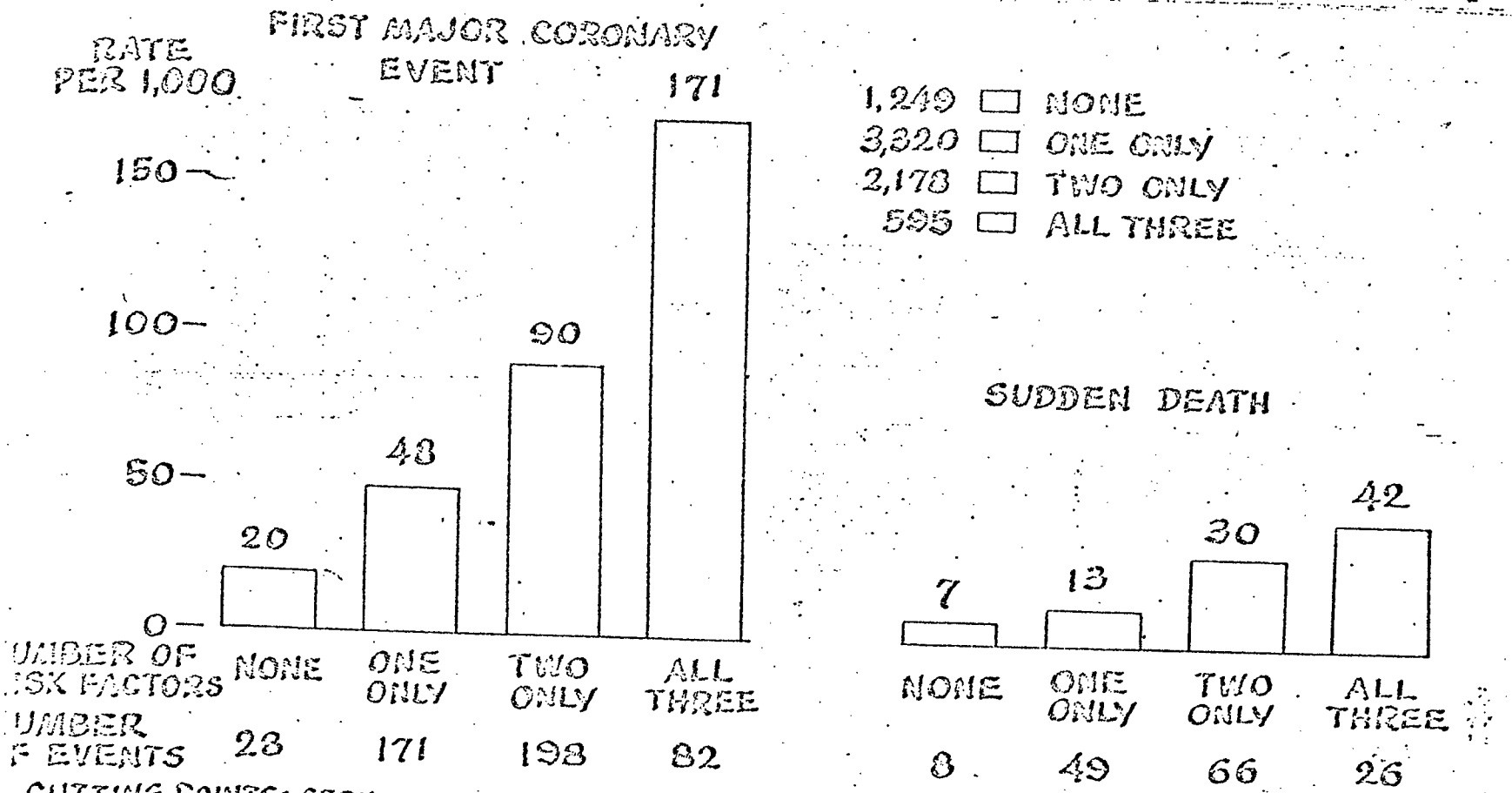

SUDDEN DEATH
7
11
15
34
9
42
NONE OF 3
S ONLY
C OR H ONLY
S+C OR S+H
C+H
C+H +S
8
25
24
61
5
26
1,249
2,018
1,302
1,794
384
595

8/70


RATE PER 1,000
150–
100–
50–
0–
ALL CHD DEATHS
ALL DEATHS
20
16
24
33
34
60
37
35
46
68
91
NEVER SMOKED
PAST ONLY
CURRENT PIPE OR CIGAR ONLY
≤½ PK. CURRENT
1 PK.
>1 PK. CIGARETTES.
NUMBER OF EVENTS
27
19
24
34
86
68
53
44
51
73
225
NUMBER OF MEN
1,188
904
878
981
2,330
1,146
POPULATION A

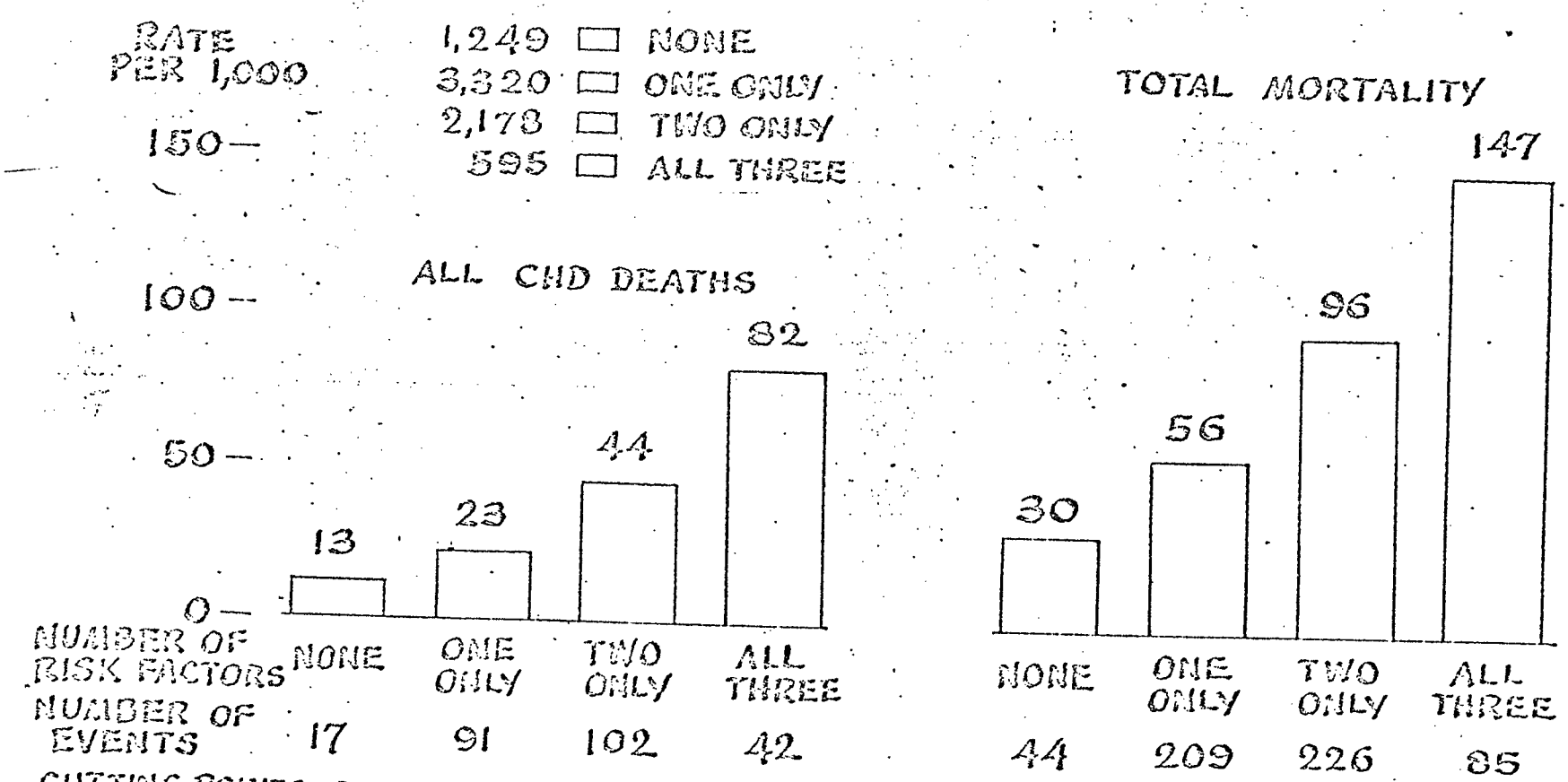
8/7


RCENT WITH
SIGNATED DEGREE
ATHEROSCLEROSIS
NEVER SMOKED REGULARLY
< 20 CIGARETTES/DAY
20-39/DAY
40+/DAY
00%-
90%-
30%-
70%-
60%-
50%-
40%-
30%-
20%-
10%-
0
71
42
35
17
21
39
41
55
7
19
25
28
NONE OR SLIGHT
MODERATE
ADVANCED



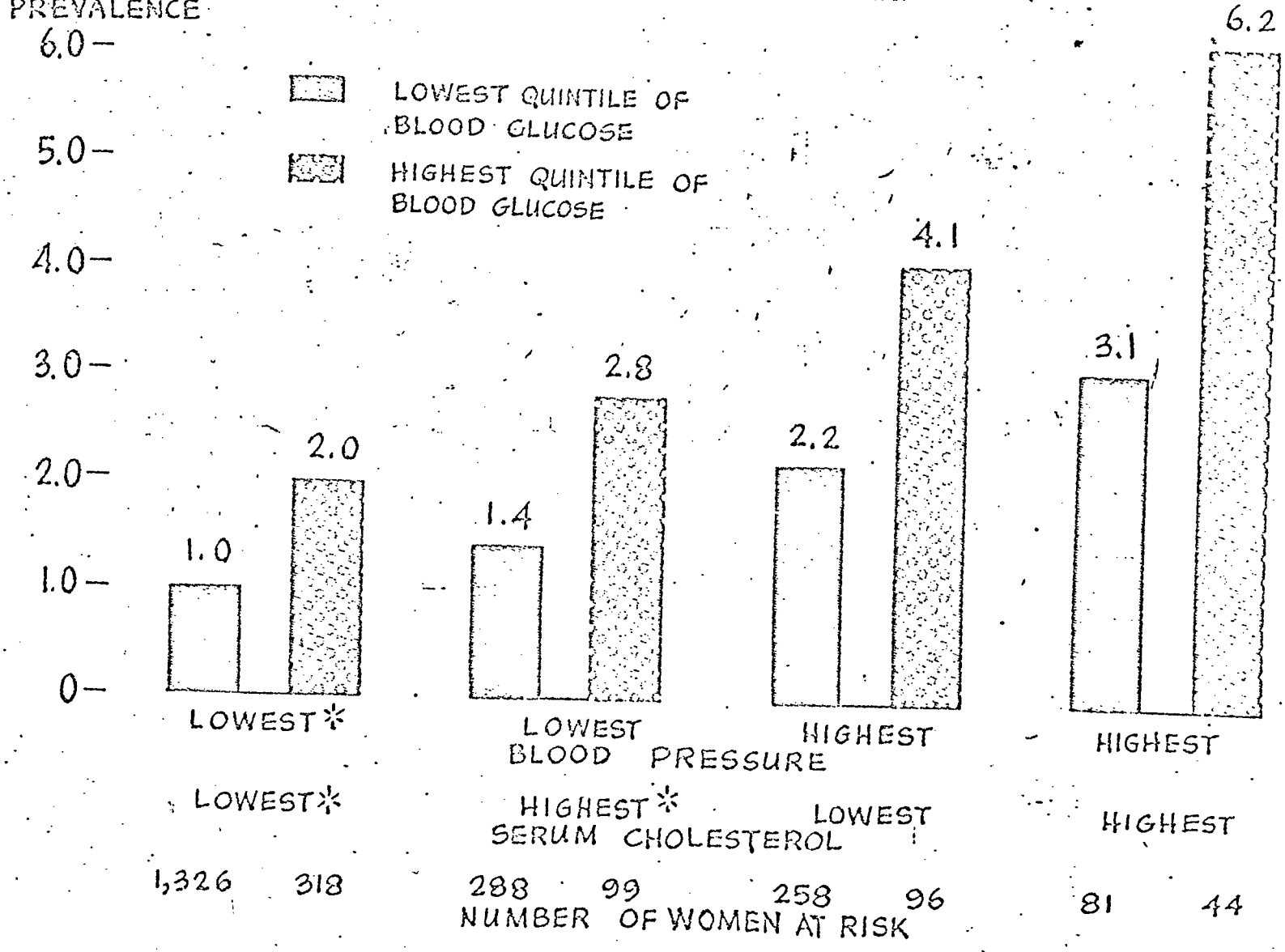
CUTTING POINTS: SERUM CHOLESTEROL ≥ 250 mg./dl; DIASTOLIC BLOOD PRESSURE ≥ 90 mm. Hg; ANY USE OF CIGARETTES AT ENTRY; POPULATION A.

8/70



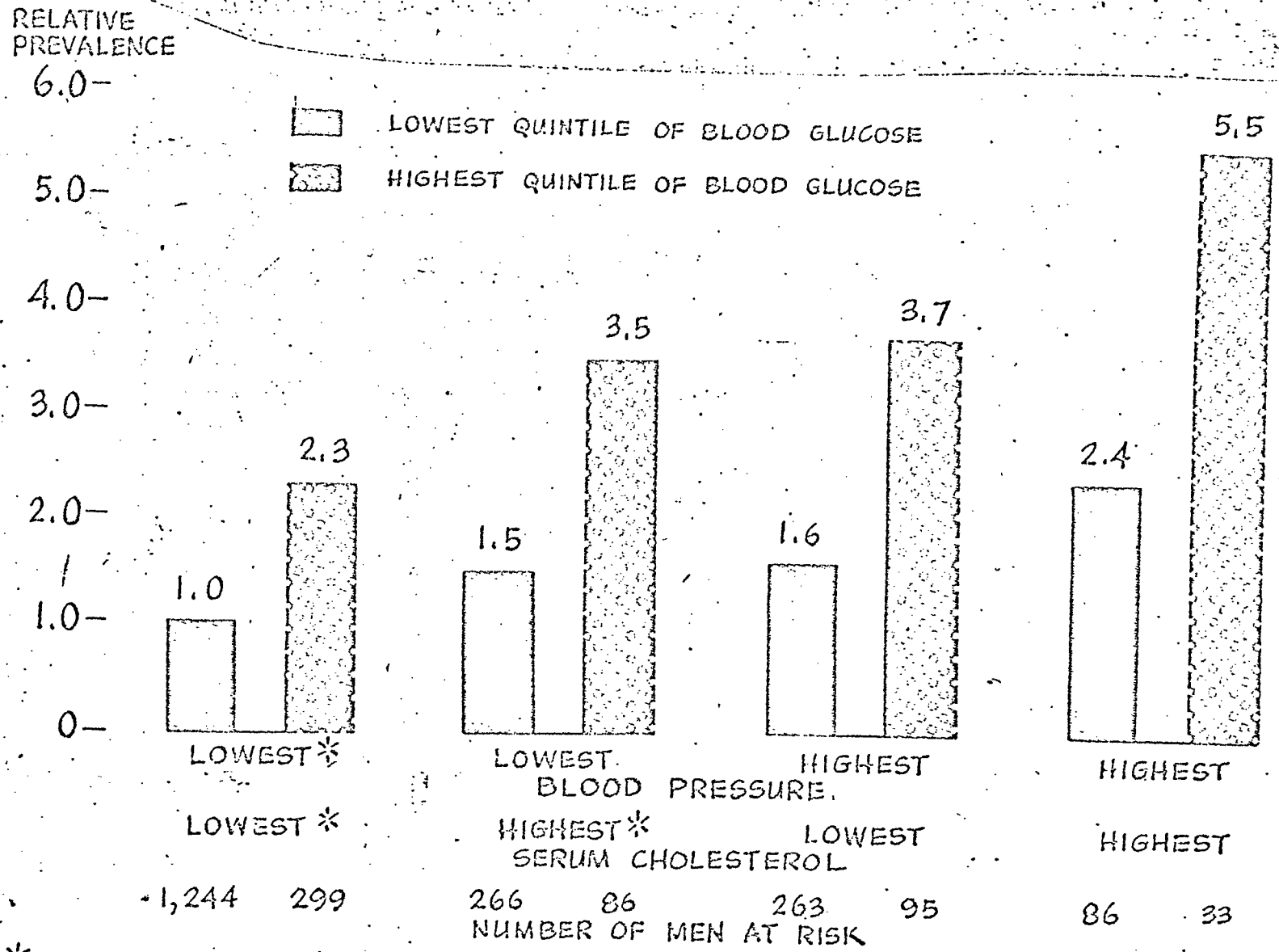
CUTTING POINTS: SERUM CHOLESTEROL ≥ 250 mg./dl.; DIASTOLIC BLOOD PRESSURE ≥ 90 mm. Hg; ANY USE OF CIGARETTES AT ENTRY; POPULATION A

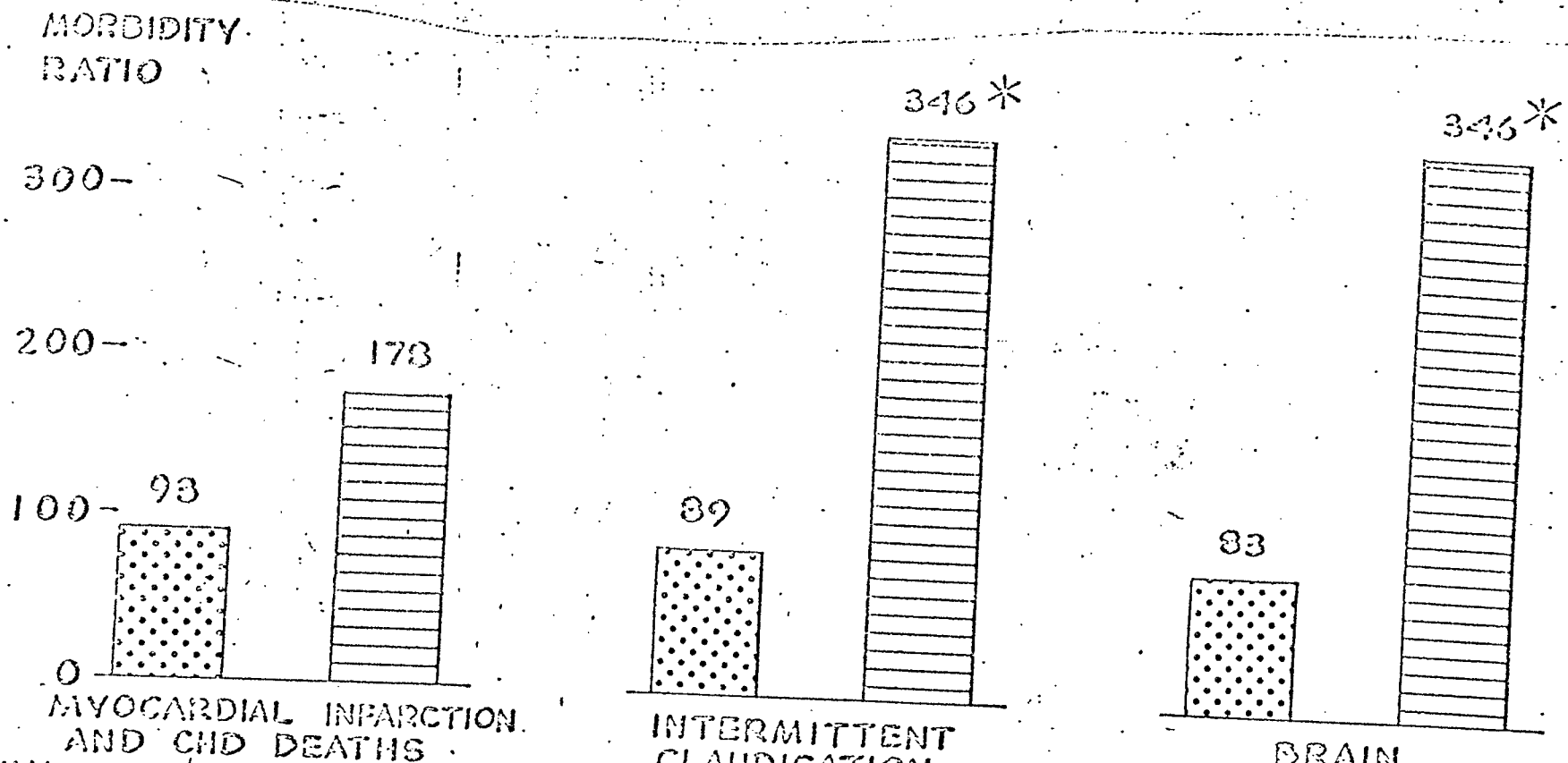
8/70



* QUINTILE

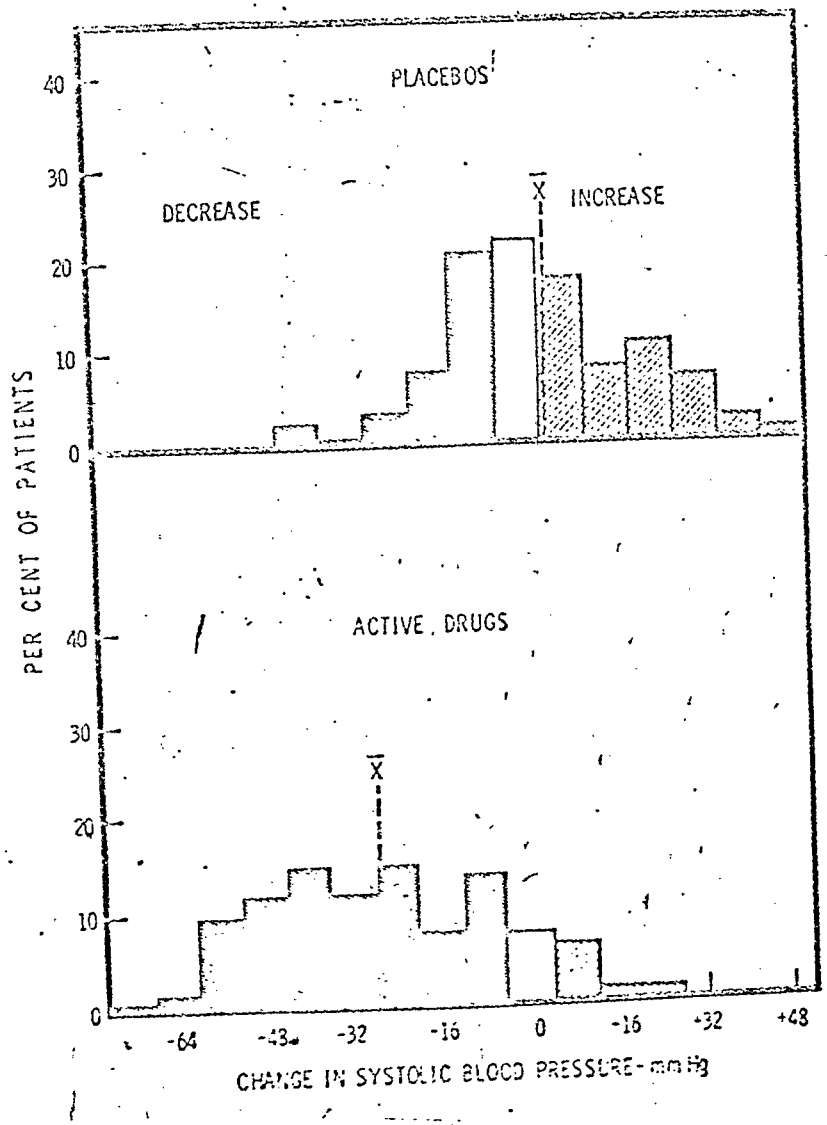
A ANN. INTERN. MED., 62, 1170 1965

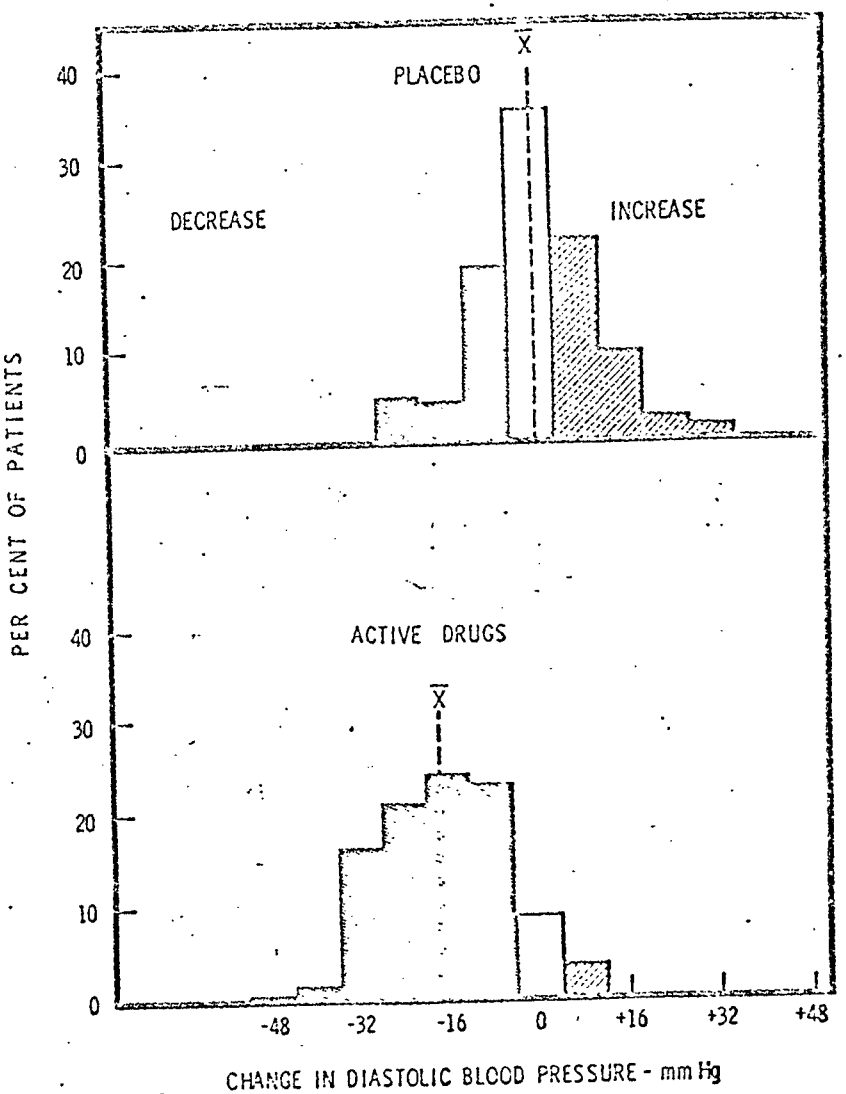

RELATIVE PREVALENCE
6.0
5.0
4.0
3.0
2.0
1.0
0
LOWEST QUINTILE OF BLOOD GLUCOSE
HIGHEST QUINTILE OF BLOOD GLUCOSE
1.0
2.3
1.5
3.5
1.6
3.7
2.4
5.5
LOWEST *
LOWEST
HIGHEST
HIGHEST
BLOOD PRESSURE
LOWEST *
HIGHEST *
LOWEST
HIGHEST
SERUM CHOLESTEROL
1,244
299
266
86
263
95
86
33
NUMBER OF MEN AT RISK
* QUINTILE



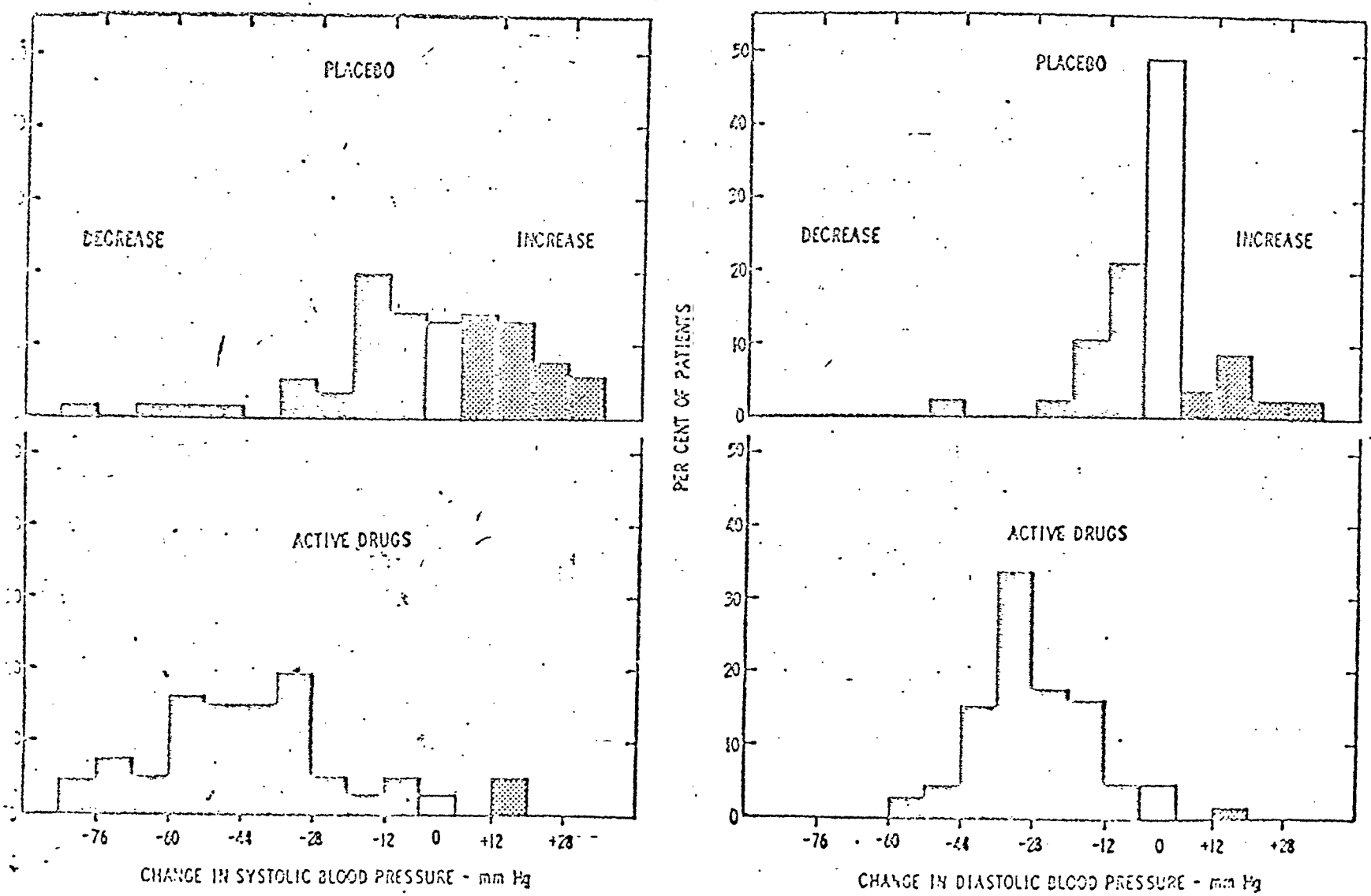
USUAL LOOS GEAR	<98	≥120	<98	≥120	<98	≥120
OBS.	172	13	44	8	40	1
EXP.	184.1	7.3	49.2	2.3	48.2	2.0

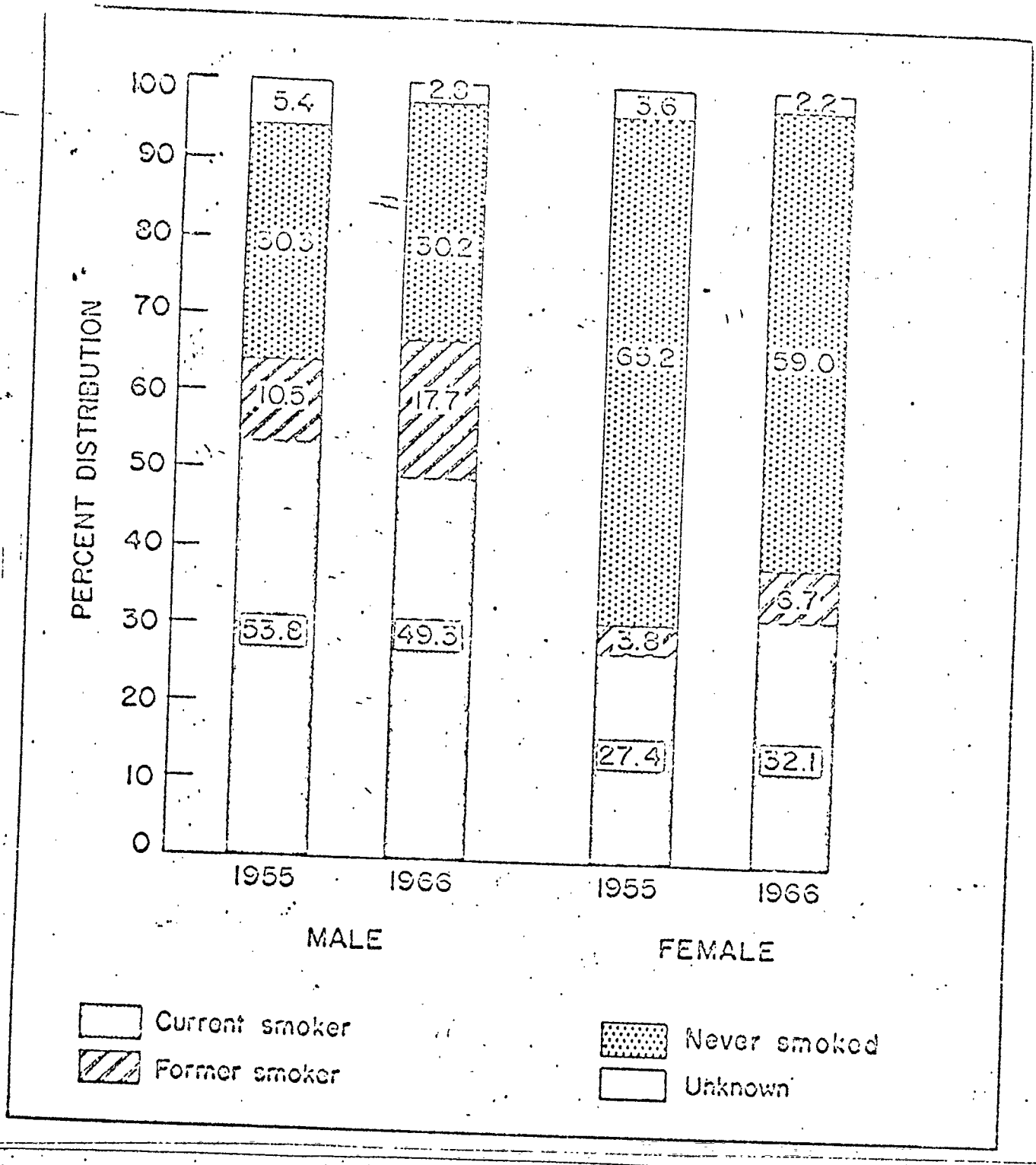
* STATISTICALLY SIGNIFICANT FROM STANDARD RISK AT 0.05


PLACEBOS
DECREASE
INCREASE
X
ACTIVE DRUGS
PER CENT OF PATIENTS
40
30
20
10
0
-64
-48
-32
-16
0
-16
+32
+48
CHANGE IN SYSTOLIC BLOOD PRESSURE - mm Hg


PLACEBO
DECREASE
INCREASE
X
ACTIVE DRUGS
PER CENT OF PATIENTS
40
30
20
10
0
-48
-32
-16
0
+16
+32
+48
CHANGE IN DIASTOLIC BLOOD PRESSURE - mm Hg

NOTE TO PRINTERS: Figure 15 has 2 glossies: they are to go on ONE SPREAD.




PERCENT DISTRIBUTION
100
90
80
70
60
50
40
30
20
10
0
5.4
30.0
10.5
53.8
2.8
30.2
17.7
49.3
3.6
65.2
3.8
27.4
2.2
59.0
6.7
32.1
1955
1966
1955
1966
MALE
FEMALE
Current smoker
Former smoker
Never smoked
Unknown

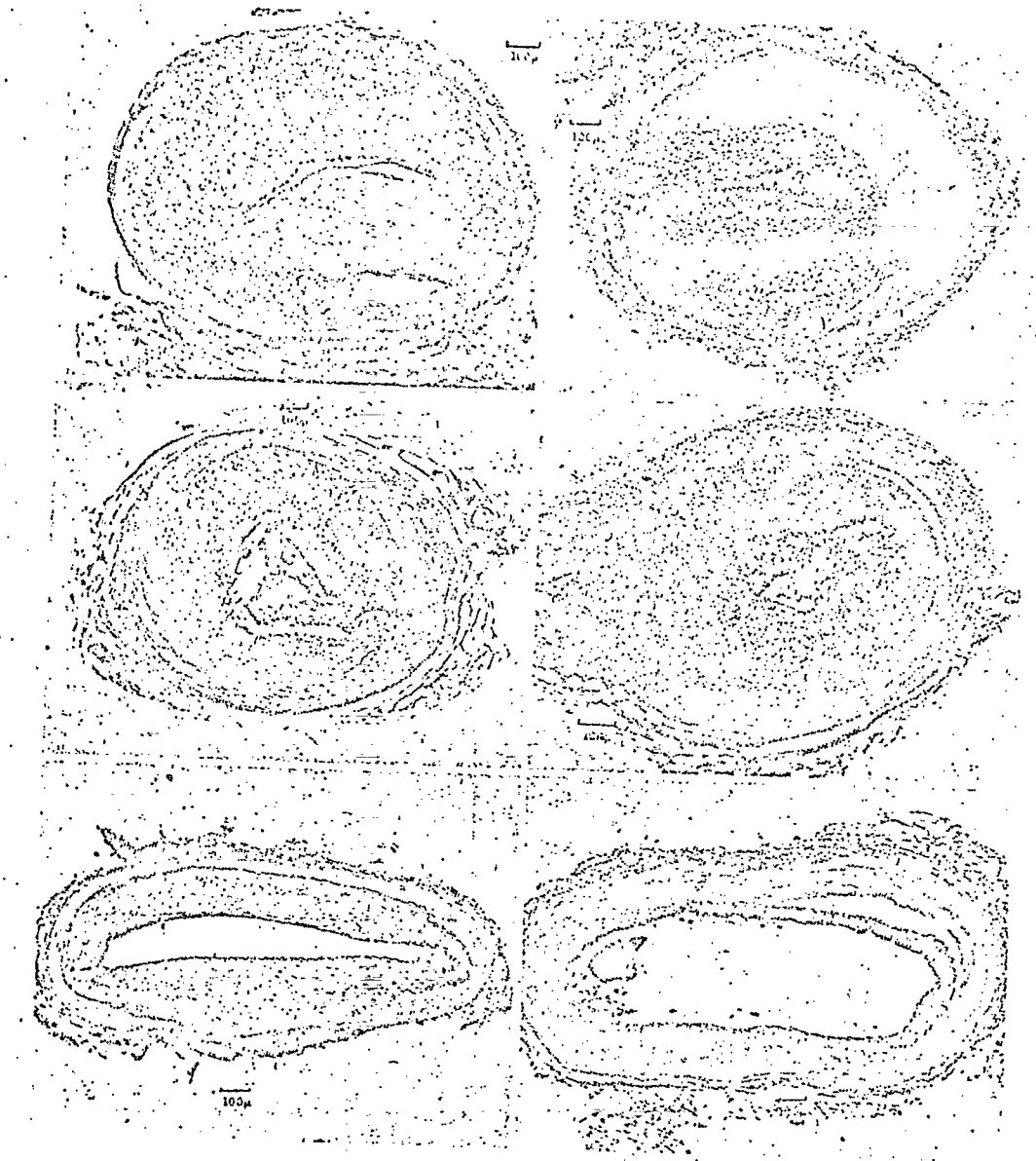


FIGURE 1 7 (8 of 7)

Top left: *Baseline atherosclerosis. Marked luminal occlusion by encroachment of intima showing several of the features found: cellular accumulation including lipid-laden macrophages, fibrous proliferation, and cellular breakdown. Hematoxylin and eosin, × 100.* **Top right:** *Baseline atherosclerosis. A downstream section from the artery shown in top left figure after staining for fat. A relatively fat-free collar of fibrous tissue encircles the lumen. Throughout the rest of the intima mixtures of fat-free and fat-bearing cells are found among varying amounts of intimal scarring. Oil-Red-O, × 90.* **Middle left:** *Baseline atherosclerosis. Large masses of acellular material are seen at the outer third of the intima. Hematoxylin and eosin, × 70.* **Middle right:** *Baseline atherosclerosis. In the larger artery a radial arrangement of the outer fibrous structure of the intima orients a mixed population of cells, the middle portion of the intimal lesion is occupied by a circumferential fibrous collar, and the innermost portion shows cellular hyperplasia. This form of intense arteritis may be seen frequently as a response to the hyperlipidemia. The portion of branch artery shown at the left has a greater acellular portion in the intimal mass. Hematoxylin and eosin, × 110.* **Bottom left:** *Regression atherosclerosis. Visible intimal lipid (black) is small within an unusually large residual mass of fibrous*

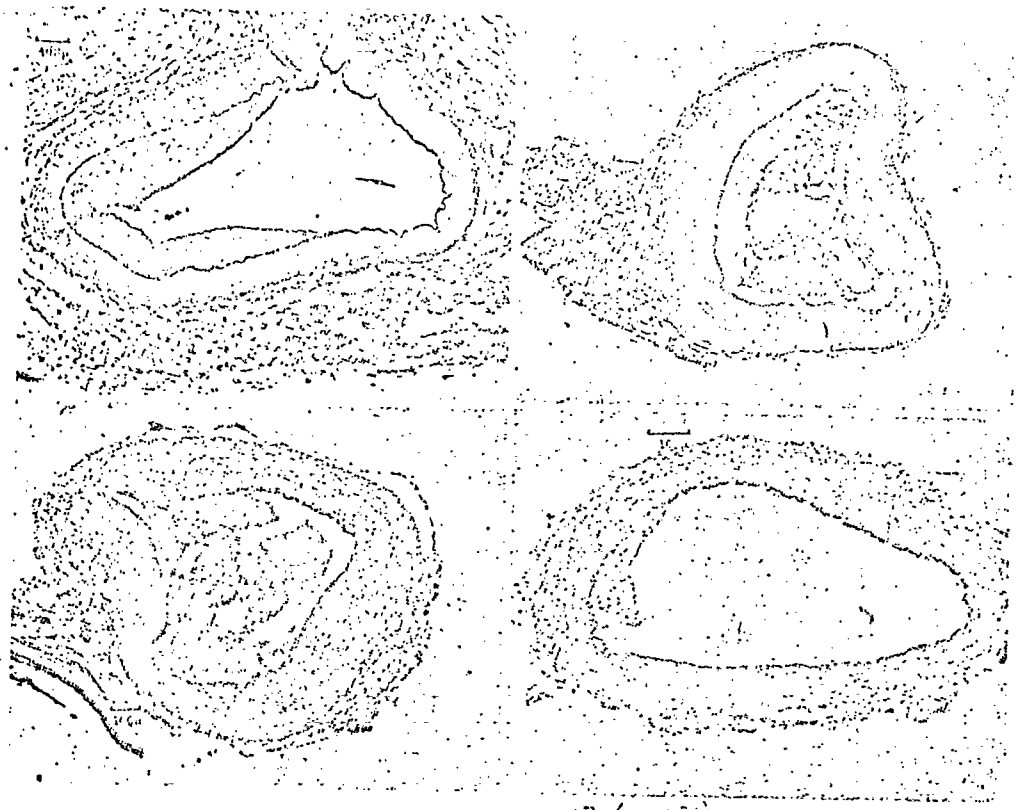


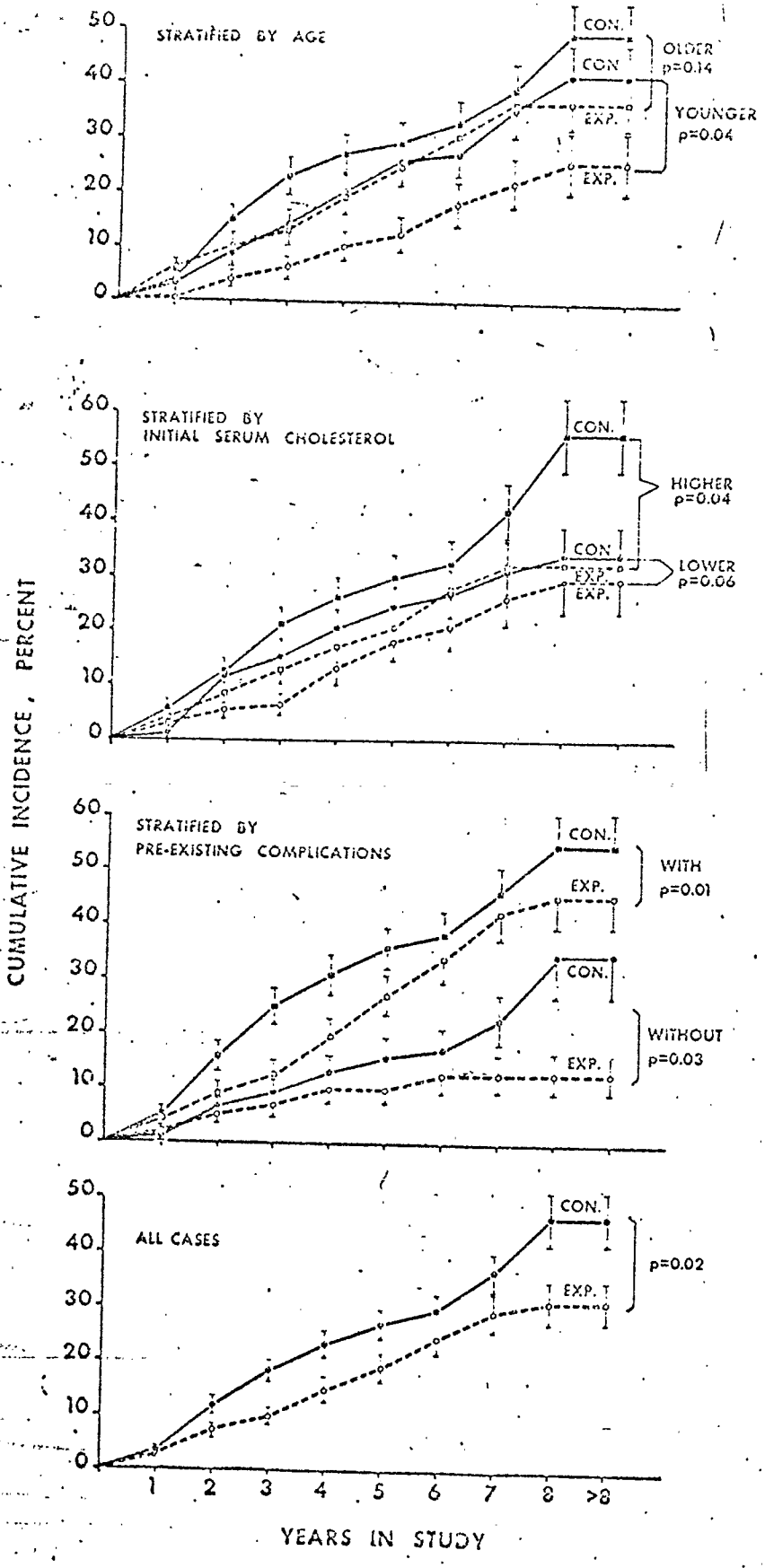
FIGURE 7, 17 (p. 62)

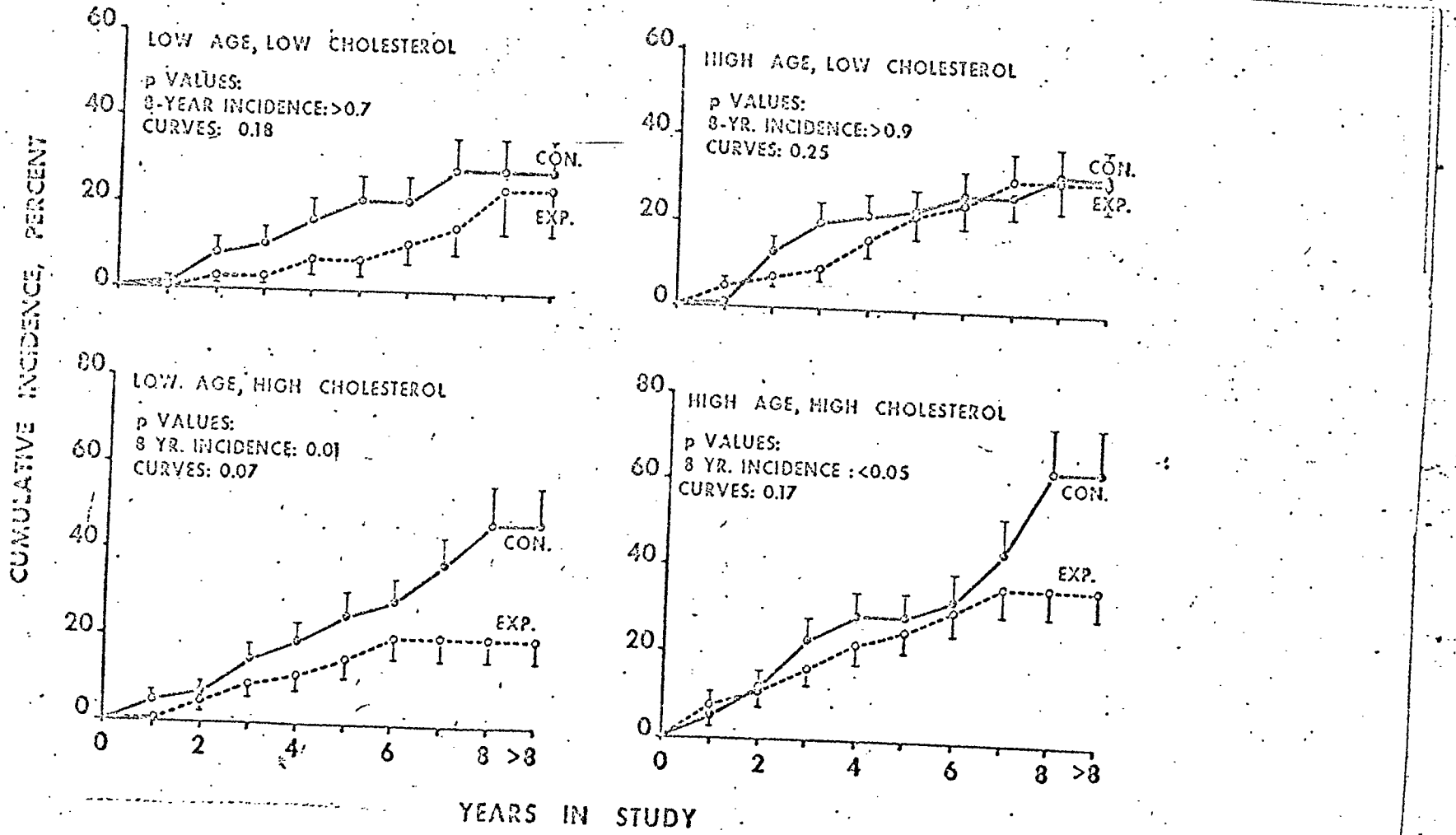
Top left: Regression atherosclerosis. Numerous small gaps occur in an otherwise intact internal elastic membrane. Residual medial damage is present at top left. Verhoeff's, × 100. Top right: Regression atherosclerosis. The intima stains dark (collagen) and the media pale (smooth muscle) with nearly intact architecture. Van Gieson, × 90. Bottom left: Regression atherosclerosis. The intima consists largely of connective tissue. Hematoxylin and eosin, × 90. Bottom right: Regression atherosclerosis. Unusually small areas of intimal thickening occur, the largest of which is at the bottom of the section. Hematoxylin and eosin, × 120.

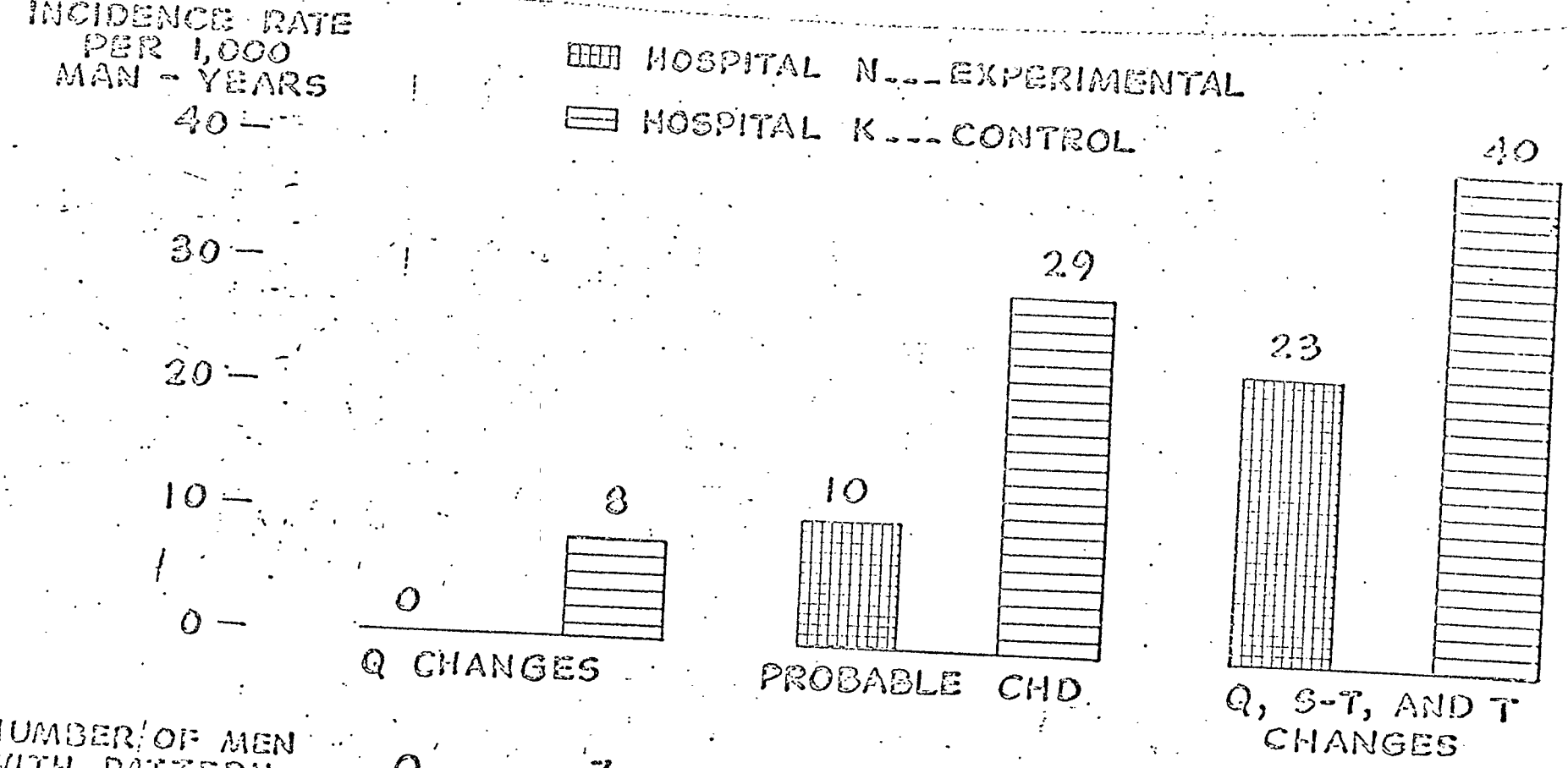
average total transverse area among the groups. Dilatation or distension cannot be ruled out in baseline atherosclerosis, however, since the average cross-sectional area of the arteries of this group was larger than in the regression animals, although the regression monkeys were more than 3 years older at autopsy.

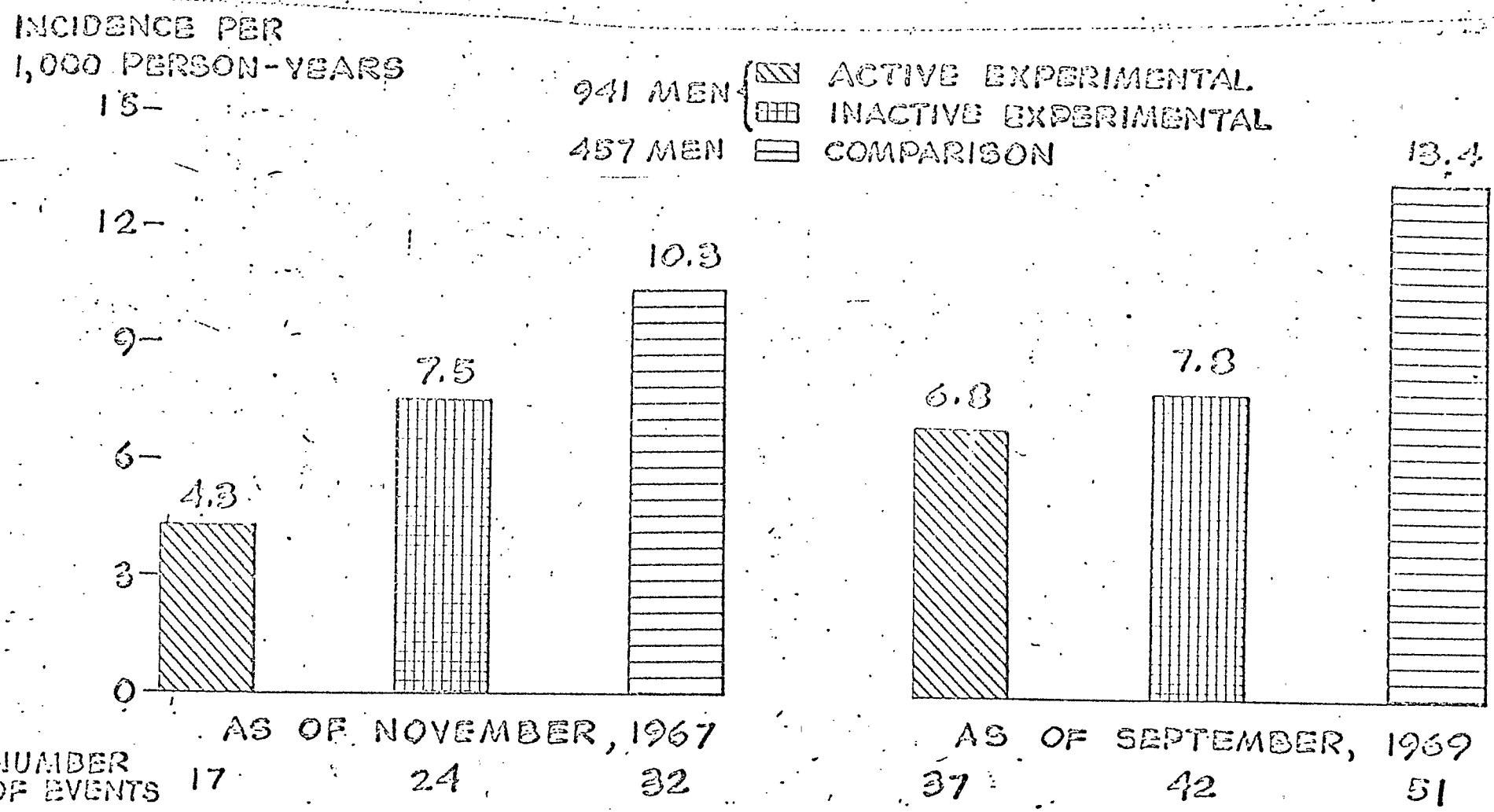
The decreased narrowing of the lumens of the coronary arteries in animals fed regression regimens was accompanied by several features that would be looked for at the end of a regression study. One was the gross observation of distinctly fewer lesions throughout the accessible arterial tree, including the aorta, in regression animals than were seen in animals with baseline atherosclerosis. This finding will be reported separately. A second observation pertains to the gross appearance of the unopened, intact coronary arteries themselves. Group 1 had beaded, ivory-colored arteries, but the regression groups had smoother, paler arteries suggesting thinner walls. The third, and to us, most notable evidence in favor of

tissue. Sudan IV, × 90. Bottom right: Regression atherosclerosis. The residual intimal lesion is rich in collagen (dark), and collagen scars are seen also in the media. Van Gieson, × 90.


STRATIFIED BY AGE
CON.
CON
OLDER
p=0.14
EXP.
YOUNGER
p=0.04
EXP.
STRATIFIED BY
INITIAL SERUM CHOLESTEROL
CON.
HIGHER
p=0.04
CON
EXP.
EXP.
LOWER
p=0.06
STRATIFIED BY
PRE-EXISTING COMPLICATIONS
CON.
EXP.
WITH
p=0.01
CON.
EXP.
WITHOUT
p=0.03
ALL CASES
CON.
EXP.
p=0.02
CUMULATIVE INCIDENCE, PERCENT
0
10
20
30
40
50
60
1
2
3
4
5
6
7
8
>8
YEARS IN STUDY

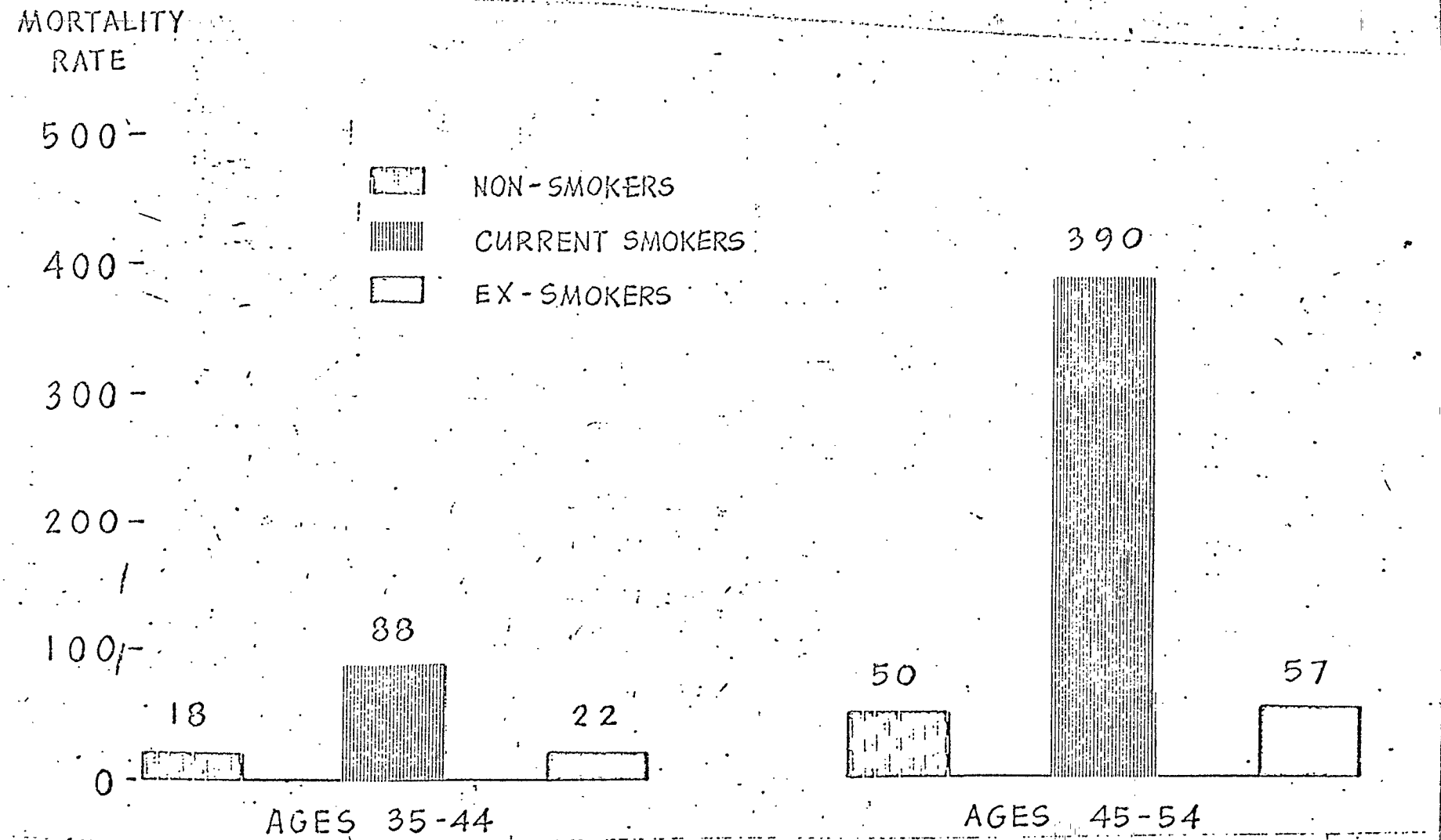

LOW AGE, LOW CHOLESTEROL
p VALUES:
8-YEAR INCIDENCE:>0.7
CURVES: 0.18
CON.
EXP.
HIGH AGE, LOW CHOLESTEROL
p VALUES:
8-YR. INCIDENCE:>0.9
CURVES: 0.25
CON.
EXP.
LOW AGE, HIGH CHOLESTEROL
p VALUES:
8 YR. INCIDENCE: 0.01
CURVES: 0.07
CON.
EXP.
HIGH AGE, HIGH CHOLESTEROL
p VALUES:
8 YR. INCIDENCE :<0.05
CURVES: 0.17
CON.
EXP.
CUMULATIVE INCIDENCE, PERCENT
0
20
40
60
80
0
2
4
6
8
>8
YEARS IN STUDY


INCIDENCE RATE PER 1,000 MAN - YEARS
HOSPITAL N---EXPERIMENTAL
HOSPITAL K---CONTROL
40
30
20
10
0
0
8
10
29
23
40
Q CHANGES
PROBABLE CHD
Q, S-T, AND T CHANGES
NUMBER OF MEN WITH PATTERN
0
7
12
25
25
33
NUMBER OF MEN AT RISK
280
219
274
213
269
210

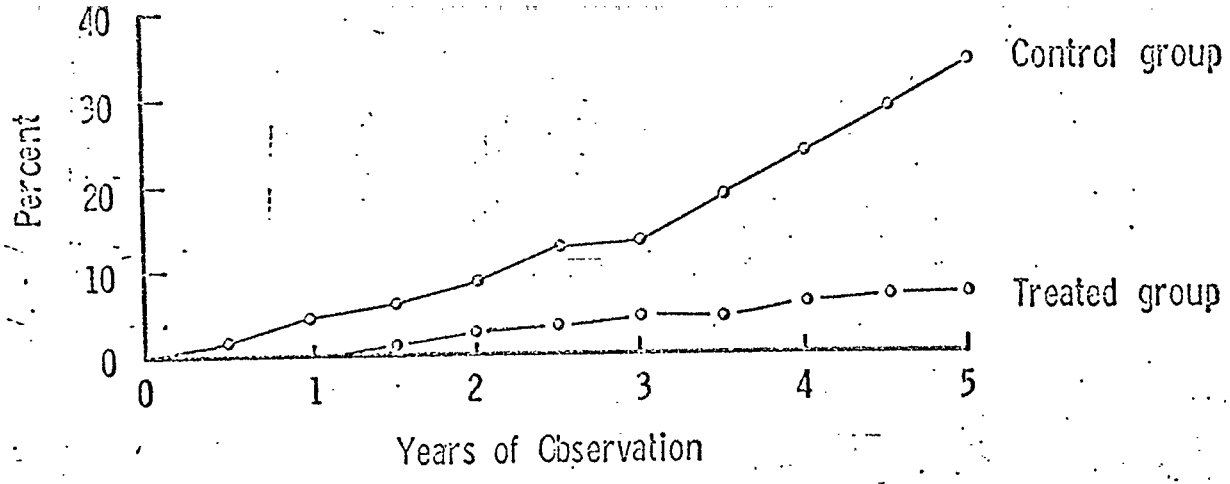


RATES FOR THE EXPERIMENTAL GROUP AGE-ADJUSTED TO COMPARISON GROUP

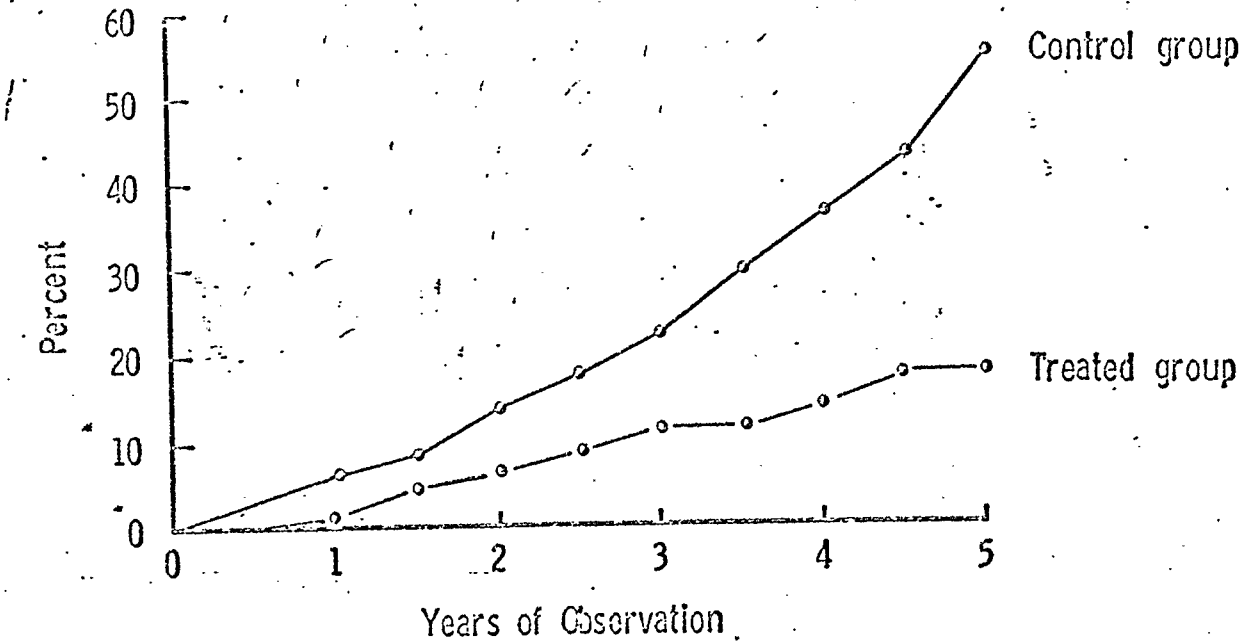
7/15/70

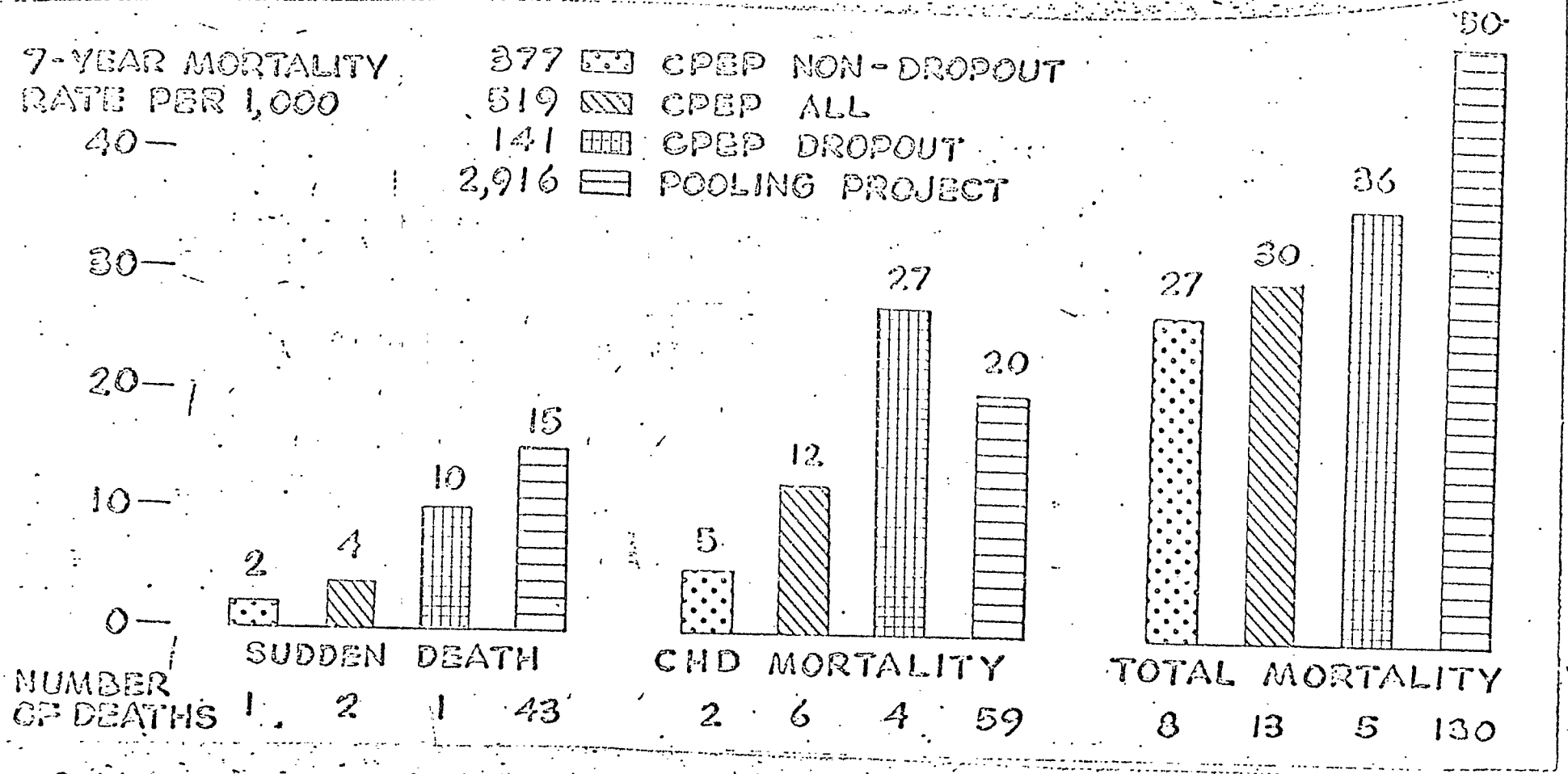

MORTALITY RATE
500
400
300
200
100
0
NON-SMOKERS
CURRENT SMOKERS
EX-SMOKERS
18
88
22
50
390
57
AGES 35-44
AGES 45-54

A. TERMINATING MORBID EVENTS



B. ALL MORBID EVENTS




7-YEAR MORTALITY RATE PER 1,000
377 CPEP NON-DROPOUT
519 CPEP ALL
141 CPEP DROPOUT
2,916 POOLING PROJECT
40
30
20
10
0
2
4
10
15
5
12
27
20
27
30
36
50
SUDDEN DEATH
CHD MORTALITY
TOTAL MORTALITY
NUMBER OF DEATHS
1 2 1 43
2 6 4 59
8 13 5 130

References

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3. Moriyama, I.M., Stamler, J. and Krueger, D.E.
The Major Cardiovascular Diseases -- An Epidemiologic Analysis.
Amer. Public Health Assoc., New York, N.Y., in press.

4. Mortality Statistics, Cardiovascular Diseases, Annual Statistics 1955-1964 by Sex and Age.
Epidemiological and Vital Statistics Report, World Health Organization, 20, 539, 1967.

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Regional Differences in Mortality, Prevalence and Incidence of Ischaemic Heart Disease. Snellen, H.A., Ed., Boerhaave Course on Ischaemic Heart Disease, 1969, Leiden, the Netherlands, in press.

6. Data from the Pooling Project, Council on Epidemiology, American Heart Association -- a national cooperative project for pooling data from the Albany civil servant, Chicago Peoples Gas Company, Chicago Western Electric Company, Framingham community, Los Angeles civil servant, Minneapolis-St. Paul business men, and other prospective epidemiologic studies of adult cardiovascular disease in the United States. The following are representative references on the individual studies and on the results of the Pooling Project presented to date:

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New York State J. Med., 63, 1317, 1963.

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Cardiovascular Diseases in the United States.
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A Longitudinal Study of Coronary Heart Disease.
Circulation, 28, 20, 1963.

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The Prediction of Coronary Heart Disease.
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6. e. Chapman, J.M. and Massey, F.J.
The Interrelationship of Serum Cholesterol, Hypertension, Body Weight, and Risk of Coronary Disease. Results of the First Ten Years Follow-up in the Los Angeles Heart Study.
J. Chron. Dis., 17, 933, 1964.

6. f. Keys, A., Taylor, H.L., Blackburn, H., Brozek, J., Anderson, J.T. and Simonson, E.
Coronary Heart Disease among Minnesota Business and Professional Men Followed Fifteen Years.
Circulation, 28, 381, 1963.

6. g. Moore, F.E.
Some Preliminary Findings from the Pooling Project of the Council on Epidemiology, American Heart Association. Paper Presented at the Conference on Cardiovascular Disease Epidemiology, Council on Epidemiology, American Heart Association, March 3-4, 1969, New Orleans, La.

6. h. Doyle, J.T. and Kinch, S.H.
Coronary Heart Disease in the United States: Some Preliminary Findings from the Pooling Project of the Council on Epidemiology of the American Heart Association. Presented at the 42nd Scientific Sessions, American Heart Association, Nov. 14, 1969.

6. i. Epstein, F.H. and Moore, F.E.
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