quitting, and the magnitude of this residual risk is proportional to the total lifetime exposure to cigarette smoke.

Populations With Low Rates of Smoking

Mortality has been studied in several population groups that have abstained from cigarette smoking for religious reasons. These include Seventh Day Adventists in California, Mormons living in Utah, members of the Reorganized Church of Jesus Christ of the Latter Day Saints living in Missouri, and Old Order Amish living in Indiana, Ohio, and Pennsylvania.

Seventh Day Adventists in California prohibit the use of tobacco and alcohol and advocate a well-balanced diet that includes a relatively large grain and fruit content. As reported by Wynder and Lemon (*285*), the Seventh Day Adventists have experienced exceptionally low coronary heart disease as well as low cancer mortality.

Cardiovascular mortality from 1969 to 1971 in Mormons and non-Mormons living in Utah was studied by Lyon et al. (*165*). Utah has the lowest per capita consumption of cigarettes and alcohol of the 50 States, and this is attributable to the Mormon Church's position against the use of tobacco and alcohol. Below the age of 65, both Mormons and non-Mormons in Utah had significantly lower coronary heart disease mortality than the average for U.S. whites, but above the age of 65 only Mormons had significantly lower rates. Mormon men and women in comparison with non-Mormon men and women living in Utah experienced 25 percent and 29 percent fewer deaths, respectively, from coronary heart disease. The rates were lower in Mormons than in non-Mormons at all ages. Below the age of 65, Mormon men and women experienced CHD mortality rates only 66 percent and 51 percent, respectively, of the rates for coronary heart disease that were experienced by U.S. whites.

The mortality of Missouri residents who were members of the Reorganized Church of Jesus Christ of Latter Day Saints (RLDS) was compared with the mortality of other white Missouri residents and of Utah residents for the period 1971–1978 (*167*). The RLDS advocates abstinence from the use of tobacco, alcohol, and hot drinks. A well-balanced diet is recommended, with ample whole grains, fruits, and vegetables but with moderate intake of meat. The total mortality rate for Missouri RLDS residents was 22.6 percent lower than that of other Missouri white residents and 14.4 percent lower than that of Utah residents. CHD mortality was 17.4 percent lower than CHD mortality for other Missouri whites. The CHD mortality of RLDS members appears to be intermediate between that of Mormons living in Utah and that of U.S. whites.

Mortality among Old Order Amish living in Ohio (1960–1975), Indiana (1967–1972), and Pennsylvania (1970–1975) was reported by

Hamman et al. (*92*). This unique population group is rooted in a rural lifestyle reminiscent of 19th century America. Their diet has been incompletely characterized, but probably is relatively high in fats and carbohydrates. Tobacco use has been widespread among men, but principally limited to pipe and cigar smoking and tobacco chewing. Alcohol intake is thought to be limited to consumption at home, and excessive intake is uncommon. Mortality of the Amish was compared with mortality of the non-Amish residents in the study counties. The non-Amish residents included an unknown proportion of those who were former members of the Amish faith and members of other conservative religious groups who shared components of the Amish lifestyle. Amish men, but not women, 40 to 69 years of age had significantly lower total mortality (61 percent and 98 percent, respectively) and cardiovascular mortality (65 percent and 89 percent) than did the non-Amish residents living in the same counties. Lower cardiovascular disease mortality for the Amish men was highly significant in all three States.

Conclusions

1. Cigarette smoking is a major cause of coronary heart disease in the United States for both men and women. Because of the number of persons in the population who smoke and the increased risk that cigarette smoking represents, it should be considered the most important of the known modifiable risk factors for CHD.
2. Overall, cigarette smokers experience a 70 percent greater CHD death rate than do nonsmokers. Heavy smokers, those who consume two or more packs per day, have CHD death rates between two and three times greater than nonsmokers.
3. The risk of developing CHD increases with increasing exposure to cigarette smoke, as measured by the number of cigarettes smoked daily, the total number of years one has smoked, and the degree of inhalation, and with an early age of initiation.
4. Cigarette smokers have a twofold greater incidence of CHD than do nonsmokers, and heavy smokers have an almost fourfold greater incidence.
5. Cigarette smoking is a major independent risk factor for CHD, and it acts synergistically with other risk factors (most notably, elevated serum cholesterol and hypertension) to greatly increase the risk of CHD.
6. Women have lower rates for CHD than do men. In particular, CHD rates for women are lower prior to the menopause. A part of this difference is due to the lower prevalence of smoking in women, and for those women who do smoke, to the tendency to smoke fewer cigarettes per day and to inhale less deeply.

Among those women who have smoking patterns comparable to male smoking patterns, the increments in CHD death rates are similar for the two sexes.

7. Women who use oral contraceptives and who smoke increase their risk of a myocardial infarction by an approximately tenfold factor, compared with women who neither use oral contraceptives nor smoke.
8. Cigarette smoking has been found to significantly elevate the risk of sudden death. Overall, smokers experience a two to four times greater risk of sudden death than nonsmokers. The risk appears to increase with increasing dosage as measured by the number of cigarettes smoked per day and diminishes with cessation of smoking.
9. The CHD mortality ratio for smokers compared with nonsmokers is greater for the younger age groups than for the older age groups. Although the smoker-to-nonsmoker mortality ratio narrows with increasing age, smokers continue to experience greater CHD death rates at all ages.
10. Cigarette smoking has been estimated to be responsible for up to 30 percent of all CHD deaths in the United States each year. During the period 1965 to 1980 there were over 3 million premature deaths from heart disease among Americans attributed to cigarette smoking. Unless smoking habits of the American population change, perhaps 10 percent of all persons now alive may die prematurely of heart disease attributable to their smoking behavior. The total number of such premature deaths may exceed 24 million.
11. Cessation of smoking results in a substantial reduction in CHD death rates compared with those of persons who continue to smoke. Mortality from CHD declines rapidly after cessation. Approximately 10 years following cessation the CHD death rate for those ex-smokers who consumed less than a pack of cigarettes daily is virtually identical to that of lifelong nonsmokers. For ex-smokers who had smoked more than one pack per day, the residual risk of CHD mortality is proportional to the total lifetime exposure to cigarette smoke.
12. Epidemiologic evidence concerning reduced tar and nicotine or filter cigarettes and their effect on CHD rates is conflicting. No scientific evidence is available concerning the impact on CHD death rates of cigarettes with very low levels of tar and nicotine.
13. Smokers who have used only pipes or cigars do not appear to experience substantially greater CHD risks than nonsmokers.

Appendix: Prediction of CHD

The probability of developing CHD may be accurately predicted within populations that are stratified by risk scores based on daily use of cigarettes and the levels of the other major risk factors. This may be accomplished efficiently using the multiple logistic equation, which provides for simultaneous consideration of multiple risk factors (*40, 80, 84, 85, 88, 91, 126, 130, 133, 135, 137, 139, 143, 159, 168, 214, 221, 246*). Furthermore, the reproducibility of the relationship between risk factors and the subsequent development of CHD may be tested among different population samples. As demonstrated in the investigations cited above, the risk of CHD in white populations in the United States and northern Europe has been shown to be predictable based on a knowledge of cigarette smoking, blood pressure, and serum cholesterol. In other population groups with lower incidences of CHD, relative risk has been predicted well, although the magnitude of risk has been overestimated. Such predictability confirms the importance of the major risk factors to the development of CHD.

Pooling Project

The relationships among a number of characteristics measured at baseline examinations and the subsequent development of CHD was studied intensively in the Pooling Project, in which the experience of five major prospective studies of defined cohorts were compared and combined. From these analyses it was concluded that the levels of the three major risk factors—cigarette smoking, blood pressure (systolic or diastolic blood pressure), and serum cholesterol—accounted for most of the risk predicted by the variables considered; the other variables were relative weight and ECG abnormalities. Furthermore, the relationships of the risk factors to CHD were similar among the cohorts considered.

Ranking of Risk

On the basis of the observed relationships among the levels of the major risk factors and the subsequent incidence of CHD in the pooled data, the men in each of the cohorts could be ranked by order of expected risk. With the men thus ranked in quintiles of estimated risk from low to high, the incidence of CHD was found to be nine times higher for the men in the uppermost quintile than for the men in the lowermost quintile.

Generalizability

To test the generalizability of the relationship between these risk factors and the subsequent incidence of CHD (in other words, the prediction of future CHD events from given individual characteris-

tics), the multiple logistic equation describing the relationship of risk factors to subsequent events in the combined data from the cohorts contributing to the pooled data were applied to other cohorts. In the cohort of U.S. railroad men, there was good correspondence between the number of first major coronary events predicted and the numbers observed by quintile of risk; 45 percent of CHD events were observed in the highest quintile and 74 percent were observed in the upper two quintiles. The total number of estimated cases was 133 as compared with 112 actually observed in the cohort of U.S. railroad men (Table 22).

Comparability of Framingham Study Results With the Results in the Other Cohorts

The mathematical relationships between the risk factors and the subsequent incidence of CHD for the Framingham study men were near the averages observed for the other four cohorts in the Pooling Project (Tables 23 and 24). The Framingham study results have been compared with the results of other cohort studies in the United States and elsewhere (*25, 77, 85, 181*); therefore, it is of interest to consider in some detail the closeness of agreement between the prediction of CHD by Framingham data and by the other cohort data in the Pooling Project. In univariate analyses for each study by CHD event and risk factor, it was found that the Framingham coefficients were not significantly different from those of the other cohorts, except for a higher coefficient for serum cholesterol in the Tecumseh cohort and a higher coefficient for cigarette smoking in the Chicago Gas Company cohort (Table 23). The Framingham coefficient for smoking was slightly lower than the average for the other cohorts.

Risk Indices for Individual Use

Multivariate risk-scoring indices for estimating the risk of CHD based on daily use of cigarettes and the levels of other characteristics have been developed for prediction of the risk of CHD in individuals. These include RISKO, developed by the Michigan Heart Association, the Framingham Risk Index, based on the Framingham study experience, and the Self-Scoring Risk Test, based on the experience of the Chicago Western Electric Company cohort (*54, 138, 178*).

The discriminative power of RISKO and the Framingham Risk Index to identify individuals who would develop CHD was evaluated in the experience of Los Angeles County safety personnel (*256*). Personnel who were free of symptoms (4,066 individuals) were examined and followed in the 1971 to 1979 time frame with a less than 3 percent loss to followup (*256*). Subsequent to initial examination, 71 developed CHD; these symptomatic cases were characterized by a higher proportion of cigarette smokers (60 percent compared with 37 percent), higher systolic blood pressures, higher serum

TABLE 22.—Prediction of 10-year risk of a first event for men of two studies (Minnesota business and professional men and Minnesota-based railroad workers) from parameters of the multivariant logistic analysis for Pool 5, age 40–59 at entry

Quintiles of expected or predicted risk	Pool 5 (6,875 men)				Minnesota business and professional men (280 men)						Minnesota-based railroad workers (2,422 men)					
	Expected		Observed		Predicted		Predicted, corrected for duration of followup[1]		Observed		Predicted		Predicted, corrected for duration of followup[2]		Observed	
I	41.3[3]	30.0[4]	29	21.1	1.0	18.4	2.0	37.6	3	53.6	16.9	34.8	8.3	17.0	8	16.5
II	71.2	51.8	71	51.6	1.6	27.9	3.3	57.0	4	71.4	30.6	63.2	15.0	31.0	5	12.4
III	101.1	73.5	106	77.1	2.2	39.6	4.5	80.9	7	125.0	44.2	91.3	21.7	44.7	15	31.0
IV	145.5	105.8	164	119.3	3.1	55.3	6.3	113.0	6	107.1	64.7	133.7	31.7	65.5	33	68.2
V	264.0	192.0	251	182.5	5.5	97.4	11.2	199.1	12	214.3	115.2	237.0	56.4	116.1	50	102.9
All	623.1	90.6	621	90.3	13.4	47.7	27.4	97.5	32	114.3	271.5	112.1	133.0	54.9	112	46.2
V/I	6.4		8.7		5.3		5.3		4.0		6.8		6.8		6.3	
V–I	222.7	162.0	222	161.4	4.5	79.0	9.2	161.5	9	160.7	98.3	202.2	48.1	99.1	42	86.4
Percentage of events in V	42.4		40.4		40.8		40.8		37.5		42.2		42.4		44.6	
Percentage of events in VI + V	65.7		66.8		64.0		64.0		56.3		66.3		66.3		74.1	

[1] Mean duration of followup for Pool 5 men was sizably less than for Minnesota business and professional men. Since the relationship between age and incidence of major coronary events is curvilinear (exponential), not linear, a correction factor was derived from the 1970 U.S. life table for white men starting at age-predicted numbers of events; rates were multiplied by this correction factor—2,044—to obtain the numbers of events and rates for different duration of followup.

[2] Mean duration of followup for Pool 5 men was sizably greater than for Minnesota-based railroad workers. A correction factor—0.$\overline{899}$—was derived by the method described in the footnote above.

[3] Number of events.

[4] Rate per 1,000.

SOURCE: Pooling Project Research Group (*214*).

TABLE 23.—Standardized univariate logistic coefficients for deaths from myocardial infarction, CHD, and all causes, by study and risk factor

	Framingham	Albany	Chicago Gas	Chicago W.E.	Tecumseh
Myocardial infarction or CHD death					
SBP	0.3373	0.2695	0.3123	0.2511	0.5633
DBP	0.3126	0.2845	0.3169	0.2797	0.5059
Cholesterol	0.3433	0.3614	0.2685	0.3271	0.7501[1]
Relative weight	0.2775	0.2385	0.1496	0.0703	-0.0136
Smoking	0.3115	0.4450	0.6984[1]	0.3049	0.5183
Death all causes					
SBP	0.4671	0.4671	0.4102	0.4196	0.2926
DBP	0.3684	0.4006	0.2426	0.3382	0.4906
Cholesterol	0.1156	0.1321	0.1815	0.0796	0.4533[1]
Relative weight	0.0540	-0.1452	-0.0921	0.1645	-0.0214
Smoking	0.3876	0.3745	0.5806	0.3229	0.5546
CHD death					
SBP	0.4880	0.3103	0.3663	0.3212	0.5831
DBP	0.4139	0.3394	0.2818	0.4056	0.5518
Cholesterol	0.2872	0.2550	0.2474	0.2344	0.8586[2]
Relative weight	0.3229	0.0490	0.1967	0.0765	0.0453
Smoking	0.3327	0.4612	0.8060	0.2311	0.4623

[1] Differs significantly from Framingham ($p < .05$).
[2] Differs significantly from Framingham ($p < .01$).
NOTE: The coefficients here are given in less precision for ease of comparison. For each coefficient in the studies other than Framingham, a test statistic was calculated to test whether it differed significantly from the comparable coefficient for Framingham. Those that did were appropriately marked. The test statistic is the difference between the coefficients divided by the standard error of the difference. The standard error of the difference is calculated by taking the square root of the sum of the variance of the coefficients. Under appropriate normality assumptions, this statistic is a standard normal deviate.
SOURCE: McGee and Gordon (*168*).

cholesterol, slightly greater prevalence of excess body fat, and less frequent regular exercise. The risk scores of cases in comparison with noncases were significantly higher with RISKO and with the Framingham Risk Index. In stepwise discriminant analysis, the Framingham Risk Index and RISKO, separately and in combination, identified the group with elevated levels of risk factors that experienced a higher incidence of CHD than the group with low levels of the risk factors.

Blacks and Whites in Evans County, Georgia

In looking for an explanation of the large difference in CHD incidence rates between black and white men in the Evans County study (see above), the incidence at different levels of risk factors was evaluated (*28, 107, 258*). Although cigarette smoking and other risk factors were strongly related to the incidence, differences in baseline characteristics did not appear to explain the higher rates of CHD in white men. However, white and black sharecroppers and farm

TABLE 24.—Standardized multivariate logistic coefficients for deaths from myocardial infarction, CHD, and all causes, by study and specified set of risk factors

	Framingham	Albany	Chicago Gas	Chicago W.E.	Tecumseh
Myocardial infarction or CHD death					
SBP	0.3432	0.2426	0.3376	0.2342	0.5524
Cholesterol	0.2905	0.3534	0.2187	0.3056	0.7989[2]
Smoking	0.3374	0.4227	0.7010[1]	0.2820	0.5509
DBP	0.3022	0.2725	0.3694	0.2680	0.5222
Cholesterol	0.2893	0.3462	0.2176	0.2979	0.7705[1]
Smoking	0.3352	0.4359	0.7240[1]	0.2934	0.5647
Death all causes					
SBP	0.5483	0.4254	0.4495	0.275[1]	0.4742
Cholesterol	0.0209	0.0992	0.1307	0.0260	0.4617[1]
Smoking	0.4845	0.3453	0.6033	0.3206	0.5614
DBP	0.4305	0.3983	0.2855	0.3382	0.4971
Cholesterol	0.0279	0.0937	0.1339	0.0145	0.4391[1]
Smoking	0.4655	0.3638	0.6012	0.3372	0.5880
CHD death					
SBP	0.5292	0.2697	0.3936	0.2981	0.5720
Cholesterol	0.2033	0.2406	0.1881	0.2025	0.9164[2]
Smoking	0.4027	0.4107	0.8076	0.2092	0.4989
DBP	0.4200	0.3126	0.3304	0.3799	9.5752
Cholesterol	0.2088	0.2324	0.1903	0.1905	0.8918[2]
Smoking	0.3806	0.4273	0.8200	0.2273	0.5140

[1] Differs significantly from Framingham ($p < .05$).

[2] Differs significantly from Framingham ($p < .01$).

NOTE: The coefficients here are given in less precision for ease of comparison. For each coefficient in the studies other than Framingham, a test statistic was calculated to test whether it differed significantly from the comparable coefficient for Framingham. Those that did were appropriately marked. The test statistic is the difference between the coefficients divided by the standard error of the difference. The standard error of the difference is calculated by taking the square root of the sum of the variance of the coefficients. Under appropriate normality assumptions, this statistic is a standard normal deviate.

SOURCE: McGee and Gordon (*168*).

laborers had similarly low incidences, but the numbers of cases were too few for more definitive analysis of the influence of occupation (*29*). At all levels of the major risk factors, the incidence of CHD was higher in white than in black men, but some differences were smaller in the higher ranges of the risk factors. The absolute rates for white men were higher than for black men whether they were smokers (including ex-smokers) or nonsmokers, but the relative risk for white male smokers compared with nonsmokers was 2, whereas the relative risk in black male smokers compared with nonsmokers was 3 (*107*).

Multivariate analyses were performed to evaluate differential risk between the black and the white men in Evans County (*146*). A multiple logistic model for the white men was developed using as

explanatory variables smoking, diastolic blood pressure multiplied by age, abnormal electrocardiogram, and cholesterol multiplied by age. This predicted the total incidence and the cases by decile of risk quite well among the white men. When this model was applied to the risk factor levels of the black men ranked by decile of relative risk, four times as many cases were predicted as had been observed (54 predicted, but only 13 actually observed). However, when the multiple logistic model was constrained by an appropriate constant, the number of cases fit the black data satisfactorily. This is consistent with the view that cigarette smoking and the other risk factors are as important in the blacks as in the whites, but that the blacks were protected by some factor that was not accounted for in the analysis (*146*).

The Seven Countries Study

In the Seven Countries study, the risk of CHD in U.S. railroad men resident in the northwest sector of the United States was compared with the risk of CHD in men living in contrasting environments in Europe and Japan. In the Pooling Project, the U.S. railroad men were found to have levels of risk factors comparable to the other principal cohorts, but the total number of cases was 16 percent lower than the number predicted by average parameters of the Pooling Project data.

The relationships of risk factors measured at entry to the subsequent incidence of CHD were less uniform in those cohorts of the Seven Countries study with a low incidence of CHD events, and the absolute incidence at specified levels of the risk factors was significantly different.

With parameters developed from the data of the U.S. railroad cohort and using the risk factors cigarette smoking, systolic blood pressure, serum cholesterol, body mass index, pulse rate, and age, 226 CHD deaths were predicted for the northern European cohorts, whereas 272 CHD deaths were actually observed. Although the predicted number of cases based on the experience of U.S. railroad men underestimated the number observed in the northern European cohorts by 20 percent, there was excellent correlation between predicted and observed cases by decile of risk. Furthermore, the absolute rate in the northern European cohorts was close to that predicted by average U.S. experience as observed in the Pooling Project.

In contrast to the northern European cohorts, the southern European cohorts had substantially fewer CHD deaths than were predicted by the multiple logistic equation based on the experience of the U.S. railroad cohort. As shown in Figure 14, 66 percent more cases were predicted than observed; however, rank order by decile of risk correlated closely ($r = 0.92$). Consistent with these differences,

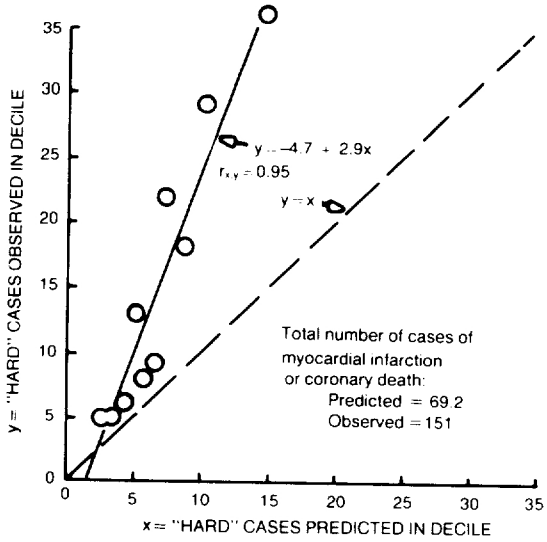

FIGURE 14.—Ten-year incidence of coronary death or myocardial infarction (hard CHD) in northern Europe, in the deciles of probability estimated from the logistic coefficients from the data on the men in southern Europe and the number of such incidence cases actually observed in those deciles

SOURCE: Keys (*143*).

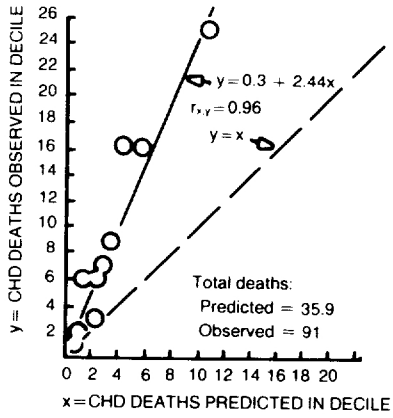

FIGURE 15.—Ten-year deaths from coronary heart disease in northern Europe, predicted in the deciles of probability estimated from the logistic coefficients from the data on the men in southern Europe and the number of coronary deaths actually found in those deciles

SOURCE: Keys (*143*).

multivariate equations for CHD incidence and for CHD deaths based on southern European experience underpredicted CHD incidence and death rates for the cohorts in northern Europe by a factor of 2.5 (Figures 14 and 15). Nevertheless, by rank order of risk, correlation between predicted and observed events was excellent ($r = 0.98$).

These detailed comparisons of the results from major epidemiologic investigations of CHD incidence do indicate that there is excellent agreement in the relationships of cigarette smoking and the other risk factors to the subsequent development of CHD in white men living in the United States and northern Europe. The agreement is close enough so that risk of CHD may be predicted well by the level of the major risk factors, using equations that are largely interchangeable among widely separated cohorts living in these different regions.

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