As part of the longitudinal study on the development of cardiovascular disease which is being conducted at Framingham, Mass., attention is being given to a variety of specific factors. This report presents evidence on national origin, educational status, and smoking and drinking habits.

SOME FACTORS ASSOCIATED WITH THE DEVELOPMENT OF CORONARY HEART DISEASE

SIX YEARS' FOLLOW-UP EXPERIENCE IN THE FRAMINGHAM STUDY

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AT FRAMINGHAM, MASS., the National Heart Institute has been conducting a prospective longitudinal study of factors related to the development of cardiovascular disease. A random sample consisting of two-thirds of the adult population, aged 29-62 years, was chosen for study. The sample size and age distribution were chosen to provide an adequate group of persons to be observed 20 or more years in which there would be a sufficient number of susceptible individuals. It was possible to bring in for examination 68.6 per cent (4,469) of the 6,510 selected. A group of 740 volunteers was added to supplement the initial group of respondents for prospective study (Table 1).[1] Follow-up of this group has been carried on for four biennial examinations representing six years of observation. A previous report has confirmed that certain factors are associated with increased risk of development of coronary heart disease.[2] Most important of these are hypercholesterolemia and hypertension. Many factors appear to be related to the development of coronary heart disease. The exact interplay of these factors and a possible common denominator important in the pathogenesis of coronary heart disease remain to be determined. No one factor has been clearly demonstrated to be essential.

Table 1—Composition of Framingham Study Group

	Number of Persons		
	Total	Men	Women
Random Sample	6,510	3,090	3,420
Respondents	4,469	2,024	2,445
Respondents free of CHD*	4,393	1,976	2,417
Volunteers free of CHD	734	307	427
Total free of CHD (Population at Risk)	5,127	2,283	2,844

* Coronary heart disease.

Table 2—Evidence of New Coronary Heart Disease in Framingham Study Group—Six-Year Follow-Up

	Number of Events		
	Total	Men	Women
All New Coronary Heart Disease*	186	125	61
Myocardial Infarction (ECG and Clinical Evidence)	71	57	14
Myocardial Infarction by ECG only	9	7	2
Sudden Death			
With preexisting evidence of CHD	9	9	—
Without preexisting evidence of CHD	18	15	3
Angina Pectoris	79	37	42

* The categories are mutually exclusive. Assignment was made according to the following priority: 1. Sudden death; 2. Myocardial infarction; 3. Angina pectoris.

At Framingham many of the factors believed to be important in the development of coronary heart disease are under study. This report is concerned with the geographical distribution of the disease within the town, the educational status and national origin of the subjects, and their smoking and drinking habits.

In order to assess factors related to the subsequent development of coronary heart disease, all persons exhibiting evidence of the disease on their initial examination were excluded from the population at risk. Criteria used for establishing a diagnosis of coronary heart disease have been defined in a previous publication.[2] In brief, they include (1) a definite history and/or definite electrocardiographic evidence of myocardial infarction; (2) definite angina pectoris; and (3) sudden death under circumstances suggesting coronary heart disease. The diagnostic categories comprising coronary heart disease occurring in the first six years of follow-up are specified in Table 2.

Socioeconomic Factors

The data on socioeconomic factors are very limited. In order to assure as complete a clinic follow-up as possible, the Framingham Study has avoided home interviews and has kept the clinic examination as short and as inoffensive as is consistent with the main purposes of the study. Only three socioeconomic factors —place of residence, education, and nativity—are reported. The study is restricted to males age 45-62 at time of entry because the incidence of coronary heart disease in the other age and sex groups studied was too low for evaluation.

Place of Residence

The residents of certain areas of Framingham differed from others within the town with respect to economic status, national origin, and education. Framingham was divided into eight voting precincts. No precise characterization of their socioeconomic features is available.

Table 3—Six-Year Incidence of Coronary Heart Disease by Precinct—Framingham Men, 45-62

Precinct	Population at Risk	New CHD	
		Observed No.	Expected No.*
All precincts	1,037	94	94.0
Precinct 1	198	14	17.5
Precinct 2	107	3	8.7
Precinct 3	174	19	15.7
Precinct 4	115	14	11.2
Precinct 5	79	8	7.7
Precinct 6	163	16	15.3
Precinct 7	108	10	9.3
Precinct 8	92	10	8.6
Outside Framingham	1	—	

* Expected numbers are calculated from the incidences in five-year age groups for all men 45–62 and the population at risk in five-year age groups for the specified precincts.

There are some less precise measurements as well as some subjective impressions of these characteristics which were studied.

One of the precincts in the town has had a lower incidence of coronary heart disease than the others (Table 3). Of 107 men in the age group 45-62 in Precinct 2, only three have developed new coronary heart disease compared to an expected number of 9 (8.7). This precinct was geographically distinct from the rest of the town. It was an area of working people, who owned small homes or occupied multiunit rental property clustered about a rug factory which had been operating at the same site for nearly 100 years. This industry employed approximately a third of the men in the study from that precinct. A number of families have been living in the area for many generations. Until 1875 this precinct was a separate town and still retains the place name. The educational level of the residents was somewhat lower than for the study group as a whole. There were fewer male graduates from high school and college. Distribution by national origin was little different from Framingham as a whole. At present there is an insufficient number of cases of newly developed disease to determine the meaning of this observation.*

Education

The data from the six-year follow-up show a significant trend in the incidence of coronary heart disease in relation to educational level (Table 4), the incidence being less at higher levels. This association was not demonstrated at the time of the four-year follow-up. The educational level was related to age, younger men having a higher educa-

* Statistical note: Tests of extreme incidences are based on the tables of Halperin, et al.[3] Tests for trend are based on a procedure prepared by Edwards.[4] Statistically significant refers to a probability less than 5 per cent.

Table 4—Six-Year Incidence of Coronary Heart Disease According to Schooling—Framingham Men, 45-62

Schooling	Population at Risk	No.	Coronary Heart Disease Observed Rate/1,000	Coronary Heart Disease Expected* Rate/1,000
Total	1,037	94	90.6	90.6
None	12	3		
4th grade or less	71	6	113.5	99.3
5th, 6th, and 7th grade	90	6		
Grade school graduate	250	33		
High school, not graduate	160	14	87.5	83.9
High school graduate	177	13	72.7	82.2
Business college	43	3		
College, not graduate	72	5		
College graduate	76	2	62.2	83.5
Postgraduate	45	5		
Unknown	41	4	97.6	106.2

* Expected rates are calculated from the incidence in five-year age groups for all men 45-62 and the population at risk in five-year age groups for the specified schooling categories.

Table 5—Six-Year Incidence of Coronary Heart Disease According to National Origin—Framingham Men 45-62

National Origin	Population at Risk	No.	Coronary Heart Disease Observed Rate/1,000	Coronary Heart Disease Expected* Rate/1,000
Total	1,037	94	90.6	90.6
Foreign-born				
Total	320	26	81.2	96.8
Italy	145	14	96.6	105.0
Other	175	12	68.6	90.1
Native-born				
Total	717	68	94.8	87.9
Great Britain	226	14	61.9	90.9
Ireland	151	19	125.8	93.6
Other	340	35	102.9	83.3

NOTE: National origin is defined by country of birth of parents and grandparents. For example, for a person to be classified as "native-born Great Britain," at least one of these antecendants must have been born in Great Britain and the others born in the United States.

* Expected rates are calculated from the incidence in five-year age groups for all men 45–62 and the population at risk in five-year age groups for the specified national origin categories.

tional level than the older men. When correction was made for this bias, the trend remained but was no longer statistically significant. Closer examination of the data indicates that the excess incidence for the group of men without any high school education is confined to those graduated from grade school and is not evident in the group whose formal schooling ended earlier. The grade school graduate in Framingham is generally the native-born American whose ancestors came from Great Britain or Ireland. The Framingham men who did not complete grade school were almost all Italian immigrants. Therefore, these data apparently suggest that in Framingham a native-born American male, 45-62 years of age and of limited education, has a higher than average risk of developing coronary heart disease.

National Origin

There are no indications of any association between national origin and the risk of coronary heart disease (Table 5). The one large distinct ethnic group, the Italians, had almost the same incidence of coronary heart disease as the rest of the population studied. There is an indication, not statistically significant, that the foreign-born Italian has a slightly lower incidence of coronary heart disease than the native-born, but since they represent different generations, it is difficult to make a direct comparison.

Smoking

A number of large studies have shown a relationship between smoking and mortality from coronary heart disease.[5,6] The data from these studies have been derived from death certificate material and consequently did not include coronary heart disease manifested simply as angina pectoris and were not restricted to new disease. Analysis of the four-year follow-up at Framingham, which showed no relation between smoking and coronary heart disease, was based exclusively

on new disease, nonfatal as well as fatal, and was therefore not strictly comparable with the findings from the mortality studies.

For purposes of comparison with these other studies, the six-year follow-up data are analyzed differently. Starting from the same population at risk, two types of new events are considered: (1) angina pectoris and (2) myocardial infarction and sudden death. These two categories of new coronary heart disease are also considered separately for the other factors treated in this paper (precinct, national origin, education, and drinking) but since the effects shown are indistinguishable for the two categories, they are combined in the final tabulations. For cigarette smoking, however, the case is different. Study of the relation of smoking to the development of all new cases of coronary heart disease continues to show lack of association, bearing out the finding of the four-year follow-up.[1] When, however, a separate analysis is made of those cases manifesting more severe degrees of coronary heart disease, (excluding those with angina pectoris alone) an association of risk with cigarette smoking seems to emerge, the risk rising with the number of cigarettes smoked per day. While these differentials are not statistically significant, they are in the same direction as the findings of the larger mortality studies.

In addition, the mortality experience in six years' follow-up is also presented. For this purpose the total Framingham Study group is considered the population at risk, and all deaths from coronary heart disease are enumerated regardless of clinical status at entry. These data do not evidence statistical significance for a trend relating incidence with amount of cigarette smoking, if the broad age group 45-62 is considered as a whole, but they do become significant when allowance is made for the fact that heavy cigarette smoking is more common among younger men, with a lesser risk of coronary heart disease. It is our opinion that these data are based on too few cases of coronary heart disease to indicate a definite association with smoking; but our findings are consistent with those involving larger populations.

The mechanisms by which smoking might be involved in the production of coronary heart disease remains obscure. There is no experimental evidence that smoking damages the healthy blood vessel.[7] It is possible that smoking is associated with some other factor which in turn may be important in the pathogenesis of the disease. At Framingham there is some evidence that smoking habits are associated with other characteristics (Table 7). Serum cholesterol levels tended to be slightly higher and relative weight slightly lower among cigarette smokers than among nonsmokers. There is evidence of a gradient of cholesterol with increasing amount of cigarette smoking in the younger men. These findings agree well with those previously reported by Gofman, et al.[8] However, men who had quit smoking also had an elevated serum cholesterol on the average. The findings with respect to relative weight, while they indicate significant variations of weight with smoking habits, do not show any clear-cut pattern. In general, weight is lower in cigarette smokers than nonsmokers except in the case of heavy cigarette smokers in whom the weight approaches that of the nonsmokers. The Framingham data indicate no association of smoking habits with blood pressure levels. All these relations were evaluated on the basis of data tabulated in five-year age groups but for convenience in presentation the data are given here in broader age groups.

The most striking association with cigarette smoking noted is the amount of alcohol consumed. A greater consumption is found with increasing use of tobacco (particularly in the younger

Table 6—Six Years' Incidence and Mortality from Coronary Heart Disease According to Smoking History—Framingham Men, 45-62

Smoking History	Incidence of new CHD: Population at Risk Number	Mean Age	Number of Events Total	AP	Other	Rate/1,000 Total	AP	Other		CHD Mortality*: Population at Risk	Deaths	Rate/1,000
Total	1,037	52.6	94	32	62	90.6	30.9	59.8	(59.8)	1,083	38	35.1
Never smoked	141	53.0	14	7	7					143	3	
Lapsed	115	53.6	8	2	6	83.1	32.3	50.8	(63.2)	121	1	24.6
Cigar or pipe only	177	53.0	14	5	9					184	7	
Smoked cigarettes	594	52.3	57	18	39	96.0	30.3	65.7	(57.3)	624	25	40.1
less than 10/day	79	53.5	3	—	3	38.0	—	38.0	(65.2)	82	2	24.4
10/day	39	52.8	2	1	1					41	1	
11–19/day	56	53.0	8	3	5	105.3	42.1	63.2	(62.3)	61	2	29.4
20/day	238	52.4	21	5	16					247	11	
21–39/day	116	51.2	12	7	5	104.8	33.3	71.4	(54.6)	124	5	45.5
40 or more/day	66	51.3	11	2	9					69	4	
Unknown	10	52.8	1	—	1					11	2	

NOTE: The rates shown in parentheses for incidence of new CHD other than AP are expected rates calculated from the incidence in five-year age groups for all men 45-62 and the populations at risk in five-year age groups for the specified smoking categories.

* Regardless of clinical status at entry.

Table 7—Mean Levels of Some Characteristics in Relation to Smoking History—Men in Framingham Study Group by Age

Tobacco History	Number of Persons 29–44	45–59	Framingham Relative Weight* 29–44	45–59	Serum Cholesterol mg per 100 ml 29–44	45–59	Systolic Blood Pressure mm Hg 29–44	45–59	Alcohol Consumed (oz/mo) 29–44	45–59
Total	1,253	1,008	101.2	102.0	223.1	229.3	133.1	140.9	24.0	23.8
No tobacco used	149	131	103.4	106.2	216.1	228.3	133.8	143.0	10.2	9.2
Cigarettes	874	589	99.9	100.1	224.8	229.5	132.5	140.3	27.7	27.4
(Less than 10/day)	75	76	100.6	100.3	217.4	229.1	134.7	144.0	23.4	26.8
10–19/day	134	95	96.8	103.0	221.1	230.0	129.4	141.6	24.0	15.5
20–39/day	551	350	99.5	98.8	225.8	227.8	132.2	138.9	25.5	28.1
40 or more/day	114	68	105.2	103.0	229.0	238.5	136.1	141.5	46.9	43.1
Pipes or cigars only	128	166	106.7	102.9	214.9	227.1	135.0	141.9	20.0	22.5
Lapse	94	112	102.2	104.8	229.2	233.1	135.6	140.1	18.0	23.4
Unknown	8	10	91.1	108.8	193.0	184.5	120.8	136.4	—	—

NOTE: These characteristics are as measured on Exam I, except that cholesterol measurements for Exam II were used for case numbers below 4,000 and the alcohol histories are as of Exam II.

* Framingham Relative Weight (FRW) = $\frac{\text{Observed Weight}}{\text{Median weight for height and sex category x 100 in the Framingham Study}}$

Table 8—Alcohol Consumption in Relation to New Coronary Heart Disease—Framingham Study Group by Age and Sex: Six Years' Incidence

Age and Sex	Number of Persons		Mean Alcohol Consumption (oz/mo)	
	Population at Risk	New CHD	Population at Risk	New CHD
Men				
30–39	754	15	23.3	23.8
40–49	703	27	24.8	29.6
50–59	555	63	23.4	23.2
60–62	60	9	22.9	12.1
Women				
40–49	890	17	6.5	1.3
50–59	737	36	4.8	2.1
60–62	54	4	7.4	1.4

NOTE: None of the means for new CHD differ significantly from the population means.

age group). Heavy smokers (two or more packages a day) showed the greatest consumption of alcohol in both age groups. Alcohol consumption per se, however, does not show any relation to the development of coronary heart disease (Table 8). Women who develop new coronary heart disease have lower alcoholic consumption than expected. While this is suggestive, it could represent a sampling fluctuation.

Summary

Several factors have been analyzed for possible association with the development of coronary heart disease. During the six years of follow-up of the population there was an inverse association with educational status, the incidence of new CHD being less at higher educational levels. There was no association between national origin and the risk of CHD. A suggestively low CHD incidence was noted in one of the eight Framingham precincts. This precinct differed from the others in some respects, but no explanation of this finding can as yet be offered.

Smoking was associated with an increased incidence of nonfatal myocardial infarction and of death from CHD in men 45-62. It was not associated with an increased incidence of angina pectoris. Cholesterol levels were higher among cigarette smokers than among nonsmokers and higher among those who had smoked and stopped than among those who had never smoked. Neither relative weight nor blood pressure showed a similar association with smoking.

Alcohol consumption per se was not associated with CHD although heavy alcohol intake was associated with heavy smoking.

REFERENCES

1. Gordon, T.; Moore, F. E.; Shurtleff, D.; and Dawber, T. R. Some Methodological Problems in the Long-Term Study of Cardiovascular Disease: Observations on the Framingham Study. (To appear in the Journal of Chronic Diseases.)
2. Dawber, T. R.; Moore, F. E.; and Mann, G. V. Coronary Heart Disease in the Framingham Study. A.J.P.H. (Part 2) 47,4:4–24 (Apr.), 1957.
3. Halperin, M.; Greenhouse, S. M.; Cornfield, J.; and Zalokar, J. Tables of Percentage Points for the Studentized Maximum Absolute Deviate in Normal Samples. J. Am. Statist. A. 50:185–195 (Mar.), 1955.
4. Edwards, J. H. A Note on the Interpretation of N x 2 Tables. Brit. J. Prev. & Social. Med. 12:141–146, 1958.

5. Hammond, E. C., and Horn, D. The Relation Between Human Smoking Habits and Death Rates. J.A.M.A. 155:1316–1328 (Aug. 7), 1954.
6. Doll, R, and Hill, A. B. Lung Cancer and Other Causes of Death in Relation to Smoking. Brit. M. J. 2:1071–1081 (Nov. 10), 1956.
7. Plotz, M. Coronary Heart Disease. New York, N. Y.: Hoeber-Harper, 1957, p. 64.
8. Gofman, J. W.; Lindgren, F. T.; Strisower, B.; deLalla, D.; Glazier, S.; and Tamplin, A. H. Cigarette Smoking Serum Lipoproteins and Coronary Heart Disease. Geriatrics 10:349–354 (Aug.), 1955.

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