FISH CONSUMPTION AND THE 30-YEAR RISK OF FATAL MYOCARDIAL INFARCTION

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ABSTRACT

Background Epidemiologic data on the possible benefit of eating fish to reduce the risk of coronary heart disease have been inconsistent. We used data from the Chicago Western Electric Study to examine the relation between base-line fish consumption and the 30-year risk of death from coronary heart disease.

Methods The study participants were 1822 men who were 40 to 55 years old and free of cardiovascular disease at base line. Fish consumption, as determined from a detailed dietary history, was stratified (0, 1 to 17, 18 to 34, and ≥35 g per day). Mortality from coronary heart disease, ascertained from death certificates, was classified as death from myocardial infarction (sudden or nonsudden) or death from other coronary causes.

Results During 47,153 person-years of follow-up, there were 430 deaths from coronary heart disease; 293 were due to myocardial infarctions (196 were sudden, 94 were nonsudden, and 3 were not classifiable). Cox proportional-hazards regression showed that for men who consumed 35 g or more of fish daily as compared with those who consumed none, the relative risks of death from coronary heart disease and from sudden or nonsudden myocardial infarction were 0.62 (95 percent confidence interval, 0.40 to 0.94) and 0.56 (95 percent confidence interval, 0.33 to 0.93), respectively, with a graded relation between the relative risks and the strata of fish consumption (P for trend = 0.04 and 0.02, respectively). These findings were accounted for by the relation of fish consumption to nonsudden death from myocardial infarction (relative risk, 0.33; 95 percent confidence interval, 0.12 to 0.91; P for trend = 0.007).

Conclusions These data show an inverse association between fish consumption and death from coronary heart disease, especially nonsudden death from myocardial infarction. (N Engl J Med 1997;336:1046-53.)

THE idea that the consumption of fish reduces the risk of coronary heart disease is supported by data from five prospective epidemiologic studies,[1-6] two case–control studies,[7,8] and one secondary-prevention trial.[9] However, the results of other studies are apparently inconsistent with these findings.[10-14] We report on the association between fish consumption and the 30-year risk of death from myocardial infarction (sudden or nonsudden), coronary heart disease, cardiovascular diseases, and all causes in the Chicago Western Electric Study.

METHODS

Population

The Chicago Western Electric Study comprises 2107 men who were 40 to 55 years old in 1957. Participants had been employed for at least two years at the Western Electric Company Hawthorne Works in Chicago and worked in occupations related to the manufacture of telephones. The selection of participants, their demographic characteristics, the initial examination, and follow-up procedures have been described elsewhere.[15,16]

Dietary Assessment

Dietary information was obtained at the first and second examinations, performed one year apart by two nutritionists using standard questionnaires.[17] The information elicited included a typical workday eating pattern, a typical weekend eating pattern, the time and place of meals, special diets, changes in eating habits over the previous 20 years, and the consumption (frequency and quantity) of 195 foods during the previous 28 days. Each participant's daily intake of nutrients was determined with the use of a food-composition table.[15-20]

Food-profile scores, based on information obtained at the second examination, indicated the level of consumption of 26 foods over the previous 28 days: soft drinks; coffee; decaffeinated coffee; whole milk; skim milk; cream; cheese; eggs; ice cream; puddings or custards; soups; fish; beef, veal or lamb; pork, ham, or bacon; liver; poultry; mixed dishes; vegetables; breads or cereals; potatoes; fruits; pastries; sweets or sugars; butter; margarine; and fried foods. Each item was coded on a four-point scale (0 for none and 1, 2, or 3 for a low, moderate, or high level of consumption, respectively). Fish consumption, in 120-g units per 28 days, was coded as 0 for none, 1 for less than 4 units, 2 for 4 to 8 units, and 3 for more than 8 units, corresponding to the following average daily intakes: none, 1 to 17 g, 18 to 34 g, or 35 g or more.

Follow-up

Vital status was determined at the annual examination for the first 10 years and by means of mailed questionnaires or telephone interviews for the next 15 years; data were available for all 2107 men. For the 31st year, data on vital status were obtained from the National Death Index, the Health Care Financing Administration, and surviving participants' responses to questionnaires; data were available for 2084 of the participants (98.9 percent). The causes of death were determined from death certificates according to codes in the *International Classification of Diseases,*

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Eighth Revision (ICD-8).[21] For the purposes of the analyses presented here, follow-up began after the second examination and continued through the 31st anniversary of the date of enrollment in the study.

End Points

The end points of the study were death from myocardial infarction (ICD-8 code 410), death from coronary heart disease (ICD-8 codes 410 through 414), and death from cardiovascular diseases (ICD-8 codes 400 through 445). Death from myocardial infarction was classified as sudden or not sudden according to the duration of the terminal illness and the place of death, as recorded on the death certificate.

Statistical Analysis

Average base-line (1957 to 1959) dietary intake and cardiovascular risk factors were calculated for four strata of fish consumption: none, 1 to 17 g, 18 to 34 g, and 35 g or more per day. Age-adjusted mortality rates for fatal myocardial infarction (all deaths, sudden deaths, and nonsudden deaths), all deaths from coronary heart disease, all deaths from cardiovascular diseases, and deaths from all causes were calculated per 10,000 person-years for each stratum of fish consumption. Cox proportional-hazards regression[22] was used to estimate the relative risk of death and 95 percent confidence interval for each stratum of fish consumption (as compared with no consumption), with adjustment for possible confounding variables, and to test for linear trend (for the four strata of fish intake classified as indicator variables). This model was also used to test for possible interactions (the statistical power was limited in this regard).

RESULTS

Of the 2107 men in the Chicago Western Electric Study, 62 were excluded because they did not attend the second examination. Another 223 men were excluded because of prior coronary heart disease (74) or missing data on diet (93), education (38), body-mass index (9), serum total cholesterol level (5), smoking status (2), or blood pressure (2), leaving a total of 1822 men.

Characteristics at Base Line

Sixty-eight percent of the study participants were blue-collar workers; 42 percent were Catholic (Table 1). (Religion was included as a variable because of religious dietary practices.) On average, the study participants were overweight, with higher-than-desirable levels of blood pressure, serum cholesterol, and intake of total fat, saturated fat, and cholesterol. Over half (58 percent) were smokers, with a mean of 18 cigarettes smoked per day. Most (85 percent) were drinkers, who consumed an average of 18.8 ml of alcohol per day (4.2 percent of kilocalories).

Religion and the intake of total energy, ethanol, several macronutrients, and several micronutrients differed significantly among the four strata (Table 1). For all the nutritional variables except carbohydrate and saturated and monounsaturated fatty acid, the highest levels were in the men with the highest level of fish consumption. Age, education, body-mass index, blood pressure, serum cholesterol level, smoking status and number of cigarettes smoked, heart rate, presence or absence of a history of diabetes, and presence or absence of electrocardiographic abnormalities did not differ significantly among the four strata.

30-Year Mortality

During 30 years of follow-up, there were 293 deaths from myocardial infarction (196 sudden deaths, 94 nonsudden deaths, and 3 that were not classifiable), 430 deaths from any type of coronary heart disease, 573 from any type of cardiovascular disease, and 1042 from any cause. Of the 137 deaths from coronary heart disease other than myocardial infarction (ICD-8 codes 411 through 414), few were sudden.

Fish Consumption and Age-Adjusted Mortality

The age-adjusted rates of death from myocardial infarction, coronary heart disease, cardiovascular diseases, and all causes were lowest for the men with the highest consumption of fish, with a trend toward lower mortality rates with higher levels of consumption (Table 2). The men who consumed 35 g or more of fish per day had a 42 percent lower rate of death from myocardial infarction than the nonconsumers, a relation accounted for by the inverse association between nonsudden death from myocardial infarction and fish consumption. In contrast, there was only a moderate association between fish intake and sudden death from myocardial infarction.

The trend toward an association between higher fish consumption and lower rates of death from coronary heart disease, cardiovascular diseases, and all causes was attributable to the inverse relation between fish consumption and death from myocardial infarction, particularly nonsudden death from myocardial infarction. Thus, when deaths from myocardial infarction were subtracted from deaths from coronary heart disease, deaths from cardiovascular diseases, and deaths from all causes, there was no significant graded relation between the four strata of fish consumption and death rates; the result was similar with the subtraction of nonsudden deaths from myocardial infarction (Table 2).

Fish Consumption and Multivariate-Adjusted Mortality

Three Cox proportional-hazards models were used to calculate the relative risks of death for the men in the four strata of fish consumption. Model 1 was adjusted only for age. Model 2 was adjusted for age; education; religion; systolic blood pressure; serum cholesterol; number of cigarettes smoked per day; body-mass index; presence or absence of diabetes; presence or absence of electrocardiographic abnormalities; daily intake of energy, ethanol, macronutrients, and cholesterol; and daily intake of iron, thiamine, riboflavin, niacin, vitamin C, beta carotene, and retinol. Model 3 was adjusted for all the non-

TABLE 1. BASE-LINE CHARACTERISTICS OF 1822 MEN ACCORDING TO THE LEVEL OF FISH CONSUMPTION.*

CHARACTERISTIC	FISH CONSUMPTION				
	0 g/DAY (N=189)	1–17 g/DAY (N=646)	18–34 g/DAY (N=745)	≥35 g/DAY (N=242)	TOTAL (N=1822)
Age (yr)	47.3	47.5	47.7	47.8	47.6±4.4
Body-mass index†	25.4	25.3	25.7	25.7	25.5±3.2
Height (cm)	174.7	174.5	174.6	174.4	174.6±6.4
Weight (kg)	77.9	77.1	78.5	78.3	77.9±10.8
Blood pressure (mm Hg)					
Systolic	133.0	131.7	131.6	133.6	132.1±16.8
Diastolic	86.3	85.1	85.4	86.7	85.6±9.8
Serum cholesterol (mg/dl)‡	242.5	239.1	242.2	245.7	241.6±45.0
Heart rate (beats/min)	73.2	72.1	71.8	72.8	72.2±10.5
History of diabetes (% of men)	1.6	1.4	1.5	1.6	1.5
Current smokers (% of men)	56.2	60.7	56.2	56.0	57.8
Current smoking (no. of cigarettes/day)	19.1	17.5	17.8	18.8	18.0±8.8
Current drinkers (% of men)§	80.4	83.4	86.0	91.2¶	85.2
Current ethanol consumption (% of kcal)	4.4	3.9	4.3	4.6	4.2±4.6
Education (yr)	10.7	11.2	11.3	11.2	11.2±2.5
Electrocardiographic abnormalities (% of men)					
Major	3.1	4.1	2.5	3.6	3.3
Minor	13.4	16.0	14.6	14.8	15.0
White-collar occupation (% of men)	26.3	30.1	34.5	35.6	32.2
Religion (% of men)					
Catholic§	27.5	40.6	46.6	46.7¶	42.5
Unknown	15.3	9.6	8.5	9.9	9.8
Daily nutritional intake					
Total energy (kcal)§	3081.6	3005.7	3126.5	3498.4¶	3128.8±842.5
Total fat (% of kcal)	42.6	43.0	42.8	43.2	42.9±4.1
Saturated fatty acid (% of kcal)	16.4	16.5	16.3	16.4	16.4±2.3
Monounsaturated fatty acid (% of kcal)	19.4	19.7	19.5	19.6	19.6±2.5
Polyunsaturated fatty acid (% of kcal)§	3.7	3.9	4.0	4.1¶	3.9±0.8
Linoleic acid§	3.3	3.5	3.5	3.6¶	3.5±0.8
Linolenic acid	0.2	0.2	0.2	0.2	0.2±0.04
Arachidonic acid§	0.2	0.3	0.3	0.3¶	0.3±0.07
Dietary cholesterol (mg/1000 kcal)	228.5	235.9	237.6	241.7	236.6±60.1
Dietary Keys score (units)‖	61.9	62.1	61.7	61.9	61.9±7.6
Carbohydrate (% of kcal)§	38.6	38.8	37.8	36.2¶	38.0±4.7
Protein (% of kcal)§	14.7	14.7	15.1	15.5¶	15.0±1.9
Animal§	11.2	11.2	11.7	12.1¶	11.5±2.0
Vegetable	3.5	3.5	3.5	3.5	3.5±0.6
Iron (mg)§	16.3	16.0	17.0	19.5¶	16.9±4.5
Thiamine (mg)§	1.6	1.6	1.6	1.8¶	1.6±0.5
Riboflavin (mg)§	2.5	2.3	2.4	2.7¶	2.4±0.8
Niacin (mg)§	21.6	21.4	23.1	26.9¶	22.8±6.2
Vitamin C (IU)§	95.4	95.7	103.2	117.2¶	101.6±40.5
Vitamin D (IU)	179.8	180.4	180.6	192.2	182.0±132.0
Beta carotene (IU)§	5252.6	5203.2	5771.8	6178.0¶	5570.0±2733.4
Retinol (IU)§	4163.3	4236.9	4950.7	5744.7¶	4753.2±3194.4

*Unless otherwise indicated, data are mean values, and plus–minus values are means ±SD. All data are for the first and second examinations, 1957–1958 and 1958–1959, except for history of diabetes, ethanol consumption, education, electrocardiographic abnormalities, and white-collar occupation, which are for 1957–1958 only, and intake of beta carotene and retinol, which are for 1958–1959 only. Values for subcategories of a characteristic may not sum to the total value for the characteristic because of rounding.

†The body-mass index is the weight in kilograms divided by the square of the height in meters.

‡To convert values for cholesterol to millimoles per liter, multiply by 0.02586.

§P≤0.01 by analysis of variance.

¶P≤0.05, by the Bonferroni method, for the comparison with no fish consumption.

‖The Keys score is calculated as $1.35\ (2S-P)+1.5\ (1000\ C/E)^{1/2}$, where S denotes saturated fatty acid, P polyunsaturated fatty acid, C dietary cholesterol, and E total energy.

TABLE 2. AGE-ADJUSTED MORTALITY RATE AT 30 YEARS ACCORDING TO BASE-LINE FISH CONSUMPTION.*

CAUSE OF DEATH	TOTAL DEATHS	FISH CONSUMPTION							
		0 g/DAY		1–17 g/DAY		18–34 g/DAY		≥35 g/DAY	
		no. of deaths	death rate	no. of deaths	death rate	no. of deaths	death rate	no. of deaths	death rate
No. of men/person-years		*189/4754*		*646/16,681*		*745/19,350*		*242/6368*	
Overall									
MI	293	36	78.6	115	69.2	113	57.9	29	45.3
All CHD	430	48	104.2	157	94.6	179	91.8	46	71.2
All CVD	573	61	132.4	208	125.5	235	120.6	69	108.2
All causes	1042	105	226.4	377	227.0	432	221.7	128	203.6
MI									
Nonsudden death	94	12	27.2	44	26.5	32	16.3	6	9.7
Nonsudden death (>12 hr)	70	8	18.0	33	19.8	23	11.7	6	9.7
Sudden death	196	24	51.5	69	41.6	80	41.1	23	35.6
Sudden death (≤12 hr)	164	15	32.5	61	36.7	66	34.0	22	34.2
Excluding MI									
CHD	137	12	25.6	42	25.4	66	33.9	17	25.9
CVD	280	25	53.8	93	56.3	122	62.7	40	62.9
All causes	749	69	147.8	262	157.8	319	163.8	99	158.3
Excluding nonsudden death from MI									
CHD	336	36	77.1	113	68.1	147	75.5	40	61.6
CVD	479	49	105.3	164	99.0	203	104.3	63	98.6
All causes	948	93	199.2	333	200.6	400	205.5	122	193.9

*Myocardial infarction (MI) was defined as ICD-8 code 410, coronary heart disease (CHD) as ICD-8 codes 410 through 414, and cardiovascular diseases (CVD) as ICD-8 codes 400 through 445. Nonsudden death from MI was defined as death occurring more than 12 hours after the onset of the terminal acute illness (70 deaths) or if information on the duration of the illness was unavailable, death occurring during the hospital stay (24 deaths). Sudden death from MI was defined as death occurring no more than 12 hours after the onset of the terminal acute illness (164 deaths) or if information on the duration was unavailable, death occurring out of the hospital or in the emergency room (32 deaths). Death rates are per 10,000 person-years.

TABLE 3. MULTIVARIATE-ADJUSTED RELATIVE RISK OF DEATH AT 30 YEARS ACCORDING TO BASE-LINE FISH CONSUMPTION.*

CAUSE OF DEATH	TOTAL DEATHS	FISH CONSUMPTION				P FOR TREND†
		0 g/DAY	1–17 g/DAY	18–34 g/DAY	≥35 g/DAY	
		relative risk (95% confidence interval)				
Overall						
MI	293	1.00	0.88 (0.60–1.28)	0.76 (0.52–1.12)	0.56 (0.33–0.93)	0.017
All CHD	430	1.00	0.88 (0.63–1.22)	0.84 (0.61–1.17)	0.62 (0.40–0.94)	0.040
All CVD	573	1.00	0.94 (0.70–1.25)	0.89 (0.67–1.19)	0.74 (0.52–1.06)	0.010
All causes	1042	1.00	1.02 (0.82–1.27)	0.98 (0.79–1.22)	0.85 (0.64–1.10)	0.175
MI						
Nonsudden death	94	1.00	1.04 (0.54–2.02)	0.67 (0.35–1.33)	0.33 (0.12–0.91)	0.007
Nonsudden death (>12 hr)	70	1.00	1.31 (0.59–2.90)	0.77 (0.34–1.76)	0.51 (0.17–1.52)	0.053
Sudden death	196	1.00	0.78 (0.48–1.24)	0.80 (0.50–1.28)	0.68 (0.37–1.25)	0.337
Sudden death (≤12 hr)	164	1.00	1.13 (0.64–1.99)	1.04 (0.59–1.85)	0.99 (0.49–1.99)	0.827
Excluding MI						
CHD	137	1.00	0.93 (0.48–1.79)	1.11 (0.59–2.08)	0.82 (0.38–1.79)	0.963
CVD	280	1.00	1.03 (0.66–1.62)	1.09 (0.70–1.70)	1.02 (0.60–1.73)	0.814
All causes	749	1.00	1.10 (0.84–1.43)	1.10 (0.85–1.44)	1.00 (0.73–1.38)	0.962

*A multivariate proportional-hazards (Cox) model was used to adjust for base-line age and education; religion; systolic pressure; serum cholesterol; number of cigarettes smoked per day; body-mass index; presence or absence of diabetes; presence or absence of electrocardiographic abnormalities; and daily intake of energy, cholesterol, saturated, monounsaturated, and polyunsaturated fatty acids, total protein, carbohydrate, alcohol, iron, thiamine, riboflavin, niacin, vitamin C, beta carotene, and retinol. The causes of death are defined in the note to Table 2. CI denotes confidence interval, MI myocardial infarction, CHD coronary heart disease, and CVD cardiovascular diseases.

†P values are for linear trend across the four strata of fish consumption.

nutrient variables in model 2 plus daily intake of energy, alcohol, and the four categories of food correlated with fish consumption and death from myocardial infarction or other coronary causes (cheese, margarine, mixed dishes, and vegetables).

The results were similar with all three models; the data from model 2 are shown in Table 3. With adjustment for multiple confounders, a significant inverse relation prevailed between fish consumption and the risk of a fatal myocardial infarction. For the men who consumed 35 g or more of fish daily as compared with the nonconsumers, the relative risk of any death from myocardial infarction was 0.56, and the relative risk of nonsudden death from myocardial infarction was 0.33 (Table 3). The results were similar with the addition of occupation to model 2 ($r=0.51$ for the correlation with education) and with the use of other definitions of sudden death (instantaneous, within one hour after the onset of symptoms, and within three hours after the onset of symptoms).

The trend toward an inverse relation between fish consumption and death from coronary causes, cardiovascular causes, and all causes was accounted for by the data on fatal myocardial infarction — specifically, by the trend toward a lower risk of nonsudden death from myocardial infarction with higher fish consumption. No significant relation was found between fish consumption and sudden death from myocardial infarction (Table 3).

In these analyses, serum cholesterol level, blood pressure, number of cigarettes smoked per day, major electrocardiographic abnormalities, age, dietary cholesterol intake, and Keys dietary lipid score[23] were also significantly and independently related to mortality from myocardial infarction.

In analyses with model 3, which was adjusted for foods (instead of nutrients) and other variables, fish consumption was significantly and independently related to the risk of any death from myocardial infarction and to the risk of nonsudden death from myocardial infarction. With the variables for consumption of cheese, margarine, mixed dishes, and vegetables included individually in the model and with all four included together, the relative risks of fatal myocardial infarction for the men who consumed 35 g or more of fish per day (as compared with the nonconsumers) ranged from 0.53 to 0.58, with 95 percent confidence intervals that excluded values of 1.00 or higher (P for linear trend = 0.004 to 0.019). The relative risks of nonsudden death from myocardial infarction ranged from 0.22 to 0.26, with 95 percent confidence intervals that excluded values of 1.00 or higher (P for linear trend = 0.001 or 0.002).

To assess the stability and independence of the relation between fish consumption and the risk of death from myocardial infarction (all deaths and nonsudden deaths), we included an interaction term in the Cox models for fish consumption and each variable listed in Table 1, as well as for each of the four food categories included in model 3. For any death from myocardial infarction, there were significant interactions between fish consumption and age, major electrocardiographic abnormalities, and consumption of mixed dishes; for nonsudden death from myocardial infarction, there was a significant interaction between fish consumption and major electrocardiographic abnormalities. No other interaction terms were statistically significant.

On the basis of these four significant interactions, Cox analyses were performed with the following dichotomized variables: an age of less than 47 years versus an age of 47 or older, the two lower strata of consumption of mixed dishes versus the two higher strata, and the absence of major electrocardiographic abnormalities versus their presence. Among the 917 men who were younger than 47 years at base line, there were 116 deaths from myocardial infarction and 32 nonsudden deaths from myocardial infarction, with no significant relation between fish consumption and either end point (P for trend = 0.678 and 0.628, respectively); among the 905 men who were 47 or older, there were 177 deaths from myocardial infarction and 62 nonsudden deaths, with fish consumption significantly related to both end points (relative risks for consumers of 35 g or more per day as compared with nonconsumers, 0.41 and 0.15 [P for trend = 0.019 and 0.005], respectively). For low and high levels of consumption of mixed dishes (946 and 875 men, respectively), the relation of fish consumption to the risk of fatal myocardial infarction was similar: the men who consumed 35 g or more of fish per day (as compared with the nonconsumers) had low relative risks (0.42 and 0.58 for any death [P for trend = 0.089 and 0.051, respectively] and 0.10 and 0.63 for nonsudden death [P for trend = 0.126 and 0.059, respectively]). For the 1761 men without major electrocardiographic abnormalities, there was a graded relation between fish consumption and the risks of any death from myocardial infarction and nonsudden death from myocardial infarction: relative risks for the men in the highest stratum of fish consumption were 0.66 and 0.43 (P for trend = 0.093 and 0.028), respectively.

Two other subgroup analyses also yielded significant associations between fish consumption and the risk of fatal myocardial infarction. Among the 1535 men who had no evidence of major organ disease at base line, the relative risks for those in the highest stratum of fish consumption were 0.55 for any death and 0.48 for nonsudden death (P for trend = 0.035 and 0.030, respectively). Among the 1693 men who were classified as light or medium drinkers (consuming less than 50 ml of alcohol per day), the relative risks for those in the highest stratum of fish consumption were 0.58 and 0.31 (P for trend = 0.040 and 0.022), respectively.

Model 2 Cox analyses were repeated for the first, second, and third decades of follow-up, with 68, 97, and 128 total deaths from myocardial infarction and 14, 34, and 46 nonsudden deaths from myocardial infarction, respectively. The findings were consistent for the three periods. In the highest stratum of fish consumption, the relative risks of any death from myocardial infarction were 0.57, 0.59, and 0.59 (P for trend = 0.563, 0.329, and 0.039) for the first, second, and third decades, respectively; the relative risks of nonsudden death from myocardial infarction were 0.16, 0.61, and 0.38, respectively (P for trend = 0.019, 0.413, and 0.109). In other words, the relation between fish consumption and the risk of fatal myocardial infarction persisted throughout the 30 years of follow-up.

DISCUSSION

We found significant, independent, inverse graded associations between base-line fish consumption and the 30-year risk of death from coronary heart disease, particularly nonsudden death from myocardial infarction. Differences in death from coronary heart disease, cardiovascular diseases, and all causes among the four strata of fish consumption were attributable to differences in death from myocardial infarction, especially nonsudden death. Correspondingly, fish consumption was not significantly associated with the risk of death from other coronary causes.

The findings from four of seven prospective population studies — the Zutphen and Rotterdam (the Netherlands) studies, the Swedish study, and the study of U.S. physicians (12-year data)[1,2,4,6] — are broadly concordant with our data showing a significant inverse relation between fish consumption and the risk of death from coronary heart disease, as are the results from the two case–control studies[7,8] and the one intervention trial.[9] However, in regard to one specific aspect of death from coronary heart disease — whether it was sudden or not sudden — our findings apparently differ from those of the Physicians' Health Study[6] and the Seattle Study.[8] Both these studies found that higher consumption of fish was associated with a lower rate of sudden death, whereas our data indicate a significantly lower rate of nonsudden but not sudden death.

In contrast to these studies, the Bergen (Norway), Hawaiian, and U.S. Health Professionals studies found no relation between fish consumption and coronary heart disease.[10,11,14] This apparent inconsistency may be due to different methods of assessing diet and categorizing fish consumption; different distributions of reported fish consumption; differences in study sites and times, with associated dietary differences (e.g., levels of intake of cholesterol, saturated fats, antioxidants, and fiber) that might influence the relation between fish consumption and the risk of coronary heart disease; and different periods of follow-up, ranging from four years to several decades.

In our analyses, we deliberately focused on the end point of fatal myocardial infarction (ICD-8 code 410) and its components of sudden and nonsudden death, rather than on overall mortality from coronary heart disease. This attention to fatal myocardial infarction was stimulated by recent research findings. In randomized, controlled trials, the lower rates of death from coronary heart disease in the intervention groups reflected, in full or in part, lower rates of death from myocardial infarction.[24-26] Most of the overall decline in the rate of death from coronary heart disease in the United States in recent decades can be attributed to a decline in the rate of fatal myocardial infarction; there has been a relatively small decrease in the rates of death from other coronary causes (ICD-8 codes 411 through 414).[27,28] Also, the results of local studies — including studies of men in Chicago cohorts — indicate that much of this decline in the rate of fatal myocardial infarction is due to decreased rates of sudden death from myocardial infarction.[29-35] On the basis of these findings, our hypothesis was that fish consumption is inversely related to sudden death from myocardial infarction. Thus, our finding that base-line fish consumption is independently and significantly related to the risk of nonsudden but not sudden death from myocardial infarction was unexpected. It will be important to determine whether this finding is reproducible. Two other observational studies recently reported an inverse relation between fish consumption and sudden death,[6,8] which is inconsistent with our results. One problem may be the definition of sudden death, which may differ among studies.

If fish consumption is indeed protective against fatal myocardial infarction, data from some of the epidemiologic studies indicate that the ingestion of small amounts of fish, including mainly lean (nonfatty) fish, provides sufficient protection.[1] Could the protective effect of consuming small amounts of fish over a period of decades be due to the very small amounts of $n-3$ long-chain polyunsaturated fatty acids ingested?[36-46] This seems unlikely, since most studies show that effects on plasma lipids and thrombogenic factors require much larger amounts of these fatty acids. Recent findings, however, suggest favorable influences on total and intermediate-density lipoprotein triglycerides (but not on cholesterol).[47] Could the protective effect be related to the influences of these fatty acids on cell membranes?[8,48] Could the components of fish protein (e.g., particular combinations of amino acids) be involved?

In conclusion, data from the Chicago Western Electric Study show a significant, graded, independent inverse association between base-line fish consumption and the 30-year risk of fatal myocardial infarction, particularly nonsudden death from myocardial infarction. This relation accounted for the lower rates of death from all coronary causes, all cardiovascular causes, and all causes in association with higher fish consumption, which persisted throughout the 30 years of the study and in analyses adjusted for potentially confounding demographic, biomedical, and dietary factors. Further studies — observational and interventional — are needed to determine whether regular ingestion of moderate amounts of fish provides substantial protection against myocardial infarction.

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