

Fish Intake and Risk of Incident Heart Failure

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OBJECTIVES	Our aim was to investigate the relation between fish consumption and incidence of congestive heart failure (CHF).
BACKGROUND	The incidence and health burden of CHF are rising, particularly in older persons. Although n-3 fatty acids have effects that could favorably influence risk of CHF, the relation between fish intake and CHF incidence is unknown.
METHODS	Among 4,738 adults age ≥ 65 years and free of CHF at baseline in 1989–90, usual dietary intake was assessed using a food frequency questionnaire. In a participant subsample, consumption of tuna or other broiled or baked fish, but not fried fish, correlated with plasma phospholipid n-3 fatty acids. Incidence of CHF was prospectively adjudicated.
RESULTS	During 12 years' follow-up, 955 participants developed CHF. In multivariate-adjusted analyses, tuna/other fish consumption was inversely associated with incident CHF, with 20% lower risk with intake 1 to 2 times/week (hazard ratio [HR] = 0.80, 95% confidence interval [CI] = 0.64 to 0.99), 31% lower risk with intake 3 to 4 times/week (HR = 0.69, 95% CI = 0.52 to 0.91), and 32% lower risk with intake ≥ 5 times/week (HR = 0.68, 95% CI = 0.45 to 1.03), compared with intake < 1 time/month (p trend = 0.009). In similar analyses, fried fish consumption was positively associated with incident CHF (p trend = 0.01). Dietary long-chain n-3 fatty acid intake was also inversely associated with CHF (p trend = 0.009), with 37% lower risk in the highest quintile of intake (HR = 0.73, 95% CI = 0.57 to 0.94) compared with the lowest.
CONCLUSIONS	Among older adults, consumption of tuna or other broiled or baked fish, but not fried fish, is associated with lower incidence of CHF. Confirmation in additional studies and evaluation of potential mechanisms is warranted. (J Am Coll Cardiol 2005;45:2015–21) © 2005 by the American College of Cardiology Foundation

Congestive heart failure (CHF) is a growing clinical and public health problem. In the U.S., nearly 5 million individuals have CHF, more than 500,000 new cases are diagnosed yearly, and CHF health care costs exceed \$28 billion annually (1). Congestive heart failure is particularly common with advancing age (2) and is the leading cause of hospitalization among adults age ≥ 65 years (3). Among older adults, CHF incidence is $\sim 2\%$ per year (4) and predicts three to six times higher mortality (5). Identification of measures for preventing CHF, particularly among older individuals, is therefore of considerable clinical and public health importance.

In experimental studies, fish oil favorably affects hemodynamics (6), inflammation (7), vascular responses (8–10), and left ventricular (LV) indices (11–17), each of which could reduce risk of CHF. In cross-sectional analyses (18),

intake of tuna or other broiled or baked fish is inversely associated with systolic blood pressure, C-reactive protein levels, and carotid intimal medial thickness, whereas fried fish intake is positively associated with systolic blood pressure and carotid intimal medial thickness, all independent risk factors for CHF (4). However, although the relation between fish intake and coronary heart disease risk has been investigated (19), little is known regarding relation of fish intake, or indeed, any dietary factor, with incidence of CHF in humans.

We investigated associations between fish consumption and incidence of CHF in the Cardiovascular Health Study, a population-based cohort study of determinants of cardiovascular disease among adults age ≥ 65 years. Our hypothesis was that consumption of tuna and other broiled or baked fish, but not fried fish, would be associated with a lower incidence of CHF.

METHODS

Design and population. In 1989 to 1990 and 1992, 5,888 men and women age ≥ 65 years were randomly selected and enrolled from Medicare eligibility lists in four U.S. communities (20,21). Baseline evaluation included health status, medical history, physical examination, electrocardiography, echocardiography, carotid ultrasonography, pulmonary function testing, and laboratory testing (2,4,5,20–22). We excluded 687 participants enrolled in 1992 (a food frequency questionnaire [FFQ] was not administered in 1992), 105

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Manuscript received December 26, 2004; revised manuscript received March 8, 2005, accepted March 10, 2005.

Abbreviations and Acronyms

CHF	= congestive heart failure
CHS	= Cardiovascular Health Study
CI	= confidence interval
DHA	= docosahexaenoic acid
EPA	= eicosapentaenoic acid
FFQ	= food frequency questionnaire
HR	= hazard ratio
LV	= left ventricular

participants with incomplete data on fish consumption, and 358 participants with baseline CHF (22) or abnormal LV ejection fraction (<45%) (5) (final $n = 4,738$). Each center's institutional review committee approved the study, and all subjects gave informed consent.

Dietary assessment. A picture-sort FFQ was administered at baseline to assess usual dietary intake of tuna fish, other fish (broiled or baked), and fried fish or fish sandwiches (fried fish burgers) (18,23). For each type, participants reported their usual intake during the past year, with response categories ranging from ≤ 4 times a year to ≥ 5 times/week. For most nutrients, the midpoint of each category was used to sum intakes of different items. On the basis of detailed assessments of fish consumption performed in a separate cohort (24) (D. Siscovick, personal communication, October 18, 2004), the median fish intakes for the two highest response categories were calculated to be slightly less than the category midpoint; this had no effect on the relative ranking of participants' fish intakes or the estimates of relative risk among participants, but likely better estimated the absolute fish intake for each participant. We have shown that as a biomarker of fish oil content, plasma phospholipid levels of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) correlate with intake of tuna fish (Spearman correlation [r] = 0.35, $p < 0.01$), other fish ($r = 0.59$, $p < 0.001$), and combined tuna/other fish ($r = 0.55$, $p < 0.001$), but not fried fish ($r = 0.04$, $p = 0.78$) (19). Dietary EPA + DHA was calculated from FFQ responses using estimates for each fish serving (3 to 5 oz) (25), including shellfish, and U.S. commercial landings data (26); this estimate correlated with plasma phospholipid EPA + DHA levels ($r = 0.52$, $p < 0.001$, $n = 65$).

Ascertainment of CHF. Potential cases of CHF were identified from annual examinations, six-month phone contacts, and hospitalization discharge summaries. Incident cases were centrally adjudicated using interviews, outpatient records, discharge summaries, history and examination data, and review of relevant diagnostic tests and consultations (4,27). Confirmation of a diagnosis of CHF required each of the following: 1) CHF symptoms (shortness of breath, fatigue, orthopnea, paroxysmal nocturnal dyspnea) and signs (edema, rales, tachycardia, gallop rhythm, displaced apical impulse) or clinical findings (such as on echocardiography, contrast ventriculography, or chest radiography); 2) diagnosis of CHF by a treating physician; and 3) medical therapy

for CHF (diuretics and either digitalis or a vasodilator [nitroglycerin, hydralazine, angiotensin-converting enzyme inhibitor]).

Analysis. Kaplan-Meier methods were used to evaluate CHF-free survival. Risk was estimated using Cox proportional hazards (time at risk until first event, death, or latest follow-up through June 30, 2001), with covariates based on clinical interest, associations with incident CHF (4), or associations with exposures/outcomes in the present analysis. The final model included age; gender; race; enrollment site; education; diabetes; body mass index; prevalent coronary heart disease; prevalent stroke/transient ischemic attack; and intakes of tuna/other fish, fried fish, and total calories. A second model was further adjusted for other behavioral and lifestyle factors including smoking; leisure-time physical activity; and intakes of saturated fat, fruits, vegetables, and alcohol. We also evaluated for potential mediation or confounding by levels of systolic blood pressure, diastolic blood pressure, baseline LV systolic function, low-density lipoprotein, high-density lipoprotein, triglycerides, and C-reactive protein. For parsimony in model construction, we excluded from the final models other covariates that did not materially alter relations between fish consumption and CHF risk, including annual income; treated hypertension; exercise intensity; forced expiratory volume in 1 s; carotid intimal medial thickness; atrial fibrillation; M-mode echocardiography-estimated LV mass; use of aspirin, beta-blockers, lipid-lowering medication, fish oil, and estrogen; serum fasting glucose, insulin, creatinine, and fibrinogen; and estimated intakes of total fat, carbohydrates, protein, linolenic acid, fiber, beef/pork, wine, thiamine, and vitamin C. Missing covariate values (typically <1%) were imputed using age, race, gender, diabetes, and prevalent cardiovascular disease; analyses using population medians or excluding missing data were not appreciably different. Tests for trend were evaluated with intake categories entered as ordinal variables. Potential effect modification was assessed using stratified analyses and likelihood-ratio testing (exposure times covariate term). Analyses were performed using Stata 8.0 (D.M.) (Stata Corp., College Station, Texas), with two-tailed $\alpha = 0.05$.

RESULTS

Mean participant age was 73 years at baseline. Median fried fish and tuna/other fish consumption were 0.5 and 1.0 servings/week, respectively. Tuna/other fish consumption was associated with younger age, female gender, higher education, and generally a more favorable cardiovascular risk profile, although higher intake was also associated with greater body mass index and higher low-density lipoprotein cholesterol (Table 1). Tuna/other fish consumption was positively associated with intakes of fruits, vegetables, alcohol, and total energy and inversely associated with saturated fat intake. Fried fish consumption was associated with male gender, non-white race, lower education, a generally less

Table 1. Baseline Characteristics According to Fish Consumption

Frequency of Intake (n)	Tuna/Other Fish					Fried Fish		
	<1/mo (510)	1-3/mo (1,095)	1-2/wk (2,210)	3-4/wk (720)	5+/wk (203)	<1/mo (2,307)	1-3/mo (1,521)	≥1/wk† (910)
Age, yrs	74.2	73.1	72.5	71.5	71.9*	72.8	72.3	72.9
Gender, % male	46	46	42	35	30*	37	45	49*
White race, %	94	95	95	97	92	97	95	91*
Diabetes, %	24	22	22	19	27	21	21	25*
Coronary heart disease, %	17	15	16	16	24	15	16	18*
Education ≥ high school, %	52	69	76	83	79*	79	70	62*
Body mass index, kg/m ²	26.0	26.3	26.4	26.7	26.8*	26.1	26.6	26.8*
Current smoker, %	16	14	11	11	7*	12	11	12
Treated hypertension, %	45	44	42	43	46	43	43	44
Systolic BP, mm Hg	138	136	136	133	134*	135	136	136
Leisure-time activity, kcal/wk	1,632	1,821	1,899	1,937	1,721	1,789	1,900	1,922
Left ventricular mass, g	151	153	151	150	145*	148	153	155*
Borderline EF (45%-54%), %	7	6	5	4	5*	4	6	7*
LDL cholesterol, mg/dl	126	127	131	137	130*	130	130	132
HDL cholesterol, mg/dl	52	53	55	55	56*	56	53	53*
C-reactive protein, mg/dl	0.37	0.37	0.32	0.29	3.0*	0.31	0.35	0.35
Total energy intake, kcal/day	1,633	1,608	1,846	2,042	2,415*	1,620	1,857	2,279*
Saturated fat, % energy	13	12	12	11	11*	11	12	13*
Alcohol, beverages/wk	1.5	2.5	2.9	3.0	2.3*	2.7	2.7	2.4
Beef/pork, servings/day	0.9	0.8	0.9	0.8	0.9	0.7	0.9	1.2*
Fruits, servings/day	1.7	1.8	2.2	2.5	2.8*	2.2	2.1	2.2
Vegetables, servings/day	1.9	1.9	2.5	3.1	4.1*	2.4	2.4	2.7*
Dietary EPA + DHA, mg/day‡	19	83	261	474	1,064*	4	22	85*

Values are mean (continuous variables) or percent (categorical variables). *p < 0.05 for ordinal trend across categories of intake. †The few individuals (n = 65) in the higher categories of fried fish intake were combined with those consuming fried fish at least once per week. ‡Estimated intake from these fish meals based on U.S. commercial landings data and estimated EPA + DHA content in each serving (3 to 5 oz) (26,27).

BP = blood pressure; DHA = docosahexaenoic acid; EF = left ventricular ejection fraction; EPA = eicosapentaenoic acid; HDL = high-density lipoprotein; LDL = low-density lipoprotein; mo = month; wk = week.

favorable cardiovascular risk profile, and higher intakes of saturated fat, beef/pork, vegetables, and total energy. Associations of these fish meals with risk of CHF were therefore evaluated with and without adjustment for each of these factors.

During 12 years of follow-up, 955 participants (20%) developed incident CHF. Among individuals consuming tuna/other fish ≥3 times/week, incidence of CHF was 19 per 1,000 person-years, compared with 30 per 1,000 person-years among individuals consuming tuna/other fish <1 time/month (p < 0.0001) (Fig. 1). Among persons consuming fried fish ≥1 time/week, incidence of CHF was 29 per 1,000 person-years, compared with 21 per 1,000 person-years among persons consuming fried fish <1 time/month (p < 0.0001) (Fig. 1).

In age-adjusted analyses, tuna/other fish consumption was inversely associated with risk of CHF (Table 2). After multivariate adjustment (Model 1), relative risks (hazards) of CHF were 0.78 (95% CI = 0.63 to 0.97), 0.68 (95% CI = 0.53 to 0.88), and 0.65 (95% CI = 0.44 to 0.97) for tuna/other fish intake 1 to 2 times/week, 3 to 4 times/week, and ≥5 times/week, compared with <1 time/month (p trend = 0.003). Further adjustment for other behavioral and lifestyle factors (Model 2) had only a small effect on these risk estimates, indicating little evidence for additional confounding by factors beyond those in Model 1. Notably, lower risk was evident with modest intake (1 to 2 times/

week). Further, the observed lower risk was similar for intakes of 3 to 4 times/week and ≥5 times/week (with borderline significance in the latter category owing to less person-time and fewer numbers of events).

In contrast, fried fish consumption was positively associated with incidence of CHF (Table 2). In age-adjusted analyses, intake ≥1 time/week was associated with a 42% higher risk (95% CI = 21% to 67%), compared with intake <1 time/month. Adjustment for other risk factors (Model 1) partly attenuated this higher risk, suggesting that it might have been partly related to differences in these factors. However, even after multivariate adjustments, there was little evidence to suggest that fried fish intake might lower the risk of CHF (Models 1 and 2).

We also evaluated the relation between dietary EPA + DHA and CHF risk. Because our focus was on diet, we excluded the few participants reporting fish oil supplement use at baseline (n = 181). After multivariate adjustment (as in Model 2), EPA + DHA intake was inversely associated with risk of CHF (p trend = 0.009) (Fig. 2). Compared with the lowest quintile of intake (<92 mg/day), individuals in the highest quintile (>487 mg/day) had a 37% lower risk of CHF (95% CI = 6% to 43%).

We evaluated for potential mediation or confounding by factors that fish intake might directly influence, including systolic blood pressure, diastolic blood pressure, baseline LV systolic function (normal vs. borderline), low-density li-

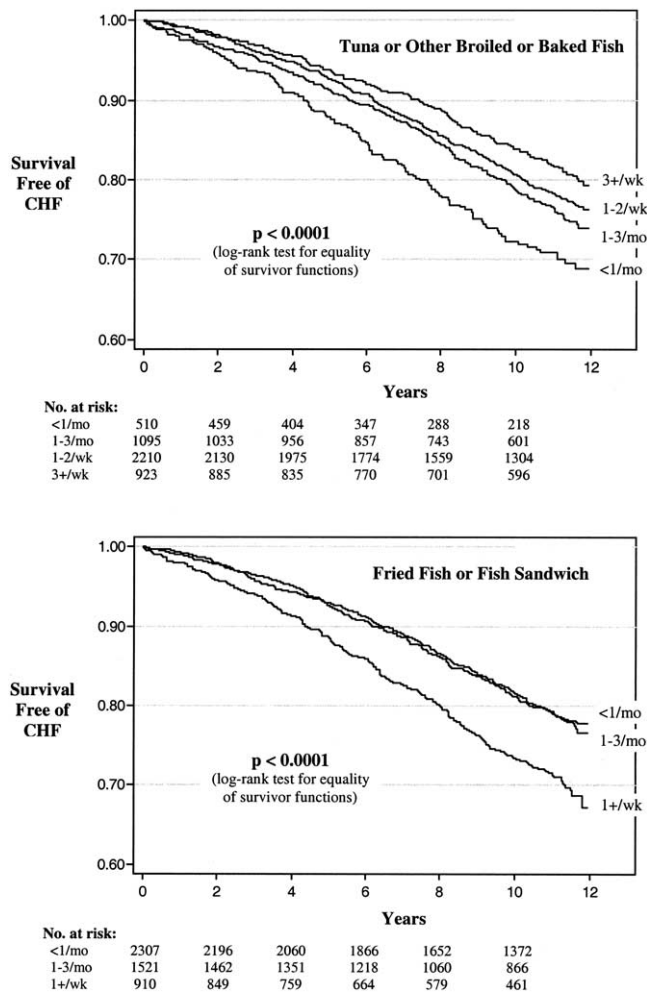


Figure 1. Survival free of congestive heart failure (CHF) according to tuna/other fish consumption and fried fish consumption (each adjusted for the other).

poprotein, high-density lipoprotein, triglycerides, and C-reactive protein. Adjustment for these factors slightly attenuated the relation between fish intake and incident

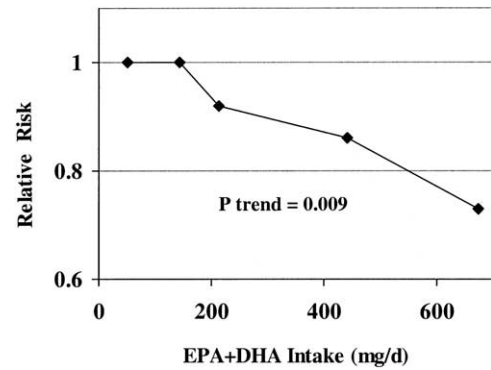


Figure 2. Risk of incident congestive heart failure according to estimated intake of dietary long-chain n-3 fatty acids (eicosapentaenoic acid [EPA] + docosahexaenoic acid [DHA]). Risk estimates are shown for quintiles of intake, with the lowest quintile as the reference category, with multivariate adjustments as in Model 2, Table 2.

CHF, with relative risks of 0.83 (95% CI = 0.67 to 1.03), 0.72 (95% CI = 0.55 to 0.95), and 0.73 (95% CI = 0.48 to 1.09) for tuna/other fish intake 1 to 2 times/week, 3 to 4 times/week, and ≥ 5 times/week, compared with < 1 time a month (p trend = 0.03), and relative risks of 0.98 (95% CI = 0.84 to 1.14) and 1.30 (95% CI = 1.08 to 1.56) for fried fish intake 1 to 3 times/month and ≥ 1 time/week, compared with < 1 time/month (p trend = 0.02) (other covariates as in Model 2).

We performed stratified analyses to further assess potential confounding or effect modification. There was little evidence that findings varied according to age, gender, education, income, diabetes, smoking, physical activity, prevalent cardiovascular disease, treated hypertension, or systolic blood pressure (p > 0.05 for each interaction; other adjustments as in Model 1), although CIs were broader in each subgroup because of fewer events. For example, the relative risk of incident CHF with tuna/other fish intake ≥ 3 times/week, compared with < 1 time/month, was 0.70 among never-smokers (95% CI = 0.49 to 1.02), 0.71 among former smokers (95% CI = 0.47 to 1.07), and 0.58

Table 2. Risk of Incident Congestive Heart Failure According to Fish Consumption

Frequency of Intake	<1/mo	1-3/mo	1-2/wk	3-4/wk	≥ 5 /wk	p Trend
Tuna/other fish						
No. events	120	228	441	131	35	
Person-years	4,051	9,751	20,319	6,930	1,878	
HR (95% CI): age-adjusted	1.0 (referent)	0.83 (0.67–1.04)	0.79 (0.65–0.97)	0.74 (0.58–0.95)	0.75 (0.51–1.09)	0.02
Model 1*	1.0 (referent)	0.84 (0.67–1.05)	0.78 (0.63–0.97)	0.68 (0.52–0.89)	0.65 (0.44–0.97)	0.003
Model 2†	1.0 (referent)	0.84 (0.67–1.06)	0.80 (0.64–0.99)	0.69 (0.52–0.91)	0.68 (0.45–1.03)	0.009
Fried fish						
No. events	441	291	223	‡	‡	
Person-years	21,227	13,936	7,765			
HR (95% CI): age-adjusted	1.0 (referent)	1.06 (0.91–1.23)	1.42 (1.21–1.67)			<0.001
Model 1*	1.0 (referent)	1.00 (0.86–1.17)	1.31 (1.09–1.57)			0.01
Model 2†	1.0 (referent)	1.02 (0.87–1.19)	1.35 (1.12–1.62)			0.005

*Adjusted for age (years), gender (male/female), race (white/nonwhite), enrollment site (four sites), education ($<$ high school, high school, $>$ high school), diabetes (yes/no), body mass index (kg/m^2), prevalent coronary heart disease (yes/no), prevalent stroke/transient ischemic attack (yes/no), total caloric intake (kcal/day), and intake of either fried fish or tuna/other fish (categories of intake). †Further adjusted for other behavioral and lifestyle factors including smoking (never, former, current), leisure-time physical activity (kcal/day), and intakes of saturated fat (percent energy), fruits (servings/day), vegetables (servings/day), and alcohol (drinks/wk). ‡The few individuals (n = 65) in the higher categories of fried fish intake were combined with those consuming fried fish one to two times per week.

CI = confidence interval; HR = hazard ratio; mo = month; wk = week.

among current smokers (95% CI = 0.28 to 1.24) (p interaction = 0.82); 0.75 among individuals with less than a high school education (95% CI = 0.47 to 1.19), 0.48 among individuals with a high school education (95% CI = 0.30 to 0.78), and 0.66 among individuals with more than a high school education (95% CI = 0.43 to 1.02) (p interaction = 0.17); and 0.66 among individuals with an annual income \geq \$35,000 (95% CI = 0.34 to 1.30) and 0.72 among individuals with an annual income $<$ \$35,000 (95% CI = 0.54 to 0.95) (p interaction = 0.77). Effect modification by fish oil supplementation could not be evaluated given the few individuals taking fish oil ($n = 181$), but exclusion of these participants had little effect (data not shown). There was little evidence for interaction between tuna/other fish intake and fried fish intake (p interaction = 0.65).

We also assessed the extent to which the relation between fish intake and CHF incidence might be related to associations between fish intake and nonfatal myocardial infarction (18) or atrial fibrillation (28). After adjustment for prevalent or incident myocardial infarction as a time-varying covariate (other adjustments as in Model 1), fish intake was still associated with an incidence of CHF, with 26% lower risk with tuna/other fish intake \geq times a week (HR = 0.74, 95% CI = 0.57 to 0.95) compared with <1 time/month, and 38% higher risk with fried fish intake ≥ 1 time/week (HR = 1.38, 95% CI = 1.15 to 1.65), compared with <1 time/month. In similar analyses adjusting for prevalent or incident atrial fibrillation, fish intake was still associated with incidence of CHF, with 34% lower risk with tuna/other fish intake ≥ 3 times/week (HR = 0.66, 95% CI = 0.51 to 0.86) compared with <1 time/month, and 28% higher risk with fried fish intake ≥ 1 time/week (HR = 1.28, 95% CI = 1.07 to 1.53) compared with <1 time/month.

DISCUSSION

Among these older adults, consumption of tuna or other broiled or baked fish was associated with a lower incidence of CHF, with $\sim 20\%$ lower a risk with intake 1 to 2 times/week and $\sim 30\%$ lower risk with intake ≥ 3 times/week, compared with intake <1 time/month. Estimated intake of marine $n-3$ fatty acids was also associated with lower CHF risk, with 37% lower risk in the highest quintile of intake compared with the lowest.

Possible mechanisms: tuna/other fish. The inverse relation between tuna/other fish intake and CHF could be due to other healthier lifestyle or socioeconomic characteristics that reduce CHF risk. We adjusted for education, smoking, physical activity, and various other clinical and behavioral risk factors. Further, findings were similar in analyses stratified by education, income, smoking, physical activity, and clinical characteristics and after adjustment for preceding nonfatal myocardial infarction or atrial fibrillation. Nevertheless, the possibility of residual confounding cannot be excluded.

There are plausible biologic mechanisms whereby tuna/other fish intake might reduce the incidence of CHF. In experimental studies, fish oil favorably affects hemodynamic, vascular, and LV indices. In rats, fish oil intake reduces peripheral vascular resistance (8), reduces myocardial oxygen consumption at given workloads (9), increases contractile recovery following ischemia-reperfusion (9), augments LV response to exercise training (10), and reduces LV hypertrophy (11). In nonhuman primates, fish oil lowers resting heart rate, increases LV ejection fraction, and improves myocardial efficiency, possibly related to enhanced diastolic filling (12,13). In humans, fish oil supplementation lowers blood pressure (6), reduces markers of inflammation (7), attenuates vasoconstrictive responses to angiotensin II (14,15), improves arteriolar compliance (16), and improves LV diastolic filling (17). Each of these mechanisms could contribute to a beneficial effect of tuna/other fish intake on the incidence of CHF.

Although these experimental effects were individually demonstrated in humans in short-term trials of fish oil supplementation (3 to 5 g/day), dietary doses (~ 0.5 g/day) may result in more modest effects that over the long term combine to reduce CHF risk. In bivariate analyses, tuna/other fish intake correlated with plasma phospholipid EPA + DHA and was inversely associated with blood pressure, C-reactive protein, LV mass, and borderline systolic function at baseline. These associations were most pronounced, and CHF risk was lowest, among persons consuming tuna/other fish at least 3 times/week, the equivalent of ~ 500 mg/day EPA + DHA. Conversely, adjustment for these factors only partly attenuated the inverse association between tuna/other fish intake and CHF risk, suggesting that differences in these factors, based upon a single measurement at baseline, do not completely mediate this association.

If tuna/other fish intake reduces the incidence of CHF, effects could be mediated by influences on systolic function, diastolic function, or both. Effects on diastolic function may be particularly relevant in older persons, as nearly two-thirds of older CHF patients have normal systolic function (2). Experimentally observed effects of fish oil on peripheral vascular resistance and LV diastolic filling (8,12-17) are intriguing, suggesting that fatty fish intake could reduce diastolic heart failure. Further investigation of these effects is warranted.

Possible mechanisms: fried fish. The association between fried fish intake and CHF risk appeared partly related to associations with higher risk clinical and lifestyle factors. However, the balance of benefit versus risk of these fish meals may also be unfavorable. Although detailed information on fish species or cooking oils was not available, the lack of correlation with plasma phospholipid $n-3$ fatty acid levels suggests that these fish meals were mostly lean (white) fish; although frying adds other fatty acids from the frying oil, it does not reduce the absolute $n-3$ content (29,30). Frying may add oxidation products (30) or, with partially

hydrogenated oils, *trans*fatty acids, and frying may also have adverse health effects when oils/fats are used repeatedly for frying (31,32). Thus, if relatively little benefit is present owing to low fish oil content, the net effect may be detrimental. In bivariate analyses in this report, fried fish intake was positively associated with C-reactive protein, LV mass, and borderline systolic function at baseline, each of which predict incident CHF (4). Further investigation is necessary to confirm these observations, determine if they are specific for certain kinds of fish or frying oils, and examine potential mechanisms and alternative explanations. Although it would be premature to conclude that fried fish intake increases the risk of CHF, our findings indicate that intake of such fish meals is unlikely to reduce CHF risk.

Strengths. The prospective cohort design reduces potential bias from recall differences or control-selection bias. The population-based recruitment strategy enhances generalizability. Standardized assessment of a variety of characteristics increases the capacity to adjust for potential confounding factors. Close follow-up, comprehensive review of potential events, and centralized adjudication reduce the potential for missed or misclassified outcomes.

Study limitations. More detailed information on fish species consumed or other preparation methods was not available. Fish intake was assessed at baseline, and consumption may have changed over time; without bias, this would result in underestimation of the relation between fish consumption and CHF risk. Precise quantification of fish intake was limited by the questionnaire response categories; however, individuals reporting greater tuna/other fish consumption had higher plasma phospholipid EPA + DHA levels, indicating reasonably accurate qualitative ranking of fish intake. Standardized assessment of LV function was not available in all participants at time of CHF diagnosis, so systolic versus diastolic heart failure could not be evaluated. Potential risks of fish intake for other health outcomes, such as from mercury contamination (33), were not evaluated. Residual confounding due to unknown or incompletely measured characteristics could not be excluded. Associations were observed in older, predominantly white individuals participating in a cohort study and may not be generalizable to other populations.

Conclusions. Our findings indicate that consumption of tuna and other broiled or baked fish, but not fried fish or fish sandwiches, is associated with lower incidence of CHF among older adults. To our knowledge, this is the first study to investigate associations between fish intake and risk of CHF, poised to become the leading cardiovascular health burden in coming decades. Just as the notion that dietary influences on coronary heart disease risk are principally related to saturated fat intake is a concept increasingly outdated (34,35), the possibility that dietary habits have important influences on other cardiovascular outcomes appears increasingly tenable. Confirmation of these findings in other studies and continued investigation of possible mech-

anisms of benefit and risk, with attention to different types of fish meals, is indicated.

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