Fish and fatty acid consumption and the risk of hearing loss in women[1–3]

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ABSTRACT

Background: Acquired hearing loss is common and often disabling, yet limited prospective data exist on potentially modifiable risk factors. Evidence suggests that higher intake of fish and long-chain omega-3 (n−3) polyunsaturated fatty acids (PUFAs) may be associated with a lower risk of hearing loss, but prospective information on these relations is limited.

Objective: We prospectively examined the independent associations between consumption of total and specific types of fish, long-chain omega-3 PUFAs, and self-reported hearing loss in women.

Design: Data were from the Nurses' Health Study II, a prospective cohort study. The independent associations between consumption of fish and long-chain omega-3 PUFAs and self-reported hearing loss were examined in 65,215 women followed from 1991 to 2009. Baseline and updated information was obtained from validated biennial questionnaires. Cox proportional hazards regression models were used to estimate multivariable-adjusted RRs and 95% CIs.

Results: After 1,038,093 person-years of follow-up, 11,606 cases of incident hearing loss were reported. Consumption of 2 or more servings of fish per week was associated with a lower risk of hearing loss. In comparison with women who rarely consumed fish (<1 serving/mo), the multivariable-adjusted RR for hearing loss among women who consumed 2–4 servings of fish per week was 0.80 (95% CI: 0.74, 0.88) (P-trend $<$ 0.001). When examined individually, higher consumption of each specific fish type was inversely associated with risk (P-trend $\leq$ 0.04). Higher intake of long-chain omega-3 PUFAs was also inversely associated with risk of hearing loss. In comparison with women in the lowest quintile of intake of long-chain omega-3 PUFAs, the multivariable-adjusted RR for hearing loss among women in the highest quintile was 0.85 (95% CI: 0.80, 0.91) and among women in the highest decile was 0.78 (95% CI: 0.72, 0.85) (P-trend $<$ 0.001).

Conclusion: Regular fish consumption and higher intake of long-chain omega-3 PUFAs are associated with lower risk of hearing loss in women. *Am J Clin Nutr* 2014;100:1371–7.

INTRODUCTION

Acquired hearing loss is a highly prevalent and often disabling chronic health condition (1) that can adversely affect social connectivity, cognitive function (2), and quality of life (3–5). Hearing loss is associated with increased burden of disease and hospitalization among older adults in the United States (6). Although a decline in hearing is often considered an inevitable aspect of aging, the identification of several potentially modifiable risk factors has provided new insight into possibilities for the prevention or delay of acquired hearing loss (7–11).

Compromise of the blood supply to the cochlea may contribute to reduced auditory sensitivities, and thus vascular factors have been implicated as important contributors to hearing loss (12). Consumption of fish and higher intakes of long-chain omega-3 PUFAs, specifically EPA (20:5n−3) and DHA (22:6n−3), have been associated with a lower risk of cardiovascular (13) and cerebrovascular disease (14) and may help in the maintenance of cochlear blood flow by similar mechanisms (15). In a study of 798 Australian men and women aged ≥50 y, the 5-y incidence of hearing loss was lower among individuals who consumed ≥2 servings of fish per week compared with those who consumed <1 serving of fish per week (RR: 0.58; 95% CI: 0.35, 0.95). Higher intake of long-chain omega-3 PUFAs was also inversely associated with a 5-y incidence of audiometrically measured hearing loss (RR: 0.76; 95% CI: 0.60, 0.97) (16). A cross-sectional study based on data from the Supplementation with Antioxidant Vitamins and Minerals 2 primary prevention trial found that higher seafood and shellfish intake was associated with better hearing thresholds in men but not in women (17). Given that prospective information on the relation between fish intake and hearing loss is limited, we prospectively examined the relation of consumption of total fish, specific types of fish, and intake of long-chain omega-3 PUFAs and the risk of self-reported hearing loss in a cohort of 65,215 US women, aged 27–44 y, who were followed for 18 y.

SUBJECTS AND METHODS

Study population

The Nurses' Health Study II is an ongoing cohort study of 116,430 female nurses who were aged 25–42 y at cohort inception in 1989. Participants have been followed by biennial mailed questionnaires that elicit information on dietary and

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lifestyle factors and various health outcomes; the follow-up rate over 22 y exceeds 90% of eligible person-time. Detailed information on diet, including fish and shellfish consumption, has been obtained every 4 y, beginning in 1991. The 2009 long-form questionnaire asked women whether they have a hearing problem and, if so, at what age a change in hearing was first noticed. Of the 90,488 women who completed this questionnaire, excluded from the analyses were those who reported a hearing problem that began before the study baseline (n = 2584); reported a history of cancer other than nonmelanoma skin cancer (attributed to possible exposure to ototoxic chemotherapeutic agents; n = 859); had not answered the 1991 baseline dietary questionnaire, left 10 or more items on the semiquantitative food-frequency questionnaire (SFFQ) blank, or reported total food intakes judged to be implausible (n = 12,160); did not answer the hearing question (n = 9364); or reported the use of fish-oil or cod liver oil supplements at baseline (n = 306). We also excluded women and censored women who reported supplement use during follow-up, as the content and quality of these supplements are not regulated and can vary considerably (18). The total number of women included in the analysis was 65,215.

Although some participants have been lost to follow-up since the inception of this cohort or did not answer the 2009 questionnaire, the baseline characteristics of participants who did and did not answer the 2009 questionnaire did not differ appreciably (data not shown). The study protocol was approved by the Institutional Review Board of the Partners HealthCare System.

Ascertainment of dietary intake of fish and fatty acids

Dietary intake was assessed by using a validated SFFQ that included more than 130 items and was first administered in 1991 and then every 4 years thereafter. The SFFQ included 4 questions about finfish and shellfish intake, with common units or portion sizes for each item: *1*) dark-meat fish, such as mackerel, salmon, sardines, bluefish, tuna steak, or swordfish; *2*) canned tuna; *3*) light-meat fish, such as cod, haddock, or halibut; and *4*) shrimp, lobster, or scallops as a main dish. For each item, participants were asked how often, on average, they had consumed a given quantity during the preceding year. Nine response options were provided, ranging from "almost never" to "6 or more per day." Total fish intake was assessed by totaling the participant's response to the finfish plus shellfish items. Individual fatty acid intake as well as average daily intake of other nutrients was calculated by multiplying the frequency of consumption of each item by its nutrient content per serving and then totaling the nutrient intake for all food items (methods described previously) (19). Nutrient estimates were based on the US Department of Agriculture (20) and Harvard University food-composition database, which is continually updated over time to reflect the composition of new foods in the marketplace. For the present study, we calculated intake of long-chain omega-3 PUFAs, EPA (20:5n−3), and DHA (22:6n−3), which are derived primarily from fish; intake of the intermediate-chain omega-3 PUFA α-linolenic acid (ALA) (18:3n−3), derived primarily from vegetarian sources; and intake of omega-6 PUFA (linoleic acid plus arachidonic acid), by using methods described in detail previously (21). Nutrient intakes were adjusted for total energy intake by the residual method (22). Intake of long-chain omega-3 PUFAs from foods was primarily from fish (>80% at baseline) and secondarily from chicken (<10% at baseline), similar to that in the US food supply data (23). To assess long-term intake and to minimize misclassification, we calculated cumulative average intake so that fish, shellfish, and nutrient intake in a given time period represented the average intake of previous and current time periods (24).

The reproducibility and validity of the SFFQ as an instrument for ranking individuals by fish and fatty acid intakes have been demonstrated in several validation studies in this and similar cohorts (22, 25, 26). Spearman rank correlation coefficients for the fish items between 2 questionnaires administered 1 y apart were 0.54 for tuna, 0.63 for dark-meat fish, 0.48 for light-meat fish, and 0.67 for shrimp, lobster, or scallops as a main dish. The mean total fish intake was 3.7 servings/wk according to the questionnaire and 3.6 servings/wk according to 2 one-week dietary records (r = 0.61, $P < 0.001$). The intake of EPA calculated from the SFFQ was correlated with the fatty acid composition of adipose tissue (r = 0.47, $P < 0.001$).

Ascertainment of outcome

The primary outcome, self-reported hearing loss, was determined based on the response to the hearing loss question on the 2009 long-form questionnaire. The question asked, "Do you have a hearing problem?" (no, mild, moderate, or severe) and, if so, "At what age did you first notice a change in your hearing?" (<30, 30–39, 40–44, 45–49, 50–54, 55–59, or 60+ y). We defined a case as a hearing problem that was first noticed after 1991. Although hearing loss can be insidious in onset, incident cases were defined as hearing loss at the age it was first noticed by the participant. We did not have information on severity of hearing loss at the time of onset, and thus we were not able to perform prospective analyses that considered severity of hearing loss as the outcome. Pure-tone audiometry is considered the gold standard for hearing loss evaluation; however, because of cost and logistic limitations of such assessment in large populations, questionnaires have been used to assess hearing loss and have been found to be reasonably reliable in previous studies (27, 28).

Ascertainment of covariates

To assess potential confounding, we evaluated multivariable models and adjusted for factors that are purported to be risk factors for hearing loss and could potentially be related to fish and fatty acid consumption. Potential confounders that were considered covariates in multivariable analyses included age (1); race (1); smoking (29); BMI (8); waist circumference (8); physical activity (8); intake of alcohol (29), folate (11), vitamin B-12, magnesium (30), potassium (31), and vitamin A (32); history of hypertension (33); history of diabetes (34); use of aspirin (7), acetaminophen (9), and ibuprofen (9); and tinnitus (35). Updated covariate information was obtained from the biennial questionnaires, and intakes of dietary factors were calculated from the SFFQ.

Statistical analysis

Descriptive analyses for baseline characteristics in 1991 were examined by categories of total fish intake. All analyses were prospective, using information on intake of fish, shellfish, and fatty acids that was collected before the date when a change in hearing was first noticed. We computed person-time of follow-up for each participant from study baseline to the date of reported hearing loss, report of cancer (other than nonmelanoma skin cancer), or end of follow-up in 2009. Date of reported hearing loss was considered the midpoint of the category for reported age of first noticing a change in hearing. Total fish consumption was divided into 5 categories (<1 serving/mo, 1–3 servings/mo, 1 serving/wk, 2–4 servings/wk, and ≥5 servings/wk), with the lowest category as the referent group. Consumption of specific types of fish was divided into 4 categories (<1 serving/mo, 1–3 servings/mo, 1 serving/wk, and ≥2 servings/wk). Fatty acid intake was categorized in quintiles, with the lowest quintile as the referent group. The highest quintile of long-chain omega-3 PUFA intake was further divided into 2 deciles to explore more extreme levels of intake. In our primary analyses, to better represent long-term dietary intake and reduce measurement error, we calculated intake of fish and fatty acids as a cumulative average of intake from all available dietary questionnaires up to the start of each follow-up interval (36). In secondary analyses, we also compared results by using the most recent reported dietary intake and baseline dietary intake in relation to hearing loss. The results were not appreciably different, and thus we report only the cumulative average results here.

Cox proportional hazards regression models adjusted for potential confounders were used to estimate the multivariable-adjusted RR of hearing loss by category of fish or fatty acid intake compared with the lowest category of intake. To test for a linear trend across categories of intake, we modeled the category medians as a continuous variable. We used the Anderson-Gill data structure, with a new data record created for each biennial questionnaire cycle in which the participant was at risk, with covariates set to represent the value from the latest returned questionnaire to handle time-varying covariates efficiently. We stratified by age and calendar time in all models. For all RRs, we calculated 95% CIs. All P values are 2-tailed. Statistical tests were performed by using SAS statistical software, version 9.3 (SAS Institute).

RESULTS

Characteristics of participants at baseline according to category of total fish intake are shown in **Table 1**. Baseline characteristics are presented to provide representative values, but updated information was used for the analyses. Women who consumed fish more frequently were more physically active; were more likely to be current or past smokers; had a higher intake of alcohol and nutrients such as vitamin B-12, folate, potassium, magnesium, and retinol activity equivalents (vitamin A); and were more likely to have hypertension. At baseline, 78.8% of the women consumed fish at least once per week.

After 1,038,093 person-years of follow-up, 11,606 cases of incident hearing loss were reported. After adjustment for potential confounders, regular fish consumption was inversely associated with the risk of hearing loss (**Table 2**). In comparison with women who consumed fish less than once per month, the multivariable-adjusted RR for hearing loss among women who consumed 1 serving/wk was 0.94 (95% CI: 0.88, 1.00), 2–4 servings/wk was 0.80 (0.74, 0.88), and ≥5 servings/wk was 0.80 (0.67, 0.95) (P-trend < 0.001).

We examined the relation between consumption of specific types of finfish or shellfish and risk of hearing loss (**Table 3**).

TABLE 1

Age-standardized baseline characteristics of women in 1991 according to category of fish intake[1]

	Fish intake (servings)				
Characteristic	<1/mo (n = 4832)	1–3/mo (n = 9017)	1/wk (n = 39,841)	2–4/wk (n = 9292)	≥5/wk (n = 2233)
Age (y)[2]	36.0 ± 4.8	36.2 ± 4.7	36.2 ± 4.6	36.5 ± 4.5	36.7 ± 4.5
BMI (kg/m^2)	24.3 ± 5.3	24.3 ± 5.2	24.4 ± 5.0	24.9 ± 5.4	25.2 ± 5.6
Waist circumference (1993) (cm)	78.1 ± 13.0	77.9 ± 12.6	77.7 ± 12.3	78.6 ± 13.0	78.2 ± 12.9
Physical activity (METs[3])	18.1 ± 25.5	17.8 ± 23.9	20.3 ± 25.5	24.3 ± 29.1	30.6 ± 37.2
Smoking status (%)					
Never	70.1	69.7	66.5	63.7	62.0
Past	19.2	19.9	22.3	25.3	25.7
Current	10.5	10.4	10.9	10.9	12.1
Alcohol (g/d)	2.2 ± 5.7	2.4 ± 5.4	3.3 ± 6.1	3.7 ± 6.5	4.0 ± 6.8
Vitamin B-12 intake (μg/d)	8.8 ± 12.6	9.1 ± 11.2	9.5 ± 10.8	10.5 ± 10.6	13.1 ± 28.4
Folate intake (μg/d)	476 ± 320	470 ± 312	474 ± 285	496 ± 275	520 ± 261
Potassium intake (mg/d)	2766 ± 595	2784 ± 526	2931 ± 498	3123 ± 518	3362 ± 585
Magnesium intake (mg/d)	301 ± 87	297 ± 74	314 ± 69	340 ± 71	370 ± 79
Retinol activity equivalents intake (μg/d)	1571 ± 1569	1563 ± 1440	1576 ± 1298	1662 ± 1292	1819 ± 1469
History of hypertension (%)	6.6	5.9	5.5	7.4	8.3
History of diabetes (%)	0.7	0.8	0.8	0.7	1.0
History of tinnitus (%)	9.8	9.5	8.4	8.4	7.2
White race (%)	93.9	94.1	94.2	93.5	89.4
Aspirin use ≥2 d/wk (%)	4.4	4.3	4.3	4.3	4.3
Ibuprofen use ≥2 d/wk (1995) (%)	9.9	9.0	9.0	9.5	9.9
Acetaminophen use ≥2 d/wk (1995) (%)	7.3	7.5	7.4	7.5	8.0

[1] Values are means ± SDs unless otherwise indicated and are standardized to the age distribution of the study population. Values of polytomous variables may not sum to 100% because of rounding.

[2] Value is not age adjusted.

[3] METs, metabolic equivalents from recreational and leisure-time activities.

TABLE 2
Age- and multivariable-adjusted RRs (95% CIs) of hearing loss according to cumulative average fish intake in 65,521 women followed from 1991 to 2009

	Cumulative average frequency of fish intake (servings)					
Characteristic	<1/mo	1–3/mo	1/wk	2–4/wk	≥5/wk	*P*-trend
No. of cases	1098	2208	7065	1078	157	
Person-years	91,537	178,178	630,597	117,447	20,334	
Age adjusted	1.00 (reference)	1.02 (0.95, 1.10)	0.95 (0.89, 1.01)	0.82 (0.75, 0.89)	0.82 (0.70, 0.97)	<0.001
Multivariable adjusted[1]	1.00 (reference)	1.02 (0.95, 1.10)	0.94 (0.88, 1.00)	0.80 (0.74, 0.88)	0.80 (0.67, 0.95)	<0.001

[1] Cox proportional hazards regression was used, and the models were adjusted for age; BMI; waist circumference; smoking; intake of alcohol, folate, vitamin B-12, potassium, magnesium, and vitamin A (retinol activity equivalents); hypertension; diabetes; tinnitus; race; use of aspirin, ibuprofen, and acetaminophen; physical activity; and calories.

More frequent consumption of any type of fish (canned tuna, dark-meat fish, light-meat fish, or shellfish) tended to be inversely associated with risk (*P*-trend ≤ 0.04).

We also examined the relation between intake of omega-3 PUFAs and the risk of hearing loss (**Table 4**). Higher intake of total omega-3 PUFAs was inversely associated with the risk of hearing loss. In comparison with women with the lowest quintile of intake, the multivariable-adjusted RR for hearing loss among women in the highest quintile of intake was 0.88 (95% CI: 0.82, 0.95) (*P*-trend < 0.001). We further examined the independent associations between long-chain omega-3 PUFAs (EPA + DHA) and between intermediate-chain omega-3 PUFAs (ALA) and risk of hearing loss. Higher intake of long-chain omega-3 PUFAs was inversely associated with risk of hearing loss. In comparison with women in the lowest quintile of long-chain omega-3 PUFA intake, the multivariable-adjusted RR for hearing loss among women in the highest quintile was 0.85 (95% CI: 0.80, 0.91) (*P*-trend < 0.001). After the highest quintile was divided into 2 deciles, the RR was 0.91 (95% CI: 0.84, 0.98) for those in the ninth decile and 0.78 (95% CI: 0.72, 0.85) for those in the highest decile of intake.

Overall, intake of ALA was not significantly associated with risk. In secondary analyses stratified by level of fish intake and level of long-chain omega-3 PUFA intake, there was no significant association between intake of ALA and risk of hearing loss, even among women with very low intake of fish or of long-chain omega-3 PUFAs (data not shown). Furthermore, the relation between long-chain omega-3 PUFA consumption and risk of hearing loss did not vary by level of omega-6 PUFA intake, nor did the relation vary by age (data not shown).

Women in the highest category of fish consumption were more likely to have hypertension, and hypertension may be a risk factor for hearing loss (33). Because of the possibility that women with hypertension changed their habits after their diagnosis, we performed analyses that excluded women with hypertension at baseline and stopped updating diet when hypertension was

TABLE 3
Age- and multivariable-adjusted RRs (95% CIs) of hearing loss according to cumulative average specific fish intake in 65,521 women followed from 1991 to 2009

	Cumulative average frequency of specific fish intake (servings)				
Characteristic	<1/mo	1–3/mo	1/wk	≥2/wk	*P*-trend
Tuna					
No. of cases	1933	6639	2701	330	
Age adjusted	1.00 (reference)	1.00 (0.95, 1.06)	0.94 (0.88, 0.99)	0.89 (0.79, 1.01)	<0.001
Multivariable adjusted[1]	1.00 (reference)	1.01 (0.96, 1.06)	0.92 (0.87, 0.98)	0.87 (0.77, 0.98)	<0.001
Light-meat fish					
No. of cases	3929	6519	1077	71	
Age adjusted	1.00 (reference)	0.94 (0.91, 0.98)	0.85 (0.79, 0.91)	0.73 (0.58, 0.92)	<0.001
Multivariable adjusted[1]	1.00 (reference)	0.95 (0.91, 1.00)	0.90 (0.83, 0.97)	0.77 (0.60, 0.99)	<0.001
Dark-meat fish					
No. of cases	7468	3688	446	—[2]	
Age adjusted	1.00 (reference)	0.97 (0.93, 1.01)	0.81 (0.74, 0.89)		<0.001
Multivariable adjusted[1]	1.00 (reference)	1.03 (0.99, 1.08)	0.94 (0.85, 1.05)		0.04
Shellfish					
No. of cases	6186	5106	311	—[2]	
Age adjusted	1.00 (reference)	0.95 (0.91, 0.98)	0.81 (0.73, 0.91)		<0.001
Multivariable adjusted[1]	1.00 (reference)	0.96 (0.92, 1.00)	0.86 (0.76, 0.97)		<0.001

[1] Cox proportional hazards regression was used, and the models were adjusted for age; BMI; waist circumference; smoking; intake of alcohol, folate, vitamin B-12, potassium, magnesium, and vitamin A (retinol activity equivalents); hypertension; diabetes; tinnitus; race; use of aspirin, ibuprofen, and acetaminophen; physical activity; calories; and intake of the other fish types.

[2] Because of the limited number of cases, the highest category of intake for dark-meat fish and shellfish was collapsed into ≥1 serving/wk.

TABLE 4
Age- and multivariable-adjusted RRs (95% CIs) of hearing loss according to cumulative average fatty acid intake in 65,521 women followed from 1991 to 2009

	Quintile of cumulative average fatty acid intake					
Characteristic	1	2	3	4	5	*P*-trend
Total omega-3 PUFAs						
Median intake (g/d)[1]	0.80	0.99	1.15	1.33	1.64	
No. of cases	2330	2416	2491	2325	2044	
Person-years	204,049	214,601	218,195	208,165	193,082	
Age adjusted	1.00 (reference)	0.94 (0.88, 0.99)	0.93 (0.88, 0.99)	0.89 (0.84, 0.95)	0.83 (0.86, 0.97)	<0.001
Multivariable adjusted[2]	1.00 (reference)	0.95 (0.89, 1.00)	0.95 (0.90, 1.01)	0.93 (0.87, 0.99)	0.88 (0.82, 0.95)	<0.001
α-Linolenic acid						
Median intake (g/d)[1]	0.65	0.79	0.91	1.07	1.35	
No. of cases	2115	2252	2442	2383	2414	
Person-years	196,251	207,813	214,944	212,536	206,549	
Age adjusted	1.00 (reference)	0.96 (0.91, 1.02)	0.98 (0.93, 1.04)	0.95 (0.90, 1.01)	0.97 (0.96, 1.08)	0.26
Multivariable adjusted[2]	1.00 (reference)	0.98 (0.92, 1.04)	1.00 (0.94, 1.07)	0.97 (0.91, 1.04)	1.00 (0.92, 1.03)	0.44
Long-chain omega-3 PUFAs (DHA + EPA)[3]						
Median intake (g/d)[1]	0.06	0.10	0.15	0.25	0.39	
No. of cases	2694	2611	2420	2346	1635	
Person-years	214,147	215,515	218,016	208,735	181,681	
Age adjusted	1.00 (reference)	0.96 (0.91, 1.02)	0.88 (0.84, 0.93)	0.88 (0.83, 0.93)	0.78 (0.74, 0.83)	<0.001
Multivariable adjusted[2]	1.00 (reference)	0.96 (0.91, 1.02)	0.92 (0.87, 0.98)	0.95 (0.90, 1.01)	0.85 (0.80, 0.91)	<0.001

[1] At baseline, 1991.
[2] Cox proportional hazards regression was used, and the models were adjusted for age; BMI; waist circumference; smoking; intakes of alcohol, folate, vitamin B-12, potassium, magnesium, and vitamin A (retinol activity equivalents); race; history of hypertension, diabetes, and tinnitus; use of aspirin, ibuprofen, and acetaminophen; physical activity; calories; and the other omega-3 fatty acids.
[3] For long-chain omega-3 PUFAs (DHA + EPA), the multivariable-adjusted RR for decile 9 (median intake 0.34 g/d) = 0.91 (95% CI: 0.84, 0.98), and the multivariable-adjusted RR for decile 10 (median intake 0.49 g/d) = 0.78 (95% CI: 0.72, 0.85).

reported during follow-up; the results were essentially unchanged (data not shown).

DISCUSSION

In this prospective study among 65,215 US women, we observed a lower risk of hearing loss among women who consumed 2 or more servings of fish per week. Consumption of any specific type of fish (tuna, dark-meat fish, light-meat fish, or shellfish) tended to be associated with lower risk. In addition, higher intake of long-chain omega-3 PUFAs was inversely associated with risk. These findings suggest that diet may be important in the pathogenesis of hearing loss.

Cochlear blood flow must be well regulated to meet the energy demands of the inner ear, ensure adequate delivery of oxygen and glucose, and effectively remove the by-products of metabolism. Compromise of cochlear blood supply can hinder maintenance of the endocochlear potential, ion transport, endolymphatic fluid balance, and the integrity of the blood-labyrinth barrier in the stria vascularis (12). Insufficient cochlear blood flow may lead to hypoxic-ischemic damage to hair cells and hearing loss. In animals, mechanisms associated with cochlear hypoperfusion, ischemia, and the formation of reactive oxygen species have been associated with mitochondrial DNA damage, anatomic changes within the inner ear, cell apoptosis, and age-related hearing loss (37, 38). Inadequate cochlear blood flow, diminished cochleovascular reactivity, and less effective autoregulation may render the ear vulnerable to stress and impaired function (12).

Fish consumption and higher intake of long-chain omega-3 PUFAs may help maintain adequate cochlear blood flow and protect against ischemic injury. These benefits may be mediated through multiple mechanisms, such as improved vascular reactivity and endothelial function; favorable influences on plasma lipids, triglycerides, and blood pressure; and protection against thrombosis and inflammation. Long-chain omega-3 PUFAs may influence membrane structure, modulate membrane ion channels and electrophysiology in response to ischemic stress, regulate gene expression, reduce arachidonic acid–derived proinflammatory or prethrombotic eicosanoids, and increase omega-3 PUFA-derived eicosanoids (13).

Our prospective results differ from those of a cross-sectional European study (n = 821) that found no association between fish intake and hearing levels in women (17). The differing findings may be the result of the small size or cross-sectional design that did not permit temporal relations to be examined. Our results in younger women are consistent with a prospective Australian study among older individuals that found consumption of ≥2 servings of fish at baseline was associated with a lower 5-y incidence of audiometrically determined hearing loss (16). Notably, no cross-sectional association between fish intake and hearing loss was observed in that study. Our findings are also consistent with those from a Dutch study that found an inverse association between higher levels of total plasma long-chain omega-3 PUFAs and a 3-y risk of hearing loss (39).

Evidence suggests regular fish consumption (1–2 servings per week) may protect against several diseases, such as coronary artery disease (40), sudden cardiac death (41), ischemic stroke (21), atrial fibrillation (42), cognitive decline (43), and dementia (44). The proposed benefits of fish intake may be attributable in large part to the long-chain omega-3 fatty acids that fish provide. Finfish and shellfish are the chief dietary sources of the major long-chain omega-3 PUFAs, EPA (20:5n−3) and DHA (22:6n−3), often referred to as "marine" fatty acids. Intake is particularly essential for DHA, because it cannot be synthesized appreciably after infancy (45). DHA appears to be important during auditory neurodevelopment, and higher dietary intake of DHA in breast milk or supplemented formula during early infancy is associated with accelerated maturation of auditory brainstem response latencies (46, 47).

Limited amounts of EPA can be synthesized from ALA (18:3n−3), the plant-derived fatty acid found in green leafy vegetables, walnuts, and flax seeds (48), and thus ALA may be a source of long-chain omega-3 PUFAs among those with very low fish intake (49). Higher intake of ALA may compensate for low fish and long-chain omega-3 PUFA intake (50), but we did not observe a relation between intake of ALA and risk of hearing loss for any amount of fish or long-chain omega-3 PUFA intake, even among women with a very low intake.

Some authors suggest that higher intake of omega-6 fatty acids can attenuate the beneficial effects of omega-3 fatty acids by competing for common metabolic enzymes, competing for incorporation into plasma lipid fractions, or serving as precursors to proinflammatory eicosanoids (44, 51). However, we did not observe that higher intake of omega-6 fatty acids modified the relation between fish or long-chain omega-3 fatty acids and risk of hearing loss.

Fish is an important part of a healthy diet, yet only approximately one-third of Americans report eating fish once per week, and almost half eat fish rarely or not at all (52). Recommendations for intake, typically ≥2 servings of fish/wk or ≥250 mg long-chain omega-3 PUFAs/d, have been incorporated into national and international dietary guidelines (13). Strikingly, intake of long-chain omega-3 PUFAs is <60 mg/d for approximately half of US adults (53). Although specific limitations are advised for pregnant and nursing women due to potential contaminants, the benefits of fish consumption greatly outweigh the possible risks for adults in the general population (41). These findings suggest a protective role for long-chain omega-3 fatty acids, but because intakes of fish and marine fatty acids are highly correlated, it is difficult to disentangle the singular effects of fish and marine fatty acid consumption. Some benefits of fish intake on hearing might be mediated through a complex interplay among a wide range of nutrients found in fish that may also confer protection against hearing loss and possibly act in synergy with omega-3 fatty acids (54).

Our study has limitations. Assessment of hearing loss was based on self-report. Pure-tone audiometry is considered the gold standard for hearing evaluation, but self-reported hearing loss has been demonstrated to be reasonably reliable (27, 28). Onset of hearing loss is usually insidious, and thus imprecision in the assessment of date of onset exists. Assessment of hearing loss was based on date of onset as reported in 2009; however, all information on exposures and covariates was collected before the reported date of onset of hearing loss, allowing all the relations to be examined prospectively. The severity of hearing loss could not be considered because we did not have information on hearing loss severity at the time of onset. Misclassification of exposure is of concern because dietary questionnaires may have errors in reporting and recall. Diet was assessed prospectively, and thus errors would likely be random with respect to the outcome and would tend to bias results toward the null. Cumulative averaging of dietary intake by using multiple validated questionnaires over time was done to reduce misclassification of the exposures and to examine the association with long-term intake. Although we recognize that measurement error still exists, the error introduced by these procedures is likely random and independent of the outcome. Women in our cohort who consumed fish more regularly may have had healthier diet and lifestyle habits. However, careful adjustment for potential dietary and lifestyle confounding variables did not appreciably alter the results, suggesting an independent association between fish and long-chain omega-3 PUFAs and risk of hearing loss. Nevertheless, the possibility of unmeasured confounding cannot be excluded. The present study examined a predominantly white population of women. Although the prevalence of acquired hearing loss in US adults is higher in men than in women in the age group of our study population, little is known about whether there are differences in the underlying pathophysiology of hearing loss between women and men or whether there are sex differences in the relation between dietary risk factors for hearing loss. Further examination of the relation between fish and long-chain omega-3 fatty acid consumption in men and in other populations would be informative.

In conclusion, regular fish consumption and higher intake of long-chain omega-3 PUFAs are associated with a lower risk of hearing loss in women. These findings provide evidence that modifiable dietary risk factors may help reduce the risk of hearing loss.

The authors' responsibilities were as follows—SGC, RDE, MW, EBR, and GCC: provided the study concept and design, analysis and interpretation of the data, and critical revision of the manuscript for important intellectual content; SGC and GCC: acquired data; SGC: drafted the manuscript; MW and GCC: provided statistical expertise; and GCC: provided study supervision and had primary responsibility for final content. All authors read and approved the final manuscript. No conflicts of interest were reported.

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