Published in final edited form as:

Nutr Metab Cardiovasc Dis. 2015 July ; 25(7): 651–658. doi:10.1016/j.numecd.2015.04.006.

Fish, omega-3 long-chain fatty acids, and all-cause mortality in a low-income US population: results from the Southern Community Cohort Study

R Villegas^a, Y Takata^a, H Murff^a, and WJ Blot^{a,b}

^aDepartment of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee

^bInternational Epidemiology Institute, Rockville, Maryland (WJB)

Abstract

Background—We examined associations between fish and n-3 LCFA and mortality in a prospective study with a large proportion of blacks with low socio-economic status.

Methods and Results—We observed 6,914 deaths among 77,604 participants with dietary data (follow-up time 5.5 years). Of these, 77,100 participants had available time-to-event data. We investigated associations between mortality with fish and n-3 LCFA intake, adjusting for age, race, sex, kcals/day, body mass index (BMI), smoking, alcohol consumption, physical activity, income, education, chronic disease, insurance coverage, and meat intake. Intakes of fried fish, baked/grilled fish and total fish, but not tuna, were associated with lower mortality among all participants. Analysis of trends in overall mortality by quintiles of intake showed that intakes of fried fish, baked/grilled fish and total fish, but not tuna, were associated with lower risk of total mortality among all participants. When participants with chronic disease were excluded, the observed association remained only between intakes of baked/grilled fish, while fried fish was associated with lower risk of mortality in participants with prevalent chronic disease. The association between n-3 LCFA intake and lower risk of mortality was significant among those with diabetes at baseline. There was an inverse association of mortality with fried fish intake in men, but not women. Total fish and baked/grilled fish intakes were associated with lower mortality among blacks while fried fish intake was associated with lower mortality among whites. Effect modifications were not statistically significant.

Conclusion—Our findings suggest a modest benefit of fish consumption on mortality.

Keywords

fish; omega-3 long-chain fatty acids; Southern Community Cohort Study

Corresponding author and requests for reprints: Raquel Villegas, PhD; Address: 2525 West End Avenue, Suite 600 (IMPH), Nashville, Tennessee 37203, USA; Phone: 615-936-1822; Fax: 615-936-8291; raquel.villegas@vanderbilt.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

None of the authors had any conflicts of interest to declare.

INTRODUCTION

The evidence linking fish intake and mortality is inconsistent. Fish intake has been associated with lower risk of total and/or cardiovascular disease mortality in some (1–4), but not all studies (5;6). Reasons for inconsistencies among studies could be related to the type of fish, cooking methods, or the amount of fish consumed in each study population. Frying fish, especially deep-frying, might produce trans-fatty acids and therefore might modify the beneficial effect of fatty acids in fish. An inverse association between broiled and baked fish, but not fried fish, and cardiovascular mortality has been reported in a study conducted in the United States (7). Among the major nutrients in fish, omega-3 long-chain fatty acids (n-3 LCFA) have been hypothesized to be beneficial for overall health (8;9). Recent studies support this association, including a large prospective study of circulating n-3 LCFA concentration and mortality (10) and another cohort study of n-3 LCFA intake and mortality (11). However, in a meta-analysis of n-3 LCFA supplementation trials, supplementation was not associated with a lower risk of all-cause mortality (12). The majority of previous studies have been conducted in populations of predominately white race/ethnicity and relatively high socioeconomic status. Data on the association between dietary fish and n-3 LCFA and mortality among blacks and low-income populations is lacking.

We investigated associations between dietary intakes of fish and n-3 LCFA with all-cause mortality in the Southern Community Cohort Study (SCCS), a population-based, prospective cohort study that includes a relatively large proportion of low-income households and blacks in the southeastern United States, where the prevalence of obesity, diabetes, and other comorbidities associated with all-cause mortality are high (13). In this report, we conducted a comprehensive evaluation of associations of intakes of tuna, fried fish, baked/grilled fish, total fish, and dietary n-3 LCFA with risk of all-cause mortality in the SCCS and further investigated potential effect modifications by gender and race. We hypothesized that high fish and dietary n-3 LCFA intakes were associated with reduced risk of mortality. We also conducted analyses among participants with prevalent diabetes and with prevalent chronic disease at baseline.

SUBJECTS and METHODS

Study participants

The SCCS is a prospective cohort study assessing health disparities among adults living in urban and rural areas of 12 states in the southeastern US (14). A detailed description of the SCCS cohort has been published (13). Briefly, from 2002 to 2009, nearly 86,000 adults were enrolled in the cohort, most (86%) were recruited at 71 participating community health centers that provide basic health services mainly to low-income and uninsured persons (13). An additional 14% of the cohort enrolled from 2004 to 2006 by responding to a mailed questionnaire sent to randomly selected residents of the same 12 states. This was done to recruit participants with more diverse incomes and education into the cohort. All SCCS participants were aged 40–79 years, able to speak English, and not under treatment for cancer during the 12 months preceding cohort enrollment. The SCCS was approved by institutional review boards at Vanderbilt University and Meharry Medical College, and all participants provided written, informed consent at enrollment.

Data collection and diet assessment

Participants completed a baseline survey via a computer-assisted personal interview for community health center enrollees and a self-administered questionnaire for mail enrollees at study enrollment. This survey contained questions about demographic, medical, family, lifestyle, and other participant characteristics.

Assessment of dietary intake

The SCCS baseline questionnaire included a 102-item food frequency questionnaire (FFQ), which was developed specifically for black and white residents of the southeastern US (15). A validation study within the SCCS to evaluate FFQ-estimated intakes of alpha-carotene, beta-carotene, beta-cryptoxanthin, lutein/zeaxanthin, lycopene, folate, and alpha-tocopherol in relation to blood levels of these nutrients has been conducted (16). The FFQ elicited information on usual frequency of consumption during the preceding year using the following scale: never, rarely, once a month, 2–3 times a month, once a week, 2–3 times a week, 4–6 times a week, once a day, and two or more times a day. The FFQ also obtained estimates of portion size (small, medium or large) for each food item. We used the mean portion size consumed by the National Health and Nutrition Examination Survey (NHANES) III sample rounded to the nearest common unit to define a medium portion. Small and large portion sizes were then defined usually as one-half (small) or twice (large) the medium portion size. When completing the FFQ, subjects would be asked to report on both their usual frequency of consumption and usual portion size as small, medium, or large. Portion sizes for each food were anchored to a specific amount of food (e.g., small = 1/2 cup, medium = 1 cup, large = 2 cups).

Data from the 24-hour dietary recalls conducted within NHANES mapped to the southern census region were used to construct food codes which were then assigned to FFQ items. Nutrient compositions of reported food sources were included within the NHANES report and were then assigned to FFQ items. When multiple NHANES items were assigned to a single FFQ food category nutrient totals were averaged (17).

Estimates of daily intakes of total energy and nutrients were calculated based on the estimated nutrient content of the foods consumed multiplied by the numbers of servings per day. Data from NHANES III, NHANES 1999–2004, and the United States Department of Agriculture's Continuing Survey of Food Intakes by Individuals were used to develop sex- and race-specific estimates of intakes of various nutrients applicable to residents of the southeastern US (18).

From the FFQ, we thus calculated estimates of average daily intake for major individual fatty acids. We calculated the total n-3 LCFA consumption by combining eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) fatty acids from the nutrient calculations. These values reflect only food sources of the nutrients, not supplement sources. Our study did not have a quantitative assessment of n-3 LCFA intake from supplements.

We calculated total fish intake by combining the average daily intakes of relevant food groups (g/day), including: 1) fried fish, based on the FFQ item that asked about intake from "fried fish, shrimp, or seafood (including sandwiches)," 2) baked/grilled fish, based on

intake from “broiled or baked fish, shrimp, or seafood (including sandwiches),” and 3) tuna, based on intake from “canned tuna fish, tuna casserole, or tuna salad (including sandwiches).”

Mortality ascertainment

Vital status was ascertained from the Social Security Administration, and the National Death Index (NDI) provided cause of death information through 2011. For analyses of all-cause mortality, follow-up was extended through December 31, 2011 (coincident with the latest NDI linkage) or date of death. For those whose vital status was reported as unknown by the Social Security Administration, follow-up was censored at the last SCCS contact with the participant or December 31, 2011 (latest linkage to the National Death Index data file). Of the 85,580 participants enrolled in the SCCS, we excluded participants who died within the first year of follow-up ($n=819$), leaving 84,761 participants for the analysis, of whom 77,604 participants had dietary intake of fish values. Of these, a total of 77,100 participants had time to event data information.

Statistical analyses

Quintiles of intakes of $n-3$ LCFA, tuna, fried fish, baked/grilled fish, and total fish were calculated. Tests for linear trend across quintiles were conducted by modeling them as continuous variables. The risk of all-cause mortality in relation to fish intake was assessed using Cox proportional hazards regression with follow-up time as the time scale to calculate relative risks (RR) and corresponding 95% confidence intervals (CI) for each quintile of intake using the lowest quintile as the reference. The final model was adjusted for age at baseline (continuous), total caloric intake (continuous), BMI (continuous), sex, race (black, white, other) smoking history (current/former/never), income in dollars/year (<15,000, 15,000–24,900, 25,000–49,999, >49,999), education (less than high school, completed high school, some college, finished college), chronic disease at baseline (i.e., prior history of diabetes, myocardial infarction, heart attack or coronary artery by-pass surgery, or stroke), physical activity level [five categories based on quintiles of metabolic equivalent (MET) hours], total meat intake (continuous), and regular alcohol consumption (none, up to one unit of alcohol per week, and more than one unit of alcohol per day). One unit of alcohol is defined as 12 g of ethanol. Subgroup analyses were conducted by the presence of diabetes or history of other chronic disease at baseline and in participants who did not report chronic disease at baseline. We conducted stratified analyses by sex and two major race groups (blacks and whites). The log-likelihood ratio test was used to evaluate the significance of the interaction terms for sex and race with fish or $n-3$ LCFA intake. All P -values were two-sided and $P < 0.05$ was considered to be statistically significant. All analyses were conducted using SAS software, version 9.3, of the SAS System for Windows (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Among 77,604 participants, a total of 6,914 deaths occurred after a mean follow-up of 5.5 years. The median intakes of total fish were 27.1 g/day among all participants, 32.7 g/day among men and 24.6 g/day among women. The median intake of total fish according to race

was 20.1 g/day in whites, 31.1 g/day in blacks, and 25.1 g/day in others. Among participants with follow-up data, there were 26,042 participants with chronic disease and 16,427 reported cases of diabetes at baseline. There were 23,698 white participants and 49,988 black participants and there were a total of 90,950 men and 46,150 women. Characteristics of the study population by n-3 LCFA intake are shown in Table 1. Higher intake of n-3 LCFA was associated with younger age, higher physical activity level, being male, and being black. Participants in the lowest quintile of n-3 LCFA had lower education level (less than high school) compared to participants in other quintiles. Participants with a higher intake of n-3 LCFA were more likely to be current smokers and consume alcohol. Chronic disease was more common among those with lower intake of n-3 LCFA. The association between diabetes and quintiles of n-3 LCFA was not significant.

We found an inverse association between total fish intake and total mortality among all participants (Table 2). Intakes of fried fish, baked/grilled fish, but not tuna, were associated with lower risk of total mortality among all participants. The association between n-3 LCFA intake with total mortality was marginally significant. When we excluded participants who reported having a chronic disease at baseline, only the inverse association of baked/grilled fish with total mortality was statistically significant.

We evaluated associations between fish intake and total mortality among participants with prevalent chronic disease at baseline (i.e., prior history of diabetes, myocardial infarction, heart attack or coronary artery by-pass surgery, or stroke) and among participants with only diabetes at baseline (Table 3). The association between total fish, tuna, or baked/grilled fish intake and total mortality was not significant among participants with chronic disease or diabetes at baseline. Fried fish intake was associated with lower risk of mortality in both groups (i.e., participants with prevalent chronic disease and participants with only diabetes at baseline). The decreasing trend for the association between fried fish intake and total mortality was statistically significant among participants with prevalent chronic disease at baseline (P -trend=0.03) and marginally not significant among participants with only diabetes at baseline (P -trend=0.06).

We evaluated the association of fish and dietary n-3 LCFA intakes with total mortality among men and women separately (Table 4). Total fish intake was not associated with mortality in men or women. Baked/grilled fish was associated with lower risk of mortality for the highest quintile compared with the lowest among women [RR (95% CI) = 0.87 (0.77–0.98)]. However, the trend was marginally not significant (P -trend=0.09). There was an inverse association of mortality with fried fish intake in men, but not women. The interactions between gender and all types of fish were not statistically significant.

When we evaluated the association between fish and n-3 LCFA intakes separately by the two major racial groups (black vs. white), total fish and baked/grilled fish were associated with lower risk of mortality among blacks only (Table 5). In contrast, among whites, fried fish intake was inversely associated with total mortality (RR=0.79, 95% CI=0.65–0.96 for the highest quintile compared with the lowest), which was not observed among blacks (RR=0.96, 95% CI=0.87–1.07). None of the interactions with race were statistically significant.

DISCUSSION

In this large cohort of low-income adults in the southeastern US, we found a modest but statistically significant inverse association between total fish, fried fish, and baked/grilled fish intakes with total mortality. The association was attenuated when we excluded participants with chronic disease at baseline, and only baked/grilled fish was statistically significantly inversely associated with total mortality. The association between total fish intake and all-cause mortality tended to differ by race, with the association being stronger among blacks and men, although the test for interaction was not statistically significant. This report includes one of the largest numbers of blacks (n=49,988) and whites (n=23,698) of similar socioeconomic status, providing a comparison group to examine association patterns across races. This helped to minimize socioeconomic-related confounding, which is common in epidemiologic studies of diet and chronic disease or mortality.

Our finding of an inverse association between total fish intake and total mortality is consistent with a case-control study in Hong Kong (19) and two previous Asian cohort studies, one in Japan (3) and the other in China (20). However, two prospective cohort studies in the United States and Britain reported no association (5;21). Reasons for inconsistent findings could be due to several factors, including differences in the amount of fish consumed or in preparation methods. As for the amount of intake, the median fish intakes in our study were 27.1 g/day in all participants, 32.7 g/day for men, and 24.6 g/day for women, which were similar to the British study (34g/day among non-vegetarians) (21) and the Chinese study (39g/day) (20) and lower than the level reported in the Japanese study (87g/day) (3). The fish intakes in our study provide a good range across which to evaluate trends in risk, and the 32-fold difference in median intake between quintiles enabled us to assess a fairly broad range of consumption levels. With regard to the cooking methods of fish, steaming, grilling, and stir-frying are the most common in Asian populations, whereas deep-frying may be more common in Western countries than in Asian countries. Broiled or baked fish, but not fried fish, has been associated with lower mortality in one study (7).

In our study, both fried fish and baked/grilled fish were associated with lower mortality among all participants. When participants with chronic disease were excluded, the observed association remained only between intakes of baked/grilled fish, while fried fish was associated with lower risk of mortality in participants with prevalent chronic disease.

A potential mechanism for the protective effect of fish consumption on mortality may be related to n-3 LCFA content in fish (8). However, because intakes of fish and n-3 LCFA are highly correlated, it is difficult to disentangle the effect of these fatty acids from the effect of fish consumption. Associations of other nutrients abundant in fish, shrimp, or seafood with total mortality have not been investigated in our cohort, which may offer further insights on specific nutrients potentially responsible for the observed associations of fish, shrimp, or seafood intake and mortality. It is possible that other potentially beneficial nutrients abundant in fish, such as vitamin D, retinol, selenium, or taurine may contribute to the protective effect of dietary fish intake on mortality (22). In another paper from the SCCS, , serum vitamin D level was inversely associated with mortality (23).

This study has several notable strengths. First, the SCCS is a well-characterized prospective cohort that included high proportions of blacks and low-income adults and a similar proportion of whites and blacks in terms of household income levels. Hence, it is well-designed for investigating dietary factors associated with chronic disease in blacks compared with whites, both of which may be affected by socioeconomic status and racial groups (24). The majority of existing prospective cohort studies often did not have sufficient numbers of black men and women to test racial differences. The SCCS population is not reflective of the socioeconomic or racial distributions in the general US population, given that our study recruitment strategy targeted community health centers and resulted in over-representation of low-income individuals. Thus, the generalizability of our findings to other study populations with different proportions of socioeconomic status and race distribution is limited. Nevertheless, the SCCS adds an important new dimension to the existing body of literature that, for the most part, has examined associations between fish and n-3 LCFA intakes and mortality in cohorts predominately consisting of middle or upper income households.

Our study also has limitations. Given that fish consumption was associated with younger age, higher socio-economic status, and higher physical activity level, the possibility of residual confounding cannot be ruled out, even after fully adjusting for confounders. Another limitation of this study is the use of self-reported dietary intake data, as misclassification of dietary information unavoidable. Specifically, in this study, differences in estimated intake for several nutrients were found, most notably among black women, which may have affected our results (18). Exposure (fish intake) was assessed through two methods: interviewer-administered FFQ in some participants and self-administered mailed questionnaire in others. This heterogeneity could introduce a differential misclassification in our results. Our study did not have a quantitative assessment of n-3 LCFA intake from supplements, and we were not able to investigate the total intake from both foods and supplements. An additional limitation is the difficulty of controlling for existing disease. We attempted to address this issue by excluding participants who died within the first year of follow-up. Another limitation of the study is that we did not have biological measures such as fatty acid composition of plasma or cells and tissues (adipose tissue) in this population.

Overall, our findings are consistent with a modest benefit of fish consumption on all-cause mortality in a population of low socioeconomic status with a high prevalence of comorbidities. Among the fish items we investigated, baked/grilled fish and fried fish, but not tuna, intake had inverse associations with total mortality among all participants. Associations between fish intake and dietary n-3 LCFA intake were more pronounced among blacks compared with whites, but these effect modification differences were not statistically significant.

ACKNOWLEDGMENTS

All authors read and approved the final manuscript. The Southern Community Cohort Study is funded by grant number R01 CA092447 from the National Cancer Institute and a special allocation from the American Recovery and Reinvestment Act (3R01 CA092447-08S1). The sponsor had no role in study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the article for publication.

Abbreviations used

BMI	body mass index
CI	confidence interval
DHA	docosahexaenoic acid
EPA	eicosapentaenoic acid
FFQ	food frequency questionnaire
ICD-9	International Classification of Diseases ninth revision
n-3 LCFA	omega-3 long-chain fatty acid
MET	metabolic equivalent
NDI	National Death Index
NHANES	National Health and Nutrition Examination Survey
RR	relative risk
SCCS	Southern Community Cohort Study

Reference List

1. Konig A, Bouzan C, Cohen JT, Connor WE, Kris-Etherton PM, Gray GM, et al. A quantitative analysis of fish consumption and coronary heart disease mortality. *Am J Prev Med.* 2005 Nov; 29(4):335–346. [PubMed: 16242600]
2. Wang MP, Thomas GN, Ho SY, Lai HK, Mak KH, Lam TH. Fish consumption and mortality in Hong Kong Chinese--the LIMOR study. *Ann Epidemiol.* 2011 Mar; 21(3):164–169. [PubMed: 21109449]
3. Yamagishi K, Iso H, Date C, Fukui M, Wakai K, Kikuchi S, et al. Fish, omega-3 polyunsaturated fatty acids, and mortality from cardiovascular diseases in a nationwide community-based cohort of Japanese men and women the JACC (Japan Collaborative Cohort Study for Evaluation of Cancer Risk) Study. *J Am Coll Cardiol.* 2008 Sep 16; 52(12):988–996. [PubMed: 18786479]
4. Zheng J, Huang T, Yu Y, Hu X, Yang B, Li D. Fish consumption and CHD mortality: an updated meta-analysis of seventeen cohort studies. *Public Health Nutr.* 2012 Apr; 15(4):725–737. [PubMed: 21914258]
5. Folsom AR, Demissie Z. Fish intake, marine omega-3 fatty acids, and mortality in a cohort of postmenopausal women. *Am J Epidemiol.* 2004 Nov 15; 160(10):1005–1010. [PubMed: 15522857]
6. Nakamura Y, Ueshima H, Okamura T, Kadowaki T, Hayakawa T, Kita Y, et al. Association between fish consumption and all-cause and cause-specific mortality in Japan: NIPPON DATA80, 1980–99. *Am J Med.* 2005 Mar; 118(3):239–245. [PubMed: 15745721]
7. Mozaffarian D, Lemaitre RN, Kuller LH, Burke GL, Tracy RP, Siscovick DS. Cardiac benefits of fish consumption may depend on the type of fish meal consumed: the Cardiovascular Health Study. *Circulation.* 2003 Mar 18; 107(10):1372–1377. [PubMed: 12642356]
8. Mozaffarian D, Wu JH. Omega-3 fatty acids and cardiovascular disease: effects on risk factors, molecular pathways, and clinical events. *J Am Coll Cardiol.* 2011 Nov 8; 58(20):2047–2067. [PubMed: 22051327]
9. Lee JH, O'Keefe JH, Lavie CJ, Harris WS. Omega-3 fatty acids: cardiovascular benefits, sources and sustainability. *Nat Rev Cardiol.* 2009 Dec; 6(12):753–758. [PubMed: 19859067]
10. Mozaffarian D, Lemaitre RN, King IB, Song X, Huang H, Sacks FM, et al. Plasma phospholipid long-chain omega-3 fatty acids and total and cause-specific mortality in older adults: a cohort study. *Ann Intern Med.* 2013 Apr 2; 158(7):515–525. [PubMed: 23546563]

11. Bell GA, Kantor ED, Lampe JW, Kristal AR, Heckbert SR, White E. Intake of long-chain omega-3 fatty acids from diet and supplements in relation to mortality. *Am J Epidemiol*. 2014 Mar 15; 179(6):710–720. [PubMed: 24496442]
12. Rizos EC, Ntzani EE, Bika E, Kostapanos MS, Elisaf MS. Association between omega-3 fatty acid supplementation and risk of major cardiovascular disease events: a systematic review and meta-analysis. *JAMA*. 2012 Sep 12; 308(10):1024–1033. [PubMed: 22968891]
13. Signorello LB, Hargreaves MK, Steinwandel MD, Zheng W, Cai Q, Schlundt DG, et al. Southern community cohort study: establishing a cohort to investigate health disparities. *J Natl Med Assoc*. 2005 Jul; 97(7):972–979. [PubMed: 16080667]
14. Signorello LB, Hargreaves MK, Blot WJ. The Southern Community Cohort Study: investigating health disparities. *J Health Care Poor Underserved*. 2010 Feb; 21(1 Suppl):26–37. [PubMed: 20173283]
15. Buchowski MS, Schlundt DG, Hargreaves MK, Hankin JH, Signorello LB, Blot WJ. Development of a culturally sensitive food frequency questionnaire for use in the Southern Community Cohort Study. *Cell Mol Biol (Noisy -le-grand)*. 2003 Dec; 49(8):1295–1304. [PubMed: 14984001]
16. Signorello LB, Buchowski MS, Cai Q, Munro HM, Hargreaves MK, Blot WJ. Biochemical validation of food frequency questionnaire-estimated carotenoid, alpha-tocopherol, and folate intakes among African Americans and non-Hispanic Whites in the Southern Community Cohort Study. *Am J Epidemiol*. 2010 Feb 15; 171(4):488–497. [PubMed: 20061366]
17. Schlundt DG, Buchowski MS, Hargreaves MK, Hankin JH, Signorello LB, Blot WJ. Separate estimates of portion size were not essential for energy and nutrient estimation: results from the Southern Community Cohort food-frequency questionnaire pilot study. *Public Health Nutr*. 2007 Mar; 10(3):245–251. [PubMed: 17288621]
18. Signorello LB, Munro HM, Buchowski MS, Schlundt DG, Cohen SS, Hargreaves MK, et al. Estimating nutrient intake from a food frequency questionnaire: incorporating the elements of race and geographic region. *Am J Epidemiol*. 2009 Jul 1; 170(1):104–111. [PubMed: 19451177]
19. Wang MP, Thomas GN, Ho SY, Lai HK, Mak KH, Lam TH. Fish consumption and mortality in Hong Kong Chinese--the LIMOR study. *Ann Epidemiol*. 2011 Mar; 21(3):164–169. [PubMed: 21109449]
20. Takata Y, Zhang X, Li H, Gao YT, Yang G, Gao J, et al. Fish intake and risks of total and cause-specific mortality in 2 population-based cohort studies of 134,296 men and women. *Am J Epidemiol*. 2013 Jul 1; 178(1):46–57. [PubMed: 23788668]
21. Key TJ, Appleby PN, Spencer EA, Travis RC, Roddam AW, Allen NE. Mortality in British vegetarians: results from the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford). *Am J Clin Nutr*. 2009 May; 89(5):1613S–1619S. [PubMed: 19297458]
22. Lund EK. Health benefits of seafood; is it just the fatty acids? *Food Chem*. 2013 Oct 1; 140(3):413–420. [PubMed: 23601384]
23. Signorello LB, Han X, Cai Q, Cohen SS, Cope EL, Zheng W, et al. A prospective study of serum 25-hydroxyvitamin d levels and mortality among African Americans and non-African Americans. *Am J Epidemiol*. 2013 Jan 15; 177(2):171–179. [PubMed: 23125439]
24. Nandi A, Glymour MM, Subramanian SV. Association among socioeconomic status, health behaviors, and all-cause mortality in the United States. *Epidemiology*. 2014 Mar; 25(2):170–177. [PubMed: 24487200]

Table 1

Characteristics of the study population by quintiles of n-3 LCFA intake, Southern Community Cohort Study

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P value ³
IQ range n-3 LCFA (g)	0.009– 0.023	0.040– 0.059	0.080– 0.103	0.135– 0.184	0.278– 0.567	
Number of deaths	1407	1364	1287	1410	1446	
Person time	29710110	30776559	31552784	31521269	31752191	
Age (yrs) (Median)	53.0	52.6	52.6	52.0	51.0	<0.001
Kcals/day (Mean)	1920.7	2080.3	2306.5	2758.7	3686.5	<0.001
BMI (Kg/m²) (Mean)	30.5	30.5	30.7	30.1	30.0	<0.001
METS¹ (Mean)	20.1	21.4	22.0	23.7	25.9	<0.001
Male (%)	27.3	35.1	35.4	50.3	52.9	<0.001
Race						<0.001
White	53.1	39.3	26.8	21.9	12.5	
Black	42.7	56.0	68.8	73.6	83.2	
Other	4.2	4.7	4.5	4.5	4.3	
Current smoker (%)	38.9	38.6	38.1	42.3	44.8	<0.001
Alcohol consumption (%)						<0.001
None	52.3	43.1	43.2	38.4	37.9	
1 unit ⁴ /day	38.4	45.1	44.0	44.9	43.0	
> 1 unit/day	9.4	11.8	12.8	16.7	19.1	
Education level (%)						
Less than high school	32.4	26.6	27.1	26.4	28.4	<0.001
Completed high school	34.0	32.4	31.2	32.8	33.4	
Some college	22.5	26.6	26.5	26.8	26.0	
Completed college	11.1	14.3	15.2	14.0	12.2	
Income level (%)²						
<\$15,000	58.3	52.8	52.3	52.8	55.7	<0.001
\$15,000–24,999	19.7	20.9	21.2	21.9	22.4	
\$25,000–49,999	13.1	15.1	14.9	14.9	14.0	
>\$49,999	8.8	11.2	11.6	10.4	7.8	

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P value ³
Diabetes (%)	21.4	21.6	21.2	21.1	20.7	0.31
Chronic disease (%)	36.6	35.4	33.8	32.9	31.3	<0.001

¹Metabolic equivalents per day

²Household income per year

³For continuous variables we used Wilcoxon test (variables were not normally distributed; for categorical variables, we used Chi-square test

⁴Unit of alcohol is defined as 12 g of ethanol

Table 2
Associations between fish⁺ and n-3 LCFA intakes and all-cause mortality, Southern Community Cohort Study*

	All participants				Chronic disease excluded			
	Median**	RR	95% CI	P trend	Median**	RR	95% CI	P trend
Total Fish								
Quintile 1	4.98	1.00		0.049	5.02	1.00		0.09
Quintile 2	15.29	0.99	0.92–1.07		15.29	1.01	0.90–1.13	
Quintile 3	27.02	0.95	0.87–1.02		27.02	0.95	0.85–1.06	
Quintile 4	46.24	0.97	0.90–1.05		46.24	0.93	0.83–1.04	
Quintile 5	108.66	0.92	0.84–1.00		109.93	0.93	0.82–1.04	
Tuna								
Quintile 1	1.10	1.00		0.86	1.47	1.00		0.76
Quintile 2	1.47	1.02	0.94–1.10		4.47	1.11	0.98–1.25	
Quintile 3	4.47	0.99	0.91–1.08		10.99	1.02	0.90–1.15	
Quintile 4	11.15	1.00	0.92–1.08		35.60	0.97	0.86–1.10	
Quintile 5	35.60	1.00	0.93–1.09			1.06	0.94–1.19	
Fried Fish								
Quintile 1	1.30	1.00		0.02	1.30	1.00		0.27
Quintile 2	5.21	0.99	0.92–1.08		5.21	1.06	0.94–1.20	
Quintile 3	13.03	0.99	0.91–1.07		13.03	1.02	0.91–1.15	
Quintile 4	22.35	0.94	0.87–1.02		22.35	0.96	0.85–1.08	
Quintile 5	55.85	0.91	0.84–0.99		55.85	0.98	0.86–1.10	
Baked/Grilled Fish								
Quintile 1	0	1.00		0.01	0	1.00		0.03
Quintile 2	1.16	0.93	0.86–1.01		1.16	0.90	0.80–1.02	
Quintile 3	3.52	0.92	0.86–0.99		3.52	0.93	0.84–1.03	
Quintile 4	8.80	0.96	0.88–1.04		10.39	0.87	0.77–0.98	
Quintile 5	33.64	0.89	0.82–0.96		33.64	0.89	0.80–1.00	
n-3 LCFA								
Quintile 1	0.02	1.00		0.07	0.02	1.00		0.30
Quintile 2	0.05	1.02	0.94–1.10		0.50	1.00	0.89–1.13	

	All participants				Chronic disease excluded		
	Median**	RR	95% CI	P trend	Median**	RR	95% CI P trend
Quintile 3	0.09	0.95	0.88–1.03		0.09	0.95	0.84–1.07
Quintile 4	0.15	0.95	0.88–1.03		0.15	0.91	0.81–1.03
Quintile 5	0.36	0.94	0.86–1.03		0.36	0.97	0.86–1.10

⁺ Based on the FFQ item that asked about intake from 1) fried fish - fried fish, shrimp or seafood (including sandwiches), 2) baked/grilled fish - broiled or baked fish, shrimp, or seafood (including sandwiches), and 3) tuna - canned tuna, tuna casserole, or tuna salad (including sandwiches)

^{*} Adjusted for age, kcal/day, BMI, smoking, alcohol consumption, physical activity level, income level, education level, presence of chronic disease, insurance coverage, race, gender, and total meat intake per day

^{**} Median units are g/day

Table 3

Associations between fish⁺ and n-3 LCFA intakes and all-cause mortality in participants with prevalent chronic disease* at baseline and diabetes at baseline, Southern Community Cohort Study**

	Participants with chronic disease at baseline			Participants with diabetes at baseline		
	RR	95% CI	P trend	RR	95% CI	P trend
Total Fish						
Quintile 1	1.00		0.23	1.00		0.22
Quintile 2	0.98	0.88–1.09		0.98	0.86–1.12	
Quintile 3	0.94	0.85–1.05		0.91	0.79–1.04	
Quintile 4	1.02	0.91–1.13		0.99	0.87–1.13	
Quintile 5	0.90	0.80–1.01		0.89	0.77–1.03	
Tuna						
Quintile 1	1.00		0.90	1.00		0.70
Quintile 2	0.94	0.84–1.05		0.99	0.87–1.13	
Quintile 3	0.97	0.87–1.09		0.96	0.84–1.11	
Quintile 4	1.02	0.91–1.14		1.08	0.94–1.24	
Quintile 5	0.96	0.86–1.07		0.99	0.87–1.13	
Fried Fish						
Quintile 1	1.00		0.03	1.00		0.06
Quintile 2	0.95	0.86–1.06		1.03	0.90–1.17	
Quintile 3	0.97	0.87–1.08		0.94	0.82–1.07	
Quintile 4	0.94	0.84–1.04		0.94	0.82–1.07	
Quintile 5	0.87	0.78–0.98		0.89	0.78–1.03	
Baked/Grilled Fish						
Quintile 1	1.00		0.16	1.00		0.12
Quintile 2	0.94	0.84–1.05		0.93	0.81–1.07	
Quintile 3	0.91	0.83–1.01		0.93	0.82–1.06	
Quintile 4	1.03	0.92–1.15		1.01	0.88–1.15	
Quintile 5	0.88	0.79–0.98		0.87	0.76–0.99	
n-3 LCFA						
Quintile 1	1.00		0.11	1.00		0.03

	Participants with chronic disease at baseline			Participants with diabetes at baseline		
	RR	95% CI	P trend	RR	95% CI	P trend
Quintile 2	1.03	0.92–1.14		1.06	0.93–1.20	
Quintile 3	0.95	0.85–1.06		0.94	0.82–1.08	
Quintile 4	0.99	0.89–1.11		0.95	0.82–1.08	
Quintile 5	0.90	0.80–1.02		0.88	0.75–1.02	

⁺ Based on the FFQ item that asked about intake from 1) fried fish - fried fish, shrimp or seafood (including sandwiches), 2) baked/grilled fish - broiled or baked fish, shrimp, or seafood (including sandwiches), and 3) tuna - canned tuna, tuna casserole, or tuna salad (including sandwiches)

^{*} Chronic disease (i.e., prior history of diabetes, myocardial infarction, heart attack or coronary artery by-pass surgery, or stroke)

^{**} RRs adjusted for age, kcals/day, BMI, smoking, alcohol consumption, physical activity, income, education, insurance coverage, race, gender, and total meat intake per day

Associations between fish⁺ and n-3 LCFA intakes and all-cause mortality among all participants stratified by sex, Southern Community Cohort Study*

Table 4

	Men			Women		
	RR	95% CI	P trend	RR	95% CI	P trend
Total Fish						
Quintile 1	1.00		0.16	1.00		0.15
Quintile 2	0.92	0.82–1.03		1.06	0.95–1.18	
Quintile 3	0.91	0.81–1.01		0.97	0.87–1.09	
Quintile 4	0.94	0.84–1.04		1.00	0.90–1.12	
Quintile 5	0.90	0.81–1.01		0.91	0.80–1.04	
<i>P interaction: 0.42</i>						
Tuna						
Quintile 1	1.00		0.86	1.00		0.97
Quintile 2	0.92	0.82–1.04		1.11	0.99–1.23	
Quintile 3	0.93	0.82–1.06		1.02	0.91–1.14	
Quintile 4	0.92	0.81–1.05		1.04	0.92–1.16	
Quintile 5	0.96	0.85–1.08		1.03	0.92–1.15	
<i>P interaction: 0.24</i>						
Fried Fish						
Quintile 1	1.00		0.03	1.00		0.14
Quintile 2	0.97	0.86–1.10		1.00	0.90–1.12	
Quintile 3	0.94	0.83–1.06		1.02	0.91–1.13	
Quintile 4	0.89	0.79–1.00		0.97	0.87–1.08	
Quintile 5	0.90	0.80–1.01		0.89	0.78–1.01	
<i>P interaction: 0.65</i>						
Baked/Grilled Fish						
Quintile 1	1.00		0.10	1.00		0.09
Quintile 2	0.89	0.77–1.03		0.96	0.87–1.07	
Quintile 3	0.89	0.81–0.97		0.99	0.88–1.11	
Quintile 4	0.92	0.82–1.03		0.99	0.89–1.11	
Quintile 5	0.91	0.82–1.01		0.87	0.77–0.98	

	Men		Women	
	RR	95% CI	RR	95% CI
<i>P</i> interaction: 0.71				
n-3 LCFA *				
Quintile 1	1.00		1.00	
Quintile 2	1.00	0.89–1.12	1.02	0.92–1.13
Quintile 3	0.90	0.80–1.01	0.99	0.89–1.10
Quintile 4	0.92	0.82–1.03	0.96	0.85–1.08
Quintile 5	0.92	0.82–1.04	0.95	0.83–1.08
<i>P</i> interaction: 0.39				

⁺Based on the FFQ item that asked about intake from 1) fried fish - fried fish, shrimp or seafood (including sandwiches), 2) baked/grilled fish - broiled or baked fish, shrimp, or seafood (including sandwiches), and 3) tuna - canned tuna, tuna casserole, or tuna salad (including sandwiches)

^{*}RRs adjusted for age, kcals/day, BMI, smoking, alcohol consumption, physical activity level, income level, education level, presence of chronic disease, insurance coverage, race, and total meat intake per day. The log-likelihood ratio test was used to evaluate the significance of the interaction terms for sex and race with fish or n-3 LCFA intake

Associations between fish⁺ and n-3 LCFA intakes and total mortality among all participants stratified by race, Southern Community Cohort Study*

Table 5

	White			Black		
	RR	95% CI	P trend	RR	95% CI	P trend
Total Fish						
Quintile 1	1.00		0.37	1.00		0.04
Quintile 2	1.01	0.89–1.14		0.97	0.88–1.08	
Quintile 3	1.01	0.88–1.16		0.90	0.82–1.00	
Quintile 4	0.98	0.85–1.12		0.95	0.86–1.05	
Quintile 5	0.92	0.78–1.09		0.90	0.81–0.99	
<i>P interaction: 0.65</i>						
Tuna						
Quintile 1	1.00		0.87	1.00		0.66
Quintile 2	0.93	0.79–1.10		1.07	0.97–1.18	
Quintile 3	0.93	0.79–1.10		1.02	0.92–1.12	
Quintile 4	0.94	0.80–1.11		1.01	0.91–1.11	
Quintile 5	0.96	0.82–1.12		1.01	0.92–1.12	
<i>P interaction: 0.45</i>						
Fried Fish						
Quintile 1	1.00		0.04	1.00		0.14
Quintile 2	0.95	0.84–1.07		1.06	0.95–1.19	
Quintile 3	0.95	0.84–1.07		1.02	0.91–1.14	
Quintile 4	0.93	0.80–1.07		0.98	0.88–1.09	
Quintile 5	0.79	0.65–0.96		0.96	0.87–1.07	
<i>P interaction: 0.73</i>						
Baked/Grilled Fish						
Quintile 1	1.00		0.94	1.00		0.006
Quintile 2	0.99	0.87–1.13		0.89	0.79–1.00	
Quintile 3	0.97	0.84–1.12		0.90	0.83–0.98	
Quintile 4	1.07	0.93–1.23		0.89	0.80–0.98	
Quintile 5	0.92	0.78–1.09		0.88	0.81–0.96	

	White			Black		
	RR	95% CI	P trend	RR	95% CI	P trend
<i>P interaction: 0.18</i>						
n-3 LCFA *						
Quintile 1	1.00			1.00		0.11
Quintile 2	1.05	0.93–1.18	0.34	0.98	0.88–1.09	
Quintile 3	0.99	0.87–1.14		0.90	0.81–1.00	
Quintile 4	0.99	0.85–1.14		0.92	0.83–1.02	
Quintile 5	0.90	0.75–1.08		0.93	0.83–1.03	
<i>P interaction: 0.74</i>						

⁺Based on the FFQ item that asked about intake from 1) fried fish - fried fish, shrimp or seafood (including sandwiches), 2) baked/grilled fish - broiled or baked fish, shrimp, or seafood (including sandwiches), and 3) tuna - canned tuna, tuna casserole, or tuna salad (including sandwiches)

^{*}RRs adjusted for age, kcals/day, gender, BMI, smoking, alcohol consumption, physical activity level, income level, education level, presence of chronic disease, insurance coverage, gender, and total meat intake per day. The log-likelihood ratio test was used to evaluate the significance of the interaction terms for sex and race with fish or n-3 LCFA intake