Published OnlineFirst July 29, 2011; DOI: 10.1158/1940-6207.CAPR-11-0241

Research Article

Cancer Prevention Research

Prospective Investigation of Poultry and Fish Intake in Relation to Cancer Risk

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Abstract

Dietary guidelines advise consumers to limit intake of red meat and choose lean protein sources, such as poultry and fish. Poultry consumption has been steadily increasing in the United States, but the effect on cancer risk remains unclear. In a large U.S. cohort, we prospectively investigated poultry and fish intake and cancer risk across a range of malignancies in men and women. Diet was assessed at baseline (1995–1996) with a food frequency questionnaire in 492,186 participants of the NIH-AARP Diet and Health Study. Over a mean follow-up of 9 years, we identified 74,418 incident cancer cases. In multivariable Cox proportional hazards regression models, we estimated the substitution and addition effects of white meat (poultry and fish) intake in relation to cancer risk. In substitution models with total meat intake held constant, a 10-g (per 1,000 kcal) increase in white meat intake offset by an equal decrease in red meat intake was associated with a statistically significant reduced (3%–20%) risk of cancers of the esophagus, liver, colon, rectum, anus, lung, and pleura. In addition models with red meat intake held constant, poultry intake remained inversely associated with esophageal squamous cell carcinoma, liver cancer, and lung cancer, but we observed mixed findings for fish intake. As the dietary recommendations intend, the inverse association observed between white meat intake and cancer risk may be largely due to the substitution of red meat. Simply increasing fish or poultry intake, without reducing red meat intake, may be less beneficial for cancer prevention. *Cancer Prev Res; 4(11); 1903–11. ©2011 AACR.*

Introduction

Meat is an integral component of the U.S. diet, and national dietary guidelines emphasize lean protein sources, such as poultry and fish (1). For the prevention of cancer, the American Cancer Society specifically advises limiting intake of red and processed meats and choosing fish and poultry instead of beef, pork, or lamb (2). However, over the last 4 decades, total meat consumption in the United States has continued to rise, mainly due to an increase in poultry consumption whereas red meat consumption is beginning to stabilize and fish consumption has remained low (3). Thus, understanding the role of poultry and fish intake in cancer risk within the U.S. population is of mounting importance.

Although red and processed meat intake in relation to cancer risk has received considerable attention in recent years, intake of "white meat" (poultry and fish) has not been as extensively investigated in epidemiologic studies and for many cancer sites there is little or no prospective evidence available (4). The 2007 report from the World Cancer Research Fund and American Institute for Cancer Research concluded that the evidence for poultry intake and cancer risk was "too limited in amount, consistency, and quality to draw any conclusions," whereas the evidence for fish intake was "limited to suggestive" of lower cancer risk and based primarily on studies of colorectal cancer (4). Poultry is generally considered a lean meat alternative to red meat, whereas the potential benefits of fish intake are linked to the anti-inflammatory and anticarcinogenic effects of long-chain *n-3* fatty acids (5). However, some species of seafood, including canned tuna, the most commonly consumed fish in the United States, may contain mercury and other environmental contaminants (6, 7).

We previously reported in the NIH-AARP Diet and Health Study, a diet and cancer cohort of half a million U.S. men and women, that red and processed meat intake was associated with an increased risk of cancers of the colorectum, lung, esophagus, and liver (8), as well as all-cause, cardiovascular disease, and cancer mortality. White meat intake was inversely associated with cancer mortality (9). Given the current dietary recommendations for meat intake and cancer prevention, as well as the rise in poultry consumption within the United States, we evaluated the substitution effect of white meat for red meat, as

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doi: 10.1158/1940-6207.CAPR-11-0241

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well as the addition effect of poultry and fish intake, in relation to cancer risk.

Materials and Methods

The NIH-AARP Diet and Health Study (10) is a large prospective cohort of U.S. men and women, aged 50 to 71 years, across 6 states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and 2 metropolitan areas (Atlanta, GA, and Detroit, MI). In 1995, AARP members were mailed a self-administered questionnaire with queries for demographics, dietary habits, and lifestyle characteristics. Of those who returned the baseline questionnaire (567,169 persons), 566,401 completed the survey satisfactorily and consented to be a part of the study. We further excluded proxy respondents ($n = 15{,}760$) and participants with prevalent cancer (as noted by cancer registry or self-report; $n = 51{,}223$) or end-stage renal disease ($n = 997$) at baseline, a death-only report for any cancer ($n = 1{,}804$), zero person-years of follow-up ($n = 36$), or implausibly high (men: >6,141 kcal; women: >4,791 kcal) or low (men: <415 kcal; women: <318 kcal) total energy intake beyond twice the interquartile range of sex-specific Box–Cox transformed intake (ref. 11; $n = 4{,}395$). Following exclusions, 293,466 men and 198,720 women ($n = 492{,}186$) were included in the present analysis. Analyses of ovarian, endometrial, and postmenopausal breast cancer excluded women who reported an oophorectomy ($n = 43{,}536$), hysterectomy ($n = 81{,}205$), and premenopausal or uncertain menopausal status ($n = 13{,}872$) at baseline, respectively. The conduct of the NIH-AARP Diet and Health Study was reviewed and approved by the Special Studies Institutional Review Board of the U.S. National Cancer Institute, and all participants gave informed consent by virtue of completing and returning the questionnaire. Follow-up for each subject began on the date of return of the baseline questionnaire (1995–1996) and continued until the date of cancer diagnosis, date of censoring due to loss to follow-up, death, or December 31, 2006, whichever came first.

Dietary assessment

Dietary intake was assessed using a 124-item food frequency questionnaire (FFQ) developed and validated by the National Cancer Institute (11). Participants were asked to report their usual dietary intake of foods and beverages over the past year in both frequency of intake and portion size. The 1994–1996 USDA Continuing Survey of Food Intakes by Individuals was used to calculate nutrient intakes (12). Total white meat intake was the sum of all poultry and fish. Total poultry intake included chicken, turkey, ground poultry, as well as the processed poultry components of turkey or chicken cold cuts and low-fat versions of hot dogs and sausage. Poultry queries included line items for breaded/deep-fried chicken, other chicken (baked, broiled, roasted, or stewed), chicken casseroles, sandwiches, and mixtures, as well as general habits of consuming skin and light or dark meat. Total fish intake included all types of finfish and shellfish, as well as canned tuna. Line items for fish differentiated breaded/deep-fried fish or fish sticks, other fish/seafood (not fried), and canned tuna. Total red meat intake included all types of fresh (beef, pork, hamburger, steak, and liver) and processed red meat (bacon, cold cuts, ham, hot dogs, and sausage, excluding low-fat versions made from poultry products).

Cancer ascertainment

During follow-up, cancer cases were ascertained through linkage with the 8 original state cancer registries and an additional 2 states (Arizona, Texas). The cancer registries are certified by the North American Association of Central Cancer Registries as being at least 90% complete within 2 years of cancer incidence. The high quality of the NIH-AARP study case ascertainment methods is described in detail elsewhere (13). Vital status was ascertained through periodic linkage of the cohort to the Social Security Administration (SSA) Death Master File in the United States, follow-up searches of the National Death Index Plus for participants matched to the SSA Death Master File, cancer registry linkage, questionnaire responses, and responses to other mailings. Invasive cancer diagnoses contributed to the incidence of the tumor site of the first diagnosis only during follow-up, excluding subsequent diagnoses at additional cancer sites. Cancer endpoints were defined by anatomic site and histology code using the third edition of the International Classification of Diseases for Oncology (ICD-0-3; ref. 14).

Statistics

All dietary variables were adjusted for total energy intake using the nutrient density method and presented for ease of interpretability as grams per 1,000 kcal of total energy intake per day. Residual energy adjustment (15) produced similar results. For cancer sites with more than 100 cases, the association between poultry and fish intake and cancer risk was evaluated with Cox proportional hazards regression models with time since entry (person-years) as the underlying time metric. We confirmed that the Cox proportional hazards assumption was met through assessment of plots and interaction terms for the exposures with follow-up time. HRs and 95% CIs are reported for 10-g (per 1,000 kcal) increments of poultry and fish intake and for sex-specific quintiles of intake (lowest intake quintile represents the referent category). In categorical models, P values for linear trend were calculated using the median value within quintiles.

We constructed 2 types of models to adjust for intake of red meat and to test alternate hypotheses of white meat intake and cancer risk. In substitution models, total meat intake was held constant, such that an increase in white meat intake is offset by an equal decrease in red meat intake (16). Addition models evaluated the effect of an independent increase in white meat intake with red meat intake held constant (16). Multivariable models also included the

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following covariables: age (modeled as a continuous covariate), education (<8 year or unknown, 8–11 years, high school graduate, some college, college graduate), marital status, family history of cancer (first-degree relative), race (non-Hispanic white, non-Hispanic black, Hispanic/Asian/Pacific Islander/American Indian/Alaskan Native or unknown), body mass index (BMI; <18.5, 18.5 to <25, 25 to <30, 30 to <35, and $\geq$35 kg/m^2), smoking status (never, quit $\geq$10 years ago, quit 5–9 years ago, quit 1–4 years ago, quit <1 year ago or currently smoking and smoked $\leq$20 cigarettes per day, quit <1 year ago or currently smoking and smoked >20 cigarettes per day), frequency of vigorous physical activity (never/rarely, 1–3 times per month, 1–2 times per week, 3–4 times per week, $\geq$5 times per week), menopausal hormone therapy (MHT; never, former, current use) in women, total energy intake (continuous), alcohol intake (none, 0 to <5, 5 to <15, 15 to <30, $\geq$30 g per day), fruit intake, and vegetable intake [MyPyramid Equivalents Database (MPED; ref. 17) servings per 1,000 kcal; modeled in quintiles]. Analyses for fish or poultry intake were mutually adjusted for the other type of white meat. We further evaluated potential confounding due to intake of fat, fiber, and calcium, as well as family history of specific cancers (first-degree relative with colon, prostate, or breast cancer), and personal history of diabetes or hypertension; and parity, age at menarche, and oral contraceptive use for female cancers. However, results did not meaningfully differ from those presented. Given that canned tuna was queried separately in the questionnaire, is commonly consumed in the United States, and may be a key source of both long-chain *n-3* fatty acids and mercury compared with other general types of fish queried (6, 7), we evaluated associations with its intake separately. We also investigated associations differentiating processed poultry components and poultry or fish that was breaded/deep-fried; and conducted a lag analysis excluding the first 2 years of follow-up. We assessed whether any of the associations varied by sex and smoking status with statistical tests for interaction evaluating the significance of cross-product terms in multivariable-adjusted models. All statistical tests were 2-sided and considered statistically significant at $P < 0.05$. All statistical analyses were conducted using SAS 9.2 (SAS Institute, Inc.).

Results

During a mean follow-up of 9.1 years, we identified 51,419 cancer cases in men and 22,999 cancer cases in women. The 10th and 90th percentiles of dietary intakes of total poultry, total fish, and canned tuna (per 1,000 kcal per day), respectively, were as follows: 4.2 to 43.8 g, 2.1 to 22.9 g, and 0 to 6.9 g in men and 4.8 to 51.6 g, 2.0 to 23.5 g, and 0.2 to 8.6 g in women. Poultry intake was only modestly correlated ($r = 0.17$) with fish intake. Less than 3% of total poultry intake was processed and approximately one-third of the total fish intake came from canned tuna (data presented in the text only). As presented in Table 1, participants in the highest quintile of total white meat (poultry and fish) intake were more likely to be college graduates and less likely to be current smokers and physically inactive than those in the lowest quintile. Red meat intake was similar across quintiles of white meat intake, whereas participants in the highest quintile of white meat intake consumed more vegetables and less alcohol than those in lowest quintile. Trends in characteristics of participants were similar across quintiles of poultry and fish intake, as well as by sex (data not shown).

Substitution of white meat for red meat

Figure 1 represents the risk associated with a 10-g increase in white meat intake offset by a 10-g decrease in red meat intake (total meat intake held constant). We observed 10% or greater reductions in risk for esophageal squamous cell carcinomas and cancers of the pleura, liver, and anus; and 3% to 7% reductions in risk for esophageal adenocarcinomas and cancers of the colon, rectum, and lung. Conversely, we observed an elevated risk (3%–8%) of melanoma and thyroid cancer. Intake of either poultry or fish, in substitution models for red meat, was similarly associated with lower risk of cancers of the esophagus, colon, rectum, liver, and lung, whereas only fish intake was associated with higher risk of melanoma (data not shown).

Addition of white meat

The results of the additive analysis represent the risk associated with an independent increase in white meat intake, while holding red meat intake constant. Total white meat intake was inversely associated with cancers of the esophagus, liver, and lung, but positively associated with melanoma (data not shown). A 10-g increase in poultry intake (Fig. 2) was associated with lower risk of liver cancer and esophageal squamous cell carcinoma, as well as laryngeal cancer in women only ($P_{\text{interaction sex}} = 0.01$). In men, poultry intake was positively associated with thyroid ($P_{\text{interaction sex}} = 0.03$) and male breast cancer. Those in the highest quintile of poultry intake had a lower risk of lung, bladder, and rectal cancer than those in the lowest quintile (Table 2). Among never smokers, the inverse association between poultry intake and lung cancer risk remained consistent [HR and 95% CI for fifth vs. first quintile: 0.78 (0.58–1.03); $P_{\text{trend}} = 0.04$, and 10-g/1,000 kcal: 0.95 (0.91–0.99); $P_{\text{trend}} = 0.03$; data in text only].

Total fish intake was associated with higher risk of melanoma (Table 2); this seemed to be driven by intake of canned tuna [HR and 95% for fifth vs. first quintile: 1.30 (1.16–1.46); $P_{\text{trend}} < 0.0001$; data in text only]. Similarly, we observed a suggestive increased risk for canned tuna intake and bladder cancer [1.13 (0.99–1.28); $P_{\text{trend}} = 0.04$], as well as ovarian cancer [1.28 (1.02–1.61); $P_{\text{trend}} = 0.05$]. Conversely, intake of canned tuna was associated with lower risk of liver cancer [0.74 (0.55–0.96); $P_{\text{trend}} = 0.05$; data in text only].

Various subanalyses including a lag analysis excluding the first 2 years of follow-up and stratified analyses by smoking status produced comparable results. We also did

Table 1. Means and proportions for selected baseline characteristics of the NIH-AARP Diet and Health Study cohort (N = 492,186) by quintiles of total white meat intake

	Total white meat				
Characteristic	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**
White meat, mean, g/1,000 kcal	8.9	18.5	27.6	40.0	72.6
Poultry, mean, g/1,000 kcal	5.3	11.5	17.7	26.6	51.2
Fish, mean, g/1,000 kcal	3.6	7.0	9.9	13.4	21.4
Canned tuna, mean, g/1,000 kcal	1.2	2.2	3.0	3.9	5.9
Red meat, mean, g/1,000 kcal	31.8	35.8	36.8	36.3	32.1
Age, mean, y	63	62	62	62	62
White, non-Hispanic, %	91	92	92	91	90
College and postcollege, %	31	35	39	42	45
Currently married, %	65	69	70	70	69
Positive family history of cancer, %	48	49	49	49	49
Never smoker, %	33	34	36	37	36
Current smoker or quit <1 y ago, %	19	16	14	12	10
Alcohol intake, mean, g/d	18.4	13.0	11.6	10.2	8.4
BMI, mean, kg/m^2	26.7	27.1	27.2	27.2	27.4
Obese, BMI ≥30, %	19	21	22	22	23
Physical activity (vigorous ≥ 20 min), %					
Never	24	20	18	17	16
≥5 times/wk	19	18	19	19	21
Current MHT use, % of women	41	44	44	46	45
Dietary intakes per day, mean					
Fruit, MPED servings/1,000 kcal	1.7	1.7	1.7	1.7	1.7
Vegetables, MPED servings/1,000 kcal	2.0	2.1	2.2	2.3	2.5
Total energy intake, kcal	1,941	1,844	1,826	1,810	1,757

NOTE: N = 293,466 men; 198,720 women.
Abbreviation: Q, quintile.

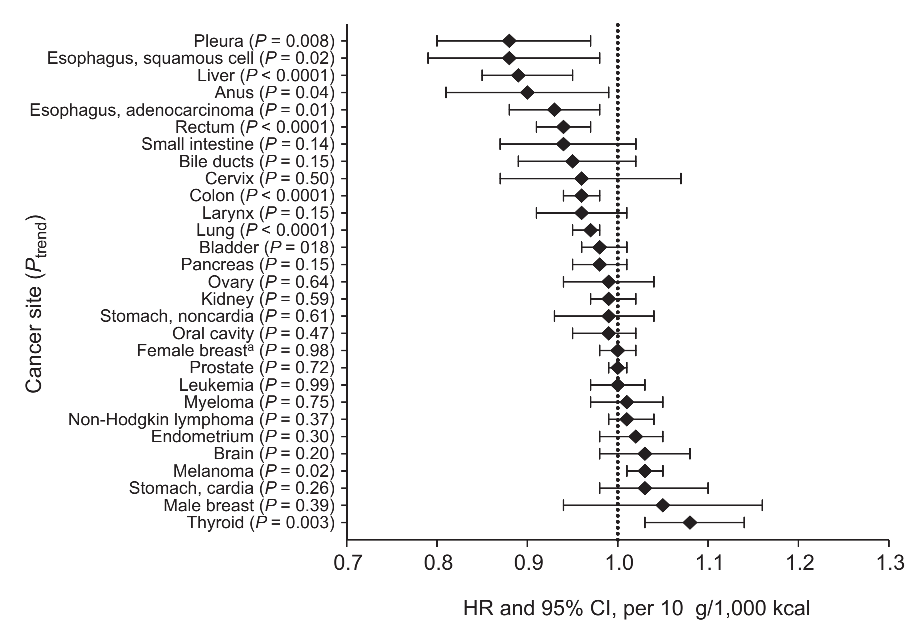

Figure 1. Multivariable HRs and 95% CIs for substitution effect of a 10-g increase in total white meat intake and cancer risk [substitution (for red meat) model: adjusted for total meat intake (10-g/1,000 kcal) and previous covariables], NIH-AARP Diet and Health Study (N = 492,186).
[a], postmenopausal cases only.

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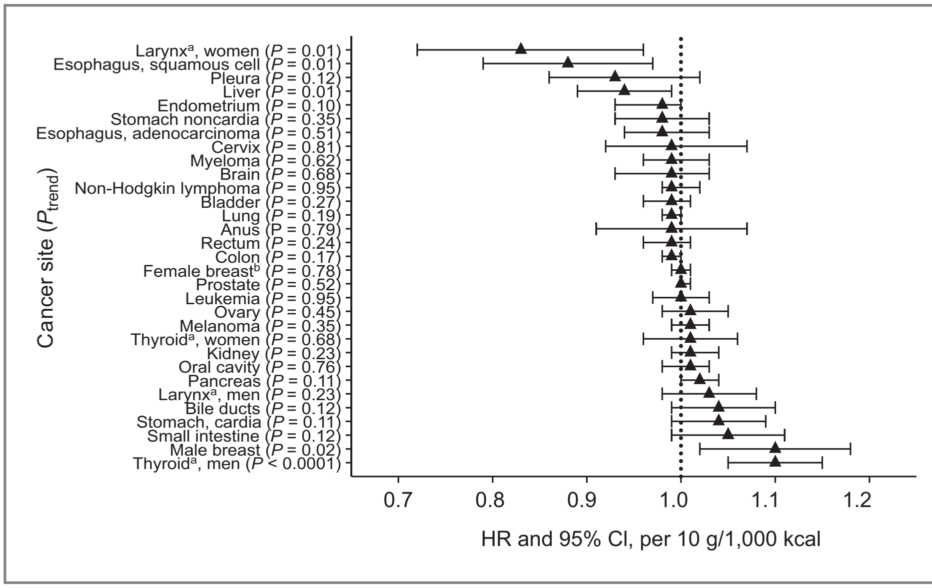

Figure 2. Multivariable HRs and 95% CIs for addition effect of a 10-g increase in poultry intake and cancer risk [addition model: adjusted for red meat intake (10-g/1,000 kcal), fish intake (10-g/1,000 kcal), and previous covariables], NIH-AARP Diet and Health Study ($N = 492{,}186$). [a], significant interaction with sex; [b], postmenopausal cases only.

not observe any striking differences in risk across cancer sites for intake of processed poultry, poultry consumed with or without skin, or fish intake excluding deep-fried fish compared with the overall results presented.

Discussion

In this large U.S. cohort, poultry and fish intake was associated with lower risk of digestive and respiratory cancers. In analyses holding total meat intake constant, such that higher intake of poultry and fish coincides with lower intake of red meat, we observed inverse associations for cancers of the esophagus, liver, colon, rectum, anus, lung, and pleura. With red meat intake held constant, poultry intake remained inversely associated with esophageal squamous cell carcinoma, liver, and lung cancer whereas associations with fish intake were mixed. Although we cannot completely rule out the possibility of residual confounding by smoking status or other factors, similar associations were observed among never smokers. Our findings for poultry and fish intake and cancer risk seemingly reflect the importance of red meat substitution but are also suggestive of an effect independent of red meat intake.

The inverse associations we observed for poultry and fish intake with lower gastrointestinal cancers seemed largely driven by the red meat substitution effect. Consistent with our findings, the ratio of (higher) red meat to (lower) poultry and fish intake has been previously associated with an increased risk of colorectal cancer (18, 19) whereas null findings in the additive analysis are consistent with summary data from a range of prospective cohorts (20). A number of studies provide possible mechanisms for these results. Poultry and fish, relative to red meat, are lower in saturated fat and heme iron, potential inducers of oxidative stress and DNA damage (21). Consumption of white meat is also likely to result in significantly lower exposure to carcinogenic *N*-nitroso compounds (NOC; ref. 22), which form more readily with red and processed meat intake due to the higher concentration of heme iron (23). Human feeding studies have shown that throughout the gastrointestinal tract intake of white meat versus red meat results in lower levels of DNA strand breaks, ileal and fecal apparent total NOCs, and DNA adducts (24–26).

Significant findings for poultry intake and lower risk of esophageal squamous cell carcinoma, liver cancer, and lung cancer in both the substitution and addition analyses suggest that other components of a high white meat diet, independent of red meat, may also be important. These findings are consistent with previous reports for total white meat intake in this cohort (27, 28). However, poultry intake was positively associated with esophageal cancer (29) and not related to lung cancer risk (30) in the European Prospective Investigation into Cancer and Nutrition (EPIC). Residual confounding by smoking status does not seem to have greatly influenced our findings, as poultry intake remained consistently associated with lower risk of lung cancer in analyses restricted to never smokers. Lower levels of prooxidant and mutagenic activity related to intake of white versus red meat may be relevant for lung and other smoking-related cancers (31, 32), but there is little mechanistic research in this area. Poultry intake was also inversely associated with laryngeal cancer in women but positively associated with thyroid and male breast cancer in men in this cohort. However, scant evidence from retrospective studies provides little support for these findings (33–35) and we cannot rule out the possibility of residual confounding by hereditary and other environmental factors.

The mechanism whereby poultry intake alone may modulate cancer risk remains unclear. We examined and adjusted for a multitude of key confounders; however, as

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Table 2. Multivariable HRs[a] and 95% CIs for the additive effect of an increase in poultry or fish intake and cancer risk, NIH-AARP Diet and Health Study ($N = 492{,}186$)

Cancer site	Dietary intake	Q1 Ref	Q2 HR	95% CI	Q3 HR	95% CI	Q4 HR	95% CI	Q5 HR	95% CI	P_{trend}
Oral cavity											
$n = 1{,}305$	Poultry	1.00	1.07	0.90–1.26	0.97	0.81–1.16	1.11	0.93–1.32	1.05	0.87–1.26	0.62
	Fish	1.00	1.03	0.87–1.22	1.00	0.84–1.18	0.97	0.81–1.16	0.90	0.75–1.09	0.17
Larynx											
$n = 472$ (M)	Poultry[b]	1.00	0.89	0.68–1.17	1.00	0.76–1.32	0.96	0.72–1.29	1.04	0.77–1.41	0.61
$n = 95$ (F)	Poultry[b]	1.00	1.04	0.61–1.77	0.72	0.39–1.34	0.79	0.42–1.50	0.27	0.10–0.71	0.004
	Fish	1.00	1.01	0.78–1.29	0.88	0.68–1.15	1.00	0.77–1.31	1.03	0.79–1.36	0.68
Esophagus, squamous cell											
$n = 185$	Poultry	1.00	0.97	0.66–1.42	0.67	0.43–1.05	0.44	0.26–0.76	0.69	0.42–1.13	0.04
	Fish	1.00	0.95	0.62–1.47	0.99	0.63–1.55	0.93	0.58–1.48	0.98	0.61–1.59	0.84
Esophagus, adenocarcinoma											
$n = 553$	Poultry	1.00	0.92	0.71–1.19	0.85	0.65–1.11	1.03	0.79–1.35	0.95	0.72–1.26	0.92
	Fish	1.00	0.94	0.73–1.21	0.88	0.68–1.14	0.83	0.63–1.09	0.78	0.59–1.03	0.06
Stomach, cardia											
$n = 418$	Poultry	1.00	0.77	0.56–1.04	0.90	0.66–1.22	0.99	0.73–1.34	1.00	0.73–1.36	0.37
	Fish	1.00	1.03	0.76–1.39	0.96	0.70–1.31	1.05	0.77–1.43	0.98	0.71–1.35	0.85
Stomach, noncardia											
$n = 510$	Poultry	1.00	1.20	0.79–1.33	0.92	0.70–1.21	0.91	0.69–1.21	0.80	0.59–1.07	0.10
	Fish	1.00	1.08	0.82–1.41	0.81	0.60–1.09	1.22	0.93–1.61	1.11	0.84–1.48	0.27
Small intestine											
$n = 379$	Poultry	1.00	0.98	0.63–1.53	1.21	0.78–1.87	1.44	0.94–2.21	1.41	0.91–2.17	0.07
	Fish	1.00	1.00	0.66–1.50	1.28	0.86–1.88	0.70	0.44–1.10	0.84	0.54–1.30	0.99
Colon											
$n = 5{,}095$	Poultry	1.00	1.04	0.96–1.13	0.96	0.88–1.05	1.03	0.95–1.13	0.97	0.89–1.07	0.43
	Fish	1.00	0.98	0.90–1.07	0.98	0.90–1.07	0.96	0.88–1.05	0.95	0.87–1.04	0.30
Rectum											
$n = 1{,}884$	Poultry	1.00	0.87	0.76–1.00	0.99	0.86–1.14	0.95	0.82–1.10	0.84	0.72–0.98	0.08
	Fish	1.00	0.95	0.82–1.09	0.81	0.70–0.94	0.87	0.75–1.01	0.96	0.83–1.11	0.88
Anus											
$n = 164$	Poultry	1.00	1.01	0.63–1.62	1.01	0.63–1.64	0.85	0.51–1.42	0.92	0.55–1.54	0.58
	Fish	1.00	1.26	0.80–2.01	1.07	0.66–1.74	0.86	0.51–1.44	0.71	0.41–1.23	0.06
Liver											
$n = 582$	Poultry	1.00	0.95	0.75–1.21	0.79	0.61–1.01	0.75	0.57–0.98	0.75	0.57–0.99	0.03
	Fish	1.00	1.00	0.78–1.28	1.01	0.79–1.30	0.95	0.73–1.24	0.86	0.65–1.13	0.16
Bile ducts											
$n = 307$	Poultry	1.00	1.10	0.76–1.59	1.14	0.78–1.65	1.06	0.72–1.55	1.27	0.87–1.85	0.25
	Fish	1.00	0.72	0.49–1.06	0.87	0.60–1.25	1.08	0.76–1.53	1.01	0.71–1.45	0.30
Pancreas											
$n = 1{,}727$	Poultry	1.00	1.03	0.89–1.20	1.02	0.87–1.19	1.11	0.95–1.30	1.10	0.94–1.29	0.22
	Fish	1.00	1.07	0.92–1.25	1.00	0.86–1.17	1.08	0.93–1.27	1.12	0.96–1.31	0.15
Lung											
$n = 9{,}751$	Poultry	1.00	0.94	0.89–1.00	0.94	0.89–1.00	0.90	0.84–0.96	0.91	0.85–0.97	0.01
	Fish	1.00	1.03	0.97–1.10	1.08	1.01–1.15	1.04	0.98–1.11	1.01	0.94–1.08	0.65
Pleura											
$n = 218$	Poultry	1.00	0.94	0.63–1.41	1.16	0.78–1.72	0.71	0.45–1.14	0.93	0.60–1.46	0.52
	Fish	1.00	1.76	1.18–2.63	1.09	0.69–1.71	1.08	0.68–1.71	1.04	0.64–1.67	0.27
Bladder											
$n = 2{,}296$	Poultry	1.00	0.86	0.76–0.98	0.89	0.78–1.01	0.92	0.81–1.05	0.83	0.73–0.96	0.07
	Fish	1.00	1.03	0.90–1.18	1.08	0.95–1.23	1.15	1.00–1.31	1.13	0.99–1.29	0.06
Kidney											
$n = 2{,}065$	Poultry	1.00	0.94	0.82–1.08	0.94	0.82–1.08	0.94	0.82–1.09	1.00	0.87–1.16	0.51

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Published OnlineFirst July 29, 2011; DOI: 10.1158/1940-6207.CAPR-11-0241

Table 2. Multivariable HRs[a] and 95 CIs for the additive effect of an increase in poultry or fish intake and cancer risk, NIH-AARP Diet and Health Study (N = 492,186) (Cont'd)

Cancer site	Dietary intake	Q1 Ref	Q2 HR	95% CI	Q3 HR	95% CI	Q4 HR	95% CI	Q5 HR	95% CI	P_{trend}
	Fish	1.00	1.01	0.88–1.16	1.07	0.93–1.24	1.12	0.97–1.29	1.10	0.93–1.28	0.15
Thyroid											
n = 250 (M)	Poultry[b]	1.00	1.23	10.79–1.93	1.23	0.78–1.93	1.46	0.94–2.26	1.74	1.14–2.67	0.005
n = 333 (F)	Poultry[b]	1.00	0.73	0.52–1.03	0.68	0.48–0.96	0.69	0.49–0.98	0.82	0.58–1.14	0.66
	Fish	1.00	1.15	0.88–1.51	1.14	0.87–1.50	1.25	0.95–1.64	1.18	0.90–1.55	0.38
Non-Hodgkin lymphoma											
n = 2,905	Poultry	1.00	1.04	0.92–1.16	1.06	0.94–1.19	0.97	0.86–1.10	0.99	0.87–1.12	0.51
	Fish	1.00	0.98	0.87–1.11	1.08	0.96–1.22	1.07	0.95–1.20	1.09	0.97–1.23	0.09
Leukemia											
n = 1,625	Poultry	1.00	0.97	0.83–1.13	0.97	0.82–1.13	1.01	0.86–1.18	1.06	0.90–1.25	0.31
	Fish	1.00	1.00	0.85–1.17	1.09	0.93–1.27	0.95	0.81–1.12	1.00	0.85–1.18	0.74
Melanoma											
n = 2,960	Poultry	1.00	1.09	0.96–1.23	1.20	1.06–1.35	1.16	1.02–1.31	1.03	0.91–1.17	0.86
	Fish	1.00	1.10	0.97–1.24	1.12	0.99–1.26	1.17	1.04–1.32	1.19	1.05–1.34	0.01
Brain											
n = 749	Poultry	1.00	1.23	0.97–1.55	1.20	0.94–1.52	1.04	0.81–1.34	1.10	0.86–1.41	0.95
	Fish	1.00	1.14	0.91–1.45	1.04	0.82–1.33	1.22	0.97–1.55	1.05	0.83–1.35	0.77
Myeloma											
n = 893	Poultry	1.00	1.09	0.88–1.33	0.98	0.79–1.21	0.92	0.73–1.14	0.93	0.74–1.15	0.19
	Fish	1.00	0.94	0.76–1.16	0.94	0.76–1.16	1.01	0.82–1.25	1.03	0.84–1.28	0.47
Male breast											
n = 129	Poultry	1.00	1.08	0.60–1.97	1.41	0.79–2.52	1.46	0.81–2.63	1.69	0.95–3.02	0.06
	Fish	1.00	1.14	0.67–1.94	0.74	0.41–1.35	0.97	0.56–1.70	0.89	0.51–1.58	0.66
Prostate											
n = 23,453	Poultry	1.00	1.06	1.02–1.10	1.04	1.00–1.09	1.04	0.99–1.08	1.05	1.00–1.09	0.23
	Fish	1.00	1.03	0.99–1.07	1.04	1.00–1.09	1.05	1.00–1.09	1.02	0.98–1.06	0.67
Female breast, postmenopausal											
n = 7,181	Poultry	1.00	0.97	0.90–1.04	0.98	0.91–1.06	0.99	0.92–1.07	0.98	0.90–1.06	0.92
	Fish	1.00	1.05	0.98–1.14	1.05	0.98–1.14	1.07	0.99–1.15	1.05	0.97–1.14	0.40
Endometrium											
n = 1,593	Poultry	1.00	1.05	0.89–1.24	1.09	0.93–1.28	1.02	0.87–1.21	0.93	0.78–1.10	0.15
	Fish	1.00	1.04	0.88–1.22	0.97	0.83–1.15	1.15	0.98–1.35	1.12	0.95–1.32	0.06
Ovary											
n = 758	Poultry	1.00	1.10	0.87–1.39	1.17	0.93–1.48	1.07	0.84–1.36	1.10	0.87–1.36	0.75
	Fish	1.00	1.00	0.80–1.26	0.86	0.68–1.09	1.04	0.83–1.31	1.04	0.83–1.32	0.41
Cervix											
n = 147	Poultry	1.00	0.81	0.47–1.40	1.33	0.81–2.19	0.97	0.56–1.67	1.10	0.65–1.88	0.66
	Fish	1.00	0.91	0.55–1.53	0.88	0.53–1.49	0.91	0.54–1.54	0.90	0.54–1.52	0.82

NOTE: N = 293,466 men; 198,720 women.

Abbreviations: M, male; F, female.

[a]Addition model: adjusted for red meat intake, age, sex, education, marital status, family history of cancer, race, BMI, smoking status, frequency of vigorous physical activity, MHT in women, and intake of alcohol, fruit, vegetables, and total energy; mutually adjusted for intake of fish or poultry.

[b]Statistically significant interaction with sex.

high intake of poultry and fish often clusters with a healthier overall eating pattern and lifestyle (36), the possibility of residual confounding by other factors remains. With intake of red meat, fish, fruit, vegetables, alcohol, and total energy held constant in multivariate additive models, it is plausible that an increase in poultry intake may represent displacement of other foods within the diet, such as refined grains and desserts. Varied risks by sex for some cancers

Published OnlineFirst July 29, 2011; DOI: 10.1158/1940-6207.CAPR-11-0241

may be related, at least in part, to overall differences in reporting, diet, and lifestyle habits (36, 37) and/or preferences related to the way the meat is prepared and consumed (38–40).

Consistent with many prospective cohort studies (4, 20, 41, 42), we found little evidence of a protective role for total fish intake and cancer risk, perhaps surprising as experimental evidence suggests that the anti-inflammatory, long-chain *n-3* fatty acids in concentrated doses of fish oil inhibit cancer development and progression (5). However the participants in our study and U.S. consumers, in general, eat very little fish (3). In addition, some species of fish may be a source of potential carcinogens, such as polychlorinated biphenyls, dioxins, and mercury (6, 7). Queries for fish intake on the standardized dietary questionnaire included little detail, and with the exception of canned tuna, did not allow us to differentiate fish types. Canned tuna intake was inversely associated with liver cancer but positively associated with ovarian cancer and melanoma in this cohort. There is little prospective evidence to support a role of fish intake in ovarian cancer (43–45); however, one other study observed a positive association between intake of cod liver oil and melanoma risk (46). Without adjustment for all the pertinent risk factors, particularly sun exposure for melanoma risk, confounding may explain the associations we observed.

The NIH-AARP cohort presented a sufficiently large sample to investigate the role of poultry and fish intake and cancer risk across a range of high- and low-incidence malignancies in U.S. men and women. With more than 70,000 cancer cases, it is unlikely that any substantial effects of white meat intake on cancer risk may have been missed. The prospective design avoids potential biases due to recall and selection that may have affected the results of previous case–control studies. However, diet and lifestyle information ascertained in the baseline questionnaire among older adults may not be entirely reflective of lifelong cumulative exposures or the most pertinent time period for cancer etiology. Given the large number of comparisons, it is possible that some of the more modestly significant results may be attributable to chance and results for cancers, particularly those with a small numbers of cases, should be interpreted with caution.

In the largest U.S. prospective investigation of white meat and cancer risk to date, intake of poultry and fish, mainly as a substitute for red meat, was associated with lower risk of cancers of the esophagus, liver, colon, rectum, anus, pleura, and lung. Independent of red meat intake, we also observed inverse associations between poultry intake and risk of esophageal squamous cell carcinoma and liver and lung cancer. Consistent with several other cohorts, we found little convincing evidence for total fish intake and cancer risk. Our findings generally support the American Cancer Society's dietary guidelines, which recommend limiting intake of red and processed meats and choosing poultry and fish as lean alternatives (2). In light of the growing popularity of poultry in the United States and the paucity of prospective evidence, additional detailed investigations are needed to clarify the role of white meat intake in the etiology of cancer.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Acknowledgments

Cancer incidence data from the Atlanta metropolitan area were collected by the Georgia Center for Cancer Statistics, Department of Epidemiology, Rollins School of Public Health, Emory University. Cancer incidence data from California were collected by the California Department of Health Services, Cancer Surveillance Section. Cancer incidence data from the Detroit metropolitan area were collected by the Michigan Cancer Surveillance Program, Community Health Administration, State of Michigan. The Florida cancer incidence data used in this report were collected by the Florida Cancer Data System (FCDC) under contract with the Florida Department of Health (FDOH). The views expressed herein are solely those of the authors and do not necessarily reflect those of the FCDC or FDOH. Cancer incidence data from Louisiana were collected by the Louisiana Tumor Registry, Louisiana State University Medical Center in New Orleans. Cancer incidence data from New Jersey were collected by the New Jersey State Cancer Registry, Cancer Epidemiology Services, New Jersey State Department of Health and Senior Services. Cancer incidence data from North Carolina were collected by the North Carolina Central Cancer Registry. Cancer incidence data from Pennsylvania were supplied by the Division of Health Statistics and Research, Pennsylvania Department of Health, Harrisburg, PA. The Pennsylvania Department of Health specifically disclaims responsibility for any analyses, interpretations or conclusions. Cancer incidence data from Arizona were collected by the Arizona Cancer Registry, Division of Public Health Services, Arizona Department of Health Services. Cancer incidence data from Texas were collected by the Texas Cancer Registry, Cancer Epidemiology and Surveillance Branch, Texas Department of State Health Services.

We thank the participants of the NIH-AARP Diet and Health Study for their outstanding cooperation. We also thank Sigurd Hermansen and Kerry Grace Morrissey from Westat for study outcomes ascertainment and management and Leslie Carroll at Information Management Services for data support and analysis. We acknowledge the loss and memory of Dr. Arthur Schatzkin, our leader, colleague, mentor, and friend.

Grant Support

This study was funded by the Intramural Research Program of the National Cancer Institute, NIH.

Received May 12, 2011; revised July 7, 2011; accepted July 21, 2011; published OnlineFirst July 29, 2011.

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Published OnlineFirst July 29, 2011; DOI: 10.1158/1940-6207.CAPR-11-0241

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Cancer Prev Res 2011;4:1903-1911. Published OnlineFirst July 29, 2011.