Polychlorinated biphenyls and omega-3 fatty acid exposure from fish consumption, and thyroid cancer among New York anglers

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ABSTRACT

Fish from the Great Lakes contain polychlorinated biphenyls (PCBs) which have been shown to disrupt endocrine function and mimic thyroid hormones, but they also contain beneficial omega-3 fatty acids that may offer protection against endocrine cancers. The purpose of this study was to examine the effects of Lake Ontario fish consumption and the estimated consumption of PCBs and omega-3 fatty acids on the risk of thyroid cancer in a group of sport fishermen. Anglers from the New York State Angler Cohort Study were followed for cancer incidence from 1991–2008. Twenty-seven cases of incident thyroid cancer and 108 controls were included in the analyses. Total estimated fish consumption, estimated omega-3 fatty acid consumption, and estimated PCB consumption from Lake Ontario fish were examined for an association with the incidence of thyroid cancer, while matching on sex, and controlling for age and smoking status. Results from logistic regression indicate no significant associations between fish consumption, short-term estimated omega-3 fatty acids, or estimated PCB consumption from Lake Ontario fish and the development of thyroid cancer, but it was suggested that long-term omega-3 fatty acid from Great Lakes fish may be protective of the development of thyroid cancer. In conclusion, fish consumption, with the possible concomitant PCBs, from the Great Lakes does not appear to increase the risk of thyroid cancer in New York anglers. Further research is needed in order to separate the individual health effects of PCBs from omega-3 fatty acids contained within the fish.

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Introduction

Polychlorinated biphenyls (PCBs) are a group of 209 synthetically produced compounds that have been shown to disrupt endocrine function and mimic thyroid hormones (Cunningham, 2012). PCBs are persistent, lipophilic, and are metabolized very slowly, resulting in a bioaccumulation in the fat stores of fish and other animals, including humans that consume contaminated fish (Cunningham, 2012).
PCBs are known endocrine disruptors, and have potential consequences on thyroid function, although studies examining the association between thyroid dysfunction and PCB exposure have produced inconsistent results (Bloom et al., 2009; Dallaire et al., 2009; Turyk et al., 2008). Even with evidence that higher concentrations of thyroid stimulating hormone (TSH), a resulting condition of thyroid dysfunction, are associated with a greater risk and more advanced stages of thyroid cancer (Boelaert et al., 2006; Haymart et al., 2008), there is a paucity of research examining the association between thyroid cancer and PCBs. One study reported a higher standardized incidence ratio for thyroid cancer among women living in an area that had previously had extensive contamination from a PCB production site (Pavuk et al., 2004), although the association was not found in men, which illustrates the complex relationship between environmental PCBs and endocrine diseases, such as thyroid cancer. Thyroid cancer is of notable concern because both the incidence and mortality of thyroid cancer in the United States have been increasing in recent years (2001–2010; Howlader et al., 2012). With its increasing incidence, understanding the risk factors for thyroid cancer is important for the prevention and treatment of this disease, and PCB exposure may be one potential preventable predictor of thyroid cancer that warrants further investigation.

Because PCBs were banned in the United States in 1979 (US EPA, United States Environmental Protection Agency, 2013), exposure since that time has come primarily from residual PCB concentrations in the environment. The consumption of fish living in polluted waters has been a notable concern, especially in regard to the development of cancer (Johnson et al., 1999). However, the association between fish consumption and cancer is complex. One study found that the incidence of breast cancer was higher for each additional 25 g of fish consumed per day (Stripp et al., 2003); while another study found that the risk of breast cancer was lowest among individuals in the highest quartile of total fish/shellfish consumption, compared to the lowest quartile of total fish/shellfish consumption (80 vs. 25 g fish per day; Gago-Dominguez et al., 2003). Similarly, another study found that the risk of colorectal cancer was lower among those in the highest quartile of fish consumption than those in the lowest quartile (Kato et al., 1997). Other studies have found no associations, positive or negative, between fish consumption and cancer incidence (Holmes et al., 2003; McElroy et al., 2003; Tomasallo et al., 2010; Willett et al., 1990). Several of these studies looked specifically at the association between Great Lake fish consumption and cancer (McElroy et al., 2003; Tomasallo et al., 2010), while most considered fish from all sources, including store-bought. Benefits of fish consumption may be due, in part, to their content of omega-3 fatty acids, which have been observed to be protective of certain types of cancers, including breast, colon, and esophageal (Tavani et al., 2003). Conversely, fish from the Great Lakes may have higher concentrations of PCBs, which are known endocrine disruptors (Cunningham, 2012), and may have an adverse effect on thyroid cancer incidence. To our knowledge, no published studies have examined the effects of fish consumption on the risk of thyroid cancer in humans. The need for research into these associations may be greater in populations with high Great Lake fish consumption patterns. Specifically, New York residents were between three and eight times more likely to consume fish more than twice a week than other states in the Great Lakes region (Imm et al., 2005). Therefore, the purpose of this study was to examine the effects of Great Lakes fish consumption, and the estimated PCB consumption or omega-3 fatty acids from these fish, on thyroid cancer incidence among sport fishermen of the New York State Angler Cohort Study.

### 1. Methods

#### 1.1. Study population

Participants were recruited from the New York State Angler Cohort Study, which is a longitudinal cohort study that was designed to examine the potential health risks in sport fishermen (anglers) and their spouses. For these analyses, a case–control design was employed. A more detailed description of the original methods and study design can be found elsewhere (Vena et al., 1996). A roster of fishing license holders residing in the 16 New York counties bordering Lakes Ontario and Erie provided names of 30,000 subjects for the sampling frame. In 1991, a baseline questionnaire queried demographics, health status, and fish consumption, along with informed consent, was completed by 18,076 anglers and their spouses.

Cases of first primary incident thyroid cancer, diagnosed and histologically confirmed between June 1, 1991 through December 31, 2008, were identified through a linkage with the New York State Cancer Registry — which requires the reporting of cancer cases from hospitals and physicians — matching on social security number, date of birth, first name, last name, soundex of first and last names, address, sex, and race. The New York State Cancer Registry has received a gold certification, which means that case ascertainment is at least 95% complete (New York State Cancer Registry, 2014). A proprietary web-based public records search tool was used to determine whether participants had moved out of the state of New York and the year they moved. Loss to follow-up was 9.8% (n = 1672), and average length of follow-up was 16.4 ± 3.1 years. Twenty-seven cases of incident thyroid cancer were identified through the search. Additionally, there was active follow-up with mailed questionnaires to identify non-reportable endpoints. In addition, vital status was ascertained by linkage with the Social Security Administration (n = 422). SAS statistical software (SAS version 9.3; SAS Institute, Carey, NC, USA) randomly selected controls from the cohort of sport anglers and spouses. There were four controls randomly selected and frequency matched on sex for every case, resulting in a total of 108 controls.

#### 1.2. Fish consumption

Fish consumption was measured using the food frequency method. A mailed questionnaire during the fall of 1991 asked both detailed and general questions regarding fish consumption. Detailed questions asked about types and patterns of Great Lakes fish consumption during the years 1990–1991; general questions asked about Great Lakes fish consumption during the years 1955–1991. The specific species asked about in the baseline survey included catfish, lake trout, Chinook...
salmon, Coho salmon, rainbow trout, brown trout, carp, white perch, and yellow perch (1990–1991). Questions asked about the usual frequency of consumption of these species over a month (1990–1991). In addition to the frequency of eating certain species, questions asked about the general size of the fish for several of these species (Coho salmon, Rainbow trout, and Brown trout). These analyses focused on the consumption of fish in Lake Ontario, since it is the most contaminated of the Great Lakes (US EPA, Environmental Protection Agency, 2012).

Usual frequency of fish eaten during the year 1990–1991 was categorized as “none”, “≤1 per month”, “2–3 per month”, “4 per month”, “5–9 per month”, and “≥9 times per month”. Because of the low fish consumption frequency, the categories were collapsed ("none", “≤1 per month”, “2–4 per month”, “>4 times per month”). The frequency of fish consumption was also evaluated as the total frequency of eating larger-sized fish (>21” for Coho salmon, >25” for rainbow trout, >20” for brown trout). A variable for fish consumption prior to 1980 was also created by summing the reported years that Lake Ontario fish was consumed from 1955 to 1980.

1.3. PCBS

An index was created, from reported fish consumption on the mailed surveys, to estimate the total exposure of PCBS from Great Lakes fish during the years of 1955 to 1991 (Buck et al., 1999; Mendola et al., 1997). The index is described as such: PCB index = years eating Lake Ontario fish × ∑ species (frequency × portion size × PCB concentration), where years = total number of years eating Lake Ontario fish, 1955 to 1991; species = 0 (not eaten) or 1 (eaten) for each of 12 species/size measured; frequency = number of species-specific fish meals in 1991; portion size = usual grams of fish per meal; and PCB concentration = milligrams/g of total PCBS, as estimated by the New York Department of Environmental Conservation/Ontario Ministry of the Environment database, 1980–1990 (Cox, 1988–1990; Skinner, 1996). Estimated PCB exposure was then categorized as high (>7.0 mg), medium (1.01–7.0 mg), and low (<1 mg), as done in other previously publish studies (Buck et al., 1999).

1.4. Omega-3 fatty acid

An index was created to estimate the amount of omega-3 fatty acids consumed from Great Lakes fish. Estimates of omega-3 fatty acids were based upon docosahexaenoic acid and eicosapentaenoic acid values reported by the US Department of Agriculture and Agricultural Research Service (2015), which is an authoritative source for the nutrient composition of foods in the United States, and are comparable to limited reported data on the omega-3 fatty acid content in Great Lakes fish (Neff et al., 2014). The reported approximate amount of omega-3 fatty acid for 4 oz of edible fish (cooked) was: 0.268 g for catfish; 1.330 g for lake trout; 2.304 g for Chinook salmon; 1.200 g for Coho salmon; 1.119 g for rainbow and brown trout; 0.630 g for carp; and 0.408 g for perch. The index was created in this manner: ∑ species (portions × omega-3 concentration × frequency/month × 12 months); where portions = number of 4 ounce servings of sport-caught fish typically eaten at each meal; omega-3 concentration = the reported amount of omega-3 fatty acid (g) per 4 ounce serving; and frequency = the number or times the fish species was eaten during a month, on average, from June 1990 through June 1991. To estimate the long-term intake of omega-3 fatty acids from Great Lakes fish, estimated omega-3 fatty acid intake (1990–1991) was then multiplied by the number of years the subject reported fish consumption from Lake Ontario between 1955 and 1991. High and low categories were created, based on the quartiles of estimated omega-3 fatty acid intake from Great Lakes fish. For short-term omega-3 intake, high intakes were those greater than 92.9 g (highest quartile), whereas, low was less than or equal to 92.9 g (lowest three quartiles). For long-term omega-3 intake, high intakes were those greater than 215.4 g (highest quartile), whereas, low was less than or equal to 215.4 g (lowest three quartiles). The lowest three quartiles were combined because many of the participants did not regularly eat fish from Lake Ontario.

1.5. Analysis

Chi-square and Fisher’s exact test were used to assess differences in categorical variables between cases and controls. Wilcoxon rank-sum tests were used to assess differences in continuous variables between cases and controls. To test whether or not variables, such as total estimated consumption of Great Lakes fish, long- and short-term estimated omega-3 consumption from Great Lakes fish, and estimated consumption of PCBS from Great Lakes fish, were able to predict thyroid cancer among anglers and their spouses, multiple logistic regression models, adjusted for sex, were used to generate odds ratios and 95% confidence intervals. Manual backward elimination using the –2 Log Likelihood method of variable selection was used to derive Chi-square values, and corresponding p-value, for the difference in model fit. A p-value of <0.20 was the cut-off for including potential covariates in the model, including interaction terms. Final adjusted models contained sex (matching variable), age, and pack-years of cigarettes. Pack-years of cigarettes was forced into the model because of its previous association with thyroid hormone abnormalities (Soldin et al., 2009). Other covariates evaluated, but not used in the final models, included previous diagnosis of a goiter or thyroid condition, education, and county of residence. Interaction between omega-3 fatty acid intake, PCB intake, and total fish intake was assessed, but not significant. The interaction of sex on the relationship between PCB or omega-3 intake and thyroid cancer was not able to be assessed due to the small sample size (9 male cases and 18 female cases), which may have resulted in a lack of statistical precision. Partially adjusted (sex) and fully adjusted (sex, age, pack-years of cigarettes) models were run for each exposure variable (e.g. fish consumption, PCB intake, or omega-3 intake). The referent categories were, respectively, none, low (<1 mg), and high (>92.9 g) for total fish consumption, PCB intake, and short-term omega-3 fatty acid intake. Reference categories were selected a priori based upon literature that indicated that low PCB and high omega-3 intakes were the low risk groups (Gago-Dominguez et al., 2003; Turyk et al., 2008). Spearman correlation coefficients between omega-3 fatty acid intake, PCB intake, and total fish consumption, as continuous variables, were calculated to assess collinearity. All analyses were
2. Results and discussion

Overall, there were no significant differences between cases and controls in regard to age, sex, previous diagnosis of thyroid condition, or smoking status. Controls reported a higher average monthly consumption of larger-sized fish, but there were no differences in the consumption of individual species of Lake Ontario fish (Table 1). Additionally, controls were more likely to have a high long-term intake of omega-3 fatty acids compared to cases, but there were no significant differences in the categories of estimated consumption of PCBS from Lake Ontario fish from Great Lakes fish between cases and controls. Generally, reported fish consumption from Lake Ontario was low, but cases reported not eating several varieties of fish, including channel catfish, Coho salmon >21″, rainbow trout >25″, and carp, whereas, controls reported eating some of these varieties. There was strong positive correlation between total fish intake and omega-3 fatty acid intake ($r = 0.99$, $p < 0.0001$), omega-3 fatty acid

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Table 1 – Descriptive characteristics between thyroid cancer cases and controls in the New York State Angler Cohort Study, 1991–2008.

<table>
<thead>
<tr>
<th></th>
<th>Thyroid cancer cases ($n = 27$) %</th>
<th>Controls ($n = 108$) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean (SD))</td>
<td>32.0 (5.1)</td>
<td>31.8 (4.9)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>33.3 (9)</td>
<td>33.3 (36)</td>
</tr>
<tr>
<td>Female</td>
<td>66.7 (18)</td>
<td>66.7 (72)</td>
</tr>
<tr>
<td>Angler status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>59.3 (16)</td>
<td>53.7 (58)</td>
</tr>
<tr>
<td>Yes</td>
<td>40.7 (11)</td>
<td>46.3 (50)</td>
</tr>
<tr>
<td>Pack-years of cigarettes (mean (SD))</td>
<td>6.2 (10.6)</td>
<td>5.1 (8.0)</td>
</tr>
</tbody>
</table>

Table 1 (continued)

<table>
<thead>
<tr>
<th></th>
<th>Thyroid cancer cases ($n = 27$) %</th>
<th>Controls ($n = 108$) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>100.0 (27)</td>
<td>90.7 (98)</td>
</tr>
</tbody>
</table>

Brown trout <20″          | 3.7 (1)                          | 11.1 (12)              |
| No                       | 96.3 (26)                        | 88.9 (96)              |

Carp                     |                                  |                        |
| Yes                      | 0.0 (0)                          | 0.9 (1)                |
| No                       | 100.0 (27)                       | 99.1 (107)             |

White perch               |                                  |                        |
| Yes                      | 3.7 (1)                          | 3.7 (4)                |
| No                       | 96.3 (26)                        | 96.3 (104)             |

Yellow perch              |                                  |                        |
| Yes                      | 7.4 (2)                          | 18.5 (20)              |
| No                       | 92.6 (25)                        | 81.5 (88)              |

Exposure of Great Lakes fish prior to 1980 |                                  |                        |
| Yes                      | 85.2 (23)                        | 79.6 (86)              |
| No                       | 14.8 (4)                         | 20.4 (22)              |

Consumption of larger sizes of fish |                                  |                        |
| Yes                      | 0.0 (0)                          | 13.0 (14)              |
| No                       | 100.0 (27)                       | 87.0 (94)              |

a Differences were calculated with Chi-square or Fisher’s exact test for categorical variables or Wilcoxon rank sum test for continuous variables.

b Standard deviation.

c 92.9 g is the cut-off for the upper quartile vs. the bottom three quartiles.

d 215.4 g is the cut-off for the upper quartile vs. the bottom three quartiles.

e Buck et al., 1999.

f >21″ for Coho salmon, >25″ for rainbow trout, >20″ for brown trout.

* The $p < 0.05$ between cases and controls.
intake and PCB intake \((r = 0.99, p < 0.0001)\), and total fish intake and PCB intake \((r = 0.99, p < 0.0001)\).

Most thyroid cancers were of the papillary carcinoma or adenocarcinoma type (Table 2). The logistic regression analyses suggested that there were no differences in short-term omega-3 fatty acid intake between cases and controls (fully adjusted \(OR = 2.07; 95\% CI = 0.64–6.72\)), although having a low estimated long-term omega-3 intake was associated with a higher odds of thyroid cancer development (Table 3; fully adjusted \(OR = 5.14; 95\% CI = 1.12–23.49\)). In addition, PCB intake was not significantly associated with the development of thyroid cancer (Table 3). The total amount of Lake Ontario fish consumed was not significantly associated with the development of thyroid cancer (Table 3). The total amount of Lake Ontario fish consumed was not significantly associated with the development of thyroid cancer (Table 3). The total amount of Lake Ontario fish consumed was not significantly associated with the development of thyroid cancer (Table 3). The total amount of Lake Ontario fish consumed was not significantly associated with the development of thyroid cancer (Table 3).

Results from these analyses suggest that there were no significant associations between estimated total fish consumption from Great Lake fish and the development of thyroid cancer. It has been a concern that Lake Ontario has been contaminated with PCB concentrations high enough to cause endocrine disruption in the fish and waterfowl residing in and near the lake (Colborn et al., 1993), but whether or not the endocrine disruption resulted in thyroid cancer has been undetermined. In these analyses, PCB consumption from Lake Ontario fish was not significantly associated with the development of thyroid cancer. It has been previously reported that long-term intake of Great Lake fish consumption, even in low amounts, could increase serum PCB concentrations for certain congeners (Bloom et al., 2005). Although, serum PCB concentrations were not associated with abnormal thyroid hormone concentrations in the anglers (Bloom et al., 2008). Since it has also been reported that higher TSH concentrations are associated with an increase in thyroid incidence (Boelaert et al., 2006; Haymart et al., 2008), it may be that the concentrations of PCBs in Lake Ontario fish did not alter thyroid hormone concentrations, and therefore, would not increase thyroid cancer incidence through this mechanism.

One study has examined the effect of PCBs on the incidence of thyroid cancer in rats (Vansell et al., 2004), and concluded that PCBs increase the incidence of thyroid cancer. However, no studies were found that examined this association in humans. The paucity of published studies in this area, in addition to the increasing incidence of thyroid cancer in the United States and around the world, has led one author to encourage scientists and researchers to investigate the contribution of PCBs to the risk of thyroid cancer (Zhang et al., 2008), specifically in epidemiological studies. The lack of published studies examining the association between PCBs and thyroid cancer in humans, in light of published animal studies, may be a result of publication bias and may therefore

### Table 2 – Types of thyroid cancer diagnosed in the New York State Angler Cohort Study, 1991–2008 (n = 27).

<table>
<thead>
<tr>
<th>Histology IDC-0-3 code</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>8050</td>
<td>8</td>
<td>30 Papillary carcinoma</td>
</tr>
<tr>
<td>8260</td>
<td>7</td>
<td>26 Papillary adenocarcinoma, not otherwise specified</td>
</tr>
<tr>
<td>8331</td>
<td>1</td>
<td>4 Follicular adenocarcinoma, well differentiated</td>
</tr>
<tr>
<td>8340</td>
<td>9</td>
<td>33 Papillary carcinoma, follicular variant</td>
</tr>
<tr>
<td>8341</td>
<td>2</td>
<td>7 Papillary microcarcinoma</td>
</tr>
</tbody>
</table>

### Table 3 – Separate logistic regression models predicting thyroid cancer from long-term Great Lakes omega-3 fatty acid consumption, Great Lakes PCB intake, and total Lake Ontario fish intake (odds ratios and 95% confidence intervals) among sport fishermen and their spouses the New York State Angler Cohort (1991–2008).

<table>
<thead>
<tr>
<th></th>
<th>Partially adjusted (n = 27) for cases; (p)-trend</th>
<th>Fully adjusted (n = 26) for cases; (p)-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated omega-3 consumption from Great Lakes fish (1955–1991)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High(^c)</td>
<td>1.00</td>
<td>0.03</td>
</tr>
<tr>
<td>Low</td>
<td>5.33 (1.19–23.94)</td>
<td>5.14 (1.12–23.49)</td>
</tr>
<tr>
<td>Estimated consumption of PCBs in Great Lakes fish (1955 to 1991)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low(^d)</td>
<td>1.00</td>
<td>0.18</td>
</tr>
<tr>
<td>Medium</td>
<td>0.27 (0.03–2.12)</td>
<td>0.29 (0.04–2.40)</td>
</tr>
<tr>
<td>High</td>
<td>0.21 (0.03–1.70)</td>
<td>0.22 (0.03–1.76)</td>
</tr>
<tr>
<td>Estimated consumption of all Lake Ontario fish (1990 to 1991)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1.00</td>
<td>0.24</td>
</tr>
<tr>
<td>&lt;1 times per month</td>
<td>0.39 (0.11–1.43)</td>
<td>0.41 (0.11–1.52)</td>
</tr>
<tr>
<td>2–4 times per month</td>
<td>0.19 (0.02–1.49)</td>
<td>0.20 (0.02–1.58)</td>
</tr>
<tr>
<td>&gt;4 times per month</td>
<td>0.99 (0.10–10.06)</td>
<td>0.97 (0.09–10.41)</td>
</tr>
</tbody>
</table>

\(^{a}\) Adjusted for sex (matching variable).

\(^{b}\) Adjusted for sex (matching variable), age, and pack-years of cigarettes.

\(^{c}\) Long-term exposure of omega-3 fatty acids: high >215.4 g vs. low ≤215.4 g.

\(^{d}\) PCB categories: high >7.0 mg, medium (1.01–7.0 mg), and low ≤1 mg.
indicate that studies have failed to find associations, perhaps because of insufficient follow-up time, or because more refined methods of determining PCB exposure are needed.

Findings from the Angler cohort analyses suggest that, among anglers and their spouses, estimated short-term omega-3 consumption from Great Lakes fish is not associated with an altered risk of thyroid cancer, although longer-term estimates were consistent with an inverse association. Several previously published studies have reported a decrease in the incidence of developing several types of cancer (Cago-Dominguez et al., 2003; Tavani et al., 2003), with higher intakes of marine and other dietary omega-3 fatty acid sources, although these studies did not report on the association between omega-3 fatty acids and thyroid cancer specifically. Conversely, other studies have found no association between omega-3 fatty acid intake and the development of cancer (Newberry et al., 2006), indicating that there is insufficient evidence to make conclusions on the effects of omega-3 fatty acids. It should be noted that because of the high correlation between omega-3 fatty acids and PCB content in this study, it is difficult to fully separate the effects of these two variables.

The relationship between omega-3 fatty acids and thyroid cancer may be mediated by inflammation. Higher omega-3 fatty acid intake has been associated with lower concentrations of inflammatory cytokines and has been shown to beneficially modulate the immune system of those with inflammatory conditions, such as rheumatoid arthritis (Simopoulos, 2002; Wall et al., 2010). Thyroid follicular cells may have alterations in oncogenes, such as RET or RAS, which may be caused by inflammation and its effects (e.g. free radicals, cytokine secretion, and cellular proliferation; Guarino et al., 2010). These alterations may, in turn, promote further inflammation, thus creating an environment favorable for cancer development and progression (Allavena et al., 2008; Guarino et al., 2010). Alterations in inflammatory genes, while not able to be accounted for in this study, may help further explain the association between omega-3 fatty acids and thyroid cancer found in this study.

Previously reported findings indicate that fish consumption is associated with a higher risk of thyroid cancer in areas with an iodine-rich diet, but fish consumption is associated with a protective effect of thyroid cancer in areas with endemic goiters (Boezaart et al., 2006; Haymart et al., 2008). Further, there were no differences between cases and controls, in regard to smoking status, which may be another explanation as to why smoking had a null effect. Also consistent with the literature is the finding that women were more likely to develop thyroid cancer in this cohort (Aschebrook-Kilfoy et al., 2011). Two-thirds of the cases in these analyses were women, while most of the total cohort was male (62%); consequently, the present analyses had cases and controls matched on sex. Family history was not assessed this study, and consequently not adjusted for, but most people who develop thyroid cancer do not have a family history of the disease (American Cancer Society, 2014).

One limitation to these analyses is that dietary data were not available to evaluate omega-3 contributions from other dietary sources, such as store-bought fish or omega-3 supplements. It seems unlikely that supplements would contribute to major differences between groups, since it has been reported that, in a cohort of male physicians interviewed around the same time as the participants in this present study, fewer than 4% reported consuming omega-3 supplements (Ascherio et al., 1999). Considering store-bought fish sources, previous studies have shown that wild-caught fish consumption increases with increasing overall fish consumption from all sources (Burger, 2000), suggesting that any misclassification in the present analysis would be non-differential, minimizing the estimate of effect. However, if there were differences in intake, and controls were to differentially consume more omega-3 fatty acids from store-bought fish that was not accounted for in the analysis, a bias towards the null and underestimation of the effect would result. Considering these points, had information on omega-3 fatty acid intake from other sources been included, it is unlikely that a null association between long-term omega-3 fatty acid consumption and thyroid cancer would have been detected.

A null association between PCB exposure and thyroid cancer was detected using our PCB exposure metric that may over-estimated PCB exposure. The index used relied on late 1980 PCB data (Buck et al., 1999; Mendola et al., 1997) and may not fully account for the declining levels of PCB in the lakes between 1991 and 2008. However, even if lower PCB values from more recent data were used in calculating exposure, a positive association between PCB and thyroid cancer is unlikely. In this cohort, there were no significant changes in fish consumption patterns due to fish advisories between cases and controls. However, if changes in fish intake over time due to fish consumption advisories existed, this would likely result in non-differential misclassification since fish intake was asked about prior to cancer ascertainment. Therefore, it is unlikely that a positive association between PCB exposure and thyroid cancer would have been seen even if the PCB metric accounted for changing fish intake patterns. The methods presented here for estimating exposure are supported by previous research that has reported that PCB congeners in both serum and breast milk are correlated with fish intake in this population (Bloom et al., 2005; Kostyniak et al., 1999).

One of the major strengths of this study is that it is a relatively large cohort that has been prospectively followed by the specific purpose of examining the associations between fish consumption and the development of cancer. Also, these analyses are some of the first to look at the consumption of fish and the development of thyroid cancer. Results from these analyses suggest that the risk of thyroid cancer development is not increased among those who consume...
Great Lakes fish. The participants in this study were relatively young (mean age of 32 years at enrollment) for the development of cancer and additional follow-up time may be needed to fully understand these associations.

3. Conclusion

In conclusion, there does not appear to be a greater risk of developing thyroid cancer among Lake Ontario sport anglers who have a higher PCB exposure from Great Lakes fish, as compared to those who have a lower estimated PCB exposure. However, long-term omega-3 fatty acid intake appears to be protective. Further studies, with longer follow-up time and better indices for quantifying PCB and omega-3 fatty acid exposure, are needed to confirm these findings.

Acknowledgment

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