Potential Exposure to PCBs, DDT, and PBDEs from Sport-Caught Fish Consumption in Relation to Breast Cancer Risk in Wisconsin

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In Wisconsin, consumption of Great Lakes fish is an important source of exposure to polychlorinated biphenyls (PCBs), dichlorodiphenyltrichloroethane (DDT), polybrominated diphenyl ethers (PBDEs), and other halogenated hydrocarbons, all of which may act as potential risk factors for breast cancer. We examined the association between sport-caught fish consumption and breast cancer incidence as part of an ongoing population-based case–control study. We identified breast cancer cases 20–69 years of age who were diagnosed in 1998–2000 (n = 1,481) from the Wisconsin Cancer Reporting System. Female controls of similar age were randomly selected from population lists (n = 1,301). Information about all sport-caught (Great Lakes and other lakes) fish consumption and breast cancer risk factors was obtained through telephone interviews. After adjustment for known and suspected risk factors, the relative risk of breast cancer for women who had recently consumed sport-caught fish was similar to women who had never eaten sport-caught fish [relative risk (RR) = 1.00; 95% confidence interval (CI), 0.86–1.17]. Frequency of consumption and location of sport-caught fish were not associated with an increased risk of breast cancer. Recent consumption of Great Lakes fish was not associated with postmenopausal breast cancer (RR = 0.78; 95% CI, 0.57–1.07), whereas risk associated with premenopausal breast cancer was elevated (RR = 1.70; 95% CI, 1.16–2.50). In this study we found no overall association between recent consumption of sport-caught fish and breast cancer, although there may be an increased breast cancer risk for subgroups of women who are young and/or premenopausal. *Key words:* breast cancer, DDT, Great Lakes, PBDEs, PCBs, sport-caught fish consumption. *Environ Health Perspect* 112:156–162 (2004). doi:10.1289/ehp.6506 available via *http://dx.doi.org/* [Online 31 October 2003]

Environmental exposure to common pollutants including polychlorinated biphenyls (PCBs), dichlorodiphenyltrichloroethane (DDT) and its most stable metabolite 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene (DDE), and polybrominated diphenyl ethers (PBDEs) has been hypothesized as a risk factor for female breast cancer (Falck et al. 1992; Wenning 2002; Wolff et al. 1996). These chemicals are ubiquitous, persistent, estrogenic, and lipophilic (Adami et al. 1995; de Boer et al. 1998; Geyer et al. 1986; Jakobsson et al. 2002; Meerts et al. 2001; Sjodin et al. 2001). Diet is a major route of human exposure, especially through consumption of sport-caught fish from contaminated waters such as the Great Lakes (Anderson et al. 1998; Darnerud et al. 2001; Geyer et al. 1986). Although the Food and Drug Administration confiscates market fish containing > 2 ppm PCBs and 5 ppm DDT/DDE (there is no regulation on PBDE levels), sport fishers' own catches are unregulated (Ahmed 1991). Consequently, consumers of Great Lakes sport-caught fish are at a higher risk of exposure to these chemicals.

Numerous epidemiologic studies have explored the relationship between body burden of PCBs, DDT, and/or DDE and risk of breast cancer with inconclusive results (Adami et al. 1995). The mean level of PCBs and DDT/DDE in adipose tissue or blood serum has declined since the banning of these chemicals in 1977 and 1972, respectively, whereas PBDE levels have dramatically increased (Noren and Meironyte 2000). Studies have consistently found a positive correlation between sport-caught fish consumption patterns and body burden of PCBs and/or DDE (e.g., Hanrahan et al. 1999). In addition, studies have shown that Great Lakes fish consumers have higher mean levels of PCB and DDE compared with nonfish consumers (He 1999; Humphrey 1983). We present data on the relationship between self-reported sport-caught fish consumption and breast cancer risk as part of an ongoing population-based case–control study.

Subjects and Methods

Identification of breast cancer cases. All participants were female Wisconsin residents 20–69 years of age with a new diagnosis of breast cancer in 1996–2000 identified by Wisconsin Cancer Reporting System. According to an institutionally approved human subjects' protection protocol, the physician of record for each eligible case was contacted by mail to inform him/her that potential participants would be contacted. Eligibility was limited to cases with listed telephone numbers and either a driver's license verified by self-report (20–64 years of age) or a Medicare card (65–69 years of age). A total of 3,753 cases (80.6% of eligible cases) participated in the study interview. The reasons for nonparticipation included subject refusal (n = 576; 12.4%), subject deceased (n = 164; 3.5%), inability to locate subject (n = 110; 2.4%), and physician refusal (n = 55; 1.2%).

Identification of population controls. Community controls were selected randomly from lists of licensed drivers (20–64 years of age) and Medicare beneficiary files compiled by the Centers for Medicare and Medicaid Services, formerly known as the Health Care Financing Administration (65–69 years of age). The controls were selected at random to yield an age distribution similar to that of the cases. Control eligibility was further limited to subjects who had a listed telephone number and had not reported a previous diagnosis of breast cancer. Of the 5,155 eligible controls, 983 (19.1%) refused, 191 (3.7%) could not be located, and 40 (0.8%) were deceased. A total of 3,941 (76.5%) controls completed the study interview.

Data collection. Introductory letters were mailed to eligible participants before they were contacted by telephone. Structured 40-min telephone interviews, conducted between February 1997 and May 2001, elicited information on known or suspected risk factors for breast cancer, including exogenous hormone use, reproductive experiences, physical activity, alcohol consumption, medical and family history, and demographics before an assigned reference date. For cases, this date was the date of diagnosis of the breast cancer. Control subjects were assigned a reference date that corresponded to the dates of diagnoses for similarly aged cases (within 5-year strata). The reference age was defined as the subject's age at the time

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of the reference date. Trained study staff conducted interviews by telephone without prior knowledge of the subjects' disease status. The interviewers reported that they were unaware of the case–control status for 90.8% of the cases and 89.1% of the controls until the end of the interview.

Beginning in 1999, questions about fish-consumption behaviors were added to the ongoing case–control study. Subjects were asked about sport-caught fish in the following way: "How often did you eat sport-caught fish in [reference year minus 5] when you were [reference age minus 5]. This does not include purchased fish." "Was any of this sport-caught fish you ate in [reference year minus 5] when you were [reference age minus 5] from the Great Lakes? (Included are Lakes Michigan, Huron, Erie, Superior, and Ontario plus mouths of rivers feeding in the lakes. Also included are Green Bay and other parts of the lakes that have separate names.)" Participants who reported consumption of Great Lakes sport-caught fish were further asked, "How often did you eat lake trout and salmon (chinook or coho) that was sport-caught from the Great Lakes in [reference year minus 5] when you were [reference age minus 5]."

Population for analysis. Information on sport-caught fish consumption was potentially available for 1,499 cases and 1,318 controls interviewed after November 1999, when the interview was expanded to include questions regarding environmental exposures. We excluded 18 cases and 17 controls who were uncertain as to whether they ate sport-caught fish. Hence, 1,481 cases and 1,301 controls were included in the analysis. The proportion of women who refused the telephone interview in this phase of the ongoing case–control study was similar to the overall study.

Analysis. We used odds ratios (ORs) and 95% confidence intervals (CIs) from logistic regression models to estimate relative risks (RR) of breast cancer (Breslow and Day 1980). A dichotomous variable described recent sport-caught fish consumption (none, any) and recent Great Lakes sport-caught fish consumption (none, any). Among recent sport-caught fish consumers and Great Lakes sport-caught fish consumers, we categorized the frequency (meals per year) of sport-caught fish consumption in approximate tertiles based on the distribution among controls and in separate models as a continuous linear term. For all sport-caught fish regression models, the reference category was defined as subjects who did not recently eat any sport-caught fish. Covariates in the models included known or suspected risk factors for breast cancer. Age was defined as age at the reference date (continuous). Family history of breast cancer was defined as having a mother, sister, or daughter who had had breast cancer (absent, present, unknown). Recent alcohol consumption was the total number of drinks of beer, wine, and hard liquor consumed per week 5 years before the reference date (three categories). Parity was defined as the number of full-term pregnancies (defined as pregnancies of > 6 months gestation resulting in a live birth or stillbirth) (three categories). Postmenopausal status was assigned to women who reported having undergone natural menopause or a bilateral oophorectomy before the reference date. Women were also categorized as postmenopausal if they had a hysterectomy alone and were ≥ 55 years of age (equal to the 90th percentile of age at natural menopause among the controls). In cases of hysterectomy without

Table 1. Characteristics of breast cancer cases (n = 1,481) and controls (n = 1,301) 20–69 years of age.

Characteristic	Cases No. (%)	Controls No. (%)	RR[a]	95% CI[a]
Age at reference date (years)				
< 40	105 (7.1)	103 (7.9)	1.00	
40–49	398 (26.9)	350 (26.9)	1.11	0.82–1.52
50–54	267 (18.0)	200 (15.4)	1.31	0.94–1.82
55–59	258 (17.4)	217 (16.7)	1.17	0.84–1.62
60–64	245 (16.5)	208 (16.0)	1.16	0.83–1.61
65–69	208 (14.0)	223 (17.1)	0.92	0.66–1.27
Family history of breast cancer				
Absent	1,161 (78.4)	1,121 (86.2)	1.00	
Present	310 (20.9)	171 (13.1)	1.76	1.43–2.15
Unknown	10 (0.7)	9 (0.7)	1.07	0.43–2.66
Recent alcohol consumption				
None	249 (16.8)	221 (17.0)	1.00	
1–6 drinks/week	1,041 (70.3)	949 (73.0)	0.97	0.80–1.19
≥ 7 drinks/week	189 (12.8)	131 (10.1)	1.28	0.96–1.71
Parity				
0	180 (12.2)	151 (11.6)	1.00	
1–2	642 (43.4)	511 (39.3)	1.06	0.83–1.35
≥ 3	658 (44.4)	638 (49.0)	0.85	0.66–1.09
Age at first full-term pregnancy (years)				
< 20	240 (16.2)	249 (19.1)	1.00	
20–24	622 (42.0)	592 (45.5)	1.09	0.88–1.34
25–29	304 (20.5)	211 (16.2)	1.50	1.17–1.93
≥ 30	132 (8.9)	97 (7.5)	1.43	1.04–1.97
Nulliparous	180 (12.2)	151 (11.6)	1.26	0.95–1.67
Lactation[b]				
Never	712 (54.8)	613 (53.4)	1.00	
1–23 months	259 (19.9)	238 (20.7)	0.93	0.76–1.15
> 24 months	329 (25.3)	298 (25.9)	0.94	0.78–1.14
Menopausal status				
Postmenopausal	838 (56.6)	757 (58.2)	1.00	
Premenopausal	577 (39.0)	490 (37.7)	1.16	0.91–1.47
Unknown	66 (4.5)	54 (4.2)	1.17	0.79–1.73
Age at menopause (years)[c]				
< 45	195 (23.3)	208 (27.5)	1.00	
45–49	190 (22.7)	170 (22.5)	1.19	0.89–1.58
50–54	235 (28.0)	225 (29.7)	1.13	0.86–1.47
≥ 55	97 (11.6)	68 (8.9)	1.55	1.07–2.25
Unknown	121 (14.3)	86 (11.4)	1.46	1.04–2.05
Age at menarche (years)				
< 12	325 (21.9)	250 (19.2)	1.00	
12	374 (25.3)	301 (23.1)	0.96	0.76–1.20
13	410 (27.7)	355 (27.3)	0.89	0.72–1.10
≥ 14	350 (23.6)	383 (29.4)	0.70	0.56–0.88
Unknown	22 (1.5)	12 (0.9)	1.41	0.68–2.90
Weight gain since age 18 (kg) in quintiles[c]				
< 5.0	121 (14.4)	147 (19.4)	1.00	
5.0–12.4	173 (20.6)	154 (20.3)	1.36	0.98–1.88
12.5–18.4	187 (22.3)	161 (21.3)	1.42	1.03–1.95
18.5–26.9	156 (18.6)	137 (18.1)	1.39	1.00–1.94
≥ 27.0	186 (22.2)	146 (19.3)	1.54	1.12–2.13
Unknown	15 (1.8)	12 (1.6)	1.53	0.70–3.39
Education				
< High school diploma	77 (5.2)	84 (6.5)	0.79	0.57–1.10
High school diploma	631 (42.6)	545 (41.9)	1.00	
Some college	395 (26.7)	366 (28.1)	0.93	0.78–1.12
College degree	372 (25.1)	302 (23.2)	1.07	0.88–1.29
Unknown	6 (0.4)	4 (0.3)	1.29	0.36–4.61

[a]Adjusted for age only. [b]Among parous women only. [c]Among postmenopausal women only.

bilateral oophorectomy, menopausal status was considered unknown if the woman's reference age was < 55 years (three categories: premenopausal, postmenopausal, unknown). Age at first full-term pregnancy (five categories), lactation (three categories), age at menarche (five categories), weight gain in kilograms from age 18 to reference age (approximate quintiles based on the distribution among controls), age at menopause (five categories), weight in kilograms at age 18 (quartiles), and education (five categories) were also covariates in the model.

Because the majority of women in this study were white (96%), we did not adjust for race/ethnicity in the models. Tests for heterogeneity in the relative risk for recent consumption of sport-caught fish (none, any) according to other covariates were conducted by comparing the change in log likelihoods in models with and without cross-product terms.

Results

Women with breast cancer were more likely to have a later age at first full-term pregnancy, have a later age at menopause (postmenopausal women), have a family history of breast cancer, gain more weight in adult years (postmenopausal women), and have a younger age of menarche compared to similarly aged controls (Table 1).

A similar proportion of women with breast cancer reported recent sport-caught fish consumption (47%) compared to age-matched controls (48%) (Table 2). The multivariate relative risk of breast cancer for women who had recently eaten sport-caught fish compared to women who had not eaten sport-caught fish in the same time period was 1.00 (95% CI, 0.86–1.17). This RR was similar to the estimate after adjustment for age only (RR = 0.98; 95% CI, 0.84–1.13). Frequency of recent sport-caught fish consumption was not associated with breast cancer risk (p-value for trend = 0.38). Compared to women who had not recently eaten any sport-caught fish, the relative risks of breast cancer for women who had recently eaten any sport-caught Great Lakes fish (RR = 1.06) or Great Lakes trout or salmon (RR = 1.00) were null. No overall association between frequency of recent Great Lakes trout or salmon consumption and risk of breast cancer was observed (p-value for trend = 0.92).

We evaluated whether any of the covariates listed in Table 1 modified the association between fish consumption and breast cancer risk by menopausal status. Regression models for any recent sport-caught fish consumption showed that a positive association with breast cancer risk was perhaps limited to younger premenopausal women (< 40 years of age), although only 98 breast cancer cases were in this category (Table 3). The interaction between menopausal status and recent Great Lake sport-caught fish consumption was significant (p-value = 0.003). A positive association was also seen for premenopausal women who recently consumed Great Lakes sport-caught fish (RR = 1.70; 95% CI, 1.16–2.50). However for postmenopausal women, the relative risk for recent Great Lake sport-caught fish consumption was 0.78 (95% CI, 0.57–1.07). Interactions between recent consumption of sport-caught fish and other covariates listed in Table 1 were not significant (data not shown).

Discussion

In our study we investigated the risk of breast cancer associated with self-reported consumption of sport-caught fish. For our population-based study, consumption of sport-caught or Great Lakes sport-caught fish was not significantly associated with breast cancer risk overall. There was a suggestion that the risk may be increased in younger or premenopausal women. Our confidence in the results is strengthened by the large sample size, high proportion of women participating in our study, validated method of assessment of sport-caught fish consumption, and information on individual-level risk factors.

To our knowledge, no study has specifically evaluated breast cancer risk in consumers of diets potentially high in PCBs, DDT/DDE, and PBDEs such as consumers of high amounts of sport-caught fish, anglers, families who operate charter fishing boats, or native populations, although several other health parameters, including fecundability (Buck et al. 2000; McGuinness et al. 2001), birth size (Fein et al. 1984), puberty growth (Gladen et al. 2000), and cognitive functioning (Jacobson et al. 1990; Schantz et al. 2001), have been investigated in these adult subpopulations as well as in children.

Our study suggested an increased breast cancer risk for young (< 40 years of age) or premenopausal women who had recently consumed sport-caught fish. Although this observed association may be due to chance, one possible explanation for this interaction is the influence of PBDE exposure at time of puberty or during early reproductive life. Because the recorded level of PBDE has dramatically increased since the 1970s (Noren and Meironyte 2000), this age cohort would be the most likely group exposed to these higher levels at puberty—a potentially vulnerable time of changing hormones and breast tissue growth (Swerdlow et al. 2002) or during early reproductive life. She et al. (2002) reported a statistically significant inverse association with age and PBDE levels in adipose tissue of women diagnosed with breast cancer. Specifically, compared with women > 48 years of age (the median age), women < 48 years of age had significantly higher PBDE levels (41.1 ng/g fat and 138.8 ng/g fat, respectively).

Table 2. Multivariate relative risks of breast cancer according to recent consumption of sport-caught fish.

	Cases No. (%)	Controls No. (%)	RR[a]	95% CI[a]	RR adjusted[b]	95% CI adjusted[b]
Recent sport-caught fish consumption						
None[c]	780 (52.7)	677 (52.0)	1.00		1.00	
Any	701 (47.3)	624 (48.0)	0.98	0.84–1.13	1.00	0.86–1.17
Recent consumption (meals per year)						
1–3	255 (17.2)	214 (16.5)	1.03	0.84–1.28	1.05	0.85–1.30
4–23	244 (16.5)	215 (16.5)	0.99	0.80–1.22	1.01	0.82–1.26
≥ 24	202 (13.6)	195 (15.0)	0.90	0.72–1.12	0.94	0.75–1.18
			$p = 0.21$		$p = 0.38$	
Recent Great Lakes fish consumption						
Any	210 (14.2)	177 (13.6)	1.03	0.82–1.29	1.06	0.84–1.33
Recent consumption of Great Lakes trout or salmon						
Any	173 (11.5)	150 (11.6)	1.00	0.79–1.27	1.00	0.78–1.28
Recent consumption of Great Lakes trout or salmon (meals per year)						
1–2	95 (6.4)	70 (5.4)	1.18	0.85–1.63	1.19	0.85–1.66
3–6	34 (2.3)	41 (3.2)	0.72	0.45–1.15	0.71	0.44–1.15
≥ 7	44 (2.8)	39 (3.0)	0.98	0.63–1.52	0.98	0.62–1.54
			$p = 0.87$		$p = 0.92$	

[a]Adjusted for age only. [b]Adjusted for age, family history of breast cancer, recent alcohol consumption, parity, age at first full-term pregnancy, lactation, menopausal status, age at menopause, weight at age 18, weight gain since age 18, age at menarche, and education. [c]Reference category.

Another possible explanation lies in the findings that young women who are diagnosed with breast cancer have a more aggressive type of breast cancer than those diagnosed at a later age (Jmor et al. 2002; Lu et al. 2002). Demers et al. (2000) suggested that exposure to organochlorines was related to breast cancer aggressiveness and prognosis as indicated by axillary lymph node involvement and tumor size. Exposure to chemicals such as PBDE might play an important role in breast cancer progression for these younger women (Lai et al. 2002; Mintzer et al. 2002).

Although we were not able to evaluate genetic characteristics of the study population, an association between breast cancer and contaminated fish consumption may be limited to women with a specific genotype. Two studies reported an association between breast cancer risk and fish consumption as indicated by body burden of PCBs when women were stratified by cytochrome P4501A1 polymorphism [*CYP1A1*—*Msp*I, the T-to-C transition at nucleotide 6235 (Laden et al. 2002) and *CYP1A1*—exon-7, the A-to-G transition at nucleotide 4889 (Moysich et al. 1999)]. In Moysich et al.'s study, the odds ratio for participants with a high PCB body burden and breast cancer risk was 1.27 (95% CI, 0.76–2.14). However, for women with high PCB body burden and the *CYP1A1* polymorphism, the odds ratio was 2.9 (95% CI, 1.18–7.45) (Moysich et al. 1999). Laden et al. (2002) reported similar results for an equivalent comparison to Moysich et al.'s subpopulation with the relative risk of 2.28 (95% CI, 1.03–5.04). In contrast to these two studies, results of evaluations of breast cancer risk and *CYP1A1* polymorphism without additional information on PCB serum levels have been positive (Fontana et al. 1998; Goth-Goldstein et al. 2000; Huang et al. 1999a, 1999b; Krajinovic et al. 2001; Ishibe et al. 1998; Taioli et al. 1999) and negative (Bailey et al. 1998; Basham et al. 2001; Dialyna et al. 2001; Rebbeck et al. 1996).

Other studies of breast cancer have imputed the DDT/DDE and PCB levels directly from serum or adipose tissue, rather than indirectly from sport-caught fish consumption patterns, with positive (Aronson et al. 2000; Demers et al. 2002; Falck et al. 1992; Guttes et al. 1998; Hoyer et al. 2000; Liljegren et al. 1998; Millikan et al. 2000; Romieu et al. 2000; Wolff et al. 1993) and negative or null associations (Bagga et al. 2000; Demers et al. 2000; Dorgan et al. 1999; Helzlsouer et al. 1999; Holford et al. 2000; Hoyer et al. 1998; Krieger et al. 1994; Lopez-Carrillo et al. 1997; Mendonça et al. 1999; Schecter et al. 1997; Unger et al. 1984; Van't Veer et al. 1997; Ward et al. 2000; Wolff et al. 2000; Zheng et al. 1999, 2000). Although individual results from these studies have not been consistent, accumulating evidence suggests that PCBs and DDT/DDE levels measured in serum or adipose tissue are not informative predictors of breast cancer in the general population. However, with regard to the subpopulation of sport-caught fish consumers, a lack of reported association does not necessarily signify that PCB, DDT, and PBDE exposure does not affect breast cancer risk because exposure to these chemicals can come from sources other than fish consumption. Further, fish contain potentially protective substances such as omega-3 fatty acids that may mask an adverse effect of halogenated organic compounds (Connor 2000).

Even though the epidemiologic studies mentioned above have reported inconsistent results, several lines of evidence support an investigation of a woman's body burden of DDT/DDE, PCB, and PBDE congeners as it influences breast cancer risk. Of the possible 209 PBDE congeners, limited testing has occurred due to the unavailability of congener-specific standards (de Wit 2002). For those PBDE congeners tested, a few have shown estrogenic mimicking behavior (Meerts 2001). In addition, 36 of the 206 PCB congeners, technical DDT, and *o,p′*-DDE are considered environmental estrogens (Hansen 1998; Kimbrough 1995; Longnecker et al. 1997). In addition, exposure to PCBs and DDT has been linked with disrupting endocrine function, interfering with intracellular communication, carcinogenesis, and perturbing immune function (Brouwer et al. 1999; Longnecker et al. 1997; Thomas 1995; Tryphonas 1995). Limited studies have evaluated the toxicity of a few brominated flame retardants, including PBDE congeners. In toxicologic studies using animals, hepatotoxicity, embryotoxicity, and endocrine disruption effects have been described (Darnerud et al. 2001; McDonald 2002). In human breast cancer cells, Meerts et al. (2001) reported estrogenic potencies of PBDE congeners similar in potency to bisphenol A, a well-known environmental estrogen.

PCBs and DDT were banned from use in the United States in the 1970s. The level of PCBs in serum sampled from a general population of men and women in Michigan significantly declined from 1979 to 1989 (Humphrey et al. 2000); however, levels remained virtually unchanged in sport-caught fish consumers. In contrast, findings from a cohort of older participants (≥ 50 years of age in 1992) recently demonstrated that a reduction in current fish consumption was associated with a monotonic decline in PCB levels in blood serum (Tee 2003). Although self-reported fish consumption has substantially declined over time, sport-caught fish intake continues to be one of the key predictors of serum PCB levels (He et al. 2001; Humphrey et al. 2000; Tee 2003). Other studies have shown a decline in organochlorinated hydrocarbons in serum,

Table 3. Multivariate relative risks of breast cancer associated with recent consumption of sport-caught fish according to age (years) and menopausal status.

	None[a]		Any			
Age (years)	Cases	Controls	Cases	Controls	RR[b]	95% CI[b]
Recent sport-caught fish consumption						
Premenopausal women						
All ages	291	273	286	217	1.24	0.96–1.59
< 40	51	69	47	31	1.92	1.01–3.66
40–44	69	70	84	72	1.54	0.90–2.65
45–49	102	73	82	69	0.87	0.53–1.42
≥ 50	69	61	73	45	1.38	0.76–2.53
Postmenopausal women						
All ages	450	382	388	375	0.91	0.74–1.11
< 55	82	65	71	67	0.81	0.48–1.38
55–59	122	90	114	106	0.89	0.58–1.35
60–64	132	112	110	94	1.11	0.74–1.67
≥ 65	114	115	93	108	0.82	0.53–1.26
Recent Great Lakes fish consumption						
Premenopausal women						
All ages	291	273	95	57	1.70	1.16–2.50
< 40	51	69	14	13	1.74	0.68–4.43
40–44	69	70	33	18	2.16	1.00–4.65
45–49	102	73	23	16	1.09	0.49–2.44
≥ 50	69	61	25	10	2.96	1.12–7.82
Postmenopausal women						
All ages	450	382	104	113	0.78	0.57–1.07
< 55	82	65	17	18	0.50	0.20–1.24
55–59	122	90	24	30	0.74	0.37–1.48
60–64	132	112	33	30	1.11	0.60–2.05
≥ 65	114	115	30	35	0.77	0.40–1.50

[a]No recent consumption of any sport-caught fish. [b]Relative to subjects with no recent consumption of any sport-caught fish within strata; adjusted for age, family history of breast cancer, recent alcohol consumption, parity, age at first full-term pregnancy, lactation, age at menarche, weight at age 18, weight gain since age 18, education, and age at menopause (postmenopausal women only).

breast milk, or adipose tissue in various populations (Dallaire et al. 2002; Fitzgerald et al. 1999; Hovinga et al. 1992; Konishi et al. 2001; Noren and Meironyte 2000; Robinson et al. 1990; Smith 1999). According to Noren and Meironyte (2000), the level of organochlorine compounds in 1997 was approximately one-tenth of the 1972 level in breast milk from Swedish mothers living in the Stockholm region.

In contrast to the PCB and DDT use and contamination trends, use of brominated flame retardant (e.g., PBDE) has increased substantially (Thomsen et al. 2002). For example, in lake sediment core samples, PBDE was detected in the 1970s and has since increased exponentially (Darnerud et al. 2001). In comparing the mean concentration of three common congeners of PBDE, Lake Michigan had 5-fold more PBDE detected in fish tissue than any other North American freshwater fish tested (Luross et al. 2002). Furthermore, Manchester-Nessvig et al. (2001) reported concentrations of PBDEs in salmon in open water of Lake Michigan as the highest in the world. In Sweden, the level of PBDEs in breast milk increased 60-fold from 1972 to 1997 (Noren and Meironyte 2000). In North America, preliminary data showed that levels of PBDE in women's breast milk appeared to be doubling every 2–5 years (Betts 2002), and the general population of California had the highest reported levels of PBDE to date (She et al. 2002).

Several studies have reported continued angling and consumption of contaminated fish from local fishing spots in spite of advisories about contamination. In other studies, respondents reported incomplete or inaccurate information about the contamination of the fish and/or lack of trust in the organization issuing the advisory (Burger 1998; May and Burger 1996; Steenport et al. 2000; Tilden et al. 1997). Furthermore, risk perceptions are usually optimistically biased; individuals believe their own risk from a voluntary activity is less than someone else's risk (Weinstein 1989). Consequently, fish-consumption behavior occurred regardless of the warnings about level of toxicants bioaccumulating in the sport-caught fish.

The design of our study had potential limitations in determining exposure from consumption of PCB-, DDT-, and PBDE-contaminated sport-caught fish. In particular, recall of past fish-consumption patterns might not have been a valid method to assess body burden of PCBs, DDT, and PBDE. However, the reported fish-consumption levels in healthy populations as well as in case–control studies have consistently correlated with body burden of PCBs, DDT/DDE, and PBDEs as determined from serum, adipose tissue, or breast milk analysis (Anderson et al. 1998; Falk et al. 1999; Fein et al. 1984; Fiore et al. 1989; Fitzgerald et al. 1999; Gerstenberger et al. 2000; Hanrahan et al. 1999; Hovinga et al. 1993; Kiviranta et al. 2002; Kosatsky et al. 1999; Kostyniak et al. 1999; Kreiss et al. 1981; Ohta et al. 2002; Schantz et al. 2001; Schwartz et al. 1983; Stewart et al. 1999; Tee et al. 2003). In addition, selective recall for cases versus controls was perhaps limited because there is little social suspicion of fish consumption in relation to breast cancer risk. Our study questions did not collect comprehensive lifetime intake of potentially contaminated fish. Although we did obtain exposure information 5 years before diagnosis, we were not able to adjust for intake in earlier life periods. In addition, problems with recall past 5 years would probably limit collection of data from earlier time periods. This limitation would bias toward the null hypothesis. It is possible that other unmeasured risk factors may play a role in breast carcinoma.

In conclusion, this study does not provide evidence for a positive association between consumption of sport-caught or Great Lake sport-caught fish and breast cancer. However, there was a suggestion of an increased breast cancer risk for young or premenopausal women who were recent consumers of sport-caught fish. Attention to the health effects of PBDEs is warranted because of the apparent increase of this emerging contaminant in the environment and some food sources, in addition to indications that consumption patterns remain high despite warnings. Further, additional studies to evaluate environment–gene interactions will contribute to our understanding of breast cancer risk factors, especially those associated with vulnerable populations.

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