

# Birth defects risk associated with maternal sport fish consumption: potential effect modification by sex of offspring<sup>☆</sup>

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## Abstract

Contaminated sport fish consumption may result in exposure to various reproductive and developmental toxicants, including pesticides and other suspected endocrine disruptors. We investigated the relation between maternal sport fish meals and risk of major birth defects among infants born to members of the New York State (NYS) Angler Cohort between 1986 and 1991 ( $n = 2237$  births). Birth defects ( $n = 125$  cases) were ascertained from both newborn medical records and the NYS Congenital Malformations Registry. For sport fish meals eaten during pregnancy, the odds ratio (OR) for all major malformations combined was slightly elevated for  $\leq 1$  meal/month (OR = 1.26, 95% confidence interval (CI): 0.84, 1.89) and  $\geq 2$  meals/month (OR = 1.51, CI = 0.74, 3.09), with no meals during pregnancy as the reference category. Higher ORs were consistently observed among male offspring compared with females. For  $\geq 2$  meals/month, the risk for males was significantly elevated (males: OR = 3.01, CI: 1.2, 7.5; females: OR = 0.73, CI: 0.2, 2.4). Exposure during pregnancy and effect modification by infants sex could be important considerations for future studies of birth outcomes associated with endocrine disruptors.

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**Keywords:** Birth defects; Effect modifiers (epidemiology); Endocrine system; Environmental pollutants; Pregnancy

## 1. Introduction

Consumption of contaminated sport fish from the Great Lakes has been associated with exposure to many persistent lipophilic chemicals including polychlorinated biphenyls (PCBs), polychlorinated dibenzo-*p*-dioxins (PCDDs), and pesticides such as dichlorodiphenyl dichloroethene (DDE), hexachlorobenzene, and mirex (Fitzgerald et al., 2001; Falk et al., 1999; Humphrey, 1988; Fiore et al., 1989; Hovinga et al., 1993; Kostyniak et al., 1999). PCBs, PCDDs, DDE, and other pesticides are known to cross the placenta and thereby serve as a prenatal source of exposure for the developing fetus (Kodama and Ota, 1977; Jacobson et al., 1984). These compounds may interfere with endocrine function (Daston et al., 1997; Peterson et al., 1993). The potential teratogenic effects of these exposures have been

**Abbreviations:** PCBs, Polychlorinated biphenyls; PCDDs, Polychlorinated dibenzo-*p*-dioxins; DDE, Dichlorodiphenyl dichloroethene; ICD 9, International classification of diseases; Ninth revision.

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observed in wildlife and laboratory animals, raising concern about human health effects (National Research Council, 1999). From a public health perspective, this body of evidence has resulted in fish consumption advisories that are issued by state and local governments. A national listing of fish and wildlife advisories indicates that most involve five primary contaminants: mercury, PCBs, chlordane, dioxins, and metabolites of dichlorodiphenyl trichloroethane, such as DDE (United States Environmental Protection Agency, 2003). These advisories typically recommend that women of reproductive age eat no fish from the most contaminated water bodies and eat limited amounts of other, less contaminated, sport fish.

PCBs, DDE, and certain other pesticides are persistent lipophilic compounds and will bioaccumulate with continued exposure (Humphrey, 1987). Exposure from contaminated fish consumption prior to pregnancy will result in a body burden of these persistent contaminants. In addition, contaminated sport fish meals cause a substantial acute increase in circulating blood levels of many potentially endocrine-disrupting compounds, levels far above the accumulated background body burden associated with chronic exposure (Humphrey, 1987, 1988). If this acute exposure occurs during a critical window of organogenesis, it may increase birth defect risk. Male fetuses may be more susceptible than female fetuses to potential perturbations in the hormonal milieu during pregnancy, since fetal androgens are critical for the normal development of the male urogenital organs.

The New York State Angler Cohort Study was implemented in 1991 to address the potential reproductive and developmental effects of contaminated sport fish consumption. The purpose of this analysis was to assess the relation between maternal consumption of sport fish meals and risk of major birth defects and to evaluate potential effect modification of this relationship by infant sex. This is the first North American epidemiologic study of sport fish consumption and birth defect risk.

## 2. Materials and methods

### 2.1. Study population

Details regarding the methods of the New York State Angler Cohort have been published elsewhere (Vena et al., 1996). Briefly, this was a population-based study of licensed anglers aged 18 to 40 years in 1991. All cohort members purchased fishing licenses in one of 16 New York State (NYS) counties surrounding Lakes Erie and Ontario and answered detailed mailed questionnaires including fish consumption and reproductive histories. Of 4229 children born to cohort members

between June 1986 and June 1991, 3758 (89%) had complete exposure and outcome data and 3366 (80%) also had complete data on potential confounders. Since neither exposures or outcomes would be independent among children born to the same mother, we restricted the analysis to the first child listed on each mother's questionnaire, resulting in 2237 (66%) of the children remaining in the analysis.

### 2.2. Exposure assessment

Sport fish consumption was ascertained at cohort enrollment in 1991 using a food frequency approach. Specifically, mothers were asked to "Please indicate the frequency with which you ate sport-caught fish from New York waters **when you were pregnant** (bold on questionnaire) anytime since June 1, 1986." This heading was followed by a request to indicate "Your average number of sport-caught fish meals eaten during pregnancy..." for each child listed. Three exposure categories were developed based on the distribution of values observed: no meals (reference), less than or equal to one meal per month, and two or more meals per month during pregnancy. This measure of fish consumption from New York waters represents a large range of potential exposure scenarios, since some fish are highly contaminated and others are not. No information was available on the specific species eaten or bodies of water fished for sport fish meals during pregnancy.

In addition to pregnancy meals, exposure was also characterized by the number of years the mother reported eating sport fish from Lake Ontario and its tributaries. Women were asked to check each year from 1955 to 1991 during which they ate Lake Ontario sport fish and the total number of years prior to the birth year of the index infant were summed for this variable. Duration was categorized into three groups based on the distribution of values: none (reference), 5 years or less, and 6 years or more. While current levels are declining, Lake Ontario sport fish were some of the most highly contaminated of all Great Lakes fish during this time, particularly with respect to dioxin (O'Keefe et al., 1983). This measure of duration reflects each mother's chronic body burden accumulated throughout her lifetime as well as her likelihood of compliance with fishing advisories. The NYS Department of Health Fishing Advisory recommends that children under 15 and women of reproductive age eat no sport fish of any species from Lake Ontario (New York State Department of Health, 2003), and this recommendation has been in place since 1976.

### 2.3. Outcome assessment

Newborn medical records were abstracted for 93% of all cohort children ( $n = 3910$ ). Over 1200 records with

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