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# Mercury diminishes the cardiovascular protective effect of omega-3 polyunsaturated fatty acids in the modern diet of Inuit in Canada<sup>☆</sup>

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## ABSTRACT

**Background:** Inuit in Canada have low reported incidence of myocardial infarction (MI) because of their traditional rich n-3 fatty acids marine diet. They are experiencing rapid nutrition transition and ischemic heart disease is now becoming a health concern.

**Objectives:** Our goal was to describe the modern Inuit diet, the eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and methyl mercury (MeHg) intake and estimate their contributions to the risk of MI. We also estimated the effect of promoting the consumption of more traditional food on Inuit's MI risk.

**Methods:** We estimated the effect of Inuit diet on MI risk with modelling. Model formulas and assumptions were extracted from various epidemiology studies and literatures. International Polar Year Inuit Health Survey (IHS) was a comprehensive health and nutrition survey conducted in 2007–8 with 2072 participants (aged 18–79) in Canada. Traditional food intake, blood biomarkers values from the IHS served as the baseline parameters of model input.

**Results:** Inuit traditional diet contained both high level of EPA, DHA and MeHg and their combined net effect was estimated to reduce the relative risk of MI by 1% for men and 2% for women. Arctic char meat provided the largest amount of EPA and DHA. Ringed seal liver was the main source for MeHg. Increase intake of selected fish, like salmon, herring and Arctic char by 75 g per day can reduce the relative risk of MI (RR 0.70, 0.78 and 0.90 respectively).

**Conclusions:** In the Inuit diet, the beneficial effect on MI of EPA and DHA is diminished by the adverse effect of MeHg. Promoting the increase consumption of fish species with high EPA+DHA and low MeHg may help to prevent MI among Inuit.

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## 1. Introduction

Inuit are a group Indigenous people sharing similar culture, heritage, and tradition (Inuit Tapiriit Kanatami, 2014). They have a total population around 200,000 and inhabit primarily in the Arctic regions of Greenland, Canada, Alaska, and Chukotka in Russia (Arctic Monitoring and Assessment Programme, 2009). The traditional Inuit diet is comprised of various marine mammals and

fish, which provide them excellent sources of protein, omega-3 polyunsaturated fatty acids (n-3 PUFAs) and vitamins (Kuhnlein and Chan, 2000). This diet pattern has been linked to high blood n-3 PUFAs levels and reduced risk of myocardial infarction (MI) (Daviglus et al., 1997). Besides the rich nutrients contained in the traditional foods, the hunting, preparing and sharing of these foods are also essential for Inuit to maintain their fitness and culture (Kuhnlein and Chan, 2000). Rapid environmental changes in the last two decades resulted in lifestyle change in Inuit. They shifted away from the traditional diet and became more sedentary (Egeland et al., 2011). Consequently, chronic conditions like obesity, diabetes and hypertension are becoming more prevalent in the Inuit communities (Brassard et al., 1993; Martinsen et al., 2006; Schumacher et al., 2003).

The cardiovascular protective effect of omega-3 polyunsaturated fatty acids (n-3 PUFAs), especially for eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) has been well documented (De Caterina, 2011; Mozaffarian and Rimm, 2014).

<sup>☆</sup> Arctic char: *Salvelinus alpinus*; Beluga: *Delphinapterus leucas*; DHA: docosahexaenoic acid; EPA: eicosapentaenoic acid; FFQ: food frequency questionnaire; Hg: mercury; IHS: International Polar Year Inuit Health Survey; ISR: Inuvialuit Settlement Region; MeHg: methyl mercury; MI: myocardial infarction; Narwhal: *Monodon monoceros*; n-3 PUFAs: omega-3 polyunsaturated fatty acids; RBC: red blood cell; RR: relative risk;

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Fish and shellfish are the most common sources of n-3 PUFAs (Kuhnlein and Chan, 2000). Various exposure assessment methods (e.g. food composition analysis; dietary intake assessment; biomarkers such as concentrations of EPA and/or DHA in plasma or red blood cell (RBC)) are commonly used to characterize n-3 PUFAs status (Lands, 1995). The inverse relationship between n-3 PUFAs and MI was first reported in Inuit from Greenland in 1970s (Bang et al., 1976; Dyerberg et al., 1978), and corroborated by numerous observational and intervention studies in other populations (Wang et al., 2006). The mechanism may involve preventing arrhythmias, lowering plasma triacylglycerol, decreasing blood pressure, decreasing platelet aggregation, improving vascular reactivity, and decreasing inflammation (Breslow, 2006).

The major route of Inuit exposure to methyl mercury (MeHg) is as also how most acquire n-3 PUFAs, i.e. through the consumption of contaminated fish and marine mammals (Chan and Egeland, 2004; Laird et al., 2013). Whole blood mercury (Hg), hair Hg and toenail Hg are the most commonly used biomarkers to estimate the biologically relevant internal dose of MeHg (Canuel et al., 2006). Fetuses, infants and children exposed to MeHg may exhibit impaired neurological development (Fernandes Azevedo et al., 2012). MeHg exposure can also induce oxidative stress, which in turn promotes inflammation and causes arrhythmias, hypertension and atherosclerotic plaque development (Houston, 2011). Consequently, long-term exposure to MeHg can increase the risk of cardiovascular diseases in the adults (Guallar et al., 2002). Increasing evidence regarding adverse cardiovascular effects of MeHg may undermine the cardio-protective, nutritional benefits conferred by Inuit traditional foods (FAO/WHO, 2010; Laird et al., 2013; Mahaffey et al., 2011). Moreover, dietary intakes of both n-3 PUFAs and MeHg are strongly dependant on the species of fish or marine mammals consumed as both concentrations vary greatly across different species (Mahaffey et al., 2011).

The primary objective of this study is to model the effect of modern Inuit diet on the relative risk of MI, using data on traditional food intake and blood biomarkers of nutrient/contaminant intake (RBC EPA+DHA and whole blood MeHg). The combined effect as well as the individual effects from n-3 PUFAs and MeHg were estimated separately to show the relative contribution of n-3 PUFAs and MeHg on the relative risk of MI. We further modelled the potential benefit of increasing intake of selected fishes with the highest EPA+DHA to MeHg ratios. The hypotheses are: 1) the net effects of n-3 PUFAs and MeHg intake from the modern Inuit diet on risk of MI is zero; and 2) there are food intake scenarios that can promote/increase the positive health effects of n-3 fatty acids.

## 2. Materials and methods

### 2.1. Sample design

The International Polar Year Inuit Health Survey (IHS) was conducted in Nunavut, Nunatsiavut and Inuvialuit Settlement Region (ISR) in Canada in 2007–2008. Details of the survey have been published elsewhere (Saudny et al., 2012). Inuit adults aged 18 and above were invited to participate in the survey. The survey covered traditional diet and nutrition, food insecurity, chronic diseases, anthropometric and lab measurements of health indicators, etc. All work was approved by the research ethics boards of the University of Northern British Columbia, McGill University and the University of Ottawa.

A total of 2595 Inuit adults agreed to participate in the survey, of whom 2172 provided blood samples and 2072 reported traditional food intake. A face-to-face food frequency questionnaire (FFQ) with 82 traditional food items was used to assess the traditional food intake during the past 12 month. The FFQ was a revised version of the Centre for Indigenous People's Nutrition and Environment's

Inuit traditional FFQ and has been validated and described elsewhere (Jamieson et al., 2012). The food lists were finalized through consultations with the IHS Steering Committees of the ISR, Nunavut, and Nunatsiavut. Pictures of species were provided to ensure appropriate documentation. For some traditional food items, the amount of intakes were truncated at the 90th percentile due to extremely high reported values. RBC fatty acids concentrations were measured by gas-liquid chromatograph according to predefined protocols at the Lipid Analytical Laboratories, University of Guelph Research Park (Zhou et al., 2011). Fatty acids were expressed as the percentage of total fatty acids in RBC phospholipids. Total blood Hg concentrations were measured by inductive-coupled plasma-mass spectrometry as described before (Laird et al., 2013).

### 2.2. Food nutrients and contaminant database

Mean EPA and DHA concentrations in listed traditional foods were extracted from the Canadian Nutrient File and a previously compiled database (Health Canada, 2014; Laird et al., 2013). Average values of EPA and DHA concentration were calculated when the serving status of food (e.g. raw, cooked, dried or frozen) was not specified in the FFQ, assuming equal consumption of each serving status. Mean total Hg concentrations (sum of inorganic Hg and methyl mercury) in various Arctic species were based on previously compiled databases (Chan, 1998; Laird et al., 2013). The arithmetic mean value was used when the Hg concentration differed among the 3 participating regions. Previous literature showed that the MeHg made up 80–95% of total Hg in fish or marine mammal meat and skin and 3–12% in marine mammal liver (Wagemann et al., 1998). We made a conservative assumption that 90% of total Hg was MeHg in the former and 12% respectively in the latter. For the small number of traditional foods without corresponding nutrients or Hg concentrations in the database, values from surrogate food items were used (Laird et al., 2013).

### 2.3. Statistical analyses

#### 2.3.1. EPA, DHA and Hg intake from Inuit traditional foods

Daily intake of EPA, DHA and MeHg from traditional foods were estimated with (Eqs. (1)–(3)), details of which has been described previously (Laird et al., 2013). The 25th and 75th percentiles of EPA, DHA, and MeHg concentrations were used to capture the uncertainty of exposure through diet. We also did a top 10 consumed foods subtotal as they composed majority of the total. Average intake of particular food was calculated using the responses of survey participants (n=2072) who reported consuming at least one traditional food. All the consumption data were averaged to represent the intake during the entire year, avoiding the seasonal fluctuation. Men and women were analyzed separately.

$$\text{MeHg Intake} = \sum_i^{82} \text{food}_i (\text{g/day}) \times [\text{MeHg}_i] (\mu\text{g/g}) \quad (1)$$

$$\text{EPA Intake} = \sum_i^{82} \text{food}_i (\text{g/day}) \times [\text{EPA}_i] (\mu\text{g/g}) \quad (2)$$

$$\text{DHA Intake} = \sum_i^{82} \text{food}_i (\text{g/day}) \times [\text{DHA}_i] (\mu\text{g/g}) \quad (3)$$

#### 2.3.2. EPA plus DHA to MeHg ratio of traditional food

Ratios of EPA+DHA to MeHg were calculated for the top 10 consumed foods, along with the next 5 most frequently consumed traditional foods in the survey with high n-3 concentrations (salmon, herring, whitefish, trout and beluga blubber). The food species with higher EPA+DHA to MeHg ratio may be more protective for cardiovascular health (Mahaffey et al., 2011).

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