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# Risk tradeoffs associated with traditional food advisories for Labrador Inuit

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ABSTRACT

The traditional Inuit diet includes wild birds, fish and marine mammals, which can contain high concentrations of the neurotoxicant methylmercury (MeHg). Hydroelectric development may increase MeHg concentrations in traditional foods. Consumption advisories are often used to mitigate such risks and can result in reduced intake of traditional foods. Data from a dietary survey, MeHg exposure assessment and risk analysis for individuals in three Inuit communities in Labrador, Canada ($n$ = 1145) in 2014 indicate reducing traditional food intake is likely to exacerbate deficiencies in n-3 polyunsaturated fatty acids and vitamins B12 and B2. Traditional foods accounted for < 5% of per-capita calories but up to 70% of nutrients consumed. Although consumption advisories could lower neurodevelopmental risks associated with an increase in MeHg exposure (90th-percentile ΔIQ = − 0.12 vs. − 0.34), they may lead to greater risks of cardiovascular mortality (90th-percentile increase: + 58% to + 116% vs. + 25%) and cancer mortality (90th-percentile increase + 2% to + 4% vs. no increase). Conversely, greater consumption of locally caught salmon mostly unaffected by hydroelectric flooding would lower all these risks (90th-percentile ΔIQ = + 0.4; cardiovascular risk: − 45%; cancer risk: − 1.4%). We thus conclude that continued consumption of traditional foods is essential for Inuit health in these communities.

## 1. Introduction

Traditional foods consumed by northern Inuit populations include locally caught fish, birds and marine mammals. These foods are critical sources of micronutrients and high-quality protein in regions that have limited access to other fresh foods. However, some traditional foods contain elevated concentrations of contaminants such as methylmercury (MeHg) that biomagnify in aquatic environments (AMAP, 2015). MeHg exposures among indigenous populations across Canada tend to be higher than the national average due to relatively greater consumption of fish and marine mammals (Lye et al., 2013; Van Oostdam et al., 2005). Fish consumption advisories are a common policy response to elevated environmental levels of MeHg (Passos and Mergler, 2008; Hydro-Québec, 2013; Hydro-Québec Production, 2014; ASS, 2013). However, even targeted food advisories can lead to decreased overall consumption of seafood (Shimshack and Ward, 2010; Teisl et al., 2011). In indigenous populations, some food consumption advisories related to elevated MeHg levels have led to decreased overall consumption of seafood (Furgal et al., 2005; Wheatley and Paradis, 1996).

MeHg has a half-life of 50–70 days in the human body and thus dietary changes can alter exposures over shorter timescales than many other hydrophobic organic pollutants such as polychlorinated biphenyls (PCBs) that persist in the body for decades (Li et al., 2016a; Binnington et al., 2014). Negative effects of MeHg exposure on the brain of the developing fetus and young children have been shown to persist into adulthood and this is the endpoint used by most regulatory agencies to establish risk thresholds (Karagas et al., 2012; Debes et al., 2016; US EPA, 2002). An association between elevated prenatal MeHg exposures and neurodevelopmental impairment has similarly been shown among Inuit children (Boucher et al., 2012; Weihe et al., 2016). MeHg exposure has also been associated with cardiovascular health risks for adults (Virtanen et al., 2007; Farina et al., 2011; Salonen et al., 1995; Roman et al., 2011).

Dietary advice to indigenous populations must balance the competing goals of minimizing contaminant exposures with ensuring nutritional sufficiency (Furgal et al., 2005; Wheatley and Paradis, 1996; Laird et al., 2013). Thus, quantitative studies quantifying the likely health risks or benefits from different dietary interventions among indigenous populations are needed and are the focus of this work. Past studies have examined risk tradeoffs between increased MeHg exposure and n-3 polyunsaturated fatty acids (n-3 PUFAs) in seafood (EFSA,

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2014; Ginsberg and Toal, 2009; Stern and Korn, 2011; Mahaffey et al., 2011). Cardiovascular and neurodevelopmental benefits of n-3 PUFAs can offset negative impacts of MeHg exposure (Mahaffey et al., 2011). The World Health Organization (WHO) and the Food and Agriculture Organization (FAO) have however recommended that risk-benefit evaluations for seafood consumption consider a broader suite of nutrients, including iron, zinc, and vitamins A, D, B2 and B12 (FAO, 2010).

Dietary changes exert changes on health endpoints through diverse, competing mechanisms. For example, red and processed meats increase cardiovascular risks by triggering the formation of proartherosclerotic trimethylamines and raise colorectal cancer risks through production of carcinogenic N-nitroso compounds in the gastrointestinal tract (Threapleton et al., 2013; Whelton et al., 2012; Koeth et al., 2013). Conversely, fruits, vegetables and nuts are rich in compounds that reduce cardiovascular risks by inhibiting platelet aggregation and oxidation of arterial cholesterol (antioxidants and polyphenols), mediating glucose homeostasis (fiber) and regulating blood pressure (potassium and magnesium) (Wang et al., 2014; Blomhoff et al., 2006; Ludwig et al., 1999; Kelly and Sabaté, 2006; Rissanen et al., 2003). There is strong evidence that vitamin D exerts a generalized cancer-protective effect through the apoptotic and antiangiogenic properties of its metabolite 1,25$(OH)_2$D (Giovannucci, 2005; Giovannucci et al., 2006; Grant, 2010). The Global Burden of Disease study synthesizes the most well-established causal relationships between intake of various foods and nutrients and different cancers and cardiovascular diseases (Forouzanfar et al., 2016).

Here, we use results from a dietary survey and food subsidy data to better understand consumption preferences and the nutritional importance of locally harvested foods for three Inuit communities in the Lake Melville region of Labrador, Canada. In this region, local Inuit are concerned about potential increases in MeHg exposure from traditional foods following completion of a hydroelectric power facility upstream of their traditional hunting and fishing territory. Flooding of hydroelectric reservoirs leads to a pulse in MeHg production in the saturated soils, which can enter the overlying water and accumulate in fish and wildlife. In previous work, we estimated increases in MeHg concentrations of traditional foods at their peak due to the local hydroelectric development using a biogeochemical model (Calder et al., 2016). Expected mean of modeled peak increases in ranged from nine times 2014 levels for some freshwater species most affected by the hydroelectric development to zero for offshore marine species (Calder et al., 2016).

In this study, we conduct a screening level analysis of potential risks associated with higher MeHg concentrations in traditional foods. We compare the estimated magnitudes of projected MeHg exposure risks to those attributable to changes in nutrient intake following a dietary transition away from traditional foods using established dose-response relationships. We conduct this analysis to better understand potential health implications of dietary consumption advisories for indigenous populations more generally.

## 2. Methods

### 2.1. Food frequency questionnaire and hair Hg analysis

We developed a food frequency questionnaire (FFQ) to measure intake of traditional foods and store-bought seafood among Labrador Inuit settled in three communities downstream from the Churchill River: 1) Happy Valley – Goose Bay, 2) North West River, and 3) Rigolet (SI Fig. S1). We enrolled a total of 1145 individuals, representing roughly 40% of the Inuit population in these communities (SI Table S1). Responses were weighted by demographic categories according to the 2011 Census to provide statistically relevant estimates for the whole population (SI Table S2) (Statistics Canada, 2011). A team of 26 trained research assistants recruited from the Inuit community administered the survey instrument.

The FFQ asked respondents to recall their intake of 64 traditional foods (locally caught seafood, land mammals, birds, plants and berries) and 24 store-bought seafood types over 24-h, one-month and three-month recall periods. Foods measured by the FFQ are listed in SI Tables S3 (locally caught seafood), S4 (other locally caught foods) and S5 (store bought seafood). The FFQ was administered across three seasons to assess seasonal variability in consumption preferences: Winter (March–April, $n = 231$), Spring (June–July, $n = 294$), and Summer (August–September, $n = 1054$). Enrollment was maximized for the Summer survey period, which we use for risk calculations unless otherwise noted. Self-reported age, sex, height and weight was included in the survey. All FFQ respondents in the Spring and Summer periods were asked to provide hair samples. In total, 656 hair samples corresponding to 571 unique individuals were collected (157 in Spring and 499 in Summer).

All work involving human subjects (recruitment, survey design, data analysis and reporting) was reviewed and approved by the Office of Human Research Administration at the Harvard T.H. Chan School of Public Health, the Newfoundland and Labrador Health Research Ethics Authority and the Nunatsiavut Government Inuit Research Advisor. The Nunatsiavut Government provided input on all research plans and has assumed responsibility for disseminating research findings to community members and provincial and federal policymakers (Durkalec et al., 2016a, 2016b). Additional information on the FFQ design and implementation, participant recruitment and hair Hg analysis is provided in the SI.

### 2.2. Modeled MeHg exposures

We modeled MeHg exposures for all Inuit individuals in 2014 using dietary recall data for the 88 traditional and store-bought foods and associated MeHg concentrations (modeled as lognormal distributions). For locally caught foods, we directly measured MeHg concentrations in 22 species representing 81% of per-capita MeHg exposures from this category in 2014. All data sources for MeHg concentrations were originally reported by Li et al. (2016b) and Calder et al. (2016) and are provided in SI Tables S3 (locally caught seafood), S4 (other locally caught foods) and S5 (store-bought seafood).

To correct for overreporting bias associated with species-specific recall, we scaled reported species-specific intakes to match reported total consumption of three food categories (local seafood, store-bought seafood and other locally caught foods) following Lincoln et al. (2011) We probabilistically simulated hair mercury concentrations (10,000 Monte Carlo trials) for each individual using the one-compartment model developed by the U.S. Environmental Protection Agency lognormal distributions for MeHg concentrations in food items (Tables S3–S5), and probabilistically distributed toxicokinetic parameters (Stern, 1997), following Li et al. (2016a)

The median ratio between measured hair Hg and simulated hair Hg was 0.96 in the larger-scale Summer survey period, suggesting that there is very little bias in the dietary model we developed (measured-to-modeled ratio close to 1). To ensure that population-wide MeHg exposures are not overestimated by the dietary model, modeled seafood intake was scaled such that simulated hair Hg matched measured Hg for all individuals with available hair Hg data. For others, seafood intake was scaled by the median bias (0.96).

### 2.3. Dietary intake of other foods

We estimated consumption of market foods other than seafood that have high nutritional content using sales data for the community of Rigolet for the same years as our dietary survey (2014–2015) (AANDC, 2016). Data on the edible supply of foods have been successfully used to estimate dietary composition and caloric sufficiency in other populations (Douglass et al., 1997; Sunderland, 2007; Sunderland et al., 2018). Data were obtained from a Canadian federal subsidy program (Nutrition North), which subsidizes 42 nutrient-dense and perishable store-bought foods or food categories in remote communities (Government of Canada, 2017). We estimated population-wide intake of nutrient-dense store-bought foods based on the magnitude of food subsidies and by subtracting retail and consumer waste fractions (Gustavsson et al., 2011) (SI Table S6). We assumed the composition of market foods sold in Rigolet was similar for the other two communities (Happy Valley-Goose Bay, Northwest River). Since traditional food intake was smaller in these communities in 2014, we allowed for proportionally greater consumption of store-bought nutrient-dense foods.

We used the relationship developed by Mifflin et al. (1990) that has been applied among indigenous populations (Kattelmann et al., 2010) to estimate total energy expenditure (*E*) of each Inuit individual based on self-reported body mass, height, and age from survey data (Eq. (1)):

$$E = (9.99W + 6.25H - 4.92A + 166\alpha)\beta \quad (1)$$

where *W* is body mass (kg), *H* is height (cm), *A* is age (years) and $\alpha = 1$ and $\beta = 1.7$ for men and $\alpha = 0$ and $\beta = 1.6$ for women. For each individual, the difference between estimated energy expenditure and the caloric intake accounted for by locally caught traditional foods (data from the FFQ) and nutrient-dense market foods (data from Nutrition North) was assumed to correspond to comparatively nutrient-sparse foods such as potato chips and sweetened beverages. There are very few foods that do not qualify for Nutrition North subsidies that have nutritional value and, in other Inuit populations, they are not widely consumed (Sheehy et al., 2014).

### 2.4. Nutritional content of store bought foods

We used the Canadian Nutrient File (Health Canada, 2018) to estimate nutrient intake from store-bought nutrient-dense foods and traditional foods. Government nutritional databases include traditional and market foods consumed by Inuit populations and have been successfully used to estimate population-wide nutrient intake for other indigenous groups (e.g., Quebec Inuit) (Rochette and Blanchet, 2004). Five foods with no data were matched to foods in the United States Department of Agriculture (USDA) Nutrient Database (USDA, 2017). Nutrient contents were available for 90% of foods by calories. For other foods, the average nutrient content of similar food categories was used. For this purpose, we group all foods (traditional and store-bought together) according to the following food categories: dairy, egg, fish liver, fish muscle, fish roe, fowl/poultry, fruit, grain, marine mammal, processed meat, red meat, shellfish, terrestrial mammal and vegetables. The compiled database of nutritional information for all foods studied here is included in the SI (Excel file: Appendix A, SI Table S6). We consider that dietary supplementation has a negligible impact on population-wide nutrient intake because dietary supplement tends to be rare among indigenous populations (Kuhnlein et al., 2008; Schaefer et al., 2011; Lepage et al.).

### 2.5. Traditional food substitution scenarios

We developed five traditional food substitution scenarios to bound the possible range of dietary changes that might occur in the future. These are: (1) Traditional foods are replaced by nutrient-dense store-bought foods subsidized by the Nutrition North program (SI Fig. S2). (2) Traditional foods are replaced by processed meat as an alternative protein source. (3) Traditional foods are replaced by vegetables. This scenario was used to provide a lower bound of nutritional risks. However, the Nunatsiavut Government identified this scenario as highly unlikely given current consumption preferences. We nevertheless include it as a best-case scenario for market-based food substitution. (4) Traditional foods are replaced by nutrient-sparse foods such as snack foods. (5) Traditional foods high in MeHg are substituted with Atlantic salmon. The Nunatsiavut Government identified Atlantic salmon as a preferred food item. We use this scenario to investigate the health impacts of traditional diet adaptation instead of replacement with store-bought foods. For all scenarios, caloric consumption is assumed to be constant at the estimated 2014 values based on Eq. (1) above.

### 2.6. Screening-level risk assessment

We quantified the magnitudes of neurodevelopmental, cardiovascular and cancer risks associated with the five dietary scenarios described above and compared them to those associated with projected future MeHg exposures at 2014 diet. Projected future MeHg exposures result from increased MeHg content in traditional foods as a result of upstream hydroelectric development calculated by Calder et al. (2016). The probabilistic projections of future MeHg levels in local traditional foods are included in SI Table S7. We do not consider cancer risks associated with MeHg in traditional foods because the U.S. EPA classifies MeHg as a possible human carcinogen, noting there is 'no persuasive evidence' for human carcinogenicity (US EPA, 2002).

Neurodevelopmental risks to children are expressed in terms of change in IQ and are modeled by considering diets of women of childbearing age (16–49 following McDowell et al., 2004). We retain the confounder-adjusted dose-response functions summarized in Table 1. We express cardiovascular and cancer risks as the relative risk (RR) of mortality compared to 2014, calculated from changes in intake of various foods and nutrients. A RR of greater than 1.0 represents an increase in risk, and a RR of less than 1.0 represents a decrease in risk.

Cardiovascular and cancer risks are quantified as the product of individual confounder-adjusted relationships following Fleming et al. (1999). RRs are presented in the literature corresponding to certain incremental doses. We assume these are proportional over the range of incremental changes explored here and scale RRs presented in the literature to changes in food substitution scenarios. We consider relative risks for cardiovascular and cancer deaths based on diet for all individuals over 25 following Forouzanfar et al. (2015). Dose-response functions for cardiovascular and cancer mortality are expressed in terms of risks of more specific causes of death (e.g., risk of cancer at certain sites). We consider the share of overall cardiovascular (Table 2) and cancer (Table 3) mortality represented by the outcome in each dose-response relationship in order to calculate net impacts on the risk of total cardiovascular and cancer mortality. A mathematical derivation (Eqs. S1–S3) is presented in the SI.

Dietary dose-response functions for risk of cardiovascular and cancer death are based on the Global Burden of Disease study (Forouzanfar et al., 2016). We excluded benefits related to increased whole grain consumption because we could not quantify the ratio of whole to processed grains in the baseline diet and intake of whole grains is small in similar northern indigenous populations (Kuhnlein et al., 2008; Gates et al., 2015). We account for cardiovascular risks associated with consumption of red and processed meats and benefits of fruits, nuts and vegetables as a function of intake of the whole food and thus do not separately consider constituent nutrients in these foods (e.g., sodium in red meat). There is strong evidence that vitamin D exerts a generalized cancer-protective effect, especially in northern

**Table 1**
Summary of dose-response relationships used for screening-level risk assessment of neurodevelopmental risk.

| Predictor | Outcome | Dose-response function[a] | Reference |
|---|---|---|---|
| MeHg | IQ points | 1.07 per 0.5 g Hg $g^{-1}$ hair (95% CI: 1.03–1.11) | Virtanen et al., 2007 |
| n − 3 PUFAs | IQ points | mode = +1.3; min = 0.8; max = 1.8 per g DHA $day^{-1}$ | Cohen et al., 2005 |

[a] MeHg dose-response function is normal distribution and n-3 PUFA dose-response function is triangular distribution following the authors. Risks accrue to children born to mothers (females aged 16–49) with modeled intakes.

**Table 2**
Summary of lognormally distributed dose-response relationships used for screening-level risk assessment risk of cardiovascular mortality.

| Predictor | Outcome | Median (95% CI) relative risk per change (+) in intake | Reference |
|---|---|---|---|
| MeHg | SCD[b] | 1.07 (1.03–1.11) per 0.5 g Hg $g^{-1}$ hair | Virtanen et al., 2007 |
| n − 3 PUFAs[a] | IHD[c] | 0.866 (0.792–0.943) per 0.1 g $day^{-1}$ | Forouzanfar et al., 2016; Chowdhury et al., 2012 |
| Fiber | IHD[c] | 0.754 (0.678–0.831) per 20 g $day^{-1}$ | Threapleton et al., 2013; Forouzanfar et al., 2016 |
| Fruit | IHD[c] | 0.867 (0.829–0.962) per 100 g $day^{-1}$ | Wang et al., 2014; Forouzanfar et al., 2016 |
| Fruit | IS[d] | 0.719 (0.604–0.8401) per 100 g $day^{-1}$ | Forouzanfar et al., 2016; Hu et al., 2014 |
| Fruit | HS[e] | 0.868 (0.661–0.762) per 100 g $day^{-1}$ | Forouzanfar et al., 2016; Hu et al., 2014 |
| Nuts | IHD[c] | 0.944 (0.845–0.914) per 4.05 g $day^{-1}$ | Forouzanfar et al., 2016; Afshin et al., 2014 |
| Processed meat | IHD[c] | 1.603 (1.022–2.271) per 50 g $day^{-1}$ | Forouzanfar et al., 2016; Micha et al., 2010 |
| Trans fatty acids | IHD[c] | 1.414 (1.281–1.567) per 2% energy intake[f] | Forouzanfar et al., 2016; Mozaffarian and Clarke, 2009 |
| Vegetables | IHD[c] | 0.96 (0.93–0.99) per 106 g $day^{-1}$ | Wang et al., 2014 |
| Vegetables | IS[d] and HS[e] | 0.89 (0.81–0.98) per 200 g $day^{-1}$ | Hu et al., 2014 |

[a] As DHA + EPA.
[b] Sudden cardiac death represents 27.4% of total cardiovascular mortality (CDC, 2010).
[c] Ischemic heart disease represents 70% of total cardiovascular mortality (CDC, 2010).
[d] Ischemic stroke represents 13% of total cardiovascular mortality (CDC, 2010).
[e] Hemorrhagic stroke represents 6% of total cardiovascular mortality (CDC, 2010).
[f] Total daily energy intake calculated from Mifflin et al. (1990) as described in methods and assuming 9 kcal $g^{-1}$ trans fatty acids (Drewnowski, 1992).

populations (Giovannucci, 2005; Giovannucci et al., 2006; Grant, 2010). We thus also consider a negative association between vitamin D and risk of cancer mortality (Kuhnlein and Chan, 2000) following earlier work by Grant et al. (2010) who calculated cancer mortality in Canada attributable to vitamin D deficiency. This analysis is carried out using probabilistically distributed parameters for relative risk of cancer and cardiovascular effects and for IQ gains and decrements, allowing for explicit calculation of the uncertainties inherent to this analysis.

## 3. Results and discussion

### 3.1. Methylmercury exposures in 2014 among Lake Melville Inuit

Measured Hg concentrations in the hair of Inuit individuals participating in our survey ranged from 6.8 ng $g^{-1}$ to 6200 ng $g^{-1}$. We find that between 67% (spring) and 71% (summer) of all measured hair Hg samples fall within the modeled ranges of exposure (Fig. 1, green circles). This is better than many recent surveys (Lincoln et al., 2011; Canuel et al., 2006; Gosselin et al., 2006; Sirot et al., 2008) and may reflect lower inter-individual variability in pharmacokinetics among a relatively homogeneous survey population and the relatively smaller range of available fish with more consistent bioaccessibility (Li et al., 2016a; Basu et al., 2014). The Inuit Health Study (IHS) previously characterized MeHg exposures among Inuit in the community of Rigolet and other communities on the Labrador Coast but excluding Happy Valley – Goose Bay and North West River. The geometric mean blood Hg (3.2 μg $L^{-1}$) reported in the IHS is equivalent to approximately 0.8 μg $g^{-1}$ hair (WHO, 1990; Chan, 2011a) and compares well to Spring and Summer mean hair levels (0.77 μg $g^{-1}$) measured in this study in Rigolet. MeHg exposures measured in 2014 are generally lower than other Inuit populations. For instance, the IHS reported geometric mean blood Hg equal to 9.0 μg $L^{-1}$ for Inuit in Nunavut (Chan, 2011b), while Dewailly et al. (2004) reported a geometric mean of 10.8 μg $L^{-1}$ for the Inuit of Nunavik (northern Quebec).

Exposures to MeHg of during the Summer survey period in 2014 were approximately double the median exposure of the general Canadian population (Lye et al., 2013; Stern, 1997). However, the majority of individuals in the survey population fall below the reference dose (RfD) for exposure established by the U.S. EPA of 0.1 μg $kg^{-1}$ $day^{-1}$ and Health Canada's provisional tolerable daily intake (pTDI) of 0.2–0.47 μg $kg^{-1}$ $day^{-1}$ (Fig. 2, SI Table S8) (Health Canada, 2017). Across the three Inuit communities, only individuals above the 90th percentile of MeHg exposures had daily intake levels that exceeded the U.S. EPA's RfD (Fig. 2). For example, the 95th percentile of MeHg exposures ranged from 0.10 μg $kg^{-1}$ $day^{-1}$ in Happy Valley–Goose Bay to 0.27 μg $kg^{-1}$ $day^{-1}$ in Rigolet, and 0.12 μg $kg^{-1}$ $day^{-1}$ when averaged across the three communities. In Summer 2014, the fractions of Lake Melville Inuit exceeding the Health Canada pTDI and the US EPA RfD were approximately 1% and 7% respectively (SI Table S8). For all survey periods, older individuals, men, and individuals residing in the community of Rigolet have higher MeHg exposures (SI Table S8). Therefore, in 2014, risks associated with MeHg exposures were generally low and concentrated among individuals at higher exposure percentiles.

Individuals with the highest MeHg exposures in 2014 had the highest intake of traditional foods. Per-capita, roughly 70% of all MeHg

**Table 3**
Summary of lognormally distributed dose-response relationships used for screening-level risk assessment of risk of cancer mortality.

| Predictor | Cancer site (mortality) | Median (95% CI) relative risk per change (+) in intake | Reference |
|---|---|---|---|
| Calcium | Colon/rectum[a] | 0.729 (0.831–0.963) per 1 g $day^{-1}$ | Forouzanfar et al., 2016; WCRF, 2015 |
| Fiber | Colon/rectum[a] | 0.809 (0.741–0.882) per 20 g $day^{-1}$ | Forouzanfar et al., 2016; WCRF, 2015 |
| Fruit | Esophagus[b] | 0.867 (0.776–0.968) per 100 g $day^{-1}$ | Forouzanfar et al., 2016; Liu et al., 2013 |
| Fruit | Trachea/bronchus/lung[c] | 0.929 (0.890–0.970) per 100 g $day^{-1}$ | Forouzanfar et al., 2016; Vieira et al., 2015 |
| Milk | Colon/rectum[a] | 0.898 (0.831–0.963) per 226.8 g $day^{-1}$ | Forouzanfar et al., 2016; WCRF, 2015 |
| Processed meat | Colon/rectum[a] | 1.179 (1.092–1.267) per 50 g $day^{-1}$ | Forouzanfar et al., 2016; WCRF, 2015 |
| Red meat | Colon/rectum[a] | 1.167 (1.033–1.309) per 100 g $day^{-1}$ | Forouzanfar et al., 2016; WCRF, 2015 |
| Sodium | Stomach[d] | 1.18 (1.02–1.38) per 1 g $day^{-1}$ | Forouzanfar et al., 2016; WCRF, 2015 |
| Vegetables | Esophagus[b] | 0.840 (0.780–0.920) per 100 g $day^{-1}$ | Forouzanfar et al., 2016; Liu et al., 2013 |
| Vitamin D | General | 0.69 (0.55–0.86) per 1429 IU $day^{-1}$ | Garland et al., 2007 |

[a] 9.1% of total cancer mortality (Howlader et al., 2016).
[b] 2.4% of total cancer mortality (Howlader et al., 2016).
[c] 26.6% of total cancer mortality (Howlader et al., 2016).
[d] 1.9% of total cancer mortality (Howlader et al., 2016).

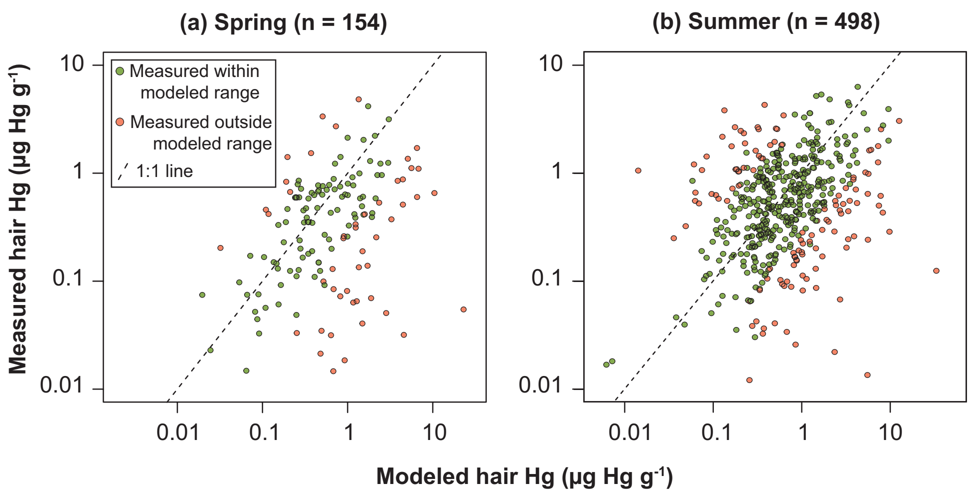


**Fig. 1.** Comparison of measured and probabilistically modeled hair Hg concentrations for Labrador Inuit in the Lake Melville Region during Spring and Summer survey periods. Green circles indicate measured values that fall within the modeled range. Red circles indicate measured values that fall outside the probabilistically modeled range of hair Hg concentrations. Individuals who did not report consuming seafood, birds or marine mammals (8 in Spring, median hair Hg = 0.036 µg g$^{-1}$ and 26 in Summer, median hair Hg = 0.049 µg g$^{-1}$) are excluded. $R^2$ = 0.13 (Spring), 0.11 (Summer). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

intake came from traditional foods. Among individuals with MeHg exposures ≥ 90th percentile, 90% of all MeHg intake came from traditional foods. In Summer 2014, individuals in the lowest quartile of traditional food intake (≤ 6.86 g day$^{-1}$) received 24% of their MeHg exposure from traditional foods compared to 80% among the highest quartile (> 41.1 g day$^{-1}$). Median MeHg exposure was 0.043 µg kg$^{-1}$ day$^{-1}$ for individuals in the highest quartile of traditional food consumption compared to 0.003 µg kg$^{-1}$ day$^{-1}$ among individuals in the lowest intake quartile. Mean MeHg per-capita exposures in the Summer survey period (0.035 µg kg$^{-1}$ day$^{-1}$) were significantly different from the Spring period (0.024 µg kg$^{-1}$ day$^{-1}$, $p < 0.001$, Wilcox rank-sum test) but not the Winter (0.046 µg kg$^{-1}$ day$^{-1}$$p > 0.05$). This mirrors trends in traditional food intake. Mean traditional food consumption was significantly lower in the Spring period (28.5 g day$^{-1}$) compared to the Summer period (36.52 g day$^{-1}$, p < 0.001, Wilcox rank-sum test). Mean traditional food consumption in Winter was 38.7 g day$^{-1}$ but was not statistically different from either Spring or Summer. Therefore, while population-wide MeHg exposure risks are generally low, these risks are sensitive to the MeHg content of local foods.

Although locally caught Atlantic salmon is relatively low in MeHg (Table S3), it was the single greatest contributor to overall MeHg intakes in all three communities including among individuals with MeHg exposures ≥ 90th percentile (24–29% of overall per-capita intake across communities in Summer 2014). Other foods contributing more than 5% to overall MeHg intakes in Summer 2014 were brook trout, Atlantic cod, tern eggs, duck and seal muscle (locally caught) and fresh cod, canned tuna and fresh tuna (store-bought). Individuals with MeHg exposures ≥ 90th percentile had similar sources of MeHg intake as the study population as a whole. SI Fig. S2 presents the breakdown of per-capita MeHg sources in Summer 2014 for all individuals in the three communities studied and for individuals in all communities with MeHg exposures ≥ 90th percentile.

### 3.2. 2014 diet composition

Survey data from the summer of 2014 suggest 91% of the

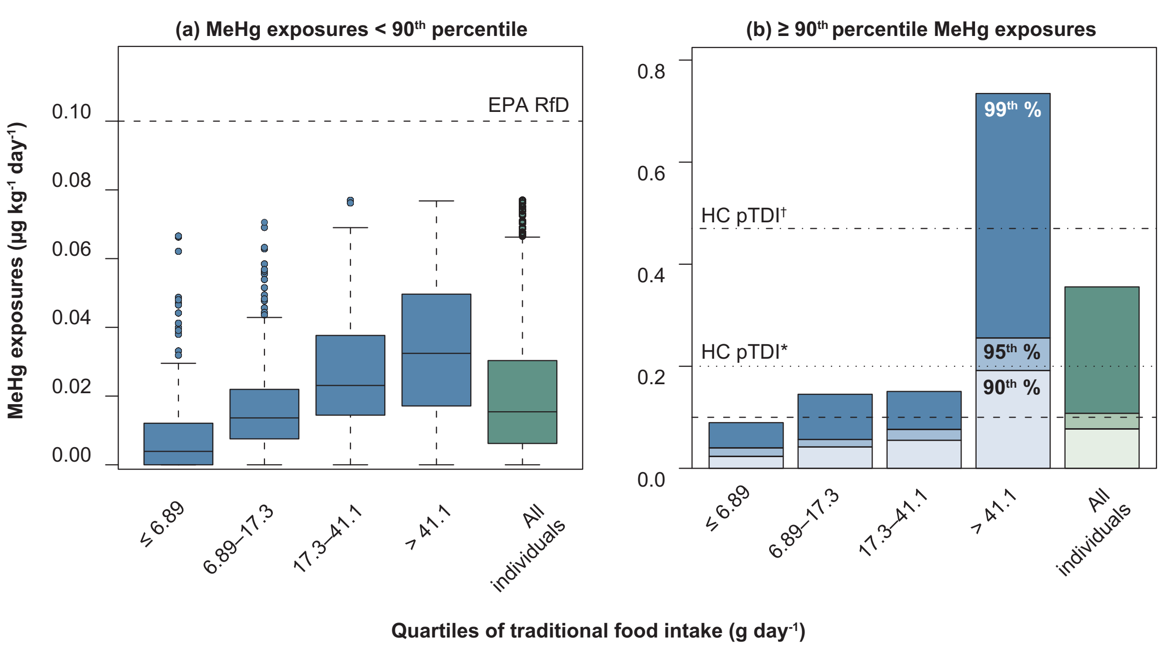


**Fig. 2.** Distributions of MeHg exposures for Inuit in the Lower Lake Melville Region of Labrador by quartile of traditional food consumption (Summer 2014). Panel (a) shows values below the 90th percentile of MeHg exposures and Panel (b) shows the distribution for highly exposed individuals in the population (at or above 90th percentile of MeHg exposures). EPA RfD denotes the U.S. EPA reference dose for methylmercury and HC pTDI indicates the Health Canada provisional tolerable daily intakes for women of childbearing age and children (*) and for everyone else (†).

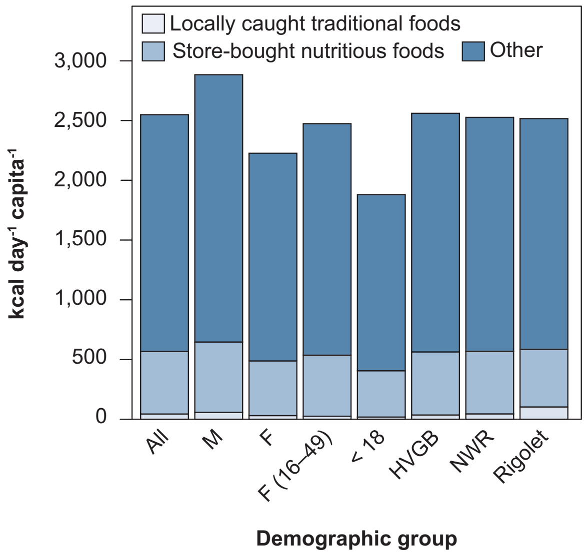


**Fig. 3.** Estimated contributions of different food types to total calories consumed by Inuit in the Lower Lake Melville region of Labrador, Canada. M = male; F = female; HVGB = Happy Valley – Goose Bay; NWR = North West River.

population consumes traditional foods. However, these foods are only account for approximately 2% of mean caloric intake and 11% for the 95th percentile consumer (Fig. 3). Across the three communities, consumption of traditional foods is highest in Rigolet (mean = 4% of total calories) and lowest in Happy Valley–Goose Bay (mean = < 1% of total calories) (Fig. 3). Prior work has reported similar findings for other Inuit communities, with higher rates of country food consumption in more northern communities that have less access to market alternatives (Chan, 2011a).

Using food subsidy data, we estimate that store-bought nutrient-dense foods account for 25% of total per-capita caloric intake. SI Fig. S3 presents the composition of this nutrient-dense store-bought food component of the diet. For store-bought seafood, dietary survey data agree to within 12% of estimates based on the food subsidy program data, providing partial validation of this method. The remaining fractions of all caloric consumption estimated from individual body weight must come from store bought food such as nutrient-sparse snack foods and sweetened beverages. We estimate that these other foods account for approximately 70% of all calories consumed across demographic groups. These findings agree with prior research that has reported Inuit populations consume traditional foods, fruits and vegetables only one third as frequently as foods with low nutrient content (Hopping et al., 2010).

Types of traditional foods consumed by individuals vary widely (Fig. 4). On a per-capita basis across the three communities, 90% of the calories from traditional foods are derived from 24 foods. Some traditional foods such as berries and seal blubber contain negligible quantities of MeHg (Fig. 4). Foods with negligible MeHg account for 40% of the total calories from traditional foods for all individuals surveyed (Fig. 5). On a per-capita basis, 11 of the 24 major traditional foods consumed contain negligible amounts of MeHg. Survey data indicate that the greatest diversity in traditional food consumption occurs among individuals with the highest MeHg exposures (Fig. 2b). Among the most highly exposed individuals to MeHg (90th percentile), traditional foods with negligible MeHg content account for only 28% of total calories (nine foods). Among all individuals, including among individuals with MeHg exposures greater than the 90th percentile, the most widely consumed traditional foods with negligible MeHg were berries, goose, partridge, moose, caribou, seal blubber and rabbit.

Consumption of traditional foods increases linearly with age, with each year of age associated with a 0.8 g $day^{-1}$ increase in traditional food intake ($R^2 = 0.10$, $p < 0.001$). Traditional foods supply a significantly higher fraction of dietary calories for men (mean = 1.9%) compared to women (mean = 1.4%, $p < 0.001$, SI Table S9). Per-capita caloric significance is reported in the SI for locally caught traditional seafood (Table S3), other locally caught traditional food (Table S4), store-bought seafood (Table S5) and other store-bought nutritious foods (Table S6).

### 3.3. Importance of traditional foods for intake of nutrients

Despite their low contribution to total caloric intake, traditional foods are the predominant source of several key nutrients (Fig. 5). Traditional foods supply approximately 70% of the n-3 PUFAs eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) across the population (Fig. 5). They are an important source of vitamins D (35%), B12 (19%), B6 (6%), A (16%), B2, B3 and C and iron (7%), and zinc (5%). Baseline dietary analysis suggests that intake on average across the population of iron, n-3 fatty acids, vitamins A, B2 and B12 and zinc are currently below dietary reference values (Kris-Etherton et al., 2009; US FDA, 2013). Other studies have similarly found traditional foods are richer in these nutrients than the market-based components of indigenous diets (Gagné et al., 2012; Kuhnlein and Receveur, 2007; Nakano et al., 2005; Sheehy et al., 2015).

### 3.4. Nutritional impact of traditional food substitution scenarios

While 2014 MeHg exposures were generally low, these exposures are likely to increase as a result of upstream hydroelectric development (Calder et al., 2016). Food consumption advisories are commonly used to control these risks but have unpredictable effects (Passos and Mergler, 2008; Furgal et al., 2005; Wheatley and Paradis, 1996). Here, we describe the nutritional impacts of several hypothetical responses to food consumption advisories.

Modeled dietary transitions to market foods, following the scenarios outlined above, generally exacerbate deficiencies in n-3 PUFA and vitamins B12, D, B2, A, iron and zinc intake among indigenous Inuit (Fig. 5b). We find a small net gain in vitamin B-2 intake in the nutrient-dense foods replacement scenario. Modeled reductions as a fraction of daily recommended intake range from 1% to 2% for vitamin A to 37% for n-3 PUFAs. Replacement of traditional foods with an equivalent amount of locally caught Atlantic salmon has a mixed impact on nutritional sufficiency. Under the Atlantic salmon replacement scenario, average intake of n-3 PUFAs and vitamin D increases by 53% and 10% of recommended daily values respectively and leads to modest declines in intake of vitamins A and B-12, iron and zinc that are less 5% of daily values (Fig. 5b).

### 3.5. Screening-level analysis of risks and benefits

In 2014, intake of traditional foods among Inuit women of childbearing age generally had a small net positive impact on child neurodevelopment due to relatively low MeHg levels in traditional foods and benefits from n-3 PUFA intake. The median IQ decrement attributable to present-day MeHg exposures from traditional foods is 0.02 points (95th population percentile: 0.14 points). After accounting for benefits from n-3 PUFAs in traditional foods, median (5th–95th population percentiles) net impact on IQ is a gain of 0.01 points (decrement of 0.014 to gain of 0.19) IQ points. Increased consumption of greater quantities of low MeHg traditional foods would further increase this net benefit.

Increased MeHg concentrations in local foods may pose neurodevelopmental and cardiovascular risks. As described above, increased exposures are likely to disproportionately impact individuals who already have high MeHg exposures and exceed regulatory reference doses. However, mitigating these risks with reduced consumption of

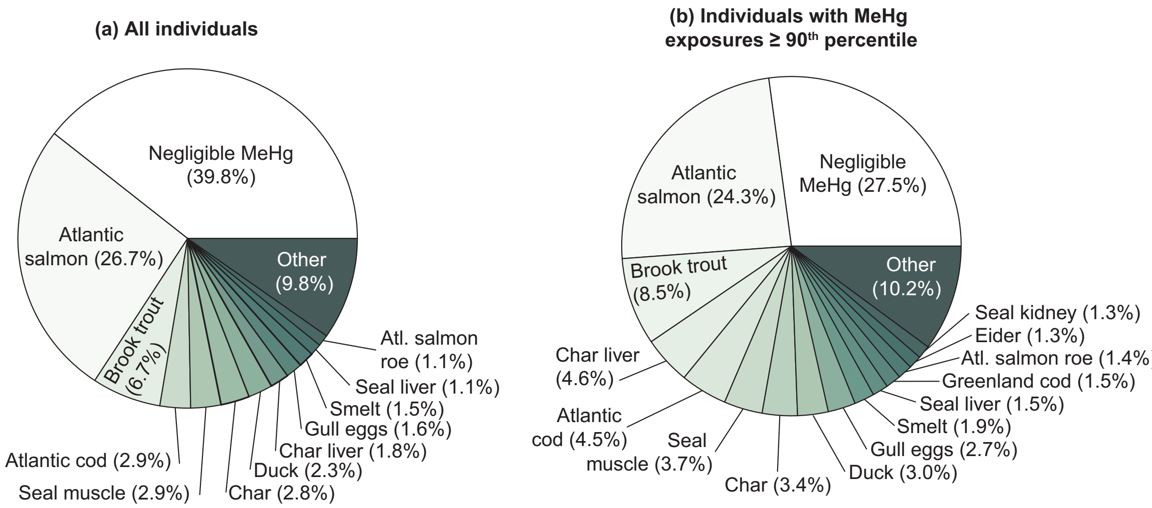


**Fig. 4.** Fraction of caloric intake from traditional foods for top 90% of foods among Lake Melville Inuit for (a) all individuals and (b) individuals with MeHg exposures above the 90th percentile in summer 2014 (0.08 μg $kg^{-1}$ $day^{-1}$). Dietary data from full-scale summer survey. Widely consumed foods (in the top 90% of contributors to overall calories from traditional foods) include berries, goose, partridge, moose, caribou, seal blubber and rabbit.

local foods may also pose risks. Here, we present the results of our analysis comparing risks from increased MeHg exposures to risks from potential dietary transitions. We conducted a screening-level estimate of the risks (Fig. 6) associated with peak forecasted increases in MeHg concentrations in traditional foods due to hydroelectric flooding by Calder et al. Calder et al. (2016). Even at peak MeHg concentrations, assuming the same magnitudes and species consumed as reported in the 2014 dietary survey, the population median IQ decrement for women of childbearing age is relatively low (0.06 points). However, among individuals with MeHg exposures greater than the 90th percentile, median impacts are much larger (loss of 1.4 IQ points). These estimates must be viewed as uncertain due to inter-individual differences in sensitivity to MeHg exposure and the toxicokinetics of MeHg absorption in the human body (Basu et al., 2014; Grandjean and Budtz-Jorgensen, 2010).

Substitution of traditional foods with store-bought alternatives represents a large reduction (70% per-capita) of n-3 PUFA intake (Fig. 6). We estimate that this may also lead to small neurodevelopmental impacts for most individuals (median IQ decrement of 0.01 across substitution scenarios). However, replacement of traditional foods with locally caught Atlantic salmon results in estimated gains of 0.08 IQ points (population-wide median) and 1.2 points (> 90th percentile

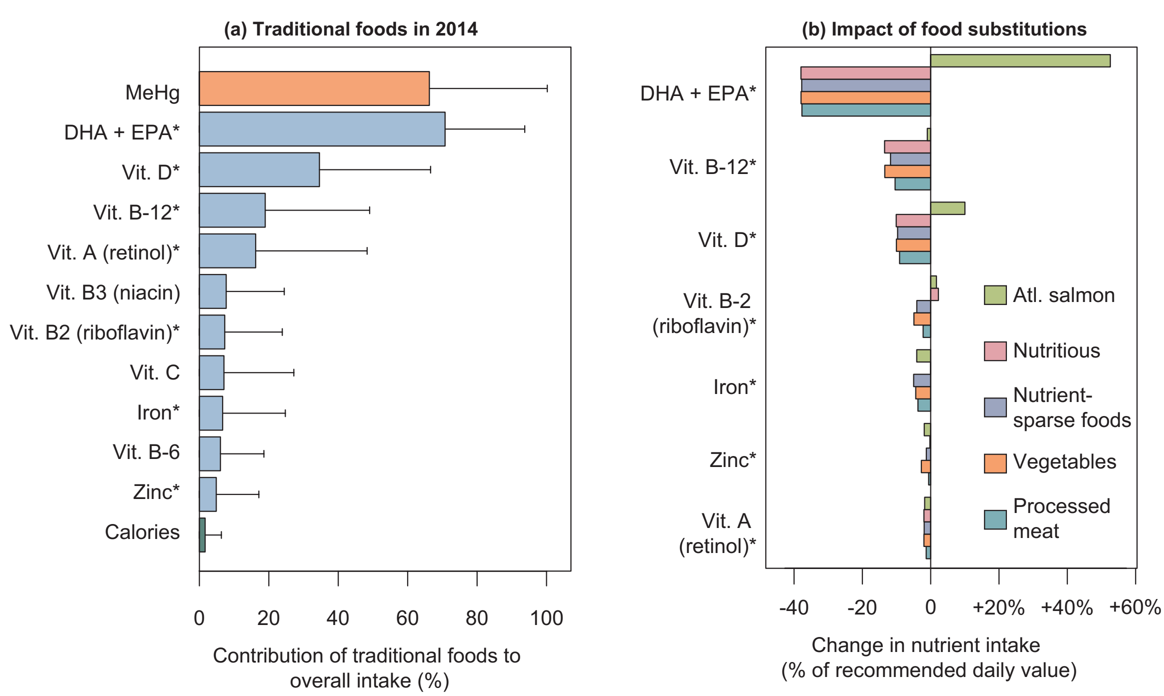


**Fig. 5.** Role of traditional foods for nutrient and MeHg intake and impacts of traditional food substitution. Panel (a) shows the estimated proportion of MeHg and several key nutrients from traditional foods based on survey data for 2014. Panel (b) shows the modeled impact of traditional food substitution on intakes relative to recommended daily values assuming several hypothetical traditional food replacement scenarios. Substitution scenarios for traditional foods include: (1) locally caught Atlantic salmon, (2) nutrient-dense store-bought foods ("Nutritious"), (3) nutrient-sparse junk foods, (4) vegetables and (5) processed meat. Shaded bars represent per-capita averages, and lines represent the 5th–95th percentile individuals. * denotes per-capita intake below recommended daily values based on US FDA recommendations (US FDA, 2013) and 500 mg $day^{-1}$ for DHA + EPA (Kris-Etherton et al., 2009).

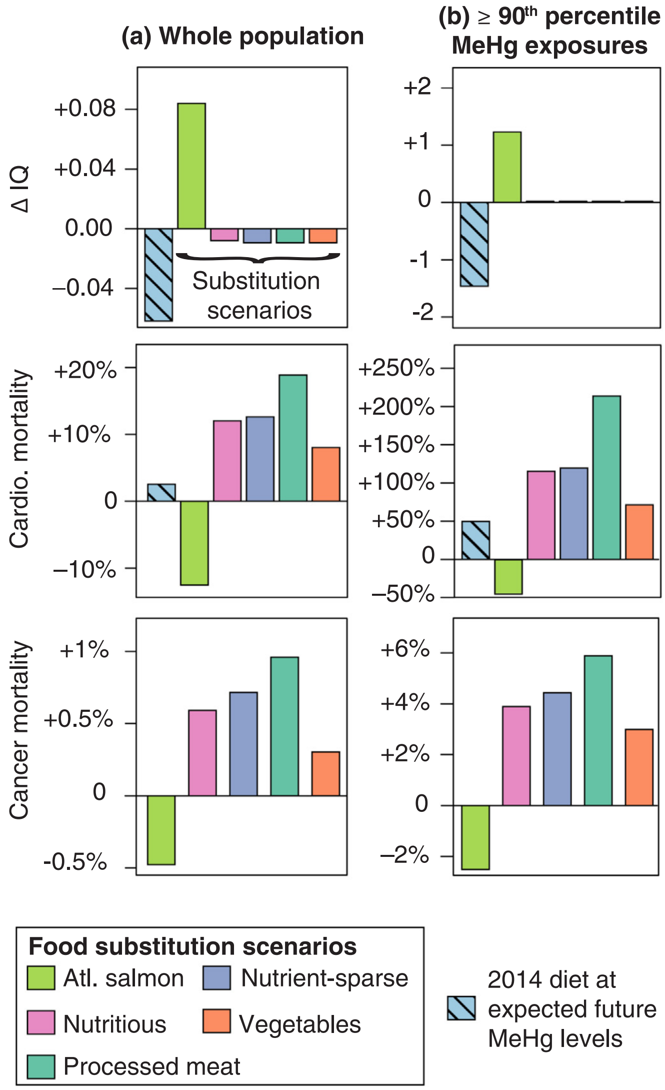


**Fig. 6.** Comparison of neurodevelopmental, cardiovascular and cancer risks for traditional food substitution scenarios compared to risks associated with projected future MeHg levels in traditional foods from Calder et al. (2016) Panel (a) shows median risks for the whole population. Panel (b) shows individuals at or above the 90th percentile of MeHg exposures in summer 2014 (0.08 μg $kg^{-1}$ $day^{-1}$). Traditional food substitution scenarios include: (1) locally caught Atlantic salmon, (2) the representative basket of subsidized nutrient-dense store-bought foods ("Nutritious"), (3) nutrient-sparse junk foods, (4) vegetables and (5) processed meat. Excess cardiovascular and cancer mortality risks are presented as fractions of present-day risks (+0% corresponds to a relative risk of 1, meaning no change relative to 2014).

MeHg exposures). This reflects a large increase in n-3 PUFA intake associated with additional Atlantic Salmon consumption that greatly outweighs minor increases in MeHg exposure (SI Table S9).

We estimate that cardiovascular risks associated with peak MeHg exposures in traditional foods are smaller than under any store-bought food replacement scenario (Fig. 6). Across the population, median risk of cardiovascular mortality associated with projected increases in MeHg in traditional foods increases by 3% relative to present-day (RR = 1.03). For individuals with MeHg exposures at the 90th percentile or greater, estimated risk of cardiovascular mortality increases dramatically (RR = 1.5). While the magnitude of these impacts is highly uncertain due to variability in susceptibility to MeHg exposure across populations, this analysis provides a quantitative estimate for the potential difference in magnitude of risks from MeHg in comparison to dietary changes. If traditional foods are replaced by processed meat, median RR of cardiovascular mortality is 1.19 across the population and 3.14 for individuals with MeHg exposures ≥ 90th percentile. Median RR of cardiovascular mortality is 1.08 at the across the population when the dietary replacement is fruits and vegetables and 1.73 for individuals with MeHg exposures ≥ 90th percentile. The replacement scenarios for nutrient-dense market foods and junk foods fall within this envelope (Fig. 6).

Replacement of high MeHg traditional foods by locally caught Atlantic salmon has the opposite impact of market foods on RR of cardiovascular mortality. This replacement scenario leads to greater net benefits for cardiovascular health than all store-bought alternative scenarios. Median RR of cardiovascular mortality under this scenario is 0.88 across the population and 0.55 for individuals with MeHg exposures ≥ 90th percentile (Fig. 6, SI Table S10).

We estimate that replacing traditional foods with store-bought foods under all scenarios will increase the RR of cancer mortality. Greater than 95% of this effect for the nutrient-dense foods scenario is attributable to reduced intake of vitamin D. Median RR of colorectal cancer is 1.01 due to reduced fiber intake (75% of individuals) and increased consumption of red and processed meat. Gains in calcium intake for 95% of individuals and increased milk consumption do not offset these risks. Increased sodium intake (97% of individuals) results in a small increase in RR of gastric cancer (RR = 0.01 at the 95th percentile). Colorectal cancers account for more than three times as many deaths as gastric cancers in Newfoundland and Labrador (Statistics Canada, 2011), and so the increased risk of colorectal cancer is a relatively stronger driver of overall cancer risks. Replacement of the representative basket of traditional foods with locally caught Atlantic salmon provides small net reductions in overall cancer risks relative to present-day (median RR = 0.995; ≥ 90th percentile individuals: RR = 0.97) (Fig. 6, SI Table S11).

### 3.6. Study strengths and limitations

To our knowledge, this study is the most comprehensive survey of Inuit diet and MeHg exposures ($n = 1145$). We provide a detailed characterization of diet variability among Lake Melville Inuit evaluated with direct hair Hg measurements. Our dietary MeHg exposure model performed better than several other recent studies, likely reflecting the relatively homogeneous sources of MeHg across the population and the use of extensive local data. This study provides an assessment of the magnitude of projected risks associated with elevated MeHg exposures in comparison with the neurodevelopmental, cardiovascular, cancer and nutritional risks posed by possible dietary changes.

We were limited by the availability of intake data for store-bought foods (other than seafood, which we measured on the FFQ), which are available only on a per-capita basis for the community of Rigolet. Therefore, our characterization of present-day nutritional sufficiency and composition of store-bought foods could not describe inter-individual variability. Dietary recall data is often biased, and although we designed the study so as to evaluate (with hair Hg measurements) and control for some biases (e.g., correcting for species-specific recall biases by asking redundant "total" recall questions) as described above, we are limited by the accuracy of the reports of survey respondents. Our evaluation of dietary model performance with respect to hair Hg and calculation of MeHg exposures from hair Hg measurements depends on self-reported measures of height and weight, which may be estimates. Although there was little evident bias in the larger-scale Summer survey round (Fig. 1), these factors likely contributed to the random error observed.

Our analysis does not account for other possible second-order effects of traditional food substitutions. For instance, isocaloric dietary substitution is associated with a mean reduction in protein intake of 2–11% across dietary scenarios. While per-capita intake of protein continues to exceed the recommended daily allowance, increasing the proportion of calories from carbohydrates and fats may lead to overall greater caloric intake via reduced satiety and higher insulin production, thus increasing weight gain and obesity-related risks (Simpson and Raubenheimer, 2012; Mozaffarian et al., 2011). Consumption rates of locally caught traditional foods in the Inuit communities studied here are lower than those for other indigenous communities across Canada. For example, British Columbia First Nations consume roughly three times the per-capita amounts reported here (Chan et al., 2011). This implies health and nutritional impacts associated with dietary transitions may be greater in other populations.

We have not addressed the physical or psychosocial dimensions of hunting and fishing and the preparation and consumption of traditional foods. Hunting traditional foods represents vigorous physical activity, and loss of access to traditional foods has been linked to adverse mental and social outcomes, implying substitution of traditional foods may present additional risks to those quantified here (Kirmayer et al., 2009; King et al., 2009; Sharma, 2010). Fruits and vegetables are not a significant part of the traditional Inuit diet (Cordain et al., 2002), and our analysis suggests they account for roughly 2% of caloric intake at present day. Replacement of traditional foods with fruits and vegetables is acknowledged to be less likely than by other foods such as red meat or other snack foods. This scenario is included as a better-case scenario for store-bought alternatives.

### 3.7. Implications for risk mitigation strategies

Food consumption advisories are routinely used to mitigate potential risks from elevated contaminant exposures. However, these advisories have unpredictable effects and can lead to reduced overall intake of traditional foods among indigenous populations. This study is the first to calculate the plausible range of health impacts from elevated MeHg exposures as compared to potential outcomes of risk-mitigation strategies. Our analysis suggests that replacing traditional foods with store-bought alternatives may lead to increases in cardiovascular and cancer risks among Lake Melville Inuit. Conversely, we estimate that replacement with locally caught Atlantic salmon will lead to net benefits for neurodevelopmental and cardiovascular health and reduce cancer risks relative to the present-day diet. Atlantic salmon is already a large component of traditional diet of our survey respondents, accounting for approximately 25% of calories from traditional foods. These results reinforce the potential benefits of dietary advice that promotes nutrient-dense, low-MeHg traditional foods. We have shown that in the local diet, there are many commonly consumed (and therefore familiar) foods with negligible levels of Hg, intake of which could be promoted in order to maximize net health benefits of the traditional diet.

Reducing the diversity of traditional foods consumed has mixed impacts on nutritional sufficiency, which must be considered when making recommendations about dietary choices among indigenous populations. Nutrient shortfalls are common in indigenous populations, and our findings suggest that this is the case among Lake Melville Inuit. Therefore, independent of contaminant levels, there may be a role for dietary interventions that promote increased intake of nutritious foods and possibly dietary supplements. Taken together, findings presented here underline the importance of protecting northern food webs from environmental contamination and of promoting traditional foods among indigenous populations.

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## Research ethics approval

This work was carried out following the approval of the following research ethics authorities:

- Office of Human Research Administration, Harvard T.H. Chan School of Public Health (case IRB13–1483).
- Newfoundland and Labrador Research Ethics Board (case 14.004).
- Nunatsiavut Government Health Research Ethics Authority.

## Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.envres.2018.09.005.

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