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Association between fish consumption, dietary omega-3 fatty acids and persistent organic pollutants intake, and type 2 diabetes in 18 First Nations in Ontario, Canada

Lesya Marushka[a], Malek Batal[b], William David[c], Harold Schwartz[d], Amy Ing[b], Karen Fediuk[e], Donald Sharp[c], Andrew Black[c], Constantine Tikhonov[d], Hing Man Chan[a,*]

[a] University of Ottawa, Canada
[b] Université de Montréal, Canada
[c] Assembly of First Nations, Canada
[d] Health Canada, Environmental Public Health Division, First Nations and Inuit Health Branch (FNIHB), Canada
[e] Dietitian and Nutrition Researcher, British Columbia, Canada

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ABSTRACT

Background: First Nations (FNs) populations in Canada experience a disproportionally higher rate of obesity and type 2 diabetes (T2D) compared to the general population. Recent data suggest that a high consumption of fish may help prevent T2D. On the other hand, fish might also be a potential source of environmental contaminants which could potentially be a risk factor for T2D.

Objective: To investigate the potential associations between self-reported T2D and consumption of locally-harvested fish, dietary long-chain omega-3 fatty acids (n-3FAs) and persistent organic pollutants intake among adult FNs living on reserve in Ontario.

Design: Data from the First Nations Food Nutrition and Environment Study, which included a cross-sectional study of 1429 Ontario FNs adults living in 18 communities across 4 ecozones in 2012 were analyzed. Social and lifestyle data were collected using household interviews. The consumption of locally-harvested fish was estimated using a traditional food frequency questionnaire along with portion size information obtained from 24hr recalls. Fish samples were analyzed for the presence of contaminants including dichlorodiphenyldichloroethylene (DDE) and polychlorinated biphenyls (PCBs). Dietary intakes of DDE and PCBs were estimated using community-specific levels of DDE/PCBs in fish species. Multiple logistic regression models adjusted for potential covariates including age, gender, body mass index, physical activity, total energy intake, smoking, and education were developed.

Results: The prevalence of T2D in Ontario FNs was 24.4%. A significant positive association between fish consumption of one portion per week and more and T2D compared to no fish consumption was found (OR = 2.5 (95% CI: 1.38–4.58). Dietary DDE and PCBs intake was positively associated with T2D (OR = 1.09 (95%CI: 1.05–1.75) for DDE and OR = 1.07 (95%CI: 1.004–1.27) for PCBs) per unit increase in DDE/PCBs while n-3-FAs intake, adjusted for DDE/PCBs intake, showed an inverse effect against T2D among older individuals (OR = 0.86 (95% CI: 0.46–0.99).

Conclusion: Our results support previous findings that exposure to DDE and PCBs may increase the risk of T2D. Elevated levels of contaminants in fish may counteract with potentially beneficial effects of n-3FAs from fish consumption. However, the overall health benefits of high consumption of fish with a high n-3 FAs content may outweigh the adverse effect of contaminants.

1. Introduction

The prevalence of type 2 diabetes (T2D) has dramatically increased worldwide over the last two decades, and it is recognized as one of the most important public health concerns. According to the World Health Organization, the global diabetes prevalence for adults aged 20 years and older was estimated to be 6.6% in 2000 and is predicted to reach 7.7% by 2030 (Wild et al., 2004). In Canada, the First Nations population experiences a disproportionally higher rate of T2D compared to the general Canadian population (Dyck et al., 2010; Young

* Corresponding author.

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et al., 2000). Age-standardized prevalence of T2D in First Nations was 17.2% compared to 6.8% in general Canadians (Pelletier et al., 2012), ranging from about 7–36% in individual First Nation communities (Dannenbaum et al., 2008; Imbeault et al., 2010; Horn et al., 2007). T2D is a multifactorial disease caused by a complex interaction between lifestyle, genetic and environmental factors. Recognized risk factors for T2D are obesity, high-calorie diets, low physical activity and smoking (Byrne et al., 2012; Day and Bailey, 2011; Chang, 2012).

Recent data from the population-based prospective cohort studies have suggested that a high consumption of fish may help prevent T2D (Patel et al., 2009; Rylander et al., 2014). Potential benefits of fish and seafood were attributed to the presence of long chain omega-3 fatty acids (n-3 FAs), specifically eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) which have shown a beneficial effects on multiple risk factors associated with diabetes, such as lipid profile, blood pressure, and inflammation, as well as on coronary heart disease and stroke (He, 2009; Panagiotakos et al., 2007). Epidemiological studies on the association between fish consumption, n-3 FAs and T2D have reported controversial results: some studies found a protective effect (Nanri et al., 2011a; Nkondjock and Receveur, 2003; Rylander et al., 2014), while others showed a negative effect (Djoussé et al., 2011; Kaushik and Mozaffarian, 2009a). Meta-analyses on the associations between fish consumption, n-3 FAs and the development of T2D found heterogeneity of the overall summary estimates based on geographical differences of the studies: an inverse association in population of Asian countries, no association in population of Western countries and a positive relation in US population (Muley et al., 2014; Wallin et al., 2012; Xun and He, 2012; Zheng et al., 2012). Differences in fish consumption patters may partially explain the inconsistency between the findings. Environmental contaminants present in fish may also influence the association between fish intake and T2D (Lee et al., 2014; Wallin et al., 2015).

Fish is a potential source of environmental contaminants, such as persistent organic pollutants (POPs) (Seabert et al., 2014). POPs are toxic substances which persist in the environment, have long half-lives, and therefore bioaccumulate and biomagnify in living organisms such as fish, mammals, predatory birds, and humans (Hardell et al., 2010; Sobek et al., 2010; Vorkamp and Rigét, 2014). This is a concern especially among First Nation populations whose diets rely on locally harvested fish and other wild foods. A study conducted on Mohawk men and women showed that local fish consumption was a major pathway of POPs exposure (Fitzgerald et al., 1999, 2004). Recently, a number of studies found positive associations between diabetes and POPs such as dioxin-like chemicals, non-dioxin-like polychlorinated biphenyls (PCBs), dichlorodiphenyltrichloroethane (DDE), and other organochlorine pesticides (Codru et al., 2007; Lee et al., 2010; Philibert et al., 2009; Silverstone et al., 2012). Pal et al. (2013) found higher POP concentrations in plasma in diabetic compared to non-diabetic Canadian First Nation individuals. Thus, First Nation people might be exposed to elevated concentrations of POPs from fish consumption which can be risk factors for T2D (Sharp, 2009).

It is clear that there is a need to evaluate the risk-benefit associated with fish consumption with respect to POPs and n-3 FAs intake, and whether it is associated with T2D. The objectives of this study are: to describe fish consumption patterns among First Nation adults in four Ontario ecozones; to estimate n-3 FAs and PCBs, and DDE intake; and to explore the associations between self-reported T2D and fish consumption, dietary n-3 FAs and POP intake among First Nations living on reserve in Ontario.

2. Methodology

2.1. Study population

Data from the First Nations Food Nutrition and Environment Study (FNFNES), a 10-year cross-sectional study (2008–2017) were used (Chan et al., 2013). The FNFNES survey was designed to assess diets, the exposure to contaminants, and food security status of First Nations people living on reserves, south of the 60th parallel across Canada. First Nations communities were sampled using a combined ecozone/cultural area framework to ensure that the diversity in ecozones and cultural areas were represented in the sampling strategy. Three stages sampling proceeded: primary sampling was carried out with random sampling of communities within each of eight Assembly of First Nation (AFN) regions of Canada; secondary sampling was conducted with the random sampling of 125 households within each selected community; and tertiary sampling when one randomly selected adult in each household who was self-identified as being a First Nations person living on reserve aged 19 and older was asked to participate in the study. Estimation weights were calculated in order to obtain representative estimates of the total population. Weighting was required to minimize nonresponse bias. The design weight was adjusted based on the assumption that the responding communities represent both responding and non-responding communities. The Bootstrap method was adopted for the estimation of the sampling error of the estimates produced for this study (Chan et al., 2013). The detailed information on the study design and methodology are publicly available online (www.fnfnes.ca). The current study analyzed data from eighteen First Nations communities across four Ontario ecozones: 1- Boreal Shield/ Subarctic, 2- Boreal Shield/Northeast, 3- Hudson Plains/Subarctic, 4- Mixed-wood Plains/ Northeast collected in the fall of 2011 and 2012 (Fig. 1). In total, 1429 participants aged 19 years and over were recruited in this study (Chan et al., 2013). The overall participation rate was 79%. To avoid potential misclassification of gestational diabetes, pregnant and breastfeeding women who reported having diabetes were excluded from the analyses. The final sample included 1426 participants (893 women and 533 men).

2.2. Ethics

Individual participation in the project was voluntary and based on informed written consent after an oral and written explanation of each project component. This survey was conducted following the “Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans” and in particular Chapter 9 research involving the First Nations, Inuit and Métis Peoples of Canada. The study was approved by the Ethical Review Boards at the University of Northern British Columbia, the University of Ottawa, the Université de Montréal, and Health Canada.

2.3. Data collection

During the household interviews, the study participants were asked to complete a series of questionnaires that collect information on dietary patterns (a 24-h recall and a Traditional Food Frequency Questionnaire (FFQ)), and social-demographic, health, and lifestyle data ((SHL) Questionnaire).

To collect the 24 h recall, the multi-pass technique with 3 stages was used as follows: the first step was to make a quick list of all foods consumed during prior 24 h; the second one was to do a detailed description of the consumed foods and beverages (brands, amounts, and amount eaten, etc..); and the third step was to review the recall with the participant to see if anything was missed (Raper et al., 2004). Three-dimensional food and beverage models were used in order to estimate corresponding quantities of the intakes. The FFQ collected data regarding consumption of locally-harvested traditional foods during the four seasons in the past year. The questionnaire was developed based on a comprehensive list of traditional foods that was representative for each participating community. In Ontario, the FFQ combined 150 traditional food items, including 30 fish species, 21 land mammals, 26 wild bird species, 22 wild berries, and 48 wild nuts, plants, tree foods, and mushrooms. In this study, only data on the frequency of

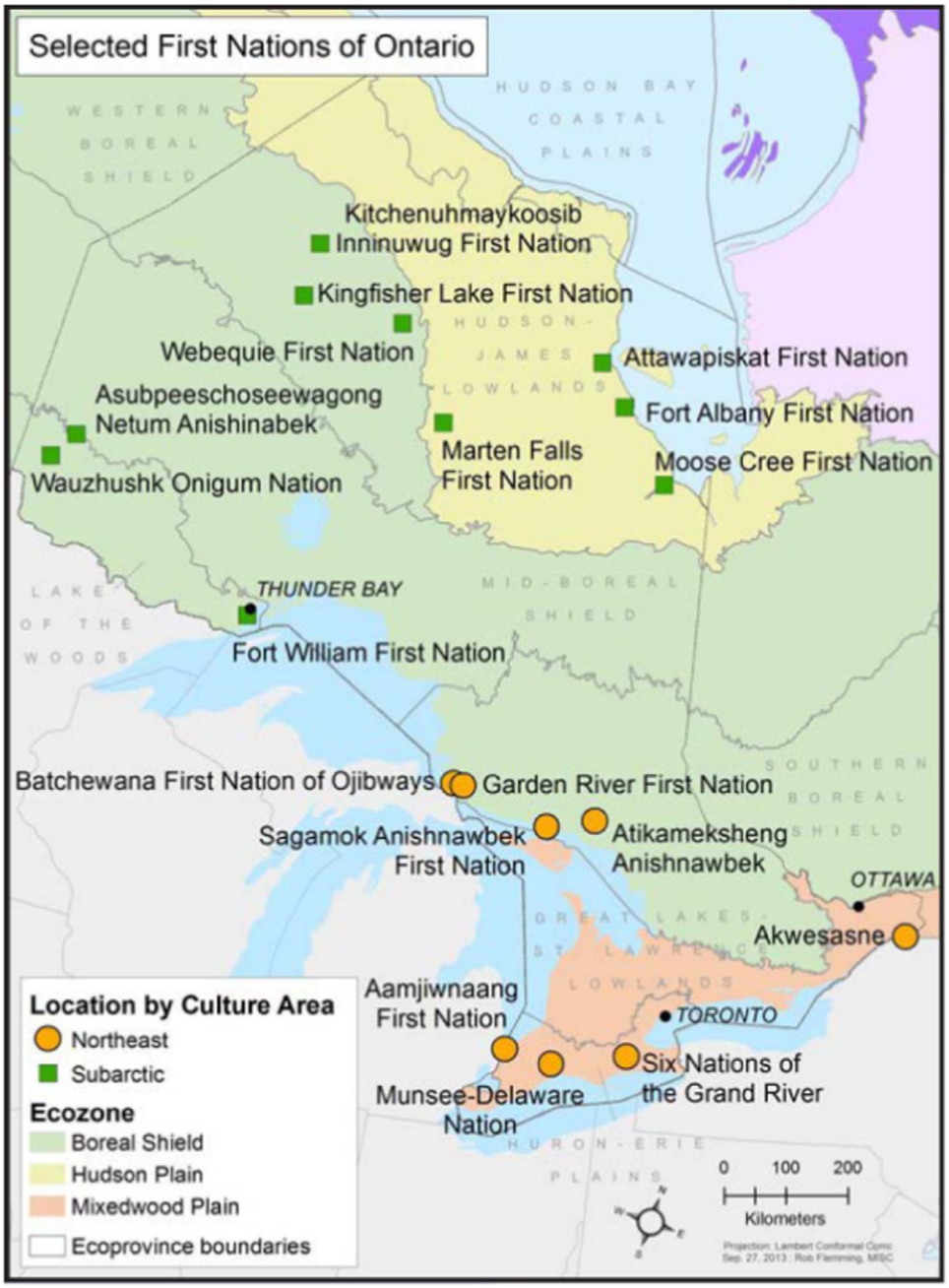

Fig. 1. Map of participating First Nations communities and four ecozones in Ontario (Chan et al., 2014).

locally-harvested fish consumption were included.

The SHL Questionnaire included information about age, gender, weight and height (measured or self-reported), physical activity level (sedentary, somewhat active, moderate, vigorous), dieting (to lose weight) on the previous day (yes/no), smoking status (yes/no), household size, source of income (wage, pension, social assistance), education (high school degree, vocational training certificate, Bachelor's degree), employment status (full time, part time, no job), and self-perceived health status (excellent, very good, good, fair, poor). All participants self-reported their level of physical activity based on provided descriptions.: a) I am usually sitting and do not walk around very much; b) I stand or walk around quite a lot, but I do not have to carry or lift things very often; c) I usually lift or carry light loads or I have to climb stairs or walk up hills often; d) I do heavy work or carry heavy loads. Body mass index (BMI) was calculated as weight (in kilograms) divided by the square of height (in meters). When available, both measured weights and heights were used in the BMI calculations. Otherwise, self-reported or a combination of self-reported and measured values were used, adjusting the BMI by the addition of the estimated bias value by gender. BMI categories were considered as follows: normal weight when BMI was < 25 kg/m^2, overweight was categorized as a BMI of 25 kg/m^2 or higher but less than 30 kg/m^2, and obesity was categorized as a BMI higher than or equal to 30 kg/m^2.

2.4. Assessment of type 2 diabetes

Data on diabetes were collected through the SHL Questionnaire. The study participants were asked if they have ever been told by a health care provider that they have diabetes. In addition, information on the type of diabetes (type 1, 2) and the onset of diabetes (how many years ago) was collected. In this study, self-reported type 2 diabetes was coded as “yes” if a participant answered to be diagnosed with type 2

diabetes (Huerta et al., 2009; Schneider et al., 2012). All participants who reported having type 1 diabetes were categorized as being non-diabetic for purpose of these analyses. The validity of self-reported T2D estimates from FNFNES survey was analyzed by comparing our estimates with those reported by the Regional Health Survey (RHS) which is the only First Nations-governed national health survey in Canada (FN RHS, 2008). In First Nations in Ontario, the age-standardized prevalence of diabetes reported by the FNFNES was 24%, which was similar to the rate of 21.6% reported by RHS (Phase II, 2008/10) (Appendix (Table A4)). Both surveys found differences in diabetes prevalence between males and females with higher rates in females (Jackson et al., 2014).

2.5. Fish sampling for contaminant content

Fish samples were collected based on the list of commonly consumed fish species in the participating communities and are representative of fish species consumed by members in each community. All fish samples were collected during the fall 2011 (September through November). Each fish sample was a composite of tissues from up to 5 different fish. The collected fish samples were analyzed for POPs including total polychlorinated biphenyls (PCBs) and dichlorodiphenyldichloroethylene (DDE) at Maxxam (2011) and ALS Global (2012), in Burnaby, British Columbia.

All fish samples were homogenized to provide a homogeneous sample for subsequent digestion. If required, a moisture value was determined gravimetrically after drying a portion of the blended sample at 105 °C overnight. Six grams of tissue was homogenized in dichloromethane (DCM) and filtered through anhydrous sodium sulphate. The extract was evaporated to 6 mL and 5 mL was injected onto the Gel Permeation Chromatography (GPC) column where a fraction of the eluent was collected, concentrated, and solvent exchanged to acetone:-hexane (1:1). Further clean-up was performed by eluting this extract through PSA columns. The final extract was concentrated and solvent exchanged to isooctane. Analysis was performed for the DDE and PCBs using GC-MS in Selective Ion Monitoring (SIM) mode with an EI source. Spiked standards and blank samples were measured for QA/QC.

2.6. Estimation of fish, dietary POPs (DDE, PCBs), and long-chain omega-3 FAs intake

Daily fish intake (g/d) for each participant was estimated as follows: firstly, by summing up the number of days in the past four seasons when fish consumption was reported (total and by fish species). Then, mean portion size of fish (g) was estimated from dietary data generated by the 24 h recalls for each gender and age group. Finally, the total number of days in the previous year when fish intake was reported was multiplied by mean portion size of fish (g) and divided by 360 days (in this study, a year included four seasons of 90 days each).

Total POPs (total PCBs, DDE) intake was calculated by multiplying the amount of PCBs and DDE (nanograms) in one gram of each fish species by the total amount of each fish species eaten per day (grams), totaling the amount of PCBs and DDE from all fish species consumed per day and dividing the obtained amount by body weight of each participant (ng/kg of body weight/day).

[Σ (Fish intake (grams/day) × total PCBs (ng/gram of fish)/body weight].

[Σ (Fish intake (grams/day) × DDE (ng/gram of fish)/body weight].

Community-specific data of POPs content in fish species were applied to calculate total PCBs and DDE intake for each participant. If the community-specific data were not available, ecozone-specific concentrations of POPs content in fish species were calculated and applied for the communities that were located within a particular ecozone. The validation of dietary assessments was performed through correlation analysis between mercury exposure from traditional food estimated using the FFQ and hair mercury levels measured in First Nations participants. Dietary intake of mercury was correlated with hair mercury (Pearson correlation coefficient = 0.53).

The concentrations of long-chain n-3 FAs in the various fish species were estimated by using the Canadian Nutrient File (Health Canada, 2014). In this analysis, n-3FAs means long-chain omega-3 fatty acids i.e. combined eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) from fish. The data are expressed as mg EPA + DHA/ gram of raw fish. Raw values were used since fish tissue EPA + DHA concentrations may vary according to cooking method. Also, using the raw values allows to compare our results with other studies. The total amount of n-3 FAs (EPA + DHA) consumed by each participant was calculated as follows:

[Σ (Fish intake (grams/day) × EPA + DHA (mg/gram of fish)]

Since walleye, lake whitefish, lake trout, and yellow perch were commonly consumed across four ON ecozones, the consumption of these fish species as well as n-3 FAs and POPs intake from these types of fish were also described.

2.7. Statistical analyses

Descriptive statistics include the calculation of proportions for categorical variables and means with standard deviation (SDs) for continuous variables. Geometric means (95%CI) were estimated for dietary DDE and PCBs intake. Medians (interquartile range) were calculated for skewed variables. Student *t*-tests, analysis of variance (ANOVA), and chi-square tests were used to test if differences between groups are statistically significant. Sub-group stratified analysis by gender, age groups and ecozones were performed to describe study population by diabetes status. Fish intake was categorized by frequency of consumption in four groups: no or < 1/month, 1/month, 2–3/month, and ≥1/week to examine dose-response relationship between fish and T2D. For this analysis, a portion of fish was considered to be 150 g. We chose 150 g since it represents two servings (of 75 g each) of fish per week recommended by Canada's Food Guide – First Nations, Inuit, and Métis (Health Canada, 2007). Pearson correlation coefficients were investigated among all continuous predictors. Collinearity was observed between fish intake with n-3 FAs, PCBs and DDE.

Bivariate analyses (simple logistic regression models) were performed between an outcome (T2D) and each primary predictor of interest (fish intake (categorical), PCBs, DDE, n-3FAs (continuous), individually) as well as all potential confounders (age, gender, BMI, total energy intake, smoking, physical activity, household size (number of people per household)), education.

Multiple logistic regression models adjusted for potential covariates were developed in order to investigate the associations between total fish, dietary POPs (PCBs and DDE) and n-3 FAs (EPA + DHA) intake, individually and T2D. Independent variables that do not fit a normal distribution were normalized using the natural logarithmic function (DDE, PCBs, and n-3FAs (EPA + DHA)). POP concentrations below the limit of quantification were imputed with a half limit of detection (LOD) of PCBs and DDE to avoid errors in the analysis. The LOD of DDE is 0.0005 μg/g and LOD of PCBs is 0.0003 μg/g (Chan et al., 2012).

To investigate the relationship between the frequency of fish consumption (4 categories) and T2D, three models were developed. Control variables were selected based on well-established risk factors for T2D reported in the literature including age, sex, body mass index (BMI), smoking, physical activity, total energy intake, education, and household size. Covariates were added into the models gradually to evaluate their relative contribution on the association between the predictors of interest and the outcome variable. Model 1 presents crude estimates; Model 2 was adjusted for age, gender, and BMI; Model 3 was additionally adjusted for physical activity, total energy intake, smoking, household size, and education. The following covariates were treated as continuous variables: age, BMI, energy intake, number of people per

household, years of education. Gender, smoking and physical activity were categorical variables. Fat, saturated fat, carbohydrate, fruit and vegetable intake were also considered as covariates but were removed from the models since they did not change the measure of the association between T2D and fish consumption.

Overall and stratified by age group (< 45y; ≥45y) logistic regression models were developed to analyze the relationship between log-transformed dietary DDE, PCBs, n-3 FAs intake and T2D. We chose to dichotomize by age below or above 45 since 45 years is median age of the study population.

The models were tested for interactions between predictors (x_1, x_2) by including the product "$x_1 \times x_2$" as an additional predictor in a model containing x_1 and x_2:

$$\log\left(p(y)/(1-p(y))\right) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_1 \times x_2.$$

Age, gender and BMI were examined as effect modifiers. The covariates did not modify associations of fish consumption, DDE, PCBs, and n-3 FAs and T2D.

Results with a p-value of less than 0.05 were considered statistically significant. All statistical analyses were performed using weighting variables in order to obtain representative estimates at the regional level. JMP version 11 and R software were used to conduct statistical analyses.

Sensitivity analyses were conducted to examine dietary characteristics and physical activity between responders who were recently diagnosed with T2D (≤5 years ago) and those who were diagnosed with T2D for a longer period of time (> 5 years) (Appendix 1: Table A1). Also, analyses of dietary and lifestyle behaviours were carried out between participants with and without T2D by dieting status (Appendix 2: Tables A2, A3).

3. Results

The study population consisted of 1426 participants (893 women and 533 men) with an average age of 46.4 ± 15 years ranging from 19 to 88 years old. Table 1 shows the characteristics of Ontario First Nations participants by diabetes status. The overall prevalence of self-reported T2D was 24.4% (327 cases out of 1426) and was slightly higher among women (24.6%) compared to men (23.5%). After standardization to the 2015 Canadian population, the prevalence of T2D was 25%. Participants with T2D were older, were more likely to be women, had a higher mean BMI, and were less likely to be physically active. In fact, a larger proportion of diabetes cases (76%) reported an inactive or sedentary lifestyle compare to 58% among participants without T2D. Mean age and BMI were comparable between males and females with and without T2D (data are not shown). The majority of the study participants, were overweight and obese (94% with T2D and 85% without T2D). Smoking was highly prevalent among both First Nations men and women reaching 50%, but was significantly lower among participants diagnosed with T2D (45.5% vs. 49.7%).

The mean number of people per household was similar between diabetic and non-diabetic participants. Regarding the education level, more participants with T2D didn't complete high school compared to those without T2D (44% vs 35%).

Individuals with T2D were more likely to be dieting on the day prior to be being interviewed compared to those without T2D (14.8% and 11.1%, respectively). Some differences in nutrient intakes between diabetic and non-diabetic cases were noted. In particular, participants with T2D reported lower saturated fat intake.

Mean fish consumption in the study population was 17 g/d (median 3.4 g/d (min-max: 0–452 g/d)) and was higher among individuals with T2D (mean 25.8 g/d, median 4.2 g/d) than without T2D (mean 14.3 g/d; median 3.1 g/d). The mean DDE and PCBs intakes were significantly higher in diabetic individuals (0.08 ng/kg/d, 0.19 ng/kg/d) compared to non-diabetic (0.03 ng/kg/d, 0.05 ng/kg/d). Similarly, subjects with T2D had higher mean intake of n-3 FAs (EPA + DHA) – 373.6 mg/d vs. 216.4 mg/d. Thus, along with fish consumption, average dietary DDE, PCBs and n-3 FAs intakes were higher in participants with T2D.

Table 1
Characteristics of Ontario First Nations participants by diabetic status (n = 1426).

	With T2D	Without T2D	p Value
N, (%)	327 (24)	1099 (76)	
Women, n (%)	217 (63)	676 (64)	0.1
Men, n (%)	110 (37)	423 (36)	
Age	55.74 (53.33,58.15)	42.96 (41.25,44.68)	0.0001*
Age groups, n (%)			
19–30	8 (1.4)	255 (24.3)	0.0001*
31–50	119 (36.5)	491 (45.6)	
51–70	155 (45.9)	282 (24.9)	
71 +	45 (16.2)	71 (5.2)	
BMI, kg/m^2	33.23 (32.34,34.12)	30.42 (29.80,31.05)	0.0001*
BMI category, n (%)			
< 25	30 (6.1)	202 (15.0)	0.0001*
25–29.99	93 (25.7)	344 (34.5)	
≥30	204 (68.2)	553 (50.5)	
Physical activity, n (%)			
inactive	97 (26.3)	227 (17.8)	0.002*
sedentary	146 (50.1)	455 (40.4)	
moderate	59 (16.0)	284 (29.0)	
vigorous	25 (7.5)	130 (12.8)	
Smoking, n (%)	147 (45.5)	576 (49.7)	0.018*
Dieting, n (%)	48 (14.8)	103 (11.1)	0.006*
Household size	4.18 (3.39,4.96)	4.16 (3.87,4.44)	0.965
Years of education	11.23 (10.36,12.10)	11.87 (11.31,12.44)	0.091
Diploma, n (%)			
Less than high school	159 (44.2)	458 (34.9)	0.003*
High school	117 (42.5)	509 (51.9)	
Post-secondary	50 (13.3)	128 (13.2)	
Employment, any (%)	196 (68.1)	753 (77.5)	0.016*
Dietary characteristics			
Energy intake (kcal/d)	1927 (1763,2091)	2015 (1918,2113)	0.442
Fruit Vegetables (g/d)	22.84 (16.74,31.17)	15.89 (13.34,18.92)	0.421
Total Fat (g/d)	79.11 (72.21,86.01)	80.39 (77.77,83.02)	0.743
Saturated Fat (g/d)	23.73 (21.68,25.77)	26.22 (25.19,27.25)	0.023*
Carbohydrate (g/d)	215.09 (202.03,228.14)	240.89 (220.30,261.49)	0.078
Protein (g/d)	92.43 (77.47,107.38)	84.56 (80.25,88.86)	0.298
Total Fish intake (g/d)	25.75 (13.11,38.40)	14.27 (4.10,24.43)	0.183
DDE (ng/kg/d)	0.08 (0.04,0.16)	0.03 (0.01,0.05)	0.002*
PCBs (ng/kg/d)	0.19 (0.07,0.47)	0.05 (0.03,0.10)	0.025*
EPA + DHA (mg/day)	373.6 (164.8582.4)	216.4 (69.7363.1)	0.36

T2D – type 2 diabetes; DDE - dichlorodiphenyldichloroethylene; PCBs - polychlorinated biphenyls.
EPA - eicosapentaenoic acid; DHA - docosahexaenoic acid; values are mean (95%CI); DDE/PCBs –geometric mean; p-values correspond to *t*-tests for continuous variables and chi-square tests for categorical variables; BMI- body mass index; weighted estimates.

Table 2 presents the characteristics of the study population by two age groups (< 45y vs ≥45y). The prevalence of T2D among older people was 34.5% compared to 13.7% in younger participants. Mean BMI was slightly higher whereas physical inactivity was statistically significantly lower in older participants compared to younger ones. Also, participants aged 45 years and over reported lower total energy and carbohydrates intake, but higher fruit and vegetables. Also, older individuals consumed two times more fish compared to younger participants.

In Table 3, the characteristics of the study population by frequency of fish consumption is presented. Higher fish consumption was associated with older age, being male and higher prevalence of self-reported T2D. The BMI, smoking status, level of physical activity and total energy intake were comparable among participants in each of the four fish frequency consumption categories.

Table 2
Characteristics of Ontario participants by age groups (< 45y/≥45y).

	< 45	≥45	p value
n	709	717	
T2D (%)	13.7	34.5	0.0001*
Body mass index	30.71 (29.97,31.46)	31.48 (30.81,32.15)	0.148
Smoking (%)	60.8	36.7	0.0001*
Physical activity (%)			0.0002*
inactive	16.1	23.5	
sedentary	40.6	44.9	
moderate	28.4	23.4	
vigorous	14.9	8.2	
Dietary characteristics			
Total energy(kcal/d)	2093 (1976,2209)	1897 (1803,1990)	0.016*
Fruit/vegetables (g/d)	11.69 (9.39,14.57)	25.38 (20.62, 31.24)	0.035*
Fat (g/d)	83.68 (79.33,88.03)	76.54 (71.38,81.70)	0.087
Protein (g/d)	84.95 (80.65,89.26)	87.94 (78.71,97.18)	0.522
Carbohydrate (g/d)	252.66 (232.34,272.98)	216.89 (203.86,229.92)	0.0001*
Fish intake (g/d)	10.5 (5.78,15.23)	23.5 (10.43,36.57)	0.012*
DDE (n/kg/d)	0.02 (0.01,0.04)	0.06 (0.03,0.13)	0.0001*
PCBs (n/kg/d)	0.04 (0.02,0.08)	0.13 (0.06,0.28)	0.0001*
EPA + DHA (g/d)	160.1 (91.7228.4)	347.4 (163.9531.0)	0.019

T2D - type 2 diabetes, DDE-dichlorodiphenyldichloroethylene; PCBs-polychlorinated biphenyls.
EPA- eicosapentaenoic acid; DHA-docosahexaenoic acid; values are mean (95%CI).
DDE/PCBs -geometric mean, p-values correspond to *t*-tests for continuous variables and chi-square tests for categorical variables; weighted estimates.

Table 4 presents self-reported prevalence of T2D, fish consumption patterns, dietary n-3 FAs, and DDE, and PCBs intakes across four Ontario ecozones: Boreal Shield/ Subarctic, Boreal Shield/Northeast, Hudson Plains/Subarctic, and Mixed-wood Plains/ Northeast (Fig. 1). The frequency of consumption of 30 different fish species was collected from the Ontario participants. Among all fish species, walleye, lake whitefish, lake trout and yellow perch were commonly consumed contributing, about 70% to the total fish intake.

Overall, 75% of participants reported eating fish over the past year, ranging within ecozones from 54% to 88%. The highest consumption of total fish was reported by participants living in the Boreal Shield/ Subarctic ecozone (mean, 31 g/d; median, 15 g/d) followed by the Hudson Plains (mean, 12.5 g/d; median, 6.2 g/d), the Boreal Shield/ Northeast (mean, 12.2 g/d; median, 5.9 g/d), and the Mixed-wood Plain/Northeast (mean, 5 g/d; median, 3.5 g/d) among fish consumers only. With respect to the commonly consumed fish species, the highest consumption of walleye and whitefish was reported in the Boreal Shield/Subarctic and the Hudson Plains/Subarctic ecozones whereas lake trout was mainly consumed by individuals living in the Boreal Shield/Northeast ecozone. In the Mixed-wood Plains/Northeast ecozone participants reported eating predominantly walleye and yellow perch. Lake trout was the primary contributor to total POPs intake across all ecozones whereas whitefish and walleye were the main sources of n-3 FAs, especially in the Boreal Shield/Subarctic ecozone.

Logistic regression model (Table 5) presents the association between frequency of fish consumption and T2D. The crude model shows a significant positive association between consumption of one portion of fish per week and more (OR: 2.34 (95%CI: 1.27–4.26)) compared to the reference group (no or < 1/month). In model 2, the results were adjusted for the following confounders: age, gender, and BMI. Model 3 was additionally controlled for physical activity, total energy intake, smoking, household size, and years of education. We were unable to control the models for DDE, PCBs, and n-3 FAs intake because of collinearity between fish intake with POPs, and with n-3 FAs variables. Overall, fish consumption of ≥1 portion per week increased the odds of T2D by about 2.5 times compared to no or < 1/mo fish consumption.

Table 6 shows the results from logistic regression models of log-transformed DDE, PCBs and n-3 FAs intakes with T2D (overall and by two age groups). A significant positive association was found between dietary DDE intake and T2D with OR =1.09 (95% CI: 1.05–1.75) overall and in older participants (OR=1.24 (95% CI: 1.12–2.54)). Similarly, dietary PCB intakes were positively associated with T2D with statistically significant ORs in overall analysis (OR=1.07 (95% CI: 1.004–1.27)) and in individuals aged 45 and over in the model adjusted for n-3 FAs intake (OR=1.13; 95% CI: 1.001–1.4). Dietary n-3 FAs intake was positively associated with T2D in the model adjusted for the risk factors only. After adjusting for dietary POPs exposure, n-3 FAs intake showed inverse, but not statistically significant effects in the total sample. However, among individuals aged 45 and over, n-3 FAs showed a protective effect against T2D (OR=0.86; 95% CI: 0.46–0.99) after adjusting for POPs intake. The dose-response relationship of

Table 3
Characteristic of Ontario participants by frequency of fish consumption.

	0 or < 1/mo	1/mo	2–3/mo	≥1/week	p trend
n	508	278	338	302	
Type 2 diabetes, %	20.2	17.3	22.8	37.3	0.02
Age, y	44.1 (42.2,45.9)	43.7 (39.4,48.0)	47.4 (45.0,49.7)	49.9 (47.3,52.6)	0.0001
Women, %	72.7	68.9	60.2	45.5	0.0001
Men, %	27.3	31.1	39.8	54.5	0.0001
Body mass index	31.5 (30.2,32.8)	30.5 (29.6,31.4)	31.1 (29.7,32.5)	30.9 (29.7,32.1)	0.3
Smoking, %	47.8	50.2	47.3	50.4	0.16
Physical activity, %					
sedentary	65.5	57.2	65.8	58.5	0.05
moderate	25.8	31	19.2	28.8	
vigorous	8.7	11.8	15	12.7	
Total energy(kcal/d)	1917 (1757,2077)	2061(1939,2183)	2071(1937,2205)	1999(1768,2229)	0.35
Fruit/vegetables (g/d)	16.6 (11.8,23.4)	21.9 (14.5,33.1)	20.0 (14.0,28.5)	16.9 (6.8,42.0)	0.69
Fat (g/d)	76.7 (71.0,82.4)	85.9 (79.4,92.5)	83.9 (79.1,88.7)	77.6 (68.8,86.3)	0.07
Protein (g/d)	78.3 (72.0,84.4)	86.5 (80.9,92.2)	90.1 (81.8,98.4)	96.6 (82.4110.8)	0.002
Carbohydrate (g/d)	230(202,258)	240(220,260)	241.9(218,266)	231(206,256)	0.8
Fish intake (g/d)	0.24 (0.19,0.28)	2.82 (2.64,2.99)	9.07 (8.62,9.51)	64.05 (47.2,80.9)	0.0001
DDE (n/kg/d)	0	0.08 (0.05,0.13)	0.26 (0.16,0.44)	1.53 (0.84,2.81)	0.0001
PCBs (n/kg/d)	0	0.30 (0.15,0.62)	0.83 (0.41,1.68)	4.8 (2.28,10.10)	0.0001
EPA + DHA (mg/d)	3.8 (2.9,4.8)	44.7 (35.8,53.6)	141 (126,155)	948 (707,1189)	0.0001

DDE - dichlorodiphenyldichloroethylene; PCBs - polychlorinated biphenyls; EPA - eicosapentaenoic acid; DHA - docosahexaenoic acid; values are mean (95%CI); DDE/PCBs -geometric mean; p-values correspond to ANOVA for continuous variables and chi-square tests for categorical variables; sedentary physical activity combines inactive and sedentary lifestyle, weighted estimates.

Table 4
Fish consumption patterns and dietary characteristics by Ontario ecozones.

	Boreal Shield/Subarctic	Boreal Shield/Northeast	Hudson Plains/Subarctic	Mixed-wood Plain/Northeast	p trend
n	356	344	266	460	
T2D (%)	23.5	24.8	28.7	24.2	0.46
Age, y	42.6 ± 15.3	47.1 ± 14.9	44.5 ± 15.6	50.0 ± 15.8	0.0001
Body mass index	29.7 ± 5.3	31.3 ± 5.5	30.5 ± 5.5	31.6 ± 6.4	0.0001
Women (%)	54	65	65	66	0.0024
Energy intake (kcal/d)	1888 (1000–3163)	1826 (958–3357)	1991 (1050–3617)	1780 (927–3150)	0.0052
Smoking (%)	55.3	62.9	51.8	32.8	0.0001
Fish consumers %	89	84	80	54	
Total fish g/d	15.0 (0.6–228)	5.9 (0.5–106.6)	6.2 (0.5–91.5)	3.5 (0.5–60.2)	0.0001
DDE ng/kg/d	0.31 (0.004–9.2)	0.21 (0.007–10.0)	0.16 (0.003–12.03)	0.14 (0.003–10.16)	0.05
PCBs ng/kg/d	1.38 (0.00931.6)	0.32 (0.005–19.6)	0.56 (0.007–34.01)	1.01 (0.001–39.99)	0.0020
EPA + DHA g/d	0.25 (0.01–2.9)	0.07 (0.003–1.29)	0.09 (0.004–1.28)	0.04 (0.002–0.79)	0.0001
Walleye consumers %	80	56	49	35	
Walleye g/d	7.5 (0.5–100.6)	2.2 (0.5–26.7)	3.3 (0.5–43.1)	2.1 (0.5–26.9)	0.0001
DDE ng/kg/d	0.06 (0.003–1.02)	0.08 (0.01–1.22)	0.02 (0.002–0.75)	0.09 (0.007–2.69)	0.1
PCBs ng/kg/d	0.09 (0.002–7.3)	0.13 (0.005–2.19)	0.05 (0.003–6.48)	0.78 (0.05–19.93)	0.023
EPA + DHA g/d	0.18 (0.01–2.33)	0.05 (0.01–0.62)	0.08 (0.01–1.00)	0.05 (0.01–0.62)	0.0001
Whitefish consumers %	38	46	15	3	
Lake Whitefish g/d	6.7 (0.5–95.8)	2.03 (0.5–55.7)	3.4 (0.5–43.9)	1.4 (0.5–4.0)	0.0001
DDE ng/kg/d	0.14 (0.008–1.90)	0.12 (0.004–3.62)	0.10 (0.01–0.88)	0.07 (0.03–0.31)	0.1
PCBs ng/kg/d	0.13 (0.006–1.91)	0.24 (0.002–9.7)	0.14 (0.02–1.53)	0.17 (0.07–0.78)	0.09
EPA + DHA g/d	0.11 (0.01–1.63)	0.03(0.01–0.94)	0.05 (0.01–0.74)	0.02 (0.01–0.07)	0.0001
Lake Trout consumers %	17	32	9	2	
Lake Trout g/d	3.3 (0.5–72.2)	2.1 (0.5–55.2)	2.5 (0.5–61.7)	2.6 (0.5–27.1)	0.2
DDE ng/kg/d	0.49 (0.02–10.08)	0.60 (0.05–4.97)	1.03 (0.14–19.19)	0.89 (0.1–8.35)	0.0171
PCBs ng/kg/d	0.51 (0.03–8.42)	0.90 (0.09–9.45)	2.50 (0.35–46.71)	2.12 (0.26–19.96)	0.0001
EPA + DHA g/d	0.04 (0.01–0.75)	0.02 (0.01–0.58)	0.03 (0.01–0.64)	0.03 (0.01–0.28)	0.26
Yellow perch consumers %	3	16	1	23	
Yellow perch g/d	1.9 (0.8–9.6)	1.7 (0.5–26.8)	1.1 (0.5–10.1)	2.36 (0.5–34.9)	0.21
DDE ng/kg/d	0.01 (0.002–0.03)	0.08 (0.02–1.57)	0.13 (0.04–1.2)	0.04 (0.01–0.67)	0.0001
PCBs ng/kg/d	0.35 (0.13–1.3)	0.12 (0.03–2.47)	1.87 (0.61–16.95)	0.26 (0.05–4.67)	0.0001
EPA + DHA g/d	0.01 (0.002–0.03)	0.004 (0.001–0.07)	0.004 (0.001–0.02)	0.01 (0.001–0.09)	0.21

DDE - Dichlorodiphenyldichloroethylene; PCBs - Polychlorinated biphenyls; EPA - eicosapentaenoic acid; DHA - docosahexaenoic acid; data are %, mean ± SD or median (2.5–97.5th percentiles); Fish, DDE, PCBs and EPA + DHA intakes estimated for fish consumers only; ng/kg/d - nanograms per kg body weight per day; p-values correspond to ANOVA for continuous variables and chi-square tests for categorical variables; weighted estimates of T2D.

Table 5
Multiple logistic regression analyses of fish consumption and type 2 diabetes.

	no or < 1/mo	1/mo	2–3/mo	≥1/week	p trend
Model 1	1 (ref)	0.82 (0.49–1.37)	1.16 (0.74–1.79)	2.34 (1.27–4.26)**	0.005
Model 2	1 (ref)	0.92 (0.56–1.48)	1.08 (0.73–1.62)	2.31 (1.32–4.02)**	0.006
Model 3	1 (ref)	0.99 (0.62–1.59)	1.14 (0.73–1.76)	2.50 (1.38–4.58)**	0.008
n	508	278	338	302	

Values are ORs (95%CI); Model 1: crude estimates; Model 2: adjusted for age, gender and BMI; Model 3 - additionally adjusted for physical activity, total energy intake, smoking, household size, and education; **- p value < 0.01; portion size is 150 g of fish.

Table 6
Logistic regression analyses of log-transformed DDE, PCBs and long-chain n-3 fatty acids intake and type 2 diabetes in total sample and stratified by age groups.

	DDE	PCBs	EPA + DHA
	Total population (n = 1426)		
Model 1	1.07* (1.03–1.29)	1.05* (1.003–1.24)	1.12 (0.99–1.20)
Model 2	1.09* (1.05–1.75)	1.07* (1.004–1.27)	0.80 (0.58–1.00)
	< 45 y (n = 709)		
Model 1	1.14 (0.99–1.50)	1.11 (0.99–1.33)	1.14 (0.95–1.35)
Model 2	1.16 (0.78–1.74)	1.12 (0.87–1.26)	0.95 (0.65–1.14)
	≥45 y (n = 717)		
Model 1	1.15* (1.002–1.3)	1.10 (0.99–1.39)	1.10 (0.93–1.26)
Model 2	1.24* (1.12–2.54)	1.13* (1.001–1.4)	0.86* (0.46–0.99)

Values are OR (95%CI); Model 1 was adjusted for age, BMI, gender, physical activity, smoking, energy intake, household size and education; Model 2: DDE and PCBs were additionally adjusted for EPA + DHA intake; EPA + DHA was adjusted for DDE/PCBs; ORs: per unit change in regression (log transformed variables); *- p value < 0.05.

dietary POPs and EPA + DHA with T2D presented in Appendix 5 Figs. A1–A3.

Average concentrations of n-3FAs (EPA + DHA), PCBs and DDE in commonly consumed fish species samples by Ontario ecozones are presented in Table A5 (Appendix 4). Overall, the concentrations of both DDE and PCBs were low in walleye across all ecozones. The highest levels of PCBs and DDE were determined to be in lake trout in the Boreal Shield/ Subarctic and Hudson Plains/ Subarctic ecozones. Total PCBs and DDE were also higher in yellow perch in the Boreal Shield/ Subarctic, Boreal Shield/Northeast and Hudson Plains/Subarctic than in other species. However, low consumption of this species was reported. In whitefish, the highest concentrations of total PCBs and DDE were found in the Boreal Shield/ Subarctic ecozone.

4. Discussion

The prevalence of T2D in Ontario First Nations living on reserve (24.4%) and was similar to that reported by the First Nation Regional Health Survey (RHS) in Ontario (21.6%) (First Nations Information Governance Centre, 2012). The prevalence of self-reported diabetes in the general Canadian population was 6.8% (95% CI: 6.6–7.1%) among individuals aged 20 years and older (Pelletier et al., 2012). In our study, more women than men reported T2D, which is compatible with other studies among First Nations in Canada (Green et al., 2003; Oster et al., 2011; Riediger et al., 2014).

We found a positive association between dietary DDE and PCBs

intakes and self-reported T2D in the whole sample and the sample stratified by age groups (> 45y vs. ≥45y). Dietary n-3 FAs intake (EPA + DHA) showed a protective effect against T2D among older participants after controlling for POPs intake. The consumption of one portion of fish and more per week was positively associated with T2D when compared to the reference group (no fish or < 1/month). This association remained significant after adjusting for the confounding factors, although we were unable to control for DDE/PCBs or fatty acids in fish.

Our findings are consistent with previous cross-sectional studies on the relationship between exposure to POPs and T2D conducted in Indigenous communities and general populations (Codru et al., 2007; Lee et al., 2006, 2007; Philibert et al., 2009). These studies investigated serum POPs concentrations in relation to the prevalence of T2D whereas we assessed dietary POPs intake from fish. However, since locally-harvested fish among Indigenous people living on reserve is considered as the main source of exposure to contaminants, dietary intake of POPs might be a good indicator of the exposure. There is also evidence in the literature that frequency of wild food consumption and serum POPs levels in First Nations communities was positively correlated (Seabert et al., 2014). Similar positive correlations between fish consumption and serum POPs levels were also reported by other studies (Duarte-Davidson, 1994; Philibert et al., 2009; Turyk et al., 2009).

Our results showed differences in the associations of POPs, n-3 FAs with T2D between younger (> 45y) and older participants (≥45y). This may be explained by low fish, and consequently, low dietary n-3 FAs and POP intake among individuals aged < 45y that resulted in the weak associations. Since older participants reported higher consumption of fish, the adverse effect of POPs and protective effect of n-3 FAs were more prominent in this age group. Also, the differences could be related to increased risk factors for T2D in older individuals. Turyk et al. reported stronger positive associations of POPs with blood glucose in persons with higher levels of diabetes risk factors (Turyk et al., 2015).

In general, the association between a single chemical and a health outcome is difficult to interpret because of co-exposure to other chemicals that might have similar or opposite effects (Ruzzin, 2012) In our study, adjustment for multiple exposure was impossible because of strong correlations between DDE and PCBs due to the same exposure route. In addition, unmeasured contaminants from other sources might also confound the associations between T2D and POPs.

Previous studies investigating fish and n-3 FAs consumption in relation to T2D reported conflicting results. A positive association between total and lean fish intake and risk of T2D was reported by van Woudenbergh et al. (2009) in a prospective cohort study of participants aged 55 y and older. Similar findings were concluded by Kaushik and Mozaffarian (2009b) in 3 prospective cohorts of adults followed for 14-18y. However, an inverse association between total (white, and oily fish) and shellfish and T2D was found in population-based cohort studies by Nanri et al. (2011b) and Villegas et al. (2011). A protective effect of n-3 FAs (EPA + DHA) against T2D was reported by several studies (Brostow et al., 2011; Paquet et al., 2014; Virtanen et al., 2014). Wallin et al. (2015) found no association between total fish consumption and T2D. However, additional adjustment for PCBs exposure resulted in lower point estimates for fish, but associations remained statistically non-significant (Wallin et al., 2015). Thus, the net effect of fish consumption on T2D may depend on the POPs content in fish.

In our study, a positive relationship between frequency of fish consumption and T2D might be due to the counteraction between the adverse effect of POPs and protective effect of n-3 FAs that co-exist in fish. In fact, the detrimental effect of POPs usually starts to appear at a lower fish consumption level whereas beneficial effects due to n-3 FAs is often more prominent at a higher fish consumption level (Lee et al., 2014). Since the study participants reported low consumption of fish (only 20% eat ≥ one portion (150 g) of fish per week that corresponds to Canada's food guide recommendations to eat at least two servings (of 75 g each) of fish a week), the overall protective effect of n-3 FAs might not be sufficient to outweigh the detrimental effects of POPs.

The fish consumption patterns differed among First Nations depending on the variety and availability of species in the Ontario regions. For example, 80–90% of participants reported eating fish at least once in the prior year in the Boreal Shield and the Hudson Plains/ Subarctic ecozones, whereas only half of participants living in the Mixed-wood Plain/ Northeast ecozone did. The highest average intake of total fish was determined to be in the Boreal Shield/Subarctic at 15 g/day compared to only about 6 g/d in the Boreal Shield/ Northeast and the Hudson Plains/ Subarctic. Walleye was the most commonly eaten fish in Ontario followed by lake whitefish and lake trout. Yellow perch was consumed only by participants in the Boreal Shield/ Northeast (16%) and the Mixed-wood Plain/ Northeast (23%) ecozones. They reported eating yellow perch about 1.7 and 2.4 g/d of, respectively.

There were differences in POPs levels in fish species (Table A5). Lake trout had the higheast POP concentrations across four regions compared to other species. Walleye, in contrast, had the lowest POPs levels in all regions. Elevated levels of POPs in lake trout were also documented by McGoldrick et al., who reported that concentrations of several POPs continue to dominate the chemical burden of Great Lakes fish (McGoldrick and Murphy, 2015). The concentrations of POPs in lake whitefish were low across all Ontario ecozones except for PCBs in Boreal Shield/Subarctic. With regards to n-3 FAs content, lake trout and whitefish have higher levels of EPA + DHA compared to walleye and yellow perch (Health Canada, 2014).

This study has several limitations. First, a cross-sectional design does not allow the conclusion of the temporality between POPs and T2D. Second, the self-reported prevalence of T2D could have resulted in underdiagnoses since some participants might not be aware of having T2D. To validate our self-reported estimates of diabetes, we compared them with prevalence rates for self-reported diabetes reported by the Regional Health Survey (RHS) which is a representative study for First Nations living on reserve conducted over the similar period of time. The RHS collected more comprehensive information on T2D including kind of treatment used to control diabetes, frequency of checking blood sugar levels, complications of diabetes, whether adopting a healthier lifestyle including (diet and exercise), attendance of a diabetes clinic and getting diabetes education (Appendices: Table A4). A study among Cree First Nations living in Northern Quebec reported that 4.5% of participants had undiagnosed diabetes based on glucose levels that indicates diabetes (≥7 mmol/L), but no mention of diabetes in their medical charts (Health et al., 2013). Finally, n-3 FAs concentrations in fish species were estimated using the Canadian Nutrient File (Health Canada, 2014). Since there is a considerable variation on reported n-3 FAs in fish species in the literature (Cladis et al., 2014; Pantazopoulos et al., 2013), the potential for error in the estimation of n-3 FAs intake from fish may occur.

In order to examine if participants diagnosed with T2D tend to change their diets, we assessed and compared their dietary and lifestyle behaviour with individuals without T2D. Thus, two sensitivity analyses were conducted. First, dietary intake and lifestyle practices were compared between participants recently diagnosed with T2D (0-5y) and those who have T2D for a long period of time (> 5y) (Appendix 1: Table A1). The analysis shows no statistically significant differences in physical activity, macronutrient intakes, and fish consumption between two groups.

The second sensitivity analysis was performed to capture differences in dietary intake and lifestyle behaviour in participants with and without T2D associated with self-reported dieting status (Appendix 2: Tables A2, A3). Overall, dieting individuals had higher mean BMI; they reported lower smoking rate, lower total energy and carbohydrate intake, and higher fruit and vegetable consumption than non-dieting subjects. Fish and n-3 FAs consumption was comparable between two groups. However, these differences were not statistically significant in further comparison of dietary intakes in dieting and non-dieting

participants with and without T2D, individually (Appendix 3: Table A4).

This is the first study investigating the relationship of fish consumption, dietary intake of n-3 FAs and POPs, and T2D in a representative sample of First Nations living on reserve across four Ontario ecozones. Our results were adjusted for the main risk factors for T2D such as age, gender, BMI, smoking, physical activity, energy intake, and education.

Most of the other studies reported a correlation between fish consumption and serum POPs levels (Duarte-Davidson, 1994; Philibert et al., 2009; Turyk et al., 2009). We found the same relationship between dietary exposure to POPs and T2D. Dietary exposure information is more useful to develop an advisory to limit exposure by changing fish intake pattern.

5. Conclusion

We found positive cross-sectional associations of fish and dietary POPs intake with T2D and a negative association of n-3 FAs with T2D in older individuals. Fish consumption of ≥1 portion per week was associated with increased odds of T2D by about 2.5 times compared to no fish consumption. DDE and PCBs dietary intake increased the risk of T2D in both younger and older participants. Long chain n-3 FAs intake showed a protective effect against T2D in older participants only. Walleye, whitefish, lake trout and yellow perch were commonly consumed fish species across four Ontario ecozones. Lake trout contained the highest levels of POPs whereas lake whitefish was the main contributor of the n-3 FAs (EPA and DHA). Our results support previous findings that exposure to DDE and PCBs may increase risk of T2D. Elevated levels of contaminants in fish may counteract with potentially beneficial effects of n-3 FAs and fish consumption, and it is important to monitor the levels of POPs in the locally harvested fish. However, the overall health benefits of high consumption of fish rich in n-3 FAs may outweigh the adverse effect of contaminants.

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Appendix A

The goal of this analysis was to examine differences in dietary intake of participants recently diagnosed with T2D and those diagnosed with T2D for a long period of time. Using data on the onset of T2D, participants were divided into two groups: 1) those who were diagnosed with T2D until 5 years ago (≤5y) and those diagnosed with T2D for more than 5 years ago (> 5y). Then, dietary and lifestyle behaviours were compared between these groups. The results presented in Table A1 show that there were no statistically significant differences in dietary characteristics between individuals recently diagnosed with T2D and those having T2D for more than 5 years.

Appendix B

Using data on self-reported dieting status (yes/no) on the previous day of an interview, a sensitivity analysis was conducted to examine whether dietary intake and lifestyle practices differed between dieting and not dieting participants (Table A2). Overall, about 12% of participants reported limiting their caloric intake on the previous day in order to lose weight. The prevalence of T2D was higher among dieting participants than non-dieting (29.8% vs 23.4%). Women tend to diet more often compared to men. Mean BMI was significantly higher among dieting responders compared to not-dieting ones (34 vs. 30.7). Also, dieting individuals reported lower smoking rate, lower total energy and carbohydrate intake, and higher fruit and vegetable consumption than non-dieting subjects. Fish and n-3 FAs consumption were similar between dieting and non-dieting participants. Also, physical activity and fat, saturated fat and protein intake were comparable.

Table A1
Dietary and lifestyle characteristics by onset of type 2 diabetes (n = 327).

	Onset of type 2 Diabetes		
	≤5 years	> 5 years	p trend
n	117	220	
Age	51.2 ± 12.9	57.0 ± 13.1	0.0001*
Body Mass Index, kg/m^2	33.1 ± 5.6	32.6 ± 6.6	0.6 12
Dieting, %	15	15	0.50
Smoking, %	51.8	44.2	0.05
Physical activity, %			0.061
Inactive	27.4	30.6	
Sedentary	41.1	45.5	
Moderate	23.1	16.7	
Vigorous	8.4	7.2	
Dietary characteristics			
Energy intake (kcal/d)	1949 (1323–2483)	1831 (1240–2176)	0.051
Total Fat (g/d)	71 (51–106)	66 (46–96)	0.061
Saturated fat (g/d)	21 (14–32)	20 (13–29)	0.052
CHO (g/d)	216 (151–270)	190 (135–253)	0.071
Protein (g/d)	77 (57–107)	72(53–104)	0.312
Fruit/Vegetables (g/d)	70 (0–176)	71 (0–213)	0.825
Fish (g/d)	5.0 (1.1–20.0)	4.2 (0–19.8)	0.513

≤5 years- diagnosed with type 2 diabetes less than 5 y ago; > 5 -diagnosed with T2D more than 5 years ago; Values are mean ± SD, or median (25–75th) percentile.

Table A2
Dietary characteristics of participants by dieting status (n = 1426).

	Dieting		
	Yes	No	p trend
Total, %	12	88	
Type 2 diabetes, %	29.8	23.4	0.020*
Female, %	66.2	62.7	0.224
Age	47.86 (44.57,51.15)	45.81 (44.58,47.04)	0.201
Body Mass Index, kg/m^2	34.01 (32.51,35.51)	30.7 (30.20,31.21)	0.0001*
Physical activity, %			0.212
inactive	23.1	19.4	
sedentary	41.1	42.9	
moderate	27.7	25.6	
vigorous	8.1	11.9	
Smoking, %	33.2	50.8	0.030*
Dietary characteristics			
Energy intake(kcal/d)	1865.5 (1609.9,2121.1)	2012.1 (1933.8,2090.4)	0.0524*
Fruit and Vegetable (g/d)	33.1 (20.8,52.5)	16.0 (13.6, 18.7)	0.0022*
Total Fat (g/d)	74.34 (63.89,84.79)	80.87 (78.22,83.51)	0.172
Saturated fat (g/d)	23.78 (20.41,27.14)	25.87 (24.79,26.95)	0.232
Carbohydrate (g/d)	221.83 (184.40,259.26)	236.4 (218.88,253.91)	0.0330*
Protein (g/d)	81.69 (72.76,90.61)	87.11 (81.47,92.75)	0.671
Fish intake (g/d)	21.86 (5.60,38.12)	16.39 (8.69,24.09)	0.254
DDE (ng/kg/d)	0.04 (0.01,0.12)	0.04 (0.02,0.06)	0.163
PCBs (ng/kg/d)	0.08 (0.02,0.28)	0.07 (0.04,0.14)	0.141
EPA + DHA (mg/d)	0.17 (0.04,0.30)	0.11 (0.05,0.17)	0.721

DDE - dichlorodiphenyldichloroethylene, PCBs - polychlorinated biphenyls, EPA - eicosapentaenoic acid, DHA - docosahexaenoic acid, values are mean (95%CI), DDE/PCBs -geometric means, weighted estimates.

Table A3
Dietary characteristics of Ontario participants by dieting status (n = 1426).

	Dieting			Not dieting		
	T2D +	T2D-	p trend	T2D +	T2D-	p trend
Total n, (%)	48	103		279	996	
Female (%)	65.5	66.4	0.851	64	62.3	0.785
Age	56.1 (51.8, 60,2)	44.4 (40.5,60.3)	0.0001*	55.6 (53.3,58.1)	42.8 (40.1,44.7)	0.0001*
Body Mass Index	36.2 (33.6,38.8)	33.1 (30.9,35,2)	0.0001*	32.8 (31.7, 33.6)	30.1 (29.4, 30.8)	0.0001*
Physical activity, %			0.0269*			0.0017*
inactive	31.3	21.4		29.4	20.6	
sedentary	45.8	32.1		44.4	42.7	
moderate	14.6	36.9		18.6	24.7	
vigorous	8.3	9.7		7.5	12.1	
Smoking (%)	40.6	30.1	0.366	46.2	52.1	0.175
Dietary characteristics						
Energy intake(kcal/d)	1558.2 (1328,1788.0)	1996.2 (1669.6,2322.7)	0.077	1991.9 (1822.5,2161.3)	2018.3 (1909.4,2127.3)	0.824
Fruit/Vegetable (g/d)	28.8 (12.6, 66.3)	35.2 (20.0, 62.2)	0.318	21.9 (15.6, 30.7)	14.6 (12.1, 17.6)	0.052
Total Fat (g/d)	60.3 (50.4,70.6)	80.3 (67.2, 93.4)	0.011	82.4 (75.6,89.1)	80.4 (77.6,83.2)	0.604
Saturated fat (g/d)	20.5 (16.1,24.0)	25.5 (21.3,29.8)	0.187	24.4 (22.3, 26.5)	26.2 (25.1,27.5)	0.114
Carbohydrate (g/d)	187.7 (160.3215.1)	236.3 (186.1286.6)	0.432	219.8 (205.4234.3)	241.5 (218.1264.8)	0.167
Protein (g/d)	70.8 (55.1,86.6)	86.3 (76.6,96.0)	0.156	89.2 (78.2108.1)	84.3 (79.7, 88.9)	0.713
Fish intake (g/d)	23.5 (8.2,38.8)	21.1 (0.8,41.5)	0.279	26.1 (11.5,40.6)	13.4 (4.3, 22.5)	0.182
DDE (ng/kg/d)	0.08 (0.03, 0.25)	0.04 (0.02, 0.08)	0.093	0.05 (0.04, 0.08)	0.03 (0.02,0.04)	0.449
PCBs (ng/kg/d)	0.15 (0.05, 0.66)	0.08 (0.04, 0.19)	0.039	0.10 (0.06, 0.16)	0.07 (0.05, 0.08)	0.601
EPA + DHA (mg/d)	320.4(146.8, 493.9)	295.4(140.2592.2)	0.241	382.8(134.5631.1)	206.5(73.1, 339.8)	0.053

DDE - dichlorodiphenyldichloroethylene, PCBs - polychlorinated biphenyls, EPA - eicosapentaenoic acid, DHA - docosahexaenoic acid, values are mean (95%CI), DDE/PCBs -geometric mean; weighted estimates.

Further analyses compared dietary intake between dieting and non-dieting individuals with and without T2D. Overall, no statistically significant differences in macronutrients intake between dieting participants with and without T2D, and non-dieting individuals with and without T2D were found. Participants with T2D (both dieting and non-dieting) tended to be less physically active compared to those without T2D. Overall, intakes of macronutrients were comparable between groups with the exception of higher fruit and vegetable consumption reported by dieting subjects without T2D (Table A3).

Table A4
Prevalence of diabetes reported by FN RHS and FNFNES.

	Ontario	
Prevalence (%)	RHS (2008/10) (18y +)	FNFNES (2011/12) (19y +)
Total	21.6	24.4
Women	23.6	24.6
Men	19.7	23.5

Appendix C. Validity of self-reported diabetes data from FNFNES

Since the estimates of diabetes prevalence are based on self-reports, there is a potential for under-reporting as some people may not be aware of having the disease. The validity of self-reported diabetes from FNFNES survey was analyzed by comparison of their estimates on the prevalence of self-reported diabetes with those reported by FN RHS (Phase II, 2008/10) which is the only First Nations-governed national health survey in Canada. RHS collected detailed data on the health and well-being of First Nations adults (aged 18 years and older). The survey sample represented the First Nations population living in First Nations communities in all provinces and territories. In phase II (2008/10) of RHS, 216 communities were included in the study. The communities were randomly selected within each First Nations "sub-region" to provide a representative sample at the regional and national levels. Individual responses were weighted, to represent a proportion of the age group and region.

In total, seven First Nations communities were surveyed by both RHS and FNFNES studies. In the RHS survey, the following information on diabetes was collected: the type of diabetes, kind of treatment used to control diabetes, frequency of checking blood sugar levels, complications of diabetes, whether adopting a healthier lifestyle including (diet and exercise), attendance of a diabetes clinic and getting diabetes education. We compared the estimates of the prevalence of diabetes in Ontario First Nations reported by RHS and FNFNES. The results are presented in Table A4. The FNFNES survey reported similar age-standardized prevalence of diabetes in Ontario First Nations (overall and by gender) compared to the RHS estimates (21.6 vs. 24%). Both surveys reported differences in diabetes prevalence between male and females with higher rates in females.

Appendix D

See Table A5 here.

Table A5
Concentration of n-3 FAs and POPs in the most consumed fish species in Ontario ecozones.

		Ecozones							
	Canada	Boreal Shield/Subarctic		Boreal Shield/Northeast		Hudson Plains/Subarctic		Mixed-wood Plain/Northeast	
Fish species	EPA + DHA g/100 g	DDE ng/g	PCBs ng/g	DDE ng/g	PCBs ng/g	DDE ng/g	PCBs ng/g	DDE ng/g	PCBs ng/g
Walleye	0.31 (0.05)	1.56 (2.22)	9.04 (10.38)	3.67 (3.26)	6.69 (7.44)	1.23 (2.06)	9.9 (18.48)	4.86 (5.30)	36.23 (27.70)
Lake whitefish	1.24 (0.56)	6.90 (9.95)	22.72 (35.52)	6.38 (5.46)	9.97 (7.49)	2.38 (1.82)	3.31 (1.76)	5.89 (7.21)	14.55 (24.27)
Lake trout	0.84 (0.14)	25.72 (34.05)	77.23 (126.1)	25.55 (24.68)	36.78 (30.25)	31.60 (24.32)	76.89 (64.67)	26.65 (24.32)	63.69 (83.54)
Yellow perch	0.29 (0.05)	3.11 (3.95)	33.17 (57.09)	3.11 (3.95)	33.17 (57.09)	3.11 (3.95)	33.17 (57.09)	1.17 (0.73)	9.80 (5.97)

EPA- eicosapentaenoic acid; DHA-docosahexaenoic acid; EPA + DHA in grams per 100 g of raw fish; ng/g -nanograms per 1 g of fish; data are mean (SD) - standard deviation.

Appendix E

See Figs. A1–A3 here.

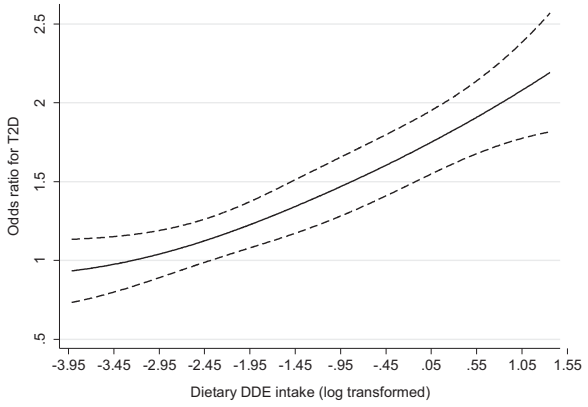

Fig. A1. Dose-response relationship between dietary DDE intake (ng/kg/bw) and type 2 diabetes (n = 1426).

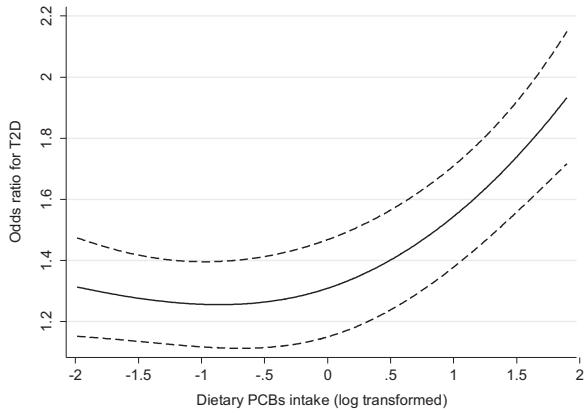

Fig. A2. Dose-response relationship between dietary PCBs intake (ng/kg/bw) and type 2 diabetes (n = 1426).

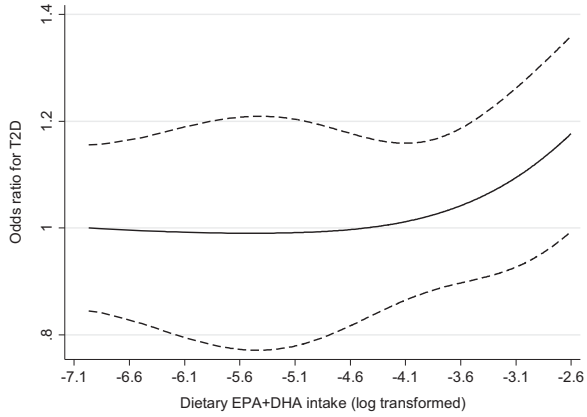

Fig. A3. Dose-response relationship between dietary EPA + DHA intake (mg/d) and type 2 diabetes (n = 1426).

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