



Contents lists available at ScienceDirect

Journal of Great Lakes Research

journal homepage: www.elsevier.com/locate/ijglr

Risk-benefit modeling to guide health research in collaboration with Great Lakes fish consuming Native American communities

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ARTICLE INFO

Article history:

Received 18 May 2020

Accepted 3 August 2020

Available online 24 August 2020

Communicated by Marc Gaden

Keywords:

Fish consumption

Native Americans

Mercury

PUFA-3

Polychlorinated biphenyls

ABSTRACT

It is well documented that fish consumption imparts both health risks and benefits. Furthermore, fish harvest and consumption are an essential part of Great Lakes Native American cultures. Quantitative models that compare risk and benefits to potential consumption scenarios can help guide future health research as well as consumption advice for potentially sensitive populations. This article presents fish consumption scenarios based on self-reported meal plans constructed by tribal members in eastern upper peninsula and northern lower Michigan Anishinaabe. Two risk–benefit models were applied to these scenarios to estimate the potential neurodevelopmental and cardiovascular risks (either increased or reduced risk) from dioxin-like polychlorinated biphenyls (DL-PCBs), methylmercury (MeHg), and omega-3 polyunsaturated fatty acids (n3-PUFA). All scenarios except maximum exposure estimates (i.e. 25th–75th percentile MeHg, DL-PCB, and n3-PUFA intakes) predicted reduced cardiovascular risk and improved neurodevelopmental outcomes. The greatest predicted benefits (adjusted for risks) occurred at the 75th percentile intake of MeHg, DL-PCB, and n3-PUFA scenarios: 5.0 visual recall memory (VRM) and 4.41 Intelligence Quotient (IQ) benefits, and 28% reduced risk of cardio-vascular disease. Scenarios based on maximum self-reported intake, however, predicted health detriments. These results suggest that most fish consumption scenarios as constructed in collaboration with Native American communities could impart health benefits despite the presence of contaminants. However, high-end consumption estimates warrant caution as well as the need for well-crafted advice. Potential benefits further underscore the value of reducing contamination burdens in Great Lakes fisheries. Future priorities of ongoing contamination monitoring and health research are discussed.

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Introduction

The Laurentian Great Lakes Basin is the ancestral, traditional, and contemporary lands and waters of many Indigenous nations, including the Anishinaabeg, the Three Fires Confederacy of Ojibwe, Odawa, and Potawatomi peoples. All environmental research seeking to engage stakeholder communities in the Basin must consider this historical context. Laurentian Great Lakes fish consumption advisories have historically focused on human health risks from persistent bioaccumulative toxic (PBT) chemicals. Standard practice is to evaluate the risks to a developing fetus as the most sensitive health endpoint responding to PBTs. In the Great Lakes, advisories appropriately focus on polychlorinated biphenyls (PCBs) and methylmercury (MeHg) as the primary PBTs of concern since

most human exposure to these contaminants occurs via fish consumption. Nevertheless, epidemiological studies have repeatedly observed health benefits associated with fish consumption (Oken et al., 2005; Mozaffarian and Rimm, 2006; Oken et al., 2008; Strain, et al., 2015). Furthermore, these beneficial endpoints align with health risk endpoints associated with fish consumption, specifically: neurodevelopment and cardiovascular health. Other health outcomes hypothesized to have countervailing responses to n3-PUFA and PBT intake include cancer, obesity, type 2 diabetes, and arthritis (Cohen et al., 2005; Weaver et al., 2008; Ginsberg and Toal, 2009; Johnson et al., 2009; Alexander et al., 2017; Wan et al., 2017).

Because PBTs and beneficial omega-3 polyunsaturated fatty acids (n3-PUFAs) vary by fish species and location (Strandberg et al., 2020), variations in response to consumption advice may have important health consequences. Recognition of these dynamics has led to a recent emphasis on risk/benefit tradeoffs along with

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a need to quantitatively estimate such tradeoffs (Ginsberg and Toal, 2009; Stern and Korn, 2011; Rheinberger and Hammitt, 2012; Ginsberg et al., 2015). Risks and benefits analyses are highly relevant to fish consuming cultures in the Great Lakes region who also report cultural and wellbeing benefits from consuming local fish (Dellinger et al. 2017, 2019). The current manuscript presents a risk/benefit analysis to inform ongoing work examining the best practices and consequences of developing fish consumption advisories in collaboration with Great Lake Native American (Anishinaabe) consortia.

Development of fish consumption advice with Anishinaabe, and similar groups, requires an acknowledgement that fish are culturally important. Furthermore, many groups including the funders of this work, National Institutes for Environmental Health Science (NIEHS), recognize the importance of community engagement with vulnerable populations (NIEHS, 2012; Finn and O'Fallon, 2015; Finn et al., 2017). The current study is a partnership between the Medical College of Wisconsin, the Chippewa Ottawa Resource Authority (CORA), and the Inter-Tribal Council of Michigan (ITCMI) to develop fish consumption advisories with the tribal community members of Upper Michigan. Since 1991, CORA has monitored PBTs in fillets of lake trout (*Salvelinus namaycush*) and lake whitefish (*Coregonus clupeaformis*) from the waters of Lakes Superior, Huron, and Michigan. They have also conducted intermittent sampling of additional species as needed to develop advice for their service area. CORA represents the fisheries interests of five Ojibwe and Ottawa tribes in eastern upper peninsula and northern lower Michigan (collectively called Anishinaabeg) whose ancestors ceded lands through the 1836 Treaty of Washington but retained the rights to hunt and fish on those territories.

We recently reported the following insights for developing community-engaged fish consumption advice: 1) that consumption of local fish is essential to Anishinaabe culture as well as a central part of Great Lakes culture broadly, 2) working in partnership with tribal communities yields advice that encourages consumption of culturally-important fish species whilst minimizing contaminant exposures, and 3) many of these culturally-important fish contain beneficial nutrients that could balance PBT risks (Dellinger et al., 2014a,b; Dellinger and Ripley, 2016; Dellinger et al., 2017; Dellinger et al., 2018a,b; Dellinger et al., 2019). A valuable next step for this work is to investigate the potential scenarios that may either optimize benefits or present excess risks. To investigate this, we have adapted three risk/benefit models to evaluate fish consumption scenarios that were generated by tribal community members. The models cover three health outcomes: visual recall memory (neurodevelopment (VRM)), coronary heart disease (CHD) (Ginsberg et al., 2015), and intelligence (IQ) (Rheinberger and Hammitt, 2012). These scenarios provide benchmarks to power future health investigations as well as refine consumption advice that is in-development.

Methods

Tribal fish monitoring data

Fish PBT and lipid data are sourced from the CORA biomonitoring program aggregated from recent (2016–2019) samples which rotate yearly between lakes. CORA protocols are detailed elsewhere (Moths et al., 2013; Dellinger et al., 2014; Dellinger and Ripley, 2016). The sampling design is based on EPA-approved methods (ITFAP, 2008) originally intended to compare to the Michigan Fish Contaminant Monitoring Program protocols (MDEQ, 1995). Normally, twelve samples per species, per source (Lake Superior, Lake Michigan, and Lake Huron) are sampled on a yearly rotation between lakes. Under the NIEHS funding, eight tra-

ditionally caught, one invasive (smelt), and four supermarket fish species from tribal fishery (CORA) areas were selected for sampling to investigate the options available to Anishinaabe fish consumers. Walleye were sampled from Lake Munuscong of the St. Marys River, a tributary of Lake Huron.

The following seven fish species from tribal fishery (CORA) areas were sampled: whitefish (*Coregonus clupeaformis*) (n = 12), lake trout (*Salvelinus namaycush*) (n = 12), walleye (*Sander vitreus*) (n = 7), yellow perch (*Perca flavescens*) (n = 7), herring (*Coregonus artedii*) (n = 7), burbot (*L. lota*) (n = 10) and smelt (*Osmerus mordax*) (n = 7). Four species of fish not caught in subsistence areas, but were available for purchase, were selected by commercial names (n = 7 each): farmed salmon, canned tuna, cod, and tilapia. Fish were weighed, measured, aged, and filleted before preservation by freezing at -20°C until sample processing. The time between capture of locally caught fish and lipid extraction was 2 weeks per US EPA/CORA protocols (ITFAP, 2008). The lipid data were analyzed at the DHA/EPA Omega-3 Institute, University of Guelph Ontario. Those methods included high performance capillary gas-liquid chromatographic analyses grade solvents and lipid standards obtained from Nu-Check Prep Inc (also described in Moths et al., 2013; Dellinger et al., 2018).

Fish consumption scenario development

ITCMI collaborated with the health and natural resource departments of the five 1836 Treaty signatory Tribes to test the fish consumption decisions of focus group participants with and without a novel fish consumption advisory (pre-post). The development and user testing of this advisory (a mobile app) is described in detail elsewhere (Dellinger et al., 2017, 2019). Data from the current study were sourced from user responses to fish consumption surveys as follows. The 1836 Treaty signatory Tribes include: Bay Mills Indian Community, Grand Traverse Bay Band of Ottawa and Chippewa Indians, Little Traverse Bay Bands of Odawa Indians, Little River Band of Ottawa Indians, and Sault Ste. Marie Tribe of Chippewa Indians. ITCMI staff set up inter-institutional contracts with each of the mentioned tribes to cover staff time in recruitment. Recruitment methods included: e-mailed newsletters, flyers at tribal offices, social media posts, and word-of-mouth as described in Dellinger et al. (2019). Sixteen app-testing sessions were facilitated by ITCMI staff and a CORA intern (all local tribal members) and held during the summer months of 2017 and April 2019. These months were targeted because more fish on average are consumed by the Anishinaabe during the spring and summer months than other seasons. Consumption peaks during the spring season, reaches a moderate rate in the summer months, and decreases during the winter months. The summer months tend to represent the overall annual average (GLIFWC, 2003). The initial fish consumption patterns from the 2017 focus groups (n = 103) were published in Dellinger et al. (2019). The current analysis updates these data with additional 39 respondents from the April 2017 focus groups (n = 142 overall respondents, n = 137 complete fish consumption data).

The pre and the post assessments recorded hypothetical monthly fish meals of various species. The participants were asked by ITCMI staff members who are Anishinaabe tribal members to consider what a typical month of fish consumption contained for them. Non-tribal research personnel were not present at focus groups to avoid undue influence from the possible perception of power dynamics. They were given a form to record first the overall number of fish meals they eat in a typical month, then to mark specifically which types of fish and how much. The form contained a matrix to represent the month with a list of fish species mentioned during past focus groups as well as a write-in option for species not listed. It included a standardized meal size referencing

a picture of a fish fillet on a plate (4 oz, 6 oz, or 8 oz; 1 oz = 28.3 g). Species historically harvested by the tribes were noted as “traditional” by CORA for later statistical analysis. This form was completed first without Gigiigoo'inaan App (see Dellinger et al., 2017 for detailed description of the advisory) and second with access to the app using an Android™ tablet. Thus, an estimate of typical fish consumption, but not a recall of any specific time was provided. When given the tablets, participants were encouraged to enter individual risk assessment data (sex, age, and bodyweight) then browse automatically generated recommendations on meal frequencies, species, and sources of fish. ITCMI staff then noted any technical or usability issues and asked a series of open-ended focus group questions and recorded the verbal responses from the group (Dellinger et al., 2019).

Intakes of n3-PUFA, Hg, PCB, fish grams, and fish meals were estimated from participant selections pre and post advisory viewing. Mean PBT and n3-PUFA data (including EPA + DHA) data per species were sourced primarily from CORA sampling but this did not cover all participant selections. Therefore, data shared with CORA by Michigan Department of Environmental Quality (MDEQ) dating back to 2004, were used to fill PBT gaps. Species for which CORA/MDEQ did not have n3-PUFA (EPA + DHA and total n3-PUFA) were accessed from USDA Food Data Central (fdc.nal.usda.gov, retrieved February 2020). These data were linked to the selected portion sizes, fish location (i.e. store or specific lake wherever available), and species of fish meal selections to generate total fish intake (grams or meals) over a hypothetical month for each participant. If data were not available for specified lakes or if no lake was specified, aggregate values of available MDEQ/CORA/USDA data were used (i.e. averaged across all three lakes).

PBT intakes were scaled against an average USA male (89 kg) or female (76 kg) body mass depending on the reported sex of the participant. The average weight of 82.5 kg (“Body Measurements.” Retrieved February 16, 2018, from <https://www.cdc.gov/nchs/fastats/body-measurements.htm>) was used for non-responders. This allowed for comparisons of PBT intake pre and post, relative to ATSDR and EPA guidelines. Mean and median pre and post PCB ($\mu\text{g}/\text{kg}/\text{day}$), Hg ($\mu\text{g}/\text{kg}/\text{day}$), n3-PUFA (mg/week), fish (g/month), and meals/month were compared separately. To confirm and update previously published findings (Dellinger et al., 2019) group differences were tested using Wilcoxon Signed-Rank. Because PBTs were expected to decrease and n3-PUFA/fish grams were hypothesized to increase posttest, $p \leq 0.05$ was considered significant.

Hg risk benefit model

Ginsberg et al. (2015) have developed a model to estimate visual recall memory (neurodevelopment (VRM)) and coronary heart disease (CHD) based on MeHg and n3-PUFA from fish (eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA)). Ginsberg and Toal (2009) selected studies from the literature (Guallar et al., 2002; Oken et al., 2005; Mozaffarian and Rimm, 2006; Oken et al., 2008) to support an integrated risk/benefit analysis for adult cardiovascular and *in utero* neuro developmental end points on a species-specific basis. These studies describe dose–response relationships between MeHg (but not other contaminants such as PCBs), n3-PUFAs, and common health endpoints for adults and fetuses. Mozaffarian and Rimm (2006) observed a 14.6% decreased relative risk to CHD per 100 mg/day of n3-PUFA, whereas a 23% increased relative risk for CHD was observed per 1 ppm hair Hg by others (Guallar et al., 2002; Ohno et al., 2007). The method therefore subtracts risk of adult CHD from MeHg (23% higher risk/1 ppm hair Hg) from the benefit (14.6% lower risk/100 mg n3-PUFA, benefit saturating at 250 mg). For fetal development (more sensitive), the method subtracts risk (3.5 VRM points/1 ppm maternal hair Hg) from the benefit (3.04 VRM

points/100 mg maternal n3-PUFA with saturation point of 8.1 VRM). This was initially based on observations of 6-month mother-infant pairs by Oken et al. (2005) in which 2.0-point VRM increase per 100 mg/day of n3-PUFA was observed contrasted with a 7.5-point VRM decrease per 1 ppm hair Hg. Ginsberg et al. (2015) updated the model for infant neural development based on a more comprehensive review of observational studies including more recent models from the World Health Organization (WHO) and USFDA (FAO/WHO, 2011).

The Ginsberg et al. (2015) equations have been modified for this study to estimate risks from steady-state intake scenarios based on focus group responses of Anishinaabe tribal members. As with the original exposure model (Ginsberg and Toal, 2000), hair Hg is predicted from dietary intake using the one compartment model (Stern, 1997). Instead of estimating risk from one fish meal, our modified model assumes a steady state daily intake ($\mu\text{g}/\text{kg}/\text{day}$) to predict a hypothetically stable hair Hg. This is possible because the Hg half-life of 40–50 days in the human body equilibrates to changed intake within months. Thus, the one compartment model, which serves as the basis for the EPA reference dose of 0.1 $\mu\text{g}/\text{kg}/\text{day}$ is considered a reasonable basis for exposure modeling. The parameters of the one-compartment model were updated to reflect the average bodyweight (82.5 kg) metric cited above and was applied to percentile Hg intakes to model steady-state hair Hg. Because the VRM and CHD coefficients were originally derived from differences in total hair Hg, the Ginsberg et al. (2015) equation was altered as follows:

Net risk/benefit for adult CHD = [(percentile: EPA + DHA mg/day) \times (14.6% lower risk/100 mg EPA + DHA)] – | [(percentile steady-state hair Hg) – (0.51 ppm hair Hg)] \times (23% higher risk/1 ppm hair Hg)

Net risk/benefit for infant VRM = [(percentile: EPA + DHA mg/day) \times (3.04 VRM points/100 mg EPA + DHA)] – | [(percentile steady-state hair Hg) \times (3.5 VRM points/1 ppm hair Hg)]

PCB + Hg risk benefit model

Rheinberger and Hammitt (2012) have presented a model that compares n3-PUFA (DHA), PCB, and MeHg intakes to various health and welfare outcomes. We have adapted the model to estimate IQ changes. Unlike Hg, PCBs and DL-PCBs persist for years in the human body (Travis and Hattemer-Frey, 1991). Furthermore, fish consumption is not the sole source of dioxin-like contaminants; whereas Hg exposure along with DHA + EPA intake come nearly exclusively from fish consumption (Ginsberg and Toal, 2009). Therefore, a timeframe-specific model was required to estimate neurodevelopmental deficits from DL-PCBs in fish relative to background exposure. Rheinberger and Hammitt (2012) put forth a model to estimate body burden changes to background DL-PCB exposure over the course of a pregnancy or lifetime risk. We estimated DL-PCB accumulation from fish over 35 years to represent a conservative estimated age of an expectant mother. This is likely an overestimation of PCB accumulation for: 1) younger mothers who have not accumulated for 35 years, and 2) mothers at 35 years of age since the intake scenarios assume an adult fish consumption rate the entire period. Time-period specific body burden changes were estimated using US EPA's central half-life estimate of 7.1 years for the TEQ-reference congener 2,3,7,8-TCDD (Rheinberger and Hammitt, 2012). Dioxin-toxic equivalents (TEQs) were estimated from total PCBs according to (Bhavsar et al., 2007) because monitoring reports often lack congener-specific PCB data. Deviating slightly from Rheinberger and Hammitt (2012) and concurring with the analysis presented in Ginsberg et al. (2015), we use the DHA benefit coefficient of 2.7 IQ points per 100 mg DHA which was derived from the FAO/WHO report. DHA benefit is hypothesized at 5.8, therefore all quantitative benefits are capped at +5.8

Table 1
Model parameters and sources.

Agent	Health Effect	Source
Hair Hg (ppm)	–3.5 VRM	Ginsberg et al. (2015)
	+23% CHD risk	Ginsberg and Toal (2009)
	–0.3 IQ	Rheinberger and Hammitt (2012), Rice et al. (2010)
EPA + DHA (mg/day)	+0.0304 VRM	Ginsberg et al. (2015)
	–0.146% CHD risk	Ginsberg and Toal (2009)
DHA (mg/day)	+0.027 IQ	Ginsberg et al. (2015), FAO/WHO (2011)
TEQ (pg/g LW)	–0.2 IQ	Rheinberger and Hammitt (2012), Stewart et al. (2008)

IQ points in the model (FAO/WHO, 2011). All model parameters appear in Table 1. Change in IQ from fish tissue TEQ exposure is relative to background which includes exposure from other sources. Thus, risk to IQ point loss from combined Hg and DL-PCBs (TEQ pg/g lipid weight (LW)) assuming percentile maternal consumption scenarios were calculated as follows:

$$\Delta \text{IQ} = [(\text{percentile: DHA mg/day}) \times (2.7 \text{ IQ points/100 mg DHA})] - [(\text{percentile steady-state hair Hg}) \times (0.3 \text{ IQ points/1 ppm hair Hg})] - [(\text{percentile: } \Delta \text{TEQ pg/g LW over 35 years}) \times (0.2 \text{ IQ points/TEQ pg/g LW})]$$

Results

Community cohort characteristics

Basic demographic and health literacy proxy data are summarized in Table 2. The pool of participants who generated the fish consumption scenarios was 65.7% female. Representation across tribal groups was substantial but with Little River and Grand Traverse Bands participating less than the other three. The most

Table 2
Demographic characteristics of study participants, N = 142.

Characteristic	N (%)
^a Sex	
Male	48 (34.3)
Female	92 (65.7)
Tribe	
Bay Mills	44 (31.0)
Sault Tribe	35 (24.7)
Little Traverse Bay	32 (22.5)
Grand Traverse	18 (12.6)
Little River	13 (9.2)
Age, years	
18–24	9 (6.3)
25–34	42 (29.6)
35–44	26 (18.3)
45–54	23 (16.2)
55 and above	42 (29.6)
Education	
Some high school or less	3 (2.1)
High school graduate	20 (14.1)
Some college	42 (29.6)
College graduate or greater	77 (54.2)
^b Income	
<25 k	24 (17.4)
25 k–49 k	54 (39.1)
50 k–99 k	45 (32.6)
100 k+	15 (10.9)

^a n = 140.^b n = 138.

frequently reported age brackets were 25–34 years and 55+ years. Relatively few young adults (ages 18–24) participated (n = 9). Many participants met the proxy criteria for baseline health literacy (\geq high school education, household income \geq \$40 k, has searched online for health information in past year) (ODPHP, 2019). Forty-two percent (42%) had obtained a college degree at minimum, and the most reported income bracket was \$25,000–\$49,000 at 39.1%.

Comparison of fish consumption scenarios

The consumption scenarios in Table 3 update our recent observations (Dellinger et al., 2019) that community-engaged advisory development, paired with mobile software to calculate personalized advice encourage consumption of culturally important fish species without exceeding ATSDR and US EPA recommendations. The current analysis includes additional 41 respondents (n = 142) to the previously reported findings and further breaks down the scenarios by quartiles. Median and mean fish consumption metrics increased pretest to posttest as expected. The same pattern was observed for quartiles except for the maximum scenario in which the consumption advisory appeared to temper, appropriately, fish intake (Table 3). Likewise, the only exceedance of US EPA/ATSDR reference doses for PCB (Minimum Risk Level (MRL): 0.02 $\mu\text{g}/\text{kg}/\text{day}$) and MeHg (MRL: 0.3 $\mu\text{g}/\text{kg}/\text{day}$, US EPA Reference Dose (RfD): 0.1 $\mu\text{g}/\text{kg}/\text{day}$) was at the maximum intake scenario (both pre and post).

Risk benefit estimations of scenarios using VRM and CHD models

Table 4 summarizes the VRM and CHD model results. All scenarios except the maximum intakes (both pre and post) predicted benefits from fish consumption using the model parameters proposed by Ginsberg et al. (2015). The highest infant neural development benefits were predicted at the 75th percentile of intakes (+5.4 VRM pre and +4.58 VRM post). The 25th percentile scenarios boasted the least benefits due to limited n3-PUFA intake despite lowered predicted hair Hg. At the maximum consumption scenario, where US EPA reference dose (RfD) and ATSDR minimum risk level (MRL) recommendations for Hg intake are exceeded, considerable risks to neurodevelopment were predicted (–16.4 VRM pre and –7.92 VRM post). The adult CHD risk estimates followed similar patterns in which only the maximum scenarios yielding net risks (115% increased risk pre and 59% increased risk post). For adults, the median scenarios of consumption yielded the highest benefits (28% reduced CHD risk pre and post). However, these benefits were comparable to the 75th percentiles whereas the 25th percentile scenarios predicted considerably less beneficial outcomes.

Risk benefit estimations of scenarios using IQ models

The predicted IQ change model for infant neurodevelopment revealed similar risk/benefit patterns to the VRM models (Table 4). All scenarios except the maximum intakes, which exceed ATSDR PCB and MeHg intake guidelines, predicted net benefits to infant cognition from DHA intake. The greatest benefits were estimated for 75th percentile intake scenarios (+4.41 IQ and +4.36 IQ post) with median intakes close behind at (+3.32 IQ pre and +3.98 IQ post). As with VRM, lowered DHA intake from the 25 h percentile consumption scenarios provided diminished IQ benefits even when accounting for reduced DL-PCB and MeHg exposure.

Table 3
Summary of scenario data derived from community engaged fish consumption projections (n = 142). Traditional denotes fish that have Anishinaabe names and are historically consumed. *n = 137, **value exceeds EPA and/or ATSDR guidelines.

Intake Metric	Before Viewing Advice						After Viewing Advice*						p-value
	Mean	Std. Dev.	25th	Median	75th	Max	Mean	Std. Dev.	25th	Median	75th	Max	
Mercury (µg/kg/day)	0.06	0.07	0.02	0.04	0.08	0.58**	0.07	0.06	0.02	0.05	0.09	0.38**	0.05
Mercury (µg/day)	4.72	5.76	1.21	3.50	6.26	51.55	5.36	5.23	1.71	4.15	7.44	33.92	0.05
PCB (µg/kg/day)	0.01	0.02	0.00	0.01	0.02	0.13**	0.02	0.02	0.00	0.01	0.02	0.13**	0.02
PCB (µg/day)	1.17	1.56	0.23	0.78	1.51	12.51	1.31	1.75	0.26	0.73	1.53	11.51	0.03
PUFA-3 (mg/wk)	2341.82	2557.53	900.94	1692.03	3130.27	19362.19	3486.49	9199.68	923.00	1968.86	3238.63	104636.70	0.38
Fish meals month	7.44	6.38	4.00	6.00	9.00	40.00	8.91	6.79	4.00	7.00	12.00	36.00	0.00
Fish g/month	1360.78	1330.53	510.29	1077.28	1700.97	9071.85	1600.40	1344.38	566.99	1360.78	2041.17	6123.50	0.00
Traditional meals/month	3.77	4.43	1.00	3.00	5.00	37.00	5.10	4.55	2.00	4.00	7.00	20.00	<0.001
Traditional fish g/month	706.74	947.11	170.10	453.59	1020.58	8391.46	945.67	934.02	226.80	680.39	1360.78	4535.92	0.00

Table 4
MeHg, DL-PCB, and PUFA-3 intake scenarios based on self-reported monthly meal plans (n = 147 participants) pre and post viewing of fish consumption advice. Risk estimates are based on hair Hg ppm using EPA's one-compartment model of steady-state daily intake of MeHg at each percentile. TEQ estimates based on 35-year accumulation at the percentile daily intake rate of PCBs. Benefit is estimated from percentile daily PUFA-3 intake (either EPA + DHA or DHA). Risk and benefit parameters for VRM and CHD originally proposed by Ginsberg et al. (2009, 2015) which exclude PCB risks. Negative number indicate increased risk. IQ modeling adapted from Rheinberger and Hammitt (2012).

Scenario		Hair Hg (ppm)	EPA + DHA (mg/week)	CHD Benefit	VRM Net	TEQ (pg/g LW)	IQ net
25th percentile	pre	0.194	709.50	15%	2.40	0.83	1.93
	post	0.263	751.33	16%	2.34	0.93	1.94
50th (median)	pre	0.539	1370.55	28%	4.07	2.84	3.32
	post	0.670	1509.76	28%	4.21	2.63	3.98
75th percentile	pre	0.969	2352.02	26%	5.01	5.48	4.41
	post	1.092	2688.84	23%	4.58	5.54	4.36
100th (max)	pre	7.104	13,327.92	-115%	-16.46	45.35	-5.40
	post	4.662	85,802.09	-59%	-7.92	41.73	-3.94

Discussion

Contextualizing scenario estimates

The estimated percentile scenarios do not stand in for a comprehensive risk assessment in these populations. Also, the predicted changes to VRM, IQ, and CHD from fish consumption are relative to other conditions. They do not account for the total complexity of factors that influence neurodevelopment and cardiovascular health. The models estimate hypothetical consumption rates from self-reported intent to consume fish. The exercise was run with and without access to culturally responsive, personalized advice. Actual behavior is not assessed. However, these estimates provide a useful benchmark for developing further advice and judging whether or not advisories meet the goals of community/academic partnerships that develop the advice. It is crucial that risk assessment and communication studies engage with the community stakeholders to align their priorities with the scientific work conducted on their behalf. For example, increasing fish consumption is a stated goal of the participating Anishinaabe consortia (Dellinger and Ripley, 2016, Dellinger et al., 2017). The scenarios in Table 3 appear to demonstrate this desired behavior.

As previously reported using a smaller dataset (Dellinger et al., 2019), the current fish meal selections conform with past attempts to characterize Anishinaabe consumption rates. During the last prospective survey of these tribes, the Ojibwe Health Study (OHS), the summer months (June-September) present a four-month window that is representative (mean 9 g/day) of overall fish consumption (mean 8.2 g/day); this was consistent across years. These Anishinaabe participants reported to eat 420 g/week of fish, but when measured prospectively they consumed 78.4 g/week of fish (Dellinger, 2004). For the current study, conducted during spring and summer months, participants selected on average

340 g/week of fish during the pre-test survey. This is closer to the recall data than the measured fish grams reported during the OHS. If participants consumed fish in accordance with the post-test estimates they would be eating 400 g/week. Overall, post-test meal selections described increased fish consumption when using personalized advice, but the maximum intake scenarios were reduced by the advice. Although the post-test maximum scenarios predict increased risks, the reduction in response to advice is encouraging.

It is possible that the participants are overestimating the amount of fish they would eat in practice. The prospective OHS data (Dellinger, 2004) could have also been under-reported. Furthermore, these populations respond to barriers to consume fish, such as contamination, which places downward pressure on their consumption habits. The current percentile estimates assist in testing scenarios that may well deviate from self-reported recall as well as projected meals. Another source of uncertainty was the need to use average U.S. body weights to scale risk assessment benchmarks. This was necessary since recruiters reassured participants that the app does not record their personal information. That data is temporarily used to generate recommendations. If these populations are heavier on average than the general population (GLITEC, 2016), using US averages would overestimate the risks to PBTs (since they are scaled by bodyweight).

Most scenarios both pre and post fell safely within recommendation limits except for the maximum intake scenario. Bearing in mind that the maximum scenario does not necessarily reflect the same individuals, this scenario was successfully attenuated by viewing the advisory. An often-cited concern for promoting the benefits of fish consumption is excess PBT exposure in pursuit of the nutrition (Mozaffarian and Rimm, 2006; FAO/WHO, 2011; Stern and Korn, 2011). However, a clear majority of Anishinaabe participants remained within reasonable Hg and PCB guidelines,

regardless of the potential to overestimate fish consumption. Furthermore, this was accomplished while increasing the consumption of local Great Lakes fish (congruent with *a-priori* community objectives) (Table 3). As with the other studies, such as OHS, the sampling of Anishinaabe fish consumers is biased towards educated women (Table 2). Differences in risk tolerance and openness to cooperating with research projects between the sexes may influence participation. ITCMI seeks new strategies to minimize this persistent sampling bias as it limits the ability to generalize study findings to the Anishinaabe public. Nevertheless, these participants (male or female) may also be more likely to act as decision makers in the home for meal selections. Therefore, the impact of these findings is likely relevant to a broader population than is sampled here.

Risks, benefits, and their implications to Great Lakes fishing cultures

The results in Table 4 align with our past observations that Great Lakes fish impart benefits relative to risks as long as they are consumed within conventional guidelines (Dellinger and Ripley, 2016). These results also follow our past analyses that demonstrate personalized advice can allow for increased fish consumption without exceeding guidelines. It is also important to consider that many tribal nations consider “heritage” (i.e. much higher than 21st century) consumption rates as a policy goal (Gagnon et al., 2018). The current analysis supports the culturally and socially important notion that heritage consumption rates would be a healthy policy goal, but this is undermined by human industrial activities. At the maximum intake scenarios, n3-PUFA intake was quite high. The theoretical benefits from high n3-PUFA intake were overshadowed by risks due to the CHD, VRM, and IQ benefit saturation points. As an interesting thought experiment, removing those saturation points would predict benefits. There is no solid evidence to support the removal of benefit saturation points. However, the juxtaposition of risks to benefits demonstrates the importance of pollution control to promote fish consumption.

Many studies have found health benefits in association with increased fish consumption including infant neurodevelopment which is presumed the most sensitive endpoint. The well-known Seychelles cohort (Davidson et al., 1998), which contributes to the basis for US EPA/ATSDR Hg chronic oral intake advice, has consistently observed neurodevelopmental benefits even at moderate maternal hair Hg levels. As of 2007, through 107 months of age, the Seychelles study of prenatal exposure to MeHg from maternal fish consumption found no consistent adverse developmental effects in the children. These mothers of the Seychelles cohort consumed fish at a mean of 12 times per week with 6.9 ppm average hair Hg levels (Myers et al., 2007). These levels closely match our pretest maximum intake scenarios (10 meals per week, 7.1 ppm predicted hair Hg). Only when controlling for n3-PUFA intake, were neurocognitive deficits associated with hair Hg in the Seychelles cohort (Stokes-Riner et al., 2011). Thus, the longstanding longitudinal Seychelles studies support the consideration of MeHg and n3-PUFAs as countervailing factors in neurodevelopment. Furthermore, the neurocognitive deficits seem masked at moderate to high hair Hg levels by high n3-PUFA intake.

Rheinberger and Hammitt (2012), analyzed the welfare consequences of adapting fish consumption advice or overcorrecting to accommodate risk-aversion. Their analysis accounted for possible health impacts of DL-PCBs as well as MeHg across multiple health and welfare models. As here, their results identified hazards both in over and under-consuming fish in response to consumption advisories. Their modeling predicted that reductions in maternal MeHg could present modest benefits to newborns whose mothers shifted dietary scenarios to match US EPA advisories. Furthermore, they noted that DL-PCB had marginal impacts on the model param-

eters including IQ and life expectancy (lifetime cancer risk). Rheinberger and Hammitt (2012) further conclude, as with the Seychelles group and Ginsberg et al. (2009, 2015), that potential benefits from fish consumption could substantially alter recommendations relating to PBT risks.

Conclusions

The models presented here do not assess the risks to the Anishinaabe public, but they provide data-driven evidence that Great Lakes fish consumption advisories can safely promote benefits, maintain the advantages of cultural continuity, and validate the Anishinaabe policy goal of increased fish consumption. Consumption scenarios that assume minimal intake, akin to a risk-averse approach, present the hazard of reduced benefits to fetal development and increased cardiovascular risk due to missed nutritional opportunities. This is in addition to the reported socio-cultural harms of attenuated fish consumption. On the other hand, maximal consumption patterns demonstrate the health-compromising consequences of PBT contamination. At this rate of intake, the modeled benefits are overshadowed by PCB and Hg health risks to fetal development and adult cardiovascular health. We note that the fish consumption advice described in Dellinger et al. (2017, 2019) tempered these risks in the maximal intake scenario.

Many tribes are seeking to address long-term issues with water quality standards that do not match their sociocultural priorities. Furthermore, CORA was established to assist their member tribes in navigating their treaty rights which include subsistence fishing practices. These challenges are part of a larger discussion including Treatment as a State provisions, adopted in the 1987 amendments to the Clean Water Act, and tribal Water Quality Standards (WQSs). These provisions are intended to help address the disconnect between federal water quality goals and the protection of tribal lands (Diver, 2018). This highlights the importance of environmental protection for these valued natural resources because PBT contamination exerts downward pressure on otherwise healthy behaviors. The information presented herein is specifically designed to empower the CORA and other Laurentian Great Lakes tribes to pursue their stated goals with respect to fish consumption.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This work was funded by the National Institute for Environmental Health Sciences (NIEHS) grant numbers: 1R21ES025788-01 and 5R01ES028255-03 with additional support from the Chippewa Ottawa Resource Authority (CORA) and the Great Lakes Native American Research Center for Health (GLNARCH) housed at the Great Lakes Inter-Tribal Council. The authors would like to thank Ms. Poupart from the Great Lakes Inter-Tribal Council for her cultural input and the Michigan Tribes for their collaboration and patience.

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