# Traditional Food Consumption and Other Determinants of Exposure for Lead, Cobalt, Manganese, and Hexachlorobenzene in Northern Canada

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ABSTRACT. Results of a 2019 human biomonitoring study indicated that several parameters, including lead, cobalt, manganese, and hexachlorobenzene, were elevated in blood and urine samples in Old Crow, Yukon, in comparison to the general Canadian population. This study aims to identify possible local determinants of levels of these parameters, including consumption of locally harvested traditional foods, lifestyle factors, and demographics, in Old Crow and, for comparison, two other northern populations: communities in the Dehcho and Sahtú regions of the Northwest Territories. We ran generalized linear models to identify possible associations between individual determinants of exposure and key biomarkers, controlling for age and sex. In Old Crow, several variables were associated with elevated exposure levels of these biomarkers, including drinking untreated river water (29% higher blood manganese levels and 120% higher blood lead levels), eating caribou kidneys (22% higher blood manganese levels and 58% higher blood lead levels), and eating whitefish (28% higher blood cobalt levels). Additionally, in order to differentiate results in Old Crow from those in other northern regions and to identify trends across regions, we observed relationships between consumption of moose and caribou organs and lead and hexachlorobenzene levels in the reference populations and pooled population groups. Though levels of particular contaminants may be elevated in some traditional foods, these foods remain an important source of nutrients for members in these communities and provide other benefits, including increased physical activity through harvesting, mental health improvements, and spiritual wellness.

Keywords: biomonitoring; contaminants; nutrients; traditional foods; lead; manganese; cobalt; hexachlorobenzene; Indigenous

RÉSUMÉ. Selon les résultats d'une étude de biosurveillance humaine réalisée en 2019, le taux de plusieurs paramètres, dont le plomb, le cobalt, le manganèse et l'hexachlorobenzène se trouvant dans des échantillons de sang et d'urine de résidents d'Old Crow, au Yukon étaient élevés par rapport à la population canadienne en général. La présente étude vise à identifier les déterminants locaux possibles attribuables aux niveaux de ces paramètres, y compris la consommation d'aliments traditionnels locaux, des facteurs liés au mode de vie et les données démographiques. Les données d'Old Crow sont comparées aux données provenant de deux autres populations nordiques, soit celles des régions du Dehcho et du Sahtú dans les Territoires du Nord-Ouest. Des modèles linéaires généralisés ont été réalisés afin de déterminer les corrélations possibles entre les déterminants individuels et les biomarqueurs clés, en tenant compte des variables de l'âge et du sexe. À Old Crow, plusieurs variables ont été associées aux taux élevés de ces biomarqueurs, notamment la consommation d'eau de rivière non traitée (taux de manganèse dans le sang plus élevé dans une mesure de 29 % et taux de plomb plus élevé de 120 %), la consommation de rognons de caribou (taux de manganèse dans le sang plus élevé dans une mesure de 22 % et taux de plomb plus élevé de 58 %) et la consommation de poissons blancs ou corégones (taux de cobalt dans le sang plus élevé dans une mesure de 28 %). De plus, afin de différencier les résultats d'Old Crow de ceux des autres régions nordiques et de cerner les tendances dans ces régions, nous avons observé des liens entre la consommation d'organes d'orignal et de caribou et les taux de plomb et d'hexachlorobenzène dans les bassins de population de référence des Territoires du Nord-Ouest. Bien que les taux de contaminants puissent être élevés dans certains aliments traditionnels, ces aliments demeurent une source importante de nutriments pour les membres de ces communautés et offrent d'autres avantages, notamment une plus grande activité physique grâce à la récolte, des améliorations sur le plan de la santé mentale et une source de bien-être spirituel.

Mots-clés : biosurveillance; contaminants; nutriments; aliments traditionnels; plomb; manganèse; cobalt; hexachlorobenzène; autochtone

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#### INTRODUCTION

In 2019, in collaboration with the Vuntut Gwitchin Government, a human biomonitoring project began in the community of Old Crow. The preliminary biological sampling results have been published previously (Drysdale et al., 2021), and this study includes further statistical analysis associating biological sample and dietary and lifestyle survey results. Old Crow is a fly-in only Gwich'in community located above the Arctic Circle in the northern Yukon, Canada. Drysdale et al. (2021) initiated the biomonitoring project in response to community concerns regarding elevated concentrations of some toxic metals and persistent organic pollutants (POPs) in locally harvested traditional foods (Indigenous and Northern Affairs Canada, 2010; Josie et al., 2015). These traditional foods, such as wild game, fish, birds, berries, and wild plants, are both nutritionally and culturally important to the residents of Old Crow and are a part of the staple diet of community members (Wein and Freeman, 1995; Wein 1996; Drysdale and Laird, 2018). Preliminary biological sample results from the human biomonitoring project showed that some parameters, including lead, cobalt, manganese, and hexachlorobenzene (HCB, an organochlorine pesticide), were elevated in comparison to the general Canadian population and other First Nations communities located outside the Northern Territories (Drysdale et al., 2021).

The Old Crow biomonitoring project was the first comprehensive biomonitoring project conducted in the Yukon and complements other previous and ongoing northern human biomonitoring programs conducted in Nunavut, the Northwest Territories, and the other northern territories. Several of those studies found elevates levels of metals, including lead, and organochlorines, in other populations when compared to those living in Canada's south (Fontaine et al., 2008; Saudny et al., 2012; Laird et al., 2013; Government of Canada, 2018). Similar to findings from the Old Crow biomonitoring project, findings from those programs showed that most participants did not have lead levels above health-based thresholds (Laird et al., 2013), and that concentrations of metal contaminants, such as lead, were decreasing over time from the 1990s to 2017 (Fontaine et al., 2008; Lemire et al., 2021).

Elevated exposure to contaminants, including lead and HCB, can cause harmful health effects, including damage to liver and thyroid function, and impairment of neurological development (Reed et al., 2007). Though cobalt and manganese are essential metal nutrients required for processes such as red blood cell formation with cobaltbearing vitamin B-12, they can also cause adverse health effects at elevated levels (Finley and Davis, 1999; Leyssens et al., 2017). No health-based guidance values for biomarkers of HCB, cobalt, or manganese have been validated. However, in the Old Crow biomonitoring project (Drysdale et al., 2021), researchers found that lead levels there were below available health-based guidance values in both blood and urine for the majority (>95%) of participants.

The aim of the current study is to build on the results of the Old Crow biomonitoring project by exploring determinants of exposure to contaminant biomarker levels. Using data collected at a biomonitoring clinic, we analyze possible local determinants of exposure for levels of key contaminant and trace nutrient biomarkers that the earlier study found to be at elevated levels in the community. In particular, this study focuses on possible local exposure factors that may be specific to Old Crow or that, potentially, are associated with exposure in other northern communities in the region. Community questions and concerns regarding contaminant levels in traditional food informed the 2019 biomonitoring project (Drysdale et al., 2019), and this work expands upon those questions by focusing on the association between consuming certain traditional foods and other lifestyle factors and levels of key biomarkers of exposure (Drysdale et al., 2021). The current study also reports on similar analyses we completed in two sub-arctic reference populations: Dene communities in the Dehcho and Sahtú regions of the Northwest Territories (Fig. 1). Understanding the most significant potential sources of exposure for contaminants and potential drivers of nutrient status can help to inform consumption notices and health promotion materials that are tailored to the community. On a broader scale, this study can be used to complement and guide other biomonitoring and environmental monitoring programs aimed at evaluating the impact of initiatives designed to reduce the contaminant burden in the sub-Arctic and Arctic.

#### MATERIALS AND METHODS

#### Community Biomonitoring Projects

This study used data from biomonitoring clinics that have been documented in other publications (Drysdale et al., 2021; Ratelle et al., 2020; Ratelle et al., 2018a; Ratelle et al., 2018b). Several of this study's researchers undertook these clinics, led by Ratelle, between 2016 and 2018 in partnership with Old Crow, Yukon, as well as six communities from the Dehcho region of the Northwest Territories and three communities in the Sahtú region. As described earlier, the impetus for this work came from the community. Local people had questions about contaminant exposure and nutrient intake in these regions. The methods used in these clinics, including study design, surveys, consent forms, biological sample collection, and sample preservation and shipment, are described elsewhere (Ratelle et al., 2018a; Ratelle et al., 2018b; Drysdale et al., 2021). Local coordinators hired from the community, along with the research team, conducted participant recruitment using both random selection by phone and passive recruitment by word of mouth, poster, and media interviews (Ratelle et al., 2018a; Ratelle et al., 2018b; Drysdale et al., 2021). The minimum age for participants in these clinics varied between communities from four



FIG. 1. Location of Old Crow and Dehcho and Sahtú reference communities.

to six years, depending on factors such as community preference and available equipment. The current study includes results for adult participants (18+ years) only. Data collected in all communities was comprised of human biological samples, including metals in whole blood and urine, and POPs in plasma, a food frequency questionnaire for traditional foods, and some risk-factor and demographic data, including smoking status, sex, and age (Ratelle et al., 2018a; Ratelle et al., 2018b; Ratelle et al., 2020; Drysdale et al., 2021). Other risk factors, including self-reported use of lead ammunition, vitamin consumption, and drinking water source, were only assessed in Old Crow and not the Dehcho and Sahtú regions.

In accordance with agreements made beforehand, we returned the results of this study to participants and each community. In addition to the community research agreements, we received approval and licensure for this study from the University of Waterloo Research Ethics Committee, which complies with the Tri-Council policy for ethical conduct for research involving humans. Additionally, we received regional approvals from the Yukon Government, the Stanton Territorial Health Authority for Human Research, and the Aurora Research Institute (Ratelle et al., 2018a; Ratelle et al., 2018b; Vuntut Gwitchin Government and University of Waterloo 2018; Drysdale et al., 2021).

#### Parameters of Interest

Preliminary results from the Old Crow biomonitoring project, that began in 2019, identified the parameters of interest (Drysdale et al., 2021). Supplementary Table S1 shows the list of parameters measured in that study. We selected parameters for further analysis in the current study when the 95% confidence intervals of both the geometric mean and 95th percentile of a reliable biomarker for the parameter were elevated relative to at least one of the Canadian Health Measures Survey (CHMS) and the First Nations Biomonitoring Initiative (Assembly of First Nations, 2013; Health Canada, 2013a, 2013b, 2015, 2017, 2019). Parameters that were elevated in Old Crow included HCB in plasma, as well as lead, cobalt, and manganese, analyzed in whole blood and creatinine-adjusted urine (Drysdale et al., 2021).

#### Reference Populations

Because of the small population of Old Crow (n = approximately 175 adults) (Statistics Canada, 2016a), and the subsequently small sample size for the biomonitoring project (n = 77 adults), it was challenging to evaluate potential relationships between contaminants and nutrients in biological samples, and consumption of traditional food and other risk factors, with sufficient power. As part of the effort to mitigate this issue, for the current study, we included two additional reference populations from northern Canada. As noted above, these reference populations include six communities from the Dehcho region of the Northwest Territories (n = 231 adults) and three communities in the Sahtú region (n = 217 adults) (Fig. 1) (Ratelle et al., 2018a, 2018b, 2020). Using reference populations can support associations observed in Old Crow, as well as differentiate trends specific to Old Crow from those in other northern communities. We integrated these communities with Old Crow to create a pooled dataset, and for comparison purposes, we also evaluated separately. Because of the cultural, dietary, and location differences among the three groups, we also compared results between regions.

#### Key Determinants of Biomarker Levels

We selected key local determinants of biomarker levels for analysis based on three criteria: (1) commonly eaten traditional foods or food categories in Old Crow, including caribou (*Rangifer tarandus*), moose (*Alces alces*), Chinook salmon (*Oncorhynchus tshawytscha*), whitefish (*Coregonus clupeaformis*), game birds, and berries; (2) a focus on the organs/parts of these foods that are eaten by more than 15% of the population and have been shown in the literature to have elevated concentrations of some or all of the key parameters; and (3) risk factors that have been shown in the literature to potentially increase exposure to some or all of the key parameters.

The biomonitoring clinics in Old Crow and the reference population included the administration of a food frequency questionnaire to identify the type, source, serving size, and frequency of consumption of traditional foods, as described by Ratelle and colleagues (Ratelle et al., 2020). The reference populations do not necessarily have the same commonly eaten foods (e.g., no Chinook salmon), but do share some of the commonly eaten foods in Old Crow (e.g., moose, whitefish, berries). When a food was eaten in Old Crow, but not the reference populations, we conducted the analysis for Old Crow only. To maintain numbers greater than n = 10 for analysis, we only included, as mentioned above, foods eaten by 15% or more of the participants in each region. We do not include frequency of consumption in this study, as the majority of participants (>85%) previously reported eating all of these foods once or less per week (Laird et al., 2019). The two most commonly eaten foods, moose and caribou muscle meat, were eaten by 93%–94% of participants in Old Crow, therefore, the small sample size of non-consumers was too small to model (n < 4).

Though commonly eaten traditional food types/species were generally similar between regions, the specific herds and migration patterns of traditional foods varied between communities. For instance, Old Crow community members primarily ate caribou from a herd of barren-ground caribou called the Porcupine herd, while community members in the Sahtú and Dehcho regions harvest both barren-ground and woodland caribou from herds that migrate farther east.

In addition to the food frequency questionnaire, we administered a survey in Old Crow to identify possible risk factors for contaminant exposure. The survey included questions regarding drinking water sources, as elevated levels of some metal contaminants have been identified in local surface waters (Environment Canada, 2021), as well as about the use of lead ammunition for hunting, vitamin consumption, and smoking status. The biomonitoring project research team (Ratelle et al, 2018b) did not administer the risk factors survey in the reference populations in the Northwest Territories.

The researchers involved in both the Old Crow and Northwest Territories biomonitoring projects adapted both the food frequency questionnaire and the risk factors survey in partnership with participating communities to ensure that questions were culturally appropriate, relevant, and clearly worded. Surveys were written in English, and translators were available based on community input (Ratelle et al., 2020). Supplementary Table S2 summarizes the rationales for each potential determinant of exposure selected for these analyses, including demographics, traditional foods, and risk factors.

## Statistical Analysis

We treated the majority of the determinants of exposure, including traditional food consumption, sex, and risk factors for exposure as binary variables, and we treated age as a continuous variable. When a participant reported that they did not know or could not remember, we excluded that data point from the analysis of that question. For concentrations of biomarkers that were below the limit of detection (LOD), we assigned values equal to half the LOD for the purposes of statistical analysis. We adjusted urine samples for creatinine levels to account for previously identified differences in hydration status among participants (O'Brien et al., 2017). Additionally, to account for previously identified interindividual variation of lipid levels in blood, we normalized POP concentrations to plasma lipid levels (O'Brien et al., 2017).

We used Spearman rank correlation coefficient (Spearman rho) to determine the strength of associations between non-log transformed biomarkers that analyzed the same parameter (e.g., blood vs. urinary manganese). We compared geometric mean biomarker concentrations between males and females using 95% confidence intervals. In addition to comparisons using means, we ran generalized linear models to identify possible correlations between independent variables, including sex, age, traditional food consumption, and risk factors, and the dependent outcome biomarker levels. We conducted forward stepwise regression modelling beginning with age and sex, which were retained in all models due to the observed differences in age and sex groups for key parameters in biomonitoring studies (Supplementary Table S3). We considered determinants significant if the p value for the regression coefficient was below 0.05, and the coefficient of determination (adjusted  $r^2$ ) value increased with the addition of the variable to the model. All significant associations represent possible sources, as this study analyzes associations not causal relationships. To normalize their distributions for modeling, we log-transformed biological sample results of key parameters.

We ran separate models for each participant group, including Old Crow, the two reference populations, and the pooled dataset for all three groups. Due to the logtransformation of the outcome variable, regression coefficients are presented as log-transformed difference in biomarker concentrations between those who did, and did not, consume the identified traditional food or have the identified lifestyle factor. For the purposes of discussion in the text and supplementary tables, we also converted regression coefficients to percent change for the non-log transformed outcome. In cases where there were multiple determinants significantly associated with the outcome variable, we used Chi-square testing to assess associations between independent variables. When the regression coefficient for a determinant of biomarker levels was significant (p <0.05), we reported the model's adjusted r<sup>2</sup>. In many of these cases, some category combinations included zero or only one participant, and therefore models include only sex, age, and one other independent variable (e.g., traditional food consumption, risk factor) each. We conducted analysis using SAS software version 9.4 (SAS Institute Inc., 2016). We checked residuals after each analysis to confirm the assumptions of linearity and homoscedasticity.

## **RESULTS AND DISCUSSION**

#### Study Population

Table 1 presents characteristics of the participating adult population in this study. Old Crow and the two reference

#### TABLE 1. Number of participants and demographics by type of sample.

Demographics and participation in surveys by sa	mple type			Referen	ce populations	
	Old C	Old Crow		Dehcho		ıtú
	Blood $(n = 54)$	Urine (n = 44)	Blood (n = 122)	Urine (n = 78)	Blood (n = 123)	Urine (n = 100)
ex Female	28 (52%)	23 (52%)	61 (50%)	35 (45%)	60 (49%)	52 (52%)
Male	28 (32%) 26 (48%)	23 (32%) 21 (48%)	61 (50%)	43 (55%)	63 (51%)	48 (48%)
ge (Years)	20 (4870)	21 (4070)	01 (3070)	45 (5570)	05 (5170)	40 (4070)
20-39	26 (48%)	20 (45%)	35 (29%)	19 (24%)	46 (37%)	29 (29%)
40-59	18 (33%)	15 (34%)	54 (44%)	36 (46%)	43 (35%)	39 (39%)
60+	10 (19%)	9 (20%)	27 (22%)	21 (27%)	31 (25%)	32 (32%)
urveys						
Food frequency questionnaire	48 (89%)	40 (91%)	74 (61%)	50 (64%)	51 (41%)	42 (42%)
Risk factors survey	44 (81%)	36 (82%)	-	_	-	-
esponses to risk factor questions by sample typ	e					
	Blood	Urine	Blood	Urine	Blood	Urine
	(n = 44)	(n = 36)	(n = 122)	(n = 78)	(n = 123)	(n = 100)
noking status (has smoked in the previous 24 h	iours)					
Yes	22 (50%)	18 (50%)	49 (40%)	52 (67%)	66 (54%)	45 (45%)
No	21 (47%)	17 (47%)	73 (60%)	26 (33%)	59 (48%)	55 (55%)
tamin usage (has taken a vitamin in the previo						
Yes	32 (73%)	25 (69%)	-	-	-	-
No	12 (27%)	11 (31%)	-	-	-	-
rinking water (drinks untreated water sometim						
Yes	37 (84%)	29 (81%)	-	-	-	-
No	7 (16%)	7 (19%)	-	-	-	_
ead ammunition usage (eats game hunted with						
Yes	24 (54%)	19 (53%)	-	-	-	-
No	7 (16%)	4 (11%)	-	-	-	-
on't know/prefer not to say	13 (30%)	13 (36%)	-	-	_	_

- Not available: risk factors survey not conducted in reference populations.

populations had between 45% and 52% female participants. Old Crow had the lowest participation levels for participants over 60 years old (19%-20% of participants who submitted biological samples) compared to the Dehcho (23%-27%) and Sahtú (26%-32%). Additionally, Old Crow had the highest participation levels for adult participants under 40 years (45%-48%) compared to Dehcho (25%-30%) and Sahtú (29%-38%), despite similar age distributions between the three regions (Statistics Canada, 2016a, b, c).

#### Survey

Table 1 includes risk factors for exposure that have been included as independent variables in the analysis. Two thirds of participants who submitted urine samples in the Dehcho reported smoking in the previous 24 hours; however, between 40% and 54% of participants submitting all other sample types in all regions were smokers. These smoking proportions are higher than those observed in the general Canadian population (10% to 15%), and similar to the proportions observed in other First Nations populations (40% to 54%) (Canadian Public Health Association, 2021). The numbers for some risk factor groups, including those who did not drink untreated water sometimes or often and those who did not eat game hunted with lead shot sometimes or often were small (n < 10 out of 44). Nearly one third of participants (n = 13 out of 44) reported that they did not know what kind of ammunition was used for the game meat they consumed.

Table 2 shows the proportions of respondents consuming traditional foods for all foods selected for analysis. Generally, a higher percentage of Old Crow participants consumed caribou organs and wild berries compared to the two reference populations. Consumption of some foods in Old Crow, including some moose organs and whitefish, were within 5% of those observed in the reference populations, with the exception of moose bone marrow and liver in the Dehcho region (8% and 13% higher, respectively) and moose liver in the Sahtú region (8% higher). Consumption of game birds was also lower in Old Crow (58%) compared to both reference populations (71%) in Dehcho, 73% in Sahtú). The most commonly eaten birds included Canada Goose (Branta canadensis) (34%), Whitewinged Scoter (Melanitta deglandi) (32%), and Ptarmigan (Lagopus sp.) (20%) in Old Crow; Canada Goose (55%), Mallard (Anas platyrhynchos) (51%), and Spruce Grouse

		Reference populations		Pooled dataset	
		Old Crow n = 69 (%)	Dehcho n = 123 (%)	Sahtú n = 71 (%)	n = 263 (%)
Game bir	de	58	71	73	68
Berries	us	84	67	55	68
Moose					
	Bones in soup/stew	43	30	41	36
	Fat	43	37	38	39
	Kidneys	35	37	27	34
	Bone marrow	38	46	38	41
	Liver	16	29	18	23
Caribou					
Barre	n-ground/Porcupine				
	Bones in soup/stew	62	2*	24	23
	Fat	65	2*	15	23
	Kidneys	51	2*	14*	18
	Bone marrow	71	3*	20	25
	Liver	30	3*	11*	12
Wood	land				
	Bones in soup/stew	_	11*	37	21
	Fat	_	11*	30	18
	Kidneys	_	13*	25	18
	Bone marrow	_	16	28	21
	Liver	_	15	13*	14
Fish	Chinook salmon	90	-	-	_
	Whitefish	83	92	80	87
	Lake trout	14*	57	79	51

TABLE 2. Proportion of adult respondents in a food frequency questionnaire who reported consuming selected traditional foods in the previous year.

\* Foods eaten by less than 15% of the population within a region were excluded in the analysis for this region.

 Food was not eaten or included in the food frequency questionnaire for this region, as these foods are not harvested in the region.

(*Falcipennis canadensis*) (31%) in the Dehcho region; and Canada Goose (63%), Ptarmigan (35%), and Black Scoter (*Melanitta americana*) and Black Duck (*Anas rubripes*) (35%), grouped because their names are used interchangeably in some communities in the Sahtú region.

#### Baseline Key Parameters

The concentrations of key parameters, including lead, cobalt, manganese, and HCB in Old Crow and both reference populations, are shown in Supplementary Table 3 and also compares results to two national studies, the Canadian Health Measures Survey (CHMS) and the First Nations Biomonitoring Initiative (FNBI) (Assembly of First Nations, 2013; Health Canada, 2013a, 2013b, 2015, 2017, 2019). Generally, blood lead levels did not differ significantly among the three regions (overlapping 95% confidence intervals of the geometric mean and 95th percentile), though blood lead levels were lower in the Dehcho region than in the Sahtú region and in Old Crow. Mean urinary lead levels in all three regions were not significantly different from those observed in the general Canadian population (CHMS) and other First Nations

communities (FNBI). All three populations had higher blood lead levels than those observed in the general Canadian population (CHMS). Blood lead levels in Old Crow and the Sahtú reference populations were also higher than those observed in other First Nations communities (FNBI). However, the majority of adult participants in Old Crow, the Dehcho, and Sahtú regions (> 95%) had lead levels below health-based guidance values of 10 µg/dL (100  $\mu$ g/L) (for women 50 and older and men) and 5  $\mu$ g/dL (for children and women of child-bearing age) in blood and 7 µg/L in urine (Haines et al., 2011; Health Canada, 2013b; World Health Organization, 2021). Blood lead levels above this threshold have been associated with adverse health effects, including cognitive impairment and hypertension (Navas-Acien et al., 2007; Sanders et al., 2009). However, adverse health effects, including cognitive impairment in both children and adults, have been observed at blood lead levels below the health-based guidance values (Lanphear et al., 2005; Sanders et al., 2009).

The majority of samples (95%) were below the analytical detection limit for blood cobalt (0.15  $\mu$ g/L) in the reference populations (Drysdale et al. 2021). Therefore, we reported only urinary cobalt levels for these groups. Generally, urinary cobalt levels were similar or lower in both the Dehcho and Sahtú compared to Old Crow, and mean urinary cobalt levels were elevated in both Old Crow and the Dehcho region in comparison to the general Canadian population. The majority of participants in all three regions (>95%) had cobalt levels below values reflecting excessive exposure  $(1 \mu g/L \text{ in blood}, 1.7 \mu g/g \text{ creatine in urine})$  (Drysdale et al., 2021; Mayo Clinic Laboratories, 2023). There is no healthbased guidance value for cobalt. However, a review of the epidemiological literature and biokinetic modeling found that blood cobalt levels below 300 µg/L have not been associated with adverse health effects in humans (Finley et al., 2012). Similarly, a clinical study involving cobalt supplementation found that no adverse health effects were detected at blood cobalt levels up to the maximum detected value of 117 µg/L (Tvermoes et al., 2015).

Urinary and blood manganese levels were similar among the three regions (Old Crow, Dehcho, and Sahtú), with the exception of elevated mean manganese concentrations in urine observed in the Dehcho region (Supplementary Table 3). Manganese is an essential nutrient. However, psychomotor development impairment has been observed in children born from mothers with manganese concentrations > 30  $\mu$ g/L in blood (Chung et al., 2015). No women of child-bearing age in any of the three regions had manganese levels above this effect threshold. Yet, the threshold for manganese sufficiency vs. toxicity has not been consistently described in the literature. Some adverse health effects, including impairment to motor function, have been observed at blood manganese levels above the median observed level of 15 µg/L in blood, with more visible effects, including tremors, observed above 25 µg/L in blood (Santos-Burgoa et al., 2001). A study of infants found that cognitive development indices peaked at blood

	Geometric mean concentration (95% CI)							
	Blood (µg/L)			Urine (µg/g creatinine)			Plasma (µg/kg lipids)	
	Mn	Čo	Pb	Mn	Со	Pb	HCB	
Old Crow	n = 54				n = 54			
Female	13 (12-16)	0.32 (0.29-0.35)	19 (16-24)	0.26 (0.17-0.31)	0.51 (0.37-0.62)	0.26 (0.11-0.40)	12 (10-15)	
Male		. ,			· /	· /		
	11 (10-12)	0.29 (0.26-0.33)	31 (26–35)	0.067 (0.055-0.08)	0.26 (0.22-0.31)	0.75 (0.63-0.83)	18 (15–21)	
Dehcho		n = 122			n = 78		n = 122	
Female	13 (12-14)	< 0.075	9.4 (7.8–11)	0.53 (0.39-0.72)	0.58 (0.47-0.71)	0.57 (0.46-0.69)	8.5 (7.4–9.8)	
Male	× /		. ,	· · · · · ·	· /	· · · ·	· · · · ·	
	9.4 (8.7–10)	< 0.075	15 (13–18)	0.30 (0.23-0.39)	$\begin{array}{c} 0.31 \\ (0.26 - 0.37) \end{array}$	0.57 (0.44-0.74)	9.0 (7.9–10)	
Sahtú		n = 123			n = 100		n = 123	
Female	10 (9.8–12)	< 0.075	24 (20-29)	0.21 (0.16-0.28)	0.48 (0.40-0.61)	0.90 (0.56-1.4)	16 (14-20)	
Male	9.2 (8.5–9.9)	< 0.075	28 (23-33)	0.14 (0.11-0.17)	0.28 (0.24-0.32)	0.81 (0.63-1.1)	15 (12-18)	

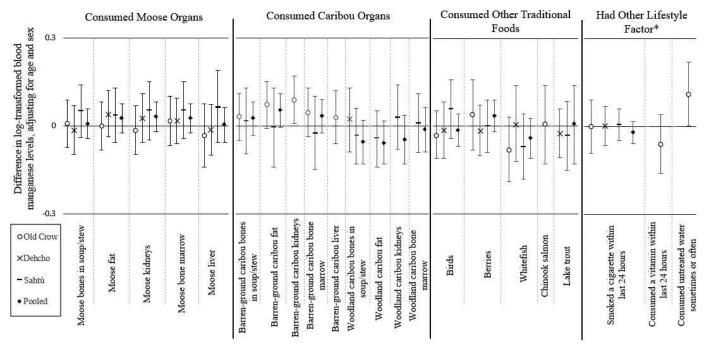
manganese levels of approximately 24  $\mu$ g/L, decreasing when biomarker levels were lower or higher than this level (Roels et al., 2012).

Similar to Old Crow, HCB levels were elevated in the Sahtú relative to the general Canadian population and other First Nations populations. Both of these groups also had elevated HCB levels compared to the Dehcho region. There is no health-based guidance value for HCB. However, reference values and biomonitoring equivalents can indicate elevated exposure levels compared to the Canadian population. Using biomonitoring data collected in 2011, Haines et al. (2017) calculated a reference value of 23 µg HCB/kg lipids in plasma using Canadian biomonitoring data for the general Canadian population. This value represents the upper margin of exposure for the population, but does not indicate the level of health risk, as it is not based on toxicological data. Similarly, Health Canada has developed a biomonitoring equivalent for HCB of 25 µg HCB/kg lipids based on neoplastic effects to the liver (Aylward et al., 2010). The majority of participants in Old Crow (>80%), Dehcho (>95%), and Sahtú (>75%) had HCB levels below these values. In epidemiological studies, HCB levels exceeding 1.0 to 1.5 µg/L in children and pregnant mothers have been associated with decreased behavioural competence and increased BMI in children (Ribas-Fito et al., 2007, Smink et al., 2008). However, in our study all participants had HCB levels below this threshold.

**Manganese**: Blood and urinary manganese were positively correlated in Old Crow (Spearman  $\rho = 0.44$ , p < 0.01). However, we observed no significant association between the two in the two reference populations or the pooled dataset. This may indicate the presence of a local source, or sources, driving manganese exposure in Old Crow. Mean blood manganese levels were not significantly different

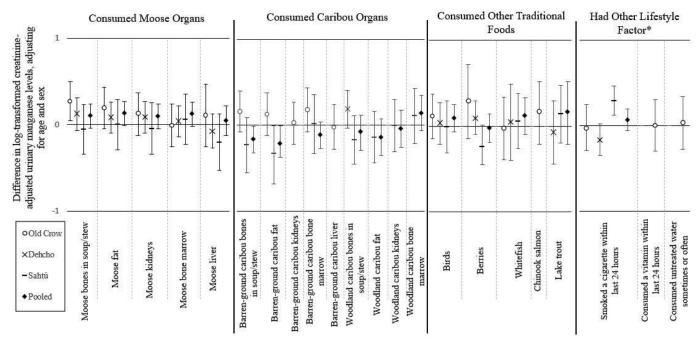
between females and males in Old Crow or in the reference populations (p > 0.05, Table 3). However, mean urinary manganese levels were higher in females than in males in all three groups. Higher manganese levels in women have been observed in the CHMS in Canada and National Health and Nutrition Examination Survey in the US, attributed to sex-related differences in manganese metabolism (Health Canada, 2013b; Oulhote et al., 2014). We observed no association between mean blood or urinary manganese levels and age in Old Crow (p = 0.95 and 0.55, respectively). However, urinary levels increased with age in the Dehcho reference population (Spearman  $\rho = 0.31$ , p < 0.001) and the pooled dataset (Spearman  $\rho = 0.20$ , p = 0.002).

For each determinant of exposure, Figures 2a and 2b show the regression coefficient and 95% confidence intervals for log-transformed blood and urinary manganese levels between those with and without the determinant, adjusting for age and sex. Confidence intervals for the regression coefficient that do not cross zero were also significant based on p < 0.05. Supplementary Tables 4–7 summarize these results using a percent difference. A positive percent difference indicates that the participants who ate the specified food, smoked, took a vitamin, or drank untreated water, as indicated, had higher average biomarker levels, by the percentage indicated, than those who did not. A negative value indicates that the participant who ate the specified food, smoked, took a vitamin, or drank untreated water, as indicated, had lower average biomarker levels, by the percentage indicated, than those who did not. In Old Crow, traditional food determinants associated with increased manganese biomarker concentrations, while adjusting for age and sex, included eating caribou kidneys (22% higher average blood manganese levels, adjusted  $r^2 = 0.44$ ) and eating soup or broth made from moose



\*Consumption of vitamins, untreated water, and food hunted using lead ammunition were only measured in Old Crow.

FIG. 2a. Regression coefficients and 95% confidence intervals for log-transformed blood manganese concentrations in a model including sex, age, and the identified determinant.



\*Consumption of vitamins, untreated water, and food hunted using lead ammunition were only measured in Old Crow.

FIG. 2b. Regression coefficients and 95% confidence intervals for log-transformed, creatinine-adjusted urinary manganese concentrations in a model including sex, age, and the identified determinant.

bones (86% higher average creatinine-adjusted urinary manganese levels, adjusted model  $r^2 = 0.51$ ).

We did not observe these associations in the reference populations. However, in the pooled dataset, participants who ate caribou fat and bones had urinary manganese levels that were 38% and 31% lower, on average, compared to those who did not eat caribou fat (adjusted model  $r^2 = 0.18$  and 0.20, respectively). The reliability of urinary manganese as a biomarker has been debated in the literature (Smith et al., 2007; Hassani et al., 2016), and therefore these trends may not represent manganese exposure levels for participants. The association between increased blood

manganese and the consumption of caribou kidneys in Old Crow is supported by literature documenting the accumulation of manganese in bones, kidneys, and livers of mammals (Budis et al., 2013; O'Neal and Zheng 2015).

In addition to caribou kidney consumption, Old Crow participants who drank untreated water often or sometimes in the past year had blood manganese levels that were 29% higher, on average, than those who drank untreated water rarely or never, adjusting for age and sex (adjusted  $r^2 =$ 0.20). Old Crow community drinking water is sourced from a local well, where it is treated using both 1) disinfectant, and 2) removal of iron and manganese (because of elevated levels of these metals in the local groundwater). However, the majority of community members (81%-84%) drank untreated surface water sometimes or often, generally in the form of ice collected from the nearby Porcupine River. The proportion of community members drinking untreated water sometimes to often (as compared to those who do not drink untreated water in the previous year) in Old Crow was higher than the proportion drinking untreated water rarely to often in the Sahtú region, the latter finding reported in Ratelle et al., (2022). Untreated groundwater analysis during well installation in Old Crow reported manganese levels exceeding the Guidelines for Canadian Drinking Water Quality of 0.12 mg/L in all samples, indicating possible manganese enrichment in local soil (TetraTech Inc. 2017). The majority (90%) of surface water samples collected from the nearby Porcupine River in the five vears previous to the biomonitoring clinic (2014-19) had manganese levels below the guideline (0.12 mg/L); however, Environment Canada (2021) observed exceedances during spring sampling events during this time period.

We observed possible significant associations between blood manganese levels and both the consumption of caribou kidneys and drinking untreated drinking water. It is important to note, though, that all participants who reported one of these determinants, also took part in the other; that is, people who drank untreated river water also ate caribou kidneys. The correlation between these two activities may be related to harvesting practices. Community members who are harvesters might drink untreated water while on the land and also consume animal organs as result of their harvests. Due to the near-perfect correlation ( $X^2 p < 0.001$ ), further environmental sampling and surveying of local water sources, particularly where community members drink the water, is necessary to determine whether manganese levels are truly associated with one or both of these determinants. As well, due to the small number of participants, it is not possible to control for both of these variables in a generalized linear model.

**Cobalt**: Blood and urinary cobalt were positively correlated in Old Crow (Spearman  $\rho = 0.35$ , p < 0.05), which may indicate more recent exposure, due to the low half-life (<12 hours) of cobalt in urine (Leyssens et al., 2017). We did not use any blood cobalt results for analysis in the Dehcho and Sahtú reference populations or the pooled dataset, as most values were below the analytical detection limit

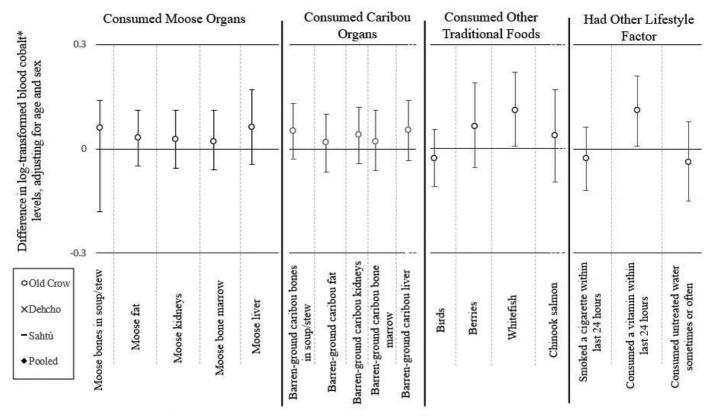
 $(0.075 \ \mu g/L)$ . Therefore, in the case of blood cobalt levels, we could not conduct regional comparisons or use the pooled dataset to identify associations with smaller effect sizes.

In Old Crow, mean blood cobalt levels were similar between females and males. However, mean urinary cobalt levels were higher in females than in males in all three regions (Table 3). High urinary cobalt concentrations in women, such as those observed in this study, have been detected in other biomonitoring studies (Health Canada, 2013b). These differences have been hypothesized as being linked to lower baseline iron levels or higher levels of iron loss in women (Fort et al., 2015), though we did not analyze iron status in Old Crow or the reference populations. We found no association between mean blood or urinary cobalt levels and age in Old Crow (p = 0.32 and 0.22, respectively) or urinary cobalt and age in the reference populations (p = 0.55 the Dehcho and p = 0.41 in the Sahtú) or the pooled dataset (p = 0.15).

Figures 3a and 3b show the regression coefficient and 95% confidence intervals for log-transformed blood and urinary cobalt levels between those with, and without, the determinant, adjusting for age and sex. Supplementary Tables 4-7 summarize these results using a percent difference. We observed no significant associations between urinary cobalt levels and eating any traditional foods in Old Crow or the reference populations. In Old Crow, the only traditional food determinant associated with increased cobalt biomarker concentrations, after adjusting for age and sex, was eating whitefish (those who ate whitefish had blood cobalt levels that were 28% higher, on average, adjusted  $r^2 = 0.15$ ). We did not find this association for the reference populations or the pooled dataset. A study of the diets of Indigenous Peoples from the Nenets Autonomous Okrug in northeastern Russia showed mean cobalt levels in whitefish more than two times higher than in other fish types that are eaten in both Russia and Old Crow, including inconnu, salmon, and northern pike (Sobolev et al., 2019). In areas where cobalt levels are elevated in the environment, dietary consumption of locally harvested foods, including, primarily, vegetables, grains, and fish, can result in elevated cobalt levels in the population (Leyssens et al., 2017) This association can be further examined in the future through the analysis of local whitefish samples for cobalt levels.

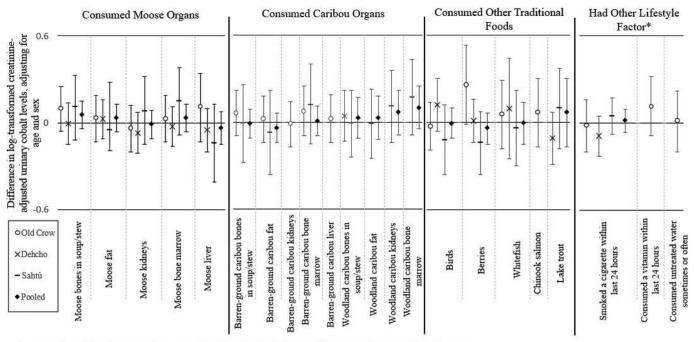
In addition to the consumption of whitefish, Old Crow participants who reported taking a vitamin in the previous 24 hours had blood cobalt levels that were 29% higher, on average, than those who did not take any vitamins, adjusting for age and sex (adjusted  $r^2 = 0.18$ ). We observed no association between vitamin consumption and the consumption of whitefish ( $X^2 p > 0.05$ ). An observed association between vitamin intake and cobalt status may be related to the inclusion of vitamin B12, a cobalt-bearing compound, in many multivitamins. Other biomonitoring studies have found that consumption of multivitamins containing B12 affects blood cobalt levels (Knoop et al., 2019). In Old Crow, 27% of respondents who provided blood samples took a vitamin that day. This is within the range

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\*Blood cobalt results are only reported in Old Crow due to values below the analytical detection limit in Dehcho and Sahtu communities.

FIG. 3a. Regression coefficients and 95% confidence intervals for log-transformed blood cobalt concentrations in a model including sex, age, and the identified determinant.



\*Consumption of vitamins, untreated water, and food hunted using lead ammunition were only measured in Old Crow.

FIG. 3b. Regression coefficients and 95% confidence intervals for log-transformed, creatinine-adjusted urinary cobalt concentrations in a model including sex, age, and the identified determinant.

of 23% to 33% observed in national-scale North American biomonitoring studies, including the CHMS and National Health and Nutrition Examination Survey (Statistics Canada, 2017; Mishra et al., 2021). Though cobalt content in vitamins may contribute to cobalt exposure, it may not explain elevated cobalt levels in Old Crow compared to the general Canadian population. Possible sources of cobalt exposure that were not included in this study include occupational exposure, exposure from surgical implants, and household exposure from dusts and soils (Agency for Toxic Substances and Disease Registry, 1992). This study did not identify a possible source of cobalt exposure with a strong association with cobalt biomarker levels in Old Crow.

Lead: Blood and urinary lead were positively correlated in Old Crow (Spearman  $\rho = 0.77$ , p < 0.001), the Dehcho (Spearman  $\rho = 0.56$ , p < 0.001) and Sahtú (Spearman  $\rho = 0.70, p < 0.001$ ) reference populations, and in the pooled dataset (Spearman  $\rho = 0.67$ , *p* < 0.001). Mean concentrations of blood lead were lower in females than males in Old Crow, but this was not the case in either the Dehcho or Sahtú (Table 3). Higher urinary and blood lead levels in men, such as those we observed in Old Crow, have been observed in other biomonitoring studies, including the National Health and Nutrition Examination Survey (Muntner et al., 2005). Some hypotheses for this trend include the biological, such as sex-specific differences in blood erythrocyte volume resulting in additional lead-bonding sites in males, or the social, including possible population-level, lifestyle-based differences between genders, including occupational exposure (Counter et al., 2001). Mean lead levels in biomarkers increased with age in Old Crow, the reference populations, and the pooled dataset for both blood lead (Spearman  $\rho = 0.41 - 0.49$ , p < 0.001) and urinary lead (Spearman  $\rho = 0.39 - 0.47$ , p < 0.001). Other large scale biomonitoring studies (Muntner et al., 2005) have observed an increase in lead with age in adults, attributed to lead retention over a lifetime of exposure.

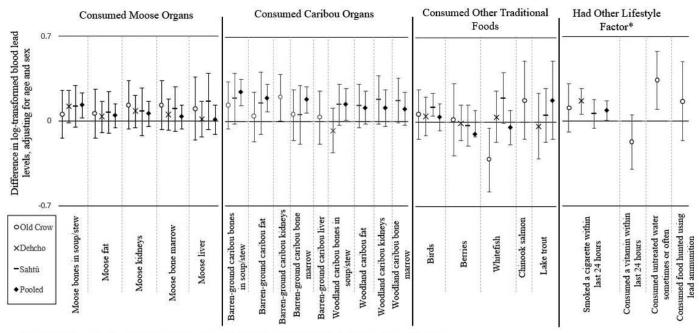
Figures 4a and 4b show the regression coefficient and 95% confidence intervals for log-transformed blood and urinary lead levels between those with and without the determinant, adjusting for age and sex. Supplementary Tables 4-7 summarize these results using a percent difference. After adjusting for age and sex, average blood lead levels were higher for Old Crow participants who ate Porcupine caribou kidney (blood lead levels that were 58% higher, on average, adjusted model  $r^2 = 0.29$ ) than those who did not. In the Dehcho, we found no association between lead levels in blood and urine and consumption of moose or caribou organs. In the Sahtú, participants who ate woodland caribou bone marrow had 230% higher urinary lead levels, on average, compared to those who did not, while accounting for age and sex (adjusted model  $r^2 = 0.17$ ). In the pooled dataset, participants who ate organs, including caribou bones, fat, and bone marrow had 38%-74% higher blood lead levels, on average, than those who did not (adjusted model  $r^2 = 0.25$ , 0.21, and 0.21,

respectively), and participants who ate moose kidneys and caribou bone marrow had 55%-91% higher urinary lead levels, on average, than those who did not (adjusted model  $r^2 = 0.12$ , and 0.16, respectively). Elevated lead levels can be found in caribou and moose organs, such as the kidneys or liver (Rabinowitz, 1991), as well as in the bones, or rumen (O'Hara et al., 2003). However, renal lead levels in Porcupine caribou bulls were generally lower than those observed in other northern herds, including the Bluenose East herd in the Sahtú region (Gamberg, 2016). Notably, ongoing caribou monitoring in northern Canada has shown decreasing renal lead levels in caribou in both of these herds (Gamberg, 2016).

We identified no association between smoking and lead levels in Old Crow. However, smokers in both of the reference populations and the pooled dataset had higher lead levels, on average, than non-smokers, adjusting for age and sex. The lack of significant association may be due to the small study population in Old Crow in comparison to the other groups, particularly the pooled dataset. Several large- and small-scale biomonitoring studies have observed elevated lead levels in current and former smokers, as lead can be found in tobacco smoke (Caruso et al., 2014; Statistics Canada, 2015; Rhee et al., 2021). As part of the return of results process for all biomonitoring clinics, health promotion materials included recommendations for reducing exposure to tobacco smoke to reduce exposure to some contaminants.

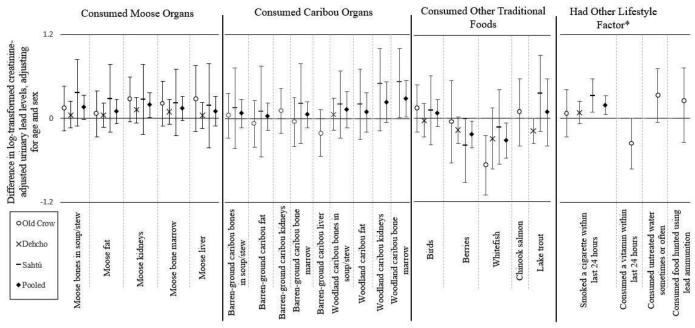
Though the majority of participants in the biomonitoring project (>75% of participants who knew the type of ammunition used in their traditional foods) ate food that had been hunted using lead ammunition, we identified no significant association between consumption of these foods and lead exposure levels. However, approximately one third of the participants in Old Crow did not know what type of ammunition was used for the game meat they consumed (Table 1). The number of participants who knew they did not consume game meat or fowl hunted using lead ammunition was small (n = 4-7) and was not sufficient to identify trends in exposure patterns in this case. Previous studies evaluating the relationship between blood lead levels and ammunition found differences in the isotopic footprint of lead in the blood of consumers of food hunted using lead shot and bullets, concluding that the use of lead ammunition can be a source of lead exposure (Tsuji et al., 2008). The small number of participants who did not consume any meat hunted using lead ammunition in Old Crow may be indicative of widespread use of lead-bearing shot or bullets for hunting in the community, resulting in elevated lead levels in the population.

Old Crow participants who often or sometimes drank untreated water had average blood lead levels 120% higher than those who rarely or never drank untreated water, adjusting for age and sex (adjusted model  $r^2 = 0.41$ ). In previous studies, elevated lead values relative to the Guidelines for Canadian Drinking Water Quality (0.005 mg/L) have been observed in surface water samples from



\*Consumption of vitamins, untreated water, and food hunted using lead ammunition were only measured in Old Crow.

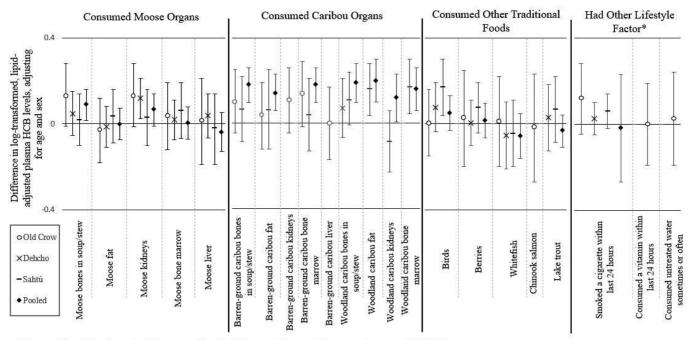
FIG. 4a. Regression coefficients and 95% confidence intervals for log-transformed blood lead concentrations in a model including sex, age, and the identified determinant.



\*Consumption of vitamins, untreated water, and food hunted using lead ammunition were only measured in Old Crow.

FIG. 4b. Regression coefficients and 95% confidence intervals for log-transformed, creatinine-adjusted urinary lead concentrations in a model including sex, age, and the identified determinant.

the nearby Porcupine River during spring sampling events between 2014–19 (Environment Canada, 2021). The Porcupine River may not be the only river community members are sourcing for untreated drinking water, and we recommend further evaluation of drinking water, including source identification, water quality analysis, and intake calculation. As discussed in the manganese section, we observed possible significant associations between blood lead levels and both the consumption of caribou kidneys and drinking untreated river water, and all of the participants who reported drinking untreated river water also reported eating caribou kidneys. Due to small numbers, it was not



\*Consumption of vitamins, untreated water, and food hunted using lead ammunition were only measured in Old Crow.

FIG. 5. Regression coefficients and 95% confidence intervals for log-transformed, lipid-adjusted plasma HCB concentrations in a model including sex, age, and the identified determinant.

possible to control for both of these variables in a regression model.

This study focuses primarily on traditional foods, with some other risk factors for exposure, and does not include all possible exposure sources. Notably, a 2021 study (Fillion et al., 2014) found that house dust and the use of lead ammunition were the primary exposure sources for Nunavut residences with elevated blood lead levels. We did not include house dusts in this analysis, but further investigation into this exposure source is warranted, given the elevated lead levels of some community members.

This paper primarily aims to identify determinants with positive associations with key parameters. It is noteworthy, however, that consumption of some traditional foods was negatively associated with lead exposure, adjusting for age and sex, including the consumption of whitefish in Old Crow (consumers had blood lead levels that were 51% lower, on average, adjusted model  $r^2 = 0.30$ ), lake trout in the Dehcho reference population (consumers had creatinineadjusted urinary lead levels that were 34% lower, on average, adjusted model  $r^2 = 0.34$ ), and berries in the Sahtú reference population (consumers had creatinine-adjusted urinary lead levels that were 59% lower, on average, adjusted model  $r^2 = 0.15$ ). In the pooled dataset, consumers who ate berries had creatinine-adjusted urinary lead levels that were 41% lower, on average (adjusted  $r^2 = 0.13$ ), and consumers who ate whitefish had blood lead levels that were 52% lower, on average (adjusted model  $r^2 = 0.13$ ). Negative associations may be relevant when identifying possible protective factors for exposure. These traditional foods are high in nutrients, including vitamin C (in the case of berries) and zinc (in the case of whitefish), which act as antioxidant defense mechanisms to reduce oxidative stress following lead exposure (Kuhnlein et al., 1995; Fediuk et al., 2002; Bashandy 2006; Prasanthi et al., 2010). In addition to the traditional food determinants, Old Crow participants who reported taking a vitamin in the previous 24 hours had creatinine-adjusted urinary lead levels that were 56% lower, on average (adjusted model  $r^2 = 0.33$ ) than those who did not, adjusting for age and sex. This result is consistent with the literature, where it noted that some vitamins, including vitamin C, vitamin E, calcium, and zinc might have protective properties against the adverse health effects of lead following exposure (Bashandy 2006; Prasanthi et al., 2010). Additionally, it is possible that broader behavioural differences, such as the replacement of higher contaminant-level foods with whitefish or berries, may account for these differences in biomarker levels.

Hexachlorobenzene (HCB): Mean concentrations of lipid-normalized HCB were lower in females than males in Old Crow, but this was not the case in either the Dehcho or Sahtú (Table 3). Generally, lipid-normalized HCB levels increased with age in Old Crow, both reference populations, and the pooled dataset (Spearman  $\rho = 0.63-0.76$ , p < 0.001).

Figure 5 shows the regression coefficient and 95% confidence intervals for log-transformed, lipid-adjusted plasma HCB levels between those with, and without, the determinant, adjusting for age and sex. Supplementary Tables 4-7 summarize these results using a percent difference. HCB is a lipophilic contaminant and is most likely to be found in the fatty tissues of long-lived biota (Mrema et al., 2013). We found some associations between HCB levels

and consumption of key traditional foods, particularly those high in fat, in several of the population groups, including the Dehcho, Sahtú, and the pooled population. However, in Old Crow, none of the selected determinants of exposure had significant associations with HCB levels. This may suggest the presence of multiple local exposure sources contributing to elevated average levels, or it could be a result of a low effect level that cannot be detected in this group due to the small sample size. The higher sample size of the pooled dataset allows for the identification of possible significant trends with smaller effect sizes, which may be the case with HCB. In the pooled dataset, participants who ate organs, including moose bones, caribou bones, fat, kidneys, and bone marrow, had 23%-58% higher blood HCB levels, on average (adjusted model r<sup>2</sup> ranged from 0.39 to 0.48), than those who did not. In the reference groups, we observed higher average HCB levels in Dehcho participants who ate moose kidneys, and, in the Sahtú, we observed higher average HCB levels for those who ate birds and woodland caribou fat and bone marrow. We found the most associations between traditional food consumption and HCB in the pooled dataset. In all regions, the consumption of most individual moose and caribou organs was positively associated with the consumption of all other individual moose and caribou organs ( $X^2$  p < 0.001). Due to these near-perfect correlations, future studies should focus on HCB analysis and intake estimation for these foods. Previous work evaluating the HCB content of some traditional foods in northern British Columbia found elevated HCB concentrations in some of the types of fish that are also eaten in Old Crow, including whitefish and chinook salmon, as well as in some game birds also hunted and consumed in Old Crow (Chan et al., 2011; Kelly et al., 2011). Generally, concentrations of HCB are low in caribou muscle tissue, but have been found in higher concentrations in kidneys, liver, and fat (Braune et al., 1999; Polder et al., 2010; Chan et al., 2011; Hassan et al., 2013;). Further studies could be conducted to estimate exposure from all these sources to determine whether intake exceeds toxicological recommendations.

We observed no association between smoking status and HCB levels in Old Crow or the reference communities. Several large- and small-scale biomonitoring studies have observed elevated HCB and lead levels in current and former smokers, as both contaminants can be found in tobacco smoke (Lackmann et al., 2000; Caruso et al., 2014; Statistics Canada 2015; Rhee et al., 2021).

## Health Promotion

In Old Crow and the reference populations, consumption of some traditional foods, including caribou and moose organs was associated with elevated levels of some of the key parameters of this study. Despite these possibly elevated levels, traditional foods are an important source of nutrients for members in all three regions, and provide other important health and wellness benefits, including increased physical activity during harvesting, cultural benefits, and improvements in mental health (Receveur et al., 1998). During the return of results process for each of the biomonitoring clinics, community members heard from researchers who validated previously held community priorities regarding the importance and benefits of these traditional foods. Community members had several occasions, including during community presentations and individual meetings, as well as through media outreach, posters, brochures, and written reports, to consider the message delivered by researchers, which was that the health benefits of eating traditional foods continue to outweigh the risks (Ratelle et al., 2018a; Drysdale et al., 2021). Community partners also collaborated with the researchers to co-develop other health promotion materials related to contaminant exposure. In particular, both parties made recommendations to reduce exposure to tobacco smoke and the use of lead-bearing ammunition in hunting. This study does not change any existing dietary recommendations in any of the participating regions.

#### Study Limitations

This study examined associations but does not reflect causal relationships between determinants and biomarker levels. Our study can be used to inform further assessment of risk for key parameters but should not be the sole factor used to issue consumption notices or health recommendations for traditional food consumption. This study drew on data from small biomonitoring projects carried out in northern communities. Although the study participants represented 44% of the population of Old Crow, and 12% to 40% of the populations of the reference populations, the numbers are not sufficient to allow analytic control for all possible factors that may impact results. Additionally, due to the nature of the recruitment process in small, community-focused biomonitoring projects, a random sample is often not possible (Ratelle et al., 2018a). Therefore, study recruitment might not reach certain members of the population, including those without phones, or those who work seasonally outside the community. This study does not include some of the most commonly eaten foods, such as moose and caribou muscle meat, as they are eaten by more than 95% of community members in Old Crow. Further study is warranted to estimate the level of contaminant exposure from these sources using modelling of intake of each contaminant through dietary and other sources at the individual and population level.

These results are intended to guide and refine future research in the North in an effort to identify determinants of exposure for contaminants found at elevated levels in humans. Any recommendations regarding changes to consumption of specific traditional foods must be done in co-development with the affected communities and taking into account their needs and experiences (Gyapay et al., 2022). These recommendations should also be informed by environmental monitoring, as well as risk assessments, in order to estimate contaminant exposure.

## CONCLUSIONS

Animal bones and organs can accumulate high concentrations of metals, and fatty tissue and organs can accumulate lipophilic compounds, such as HCB (Chan et al., 2011; O'Hara et al., 2005; Robillard et al., 2002). Informed by community concerns about the relationship between traditional foods and potentially elevated exposure to these contaminants, this study aimed to identify possible determinants of exposure. We sought to complement sampling of local traditional foods in Old Crow and to inform risk assessments in the community based on their level of intake of these foods. We found that consumption of some traditional foods in Old Crow was positively associated with biomarker levels to some contaminants and nutrients, including manganese, cobalt, and lead. Members of our research team are now engaged with community partners in further HCB analysis in traditional food samples in Old Crow in an effort to estimate intake and identify possible driver(s) for elevated levels in community members.

In addition to the consumption of some traditional foods, several other determinants of exposure were associated with elevated levels of key parameters. These included the consumption of untreated river water, vitamins, and smoking. The federal government monitors local surface water in Old Crow and has found elevated levels of some metals, including manganese and lead during spring runoff (Environment Canada, 2012). However, based on our results, we recommend additional monitoring in locations where the local community consumes untreated water. Smoking rates in northern communities are higher than those in the general Canadian population, and this may contribute to elevated levels of some contaminants, including lead, in these populations.

Traditional foods remain an important source of nutrients in the diets of community members in Old Crow and the reference populations and confer other benefits, including toward maintaining spiritual wellness (Receveur et al., 1998; Kuhnlein and Receveur, 2007). Given the importance to the communities of these traditional foods, future efforts should focus on monitoring the levels of contaminants they contain followed by generating exposure estimates to further increase understanding of the benefits and risks of their consumption.

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# REFERENCES

- Agency for Toxic Substances and Disease Registry. 1992. Toxicological profile for cobalt. U.S. Department of Health and Human Services, Agency for Toxic Substances and Disease Registry. https://www.atsdr.cdc.gov/toxprofiles/tp33.pdf
- Arrebola, J.P., Martin-Olmedo, P., Fernandez, M.F., Sanchez-Cantalejo, E., Jimenez Moreno, J.A., Torne, P., Porta, M., and Olea, N. 2009. Predictors of concentrations of hexachlorobenzene in human adipose tissue: A multivariate analysis by gender in southern Spain. Environment International 35(1):27–32.

https://doi.org/10.1016/j.envint.2008.05.009

Assembly of First Nations. 2013. First Nations biomonitoring initiative: National results (2011). Ottawa. https://www.fehncy.ca/wp-content/uploads/2020/07/AFN-biomonitoring-initiative-\_fnbi\_en\_-\_2013-06-26.pdf

Aylward, L.L., Hays, S.M., Gagne, M., Nong, A., and Krishnan, K. 2010. Biomonitoring equivalents for hexachlorobenzene. Regulatory Toxicology and Pharmacology 58(1):25–32. https://doi.org/10.1016/j.yrtph.2010.06.003

Bashandy, S.A.E. 2006. Beneficial effect of combined administration of vitamin C and vitamin E in amelioration of chronic lead hepatotoxicity. The Egyptian Journal of Hospital Medicine 23(1):371–384. https://ejhm.journals.ekb.eg/article 17948.html

Braune, B., Muir, D., DeMarch, B., Gamberg, M., Poole, K., Currie, R., Dodd, M., et al. 1999. Spatial and temporal trends of contaminants in Canadian Arctic freshwater and terrestrial ecosystems: A review. Science of the Total Environment 230(1-3):145-207. https://doi.org/10.1016/S0048-9697(99)00038-8

- Brown, M.J., and Margolis, S. 2012. Lead in drinking water and human blood lead levels in the United States. Centers for Disease Control and Prevention. Morbidity and Mortality Report (MMWR) 61(4):1–9. https://www.cdc.gov/mmwr/preview/mmwrhtml/su6104a1.htm
- Budis, H., Kalisinska, E., Lanocha, N., and Kosik-Bogacka, D. 2013. The concentration of manganese, iron and strontium in bone of red fox *Vulpes vulpes* (L. 1758). Biological Trace Element Research 155:361–369. https://doi.org/10.1007/s12011-013-9809-2
- Canadian Public Health Association. 2021. Tobacco and vaping use in Canada: Moving forward. Ottawa. https://www.cpha.ca/tobacco-and-vaping-use-canada-moving-forward
- Caruso, R.V., O'Connor, R.J., Stephens, W.E., Cummings, K.M., and Fong, G.T. 2014. Toxic metal concentrations in cigarettes obtained from U.S. smokers in 2009: Results from the international tobacco control (ITC) Unites States survey cohort. International Journal of Environmental Research and Public Health 11(1):202–217. https://doi.org/10.3390/ijerph110100202
- Chan, L., Receveur, O., Sharp, D., Shwartz, H., Ing, A., and Tikhonov, C. 2011. First Nations food, nutrition and environment study: Results from British Columbia. Prince George: University of Northern British Columbia.

http://www.fnfnes.ca/docs/FNFNES\_British\_Columbia\_Regional\_Report\_ENGLISH\_2019-12-06.pdf

Chung, S.E., Cheong, H.K., Ha, E.H., Kim, B.N., Ha, M., Kim, Y., Hong, Y.C., Park, H., and Oh, S.Y. 2015. Maternal blood nanganese and early neurodevelopment: The mothers and children's environmental health (MOCEH) study. Environmental Health Perspectives 123(7):717–722.

https://doi.org/10.1289/ehp.1307865

- Counter, S.A., Buchanan, L.H., and Ortega, F. 2001. Gender differences in blood lead and hemoglobin levels in Andean adults with chronic lead exposure. International Journal of Occupational Environmental Health 7(2):113–118. https://doi.org/10.1179/107735201800339551
- Drysdale, M., and Laird, B. 2018. Community report—Dietary and health messages surveys in Old Crow, Yukon Territory: Results. Brian.laird@waterloo.ca
- Drysdale, M., Ratelle, M., Skinner, K., Garcia-Barrios, J., Gamberg, M., Williams, M., Majowicz, S., et al. 2021. Human biomonitoring results of contaminant and nutrient biomarkers in Old Crow, Yukon, Canada. Science of the Total Environment 760: 143339. https://doi.org/10.1016/j.scitotenv.2020.143339
- Fediuk, K., Hidiroglou, N., Madère, R., and Kuhnlein, H.V. 2002. Vitamin C in Inuit traditional food and women's diets. Journal of Food Composition and Analysis 15(3):221–235. https://doi.org/10.1006/jfca.2002.1053
- Fillion, M., Blais, J.M., Yumvihoze, E., Nakajima, M., Workman, P., Osborne, G., and Chan, H.M. 2014. Identification of environmental sources of lead exposure in Nunavut (Canada) using stable isotope analyses. Environment International 71:63-73. https://doi.org/10.1016/j.envint.2014.06.004
- Finley, J.W., and Davis, C.D. 1999. Manganese deficiency and toxicity: Are high or low dietary amounts of manganese cause for concern? Biofactors 10(1):15–24.

https://doi.org/10.1002/biof.5520100102

Finley, B.L., Monnot, A.D., Gaffney, S.H., and Paustenbach, D.J. 2012. Dose-response relationships for blood cobalt concentrations and health effects: A review of the literature and application of a biokinetic model. Journal of Toxicology and Environmental Health - Part B: Critical Reviews 15(8):493–523.

htps://doi.org/10.1080/10937404.2012.744287

- Fontaine, J., Dewailly, É., Benedetti, J.-L., Pereg, D., Ayotte, P., and Dery, S. 2008. Re-evaluation of blood mercury, lead and cadmium concentrations in the Inuit population of Nunavik (Quebec): A cross-sectional study. Environmental Health 7: 25. https://doi.org/10.1186/1476-069X-7-25
- Fort, M., Grimalt, J.O., Casas, M., and Sunyer, J. 2015. Interdependence between urinary cobalt concentrations and hemoglobin levels in pregnant women. Environmental Research 136:148–154. https://doi.org/10.1016/j.envres.2014.10.013
- Gamberg, M. 2016. Arctic caribou contaminant monitoring program. Whitehorse. https://nwtdiscoveryportal.enr.gov.nt.ca/geoportaldocuments/Synopsis%20Report%20Contaminants%20in%20Arctic%20 Caribou%202016-17.pdf
- Garcia-Barrios, J., Drysdale, M., Ratelle, M., Gaudreau, È., LeBlanc, A., Gamberg, M., and Laird, B.D. 2021. Biomarkers of polyand perfluoroalkyl substances (PFAS) in sub-Arctic and Arctic communities in Canada. International Journal of Hygiene and Environmental Health 235: 113754.

https://doi.org/10.1016/j.ijheh.2021.113754

Government of Canada. 2014. Freshwater quality monitoring and surveillance—Online data: Filtered site variable data, Porcupine River above Old Crow River (YT09FB0003).

http://aquatic.pyr.ec.gc.ca/webdataonlinenational/en/Measurements/LastDataResultsHtml/Sites/YT09FB0003/Projects/PYLTM/ Regions/0/vars/679a589a683a591/from/19921127/to/20200116/utcToLocal/0/page/1?linesPerPage=6 -----. 2018. Canadian Arctic contaminants assessment report: Human health assessment. Ottawa. http://publications.gc.ca/collections/collection 2018/rcaanc-cirnac/R74-2-4-2017-eng.pdf

- Gyapay, J., Noksana, K., Ostertag, S., Wesche, S., Laird, B., and Skinner, K. 2022. Informing the co-development of culture-centered dietary messaging in the Inuvialuit Settlement Region, Northwest Territories. Nutrients 14(9): 1915. https://doi.org/10.3390/nu14091915
- Haines, D.A., Arbuckle, T.E., Lye, E., Legrand, M., Fisher, M., Langlois, R., and Fraser, W. 2011. Reporting results of human biomonitoring of environmental chemicals to study participants: A comparison of approaches followed in two Canadian studies. Journal of Epidemiology and Community Health 65(3):191–198. http://dx.doi.org/10.1136/jech.2008.085597
- Haines, D.A., Khoury, C., Saravanabhavan, G., Werry, K., Walker, M., and Malowany, M. 2017. Human biomonitoring reference values derived for persistent organic pollutants in blood plasma from the Canadian health measures survey 2007–2011. International Journal of Hygiene and Environmental Health 220(4):744–756. https://doi.org/10.1016/j.ijheh.2017.03.004
- Hassan, A.A., Rylander, C., Brustad, M., and Sandanger, T.M. 2013. Persistent organic pollutants in meat, liver, tallow and bone marrow from semi-domesticated reindeer (*Rangifer tarandus tarandus* L.) in northern Norway. Acta Veterinaria Scandinavica 55: 57. https://doi.org/10.1186/1751-0147-55-57
- Hassani, H., Goldbabaei, F., Shirkhanloo, H., and Tehrani-Doust, M. 2016. Relations of biomarkers of manganese exposure and neuropsychological effects among welders and ferroalloy smelters. Industrial Health 54(1):79-86. https://doi.org/10.2486/indhealth.2014-0250
- Health Canada. 2010. Report on human biomonitoring of environmental chemicals in Canada: Results of the Canadian health measures survey cycle 1 (2007–2009). Ottawa.

https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/report-human-biomonitoring-environmental-chemicals-canada-health-canada-2010.html

-----. 2013a. Second report on human biomonitoring of environmental chemicals In Canada: Results of the Canadian health measures survey cycle 2 (2009–2011). Ottawa.

https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/ewh-semt/alt\_formats/pdf/pubs/contaminants/chms-ecms-cycle2/chms-ecms-cycle2-eng.pdf

. 2013b. Final human health state of the science report on lead. Ottawa.

https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/ewh-semt/alt\_formats/pdf/pubs/contaminants/dhhssrl-rpecscepsh/dhhssrl-rpecscepsh-eng.pdf

-----. 2015. Third report on human biomonitoring of environmental chemicals in Canada: Results of the Canadian health measures survey cycle 3 (2012–2013). Ottawa.

https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/ewh-semt/alt\_formats/pdf/pubs/contaminants/chms-ecms-cycle3/chms-ecms-cycle3-eng.pdf

-----. 2017. Fourth report on human biomonitoring of environmental chemicals in Canada: Results of the Canadian health measures survey cycle 4 (2014–2015). Ottawa.

https://www.canada.ca/content/dam/hc-sc/documents/services/environmental-workplace-health/reports-publications/ environmental-contaminants/fourth-report-human-biomonitoring-environmental-chemicals-canada/fourth-report-humanbiomonitoring-environmental-chemicals-canada-eng.pdf

-----. 2019. Fifth report on human biomonitoring of environmental chemicals in Canada: Results of the Canadian health measures survey cycle 5 (2016–2017). Ottawa.

https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/fifth-report-human-biomonitoring.html

——. 2021. Sixth report on human biomonitoring of environmental chemicals in Canada: 8 summaries and results for metals and trace elements. Ottawa.

https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/sixth-report-human-biomonitoring/page-2.html #s8-1

Indigenous and Northern Affairs Canada. 2010. Metals of concern fact sheet (Yukon Territory).

https://pubs.aina.ucalgary.ca/ncp/85905.pdf

Iyare, P.U. 2019. The effects of manganese exposure from drinking water on school-age children: A systematic review. NeuroToxicology 73:1-7.

https://doi.org/10.1016/j.neuro.2019.02.013

Josie, W., Gamberg, M., Suitor, M., Wang, X., and Muir, D. 2015. Mercury in fish from Old Crow (Old Crow, YT). Brian.laird@waterloo.ca

Kelly, B.C., Ikonomou, M.G., MacPherson, N., Sampson, T., Patterson, D.A., and Dubetz, C. 2011. Tissue residue concentrations of organohalogens and trace elements in adult Pacific salmon returning to the Fraser River, British Columbia, Canada. Environmental Toxicology and Chemistry 30(2):367–376.

https://pubmed.ncbi.nlm.nih.gov/21086554/

- Knoop, A., Görgens, C., Geyer, H., and Thevis, M. 2020. Elevated urinary cobalt concentrations identified in routine doping controls can originate from vitamin B<sub>12</sub>. Rapid Communications in Mass Spectrometry 34(7): e8649. https://doi.org/10.1002/rcm.8649
- Kuhnlein, H.V., and Receveur, O. 2007. Local cultural animal food contributes high levels of nutrients for Arctic Canadian Indigenous adults and children. The Journal of Nutrition 137(4):1110–1114. https://doi.org/10.1093/jn/137.4.1110
- Kuhnlein, H.V., Receveur, O., Morrison, N.E., Appavoo, D.M., Soueida, R., and Pierrot, P. 1995. Dietary nutrients of Sahtú Dene/Métis vary by food source, season and age. Ecology of Food and Nutrition 34(3):183–195. https://doi.org/10.1080/03670244.1995.9991459
- Lackmann, G.M., Angerer, J., and Tollner, U. 2000. Parental smoking and neonatal serum levels of polychlorinated biphenyls and hexachlorobenzene. Pediatric Research 47:598-601. https://doi.org/10.1203/00006450-200005000-00007
- Laird, B.D., Goncharov, A B., and Chan, H.M. 2013. Body burden of metals and persistent organic pollutants among Inuit in the Canadian Arctic. Environment International 59:33–40. https://doi.org/10.1016/j.envint.2013.05.010
- Laird, B., Ratelle, M., Skinner, K., Brandow, D., and Packull-McCormick, S. 2019. Contaminant biomonitoring in the Northwest Territories Mackenzie Valley: Investigating the links between contaminant exposure, nutritional status, and country food use. University of Waterloo, Ontario.

https://uwaterloo.ca/human-exposure-and-toxicology-research-group/sites/default/files/uploads/files/community\_report\_-\_ mackenzie\_final\_review\_1.pdf

- Lanphear, B.P., Hornung, R., Khoury, J., Yolton, K., Baghurst, P., Bellinger, D.C., Canfield, R.L., et al. 2005. Low-level environmental lead exposure and children's intellectual function: An international pooled analysis. Environmental Health Perspectives 113(7):894–899. https://doi.org/10.1289/ehp.7688
- Lemire, M., Lavoie, A., Pontual, M., Little, M., Levesque, B., and Ayotte, P. 2021. Environmental contaminants: Metals, Qanuilirpitaaq? 2017, Nunavik Inuit health survey. Kuujjuaq, Quebec: Nunavik Regional Board of Health and Social Services. https://nrbhss.ca/sites/default/files/health surveys/Environmental Contaminants-Metals report en.pdf
- Leyssens, L., Vinck, B., Van Der Straeten, C., Wuyts, F., and Maes, L. 2017. Cobalt toxicity in humans: A review of the potential sources and systemic health effects. Toxicology 387:43-56. https://doi.org/10.1016/j.tox.2017.05.015
- Manninen, S., and Tankskanen, N. 1993. Transfer of lead from shotgun pellets to humus and three plant species in a Finnish shooting range. Archive of Environmental Contamination and Toxicology 24:410–414. https://doi.org/10.1007/BF01128741
- Mayo Clinic Laboratories. 2023. Rochester 2023 interpretive handbook. Minnesota. https://www.mayocliniclabs.com/test-catalog/pod/MayoTestCatalog-Rochester--SortedByTestName-duplex-interpretive.pdf
- Mishra, S., Stierman, B., Gahche, J.J., and Potischman, N. 2021. Dietary supplement use among adults: United States, 2017–2018. Nation Center for Health Statistics.

https://www.cdc.gov/nchs/products/databriefs/db399.htm#:~:text=During%202017%E2%80%932018%2C%20 57.6%25,supplement%20use%20increased%20with%20age

- Mrema, E.J., Rubino, F.M., Brambilla, G., Moretto, A., Tsatsakis, A.M., and Colosio, C. 2013. Persistent organochlorinated pesticides and mechanisms of their toxicity. Toxicology 307:74–88. https://doi.org/10.1016/j.tox.2012.11.015
- Muntner, P., Menke, A., DeSalvo, K.B., Rabito, F.A., and Batuman, V. 2005. Continued decline in blood lead levels among adults in the United States: The national health and nutrition examination surveys. Archives in Internal Medicine 165(18):2155–2161. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/486734
- Navas-Acien, A., Guallar, E., Silbergeld, E.K., and Rothenberg, S.J. 2007. Lead exposure and cardiovascular disease—A systematic review. Environmental Health Perspectives 115(3):472–482. https://doi.org/10.1289/ehp.9785
- O'Brien, K.M., Upson, K., and Buckley, J.P. 2017. Lipid and creatinine adjustment to evaluate health effects of environmental exposures. Current Environmental Health Reports 4(1):44–50. https://doi.org/10.1007/s40572-017-0122-7
- O'Hara, T.M., George, J.C., Blake, J., Burek, K., Carroll, G., Dau, J., Bennett, L., McCoy, C.P., Gerard, P., and Woshner, V. 2003. Investigation of heavy metals in a large mortality event in caribou of northern Alaska. Arctic 56(2):125-135. https://doi.org/10.14430/arctic608
- O'Hara, T.M., Hoekstra, P.F., Hanns, C., Backus, S.M., and Muir, D.C.G. 2005. Concentrations of selected persistent organochlorine contaminants in store-bought foods from northern Alaska. International Journal of Circumpolar Health 64(4):303-313. https://doi.org/10.3402/ijch.v64i4.18008

O'Neal, S.L., and Zheng, W. 2015. Manganese toxicity upon overexposure: A decade in review. Current Environmental Health Reports 2(3):315-328.

https://doi.org/10.1007/s40572-015-0056-x

Osdjo, T., and Bignert, A. 2002. Time trends of metals in liver, kidney and muscle of moose (*Alces alces*) from Sweden, 1980–2000. Sweden Museum of Natural History.

http://naturvardsverket.diva-portal.org/smash/get/diva2:657863/FULLTEXT01.pdf

- Oulhote, Y., Mergler, D., and Bouchard, M. 2014. Sex- and age-differences in blood manganese levels in the U.S. general population: National health and nutrition examination survey 2011–2012. Environmental Health13: 87. https://doi.org/10.1186/1476-069X-13-87
- Pappas, R.S., Fresquez, M.R., Martone, N., and Watson, C.H. 2014. Toxic metal concentrations in mainstream smoke from cigarettes available in the USA. Journal of Analytical Toxicology38(4):204–211. https://doi.org/10.1093/jat/bku013
- Polder, A., Savinova, T.N., Tkachex, A., Løken, K.B., Odland, J.O., and Skaare, J.U. 2010. Levels and patterns of persistent organic pollutants (POPS) in selected food items from northwest Russia (1998–2002) and implications for dietary exposure. Science of the Total Environment 408(22):5352–5361.

https://doi.org/10.1016/j.scitotenv.2010.07.036

Prasanthi, R.P.J., Devi, C.B., Basha, D.C., Reddy, N.S., and Reddy, G.R. 2010. Calcium and zinc supplementation protects lead (Pb)induced perturbations in antioxidant enzymes and lipid peroxidation in developing mouse brain. International Journal of Developmental Neuroscience 28(2):161–167.

https://doi.org/10.1016/j.ijdevneu.2009.12.002

Rabinowitz, M.B. 1991. Toxicokinetics of bone lead. Environmental Health Perspectives 91:33-37. https://doi.org/10.1289/ehp.919133

- Ratelle, M., Laird, M., Majowicz, S., Skinner, K., Swanson, H., and Laird, B. 2018a. Design of a human biomonitoring community-based project in the Northwest Territories Mackenzie Valley, Canada, to investigate the links between nutrition, contaminants and country foods. International Journal of Circumpolar Health 77(1): 1510714. https://doi.org/10.1080/22423982.2018.1510714
- Ratelle, M., Skinner, K., Laird, M.J., Majowicz, S., Brandow, D., Packull-McCormick, S., Bouchard, M., et al. 2018b. Implementation of human biomonitoring in the Dehcho region of the Northwest Territories, Canada (2016–2017). Archives of Public Health 76: 73. https://doi.org/10.1186/s13690-018-0318-9
- Ratelle, M., Skinner, K., Packull-McCormick, S., and Laird, B. 2020. Food frequency questionnaire assessing traditional food consumption in Dene/Métis communities, Northwest Territories, Canada. International Journal of Circumpolar Health 79(1): 1760071. https://doi.org/10.1080/22423982.2020.1760071
- Ratelle, M., Spring, A., Laird, B.D., Andrew, L., Simmons, D., Scully, A., and Skinner, K. 2022. Drinking water perception and consumption in Canadian subarctic Indigenous communities and the importance for public health. Facets 7(1):343–359. https://doi.org/10.1139/facets-2021-0094
- Receveur, O., Kassi, N., Chan, H.M., Berti, P.R., and Kuhnlein, H. 1998. Yukon First Nations' assessment of dietary benefit/risk. Montreal: CINE, McGill University. Brian.laird@uwaterloo.ca
- Reed, L., Buchner, V., and Tchounwou, P.B. 2007. Environmental toxicology and health effects associated with hexachlorobenzene exposure. Reviews on Environmental Health 22(3):213–243. https://doi.org/10.1515/REVEH.2007.22.3.213
- Rhee, J., Graubard, B.I., and Purdue, M.P. 2021. Blood lead levels and lung cancer mortality: An updated analysis of NHANES II and III. Cancer Medicine 10(12):4066–4074. https://doi.org/10.1002/cam4.3943
- Ribas-Fitó, N., Torrent, M., Carrizo, D., Júlvez, J., Grimalt, J.O., and Sunyer, J. 2007. Exposure to hexachlorobenzene during pregnancy and children's social behavior at 4 years of age. Environmental Health Perspectives 115(3):447-450. https://doi.org/10.1289/ehp.9314
- Robillard, S., Beauchamp, G., Paillard, G., and Bélanger, D. 2002. Levels of cadmium, lead, mercury, and cesium in caribou (*Rangifer tarandus*) tissues from northern Quebec. Arctic 55(1):1–9. https://doi.org/10.14430/arctic686
- Roels, H., Bowler, R.M., Kim, Y., Claus Henn, B., Mergler, D., Hoet, P., Gocheva, V.V., et al. 2012. Manganese exposure and cognitive deficits: A growing concern for manganese neurotoxicity. NeuroToxicology 33(4):872–880. https://doi.org/10.1016/j.neuro.2012.03.009
- Sanders, T., Liu, Y., Buchner, V., and Tchounwou, P.B. 2009. Neurotoxic effects and biomarkers of lead exposure: A review. Reviews on Environmental Health 24(1):15-45. https://doi.org/10.1515/REVEH.2009.24.1.15

- Santos-Burgoa, C., Rios, C., Mercado, L.A., Arechiga-Serrano, R., Cano-Valle, F., Eden-Wynter, R.A., Texcalac-Sangrador, J.L., Villa-Barragan, J.P., Rodriguez-Agudelo, Y., and Montes, S.2001. Exposure to manganese: Health effects on the general population, a pilot study in central Mexico. Environmental Research 85(2):90–104. https://doi.org/10.1006/enrs.2000.4108
- Saudny, H., Leggee, D., and Egeland, G. 2012. Design and methods of the adult Inuit health survey 2007–2008. International Journal of Circumpolar Health 71(1): 19752.

https://doi.org/10.3402/ijch.v71i0.19752

- Smink, A., Ribas-Fito, N., Garcia, R., Torrent, M., Mendez, M.A., Grimalt, J.O., and Sunyer, J. 2008. Exposure to hexachlorobenzene during pregnancy increases the risk of overweight in children aged 6 years. Acta Pædiatrica 97(10):1465–1469. https://doi.org/10.1111/j.1651-2227.2008.00937.x
- Smith, D., Gwiazda, R., Bowler, R., Roels, H., Park, R., Taicher, C., and Lucchini, R. 2007. Biomarkers of Mn exposure in humans. American Journal of Internal Medicine 50(11):801-811. https://doi.org/10.1002/ajim.20506
- Sobolev, N., Aksenov, A., Sorokina, T., Chashchin, V., Ellingsen, D.G., Nieboer, E., Varakina, Y., Veselkina, E., Kotsur, D., and Thomassen, Y. 2019. Essential and non-essential trace elements in fish consumed by Indigenous peoples of the European Russian Arctic. Environmental Pollution 253:966-973. https://doi.org/10.1016/j.envpol.2019.07.072

Sorrell, M., Rosen, J.F., and Roginsky, M. 2013. Interactions of lead, calcium, vitamin D, and nutrition in lead-burdened children. Archives of Environmental Health 32(4):160–164.

https://doi.org/10.1080/00039896.1977.10667274

Statistics Canada. 2015. Blood lead concentrations in Canadians, 2009 to 2011. https://www150.statcan.gc.ca/n1/pub/82-625-x/2013001/article/11779-eng.htm

-----. 2016a. Aboriginal population profile, 2016 census: Sahtu Dene Council (First Nation/Indian band or tribal council area), Northwest Territories.

https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/abpopprof/details/page.cfm?Lang=E&Geo1=AB&Code1=2016C 1005752&Data=Count&SearchText=Sahtu%20Dene%20Council&SearchType=Begins&B1=A11&C1=A11&SEX\_ID=1&AGE\_ID=16&RESGEO\_ID=1

-----. 2016b. Aboriginal population profile, 2016 census: Deh Cho First Nations (First Nation/Indian band or tribal council area), Northwest Territories.

https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/abpopprof/details/page.cfm?Lang=E&Geo1=AB&Code1=2016C100 5713&Data=Count&SearchText=Deh%20Cho%20First%20Nations&SearchType=Begins&B1=A11&C1=A11&SEX\_ID=1&AGE\_ID=17&RESGEO\_ID=1

——. 2016c. Census profile, 2016 census: Old Crow settlement [census subdivision], Yukon and Yukon [territory]. https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/prof/details/page.cfm?Lang=E&Geo1=CSD&Code1=6001043&Geo2= PR&Code2=60&SearchText=Old%20Crow&SearchType=Begins&SearchPR=01&B1=All&GeoLevel=PR&GeoCode=6001043&T ABID=1&type=0

—. 2017. Health fact sheets: Use of nutritional supplements, 2015.

https://www150.statcan.gc.ca/n1/pub/82-625-x/2017001/article/14831-eng.htm

TetraTech Inc. 2017. Overarching Yukon source water supply and protection study—Summary report.

https://open.yukon.ca/sites/default/files/env-overarching-yukon-source-water-supply-protection-study-summary-report.pdf

Tsuji, L.J.S., Wainman, B.C., Martin, I.D., Sutherland, C., Weber, J.-P., Dumas, P., and Nieboer, E. 2008. Lead shot contribution to blood lead of First Nations people: The use of lead isotopes to identify the source of exposure. Science of the Total Environment 405(1-3):180-185.

https://doi.org/10.1016/j.scitotenv.2008.06.048

- Tvermoes, B.E., Paustenbach, D.J, Kerger, B.D, Finley, B.L., and Unice, K.M. 2015. Review of cobalt toxicokinetics following oral dosing: Implications for health risk assessments and metal-on-metal hip implant patients. Critical Reviews in Toxicology 45(5):367–387. https://doi.org/10.3109/10408444.2014.985818
- Venäläinen, E.-R., Anttila, M., and Peltonen, K. 2005. Heavy metals in tissue samples of Finnish moose, *Alces alces*. Bulletin of Environmental Contamination and Toxicology 74:526-536. https://doi.org/10.1007/s00128-005-0616-0
- Vuntut Gwitchin Government and University of Waterloo. 2018. Vuntut Gwitchin Government research agreement, Old Crow, Yukon. Brian.laird@uwaterloo.ca
- Wein, E.E. 1996. Foods and nutrients in reported diets versus perceived ideal diets of Yukon Indian people. Journal of Nutrition Education 28(4):202-208.

https://doi.org/10.1016/S0022-3182(96)70071-7

Wein, E., and Freeman, M.M.R. 1995. Frequency of traditional food use by three Yukon First Nations living in four communities. Arctic 48(2):161–171.

https://doi.org/10.14430/arctic1238

World Health Organization. 2021. Guideline for clinical management of exposure to lead: Executive summary. https://www.who.int/publications/i/item/9789240036888