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Accepted Manuscript

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TABLE OF CONTENTS ENTRY

Blood cadmium concentrations, dietary patterns, and personal information for nine Cree First Nations communities of northern Quebec (Canada) are used to investigate sources of the toxic metal cadmium.

ENVIRONMENTAL IMPACT STATEMENT

Cadmium (Cd) is a non-essential metal found naturally in the environment and thus mining/refining operations, such as of zinc, constitute primary sources. It is a constituent of some industrial, commercial and household products, and recycling of cadmium in Ni-Cd batteries is gaining importance. Cd toxicity has been associated with irreversible kidney damage, cancers, and other health ailments. The relative contributions to blood cadmium levels of consuming traditional foods (wild game including organs) and cigarette smoking prevalence is explored in a large (n = 1429) cross-sectional study of nine northern Quebec Cree First Nations communities.

An examination of traditional foods and smoking as cadmium sources among the nine First Nations of *Eeyou Istchee*, Northern Quebec, Canada

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Abstract

Cadmium (Cd), a nonessential toxic metal present in the environment, accumulates in the organs of herbivorous mammals which typically are consumed by Aboriginal populations. The relative contribution of this potential exposure source to concentrations of blood Cd was investigated in 1429 participants (age > 7 y) residing in the nine Cree First Nations communities of *Eeyou Istchee*, northern Quebec, Canada. Analysis of variance identified significant Cd concentration differences between Communities, Sex, and Age Groups, although these were complicated by significant 2-way interactions. The percentage of participants with Cd concentrations within the adopted health-based guideline categories of 'acceptable', 'concern' and 'action' pertaining to kidney damage was 56.2%, 38.3%, and 5.5%, respectively. Partial correlations (controlling for age as a continuous variable) did not show a significant association between consumption of traditional foods and Cd concentrations ($r = 0.014$, $df = 105$, $p = 0.883$). A significant and positive partial correlation ($r = 0.390$, $df = 105$, $p<0.001$) was observed between Cd concentrations and number of cigarettes smoked daily. Analysis of covariance (with mean daily organ meat consumption over the year as a covariate) confirmed that smokers had significantly higher levels of blood Cd than non-smokers ($F_{1,1109} = 1918.2$, $p<0.001$), and that traditional food consumption was not a good predictor of Cd exposure. Our findings suggest that consumption of traditional foods should not be restricted in *Eeyou Istchee* for fear of increased Cd exposure risk. Further studies of smoking prevalence among the Cree First Nations and additional public health initiatives to reduce smoking are recommended.

Introduction

Cadmium (Cd) is a non-essential metal that is nephrotoxic and carcinogenic, and is found in rocks, sediments, soils and dust.[1,2] In soil, Cd is taken up by plants, primarily cereal grains, vegetables, and tobacco.[1] For most non-occupationally exposed persons, the primary source of Cd is from cigarette smoking and eating foodstuffs from soil or water rich in and/or contaminated with this toxic metal (e.g., leafy green vegetables, potatoes, shellfish, seeds and nuts, etc.).[1,3,4,5] Owing to the manufacturing process of various products (e.g., batteries, plastics, alloys) and agricultural practices (e.g., fertilizers), Cd has been widely dispersed. Consequently, trace amounts of Cd are present in the environment and human food products.[2,3,6]

Once exposed to Cd by way of the respiratory or gastrointestinal tract,[4,7] it is absorbed with variable efficiency depending on the person's age and level of micronutrients and essential elements.[6] Cd primarily accumulates in the liver and kidneys bound to metallothionein, an inducible metal-binding protein,[4,8] which is excreted inefficiently (biological half-lives of 10–30 years have been reported in kidney Cd[4,9,10,11]). Urinary Cd levels are reflective of the total body burden or long-term exposure, although recent findings challenge this for low-level exposures.[12] By contrast, blood Cd responds primarily to more recent exposures (last few months) and has a half-life of 40–90 days.[11,13,14] Cd toxicity manifests in different ways, depending on the route of exposure, the extent of exposure (acute or chronic), its chemical form, dose, tissue affinity, as well as the age and sex of the individual.[4,10,15] Studies have shown that females, older adults, and those with renal disease typically have an increased Cd body burden.[1]

Long-term occupational or environmental exposure to Cd has been associated with irreversible kidney damage involving renal tubular dysfunction (impaired reabsorption of low molecular weight proteins), glomerular damage (loss of high molecular weight plasma proteins), and reduced glomerular filtration rate.[4,10,16] Severe Cd exposure has been associated with renal, lung, breast, prostate, gastric, and endometrial cancers.[10,15] Chronic exposure has been linked to effects on bone and may well constitute a potential risk factor for diabetes mellitus and cardiovascular diseases.[4]

Cd is a major toxic pollutant in the northern environment,[17,18] is taken up by lichens and other plants, and thereby accumulates in the liver and kidneys of herbivorous mammals.[6,19,20] Indigenous populations living in northern geographic regions typically harvest, share, and consume traditional foods, including mammalian organ meats. The traditional northern diet may thus potentially expose indigenous peoples to high levels of Cd, thereby putting them at risk of developing the associated health complications.[17,20,21] Based on a survey of consumption of traditional foods among First Nations Cree schoolchildren of the western James Bay Region of Ontario, there is indeed concern about potential environmental contamination in wild game.[22] However, the practice of harvesting and consuming traditional foods has many physical, social, spiritual, cultural, economic, and nutritional benefits.[17,21,23,24] For instance, many traditional foods have higher nutrient values compared to those of market foods.[25] Consequently, the contamination of traditional foods raises issues beyond public health food advisories, since potential health risks need to be assessed in light of the wide array of benefits associated with the consumption of traditional foods.[21] In support of public health efforts, it is therefore imperative to fully understand the relationship between sources of Cd exposure from traditional foods and other exposure sources for indigenous populations. Here, we present findings on blood Cd

concentrations and potential sources of Cd exposure among nine Cree First Nations communities of *Eeyou Istchee* in northern Quebec, Canada.

Methods

Study design and sample population

A cross-sectional study was carried out in nine First Nations Cree communities of *Eeyou Istchee* (coded A–I for anonymity) located on the eastern coast of James Bay in northern Quebec, Canada (Figure 1). The presented study is part of a larger regional environmental health study, entitled "*Nituuchischaayihtitaau Aschii*. Multi-community Environment-and-Health Study in *Eeyou Istchee*" conducted from the summer of 2005 to autumn 2009. This study was preceded by a pilot study of Communities A and B in 2002.[26] The characteristics of the participants, population proportion enrolled, and the month and year when the field work was completed (as all nine communities were not sampled at the same time due to logistical constraints) are summarized in Table 1.[27,28]

The project was approved by the Research Ethics Committees of Université Laval and McGill University, in partnership with McMaster University, and by the Research Committee of the Cree Board of Health and Social Services of James Bay. Written informed consent was obtained from all participating subjects or guardians. Cree speaking (*Eeyou Ayimuwin)* translators were always present to aid those participants who did not speak English.

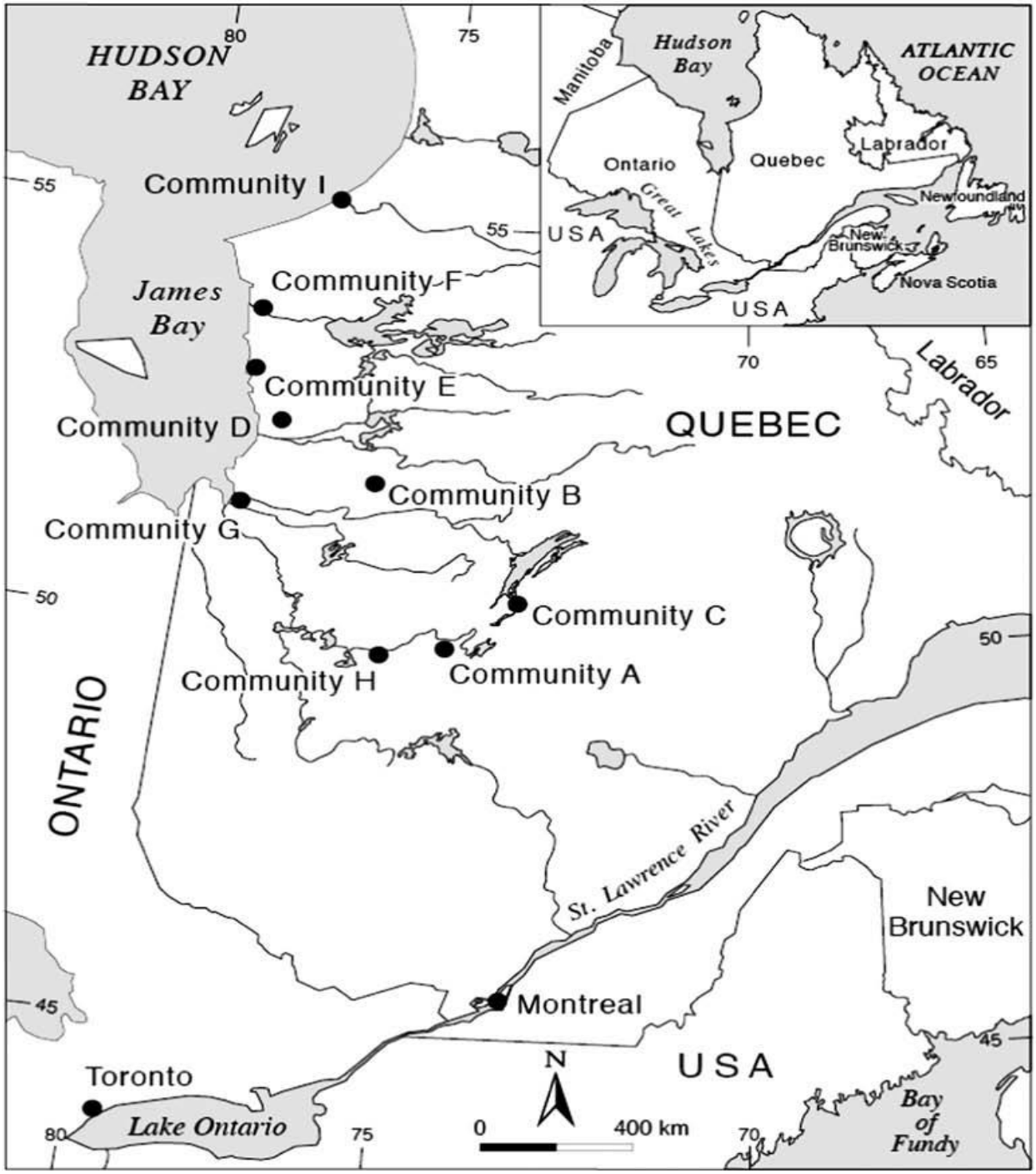

Figure 1 Map of the 9 Cree First Nations of *Eeyou Istchee*, Quebec, Canada. [Reproduced with permission from: E. N. Liberda, L. J. S Tsuji, I. D. Martin, S. Coté, P. Ayotte, E. Dewailly and E. Nieboer, *Sci. Total Environ*., 2014, **470-471**, 818-828.]

Table 1 Characteristics of participants, percentage of population included, and date of completed field work

		n	Community Population[a] (% of population included)	Month, Year Sampled
Community	A	190	622 (30.5)	October, 2002
	B	82	616 (13.3)	November, 2002
	C	229	2679 (8.5)	June 2005
	D	134	561 (23.9)	August, 2007
	E	170	1178 (14.4)	June, 2007
	F	221	3820 (5.8)	June-July, 2008
	G	140	1967 (7.1)	June, 2008
	H	128	1473 (8.7)	August-September 2009
	I	135	798 (16.9)	August, 2009
Sex	Female	809	---	----
	Male	620	---	---
Age Group	8 – 14 y	245	---	---
	15 – 39 y	757	---	---
	Above 40 y	427	---	---

[a]Population entries refer to the year the field work was conducted (from Cree Beneficiaries Lists as per the James Bay and Northern Quebec Agreement 2002, 2005, 2007, 2008 and 2009; Ministère de la Santé et des Services sociaux (www.msss.gouv.qc.ca)).

A random sampling without replacement design was used for recruitment based on the Cree Beneficiary Lists of each community (Community A was oversampled upon request of the Band Council, the locally elected government). Sampling of participants was stratified by sex and age group (children between 0–7 y, children between 8–14 y, adults between 15–39 y, and adults >39 y). A total of 1429 participants were included in the component of the study presented here and this excludes the children below 8 y for whom the blood sampling was limited.

Questionnaires and biological sample collection

The regional environmental health study investigated the health risks to the *Eeyou Istchee* population; thus, a wide array of health-related information was collected from participants.[29] Of interest to the present study, participants completed a dietary questionnaire to document their frequency of consumption of market foods and traditional game harvest of species, such as, moose (*Alces alces*) and caribou (*Rangifer tarandus*). Participants were asked to identify themselves as a smoker (daily or occasionally), ex-smoker, or non-smoker. Smokers were requested to indicate the number of cigarettes smoked per day.

Whole blood samples were drawn from participants to measure concentrations of Cd and other metals and were frozen at -20ºC and/or -80ºC until analyzed at the Institut National de Santé Publique du Québec (INSPQ) Human Toxicology Laboratory, which serves as one of the Arctic Monitoring and Assessment Programme (AMAP) reference laboratories.[30,31] Metal concentrations (nmol/L) were measured by inductively coupled plasma mass spectrometry (ICP-MS) using a Perkin Elmer Sciex Elan 6000 ICP-MS instrument. Prior to being quantified by ICP-MS, the collected blood samples were diluted in ammonium hydroxide and metals were converted to elemental form by aspirating the sample into an argon plasma. The limit of detection (LOD) for Cd was 0.04 nmol/L. Additional details pertaining to the analytical methods, including quality assurance and control measures, have been described in previously published technical reports and articles.[30,31,32]

Statistical analysis

We calculated the frequency of blood Cd concentrations in several categories: below the LOD (<0.04 nmol/L); acceptable levels (0.40 to <10 nmol/L); above level of concern (10.0 to <45.0 nmol/L); and, above the action level for medical review (≥45.0 nmol/L). The latter is equivalent to the biological exposure index (BEI) of 44.5 nmol/L (5 µg/L) in whole blood adopted by the American Conference of the Governmental Industrial Hygienists.[33] In promulgating this BEI, it was concluded that subclinical renal changes, such as micro-proteinuria, can be predictive of exacerbating the age-related decline in renal function.[34] Interestingly, the concentrations of 4.4 and 5.3 µg/L (39.1 and 47.2 nmol/L, respectively) have served as points of departure in the calculation of a biomonitoring equivalent blood screening criteria for Cd-related health outcomes.[35] The selected level of concern of 10 nmol/L (1.12 µg/L) (the threshold for the follow-up protocol in our study[36]) corresponds to the geometric mean observed for smokers (n =228) and the 96th percentile for non-smokers (n = 244) of adults (≥ 18 y) living in the greater Quebec City region, Quebec, Canada in 2001.[37] Our choice of 10 nmol/L (1.12 µg/L) as the level of concern is affirmed by the biomonitoring equivalent estimates for kidney damage proposed by Hays et al. (2008)[35], namely 1.4 and 1.7 µg/L (12.4 and 15.1 nmol/L, respectively).

The actual sample size for individual statistical analyses varied as not all 1429 participants took part in all components of the study. Simple descriptive statistics (arithmetic mean ± 95% confidence limits) are portrayed graphically, subdivided by Community, Sex, and Age Group. For statistical comparisons, blood Cd concentrations were log transformed before analysis of variance (ANOVA) or covariance (ANCOVA). Using ANOVA, we examined differences in blood Cd concentrations attributable to the main effects of Community, Sex, and Age Group. Comparisons between groups were conducted by *post-hoc* pair-wise Bonferroni-adjusted tests using estimated marginal means (EMMs) when interactions between main effects were significant. EMMs (means adjusted for the effects of other variables and for unbalanced sample size) were calculated for main-effects groups of individuals in the ANOVA design. These EMMs were compared using pair-wise Bonferroni-adjusted tests of the equality of group means. Within each Community, EMMs of the three Age Groups were compared in this pair-wise fashion, as were Sexes within Communities, and Sexes within Age Groups.

Partial correlations were conducted to identify significant sources of Cd exposure. ANCOVA was used to examine the possible influence of self-reported smoking status over the reported range of wild game organ meat consumption. Blood Cd concentrations were compared between

smokers and non-smokers after adjustment for organ meat consumption. Analyses were carried out using SPSS version 21 (SPSS Inc., Chicago, Illinois, U.S.A.).

Results

Blood cadmium concentrations by Community, Age Group, and Sex

The observed mean blood Cd concentrations (± 95% confidence limits) in participants partitioned by Community, Sex, and Age Group are presented in Figure 2. It is apparent from this figure that mean blood Cd concentrations (nmol/L) did not increase monotonically with age, as the 15–39 y Age Group generally had the highest blood Cd concentrations in both Sexes and across Communities. Differences between male and female groups were minimal, but varied widely between communities.

The total frequency and percentage of participants with blood Cd concentrations within the acceptable level (56.2%), concern level (38.3%) and action level (5.5%) are listed in Table 2, as are the pertinent values within the grouping factors of Community, Sex, and Age Group. In Figure 3, the percentage of participants with blood Cd concentrations within each level are shown graphically. It is apparent that participants in Community B (15.9%) and the 15–39 y Age Group (8.3%; all communities) had the greatest percentage of participants above the action level, whereas seemingly comparable proportions of males and females were represented above the action level (5.6% and 5.4%, respectively; all communities) (Table 2; Figures 3a, b, c). None of the participants had blood Cd concentrations less than the LOD of 0.04 nmol/L.

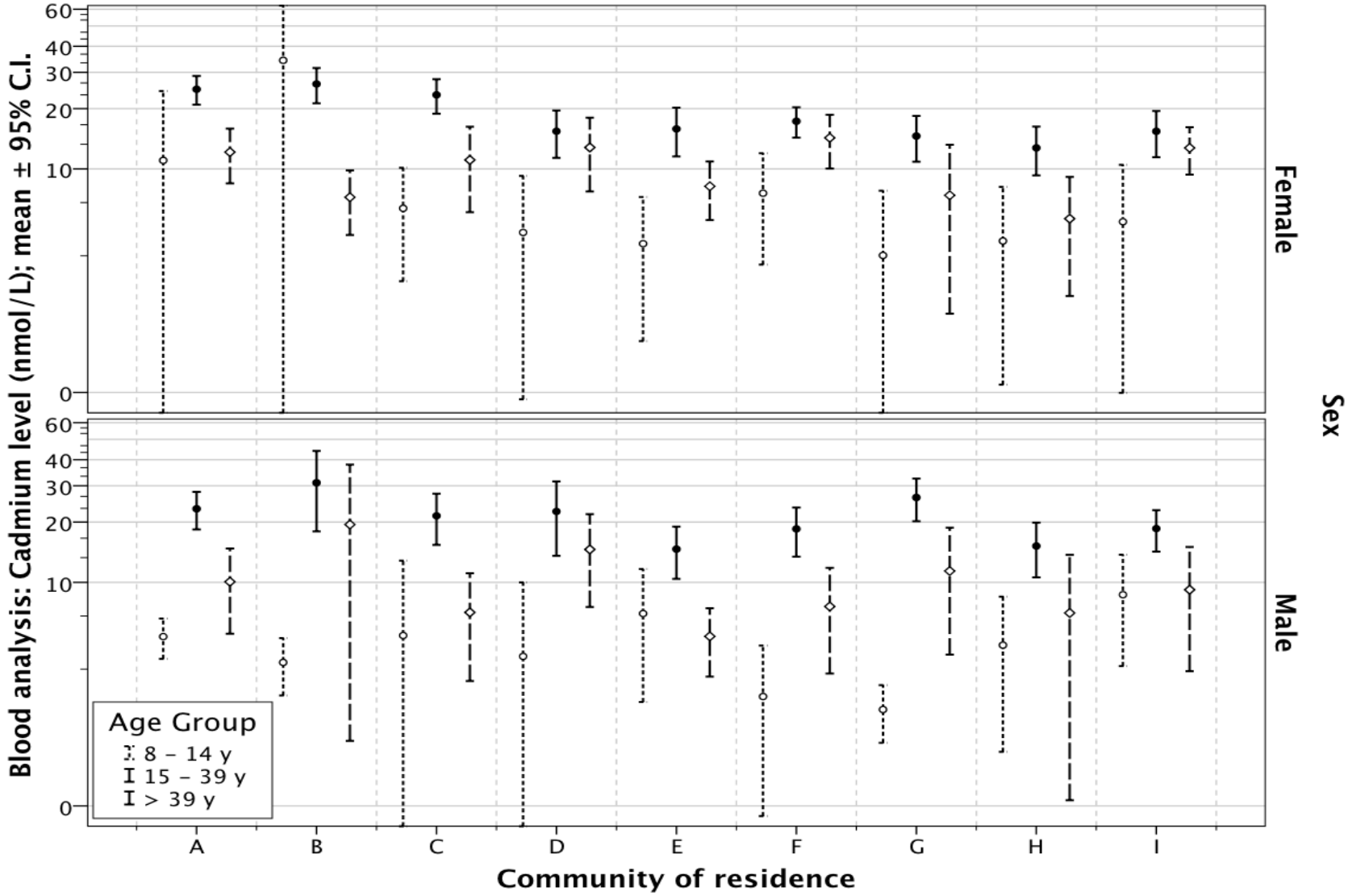

Figure 2 Blood cadmium concentrations (nmol/L) by Community, Age Group, and Sex. Age Groups (8-14 y, 15-39 y, and above 39 y) are presented from left to right within each Community.

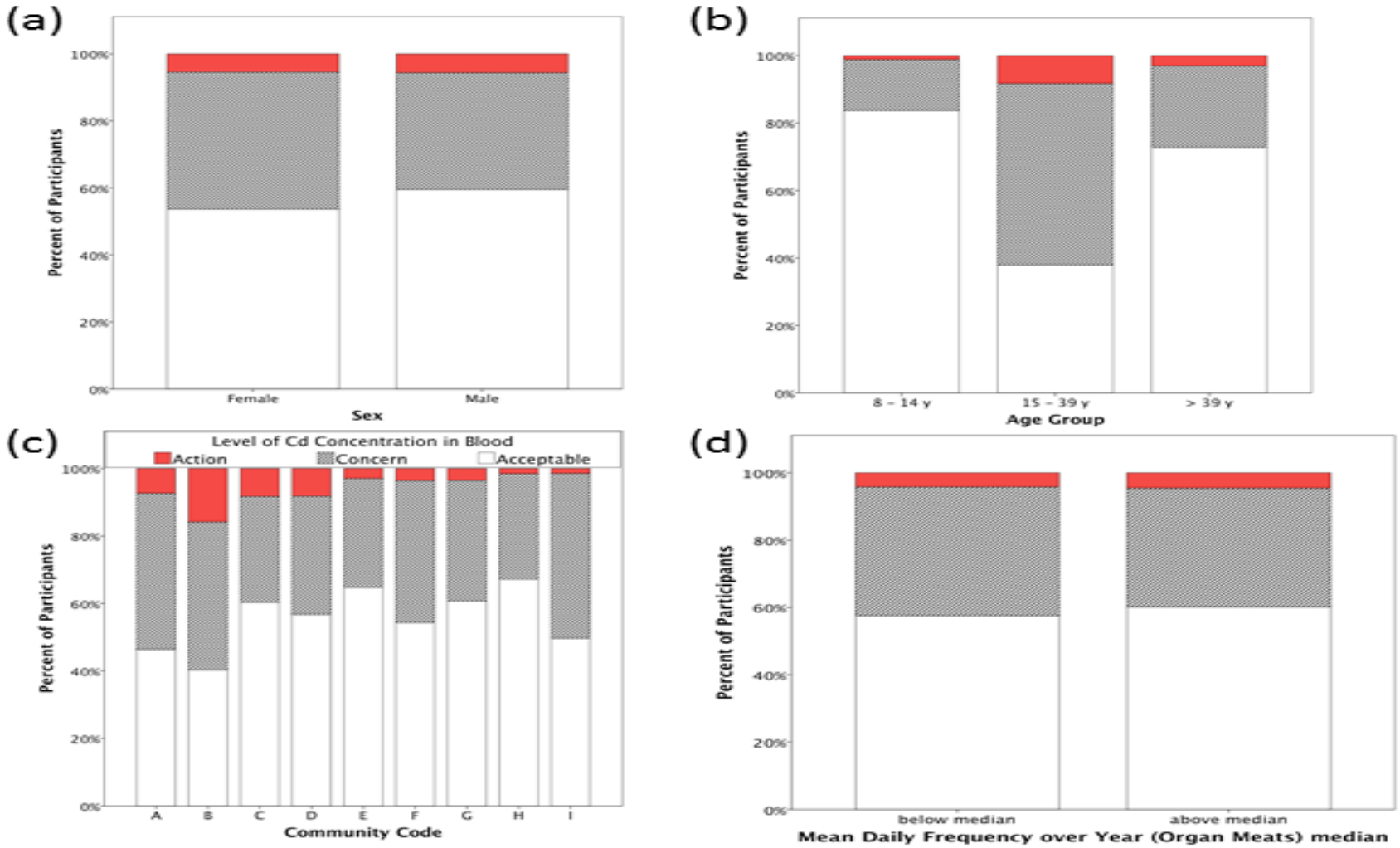

Figure 3 Percentage of occurrence of blood cadmium concentrations (log nmol/L) of participants within acceptable (open), concern (gray), and action (red) levels by Sex (a), Age Group (b), Community (c), and organ meat consumption (d).

Table 2 Frequency of occurrence of blood Cd concentrations (nmol/L) of participants within acceptable, concern, and action levels by Community, Age Group, and Sex

			Level of Cd Concentration in Blood[a]			
			Acceptable (0.04-9.99)	Concern (10.0-44.99)	Action (>45.0)	Total
Community	A	Count	88	88	14	190
		%	46.3%	46.3%	7.4%	100.0%
	B	Count	33	36	13	82
		%	40.2%	43.9%	15.9%	100.0%
	C	Count	138	72	19	229
		%	60.3%	31.4%	8.3%	100.0%
	D	Count	76	47	11	134
		%	56.7%	35.1%	8.2%	100.0%
	E	Count	110	55	5	170
		%	64.7%	32.4%	2.9%	100.0%
	F	Count	120	93	8	221
		%	54.3%	42.1%	3.6%	100.0%
	G	Count	85	50	5	140
		%	60.7%	35.7%	3.6%	100.0%
	H	Count	86	40	2	128
		%	67.2%	31.3%	1.6%	100.0%
	I	Count	67	66	2	135
		%	49.6%	48.9%	1.5%	100.0%
Age Group	8 - 14 y	Count	205	37	3	245
		%	83.7%	15.1%	1.2%	100.0%
	15 - 39 y	Count	287	407	63	757
		%	37.9%	53.8%	8.3%	100.0%
	> 39 y	Count	311	103	13	427
		%	72.8%	24.1%	3.0%	100.0%
Sex	Female	Count	434	331	44	809
		%	53.6%	40.9%	5.4%	100.0%
	Male	Count	369	216	35	620
		%	59.5%	34.8%	5.6%	100.0%
Total		Count	803	547	79	1429
		%	56.2%	38.3%	5.5%	100.0%

[a]See text for the basis of the acceptable, concern, and action levels.

Analysis using ANOVA identified significant differences in blood Cd concentrations between groups for all three main effects: Community, Age Group (both $p<0.001$), and Sex ($p = 0.016$; Table 3). Interpretation of differences owing to these main effects was complicated by the significant 2-way interaction terms observed for Community X Sex ($p = 0.002$), Community X

Age Group (p = 0.025), and Sex X Age Group (p = 0.036); however the 3-way interaction of Community X Sex X Age Group was not statistically significant (p = 0.120; Table 3).

Table 3 ANOVA of blood Cd concentration (log nmol/L) between Communities, Sexes, and Age Groups

Source	df	F-ratio	p-value	Power
Community	8	7.484	<0.001	1.000
Sex	1	5.765	.016	.670
Age Group	2	140.713	<0.001	1.000
Community X Sex	8	3.004	.002	.960
Community X Age Group	16	1.809	.025	.952
Sex X Age Group	2	3.333	.036	.632
Community X Sex X Age Group	16	1.427	.120	.875

Tests of differences between EMMs for Age Groups within Communities showed that the 15–39 y Age Group had significantly greater concentrations of blood Cd than was found in the 8–14 y Age Group for all but Community B. This middle age group also had concentrations significantly greater than did the >39 y Age Group in all communities, with the exception of Communities D and I (Table 4). The 8–14 y and >39 y Age Groups were less often distinguishable, with significant differences between these two groups found only at Communities C, D, F, G, and I (Table 4).

Table 4 Pair-wise Bonferroni-adjusted comparisons of estimated marginal means for blood Cd concentrations (log nmol/L) for Age Groups within specific Communities[a]

Community	Age Group (I)	Age Group (J)	Mean Difference (I-J)	Std. Error	p-value	95% Confidence Interval for Difference[b]	
						Lower Bound	Upper Bound
A	8 - 14 y	15 - 39 y	-0.431	0.098	<0.001	-0.665	-0.197
	8 - 14 y	> 39 y	-0.127	0.106	0.693	-0.380	0.127
	15 - 39 y	> 39 y	0.305	0.067	<0.001	0.144	0.465
B	8 - 14 y	15 - 39 y	-0.264	0.163	0.318	-0.654	0.127
	8 - 14 y	> 39 y	0.093	0.188	1.000	-0.358	0.545
	15 - 39 y	> 39 y	0.357	0.125	0.014	0.056	0.657
C	8 - 14 y	15 - 39 y	-0.566	0.072	<0.001	-0.740	-0.393
	8 - 14 y	> 39 y	-0.210	0.078	0.022	-0.398	-0.022
	15 - 39 y	> 39 y	0.356	0.060	<0.001	0.213	0.500
D	8 - 14 y	15 - 39 y	-0.555	0.094	<0.001	-0.781	-0.328
	8 - 14 y	> 39 y	-0.513	0.103	<0.001	-0.760	-0.266
	15 - 39 y	> 39 y	0.042	0.079	1.000	-0.149	0.232
E	8 - 14 y	15 - 39 y	-0.433	0.084	<0.001	-0.635	-0.232
	8 - 14 y	> 39 y	-0.158	0.089	0.230	-0.373	0.056

	15 - 39 y	> 39 y	0.275	0.068	<0.001	0.113	0.437
F	8 - 14 y	15 - 39 y	-0.570	0.076	<0.001	-0.752	-0.388
	8 - 14 y	> 39 y	-0.340	0.080	<0.001	-0.531	-0.149
	15 - 39 y	> 39 y	0.230	0.059	<0.001	0.089	0.370
G	8 - 14 y	15 - 39 y	-0.750	0.086	<0.001	-0.955	-0.544
	8 - 14 y	> 39 y	-0.378	0.096	<0.001	-0.608	-0.149
	15 - 39 y	> 39 y	0.371	0.079	<0.001	0.182	0.560
H	8 - 14 y	15 - 39 y	-0.500	0.093	<0.001	-0.722	-0.277
	8 - 14 y	> 39 y	-0.157	0.099	0.342	-0.395	0.081
	15 - 39 y	> 39 y	0.343	0.079	<0.001	0.154	0.531
I	8 - 14 y	15 - 39 y	-0.502	0.090	<0.001	-0.717	-0.288
	8 - 14 y	> 39 y	-0.319	0.097	0.003	-0.551	-0.086
	15 - 39 y	> 39 y	0.184	0.078	0.054	-0.002	0.370

[a]Based on estimated marginal means (EMMs).

[b]Adjustment for multiple comparisons by Bonferroni.

Sex differences within individual communities were not common, as only Community C and Community F showed significant differences, with females having greater blood Cd concentrations than males (Table 5). Within the Age Groups, significant differences existed between females and males only in the youngest (8–14 y) Age Group, again with females registering greater concentrations of blood Cd than did males (Table 6).

Table 5 Pair-wise Bonferroni-adjusted comparisons of estimated marginal means for blood Cd concentrations (log nmol/L) for Sexes within specific Communities[a]

						95% Confidence Interval for Difference[b]	
Community	**Sex (I)**	**Sex (J)**	**Mean Difference (I-J)**	**Std. Error**	**p-value**	**Lower Bound**	**Upper Bound**
A	Female	Male	0.096	0.075	0.198	-0.051	0.243
B	Female	Male	0.216	0.132	0.101	-0.042	0.474
C	Female	Male	0.152	0.058	0.008	0.039	0.265
D	Female	Male	0.008	0.076	0.913	-0.140	0.157
E	Female	Male	0.017	0.066	0.798	-0.113	0.146
F	Female	Male	0.244	0.059	<0.001	0.129	0.360
G	Female	Male	-0.122	0.071	0.087	-0.261	0.018
H	Female	Male	-0.026	0.074	0.730	-0.171	0.120
I	Female	Male	-0.021	0.072	0.772	-0.163	0.121

[a]Based on estimated marginal means (EMMs).

[b]Adjustment for multiple comparisons by Bonferroni.

Table 6 Pair-wise Bonferroni-adjusted comparisons of estimated marginal means for blood Cd concentrations (log nmol/L) for Sexes within Age Groups[a]

Age Group	Sex (I)	Sex (J)	Mean Difference (I-J)	Std. Error	p-value	95% Confidence Interval for Difference[b]	
						Lower Bound	Upper Bound
8 - 14 y	Female	Male	0.139	0.058	0.017	0.025	0.253
15 - 39 y	Female	Male	-0.017	0.030	0.569	-0.077	0.042
> 39 y	Female	Male	0.067	0.043	0.122	-0.018	0.152

[a]Based on estimated marginal means (EMMs).

[b]Adjustment for multiple comparisons by Bonferroni.

Blood cadmium concentrations, consumption of organ meat, and smoking

Categories and species of animals which typically are harvested by the communities included birds, fish, and mammals. The latter category included moose, caribou, rabbit (*Lepus curpaeums*), beaver (*Castor canadensis*), and bear (*Ursus americanus and U. maritimus*; ranked from highest to lowest mean daily frequency of consumption over a year). For all species consumed, the mean daily frequency was generally the greatest by male participants and for the >39 y Age Group. Consumption patterns of the harvested species varied widely between communities.

Percentages above and below the median Cd concentrations for participants who consumed wild game organ meats are shown in Figure 3d. The percentage of participants within the acceptable, concern, and action levels of Cd who reportedly consumed traditional foods were 58.7%, 36.9%, and 4.4% respectively. Since the consumption of the traditional foods (wild game) itemized above showed significant positive correlations with age (r range: 0.141- 0.247, all $p<0.001$), partial correlations between blood Cd concentration and consumption of wild game organ meats were controlled for age of the participants. After such adjustment, there was no significant association between wild game organ meat consumption and blood Cd ($R = 0.014$, $df = 105$, $p = 0.883$).

Using self-reported smoking status, a common trend was observed for both current smokers and non-smokers groups in the relationship between organ meat consumption and blood Cd concentrations (homogeneity of slopes, $F_{1,1108} = 0.320$, $p = 0.572$). The homogeneity of slopes pre-condition for ANCOVA was thus satisfied. The resultant ANCOVA found that current smokers had significantly greater levels of blood Cd than did non-smokers ($F_{1,1109} = 1918.2$, $p<0.001$). Blood Cd concentrations (log nmol/L) in relation to smoking status and consumption of organ meats clearly show a clear separation between smokers and non-smokers, and indicate that the greater consumption of these traditional foods is not a good predictor of blood Cd concentration (Figure 4).

After controlling for age of the participants, a significant positive partial correlation was observed between blood Cd concentrations and number of cigarettes smoked per day ($r = 0.390$, $df = 105$, $p<0.001$). It is apparent from Figure 5 that the majority of smokers exceeded the concern level and some smokers even exceeded the action level.

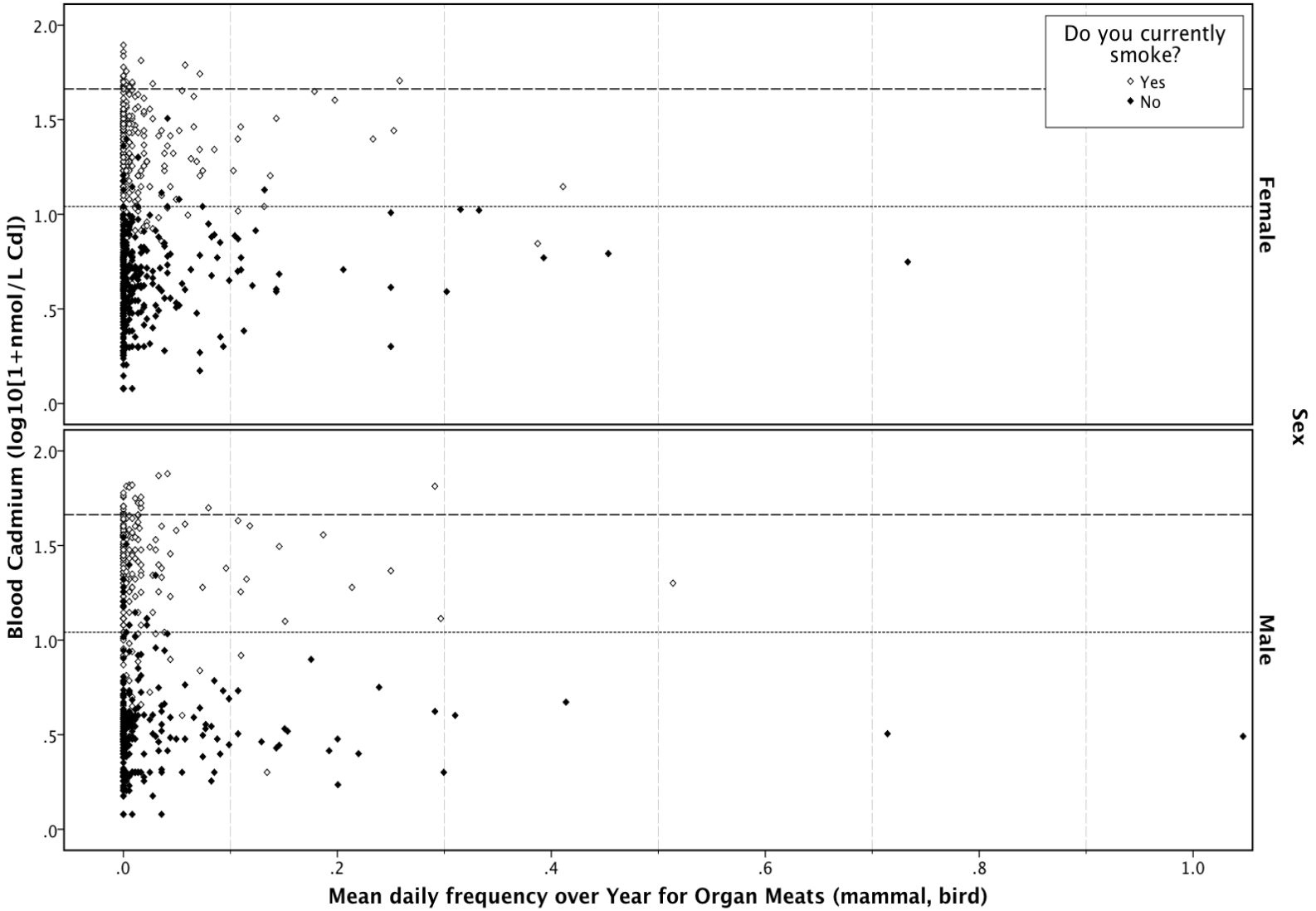

Figure 4 Blood cadmium concentrations (log nmol/L) in relation to organ meat consumption and current smoking status. The concern (10.0 nmol/L) and action (45.0 nmol/L) levels for Cd, transformed as log values, are indicated by horizontal broken lines.

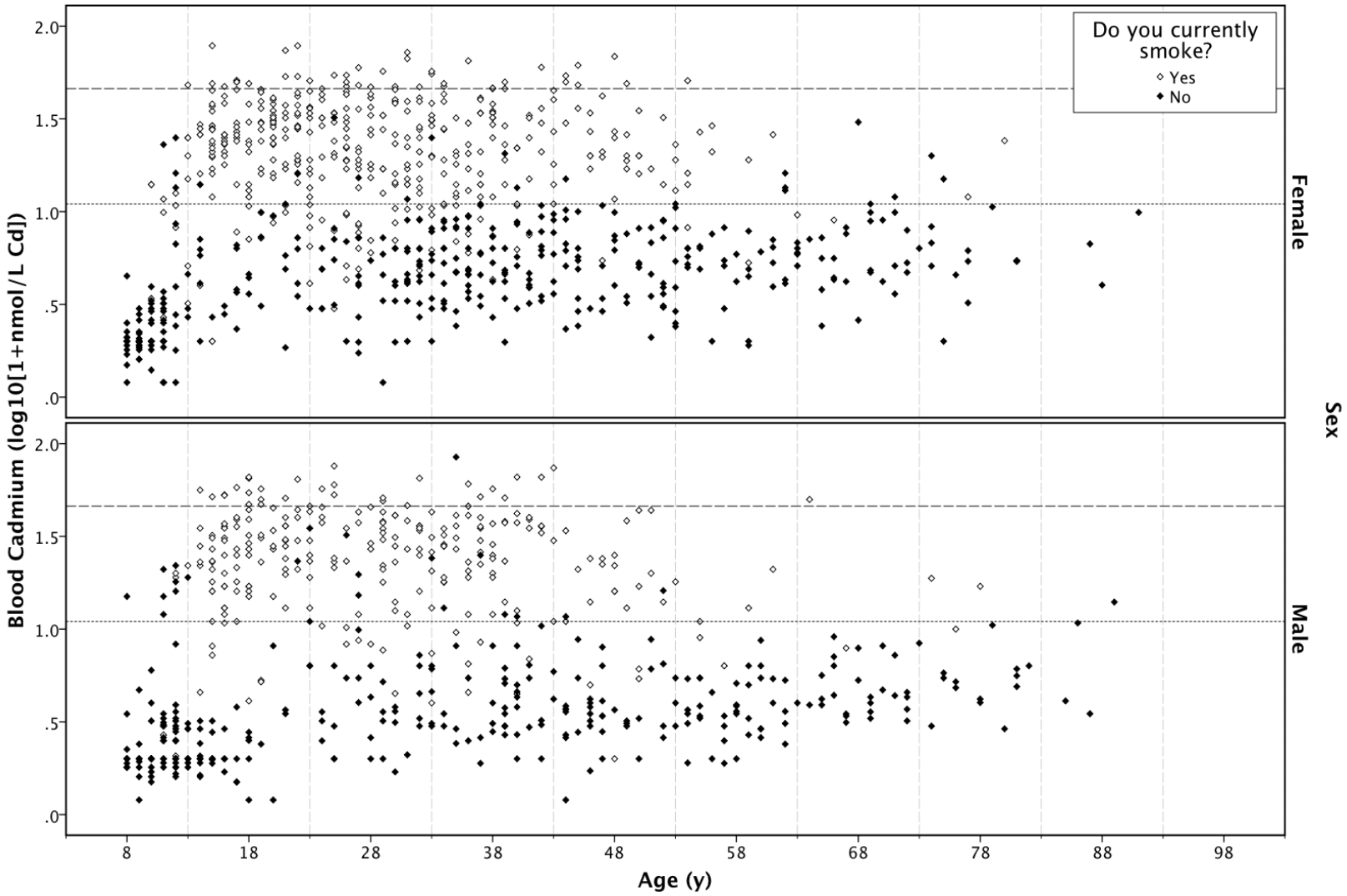

Figure 5 Blood cadmium concentrations (log nmol/L) in relation to age and current smoking status. The concern (10.0 nmol/L) and action (45.0 nmol/L) levels for Cd, transformed as log values, are indicated by horizontal broken lines.

Discussion

Blood cadmium concentrations by Community, Age Group, and Sex

The ANOVA main effects show significant differences between Communities, Age Groups, and Sex, although this is complicated by significant 2-way interactions. This analysis indicated that mean blood Cd concentrations varied widely between Communities, potentially because of factors such as smoking status and community-specific consumption patterns of Cd-containing foods. Different environmental Cd exposures attributable to local geology and/or industrial activities cannot be entirely discounted as this region has experienced many large-scale industrial activities, including mining operations and military radar sites.[38,39,40]

The 15–39 y Age Group generally had the greatest mean blood Cd concentrations and percentage of participants exceeding the action level of all age groups, which may be owing to the high prevalence of smoking seen in this age range in Canada and the USA.[41] Indeed, the smoking prevalence across the communities surveyed was 70.2% in females and 67.8% in males among the 15-39 Age Group, much higher than in either those >39 y (28.0% in females; 25.5% in males) or the 8–14 y (21.3% in females; 11.7% in males). By contrast, previous studies have reported that increasing age has been associated with higher urine Cd concentrations.[1,42] This discrepancy may be attributable to the understanding that measurement of blood Cd is more sensitive to current exposure than is urine. Furthermore, previous studies have reported that renal Cd concentration reached a plateau in 50–60 y, and coincides with age-related kidney degeneration.[12,43]

In the present study, we found that mean blood Cd concentrations were often similar for males and females across the nine Communities and the three Age Groups, with the exception of two communities (Community C and Community F) and the youngest Age Group (8–14 y), where females had significantly greater concentrations than males. This finding may be attributed to the higher smoking prevalence in females compared to males across the communities surveyed. Moreover, the rate of Cd intestinally absorbed has been shown to increase in people with low nutritional status of calcium, iron, or zinc.[5,7] Mortensen et al. (2011)[1] summarized that, regardless of smoking status, the adjusted geometric means of urine Cd levels are higher in females compared to males, presumably because iron deficiency and lower calcium intakes are typical of females, and promote increased absorption of Cd in the intestinal tract.

Blood cadmium concentrations and consumption of organ meat

Our study did not show a significant association between blood Cd concentrations and the consumption of organ meats. The concern reported in previous studies that indigenous populations living in northern regions might potentially be exposed to Cd from the consumption of mammalian organ meats is therefore not borne out in the presented study.[17,18,20,21,38,44,45,46,47] Neither are our results consistent with those of Haswell-Elkins et al. (2007a; 2007b)[48,49], who found a strong relationship between urinary Cd levels (adjusted for creatinine) and dietary intake of traditional seafood for a distinct group of indigenous people living on islands located in the Torres Strait off the northern coast of Queensland, Australia. Specifically, higher consumption of turtle liver and kidney and locally gathered clams ($p<0.05$), and possibly dugong kidney ($p = 0.06$), were identified.[48,49] Available food item analyses for Cd supported these observations.[49] Rather than from seafood, the traditional foods consumed by the *Eeyou Istchee* Cree are from

land-based animals. The quantity of Cd ingested appears to be dependent on the species and age of the consumed animal and the type of organ meat consumed. Studies have reported that caribou kidney samples have higher Cd concentrations when compared to other animal organ meats.[20,21,47] Some studies have also reported that the age of the caribou positively correlated with Cd levels in the animals' livers and kidneys, inferring that the age of the ingested animal impacts the intake amount of Cd.[20,44] In our study, the communities, age group, and sex that had the highest mean caribou consumption did not have the highest mean blood Cd concentrations. A second reason for the divergent observations between our study and those of Haswell-Elkins et al. (2007a; 2007b)[48,49] relates to the fact that they employed urinary Cd as the exposure biomarker, while ours was whole blood. As pointed out in the introduction and earlier in this section, blood Cd primarily reflects current exposure as opposed to long term accumulation by urinary Cd. As explained below, seasonal-dependent consumption practices may constitute a third difference.

To minimize the risk of Cd-associated kidney disease, the World Health Organization (WHO) established a provisional tolerable weekly intake (PTWI) of 400-500 μg of Cd for an adult, or 7 μg/kg of body weight.[50] As Cd is a contaminant in most human foodstuffs, consuming foods ranging from oilseeds and cocoa beans to vegetables can result in a typical total exposure of 30 μg Cd per day (210 μg Cd per week).[6] The frequency of consuming organ meats might also be relevant. For instance, game animals are typically only eaten during certain seasons and, as shown previously for the western James Bay coast of Ontario,[24] exposure can be seasonally limited. A study pertaining to the James Bay Cree of Canada estimated that a regular consumer of liver and kidney, assumed to be from 2 moose and 3 caribou per family of five per year, could add 300 μg of Cd to the weekly intake of 210 μg of Cd from an average diet resulting in a slight exceedance of the established PTWI for Cd.[23] Based on published findings, the following wet-weight tissue Cd concentrations (in mg/kg) were selected in this assessment: kidney, 15.0 (moose) and 8.8 (caribou); liver, 2.0 (moose) and 0.82 (caribou).[23] Similarly, concentrations of Cd in the liver and kidney of wild moose in Alaska ranged from 0.06–9.0 and 0.10–65.7 μg/g wet weight, respectively.[51] However, after accounting for relevant dietary information, these findings indicated that most individuals would not exceed the WHO's PTWI.[51] Our findings, which show a lack of any dependence of blood Cd on organ meat consumption, suggest that these various Cd intake calculations constitute overestimates for the current situation in *Eeyou Istchee.*

Blood cadmium concentrations and smoking status

Our observation that the majority of current smokers exceeded established acceptable levels of blood Cd is consistent with the findings of Mortensen et al. (2011)[1] for U.S. adults without chronic kidney disease. Consequently, smokers are at a higher risk of kidney damage.

Exposure to Cd from traditional dietary sources has been reported to be less than that from smoking cigarettes.[38] Tobacco plants readily absorb Cd from soil and thus smoking cigarettes is a common source of this toxic metal for non-occupationally exposed individuals.[1,3,4,52] For instance, cigarettes produced in Canada may contain 1.39–1.66 μg Cd per cigarette.[53] This is one reason for smokers having greater Cd body burdens than non-smokers.[52] Another factor is that absorption of inhaled Cd is much higher than from gastrointestinal intake.[54] Elinder et al. (1983)[54] calculated that smoking one cigarette containing 1.7 μg Cd would result in inhaling 0.14–0.19 μg Cd, or about 10% of the Cd content in the cigarette, and 25–50% of that Cd would

be absorbed. This potentially adds approximately 2 μg of Cd per day to the body burden for an individual who smokes a pack of cigarettes per day.[1]

Study strengths and limitations

Questionnaire studies have their limitations. The randomized approach taken to select the study subjects and the sample size strengthen the assertion that our findings are representative of the Cree population residing in *Eeyou Istchee.* Furthermore, the data collection in the field was performed by trained interviewers using a reliable questionnaire.[55] As a quality control measure, completed questionnaires were reviewed by members of the research team to ensure completeness and appropriateness (medical information was also checked against patient's records).[55] Moreover, standardized methods were used to analyze the samples by an accredited reference laboratory.[30]

Some study limitations are noted. First, the percentage of population included differed between communities. It is unlikely that the characteristics of the participants collected varied much from all eligible candidates of the same age and gender since the *Eeyou Istchee* population is quite homogeneous and only First Nations Cree were eligible and selected. Secondly, we used self-reported smoking status to estimate tobacco exposure, which is a more subjective method compared to the use of biomarkers of tobacco exposure such as, nicotine and cotinine levels.[56] Some participants may not have accurately recalled their smoking habits or may have recalled it with bias (such as, parents of young children who may have been reluctant to disclose their true smoking status[56,57]). Nevertheless, the collected smoking habits data appears to be reliable as consistent differences of Cd content were noted between smokers and non-smokers. Also, our multivariate analyses of essential and toxic elements in whole blood (unpublished work) showed that Cd had a distinct pattern of variation - suggestive of a unique source - when compared to mercury, lead, and a group of elements that included the toxic metals (nickel and cobalt) and selected essential elements (selenium, molybdenum, copper and zinc).

Conclusion

In general, mean blood Cd concentrations varied widely between communities, were often similar for male and female participants, and were highest in the 15–39 y age group. Our study did not reveal a significant association between consumption of traditional foods (specifically, wild game organ meats) and blood Cd concentrations. Reducing the intake of traditional foods in *Eeyou Istchee* to limit Cd exposure is not warranted. However, a significant positive association was observed with the number of cigarettes smoked per day. Exceedances of established blood Cd guidelines suggest that smokers are at risk for kidney damage. This is especially worrying in the context of the high prevalence of Type-2 diabetes in the Cree communities[29], since there is evidence that diabetes-related kidney tubular dysfunction may increase the risk of cadmium-induced kidney damage.[58,59] Clearly, further research on the prevalence of smoking among Cree First Nations is warranted, as well as public health initiatives to reduce primary and second-hand exposure to tobacco smoke.

Acknowledgments

We hereby thank the participants of the nine eastern James Bay Cree communities for their participation in the presented study, the Band Councils for their support and facilitation of the

field work, and the local recruiters/interviewers/interpreters and other support staff for their invaluable help. We also acknowledge the hard work of many others: co-investigators, field project managers (Mathieu Trépanier, Laurie Lavallée and Laura Atikessé), assistant project manager (Reggie Tomatuk), clinical staff and technical support team. This scientific communication constitutes a report from the *Nituuchischaayihtitaau Aschii* Multi-Community Environment-and-Health Study in *Eeyou Istchee* supported by the Cree peoples (*Eeyouch*) of northern Quebec, the Cree First Nations and the Cree Board of Health and Social Services of James Bay through financial contributions from the Niskamoon Corporation.

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