Examining Relationships between Pb and Nutrient Intake and Sources of Pb in the Sahtú, NWT

by

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Author's Declaration

This thesis consists of material all of which I authored or co-authored: see Statement of Contributions included in the thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Statement of Contributions

This thesis presents the work of Calin Lazarescu in direct collaboration with his supervisor Dr. Brian Laird and his committee members, Dr. Kelly Skinner, Dr. Mylène Ratelle, and Dr. Warren Dodd.

Research presented in Section 2:

Section 2, Assessing Relationships between Pb Levels and Various Nutrient Biomarkers in the Sahtú, NWT was informed by Dr. Brian Laird, Dr. Mylène Ratelle, Dr. Yvonne Lamers, and Larisse Melo. Dr. Laird was the primary investigator of the Contaminant Biomonitoring Study in the Northwest Territories Mackenzie Valley and was involved in all aspects of the section writing. Dr. Mylène Ratelle assisted through database creation related to nutrient biomarkers, and chemical analysis seeking. Dr. Yvonne Lamers, and Larisse Melo, from the Nutritional Biomarker Laboratory, Faculty of Land and Food Systems, at the University of British Columbia were responsible for analysis vitamins and nutrients in biobanked blood samples.

Research presented in Section 3:

Section 3, The development of a Pb exposure survey for Northern Indigenous Populations in Canada, was informed by Dr. Kelly Skinner, Dr. Mylène Ratelle, Dr. Brian Laird, Dr. Kirsty Gurney, and Dr. Jérôme Comte. Dr. Kelly Skinner was the principal investigator for the project, Preliminary study: Investigating Lead Exposure in Northern Canada and the Sahtú region, NWT, funded by the Northern Contaminants Program and was involved in all aspects of the project. Dr. Mylène Ratelle assisted throughout the survey development and finalization processes by creation of the first draft of the survey, co-leading feedback interviews, taking notes during interviews, developing a plan for calling stores in the region, and providing feedback on survey drafts. Dr. Brian Laird assisted throughout the survey development and finalization processes and calling stores by providing feedback and edits. Drs. Kirsty Gurney, and Jérôme Comte assisted during the survey development stage by providing feedback to existing questions and the development of questions related to Pb ammunition usage, and water consumption respectively.

Abstract

Background

The Sahtú is a subarctic region located in the Northwest Territories, Canada. It is comprised of five remote communities, with a total population of approximately 2600 people. Over 75% of the total population is Indigenous, with the largest group being Dene First Nation. Previous human biomonitoring work in the region had indicated lead (Pb) levels in both blood and urine were higher when compared to both the neighbouring Dehcho region, and the general Canadian population.

Pb is an element that is toxic to humans in high concentrations. Pb is commonly absorbed through inhalation, ingestion, and dermal exposure, and is distributed in bone and blood. Negative health implications related to chronic exposure include neurological, cardiovascular, and renal impacts. Pb is still widespread in environmental media including soil, air, and water, from anthropogenic releases into the environment, as well as use in industry and hobbies. Specific to the Northern Canada, diet, and hunting practices, such as the use of Pb ammunition, are key routes of exposure.

Methods

Using data collected from the biomonitoring project, and supplemental analysis on biobanked blood samples, statistical analysis to determine the correlations and associations between nutrient biomarkers and Pb was conducted. Nonparametric and parametric correlations were conducted between age, BMI, sex, smoking status, alcohol consumption status, zinc, iron, vitamin D with Pb, followed by multivariate linear regression. Nutritional levels of zinc, iron, and vitamin D were assessed and compared to national averages and deficiency thresholds.

An exposure survey adapted for Northern Canadian Indigenous populations was developed through supplementing and adapting questions collated from existing tools and information from a literature review. The survey was piloted, and feedback was gathered from community members after interviews with research team members. The survey was finalized and ready for future implementation.

Results

128 biobanked blood samples were used for analysis. Geometric mean values for blood Pb in the Sahtú were 2.3 ug/dL, which were more than twice higher than those in the Dehcho (1.1 ug/dL) and almost twice higher than the Canadian population (1.2 ug/dL). Non-parametric and parametric testing indicated positive correlations existed between age, vitamin D, and zinc, with Pb, and mean differences existed across sex. A linear regression model was created using age, sex, smoking status, and zinc levels as explanatory variables. Comparison of Akaike information criterion (AIC) and R^2 values indicated it was the best model at exploring Pb values.

Averages for all nutritional biomarkers, zinc, iron, and vitamin D, were lower in the Sahtú population compared to the Canadian Health Measures Survey. Based on nutritional thresholds, 10% of adults and 27% of children had probable zinc deficiency, 19% adults and 18% children had probable iron deficiency, and 69% of adults and 100% of children had probable vitamin D deficiency.

The development process of the survey resulted in a draft survey with 62 total questions across five sections: socio-demographic, harvesting practices and food preparation, other Pb exposure determinants, and symptoms of Pb poisoning and a supplementary 12 questions in an option hunter only sections. A total of six participants from the community assisted in the feedback gathering through remote interviews indicating change was necessary to 43.5% of questions. During the finalization process, 66/74 existing questions were changed, and or adapted, and the survey was finalized to a total of 63 + 12 questions in five sections.

Conclusions

Positive correlations between Pb and nutritional biomarkers were contrary to what was found in literature. These results may point towards a shared exposure and intake pathway. A possible pathway by which this occurs is the consumption of traditional food which is hunted with Pb ammunition. The development of an adapted and specific exposure survey to Pb in a Northern Indigenous context was vital towards the future implementation of the survey, and towards assessing Pb exposure within the region. Future work into assessing other routes of exposure to Pb in the community is recommended.

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List of Abbreviations

25(OH)D	25-hydroxyvitamin Vitamin D3
AIC	Akaike Information Criterion
ALAD	Aminolevulinate Dehydratase
BMI	Body Mass Index
CDC	Centers for Disease Control
CHMS	Canadian Health Measures Survey
CI	Confidence Intervals
CIHR	Canadian Institutes of Health Research
DNA	Deoxyribonucleic acid
DMT1	Divalent Metal Transporter 1
Egr-1	Early Growth Response Transcription Factor 1
EFSA	European Food Safety Authority
NWT	Northwest Territories
FFQ	Food Frequency Questionnaire
Pb	Lead
PbB	Blood Lead Concentration
TRV	Toxicological Reference Value

1 Literature Review and Project Background

1.1 The Sahtú Region and Indigenous Populations

1.1.1 Geography

The Sahtú is a settled land claim region (283,000 km^2) located in the Northwest Territories (NWT) of Canada, as depicted in Figure 1 below (1). The climate of the Sahtú is subarctic continental resulting in little precipitation, mean annual temperatures below freezing, and max temperatures in summer months average between 10-15° C (2, 3). The Sahtú is part of the Mackenzie River basin, and Great Bear Lake is the largest lake in the region; water bodies are typically frozen for over half the year (2, 4). Western parts of the Sahtú have the Mackenzie mountains, while the eastern region is tundra (1). Various vegetation including boreal forests is present in the centre of the region in the Mackenzie Valley (1, 2, 4).

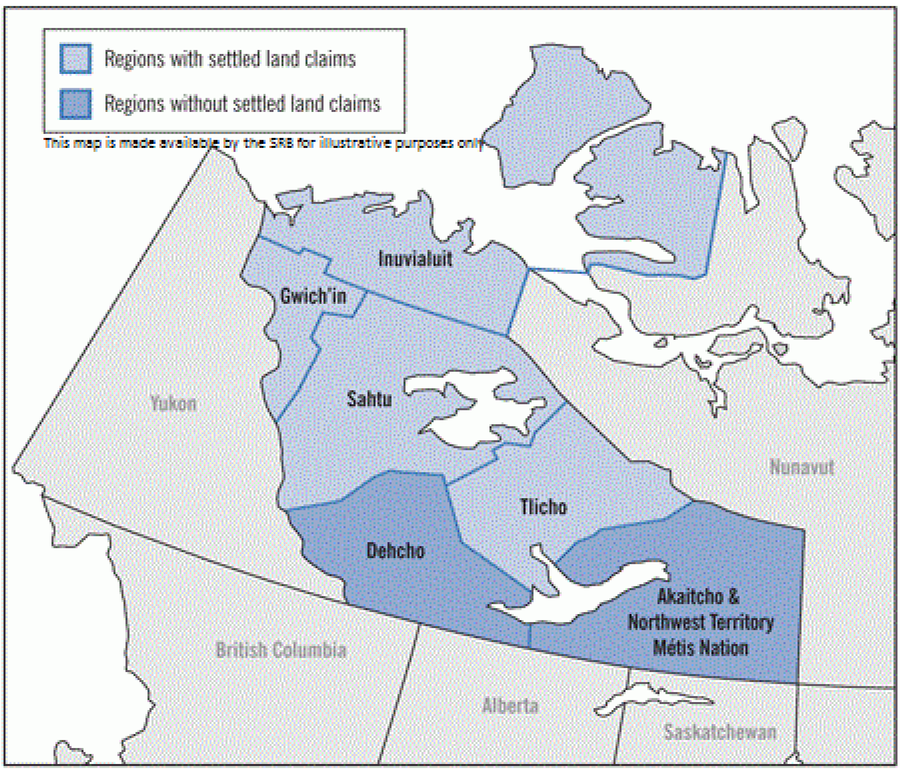

Figure 1: Map of Northwest Territories Indigenous land claims as of 2016 (5)

1.1.2 Demographics

As shown in Figure 2, the Sahtú is home to five communities: Colville Lake, Deline, Fort Good Hope, Norman Wells, and Tulita (6). Communities are accessible by road only during the winter and rely on scheduled air service for the rest of the year, and summer river barge service (1, 7). As of July 2021, the population of the Sahtú Region was 2,668, the least populated organized region of the NWT, representing 5.83% of the total population of the territory (6). Norman Wells is the most populated community (768), followed by Deline (627), Fort Good Hope (601), Tulita (513), and the smallest and most northern community, Colville Lake (159) (6). 76% of the total population is Indigenous; with the largest group being Dene (First Nations) which represents 68.5% of the total population, and 90.0% of the Indigenous population (6). Other Indigenous groups include Métis (5.2% of the total population) and Inuit (2.3% of the total population) (6). A majority of the non-Indigenous population (73.0%) lives in the largest community, Norman Wells (6). Norman Wells is a major oil field, one of the largest in the territory, and as a result, has attracted residents born outside of the region (8). Oil extraction in and around the area of Norman Wells is still ongoing, with about 120 total employees (9). All other Sahtú communities have over 90% Indigenous populations (6). Population demographics of the region are similar to those of the NWT, with adults 25 – 44 representing the largest section (33.1%) of the total population (6). 47.1% of the population is female, and 52.9% is male (6).

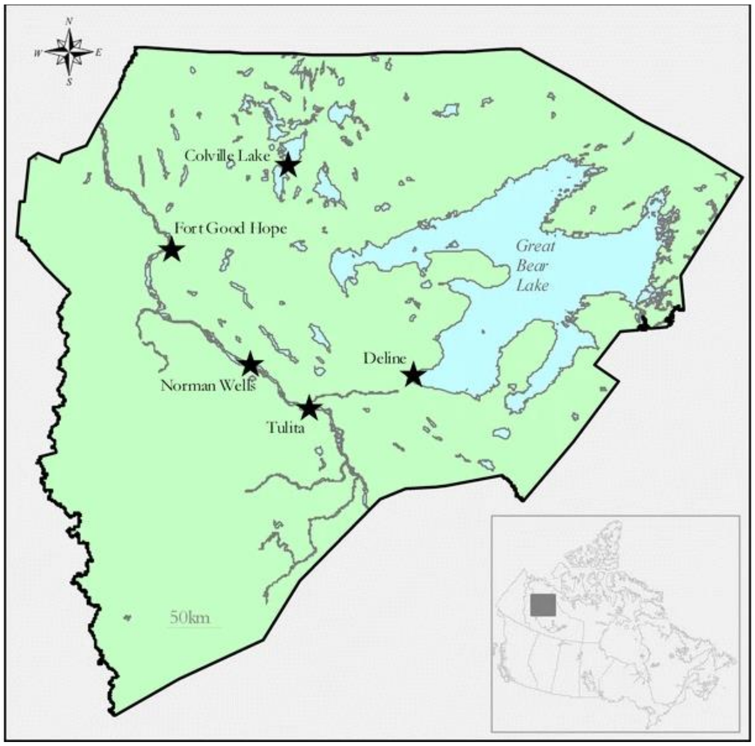

Figure 2: Detailed map of the Sahtú Region with the five communities indicated (1)

1.1.3 Indigenous populations and history

The Sahtú Region has been inhabited by Dene populations for generations, and more recently by Métis and non-Indigenous populations (7). Historically, Dene populations were nomadic, often traveling great distances, and living solely off the land (7). Dene people were the first groups to settle in the NWT, and are now organized in various regions of the territory (10). Throughout time, Dene populations of the Sahtú adapted to environmental conditions that are demanding and challenging (7). These traditions, practices, and stories have been shared among generations and continue to be used and adapted to a modern context (7). Those living in the Sahtú are part of the major Sahtúot'ı̨nę Yatı̨́ (North Slavey) language group, and three different dialects are spoken across the region (10).

Dene people's relationship with the land and wildlife is a vital part of traditions and practices that have spanned hundreds if not thousands of years (7, 11). Trails, water routes, hunting, and gathering, are all deeply rooted parts of Dene culture with high significance (7). The land itself is important in transmitting knowledge from generation to generation (7). In 1993, Dene and Métis populations signed a land claim agreement with the Canadian government (1, 7, 12). This gave title to over 41, 400 km^2 of land to Indigenous populations, federal government payments to designated land claim institutions, and rights to hunt throughout the region (12). The land was selected per various criteria including resource selection, spiritual sites, traditional land, and harvesting areas (7). As a result, seven land corporations exist within the region and act as the main source of contact for education, health, environmental, and economic development (7).

1.1.4 Economical and environmental history

Trapping and fur trade was a large part of the economy in the region prior to the 1900s (7). In the 1920s, the discovery of oil in the Norman Wells area, followed by the opening of the Port Radium Mine on Great Bear Lake in 1933 increased industry and the economy in the region (7). Oil production quickly increased and by the 1940s, mineral and oil production exceeded fur production (7). Presently, much of the economy of the region is based on a mix of industrial resource extraction, tourism, and subsistence harvesting (7).

However, much of the industry of the Sahtú was cause for environmental concern including the over-trapping and hunting of wildlife and ecological impacts of mining and oil drilling. Additionally, the industrialization of the region brought in non-Indigenous populations to the area, resulting in an acceleration of loss of language and culture for the Dene populations (7, 8). Wildlife and language are sources of survival for Dene populations in the Sahtú, and as a result, industry had negative impacts on the health of these populations (7, 8).

Facing harsh environmental conditions due to the subarctic climate, and environmental concerns related to resource extraction, Northern populations face different challenges than those living in southern areas. One set of challenges faced by such populations is the presence of contaminants, like lead (Pb), in the environment (13-15). In the Sahtú, elevated Pb levels have been found in soils and sediments of the region (16). Elevated Pb levels have been found near former mines within the region, in the silver-bearing deposits off of the east shore of Great Bear Lake near the former Port Radium mine (17). Furthermore, it is documented that some mine waste was directly deposited into Great Bear Lake until the 1970s (17).

As a result of contaminant exposure, ongoing governmental and research work occurs in many Northern regions, to assess contaminant exposure. These projects are often focused on environmental, and human biomonitoring. These projects are essential for understanding the impacts on human health while balancing the importance of Indigenous lifestyle and traditions. In the Sahtú specifically, little work on human biomonitoring was completed prior to the Northwest Territories Human Biomonitoring Project completed between 2016 – 2019.

1.2 The Northwest Territories Human Biomonitoring Project

The data and sample collection of the human biomonitoring project was completed between 2016 – 2019. The description below provides a synopsis of the methods and results of the project.

1.2.1 Rationale and study participation

The goal of the project was to understand environmental challenges faced by Indigenous populations living in the NWT by determining contaminant concentrations in biological samples and quantifying the consumption of traditional food. Elevated fish mercury levels were found in waterbodies of the Mackenzie River basin of the NWT which resulted in the local population wanting to learn more on the safety of fish and other traditional foods (14). To address community concerns, the human biomonitoring project was designed and implemented. The focus of the project included all traditional foods, not just fish, and additional metals alongside mercury (14). The investigation was designed in close collaboration with community leaders and members of communities in the Mackenzie Valley (14).

Any community member within the respective communities from both the Sahtú and Dehcho regions was eligible to participate in the study. Participation was voluntary, and participants must have been over the age of six and provided informed consent. Informed consent required participants over 18 years of age to not be under the influence of alcohol or drugs and to have sufficient capacity to consent to the study; participants between six to 17 years old required a parent or guardian to consent on their behalf. Participants were able to withdraw their consent at any point during the study, and those who did not want to receive further communication were removed from the study. Participants were recruited through various methods, mostly by randomized selection, and passively through local radio; walk ins during sample collection were also allowed. Participants were compensated for their participation based on the samples provided (13, 15).

1.2.2 Sample collection

Samples were collected by researchers at community centres during the winter between 2016 – 2018, local coordinators were hired to assist with participant recruitment and sample collection throughout. A total of 537 residents from both regions took part in the study which represented a total of 8.9% of all residents from the Dehcho and Sahtú regions. Population demographics between samples and total populations were similar, aside from the 6 – 14-year-old age group, as children under the age of six were excluded from the study in both the Dehcho and Sahtú regions. Three types of samples were collected: hair, blood, and or urine, and participants could provide any or all three types of samples. A total of 917 samples were collected, 443 hair, 198 urine, and 276 blood. Alongside sample collection, demographic information including age, sex, weight, height, and alcohol and smoking consumption were asked for all participants (13, 15). The analysis done in chapter 1 used only biobanked blood samples collected from the Sahtú, as the additional nutrient analysis was done on only these samples.

1.2.3 Survey data collection

Participants were invited to complete two dietary surveys: a 24-hour recall survey, and a food frequency questionnaire (FFQ) (15). The 24-hour recall survey, in which 199 people participated, was used to determine eating behaviors, specifically outlining food consumption, methods of preparation, and portion sizes, local traditional food was included in the recall survey. The FFQ considered food intake over a week, including that of traditional food, and asked questions about specific types of eating practices including which parts of harvested and hunted meat were consumed and was answered by 238 people (15, 18). In addition to the food surveys, a health messages survey was used to quantify the public perception of traditional food, including the nutritional and health benefits of traditional foods, and perception of advisories placed on traditional foods with 87 participants completing the survey (13, 15). While the data from these surveys are not directly used for any analysis as part of chapter 1, information was drawn from these surveys for the development of the exposure survey outlined in chapter 2, for example including the most consumed types of traditional food, and cooking methods. Additionally, information from these surveys was used to understand community perception and consumption of traditional food.

1.2.4 Results

Overall, levels of contaminants in all matrixes of samples were similar to those from other biomonitoring studies across Canada (13). However, some samples were found to be above the guidance values for cadmium, mercury, and Pb (13). While only a small percentage, 3.6% of all samples were found to be above guidance values for these contaminants, they were still of concern as prior evidence has suggested negative impacts can occur before these thresholds (13).

Specifically for Pb, average levels in blood and urine were higher than in other populations in Canada (13). Looking across communities and regions from the project, data collected on Pb during this project indicated elevated blood levels in the Sahtú population, when compared to the Dehcho Region (13). The comparison of Pb values between both regions, and to the Canadian Health Measures Survey (CHMS) is highlighted in Table 1, below. Overall, Pb values in the Sahtú were higher than both the Dehcho and the general Canadian population for both blood and urine. As a result, Pb levels warranted further investigation in the Sahtú, and thus a further project on the exposure to Pb was developed.

Table 1: Pb levels (ug/L) in samples from the Sahtú vs levels in samples from the Dehcho and levels in Canadians aged 6 – 79 from CHMS Cycle 2, 2009 – 2011 (19)

LEAD	**Sahtú Samples**			**Dehcho Samples**			**Canadian population**		
	Detection (%)	GM	P95	Detection (%)	GM	P95	Detection (%)	GM	P95
Blood	100	2.3	8.2	100	1.1	4.3	100	1.2	3.2
Urine	98.2	0.67	4.6	100	0.50	2.0	83.8	0.52	1.9

1.3 Toxicokinetics of Lead

To better understand the movement of Pb into and out of the body including absorption, distribution, metabolism, and excretion, this section focuses on the toxicokinetics of Pb.

1.3.1 Absorption

The two most common ways by which Pb is absorbed into the body are inhalation and oral exposure routes. A third, less common absorption of Pb is through dermal exposure (19). Relating these absorption pathways to the NWT, all three are possible pathways of absorption. The route of absorption depends on particle size. With a small enough size, Pb particles can be absorbed through the respiratory tract (20). Large particles are ingested through swallowing and are absorbed in the gastrointestinal tract (21).

Airborne Pb is typically found in aerosols; aerosols are absorbed and deposited in the respiratory tract after being inhaled. Particles between 1 and 2.5 microns are deposited in the alveolar region and absorbed after extracellular dissolution. Larger particles, 2.5 microns and above are transferred via mucociliary transport into the esophagus and swallowed (22). Airborne Pb absorption can also occur through indoor dust (23, 24).

Gastrointestinal absorption of ingested Pb inside of the body varies based on several factors. Absorption of ingested Pb is approximately 40-50% in children, and 3 – 10% in adults (25, 26). Generally, the presence of food in the digestive tract reduces the absorption of Pb (27). Interactions of Pb with essential molecules and macronutrients are explored in section 1.4. Although not typically an important route of exposure, when dermal exposure is significant, it is often in occupational settings, such as those working with batteries (28). Notably, hand-to-mouth behavior in children is sometimes quantified under dermal exposure, even though absorption follows the same route as ingested Pb (19, 29).

1.3.2 Distribution

Regardless of the route of exposure, absorbed Pb is distributed similarly throughout the body with distribution dependent instead on the physiological characteristics of the receptor (30, 31). The term body burden is used to represent the total amount of Pb in the body (19, 29). Following exposure, most Pb in the body is deposited in the bones, and red blood cells (32). Pb deposits in bone during the mineralization process of bone growth, replacing calcium and forming stable complexes with phosphate. Concentrations of Pb in bone increase with age (33-35). Pb in blood readily exchanges with Pb in bone; as a result, bone Pb acts as a reservoir for Pb and can maintain elevated blood Pb levels even after exposure has ended (30, 36). Concentrations of Pb in blood vary with age, physiology, life stage, and exposure to Pb (31). Up to 99% of Pb in blood is distributed in red blood cells, with the remainder in plasma (37, 38). Pb crosses cell membranes through saturable transport occurring via membrane carriers. The major pathways in which Pb enters red blood cells is through the ligand Aminolevulinate Dehydratase (ALAD) and via facilitated transfer of ion exchangers such as Divalent metal transporter 1 (DMT1) (37, 39, 40).

1.3.3 Metabolism and excretion

Pb is not broken down or synthesized into other substances in the body. Relatively few studies have addressed the metabolism of organic Pb in humans (19). Organic Pb is metabolized in the liver through the formation of various protein and non-protein ligands. Typically, Pb is excreted through bodily fluids, primarily through urine and feces (19). Sweat, saliva, hair, nails, breast milk, and seminal fluid represent other, more minor routes of elimination (19). For Pb inhaled as submicron particles, excretion occurs primarily through urine and feces, with approximately 50% of daily Pb intake being eliminated (30, 41). Following ingestion, most excreted Pb is eliminated in fecal matter (90%) while approximately 10% is eliminated by urine (42). Minor methods of excretion, accounting for less than 2.5%, are through saliva and bile (42). Retention times in the body vary based on physical factors such as age and exposure history (43). The elimination of Pb from blood is faster than that from bone (44). The half-time of Pb in blood is impacted by age (age increasing half-time) and exposure history (with increased exposure and body burden increasing half-time) and can range anywhere from 1 week, to several years (44). Elimination of Pb from bone has a half-time of 10-20 years and is based on similar factors to that of Pb from blood half-time (44).

1.4 Toxicodynamics of Lead

1.4.1 Duration of exposure

Complete exposure history to Pb is almost always unknown, especially when looking at longer-term cumulative exposure. As such, the duration of exposure is sometimes estimated according to the clinical and sub-clinical outcomes observed (19). Acute exposure to Pb often comes from a direct point source leading to a high influx of Pb into the body. Acute exposures are often associated with severe gastrointestinal issues (19). Acute Pb exposure and toxicity is outside the scope of this thesis.

Chronic exposures are prevalent with lower concentrations of exposure over longer periods of time. Chronic exposure to Pb can be associated with short-term memory loss, concentration problems, depression, and numbness or tingling in the hands and feet (45). Other symptoms, including renal, neurological, gastrointestinal, and cardiovascular health impacts are also associated with chronic exposure (45). While chronic exposure is related to lower exposure levels, no level of Pb in the system is considered safe, and health consequences can arise at any blood Pb (PbB) level (45).

1.4.2 Biomarkers and concentrations of lead in the body

Biomarkers of exposure for Pb include Pb levels in human tissue and fluid, such as concentrations of Pb in blood, bone, and urine (19). PbB in whole blood is the most widely used biomarker for determining association and health outcomes. PbB are strongly influenced by recent exposures over the previous 30 days and are based on the half-life of Pb in blood (29). The current blood Pb intervention level in Canada is 10 μg/dL; however, sufficient evidence indicates that PbB below the 10 μg/dL thresholds may still be associated with adverse health effects, and as a result, there is no safe value of Pb in blood (19, 29). Furthermore, as negative health impacts occur even below the commonly established 5 ug/dL level, Minimal Risk Levels, the estimate of daily exposure of a substance that will not result in a detectable risk of adverse (non-cancerous) health effects over repeated exposure, have not been derived by the Agency for Toxic Substances and Disease Registry (19, 46).

Bone Pb has a long half-life and represents chronic exposure or total body burden of Pb. However, bone Pb is not an optimal biomarker as there is limited availability and means of getting it through non-invasive assessments (29). Children's teeth may provide measurements that may be informative, and less invasive, but are not as reliable as blood or bone. Pb in urine is another biomarker, but not as common or reliable as blood or bone. Urine reflects recent exposure. However, since urine acts as a method of excretion for Pb, urine Pb levels may exhibit large variability when compared to PbB (19).

Additionally, when working with specific populations, advantages, and disadvantages of matrices for biomarkers are related to cultural sensitivity. Populations may be reluctant to provide specific samples based on previous history, and or cultural taboos or beliefs. Since the research in this thesis has a major focus on Indigenous populations, cultural sensitivity towards the collection of hair, and urine samples needs to be addressed. While blood may be more invasive than both hair and urine samples, it can sometimes be the preferred matrix, as was evident in the human biomonitoring project of the NWT.

1.4.3 Neurobehavioral health impacts

Much of the literature looking at Pb exposure and neurobehavioral impacts sets thresholds of exposure as 5 and 10 μg/dL respectively. However, alteration of neurological behaviour because of Pb toxicity appears to not have a threshold, especially in children. In Canada, older government reports, such as the Final human health state of the science report on Pb published in 2013, used indicates concern exists around Pb levels of 5 and 10 µg/dL (29). These values were also echoed by governing bodies in the United States, such as the Centers for Disease Control (CDC) (19).. Recent updates to the toxicological reference values (TRV) in Canada, as well as the release of the toxicological profile for Pb from the United States have now aligned with the stance from the EFSA (19, 47). Specifically, while Health Canada has not derived a TRV for Pb, they have set a provisional value (risk-specific dose) of an oral tolerable daily intake of 0.0005 mg/kg body weight, as per the risk specific dose from the EFSA (47). Additionally, Health Canada reiterated that no threshold has been established for a critical effect of Pb thus meaning Pb should be considered a non-threshold substance (47). As a result, the effects of Pb on intellectual function and neurological behaviour may be present at any level of chronic Pb toxicity (47).

Literature on the human neurobehavioral impacts of Pb is the most extensive as neurological effects are of greatest concern when observed in infants and children as they may result in life-long decrements to neurological function (45, 48). In children, the effects of chronic exposure to Pb vary. Chronic exposure to elevated levels of Pb may be associated with decreased IQ, reduced verbal comprehension, lack of language development, slowed processing speed, hyperactivity, ADHD, and emotional functioning in children (19, 49, 50). Symptoms are similar in adults, but typically occur at higher concentrations. Other neurobehavioral impacts on adults may include intellectual deficits, reduced cognitive function, logic, and memory, and altered mood and behaviour (51-53).

1.4.4 Cardiovascular health impacts

Cardiovascular effects associated with chronic exposure to Pb in humans are similar among both children and adults. However, adults often experience increased symptoms as known confounders (age, alcohol consumption, and smoking status) are associated with adult behaviours (19, 54). Pb effects on blood pressure are the most studied cardiovascular consequence; results indicate that a positive association between Pb and blood pressure exists (55).

Increased blood pressure and hypertension are typically evident in both adults and children with chronic exposure to Pb and PbB of ≤10 µg/dL (56-58). Results from the Canadian Health Measures Survey from 2007 to 2011 identified that average PbB levels were higher in hypertensive people, and that blood pressure began increasing with chronic exposure above 1 µg/dL PbB (59).

1.4.5 Renal and other health impacts

Renal damage and reduced renal function are associated with a wide range of Pb blood levels in those with chronic exposure (19). Renal effects associated with PbB of ≤10 µg/dL are changes to glomerular filtration rate, and proteinuria chronic kidney disease (60). As PbB increases, renal effects are further amplified.

Other impacts of Pb toxicity in humans include developmental effects, which are more commonly seen at the highest levels of Pb exposure. These include decreased birth weight, and delayed puberty in both females and males, with the magnitude of effects increasing as PbB increased (61-63). Reproductive effects have also been observed in both females and males. For females, these effects include decreased fertility, spontaneous abortion, preterm births, and earlier age of menopause (64-66). For males, effects include changes to testosterone levels, decreased sperm count, and overall decreased fertility (67, 68).

1.5 Lead in the Environment, Bioavailability, and Uptake

1.5.1 Lead in environmental medias

Pb is found in all environmental media, as well as food and drinking water in Canada. Pb is naturally occurring in the environment, but levels in environmental medias are higher than natural levels due to anthropogenic emissions. Once anthropogenic Pb is released into the atmosphere, which is the main environmental transport media for Pb, Pb will deposit onto surfaces including land and water (69). Table 2 below outlines various concentrations of Pb in environmental medias across Canada prior to 2010.

Table 2: Levels of Pb in environmental medias in Canada (29)

Environmental Media	Range concentration	Study Characteristics
Air	0.0023 – 0.014 µg/m^3	5th – 9th percentile concentration of Pb in $PM_{2.5}$ across Canada in 2009
Air	0.0004 – 0.0027 µg/m^3	Indoor air concentrations of non-smokers in rural residences of Ottawa, Ontario
Air	0.0010 – 0.0051 µg/m^3	Indoor air concentrations of non-smokers in urban residences of Ottawa, Ontario
Soil	1 – 152 mg/kg	Natural Resources Canada's Geological Survey of Canada, Pb concentrations in glacial till
Soil	35.6 – 766 mg/kg	Arithmetic means concentrations of Pb in soils surrounding residential and parkland, data from studies conducted in BC, NL, NS, ON, and QC. Highest value from St. Johns NL dripline, lowest in Lake Claire QC watershed
Soil	5.3 – 750 mg/kg	Arithmetic means concentrations of Pb in soils surrounding anthropogenic sources, data from studies conducted in AB, BC, NL, NS, NU, ON, MB, QC, and SK. Highest value from Trial BC, lowest in Bankers Narrow MB

Since 1970s, $PM_{2.5}$ levels of Pb in ambient air have decreased by 97% and have been below 0.02 µg/m^3 since 1994 (29). Indoor air levels tend to be higher in urban areas compared to rural areas (29). Most soil samples in Canada are below the Canadian Council of Ministers of the Environment soil quality guideline for human health of 140 mg/kg, but some variation exists across the country and soil type (29). No large, country wide testing has been done for Pb in either freshwater and saltwater systems as concern for Pb in water is primarily related to drinking water (29).

Airborne Pb tends to be in the form of submicron aerosols, as previously mentioned, while in the atmosphere, compounds of Pb exist as particulates (70). Once in the atmosphere, particles are removed via either dry or more commonly wet deposition (19). Transport of Pb is based on particle size, large particles will deposit much closer to emission sources, while smaller particles are transported to much further distances (69). After deposition occurs, particles may be resuspended or redeposited, and thus Pb is persistent in the environment (69). Additionally, long-range transport results in Pb in the air, as well as water (71).

In water, concentrations of soluble Pb will depend on the pH and ionic strength of water, with neutral and basic pH levels having less soluble Pb than acidic pH water (69). As pH increases, Pb carbonates are formed which limits the concentration of soluble Pb (69). Additionally, the adsorption of Pb to organic matter, substrate, clay, and mineral surfaces increases in higher pH waters (72).

Levels of Pb in soil are dependent on both natural and anthropogenic factors. Natural levels of Pb in soil are related to the geological setting of the soil. Pb is naturally occurring in the form of Pb sulfide, most commonly as galena, an ore that is commonly mined as a source of silver (73). Pb is commonly found in oil sands (in Pb-zinc bedrock) and mines (as Pb-zinc ore and galena) as a result of Pb-zinc mineralization in soils and rocks (16). Thus, soils surrounding areas in which Pb formations are distributed, for example, silver mining and smelting practices. will often have higher levels of Pb (74). Pb has low soil mobility and will often be persistent, and thus typically, soils and sediments act as environmental sinks for Pb compounds (19, 75). Pb can remain in soil indefinitely because of low soil mobility and non-volatility thus deposition is irreversible and permanent unless it is removed through remediation (69). Pb is found in all surface soils in Canada, specifically in the upper levels of soils (29).

Plants may accumulate low levels of Pb when growing in Pb-contaminated soil, as well as from atmospheric deposition (76, 77). For example, bog blueberry plants around a Pb zinc mine in the Yukon had levels between 0.1-20 ug/g dry weight, while Labrador tea in the same area contained 0.1 – 53 ug/g dry weight (78). Plants can be indicators of atmospheric Pb of local sources, as well as indicators for long-range transport, as levels of Pb change in the atmosphere, so do they in plant material (79). Additionally, plants may be a method of remediation of soil contaminated with Pb, specifically by method of phytoremediation including subarctic and Arctic vegetation (80). Plants near higher pH waters, those with increased organic matter and Pb carbonate complexes, may more readily uptake Pb (19).

1.5.2 Accessibility, chemical activity, and retention

The accessibility of Pb depends on several factors such as geography, environmental media, and time since emission. Deposition of Pb is greatest closer to Pb emission sources (69). The geographical differences of Pb availability are typically associated with activities that use Pb (which are explored in the following section, 1.6). Additional Pb exposures may occur in urban environments, which can directly contribute to increased Pb exposure (such as soil in urban areas as a source of airborne Pb) and indirect causes (such as urban runoff of Pb found in aquatic environments) (19). While many anthropogenic sources of Pb have been eliminated, the former uses continue to be a potential source for Pb exposure as a result of Pb's persistence in environmental media (19, 29). Compared to air and water, soil has the highest ability to retain Pb (81).

1.5.3 Bioconcentration, magnification, and accumulation

The elevated retention time of Pb in tissues results in bioconcentration and accumulation. The highest Pb concentrations are found in aquatic and terrestrial organisms who live near activities that use Pb. These include mining, smelting, and refining facilities, battery recycling plants, areas with high automobile and truck traffic, sewage sludge, areas of heavy hunting and fishing with the use of Pb sinkers, and Pb ammunition (19). Biomagnification of Pb does not occur in aquatic or terrestrial food chains, including both inorganic and organic Pb. However, because Pb is persistent, it has a highly bioaccumulative nature (19).

1.6 Lead Emissions and Anthropogenic Emissions

1.6.1 Emission history

Global atmospheric deposition of Pb was highest during the 1970s and has since begun to decline (69). As of 2009, emissions and releases of Pb into the environment in Canada were approximately 436,000 kg, per year; a breakdown of the years 2000 – 2009 is evident in Figure 3, below. A more in-depth overview of air releases, including sources of emission, follows in Figure 4.

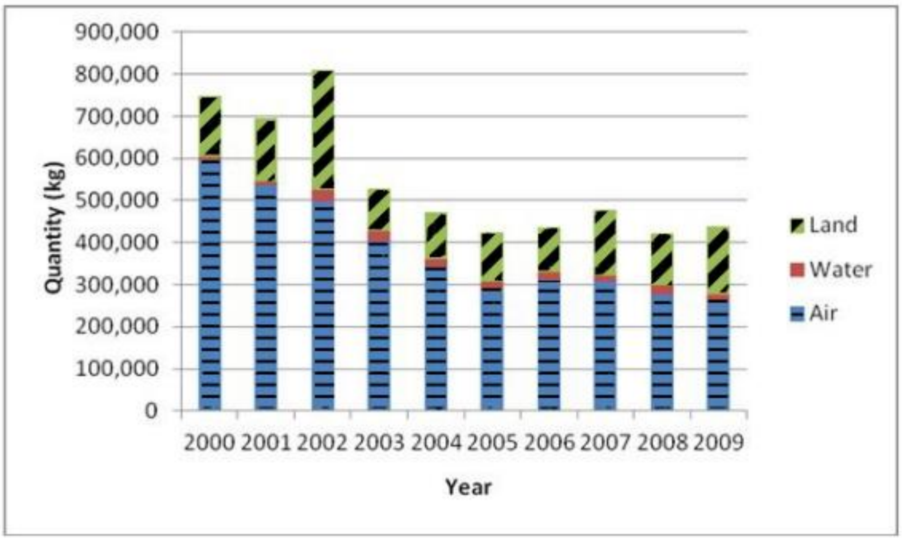

Figure 3: Canadian Pb emissions in land, water, and air between 2000 – 2009 quantified and graphed for the Final Human Health State of the Science Report on Lead (29)

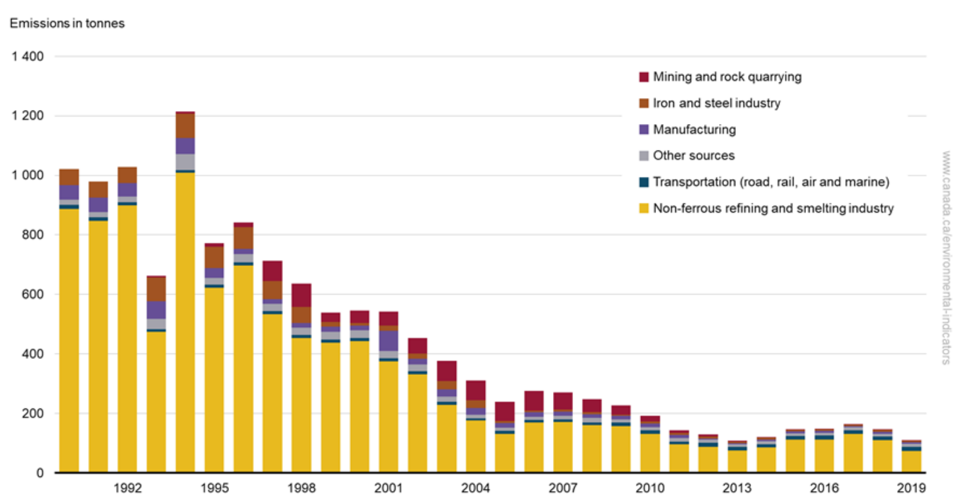

Figure 4: Canadian Pb air emissions between from 1990 – 2019 and breakdown of emissions sources from the releases of harmful substances to air as of November 2021 (82)

Canadian emissions are majority into the air, followed by land, and lastly water, as based on Figure 3. In 2019, the most recent available data on total releases of Pb in Canada were 204,512 kg, which represented a 46% decrease from levels in 2010 of 380,208 (83). As is evident in both Figures 3 and 4, levels are generally decreasing. In the NWT specifically, Pb emissions to air in 2019 were higher than in 2009 (0.38 tonnes vs 0.35 tonnes), while Pb emissions to water were lower in 2019 than 2009 (0.1 tonnes vs 0.6 tonnes) (82, 84).

1.6.2 Naturally occurring emissions

Naturally occurring emissions are a result of volcanic emissions, and from rocks and soil as dust (in soils that naturally contain higher levels of Pb) (85).

1.6.3 Anthropogenic emissions

While the use of Pb has significantly decreased over several decades, Pb continues to be used in several methods, which continue to contribute to anthropogenic releases to air, land, and water. Pb concentrations in ambient air have seen a reduction of 99% from 1984 to 2008. This reduction was in large part related to the introduction of unleaded gasoline in 1975 (29). Leaded gas was banned for use in vehicles in the 1990s (29). The only use today for leaded fuel is in aviation fuels for small aircrafts which is one of the main emission sources for Pb in air (29, 83). Living in proximity to an airport has been explored in literature as a potential exposure source to Pb (86, 87). A significant and positive association with proximity to an airport and PbB has been found in American children living within 0.5 – 1.5 km and or downwind of an airport where leaded aviation gasoline was used (86). Specifically, children living within 0.5, 1.0, and 1.5 km had on average PbB levels that were 4.4, 3.8, or 2.1% higher, respectively, than other children (86). The other main causes of Pb emissions to air are as a result of mining activities, specifically releases from the mining and smelting of Pb ores and ores where Pb is a by-product (such as galena) (83). Releases from mining and smelting have also been reduced for decades (83). As a result, Canadian Pb concentrations in air are now consistently below 0.02 μg/m3. Of releases to ambient air in Canada, 70% was by mining, and metals production, 17% was released by air transportation, and 13% by other sources (29).

The highest contributor of Pb releases to land is the use of Pb ammunition (83). More specifically, the largest emitters of Pb to land are from shooting ranges, with a large majority being from the Department of National Defence military training ranges (83). Looking at levels of Pb in soil, unlike air emissions, levels of Pb in soil have not decreased (12). This is concerning as Pb in soil and contaminated road dust can be resuspended and act as further emissions into the air (19, 69, 81). Pb levels tend to be higher in cities, roadways, and industrial sources that emit Pb (29). In Canada, releases of Pb to water are lower than in both air and land (29, 83). Pb emissions to water are a result of mining by-products and runoff, as well as fishing activities, such as the loss of Pb sinkers and jigs (83).

Disposal, transfers, and treatment and recycling of Pb are much higher than emission levels in Canada. Specifically, in 2019, 24,739,847 kg of Pb were disposed of in facilities, and 34,797,784 kg were transferred off-site for treatment or recycling; this represents a 33% and 21% reduction of values in 2010 (83). The reduction in values also indicates the reduced use of Pb overall (83). Other commercial and manufacturing uses for Pb, are also responsible for emissions to air, water, and land, including rolled and extruded products in the construction industry, Pb sheeting in the building industry, batteries in the automotive industry, paint primers, manufacturing of Pb ammunition, stamping, pressing, and castings (88, 89).

1.7 Lead Sources and Human Exposures

Sources of exposure to Pb are linked to consumption of food and or water that has elevated Pb levels, exposure to air and dust containing Pb aerosols or Pb soil particles, occupational exposures, and exposure through personal and recreational activities which use Pb.

1.7.1 Food and water

Water and food currently represent the predominant route of Pb intake for the general adult population even though there is no permissible Canadian food use for Pb. However, the dietary intake of Pb in Canada decreased from 0.8 ug/kg body weight in 1981, to 0.1 in 2007 (29). 2007 values of 0.1 ug/kg body weight equate to 0.0001 mg/kg body weight, which are five times below the EFSA threshold of 0.0005 mg/kg body weight which is the provisional TRV also used by Health Canada (47). Major reasons for this reduction include the replacement of Pb soldered cans for food storage and the prohibition of the use of Pb-based water service pipes and solder (29). Changes to Pb water pipes however is a relatively new change, and thus, homes built before 1990 may have existing distribution and plumbing materials that can act as a source of Pb in domestic tap water (29). The age of the plumbing system, the chemistry of water, including temperature, and pH, and the length of time water sits in the Pb pipes impact Pb consumption from tap water (29). No simple relationship exists between these factors and Pb exposure, but corrosion of Pb pipes is most impacted by contact time of the water and material; thus, flushing plumbing materials prior to human consumption can assist with reducing exposure to contaminants from drinking water (90).

The current primary source of Pb in food is uptake from soil in edible plants (29). The food groups contributing most to dietary Pb intake aside from beverages include cereal products, and vegetables (29). (91, 92). Testing from the Canadian Food Inspection Agency found highest Pb levels in grain-based products, with 162 of 265 samples having levels above the detection limit, with a mean concentration of 25 ug/kg and a range of 2 – 977 ug/kg (29). However, while Pb in food is the mostly predominant route of Pb intake, it may not lead to Pb levels of concern (29). In plants, only low levels of Pb accumulate in edible portions, even when grown in Pb-contaminated soils (76). Thus, Pb levels in plants are often lower than guidelines for human consumption, including in the Canadian circumpolar north, and vegetation represents a minor pathway of exposure to Pb for humans. In general, domestic Canadian food do not have levels have low or non-detectible levels of Pb (29). Deposition in plants may be of concern when hunting herbivore animals who have consumed high quantities of contaminated plants. Additionally, any fish intake from contaminated waters and the consumption of wild game which has been hunted with the use of Pb ammunition are also sources of exposure to Pb through food (29). Using data from the Canadian Total Diet Study (from Vancouver, Halifax, Toronto, Winnipeg, and Montreal between 2003 – 2007), levels of Pb are highest in marine fish 2.5 – 20.7 ug/kg, followed by shellfish 3.87 – 8.00 ug/kg, canned fish 1.70 – 3.69 ug/kg, and then freshwater fish 0.50 – 2.55 ug/kg, across Canada (29). The use of Pb shot has been banned for the hunting of migratory birds in Canada since 1999, no further national restrictions exist on the use of Pb ammunition (93). The use of Pb ammunition and harvesting of wild game has been hypothesized to be of highest concern for Indigenous populations (29).

1.7.2 Indoor air and house dust

While concentrations of Pb in ambient air are at their current lowest levels, Canadians spend up to 90% of their time indoors at home, school, or the workplace, and thus, Pb in indoor environments may be a more significant source of exposure (29). Pb-based paint is a the most significant source of household exposure to Pb, dispersed as a result of paint degradation or from home renovation activities such as scraping and sanding that cause the formation of dust (29). The composition of dust from four homes built between 1905 – 2000 with Pb concentrations above 1000 mg/kg from the Canadian House Dust Study identified minerals commonly found in Pb based paint (94). Settled dust from home renovations, as well as other sources such as contaminated soils or hobbies releasing aerosols, can act as a route of exposure if ingested, and may be one of the biggest exposure routes for children (29, 95). Pb ammunition can also contribute to household dust, if ammunition is casted at home, or consumed near the home (96). Smoking and e-cigarettes can contribute to higher concentrations of Pb in indoor air (81).

1.7.3 Occupational exposures

Occupations related to mining, smelting, and refinery of Pb ores, as well as people working in hazardous waste sites, or with automotive batteries may result in exposure to Pb in the workplace (19, 29, 89).

1.7.4 Other sources of exposure

Other less common sources of Pb exposure may result from engaging in hobbies and artistic activities that use Pb or Pb-based products, such as hobby soldering, stained-glass making, as well as target shooting using Pb ammunition (29). Dermal exposure may occur when using hair dyes, hand creams, and other products containing Pb pigments. Pb may also leach from crystal decanters, bowls, and glasses into the foods and liquids they contain and provide a route of exposure through ingestion (19). Smoking status is also an exposure to Pb (19, 56, 97, 98)

1.7.5 Sources and regulations in the north and the Sahtú

Sources such as the use of Pb paint, or Pb water pipes may be methods of exposure regardless of geographical location and pertain to the North. However, diet and hunting practices appear to be key reasons for elevated PbB among Indigenous populations (99). Consumption of traditional food in Indigenous populations can act as a potential source of exposure to contaminants (14, 15). Levels of Pb may be elevated in game animals. For large mammals, the muscles and livers of deer and caribou that were harvested with Pb bullets may result in increased Pb concentrations (100). The use of Pb shot on game birds is another common method of exposure to Pb (101, 102). Due to the size of Pb shot, fragments may remain in the bird tissue, and be ingested, specifically meat around the wound channel (103). Migratory birds may be capable of bringing Pb to Northern environments through long-range transport, based on where their wintering grounds are located (104). Further, birds may ingest excess and expended Pb shot (including those from target shooting) located at the bottom of water bodies, or in other parts of their habitat (105). Prior work in the Sahtú has indicated the consumption of traditional food is still frequent, and the use of Pb ammunition may still be present (13).

All the communities within the Sahtú, which were part of the previous biomonitoring project have no access to all season roads and are thus fly-in communities (as compared to all but one Dehcho community which participated in the study having all season road access). This means all communities in the Sahtú also have airports. Each of the airports in the community is serviced by North-Wright Airways, as well as private chartered flights. Presently, none of the aircraft fleet of North-Wright Airways are piston airplanes, and or operate on leaded fuel (106). However, as previously mentioned, Pb is persistent in the environment and as a result, would remain in the area if piston and or leaded fuel airplanes were used in the area before. This may be especially of concern in Tulita, as some residential homes are within one kilometer of the airport (while those in Fort Good Hope and Deline are within three kilometers of the airport).

As Pb is a known toxic substance in the NWT, rules, and regulations existing in the North are a combination of national laws and local programs. As per Canadian law, Pb shot cannot be used for hunting migratory birds or when hunting in wetlands (107). However, no rules exist for the use of Pb ammunition for small game, game birds, or on larger animals. Food consumption recommendation documents exist for traditional foods and include methods of reducing Pb (such as a diet rich in vitamin D, zinc, and iron) (13). Further, a guideline for the management of waste Pb (including Pb-based paints) is available online and outlines regulatory agencies which monitor, and facilitate the exchanging of waste items (108). Additional research and assessment of exposures to Pb within the Sahtú are explored throughout the rest of the thesis, in both chapters one and two.

1.8 Interactions Between Lead and Nutrients in Humans

1.8.1 Lead and Iron

Nutritional iron status impacts Pb absorption, with higher Pb levels being observed in people with iron deficiencies (109). For example, results from the second National Health and Nutritional Examination Survey of the United States, indicate that people with the highest Pb values and low iron values had over six times higher odds of developing complications compared to people with normal iron levels (109). Gastrointestinal absorption of ingested Pb is also impacted by iron status. The more iron present in a diet, and/or the higher one's iron status is, the less Pb is absorbed into the body (109). Therefore, people with an iron deficiency may experience higher absorption of Pb. Additionally, other changes may occur in the biokinetics of Pb in the absence of iron, which would increase Pb retention and absorption levels (109, 110).

1.8.2 Lead and Zinc

Zinc and Pb complete with one another for uptake in the intestine. Pb can substitute and or displace zinc in some enzymes or proteins where zinc cations are found, such as those essential for the ALAD gene activity (111). Pb substitution impacts gene expression, resulting in neurological conditions developing (111). The relationship between Pb exposure and Zn deficiency and dietary levels are not well studied. However, based on current literature, like iron, zinc experiences an inverse relationship with Pb intake; increased Pb levels are associated with lower zinc levels (112-114). A study focusing on PbB of Australian children found a significant negative correlation (coefficient -0.209) between zinc in diet and PbB, even after adjusting for important covariates such as interior house dust (115). Additionally, zinc had the highest effect on PbB variance among all variables assessed with 4.23%, followed by calcium with 3.91%, and iron with 2.20% (115).

1.8.3 Lead and Vitamin D

A negative relationship between vitamin D intake and or levels with Pb levels in the body has been studied in literature in children, adults, and pregnant women (116-119). A study conducted in New York on children aged one to five years old found a link between higher PbB and reduced dietary intake of vitamin D (116). Children with the highest PbB (mean 74 ug/dL) had the lowest vitamin D intake (245 IU/day) and lowest serum 25-hydroxyvitamin D (25(OH)D) concentration (20 ng/mL) compared to their counterparts (PbB 18 and 47 ug/dL, intake 340 and 325 IU/day, 25(OH)D 27 and 29 ng/mL) (116). In adult men, those with higher daily vitamin D intake (more than 589 IU/day) had bone Pb levels that were 5.6 – 6.0 ug/g lower than those with vitamin D intake below 179 IU/day (118). A negative relationship between vitamin D intake and maternal PbB was found in pregnant women in New York (119). Overall, the association between Pb and vitamin D concentrations indicates an inverse relationship. Therefore, the reduction of vitamin D concentration can result in increased Pb absorption and elevated Pb concentrations in the blood and vitamin D intake may be a protective factor against Pb exposure

2 Assessing Relationships between Pb Levels and Various Nutrient Biomarkers in the Sahtú, NWT

2.1 Introduction

Micro-elements like iron and zinc, and vitamins including vitamin D, are essential for the body and the regulation of these nutrients is important for health. Iron helps maintain blood, specifically as it is a major component of hemoglobin and myoglobin (120). Iron in food is found in meat and organs, as well as beans, nuts, seeds, and certain vegetables such as spinach (121). Zinc is a trace mineral necessary for growth and specifically for the regulation of gene expression as it is a component of various enzymes and proteins (120). Meats, poultry, and seafood are rich in zinc, as well as legumes and whole grains (121). Vitamin D works in conjunction with calcium and phosphorus to maintain bone structure (122). Vitamin D is a unique nutrient that can be synthesized by the human body when exposed to sunlight and is found in human diets (122). Dietary sources of vitamin D include fatty fish and liver oils, and small amounts in eggs; few foods are naturally rich in vitamin D (121, 122).

In Northern regions, such as the Sahtú NWT, populations face greater prevalence of nutrient and vitamin deficiencies due to differences in diet, environmental factors, lack of affordable nutrient-rich market food, and the presence of many nutrient-poor market foods (123). While some traditional foods may be a source of vitamin D, not all are. As a result, vitamin D levels often have to be supplemented through market foods, which are expensive and may not always be available (124). However, even when vitamin D are often is supplemented by market foods, levels are still low in regions of the NWT (125-128). Further, vitamin D levels are not adequately supplemented by sun exposure in Northern regions as less absorption of vitamin D occurs during the winter months due to a reduction of hours of sunlight during, and low temperatures resulting in less skin is exposed to the sun (129). However, vitamin D levels may increase during the summer season as a result of increased sun exposure in subarctic (130). The consumption of traditional food, on the other hand, most typically the consumption of game meat and fish, has often resulted in adequate levels of iron and zinc in Northern populations (126, 127, 131, 132).

However, the consumption of traditional food, partnered with contaminant exposure, has resulted in the phenomenon known as the “Arctic Dilemma” becoming of concern. The Arctic Dilemma describes the balance between the importance of traditional foods to Indigenous populations with exposure to environmental contaminants through the consumption of traditional food (133). The Arctic Dilemma is also of concern for infant exposure, specifically throughout maternal transmission through breastmilk consumption (133). While traditional foods are high in nutrients, they may also be high in contaminants including heavy metals, and persistent organic pollutants (123, 133). In the Sahtú, prior work has identified Pb as a contaminant of concern as levels of Pb in blood were higher than those in the general Canadian population as assessed through the CHMS (13, 134). Additionally, prior evidence indicates that nutritional deficiencies of, iron, zinc, and vitamin D can be linked to elevated PbB (135-137).

Pb is dietarily linked to iron, zinc, and vitamin D; the more nutrients in a diet, the less Pb is absorbed (135-137). Substitution of Pb for essential elements and vitamins occurs during membrane transport and allows for additional Pb to be absorbed into the body (109, 112, 138). As a result, the concentrations and nutritional level zinc, iron, and vitamin D is important to the absorption of Pb, Pb availability in the body, and health consequences of Pb onto the body.

Levels and accessibility of nutrients and vitamins may differ in Northern people, such as those living in the Sahtú, when compared to people in less remote and Northern communities. Therefore, analysing the relationships between nutrient concentrations, using various biomarkers, may assist with determining exposure pathways and susceptibility to Pb in Northern populations. The pathways by which interactions with Pb and these nutrients occur vary. Research on the nutritional deficiencies of Northern populations and elevated contaminant concentrations is limited, and the interactions below are from studies in the general population.

Iron is fundamental for the carrying of oxygen in blood as it is a key piece in the formation of hemoglobin (139). Additionally, it is necessary for Deoxyribonucleic acid (DNA) synthesis and electron transport (139). Pb and iron have a competitive relationship, and Pb is pernicious to iron metabolism (139, 140). This competitive relationship occurs through intestinal absorption, as Pb is taken up by iron absorption machinery instead of iron thus blocking the absorption of iron into the body (139). Once present in the body, Pb interferences with DNA synthesis and heme production (139). Individuals with reduced iron intake or those who are iron deficient, can absorb more Pb when exposed to it, while contrastingly, a diet enriched with iron, or those with higher levels of iron, typically absorb less Pb than their deficient counterparts (109, 141). For example, in a study of 457 children from the United States, children who ate biscuits fortified with iron at endpoint had half the odds of having PbB above 3 ug/dL compared to children who ate regular biscuits (141).

While zinc is a metal that in high concentrations is of toxicological concern as it is damaging to the environment and to human health, for the scope of this thesis, zinc is treated as an essential nutrient. Zinc is an essential element in the maintenance of the immune system, cell growth, and DNA creation (142). When Pb and zinc interact in a biologically active system, they typically have a negative correlation (113). When absorbed into the body, Pb competes with zinc for finger sites in early growth response transcription factor 1 (Egr-1), which is the gene important for learning and memory formation during growth (113). Additionally, Pb disrupts zinc signalling in immune cells, which slows body response and healing, and is especially prevalent in skin diseases (113). Adequate intake of essential minerals, including zinc, have been linked to reductions in concentrations of Pb in various tissues of animals, including kidneys, heart, and brain, and in human blood, while consequently, zinc deficiency has been linked to increased absorption of Pb (113, 143-145). In a study of children in Mexico, a negative association between Pb and Zinc was observed (146). While Pb values were not significantly different between deficient and non-deficient zinc groups, complications related to Pb exposure (specifically stunted growth rate) were three times higher, statistically significant, in the zinc deficient group (146).

Vitamin D is a fundamental nutrient in the development and maintenance of bone structure and is closely related to many calcium pathways (122). Studies state that like both iron and zinc, vitamin D has been observed to reduce health impacts and levels of absorption of body Pb (147, 148). Pb impacts vitamin D metabolism, with a negative association being evident (149). As a result, when vitamin D levels are lower, Pb is absorbed at higher levels when available (149). Children in New

York with the lowest 25(OH)D levels subsequently had the highest PbB, and the lowest daily intake of Vitamin D (148). Mean serum 25(OH)D levels in children with PbB above 60 ug/dL were 9.08 ng/mL compared to 9.96 and 9.85 ng/mL in children with PbB of 30 – 59 ug/dL and less than 30 ug/dL respectively (148). Additionally, Vitamin D has also been linked to a protective effect against neurotoxicity of Pb (150).

The objective of this chapter was to evaluate relationships between various explanatory variables including demographic information, nutrients, and elements with blood Pb levels by determining the associations between various macro-element, micro-element, and vitamin biomarker data and comparing to the level of Pb biomarker. This was based on secondary data analysis of previously gathered data from the human biomonitoring project in the NWT, as well as additional chemical analysis of specific nutrients. The proposed hypotheses of this objective were as follows:
H_O: there is no association between explanatory variables and Pb concentrations
H_1: there is at least one association between explanatory variables and Pb concentrations

2.2 Methods

The methods used in the study participation, sample collection, and chemical analysis of primary samples are those implemented in the human biomonitoring project in the NWT between 2016 – 2018 (13-15). The description below provides a brief synopsis of the methods used in that project.

2.2.1 Study Participation

Any community member from the Sahtú and Dehcho region of the NWT was eligible to participate in the study. Participation in the study was voluntary, and participants were accepted if they were over the age of six and could provide informed consent. Informed consent required participants to not be under the influence of alcohol or drugs have sufficient capacity to consent and require a parent or guardian to consent on the behalf of a minor. Participants who did not want to receive their results were excluded from further participation. Participants were recruited actively through random contact, and passively through local radio, and reimbursed for their participation (13-15).

2.2.2 Sample collection and initial Analysis

Samples were collected in the wintertime at various community centers in the Sahtú and Dehcho regions by members of the research team and local research coordinators. 537 residents took part in the study, a total of 8.9% of all residents from the Dehcho and Sahtú regions. Participants had the choice to provide hair, blood, and or urine samples; 917 samples were collected, 443 hair, 198 urine, and 276 blood. Alongside sample collection, demographic questions including age, sex, weight, height, and alcohol and smoking consumption were asked (13-15).

2.2.3 Chemical analysis of primary samples

For the 917 collected samples, a range of metal nutrients (including zinc) and toxic metals (such as Pb) were measured between February 2016 and March 2018. For each measurement, the detection rate, the geometric mean, and the 95th percentile were calculated (where the 95th percentile indicates the upper limit of typical exposures). Whole blood and urine samples were analyzed at the Université de Montréal by Inductively Coupled Plasma Mass Spectrometer, and funder by the Northern Contaminants Program (13-15).

2.2.4 Additional Analysis of Biobanked Samples

The preliminary assessment of nutrition markers in biobank samples from the Sahtú region occurred in 2020. All three communities from the Sahtú Region were included in the biobanked samples. The original scope of this assessment was to focus on the nutritional benefits of traditional food consumption and food security, and the work was conducted as part of a Canadian Institutes of Health Research (CIHR) grant.

The biobank plasma samples were held in a -80^{O}C freezer at the University of Waterloo. The additional analyses were completed only on samples from participants in the Sahtú region who consented to have their samples kept in a biobank for additional contaminant and nutritional marker testing if more funding was received. Three participants withdrew their consent, and thus 128 biobanked blood samples underwent further analysis.

Vitamin D was measured in samples by the Canada Research Chair in Human Nutrition and Vitamin Metabolism at the University of British Columbia. Analysis on all biobanked samples was done in plasma and completed in 2020. For many nutrients, biomarkers of supply, function, and outcome differ. For the purpose of this study, biomarkers of supply were considered. For vitamin D in plasma, 25(OH)D is the most commonly used indicator of body levels of vitamin D, as it can be used as a metric for both food (ergocalciferol) and sunlight-based (cholecalciferol) vitamin D (151, 152). More specifically, regardless of the intake (though diet and or sunlight exposure), after vitamin D undergoes hydroxylation in the liver, it becomes 25(OH)D (152). Thus, using 25(OH)D as the biomarker of choice represented whole-body count of levels available to become active vitamin D and provided information on nutrient supply to target tissues, and was thus most applicable to compare to contaminant exposure (151, 152).

In 2021, ferritin was quantified by the Nutritional Biomarker Laboratory, Faculty of Land and Food Systems, University of British Columbia. Ferritin analysis was performed as biobanked samples were plasma as opposed to whole blood. Ferritin is a common indicator of iron deficiency, and is the protein that stores and releases iron in cells (153, 154). After whole iron is processed and absorbed in the small intestine, it is stored in ferritin, which then binds to cells and releases iron into the blood as needed (155). Contrary to other biomarkers for iron, specifically hemoglobin, ferritin represents total amount of iron stores in the body, not just that found in blood; this relationship between ferritin and iron has been proven in literature before indicating that ferritin is a good indicator of iron levels in the body (153, 154).

2.2.5 Data Management

All gathered results on biomarkers were compiled together into one database which was used for statistical purposes related to this thesis. Data on Pb and zinc was from only the 128 biobanked, not all 140 samples collected in the Sahtú. Each sample was matched with its respective sample ID and demographic variables.

2.2.6 Data Analysis of Biobanked Samples

Using the compiled database, associations between vitamin D, iron, and zinc and Pb were evaluated to help describe possible associations with Pb levels in participants. Additional variables included demographic information: age, sex, Body Mass Index (BMI), smoking, and alcohol consumption in the last 24 hours were used as variables. All biomarker variables were continuous, and non-normally distributed. For correlations which included Pb, Pb was the dependent variable.

Age and BMI were continuous, while sex (female, male), smoking in the last 24 hours (yes, no), and alcohol consumption in the last 24 hours (yes, no) were all binary.

Summary statistics were compiled for variables and exploratory data analysis was performed to determine distributions of variables, assess normality, and determine outliers. All biomarker variables were compared to CHMS data to determine how values in the Sahtú compare to national levels. Further, levels were assessed to threshold values from literature to determine the percentage (total, children, adult) that fell above, below, or between blood nutrient and exposure thresholds These thresholds are stated below, in Table 3.

Table 3: Blood threshold of deficiency, normal, and overload/toxicity levels for iron, zinc, and vitamin D based on matrix used in chemical analysis

Nutrient/Vitamin	Matrix	Thresholds
Ferritin (Iron) (156-158)	Serum/plasma	<15 adults / <12 children ug/L – diagnosis of deficiency 15-30 adults / 12 – 20 children ug/L – probable deficiency >30 adults / > 20 children ug/L – deficiency unlikely >100 ug/L – normal ≥600 ug/L – concern for iron overload
Zinc (159)	Whole blood	<440 ug/dL – probable deficiency 440 - 860 ug/dL – normal >860 ug/dL concern for toxicity
25(OH)D (Vitamin D) (122, 160)	Serum/plasma	<30 nmol/L – probable deficiency 30-50 nmol/L – inadequate ≥50 nmol/L – normal > 125 nmol/L – concern for toxicity

Normality of data was assessed through visual inspection, and QQ plot analysis. Nonparametric analysis (Spearman) was done between continuous data to determine correlations between biomarker and Pb concentrations, and continuous demographic characteristics. Nonparametric analysis (Mann-Whitney) was done between biomarker and Pb concentrations and categorical demographic data (sex, smoking status, alcohol status) (H_o: $\mu 1 = \mu 2$; H_1: $\mu 1 \neq \mu 2$; where μ = mean nutrient biomarker/Pb concentration in biobanked blood samples). Nonparametric analysis was completed as part of a preliminary presentation of the data and is presented alongside all other statistical approaches. However, final conclusions for correlations, and subsequent associations between variables was determined via the results of parametric and regression testing.

Following nonparametric testing, all biomarker data were transformed ($\log_{10}$) and converted to a normal distribution so that parametric tests could be applied. Using the transformed biomarker data, a univariate parametric analysis (Pearson) was done between continuous variables (age, BMI, zinc, iron, vitamin D) and Pb. Independent sample t-tests were conducted between Pb and binary data, sex, smoking status, and alcohol status (H_o: $\mu 1 = \mu 2$; H_1: $\mu 1 \neq \mu 2$; where μ = mean nutrient biomarker/Pb concentration in biobanked blood samples).

After all variables were assessed and significance determined, a multilinear regression model was created using stepwise regression. Models were assessed based on Akaike Information Criterion

(AIC) and R^2 values. Two sets of forward stepwise regression were completed, a first including all explanatory variables, and a second which removed BMI from the possible list of variables. The removal of BMI allowed additional data points to be considered in the regression model. As a result, a final model containing age, sex, smoking status, and zinc as explanatory variables was created. All statistical analysis was done in SPSS, aside from confidence interval calculations, which were done in Excel.

2.2.7 Ethics

Original sample collection occurred as part of the broader human biomonitoring project in the NWT between 2016 – 2018 (13-15). Analysis of biobanked samples occurred as part of additional work for which ethics approval was received from the University of Waterloo (#20173, 20950). Research licenses were obtained from the Aurora Research Institute (#3043, 3118, 3498, 3506, 3540, 3845). All data were confidential as no names were kept within any datasets. All datasets were kept at the University of Waterloo on password-protected computers.

2.3 Results and Discussion

2.3.1 Participation

Of 276 samples of blood collected, 140 (50.7%) were in the Sahtú, and 136 (49.3%) were from Dehcho. A total of 246 (89%) of participants opted to have their samples stored within the biobank at the University of Waterloo for the future testing of additional biomarkers when funding became available. A total of 131 (93.5%) samples of plasma from the Sahtú were available in the biobank for further analysis. Of 131 samples, 3 no longer wanted analysis to be completed and were removed from the study. Thus, all further analysis was then done with 128 biobanked samples.

2.3.2 Summary statistics

A total of 128 samples were used during the statistics section. A breakdown of the summary statistics for continuous demographic variables can be found in Table 4, below.

Table 4: Summary statistics for 128 blood samples that were biobanked during the human biomonitoring project from 2016-2018

	Age (years; n=125)	BMI (kg/m^2; n=108)
Arithmetic Mean	44.36	25.77
Standard deviation	19.88	5.25
Median	44	24.87
Range	8 - 88	16.9 – 46.4

*Counts for age and BMI are not equivalent to 128 as only a subset of participants chose to provide weight, height, and/or age

Of the 128 participants, 11 (8.6%) were aged 17 years and under and were classified as children. A total of 114 (89.0%) of the participants were aged 18 years or older and were classified as adults. Three participants who did not provide their specific ages were included in the total analysis and were coded as adults since they indicated being over 18 years old. The youngest participant was eight years old, and the oldest was 88 years old, with the median being 44 years of age. These statistics related to the population of the region (as of 2021) (161). The largest difference in study population and population statistics of the Sahtú was in children. In total, 29% of the Sahtú are aged 19 and under, while only 6% of the study population was 19 and under. All other age breakdowns were similar. 14% of the Sahtú and 16% of the study population were between the ages of 20 – 29, 16% for both were between ages 30 – 39, 12% and 15% were between ages 40 – 49, 14% and 17% for ages 50 – 59, 8% and 12% for ages 60 – 69, 6% and 7% for ages 70 – 79, and 2% and 3% for ages 80+. Overall, the study population was similar to the current population of the Sahtú. BMI central tendencies fluctuated between the upper end of normal, and lower end of overweight, as average, geometric mean, and median all surrounded 25 kg/m^2 (162).

Alongside sample collection during the human biomonitoring project in the Sahtú, data were collected on certain demographics. Questions related to sex, smoking within 24 hours of sample collection, and alcohol consumption within 24 hours of sample collection, were included alongside the information asked during sample collection. As a result, answers were recorded for all participants and the percentages of each category can be found in Table 5, below.

Table 5: Percentage in categories for categorical variables of information of participants who provided a blood sample and had their samples biobanked for further use (n=128)

		Count	Percentage
Sex	Female	64	50%
	Male	64	50%
Smoking within the past 24 hours	Yes	64	50%
	No	64	50%
Alcohol consumption within the past 24 hours	Yes	18	14.1%
	No	110	85.9%

The sex of participants was an even split, which is similar to the 47.1% female and 52.9% male population breakdown of the Sahtú (6). The percentage of the study population who smoked in the 24 hours prior to providing the sample was the same as the percentage who did not smoke, while the percentage of those who consumed alcohol was much lower than those who did not.

Table 6 below, presents the key summary statistics for central tendency (mean including confidence intervals (CI), median), and spread (standard deviation, minimum, maximum, 5th percentile, 95th percentile) for all biomarker variables. Discussion on all biomarker concentrations proceeds in the following sections. Confidence intervals were calculated using average log concentrations and margin of error.

Table 6: Summary statistics for biomarker concentrations in 128 blood samples collected during the human biomonitoring project from 2016-2018, and further analyzed in 2020 – 2022

	Pb (ug/L)	Zn (ug/L)	VitD (ug/L)	Ferritin (ug/L)
Count	128	128	128	128
Arithmetic Mean	31.73	5476.63	9.88	115.76
Geometric Mean (95% CI)	23.02 (19.98 – 26.53)	5393.32 (5228.66 – 5563.19)	8.60 (7.85 – 9.44)	69.25 (56.74 – 84.53)
Standard Deviation	27.47	921.55	5.04	121.64

Median	20.97	5457.90	8.75	85.51
Minimum	3.16	2825.90	2.30	1.02
Maximum	193.73	7965.40	31.10	757.31
5th Percentile (95% CI)	6.84 (5.93 – 7.89)	4032.99 (3909.84 – 4160.00)	3.40 (3.10 – 3.72)	7.77 (6.36 – 9.48)
95th Percentile (95% CI)	81.35 (70.58 – 93.76)	6877.51 (6667.52 – 7094.11)	20.49 (18.68 – 22.48)	309.06 (253.18 – 377.16)

2.3.3 Pb values vs CHMS and Dehcho

A breakdown of Pb blood values compared to CHMS data, and the neighbouring Dehcho region follows, in Table 7. The geometric mean in the Sahtú was over twice that of the Dehcho, and almost twice that of the general Canadian population; it fell above both confidence intervals (163). The 95th percentile value in the Sahtú was 1.88 fold higher than the Dehcho and more than two and a half fold the general Canadian population; 95th percentile values in the Dehcho were higher than those of the CHMS, but geometric mean values lower (163).

Table 7: Blood Pb levels (ug/dL) in 128 biobanked samples from the Sahtú region, NWT collected during the human biomonitoring project 2016 – 2018 vs blood Pb levels (ug/dL) in 136 samples from the Dehcho region, NWT collected during the human biomonitoring project 2016 – 2018 vs blood Pb levels in 5575 Canadians aged 6 – 79 from the CHMS Cycle 2, 2009 – 2011 (163)

	Sahtú	Dehcho	CHMS
Detection (%)	100	100	100
Geometric Mean (95% confidence interval)	2.3 (2.0 – 2.6)	1.1 (0.9 – 1.3)	1.2 (1.1 – 1.3)
95% percentile (95% confidence interval)	8.1 (7.1 – 9.4)	4.3 (4.1 – 4.5)	3.2 (3.0 – 3.5)

Additionally, of 128 blood Pb samples from the Sahtú, 79% (n=101) of samples fell below 5 ug/dL. 19% (n=25) of samples fell between 5-10 ug/dL, and 2% (n=2) of samples were above 10 ug/dL, which is the Canadian intervention level for blood Pb (29). If participants had levels falling above the Canadian intervention for blood Pb, participants were contacted as part of the follow-up protocol described elsewhere (13). During follow-ups, individual meetings which provided information on methods to reduce Pb exposure, as well as re-testing opportunities were offered to participants. However, as previously mentioned, these thresholds are outdated, and health impacts can occur at much lower concentrations. No children aged 17 and under, (n=11) had blood Pb values above 5 ug/dL. Comparing this to both the Dehcho and Canadian populations, where no samples within the 95th percentile from either study population were higher than 5 ug/dL (163). As a result, 21% of samples in the Sahtú being above 5 ug/dL was concerning.

2.3.4 Nutritional Biomarker Values vs CHMS and Assessment of Deficiencies

Comparing zinc, vitamin D, and ferritin values to those from the CHMS, both mean and 95th percentile values were lower than the respective Canadian general population geometric mean and their 95th percentile. The comparison of these values is evident in Figure 5, below. Levels of both ferritin and zinc at the geometric mean and 95th percentile were slightly lower in the Sahtú than those in the CHMS. However, levels of ferritin and zinc were within normal thresholds and the confidence intervals of what is evident in the CHMS. Specifically, both the geometric means and 95th percentile for ferritin and zinc fell within the confidence intervals of the respective general Canadian population level. In contrast, vitamin D levels were significantly lower than national averages. Specifically, both geometric mean and 9th percentile values from the Sahtú fell below the geometric mean and 95th percentile values from CHMS, including the lower limits of the confidence interval. These results align with what is found in literature, as Indigenous populations living in subarctic and Arctic areas typically have adequate levels of iron and zinc within their diets, and insufficient vitamin D (123).

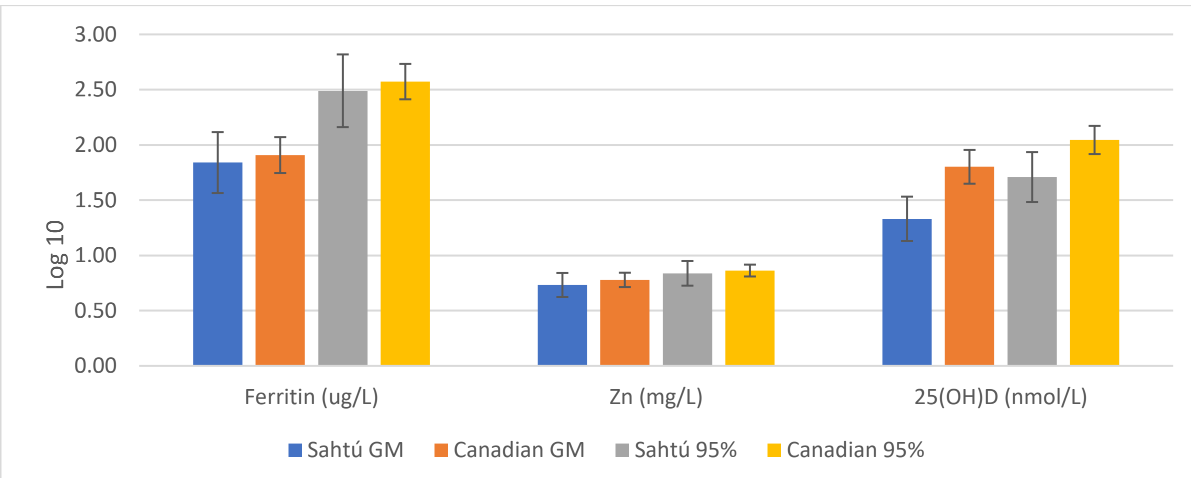

Figure 5: Geometric means and 95th % for the Sahtú, and general Canadian population of nutritional biomarkers

As a result, the assessment of nutritional status and deficiencies for each micro, macro-element, and vitamin was done by comparing independent values from the study population to present thresholds existing in literature as found in Table 3, in the methods sections. Table 8, below, outlines the percentages of total, adults, and children, from the study population of 128 biobanked and their nutritional status according to the thresholds set out above, in Table 3.

Table 8: Percentage of all (n=128), adults (n=117), and children (n=11) falling within blood ranges for iron, zinc, and vitamin D in the Sahtú

Nutrient/Vitamin	Range	All	Adults	Children
Ferritin (Iron) ug/L	<15 adults <12 children	11%	12%	0%
	15 – 30 adults 12 – 20 children	8%	7%	18%
	30 – 99 adults 20 – 99 children	39%	38%	55%
	100 - 599*	41%	42%	27%
	≥600	2%	2%	0%

Zinc ug/dL	<440	12%	10%	27%
	440 - 860*	88%	90%	73%
	>860	0%	0%	0%
25(OH)D (Vitamin D) nmol/L	<30	72%	69%	100%
	30-49	22%	24%	0%
	50 - 125*	6%	7%	0%
	≥ 125	0%	0%	0%

*****Indicates normal/healthy range

Overall, 74 (58%) of all samples fell below normal ferritin levels of 100 ug/L. However, levels above 30 ug/L for adults, and 20 ug/L for children are unlikely for deficiency. When adjusting for this threshold, only 22 (19%) adults and 2 (18%) children had concerning iron levels. As a result, less than one-fifth of the study population had probable iron deficiency. Comparing this to literature, iron sufficiency levels are similar in the Sahtú (164). 96% of Canadians had sufficient serum ferritin concentrations using data collected from CHMS Cycle 2, with a 15 ug/L threshold for anyone aged 6 and older (164). In the Sahtú, 89% of the total population fell above this threshold. Few studies have looked at iron levels in Northern and Indigenous populations, with a vast majority focusing on children iron levels. One study based on 115 Cree and Inuit children in Northern Ontario and Nunavut found iron deficiency in 27.6% of their study population, while another study on 198 First Nations children in Quebec found 20.5% of their population with iron deficiency (165, 166). In adults, a study looking at the association between iron status and fatty acids which used data collected from the International Polar Year Inuit Health Survey found that 13.7% of 1511 Canadian Inuit had iron deficiency (167).

When looking at zinc, 15 (12%) of samples in the study population had zinc values in the probable deficiency category, while 3 (27%) children had a probable deficiency. Few studies exploring blood zinc levels (where zinc is considered a micronutrient) are prevalent in literature. Zinc's inclusion in the CHMS is as an environmental chemical, not as a nutrient, and thus, levels of deficiency are not alluded to (163). Literature assessing zinc intake, however, is more prevalent. A report outlining nutrient requirements from food intake among Canadians 19 and older, found that approximately 10 – 35% consumed zinc in inadequate amounts (168). However, the data presented in this report contains high variation between age and sex groups (168). A study in Dene, Metis, and Yukon First Nations found 7.7% of pregnant women, and 2.0% of lactating women had dietary micronutrient inadequacy (131).

Overall, for both iron and zinc levels, statistics aligned with the literature outlined above. Additionally, many studies conducted in Northern regions have indicated both iron and zinc levels are near normal, and most samples are above deficiency levels or average intakes (126, 127, 131, 132). Levels of iron and zinc are often associated with the consumption of meat, which in prior work has indicated most of the population of the Sahtú consumes often, including the consumption of hunted game and traditional foods (13). As such, populations levels of both iron and zinc in the Sahtú aligned with those observed in general, and other Northern populations.

When looking at vitamin D levels, most of the population, 94% had vitamin D levels under normal values, with 72% fell in the probable deficiency category. As vitamin D is an essential nutrient for growth, these results are especially concerning as 100% of children were getting insufficient levels of vitamin D and were in the probable deficiency category. According to Statistics Canada, 68% of Canadians had blood vitamin D levels above 50 nmol/L, as well as 76% of children aged 6 to 11, and 71% aged 12 to 19 (169). As such, vitamin D levels in the Sahtú were significantly lower than the general Canadian Population. Vitamin D levels in other Northern and Indigenous communities, like the Sahtú, are also significantly lower than general population levels. For example, 61% of Dene participants in a Northern Canadian cohort were found to have serum 25(OH)D levels below 75 nmol/L during the wintertime (170). It is important to note that the biomarker data presented in this paper was collected during the wintertime, when vitamin D levels are naturally lower as a result of reduced exposure to sunlight and less sun hours. Coupled with the reduction of sunlight as a result of latitude, the difference between these results and what is found in literature, such as the CHMS (for which data collection occurred not only during the winter) may be amplified.

2.3.5 Correlation Analysis

Biomarker concentrations of Pb, iron, zinc, and vitamin D were not normally distributed, while age and BMI followed an approximately normal distribution. As a result, a nonparametric test, Spearman, was conducted between all continuous variables to determine correlations. Outliers, values that were much higher compared to the rest of samples collected, were removed using visual inspection and resulted in n=128 for zinc, n=127 for Pb, n=127 vitamin D, and n=126 for iron. At alpha = 0.05, the Spearman Rank test showed that Pb was significantly correlated with age (p = 1.4E-9), zinc (p = 4.6E-3), and vitamin D (p = 1.7E-2). Other significant associations included vitamin D with age (p = 1.0E-13) and BMI (p = 2.7E-2), and zinc with age (p = 1.5E-3) and BMI (p = 8.8E-5). No nutrient biomarkers had correlations with one another, and iron levels were not related to any biomarker or demographic characteristic. A full breakdown of the spearman correlation coefficients is in Table 9, where all significant results, at alpha = 0.05 are bolded.

Table 9: Spearman rank test results (rho values) for blood samples collected during the human biomonitoring project from 2016-2018

	Age	BMI	Pb	Vitamin D	Zinc	Iron
Age		**.38**	**.51**	**.62**	**.28**	.15
BMI	**.38**		.09	**.23**	**.35**	.14
Pb	**.51**	.09		**.25**	**.21**	.11
Vitamin D	**.62**	**.23**	**.25**		.14	.01
Zn	**.28**	**.35**	**.21**	.14		.04
Fe	.15	.14	.11	.01	.04	

Pearson correlation testing was also completed between continuous variables, after biomarker data was transformed. Normality was assessed visually, with the removed outliers from the previous calculations omitted in these tests, and all variables were assumed to follow a normal distribution. Just like the nonparametric testing, significant correlations were found between Pb and age, zinc, and vitamin D. At alpha = 0.05, the Pearson test shows that Pb is significantly correlated with age (p = 1.8E-9), zinc (p = 9.8E-3), and vitamin D (p = 2.2E-2). Additionally, just like the nonparametric analysis, vitamin D was significant associated with age (p = 2.6E-14) and BMI (p = 3.8E-2), and zinc with age (p = 4.8E-3) and BMI (p = 2.9E-3). Once again, no nutritional biomarkers were correlated to one another, and iron had no significant correlations. A full breakdown of the Pearson correlation coefficients is in Table 10 below, with all significant results at alpha = 0.05 bolded.

Table 10: Pearson correlation test results for log-transformed variables

	Age	BMI	Pb	Vitamin D	Zinc	Iron
Age		**.36**	**.51**	**.62**	**.25**	.12
BMI	**.36**		.07	**.20**	**.29**	.16
Pb	**.51**	.07		**.21**	**.23**	.09
Vitamin D	**.62**	**.20**	**.21**		.10	.06
Zn	**.25**	**.29**	**.23**	.10		.07
Fe	.12	.16	.09	.06	.07	

For Pb and age, the correlation coefficients were 0.51 for both nonparametric and parametric testing. As the rho value was positive, the monotonic relationship between these two variables indicated that Pb concentrations increased as age increased. This result is consistent with what is expected in literature as Pb will continue to accumulate in bone (33-35). Exploring the data, Pb levels were higher overall higher in older adults. Additionally, as previously mentioned, no children had blood Pb levels above 5 ug/dL while on the other hand, 23.6% of adults did. This result would indicate exposure is ongoing throughout the lifetime. Low level environmental, and community exposure would support these results. Possible routes of exposure could also align with the consumption of traditional food, for which adults also have higher consumption compared to children (171).

For Pb and zinc, the correlation coefficients were 0.21 (nonparametric) and 0.23 (parametric), while the correlation coefficients between Pb and vitamin D were 0.25 (nonparametric) and 0.21 (parametric). Both correlations with Pb were not as strong as age, as rho values were closer to 0, but monotonic relationships were still evident. Just like with age, since these rho values were positive, Pb concentrations increased as zinc and vitamin D levels increased respectively. However, unlike age, these results were contrary to what is expected; as was expressed in the introduction, both zinc and vitamin D have an inverse physiochemical relationship with Pb, and when Pb intake is elevated, zinc and vitamin D levels are usually lowered. As a result, in the presence of elevated Pb levels, a negative correlation coefficient would be expected.

Instead, based on the coefficient, Pb levels increased when zinc and vitamin D levels increased. Positive correlations between vitamin D with Pb have been found in literature as well. For example, a study conducted in children in the United States found Pb levels increase in the summer, which correlated to an increase in vitamin D concentrations as a result of increased sun exposure (172). This correlation would indicate that a surplus of vitamin D that is different than normal, may result in increased Pb absorption when exposed (172). However, while a positive relationship was evident, this does not mean that the established physiological processes that have been established before, more specifically the negative relationship between vitamin D, zinc and Pb, were not present. Instead, the net resulting relationship was positive. Instead, the biochemical interactions between vitamin D, zinc and Pb were still occurring, but were masked by an alternative cause resulting in a slightly net positive relationship between the nutrients and Pb.

The association between these biomarkers may be indicative of a shared exposure or consumption pathway. More specifically, exposure to Pb could be related to zinc and vitamin D intake. This equates to food sources containing essential nutrients such as zinc, and vitamin D, to also act as exposure sources for Pb. A possible pathway that would explain this relationship would be the use of Pb ammunition when hunting, which may result in Pb contamination of harvested traditional foods. This is a well-documented reason that has resulted in elevated Pb blood levels in other Indigenous populations, including Cree First Nations populations in Quebec and James Bay in Ontario, and Inuit in Nunavik (99, 102, 173). While this may present a possible pathway, some elements do not align. For example, vitamin D is not naturally high in land animal game meat (and as mentioned before, few foods contain naturally high levels of vitamin D), and thus, the consumption of game meat hunted with Pb ammunition would not explain the correlation with vitamin D. However, vitamin D is high in fish, and the use of Pb jigs and sinkers may act as an exposure though the consumption of fish. Additionally, those who consume traditional foods are likely to consume various types, including fish, and as such, may be exposed. Further, iron is typically high in traditional food, and especially in game meat (174). However, no significant correlation was found between Pb and iron in the data, and a correlation between increased levels of Pb and iron would likely be prevalent if Pb ammunition use was the cause for increased exposure. As a result, the assessment of additional pathways of exposure is crucial for determining the exposure pathways related to increased Pb blood levels.

Exploring the correlation results of other biomarkers, the results gleaned from this data were different from those found within literature. Aging is known to reduce vitamin D production in skin, and absorption from food, and additionally zinc levels decrease with age (120, 122, 175). However, based on the correlation coefficients evident in Table 9 and 10 respectively, this dataset did not support these findings. The correlation coefficient between age and vitamin D was 0.62 in both parametric and nonparametric, which happens to be the highest and thus strong correlation between any two variables. This result means that as age increased, so did vitamin D levels. Overall, vitamin D levels were much higher in older adults; three of the four highest values were evident in people aged over 60, while all four of the lowest samples occurred in people between 20 – 30 years old. A possible reason may be due to the higher consumption of fish, a traditional food which may be an exposure to Pb. The correlation between zinc and age was once again positive, being 0.28 in nonparametric testing, and 0.25 in parametric testing, indicating both zinc and age increased together.

Additionally, the results also did not align with literature on the relationship between vitamin D, zinc, and BMI levels. The relationship between vitamin D levels and BMI in literature indicates that the prevalence of vitamin D deficiency is higher in populations with higher BMI, which is also echoed by the relationship between zinc and BMI (176-178). Once again, however, the correlation coefficients were positive for both significant results, between vitamin D and BMI as 0.23/0.20 (nonparametric/parametric) and zinc and BMI as 0.35/0.29.

These results do however align with the concept of a nutritional transition away from traditional foods. More specifically, younger Indigenous populations have an increased reliance on market foods and consume less traditional foods than older Indigenous adults in the same communities (171, 179). Additionally, as previously mentioned, market foods are often poor in nutrients compared to traditional foods. This transition could explain the positive correlation between nutrient concentrations and age being different than that represented in literature. Additionally, as BMI and age were also positively correlated, with coefficients of 0.38 (nonparametric) and 0.36 (parametric), this would indicate BMI was higher in older adults, and thus why nutrients were also higher in those with higher BMIs. Looking at the magnitudes between these correlations, the correlation that was strongest for vitamin D was with age (0.62 for both nonparametric and parametric) and for zinc with BMI (0.35 nonparametric, 0.29 parametric). This would then indicate the importance of age in the relationship of vitamin D and Pb, and the importance of BMI in the relationship of zinc and Pb. Overall, these results should continue to be explored further, outside the scope of this thesis.

2.3.6 Mean Differences Analysis

Next, using Mann-Whitney and independent-samples t-tests, continuous variables were assessed for their relationship with categorical data. Levene's test was used to determine if equal variances were assumed or not assumed. For all parametric testing, the significance was greater than alpha, and equal variances were assumed and thus pooled independent-samples t-tests were used. Specifically, Pb and biomarker values were compared across sex, smoking status, and alcohol status, by comparing the differences in means between groups. Performing these tests allowed to determine how categorical factors impact Pb concentrations, and if trends existed. Table 11, below, identifies the which differences in means were found. All test statistics related to mean differences are included in Appendix A as Table 20.

Table 11: Nonparametric and parametric testing between biomarker and categorical data and significant mean differences

	Pb	Vitamin D	Zinc	Iron
Sex	**N, P**	-	**N, P**	-
Smoking Status	-	**N, P**	**N, P**	**P**
Alcohol Consumption	-	-	-	-

*N indicates test was significant at using Mann-Whitney test

*P indicates was significant using independent samples t-test

A difference in Pb concentration was found between sexes in both nonparametric and parametric testing. The geometric mean for all 128 Pb samples was 23.02 ug/L. When stratifying the data, however, as evident in Table 12, the geometric means between males are females were different. Specifically, Pb concentrations were higher in males than in females with the geometric mean for males being 27.68 ug/L while for females was 19.15 ug/L. Looking at the geometric mean confidence intervals, very little overlap was evident. Comparing other summary statistics between the two sexes, all values, except for the maximum value, were higher in men. The 194 ug/L value on the women's side was the highest across all samples, with the next highest being the maximum on the men's side. This extreme outlier was removed in the calculations used for statistical analysis but included in the summary statistics table below. These results were consistent with those from the CHMS, where males tended to have higher Pb levels than females in all age groups (163).

Table 12: Pb summary statistics (count, average (arithmetic mean), geometric mean, standard deviation, median, minimum, maximum, 5th percentile, 95th percentile) for 128 blood samples collected during the human biomonitoring project from 2016-2018 stratified by sex

	Pb (ug/L)	
	Males	Females
N	64	64
AVG	35.24	28.22
GM (95% CI)	27.68 (23.11 – 33.16)	19.15 (15.54 – 23.59)
Max	100	194
Min	4	3
Median	31	19
SD	23.56	30.17
5th % (95% CI)	7.94 (6.63 – 9.50)	5.30 (4.30 – 6.52)
95th % (95% CI)	83.82 (69.92 – 100.28)	80.12 (65.01 – 98.65)

When looking at nutritional biomarkers, the distribution of zinc was also not the same across the categories of sex. Comparing both the geometric means and 95^{th} % between sexes, both values were higher in men. For men, the geometric mean and P95 were 5581 ug/L and 7109 ug/L, while for females they were 5211 ug/L and 6606 ug/L respectively. This result was consistent with literature, as most often, men of the same age will have higher zinc levels than females (180). A full breakdown of the difference between sexes for zinc is found in Table 13, below. Iron and vitamin D, however, had no significant difference between sexes.

Table 13: Zinc summary statistics (count, average (arithmetic mean), geometric mean, standard deviation, median, minimum, maximum, 5th percentile, 95th percentile) for 128 blood samples collected during the human biomonitoring project from 2016-2018 stratified by sex

	Zn (ug/L)	
	Males	Females
N	64	64
AVG	5677.20	5276.06
GM (95% CI)	5581.61 (5327.98 – 5847.34)	5211.39 (5010.09 – 5420.80)
Max	7965	7249
Min	3362	2826
Median	5788	5225

SD	1016.87	805.29
5th % (95% CI)	3995.03 (3813.47 - 4185.20)	4233.76 (4070.16 - 4403.80)
95th % (95% CI)	7109.35 (6786.279 - 7447.90)	6606.23 (6351.05 - 6871.66)

No differences in Pb concentrations were found between smokers and non-smokers in either nonparametric or parametric testing. However, literature has identified smoking as a possible route of exposure; smoking has also been related to increased Pb levels in blood (81, 181). As such, no significant correlation between these two variables was unexpected. When stratifying by smoking status, Pb levels were similar among the groups, but generally higher for smokers. Specifically, everything except for the arithmetic means and maximum values are higher in smokers. All results are evident in table 14 below.

Table 14: Pb summary statistics (count, average (arithmetic mean), geometric mean, standard deviation, median, minimum, maximum, 5th percentile, 95th percentile) for 128 blood samples collected during the human biomonitoring project from 2016-2018 stratified by smoking status

	Pb (ug/L)	
	Smokers	Non-smokers
N	64	64
AVG	31.49	31.97
GM (95% CI)	24.14 (20.13 – 28.93)	21.96 (17.63 – 27.35)
Max	96	194
Min	5	3
Median	22	20
SD	23.79	30.72
5th % (95% CI)	8.08 (6.74 – 9.68)	4.87 (3.90 – 6.06)
95th % (95% CI)	81.40 (67.90 – 97.58)	72.74 (58.41 – 90.58)

It is important to note that smoking status was treated as a yes/no binary variable, which was assessed as having smoked within the previous 24 hours to sample collection. This collection method made it straightforward to compare between smokers and non-smokers but did not allow for any analysis looking into the extent of tobacco usage. More specifically, no data on number of cigarettes and or qualifiers smoking level was collected, nor was cotinine, the chemical that is produced in the body after exposure to nicotine, quantified. Thus, it is possible that differences in Pb levels do exist between smokers and non-smokers in the study population but were not found due to the limitation of smoking status being a binary variable, as opposed to categorical and or continuous.

Looking at the nutritional biomarkers, significant differences were found for all three biomarkers. For zinc, and vitamin D, significant differences were found for both nonparametric and parametric testing, while for iron, a significant difference was found only in parametric testing (the only result that differed between nonparametric and parametric testing overall). Average concentrations of all three nutrient biomarkers were higher in the non-smoking group.

The geometric mean for smokers for vitamin D was 7.32 ng/mL compared to 10.11 ng/mL for non-smokers. The results for vitamin D align with those found in literature, which indicate vitamin D levels are lower in smokers (182, 183). The geometric mean for smokers for zinc was 5219 ug/L compared to 5572 ug/L for non-smokers. The relationship between smoking and zinc is not clear in literature since zinc is found in cigarettes (184). For iron, the ferritin geometric mean was 123.2 ug/L for non smokers, compared to 90.6 ug/L for smokers. Literature on smoking and iron levels is inconclusive; some studies have indicated higher levels of iron in smokers as iron is found in cigarettes, while other studies have associated iron deficiencies and anemia with smoking status as a result of damage to cells (185-187). Hence, the result from this data set indicates smoking was associated with lower levels of iron and aligned with some literature.

When it comes to exploring the difference between people who consumed alcohol in the 24 hours prior to sample collection vs those who did not, there were no difference in means for any nutritional biomarker and or Pb.

2.3.7 Linear Regression

Using the results determined in the above sections, a multi-linear regression model using a forward stepwise regression approach was developed using SPSS. A forward stepwise approach was selected as there were many potential predictor variables. Using transformed Pb data as the dependent variable, each of the following independent variables was considered in the model: age, BMI, sex, smoking status, alcohol status, zinc, iron, and vitamin D (transformed data was used for all biomarker concentrations so a more normal distribution was followed and used in analysis). Statistical analysis determined two possible models:

$Model\ 1: Y_i = \beta_0 + \beta_1 X_{1i} + \varepsilon_i;$ $\quad i = 1, \ldots, n$

$Model\ 2: Y_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \varepsilon_i;$ $\quad i = 1, \ldots, n$

Y_i is the observed log outcome value for blood Pb,

X_{1i} is the observed predictor value for Age (in number of years),

X_{2i} is the observed predictor value for smoking status (binary, 0 = no, 1 = yes)

β_0 is the fixed unknown intercept,

β_1 is the fixed unknown regression coefficient of age,

β_2 is the fixed unknown regression coefficient of smoking status, and

ε_i is the unknown random noise where $\varepsilon_i \overset{iid}{\sim} N(0, \sigma^2)$ and for any $i \neq j,\ (X_i, Y_i) \perp (X_j, Y_j)$ and $\varepsilon_i \perp X_1, X_2, X_3$

To determine which model would be best to use, a comparison of AIC values was done. AIC values are a set of model section criteria that is used in the selection of a best predictive model (188). For Model 1, AIC = 56.53 and Model 2, AIC = 53.60. The AIC for Model 2 was slightly higher, which meant Model 2 was better at explaining blood Pb values. Next, a comparison of the R^2 values was also conducted. For Model 1, R^2 = 0.25, and for Model 2, R^2 = 0.28. Since Model 2 had a higher R^2 value, this meant it could explain the most amount of the variance in blood Pb levels, thus determining it as the best model. However, R^2 will always increase with the number of predictor variables added to a model, and thus the inclusion of smoking must be justified. Thus, Model 2 was selected as the model for best-explaining blood Pb values including age, and smoking status as explanatory variables. Model 2 then was:

$$Pb_i = \beta_0 + \beta_1 Age_i + \beta_2 SMK_i + \varepsilon_i; \qquad i = 1, \ldots, 108$$

Where:

Pb_i is the observed log outcome value for blood Pb level,
Age_{1i} is the observed predictor value for Age (in number of years),
SMK_i is the observed predictor value for smoking status in the 24 hours prior to sample collection (binary, 0 = no, 1 = yes)
β_0 is the fixed unknown intercept,
β_1 is the fixed unknown regression coefficient of age
β_2 is the fixed unknown regression coefficient of smoking status
ε_i is the unknown random noise where $\varepsilon_i \overset{iid}{\sim} N(0, \sigma^2)$ and for any $i \neq j$, $(X_i, Y_i) \perp (X_j, Y_j)$ and $\varepsilon_i \perp X_1, X_2$

The model above incorporates all predictor variables from a total of 108 samples. While there was a total of 128 samples, BMI was the variable with the lowest count, and thus, the model only considers samples for which there was complete data. However, BMI did not have any correlation with Pb levels in prior testing, nor was it included in any of the models. As a result, by excluding BMI in the variable list, and running a second stepwise regression, more data points were considered. Specifically, the next lowest variable count was 120, which came from Age (a variable that has been determined to be significant in correlation testing). When BMI was excluded, and 120 samples were considered, different models were presented. As a result of running a forward stepwise regression, four possible models existed:

$Model\ 1$: $Y_i = \beta_0 + \beta_1 X_{1i} + \varepsilon_i; \qquad i = 1, \ldots, n$
$Model\ 2$: $Y_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \varepsilon_i; \qquad i = 1, \ldots, n$
$Model\ 3$: $Y_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \beta_3 X_{3i} + \varepsilon_i; \qquad i = 1, \ldots, n$
$Model\ 4$: $Y_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \beta_3 X_{3i} + \beta_4 X_{4i} + \varepsilon_i; \qquad i = 1, \ldots, n$
Y_i is the observed log outcome value for blood Pb,
X_{1i} is the observed predictor value for Age (in number of years),
X_{2i} is the observed predictor value for sex (binary, 0 = female, 1 = male)
X_{3i} is the observed predictor value for smoking status (binary, 0 = no, 1 = yes)
X_{4i} is the observed predictor continuous log value for zinc level
β_0 is the fixed unknown intercept,
β_1 is the fixed unknown regression coefficient of age,
β_2 is the fixed unknown regression coefficient of sex,
β_3 is the fixed unknown regression coefficient of smoking status,
β_4 is the fixed unknown regression coefficient of zinc, and
ε_i is the unknown random noise where $\varepsilon_i \overset{iid}{\sim} N(0, \sigma^2)$ and for any $i \neq j$, $(X_i, Y_i) \perp (X_j, Y_j)$ and $\varepsilon_i \perp X_1, X_2, X_3$

Model 1 here was the same as before, with Age being the only predictor. However, Model 2 now included a different variable with age, and sex instead of smoking status. Smoking status reappears and was included in Model 3, and zinc was introduced with the three previous variables for the fourth Model. A breakdown of AIC and R^2 values for the four models is found below, in Table 15.

Table 15: Regression Models with AIC and R^2 value comparisons

Model Number	Variables	AIC	R^2	F	Significance
1	Age	56.53	0.28	45.61	5.61E-10
2	Age, Sex	52.78	0.31	26.32	3.54E-10
3	Age, Sex, Smoking	49.01	0.33	19.60	2.32E-10
4	Age, Sex, Smoking, Zinc	48.60	0.36	16.17	1.49E-10

All these models were determined using the same stepwise regression in SPSS. Once models were identified, AIC and R^2 values were determined by running each model sequentially. All models had statistically significant R^2 values. Once again, like the models which also considered BMI, the model with the most predictor variables (Model 4) has the highest R^2 value, and the lowest AIC value, which as previously mentioned, are expected as more terms will increase the R^2 value and assist in explaining the predictor variable better (lower AIC). Therefore, when using the count as 120, by not including BMI in the list of possible variables, Model 4 would be best at explaining blood Pb values. The final model was:

$$\boldsymbol{Pb_i = \beta_0 + \beta_1 Age_{1i} + \beta_2 Sex_{2i} + \beta_3 SMK_{3i} + \beta_4 Zn_{4i} + \varepsilon_i}; \qquad \boldsymbol{i = 1, \ldots, 120}$$

Pb_i is the observed log outcome value for blood Pb,
Age_{1i} is the observed predictor value for Age (in number of years),
Sex_{2i} is the observed predictor value for sex (binary, 0 = female, 1 = male)
SMK_{3i} is the observed predictor value for smoking status (binary, 0 = no, 1 = yes)
Zn_{4i} is the observed predictor continuous log value for zinc level
β_0 is the fixed unknown intercept,
β_1 is the fixed unknown regression coefficient of age,
β_2 is the fixed unknown regression coefficient of sex,
β_3 is the fixed unknown regression coefficient of smoking status,
β_4 is the fixed unknown regression coefficient of zinc, and
ε_i is the unknown random noise where $\varepsilon_i \overset{iid}{\sim} N(0, \sigma^2)$ and for any $i \neq j$, $(X_i, Y_i) \perp (X_j, Y_j)$ and $\varepsilon_i \perp X_1, X_2, X_3$

Exploring this model further, the standardized beta coefficients, t values, and significance values are laid out in Table 16 below. At an alpha of 0.05, the beta coefficient was significant for all four variables.

Table 16: Standardized coefficient values for model 4 with logPb as dependent variable

Variable	Beta	t	Significance
(Constant)	N/A	-1.44	0.15
Age	0.50	6.30	5.49E-9
Sex	0.16	2.15	0.03
Smoking	0.18	2.40	0.02
logZn	0.16	2.07	0.04

This model aligned more closely with the previous results explored. Specifically, a significant difference in mean Pb concentration values was found between sexes in the data set. Further, age was significantly correlated with Pb as well. Additionally, a significant correlation between Pb and zinc values was also found. All these variables were included in the final model.

While no significant difference in Pb concentrations was found between smoking status, the inclusion of smoking status in the model was supported by two other reasons. Firstly, prior literature had established smoking as an exposure pathway to increased Pb levels, and therefore a known confounder (81, 181). Secondly, ongoing work within the research group, including the use of the entire dataset from the human biomonitoring project in the NWT, as well as another in Old Crow, Yukon, had indicated smoking levels may be associated with increased Pb levels.

Interestingly, even though vitamin D levels were significantly correlated to Pb values in both nonparametric and parametric testing, the inclusion of vitamin D as a predictor variable did not make the model stronger. When doing a separate regression after adding in vitamin D to the model above, containing four explanatory variables, the AIC value raised slightly to 48.664. Thus, the inclusion of vitamin D only complicated the model further and raised the AIC and thus did not assist in better explaining and predicting Pb levels. The explanation on why vitamin D was not included in the final model likely comes from strong, positive correlation between vitamin D and age, which had the highest correlation coefficient in both nonparametric and parametric testing. As such, the positive correlation between Pb and vitamin D was likely drive by the role of age. Contrasting this to zinc, which was included in the model, the correlation coefficients between zinc and age were much closer to zero than those of vitamin D and age (0.28 and 0.25 vs 0.62 and 0.62). In comparison, the correlation coefficient with age was more than double with vitamin D than zinc.

Additionally, a regression of a model with only the variables that had significant nonparametric and parametric tests with Pb (age, vitamin D, zinc, sex) was run and had an AIC of 52.05. Once again, this AIC value was higher than that of the final model, thus meaning it was not as good at explaining Pb values as the final model was. This also further illustrates the importance of including smoking status in the final model, as the AIC was much higher when smoking was not included in the model.

2.4 Conclusion

The objectives of this were to evaluate relationships between various nutrients and elements and Pb levels by determining the associations between various macro-element, micro-element, and vitamin biomarker data and comparing them to the level of the Pb biomarker. Using previously gathered data, and additional chemical analysis of further biomarkers, these objectives were met. Specifically, it was determined that relationships exist between blood Pb and blood zinc and vitamin D and elements. Further research on concentrations of iron, zinc, and vitamin D levels in blood in Northern populations need to be explored further in literature and are a current literature gap. Current Information that is available mostly focuses on dietary intake as opposed to biomarker concentrations. The consideration of dietary intake of nutrients in this study population would assist in strengthening the understanding of the relationships that exist between Pb, zinc, vitamin D, and iron.

The levels of Pb in biobanked blood samples of the Sahtú were higher than those in both the neighboring Dehcho region and the general Canadian population. Conversely, nutritional biomarker levels were lower than the general Canadian population. Established trends from statistical analysis have determined the relationship between Pb and biomarker levels are contrary to those established in literature. Instead, these results may be indicative of a shared exposure pathway to Pb and other nutrients. As a result, further investigation into possible exposure pathways, including the consumption of traditional food, should occur. Testing of Pb levels in various commonly consumed food, including fish and game animals, and water has occurred, and will be presented in future work.

Overall, using a regression model, four variables were associated with Pb concentrations: age, sex, smoking status in the 24 hours prior to sample collection, and zinc levels. These associations will assist with better understanding the pathways of exposure to Pb in the Sahtú, and with future investigations into Pb exposure within the region by identifying factors of concern and more interest. Further data on smoking status should be collected and explored, specifically data which would indicate magnitude of smoking status. This would allow to explore the correlations between smoking status and Pb in the community further and determine what impacts magnitude of smoking may have on Pb levels.

3 The development of a Pb exposure survey for Northern Indigenous Populations in Canada

3.1 Introduction

Exposure assessment is the process by which the characteristics of exposure, such as pathways, and routes of exposure, duration, frequency, and magnitude, are measured and assessed (189, 190). Exposure assessment is used to answer what the sources of exposure are, who is exposed and to what, where, when, and how exposure occurs (191). However, environmental exposures are often hard to assess, and therefore, many tools and methods exist in the process of exposure assessment (189, 190). These methods include both direct methods such as biomonitoring and data collection, such as environmental media sampling, and indirect tools such as the use of surveys (189).

Biomonitoring is a direct method of exposure assessment that is predominantly used to estimate internal dose resulting from external exposures across multiple routes (191). Biomonitoring is the measurement of a chemical in a biological matrix and is done by the collection and subsequent testing of samples, in matrixes such as urine, blood, hair among others (14, 189). While biomonitoring is useful in understanding levels of exposure, it does not provide the necessary information in understanding predominant pathways of exposure (189). Instead, the use of other direct data collection, such as environmental sampling, is better in determining possible pathways of exposure (189). Additionally, the use of surveys, an indirect method of exposure assessment, is needed to acquire information when working with a human population. This information, such as demographics, lifestyle activities, and other factors can then be used to assess possible routes of exposure, and the information collected is then complementary to what has been gathered through direct exposure assessments methods (189). Surveys are also useful in determining the frequency and duration of exposure (189).

Surveys are a method of assessing exposure when no other source of information may be present (192). Surveys can be very effective when looking at specific exposures and assessing existing and known pathways of exposure (192). Surveys can be used at both a large scale, adapted across smaller populations, and become specific (189, 192, 193). Surveys work well paired with biomonitoring and environmental data collection. When these tools are used in tandem with one another, they each target different aspects allowing for a more complete approach to exposure assessment (189). As a result, using several methods and tools to assess exposure will result in additional data assisting with determining more complete routes, methods, and reasons for exposure. While surveys are a very useful tool used in exposure assessment, the development of a survey requires a high level of application (189). At the same time, they must be used to obtain clear information, can be easily applied, and connected to other gathered information while not being too lengthy for a participant (189).

Surveys have been used to assess Pb exposure in various populations and settings, such as in children, pregnant women, and occupational settings (194-196). The use of surveys in context to Pb exposure is beneficial in determining which possible pathways of exposure may be present; Pb has numerous routes of exposure, and the pathways may not often be evident. Questions in health based surveys related to Pb exposure often focus on common exposure pathways, such as Pb pipes, paint, and other commercial uses, as well as symptoms related to chronic Pb exposure (197-199). These types of surveys are used towards developing mitigation techniques at a large scale. Surveys that assess exposure to Pb in the work settings contain questions related to the type of work, and exposure duration (195, 200). These surveys are used to determine which occupations and settings may be at higher risk for Pb exposure. Surveys related to the use of Pb ammunition have been used to assess effects on animals and wildlife (100, 201). Populations living in Northern regions lining in close proximity with their environmental often face different environmental challenges compared to those living in more southern communities.

The Sahtú is a subarctic region located in the Northwest Territories (NWT) of Canada. In July 2021, the population of the Region was 2,668 (6). The Sahtú is comprised of five communities, and 76% of the population is Indigenous, with Dene being the largest ethnicity representing 68.5% of the total population and 90% of the Indigenous population (6). Both Indigenous and non-Indigenous people live in all five of the communities. In Norman Wells, the most populated community a majority of the population (60.9%) is not Indigenous which represents a total of 73% of the non-Indigenous population of the Sahtú (6). Three communities have previously worked with the research teams as part of the human biomonitoring project: Deline (91.6% Indigenous population), Fort Good Hope (91.7% Indigenous population), and Tulita (92.2% Indigenous population) (6). Throughout a human biomonitoring research project between 2016 – 2018, blood and urine samples were collected from these three communities. Data collected on Pb during this project indicated elevated blood levels in the Sahtú population when compared to both the Dehcho Region and national averages (13). Thus, Pb was identified as a contaminant of interest in the Sahtú, warranting further investigation. As the biomonitoring data revealed higher than normal Pb levels within a segment of the population, the application of a survey would be vital in defining the key determinants of exposure and working towards the implementation of future programs to mitigate the exposure.

The objective of this study was to create a survey that will allow future research projects to explore Pb determinants and exposure pathways in Sahtú Dene communities of the Northwest Territories, Canada. This objective was met through a three-step process. Firstly, a survey was developed with questions divided into four sections: socio-demographic status, harvesting practices and food preparation, household Pb exposure, and knowledge on the symptoms of Pb poisoning. Next, feedback was gathered on the survey contents through individual interviews with members of the Sahtú. Lastly, the survey was edited and refined using gathered feedback to create a finalized draft.

3.2 Methods

The process of the creation of the survey occurred in three distinct parts: 1) survey drafting, 2) participant interviews for feedback gathering, and 3) refinement and finalization. The timeline of the project occurred from October 2020 – February 2022.

3.2.1 *Survey Drafting*

The survey drafting process occurred between October 2020 – February 2021. For the drafting of the survey, several sources were used to develop questions. Firstly, questions were included from prior surveys implemented by the research team, specifically from an exposure survey that was used in the Old Crow region of Yukon. Next, questions were included from clinical and subclinical practitioner and or governmental agencies surveys on Pb exposure. Lastly, questions were also specifically developed for the survey based on background and supporting literature, and researcher expertise. The questions on the survey were categorized into four sections: socio-demographic, harvesting practices, food preparation, other Pb exposure determinants, and symptoms of Pb poisoning. Questions on the symptoms of Pb poisoning were included to gauge local awareness of the health hazards associated with chronic Pb exposure and are included in the survey to assist when providing the research to those responsible for interventions and policy making.

Many of the questions drafted for the survey were based on an extensive literature review. Literature included reports from various government organizations (including Health Canada, and the CDC), and various peer-reviewed work, with some specific to Indigenous populations (19, 29, 107, 202, 203). Possible and applicable determinants of exposure were identified and formulated into multiple choice questions to be included in the survey. A large focus on questions specific to the consumption of game birds, and the use of Pb ammunition were included as they had been identified by researchers and supporting literature as a possible determinant of Pb exposure in the region, and prior conversations with people of the community indicated that Pb ammunition may still be used. Further, the research team acquired a previous Pb and game bird exposure survey from the CDC and adapted questions for use (194, 204).

An additional section of the survey, specific to hunters, was also included in the survey. This section was created as an optional section as questions do not apply to those who do not hunt. Instead, this section facilitates more in-depth exploration of topics related to hunting, such as ammunition usage, and storage. In total, six drafts of the survey were developed and edited. From this process, a final survey, ready for feedback gathering from community members, was produced.

3.2.2 *Study population and consent*

The study population for this project included all residents in the Sahtú Region over the age of 18 years old, regardless of their sex, family status, and ethnicity. Participants were required to be able to receive an e-transfer for compensation to partake in interviews.

An information letter detailing the background of the study, involvement in the project, benefits for doing the study, the privacy of information, reporting of the finding, withdrawing from the study, and other details was read to participants before commencement of the interview. Following the information letter, participants were read a consent form, and provided informed oral consent, which was recorded, for proceeding with the interview. Participants were sent the consent form and information letter by email post-discussion if wanted. Participants were made aware that they could ask questions, and/or stop the interview at any point.

3.2.3 *Recruitment*

A digital poster was posted in the various buy and sell groups on Facebook for both Fort Good Hope and Tulita. The poster was posted in both groups twice, once at the beginning of October 2021, with a follow-up post made near the end of October 2021. These Facebook groups are commonly used by people in the communities, and typically have several posts each day. The poster was also published on the page of the Sahtú Renewable Resources Board. These communication methods have been previously used by the research group to gather participants for studies (15). The poster contained information on the background of the study (the development of a study looking at how people in the region are exposed to Pb), the details surrounding the interview, and contact information.

3.2.4 *Compensation*

Once all survey questions were asked to participants, and discussions between participants and researchers finished, the interview was concluded. Participants were then provided with compensation of $100 for their time, which was sent via e-transfer in the following hour.

3.2.5 *Interview Process*

Once the survey was ready for the refinement process, recruitment for the feedback gathering session of the survey began. The purpose of the refinement process was to ensure the survey was easy to understand and complete, while also at the same time applicable to people living in the Sahtú, and appropriate and respectful of Dene populations.

Interested participants reached out to the researchers and scheduled a phone interview with two researchers at a time that was best for them. All interviews were conducted between October – November 2021. Participants were asked to voluntarily provide information on their sex, age, and community of residence. Audio recording was not used to ensure participants were comfortable when talking to researchers alone, and instead verbatim notes were taken throughout all sessions.

Questions and the selectable options were read out to participants. Participants were told they did not have to respond to the question, and instead to provide feedback on the actual questions and options. However, if participants elected to answer the question based on the options provided, their answers were recorded. Follow-up discussion and or questions were asked of interview participants for select survey questions that were deemed to be of relevance to understand Pb exposure in the NWT. After a section of the survey was finished, the discussion questions in Table 17 were asked to participants. Once the first four sections of the survey were complete, participants were asked if they were hunters, and if answered yes, they were asked to provide feedback on the additional hunter section of the survey. Once the survey was completed, and all sections had concluded, a follow-up discussion period with participants began. Further questions were asked, and prompts were used which are outlined in the second part of Table 17 below.

Table 17: Questions and prompts asked during feedback interviews

Questions asked after the completion of each section	1. Are the questions understandable? - Is it easy to understand what the questions mean? - Can you reformulate the question in your own words? - Are there any terms difficult to understand? 2. Are the options of the answers complete? - Would you have replied something else than written here? 3. Are the questions and answers culturally appropriate? - Are there any questions or options that made you uncomfortable? - Is there anything you believe we should modify?
Questions asked after the completion of the final section	1. Are the terms used through the survey familiar to you? - For example, the difference between shot, bullet, ammunition? - Drinking water, tap water, untreated water, reverse osmosis water 2. What do you think about the length and number of questions? 3. Is there any other information you think the survey should include to document the contact with Pb? 4. Are you aware of any contaminated or potentially contaminated site we should document the contact in the survey?

	5. Is there any other information or comment you would like to share with us?

3.2.6 *Survey refinement and finalization*

Between December of 2021 – February 2022, interview feedback was synthesized across interviews, aggregating all suggestions made for an individual survey question, and edits were made to the survey. Post-interview refinements to the survey occurred in several steps. The first step was incorporating straightforward edits and changes to questions based on the received feedback. These edits included rephrasing and clarifying questions or adding additional selectable options. Further, changes were made to ensure language between questions was consistent throughout the survey. The next step was resulting discussion amongst the research team related to questions that received differing feedback from interview participants, or questions where received feedback was different than what the question intended to ask. After this, questions were added and removed to improve the flow of the survey and to ensure questions were asked in the same format between all sections. A final language review of all questions and minor changes to the formatting of the survey occurred as the last step.

3.2.7 *Adaptations due to COVID-19*

As a result of the ongoing COVID-19 pandemic, several changes throughout the survey refinement process occurred. Originally, a focus group (n=10) was planned to be used for feedback gathering. This session would have been audio recorded, and researchers would have been present remotely to communicate with participants and ask follow-up questions, while a local research coordinator would be present in-person to facilitate the gathering. However, to comply with COVID-19 protocols set out by the University of Waterloo on human participation and research as to limit social gatherings, all interviews were conducted by the researchers remotely, over the phone, on an individual basis.

3.2.8 *Assessing Availability of Pb Ammunition*

To determine the usage, consumption, and availability of Pb ammunition in the region, stores in all five communities of the Sahtú were called. The purpose of this task was to determine if Pb ammunition is available to be purchased in the Sahtú. A list of all the stores in the region, hours of operation, and contact information was compiled into a document, and was collected from Google. Businesses that identify as a store, including convenience stores, were included in the list, while businesses that did not identify as a store on Google were not included. Each of the businesses were called during their hours of operations approximately 1-2 hour(s) after opening. After calling each store, a script was used asking to speak to the store owner or manager, and the questions listed in Table 18, below, were asked.

Table 18: Questions and prompts asked during store calls

1. Do you sell lead ammunition? 1.1. If yes, what type? Bullets, shot? 1.1.1. If yes, how much does it cost? 1.2. If no, did you ever sell lead ammunition? 1.2.1. If yes, when did you stop selling? 2. Do you sell non lead ammunition? 2.1. If yes, what type? Steel? 2.1.1. If yes, how much does it cost?

2.2. If no, do you know where ammunition is sold in the community?
3. Do you know if lead ammunition is still being used for hunting?
   3.1. If yes, is it commonly used, or are alternatives more commonly used?
4. Do you know if lead ammunition is being used for any other purposes?
   4.1. If yes, for what? Target shooting?

3.2.9 *Ethics*

Ethics approval was obtained by the University of Waterloo Research Ethics Committee (#42741), and the Aurora Research Institute (#4902). Confidentiality was ensured within interview methods, and feedback from participants and the synthesized document containing all feedback has participant identifiers removed.

3.3 Results and Discussion

3.3.1 *Survey Drafting*

The drafting process of the survey resulted in a preliminary survey with 62 questions in four core sections, and 12 questions in the optional hunter section. The questions on the survey were categorized into four sections: socio-demographic, harvesting practices and food preparation, other Pb exposure determinants, and symptoms of Pb poisoning.

Questions in the socio-demographic portion of the survey were used to determine the characteristics of the people being surveyed. These characteristics include physical factors such as age, sex, weight, and height. Questions on education, job status, and main sources of income were also included. Harvesting practice and food preparation questions were based on specific questions related to the target population (Dene people of the Sahtú) and general consumption patterns. Questions were developed to consider water intake and food consumption. For the question set related to water, questions included asking about the source of drinking water, methods of water collection and treatment, and use of untreated water from lakes, rivers, or snow. Food questions were related to harvesting practices for traditional food. Special focus was placed on hunting using Pb ammunition and consumption of game meat that has been hunted with Pb ammunition, specifically wild birds, with an additional question on Pb jigs or sinkers used for fishing. Aside from questions related to game meat hunted with Pb ammunition, specific questions on food frequency consumption or types of food eaten were not asked, and these had already been assessed through the use of food frequency questionnaire in the human biomonitoring project (13) .

Questions related to other methods of Pb exposure determinants were based on literature external to the human biomonitoring project. Questions were focused on the exposure to common Pb sources, including smoking, medications, and personal care products such as face creams. Other questions included hobbies and activities, including careers that may have higher exposure to Pb. The last set of questions was related to the physical home. These questions asked about age of the home, condition, and renovation history. The purpose of these questions was to determine household contaminants such as Pb water pipes, paint, or wood stoves which are sources of Pb. A few questions on the symptoms of Pb poisoning were included in the survey. These questions were not to indicate or diagnose that a person has Pb poisoning. Instead, these questions were asked to gauge the knowledge of those surveyed on the symptoms of Pb poisoning. The supplementary section for hunters goes more in-depth about hunting practices. Specifically looking at storage, usage, and purchasing of ammunition, and included details such as price and type of ammunition.

The development of questions related to many common pathways of exposure to Pb (such as Pb pipes, paints) from these sources was straightforward as information on Pb poisoning and exposure was readily available since Pb has been a contaminant of concern for decades. This literature was readily available, and several government agencies had human reports or toxicological profiles on Pb (19, 29). However, much of the literature looking at Pb exposure was not within the context of either an Indigenous lifestyle or from the perspective of a rural Northern community, instead focusing on occupational or commonly known sources of exposure (only some of which may be applicable to Northern populations). For example, the Final Human Health State of the Science Report on Pb, a comprehensive document outlining Pb uses, releases, sources, health impacts, and levels in environmental media and concentrations in the general population, did not include results of studies which completed testing in the Territories, nor did the report mention specific pathways of exposure to Indigenous populations (29). Additionally, other research working with Indigenous populations and or Northern populations is often biomonitoring research (49, 50, 62). As such, literature and other Pb surveys was not always applicable, or appropriate to ask on a survey for people living in the Sahtú. Questions needed to be developed with a different cultural perspective, and thus could only use limited supporting literature, on exposure pathways that are specific to this audience. As a result, the creation of an exposure survey that is comprehensive, applicable, and appropriate to a Northern, rural Indigenous population was a challenging process.

The first difficulty with the making of the survey was ensuring it was both comprehensive, but at the same time relevant to people living in the Sahtú. For example, while it was important to consider all the possible routes of exposure, a balance between the comprehensiveness versus the length and relevance of the survey needed to happen; it was important to ensure the survey would not be too long, as the longer a survey will be, the less likely to obtain quality data (205). Including all Pb, determinants was important so that all possible routes of exposure were considered. At the same time, making the survey applicable was important to ensure the survey is feasible to do within a certain time frame, and was neither too long nor difficult to ensure a large study sample.

Since much of the literature used to develop the exposure survey did not incorporate an Indigenous and or Northern perspective, many new questions needed to be drafted for the survey. For the most part, the expertise of the research team, as well as prior work in the community, was often used in the development of questions. These topics included the use of Pb ammunition (especially in wild game birds), and traditional food consumption. Literature on the use of Pb ammunition was used to develop some questions, but the supplementary hunter section was drafted in response to the need for additional questions by a research partner during the survey development process. Additionally, questions specific to the consumption of game birds were added to a large extent to the survey, as the consumption of game birds harvested with Pb ammunition was identified as the leading possible source of increased exposure. Questions on other traditional food consumption were incorporated from food frequency questionnaires used throughout other human biomonitoring projects in Northern Canada (13-15, 206).

Another important consideration when drafting the survey was to ensure questions were culturally appropriate. This was an extremely important consideration as questions needed to be respectful, and had to follow the guidelines set by the Tri-Council on research involving Indigenous populations (207). The relationship between researchers and the community had been developing through previous projects, and prior survey data has shown that there is trust between researchers and the community (13-15). As a result, some determinants were omitted from being included in the survey to ensure the survey remains respectful. For example, a common determinant to Pb exposure is through the consumption of non-food items such as paint, plaster, dirt, and or clay (29, 43). This question was one that was asked by the CDC in prior Pb surveys and identified as a possible route of exposure to Pb in children (194, 202). However, this question would not be appropriate to ask Indigenous audiences for several reasons. Indigenous food sovereignty, including the consumption of traditional food, and food insecurity are ongoing issues Indigenous populations face, partnered with the discriminatory and racist attitudes that have pervaded Canada's colonial history with Indigenous populations, asking a question on the consumption of non-food items may seem ill-intended (125, 208-211). As such, even though this question has been used to assess Pb exposure in the past surveys, it was deemed inappropriate to ask in this context, and omitted from the survey by researchers. Other questions, for example, related to exposure via household or domestic animals were not included in the survey, even though they have previously been identified as potential exposure pathways. This is both a further example of ensuring cultural sensitivity when drafting the survey, as Canada's colonial history with Indigenous populations has resulted in the discussion surrounding pets, domesticated and or companion animals to be one that must be approached with cultural sensitivity.

It was also important to ensure questions were appropriate specifically to Dene people, the largest population of Indigenous people in the Sahtú. For example, all questions were evaluated according to their compatibility with Dene laws, and other principles and values that outline Dene culture and way of life (212, 213). Dene laws are an important part of the history and traditions of Dene people and represent guiding values and principles that Dene people live by, including the people of the Sahtú (11, 214, 215). A breakdown of Dene Laws is available in Table 19. Questions that would insinuate any divergence from traditions or Dene laws were not included in the survey during the development stage, and further conversations between researchers occurred post-interviews to further assess questions that should not be included. An example was the removal of a question that asked what was done with meat that was removed from the wound channel, as discarding the meat and not using it in any form would be wasteful and could be contrary to Dene values. The Dene laws also relate to the translation of knowledge that occurs between the research team and Indigenous People. Specifically, the importance of listening, oral traditions of Indigenous populations, and storytelling as methods of communicating information are all important in the notion of feedback gathering between participants and researchers. As a result, the values were important both during survey creation and finalization, as well as during the refinement stage.

Table 19: Outline of Dene Laws (213)

Share what you have
Help each other
Love each other as much as possible
Be respectful of elders & everything around you
Pass on the teachings
Be happy at all times
Sleep at night and work during the day
Be polite and don't argue with others
Young girls and boys should behave respectfully

Another important factor related to the types of questions asked on the survey is researcher and community trust. University researchers are one of the top trusted sources of information on messages related to contaminants in the environment and traditional foods in the Sahtú (17). Thus, the survey needed to be framed so that the inclusion of a determinant should not result in actions to attempt to mitigate or eliminate the possible determinant from community members. Questions that may have resulted in community concern and or actions were not included in the survey (such as those related to household domestic animals and pets, which were mentioned above). However, questions on important determinants (deemed so by both previous work in the community and literature), such as the consumption of traditional food were included, even if the intention of the research team was not to limit the consumption of traditional food. As such, an information statement prior to the beginning of the survey was included and uses language that indicates the survey is assessing pathways that *may* result in elevated Pb levels (as opposed to using definitive language such as *will* result in elevated Pb levels). Additionally, questions related to symptoms of Pb poisoning in section D, a further information statement was included to indicate the questions are not used for diagnosis purposes nor that if a person has said symptoms, that they have Pb poisoning.

Overall, throughout the survey development process, many considerations needed to be made. As a result, the survey that was prepared and used for the refinement stage was applied to the Dene people of the Sahtú and contained a comprehensive list of determinants of exposure to Pb.

3.3.2 *Survey interviews*

A total of seven individuals reached out to participate in the study. After three attempts, a participant was unable to connect with the researchers to complete the interviews, resulting in six total interviews completed. All participants provided their age, sex, and community. Participant ages ranged from 29 – 59 years old, with four participants identifying as women and two as men, and two located in Tulita, with four located in Fort Good Hope. Interviews ran between October 14th to November 3rd, 2021. Interviews were scheduled for two hours during any time of day that was most convenient for participants. The earliest an interview ran was from 10:00 to 12:00 MT (12:00 to 14:00 ET) and latest was from 18:00 – 20:00 MT (20:00 to 22:00 ET). All interviews were conducted over the phone. The shortest interview was 42 minutes in length, and the longest 1:45.

All six participants provided answers to the first four sections of the survey; five participants provided feedback on all questions during the allotted time. Two participants identified as hunters and provided information on the supplemental hunter section during the two-hour time frame; one hunter provided feedback on all questions during the allotted time.

Feedback was received for all questions, including those in the hunter section, by at least one person. A total of 40 pieces of feedback were received in total for the four core sections of the survey, of which 30 were unique (indicating that only one participant had mentioned that change or comment). 35/62 (56.5%) questions had feedback indicating no change was needed while 27/62 (43.5%) questions had feedback with comments or recommended changes. Only one piece of feedback was received for 1/12 (8.3%) questions in the optional hunter section. A full breakdown of all the received feedback coded to each question is in presented Appendix C.

The process of virtual discussions and interviews was beneficial for two reasons. The first benefit was, directly receiving feedback to make questions more applicable in the survey. The second benefit was learning more about the culture of people living in the Sahtú and their experiences which then assisted with contextual pieces and a better understanding of how to develop the survey.

The original target for interviews was between eight to 10 participants. This target was not achieved as only six interviews occurred. Limiting factors to have a lower number of interviews than targeted was due to, the low adult population of the two communities (less than 800), the total time commitment of two hours, and needing to use a phone for the interviews. However, even with fewer than expected participants, all questions received feedback and overall were provided with extensive feedback across the interviews, and many edits were made to the survey. Thus, the main goal of the interview process of refining the survey to make it more applicable to the population still occurred, regardless of the number of participants. The process of making the survey more applicable then happened through various methods.

Firstly, the feedback received from the participants was directly applicable to making changes to the survey. Piloting a survey and feedback gathering was an essential element of the development process to ensure clarity and appropriateness of the survey was achieved (216). Several situations arose in which participants indicated clarity of questions, and selectable response options, could be improved. This included making questions more specific (such as adding options of wild plant food, or the inclusion of other water treatment options). Further, participants suggested the standardization of questions as the survey used for the refinement stage had similar questions which were asked in different ways with different options to select. This was an instance that occurred in questions where selectable response options were indefinite adverbs (never, rarely, frequently, etc.), as questions in different parts of the survey, and between the general and hunter survey, had a different list of adverbs to select from. Other comments and refinements include changes to question phrasing and wording; suggestions for changes arose when question-wording was either complex, unclear, or contained needless words (such as changing the term wild game bird to just game bird).

Through the follow-up discussions after each section, and after the end of the survey, the overall feeling of the survey, and perceived reception of the survey were further assessed. Specifically, determining if questions were appropriate to ask and if community members would be willing to answer the questions; participants were asked if questions were appropriate, and if any words needed to be changed as a result. Participants indicated no language was inappropriate, or questions that were uncomfortable to answer. Additionally, the length of time and number of questions on the survey were gauged throughout the interview process, and feedback indicated the length of the survey and time commitment were accurate and suitable. Undue burden is necessary to avoid, as this would lead to boredom and likely inaccurate information (189).

Next, another subset of edits needing to be made on the survey was identified by piloting the survey and asking the questions to participants. Since interviews were done over the phone, participants did not have access to a copy of the survey. As such, questions and options had to be read to participants. This process, and the repetition of the process throughout several surveys, allowed for existing mistakes to the surface when asking the questions. This included realizing questions were repetitive, noticing spelling or grammar mistakes, and where options were inconsistent between similar questions. To track the edits that needed to be made, researcher notes were taken alongside the verbatim notes of participants' answers.

Additionally, since questions were read out to participants when a question needed to be repeated and or rephrased to participants, this indicated that the question was not clear, and thus needed to be reworded. If a participant was confused by the language of the question, questions were then worded differently so that participants could answer them. As well, question-wording needed to be adapted based on a person's interpretation of a question. For instance, a question asking about herbal remedies included asking about the use of plant-based traditional medicine. Conversely, the term herbal remedies was interpreted by a participant as referring to cannabis usage. This was not the target of the question, nor was there intention of collecting information on cannabis usage on the survey. Thus, the question needed to become more specific to not allow there to be room for interpretation, and the refinement of the language of the question was necessary. These edits were crucial as during the future application and implementation of the survey, it will not be possible to explain every option and question in detail, as the survey will be implemented digitally, and researchers will not be present, and thus, they survey must be clear to all participants (205, 217). While the survey has gone through many drafts before the interview stage, several errors (or questions that could be interpreted) were missed, and thus proceeding with interviews allowed for the errors to be rectified.

Interviewing participants of the Sahtú assisted with providing a better context to how questions need to be applied to this specific population. Having the opportunity to speak with people who directly live in the region was very beneficial as it assisted with the context necessary throughout the writing, not only of the survey but supplementary work as well as it helps in understanding the perspective of someone living in a Northern community. For example, some participants spoke about their experiences and relationships with the land surrounding them, and the importance of things such as flowing water, and wildlife, for their identity and way of living. The interviews were then used in a qualitative way to collect data on things such as the attitudes and experiences towards the survey, which were beneficial to better understand the research population (218).

While literature may outline the difficulties of living in Northern communities and the differences compared to more southern communities, a community research approach is more effective at understanding the challenges of a specific population. As such, being able to speak to somebody who lives in the Sahtú about their life and how things were different allows for a reflective process that is different what would be gained from reading literature. Though this part of the interviews did not provide direct edits that can be made on the survey, they do assist the understanding and context pieces that were apparent in the survey. As traveling was limited due to COVID-19, interviews were a good method towards developing a better background and context; the interviews assist in learning and understanding key components vicariously through people who were currently living there.

Further, having the ability to speak to people from the region allowed asking questions that were specific to the Sahtú, to learn more about the community. These small interactions were very insightful, and connections allow the interviews to run better while gathering contextual background information. It was during these conversations that Dene laws were also mentioned, which were an important guiding principle for the finalization process. Of course, while this topic may have come up during literature review, this was brought up quickly in the interview and lead to a higher understanding of the population by indicating the personal importance. Specifically, when Dene laws were brought up in interviews, it was connected to the concept of sharing experiences, which was what was happening during the interview process. Therefore, these interviews allow the capturing of the emotion and thinking behind several topics which is not often elaborated in literature and previous works.

3.3.3 *Survey refinement and finalization*

The process of incorporating feedback and making edits to the survey was iterative. Throughout this finalization process, a total of 120 edits were made to the survey. Edits were made to 66/74 questions between all sections of the survey, including the optional hunter section.

Overall, 16/66 questions had one edit made, 40/66 two edits, and 8/66 questions three edits. Specific changes to questions included: 35 questions had prompts added (e.g., please specify, please circle, etc.), 35 questions had changed to their selectable response options, 30 questions had grammar changes and or were reworded, four moved within their section, three questions were added, two questions were deleted, and one changed format. As a result, this yielded a finalized survey consisting of 75 questions, 63 questions in the first four sections of the survey, and the supplementary hunter section with 12 questions.

While all information gathered during the refinement stage was valuable, not all pieces of feedback could be implemented. Of the 40 pieces of feedback received, seven were not incorporated as edits to the survey. Most of the pieces of feedback that were not implemented were changes to questions which use standardized language (for example, clarifying the term self-employment which is the recognized and governmental term for an individual who works independently) or suggestions to remove and or change standard demographic questions such as those related to sex, height, and weight. Additionally, other feedback that was not included was feedback which would make the survey too long. For example, a participant suggested asking questions related to hunting practices and the use of Pb ammunition based on season, and type of gun. Separating hunting and Pb ammunition questions by additional factors such as rifle, ammunition type, and season, would complicate the survey, and extend the number of questions. As such, to ensure the survey remains applicable to a large portion of community members and avoiding the concept of undue burden on survey-takers during the implementation, this feedback was not used.

Additionally, it is important to acknowledge that throughout the refinement process, the decisions on which feedback would be incorporated was determined by researchers. In general, almost all feedback was incorporated into the survey. However, the decisions made by the research team may be a form of bias, specifically interviewer bias since the survey was developed by the research team, and there was a target in mind of the type feedback wanted to be collected. Informal discussion about the survey, for example sharing stories or personal experiences during the interviews, also occurred and were important pieces of information that could be used for contextual understanding in the survey, as have been expanded on previously. As a result, all points of view were considered valid, even if they were not a clear point of view that aligned with the researchers' interests and thinking and as such, a majority of the feedback was incorporated into the survey.

Next, since the results gathered from the exposure survey will be self-reported with researchers not present, and will be administer as an email survey, it was important to ensure questions were specific and succinct. A nonspecific question will be interpreted differently by people, and the difference in interpretation between participants will make it less likely for that factor to be observed a as predictor of any outcome. As such, based on this and the feedback received by participants, some questions, were made to be more specific. For example, questions related to the consumption of traditional foods now provide examples of traditional foods of various types.

Overall, most of the comments received during the refinement stage were easy to incorporate into the survey. Many comments indicated clarification on questions was needed. This was an important piece as questions need to be as clear as possible since researchers will not be present during future survey implementation. All comments which indicated clarification was necessary were incorporated into the final survey version. Additionally, other questions were simplified, and language was made consistent throughout. Other edits, which required further consideration were discussed amongst the research team. These included comments which were specific, as well as comments which were unclear if edits would be beneficial to the survey. Errors from previous drafts were assessed and corrected. The resulting finalized draft is a complete product that is now ready for implementation to explore routes of exposure to Pb in the Sahtú.

3.3.4 *Store Calling*

A total of 10 stores were classified as potentially selling ammunition in the region and compiled into a list. Using this list, each store was called in January 2022, to assess availability of Pb ammunition. Calls were connected to nine stores, and discussions with store managers and/or owners happened at eight stores. Communication with store managers, including their willingness to response and knowledge of products varied from store to store. Five stores total currently sold ammunition, three of which currently sold Pb ammunition, while the other two used to sell Pb ammunition in the past. No patterns existed between store type, or community regarding the availability of Pb ammunition, however, at least one type Pb ammunition (shotgun shells, bullets, or shot) was available for purchase from at least one store in the three communities from which biomonitoring data was collected (Deline, Fort Good Hope, and Tulita). Cost of ammunition varied depending on gun type, and only one store indicated that Pb ammunition was more expensive than alternatives. These results align with prior accounts communicated with the research team, which indicated that the availability of Pb ammunition may differ from community to community, and thus indicated the importance of the inclusion of questions related to Pb ammunition and hunting on the survey.

3.4 Conclusion

The objectives of this study have been met. A survey tool was created through an entire process designed to make the survey appliable to populations of the Sahtú and can be used to determine Pb exposure pathways. All components related to the development, refinement, and finalization of the survey have occurred, and a comprehensive survey containing questions socio-demographic status, harvesting practices and food preparation, household Pb exposure, and symptoms of Pb poisoning, and an additional supplementary individual survey for hunters have been created.

The beginnings of the survey underwent several drafts with the addition and removal of numerous questions over several months. After a final draft was organized, it was refined through individual participant interviews. Once all interviews were conducted, the survey was finalized, and ready for future use. The existence of this survey is extremely significant, as a complete exposure assessment survey for Pb with consideration and focus on an Indigenous Northern population is not evident in literature. The process of the survey creation has yielded a comprehensive product, totaling 63 questions, as well as a 12-question supplementary section for hunters, which will both be critical in assessing routes of exposure to Pb. The survey has been significantly adapted and edited to ensure its application to a Northern and Indigenous population while being inclusive of a wide array of Pb exposure pathways. This information will then be used in conjunction with previously gathered biomonitoring data to determine routes of exposure to Pb causing elevated Pb levels. It is important to note that while much of the work was conducted with the target population in mind, and input was received from the population, the final decisions on the inclusion of content, structure, and overall composition of the survey was made by the researchers. As such, the information gathered during the survey refinement, and subsequently what is presented in the survey may not represent the original contributions and aims of the participants but reflected what researchers considered should be included and assessed through the survey.

On the whole, a comprehensive exposure survey specific to Northern Indigenous populations, and the development of such a survey is a current literature gap. The development, refinement, and finalization of this survey were important pieces towards assessing exposure to Pb for this specific population. The future implementation of the survey will assist with collecting supplementary information, which alongside human biomonitoring, and environmental monitoring data, will ensure a better understanding of the reasons for elevated Pb levels in the Sahtú Northwest Territories, Canada.

4 Thesis conclusions

This thesis project focused on Pb exposure in communities of the Sahtú, NWT by assessing nutrient biomarker concentrations and their relationship to Pb in blood, as well as developing future tools for assessing these elevated levels in the form of a comprehensive exposure survey. The results and work conducted as part of this thesis have directly contributed to a further understanding the levels of Pb, and exposure to Pb in the Sahtú.

This thesis is situated at the intersection of several completed and ongoing projects occurring within the subarctic regions of Canada. Much of the work compiled in this project uses data collected from the human biomonitoring project conducted in the NWT. This project had a direct focus on contaminant monitoring in the NWT, which would lead to supplementary work based on observed levels. From here, based on elevated Pb levels that were observed, additional analysis was set to occur, and further research was necessary. The supplemental analysis of biobanked samples in the region was done as part of a project focusing on food security and climate change in the Canadian North. The original scope of this work was to assess biomarkers in relation to nutritional status. While this work is not directly related to the understanding of food security in the region, the assessment of nutritional status was important in understanding the relationships with Pb. Specifically, the determination of a shared pathway of exposure to Pb, and intake of nutrients, likely through the consumption of traditional food hunted with Pb ammunition. Additionally, the development of an exposure survey to assess determinants of Pb exposure was part of a larger and ongoing project assessing Pb exposure in the Sahtú. The survey is a major part of this project, which also contains a synthesis report, environmental, and food sampling. As such, the combination of many projects and pieces of prior, existing, and ongoing research have resulted in a thesis project that is multi-faceted and geared towards assessing Pb levels and exposures in the Sahtú.

4.1 Key Findings

In the first chapter, statistical analysis between demographic information, various biomarkers, and Pb blood levels occurred. The results gathered indicated that age and sex and smoking status, all were associated with blood Pb levels. Specifically, older people, men, and smokers, all had higher levels of blood Pb than their counterparts (younger people, women, and those who do not smoke). Smoking, as previously mentioned, is a known cause of increased Pb exposure. The exploration on why differences in Pb levels exist between age and sex needs to be further examined. Additionally, positive correlations between zinc and Pb, and vitamin D and Pb, were found meaning that both levels of Pb and zinc/vitamin D increase together. These associations, unlike those of age, sex, and smoking status, were contrary to what was found in literature. These slightly net positive correlations may be indicative of a shared exposure pathway exists between the intake of nutrients and vitamins, and exposure to Pb. The determination of this shared pathway needs to be further investigated. Specifically, the consumption of traditional food, which are higher in nutrients and vitamins compared to market foods, needs to be assessed to determine if traditional food consumption is a cause for increased Pb levels compared to available and affordable market foods. Incorporating all factors, a regression model containing age, sex, smoking status, and zinc, was developed, which can be used in explaining Pb levels in the population.

Chapter two focused on collecting information on possible Pb exposure pathways through the development and feedback gathering of an individual questionnaire, containing questions on socio-demographic status, harvesting practices and food preparation, household Pb exposure. An additional section on the symptoms of Pb poisoning is used to gauge local understanding on the impacts of Pb. Extensive literature review, researcher expertise, and interviews with community members all contributed to the development of the exposure survey. This process resulted in a survey adapted to the perspective of subarctic Indigenous populations and their exposure to Pb. Overall, through an extensive development of drafting and refinement process, a survey was finalized with 63 questions in four core sections and an additional 12 questions as an optional section for hunters.

The two chapters present factors that underpin the elevated Pb levels observed among participants in the Sahtú region. While the chapters have very different results and work completed, together they can be used to better understand trends related to nutrients and vitamins and Pb, intake sources, and exposure methods of Pb to people living in the Sahtú. The connection between these two chapters exists beyond the fact that they are both additional works completed on Pb exposure in the Sahtú. Instead, these two chapters are applied to tackle the understanding of sources of exposure to Pb, and the future development of a Pb monitoring program in the region. Additionally, the research generated directly addresses community concerns, who have expressed concern in identifying why Pb levels are high and methods in reducing Pb concentrations in the future.

The results of this research explore the correlation between nutrient biomarkers and Pb levels and work towards the future implementation of an in-depth exposure survey on Pb to assess the reasons behind elevated levels in the blood. The results have indicated that exposures in the community are present, and the determinants of exposure may not be those traditionally associated with elevated Pb levels. This work continues to build the foundation for future projects, and active work towards identifying key exposure pathways. However, while much of the work in this thesis has been vital towards future goals, with some questions being answered, changes to the scope, timeline and process of the work have resulted in many pieces remaining unknown.

4.2 Impacts of COVID-19 and Limitations

As a result of the ongoing COVID-19 pandemic, several changes and limitations associated with the completion of this project occurred. The scope of the thesis changed numerous times. The original data collection plan for the project has been adjusted several times, due to required precautions from university ethics and governmental agencies. Specifically, no collection of animal tissues, to determine the use of Pb ammunition, was conducted as part of this work, and was instead collected outside of the scope of the thesis, and results are still being finalized. As such, the assessment of the use of Pb ammunition, and thus the link that may exist between nutritional levels and Pb levels, as explored in section 2, will occur outside the scope of this thesis.

Furthermore, timeline changes and drawbacks resulted in a reduced quantity of biomarkers analyzed. Specifically, calcium was not categorized in relation to Pb levels. While calcium and vitamin D are usually closely related, the relationship between calcium and Pb is uncertain. As a result, statistical analysis would either reinforce the relationships that have already been explored between nutrients and Pb or be different. Either result would indicate further investigation to be necessary.

The largest piece impacted by COVID-19 was the implementation of the survey. The future implementation of the survey will be vital towards assessing which determinants are applicable in the community. The process of developing and finalizing a survey that is specific to a unique population was both challenging and fulfilling but feels incomplete without implementation. As a result, the implementation of the survey would result in this piece being complete. However, once again, delays caused by the pandemic meant that the survey would not be implemented in time to be included in the thesis. Overall, the implementation of the survey would have resulted in additional connection between the two chapters presented in the thesis. While the two chapters are connected in the broader sense as they both relate to the common topic of Pb exposure, statistical analysis of exposure pathways as assessed by the survey and relating them to both biomarker and Pb levels from biomonitoring data, would provide a much larger idea on the causes of elevated Pb levels. The connection between the two pieces would have made the work in the thesis more cohesive and presented the bigger picture from start to finish.

4.3 Next steps

Statistical analysis of nutrient concentrations and comparisons of Pb values is the preliminary step in a further Pb investigation in the community. Even though some correlations were found, these are not fully indicative of the routes of exposure to Pb. The resulting net positive relationships between Pb and nutrient biomarkers, as opposed to the negative ones found in literature need to be further explored. More specifically, the causes resulting in a positive relationship. Ongoing work exploring Pb levels in environmental media such as water, as well as food sources (including fish, and game animals) will assist in strengthening conclusions. Research into the use of Pb ammunition in the community (as assessed through the survey) and Pb levels in hunter shot birds (both in meat and fragments of Pb ammunition) will additionally support the notion of a shared exposure pathway. Connection of the results gleaned from this thesis, alongside other data was collected in conjunction with this work, should be connected to the data available in both the Yukon, and Dehcho regions. As a result, a comparison between the data, to determine if trends exist, should be completed, and may assist with identifying possible pathways of exposure. Furthermore, information collected from the FFQ could be used in conjunction with Pb data to determine if trends exist.

While the implementation of the survey and subsequent results will provide additional data and generate further correlations with Pb values, other considerations and research into exposures which could not have yet been studied, nor could be included in the survey, must occur. For example, exposure to Pb from aviation fuel and airplanes flying in the communities. This would include distance of homes from airports, flight paths (including if they fly over the communities directly and or if communities are downwind of the airport) of airplanes and determining if aviation fuel containing Pb is used in airplanes that service the airport. As well, how, and where fuel might be stored. Other factors that should be considered include data collection to determine composition of soil, and house dust. These medias may present an exposure pathway that have not presently been explored, and the magnitude of their effect cannot be measured via the survey. An additional pathway of exposure which was identified of interest during research was the disposal of car batteries. More research on how, and where car batteries are stored and disposed of, including their proximity to water bodies, should be conducted.

Results and work from this thesis have been presented to the scientific community (through conferences and presentations) and most importantly, will be presented to communities as results are returned, and information is shared with community members. While some drawbacks have resulted in the scope and the work presented in the thesis to be different than expected the work that has been completed was still widely applicable. In particular, nutrients and Pb levels have been explored and correlations have been found, as well as a regression model has been created. Moreover, a survey ready for implementation has been created that has been adapted to be specific to the Indigenous groups of the Sahtú and assessing their Pb exposure. Thus, overall, the relationships between nutrients and Pb data were explored, and a survey examining Pb exposure pathways that resulted in elevated blood of people in the Sahtú Region of the NWT Canada was created.

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Appendices

Appendix A: Mean differences test statistics

Table 20: Nonparametric (Mann-Whitney) and Parametric (independent samples t-test) testing statistics for mean differences

Continuous Variable	Categorical Variable	Nonparametric testing	Parametric testing
Pb	Sex	**U = 1447.00, p = 6.1E-3, n = 64, 63**	**t = -2.94, p = 3.9E-3, d.f. = 125**
	Smoking Status	U = 2174.00, p = 0.446, n = 63, 64	t = -0.91, p = 0.365, d.f. = 125
	Alcohol Consumption	U = 1241.00, p = 0.72, n = 109, 18	t = -1.843, p = 0.068, d.f. = 125
Vitamin D	Sex	U = 2012.00, p = 0.985, n = 64, 63	t = 0.185, p = 0.854, d.f. = 125
	Smoking Status	**U = 1342.0, p = 1.1E-3, n = 64, 63**	**t = 3.42, p = 8.5E-4, d.f. = 125**
	Alcohol Consumption	U = 823.50, p = 0.276, n = 109, 18	t = 1.311, p = 0.192, d.f. = 125
Zinc	Sex	**U = 1491.00, p = 8.0E-3, n = 64, 64**	**t = -2.098, p = 3.8E-2, d.f. = 126**
	Smoking Status	U = 1562.0, p = 2.1E-2, n = 64, 64	**t = 2.10, p = 3.9E-2, d.f. = 126**
	Alcohol Consumption	U = 1183.00, p = 0.186, n = 110, 18	t = -0.652, p = 0.516, d.f. = 126
Iron	Sex	U = 2038.00, p = 0.794, n = 64, 63	t = -0.484, p = 0.692, d.f. = 124
	Smoking Status	U = 1639.00, p = 0.92, n = 62, 64	**t = 2.12, p = 3.5E-2, d.f. = 124**
	Alcohol Consumption	U = 846.00, p = 0.380, n = 108, 18	t = 0.231, p = 0.817, d.f. = 124

*Bolded indicate significant difference

Appendix B: Finalized Exposure Survey Post Refinement

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Lead exposure survey

Lead is a heavy metal that can be found in the environment, but its concentration can be enriched from industrial sources. This project investigates how people might be exposed to lead. and will help identify how people might reduce their exposure to lead.

This survey includes 63 questions and should take about 45 minutes to complete. The questions are separated into 4 sections:

a) socio-demographic questionnaire
b) harvesting practices and food preparation
c) other lead exposure determinants
d) symptoms of lead poisoning

You can ask for help from a research team member at any time.

Participant ID:

ID: ____________________

Part A: Socio-Demographic Questions

1. How did you hear about the project? (*Circle one*):
    a) Posters in town
    b) Information on Facebook
    c) Phone call from the local study coordinator
    d) From a friend or relative
    e) I prefer not to say
    f) Other: ____

2. What is your sex? (*Circle one*):
    a) Man
    b) Woman
    c) Other, please specify: __________________________________
    d) I prefer not to say

<u>For WOMEN only *(circle applicable)*</u>:

3. Currently pregnant:	a) Yes	b) No	c) I prefer not to say
4. Currently breastfeeding:	a) Yes	b) No	c) I prefer not to say

5. How old are you (in years)?
   Age: ____________ I prefer not to say □

6. What is your weight? (Please mention the unit: kg/pounds):
   Weight: _________________________
   I don't know □
   I prefer not to say □

7. What is your height? (Please mention the unit: meter/feet):
   Height: _________________________
   I don't know □
   I prefer not to say □

8. What is your marital status? (*Circle one*):
    a) Married
    b) Common-law
    c) Widowed
    d) Separated
    e) Divorced
    f) Single
    g) I prefer not to say
    h) Other. Please specify: _______________________

9. What is the highest level of formal schooling you have completed? (*Circle one*):
    a) No formal education or some elementary school. Specify grade: _________
    b) Elementary school completed or some high school. Specify grade: _________

c) High school diploma or high school equivalency certificate
d) Some postsecondary education
e) Diploma/certificate from trade or vocational school
f) Diploma/certificate from community college or CEGEP
g) University Degree or diploma (undergraduate)
h) University Degree (graduate studies, master, or doctorate)
i) I prefer not to say
j) Other, please specify: ______________________________________

10. How many persons (adults and children), including yourself, live in your household this month?
    Number of persons: ______________ I prefer not to say □

11. How many children, aged less than 18, live in your household this month?
    Number of children: ______________ I prefer not to say □

12. Are you currently employed? *(Circle one):*
    a) Yes, full time (at least 35 hours/week)
    b) Yes, part time (less than 35 hours/week)
    c) Retired
    d) No, laid off or temporarily unemployed
    e) No, unemployed
    f) I prefer not to say

13. What is your main employment or source of income? *(Circle one):*
    a) Wages/salary/self-employment - FULL TIME (at least 35 hours/week)
    b) Wages/salary/self-employment - PART TIME (less than 35 hours/week)
    c) Pension/seniors benefits
    d) Social assistance
    e) Worker's compensation/employment insurance
    f) Family care
    g) Traditional economy. Please specify main activity: _______________________________
    h) Other, please specify____
    i) I prefer not to say

14. Where do you spend most of your awake time? *(Circle one)*:
    a) At home
    b) At work
    c) At school
    d) Other, please specify: ____
    e) It changes between the seasons, please specify: ____
    ____
    ____
    f) I prefer not to say

Part B: Harvesting and Food Preparation

15. What types of water do you use for drinking in your house? (*Select all that apply*):

    a) Tap water
    b) Reverse Osmosis water (from a machine at the store)
    c) Filter station (e.g., at the Yamoga building in FGH)
    d) At home filter (e.g., Brita)
    e) Bottled water
    f) Stream/river
    g) Lake/pond
    h) Ice/snow
    i) Other, please specify: ______________________________
    j) I prefer not to say

16. In the last year, what was your main source of drinking water? *(Circle one):*

    a) Tap water
    b) Reverse Osmosis water (from a machine at the store)
    c) Filter station (e.g., at the Yamoga building in FGH)
    d) At home filter (e.g., Brita)
    e) Bottled water
    f) Stream/river
    g) Lake/pond
    h) Ice/snow
    i) Other, please specify: ______________________________
    j) I prefer not to say

17. How do you receive tap water? *(Circle one)*:

    a) Delivered and stored in a water tank
    b) Municipal pipes
    c) Other: ______________________________
    d) I prefer not to say

18. What types of water do you use for cooking in your home? *(Circle one)*:

    a) Tap water
    b) Reverse Osmosis water (from a machine at the store)
    c) Filter station (e.g., at the Yamoga building in FGH)
    d) At home filter (e.g., Brita)
    e) Bottled water
    f) Stream/river
    g) Lake/pond
    h) Ice/snow
    i) Other, please specify: ______________________________
    j) I prefer not to say

19. In the last year, what main source of water used to cook in your home? *(Circle one)*:

    a) Tap water
    b) Reverse Osmosis water (from a machine at the store)

c) Filter station (e.g., at the Yamoga building in FGH)
d) At home filter (e.g., Brita)
e) Bottled water
f) Stream/river
g) Lake/pond
h) Ice/snow
i) Other, please specify: ___________________________________
j) I prefer not to say

20. Do you treat the water you drink or use to cook in your house (e.g., filters, boil, tablets, softeners)? *(Circle one):*
    a) Yes, please describe: ________________________________
    b) No
    c) I prefer not to say

21. In the last year**,** how often did you drink, or cook with untreated water (this would be water you get directly from the lake, the river, snow, or ice) while at home? *(Circle one)*:
    a) Not at all
    b) Rarely
    c) Sometimes
    d) Often
    e) Very often
    f) All the time
    g) I don't know
    h) I prefer not to say

22. If you drink water from an untreated source, what are the main types of waterbodies you drink from (Please specify lake or river and name which one(s)):

    ____

    ____

    I do not know the waterbody name □   Not applicable □   I prefer not to say □

23. In the past year, did you personally (*select all that apply*):
    a) Hunt or set snares for food
    b) Fish
    c) Collect wild plants (e.g., berry picking, or for traditional medicines)
    d) Plant a garden
    e) Can or jar your own food
    f) None of these
    g) I prefer not to say

24. In the past year, did anyone else in your household (*select all that apply*):
    a) Hunt or set snares for food
    b) Fish
    c) Collect wild plants (e.g., berry picking, or for traditional medicines)

d) Plant a garden
e) Can or jar your own food
f) None of these
g) I prefer not to say
h) Not applicable (participant lives alone)

25. During the past year, did you eat any locally harvested traditional foods? *(Circle one)*:
    a) Yes
    b) Not this year, but I have in the past
    c) No
    d) I prefer not to say

26. During the past year, did you eat any locally harvested game birds (e.g., goose, duck, ptarmigan, grouse, swan, pintail, canvasback, wigeon, etc.)? *(Circle one)*:
    a) Yes. Please specify what birds:____
    b) Not this year, but I have in the past
    c) No
    d) I prefer not to say

27. During the past year, how often did you eat game birds? *(Circle one)*:
    a) Not at all
    b) Rarely
    c) Sometimes
    d) Often
    e) Very often
    f) All the time
    g) I don't know
    h) I prefer not to say

28. This past year, when you ate wild game bird, how was the meat usually prepared (e.g., cooked, smoked, baked, grilled, on a campfire, etc.)?

____

____

I did not eat any game bird in the last year □
I don't know □
I prefer not to say □

29. Do you remove shot-damaged meat before preparing it? *(Circle one)*:
    a) Yes
    b) No
    c) I don't know
    d) I prefer not to say

30. This past year, did you eat bird organs or parts other than meat? If yes, please specify:

____

____

No, I only ate meat from game bird in the last year □
No, I did not eat any game bird in the last year □
I don't know □
I prefer not to say □

31. This past year, if you ate game bird, how were the organs and other parts usually prepared?

____

____

I only ate meat from game bird in the last year □
I did not eat any game bird in the last year □
I don't know □
I prefer not to say □

32. This past year, how often did you eat locally caught fish? *(Circle one)*:

a) Not at all
b) Rarely
c) Sometimes
d) Often
e) Very often
f) All the time
g) I don't know
h) I prefer not to say

33. This past year, how often did you eat locally harvested land animal? *(Circle one)*:

a) Not at all
b) Rarely
c) Sometimes
d) Often
e) Very often
f) All the time
g) I don't know
h) I prefer not to say

34. This past year, how often did you consume locally harvested plants or vegetables (including traditional medicine)? *(Circle one)*:

a) Not at all
b) Rarely
c) Sometimes
d) Often
e) Very often
f) All the time
g) I don't know
h) I prefer not to say

35. In the last year**,** how often did you hunt? *(Circle one)*:
    a) Not at all
    b) Rarely
    c) Sometimes
    d) Often
    e) Very often
    f) All the time
    g) I prefer not to say

36. In the last year**,** did you hunt or fire on a target, with LEAD ammunition? *(Circle one)*:
    a) Not at all
    b) Rarely
    c) Sometimes
    d) Often
    e) Very often
    f) All the time
    g) I don't know the bullet type
    h) I prefer not to say

37. In the last year, did you eat animals harvested with LEAD ammunition? *(Circle one)*:
    a) Not at all
    b) Rarely
    c) Sometimes
    d) Often
    e) Very often
    f) All the time
    g) I don't know the bullet type
    h) I prefer not to say

38. Do you, or anyone who shares traditional food with you, use lead-ammunition alternatives (example: steel shot)? *(Circle one)*:
    a) Yes. Please specify: ___________________________
    b) No
    c) I don't know
    d) I prefer not to say

39. In the last year**,** how often did you fish? *(Circle one)*:
    a) Not at all
    b) Rarely
    c) Sometimes
    d) Often
    e) Very often
    f) All the time
    g) I prefer not to say

40. In the last year**,** did you fish with LEAD jigs and or sinkers? *(Circle one)*:

a) Not at all
b) Rarely
c) Sometimes
d) Often
e) Very often
f) All the time
g) I don't know the jig or sinker type
h) I prefer not to say

41. How often do people regularly share traditional food with you or your household? *(Circle one)*:
    a) Not at all
    b) Rarely
    c) Sometimes
    d) Often
    e) Very often
    f) All the time
    g) I prefer not to say

42. What kind of traditional food do people share with you? (*Select all that apply)*:
    a) Big game (e.g., moose, caribou, elk, deer, bison, etc.)
    b) Small game (e.g., rabbit, muskrat, beaver, etc.)
    c) Fish
    d) Game bird (e.g., goose, duck, ptarmigan, grouse, swan, pintail, canvasback, wigeon, etc.)
    e) Wild plants (e.g., berries, traditional medicine)
    f) Garden produce
    g) Other. Please specify: ____
    h) Not applicable (do not receive traditional food)
    i) I prefer not to say

Part C: Other Lead Exposure Determinants

43. What is your smoking status? *(Circle one)*:
    a) A smoker
    b) A non-smoker: I have smoked less than 100 cigarettes in total in my life
    c) An occasional smoker
    d) A former smoker - I stopped in the last year
    e) A former smoker - I stopped 1 to 2 years ago
    f) A former smoker - I stopped 3 to 5 years ago
    g) A former smoker - I stopped more than 5 years ago
    h) I prefer not to say

44. How many cigarettes (or any other tobacco and nicotine products) do you typically smoke in a day? *(Circle one)*:
    a) 0
    b) 1 to 10
    c) 11 to 19
    d) 20+
    e) I prefer not to say

45. Are you exposed to second-hand tobacco smoke at home? *(Circle one)*:
    a) Yes
    b) No, members who smoke in household do not smoke indoors
    c) No, no members of household smoke
    d) I prefer not to say

46. In the last month, did you take or use any store-bought supplements and or vitamins? *(Circle one):*
    a) Yes. Please specify: ____
    b) No
    c) I prefer not to say

47. In the last month, did you take or use any traditional medicines? *(Circle one):*
    a) Yes. Please specify: ____
    b) No
    c) I prefer not to say

48. In the last month, did you use any make-up or any cosmetics that contain dyes, pigments, coloring with heavy metals? *(Circle one):*
    a) Yes. Please specify: ____
    b) No
    c) I don't know
    d) I prefer not to say

49. In the past 10 year, have you worked in any of these settings for more than one year? *(<u>Select all that apply</u>):*

   a) Soil decontamination
   b) Waste disposal
   c) Recycling services or facilities
   d) Mining industry
   e) Metals working
   f) Oil and gas business
   g) Laboratory research or chemical production
   h) Automobile repair
   i) Power Plant
   j) Battery manufacture or repair
   k) Gardening or farming
   l) Road pavement or roof construction
   m) None of these
   n) I prefer not to say

50. Have you ever participated in any of the hobbies listed below? (Select all that apply):

   a) Car/boat repair
   b) Casting (bullets, fishing weights, etc.)
   c) Casting lead figures (toys, soldiers)
   d) Furniture finishing
   e) Home remodeling/painting
   f) Hunting
   g) Jewelry making
   h) Lead soldering
   i) Pottery/stained glass making
   j) Reloading
   k) Target shooting
   l) Welding
   m) None of these
   n) I prefer not to say

51. Do you have and use a wood stove or fireplace at home? *(Circle one):*

   a) Yes, that I use frequently
   b) Yes, that I barely use
   c) No
   d) I prefer not to say

52. How old is the house you currently live in? *(Circle one):*

   a) Less than 20 years
   b) Between 20 and 40 years
   c) Older than 40 years
   d) I don’t know

e) I prefer not to say

53. How long have you lived at your current residence (please mention the unit: months/years)?
    Length of time: ______________ I prefer not to say □
54. Has your home been renovated since its construction? *(Circle one):*
    a) Yes, major renovation (causing construction debris)
    b) Yes, minor renovation (for example, new paint, new flooring etc.)
    c) No
    d) I don't know
    e) I prefer not to say

55. Does your home have any paint that is old, peeling, or in poor condition? *(Circle one):*
    a) Yes
    b) No
    c) I don't know
    d) I prefer not to say

56. In the last 20 years, have you lived over one year in a house that is built before 1980s? *(Circle one):*
    a) Less than 20 years
    b) Between 20 and 40 years
    c) Older than 40 years
    d) I don't know
    e) I prefer not to say

57. In the last 20 years, did you ever live in a house with lead component water pipes? *(Circle one):*
    a) Yes
    b) No
    c) I don't know
    d) I prefer not to say

58. In the past 10 years, have you lived in a location within 100km of a mine? *(Circle one):*
    a) Yes
    b) No
    c) I don't know
    d) I prefer not to say

59. Do you think there are specific areas or waterbodies that might be contaminated by lead in your region? If yes, please specify:

    ____

    ____

    ____

    ____

60. Do you think there are any industrial or human activities that might have released lead in the environment in your region in the last 30 years? If yes, please specify:

61. Is there any historical information on lead contamination you believe we should be aware of? If yes, please specify:

Part D: Symptoms of Lead poisoning

62. Do you have any of the following symptoms? Please mention only if frequent and recurrent for at least 3 months (*select all that apply*)

    NOTE THAT IF YOU ARE HAVING THESE SYMPTOMS, IT DOES NOT MEAN YOU HAVE LEAD POISONING. OTHER FACTORS CAN CAUSE THESE SYMPTOMS.

    a) Abdominal pain
    b) Constipation
    c) Tiredness
    d) Headaches
    e) Irritability
    f) Depression or mood
    g) Loss of appetite
    h) Memory loss
    i) Pain or tingling in the hands and/or feet
    j) None of these
    k) I prefer not to say

63. Did you ever receive a medical diagnosis from a doctor of the following condition which may be associated in some cases with prolonged exposure to lead?

    a) High blood pressure
    b) Heart disease
    c) Kidney disease
    d) Reduced fertility

The survey is now completed. Thank you for your time.

Use of lead in harvesting practices

<u>Interview for hunters</u>

Lead is a heavy metal that can be found in the environment, but its concentration can be enriched from industrial sources. This project investigates how people might be exposed to lead. and will help identify how people might reduce their exposure to lead.

Using lead tool to harvest food might sometimes be associated with higher lead intake in people. We will invite you to answer questions to know the extent of lead harvesting tool use in the Sahtú region (e.g., lead shot).

This interview should take about 45 minutes to complete.

You can ask for help from a research team member at any time.

Participant ID:

ID: ____________________

1. In the past year, did you personally hunt? *(Circle one):*
    a) Yes
    b) No
    c) Not in the past year, but I have in the past
    d) I prefer not to say

2. In the last year**,** did you harvest game birds or any other animal, with LEAD SHOTS? *(Circle one):*
    a) Not at all
    b) Rarely
    c) Sometimes
    d) Often
    e) Very often
    f) All the time
    g) Not in the past year, but I have in the past
    h) I don't know the bullet type
    i) I prefer not to say

3. In the last year, did you harvest any animals with LEAD BULLETS? *(Circle one):*
    a) Not at all
    b) Rarely
    c) Sometimes
    d) Often
    e) Very often
    f) All the time
    g) Not in the past year, but I have in the past
    h) I don't know the bullet type
    i) I prefer not to say

4. In the last year, what animal species were harvested with LEAD BULLETS? Please specify:

____

____

I don't know □ I prefer not to say □

5. Where do you buy your LEAD ammunition? Please specify:

____

____

I don't know □ I prefer not to say □

6. How many bullets and shots do you tend to use during a harvest trip? Please specify:

____

____

I don't know □ I prefer not to say □

7. Where do you store your ammunition? Please specify:

____

____

I don't know ☐ I prefer not to say ☐

8. How are your ammunition disposed of, if not used? Please specify:

____

____

I don't know ☐ I prefer not to say ☐

9. Do you load your own bullets? (*Circle one):*

  a) Yes. Please specify how: ______________________________
  b) No
  c) I prefer not to say

10. What is the cost of the LEAD bullets and shot? Please specify:

____

____

I don't know ☐ I prefer not to say ☐

11. Do you think the cost of the LEAD ammunition is fair? Please specify:

____

____

I don't know ☐ I prefer not to say ☐

12. What ammunition type do you use instead of LEAD ammunition? Please specify:

____

____

I don't know ☐ I prefer not to say ☐

The survey is now completed. Thank you for your time.

Appendix C: Survey Refinement Individual Question Results

Part A: Socio-demographic questions

1. 6/6 participants did not suggest changes
2. 5/6 participants did not suggest changes
   1/6 participants suggested to be able to identify as "Aboriginal [SEX]"
3. 6/6 participants did not suggest changes
4. 6/6 participants did not suggest changes
5. 6/6 participants did not suggest changes
6. 4/6 participants did not suggest changes
   1/6 participants suggested people might be reluctant to provide identification on weight and height
   1/6 participants did not know their height or weight and suggested other people might not know either
7. 4/6 participants did not suggest changes
   1/6 participants suggested people might be reluctant to provide identification on weight and height
   1/6 participants did not know their height or weight and suggested other people might not know either
8. 5/6 participants did not suggest changes
   1/6 participants suggested asking how many children live in the household
9. 5/6 participants did not suggest changes
   1/6 participants suggested separating options such as elementary school completed vs partial high school (and further suggested separating based on highest grade in elementary/high school finished)
10. 6/6 participants did not suggest changes
11. 6/6 participants did not suggest changes
12. 6/6 participants did not suggest changes
13. 5/6 participants did not suggest changes
    1/6 participants suggested adding options that are temporary (for example, if someone is usually employed but is currently unemployed or laid off)
14. 5/6 participants did not suggest changes
    1/6 participants suggested clarifying what is meant by self-employed
15. 5/6 participants did not suggest changes
    1/6 participant suggests that this answer will change based on the season or time of year (for example, hunting during the summer means people will be on the land)

Part B: Harvesting practices and food preparation

16. 5/6 participants did not suggest changes
    1/6 participants suggested adding "Brita water" to the question as this is what most people drink
17. 6/6 participants did not suggest changes
18. 5/6 participants did not suggest changes
    1/6 participants suggested adding at home filters (for example, Brita)
19. 6/6 participants did not suggest changes
20. 6/6 participants did not suggest changes
21. 6/6 participants did not suggest changes

22. 5/6 participants did not suggest changes
    1/6 participants suggested this will depend on if they are on the land or not
23. 5/6 participants did not suggest changes
    1/6 participants suggested "I am not sure" as an option
24. 5/6 participants did not suggest changes
    1/6 participants suggested adding "berry picking" as well as jam making or canning as options
25. 5/6 participants did not suggest changes
    1/6 participants suggested adding "berry picking" as well as jam making or canning as options
26. 6/6 participants did not suggest changes
27. 3/6 participants did not suggest changes
    1/6 participants suggested providing examples of wild game birds, or just using the bird names instead of wild game bird (for example, ptarmigan, duck, goose) and also suggested using the word traditional food in the question
    1/6 participants suggested using migratory birds as chickens and crows are still birds and providing examples (swan, geese, duck)
    1.6 participants suggested saying wild animal instead of wild game bird
28. 6/6 participants did not suggest changes
29. 4/6 participants did not suggest changes
    1/6 participants suggested this will change based on the season
    1/6 participants suggested changing the term "preparation" to "cooked"
30. 6/6 participants did not suggest changes
31. 6/6 participants did not suggest changes
32. 3/6 participants did not suggest changes
    2/6 participants suggested using just terms (rarely, sometimes etc.) is better than numbers
    1/6 participants suggested there were too any options
33. 4/6 participants did not suggest changes
    2/6 participants suggested terms (rarely, sometimes etc.) is better than numbers
34. 4/6 participants did not suggest changes
    2/6 participants suggested terms (rarely, sometimes etc.) is better than numbers
35. 1/3 participants did not suggest changes
    2/3 participants suggested terms (rarely, sometimes etc.) is better than numbers
    *Question 35 was noticed to be a duplicate to question 28 and was not asked to 3 participants to save time
36. 6/6 participants did not suggest changes
37. 5/6 participants did not suggest changes
    1/6 participants suggested the question be asked in categories since each gun (rifle, shotgun) will be different
38. 6/6 participants did not suggest changes
39. 6/6 participants did not suggest changes
40. 5/6 participants did not suggest changes
    1/6 participants suggested the answer will be different based on the season
41. 4/6 participants did not suggest changes
    1/6 participants suggested not saying "your household" since they might consume traditional foods while other people in their household do not

1/6 participants suggested that this will change based on season (for example, during the summer people often get together and enjoy traditional food)

42. 6/6 participants did not suggest changes

Part C: Other lead exposure determinants

43. 4/6 participants did not suggest changes
    2/6 participants suggested that having only qualifiers would be better
44. 6/6 participants did not suggest changes
45. 6/6 participants did not suggest changes
46. 6/6 participants did not suggest changes
47. 5/6 participants did not suggest changes
    1/6 participants suggested changing the term “herbal”, so it is not interpreted as marijuana
48. 5/6 participants did not suggest changes
    1/6 participants suggested to provide examples of some creams with pigments
49. 5/6 participants did not suggest changes
    1/6 participants suggested the term “smelting” may be confusing and to change it metal melting
50. 5/6 participants did not suggest changes
    1/6 participants suggested making the question yes or no for each option as opposed to selecting which apply
51. 6/6 participants did not suggest changes
52. 6/6 participants did not suggest changes
53. 6/6 participants did not suggest changes
54. 6/6 participants did not suggest changes
55. 5/5 participants did not suggest changes
56. 5/5 participants did not suggest changes
57. 5/5 participants did not suggest changes
58. 5/5 participants did not suggest changes
59. 5/5 participants did not suggest changes
60. 5/5 participants did not suggest changes

* Questions 55 – 62 were not asked to one participant who ran out of time

Part D: symptoms of lead poisoning

61. 5/5 participants did not suggest changes
62. 5/5 participants did not suggest changes

Interview for Hunters

1. 2/2 participants did not suggest changes
2. 2/2 participants did not suggest changes
3. 2/2 participants did not suggest changes
4. 2/2 participants did not suggest changes
5. 2/2 participants did not suggest changes
6. 1/2 participants did not suggest changes
   1/2 participants suggested clarifying what is meant by a harvest trip
7. 2/2 participants did not suggest changes
8. 2/2 participants did not suggest changes

9. 2/2 participants did not suggest changes
10. 1/1 participants did not suggest changes
11. 1/1 participants did not suggest changes
12. 1/1 participants did not suggest changes
    * Questions 10 – 12 were not asked to one participant who ran out of time

Appendix D: Poster used for Survey Refinement Recruitment

UNIVERSITY OF WATERLOO

Do you have 2h to talk about a survey?

You could receive $100 for it!

Would you like to help design a study looking at how people in the region are exposed to lead?

We would like you to participate in a discussion about a survey developed by the research team that will be used in the future as part of a larger project to document lead exposure in people.

We are looking for **10 adults**, living in Fort Good Hope.

The **virtual discussion** (via phone or Zoom) will be on the survey design (questions, options and format), as well as any complementary information you believe is worth integrating in the survey that we may have missed.

Your involvement in this study will take **about 2h**.

To show appreciation for your time, you will receive **$100**, paid by e-transfer. Participants must be able to accept either text or email e-transfer.

Study time: according to your availability, anytime from October 4 to 29, 2021.

Are you interested? Please contact the researcher via the contact information below.

Contact:

**This study is a collaboration between Fort Good Hope, Environment and Climate Change Canada, University of Waterloo, and the Sahtú Renewable Resources Board. Participation is completely voluntary and your participation and name will be kept confidential. This study has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee.*

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Appendix E: Information Letter for Survey Interviews

INFORMATION LETTER

Would you like to take part in a study looking at how people in the region are exposed to lead? Kelly Skinner, a researcher from the University of Waterloo in Ontario is doing a project to answer community concerns on lead sources in the Sahtú.

This project is the next step following the human biomonitoring research conducted in the NWT from 2015-2019 (by Brian Laird). Elevated lead levels were measured in people in participating Sahtú communities (Déline, Tulít'a and Fort Good Hope), but lead levels were generally below those known to cause illness. Community members raised concerns regarding the sources of lead. This proposed project is a preliminary study to initiate work to prepare for a following project monitoring lead in the Sahtú region, which will involve a survey to identify sources of lead for people, and the measurement in environmental medias such as water and country food.

The research team has created a first draft of a survey to document lead exposure for people. This survey includes questions on occupation, country food consumption, harvesting, and household characteristics. These parameters are essential to assess the sources of lead exposure. We are inviting you to review and discuss the survey (questions, options and format), as well as complementary information you believe it worth integrating in the survey that we might have missed. We want to create the most relevant survey possible for the region and we need you help to do so. Your involvement in this study will take up to 4h and the study discussion will be audio-recorded. You are eligible to participate if you are an adult resident from the Sahtú region.

Taking part in the project will involve:

In a group of about 10 people (focus group), researchers and a local coordinator will ask you if the survey questions:

i. Were complete (Any questions we forgot?)
ii. Were understandable
iii. Were appropriate (Any questions not relevant to the Sahtú? Culturally right?)

Group discussions might involve housing factors (i.e., house age, water system), harvesting practices, the use of lead bullets, the lead-shot alternatives, other lead exposure sources in or near the community, historical information on these sources, and how/when you have come into contact with these sources. The focus group discussion will be audio-recorded so that answers can be reviewed at a later time.

Benefits for doing the study

You will not directly benefit from the research project. However, to show appreciation for your time, you will receive $100 from the coordinator for your participation.

This amount is taxable. It is your responsibility to report the amount received for income tax purposes and University of Waterloo will not issue a tax receipt.

Privacy of the information

Since parts of this study may be done in a public space (e.g., in the community center), your involvement may not be completely private, but researchers will keep your participation confidential. Your name will not appear in any paper or publication resulting from this study.

Given the group format of this session, we will ask all the participants to keep in confidence information that identifies or could potentially identify another participant and/or their comments, however we cannot guarantee that everyone will honour this request.

Your answers and the audio file will be sent to a secure online server at University of Waterloo, with the consent form. All information from this study will be kept at the University of Waterloo on a password-protected computer in a locked room. The discussion transcript, without name, might be shared with co-investigators (see the list below). If you agree to do the study, your answers will be kept for at least 7 years.

Reporting of the findings
No research performed under this project, no research products, and no traditional or Indigenous knowledge will be used for commercial purposes. A results report will be returned to the community one year from now. After the results have been returned to the community, de-identified results may be presented in thesis, papers, and presentations at national and international meetings.

Withdraw from the study
Your participation in this study is completely voluntary. You may decline to answer any question(s) you prefer not to answer and you may stop participating at any time by informing the coordinator of this decision.

You can withdraw from the study by contacting Kelly Skinner by phone or email, contact information found below. If you withdraw from the study, your name will be permanently erased from our study records, however please note that because comments made during the study session will not be linked to individual participants, it will not be possible to identify and/or remove participants' data once the session ends. If you change your mind, you will still keep the money previously given for your time.

Other details
Participation in this study will not provide any personal benefit to you. There are no known or anticipated risks associated with participation in this study.

This project in funded by the Northern Contaminants Program.

This study has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee (ORE#42741). If you have any questions for the Committee contact the Office of Research Ethics at 1-519-888-4567 ext. 36005 or ore-ceo@uwaterloo.ca. This study has been approved by the Fort Good Hope leadership.

Contact Information
Feel free to contact Kelly Skinner for more information at any time during the study.

We thank you for your interest in this study.

Yours sincerely,

Kelly Skinner, PhD

Co-investigators:
Kirsty Gurney (Environmental and Climate Change Canada), Brian Laird, PhD (University of Waterloo), Mylène Ratelle, PhD (University of Waterloo), Jerome Conte (INRS), Leon Andrew (SRRB), Deborah Simmons (SRRB).

Appendix F: Consent Form for Survey Interviews

CONSENT FORM (Participant 18+)

By agreeing to do this study, you are not giving up your legal rights or releasing the researchers or involved institutions from their legal and professional responsibilities. This study has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee. If you have any questions or ethics concerns, you may contact the Office of Research Ethics, at the contact information on the information letter.

By agreeing to participate, you are agreeing to the following:

- *You have read and received a copy of the information letter*
- *You had a chance to ask questions and discuss the study*
- *You understand your involvement in the research study*
- *You understand this discussion will be audio-recorded*
- *The privacy of your answers and information has been explained to you*
- *You understand who will have access to your answers*
- *You are aware you can refuse to answer any question*
- *You are aware you can withdraw at any time during the study, by contacting Kelly Skinner*

Do you agree to take part in this study? ☐ **Yes** ☐ **No**

NAME OF THE PARTICIPANT:

____

Did the participant receive 100$ for the time participating in the study (mandatory)?

☐ **Yes** ☐ **No**

Signature of the researcher:___________________________________ Date: _____________

Project Title: Investigating Lead Exposure in the Sahtú– survey refinement
(Page to be detached and be kept at University of Waterloo)

Appendix G: Store Information Collection Process

Introduction and Purpose

Lead ammunition (bullets and shot) presents a method of exposure to lead. The use of lead ammunition in hunting, and the consumption of meat in and around the wound channel (especially that which has not been cleaned properly) of animals hunted using lead ammunition, represents an exposure pathway to lead for Northern Indigenous populations. While the use of lead ammunition has decreased over time as alternatives have become more apparent, lead ammunition may still be available in Northern regions, and no rules exist for its use. The only regulation on the use of lead ammunition is the use of lead shot in hunting migratory birds or when hunting in wetlands.

The purpose of this task is to determine if lead ammunition is available to be purchased in the Sahtú. This will assist in understanding what the current use of lead ammunition is in the Sahtú. Specifically, if no lead ammunition is being sold, the only lead ammunition that is being used is older ammunition that was purchased when it was available, or ammunition not purchased at the stores.

Methods

The first step is to compile a list of all the stores in the Sahtú Region that could possibly sell ammunition. The list, including hours of operations (if available) in Mountain Time, and their phone numbers is as following:

Colville Lake
1. Kapami Co-Op Assn
Phone: (867) 709-2900

Deline
1. Northern Store
Hours: 10AM-6PM
Phone: (867) 589-3311

2. Great Bear Co-op
Hours: 10AM-6PM
Phone: (867) 589-3361

Fort Good Hope
1. Northern Store
Hours: 10AM-6PM
Phone: (867) 598-2291

2. Fort Good Hope Co-op
Hours: 10AM-6PM
Phone: (867) 598-2543

Norman Wells
1. Northern Store
Hours: 10AM-8PM
Phone: (867) 587-2345

2. Rampart Rentals
Hours: 9AM-1PM
Phone: (867) 587-2822

Tulita
1. Northern Store
Hours: 10AM-6PM
Phone: (867) 588-4331

2. BJ's Market
Hours: 9AM-7PM
Phone: (867) 588-3504

3. Wright’s Convenience
Hours: 7PM-12AM
Phone: (867) 588-4927

The information included on the list is all gathered from a Google search. Businesses that identify as a store, including convenience stores, were included in the list, while businesses that did not identify as a store on Google were not included. If during the phone calls, people identify a different location that may sell lead ammunition (or ammunition as a whole), I will find the information for those stores and call them as well.

Each of these businesses will be called during their hours of operations. I will attempt to call stores when they are not at their busiest. To do so, I will call approximately 1-2 hour(s) after opening. I will follow a script and ask to speak to the store owner/manager if available. The call should last about 5 minutes in total.

"Good morning/afternoon/evening. How are you doing today? My name is Calin, I am a researcher from the University of Waterloo, in Ontario. I am curious about some of the products you are selling. Is the store manager or yourself available for a quick talk? Thank you. I would like to know if lead ammunition is still being sold in the region. I will only take few minutes of your time"

While the conversation may guide away from the script, I will ask the following questions:

5. Do you sell lead ammunition?
    - 5.1. If yes, what type? Bullets, shot?
        - 5.1.1. If yes, how much does it cost?
    - 5.2. If no, did you ever sell lead ammunition?
        - 5.2.1. If yes, when did you stop selling?
6. Do you sell non lead ammunition?
    - 6.1. If yes, what type? Steel?
        - 6.1.1. If yes, how much does it cost?
    - 6.2. If no, do you know where ammunition is sold in the community?
7. Do you know if lead ammunition is still being used for hunting?
    - 7.1. If yes, is it commonly used, or are alternatives more commonly used?
8. Do you know if lead ammunition is being used for any other purposes?
    - 8.1. If yes, for what? Target shooting?

After asking the questions, I will ask if there is any other information, they would like to share with me that they think is important for me to know or would help me in my research. Then, I will thank them for their time. Throughout the phone call, I will be taking notes on their answers and compile the information from all the stores into a document.

Appendix H: Northern Contaminants Program Systematic Review Title Pages

Northern Contaminants Program

Investigating Lead Exposure in Northern Canada

Report:

Human lead exposure sources in Arctic and subarctic regions

Systematic Literature Review

Collaboration of:
University of Waterloo
Environment and Climate Change Canada
Institut National de Recherche Scientifique (INRS)

March 2022
(Version 1: reviewed on March 31, 2021)
(Version 2: reviewed on November 3, 2021)
(Version 3: reviewed on March 2, 2022)

School of Public Health Sciences
University of Waterloo
200 University Avenue West, Waterloo (Ontario), Canada, N2L 3G1

Environment and Climate Change Canada
Prairie and Northern Wildlife Research Centre
115 Perimeter Road, Saskatoon (Saskatchewan), Canada, S7N 0X4

Institut National de Recherche Scientifique (INRS)
Eau Terre Environnement Centre
490 rue de la Couronne, Québec (Quebec), Canada, G1K 9A9

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Kelly Skinner, Principal Investigator
Jordyn Stalwick, main author

Cover photo: Nunavik community in 2014. Photo taken by Mylène Ratelle.

Suggested citation:

Stalwick J, Ratelle M, Gurney K, Drysdale M, Lazarescu C, Laird B, Comte J, Skinner K (2022). Human lead exposure sources in Arctic and subarctic regions - Systematic Literature Review. Preliminary study: Investigating Lead Exposure in Northern Canada and the Sahtú region, NWT. University of Waterloo, Ontario (Canada).

Appendix I: Plain Language Report for Communities

Investigating Lead Exposure

Preliminary project in Fort Good Hope

Introduction

Findings from the human biomonitoring project conducted in 2015-2019 indicated that lead levels in blood and urine were elevated in Sahtú region participating communities compared to the general Canadian population, and the Dehcho (Ratelle et al., 2018). Fort Good Hope was a participating community. Those results were shared with the leadership and the community residents during a public meeting in February 2019.

Lead is a toxic metal. At elevated exposure, lead can be associated with a range of health issues, including anemia, kidney damage, and intellectual and behavioural development issues. Contact with lead can occurred through various sources, such as lead ammunitions use, lead pipe plumbing, lead-based paint, lead-contaminated dust and soil. While we know about general lead exposure determinants, less is known regarding the sources of exposure to lead in northern regions. Sources of elevated lead levels in the Sahtú are still unknown.

Methods

This project aims to address concerns from the Sahtú communities. Research happened between 2020 and 2022.

- We completed a literature review of all the available information on lead exposure in the North.
- We also established a community-based research in Fort Good Hope to harvest birds.
- We analyzed birds, water and fish for lead.
- In parallel, we created and refined a survey to be used later.

John Tobac, Indigenous Guardian. Mr Tobac was in charge of the bird harvest project

Findings

- **Review of studies**

We created a knowledge synthesis of lead exposure levels and determinants in northern Canada to understand how people living in northern communities might be exposed to lead, with a focus on Canadian groups. The literature report is over 100 pages long and includes information on potential exposure sources from the Land, potential sources from other pathways and lifestyles and human health in the north (Stalwick et al., 2022).

These studies also tell us that for people living in the north, lead levels are higher than people who live in the south but those levels are decreasing. Most studies show that lead levels in northern people are below levels that cause harm.

The review indicated that the consumption of hunted food has been associated with higher lead levels in humans in a multitude of studies. Elevated levels of lead have been associated with hunting practices (e.g., Liberda et al., 2018). The review indicated that while the consumption of hunted food has been associated with higher lead levels in humans in a multitude of studies, there might be some other sources of exposure essential to consider.

- **Community-based bird harvest**

During the 2021 Spring hunt, hunters in Fort Good Hope were contacted and invited to contribute harvested game birds for testing. Each hunter received financial compensation for harvesting activities. For each animal, the hunter was asked to complete short (e.g., the date of collection, bird species, tissue type, approximate weight, what bullet type was used).

To understand how harvesting practices might affect lead in people in Fort Good Hope, we surveyed hunters. We found out that the hunters we surveyed use non-lead ammunition for bird-hunting and no hunters reported using lead ammunition for bird-hunting in the last 2 years.

X-ray radiographs were done on the bird carcasses. It is very interesting to confirm the birds do not have any trace of lead fragments found in their digestive system. However, we did see potential lead fragments in one goose wing and are currently investigating further.

- **Lead in birds, water and fish**

A total of 20 birds were collected, including lesser snow geese, greater white-fronted geese, and Canada geese. The levels in most breast muscle samples were under the analytical limit and as such, not detected. The average of lead concentration in gizzard was slightly higher than in breast meat at 0.008 mg/kg. The analysis of the bird meat (breast and gizzard) showed low levels of lead. In fact, all the samples were below the Canadian Maximum level recommended and monitored by Health Canada's Bureau of Chemical Safety, Food Directorate (Canada, 2020). By example, the acceptable maximum level for lead in solid food being 0.5 mg/kg in fish protein and whole tomatoes.

Water sampling was done at different points of the water system, from the Mackenzie River, at the water treatment plant, and at house taps (by Dr. Jerome Comte’s group). In total, lead in water was tested in 30 different spots in an around Fort Good Hope. The source of water with the most elevated lead concentration, as well as other metals, is from water from the Mackenzie River. The sample with the second most lead was collected in a nearby wetland to the Mackenzie. All the tap water samples were below the Canadian Maximum Acceptable Concentration.

Additionally, as part of ongoing monitoring activities, fish were collected in Mackenzie River at Rampart Rapids, near Fort Good Hope (by Dr. Gary Stern’s group). Lead levels measured in fish were also very low. From the 10 burbot fish samples analyzed, only one muscle sample had detectable level of lead. All samples fall below the European Union recommendation limit of 0.030 mg/kg of lead in fish muscle (EUC, 2006). Liver samples had higher lead levels than muscles, with a maximum of 1.002 mg/kg.

- **Survey preparation**

Our research team worked on developing a survey to look at lead exposure. Questions include occupation and hobbits, country food preparation and consumption, harvesting practices, other potential sources of exposure (e.g., household characteristics). Feedbacks from six Sahtú residents on the format, content, relevance, cultural and local appropriateness were gathered on the survey contents through individual interviews. The survey was edited and a final version is ready for implementation.

Conclusions

The creation of a literature review on the sources of lead in arctic and subarctic regions is the most comprehensive on the topic to date. The preliminary findings from the environmental samples tested for lead around Fort Good Hope do not indicate any bird, fish and water samples with high levels of lead.

As a next step, we will extend the community-based bird harvest project in Deline and Tulit'a. We will also invite people in the Sahtú to complete a survey on possible lead exposure. The future implementation of the survey, the expansion of the bird harvest, alongside with previous human biomonitoring, and environmental monitoring data, will ensure a better understanding of the reasons for elevated lead levels in the Sahtú.

Overall, this project provided some data to assess sources of lead for people living in the Sahtú region. Further work is required to assess all sources of lead and further develop efficient communication to share those findings and promote safe traditional/country food consumption.

For more information, please contact:

References

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Appendix J: Result Letter for Nutritional Markers

UNIVERSITY OF WATERLOO | School of Public Health Sciences

200 University Avenue West,
Waterloo, ON, Canada N2L 3G1

DATE

Subject: Nutrition markers results from the Northwest Territories biomonitoring project

Dear NAME,

During the biomonitoring project that took place in 2016-2018, you agreed to participate in a human biomonitoring project led by Dr. Brian Laird and funded by the Northern Contaminants Program. This research project investigated people's exposures to contaminants by measuring levels of contaminants and nutrients in samples of hair, blood, and urine. You have received the main results of the project in a previous letter. When you decided to take part in the project, you agreed that we could keep your biological sample(s) in a biobank for future analysis of contaminants and nutrition markers, if we got the funding to do so. We received funding from the Canadian Institutes of Health Research to measure nutrition markers in the plasma samples.

In this letter, you will find your sample results. The results can be compared with the deficiencies threshold, with the normal range or with the normal population levels. For some of those nutrition markers we don't have any comparative clinical values. If the case you have a vitamins' deficiency, you can look at recommendations in the following table.

Unbalanced nutrition status is not an indicator for any disease or health condition. In addition, these results represent your nutrition status at the time you provided the sample, years ago, and nutrition status changes over time. If you have health concerns, we suggest you contact your doctor and bring this letter with you. This letter does not replace regular visits to your doctor or health care professional.

We are available to discuss the results of the project to-date and answer your questions. As the project continues, Dr. Laird's research team will be able to provide more information on the exposure levels of people living in the Northwest Territories. If we receive any additional information about your samples, we will provide another letter with those results too. We recommend keeping this letter in a safe place for potential future monitoring.

Thank you very much for your participation in this project.

Regards,

Brian Laird, Mylène Ratelle,

YOUR RESULTS		
Participant XXX000		
NUTRITION MARKERS IN PLASMA		
Biomarker	**Level**	**Clinical Individual References Values[a]**
25 hydroxy vitamin D3 (ng/mL)	**X**	DEFICIENCY THRESHOLDS: <10 ng/mL (severe deficiency) 10-19 ng/mL (mild to moderate deficiency) 20-50 ng/mL (optimum levels) 51+ ng/mL (increased risk of toxicity possible) NORMAL RANGE: Not available. POPULATION ESTIMATE: The central estimate of the adult Canadian population is 26 ng/L[b]
5,10-methenyl THF (nmol/L)	**X**	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: Not available. POPULATION ESTIMATE: Not available.
5-formyl THF (nmol/L)	**X**	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: Not available. POPULATION ESTIMATE: Not available.
5-methyl THF (nmol/L)	**X**	DEFICIENCY THRESHOLDS: Below 8.7 nmol/L in serum NORMAL RANGE: Not available. POPULATION ESTIMATE: Not available.
Albumin (g/L)	**X**	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: 35-50 g/L POPULATION ESTIMATE: Not available.
alpha tocopherol (ug/mL)	**X**	DEFICIENCY THRESHOLDS: Below 3.0 ug/mL NORMAL RANGE: 0-17 years: 3.8-18.4 ug/mL 18 years and over: 5.5-17.0 ug/mL POPULATION ESTIMATE: Not available.
B1/ thiamine (nmol/L)	**X**	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: Not available. POPULATION ESTIMATE: Not available.

B2 (nmol/L)	X	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: 2.7-50.5 nmol/L POPULATION ESTIMATE: Not available.
B12 (pmol/L)	X	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: 133-674 pmol/L POPULATION ESTIMATE: The central estimate of the adult Canadian population is 306 pmol/L[b]
FA (nmol/L)	X	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: Not available. POPULATION ESTIMATE: Not available.
FAD (nmol/L)	X	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: Not available. POPULATION ESTIMATE: Not available.
Ferritin (ug/L)	X	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: Males: 24-336 ug/L in serum Females: 11-307 ug/L in serum POPULATION ESTIMATE: Not available.
FMN (nmol/L)	X	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: Not available. POPULATION ESTIMATE: Not available.
MeFox (nmol/L)	X	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: Not available. POPULATION ESTIMATE: Not available.
PA (nmol/L)	X	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: Not available POPULATION ESTIMATE: Not available.
Phosphorus (mmol/L)	X	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE:

		While critical values vary by age and sex, the normal range for adults of both sex is 0.81-1.45 mmol/L POPULATION ESTIMATE: Not available.
PL (nmol/L)	X	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: Not available. POPULATION ESTIMATE: Not available.
PLP (nmol/L)	X	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: 20-202 nmol/L POPULATION ESTIMATE: Not available.
Retinol (ug/mL)	X	DEFICIENCY THRESHOLDS: Severe deficiency below 0.100 ug/mL (WHO) Potential toxicity potential above 0.120 ug/mL (WHO) NORMAL RANGE: 7-12 years: 0.128-0.812 ug/mL 13-17 years: 0.144-0.977 ug/mL > or =18 years: 0.325-0.780 ug/mL POPULATION ESTIMATE: Not available.
Sodium (mmol/L)	X	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: 135-145 mmol/L POPULATION ESTIMATE: Not available.
THF (nmol/L)	X	DEFICIENCY THRESHOLDS: Not available. NORMAL RANGE: Not available. POPULATION ESTIMATE: Not available.

NOTES:

If *: your nutrition marker level is considered as deficient. See the next section for any nutrition recommendations.

[a] This information comes from the Mayo labs (https://www.mayocliniclabs.com/test-catalog/index.html)

[b] Canadian Health Measure Survey for nutrition central estimate: Statistics Canada. Table 13-10-0336-01 Nutritional status of the household; https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310033601

5- Methyl THF (5-Methyl-tetrahydrofolate), FA (Folic Acid), FA (flavin adenine dinucleotide), FMN (flavin mononucleotide), MeFox (Oxidation product of 5-methyltetrahydrofolate), PA (Pyridoxic Acid), PL (Pyridoxal), PLP (Pyridoxal 5-phosphate), THF (Tetrahydrofolate/Tetrahydrofolic acid)

Table 1. Interpretation table to support the assessment of the nutrition markers.

Nutrient	Marker	Information[a]	Recommendation to improve dietary intake[b]
Vitamin D	25hydroxy vitamin D3	Vitamin D acts as a hormone. This test measures vitamin D status and describes the body's vitamin D stores. Severe deficiency could be associated with osteomalacia or rickets. Mild deficiency may be associated with increased risk of osteoporosis or hyperparathyroidism. Sustained levels >50 ng/mL along with prolonged calcium supplementation may lead to hypercalciuria and decreased renal function.	The best sources are fatty fish and fish liver oils. Smaller amounts are found in egg yolks, cheese, and beef liver. Certain mushrooms contain vitamin D. Many foods and supplements are fortified with vitamin D like dairy products and cereals. Vitamin D is also available in supplements. Vitamin D is also the "sunshine vitamin" and is converted during exposure to sunlight. A sensible sun exposure is recommended.
B12	B12	Vitamin B12 is necessary to produce blood cells and for neuronal function. Vitamin B12 deficiency frequently causes anemia, weakness, mood changes.	In humans, it is obtained only from animal proteins. There is a variety of vitamin B12 supplements available. Food sources are fish and shellfish, red meat and liver, eggs, poultry, dairy products such as milk, cheese, and yogurt, and fortified foods.
Vitamin A	Retinol	Retinol levels reflects the quantities of vitamin A and carotene ingested and absorbed. Vitamin A plays an essential role in the function of the retina and is necessary for growth. Vitamin A enhances immune function. Vitamin A deficiency is a cause of blindness. Deficiencies may arise from poor nutrition or from intestinal malabsorption.	The World Health Organization recommends supplementation when this biomarker is below 0.200 ug/ml. Many breakfast cereals, juices, dairy products, and other foods are fortified with retinol. Vegetables and fruits are sources of vitamin A precursors, such as leafy green vegetables (kale, spinach, broccoli), orange and yellow vegetables (carrots, sweet potatoes, pumpkin and other winter squash, summer squash), tomatoes, red bell pepper, cantaloupe, mango. In addition, there are some in beef liver, fish oils, milk and eggs.
Vitamin E	alpha tocopherol	Vitamin E contributes to the normal maintenance of the vascular and nervous systems, and provides antioxidant protection. Deficiency of vitamin E leads to reversible motor and sensory neuropathies. Deficiencies may arise from poor nutrition or from intestinal malabsorption.	Vitamin E is found in plant-based oils (e.g., sunflower oil), nuts, seeds. That includes: sunflower seeds, almonds, peanuts, peanut butter. There is also some amount in fruits and vegetables, such as beet greens, collard greens, spinach, pumpkin, red bell pepper, asparagus, mango and avocado.
B2	Riboflavin	Dietary deficiency of B2 is characterized by sore throat, lesions on the lips, patches	Riboflavin is found mostly in meat and fortified foods but also in some

		on the skin and anemia. Severe riboflavin deficiency may affect also affect other vitamins' level (e.g. vitamin B6, niacin).	nuts and green vegetables. Sources are: dairy products (milk, yogurt, cheese), eggs, lean beef and pork, organ meats (beef liver), chicken breast, salmon and other fish, fortified cereal and bread, almonds and spinach.
B6	FAD FMN PLP PL PA	Vitamin B6 deficiency is a potential cause of burning mouth syndrome and a possible potentiating factor for carpal tunnel. Vitamin B6 deficiency is associated with symptoms skin scaling, severe gingivitis, irritability, weakness, depression, dizziness, peripheral neuropathy, and seizures. In children, deficiencies can lead to diarrhea, anemia, and seizures. Pyridoxal 5-phosphate (PLP) is the biologically active form of vitamin B6. Pyridoxic Acid (PA) is also a marker of vitamin B6.	Vitamin B6 is found in a variety of animal and plant foods, including meat (e.g., beef liver, poultry), fish (e.g., tuna, salmon). Some vegetables and fruits are good sources especially dark leafy greens, bananas, papayas, oranges, and cantaloupe and chickpeas. It can also be found in fortified cereals.
Iron	Ferritin	Ferritin is a molecule binding iron and storing it. Its concentration is directly proportional to the total iron stores in the body. Ferritin level below the ranges might reveal iron deficiency and anemia, level abovepoint to liver disease, inflammatory conditions or hyperthyroidism.	Meats, poultry, seafood, grains, nuts, seeds, legumes, and vegetables are good sources of iron. Many breads, cereals, and infant formulas are fortified with iron. Sources include: oysters, clams, mussels, beef or chicken liver, organ meats, beef, poultry, canned sardines, canned light tuna, beans, lentils, dark chocolate (at least 45%), spinach, potato with skin, nuts, seeds. Iron is also available in supplements.
Folate/ vitamin B9	5-methyl THF	This test is useful for determining a deficiency of folate in the central nervous system. Serum folate is almost entirely in the form of N-(5)-methyl tetrahydrofolate. Low levels are associated with inborn errors of metabolism affecting folate metabolism, dietary deficiency of folate, cerebral folate syndromes and Kearns-Sayre syndrome. Symptoms may include, anemia, developmental delay, seizures, depression and dementia.	Folic acid is sometimes added to foods commonly eaten, including breads, cereals, pasta, rice, and other grain products. Good sources of folate include: dark green leafy vegetables (turnip greens, spinach, romaine lettuce, asparagus, Brussels sprouts, broccoli), beans, peanuts, sunflower seeds, fresh fruits, fruit juices, whole grains, liver, seafood, eggs, fortified foods and supplements.
Folate	THF; 5,10-methenyl THF; FA; 5-formyl THF MeFox	Folate refers to all derivatives of folic acid. Approximately 20% of the folate absorbed daily is derived from dietary sources; the remainder is synthesized by intestinal microorganisms. Significant folate deficiency is characteristically associated with anemia, and low levels have beenreported in patients with neuropsychiatric disorders, and pregnancy	(see above for folate/vitamin B9)

		disorders. Folate deficiency is most commonly due to insufficient dietary intake and is most frequently encountered in pregnant women or with people having a high alcohol consumption.	
Vitamin B1	Thiamine (B1)	Vitamin B1 is essential for metabolism, brain function, and the nervous system. Beside poor nutrition, deficiency can occur in the elderly, those with chronic gastrointestinal problems, anorexia, on cancer treatment, or receiving diuretic therapy. The signs and symptoms of a deficiency may include poor sleep, malaise, weight loss, irritability, and confusion. Newborns breast fed from deficient mothers may develop dyspnea and cyanosis; diarrhea, vomiting, and aphonia may follow. Moderate deficiency can affect intellectual performance and well-being, despite a lack of apparent clinical symptoms.	Thiamin is found naturally in meats, fish, and whole grains. It is also added to breads, cereals, and baby formulas. Sources are: fortified breakfast cereals, pork, fish, beans, lentils, green peas, enriched cereals, breads, noodles, rice, sunflower seeds and yogurt.
Sodium	Sodium	Sodium plays a central role in maintaining the normal distribution of water and the osmotic pressure. The amount of sodium in the body is a reflection of the balance between sodium intake and output.	People usually have high intake of sodium and some might try to limit their intake. Unprocessed food like fruits, vegetables, whole grains, nuts, meats, and dairy foods is low in sodium. Most of the salt in our diets comes from commercially prepared foods. Foods with highest sodium levels include breads/rolls, pizza, savory snacks (chips, popcorn, pretzels, crackers).
Albumin	Albumin	This test is useful for assessing general nutritional status. Albumin is a protein. It is involved in the transport and storage of a wide variety of compounds, and is a source of endogenous amino acids.	Most good quality protein sources are also good sources of albumin (e.g., meat, poultry, fish, eggs, peanut butter, etc.).
Phosphorus	Phosphorus	A large portion of phosphorus contained in the body is localized in bone. The remainder is involved in metabolism. Phosphate concentrations are dependent on meals and may vary widely. Levels below 15 mg/L may result in muscle weakness, hemolysis of red cells, coma, and bone deformity and impaired growth.	The richest sources are dairy (e.g., milk, yogurt, cheese), meat (e.g., beef, poultry, pork), seafood and fish (e.g., salmon), legumes, seeds and nuts. There is also phosphorus in whole wheat breads and cereals, and in some vegetables (e.g., asparagus, tomatoes, cauliflower). Phosphate additives and preservatives in foods are a significant contributor to phosphorus intakes, especially deli meats, bacon, sausage, sodas, sports drinks, and other bottled beverages. Phosphorus is also available in supplements.

[a] This information comes from the Mayo labs (https://www.mayocliniclabs.com/test-catalog/index.html)

[b] Harvard T.H. Chan School of Public Health. The Nutrition Sources (https://www.hsph.harvard.edu/nutritionsource/)

5- Methyl THF (5-Methyl-tetrahydrofolate), FA (Folic Acid), FA (flavin adenine dinucleotide), FMN (flavin mononucleotide), MeFox (Oxidation product of 5-methyltetrahydrofolate), PA (Pyridoxic Acid), PL (Pyridoxal), PLP (Pyridoxal 5-phosphate), THF (Tetrahydrofolate/Tetrahydrofolic acid)

Table 2. Nutrition markers quantified in plasma samples from all the Sahtú participants (n=128)[a]

	Unit	Min	Mean	Max	% deficiency
5-formyl THF	(nmol/L)	0.010	0.12	1.0	-
5-methyl THF	(nmol/L)	2.6	15	33	21
5,10-methenylTHF	(nmol/L)	0.040	0.11	0.35	-
25-hydroxy vit. D3	(ng/ml)	2.3	9.9	31	94
Albumin	(g/L)	37	48	57	-
alpha tocopherol	(ug/ml)	3.6	9.8	17	0
B1 /thiamine	(nmol/L)	0.40	4.5	36	-
B2	(nmol/L)	1.2	27	320	-
B12	(pmol/L)	94	310	730	-
FA	(nmol/L)	0.30	1.0	17	-
FAD	(nmol/L)	45	82	200	-
Ferritin	(ug/L)	1.0	120	760	-
FMN	(nmol/L)	14	22	72	-
MeFox	(nmol/L)	0.46	4.4	14	-
PA	(nmol/L)	20	45	770	-
PL	(nmol/L)	24	56	610	-
PLP	(nmol/L)	7.0	92	620	-
Retinol	(ug/ml)	0.30	0.83	1.4	0
Sodium	(mmol/L)	130	140	140	-
Phosphorus	(mmol/L)	0.75	1.2	1.7	-
THF	(nmol/L)	0.25	1.6	7.1	-

NOTES:

[a] Detection of 100% beside for phosphorus which is 99%.

Mean (Arithmetic Mean); Min (Minimum); Max (Maximum)

5- Methyl THF (5-Methyl-tetrahydrofolate), FA (Folic Acid), FA (flavin adenine dinucleotide), FMN (flavin mononucleotide), MeFox (Oxidation product of 5-methyltetrahydrofolate), PA (Pyridoxic Acid), PL (Pyridoxal), PLP (Pyridoxal 5-phosphate), THF (Tetrahydrofolate/Tetrahydrofolic acid)

Appendix K: Ethics Clearance Certificate

UNIVERSITY OF WATERLOO

Notification of Ethics Clearance to Conduct Research with Human Participants

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Principal Investigator: Kelly Skinner (School of Public Health and Health Systems)

Co-Investigator: Mylene Ratelle (School of Public Health and Health Systems)

Co-Investigator: Brian Laird (School of Public Health and Health Systems)

Student investigator: Calin Lazarescu (School of Public Health and Health Systems)

Co-Investigator: Kirsty Gurney (Environment and Climate Change Canada (ECCC) / Government of Canada)

Co-Investigator: Jerome Comte (INRS- Centre - Eau Terre Environnement)

Collaborator: Leon Andrew (Sahtu Renewable Resources Board)

Collaborator: Deborah Simmons (Sahtu Renewable Resources Board)

Research assistant: Jordyn Stalwick (University of Saskatchewan)

File #: 42741

Title: Investigating Lead Exposure in the Sahtú region

The Human Research Ethics Committee is pleased to inform you this study has been reviewed and given ethics clearance.

Initial Approval Date: 02/23/21 (m/d/y)

University of Waterloo Research Ethics Committees are composed in accordance with, and carry out their functions and operate in a manner consistent with, the institution's guidelines for research with human participants, the Tri-Council Policy Statement for the Ethical Conduct for Research Involving Humans (TCPS, 2nd edition), International Conference on Harmonization: Good Clinical Practice (ICH-GCP), the Ontario Personal Health Information Protection Act (PHIPA), the applicable laws and regulations of the province of Ontario. Both Committees are registered with the U.S. Department of Health and Human Services under the Federal Wide Assurance, FWA00021410, and IRB registration number IRB00002419 (HREC) and IRB00007409 (CREC).

This study is to be conducted in accordance with the submitted application and the most recently approved versions of all supporting materials.

Expiry Date: 02/24/22 (m/d/y)

Multi-year research must be renewed at least once every 12 months unless a more frequent review has otherwise been specified. Studies will only be renewed if the renewal report is received and approved before the expiry date. Failure to submit renewal reports will result in the investigators being notified ethics clearance has been suspended and Research Finance being notified the ethics clearance is no longer valid.

Level of review: Delegated Review

Signed on behalf of the Human Research Ethics Committee