HEALTH EFFECTS
MONITORING PROGRAM

YELLOWKNIFE, NDILQ, AND DETTAH

PROGRESS REPORT 2023

Follow-up to Progress Report 2020

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uOttawa
Faculté des sciences
Faculty of Science

The Health Effects Monitoring Program acknowledges that our work takes place in Chief Drygeese territory. From time immemorial, it has been the traditional land of the Yellowknives Dene First Nation. We respect the histories, languages, and cultures of all other Indigenous Peoples including the North Slave Métis, and all First Nations, Métis, and Inuit.

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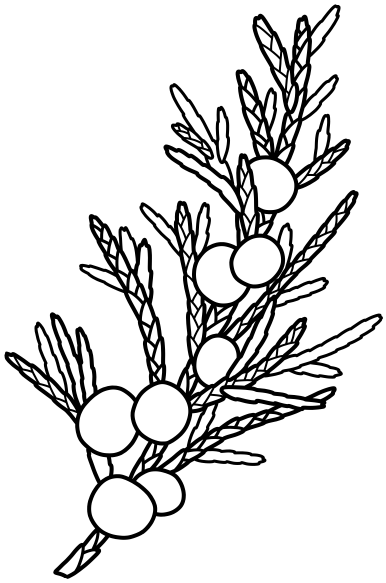


THE HEALTH EFFECTS MONITORING PROGRAM AT A GLANCE

This is the third progress report for the Yellowknife Health Effects Monitoring Program (YKHEMP). You can find our previous reports on our website by visiting ykhemp.ca/results

Why a monitoring program?

YKHEMP is guided by two main objectives:

1) To find out if local residents are exposed to higher levels of arsenic and other metals compared to other Canadians; and

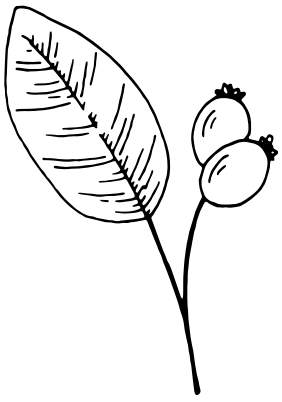
2) To investigate the long-term relationships between exposure to arsenic and health outcomes.

YKHEMP is a result of the 2013 Report of Environmental Assessment for Giant Mine. published by the Mackenzie Valley Environmental Impact Review Board, which identified public concern about the potential health impacts of environmental arsenic and Giant Mine clean-up activities. As a result, the Giant Mine Remediation Project (GMRP) was required to design and implement a broad health effects monitoring program in the Yellowknife area.

In 2017, YKHEMP was launched to establish a baseline of contaminant exposures and potential health effects for people living in Yellowknife, Ndılǫ, and Dettah, to ensure that the GMRP does not negatively impact the health of the local residents during its remediation activities.

What's the purpose of YKHEMP?

The purpose of YKHEMP is to establish baseline levels of contaminant exposure and examine possible health effects among the residents of Yellowknife, Ndılǫ, and Dettah in the Northwest Territories, before remediation work begins. Then, during remediation, as monitoring continues, new results will be compared to the baseline to ensure participants' arsenic levels are not increasing because of work being done at Giant Mine.



YKHEMP focuses on arsenic and other contaminants of concern, including cadmium, lead, antimony, manganese and vanadium. To characterize any trends between contaminant exposure and health effects, the study will be repeated every five years in children and youth, and every ten years in adults.

Who is leading YKHEMP?

The study is led by Dr. Laurie Chan, Professor and Canada Research Chair in Toxicology and Environmental Health at the University of Ottawa. A Health Effects Monitoring Program Advisory Committee (HEMPAC) was created as a mechanism for GMRP rights holders and stakeholders to contribute to the development and implementation of the study by utilizing their health expertise and knowledge of regional and community level issues.

HEMPAC members include:

- Crown-Indigenous Relations and Northern Affairs Canada (CIRNAC)
- Government of the Northwest Territories, Environment and Natural Resources (GNWT - ENR)
- Government of the Northwest Territories, Health and Social Services (GNWT - HSS)
- Health Canada (HC)
- Yellowknives Dene First Nation (YKDFN)
- North Slave Métis Alliance (NSMA)
- City of Yellowknife
- Giant Mine Oversight Board (GMOB)
- University of Ottawa (uOttawa)

INTRODUCTION

Welcome to our third Progress Report (2023). Previous results, including details about other metals like cadmium and lead, have been reported in our 2020 and 2019 Progress Reports.

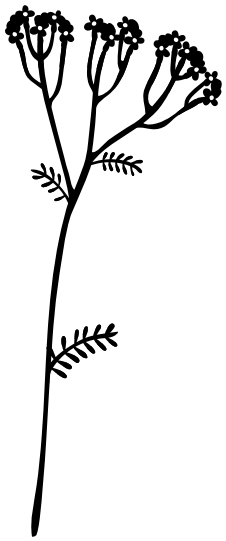
In this report, you will find:

- How the study was done
- New results from toenail and saliva samples
- A review of medical files to identify possible links between arsenic and certain health conditions
- An introduction to biomarkers of effect: KIM-1 (kidney) and CC16 (lung) function-related proteins
- What these results could mean for local residents

Additional details on the 2017-2018 baseline study can be found in our 2023 Technical Report at ykhemp.ca/results.

Overview of activities 2017-2028

2017 - 2018	• Engagement meetings in Yellowknife, Ndılǫ, and Dettah • 2037 people participate in the baseline study • Analysis of urine and toenail samples at uOttawa lab • Analysis of saliva samples at Génome Québec lab
2019	• Personal results letters sent to 2037 participants • Community results meetings in Yellowknife, Ndılǫ, Dettah • Progress Report #1 (2019)
2020 - 2022	• Progress Report #2 (2020) • Three scientific papers published (2020)
2023	• Resample children and youth from 2017-18 baseline • Sample a new group of children and youth • Community results meetings in Yellowknife, Ndılǫ, Dettah • Progress Report #3 (2023), Technical Report (2023) • Community results meetings in Yellowknife, Ndılǫ, Dettah
2028	• Children, youth, and adults are re-sampled



BACKGROUND

Arsenic is a natural component of the Earth's crust and is common in the environment. In the area surrounding Yellowknife, Ndılǫ, and Dettah, arsenic has always been in the rocks — the bedrock in this area contains a mineral called arsenopyrite and is usually associated with mineralized zones containing gold.

Giant Mine, Con Mine, and Negus Mine, in particular, operated in the area for many decades. In order to extract the Yellowknife gold, mines roasted the ore at extremely high temperatures. These high temperatures released arsenic from the rocks in a different form called arsenic trioxide, a highly toxic form of arsenic. This process released many thousands of tonnes of arsenic trioxide into the environment (with Giant contributing the vast majority). In 1951, Giant Mine began capturing the arsenic and storing it in underground stopes and chambers, that is why today, there are over 237,000 tonnes of arsenic trioxide waste stored underground.

Arsenic can be released from rock by natural weathering, volcanic eruptions, and human activities such as mining and smelting.

In 1999, the owners of Giant Mine went into receivership, and the federal government took over care, custody, and control of the Site. Today, ongoing care, maintenance, and remediation of the Site is a joint partnership between the Government of Canada and the Government of the Northwest Territories (GNWT), along with their main construction manager, Parsons. Remediation of the Site officially began in 2021.

How people are exposed to arsenic

People get exposed to some levels of arsenic from the food and water they eat and drink. Arsenic is also present in tobacco and is inhaled with cigarette smoke. Additionally, people can be exposed to arsenic from inhaling dust and ingesting contaminated soil. Arsenic is found at very low levels in many foods, including animal products, baked goods and cereals, vegetables, and fruits and fruit juices. Higher levels of arsenic are found in rice, seafood, and mushrooms.

Mushrooms should not be eaten if harvested within 10km of Giant and Con mines.

Arsenic does not accumulate in the body

At present, YKHEMP saw no evidence that people's health is at risk at the arsenic levels we are seeing in the Yellowknife area.

It is not possible to measure a lifetime exposure to arsenic, because most arsenic that enters the body leaves the body in the urine within three to five days. Some arsenic binds to keratin in the hair and nails; that is why in addition to collecting urine, we also collect toenail samples to measure for arsenic. Levels of arsenic in toenails can show us exposure to arsenic between two to twelve months.

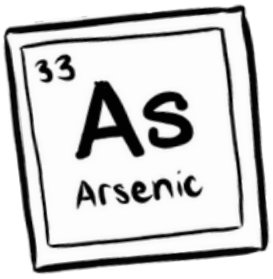
Different forms of arsenic

In the environment, arsenic exists as both organic and inorganic forms. **Organic arsenic compounds**, like arsenobetaine, arsenocholine, arsenosugars, and arsenolipids, are much less toxic than inorganic forms. These organic arsenic compounds are considered not harmful to people or wildlife. Foods such as seaweed, fish and shellfish have higher proportions of arsenic in organic forms.

Inorganic arsenic compounds are toxic and can be very harmful to human health if ingested in high amounts over a long period of time. Inorganic arsenic naturally occurs as either pentavalent arsenate (arsenic V), or trivalent arsenite (arsenic III) forms. Arsenic in minerals, rocks, plants, mushrooms, and water are mostly in inorganic form.

Arsenic III is considered more toxic than arsenic V, and MMA is more toxic than DMA.

Arsenic enters the body mainly through food, where it is absorbed in the small intestines and travels throughout the body in the blood stream. Inorganic arsenic is metabolized by the body into dimethylarsinic acid (DMA) and monomethylarsonic acid (MMA), which are both known **arsenic metabolites**. However, not all arsenic is metabolized, as both inorganic arsenic and arsenic metabolites are found in urine.



Acute arsenic exposure

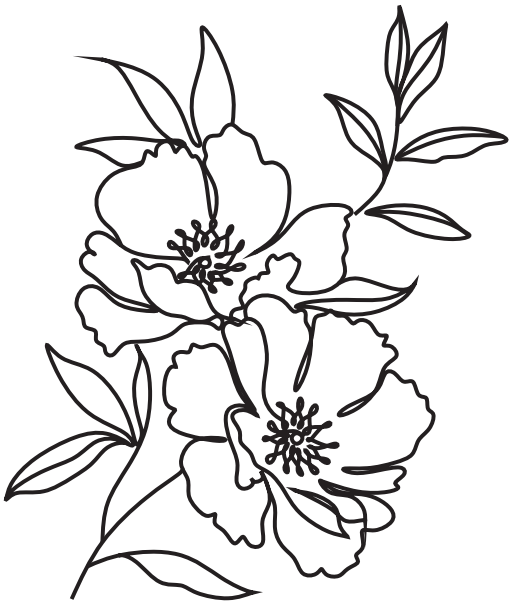
Acute exposure to high amounts of inorganic arsenic over a short period of time is usually only seen in workplaces that involve arsenic. Symptoms of acute arsenic exposure include:

- Vomiting, abdominal pain, and diarrhea
- Numbness and tingling of hands and feet
- Muscle cramping and death, in extreme cases

Chronic arsenic exposure

Chronic exposure to small amounts of inorganic arsenic over months or years may result in the following conditions:

- Skin conditions such as lesions (wounds), changes in skin colour, and hard patches on the palms of hands and the soles of feet
- Harm to the nervous system and impacts on learning in children
- High blood pressure (hypertension) and heart disease
- Bladder, kidney, liver, lung, and skin cancer
- Diabetes



METHODS

Study population

The 2017-2018 baseline study tested a total of 2037 children and adults living in Yellowknife, Ndılǫ, and Dettah, including members of the Yellowknives Dene First Nation (YKDFN) and North Slave Métis Alliance (NSMA).

POPULATION	CHILDREN (ages 3-19)	ADULTS (ages 20+)	TOTAL
YK randomly selected participants	217	673	890
YK volunteer participants	191	685	876
Yellowknives Dene First Nation	87	138	225
North Slave Métis Alliance	11	35	46
Total	506	1531	2037

For the Yellowknife general population, households were randomly selected from a list of residential addresses. In response to the request of the Yellowknife residents during the consultation period, the study also included individuals who were not selected for random sampling but who still wanted to participate in the study, these individuals formed a separate sample group labelled as "YK Volunteer Population". All members of the YKDFN and NSMA, above the age of 3, were invited to participate in the study.

Data collection

Participants were asked to complete a lifestyle and food frequency questionnaire. They were also asked to provide samples of urine and toenails to get tested for arsenic and other metals. Saliva samples were collected to look at specific genes related to arsenic. Participants also provided consent to have their medical records from the previous 5 years be reviewed by the research team. At the request of the Yellowknives Dene First Nation leadership, YKDFN members also completed a medical questionnaire and a brief medical exam that included measurements of height, weight, and blood pressure.

The study can measure only recent levels of arsenic in the body.

There is no way to measure past exposures to arsenic; for example, over a lifetime of living in Yellowknife, because there is no existing technology that can help us to do that.

Sample analysis

Samples of urine and toenails were shipped to the University of Ottawa for contaminant testing. Saliva samples were sent to Génome Québec in Québec City to test for specific genes related to arsenic.

Following analysis, each participant received their individual test results in a personal letter, with an explanation of their results and appropriate health advice and tips. Participants with metal levels above reference values were invited for follow-up testing. We use reference values set by Health Canada to compare metal results from study participants to other Canadians.

Timeline

YKHEMP is designed to investigate the relationships between exposure to arsenic and other metals, and the health of local residents over the long-term. The project will re-sample children in Spring 2023 and will re-sample children and adults in 2028. Results from these studies will be compared to the 2017-2018 (baseline) sample, and will be used to ensure that the Giant Mine clean-up activities are not negatively affecting the health of local residents.

RESULTS: ARSENIC IN TOENAIL SAMPLES

Arsenic binds to keratin in our bodies, and since fingernails and toenails are made of keratin, they are useful for measuring arsenic over a longer period of time than urine.

Diet plays a major role in the amount of arsenic that ends up in the urine, and the levels change depending on the types of food we have recently eaten. In comparison, toenails are more stable and reflect chronic or long-term arsenic exposure. Together, both toenails and urine are useful for measuring different types of exposures.

Methods

Toenails are a useful biomarker in assessing arsenic levels as they can reflect exposures of up to several months compared to urine which reflects exposures of only the previous few days.

A total of 1872 samples of toenail clippings were collected from local residents ages 3-79 living in Yellowknife, Ndılǫ, and Dettah. These samples were then processed at the laboratory and analyzed for different kinds of arsenic: arsenic III, arsenic V and their methylated metabolites, MMA, and DMA.

The Canadian Health Measures Survey study did not measure arsenic in toenails, therefore our team could not compare YKHEMP results to the general Canadian population. Without a reference level, we set levels for total arsenic in toenails based on data collected from Yellowknife. Participants were asked for a follow-up if they were in the top 5% of arsenic levels among adults, and the top 20% for children. The top 20% was chosen for children to be more cautious, allowing more children to be retested.

We also tested the different layers of the toenail to understand how people are being exposed to arsenic. Arsenic found at the core of the toenail was likely ingested and processed by the body, while arsenic found on the outside layers of the toenails most likely came from the environment, for example, from walking in soil or sediment that contained arsenic.

Key observations

- Arsenic toenail concentrations were higher in children than in adults.
- Activities identified as risk factors for children with higher toenail arsenic levels included: recreational water activities, fishing, eating garden-grown produce, and eating local wild plants.
- Activities identified as risk factors for adults with higher toenail arsenic levels included: lake water as a main drinking water source, working at Giant Mine, and eating locally harvested meat, mushrooms, and wild plants.
- Toenails collected in the spring and summer had higher arsenic levels.
- In toenails, most of the arsenic we measured was in the form of arsenic III and arsenic V, while in urine, arsenic was mostly in the form of organic arsenic and DMA.
- Study participants had higher rates of arsenic V in their toenail samples compared to arsenic III.

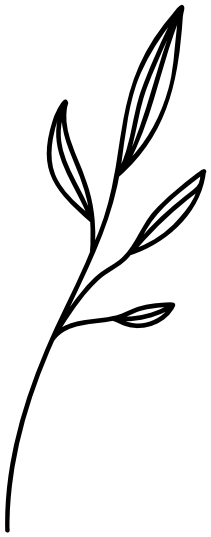
Toenail arsenic levels in our study were generally lower than other populations living near mining operations or contaminated sites.

What this could mean

Our bodies process much of arsenic III and arsenic V to which we are exposed, into MMA and DMA through a process called methylation. If people are ingesting and metabolizing arsenic, we would expect to see proportional levels of MMA and DMA in toenails. Overall, most of the arsenic in toenails was present as arsenic III and arsenic V. Less was present as MMA and DMA. This could mean that the arsenic may come from soil or dust depositing onto toenails, rather than being absorbed into the body. It is possible that children have higher toenail arsenic levels due to activities such as playing outdoors, being barefoot, and crawling on the ground.

These results add to the understanding of arsenic exposure in the Yellowknife area. Measuring arsenic in toenails gives us a understanding of arsenic exposure over the past 2-12 months.

Exposure to arsenic in Yellowknife is most likely coming from external sources like dust, soil, or sediment.



RESULTS: BIOMARKERS OF EFFECT

A biomarker is something in the body that can be measured and gives us information about a chemical, process, condition, or disease. A type of biomarker, called a **biomarker of effect**, can tell us how exposure to a chemical may impact our bodies. Blood pressure and blood glucose are examples of biomarkers of effect.

Some biomarkers of effect, when measured early in life, can be used to help detect future illnesses.

We looked for potential biomarkers of effect that could tell us about the health impacts of arsenic. We chose to look at two candidates: Kidney injury molecule-1 (KIM-1) in the kidney and club cell secretory protein (CC16) in the lung. We wanted to see if arsenic levels were related to levels of these proteins so that in the future, they may be used as indicators of lung and kidney function from arsenic exposure. We did not study these biomarkers in adults because they are affected by certain life factors, such as smoking, which can impact levels of these proteins.

KIM-1 is a protein produced by our kidneys when they are injured. KIM-1 has been shown to be a marker of reduced kidney function and chronic kidney disease. Arsenic has previously been shown to impact the kidneys, making KIM-1 a potential biomarker for detecting reduced kidney function from arsenic exposure.

CC16 is a protective protein that is produced in the lungs when the lungs and airway are disturbed. Over time, people who are repeatedly exposed to these sources tend to produce less CC16. Reduced levels of CC16 can potentially predict lung disease, cancer, and related health issues.

Methods

YKHEMP measured levels of KIM-1 and CC16 in urine samples of 244 children, ages 3 to 11, living in Yellowknife, Ndılǫ, and Dettah. The study team looked to see if there was a relationship between levels of KIM-1 and CC16, and levels of arsenic and other contaminants.

Key observations

- High KIM-1 levels were associated with higher levels of inorganic arsenic in the urine.
- High CC16 levels were associated with higher levels of inorganic arsenic, lead, and manganese in the urine.

What this could mean

Our results suggest that KIM-1 could be used as a potential biomarker for detecting early effects of arsenic exposure on kidney function in children. Using the biomarker KIM-1 to measure impact on kidney function may be a valuable tool in assessing arsenic exposures in children who showed higher levels of arsenic. In comparison, CC16 is not as specific, but may be a potential biomarker of reduced lung function from multiple contaminants such as inorganic arsenic, lead, and manganese.

RESULTS: GENETICS

The same level of arsenic exposure could impact different people in different ways, depending on how well their bodies are able to metabolize arsenic. After inorganic arsenic enters into the human body, primarily through ingestion or inhalation, it undergoes methylation in the liver. Afterwards, the arsenic is mainly excreted in urine as MMA and DMA. Methylation is one of the processes in our body which makes arsenic less toxic to us.

Arsenite methyltransferase (AS3MT) is an important protein enzyme in arsenic metabolism. If a person's body produces more AS3MT, they have a higher arsenic metabolism and are better at getting rid of the arsenic from their body. Studies have shown that some ethnicities may metabolize arsenic more efficiently in their body.

Methods

Using buccal swabs, the team collected saliva samples from participants on the inside of the person's cheek. The samples were shipped to a lab called Génome Québec in Québec City in order to look at specific genes related to arsenic. The analysis provided the team with information on how the genetic makeup of an individual may affect their interaction with arsenic.

Results are provided for Yellowknife and the Yellowknives Dene populations. Results from the North Slave Métis population were not included in this report due to the sample size being too small to yield reliable estimates.

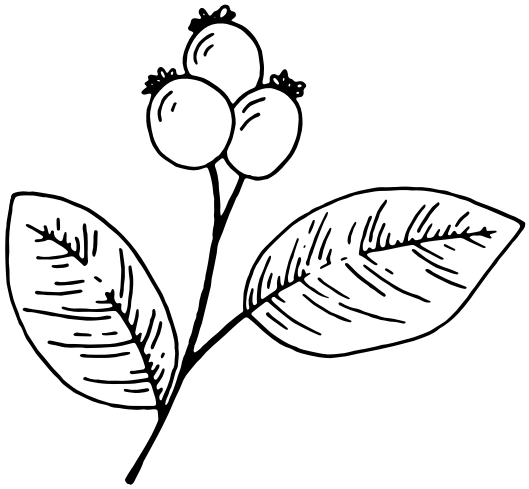
Key observations

- We found that some people in the study are less efficient at metabolizing arsenic because of a group of genes called Haplotype-AS3MT, which results in them producing less AS3MT.
- In total, 282 participants (18%) from the Yellowknife population and 61 (34%) Yellowknives Dene First Nation participants carry Haplotype-AS3MT.

What this could mean

Having copies of Haplotype-AS3MT and producing less AS3MT does not necessarily mean that the individual is at risk of being affected by arsenic exposure. At the population level, those people having the Haplotype-AS3MT means that they may be more sensitive to arsenic exposure.

At the population level, we can use genetic information as a potential risk factor for disease outcomes like skin cancer or other health problems. This information will help the research team to adjust for the differences in genes that affect arsenic metabolism. As well, it will help in future interpretation of results when investigating the relationship between arsenic exposure and health outcomes.



RESULTS: MEDICAL FILES

We wanted to see if there was a relationship between people's medical conditions and the arsenic levels that we measured in their urine and toenails. Long-term exposure to inorganic arsenic is associated with diseases and symptoms affecting most body systems and major organs.

Methods

The research team asked participants for their permission to review the previous 5 years of their medical files. Researchers only accessed health conditions that are potentially related to arsenic exposure.

In addition to the medical files, YKDFN participants were also asked to complete a medical questionnaire, and invited to undergo a brief medical exam that included measuring a person's height, weight, and blood pressure. The medical questionnaire covered diagnosed diseases, including hypertension, diabetes, cancer and common clinical symptoms potentially related to arsenic exposure.

Results from the medical files for participants living in Yellowknife, Ndılǫ, and Dettah were compared to the national and NWT data. The research team also looked at whether the measured arsenic levels in urine and toenail samples were related to the incidence, or frequency, of the various diseases. For YKDFN participants, the results obtained from the medical questionnaires were compared to the medical files of each participant to see if there were any differences between what the participant remembered and what was recorded in their files.

Key observations

- Health outcomes were similar between the randomly selected and volunteer participants in Yellowknife.
- Similar to the rest of Canada, hypertension and diabetes were the most commonly reported chronic health conditions.
- The rate of melanoma and other skin cancers was higher in the Yellowknife population compared to NWT and national data.
- Arsenic levels measured in urine or toenails were not a predictor of diseases, including skin cancer.
- For YKDFN participants, medical file results matched what people reported in their medical questionnaires. The main exceptions were skin conditions and difficulty breathing, which were reported more often in the questionnaire.
- The rate of heart conditions and hypertension was lower in the Yellowknife population compared to the NWT and national data.

What this could mean

In general, people in Yellowknife, Ndılǫ, and Dettah had health outcomes similar to others in Canada. The main difference was that there were higher rates of skin cancer in people in Yellowknife. Arsenic exposure may play a role, but we did not see a relationship in this phase of the study. The long-term results will provide a more definitive answer. Other factors, such as the amount of time that people spend outdoors and the amount of sunlight people are exposed to, may be significant contributing factors. The best way for people to reduce their risk of developing skin cancer is to use sunscreen every day.

Arsenic in the environment around Yellowknife is higher than in other areas of the NWT and Canada but much lower (up to one hundred times) than in places where people are at risk for cancer and other arsenic-related illnesses.

We did not find a relationship between the levels of arsenic measured in people's urine and toenails and the health conditions reported in medical files at this time. The study is designed to look at the long-term relationships; therefore, future waves of resampling will help provide more information about the pattern of health conditions and their relationship to measured levels of arsenic.

TRUTH AND RECONCILIATION

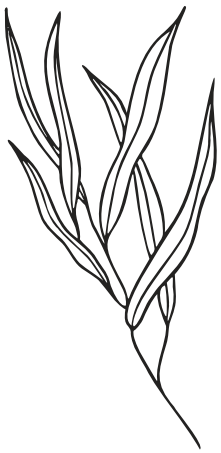
YKHEMP is committed to working together with the YKDFN and the NSMA to promote and implement some of the actions set out in the reports of the Truth and Reconciliation Commission of Canada (particularly Calls to Action 18 and 19 under the Health section).

YKDFN and NSMA are key partners in the study, representing their communities. Sitting on our advisory committee, the HEMPAC, they help to determine research priorities, provide strategic advice on study protocols, and review all communication materials.

Copies of the YKDFN-specific and NSMA-specific baseline data were provided to our respective partners in May 2022. The arsenic and health data will help to better position YKDFN and NSMA members to develop health mitigation measures that are evidence and community based. YKHEMP will be repeated every 5 years and future results will be compared to the baseline, providing important information towards the investigation of the long term relationships between arsenic and health effects.

Ownership, control, access, and possession (OCAP)

The OCAP principles assert that First Nations have control over data collection processes, and that they own and control how collected information can be used. YKHEMP employs OCAP principles with both the YKDFN and NSMA. Following data collection, the YKDFN has ownership, control, access, and possession of data collected from their members; the NSMA has the same for their members.



UNDRIP

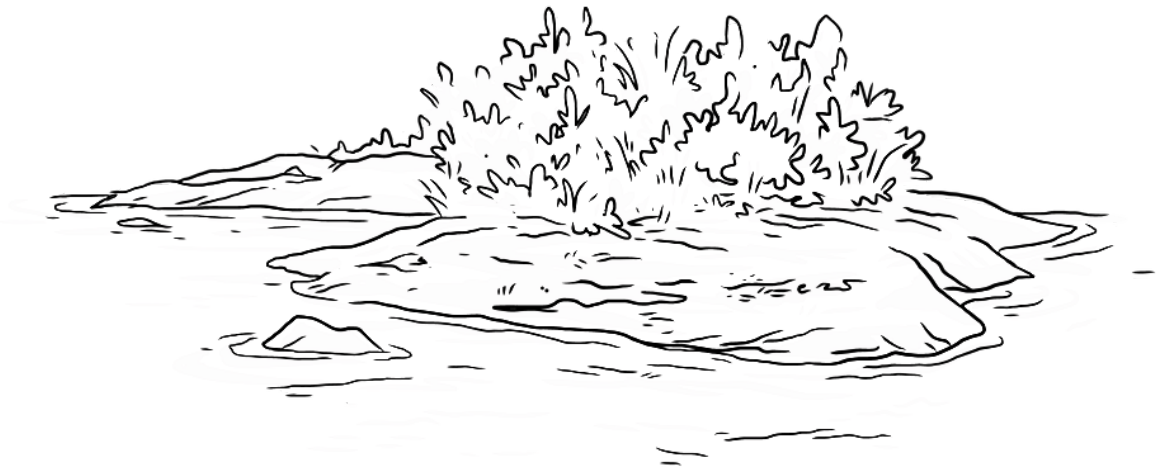
YKHEMP supports the implementation of UNDRIP Articles 23 and 29, which assert that Indigenous peoples have the right to be actively involved in developing and implementing programs which aim to support the health and wellbeing of their communities, and that health-related programs are implemented, as needed.

ETHICAL CONSIDERATIONS

Our research was conducted following the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans and, in particular Chapter 9, research involving the First Nations, Inuit and Métis Peoples of Canada, and the document entitled: Indigenous Peoples & Participatory Health Research: Planning & Management, Preparing Research Agreements published by the World Health Organization.

The study was approved by the Health Sciences and Sciences Research Ethics Board of the University of Ottawa and the Aurora College Research Ethics Committee. In addition, the study has been granted a Scientific Research License from the Aurora Research Institute in Northwest Territories. Participation in the project was voluntary and based on informed written consent following an oral and written explanation of each part of the project.

All information collected is kept confidential throughout the study at the University of Ottawa.



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