Environment International 152 (2021) 106510

Contents lists available at ScienceDirect

Environment International

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

Essential and non-essential elements in biological samples of inhabitants residing in Nenets Autonomous Okrug of the Russian Arctic

Nikita Sobolev[a,*], Dag G. Ellingsen[b], Natalia Belova[a,c], Andrey Aksenov[a], Tatiana Sorokina[a], Anna Trofimova[a], Yulia Varakina[a], Dmitriy Kotsur[a,d], Andrej M. Grjibovski[c,e,f,g], Valerii Chashchin[a,h,i], Konstantin Bogolitsyn[a,d], Yngvar Thomassen[a,b,i]

[a] Northern (Arctic) Federal University Named After M. V. Lomonosov, Naberezhnaya Severnoy Dvini 17, 163002 Arkhangelsk, Russia
[b] National Institute of Occupational Health, Gydas vei 8, N-0363 Oslo, Norway
[c] Northern State Medical University, Troitskiy Ave. 51, 163000 Arkhangelsk, Russia
[d] N. Laverov Federal Center for Integrated Arctic Research, Ural Branch of the Russian Academy of Sciences, Naberezhnaya Severnoy Dvini 23, 163000 Arkhangelsk, Russia
[e] Sechenov First Moscow State Medical University (Sechenov University), Moscow 119991, Russia
[f] Al-Farabi Kazakh National University, Almaty 050040, Kazakhstan
[g] West Kazakhstan Marat Ospanov Medical University, Aktobe 030019, Kazakhstan
[h] North-Western State Medical University named after I.I. Mechnikov, Kirochnaya ul. 41, 191015 Saint-Petersburg, Russia
[i] Institute of Ecology, HSE University, Myasnitskaya str. 20, 101000 Moscow, Russia

ARTICLE INFO

Handling Editor: Lesa Aylward

Keywords:
Essential elements
Non-essential elements
Russian Arctic
Whole blood
Urine
Indigenous people

ABSTRACT

Exposure of Arctic residents to environmental pollutants is an emerging public health problem receiving little global attention. The objective of this study was to assess whole blood concentrations of nine selected essential (Co, Cu, Mn, Se, Zn) and non-essential (As, Cd, Hg, Pb) elements among Nenets and non-Nenets adult residents of the Nenets Autonomous Okrug (NAO) living in seven coastal and inland settlements. Urine was collected in two settlements for assessment of iodine status. Altogether 297 whole blood and 68 urine samples were analysed by inductively coupled mass spectrometry and the accuracy of the measurements was assessed by use of human whole blood and urine quality control materials. Several essential and non-essential showed significant variations in whole blood concentrations characterized by gender, population group and locality. Cd levels among non-Nenets non-smokers (0.19 μg/L) indicated a dietary intake at a natural global background level. Hg concentrations in whole blood show that not more than 10% of women in the fertile age had a Hg intake above the EFAS's recommendation. The Pb concentrations were in the range of, or partly exceeding reference values for increased risk of nephrotoxicity, and there is a need for a continued effort to reduce Pb exposure among the population groups in NAO. With high prevalence of obesity among the Nenets and non-Nenets population, a high prevalence of Fe-deficiency among menstruating women (<50 years) (37.2%) and a lower I status than recommended by WHO, these nutritional dependent components deserve further attention.

1. Introduction

Exposure of the Arctic residents to environmental pollutants is a public health problem receiving little global attention. The Arctic Monitoring Assessment Program (AMAP) reported already in 1998 that indigenous inhabitants who hold onto traditional lifestyles are exposed to environmental contaminants to much greater extent than non-indigenous inhabitants in Arctic regions (AMAP assessment, 2015). AMAP's biomonitoring has provided unique data suggesting that concentrations of persistent inorganic pollutants (PIPs) such as lead (Pb), cadmium (Cd) and mercury (Hg) as well as most of persistent organic pollutants (POPs) have decreased over the last decades across the Arctic, while Hg concentrations remain stable in Inuit populations in Canada and Greenland (Abass et al., 2018; Donaldson et al., 2016). Large variations in whole blood Hg (B-Hg) have been reported from the Arctic regions of Russia (Abass et al., 2018) with mean concentrations ranging from 1.6 μg/L in pregnant women in Chukotka to 11.2 μg/L in indigenous men in the Yamalo-Nenets Autonomous district (Agbalyan

* Corresponding author.
E-mail address: n.a.sobolev@outlook.com (N. Sobolev).

https://doi.org/10.1016/j.envint.2021.106510
Received 19 November 2020; Received in revised form 10 February 2021; Accepted 6 March 2021
Available online 21 March 2021

and Shinkaruk, 2018; Gibson et al., 2016).

Human consumption of sea mammals, fish and other seafood has been consistently shown as main sources of POPs, Hg and arsenic (As) for Arctic residents (Dudarev et al., 2019; Lockhart et al., 2005; Sobolev et al., 2019). Tobacco smoking and recreational shooting, hunting, preparation of angling and fishing equipment/ammunition are important sources of Cd and Pb (AMAP assessment, 2015; Laidlaw et al., 2017; Mertz, 2012; Smith et al., 1997). Although AMAP's activities provide information on exposure of the Arctic populations to PIPs and POPs, the information on concentrations of environmental contaminants in human biological fluids, particularly in residents of the Russian part of the Arctic, is still scarce (AMAP assessment, 2015).

The Russian Federation is the largest country in the world with a multi-ethnic population unevenly distributed across the country with large socioeconomic, environmental, nutritional, and cultural differences between the settlements. There are more than 180 ethnicities permanently residing on the territory of Russia. Forty of them are officially registered as "indigenous minorities of the North, Siberia and the Far East". These ethnic groups maintain their traditional lifestyles and live predominantly in the Northern part of the country. The total population of these ethnic groups is ~260 thousand individuals accounting for ~0.2% of the Russian population.

Residents of the Russian Arctic have considerably lower life expectancy and poorer general health than national average. Although poor socioeconomic conditions seem to be responsible to the major part of the disease burden among the Arctic residents, exposures to environmental pollutants through traditional foods also contribute to poorer health of the residents of the North compared to their counterparts living in Central and Southern parts of the country. Indigenous people may be at greater risk of being exposed to environmental hazards than non-indigenous residents of the Arctic due to their lifestyle, nutrition and living conditions (Webster, 2005, Bjerregaard, 2019). However, significant changes in lifestyles have occurred over the last two decades, which have distanced them from their ancestors in economic, social, cultural, and even anthropometrical respects (AMAP assessment, 2004).

Although Russia has a national system of so-called socio-hygienic monitoring (http://43.rospotrebnadzor.ru/directions/sgm/), data on exposure of the population to PIPs and POPs are not routinely collected. Thus, the information related to the amount of these environmental pollutants are missing for the Russian part of the Arctic region. To fill this gap of knowledge an international biomonitoring laboratory was established in 2017 at the Northern (Arctic) Federal University (NArFU) in Arkhangelsk with the main purpose to perform regular quantitative assessments of exposures to and measurement of concentrations of chemical compounds in the environments, plant- and animal species as well as in humans with the further aim to provide the basis for development of the evidence-based health risk management programs in the Russian Arctic.

Biomonitoring is of fundamental importance in environmental and nutritional sciences for identification and quantitative assessment of exposure to chemical compounds providing important information for health risk management. Iodine (I), iron (Fe) and zinc (Zn) deficiencies have similar effects on the development of the human brain as POPs, Hg and Pb (Black, 2003). However, the information on concentrations of these elements in Russian Arctic populations is almost non-existent in international peer-reviewed literature.

The aim of this study was to assess blood concentrations of selected essential and non-essential elements among Nenets and non-Nenets residents of the Nenets Autonomous Okrug (NAO) – a federal subject of Russia located in the Arctic.

2. Materials and methods

2.1. Site description and study design

NAO is one of the northernmost and the least populated (44.1 thousand in 2020) federal subject of the Russian Federation according to Federal State Statistics Service of Russian Federation. The town Naryan-Mar is the administrative center of the region accounting for 51.4% of the NAO's population (Fig. 1). Most settlements in NAO are located far from Naryan-Mar, have poor infrastructure and almost non-existent connections with the regional center for most of the year. NAO has a sub-Arctic climate with long and cold winters and short and wet summers, strong winds and frequent weather changes. Russians (63.3%), Nenets (17.8%) and Komi (8.6%) are the three major population groups. Lifestyles of people in the remote areas have been significantly influenced by climate change (Smith et al., 2014). Reindeer, fish and birds are main food sources for the rural population of NAO (Petrenya et al., 2012). Meat and fish account for as much as 75% of daily caloric intake in some settings (Murashko and Dallmann, 2011).

The sites selected included all island settlements (Bugrino, Varnek), coastal settlements in the western (Shoina) and eastern (Amderma) regions of NAO and inland settlements in the central region (Indiga, Nelmin-Nos, Krasnoe). The selected settlements should also reflect differences in the traditional way of living; "indigenous" (Bugrino, Varnek); "urban" (Krasnoe), "industrially developed" (Shoina, Amderma) and "mixed". The industrially developed settlements consisted mainly of non-indigenous people in the past, but the percentage of indigenous residents has later significantly increased mainly due to a large reduction of the population as a whole. The Nelmin-Nos and Indiga settlements represents populations with no dominating indigenous or non-indigenous lifestyles. The settlements which have previously been part of AMAP studies were also chosen (Nelmin-Nos, Krasnoe) (AMAP assessment, 2004) (Fig. 1).

Indiga arose on the site of the seasonal fishing area of the Mezen Pomors and is located in the northwestern part of the NAO at the confluence of the Indiga and Shchelikha rivers. As a settlement it was first officially mentioned in 1926. The population of Indiga is 726 people (2019) of which 434 are Nenets (59.8%). Main activities of the inhabitants are reindeer breeding, hunting, and fishing. The distance to Naryan-Mar is 170 km and transportation is organized by air.

Krasnoe is located on the right bank of the Krasnaya River 16 km from the confluence to the Pechora River. As a base of the kolkhoz Kharp, Krasnoe was founded in 1956. The population is 1840 people (2020) including 450 Nenets (24.5%) (Data provided by the municipality "Primorsko-Kuy village council" in October 2020). The main occupation of the population is reindeer and cattle husbandry. Hunting and fishing are also common activities in this settlement. During open water periods, the travel between Krasnoe and Naryan-Mar is carried out by boat along the Pechora River (33 km) or year around by road (41 km).

Nelmin-Nos was founded in 1937 as a base for the first Nenets reindeer breading collective farm and is located downstream of the Pechora River, on the left bank of the Tundra Shar. The population of Nelmin Nos is 864 people (Data provided by the municipality "Malozemelskii village council" in October 2020) and the overwhelming majority of residents are Nenets (n = 777, 89.9%). The main activities of the inhabitants are reindeer husbandry, hunting and fishing. The distance to Naryan-Mar is 60 km and transportation is possible by boat during summer and by car during winter.

Shoina is located on the shore of the White Sea on the Kanin Peninsula at the mouth of the river Shoina. By 1950 more than 1500 inhabitants lived in the settlement when it was a base for the fishing fleet of the kolkhozes of Arkhangelsk Oblast. The village has today 352 residents with 31.8% as Nenets. The main activities of both indigenous- and non-indigenous residents are fishing and hunting. There are no reindeer breeding in the village. The distance to Naryan-Mar is 380 km and transportation is by air.

Amderma is located on the coast of the Kara Sea at the geographical border between Europe and Asia. The population of the village founded in 1933 for fluorite mining is 623 with 39.8% as Nenets. Local residents are mainly engaged in hunting and fishing although some reindeer herding is also present. The distance to Naryan-Mar is 490 km and

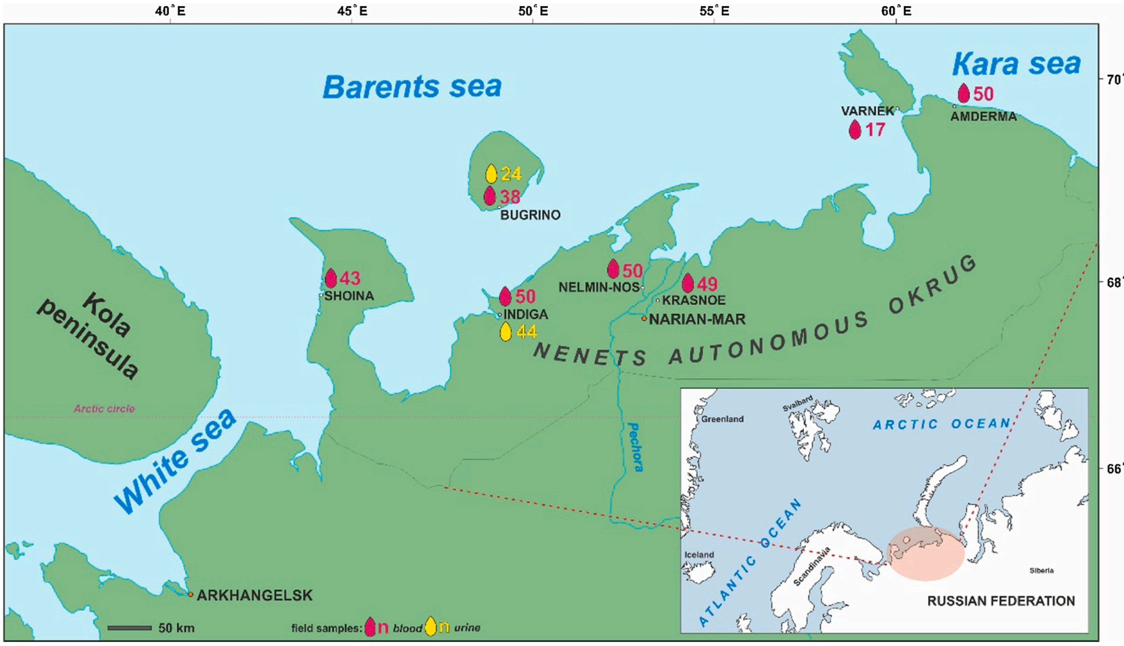

Fig. 1. Map of the Nenets Autonomous Okrug with study sites, number of samples collected and footnotes with ethnicity and gender information. Shoina: *Ethnicity*: 12 Nenets, 25 Russian, 6 others; *Gender*: 11 men, 32 women. Bugrino: *Ethnicity*: 35 Nenets, 3 Russian; *Gender*: 14 men, 24 women. Indigia: *Ethnicity*: 21 Nenets, 25 Russian, 4 others; *Gender*: 15 men, 35 women. Varnek: *Ethnicity*: 16 Nenets, 1 Russian; *Gender*: 6 men, 11 women. Amderma: *Ethnicity*: 16 Nenets, 26 Russian, 8 others; *Gender*: 17 men, 33 women. Nelmin-Nos: *Ethnicity*: 42 Nenets, 6 Russian, 2 others; *Gender*: 22 men, 28 women. Krasnoe:*Ethnicity*: 23 Nenets, 15 Russian, 11 others; *Gender*: 8 men, 41 women.

transportation is by sea or air.

Bugrino is situated on the south of the Kolguev island in the Barents Sea. Although it was founded in 1875, most of the Nenets population came from Novaya Zemlya archipelago in the 1950s. The majority of the total population (n = 470) are Nenets (95.7%). Reindeer herding, hunting, fishing, gathering wild plants and folk crafts are the main activities of the indigenous population while the non-indigenous residents work at the Peschanoozerskoye oil field located 60 km from the village. Kolguev island is a “territory of traditional nature management”, that means that the territory is protected by the state. All industrial activities are carried out without violating the rights and legitimate interests of the Nenets people. The distance to Naryan-Mar is 370 km and communication with the island is organized by helicopter.

Varnek is located on the Vaygach Island which separates the Barents Sea from the Kara Sea. Historically, Vaygach was the sacred land for the Nenets people and was not used for permanent residence until the 20th century. Varnek is the only settlement on the island. It was founded in 1930 to house the GULAG administration and prisoners who worked in the Pb- and Zn mines (Svetlichnaya and Vorobyeva, 2019). Nenets account for 90% of the 118 inhabitants. (Data provided by the municipality “Yusharsky village council” in October 2020). All local residents have similar lifestyles with hunting, fishing and gathering berries and plants being the main activities. The entire Vaygach Island, like Kolguev, is a territory of traditional nature management.

The travel to Bugrino and Varnek within the framework of this study was by sea with the help of NArFU’s “Arctic Floating University” expedition.

2.2. Recruitment of participants

Residents of the settlements were invited to participate in the study through the information campaigns in the villages. We planned to recruit 50 individuals from each village, but in some places, this was not feasible due to the total number of inhabitants and their interest to participate. According to the study protocol participants were recruited based on only two criteria: i) age should be 18 years (the age of maturity under Russian law) or older, and ii) permanent residence in the settlement. There were no specific requirements for gender, nationality, profession, lifestyle and nutrition, etc. Due to more than 10 years’ gender difference in life expectancy in the Russian North, the known general situation that women are more concerned and interested in own and family health (Ek, 2013) and lack of men in the day of collection of biological samples due to their involvement in reindeer breeding, fishing and hunting it was a predominance of females in the sample.

NArFU formally contracted the regional hospital to provide services for blood sampling of the population of the seven villages. Those who agreed to participate filled out a self-administrated food frequency questionnaire to record demographic and nutritional variables. Trained medical personnel checked the completeness of the questionnaires.

This study was approved by the Ethical Committee at the Northern Medical State University, Arkhangelsk, Russia (protocol no. 06/09-17 of Sept. 27, 2017). All the participants signed a written informed consent.

2.3. Examinations

Examinations were conducted in 2018 at the medical units of the seven villages where whole blood was collected by local authorized health staff. A total of 68 spot urine samples were collected among the study participants in Bugrino (n = 24) and Indiga (n = 44). The numbers of individuals participating in the study are presented in Fig. 1.

2.4. Collection of biological samples

Whole blood was collected from the cubital vein into 9.5 mL plastic vacutainer tubes with EDTA (Lind-Vac, InterVac Technology, Estonia) after cleaning of the skin with 0.05% solution of chlorhexidine in ethanol and water. The samples were immediately frozen at −25 °C. To obtain serum samples for ferritin measurements whole blood was collected into 9.5 mL plastic vacutainer tubes with clot activator ((Lind-Vac, InterVac Technology, Estonia). After collection, the tubes were left for 30 min at room temperature for clot formation and then centrifuged at 3000 rpm for 10 min. Serum was then transferred to 2 mL cryogenic tubes (type and manufacturer) and frozen at −25 °C. The first voided morning urine sample were collected from the participants in Burgino and Indiga in 125 mL polypropylene screw cap urine containers (Litoplast-Med, Minsk, Belarus) and immediately frozen. All samples were transported in medical cooler bags to NArFU for long-term storage at −25 °C until analysis.

2.5. Measurement of elements in biological samples

Whole blood was analysed at NArFU for the content of Hg, Cd, Pb, As, cobalt (Co), copper (Cu), manganese (Mn) and zinc (Zn) while iodine (I) was measured in urine. Whole blood was prepared for analysis by pipetting one mL into a 15 mL polypropylene screw cap tube (Sarstedt AG, Numbrecht Germany) before adding 2 mL of in-house double sub-distilled nitric acid (Puriss PA, Merck, Darmstadt, Germany). After gentle heating to 90 °C in a DigiBlock heating block (LabTech, Sorisole, Italy) with temperature rate 3 °C/min for 90 min and cooling to room temperature 100 μL of both an internal standard mixture, containing 1.25 μg/mL of scandium (Sc), yttrium (Y), indium (In), and bismuth (Bi) (Bruker Daltonics, Fremont, CA, USA) and a 2.5 μg/mL ^{74}Se enriched stable isotope solution (99.9% of ^{74}Se from STB Isotope Germany GmbH, Hamburg, Germany) were added before final dilution to 10 mL with deionized water.

Two mL of urine were added aliquots of the 2.5 μg/mL ^{74}Se enriched stable isotope and a 1 μg/mL tellurium internal standard solutions before dilution with deionized water to 10 mL.

The measurements were performed with an Aurora Elite inductively coupled plasma mass spectrometer (Bruker Daltonik GmbH, Bremen, Germany) equipped with a collision reaction interface (CRI) for reducing polyatomic interferences, a concentric glass nebulizer and a Peltier cooled Scott double-pass spray chamber. The instrument was calibrated with nitric acid, whole blood and urine matrix matched standards solutions diluted from primary certified standard solutions (Spectrapure Standards AS, Oslo, Norway). The following isotopes with internal standards in brackets; ^{202}Hg (^{209}Bi), ^{114}Cd (^{115}In), ^{206,207,208}Pb (^{209}Bi), ^{59}Co (^{45}Sc), ^{65}Cu (^{89}Y), ^{127}I (^{125}Te) and ^{55}Mn (^{45}Sc) were measured in no gas mode. To reduce polyatomic mass interferences for the ^{75}As (^{74}Se) and ^{78}Se (^{74}Se) isotopes the CRI was used with a hydrogen flow rate of 115 mL/min in the skimmer cone. The isobaric interference from ^{114}Sn on ^{114}Cd was automatically corrected by the instrumental set-up, but there was no need for any correction for molybdenum monoxide (^{98}Mo^{16}O) since whole blood concentration of Mo is about 1 μg/L.

For quality assurance of the measurements Seronorm Trace Elements Whole Blood L-1 (Lot:010010) and L-2 (Lot: 010011) and Seronorm Trace Elements Urine L-1 (Lot:1403080) and L-2 (Lot:1403081) reference materials (Sero AS, Billingstad, Norway) were used. The results obtained for the elements were within the producer's recommended reference ranges.

Limit of quantification (LOQ) for elements in whole blood in μg/L were Mn (1.2), Co (0.05), Cd (0.004), Hg (0.2), Pb (0.05), As (0.1), Se (1.4) and 0.1 mg/L of Cu and Zn, respectively. The LOQ for I in urine was 1 μg/L.

Serum ferritin was measured by Random Access automatic biochemical analyzer using ferritin assay kits at the central research hospital of the Northern State Medical University in Arkhangelsk (Biosystems, Barcelona, Spain).

2.6. Statistical analysis

The concentrations of the non-essential elements had generally skewed distributions. To achieve a normal distributions these analytes were log-transformed when skewness exceeded 2.0. The geometric means (GM) are presented for these while arithmetic means (AM) are otherwise reported. The differences between groups were assessed with the Student's *t*-test. Multiple linear regression analysis (backward procedure) was used to assess associations between elemental concentrations as dependent variables and a set of independent variables, including sex (1/0), being indigenous (1/0), living in a coastal settlement (1/0), age, body mass index (BMI) and being active smoker (1/0). Univariate associations were obtained by least squares linear regression analysis and Pearson's correlation coefficient as a measure of association. For adjustment of relevant covariates between groups P-values $<$ 0.05 were considered to be significant. All statistical calculations were performed using SPSS software, version 25.0 (IBM Corp., Armunk, NY, USA).

3. Results

The sample consisted of 204 women and 93 men aged 18–87 years. Nenets (54.2%), Russians (35.7%) and Komi (7.1%) were the main population groups. The remaining participants were of Ukrainian (n = 7), Mariy (n = 1) and Udmurt (n = 1) descent. For further analyses Nenets were merged into one group representing the indigenous population (n = 161) while Russians, Ukrainians, Komis, one Maryi and one Udmurt were combined into a non-Nenets group (n = 136). Background characteristics of the population are summarized in Table 1.

The women were significantly older than men. There was no statistical significant difference between the genders of the two population groups for BMI, but smoking was significantly more common among the male Nenets participants. The prevalence of obesity, using the World Health Organization's definition ($>$30 kg/m^2) is significantly higher among non-Nenets women and men, 30.5 and 29.3%, respectively. S-ferritin was significantly lower among women of both population groups and 20.2 and 12.6% of those were Fe deficient ($<$15 μg/L of S-ferritin). Grouping the women of all ethnicities in two age groups, $\leq$ 50 (n = 94) and $>$50 years (n = 110), the prevalence of Fe deficiency were 26.6 and 8.2%, respectively.

Whole blood concentrations of Mn, Cu, Cd, Hg and Pb were higher in the Nenets group while Zn, As and Se were lower (Table 2).

Women had significantly higher amounts of Co and Cu in their whole blood, while men showed higher concentrations of Zn and Pb. For other elements there were no significant differences (Table 3).

There were significant group differences for a number of elements between the settlements; e.g. the inhabitants from Varnek and Bugrino had the highest B-Pb concentrations. For B-Hg, the lowest concentrations were among the inhabitants of the coastal villages Bugrino, Amderma and Shoina although the 17 participants in Varnek displayed a significant higher average value. Since there were large discrepancies in the requirement of participants from the different villages with respect to age, gender and ethnicity, it is difficult to compare group differences using a geographical factor as *settlement*. Thus, it is sounder to stratify the population to live in either a coastal (Burgino, Amderma, Shoina, Varnek) or in an inland settlement (Indiga, Nelmin-Nos, Krasnoe).

The whole blood concentrations of Mn, Zn, Pb and As in the coastal sub-group were significantly higher while concentrations of Cu and Hg were higher in the inland population. For Co, Cd and Se there were no significant difference (Table 4).

Multiple linear regression analysis including all participants was used to assess several factors simultaneously (Table 5). As an example of how this table should be understood, we may use Hg as an example: the concentrations of Hg was 0.95 μg/L higher among Nenets than non-Nenets and 2.7 μg/L higher among the inland populations compared to the coastal population. The results show that not only the geographical factor, but also being Nenets or non-Nenets, gender, smoking and to a lesser extent, age and BMI, had impact on the concentrations. Being male, smoking and coastal, Nenets were associated with higher concentration of B-Pb, while coastal non-Nenets males had significantly higher amounts of Zn in the blood. While B-Hg was significantly higher among the inland Nenets, the B-Pb was highest among the Nenets in the coastal settlements after adjusting for smoking and gender (Fig. 2a-b). B-As was significantly higher in the coastal

Table 1
Background data of the 297 study participants from seven villages of the Nenets Autonomous Okrug.

	Nenets (n = 161)				Non-Nenets (n = 136)			
	Women (n = 109)		Men (n = 52)		Women (n = 95)		Men (n = 41)	
	AM	Min-Max	AM	Min-Max	AM[a]	Min-Max	AM	Min-Max
Age (y)	46.5	20–79	42.9	20–78	54.3	19–87	43.6	18–72
BMI (kg/m^2)	27.0	16.2–42.9	26.4	19.8–37.1	28.5	19.2–46.0	27.1	19.4–40.0
BMI ≥ 30 (kg/m^2), (%)	21.3	–	19.2	–	30.5	–	29.3	–
S-ferritin (μg/L)	75.9	0.5–342	134.7	17–506	83.7	3–463	154.1	13–506
Prevalence of Fe deficiency (%)[b]	20.2	–	0	–	12.6	–	2.4	–
Current smoker (%)	25.7	–	63.5	–	24.2	–	31.7	–
Former smoker (%)	12.0	–	9.6	–	7.4	–	34.1	–

[a] Arithmetic mean.
[b] S-ferritin < 15 μg/L.

Table 2
The arithmetic mean (AM) and minimum and maximum concentrations of elements in whole blood (μg/L) among Nenets and non-Nenets in the Nenets Autonomous Okrug.

Element	Non-Nenets (n = 136)		Nenets (n = 161)		p-value
	AM	Min-Max	AM	Min-Max	
Co[a]	0.52	0.25–1.7	0.53	0.30–2.5	0.64
Cu	1.05	0.58–1.9	1.13	0.73–2.4	0.003
Mn	12.1	4.4–26.7	15.1	4.3–35.0	<0.001
Se	128	89–227	122	85–192	0.004
Zn	9.1	4.2–13.7	8.6	4.1–14.5	0.03
As[a]	5.9	<LOQ –143	3.9	<LOQ –163	0.009
Cd[a]	0.27	<LOQ – 4.2	0.40	<LOQ –3.0	0.004
Hg	4.6	0.52–18.4	5.6	0.28–24.3	0.03
Pb[a]	19.8	5.4–356	28.9	5.2–281	<0.001

Abbreviations: <LOQ – less than limit of quantification.
[a] Geometric mean.

Table 3
The arithmetic mean (AM) and minimum and maximum concentrations of elements in whole blood (μg/L) among women and men in the Nenets Autonomous Okrug.

Element	Women (n = 204)		Men (n = 93)		p-value
	AM	Min-Max	AM	Min-Max	
Co[a]	0.56	0.26–2.5	0.47	0.25–0.94	<0.001
Cu	1.14	0.69–2.4	1.01	0.58–1.5	<0.001
Mn	14.0	4.3–35.0	13.2	4.5–24.0	0.19
Se	125	85–227	124	89–192	0.70
Zn	8.6	4.2–14.5	9.4	4.1–12.9	<0.001
As[a]	5.2	<LOQ – 163	3.9	<LOQ – 143	0.09
Cd[a]	0.32	<LOQ-4.2	0.37	<LOQ – 2.6	0.29
Hg	5.1	0.3–24.3	5.4	0.64–23.8	0.55
Pb[a]	20.6	5.2–356	34.8	5.4–281	<0.001

Abbreviations: <LOQ – less than limit of quantification
[a] Geometric mean.

Table 4
The arithmetic mean (AM) and minimum and maximum concentrations of elements in whole blood (in μg/L) among participants from inland or coastal settlements in the Nenets Autonomous Okrug.

Element	Inland (n = 149)		Coastal (n = 148)		p-value
	AM	Min-Max	AM	Min-Max	
Co[a]	0.51	0.29–1.2	0.54	0.25–2.5	0.12
Cu	1.13	0.69–1.9	1.07	0.58–2.4	0.008
Mn	12.0	4.3–26.7	15.4	5.3–35.0	<0.001
Se	123	89–227	127	85–192	0.17
Zn	8.4	4.1–14.5	9.3	4.9–13.7	<0.001
As[a]	3.0	<LOQ-50	7.6	<LOQ-163	<0.001
Cd[a]	0.34	0.07–3.0	0.33	<LOQ-4.2	0.86
Hg	6.5	0.86–24.3	3.8	0.28–21.4	<0.001
Pb[a]	17	5.2–164	34	7.2–356	<0.001

Abbreviations: <LOQ – less than limit of quantification.
[a] Geometric mean.

population after adjusting for age. B-Mn concentrations of the female coastal Nenets were also higher compared with any other sub-groups. As expected, smoking habits was the dependent variable with highest impact on B-Cd concentrations. The Nenets had in average 6 μg/L lower amounts of Se compared with non-Nenets.

The median concentration and GM of I in the urine samples (n = 68) was 103 μg/L of 122 μg/L, range 21 – 2930.

4. Discussion

4.1. General description of the population

This is to our knowledge the largest study of essential and non-essential trace element concentrations in human biological fluids collected from residents in rural settlements of the Russian Arctic.

Nenets Autonomous Okrug is home to Russian, Nenets and other ethnic groups with presumably similar lifestyles and diets including reindeer, game and fish. Several studies have reported on unhealthy diets with high-fat, high cholesterol, low fibre, high consumption of dairy, meat, sugar and alcohol among most Russians (Lunze et al., 2015). This may have contributed to the present high prevalence of overweight (57.1%) and obesity (23.1%) in Russian adults (2016). However, most of the studies did not include Arctic populations. In our study, 30.5 and 29.3% of the non-Nenets women and men were obese which is somewhat higher than the national average. The prevalence among female (21.3%) and male (19.2%) Nenets was however similar to the national average, but considerably lower compared with a recent study among urban Russian women (n = 132) living in Arkhangelsk – a large regional centre in the Russian Arctic zone – and Nenets women (n = 93) in Nelmin-Nos. In that study Petrenya et al. (2014) reported prevalence of general obesity of 34.4% in Russians and 42.5% in Nenets, respectively. Thus, our results in combination with the results of earlier studies suggest that obesity is a public health problem in the European part of the Russian Arctic being obvious among both population groups. Whether this is true for the Asian part of Arctic Russia populated with different ethnic groups remains to be studied.

The evidence of the role of essential and non-essential elements on developing obesity is review by Karatela et al. 2016. They conclude that the literature provides information that essential elements in developing obesity is possible, e.g. for Fe and Zn. There is, however, in their view, a lack of evidence for non-essential elements. It is interesting to note that in our study there is a statistically significant association between BMI and the concentrations of Cu and Mn, but for S-ferritin and Zn (Table 5).

Iron deficiency is an important risk factor for adverse health outcomes among humans worldwide and is a diagnostic challenge since it may be unrecognized for a long period particularly in rural areas.

Table 5
Multiple regression α and β coefficients with 95% confidence intervals in brackets for the associations between selected socio-demographic factors and whole blood concentrations of elements among the residents of Nenets Autonomous Okrug. Presented are the respective β-coefficients of statistical significance, multiple r and the corresponding p-values.

Element	α	β						Multiple r
		Population group	Sex	Community	Smoking	Age	BMI	
Co[a]	−0.16***	–	−0.09*** (−0.12, −0.06)	–	–	−0.002** (−0.003, −0.001)	–	0.33***
Cu	0.79***	0.08** (0.03, 0.13)	−0.13*** (−0.19, −0.08)	0.07** (0.03, 0.12)	0.07** (0.02, 0.13)	–	0.009** (0.004, 0.01)	0.41***
Mn	18.2***	3.0*** (1.9, 4.1)	−1.2 * (−2.3, −0.01)	−3.7*** (−4.7, −2.6)	–	–	−0.14** (−0.24, −0.04)	0.47***
Se	128***	−6.3** (−10.6, −1.5)	–	–				0.17***
Zn	9.2***	−0.46* (−0.87, −0.05)	0.84*** (0.40, 1.3)	−0.80*** (−1.2, −0.39)	–	–		0.33***
As[a]	0.48***	–	–	−0.43*** (−0.55, −0.31)	–	0.009*** (0.004, 0.01)	–	0.41***
Cd[a]	−0.71***	0.12* (0.02, 0.22)	–	–	0.53*** (0.42, 0.63)	–	–	0.52***
Hg	3.3***	0.95* (0.05, 1.8)	–	2.7*** (1.8, 3.5)	–	–	–	0.34***
Pb[a]	1.36***	0.16*** (0.09, 0.23)	0.20*** (0.12, 0.27)	−0.30*** (−0.36, −0.23)	0.08* (0.006, 0.15)	–	–	0.58***

Note: Ethnicity: 1/0, 1 = Nenets, 0 = non-Nenets: Sex: 1/0, 1 = men, 0 = women; Community: 1/0, 1 = inland, 0 = coastal; Smoking: 1/0, 1 = current smoker, 0 = non-smoker.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.
[a] lg-transformed dependent variable.

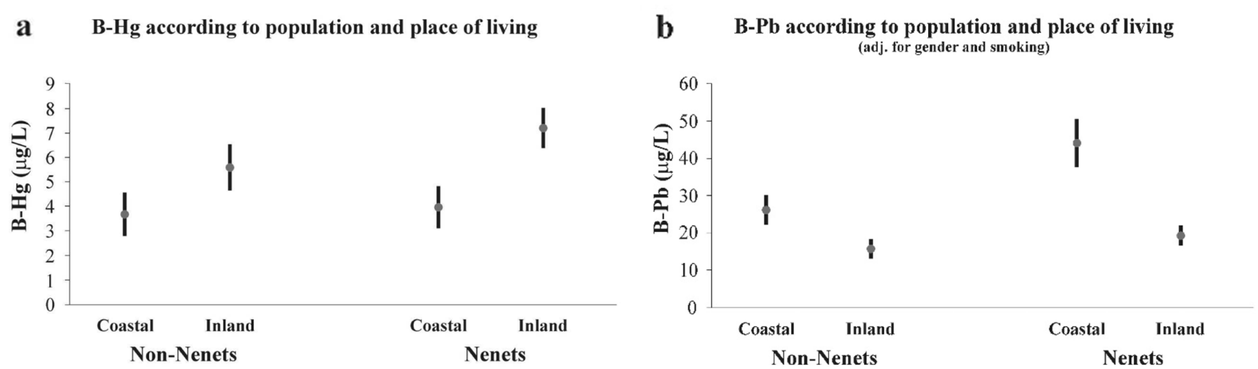

Fig. 2. a-b. The GM (and 95% CI) concentrations of mercury and lead (adjusted for gender and smoking) according to population and place of living.

Measurement of S-ferritin concentrations is a sensitive and specific test used for identification of Fe deficiency and or depleted Fe stores as indicated by values < 15 µg/L (Camaschella, 2015; World Health Organization, 2011; Zimmermann and Hurrell, 2007). Blood loss from menstruation is a well-known cause of Fe-deficiency which may explain the significant difference in S-ferritin between women before menopause and men. The prevalence of Fe-deficiency in the present study using the aforementioned criteria, is 26.6% among menstruating women (≤50 years). We have not been able to find any scientific information of S-ferritin values in Russia, except for measurements in maternal and cord blood collected among indigenous populations (AMAP assessment, 2004). In Europe the prevalence of Fe deficiency (<15 µg/L of S-ferritin) among healthy reproductive-aged women varies between countries with values reported between 3.1 (Poland) and 32.1% (Finland) (Milman et al., 2017). Thus, our estimates of the prevalence of Fe deficiency in NAO can be used for further comparisons and warrants further research.

4.2. Non-essential elements

Since the beginning of the 2000 s Russia has been among countries with most daily smokers with prevalences of current adult (>15y) smokers of 60.2% among men and 21.7% among women (Giovino et al., 2012). The implementation of comprehensive tobacco control strategies was initiated in 2008 and has contributed to reduction of the prevalence of smoking to 48% among men and 19% among women (Shkolnikov et al., 2020). Data on smoking among indigenous people are scarce on the global scale. In Canada, the prevalence of daily smoking among Inuits older than 15 years, was 63.8% and 64.2% among men and women, respectively, in 2012 (Bougie and Kohen, 2018). Russian studies on smoking among indigenous people suggest, however, substantially higher prevalence of smoking among men than in Canada. Glover et al., 2020, has reported the prevlence of smoking to be 23.7% among Evenk women and 74% among Nenets men. In the period 2008–2009, the prevalence of current male and female smokers was in Arkhangelsk 42.9 and 15.5%, and 50.0 and 16.9% in Nelmin-Nos, respectively (Petrenya et al., 2012). This indicates that the prevalence of daily smoking among males in NAO has not changed during the time period 2008–2017. In contrast to men, the prevalence of female smokers has increased to 25% suggesting that the current national measures to reduce the prevalence of smoking do not reach Arctic populations.

Smokers are exposed to numerous harmful constituents including Cd by inhalation of tobacco smoke, which is the main non-occupational source of its exposure. While the concentration of Cd in urine is associated with chronic exposure, the whole blood concentrations reflects recent exposures (Richter et al., 2017). In regions with low Cd concentrations in the diet, smokers have considerably higher concentrations of B-Cd than never-smokers (0.21 µg/L) (Hoffmann et al., 2000). The GM concentration of B-Cd for non-smoking non-Nenets men and women in the present study is 0.19 µg/L which is slightly lower than 0.26 µg/L for non-smoking Nenets (Table 5). The B-Cd concentrations among Nenets and non-Nenets smokers are 0.87 and 0.66 µg/L of Cd, correspondingly. Among Canadian Inuits, smoking has also been identified as the main contributor to the enhanced B-Cd concentrations (Fontaine et al., 2008; Ratelle et al., 2018). The Cd levels in non-smokers in the current study are among the lowest measured internationally. This may indicate that the daily intake, either through water or food is low and reflects a natural background level.

Mercury is naturally present in the environment in three chemical forms; either as inorganic (metallic), ionic or as metal-organic Hg with methyl-Hg being the most important. Mercury bio-accumulates and biomagnifies through food webs. Humans are exposed to Hg mainly through consumption of marine and freshwater fish, other seafood and marine mammals in particular. The predominant chemical form of Hg in food and in blood of non-occupationally exposed humans is methyl-Hg (UNEP 2008). With measurements of blood concentrations of Hg (as total Hg) and corresponding intakes of methyl-Hg it has been suggested that a daily intake of 0.02 µg of Hg per kg body weight corresponds to B-Hg of about 1 µg/L (UNEP 2008). Thus, an intake of the EFSA recommended tolerable weekly intake (TWI) amount of 1.3 µg of Hg per kg body weight would results in a B-Hg level of 10 µg/L. This recommendation is based on prenatal neurodevelopment as the critical health effect (EFSA Scientific Committee, 2015). In all settlements, the AM B-Hg concentrations are below this level with individual B-Hg concentrations ranging from 0.28 to 24.3 µg/L of Hg. Among the 54 women ≤50 years the median B-Hg concentration was 3.5 µg/L with minimum and maximum values of 0.28 and 24.3 3 µg/L, respectively; seven women had B-Hg exceeding 10 µg/L. Even though the traditional diet of Arctic populations includes much seafood and freshwater fish, the Hg concentrations measured in whole blood in this study may indicate that not more than about 10% of women in the fertile age have a Hg intake above the EFAS's recommendation. The measured B-Hg concentrations are, however, in line with the findings in other Arctic populations or seafood consumers in Norway and Spain (Abass et al., 2018; Birgisdottir et al., 2013; Castaño et al., 2019). In Europe, the average B-Hg concentrations among the adult population declined significantly from 1966 with and estimated annual change of 5.3% to a level of 0.75 µg/L (Sharma et al., 2019).

Lead is also considered as a good measure of Pb exposure. Since the bans of Pb in gasoline in the 1980s and 1990s, the B-Pb concentrations have decreased in the general population. The B-Pb concentration among the US population dropped from 16.5 in 1999 to 8.6 µg/L in 2014 (Tsoi et al., 2016). In the period 2011–2016 the B-Pb among women of reproductive age in the US was 6.1 µg/L compared to 103.7 µg/L in the period 1976–1980 (Ettinger et al., 2020). Similar time trends have been shown among German students from 70 µg/L in 1981 to 15 µg/L in 2009 (Becker et al., 2013) and among the Nunavik population in Canada (1996–2013) (Abass et al., 2018). Very little information is, however, available from Russian Arctic populations. AMAP reported in 2004 a B-Pb level of 47 µg/L in indigenous adults from Nelmin-Nos and 32 µg/L in maternal blood. These concentrations are similar to those measured among the coastal population in our study. The participants from Nelmin-Nos in our study showed a GM B-Pb concentration 50% lower than reported in 2004 indicating a substantial reduction in the B-Pb among the inland Nenets (data not shown). The spatial trend of higher B-Pb among the coastal population and the large range in concentrations (up to 356 µg/L) may be due to Pb pellets used for waterfowl and seabirds hunting, which is well known to contaminate the meat with Pb fragments, and preparation of Pb fishing sinkers (Verbrugge, 2009). Some of the highest B-Pb concentrations were measured among residents in Varnek. Lead contamination of drinking water sources in this settlement from previous mining activities may also have contributed to the enhanced B-Pb amounts. This merits further assessment.

The EFSA Panel on Contaminants in the Food Chain (CONTAM) identified the developmental neurotoxicity (DN) in young children and systolic blood pressure (SBP) and nephrotoxicity and chronic kidney disease (CKD) in adults as most important adverse health effects in risk assessment of exposure to Pb with following B-Pb benchmark dose levels (BMDL); DN: $BMDL_{01}$ = 12 µg/L; SBP: $BMDL_{01}$: 36 µg/L and CKD: $BMDL_{10}$ = 15 µg/L, respectively (EFSA, 2014). The B-Pb concentrations in this study are in the range of, or partly exceeding these reference values for increased risk for SBP and CKD. Thus, there is a need for a continued effort to reduce Pb exposure among the population groups in NAO.

Inorganic As is present naturally at high concentrations in the environment. (Ravenscroft et al., 2009). Especially the occurrence of As in the groundwater in Bangladesh has attracted much attention where still millions of inhabitants are exposed to high amounts through drinking water (Hossain, 2006). For humans not exposed through drinking water, fish and seafood are the main sources of As with concentrations vastly exceeding those present in other foods (Taylor et al., 2017). Arsenic in marine and freshwater fish is present as various organo-As compounds and arsenobetaine has been shown to be the main compound (de Rosemond et al., 2008; Taylor et al., 2017). Although there is a need of As speciation analysis both in seafood and fish as well as in human blood, As is usually reported as total As. It has been shown that B-As reflects seafood consumption even better than B-Hg (Brantsæter et al., 2010). The significantly higher B-As concentration among coastal residents compared with those living inland may reflect a higher intake of As from seafood. This compares well with finding from Norway where a similar coast-inland spatial difference in B-As was found among pregnant women; 11.6 versus 3.0 µg/L (Birgisdottir et al., 2013). Seafood consumers have been shown to be older and this may explain the slight significant increase in whole blood concentration of As with age (Table 5; Govsman et al., 2020).

In spite of limited information of the toxicity of As present in seafood, its compounds have historically been considered harmless. Recent studies may, however, indicate that the organo-As compounds undergo biotransformation that might involve formation of trivalent toxic As intermediates (Molin et al., 2015).

4.3. Essential elements

Selenium is utilised through a number of selenoproteins essential for antioxidant/redox reactions, thyroid hormone metabolism, reproduction and immune functions. Se deficiency in humans is rare, but low Se status has been associated with increased incidence of some cancers and cardiovascular disease (Rayman, 2012). The main criterion for estimating recommended intake for Se is maximization of plasma glutathione peroxidases (GPx) activity which plateaued at a B-Se concentration of 1.13 µmol/L (89 µg/L) in Finnish subjects and at 1.15 µmol/L (91 µg/L) in New Zealand subjects, respectively. Selenoprotein P is also an informative biomarker of Se status and in the New Zealand study it maximized little lower than for GPx. It should, however, be noted that the B-Se may vary with different forms of dietary Se and among population groups (Thomson, 2004).

The concentrations of B-Se among the non-Nenets (128 µg/L) and Nenets (122 µg/L) participants in the present study were similar and higher than needed for optimizing the amount of important selenoproteins. The observed Se concentrations are also comparable with the results of pooled data analysis of 75 global studies (121 µg/L) (Noisel et al., 2014). Few data on the Se status among inhabitants of the Arctic regions of Russia are available. Rylander et al. (2011) reported B-Se GM concentrations between 87 and 100 µg/L for men and women living in Izhma and Usinsk of the Komi Republic. In a study of human Se status in

27 regions of Russia only few areas showed low serum Se concentrations with Pskov with the lowest amount (0.91 μmol/L (72 μg/L)) and Sakhalin (1.74 μmol/L (137 μg/L)) with the highest value. The Se concentrations measured seemed to be associated with the Se amount in the consumed wheat indicating that this grain had a predominant influence on the Se status (Golubkina and Alfthan, 1999). In a previous study we have shown that the Se tissue concentrations in marine fish are about twice as high as in freshwater fish consumed in the NAO (Sobolev et al., 2019). Since there was no significant difference in B-Se between coastal and inland subjects in our study, fish consumption may not be a predominant source of Se for this population. As a protective role of Se on methyl-Hg bioaccumulation has been observed and fish consumption is the primary human exposure route for Hg, Se concentrations and the Hg/Se ratio are considered to be bioindicators of human risks associated with the consumption of Hg in fish (Kasuya, 1976, Burger and Gochfeld, 2011).

Reliable and sensitive biomarkers of assessing Cu and Zn status in humans are not available. Most commonly, the total concentrations are measured in serum or plasma and it is difficult to evaluate any deficiency or excess (Harvey et al., 2009; Lowe et al., 2009). Whole blood contains about eight times as high amount of Zn as serum/plasma while the Cu concentration is similar in these body fluids (Hinks et al., 1983). Since only whole blood was available for trace element measurements in our study, this prevents an appropriate characterization of these two elements. Though, it is interesting to note that women have statistically significantly higher B-Cu than men. This is in line with other studies (Beneš et al., 2005, Bocca et al., 2011, Zhang et al., 2015, Kim et al., 2017) and may be at least partly explained by estrogen-induced ceruloplasmin synthesis in the liver of women that may lead to an enhanced B-Cu (Martín-Lagos et al., 1998). It is also interesting to observe the significantly higher B-Cu among the Nenets and non-Nenets living inland and that smoking contributes to a higher B-Cu. In another large population study the gender difference between men and women and the enhanced B-Cu among smoker have been confirmed (Beneš et al., 2005).

There is a significant geographical difference in B-Zn with higher concentrations in the coastal population. The significantly higher B-Zn among men is also confirmed by Beneš et al. (2005). Hormone regulation (e.g. by testosterone and prolactin) of the expression of the Zn transporter mRNA has been suggested to play a role in the gender difference of serum Zn, but this has not been extensively studied and merits further investigation (Foster et al., 2011).

Several interactions between Fe status and whole blood concentrations of e.g. Co, Cd, Mn and Pb have been described (Melzter et al., 2010; Le and Kim, 2014). Such interactions have also been demonstrated in this study, specifically between ferritin, Co and Mn in women younger than 50 years of age. There is, however, no statistically different difference between men and women for B-Mn even when women have generally lower S-ferritin, but the B-Co concentrations are somewhat higher among women.

The significantly higher B-Mn among the Nenets and the coastal populations are difficult to explain and should be further studied in relation to Fe status and dietary habits. All participants in this study have also responded to a validated nutrition questionnaire that allows us to investigate these interactions more closely. This work is, however, too extensive to be included in this article.

Iodine deficiency is a major global health challenge but difficult to assess. Urinary I excretion is presently the most appropriate population indicator but difficult to use for individual evaluation due to a daily substantial variation. The limited number of urine samples collected in Indiga and Bugrino (n = 68) showed a median concentration of 103 μg/L and GM of 122 μg/L of I. According to the WHO epidemiological criteria almost half of the participants in this study (n = 33) had urinary I concentration (UIC) <100 μg/L which is considered as an adequate I nutrition for adults (UIC: 100–199 μg/L) (WHO, 2007). Specifically, 15% (n = 10) of the participants had UIC in the range 20–49 μg/L considered as insufficient and moderate I deficiency; 34% (n = 23) as mild I deficiency (UIC: 50–99 μg/L); 28% (n = 19) as adequate iodine intake (UIC: 100–199 μg/L); 10% (n = 7) above the adequate iodine intake (UIC: 200–299 μg/L) and 13% (n = 9) with excessive intake with an excessive risk of adverse health consequences (UIC greater than 300 μg/L). Out of the 68 participants 14 were women in reproductive age (younger than 50 years). The median and GM UIC for this group was 89 and 111 μg/L, respectively. A substantial variability in UIC below WHO recommendation for adequate I intake among Russian women and infants across the country with no clear geographical pattern has been observed (Korobitsyna et al., 2020). About 1.5 million people in Russia may have mental retardation and related disability due to I deficiency (Melnichenko et al., 2019). In light of this and the indication of both low and excessive UIC among inhabitants of NAO demonstrate that the relevance and consequences of I status deserve further attention.

5. Conclusions

Assessment of nine essential and non-essential shows significant variations in whole blood concentrations of several elements characterized by gender, population group and locality.

Cd levels among non-smokers indicate that the daily intake, either through water or food is low and reflects a natural global background level.

The Hg concentrations in whole blood show that not more than 10% of women in the fertile age have a Hg intake above the EFAS's recommendation. The observed B-Hg concentrations are in line with findings in other Arctic populations.

The B-Pb concentrations are in the range of, or partly exceeding reference values for increased risk of nephrotoxicity and there is a need for a continued effort to reduce Pb exposure among the population groups in NAO.

Both the high prevalence of Fe-deficiency among menstruating women (<50 years) and a lower I status than recommended by WHO deserve further attention.

CRediT authorship contribution statement

Nikita Sobolev: Writing - original draft, Writing - review & editing, Data curation, Resources, Investigation, Formal analysis, Validation, Methodology, Conceptualization, Visualization. **Dag G. Ellingsen:** Writing - original draft, Writing - review & editing, Data curation, Investigation, Visualization, Formal analysis. **Natalia Belova:** Resources, Investigation, Validation. **Andrey Aksenov:** Writing - original draft, Visualization, Resources, Investigation, Conceptualization. **Tatiana Sorokina:** Writing - original draft, Project administration, Writing - review & editing, Resources, Investigation, Conceptualization. **Anna Trofimova:** Resources, Investigation. **Yulia Varakina:** Resources, Investigation. **Dmitriy Kotsur:** Resources, Investigation. **Andrej M. Grjibovski:** Writing - original draft, Writing - review & editing, Investigation, Formal analysis. **Valerii Chashchin:** Writing - original draft, Conceptualization, Funding acquisition, Methodology. **Konstantin Bogolitsyn:** Writing - original draft, Investigation. **Yngvar Thomassen:** Supervision, Writing - original draft, Writing - review & editing, Data curation, Resources, Investigation, Formal analysis, Validation, Methodology, Conceptualization, Visualization.

Declaration of Competing Interest

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

Acknowledgements

This work was supported by the Government of the Russian

Federation in compliance with the Resolution of April 09, 2010 No. 220 (the contract from 14.03.2017 No. 14.Y26.31.0009). The analyses were conducted using the instrumentation of the Core Facility Center "Arktika" of the Northern (Arctic) Federal University named after M.V. Lomonosov.

References

Abass, K., Emelyanova, A., Rautio, A., 2018. Temporal trends of contaminants in Arctic human populations. Environ. Sci. Pollut. Res 25 (29), 28834–28850. https://doi.org/10.1007/s11356-018-2936-8.

Agbalyan, E.V., Shinkaruk, E.V., 2018. The mercury content in the blood of inhabitants of the Yamalo-Nenets autonomous district. Hygiene & Sanitation (Russian Journal) 799.

AMAP assessment, 2004: Persistent toxic substances, food security and indigenous peoples of the Russian North. Final Report, 2004. Arctic Monitoring and Assessment Programme (AMAP), Oslo. AMAP Report 2004:2. 192 pp.

AMAP assessment, 2015: Human health in the Arctic, 2015. Arctic Monitoring and Assessment Programme (AMAP). https://doi.org/10.3402/ijch.v75.33949.

Becker, K., Schroeter-Kermani, C., Seiwert, M., Rüther, M., Conrad, A., Schulz, C., Wilhelm, M., Wittsiepe, J., Günsel, A., Dobler, L., Kolossa-Gehring, M., 2013. German health-related environmental monitoring: Assessing time trends of the general population's exposure to heavy metals. Int. J. Hyg. Environ. Health 216 (3), 250–254. https://doi.org/10.1016/j.ijheh.2013.01.002.

Beneš, B., Spěváčková, V., Šmíd, J., Batáriová, A., Čejchanová, M., Zítková, L., 2005. Effects of age, BMI, smoking and contraception on levels of Cu, Se and Zn in the blood of the population in the Czech Republic. Cent. Eur. J. Publ. Health 13 (4), 202–207.

Birgisdottir, B.E., Knutsen, H.K., Haugen, M., Gjelstad, I.M., Jenssen, M.T.S., Ellingsen, D.G., Thomassen, Y., Alexander, J., Meltzer, H.M., Brantsæter, A.L., 2013. Essential and toxic element concentrations in blood and urine and their associations with diet: Results from a Norwegian population study including high-consumers of seafood and game. Sci. Total Environ. 463, 836–844. https://doi.org/10.1016/j.scitotenv.2013.06.078.

Bjerregaard, P., 2019. Regional studies of indigenous health: Europe and Russia, Oxford Research Encyclopedia, Global Health, Online Publication, doi: 10.1093/acrefore/9780190632366.013.7.

Black, M.M., 2003. Micronutrient deficiencies and cognitive functioning. J. Nutr. 133 (11), 3927S–3931S. https://doi.org/10.1093/jn/133.11.3927S.

Bocca, B., Madeddu, R., Asara, Y., Tolu, P., Marchal, J.A., Forte, G., 2011. Assessment of reference ranges for blood Cu, Mn, Se and Zn in a selected Italian population. J. Trace Elem. Med. Biol. 25 (1), 19–26. https://doi.org/10.1016/j.jtemb.2010.12.004.

Bougie, E., Kohen, D., 2018. Smoking correlates among Inuit men and women in Inuit Nunangat, Health Reports, 29(3), 3-10, Statistic Canada, Catalogue 82-003-x, ISSN 1209-1367.

Brantsæter, A.L., Haugen, M., Thomassen, Y., Ellingsen, D.G., Ydersbond, T.A., Hagve, T.A., Alexander, J., Meltzer, H.M., 2010. Exploration of biomarkers for total fish intake in pregnant Norwegian women. Public Health Nutr. 13, 199–210. https://doi.org/10.1017/S1368980009005904.

Burger, J., Gochfeld, M., 2011. Mercury and selenium levels in 19 species of saltwater fish from New Jersey as a function of species, size, and season. Sci. Total Environ. 409 (8), 1418–1429. https://doi.org/10.1016/j.scitotenv.2010.12.034.

Camaschella, C., 2015. Iron-deficiency anemia. N Engl. J. Med. 372 (19), 1832–1843. https://doi.org/10.1056/NEJMra1401038.

Castaño, A., Pedraza-Díaz, S., Cañas, A.I., Pérez-Gómez, B., Ramos, J.J., Bartolomé, M., Pärt, P., Soto, E.P., Motas, M., Navarro, C., Calvo, E., Esteban, M., 2019. Mercury levels in blood, urine and hair in a nation-wide sample of Spanish adults. Sci. Total Environ. 670, 262–270. https://doi.org/10.1016/j.scitotenv.2019.03.174.

de Rosemond, S., Xie, Q., Liber, K., 2008. Arsenic concentration and speciation in five freshwater fish species from Back Bay near Yellowknife, NT, Canada. Environ. Monit. Assess. 147 (1–3), 199–210. https://doi.org/10.1007/s10661-007-0112-6.

Donaldson, S., Adlard, B., Odland, J.Ø., 2016. Overview of human health in the Arctic: Conclusions and recommendations. Int. J. Circumpolar Health 75 (1), 33807. https://doi.org/10.3402/ijch.v75.33807.

Dudarev, A., Chupakhin, V., Vlasov, S., Yamin-Pasternak, S., 2019. Traditional diet and environmental contaminants in coastal Chukotka II: Legacy POPs. Int. J. Environ. Res. Public Health 16 (5), 695. https://doi.org/10.3390/ijerph16050695.

EFSA, 2014. Scientific opinion on dietary reference values for iodine. EFSA J. 12 (5), 3660. https://doi.org/10.2903/j.efsa.2014.3660.

EFSA Scientific Committee, 2015. Statement on the benefits of fish/seafood consumption compared to the risks of methylmercury in fish/seafood. EFSA J. 13 (1), 3982. https://doi.org/10.2903/j.efsa.2015.3982.

Ek, S., 2013. Gender differences in health information behaviour: a Finnish population-based survey. Health Promotion Int. 30 (3), 736–745. https://doi.org/10.1093/heapro/dat063.

Ettinger, A.S., Egan, K.B., Homa, D.M., Brown, M.J., 2020. Blood lead levels in U.S. women of childbearing age, 1976–2016. Environ. Health Perspect. 128(1), 017012. https://doi.org/10.1289/EHP5925.

Fontaine, J., Dewailly, É., Benedetti, J.L., Pereg, D., Ayotte, P., Déry, S., 2008. Re-evaluation of blood mercury, lead and cadmium concentrations in the Inuit population of Nunavik (Québec): A cross-sectional study. Environ. Heal. A Glob. Access Sci. Source. 7 (1), 1–13. https://doi.org/10.1186/1476-069X-7-25.

Foster, M., Hancock, D., Petocz, P., Samman, S., 2011. Zinc transporter genes are coordinately expressed in men and women independently of dietary or plasma zinc. J. Nutr. 141 (6), 1195–1201. https://doi.org/10.3945/jn.111.140053.

Gibson, J., Adlard, B., Olafsdottir, K., Sandanger, T.M., Odland, J.Ø., 2016. Levels and trends of contaminants in humans of the Arctic. Int. J. Circumpolar Health. 75 (1), 33804. https://doi.org/10.3402/ijch.v75.33804.

Giovino, G.A., Mirza, S.A., Samet, J.M., Gupta, P.C., Jarvis, M.J., Bhala, N., Peto, R., Zatonski, W., Hsia, J., Morton, J., Palipudi, K.M., Asma, S., 2012. Tobacco use in 3 billion individuals from 16 countries: An analysis of nationally representative cross-sectional household surveys. Lancet 380 (9842), 668–679. https://doi.org/10.1016/S0140-6736(12)61085-X.

Glover, M., Patwardhan, P., Selket, K., 2020. Tobacco smoking in three "left behind" subgroups: indigenous, the rainbow community and people with mental health conditions. Drugs and Alcohol Today. https://doi.org/10.1108/DAT-02-2020-0004.

Golubkina, N.A., Alfthan, G.V., 1999. The human selenium status in 27 regions of Russia. J. Trace Elem. Med. Biol. 13 (1–2), 15–20. https://doi.org/10.1016/S0946-672X(99)80018-2.

Govzman, S., Looby, S., Wang, X., Butler, F., Gibney, E.R., Timon, C.M., 2020. A systematic review of the determinants of seafood consumption. Br. J. Nutrition, First View 1–15. https://doi.org/10.1017/S0007114520003773.

Harvey, L.J., Ashton, K., Hooper, L., Casgrain, A., Fairweather-Tait, S.J., 2009. Methods of assessment of copper status in humans: a systematic review. Am. J. Clin. Nutr. 89 (6), 2009S–2024S. https://doi.org/10.3945/ajcn.2009.27230E.

Hinks, L.J., Clayton, B.E., Lloyd, R.S., 1983. Zinc and copper concentrations in leucocytes and erythrocytes in healthy adults and the effect of oral contraceptives. J. Clin. Pathol. 36 (9), 1016–1021. https://doi.org/10.1136/jcp.36.9.1016.

Hoffmann, K., Becker, K., Friedrich, C., Helm, D., Krause, C., Seifert, B., 2000. The German Environmental Survey 1990/1992 (GerES II): Cadmium in blood, urine and hair of adults and children. J. Expo. Anal. Environ. Epidemiol. 10, 126–135. https://doi.org/10.1038/sj.jea.7500081.

Hossain, M.F., 2006. Arsenic contamination in Bangladesh - An overview. Agric. Ecosyst. Environ. 113 (1–4), 1–16. https://doi.org/10.1016/j.agee.2005.08.034.

Karatela, S., Ward, N.I., 2016. Trace elements and human obesity: An overview. Manipal J. Nursing Health Sci. 2 (2), 50–59.

Kasuya, M., 1976. Effect of selenium on the toxicity of methylmercury on nervous tissue in culture. Toxicol. Appl. Pharmacol. 35 (1), 11–20. https://doi.org/10.1016/0041-008X(76)90106-X.

Kim, H.-J., Lim, H.-S., Lee, K.-R., Choi, M.-H., Kang, N.M., Lee, C.H., Oh, E.-J., Park, H.-K., 2017. Determination of trace metal levels in the general population of Korea. Int. J. Environ. Res. Public Health 14 (7), 702. https://doi.org/10.3390/ijerph14070702.

Korobitsyna, R., Aksenov, A., Sorokina, T., Trofimova, A., Sobolev, N., Grjibovski, A., Chashchin, V., Thomassen, Y., 2020. Iodine status of women and infants in Russia: A systematic review. Int. J. Environ. Res. Public Health 17, 8346. https://doi.org/10.3390/ijerph17228346.

Laidlaw, M.A.S., Filippelli, G., Mielke, H., Gulson, B., Ball, A.S., 2017. Lead exposure at firing ranges - a review. Environ. Heal. 16 (1), 34. https://doi.org/10.1186/s12940-017-0246-0.

Le, B.-K., Kim, Y., 2014. Sex-specific profiles of blood metal levels associated with metal-iron interactions. Saf. Health Work 5, 113–117. https://doi.org/10.1016/j.shaw.2014.06.005.

Lockhart, W.L., Stern, G.A., Low, G., Hendzel, M., Boila, G., Roach, P., Evans, M.S., Billeck, B.N., DeLaronde, J., Friesen, S., Kidd, K., Atkins, S., Muir, D.C.G., Stoddart, M., Stephens, G., Stephenson, S., Harbicht, S., Snowshoe, N., Grey, B., Thompson, S., DeGraff, N., 2005. A history of total mercury in edible muscle of fish from lakes in northern Canada. Sci. Total Environ. 351, 427–463. https://doi.org/10.1016/j.scitotenv.2004.11.027.

Lowe, N.M., Fekete, K., Decsi, T., 2009. Methods of assessment of zinc status in humans: a systematic review. Am. J. Clin. Nutr. 89 (6), 2040S–2051S. https://doi.org/10.3945/ajcn.2009.27230G.

Lunze, K., Yurasova, E., Idrisov, B., Gnatienko, N., Migliorini, L., 2015. Food security and nutrition in the Russian Federation - A health policy analysis. Glob. Health Action. 8 (1), 27537. https://doi.org/10.3402/gha.v8.27537.

Meltzer, M.H., Brantsæter, A.L., Borch-Iohnsen, B., Ellingsen, D.G., Alexander, J., Thomassen, Y., Stigum, H., Ydersbond, T.A., 2010. Low iron stores are related to higher blood concentrations of manganese, cobalt and cadmium in non-smoking, Norwegian women in the HUNT 2 study. Environ. Res. 110 (5), 497–504. https://doi.org/10.1016/j.envres.2010.03.006.

Martín-Lagos, F., Navarro-Alarcón, M., Terrés-Martos, C., López-García De La Serrana, H., Pérez-Valero, V., López-Martínez, M.C., 1998. Zinc and copper concentrations in serum from Spanish women during pregnancy. Biol. Trace Elem. Res. 61 (1), 61–70. https://doi.org/10.1007/BF02784041.

Melnichenko, G.A., Troshina, E.A., Platonova, M.N., Panfilova, E.A., Rybakova, A.A., Abdulkhabirova, F.M., Bostanovaet, F.A., 2019. Iodine deficiency thyroid disease in the Russian Federation: the current state of the problem. Analytical review of publications and data of official state statistics (Rosstat). Consilium Medicum 21 (4), 14–20. https://doi.org/10.26442/20751753.2019.4.190337.

Mertz, W., 2012. Trace Elements in Human and Animal Nutrition: Fifth Ed., Trace Elements in Human and Animal Nutrition: Fifth Ed. https://doi.org/10.1016/C2009-0-02917-1.

Milman, N., Taylor, C.L., Merkel, J., Brannon, P.M., 2017. Iron status in pregnant women and women of reproductive age in Europe. Am. J. Clin. Nutrit. 106 (6), 1655S–1662S. https://doi.org/10.3945/ajcn.117.156000.

Molin, M., Ulven, S.M., Meltzer, H.M., Alexander, J., 2015. Arsenic in the human food chain, biotransformation and toxicology - Review focusing on seafood arsenic.

J. Trace Elem. Med. Biol. 31, 249–259. https://doi.org/10.1016/j.jtemb.2015.01.010.

Murashko, O.A., Dallmann, V.K., 2011. Transformation of the traditional way of life and nutrition of the indigneous population of the Nenets Autonomous Okrug. Moscow Univ. Anthropol. Bull. (Vestnik Moskovskogo Universiteta. Seria XXIII. Antropologia). 4, 4-24. (in Russian).

Noisel, N., Carrier, G., Bouchard, M., 2014. Study of selenium intake and disposition in various matrices based on mathematical algorithms derived from pooled biomonitoring data. Int. J. Hyg. Environ. Health. 217 (7), 796–804. https://doi.org/10.1016/j.ijheh.2014.04.005.

Petrenya, N., Brustad, M., Cooper, M., Dobrodeeva, L., Bichkaeva, F., Lutfalieva, G., Odland, J.O., 2012. Serum apolipoproteins in relation to intakes of fish in population of Arkhangelsk County. Nutr. Metab. 9 (1), 51. https://doi.org/10.1186/1743-7075-9-51.

Petrenya, N., Brustad, M., Dobrodeeva, L., Bichkaeva, F., Lutfalieva, G., Cooper, M., Odland, J.Ø., 2014. Obesity and obesity-associated cardiometabolic risk factors in indigenous Nenets women from the rural Nenets Autonomous Area and Russian women from Arkhangelsk city. Int. J. Circumpolar Health 73 (1), 23859. https://doi.org/10.3402/ijch.v73.23859.

Ratelle, M., Li, X., Laird, B.D., 2018. Cadmium exposure in First Nations communities of the Northwest Territories, Canada: smoking is a greater contributor than consumption of cadmium-accumulating organ meats. Environ. Sci. Process. Impacts. 20 (10), 1441–1453. https://doi.org/10.1039/c8em00232k.

Ravenscroft, P., Brammer, H., Richards, K., 2009. Arsenic Pollution: A Global Synthesis, Arsenic Pollution: A Global Synthesis. https://doi.org/10.1002/9781444308785.

Rayman, M.P., 2012. Selenium and human health. The Lancet. 379 (9822), 1256–1268. https://doi.org/10.1016/S0140-6736(11)61452-9.

Richter, P., Faroon, O., Pappas, R.S., 2017. Cadmium and cadmium/zinc ratios and tobacco-related morbidities. Int. J. Environ. Res. Public Health 14 (10), 1154. https://doi.org/10.3390/ijerph14101154.

Rylander, C., Sandanger, T.M., Petrenya, N., Konoplev, A., Bojko, E., Øyvind Odland, J., 2011. Indications of decreasing human PTS concentrations in North West Russia. Glob. Health Action 4 (1), 1–9. https://doi.org/10.3402/gha.v4i0.8427.

Sharma, B.M., Sáňka, O., Kalina, J., Scheringer, M., 2019. An overview of worldwide and regional time trends in total mercury levels in human blood and breast milk from 1966 to 2015 and their associations with health effects. Environ. Int. 125, 300–319. https://doi.org/10.1016/j.envint.2018.12.016.

Shkolnikov, V.M., Churilova, E., Jdanov, D.A., Shalnova, S.A., Nilssen, O., Kudryavtsev, A., Cook, S., Malyutina, S., McKee, M., Leon, D.A., 2020. Time trends in smoking in Russia in the light of recent tobacco control measures: Synthesis of evidence from multiple sources. BMC Public Health. 20 (1), 1–11. https://doi.org/10.1186/s12889-020-08464-4.

Smith, C.J., Livingston, S.D., Doolittle, D.J., 1997. An international literature survey of “IARC group I carcinogens” reported in mainstream cigarette smoke. Food Chem. Toxicol. 35 (10–11), 1107–1130. https://doi.org/10.1016/S0278-6915(97)00063-X.

Smith, K.R., Woodward, A., Campbell-Lendrum, D., Chadee, D.D., Honda, Y., Liu, Q., Olwoch, J.M., Revich, B., Sauerborn, R., Confalonieri, U., Haines, A., Chafe, Z., Rocklov, J., 2014. Human health: Impacts, adaptation, and co-benefits. In: Climate Change 2014 Impacts, Adaptation and Vulnerability: Part A: Global and Sectoral Aspects. Cambridge University Press (CUP), pp. 709–754. https://doi.org/10.1017/CBO9781107415379.016.

Sobolev, N., Aksenov, A., Sorokina, T., Chashchin, V., Ellingsen, D.G., Nieboer, E., Varakina, Y., Veselkina, E., Kotsur, D., Thomassen, Y., 2019. Essential and non-essential trace elements in fish consumed by indigenous peoples of the European Russian Arctic. Environ. Pollut. 253, 966–973. https://doi.org/10.1016/j.envpol.2019.07.072.

Svetlichnaya, T.G., Vorobyeva, N.A., 2019. Lifestyle and self-perceived health of the Nenets population living on the Arctic island of Vaigach. Ekologiya cheloveka (Human Ecology). 12, 20–25. https://doi.org/10.33396/1728-0869-2019-12-20-25 (in Russian).

Taylor, V., Goodale, B., Raab, A., Schwerdtle, T., Reimer, K., Conklin, S., Karagas, M.R., Francesconi, K.A., 2017. Human exposure to organic arsenic species from seafood. Sci. Total Environ. 580, 266–282. https://doi.org/10.1016/j.scitotenv.2016.12.113.

Thomson, C.D., 2004. Assessment of requirements for selenium and adequacy of selenium status: A review. Eur. J. Clin. Nutr. 50 (3), 391–402. https://doi.org/10.1038/sj.ejcn.1601800.

Tsoi, M.F., Cheung, C.L., Cheung, T.T., Cheung, B.M.Y., 2016. Continual decrease in blood lead level in Americans: United States national health nutrition and examination survey 1999–2014. Am. J. Med. 129 (11), 1213–1218. https://doi.org/10.1016/j.amjmed.2016.05.042.

UNEP, 2008, Guidance for identifying populations at risk from mercury exposure, WHO, UNEP Chemicals, http://www.chem.unep.ch.

Verbrugge, L., 2009. Human exposure to lead from ammunition in the circumpolar. North. https://doi.org/10.4080/ilsa.2009.0110.

Webster, P., 2005. Health in the Arctic. World Report 365 (9461), 741–742. https://doi.org/10.1016/50140-6736(05)18003-9.

World Health Organization, 2007. Assessment of iodine deficiency disorders and monitoring elimination: a guide for programme managers. Third edition. ISBN 9789241595827.

World Health Organization, 2011. Serum ferritin concentrations for the assessment of iron status and iron deficiency in populations. Vitamin and Mineral Nutrition Information System. WHO/NMH/NHD/MNM/11.2.

Zhang, L.L., Lu, L., Pan, Y.J., Ding, C.G., Xu, D.Y., Huang, C.F., Pan, X.F., Zheng, W., 2015. Baseline blood levels of manganese, lead, cadmium, copper, and zinc in residents of Beijing suburb. Environ. Res. 140, 10–17. https://doi.org/10.1016/j.envres.2015.03.008.

Zimmermann, M.B., Hurrell, R.F., 2007. Nutritional iron deficiency. The Lancet 370 (9586), 511–520. https://doi.org/10.1016/S0140-6736(07)61235-5.