

ARTICLE OPEN



Identifying dietary sources and patterns of exposure to toxic metals and other trace elements in Swedish toddlers and young children

Mohammad Redwanul Islam^{1,4}, Mercedes Trask^{1,4}, Maria Kampouri¹, Michael Levi¹, Taranbir Singh¹, Klara Gustin¹, Helena Bjermo², Pernilla Almerud³, Florencia Harari³, Marie Vahter¹, Sanna Lignell² and Maria Kippler¹✉

© The Author(s) 2026

BACKGROUND: Diet is a source of many toxic compounds, but dietary sources of toxic metal exposure in young children are largely unknown.

OBJECTIVE: To explore dietary sources and patterns of the most commonly occurring toxic metals and key elements of antioxidant defense.

METHODS: We studied 1.5-year-olds ($n = 305$) and 4-year-olds ($n = 288$) in the Swedish national dietary survey “Riksmaten Young Children”. From a 2-day web-based food diary, habitual consumption (g/day) of specific food groups was estimated using the Multiple Source Method. Dietary patterns were derived using age-specific principal component analysis (PCA) and k-means clustering. Toxic (arsenic, cadmium, cobalt, lead, mercury) and essential elements (copper, manganese, selenium, and zinc) in blood and/or urine were measured with inductively coupled plasma-mass spectrometry, arsenobetaine and inorganic arsenic metabolites [methylarsonic acid (MMA), dimethylarsinic acid (DMA) and remaining inorganic arsenic] after separation by reversed-phase/ion exchange high-performance liquid chromatography, and fluoride with an ion-specific electrode.

RESULTS: Biomarker concentrations of toxic metals varied, and blood selenium was suboptimal in many children (median: 103 µg/L at both ages). Spearman rank correlation with unsupervised hierarchical cluster analysis revealed that urinary arsenobetaine and blood arsenic, mercury, and selenium correlated positively with seafood and vegetable consumption, particularly among 4-year-olds, where seafood and vegetables clustered together. In children with <80% DMA in urine, inorganic arsenic metabolites correlated positively with vegetables. In multivariable-adjusted regression models, the PCA-derived fruits-vegetables-seafood pattern was positively associated with blood arsenic (mainly arsenobetaine) among 4-year-olds as well as mercury (mainly methylmercury) and selenium at both ages. Dietary clusters dominated by plant-based meat and milk alternatives showed higher cadmium concentrations, and clusters characterized by a western-style diet (meat, cereals, and sweets) showed lower selenium concentrations than clusters with a high-diversity diet.

SIGNIFICANCE: Diet contributes to exposure to arsenic compounds, methylmercury, cadmium, and selenium in small Swedish children.

IMPACT: Concentrations of toxic metals in the blood and urine of young Swedish children were generally low, though they exhibited considerable variability. Simultaneously, around half of the children appeared to have suboptimal selenium status, a key element in antioxidant defense against metal toxicity. Diets rich in plant-based alternatives, nuts, and seeds were associated with increased cadmium exposure, while high-diversity diets rich in fruits, vegetables, and seafood were associated with increased arsenobetaine and methylmercury exposure, in combination with improved selenium status. Furthermore, after excluding the contribution of arsenic compounds from fish, low concentrations of inorganic arsenic appeared to originate from vegetable consumption.

Keywords: Metals; Selenium; Plant-based alternatives; Seafood; Vegetables.

Journal of Exposure Science & Environmental Epidemiology; <https://doi.org/10.1038/s41370-026-00973-5>

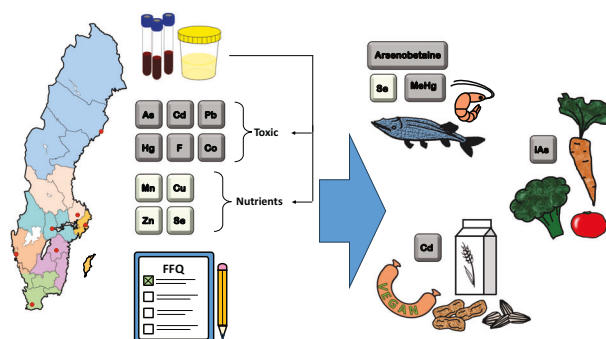
¹Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden. ²Department of Risk and Benefit Assessment, Swedish Food Agency, Uppsala, Sweden.

³Occupational and Environmental Medicine, School of Public Health and Community Medicine, University of Gothenburg and Sahlgrenska University Hospital, Gothenburg, Sweden. ⁴These authors contributed equally: Mohammad Redwanul Islam, Mercedes Trask.✉email: maria.kippler@ki.se

Received: 29 December 2025 Revised: 20 August 2026 Accepted: 26 August 2026

Published online: 25 September 2026

Graphical Abstract



INTRODUCTION

Early childhood development requires adequate nutrition as well as limited exposure to environmental hazards and other environmental stressors. Whereas diet provides nutrition, it can also be a source of exposure to toxic metals, as their presence in soil, water, and air allows their entry into the food chain seamlessly [1]. The U.S. Food and Drug Administration (FDA) and the U.S. Department of Agriculture (USDA) have made a joint effort to reduce levels of commonly occurring food toxicants (arsenic, cadmium, mercury, and lead) in infant food throughout the whole supply chain, while ensuring the availability of essential elements [2]. Children's vulnerability to toxic metals, however, extends far beyond infancy. Several studies report that childhood exposure to toxic metals is associated with altered childhood immune function, growth, cognition, and behaviour [3–5]. Notably, a Finnish study reported that many 3- and 6-year-olds exceeded the European Food Safety Authority's (EFSA) health-based guidance values for dietary intake of inorganic arsenic (43% and 29% of the 3- and 6-year-olds, respectively), cadmium (88% and 64%), and lead (14% and 1%) [6]. As the health-based guidance value of inorganic arsenic has been lowered since then, from 0.3 to 0.06 µg/kg body weight/day [7], the dietary intake of arsenic is even more worrying.

The type of food contributing the most to children's toxic metal exposure is largely unknown, but is believed to vary regionally due to differences in dietary habits as well as agricultural, manufacturing, and cooking processes [8]. There are some studies that have linked metal concentrations in children's blood or urine with intake of specific foods in restricted European regions [9–12]. Even less is known about the contribution of certain dietary patterns, defined as regularly consumed foods and drinks [13], to children's metal exposure. The focus of existing child studies in a few European countries has been on Mediterranean [14], pro-vegetarian [15], or healthy versus non-healthy diets [16]. The aim of the present study was to identify the dietary sources of young children's exposure to multiple toxic metals, measured through concentrations in blood and urine, and to identify dietary patterns of major concern in a sample of 1.5- and 4-year-olds participating in a Swedish national dietary survey. We also aimed to compare the dietary sources of toxic metals with those related to children's status of copper, manganese, selenium, and zinc. These essential elements are cofactors of antioxidant enzymes, which play a crucial role in the body's defense against several toxic metals [17].

MATERIALS AND METHODS

Study design and population

During 2021–2023, the Swedish Food Agency carried out Riksmaten Young Children, a national cross-sectional dietary survey of young children aged 1.5 and 4 years. Details of the survey design, sampling, and implementation have been published elsewhere [18]. Briefly, a register-based random nationwide sample of participants was drawn by the governmental agency Statistics Sweden. Participants were asked to complete a dietary survey, including a 2-day web-based food diary and a food habit questionnaire. A

subsample of families was also invited to participate in biological sampling (blood and urine), consisting of children residing in municipalities within 50 km of the seven regional Environmental and Occupational Medicine clinics located across Sweden (Lund, Gothenburg, Linköping, Örebro, Stockholm, Uppsala, and Umeå). The goal was to include approximately 1000 children per age group in the entire dietary survey, and to collect blood and urine from 300 children per age group in a subsample.

This study on dietary exposure to toxic and essential elements comprises all 1.5- and 4-year-olds in Riksmaten Young Children who completed the dietary survey and provided a blood and/or urine sample (Fig. S1). Of 5,506 eligible 1.5-year-olds in the subsample drawn by Statistics Sweden, 305 completed the dietary survey and donated blood ($n = 294$) and/or urine ($n = 65$). Of 4,544 eligible 4-year-olds in the subsample, 288 completed the dietary survey and donated blood ($n = 273$) and/or urine ($n = 276$). We examined whether the likelihood of providing a urine sample (available for only 65 out of 305) among 1.5-year-olds differed by background characteristics (Table S1). Only the difference by region of residence ($n = 7$) reached statistical significance ($p = 0.015$). Ethical approval for the Riksmaten Young Children study, including the present analysis, has been obtained from the Swedish Ethical Review Authority (2020-05293).

Dietary assessment

Dietary intake data of the included 1.5- and 4-year-olds were collected through a food diary according to recommendations made by the European Food Safety Authority [19]. The food diary RiksmatenFlexDiet has been developed by the Swedish Food Agency [18], and it has previously been validated among Swedish adolescents [20]. The web-based dietary diary covers data from two non-consecutive days (initiated during the weekend, followed by one weekday 4–11 days later) [18]. In brief, guardians were asked to enter the time and place of food consumption, and the type of all food consumed. Food items were searchable in the linked food composition database, and portion sizes could be identified from photographs and common household measures. Before submitting the diary, guardians were presented with a list-based reminder of commonly forgotten food items to minimize recall bias. The food list employed in Riksmaten Young Children included 1218 food items and composite dishes, based on the Swedish Food Agency's food composition database version Riksmaten Young Children 2021–24. Reported consumption from two days of dietary recall was converted to habitual (long-term) consumption (g/day) using the Multiple Source Method [21].

To identify dietary patterns contributing the most to children's exposure, we selected habitual intake of 14 major food groups: vegetables, fruits and berries, cereals (cereal-based products including rice), potatoes, nuts and seeds, chicken, fish and seafood, eggs, plant-based meat alternatives, dairy (liquid), sugary drinks, sweet snacks, juice and plant-based milk alternatives, and red and processed meat. Despite differences in origin and ingredient profiles, juice and plant-based milk alternatives can be grouped together in dietary patterns since they share consumption context [22] and load together [23]. For more rarely consumed food items, like canned tuna and game meat, known to contribute to toxic metal exposure, we used data from a questionnaire on consumption frequencies (RiksmatenFlexQ).

Element analysis

Upon completion of the first day of the 2-day food diary, participants were invited to blood sampling at the nearest Environmental and Occupational Medicine clinic. A 2 mL non-fasting venous blood sample (Vacuette® tubes

2 ml Lithium Heparin) was collected from either the back of the hand or the antecubital fossa by registered nurses or other certified personnel after applying local anaesthetic patches containing lidocaine and prilocaine. A spot urine sample was collected into a 50 mL tube at home before attending the clinic. If this was difficult, it was allowed to transfer urine from a clean potty to the tube as long as no stool was produced. The median interval between the first day of food diary registration and blood sampling was 32 days (10th–90th percentile: 15–81 days). Long intervals for some children reflect practical constraints: few sampling occasions, limited availability of personnel certified to sample young children, and missed occasions due to illness. Blood and urine samples were stored at -80°C awaiting analyses at Karolinska Institutet, Stockholm.

Whole blood concentrations were measured in the present study as they are preferred over serum or plasma concentrations as exposure biomarkers of most toxic metals [24]. While concentrations of essential elements in plasma or serum are generally the preferred measures in the clinical setting, whole blood concentrations reflect more long-term status, especially for selenium and copper [25–27]. Concentrations of arsenic (sum of inorganic arsenic metabolites and arsenobetaine) and cadmium were also measured in urine, along with fluoride. Cadmium concentration in urine reflects long-term exposure since cadmium accumulates in the renal cortex with a half-life of decades [28]. Urinary concentrations of arsenic and fluoride, on the other hand, are reflective of short-term exposure [24, 29].

Concentrations of elements in whole blood [toxic elements: arsenic (B-As), cadmium (B-Cd), cobalt (B-Co), mercury (B-Hg), lead (B-Pb); essential elements: copper (B-Cu), manganese (B-Mn), selenium (B-Se), and zinc (B-Zn)] and urine [cadmium (U-Cd)] were measured using inductively coupled plasma mass spectrometry (ICP-MS; Agilent 7900, Agilent Technologies, Tokyo, Japan). Cobalt is grouped with the toxic elements, as humans are incapable of *de novo* synthesis of the essential vitamin B12, of which cobalt is a part, and inorganic cobalt has been shown to have toxic properties [30]. Blood was diluted 1:20 in an alkali solution as described in detail elsewhere [31], while urine was diluted 1:10 in 1% nitric acid (67–69% w/w, NORMATOM®, VWR, Butterworth, UK). The limit of detection (LOD; calculated as three times the standard deviation of blank concentrations) for each element is presented in Table S2 together with the matrix-specific commercial reference materials used for quality control. Concentrations below LOD were kept as measured, apart from when they were negative and replaced with $\text{LOD}/\sqrt{2}$ [B-As ($n=6$), B-Co ($n=3$), and B-Hg ($n=6$)]. As the blood collection tubes used (Vacuette®, 2 ml, with lithium-heparin, Greiner Bio-One GmbH, Austria) were not marketed as trace-element-free, we performed an overnight leaching test using 0.2% nitric acid (67–69% w/w, NORMATOM®, VWR, Butterworth, UK) in tubes from different batches. ICP-MS measurements showed that the average leakage was very low for all measured elements (Table S2), resulting in negligible contributions to the blood concentrations.

Urinary metabolites of inorganic arsenic [methylarsonic acid (MMA), dimethylarsinic acid (DMA), and remaining inorganic arsenic (iAs)] and arsenobetaine (U-AsB) were measured using high-performance liquid chromatography (HPLC; Agilent 1260 Infinity II, Agilent Technologies) coupled to ICP-MS (Agilent 7900, Agilent Technologies) [32]. The sum concentration of MMA, DMA, and iAs (hereafter referred to as U-iAs metabolites) was used as a biomarker of inorganic arsenic exposure. Commonly, U-iAs metabolites consist of 10–20% MMA, 60–80% DMA, and 10–20% iAs [33]. Twenty μL hydrogen peroxide (Merck, Darmstadt, Germany) was added to a 200 μL urine sample to oxidize inorganic arsenic(III) to arsenic(V) to facilitate peak evaluation. Separation of the arsenic compounds was improved by serially connecting two types of Hamilton columns, reversed-phase PRP-C18 and anion-exchange PRP-X110 (Hamilton, Bonaduz, Switzerland) using stainless-steel tubing. The mobile phase consisted of a water/ammonium carbonate or water/ammonium bicarbonate (Fisher Scientific, Waltham, MA, USA) gradient at pH 9.6 and 8, respectively. External standards of MMA, DMA (NIST, Gaithersburg, MD, USA), arsenic(V), and arsenobetaine (LGC Standards, Teddington, UK) ranged between 0.312–409 $\mu\text{g/L}$. An internal standard of 200 ppb rhodium (Rh) was added online. LODs and results of the reference materials (Urine 2669 NIST L-1 and L-2, Gaithersburg, MD, USA) are presented in Table S2.

Fluoride exposure was assessed by urinary concentrations (U-F) measured using a fluoride-specific electrode (Orion 9609BNWP and Orion Star A214 pH/ISE meter; Thermo Fisher Scientific, Waltham, MA, USA) [34]. Urine was diluted 1:1 with a total ionic strength adjustment buffer (TISAB II, Thermo Fisher Scientific). The external calibration curve was prepared daily through serial dilution of a 100 mg/L fluoride standard solution (Thermo Fisher Scientific) in deionized water and adjustment buffer (50% TISAB II)

and ranged between 0.05–2 mg/L. The LOD was 0.011 mg/L. Results of two different reference materials [fluoride in water; Product number: QC3162; Sigma-Aldrich, USA (certified fluoride concentration: 0.42 mg/L) and SeroNorm Trace Elements Urine L-2; LOT: 1011645; Sero AS, Norway (recommended fluoride concentrations: 4 mg/L)], analyzed before and after each run were 0.43 ± 0.02 mg/L ($n=24$, recovery 102.4%) and 3.9 ± 0.06 mg/L ($n=24$, recovery 97.5%), respectively.

To compensate for variation in urine dilution of the spot urine samples, all obtained concentrations were adjusted to the median specific gravity [adjusted urinary element concentration = unadjusted concentration $\times (\text{specific gravity}_{\text{median}} - 1) / (\text{specific gravity}_{\text{sample}} - 1)$] measured using an ATAGO PAL-10S refractometer (Thermo Fisher Scientific, Waltham, MA, USA). Overall median specific gravity was 1.020 (1.018 in 1.5-year-olds and 1.022 in 4-year-olds).

Covariates

The RiksmatenFlex questionnaire included sociodemographic information, such as the birthplace of the parents (categorized as both or only parent born in Sweden; one parent born in Sweden, the other outside of Sweden; both or only parent born outside of Sweden), number of children and adults in the household, area of residence (geographical region), smoking household members (yes/no), source of drinking water (public, private well, other), as well as breastfeeding [currently breastfed (yes/no) and duration of exclusive breastfeeding (months)] and child anthropometry [weight (kg) and height (cm) measured at the most recent visit to the child health care center at either 1.5 or 4 years of age or, for a few children, measured at home]. Body mass index (BMI, kg/m^2) at 4 years of age was defined according to the International Obesity Task Force's guidelines [35]. Parental education (≤ 12 years or at least one parent with >12 years) was based on register data provided by Statistics Sweden. The date of biological sample collection was used to generate the season of sampling [spring (March–May), summer (June–August), autumn (September–November), winter (December–February)].

Statistical analysis

Statistical analyses were performed using STATA 17 (StataCorp, LP, College Station, Texas, USA) and R 3.6.2 and 4.3.0. All tests were two-tailed, and p -values < 0.05 were considered statistically significant. Complete case analysis was adopted for addressing missing data. We conducted all statistical analyses and present data for 1.5- and 4-year-olds separately, as dietary patterns usually differ between these age groups. Categorical variables were described by frequency or percentage, and continuous variables by mean and standard deviation (SD) or median and 5th–95th percentiles. Distributions of element concentrations in blood and urine were examined by histograms and quantile-quantile plots. Differences in element concentrations by categorical background characteristics (child sex, parental origin, parental education, region of residence, smokers in the household, and water source) were assessed using either the Mann-Whitney U test or the Kruskal-Wallis Test. Correlations between element concentrations were assessed using the Spearman rank correlation test.

Correlations between individual element concentrations (toxic elements: B-As, U-AsB, U-iAs, B-Cd, U-Cd, B-Co, U-F, B-Pb, B-Hg; essential elements: B-Cu, B-Mn, B-Se, B-Zn) and habitual consumption of specific food groups (intake in grams/day) were analyzed using Spearman rank correlation in combination with unsupervised hierarchical cluster analysis, which were visualized in heat maps using R package “pheatmap” (version 3.6.2). The unsupervised hierarchical cluster analysis automatically structures the dietary data based on correlations between different food groups, forming clusters. The direction of the correlation between element concentrations and dietary intake data is represented by color: red for positive correlations and blue for negative correlations. Color intensity signifies the strength of correlations, and significance is indicated by stars.

To derive *a posteriori* dietary patterns [36], we adopted two data-driven approaches: (i) principal component analysis (PCA) using the `princomp()` function, and (ii) k-means clustering using the `kmeans()` function from the R package “stats”. The “factoextra” package was used for visualization. While PCA yields a component score for each child, which reflects their adherence to specific dietary patterns, the clustering algorithm generates mutually exclusive groups of children based on underlying dietary patterns [36]. Thus, these two approaches address different, but equally relevant, questions: “which combinations of foods tend to be consumed together?” (PCA) versus “which types of diets do participants mainly consume?” (clustering) [36], and therefore, the combination of both methods may give a more comprehensive, nuanced understanding of dietary patterns [37].

Based on cluster and scree plots (Figs. S2 and S3), size of the groups, and interpretability [38], we retained three principal components and three clusters (each representing a dietary pattern) among both 1.5- and 4-year-olds. Prior to running the PCA, the 14 food-group variables were standardized using the `scale()` function in R to ensure that food groups with larger absolute consumption (in g/day) did not disproportionately influence the extracted dietary patterns. Factor loadings were not rotated. For the PCA-derived dietary patterns, food groups with factor loadings ≥ 0.3 were considered important contributors in characterizing that specific pattern [38, 39].

Linear regression analyses were used to explore associations of the PCA- and clustering-derived dietary patterns with the individual element concentrations [presented as mean concentrations with associated 95% confidence intervals (CI)]. The three different principal component scores were converted into tertiles and used as predictors in the models, resulting in three separate models (one per component) fitted per age group for each element concentration. From k-means clustering, we generated one categorical variable (comprising three diet clusters) for each age group, which was used as the predictor for each element concentration. In total, the contribution to eight toxic element biomarkers (B-As, U-iAs, B-Cd, U-Cd, B-Co, U-F, B-Pb, B-Hg) and four essential biomarkers (B-Cu, B-Mn, B-Se, B-Zn) was explored in each age group. The element concentrations of B-As, U-iAs, B-Cd, U-Cd, U-F, and B-Pb were right-skewed, and they were therefore natural log-transformed to obtain normally distributed residuals in the models, and then back-transformed estimates were retrieved directly using the “`emmeans`” package. Covariates were selected using a directed acyclic graph (Fig. S4). The final models were adjusted for child sex, age (years), parental education (≤ 12 years or >12 years of formal education), season of sampling (spring from March–May, summer from June–August, autumn from September–November, and winter from December–February), and the children’s daily energy intake (continuous, kJ/day).

In sensitivity analysis, models based on U-iAs metabolites were further adjusted for U-AsB concentrations in an attempt to compensate for the influence of arsenic species other than iAs originating from seafood intake [40]. A second analysis involved restriction of U-iAs metabolites models to children with less than 80% DMA (% of the sum of iAs metabolites) because arsenosugars and arsenolipids, which commonly occur in seafood, are metabolized in the body to DMA [41]. The fraction of DMA has been shown to generally vary between 60–80% in populations exposed to iAs [33], and therefore, it can be assumed that a higher %DMA indicates influence from seafood consumption. Notably, these sensitivity analyses were only done in 4-year-olds, for whom we had sufficient power. Quantile-quantile plots of the residuals and residuals versus fitted plots were used to ensure that there were no violations of regression assumptions.

RESULTS

Background characteristics and element concentrations

The study included a similar proportion of boys and girls both at 1.5 and 4 years of age (Table S1). Most of the parents were born in Sweden, had more than 12 years of education, and were non-smokers, and most children consumed public drinking water. The median duration of exclusive breastfeeding was 6 months (10–90th percentile: 3–8 months). Only 54 of the 1.5-year-olds (17.7%) were still breastfed to some extent during the survey. Based on the children’s BMI at 4 years of age, 18% were underweight (< 14.51 kg/m² for boys and < 14.30 kg/m² for girls), 77% were of normal body weight, 5% were overweight (≥ 17.52 kg/m² for boys and ≥ 17.36 kg/m² for girls), and less than 1% were obese (≥ 19.23 kg/m² for boys and ≥ 19.16 kg/m² for girls).

There were marked variations in both toxic and essential element concentrations in children’s blood and urine at both ages (Table 1). Compared to 1.5-year-olds, 4-year-old children had significantly higher B-Cd, B-Co, and U-F concentrations. The concentrations of U-iAs metabolites were 4.6 and 4.2 µg/L at 1.5 and 4 years, respectively. Although U-AsB showed a considerably wider concentration range (5th–95th percentile: 0.13–181 µg/L for all children) than that of U-iAs metabolites (1.9–16.9 µg/L), they were significantly correlated in both age groups

(Tables S3 and S4, and Figs. S5 and S6). However, the correlation was markedly weakened after restriction to children with less than 80% DMA in urine [ρ : 0.02 ($n = 31$) and 0.20 ($n = 188$) at 1.5 and 4 years, respectively]. For these children, the median concentrations of U-iAs metabolites were 2.8 versus 3.6 µg/L at 1.5 and 4 years, respectively (Table 1). 4-year-olds had also marginally higher B-Zn, but slightly lower B-Cu and B-Mn concentrations than 1.5-year-olds.

In both age groups, B-As and B-Hg were moderately correlated, as were B-Hg and B-Se, and B-Mn and B-Zn (Tables S3 and S4, and Figs. S5 and S6). Among 4-year-olds, B-Co was moderately correlated with B-Cd and B-Mn. B-Cd and U-Cd correlated in 4-year-olds, but not in 1.5-year-olds. In both age groups, the correlation of B-As with U-AsB was markedly stronger than that with U-iAs metabolites. U-AsB concentrations were also strongly correlated with both B-Hg and B-Se.

Detailed information on differences in element concentrations by demographic background data is presented in detail in Tables S5–S7. The most consistent finding was the variation by region of residence for most of the toxic and essential elements among both 1.5- and 4-year-old children, while correlations with other demographic factors were less consistent.

Element concentrations and food consumption

Correlations between toxic and essential element concentrations and the children’s habitual consumption of different food groups at 1.5 and 4 years of age, estimated based on the parent-reported dietary questionnaire, are summarized in Fig. 1 and Table S8. Among 1.5-year-olds, B-As was positively correlated with fish and shellfish consumption. On the other hand, U-AsB and U-iAs metabolites showed no correlations with food groups, but only 65 children at 1.5-years had donated urine. Among 4-year-olds, B-As was not significantly correlated with fish and shellfish consumption but was positively correlated with total vegetable consumption, which clustered together with fish and shellfish consumption. However, U-AsB and, to some extent, U-iAs metabolites at 4 years were positively correlated with fish and shellfish as well as total vegetable consumption. When only 4-year-olds with $< 80\%$ DMA in urine were considered, the correlation of U-iAs metabolites with fish and shellfish was attenuated (from ρ : 0.15 to 0.07; $p = 0.37$), whereas the correlation with vegetables remained essentially unchanged (ρ : 0.20; $p = 0.007$). B-Hg concentrations were positively correlated with fish and shellfish and total vegetable consumption among both 1.5- and 4-year-olds. To note, fish and shellfish consumption clustered more closely together with vegetable consumption among 4-year-olds than among 1.5-year-olds (Fig. 1). When considering data from the questionnaire on consumption frequencies (RiksmatenFlexQ), B-Hg was slightly higher among children who consumed canned tuna compared with those who did not [median: 1.12 ($n = 103$) versus 0.91 µg/L ($n = 144$) at age 1.5; median 1.22 ($n = 90$) versus 0.91 µg/L ($n = 165$) at age 4, p for all < 0.05].

U-Cd in 1.5-year-olds was positively correlated with plant-based milk alternatives and nuts and seeds, and inversely correlated with chicken consumption. In 4-year-olds, U-Cd was inversely correlated with chicken and eggs, both of which clustered together with total red meat consumption. Neither B-Cd nor B-Co ($\rho \leq 0.15$) showed evident correlation with any food groups at any age. B-Pb was inversely correlated with total cereal consumption among 1.5-year-olds, while this correlation was weaker among 4-year-olds. Furthermore, children with reported game meat consumption (RiksmatenFlexQ) had slightly higher B-Pb than children who did not report any consumption both among 1.5-year-olds [median: 7.61 µg/L ($n = 102$) versus 6.35 µg/L ($n = 163$), $p = 0.001$] and among 4-year-olds [median: 6.54 µg/L ($n = 119$) versus 5.82 µg/L ($n = 147$), $p = 0.081$].

B-Se concentrations were positively correlated with fish and shellfish, as well as with total vegetable consumption in both age

Table 1. Concentrations of metals and other trace elements in the blood and urine of the 1.5- and 4-year-olds in Riksmaten young children.

Elements	All children N	Median	5th–95th percentile	1.5-year-olds N	Median	5th–95th percentile	4-year-olds ^a N	Median	5th–95th percentile	p ^b
Toxic elements										
B-As (µg/L)	538	1.4	0.38–9.3	269	1.4	0.42–10.0	269	1.6	0.34–8.8	0.139
U-AsB (µg/L) ^c	336	7.8	0.13–181	65	8.2	0.04–178	271	7.6	0.16–181	0.58
U-IAs (µg/L) ^c	336	4.4	1.9–16.9	65	4.6	1.8–18.2	271	4.2	2.0–16.0	0.88
U-IAs (µg/L) ^{c,d}	219	3.6	1.7–8.3	31	2.8	1.54–7.02	188	3.6	1.8–8.4	0.021
B-Cd (µg/L)	538	0.10	0.03–0.26	269	0.07	0.02–0.21	269	0.14	0.05–0.28	<0.001
U-Cd (µg/L) ^c	341	0.11	0.05–0.24	65	0.12	0.05–0.29	276	0.10	0.05–0.24	0.554
B-Co (µg/L)	538	0.28	0.12–0.48	269	0.23	0.09–0.44	269	0.31	0.18–0.49	<0.001
U-F (µg/L) ^c	341	0.89	0.34–2.3	65	0.68	0.30–2.1	276	0.93	0.35–2.4	0.005
B-Pb (µg/L)	538	6.4	3.2–15.4	269	6.6	3.2–16.4	269	6.1	3.4–12.9	0.111
B-Hg (µg/L)	538	0.99	0.16–2.4	269	0.99	0.11–2.5	269	0.99	0.24–2.4	0.516
Essential elements										
B-Cu (µg/L)	538	1074	868–1395	269	1099	878–1458	269	1052	863–1294	<0.001
B-Mn (µg/L)	538	11.9	6.8–20.3	269	12.7	8.3–21.2	269	11.0	5.6–17.3	<0.001
B-Se (µg/L)	538	103	79.5–127	269	103	77.1–133	269	103	81.3–124	0.915
B-Zn (mg/L)	538	4.8	3.4–5.9	269	4.7	3.2–5.6	269	4.9	3.7–6.2	<0.001

B-As blood arsenic, U-AsB urinary arsenobetaine, U-IAs sum of inorganic arsenic metabolites [dimethylarsinic acid (DMA), methylarsonic acid (MMA), and remaining inorganic arsenic (III + V)], B-Cd blood cadmium, U-Cd urinary cadmium, B-Co blood cobalt, U-F urinary fluoride, B-Pb blood lead, B-Hg blood mercury, B-Cu blood copper, B-Mn blood manganese, B-Se blood selenium, B-Zn blood zinc.

^aNumber of 4-year-olds who donated blood $n = 269$ and urine $n = 276$ (U-IAs and U-AsB only measured in 271 children due to insufficient amount of sample).

^bMann-Whitney U-test was used to assess the difference between 1.5- and 4-year-olds.

^cConcentrations adjusted for specific gravity (median 1.021).

^dRestricted to children with urinary DMA < 80% of total U-IAs metabolites (total $n = 219$, 1.5-year-olds $n = 31$, 4-year-olds $n = 188$).

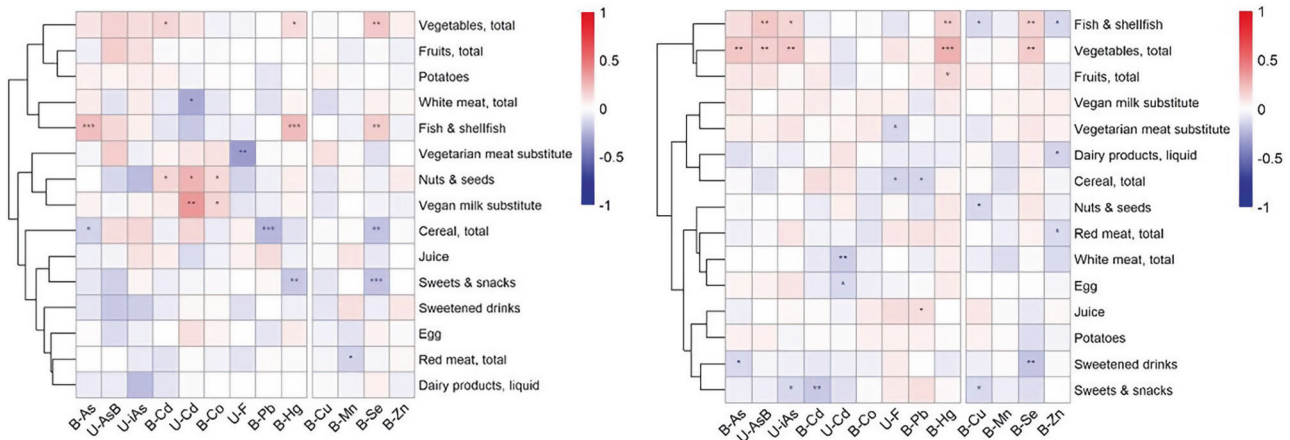


Fig. 1 Clustered heat map of correlations. Bivariate correlations between consumption of different food groups and concentration of toxic and essential elements in blood and/or urine [toxic elements: blood arsenic (B-As), urinary arsenobetaine (U-AsB), urinary sum of inorganic arsenic metabolites (U-iAs), blood cadmium (B-Cd), urinary cadmium (U-Cd), blood cobalt (B-Co), urinary fluoride (U-F), blood lead (B-Pb), blood mercury (B-Hg); essential elements: blood copper (B-Cu), blood manganese (B-Mn), blood selenium (B-Se), blood Zn (B-Zn)] are shown among 1.5- (left) and 4-year-olds (right). The correlations are based on the Spearman rank correlation test, and the direction and magnitude are denoted by color, with red representing positive correlations and blue representing negative correlations, and deeper colors signifying stronger correlations. Asterisks denote statistical significance: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

groups. These two food groups clustered together in both age groups. Additionally, B-Se concentrations were inversely correlated with the consumption of cereals, sweets, and snacks (which clustered together) among 1.5-year-olds and with sweetened drinks consumption among 4-year-olds. B-Cd, B-Mn, and B-Zn showed no evident correlations with food groups ($\rho < 0.15$).

Dietary patterns derived using PCA and k-means clustering among 1.5-year-olds

A comparison between the dietary patterns obtained using PCA and k-means clustering among 1.5-year-olds is shown in Table S9. For PCA, three principal components were retained and characterized based on food groups with factor loadings ≥ 0.3 (Tables S9 and S10). Principal Component 1 loaded high on plant-based meat and milk alternatives; Principal Component 2 on vegetables, fruits and berries, and fish and shellfish; and Principal Component 3 on eggs, sugary drinks and sweet snacks. The k-means clustering analysis identified three dietary clusters (Table S9 and Fig. S2). As shown in Tables S11 and S12, Cluster 1 ($n = 43$) was mainly characterized by the highest consumption of plant-based meat and milk alternatives, juice, and nuts and seeds; Cluster 2 ($n = 116$) by a high-diversity diet with consumption of fruits and vegetables along with potato, fish and shellfish, chicken, and milk products; and Cluster 3 ($n = 146$) by a western-style diet with consumption of red and processed meat, cereals, sweet snacks, and sugary drinks. There were very small differences in median energy intake across the clusters, with a marginally higher value in Cluster 2 than in Clusters 1 and 3 (Table S11).

Dietary patterns and associations with element concentrations among 1.5-year-olds

In the multivariable-adjusted linear regression models (Table 2), increased adherence to Principal Component 1 was associated with increasing U-Cd and B-Cd concentrations (p -trend 0.018). Increased adherence to Principal Component 2 was associated with increasing B-Hg and B-Se concentrations (p -trend 0.001 and < 0.001 , respectively). B-As showed a similar trend, although non-significant (p -trend 0.069).

As indicated in Table 3, we found that children in Cluster 1 (plant-based alternatives diet) had higher U-Cd concentrations, but not B-Cd, than those in Cluster 2 (high-diversity diet) and Cluster 3 (western-style diet). Concerning the essential elements, children in Cluster 1 (plant-based alternatives diet) had higher B-Mn

concentrations than children in Cluster 2 (high-diversity cluster). Children in Cluster 2 had, on the other hand, higher B-Hg and B-Se concentrations than children in Cluster 3 (western-style diet).

Dietary patterns derived using PCA and k-means clustering among 4-year-olds

A comparison between the dietary patterns obtained using PCA and k-means clustering is shown in Table S9. Three principal components were retained and characterized based on food groups with factor loadings ≥ 0.3 (Tables S9 and S13). Principal Component 1 loaded high on chicken, dairy, and red and processed meat; Principal Component 2 on vegetables, fruits and berries, and fish and shellfish; and Principal Component 3 on fruits and berries, potatoes, and juice and plant-based milk alternatives. The k-means clustering analysis identified three dietary clusters (Table S9 and Fig. S3). As shown in Tables S14 and S15, Cluster 1 ($n = 35$) was mainly characterized by plant-based meat and milk alternatives (including juice) with consumption of nuts, seeds, and cereals; Cluster 2 ($n = 112$) by a western-style diet with consumption of milk products, sugary drinks, sweet snacks, and red and processed meat; and Cluster 3 ($n = 141$) by a high-diversity diet with consumption of fruits and vegetables, potato, chicken, fish and seafood, and eggs. There was no significant difference in energy intake across these clusters (Table S14).

Dietary patterns and associations with element concentrations among 4-year-olds

In the multivariable-adjusted linear regression models (Table 4), increased adherence to Principal Component 2 was associated with increasing B-As concentrations (p -trend 0.002). Similarly, increased adherence to Principal Component 2 was associated with increased U-iAs metabolites (p -trend 0.006). In sensitivity analysis (Table S16), this positive trend remained after further adjustment for U-AsB, but when the analysis was restricted to children with $< 80\%$ DMA in urine, the trend was attenuated. Furthermore, increased adherence to Principal Component 2 was associated with increasing B-Hg and B-Se concentrations (p -trend < 0.001 ; Table 4). In Principal Component 3, B-As concentrations increased from the first to the second tertile but then leveled off (p -trend 0.036), and U-Cd concentrations decreased marginally in the highest tertile (p -trend 0.003), while B-Hg and U-F increased across the tertiles (p -trend < 0.05).

Table 2. Predicted mean concentrations (95% confidence intervals) of toxic metals and essential elements in blood or urine at 1.5 years of age by tertiles of PCA-derived factor scores for the dietary patterns from multiple linear regression models.

Elements ^a	Component 1 (Plant-based alternatives)			Component 2 (Vegetables, fruits & berries, seafood pattern)			Component 3 (Eggs, sugary snacks, drinks pattern)		
	Mean (95% CI)			Mean (95% CI)			Mean (95% CI)		
	T1	T2	T3	T1	T2	T3	T1	T2	T3
Toxic elements (µg/L)									
B-As	1.42 (1.09, 1.85)	1.41 (1.05, 1.90)	1.40 (1.05, 1.86)	1.25 (0.97, 1.63)	1.49 (1.11, 2.00)	1.65 (1.23, 2.20)	1.51 (1.14, 2.02)	1.47 (1.11, 1.93)	1.29 (0.98, 1.69)
U-IAs ^b	5.95 (3.44, 10.28)	3.85 (2.31, 6.44)	5.44 (3.33, 8.86)	4.32 (2.82, 6.60)	7.26 (3.92, 13.4)	6.44 (3.75, 11.1)	6.65 (3.84, 11.52)	4.74 (2.93, 7.66)	4.76 (2.91, 7.77)
B-Cd	0.06 (0.05, 0.07)	0.06 (0.05, 0.08)	0.07 (0.06, 0.09)*	0.06 (0.05, 0.07)	0.06 (0.05, 0.08)	0.07 (0.05, 0.08)	0.06 (0.05, 0.07)	0.06 (0.05, 0.08)	0.06 (0.05, 0.07)
U-Cd ^b	0.08 (0.05, 0.11)	0.09 (0.07, 0.13)	0.13 (0.09, 0.18)*	0.09 (0.07, 0.13)	0.11 (0.07, 0.17)	0.11 (0.08, 0.16)	0.08 (0.06, 0.12)	0.10 (0.07, 0.14)	0.10 (0.07, 0.15)
B-Co	0.23 (0.21, 0.26)	0.26 (0.23, 0.29)	0.25 (0.22, 0.28)	0.25 (0.22, 0.27)	0.25 (0.22, 0.28)	0.24 (0.21, 0.27)	0.23 (0.20, 0.26)	0.26 (0.23, 0.29)	0.24 (0.21, 0.27)
U-F	914 (625, 1338)	580 (405, 829)	684 (487, 962)	687 (505, 935)	705 (451, 1103)	801 (541, 1186)	676 (455, 1003)	756 (535, 1068)	686 (482, 977)
B-Pb	7.29 (6.37, 8.35)	6.79 (5.84, 7.91)	6.99 (6.04, 8.10)	6.96 (6.08, 7.97)	7.46 (6.42, 8.68)	6.93 (5.96, 8.05)	6.89 (5.94, 7.98)	7.18 (6.23, 8.27)	7.14 (6.20, 8.22)
B-Hg	0.94 (0.76, 1.14)	1.04 (0.83, 1.28)	1.02 (0.82, 1.25)	0.86 (0.69, 1.05)	0.99 (0.79, 1.21)	1.23 (1.01, 1.48)*	0.99 (0.79, 1.21)	1.00 (0.81, 1.22)	0.98 (0.78, 1.19)
Essential elements (µg/L)									
B-Cu	1078 (1034, 1122)	1079 (1031, 1129)	1095 (1047, 1144)	1070 (1028, 1115)	1106 (1057, 1157)	1084 (1036, 1134)	1102 (1055, 1152)	1075 (1030, 1122)	1075 (1030, 1121)
B-Mn	11.8 (10.8, 12.8)	12.1 (11.0, 13.3)	12.7 (11.6, 13.9)	12.0 (11.0, 13.0)	13.1 (11.9, 14.2)	11.6 (10.5, 12.7)	12.4 (11.3, 13.5)	11.9 (10.8, 12.9)	12.2 (11.2, 13.3)
B-Se	102 (97.3, 107)	103 (97.3, 108)	102 (96.9, 107)	97 (93, 102)	104 (99, 109)	108 (103, 113)**	101 (96, 106)	104 (99, 109)	101 (96, 106)
B-Zn	4473 (4268, 4677)	4250 (4021, 4478)	4477 (4255, 4699)	4426 (4221, 4631)	4472 (4242, 4702)	4355 (4127, 4583)	4402 (4178, 4625)	4490 (4274, 4705)	4360 (4146, 4574)

T tertile, B-As blood arsenic, U-IAs sum of inorganic arsenic metabolites (dimethylarsinic acid (DMA), methylarsonic acid (MMA), and remaining inorganic arsenic (III + V)), B-Cd blood cadmium, U-Cd urinary cadmium, B-Co blood cobalt, U-F urinary fluoride, B-Pb blood lead, B-Hg blood mercury, B-Cu blood copper, B-Mn blood manganese, B-Se blood selenium, B-Zn blood zinc.

^aModels adjusted for age, sex, parental education, season and energy intake

^bUrinary concentrations were specific-gravity-adjusted (median 1.021).

*Statistically significant p for linear trend <0.05 to 0.001, and **<0.001 appear in bold.

Table 3. Predicted mean concentrations (95% confidence intervals) of toxic and essential elements in blood or urine at 1.5 and 4 years by k-means-derived dietary clusters from multiple linear regression models.

	1.5-year-olds ^{a,b}			4-year-olds ^{a,c}		
	Cluster 1 (Plant-based alternatives diet)	Cluster 2 (High-diversity diet)	Cluster 3 (Western-style diet)	Cluster 1 (Plant-based alternatives diet)	Cluster 2 (Western-style diet)	Cluster 3 (High-diversity diet)
Elements ^a	Predicted mean (95% CI)			Predicted mean (95% CI)		
Toxic elements (µg/L)						
B-As	1.11 (0.77–1.59)	1.49 (1.13–1.96)	1.44 (1.12–1.84)	2.6 (1.7–3.9) ^{*d}	1.3 (1.0–1.8) ^{*f}	2.1 (1.6–2.7)
U-iAs	5.13 (2.65–9.93)	6.60 (3.97–10.96)	4.46 (2.87–6.91)	5.1 (4.0–6.5)	4.5 (3.9–5.3)	5.1 (4.4–5.9)
B-Cd	0.07 (0.05–0.10)	0.06 (0.05–0.08)	0.06 (0.05–0.07)	0.15 (0.12–0.18)	0.13 (0.11–0.15)	0.13 (0.12–0.15)
U-Cd	0.15 (0.10–0.24) ^{*d, e}	0.09 (0.07–0.13)	0.09 (0.07–0.12)	0.11 (0.10–0.14) ^{*e}	0.11 (0.10–0.13) ^{*f}	0.09 (0.08–0.10)
B-Co	0.27 (0.23–0.30)	0.25 (0.22–0.27)	0.24 (0.22–0.27)	0.33 (0.30–0.37)	0.30 (0.27–0.32)	0.31 (0.29–0.34)
U-F	948 (595–1510)	776 (543–1110)	632 (464–862)	857 (690–1064)	834 (723–962)	919 (801–1055)
B-Pb	6.7 (5.5–8.1)	6.8 (5.8–7.8)	7.3 (6.5–8.3)	6.3 (5.3–7.4)	6.1 (5.5–6.8)	6.4 (5.7–7.1)
B-Hg	0.92 (0.68–1.2)	1.12 (0.91–1.35) ^{*f}	0.93 (0.76–1.11)	1.01 (0.79–1.27)	0.79 (0.66–0.94) ^{*f}	0.99 (0.84–1.15)
Essential elements (µg/L)						
B-Cu	1113 (1052–1178)	1081 (1035–1128)	1078 (1038–1120)	1063 (1014–1114)	1063 (1031–1095)	1059 (1027–1091)
B-Mn	13.7 (12.2–15.2) ^{*d}	12.2 (11.0–13.3)	12.6 (11.6–13.6)	11.2 (9.9–12.5)	11.3 (10.4–12.1)	11.5 (10.7–12.4)
B-Se	103 (96.5–109)	107 (102–112) ^{**f}	99 (94.7–103)	104.3 (99.4–109.2) ^{*d}	98.9 (95.7–102)	102 (98.9–105.1)
B-Zn	4472 (4186–4759)	4357 (4140–4573)	4445 (4250–4639)	4856 (4576–5143)	4844 (4662–5030)	4796 (4616–4978)

CI confidence interval, B-As blood arsenic, U-iAs sum of inorganic arsenic metabolites [dimethylarsinic acid (DMA), methylarsonic acid (MMA), and remaining inorganic arsenic (III + V)], B-Cd blood cadmium, U-Cd urinary cadmium, B-Co blood cobalt, U-F urinary fluoride, B-Pb blood lead, B-Hg blood mercury, B-Cu blood copper, B-Mn blood manganese, B-Se blood selenium, B-Zn blood zinc.

^aModels are adjusted for age (years), sex (boy/girls), parental education (≤ 12 years and >12 years), and daily energy intake (kJ/day);

^bChildren aged 1.5 years ($n = 305$): 269 children donated blood [Cluster 1 ($n = 41$), Cluster 2 ($n = 103$), and Cluster 3 ($n = 125$)], and 65 children donated urine [Cluster 1 ($n = 10$), Cluster 2 ($n = 28$), and Cluster 3 ($n = 27$)], in which all elements concentrations were specific-gravity-adjusted (median: 1.021).

^cChildren aged 4 years ($n = 288$): 269 children donated blood [Cluster 1 ($n = 33$), Cluster 2 ($n = 103$), and Cluster 3 ($n = 133$)], and 276 children donated urine [Cluster 1 ($n = 35$), Cluster 2 ($n = 107$), and Cluster 3 ($n = 134$)], in which all element concentrations were specific-gravity-adjusted (median 1.021).

^dDifference between Cluster 1 and 2 (* < 0.05 to 0.001, and ** < 0.001).

^eDifference between Cluster 1 and 3 (* < 0.05 to 0.001, and ** < 0.001).

^fDifference between Cluster 2 and 3 (* < 0.05 to 0.001, and ** < 0.001).

As shown in Table 3, children in Cluster 1 (plant-based alternatives diet) and Cluster 3 (high-diversity diet) had similar B-As concentrations, which were higher than those of children in Cluster 2 (western-style diet). The U-iAs metabolites did not differ between the clusters. In sensitivity analysis (Table S17), further adjustment for U-AsB or restricting the model to children with $<80\%$ DMA did not significantly alter the U-iAs metabolite estimates. Children in Cluster 1 (plant-based alternatives diet) and Cluster 2 (western-style diet) had similar U-Cd concentrations, which were higher than those in children in Cluster 3 (high-diversity cluster; Table 3). B-Cd did not differ across the clusters. Children in Cluster 3 (high-diversity diet) had higher B-Hg concentrations than children in Cluster 2 (western-style diet). Children in Cluster 1 (plant-based alternatives diet) had higher B-Se concentrations than children in Cluster 2 (western-style diet).

DISCUSSION

We combined a Swedish nation-wide dietary survey with biomonitoring data for commonly occurring toxic metals and certain essential elements from children aged 1.5 and 4 years and examined cross-sectional associations with consumption of specific food groups and dietary patterns. Concentrations of toxic metals in blood and/or urine showed a wide range and differed by geographical region. Concerning correlations with specific food groups, children's U-AsB and B-As (mainly arsenobetaine), B-Hg (mainly methylmercury), and B-Se correlated moderately with both seafood and vegetable intake, which clustered together. Similarly, in the adjusted analysis, increasing adherence to a dietary pattern rich in seafood, fruits and berries, and vegetables

was associated with increasing B-As, B-Hg, and B-Se concentrations. Children's U-iAs metabolites (restricted to those with $<80\%$ DMA) correlated mainly with vegetable consumption. The adjusted associations with dietary patterns revealed higher cadmium exposure from diets characterized by plant-based meat and milk alternatives, nuts, and seeds.

Fish and other seafood are well-known sources of exposure to certain organic arsenic compounds and methylmercury [32, 41, 42]. Among the measured arsenic species in the present study, seafood intake was most strongly correlated with B-As and U-AsB, which correlated strongly, showing that the dominant form of children's arsenic exposure was arsenobetaine. This arsenic analogue of glycine betaine originates almost exclusively from marine fish and other seafood [41]. Nonetheless, among 4-year-olds, U-iAs metabolites, a commonly used measure of exposure to inorganic arsenic, were also weakly correlated with seafood consumption ($\rho = 0.15$), suggesting that some of the urinary DMA originated from seafood, especially through metabolism of ingested arsenolipids and arsenosugars [41]. Therefore, it has been proposed to adjust the exposure models with U-iAs metabolites for U-AsB to reduce the impact of seafood-derived DMA [40]. However, seafood-specific sources of arsenobetaine and DMA are not the same [41], although consumption often overlaps as people vary the type of fish and other seafood consumed. Indeed, the positive association of total U-iAs metabolites with adherence to a dietary pattern rich in seafood, fruits and berries, and vegetables remained essentially the same after adjustment for U-AsB. We therefore tested another approach where we restricted our analysis to 4-year-olds with $<80\%$ DMA in urine ($n = 188$), since it is known that the relative amount of DMA in urine following

Table 4. Predicted mean concentrations (95% confidence intervals) of toxic metals and essential elements in blood or urine at 4 years of age by tertiles of PCA-derived factor scores for the dietary patterns from multiple linear regression models.

Elements ^a	Component 1 (Meat and dairy pattern)			Component 2 (Vegetables, fruits & berries, seafood pattern)			Component 3 (Fruits & berries, potatoes, plant-based milk pattern)		
	Mean (95% CI)			Mean (95% CI)			Mean (95% CI)		
	T1	T2	T3	T1	T2	T3	T1	T2	T3
Toxic elements (µg/L)									
B-As	2.10 (1.57, 2.81)	1.67 (1.24, 2.25)	1.60 (1.20, 2.14)	1.39 (1.06, 1.83)	1.93 (1.44, 2.55)	2.42 (1.78, 3.30)*	1.38 (1.04, 1.83)	2.03 (1.51, 2.72)	2.06 (1.54, 2.75)*
U-As ^b	4.80 (4.05, 5.69)	5.06 (4.26, 6.02)	4.76 (4.02, 5.63)	4.24 (3.61, 4.99)	4.95 (4.20, 5.84)	5.76 (4.83, 6.87)*	4.47 (3.78, 5.29)	4.95 (4.16, 5.88)	5.18 (4.38, 6.12)
B-Cd	0.15 (0.13, 0.17)	0.12 (0.11, 0.14)	0.13 (0.11, 0.15)	0.13 (0.11, 0.15)	0.13 (0.11, 0.15)	0.15 (0.13, 0.17)	0.14 (0.12, 0.15)	0.14 (0.12, 0.15)	0.13 (0.11, 0.15)
U-Cd ^b	0.12 (0.10, 0.13)	0.11 (0.09, 0.12)	0.10 (0.09, 0.12)	0.12 (0.10, 0.13)	0.11 (0.09, 0.12)	0.11 (0.09, 0.12)	0.12 (0.10, 0.13)	0.12 (0.10, 0.13)	0.10 (0.08, 0.11)*
B-Co	0.32 (0.30, 0.35)	0.31 (0.29, 0.34)	0.30 (0.27, 0.32)	0.31 (0.29, 0.34)	0.31 (0.28, 0.33)	0.31 (0.29, 0.34)	0.30 (0.27, 0.32)	0.31 (0.28, 0.33)	0.32 (0.30, 0.35)
U-F	910 (781, 1061)	851 (727, 995)	863 (741, 1004)	949 (819, 1100)	822 (706, 957)	844 (719, 991)	788 (678, 915)	841 (721, 981)	1003 (864, 1166)*
B-Pb	6.43 (5.73, 7.22)	5.88 (5.23, 6.62)	6.36 (5.67, 7.14)	6.38 (5.71, 7.13)	6.18 (5.50, 6.93)	6.09 (5.38, 6.90)	5.83 (5.21, 6.53)	6.85 (6.09, 7.70)	6.15 (5.48, 6.89)
B-Hg	0.93 (0.77, 1.10)	0.86 (0.71, 1.03)	0.92 (0.76, 1.09)	0.73 (0.60, 0.86)	1.00 (0.84, 1.17)	1.10 (0.93, 1.30)**	0.80 (0.66, 0.96)	0.93 (0.77, 1.10)	0.99 (0.83, 1.17)*
Essential elements (µg/L)									
B-Cu	1066 (1032, 1102)	1066 (1031, 1102)	1051 (1018, 1086)	1068 (1035, 1102)	1061 (1027, 1096)	1050 (1014, 1087)	1057 (1024, 1092)	1063 (1028, 1099)	1063 (1029, 1098)
B-Mn	11.7 (10.8, 12.6)	11.0 (10.0, 11.9)	11.4 (10.5, 12.3)	11.5 (10.7, 12.4)	11.1 (10.2, 12.0)	11.5 (10.5, 12.5)	10.9 (10.0, 11.8)	11.3 (10.4, 12.2)	11.9 (11.0, 12.8)
B-Se	100 (97, 104)	101 (97, 104)	102 (98, 105)	97 (94, 100)	102 (99, 105)	106 (102, 109)**	102 (98, 105)	101 (98, 105)	100 (96, 103)
B-Zn	4979 (4784, 5179)	4685 (4491, 4883)	4796 (4604, 4992)	4944 (4756, 5136)	4715 (4524, 4910)	4784 (4577, 4996)	4863 (4672, 5058)	4659 (4465, 4857)	4934 (4739, 5132)

T tertile, B-As blood arsenic, U-As sum of inorganic arsenic metabolites (dimethylarsinic acid (DMA), methylarsonic acid (MMA), and remaining inorganic arsenic (III + V)), B-Cd blood cadmium, U-Cd urinary cadmium, B-Co blood cobalt, U-F urinary fluoride, B-Pb blood lead, B-Hg blood mercury, B-Cu blood copper, B-Mn blood manganese, B-Se blood selenium, B-Zn blood zinc.

^aModels adjusted for age, sex, parental education, season, and energy intake; and

^bUrinary concentrations were specific-gravity-adjusted (median 1.021).

*Statistically significant p for linear trend <0.05 to 0.001, and **<0.001 appear in bold

exposure to inorganic arsenic is usually 60–80% [33]. Subsequently, the association was markedly attenuated and no longer significant.

Collectively, exposure to inorganic arsenic from food, as well as other sources, was low among young Swedish children (median U-iAs metabolites: 3.6 µg/L, range 1.3–15.4 µg/L, for 4-year-old children with <80% DMA). In U.S. children (aged 6–12 years) from NHANES cycles 2007–2020, the median U-iAs metabolite concentration was 6.40 µg/L, irrespective of their percent DMA, which may have overestimated the actual inorganic arsenic exposure. According to diet studies from Germany and Spain, rice-based foods were the most important dietary contributors to children's inorganic arsenic exposure [43–45]. Similarly, assessment of food products on the Swedish market showed that rice contained the highest amount of inorganic arsenic among all cereals assessed [46], and gluten-free rice-based baby porridge contained the highest arsenic concentrations of all infant foods, alongside products containing fish [47]. In the present study, rice was included among other cereals, and this food group did not correlate with any arsenic biomarkers. To note, the Swedish Food Agency recommends that children restrict their consumption of rice and rice products due to the presence of inorganic arsenic [48]. In a U.S. study of changes in child exposure to inorganic arsenic during weaning, rice cereal, fruit, and vegetable consumption were each strongly positively correlated with U-iAs metabolites (ρ : 0.90, 0.70, and 0.86, respectively), also suggesting inorganic arsenic intake from plant-based foods other than rice [49]. Correspondingly, we found that the present 4-year-olds' U-iAs metabolites (<80% DMA) correlated with their total vegetable intake.

The main form of mercury exposure in Sweden is methylmercury, which almost exclusively originates from fish, especially large predatory fish from both freshwater and oceans [50]. Mercury levels in fish and shellfish from the North-East Atlantic, predominantly consumed in Nordic countries, do not appear to decrease, despite a decades-long ban on mercury emissions [51]. Likewise, B-Hg concentrations in 4–9-year-old children in southern Sweden have not decreased since the beginning of this century (median values around 0.7 µg/L) [52]. Similar exposure levels were found in 4-year-olds in the northernmost region of Sweden in 2019–2022 (erythrocyte median 1.5 µg/kg, corresponding to about 0.6 µg/L in whole blood) [53]. In the present study, the median B-Hg concentration was somewhat higher (0.99 µg/L in both age groups), which is also higher than that in 4-year-old Greek children (median 0.73 µg/L) [54], 3–4-year-old Canadian children (median 0.19 µg/L) [55], and 1–5-year-old U.S. children (geometric mean 0.34 µg/L) [56]. Still, the exposure is lower than the U.S. health-based guidance value of 5.8 µg/L in blood [57]. Interestingly, canned tuna was associated with elevated B-Hg among children in both age groups, although it was not possible to disentangle the role of tuna from the consumption of other types of fish. While European regulations limit mercury levels in canned tuna products to 1 mg/kg (0.3 mg/kg for other fish), some products of Italian (0.04 to 1.8 mg/kg wet weight) and Spanish (0.031–1.176 mg/kg) origin have been shown to exceed this limit [58]. Unexpectedly, the children's B-Hg concentrations were also correlated with vegetable intake, but whether this was due to the close linkage between fish and vegetable intake (healthy diet) or the presence of inorganic mercury in vegetables is unknown. The dietary intake of inorganic mercury is usually very low, and when ingested, it is poorly absorbed in the gastrointestinal tract [59].

Among the youngest children, adherence to dietary patterns characterized by high intake of plant-based meat and milk alternatives, and nuts and seeds was associated with increased cadmium and manganese exposure. This was less obvious in 4-year-olds who had more varied diets [60]. The main building blocks of plant-based meat alternatives are reconstructed vegetable proteins from soy, pea, and other legumes, which

easily take up cadmium and manganese from soil [61]. Studies from Portugal and the U.S. have reported elevated cadmium concentrations in soy milk [62, 63]. Some plant-based meat alternatives contain an array of additives necessary for orosensory properties resembling natural meat [64]. Certain additives—for instance, carrageenans extracted from red seaweed—have been found to accumulate cadmium [65]. In the Swedish market basket survey in 2022 (all ages), the mean cadmium concentrations in meat and milk alternatives were 11 µg/kg and 1.9 µg/kg, respectively, while the corresponding values for traditional meat and meat products and lean dairy products were 1.3 µg/kg and 0.05 µg/kg [66]. Nuts and seeds are also known sources of cadmium [67], as the phytate present in them can bind divalent cations, including cadmium [68], thereby also potentially lowering bioavailability. In addition, the higher cadmium burden among children with a diet high in plant-based alternatives could be linked to avoidance of meat and an associated lower iron status, which, in turn, has been associated with increased gastrointestinal absorption of cadmium among Swedish adolescents [69]. Studies of Swedish pregnant women and adolescents demonstrate that cadmium exposure is mostly related to the consumption of plant-derived foods, including cereals and seeds [69, 70].

The highest U-F concentrations were generally found in children in Uppsala, which agrees with the elevated fluoride concentrations in public drinking water in the area [71]. Moreover, consuming well water was related to higher U-F in comparison with consuming public water, especially among 4-year-olds. Fluoride levels in groundwater are elevated in many parts of Sweden. In the southeast of Sweden, 24% of approximately 4800 private wells contained fluoride concentrations above the WHO's drinking water guideline of 1.5 mg/L [72]. In 4-year-olds, U-F increased with increasing adherence to a diet rich in fruits and berries, potatoes, as well as juice and plant-based milk alternatives. One can speculate that this may be due to the presence of fluoride in drinking water used to dilute juice concentrates. Moreover, we found that 4-year-olds with both parents born in Sweden had higher U-F than those with both parents born abroad, which may reflect different dietary habits and cultural attitudes regarding the use of fluoridated dental products [73]. Toothpaste is often swallowed by smaller children, leading to increased fluoride exposure, as toothpaste for children generally contains about 1000 µg/g of fluoride [74].

The four essential elements (copper, manganese, selenium, and zinc) studied are of importance for antioxidant defense. Sufficient selenium intake has been proposed to alleviate potential toxic effects of methylmercury [75]. Only selenium was clearly associated with specific dietary groups and patterns, including seafood, fruits and berries, and vegetables. Fish, especially marine fish, have been shown to be a good source of selenium [32]. Surprisingly, children with consumption of plant-based alternatives had similar B-Se as children with a highly diverse diet, especially among 4-year-olds, likely due to a higher consumption of seeds, nuts, and legumes, which are known to contribute to selenium intake [32, 76]. A recent Swedish study showed that plant-based alternatives did not meet the Nordic Nutrition Recommendations for selenium intake [77].

Plasma and serum selenium are the most common biomarkers for selenium status, and plasma concentrations below 60 µg/L, corresponding to a whole blood concentration of about 100 µg/L [78], seem to reflect deficiency based on glutathione peroxidase 3 activity [79]. The present children's median B-Se, more reflective of long-term intake [80], was 103 µg/L at both ages. Thus, around half of the children appear to have suboptimal selenium status, which agrees with our previous findings from the north of Sweden, and which may be attributed to the low selenium content in Swedish soils [76]. Selenium deficiency has been associated with poorer neurodevelopment and impaired growth and immune function [81].

A strength of the study is that recruitment was conducted nationally, and the children were recruited across different parts of Sweden. Further, we estimated individual exposure to toxic metals and the status of essential elements in children using well-established biomarkers. We used two different statistical approaches to assess dietary patterns, accounting for the overall dietary consumption, instead of putting all food groups into the same regression model, which may raise issues with collinearity. Application of both PCA and k-means clustering enables a comprehensive assessment of how dietary patterns in young children contribute to both toxic and essential elements in blood and/or urine. PCA offers a “food-group-centered perspective” by identifying underlying combinations of foods consumed together, resulting in dietary patterns that more or less all children adhere to at a certain age. Moreover, dividing the PCA component scores into tertiles allowed us to assess potential dose–response relationships between adherence to specific dietary dimensions and biomarker concentrations. K-means clustering provided a “participant-centered” perspective by identifying mutually exclusive subgroups of children with distinct dietary profiles (e.g., plant-based, high-diversity, and western-style diets), facilitating comparison of biomarker concentrations between the different dietary profiles. Interestingly, both statistical methods identified some similar dietary patterns as important contributors to children’s element concentrations in blood and/or urine, implying consistency of the observed associations. However, only the k-means clustering was able to identify the higher urinary cadmium and higher blood arsenic and blood selenium concentrations in the few 4-year-old children consuming a diet dominated by plant-based alternatives. Similarly, k-means clustering demonstrated higher B-Mn concentrations among 1.5-year-old children belonging to the small cluster with the highest intake of plant-based alternatives.

The main limitations of the present study include the cross-sectional design, which precludes the establishment of temporality and causal inferences, and the low participation rate among 1.5-year-olds due to challenges of obtaining urine samples, which hampered the statistical power and the generalizability of our findings. The web-based food diary (RiksmatenFlexDiet) only covered two non-consecutive days, including one weekday and one weekend day. Still, when combined with statistical methods for estimating habitual intake such as the Multiple Source Methods used herein, such assessments have demonstrated comparable reliability to several days of assessment in large-scale studies [82]. Secondly, our analytical framework mitigates the influence of episodic consumption, as the a posteriori dietary patterns represent combinations of multiple correlated food groups and are likely less sensitive to day-to-day variation in any single item. Nevertheless, diet is a complex exposure, inherently challenging to ascertain with complete accuracy. Therefore, we acknowledge that some degree of misclassification, especially when it comes to less frequently consumed foods, was unavoidable, which may have biased our associations towards null. Moreover, despite the documented validity of RiksmatenFlex [20] and its built-in reminders, recall and social desirability bias are unavoidable to some extent when estimating dietary intake. For some children, the time between dietary recall and biological sampling was rather long. However, as most of the biomarkers were measured in whole blood, with many elements mainly being present in the erythrocyte fraction, the half-lives are in the order of months [83]. Concentrations of arsenic and fluoride, on the other hand, are reflective of short-term exposure, although during daily intake via food and/or water, urinary concentrations usually reflect ongoing exposure rather well [24, 84]. While the regression models were controlled for relevant confounders, including energy intake, residual confounding cannot be ruled out entirely. For instance, we lacked detailed information on supplement use as well as potential soil or dust contamination. Finally, even

though multiple associations were explored in the present study, we did not adjust for multiple comparisons, as we adopted an exploratory, data-driven approach focusing instead on the magnitude, direction, and consistency of associations across complementary statistical methods.

In conclusion, biomarker concentrations of toxic metals in young Swedish children were generally low, although with wide variations. Selenium status seemed suboptimal in many children. Seafood consumption was associated with higher biomarker concentrations of arsenobetaine, methylmercury, and selenium, whereas dietary patterns high in consumption of plant-based meat and milk alternatives, nuts, and seeds were associated with higher cadmium concentrations. Furthermore, vegetable consumption appeared to be a source of low-level inorganic arsenic exposure, which has previously not been highlighted and assessed in detail. There is a need for further investigations regarding the metal contents of specific dietary items, particularly plant-based meat and milk alternatives as well as vegetables.

DATA AVAILABILITY

Data can be made available upon reasonable request.

REFERENCES

- Scutarasu E, Trinca L. Heavy Metals in Foods and Beverages: Global Situation, Health Risks and Reduction Methods. *Foods*. 2023;12:3340.
- FDA. Closer to Zero: Reducing Childhood Exposure to Contaminants from Foods. 2025. <https://www.fda.gov/food/environmental-contaminants-food/closer-zero-reducing-childhood-exposure-contaminants-foods>
- Feiler MO, Kulick ER, Sinclair K, Spiegel N, Habel S, Castello O. Toxic metals and pediatric clinical immune dysfunction: a systematic review of the epidemiological evidence. *Sci Total Environ*. 2024;927:172303. <https://doi.org/10.1016/j.scitotenv.2024.172303>.
- Grandjean P, Landrigan P. Developmental neurotoxicity of industrial chemicals. *Lancet*. 2006;368:2167–78. [https://doi.org/10.1016/S0140-6736\(06\)69665-7](https://doi.org/10.1016/S0140-6736(06)69665-7).
- Malin Igra A, Warnqvist A, Rahman SM, Ekström E-C, Rahman A, Vahter M, et al. Environmental metal exposure and growth to 10 years of age in a longitudinal mother–child cohort in rural Bangladesh. *Environ Int*. 2021;156:106738. <https://doi.org/10.1016/j.envint.2021.106738>.
- Suomi J, Tuominen P, Niinistö S, Virtanen SM, Savela K. Dietary heavy metal exposure of Finnish children of 3 to 6 years. *Food Addit Contam Part A*. 2018;35:1305–15. <https://doi.org/10.1080/19440049.2018.1480065>.
- Schrenk D, Bignami M, et al. EFSA Panel on Contaminants in the Food Chain (CONTAM). Update of the risk assessment of inorganic arsenic in food. *EFSA J*. 2024;22:e8488. <https://doi.org/10.2903/j.efsa.2024.8488>
- Kordas K, Cantoral A, Desai G, Halabicky O, Signes-Pastor AJ, Téllez-Rojo MM, et al. Dietary exposure to toxic elements and the health of young children: methodological considerations and data needs. *J Nutr*. 2022;152:2572–81. <https://doi.org/10.1093/jn/nxac185>.
- Boon PE, Pustjens AM, Te Biesebeek JD, Brust GMH, Castenmiller JJM. Dietary intake and risk assessment of elements for 1- and 2-year-old children in the Netherlands. *Food Chem Toxicol*. 2022;161:112810. <https://doi.org/10.1016/j.fct.2022.112810>.
- Junqué E, Tardón A, Fernández-Somoano A, Grimalt JO. Environmental and dietary determinants of metal exposure in four-year-old children from a cohort located in an industrial area (Asturias, Northern Spain). *Environ Res*. 2022;214:113862. <https://doi.org/10.1016/j.envres.2022.113862>.
- Roca M, Sánchez A, Pérez R, Pardo O, Yusá V. Biomonitoring of 20 elements in urine of children. Levels and predictors of exposure. *Chemosphere*. 2016;144:1698–705. <https://doi.org/10.1016/j.chemosphere.2015.10.008>.
- Sharma BM, Komprdová K, Lörinczová K, Kuta J, Příbylová P, Scheringer M, et al. Human biomonitoring of essential and toxic trace elements (heavy metals and metalloids) in urine of children, teenagers, and young adults from a Central European Cohort in the Czech Republic. *J Expo Sci Environ Epidemiol*. 2025;35:730–45. <https://doi.org/10.1038/s41370-024-00724-4>.
- Schulze MB, Martínez-González MA, Fung TT, Lichtenstein AH, Forouhi NG. Food-based dietary patterns and chronic disease prevention. *BMJ*. 2018;361:k2396. <https://doi.org/10.1136/bmj.k2396>.
- Notario-Barandiaran L, Irizar A, Begoña-Zubero M, Soler-Blasco R, Riutort-Mayol G, Fernández-Somoano A, et al. Association between Mediterranean diet and metalloid exposure in 4–5-year-old children living in Spain. *Environ Res*. 2023;233:116508.

15. Oncina-Cánovas A, Vioque J, Riutort-Mayol G, Soler-Blasco R, Irizar A, Barroeta Z, et al. Pro-vegetarian dietary patterns and essential and heavy metal exposure in children aged 4–5 years from the Infancia y Medio Ambiente cohort (INMA). *Int J Hyg Environ Health*. 2024;257:114344. <https://doi.org/10.1016/j.ijheh.2024.114344>.
16. Paulsen MM, Haug LS, Sakhi AK, Thomsen C, Brantsæter AL. Associations between dietary patterns and environmental contaminants in children from the Norwegian Environmental Biobank: a cross-sectional analysis. *Environ Res*. 2025;280:121871. <https://doi.org/10.1016/j.envres.2025.121871>.
17. Jan AT, Azam M, Siddiqui K, Ali A, Choi I, Haq QMR. Heavy metals and human health: mechanistic insight into toxicity and counter-defense system of antioxidants. *Int J Mol Sci*. 2015;16:29592–630. <https://doi.org/10.3390/ijms161226183>.
18. Bjermo H, Patterson E, Petrelius Sipinen J, Lignell S, Karin S, Larsson E, et al. Design, methods, and participation in Riksmatsen young children—a Swedish national dietary survey. *Curr Dev Nutr*. 2024;8:102150. <https://doi.org/10.1016/j.cdnut.2024.102150>.
19. European Food Safety Authority. Guidance on the EU Menu methodology. EFSA J. 2014;12:3944 <https://doi.org/10.2903/j.efsa.2014.3944>.
20. Lindroos AK, Sipinen JP, Axelsson C, Nyberg G, Landberg R, Leanderson P, et al. Use of a web-based dietary assessment tool (RiksmatenFlex) in Swedish adolescents: comparison and validation study. *J Med Internet Res*. 2019;21:e12572 <https://doi.org/10.2196/12572>.
21. Harttig U, Haubrock J, Knüppel S, Boeing H. The MSM program: a web-based statistics package for estimating usual dietary intake using the multiple source method. *Eur J Clin Nutr*. 2011;65:S87–91. <https://doi.org/10.1038/ejcn.2011.92>.
22. Babio N, de Las Heras-Delgado S, De Miguel-Etayo P, Pastor-Villaescusa B, Leis R, Garcidueñas-Fimbres TE, et al. Reproducibility and relative validity of a semi-quantitative food and beverage frequency questionnaire for Spanish children aged 3 to 11 years: the COME-Kids F&B-FQ. *Eur J Pediatr*. 2023;182:5577–89. <https://doi.org/10.1007/s00431-023-05220-9>.
23. Lioret S, Betoko A, Forhan A, Charles M-A, Heude B, de Lauzon-Guillain B. Dietary patterns track from infancy to preschool age: cross-sectional and longitudinal perspectives. *J Nutr*. 2015;145:775–82. <https://doi.org/10.3945/jn.114.201988>.
24. Martínez-Morata I, Sobel M, Tellez-Plaza M, Navas-Acien A, Howe CG, Sanchez TR. A state-of-the-science review on metal biomarkers. *Curr Environ Health Rpt*. 2023;10:215–49. <https://doi.org/10.1007/s40572-023-00402-x>.
25. Skróder H, Kippler M, Nermell B, Tofail F, Levi M, Rahman SM, et al. Major limitations in using element concentrations in hair as biomarkers of exposure to toxic and essential trace elements in children. *Environ Health Perspect*. 2017;125:067021. <https://doi.org/10.1289/EHP1239>.
26. Pfeiffer CM, Schleicher RL, Caldwell KL Biochemical Indices. In: Caballero B, ed. *Encyclopedia of human nutrition*. Amsterdam: Academic Press, Elsevier, 2013.
27. Schultze B, Lind PM, Larsson A, Lind L. Whole blood and serum concentrations of metals in a Swedish population-based sample. *Scand J Clin Lab Invest*. 2014;74:143–8. <https://doi.org/10.3109/00365513.2013.864785>.
28. Akerstrom M, Barregard L, Lundh T, Sällsten G. The relationship between cadmium in kidney and cadmium in urine and blood in an environmentally exposed population. *Toxicol Appl Pharmacol*. 2013;268:286–93. <https://doi.org/10.1016/j.taap.2013.02.009>.
29. Aldana SI, Colicino E, Cantoral Preciado A, Tolentino M, Baccarelli AA, Wright RO, et al. Longitudinal associations between early-life fluoride exposures and cardiometabolic outcomes in school-aged children. *Environ Int*. 2024;183:108375. <https://doi.org/10.1016/j.envint.2023.108375>.
30. Simonsen LO, Harbak H, Bennekou P. Cobalt metabolism and toxicology—a brief update. *Sci Total Environ*. 2012;432:210–5. <https://doi.org/10.1016/j.scitotenv.2012.06.009>.
31. Lu Y, Kippler M, Harari F, Grandér M, Palm B, Nordqvist H, et al. Alkali dilution of blood samples for high-throughput ICP-MS analysis—comparison with acid digestion. *Clin Biochem*. 2015;48:140–7. <https://doi.org/10.1016/j.clinbiochem.2014.12.003>.
32. Stråvik M, Gustin K, Barman M, Levi M, Sandin A, Wold AE, et al. Biomarkers of seafood intake during pregnancy – Pollutants versus fatty acids and micro-nutrients. *Environ Res*. 2023;225:115576. <https://doi.org/10.1016/j.envres.2023.115576>.
33. Vahter M. Mechanisms of arsenic biotransformation. *Toxicology*. 2002;181–182:211–7. [https://doi.org/10.1016/S0300-483X\(02\)00285-8](https://doi.org/10.1016/S0300-483X(02)00285-8).
34. Kampouri M, Gustin K, Stråvik M, Barman M, Levi M, Daraki V, et al. Association of maternal urinary fluoride concentrations during pregnancy with size at birth and the potential mediation effect by maternal thyroid hormones: the Swedish NICE birth cohort. *Environ Res*. 2022;214:114129. <https://doi.org/10.1016/j.envres.2022.114129>.
35. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. *Pediatr Obes*. 2012;7:284–94. <https://doi.org/10.1111/j.2047-6310.2012.00064.x>.
36. Zhao J, Li Z, Gao Q, Zhao H, Chen S, Huang L, et al. A review of statistical methods for dietary pattern analysis. *Nutr J*. 2021;20:37. <https://doi.org/10.1186/s12937-021-00692-7>.
37. Devlin UM, McNulty BA, Nugent AP, Gibney MJ. The use of cluster analysis to derive dietary patterns: methodological considerations, reproducibility, validity and the effect of energy mis-reporting. *Proc Nutr Soc*. 2012;71:599–609. <https://doi.org/10.1017/S0029665112000729>.
38. Fransen HP, May AM, Stricker MD, Boer JMA, Hennig C, Rosseel Y, et al. A posteriori dietary patterns: how many patterns to retain? *J Nutr*. 2014;144:1274–82. <https://doi.org/10.3945/jn.113.188680>.
39. Edefonti V, De Vito R, Salvatori A, Bravi F, Patel L, Dalmartello M, et al. Reproducibility of a posteriori dietary patterns across time and studies: a scoping review. *Adv Nutr*. 2020;11:1255–81. <https://doi.org/10.1093/advances/nmaa032>.
40. Jones MR, Tellez-Plaza M, Vaidya D, Grau M, Francesconi KA, Goessler W, et al. Estimation of inorganic arsenic exposure in populations with frequent seafood intake: evidence from MESA and NHANES. *Am J Epidemiol*. 2016;184:590–602. <https://doi.org/10.1093/aje/kww097>.
41. Molin M, Ulven SM, Meltzer HM, Alexander J. Arsenic in the human food chain, biotransformation and toxicology—review focusing on seafood arsenic. *J Trace Elem Med Biol*. 2015;31:249–59. <https://doi.org/10.1016/j.jtemb.2015.01.010>.
42. Næss S, Aakre I, Lundebye A-K, Ørnsrud R, Kjelleveid M, Markhus MW, et al. Mercury, lead, arsenic, and cadmium in Norwegian seafood products and consumer exposure. *Food Addit Contam Part B*. 2020;13:99–106. <https://doi.org/10.1080/19393210.2020.1735533>.
43. García-Villarino M, Fernández-Iglesias R, García AV, Villa-Fernández E, Fernández-Arce L, Riaño-Galán I, et al. Exposure to a mixture of arsenic species and growth indicators in 6–12-year-old children from the cycles 2007–2020 NHANES. *Environ Int*. 2025;197:109347. <https://doi.org/10.1016/j.envint.2025.109347>.
44. Hackethal C, Kopp JF, Sarvan I, Schwerdtle T, Lindtner O. Total arsenic and water-soluble arsenic species in foods of the first German total diet study (BfR MEAL Study). *Food Chem*. 2021;346:128913. <https://doi.org/10.1016/j.foodchem.2020.128913>.
45. Signes-Pastor AJ, Vioque J, Navarrete-Muñoz EM, Carey M, García De La Hera M, Sunyer J, et al. Concentrations of urinary arsenic species in relation to rice and seafood consumption among children living in Spain. *Environ Res*. 2017;159:69–75. <https://doi.org/10.1016/j.envres.2017.07.046>.
46. Kollander B, Sand S, Almerud P, Halldin Ankarberg E, Concha G, Barregård L, et al. Inorganic arsenic in food products on the Swedish market and a risk-based intake assessment. *Sci Total Environ*. 2019;672:525–35. <https://doi.org/10.1016/j.scitotenv.2019.03.289>.
47. Gustin K, Trask M, Bjermo H, Levi M, Lignell S, Vahter M, et al. Estimating daily intakes of toxic metals and essential elements from infant formula, gruel, porridge and ready-to-eat baby food. *Food Chem*. 2026;509:148337. <https://doi.org/10.1016/j.foodchem.2026.148337>.
48. Halldin Ankarberg E, Foghelberg P, Gustafsson K, Nordenfors H, Bjerselius R. Inorganic arsenic in rice and rice products on the Swedish market 2015. Uppsala: Livsmedelsverket; 2016.
49. Signes-Pastor AJ, Cottingham KL, Carey M, Sayarath V, Palys T, Meharg AA, et al. Infants' dietary arsenic exposure during transition to solid food. *Sci Rep*. 2018;8:7114. <https://doi.org/10.1038/s41598-018-25372-1>.
50. Berglund M, Lind B, Björnberg KA, Palm B, Einarsson O, Vahter M. Inter-individual variations of human mercury exposure biomarkers: a cross-sectional assessment. *Environ Health*. 2005;4:20. <https://doi.org/10.1186/1476-069X-4-20>.
51. Larsen MM. Hjermann DØ Status and Trend for Heavy Metals (Mercury, Cadmium and Lead) in Fish, Shellfish and Sediment. London: OSPAR Commission; 2022.
52. Stajnik A, Lundh T, Assarson E, Krook EA, Broberg K. Lead, cadmium, and mercury blood levels in schoolchildren in southern Sweden: time trends over the last decades. *Chemosphere*. 2024;346:140562. <https://doi.org/10.1016/j.chemosphere.2023.140562>.
53. Vahter M, Mossegård KG, Levi M, Kippler M. Exponering för toxiska metaller och andra spårämnen vid 4 års ålder—data från NICE-studien i Norrbotten. Stockholm: Karolinska Institutet & Naturvårdsverket; 2024.
54. Yim G, Margetaki K, Romano ME, Kippler M, Vafeiadi M, Roumeliotaki T, et al. Metal mixture exposures and serum lipid levels in childhood: the Rhea mother-child cohort in Greece. *J Expo Sci Environ Epidemiol*. 2024;34:688–98. <https://doi.org/10.1038/s41370-024-00674-x>.
55. Packull-McCormick S, Ashley-Martin J, Singh K, Fisher M, Arbuckle TE, Lanphear B, et al. Prenatal and concurrent blood mercury concentrations and associations with IQ in Canadian preschool children. *Environ Res*. 2023;233:116463. <https://doi.org/10.1016/j.envres.2023.116463>.
56. Schober SE, Sinks TH, Jones RL, Michael Bolger P, McDowell M, Osterloh J, et al. Blood mercury levels in US children and women of childbearing age, 1999–2000. *JAMA*. 2003;289:1667 <https://doi.org/10.1001/jama.289.13.1667>.
57. Nielsen SJ, Aoki Y, Kit BK, Ogden CL. More than half of US youth consume seafood, and most have blood mercury concentrations below the EPA reference level, 2009–2012. *J Nutr*. 2015;145:322–7. <https://doi.org/10.3945/jn.114.203786>.

58. García MÁ, Núñez R, Alonso J, Julia Melgar M. Total mercury in fresh and processed tuna marketed in Galicia (NW Spain) in relation to dietary exposure. *Environ Sci Pollut Res*. 2016;23:24960–9. <https://doi.org/10.1007/s11356-016-7634-9>.
59. Björnberg KA, Vahter M, Petersson-Gråwé K, Glynn A, Cnattingius S, Darnerud PO, et al. Methyl mercury and inorganic mercury in Swedish pregnant women and in cord blood: influence of fish consumption. *Environ Health Perspect*. 2003;111:637–41. <https://doi.org/10.1289/ehp.111-1241457>.
60. Moraeus L, Bjermo H, Petrelius Sipinen JP, Patterson E, Larsson E, Stenberg K, et al. Riksmaten småbarn 2021–24 – Så äter småbarn i Sverige. Uppsala: Livsmedelsverket; 2024.
61. Sha L, Xiong YL. Plant protein-based alternatives to reconstructed meat: Science, technology, and challenges. *Trends Food Sci Technol*. 2020;102:51–61. <https://doi.org/10.1016/j.tifs.2020.05.022>.
62. Andrade VL, Ribeiro I, dos Santos APM, Aschner M, Mateus ML. Metals in cow's milk and soy beverages: is there a concern? *Toxics*. 2023;11:1013 <https://doi.org/10.3390/toxics11121013>.
63. Redan BW, Zuklic J, Hryshko J, Boyer M, Wan J, Sandhu A, et al. Analysis of eight types of plant-based milk alternatives from the United States market for target minerals and trace elements. *J Food Compos Anal*. 2023;122:105457. <https://doi.org/10.1016/j.jfca.2023.105457>.
64. Bogueva D, McClements DJ. Safety and nutritional risks associated with plant-based meat alternatives. *Sustainability*. 2023;15. <https://doi.org/10.3390/su151914336>.
65. Besada V, Andrade JM, Schultze F, González JJ. Heavy metals in edible seaweeds commercialised for human consumption. *J Mar Syst*. 2009;75:305–13. <https://doi.org/10.1016/j.jmarsys.2008.10.010>.
66. Bjermo H, Edgar D, Lignell S, Kollander B. Exposure to silver, aluminum, arsenic, cadmium, mercury, nickel, and lead from food in Swedish children, adolescents, and adults. *Food Chem Toxicol*. 2025;206:115728. <https://doi.org/10.1016/j.fct.2025.115728>.
67. Bielecka J, Puścion-Jakubik A, Markiewicz-Żukowska R, Soroczyńska J, Nowakowski P, Grabia M, et al. Assessment of the safe consumption of nuts in terms of the content of toxic elements with chemometric analysis. *Nutrients*. 2021;13:3606 <https://doi.org/10.3390/nu13103606>.
68. Knutsen HK, Amlund H, Brantsæter AL, Engeset D, Fæste CK, Holene E, et al. Risk assessment of dietary cadmium exposure in the Norwegian population. *Eur J Nutr Food Saf*. 2018;8:157–61. <https://doi.org/10.9734/EJNFS/2018/42537>.
69. Almerud P, Zamaratskaia G, Lindroos AK, Bjermo H, Andersson EM, Lundh T, et al. Cadmium, total mercury, and lead in blood and associations with diet, socio-demographic factors, and smoking in Swedish adolescents. *Environ Res*. 2021;197:110991. <https://doi.org/10.1016/j.envres.2021.110991>.
70. Gustin K, Barman M, Stråvik M, Levi M, Englund-Ögge L, Murray F, et al. Low-level maternal exposure to cadmium, lead, and mercury and birth outcomes in a Swedish prospective birth cohort. *Environ Pollut*. 2020;265:114986. <https://doi.org/10.1016/j.envpol.2020.114986>.
71. Helte E, Donat Vargas C, Kippler M, Wolk A, Michaëlsson K, Åkesson A. Fluoride in drinking water, diet, and urine in relation to bone mineral density and fracture incidence in postmenopausal women. *Environ Health Perspect*. 2021;129:47005 <https://doi.org/10.1289/EHP7404>.
72. Augustsson A, Berger T. Assessing the risk of an excess fluoride intake among Swedish children in households with private wells—expanding static single-source methods to a probabilistic multi-exposure-pathway approach. *Environ Int*. 2014;68:192–9. <https://doi.org/10.1016/j.envint.2014.03.014>.
73. Östberg A-L, Skeie MS, Skaare AB, Espelid I. Caries increment in young children in Skaraborg, Sweden: associations with parental sociodemography, health habits, and attitudes. *Int J Paediatr Dent*. 2017;27:47–55. <https://doi.org/10.1111/tpd.12225>.
74. Zohoori FV, Buzalaf MAR, Cardoso CAB, Olympio KPK, Levy FM, Grizzo LT, et al. Total fluoride intake and excretion in children up to 4 years of age living in fluoridated and non-fluoridated areas. *Eur J Oral Sci*. 2013;121:457–64. <https://doi.org/10.1111/eos.12070>.
75. Barone G, Storelli A, Meleleo D, Dambrosio A, Garofalo R, Busco A, et al. Levels of mercury, methylmercury, and selenium in fish: insights into children's food safety. *Toxics*. 2021;9. <https://doi.org/10.3390/toxics9020039>.
76. Stråvik M, Gustin K, Barman M, Skråder H, Sandin A, Wold AE, et al. Infant iodine and selenium status in relation to maternal status and diet during pregnancy and lactation. *Front Nutr*. 2021;8. <https://doi.org/10.3389/fnut.2021.733602>.
77. Bunge AC, Mazac R, Clark M, Wood A, Gordon L. Sustainability benefits of transitioning from current diets to plant-based alternatives or whole-food diets in Sweden. *Nat Commun*. 2024;15:951. <https://doi.org/10.1038/s41467-024-45328-6>.
78. Combs GF. Selenium in global food systems. *Br J Nutr*. 2001;85:517–47. <https://doi.org/10.1079/bjn2000280>.
79. Fairweather-Tait SJ, Bao Y, Broadley MR, Collings R, Ford D, Hesketh JE, et al. Selenium in human health and disease. *Antioxid Redox Signal*. 2011;14:1337–83. <https://doi.org/10.1089/ars.2010.3275>.
80. Hays SM, Macey K, Nong A, Aylward LL. Biomonitoring equivalents for selenium. *Regul Toxicol Pharmacol*. 2014;70:333–9. <https://doi.org/10.1016/j.yrtph.2014.07.017>.
81. Batyrova G, Taskozhina G, Umarova G, Umarov Y, Morenko M, Iriskulov B, et al. Unveiling the role of selenium in child development: impacts on growth, neurodevelopment and immunity. *J Clin Med*. 2025;14:1274 <https://doi.org/10.3390/jcm14041274>.
82. Singh R, Verest MTE, Salathé M. Minimum days estimation for reliable dietary intake information: findings from a digital cohort. *Eur J Clin Nutr*. 2025;79:1007–17. <https://doi.org/10.1038/s41430-025-01644-8>.
83. Nève J. Human selenium supplementation as assessed by changes in blood selenium concentration and glutathione peroxidase activity. *J Trace Elem Med Biol*. 1995;9:65–73. [https://doi.org/10.1016/S0946-672X\(11\)80013-1](https://doi.org/10.1016/S0946-672X(11)80013-1).
84. Buzalaf MAR, Rodrigues MHC, Pessan JP, Leite AL, Arana A, Villena RS, et al. Biomarkers of fluoride in children exposed to different sources of systemic fluoride. *J Dent Res*. 2011;90:215–9. <https://doi.org/10.1177/0022034510385937>.

ACKNOWLEDGEMENTS

The regional Environmental and Occupational Medicine clinics in Lund, Gothenburg, Linköping, Örebro, Stockholm, and Umeå are acknowledged for their help with blood and urine sampling. We are also grateful to the families who participated in and showed dedication to the study.

AUTHOR CONTRIBUTIONS

MRI statistical analysis, interpretation and drafted the manuscript; MT statistical analysis, interpretation and drafted the manuscript; MKA statistical analysis, visualization, drafted and review manuscript; TS fluoride analysis and drafted related method, review and editing manuscript; KG visualization and review and editing manuscript; HB conceptualization, study design, data cleaning, reviewing and editing manuscript; PA data collection and reviewing and editing manuscript; FH data collection and reviewing and editing of manuscript; MV: interpretation and reviewing and editing manuscript; SL conceptualization, methodology, data cleaning, funding and reviewing and editing manuscript; MKI conceptualization, methodology, funding, project administration, supervision, and writing and editing manuscript.

FUNDING

The Riksmaten Young Children study was conducted by the Swedish Food Agency with funding from the Swedish Environmental Protection Agency (agreement number 215-21-005). Funding for the present work has also been received from the Swedish Research Council Formas (project no. 2022-00808) and Karolinska Institutet. Open access funding provided by Karolinska Institute.

COMPETING INTERESTS

The authors declare no competing interests.

ETHICAL APPROVAL

All methods were performed in accordance with the relevant guidelines and regulations. Ethical approval for the Riksmaten Young Children study, including the present analysis, has been obtained from the Swedish Ethical Review Authority (2020-05293). Informed consent was obtained from all parents of participating children.

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at <https://doi.org/10.1038/s41370-026-00973-5>.

Correspondence and requests for materials should be addressed to Maria Kippler.

Reprints and permission information is available at <http://www.nature.com/reprints>

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

© The Author(s) 2026