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Lead exposure in an Italian population: Food content, dietary intake and risk assessment

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Title: Lead exposure in an Italian population: food content, dietary intake and risk assessment

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Abstract

Background and aim: Lead is a highly toxic heavy metal released into the environment after natural and anthropogenic activities. Excluding populations in occupations where there is possible lead contamination, food is the major source of human exposure. In this study, we determined lead contamination in food and beverages consumed in a Northern Italy community and performed a health risk assessment. Methods: We collected a total of 908 food samples and measured lead levels using inductively coupled plasma mass spectrometry. Using a validated food frequency questionnaire, we assessed the dietary habits and estimated daily lead dietary intakes in a sample of 719 adult individuals. We performed risk assessment using a benchmark dose and margin of exposure approach, based on exposure levels for both adverse effect of systolic blood pressure and chronic kidney disease. Results: Foods with the highest lead levels include non-chocolate confectionery (48.7 µg/kg), leafy (39.0 µg/kg) and other vegetables (42.2 µg/kg), and crustaceans and molluscs (39.0 µg/kg). The estimated mean lead intake was 0.155 µg/kg bw-day in all subjects, with little lower intakes in men (0.151 µg/kg bw-day) compared to women (0.157 µg/kg bw-day). Top food contributors were vegetables, cereals, and beverages, particularly wine. In relation to risk assessment, the estimated dietary intake was lower than levels associated with cardiovascular risk and nephrotoxicity. Conclusions: Our study provides an updated assessment of lead food contamination and dietary exposure in a Northern Italian community. The margin of exposure risk assessment approach suggests that risk of detrimental effects due to dietary lead intake is low in the investigated population. Nonetheless, these exposure levels for adverse effects are not reference health standards, and no safety threshold value can be established for lead. As a consequence, other and more subtle adverse effects may still occur in vulnerable and occupationally exposed individuals, particularly in relation to the nervous system.

Keywords: lead; food contamination; dietary intake: margin of exposure; risk assessment

1. Introduction

Lead is a toxic heavy metal that occurs in the environment from both natural and anthropogenic sources (EEA, 2019; Jarvis et al., 2018). Monitoring data show that from the mid-1970s onwards lead concentration in the atmosphere decreased as a result of the phasing out of leaded gasoline, consequently reducing human exposure in non-occupationally exposed individuals (EEA, 2019; UNEP, 2019). However, lead pollution and contamination still pose a serious global threat to public health, and is included in the top ten chemicals due to its poisonous and deleterious effects, particularly for children (O'Connor et al., 2018; WHO, 2010). Sources and routes of exposure are inhalation or ingestion of lead in food, water, dust, and lead particles released during burning of lead contaminated materials (WHO, 2010).

Food intake is the primary route of chronic exposure in non-occupationally exposed individuals (EFSA, 2010). In plants, the uptake of lead from contaminated soils is generally low, and any heavy metals absorbed through the root systems generally remain within root tissue (Finster et al., 2004; Khan et al., 2015; Peralta-Videa et al., 2009; Zaprjanova et al., 2010) with variable translocation to the edible parts (Cristaldi et al., 2020). Lead particles that have been deposited on plant surfaces are difficult to remove, even after washing, which explains the higher levels generally found in leafy vegetables, herbs and fruits (ATSDR, 2019; Finster et al., 2004; Khan et al., 2015; Li et al., 2006). Lead uptake by animals may occur through inhalation of ambient air or ingestion of contaminated plants (ATSDR, 2019). However, lead is not biomagnified into the food chain, mainly because its distribution and metabolism in animals is associated with calcium metabolism (WHO, 1989). Lead is stored mainly in bone, thus decreasing the risk of transmission through the food chain; other tissues and organs with high levels include blood, kidney, and liver (Lee et al., 2019). In aquatic organisms, higher lead levels are found in algae and benthic organisms such as bivalves, or crabs, whilst lower levels are found in upper trophic levels organisms, such as piscivorous fish (Lee et al., 2019; Rahmani et al., 2018). Lead contamination in drinking water is due to human activities causing environmental contamination in soil or directly in underground waters, e.g. due to atmospheric deposition (ATSDR, 2019) or the internal corrosion of pipes used for water distribution systems, especially in plumbing of older properties (ATSDR, 2017).

National and International agencies have attempted to provide health-based guidelines for tolerable dietary exposure to lead (EFSA, 2012; WHO, 2016). However, there is no level of exposure to lead that is known to be without harmful effects (EFSA, 2012; WHO, 2010). In this study, we assessed the dietary intake of lead in an Italian community located in the Emilia-Romagna region in the North of the country, taking into account the lead levels in foods and the dietary habits characterizing this community.

2. Materials and Methods

2.1 Food collection

Food samples were obtained from marketplaces in the study area, namely grocery stores and markets, in two Northern Italian provinces of Emilia-Romagna region (Modena and Reggio Emilia). Between October 2016 and February 2017 we purchased the most frequently consumed foods in a typical Italian diet, as previously described (Filippini et al., 2019b; Filippini et al., 2019c). The relevant food items were selected from those characterizing the diet of a Northern Italian population identified in previous population-based studies addressing the dietary habits of this community from the Emilia-Romagna region (Bottecchi et al., 2012).

2.2. Food analysis

To determine the lead content in collected food samples, we avoided metal cross-contamination by using plastic food containers (i.e. plastic tubes or jars) as well as plastic cutlery or stainless steel knives during the handling and collection of food samples. We homogenised the samples using a food blender equipped with a stainless steel blade and 0.5 g portions (wet weight) were aliquoted into quartz containers previously washed with MilliQ water (MilliQPlus, Millipore, MA, USA) and HNO_3. Samples were digested with 10 ml solution (5 ml HNO_3 + 5 ml H_2O) in a microwave system (Discover SP-D, CEM Corporation, NC, USA), then stored in plastic tubes and diluted to 50 ml with deionised water before analysis. We measured the lead content using an inductively coupled plasma-mass spectrometer (Agilent 7500ce, Agilent Technologies, CA, USA). All analyses were performed in duplicate, implementing quality controls as previously described (Filippini et al., 2018a; Filippini et al., 2018b). The limit of quantification was 0.012 µg/kg, and the corresponding limit of detection (LOD) of 0.003 µg/kg.

2.3 Study population and assessment of dietary habits

We identified 2,825 potential subjects from the population database of the Emilia-Romagna Region residents, using the National Health Service directories, namely from the provinces of Bologna, Ferrara, Modena, Parma and Reggio Emilia. A total of 747 (26.4%) suitable subjects were selected among all residents in the study provinces to participate. Written informed consent was obtained and study material returned for assessment of individual characteristics and dietary intakes. In subjects who agreed to participate, we evaluated habitual dietary habits (Filippini et al., 2019a; Malagoli et al., 2015). In order to assess dietary patterns, we used the food frequency questionnaires (FFQ) implemented within the 'European Prospective Investigation into Cancer and Nutrition' project. The EPIC FFQ is a validated semi-quantitative FFQ specifically developed for the Central-Northern Italy population (Pala et al., 2003; Pasanisi et al., 2002). It was designed to estimate frequency and amount of consumption of 188 food items over the previous year, also providing photos of serving sizes to aid more accurate completion by participants. We also undertook quality control of data reliability by excluding incomplete FFQs or reporting extreme and implausible values of energy intake, namely lower than the 0.5th percentile or higher than the 99.5th percentile, based on the ratio between total energy intake and calculated basal metabolic rate. Out of those who agreed to participate, we excluded twenty-eight subjects after the quality control exercise, leaving 719 adult participants (319 men and 400 women) for subsequent analysis.

2.4 Estimation of dietary intake and risk assessment

We combined data from the determination of lead levels in foods and dietary habits assessed using the FFQ to compute daily dietary intake (DDI) of lead using the following equation (Filippini et al., 2018a):

Eq. (1) $$DDI\left(\frac{\mu g}{kg\ bw/day}\right) = \sum \frac{lead\ level\ in\ food\left(\frac{\mu g}{kg}\right) \times\ food\ intake\left(\frac{g}{day}\right)}{1000\ \times\ bw\ (kg)}$$

In detail, we multiplied the measured lead content of foods (μg/kg) with the intake as estimated by the FFQ (g/day), and we divided this by body weight (bw) to obtain the daily dietary intake by weight of study participants (in μg/kg of bw-day).

2.5 Risk assessment

Previous reference health standards for lead were withdrawn as they were considered to be no longer appropriate and no health-based guidance value for lead has been identified so far (EFSA, 2010, 2012; FSANZ, 2019; US-EPA; WHO, 2010). Hence, we used the margin of exposure methods (MOE) in order to assess the health risks of dietary lead exposure (Aylward et al., 2008; EFSA, 2005; FSANZ, 2019; Lachenmeier et al., 2011; Yousefi et al., 2018). According to this approach, we calculated the MOE as the ratio of the observable effect level of the dose-response curve to the critical effect (measured using the lower bound of the benchmark dose of extra risk-BMDL) and the exposure level of the population using the following equation (FSANZ, 2019; Yousefi et al., 2018):

Eq. (2) $$MOE = \frac{BMDL}{DDI}$$

For MOE estimation, we considered the dietary exposure of 80 µg/day, corresponding to approximately 1.2 µg/kg bw-day assuming a body weight of 60 kg. This threshold corresponds to the lower bound of the benchmark dose of an extra risk of 1% ($BMDL_{01}$) which has been associated with an increase in systolic blood pressure of 1 mmHg in the adult population suggested by the Joint FAO/WHO Expert Committee on Food Additive evaluation (JECFA, 2011). We additionally estimated the MOE associated with nephrotoxic effects using the lower bound of the benchmark dose of an extra risk of 10% ($BMDL_{10}$) of 0.63 µg/kg bw-day based on the EFSA evaluations (EFSA, 2010, 2012). We performed a sensitivity analysis by adding the contribution of water to the food dietary intake; we took 1L as the average daily consumption in Italian population (Mistura et al., 2016). Thus, we assumed a lead content of 10 µg/L, the European Union standard, resulting in an additional intake of 10 µg/day per person. Finally, we performed a sensitivity analysis considering lower thresholds of dietary exposure for adverse effects, namely 1.14 µg/kg bw-day for effects on systolic blood pressure, and 0.55 µg/kg bw-day for nephrotoxic effects assuming a higher average body weight of 70 kg per person. These thresholds for adverse effects are not reference health standards but approximate estimates of the level at which the risk of an adverse effect is considered to be low. Hence, with an exposure equal or lower than these levels, the risk might be considered to be acceptably low (Aylward et al., 2008; FSANZ, 2019; Lachenmeier et al., 2011).

3. Results

We measured lead contamination in a total of 908 samples. Distribution of lead levels according to food categories are reported in Table 1. Foods with the highest percentage of samples below the LOD were eggs (44%) and nuts and seeds (27%), followed by crackers and crispbread (19%) and soft drinks (14%). The highest mean values were found in non-chocolate confectionery

(48.7 µg/kg), other vegetables (e.g. eggplant, zucchini, etc. – 42.2 µg/kg), leafy vegetables (39.0 µg/kg) and crustaceans and molluscs (39.0 µg/kg). The highest median values were found in mushrooms (20.2 µg/kg), chocolate-based sweets (19.7 µg/kg), leafy vegetables (14.2 µg/kg) and dry fruit (14.5 µg/kg). The highest values for maximum contamination levels (95 percentile) were found in not-chocolate confectionery (307.0 µg/kg), leafy vegetables (160.1 µg/kg), red meat (121.2 µg/kg) and crustaceans/molluscs (120.9 µg/kg).

In relation to dietary habits, none of the participants in our study population (Emilia-Romagna region) reported 'special' dietary requirements or habits (e.g. weight control diet, low salt diet, or vegetarian/vegan diet) during the survey. The median energy intake was 1906 kcal/day (interquartile range-IQR: 1538-2364 kcal/day) in all participants, 2024 kcal/day (IQR: 1649-2462 kcal/day) in men and 1800 kcal/day (IQR: 1455-2296 kcal/day) in women, respectively.

Details of dietary intakes are reported in Supplemental Table S1. In general, comparable intakes between sexes were reported for the main food categories. However, men had a higher consumption of cereal products, meat products, and alcoholic beverages (mainly wine). Conversely, women had higher intakes of milk and dairy products (in particular yogurt), vegetables, coffee and tea and sweets.

Table 2 shows the mean estimate of daily lead dietary intakes. Mean and median values were 0.155 µg/kg bw-day and 0.148 µg/kg bw-day, respectively. Top contributors, accounting for more than half of lead intake, were vegetables (27.7%: mainly leafy and other vegetables), cereals products (19.4%: all except rice), and beverages (18.7%, particularly wine) (Figure 1). Substantially comparable results were found in sex-stratified analysis (Tables 3-4) with mean and median lead intake of 0.151 µg/kg bw-day and 0.146 µg/kg bw-day in men, and 0.157 µg/kg bw-day and 0.148 µg/kg bw-day, respectively in women. For individual food categories, in men, vegetables had a lower and beverages a higher contribution, whilst the findings in women were the opposite.

The risk assessment using the MOE approach is reported in Table 5. MOE values for both adverse effect of systolic blood pressure (SBP) and nephrotoxic effects (NE) were above 1, either using the mean (7.7 for SBP and 4.1 for NE), median (8.1 for SBP and 4.3 for NE), or the highest (4.4 for SBP and 2.3 for NE) estimation of dietary lead intake. Sensitivity analysis with the addition of water contribution generally showed lower estimates within the MOE risk assessment for both SBP and NE effects, although all values are still above 1 (Table S2). Finally, sensitivity analysis assuming lower thresholds of dietary intake for adverse effects showed comparable results (Table S3-S4).

4. Discussion

In this study, we estimated the dietary intake of lead in a Northern Italy community through the assessment of its content in food and beverages that characterize habitual dietary habits. The most important sources of intake were vegetables, cereal products and beverages. Our results are consistent with previous findings indicating that lead contamination is generally higher in foods of plant origin, especially leafy vegetables and herbs, partly due to absorption by the growing plant from contaminated soil but mostly through atmospheric deposition on edible parts (Finster et al., 2004; Khan et al., 2015). Similarly, the relatively high contribution of beverages compared to other foods may also be related to both environmental contamination of soil and subsequently water, and also to lead deposition from particulate matter, especially on grapes used for wine (ATSDR, 2019).

In the investigated study population, lead intake fell within the range of values reported by EFSA for European populations (EFSA, 2012), and it was substantially consistent with values computed in studies carried out in different Western populations (Arnich et al., 2012; FSANZ, 2019; Health Canada, 2020; Leblanc et al., 2005; Marin et al., 2017; Nasreddine et al., 2006). However, some studies have yielded higher values (Aung et al., 2006; Bocio et al., 2005; Brussaard et al., 1996; Cuadrado et al., 1995; Leblanc et al., 2000; Llobet et al., 2003; Marti-Cid et al., 2008; Marzec et al., 2004; Munoz et al., 2005; Rubio et al., 2005; Turconi et al., 2009; Ysart et al., 1999; Ysart et al., 2000), whereas lower values are reported in a few investigations (Rose et al., 2010). The generally higher intake reported in many previous reports in the past decades compared with most recent studies, including ours, may reflect the success of measures taken by the European Commission and by single European countries to reduce lead exposure and contamination of food, e.g. the use of leadfree gasoline. Studies investigating time trends of dietary lead intake in the same population generally reported decreasing levels (Gonzalez et al., 2019; Larsen et al., 2002; Martorell et al., 2011; Nasreddine et al., 2006), which supports this hypothesis.

Variations in dietary exposure may be related to differences in soil composition in the regions where food is produced or in individual dietary patterns. Since our sample population is generally characterized by moderate-to-high adherence to the Mediterranean diet (Malagoli et al., 2015), this may have influenced the frequency and amount of consumption of the types of foods that we observed as top contributors of lead intake, namely cereals, (leafy) vegetables, and wine (among beverages). It is noteworthy that similar results have been reported for the Spanish population, probably sharing similar dietary Mediterranean habits (Llobet et al., 2003; Marin et al., 2017; Rubio et al., 2005). Although a comparison of contribution of individual foods is hampered by the presentation of summary data with slightly different food categories, it is noteworthy that the average lead intake was generally comparable, with the highest lead contamination found in cereal products (Llobet et al., 2003; Marin et al., 2017; Martorell et al., 2011), but also in vegetables, meat products and seafood (Fakhri et al., 2018; Llobet et al., 2003; Martorell et al., 2011). Previous studies carried out in Italian populations showed a higher lead concentration in pasta and bread, followed by meat and cheese, resulting in a higher contribution to total lead intake from cereal and meat products (Alberti-Fidanza et al., 2002; Turconi et al., 2009), but also seafood and vegetables (Storelli et al., 2010; Turconi et al., 2009).

The MOE risk assessment estimation suggested that risks for cardiovascular disease and chronic kidney disease predicted at this exposure level should be low in our population. However, there is no evidence of a threshold below which adverse effects are not experienced (JECFA, 2011; US-EPA, 2020b; WHO, 2010). As a consequence, other and more subtle adverse effects may still occur, specifically in vulnerable population such as children. Indeed the exposure level for neurodevelopmental adverse effects is much lower than those associated with the onset of cardiovascular risk and chronic kidney diseases (EFSA, 2012; WHO, 2010). Additionally, the cumulative exposure of dietary intake with other sources of lead, especially from the occupational environment (IARC, 2006), may still cause adverse effects in highly exposed individuals.

Some study limitations must be noted. In the estimation of lead dietary intake we included only foods and beverages, and the contribution of drinking water as a source of lead exposure was not considered. This might have biased our results toward a lower estimation of lead intake, since drinking water may be a significant source of lead ingestion when tap water is contaminated by lead or distributed through lead pipes (Guidotti et al., 2007; Jarvis et al., 2018; Rosen et al., 2017). Despite the fact that the lead concentration of public municipal drinking water is strictly and periodically assessed and must be lower than 10 µg/L according to EU (EC, 1998) and Italian (Italy, 2001) legislation, we cannot entirely rule out a high level of contamination in private plumbing household distribution systems still using lead pipes. These will expose people to higher intakes of lead via the drinking water (Jarvis et al., 2018). However, it should be noted that consumption of bottled mineral water has risen in the last decades despite good tap water quality (Doria, 2006; Doria et al., 2009; Vinceti et al., 2000), especially in Italy, in spite of the issue of environmental contaminants which has recently been pointed out (Chapa-Martinez et al., 2016; Zuccarello et al., 2019). Nonetheless, considering an average daily consumption of 1 L with a lead content as high as the European standard of 10 µg/L, we found a substantially increased intake but the MOE assessment for both cardiovascular and nephrotoxic effects still suggests a substantially low risk.

Another study limitation is the lack of information on lead bioavailability in foods (Li et al., 2019). We did not carry out any speciation analysis thus we are unable to provide any estimates of inorganic and organic lead (e.g. tetraethyl lead) (ATSDR, 2017), the latter being characterized by dangerous toxicological features due to its higher neurotoxicity (IARC, 2006; Vinceti et al., 2017). Finally, we included in our study adult participants only, thus we cannot perform any safety assessment of the intake in vulnerable populations such as children or pregnant women (Gonzalez et al., 2019; Vinceti et al., 2001).

It should also be noted that the measurements made in this study cannot be considered a comprehensive assessment of overall lead exposure, since other sources of lead exposure such as skin or inhalation from environmental and occupational sources, must be considered (IARC, 2006; Mielke et al., 2010; Pan et al., 2010).

Our study also has some strengths. We collected and analyzed a large number of samples of foods and beverages representing habitual dietary patterns of Northern Italy. In addition, we estimated dietary intakes in a large randomly selected population sample with overall dietary characteristics similar to those observed in other Italian populations (Agnoli et al., 2011; Filippini et al., 2018c). Finally, we implemented a validated dietary questionnaire, specifically developed for the Northern Italian population (Pala et al., 2003; Pasanisi et al., 2002). We could therefore estimate both overall and food-specific intake in our study population, also allowing our findings to be compared with other studies.

5. Conclusions

Our study provides comprehensive and updated information on the lead concentration of foods consumed by an adult Northern Italy population, which may be of interest for both risk assessment and periodical food surveillance of toxic metals, and which is based on a validated and reliable methodology for the assessment of dietary intakes. Due to the absence of a safety threshold value for this highly toxic heavy metal no level of intake, including the one we determined in the present study, can be considered safe. However, it appeared to be not high enough to elicit adverse cardiovascular risk and nephrotoxic effects, and we can conclude that these are unlikely to occur at these exposure levels.

Author contribution: Conceptualization: MV and TF; Data curation: CM, LV, MM and TF; Formal analysis: LV, MM and TF; Funding acquisition: MV; Investigation/Methodology: CM, LV and SJFT; Roles/Writing - original draft MM, MV, SJFT and TF; Writing - review & editing: all authors.

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Declarations of interest: none.

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Table 1. Distribution of lead contamination (µg/kg wet weight) according to food categories.

Food	N	Mean	P5	P25	P50	P75	P95	<LOD N	<LOD %
Cereals and cereal products	**112**	**11.427**	**0.002**	**3.639**	**7.285**	**12.193**	**39.581**	**7**	**6.3%**
Pasta, other grains	41	11.414	0.133	1.089	4.947	10.323	40.509	2	4.9%
Rice	8	8.840	0.002	0.283	4.396	10.891	39.581	1	12.5%
Bread and rolls	42	11.870	2.256	6.203	9.965	13.773	31.038	0	0.0%
Crackers, crispbread, salty snacks	21	11.552	0.002	3.98	6.454	14.317	35.423	4	19.0%
Meat and meat products	**86**	**12.520**	**0.613**	**2.399**	**5.255**	**9.562**	**43.815**	**2**	**2.3%**
Red meat	28	16.290	0.511	1.215	4.311	8.321	121.718	1	3.6%
White meat	12	3.189	0.584	0.975	2.007	4.271	11.601	0	0.0%
Processed meat	36	9.817	1.537	4.550	7.658	9.941	31.397	1	2.8%
Offal	10	22.889	0.613	1.644	7.894	38.164	91.601	0	0.0%
Milk and dairy products	**72**	**6.792**	**0.322**	**1.915**	**4.249**	**8.346**	**26.636**	**1**	**1.4%**
Milk and yogurt	13	0.556	0.556	0.354	0.420	0.630	1.950	1	7.7%
Cheeses	59	8.166	1.360	3.310	5.447	9.106	28.093	0	0.0%
Fresh cheese	17	5.446	0.322	1.800	3.230	4.780	28.093	0	0.0%
Aged cheese	42	9.267	2.184	4.171	7.013	9.139	26.636	0	0.0%
Eggs	**9**	**0.442**	**0.002**	**0.002**	**0.307**	**0.861**	**1.494**	**4**	**44.4%**
Fish and seafood	**62**	**18.713**	**0.462**	**1.877**	**6.197**	**13.83**	**104.959**	**2**	**3.2%**
Fish	41	8.326	0.152	1.228	3.779	6.973	24.104	2	4.9%
Preserved and tinned fish	9	7.823	0.152	1.228	5.752	6.394	40.914	0	0.0%
Non-piscivorous fish	15	14.443	0.002	1.337	6.783	17.752	104.959	1	6.7%
Piscivorous fish	17	3.196	0.002	0.676	2.558	4.551	7.526	1	5.9%
Crustaceans and molluscs	21	38.992	2.316	7.694	13.83	40.284	120.873	0	0.0%
All vegetables	**196**	**24.948**	**0.343**	**1.918**	**4.922**	**13.865**	**93.621**	**6**	**3.0%**
Leafy vegetables	40	38.953	2.316	9.920	14.169	51.947	160.127	0	0.0%
Tomatoes	19	6.166	0.002	0.844	1.688	5.978	66.342	2	10.5%
Root vegetables	14	10.546	0.455	3.058	7.023	13.277	44.248	0	0.0%
Cabbage	28	11.628	0.345	1.282	4.138	10.823	58.334	0	0.0%
Onion and garlic	32	2.627	0.002	0.885	1.956	3.062	6.038	3	9.4%
Other vegetables (eggplant, zucchini, etc.)	63	42.179	0.574	2.454	5.001	21.725	93.621	1	1.6%
Mushrooms	**5**	**24.997**	**9.362**	**18.825**	**20.119**	**38.15**	**38.529**	**0**	**0.0%**
Pulses	**43**	**7.615**	**0.072**	**1.493**	**7.219**	**11.032**	**21.227**	**1**	**2.3%**
Potatoes	**14**	**4.056**	**1.300**	**2.927**	**3.627**	**4.656**	**9.653**	**0**	**0.0%**
Fresh fruit	**60**	**2.450**	**0.002**	**0.642**	**1.682**	**3.063**	**7.263**	**5**	**8.3%**
Citrus fruit	12	4.618	0.339	1.006	2.036	5.362	23.112	0	0.0%
All other fruit	48	1.908	0.002	0.567	1.682	2.713	4.595	5	10.4%
Dry fruit, nuts and seeds	**45**	**9.373**	**0.002**	**1.099**	**2.355**	**5.602**	**56.524**	**10**	**22.2%**
Dry fruit	8	32.254	1.736	6.557	14.522	51.465	111.210	0	0.0%
Nuts and seeds	37	4.425	0.002	0.002	1.803	3.056	29.725	10	27.0%
Sweets, chocolate, cakes, etc.	**79**	**15.306**	**0.417**	**3.630**	**6.980**	**14.398**	**49.014**	**0**	**0.0%**
Sugar, non-chocolate confectionery	8	48.687	0.790	4.409	12.098	24.369	306.959	0	0.0%
Chocolate, candy bars, etc.	21	22.456	3.630	9.848	19.721	31.288	49.014	0	0.0%
Ice-cream	5	2.708	0.110	1.669	3.535	3.667	4.560	0	0.0%
Cakes, pies and pastries	30	6.116	0.417	2.599	4.189	8.368	16.660	0	0.0%
Biscuits, dry cakes	15	10.072	0.157	4.727	6.160	9.722	58.446	0	0.0%
Oils and fats	**23**	**1.658**	**0.149**	**0.249**	**0.900**	**2.640**	**4.400**	**1**	**4.3%**
Vegetables fats and oils (non-olive)	12	1.469	0.002	0.275	0.760	2.339	6.846	1	6.3%
Olive oil	4	1.154	0.149	0.189	0.635	2.118	3.195	0	0.0%
Butter and other animal fats	7	2.269	0.240	0.900	2.458	3.221	4.400	0	0.0%
Beverages	**102**	**7.957**	**0.058**	**0.726**	**2.489**	**8.761**	**31.735**	**1**	**1.0%**
Coffee and tea	8	1.691	0.043	0.073	0.440	2.057	8.345	0	0.0%
Wines	50	13.900	1.0131	3.509	8.022	19.513	43.816	0	0.0%
Red wine	27	17.164	3.125	3.747	12.425	27.064	43.816	0	0.0%
White wine	23	10.068	0.958	1.770	5.849	9.895	26.232	0	0.0%
Aperitif wines and beers	8	7.021	0.456	0.544	1.129	5.664	41.04	0	0.0%
Spirits and liqueurs	21	1.962	0.089	0.656	1.172	2.453	6.536	0	0.0%
Fruit juices	8	0.371	0.051	0.070	0.162	0.668	1.115	0	0.0%
Soft drinks	7	0.386	0.002	0.095	0.277	0.650	0.771	1	14.3%

Table 2. Estimation of lead daily dietary intake in all subjects (in µg/kg of body weight/day) and percentage contribution (%) of each food to total intake.

Food	Mean	P5	P25	P50	P75	P95	%
Total intake	***0.155***	***0.072***	***0.111***	***0.148***	***0.188***	***0.273***	***100***
Cereals and cereal products	**0.030**	**0.007**	**0.017**	**0.027**	**0.039**	**0.063**	**19.35**
Pasta, other grains	0.009	0.001	0.005	0.008	0.012	0.021	5.81
Rice	0.001	0.000	0.000	0.000	0.001	0.002	0.65
Bread and rolls	0.013	0.000	0.004	0.011	0.019	0.035	8.39
Crackers, crispbread, salty snacks	0.007	0.000	0.002	0.004	0.008	0.025	4.52
Meat and meat products	**0.015**	**0.003**	**0.008**	**0.013**	**0.018**	**0.034**	**9.68**
Red meat	0.009	0.001	0.004	0.007	0.011	0.023	5.81
White meat	0.001	0.000	0.000	0.001	0.002	0.004	0.65
Processed meat	0.004	0.000	0.002	0.003	0.005	0.011	2.58
Offal	0.001	0.000	0.000	0.000	0.000	0.003	0.65
Milk and dairy products	**0.006**	**0.001**	**0.003**	**0.005**	**0.008**	**0.015**	**3.87**
Milk and yogurt	0.002	0.000	0.000	0.001	0.002	0.005	1.29
Cheese	0.005	0.000	0.002	0.004	0.006	0.012	3.23
Fresh cheese	0.001	0.000	0.000	0.001	0.001	0.004	0.65
Aged cheese	0.003	0.000	0.001	0.003	0.005	0.009	1.94
Eggs	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.00**
Fish and seafood	**0.006**	**0.000**	**0.002**	**0.004**	**0.008**	**0.018**	**3.87**
Fish	0.003	0.000	0.001	0.002	0.004	0.009	1.94
Preserved and tinned fish	0.001	0.000	0.000	0.000	0.001	0.002	0.65
Non-piscivorous fish	0.002	0.000	0.000	0.001	0.002	0.007	1.29
Piscivorous fish	0.000	0.000	0.000	0.000	0.001	0.001	0.00
Crustaceans and molluscs	0.003	0.000	0.000	0.001	0.004	0.013	1.94
All vegetables	**0.043**	**0.012**	**0.024**	**0.038**	**0.057**	**0.095**	**27.74**
Leafy vegetables	0.018	0.002	0.007	0.014	0.024	0.046	11.61
Tomatoes	0.004	0.000	0.002	0.004	0.006	0.011	2.58
Root vegetables	0.002	0.000	0.000	0.001	0.003	0.008	1.29
Cabbage	0.001	0.000	0.000	0.000	0.001	0.003	0.65
Onion and garlic	0.001	0.000	0.000	0.000	0.001	0.002	0.65
Other vegetables (eggplant, zucchini, etc.)	0.018	0.003	0.008	0.014	0.024	0.044	11.61
Mushrooms	**0.001**	**0.000**	**0.000**	**0.000**	**0.001**	**0.003**	**0.65**
Pulses	**0.002**	**0.000**	**0.001**	**0.001**	**0.003**	**0.006**	**1.29**
Potatoes	**0.001**	**0.000**	**0.001**	**0.001**	**0.002**	**0.004**	**0.65**
Fresh fruit	**0.010**	**0.002**	**0.006**	**0.009**	**0.014**	**0.022**	**6.45**
Citrus fruit	0.006	0.001	0.003	0.005	0.008	0.013	3.87
All other fruit	0.004	0.000	0.002	0.004	0.006	0.010	2.58
Dry fruit, nuts and seeds	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.001**	**0.00**
Dry fruit	0.000	0.000	0.000	0.000	0.000	0.001	0.00
Nuts and seeds	0.000	0.000	0.000	0.000	0.000	0.000	0.00
Sweets, chocolate, cakes, etc.	**0.009**	**0.001**	**0.003**	**0.006**	**0.012**	**0.026**	**5.81**
Sugar, non-chocolate confectionery	0.002	0.000	0.000	0.001	0.002	0.007	1.29
Chocolate, candy bars, etc.	0.002	0.000	0.000	0.001	0.002	0.008	1.29
Ice-cream	0.001	0.000	0.000	0.000	0.001	0.002	0.65
Cakes, pies and pastries	0.003	0.000	0.000	0.001	0.004	0.011	1.94
Biscuits, dry cakes	0.002	0.000	0.000	0.001	0.003	0.007	1.29
Oils and fats	**0.000**	**0.000**	**0.000**	**0.000**	**0.001**	**0.001**	**0.00**
Vegetables fats and oils (non-olive)	0.000	0.000	0.000	0.000	0.001	0.001	0.00
Olive oil	0.000	0.000	0.000	0.000	0.000	0.001	0.00
Butter and other animal fats	0.000	0.000	0.000	0.000	0.000	0.000	0.00
Beverages	**0.029**	**0.002**	**0.005**	**0.017**	**0.044**	**0.090**	**18.71**
Coffee and tea	0.004	0.000	0.002	0.003	0.004	0.009	2.58
Wine	0.024	0.000	0.000	0.010	0.040	0.085	15.48
Red wine	0.017	0.000	0.000	0.004	0.027	0.072	10.97
White wine	0.007	0.000	0.000	0.000	0.007	0.036	4.52
Aperitif wines and beers	0.001	0.000	0.000	0.000	0.000	0.004	0.65
Spirits and liqueurs	0.000	0.000	0.000	0.000	0.000	0.000	0.00
Fruit juices	0.000	0.000	0.000	0.000	0.000	0.001	0.00
Soft drinks	0.000	0.000	0.000	0.000	0.000	0.001	0.00

Table 3. Estimation of lead daily dietary intake in men (in µg/kg of body weight/day) and percentage contribution (%) of each food to total intake.

Food	Mean	P5	P25	P50	P75	P95	%
Total intake	***0.151***	***0.069***	***0.107***	***0.146***	***0.186***	***0.244***	***100***
Cereals and cereal products	**0.030**	**0.008**	**0.017**	**0.026**	**0.039**	**0.060**	**19.87**
Pasta, other grains	0.010	0.001	0.006	0.009	0.013	0.023	6.62
Rice	0.001	0.000	0.000	0.000	0.001	0.002	0.66
Bread and rolls	0.013	0.000	0.003	0.010	0.019	0.034	8.61
Crackers, crispbread, salty snacks	0.006	0.000	0.001	0.003	0.007	0.023	3.97
Meat and meat products	**0.015**	**0.004**	**0.009**	**0.013**	**0.018**	**0.033**	**9.93**
Red meat	0.009	0.001	0.004	0.007	0.011	0.022	5.96
White meat	0.001	0.000	0.000	0.001	0.002	0.003	0.66
Processed meat	0.004	0.000	0.002	0.003	0.005	0.011	2.65
Offal	0.001	0.000	0.000	0.000	0.001	0.003	0.66
Milk and dairy products	**0.006**	**0.001**	**0.003**	**0.005**	**0.008**	**0.013**	**3.97**
Milk and yogurt	0.001	0.000	0.000	0.001	0.002	0.004	0.66
Cheese	0.004	0.001	0.002	0.004	0.006	0.011	2.65
Fresh cheese	0.001	0.000	0.000	0.001	0.001	0.003	0.66
Aged cheese	0.004	0.000	0.001	0.003	0.005	0.009	2.65
Eggs	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.00**
Fish and seafood	**0.005**	**0.000**	**0.002**	**0.004**	**0.007**	**0.014**	**3.31**
Fish	0.003	0.000	0.001	0.002	0.003	0.009	1.99
Preserved and tinned fish	0.001	0.000	0.000	0.000	0.001	0.002	0.66
Non-piscivorous fish	0.002	0.000	0.000	0.001	0.002	0.008	1.32
Piscivorous fish	0.000	0.000	0.000	0.000	0.000	0.001	0.00
Crustaceans and molluscs	0.003	0.000	0.000	0.001	0.004	0.011	1.99
All vegetables	**0.036**	**0.011**	**0.021**	**0.032**	**0.046**	**0.076**	**23.84**
Leafy vegetables	0.014	0.001	0.006	0.011	0.020	0.038	9.27
Tomatoes	0.005	0.001	0.002	0.004	0.007	0.012	3.31
Root vegetables	0.001	0.000	0.000	0.001	0.002	0.006	0.66
Cabbage	0.001	0.000	0.000	0.000	0.001	0.003	0.66
Onion and garlic	0.001	0.000	0.000	0.000	0.001	0.002	0.66
Other vegetables (eggplant, zucchini, etc.)	0.014	0.002	0.006	0.012	0.020	0.033	9.27
Mushrooms	**0.001**	**0.000**	**0.000**	**0.000**	**0.001**	**0.003**	**0.66**
Pulses	**0.002**	**0.000**	**0.001**	**0.001**	**0.002**	**0.005**	**1.32**
Potatoes	**0.001**	**0.000**	**0.001**	**0.001**	**0.002**	**0.004**	**0.66**
Fresh fruit	**0.009**	**0.001**	**0.005**	**0.008**	**0.012**	**0.019**	**5.96**
Citrus fruit	0.005	0.001	0.003	0.004	0.007	0.011	3.31
All other fruit	0.004	0.000	0.002	0.003	0.005	0.009	2.65
Dry fruit, nuts and seeds	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.001**	**0.00**
Dry fruit	0.000	0.000	0.000	0.000	0.000	0.001	0.00
Nuts and seeds	0.000	0.000	0.000	0.000	0.000	0.000	0.00
Sweets, chocolate, cakes, etc.	**0.008**	**0.000**	**0.002**	**0.006**	**0.010**	**0.024**	**5.30**
Sugar, non-chocolate confectionery	0.002	0.000	0.000	0.001	0.002	0.006	1.32
Chocolate, candy bars, etc.	0.001	0.000	0.000	0.000	0.002	0.007	0.66
Ice-cream	0.000	0.000	0.000	0.000	0.001	0.002	0.00
Cakes, pies and pastries	0.003	0.000	0.000	0.001	0.004	0.009	1.99
Biscuits, dry cakes	0.002	0.000	0.000	0.001	0.003	0.006	1.32
Oils and fats	**0.000**	**0.000**	**0.000**	**0.000**	**0.001**	**0.001**	**0.00**
Vegetables fats and oils (non-olive)	0.000	0.000	0.000	0.000	0.000	0.000	0.00
Olive oil	0.000	0.000	0.000	0.000	0.000	0.001	0.00
Butter and other animal fats	0.000	0.000	0.000	0.000	0.000	0.000	0.00
Beverages	**0.039**	**0.002**	**0.009**	**0.030**	**0.061**	**0.105**	**25.83**
Coffee and tea	0.003	0.000	0.001	0.002	0.004	0.006	1.99
Wine	0.034	0.000	0.003	0.025	0.055	0.102	22.52
Red wine	0.025	0.000	0.000	0.012	0.043	0.082	16.56
White wine	0.009	0.000	0.000	0.003	0.013	0.042	5.96
Aperitif wine and beer	0.001	0.000	0.000	0.000	0.001	0.003	0.66
Spirits and liqueurs	0.000	0.000	0.000	0.000	0.000	0.001	0.00
Fruit juices	0.000	0.000	0.000	0.000	0.000	0.001	0.00
Soft drinks	0.000	0.000	0.000	0.000	0.000	0.001	0.00

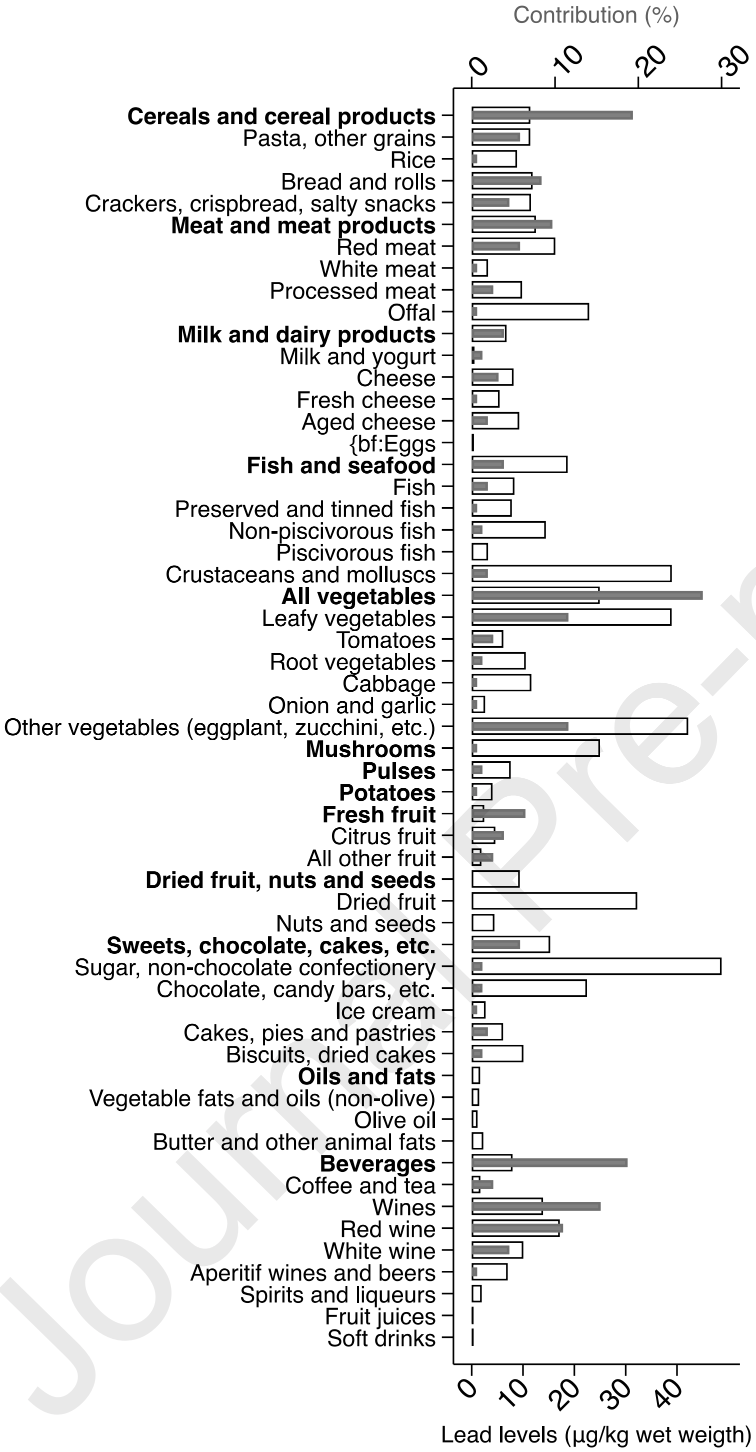
Table 4. Estimation of lead daily dietary intake in women (in µg/kg of body weight/day) and percentage contribution (%) of each food to total intake.

Food	Mean	P5	P25	P50	P75	P95	%
Total intake	***0.157***	***0.076***	***0.114***	***0.148***	***0.189***	***0.28***	***100***
Cereals and cereal products	**0.030**	**0.006**	**0.017**	**0.027**	**0.039**	**0.065**	**19.87**
Pasta, other grains	0.008	0.001	0.004	0.007	0.012	0.020	5.30
Rice	0.001	0.000	0.000	0.000	0.001	0.002	0.66
Bread and rolls	0.014	0.000	0.004	0.011	0.019	0.036	9.27
Crackers, crispbread, salty snacks	0.008	0.000	0.002	0.004	0.009	0.026	5.30
Meat and meat products	**0.015**	**0.003**	**0.008**	**0.012**	**0.019**	**0.037**	**9.93**
Red meat	0.009	0.001	0.003	0.006	0.011	0.027	5.96
White meat	0.001	0.000	0.001	0.001	0.002	0.004	0.66
Processed meat	0.004	0.000	0.002	0.003	0.006	0.011	2.65
Offal	0.001	0.000	0.000	0.000	0.000	0.003	0.66
Milk and dairy products	**0.007**	**0.001**	**0.004**	**0.006**	**0.008**	**0.016**	**4.64**
Milk and yogurt	0.002	0.000	0.001	0.002	0.003	0.006	1.32
Cheeses	0.005	0.000	0.002	0.004	0.006	0.012	3.31
Fresh cheese	0.001	0.000	0.000	0.001	0.002	0.005	0.66
Aged cheese	0.003	0.000	0.001	0.002	0.004	0.008	1.99
Eggs	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.00**
Fish and seafood	**0.007**	**0.000**	**0.002**	**0.004**	**0.008**	**0.021**	**4.64**
Fish	0.003	0.000	0.001	0.002	0.004	0.009	1.99
Preserved and tinned fish	0.001	0.000	0.000	0.000	0.001	0.002	0.66
Non-piscivorous fish	0.002	0.000	0.000	0.001	0.003	0.007	1.32
Piscivorous fish	0.000	0.000	0.000	0.000	0.001	0.002	0.00
Crustaceans and molluscs	0.004	0.000	0.000	0.002	0.005	0.014	2.65
All vegetables	**0.049**	**0.013**	**0.027**	**0.044**	**0.065**	**0.105**	**32.45**
Leafy vegetables	0.020	0.002	0.008	0.016	0.028	0.052	13.25
Tomatoes	0.004	0.000	0.002	0.003	0.006	0.010	2.65
Root vegetables	0.003	0.000	0.000	0.002	0.004	0.010	1.99
Cabbages	0.001	0.000	0.000	0.000	0.001	0.003	0.66
Onion and garlic	0.001	0.000	0.000	0.000	0.001	0.002	0.66
Other vegetables (eggplant, zucchini, etc.)	0.021	0.004	0.010	0.017	0.028	0.049	13.91
Mushrooms	**0.001**	**0.000**	**0.000**	**0.000**	**0.001**	**0.003**	**0.66**
Pulses	**0.002**	**0.000**	**0.001**	**0.002**	**0.003**	**0.006**	**1.32**
Potatoes	**0.001**	**0.000**	**0.001**	**0.001**	**0.002**	**0.004**	**0.66**
Fresh fruit	**0.011**	**0.002**	**0.006**	**0.010**	**0.015**	**0.024**	**7.28**
Citrus fruit	0.007	0.001	0.004	0.006	0.009	0.014	4.64
All other fruit	0.005	0.000	0.002	0.004	0.006	0.012	3.31
Dry fruit, nuts and seeds	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.001**	**0.00**
Dry fruit	0.000	0.000	0.000	0.000	0.000	0.001	0.00
Nuts and seeds	0.000	0.000	0.000	0.000	0.000	0.000	0.00
Sweets, chocolate, cakes, etc.	**0.010**	**0.001**	**0.004**	**0.007**	**0.014**	**0.028**	**6.62**
Sugar, non-chocolate confectionery	0.002	0.000	0.000	0.001	0.002	0.008	1.32
Chocolate, candy bars, etc.	0.002	0.000	0.000	0.001	0.002	0.009	1.32
Ice-cream	0.001	0.000	0.000	0.000	0.001	0.002	0.66
Cakes, pies and pastries	0.003	0.000	0.001	0.002	0.005	0.013	1.99
Biscuits, dry cakes	0.002	0.000	0.000	0.001	0.004	0.009	1.32
Oils and fats	**0.001**	**0.000**	**0.000**	**0.000**	**0.001**	**0.001**	**0.66**
Vegetables fats and oils (non-olive)	0.000	0.000	0.000	0.000	0.000	0.000	0.00
Olive oil	0.000	0.000	0.000	0.000	0.001	0.001	0.00
Butter and other animal fats	0.000	0.000	0.000	0.000	0.000	0.000	0.00
Beverages	**0.022**	**0.002**	**0.004**	**0.010**	**0.033**	**0.074**	**14.57**
Coffee and tea	0.004	0.001	0.002	0.004	0.005	0.011	2.65
Wine	0.016	0.000	0.000	0.003	0.025	0.068	10.60
Red wine	0.011	0.000	0.000	0.000	0.011	0.059	7.28
White wine	0.005	0.000	0.000	0.000	0.004	0.028	3.31
Aperitif wine and beer	0.001	0.000	0.000	0.000	0.000	0.004	0.66
Spirits and liqueurs	0.000	0.000	0.000	0.000	0.000	0.000	0.00
Fruit juices	0.000	0.000	0.000	0.000	0.000	0.002	0.00
Soft drinks	0.000	0.000	0.000	0.000	0.000	0.001	0.00

Table 5. Margin of exposure (MOE) estimation using the lower bound of the benchmark dose (BMDL) of an extra risk of 1% ($BMDL_{01}$) for adverse effect on systolic blood pressure (SBP) and the BMDL for an extra risk of 10% ($BMDL_{10}$) for the nephrotoxic effects (NE) using either mean, median (P50) and 95 percentiles (P95) values of daily dietary intake (DDI) in overall population and divided by sex. DDI and BDML are in µg/kg bw-day.

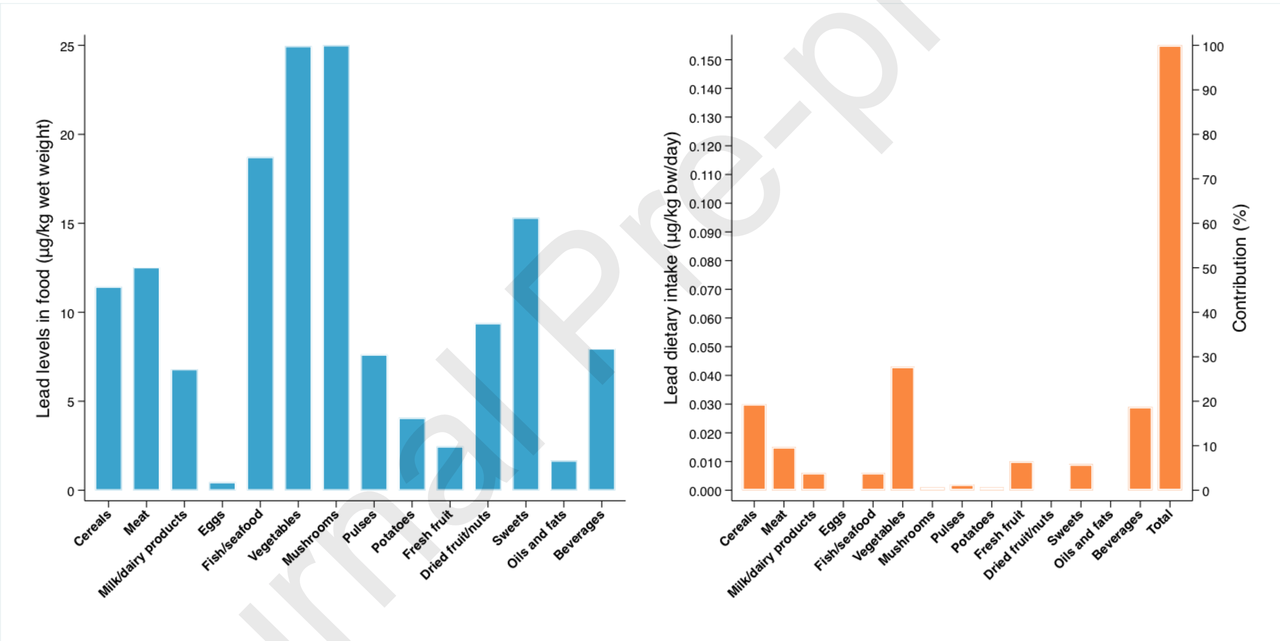
	DDI			BMDL		MOE					
						SBP			NE		
	Mean	P50	P95	SBP	NE	Mean	P50	P95	Mean	P50	P95
All subjects	0.155	0.148	0.273	1.2	0.63	7.7	8.1	4.4	4.1	4.3	2.3
Men	0.151	0.146	0.244	1.2	0.63	7.9	8.2	4.9	4.2	4.3	2.6
Women	0.157	0.148	0.280	1.2	0.63	7.6	8.1	4.3	4.0	4.3	2.3

Figure 1. Lead levels in food (µg/kg wet weight– white bars) and contribution to daily dietary intake of each food category (percentage – gray bars).



Highlights

- Foods with the highest lead content included sweets, leafy vegetables and seafoods
- The estimated mean lead intake in the investigated population was 0.155 µg/kg bw-day
- Top contributors of lead intake were vegetables, cereals, and alcoholic beverages
- Risk assessment was performed using the margin of exposure (MOE) approach
- The MOE assessment suggested almost low risk in the study community



Author contribution: Conceptualization: MV and TF; Data curation: CM, LV, MM and TF; Formal analysis: LV, MM and TF; Funding acquisition: MV; Investigation/Methodology: CM, LV and SJFT; Roles/Writing - original draft MM, MV, SJFT and TF; Writing - review & editing: all authors.