

RESEARCH ARTICLE

# Predictors of mercury, lead, cadmium and antimony status in Norwegian never-pregnant women of fertile age

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## Abstract

### Background

The toxic trace elements mercury (Hg), lead (Pb), cadmium (Cd) and antimony (Sb) are transferred over the placenta to the fetus and secreted into the breastmilk. All four elements bioaccumulate in the body and as maternal age at delivery is increasing in industrialized countries, the burden of toxic trace elements in never-pregnant women of fertile age is of concern.

### Methods

Healthy, never-pregnant women aged 18 to 40 years (n = 158) were recruited between June 2012 and March 2015 in Bergen, Norway. Clinical data were collected and non-fasting venous blood samples were analyzed for whole blood Hg, Pb and Cd and serum Sb by ICP-MS and related to diet and life style factors.

### Results

In a multiple linear regression model, increasing age was associated with higher levels of Hg and Sb, but diet and life style factors were more important predictors. Median whole blood Hg was increased by a factor of 70 in women who had fish for dinner  $\geq 1$ /week, compared to women who rarely or never ate fish ( $p < 0.001$ ). Alcohol intake was the strongest predictor for whole blood Pb, while use of tobacco was the strongest predictor for whole blood Cd. Being a vegetarian was associated with lower levels of both Hg and Sb.

### Conclusions

As toxic trace elements tend to bioaccumulate in the body, increasing maternal age at delivery may represent a threat to the next generation. In a group of healthy Norwegian never-pregnant women, age contributed to Hg and Sb levels, but diet and life style factors were stronger determinants of whole blood Hg, Pb, Cd and serum Sb levels. Continuous public

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actions are needed to reduce modifiable and preventable sources of potentially deleterious toxins to minimize the exposure in children and fertile women.

## Introduction

Mercury (Hg), cadmium (Cd), lead (Pb) and antimony (Sb) are toxic trace elements associated with negative health effects on the nervous, renal, cardiovascular and immune system [1–3]. Element interactions may also amplify the effect of even low dose concentrations [4]. The half-lives of the elements vary from 3 months for Hg [5], 2.7 years for Sb [6], while Pb and Cd have half-lives of about 30 years, so body stores tend to increase with age [7, 8].

As Hg and Pb and to a lesser degree also Cd and Sb are transferred over the placenta to the fetus [9, 10] and after birth secreted into the breastmilk [11, 12], pregnancy represents a detoxification process for the mother, and higher parity is associated with lower levels of Hg, Pb and Cd [13]. Exposure to heavy metals during fetal life and infancy is associated with impairment of growth and central nervous system development, as well as pulmonary and nephrotic damage, and may have serious long-term health consequences for the child [14–17]. There are limited data on fetal exposure of Sb, but higher levels of Sb are reported in cord blood of pregnancies with an adverse outcome [18], but in general there are limited data on fetal and infant exposure of Sb.

Mean maternal age at delivery has increased during the last years and primiparas above 35 years are becoming increasingly common in industrialized countries [19]. A higher maternal age is associated with higher maternal morbidity, pregnancy complications [20], and later disease in the child [21]. Since 1980 there has been an increasing prevalence of autism spectrum disorders [22], a mental dysfunction that has been associated with advanced maternal age [23] and also higher levels of Hg, Pb, Cd and Sb in the children with autism spectrum disease compared to normal children [24].

As the age for giving birth to the first child is increasing, the burden of toxic elements in never-pregnant women of fertile age is of interest. We have evaluated the Hg, Pb, Cd and Sb status in healthy, never-pregnant Norwegian women aged of fertile age (18–40 years) and related this to age and life style factors associated with toxic trace element exposure [25–30].

## Materials and methods

### Study population and design

Between June 2012 and March 2015, healthy, never-pregnant women aged 18 to 40 years were recruited among employees and students at Haukeland University Hospital and the University of Bergen, Norway. In addition, healthy never-pregnant women in the same age-group with a vegetarian diet were recruited through Facebook, and complied with [Facebook.com's](https://www.facebook.com/policies/ads/) terms of service for recruiting participants on their website ([www.facebook.com/policies/ads/](https://www.facebook.com/policies/ads/)).

Ethical approval of the protocol was granted by the Regional Committee of the Norwegian National Research Ethics Committee for Medical and Health Research (NEM) (2011/2447), and written informed consent was obtained from all women before enrollment.

The women completed a questionnaire concerning age, years of completed education, height, weight, use of medications, including oral contraceptives and hormone implants, diet, intake of alcohol, regular use of tobacco, including cigarettes and snuff, use of multiple micro-nutrient supplements (MMN), including vitamins, minerals, omega-3 fatty acids and cod oil. Use of supplements more than three days per week was defined as a regular user.

## Blood sampling and analyses

Non-fasting blood samples were obtained by antecubital venipuncture and collected into vacutainer tubes with EDTA and without additives approved for trace metal analysis (Terumo®, US). Five-hundred  $\mu\text{L}$  of whole blood and serum was aliquoted and stored at  $-80^{\circ}\text{C}$  until analysis. Whole blood Hg, Pb and Cd and serum Sb were analyzed by ICP-MS on Perkin Elmer DRC-e (Perkin Elmer®, USA) in standard mode [31].

Plasma levels of cotinine were assayed using a LC-MS/MS method [32]. A plasma cotinine level  $\geq 85$  nmol/L is commonly used as a cut off to define regular smokers [33], however use of smokeless tobacco is associated with similar cotinine levels [34].

## Statistical analysis

Results are presented as mean and standard deviation (SD), compared by Student's t-test or Anova, and median and interquartile range (IQR), compared by Mann-Whitney U test or Kruskal Wallis test. Chi-square test was used for categorical data. Spearman correlations and multiple linear regression models were used to explore relationships between data.

Graphical illustration of the relationship between whole blood Pb and alcohol units consumed per week was obtained by generalized additive models (GAM).

The SPSS statistical program (version 23) and the packages “mgcv” in R®, version 3.3 (The R Foundation for Statistical Computing) were used for the statistical analyses. Two-sided p-values  $< 0.05$  were considered statistically significant.

## Results

### Demographics, nutrition and life style factors

A total of 158 healthy, never-pregnant women with an age range of 18 to 40 years, were included in the study. The majority 122/158 (78%) had a normal BMI (18.5 to 25.0), 6/158 (4%) were underweight (BMI  $< 18.5$ ), 24/158 (15%) were overweight (BMI: 25.0 to  $< 30.0$ ) and four women (3%) were obese (BMI  $\geq 30.0$ ).

Most women, 124/158 (78%), had an omnivore diet, whereas 34/158 (22%) had used a vegetarian diet for a median of 36 months (IQR 16, 132), range 2–240 months. Fifteen of the 34 vegetarians (44%) were vegans and did not eat any animal products, including eggs and milk. Demographic data according to an omnivore or a vegetarian diet are given in [Table 1](#).

Omnivorous were younger, had a higher educational level and were less likely to use tobacco compared to vegetarians ([Table 1](#)). A total of four women (2.5%) reported regular daily smoking, two from each diet group, however, based on plasma cotinine levels  $\geq 85$  nmol/L, 17/158 (11%) women were defined as regular tobacco users. Use of alcohol ranged from 0 to 12 units per week, with no difference between the groups ([Table 1](#)). Two thirds (105/158) of the women reported regular use of micronutrient supplements, with no difference between omnivores and vegetarians ( $p > 0.07$ ) ([Table 1](#)).

Among the omnivores, the majority 86/124 (69%) had fish for dinner  $\geq 1$ /week, while 38/158 (24%) rarely or never ate fish. The majority of the regular tobacco-users (10/17, 59%) rarely or never ate fish compared to non-users (28/140, 20%,  $p = 0.002$ ). The most frequently eaten fish was farmed salmon (72%), followed by lean fish (17%) and other types of fatty fish (11%).

### Toxic trace element levels according to age, diet and life style factors

Levels of Hg, Pb, Cd and Sb according to age, diet, use of alcohol and tobacco are given in [Table 2](#). Age was positively correlated to Hg ( $r = 0.18$ ,  $p = 0.02$ ), Cd ( $r = 0.27$ ,  $p = 0.001$ ) and Sb

**Table 1. Baseline characteristics of healthy, never-pregnant women according to diet (n = 158).**

	Omnivore diet N = 124	Vegetarian diet N = 34	P value
Age, years, mean (SD)	25.3 (4.8)	31.5 (4.3)	<0.001 <sup>a</sup>
BMI, kg/m <sup>2</sup> , median (IQR)	21.7 (20.5, 23.7)	22.1 (20.7, 23.4)	0.88 <sup>b</sup>
Education, n (%)			
≤12 years	5 (4)	9 (27)	<0.001 <sup>c</sup>
13–17 years	32 (26)	18 (53)	
≥17 years	87 (70)	7 (21)	
Regular users of supplements, (≥3 days/week), n (%)			
Omega 3 fatty acids	59 (48)	11 (32)	0.11 <sup>c</sup>
Multivitamins/minerals	27 (22)	8 (24)	0.85 <sup>c</sup>
Alcohol, number of units/week, median (IQR)	2.0 (0.5, 4.0)	2.0 (0.8, 3.0)	0.99 <sup>b</sup>
Smokers, based on plasma cotinine ≥85 nmol/L, n (%)	8 (7)	9 (27)	0.001 <sup>c</sup>

<sup>a</sup>Comparison by Student's t-test

<sup>b</sup>Comparison by Mann-Whitney U test

<sup>c</sup>Comparison by Pearson Chi-square test

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( $r = 0.23, p = 0.004$ ) by Spearman correlation, but only Cd and Sb levels were higher in women ≥25 years, when compared by Mann-Whitney to the younger age-group (Table 2).

Age remained a significant predictor for Hg and Sb in a multiple linear regression model, which additionally included type of diet, fish intake, alcohol intake, use of tobacco, education, BMI and use of omega 3/cod oil supplements (Table 3).

Vegetarians had lower levels of Hg and Sb compared to omnivores (Table 2), and this was evident also in the multiple linear regression model (Table 3). No differences in levels of toxic trace elements were seen between vegans and vegetarians ( $p > 0.22$ , data not shown).

Fish intake was the strongest predictor for Hg in the multiple linear regression model (Table 3). Median whole blood Hg was increased by a factor of 70 in women who had fish for dinner ≥ 1/week, compared to women who rarely or never ate fish (Table 4).

**Table 2. Levels of toxic trace elements according to age, diet, intake of alcohol and use of tobacco in healthy never-pregnant women (n = 158).**

Parameters <sup>a</sup>	Age, years			Diet			Intake of alcohol, units per week			Use of tobacco determined by cotinine level		
	18–24 N = 87	25–40 N = 71	P value	Omnivore N = 124	Vegetarian N = 34	P value	<2 N = 65	≥2 N = 81	P value	<85 nmol/L N = 140	≥85 nmol/L N = 17	P value
Whole blood mercury, nmol/L	4.31 (1.55, 7.73)	4.92 (2.41, 9.19)	0.30	5.83 (3.85, 9.25)	0.13 (0, 0.93)	<0.001	4.85 (1.85, 8.70)	4.67 (1.73, 8.20)	0.93	4.93 (2.32, 8.82)	1.17 (0, 6.72)	0.04
Whole blood lead, μmol/L	0.04 (0.03, 0.05)	0.04 (0.03, 0.05)	0.62	0.04 (0.03, 0.05)	0.04 (0.03, 0.06)	0.30	0.03 (0.03, 0.05)	0.04 (0.04, 0.06)	<0.001	0.04 (0.03, 0.05)	0.05 (0.03, 0.06)	0.14
Whole blood cadmium, nmol/L	1.43 (1.11, 1.88)	1.88 (1.25, 2.59)	0.008	1.50 (1.15, 2.17)	1.70 (1.23, 2.57)	0.15	1.51 (1.14, 2.32)	1.51 (1.19, 1.98)	0.56	1.51 (1.14, 2.10)	2.47 (1.50, 7.66)	0.009
Serum antimony, nmol/L	28.7 (26.3, 31.8)	31.2 (28.7, 33.6)	0.002	30.2 (27.3, 33.6)	29.2 (26.4, 31.0)	0.09	31.2 (28.0, 33.6)	29.5 (27.0, 32.7)	0.06	30.0 (27.0, 32.7)	30.6 (27.6, 34.1)	0.24

<sup>a</sup>Median and IQR, compared by Mann-Whitney test

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**Table 3. Determinants of toxic trace elements levels in healthy never-pregnant women (n = 158) by multiple linear regression.**

Variables included in the model	Whole blood mercury, nmol/L		Whole blood lead, $\mu\text{mol/L}$		Whole blood cadmium, nmol/L		Serum antimony, nmol/L	
	Beta	P	Beta	P	Beta	P	Beta	P
Age <sup>a</sup>	0.18	0.03	0.10	0.22	0.08	0.32	0.19	0.02
Diet <sup>b</sup>	-0.04	0.80	0.09	0.53	0.03	0.86	-0.37	0.01
Fish consumption <sup>c</sup>	0.45	0.002	-0.01	0.95	0.15	0.26	-0.24	0.10
Alcohol intake <sup>d</sup>	0.04	0.66	0.37	<0.001	0.16	0.048	-0.06	0.51
Regular use of tobacco <sup>e</sup>	-0.04	0.63	0.04	0.63	0.45	<0.001	0.19	0.03
Education <sup>f</sup>	-0.13	0.13	0.10	0.28	-0.20	0.02	-0.04	0.69

BMI and use of omega 3 supplements/cod oil were additionally included in the model

<sup>a</sup> Age in years

<sup>b</sup> Omnivore versus vegetarian diet

<sup>c</sup> Fish consumption categorized; Fish for dinner: <1/month, 1-3/month or  $\geq 1/\text{week}$

<sup>d</sup> Intake of alcohol units/week

<sup>e</sup> Based on plasma cotinine levels, categorized; <85 nmol/L,  $\geq 85$  nmol/L

<sup>f</sup> Education, categorized;  $\leq 12$  years, 13–17 years,  $\geq 17$  years.

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Alcohol intake was correlated to Pb by Spearman correlation ( $r = 0.37, p < 0.001$ ), and median Pb was significantly higher in women who drank 2 or more units of alcohol per week (Table 2). There was a dose-response relationship between intake of alcohol in units per week and Pb, as shown by GAM corrected for age (Fig 1). Alcohol was also the only significant predictor for Pb in the multiple linear regression model (Table 3).

Regular use of tobacco resulting in plasma cotinine levels  $\geq 85 \mu\text{mol/L}$  was associated with higher Cd and lower Hg levels (Table 2). In the multiple linear regression models, tobacco use was strongly related to Cd and less to Sb.

A longer education was a negative predictor for Cd, while no significant associations to any of the trace elements were seen for BMI or use of omega 3 fatty acids/ cod oil supplements by multiple linear regression models (Table 3).

## Discussion

In this group of never-pregnant women of fertile age, age was associated with higher levels of Hg and Sb, but the strongest predictor for Hg status was fish intake, alcohol intake for Pb, use of tobacco for Cd status, while the strongest predictor for Sb was an omnivore diet.

## Strength and limitations

This was an observational study with self-reported clinical data, known to have disadvantages, as highlighted by the discrepancy between reported smoking status and plasma cotinine levels.

**Table 4. Levels of toxic trace elements according to fish intake in healthy never-pregnant women (n = 158).**

Toxic trace elements <sup>a</sup>	Consumption of fish for dinner			P value
	<1 meal/month N = 38	1–3 meals/month N = 34	$\geq 1$ meal/week N = 86	
Whole blood mercury, nmol/L	0.1 (0, 1.1)	4.4 (2.5, 7.1)	7.0 (4.3, 11.0)	<0.001
Whole blood lead, $\mu\text{mol/L}$	0.04 (0.03, 0.06)	0.04 (0.03, 0.05)	0.04 (0.03, 0.05)	0.73
Whole blood cadmium, nmol/L	1.8 (1.2, 2.4)	1.4 (1.1, 2.0)	1.5 (1.2, 2.2)	0.27
Serum antimony, nmol/L	29.4 (27.0, 31.3)	31.2 (27.5, 33.8)	30.0 (27.0, 32.9)	0.33

<sup>a</sup> Median and (IQR) compared by Kruskal-Wallis test

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**Fig 1. The association of alcohol intake in units per week with Pb levels by generalized additive model (GAM), adjusted for age.** The solid line shows the fitted model and the area between the dotted lines indicate 95%.

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However, as we were able to measure plasma cotinine this problem was diminished. This study included women of fertile age, ranging from 18 to 40 years, however, the majority of our population was below 30 years, which disabled us to fully investigate the effect of a more advanced age on toxic trace element status.

### An omnivore versus a vegetarian diet

Published data concerning toxic element status in vegetarians compared to omnivores are somewhat conflicting [28, 35, 36]. In a non-smoking population, vegetarians had higher levels of Cd compared to omnivores [28], and both vegan and vegetarian diets have been proposed to be a risk factor for increasing the level of several toxic trace elements in the body [35]. However, in a Swedish study, a change from a mixed to a lactovegetarian diet for 3 months was associated with lower hair concentrations of mercury, lead, and cadmium [36].

We did not find any difference in Pb and Cd according to diet. An omnivore diet was a predictor for Sb, and the negligible Hg levels we found in our vegetarian population compared to omnivores with a high fish intake, confirms the notion that Hg levels are primarily the result of intake of fish and seafood [27] and therefore reduced in vegetarians.

### Mercury

The level of Hg is reported to increase with age [37], confirmed by our data on women aged 18 to 40 years. Compared to published studies (Table 5), the median Hg value (4.91 nmol/L) in our population was low. Hg levels vary in different populations according to published studies

**Table 5. Concentrations of whole blood mercury, lead, cadmium and serum antimony in different populations.**

Value	Statistical	Number	Year	Sex	Age group	Nationality	Reference
<b>Whole blood mercury, nmol/L</b>							
13.1 (12.3, 13.8)	GM (95% CI)	3531	2008	Female	>20	Korean	[41]
11.47 (1.1, 3.5)	P95 (95% CI)	1229	2012–2013	Mixed	20–79	Canadian	[44]
9.22 (8.43, 10.02)	Mean (95% CI)	123	1997	Female	31	Finnish	[38]
7.98	Median	30	2013	Mixed	Adults < 40 years	Norwegian	[37]
7.93 (3.44, 25.92)	GM (10–95 percentile)	73	2011–2012	Female	18–40	Danish	[43]
6.88 (6.58, 7.23)	Mean (95% CI)	1992	2008–2010	Mixed	20–59	French	[42]
4.91 (0, 19.34)	Median (2.5, 97.5 percentile)	158	2011–2015	Female	18–39	Norwegian	Fløtre et al
4.69	GM	185	2006	Women	18–39	Brazilian	[40]
3.74	Median	1227	2009	Mixed	18–58	Czech	[39]
<b>Whole blood lead, µmol/L</b>							
0.16 (0.15, 0.17)	P95 (95% CI)	3142	2012–2013	Mixed	20–79	Canadian	[44]
0.09 P95 (95% CI)	GM	1992	2008–2010	Mixed	20–59	French	[42]
0.09	Median	30	2013	Mixed	Adults < 40 years	Norwegian	[37]
0.08	GM	158	2006	Female	18–39	Brazilian	[40]
0.07	Median	494	2009	Female	18–58	Czech	[39]
0.05	GM	2892	2007–2010	Mixed	20–39	American	[45]
0.04 (0.02, 0.11)	Median (2.5, 97.5 percentile)	158	2011–2015	Female	18–39	Norwegian	Fløtre et al
0.04 (0.03, 0.08)	GM (10–95 percentile)	73	2011–2012	Female	18–40	Danish	[43]
0.04 (0.04, 0.05)	GM (95% CI)	123	1997	Female	31	Finnish	[38]
<b>Whole blood cadmium, nmol/L</b>							
7.38 (6.40, 8.45)	P95 (95% CI)	2507	2012–2013	Mixed	20–79	Canadian	[44]
3.47 (3.38, 3.65)	GM (95% CI)	1992	2008–2010	Mixed	20–59	French	[42]
2.94	Median	30	2013	Mixed	Adults < 40 years	Norwegian	[37]
2.76	GM	2892	2007–2010	Mixed	20–39	American	[45]
2.67	Median	896	2009	Mixed	18–58 years, non-smokers	Czech	[39]
1.78 (0.63, 6.76]	GM (10–95 percentile)	73	2011–2012	Female	18–40	Danish	[43]
1.53 (0.68, 7.75)	Median (2.5, 97.5 percentile)	158	2011–2015	Female	18–39	Norwegian	Fløtre et al
1.07 (0.89–1.25)	GM (95% CI)	123	1997	Females	31	Finnish	[38]
0.9	GM	185	2006	Females	18–39	Brazilian	[40]
<b>Serum antimony, nmol/L</b>							
30.1 (21.2, 38.7)	Median (2.5, 97.5 percentile)	158	2011–2015	Female	18–39	Norwegian	Fløtre et al
14.78 ± 8.9	GM ± SD	24	2014	Female	23–64	Chinese	[46]

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[37–43] (Table 5). A considerable higher Hg level, geometrical mean (GM) 13.1 nmol/L, was reported in Korean women above 20 years in 2008 [41], while a lower level, median 3.74 nmol/L, was found in a Czech mixed population aged 18–58 years in 2009 [39] (Table 5).



The high level of blood mercury in the Korean study has been explained by a high seafood consumption in this population [41]. Fish consumption is generally high in Norway [47], but the lower median Hg level in our population might be due to a high percentage of vegetarians (22%). Omnivores with a high fish intake had a median Hg level of 7.0 nmol/L, comparable to Danish women of fertile age (geometrical mean (GM) 7.93 nmol/L) [43] (Table 5). Tobacco-users had also lower levels of Hg and conversely a lower intake of fish, compared to non-users of tobacco. Smoking is associated with overall unhealthy behavior, including poor nutrition [48], while eating fish and seafood is considered to be beneficial [49]. According to current Nordic recommendations, Norwegians should have an intake of 300–450 g fish per week, of which at least 200 g should be fatty fish, with no discrimination according to age and sex [50]. Fish provides important nutrients, it is however important to consider the fact that fish is also the most important contributor of Hg, known to have serious negative health effects, even in low doses [3].

## Lead

The median Pb value of 0.04  $\mu\text{mol/L}$  was low in our population and comparable to published data from Nordic female populations [38, 41, 43, 44] (Table 5). Pb levels in premenopausal, non-pregnant women are primarily due to exposures to contaminated food or water [51]. Pb are commonly found in brewed tea [52], reported to be a popular drink among women [53], however, as we did not have any data on tea consumption, we were unable to evaluate this factor. Pb is also commonly found in red wine [54], which corroborate with our finding of alcohol intake being the only significant predictor for Pb level. According to 2014 data from the Norwegian Institute of Public Health, the alcohol consume has increased by approximately 40% in Norway during the last 20 years, particularly among women, who preferably drink wine [55].

## Cadmium

We found a median Cd value of 1.53 nmol/L, which is low compared to other countries (Table 5). As smoking has been associated with higher levels of Cd [25], this finding might be related to a low prevalence of smokers in our population. The use of snuff is becoming increasingly popular in Norway [56], but studies on how use of smokeless tobacco affect toxic element status are difficult to find [57]. We found a 63% higher median Cd level in regular users of tobacco, confirmed by cotinine levels, compared to non-users. The median cadmium level in our non-users of tobacco, 1.51 nmol/L, was about twice as high as the value of Finnish non-smokers aged 31 years, 0.62 nmol/L, while the median level in our current tobacco-users, 2.47 nmol/L, was substantially lower than in the Finnish smokers, 6.04 nmol/L [38].

## Antimony

Our median Sb levels (30.1 nmol/L) was comparable, but higher than in Chinese females aged 23–64 years in a study from 2014, where they found a geometric mean (SD) of 14.78 ( $\pm$  8.9) nmol/L [46] (Table 5). The most significant predictor for Sb in our population was an omnivore diet, followed by age and use of tobacco. Sb has been found in all food groups, with the highest concentrations in dairy products [26]. Sb levels are also reported to be higher in smokers [58], as confirmed by our results.

Occupational exposure in electronic waste recycling was the most important source of Sb in the Chinese population, while dietary exposure was considered to be low [58]. Data on environmental exposure sources of Sb is scarce and further studies are obviously needed. Sb is frequently found in mobile phones [58], a popular electronic article, however, whether the use of mobile phones may contribute to higher serum levels is unknown.



Sb has been reported to cause neurotoxicity, liver and respiratory disease and has been associated with an increased cardiovascular risk [1, 10]. Sb may cross the placenta [1], and is also found in breastmilk [11]. It has been suggested that antimony trioxide may interfere with fetal development [1, 59] and higher concentrations of Sb have been found in cord blood in pregnancies with an adverse outcome [18].

## Implications

Element interactions may amplify the effect of even low dose concentrations of toxic elements [4] and safe limits are considered to be unlikely [60]. As toxic elements tend to bioaccumulate in the body [37, 61], a higher maternal age may have an impact on the burden of environmental toxins transferred to the next generation. However, we find that fish intake, alcohol consumption and use of tobacco, are more important determinants for Hg, Pb and Cd status than age in females from 18 to 40 years.

As the only possible way to protect a fetus is to minimize the exposure of toxic elements in fertile women [62], continuous public actions are needed for reducing these modifiable and preventable sources of potentially deleterious toxins.

## Conclusion

As toxic trace elements tend to bioaccumulate in the body, increasing maternal age at delivery may represent a threat to the next generation. In this study of Norwegian never-pregnant women aged 18 to 40 years, older age was associated with higher levels of Hg and Sb, but the main predictor for Hg levels was fish intake, for Pb alcohol intake, for Cd regular use of tobacco, while an omnivorous diet was the strongest predictor for Sb levels. As these are modifiable and preventable sources of harmful toxic elements in fertile women, public consideration and actions are needed to minimize the potential transfer of toxins to the next generation.

## Supporting information

**S1 Data. Fløtre et al data, containing the data for the study.**  
(XLSX)

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## Author Contributions

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