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Time trends of cadmium, lead and mercury in the population of Northern Sweden 1990-2009 and blood levels of rhodium and platinum in 2009

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Abstract

Background: Knowledge of time trends in burdens of the heavy metals cadmium (Cd), lead (Pb) and mercury (Hg) are important to evaluate effects of preventive actions. This has previously been monitored in northern Sweden in samples from 1990-1999. Alpha-1-microglobuline (A1M) in urine is a potential biomarker of tubular dysfunction, presumed to be effected by body burdens of cadmium. It is unknown if elements from catalytic converters, platinum (Pt), rhodium (Rh) and palladium (Pd), cause human exposure.

Objective: To continue the time trend series of body burdens of Cd, Pb and Hg and to quantify levels of Pt, Rh and Pd and alpha-1-microglobuline in samples from northern Sweden.

Design: Biobanked blood samples from health screenings in the WHO MONICA-project in northern Sweden were analyzed for Cd, Pb and Hg, in two age-groups; 25-35 years and 50-60 years. In 2004, blood samples from 287 women were analysed and in 2009, blood samples from 150 men and 177 women were analyzed. Also, cadmium and A1M were analysed in urine for the 2004 and 2009 participants. Pt, Rh and Pd were analysed in blood for 26 women in ages 55-59 years from the 2009 screening.

Results: There was a decline in blood levels of Pb in both men and women. Blood levels of Cd did not change over time. However, in women, levels of U-Cd were lower in 2009 as compared to 2004, also in never-smokers in the younger age-group. Due to use of erythrocytes in the previous report on data from 1990-99, body burdens of Hg could not be compared to previous data. A decrease from 2004 to 2009 was detected in B-Hg in women in the older age-group. Levels of Pd could not be quantified due to high uncertainty in the analysis. Blood levels of Pt and Rh were at levels of about one thousandth of the heavy metals. Levels of protein A1M in urine could not be compared over time, due to changes in analytical method. Levels of the protein were higher in the older age-group and men had higher levels than women in samples from 2009.

Conclusion: The previously detected decline in body burdens of Pb continued from 1999 to 2009, while there is still no evident change in body burdens of Cd. We cannot evaluate the time trend of Hg body burdens after 1999 with these data. Levels of Pt and Rh are detectable. Surprisingly, men in the older age-group had higher levels than women of protein A1M. For Cd, there are indications of risk of adverse health effects at the reported levels. Efforts to reduce pollution and human exposure to all three heavy metals are important, but this is especially important for cadmium.

Introduction

Cadmium, lead and mercury are heavy metals that are toxic to humans. Exposure to cadmium primarily affects the kidney (tubular dysfunction) and bone tissue (osteoporosis) and may also be associated with oestrogen related cancer (1, 2). Lead can damage the kidney and the central nervous system (3) and mercury is related to damages in the nervous system (4). In addition, cardiovascular diseases have been associated to organic mercury from fish consumption (5, 6). Preventive actions have been conducted in industrialized countries to decrease the environmental exposure of the general population. One example of a preventive action taken in Sweden was the legislation in 1994 against using lead as an additive in petrol. More examples are recommendations from the Swedish National Food Administration on limited consumption of predatory fish species, higher in methylmercury, and the introduction of a special environmental tax on cadmium in fertilizers in the beginning of the 1990´s, to reduce the use of cadmium containing fertilizers. However, this environmental tax was removed in January 2009, despite that the Swedish soils naturally contains Cd and that the European Food Safety Authority (EFSA) recently lowered its recommended maximum weekly intake from 7 µg Cd/kg body weight to 2.5 µg. To evaluate the effects of actions like these, it is of importance to conduct time trend studies.

The main exposure pathways for the general population are; for cadmium via food and smoking; for lead via food and air; and for mercury via fish and dental amalgam (7). Cadmium, lead and organic mercury in blood (B-Cd, B-Pb and B-Hg) are generally associated to erythrocytes, while inorganic mercury may be present in plasma (8). B-Cd and B-Pb reflect current exposure but are affected if the body burdens of these metals are elevated. Cd in urine (U-Cd) reflects body burden, whilst Hg in urine (U-Hg), on the contrary, is more related to recent exposure of inorganic mercury (7). Because of bioaccumulation of Cd (kidney) and Pb (bone tissue), older people have higher concentrations in blood than younger, with an exception of small children (1 to 4 years) who may have the highest B-Pb levels due to an intake of soil and dust (9).

The population of Northern Sweden has previously been monitored between 1990 and 1999 for heavy metals (10). Declining trends for Pb and Hg, which each showed an annual decrease of 5-6% in erythrocytes, were found. No declining trend was detected for Ery-Cd, except for in smoking men.

During recent years the use of automobile catalytic converters has increased environmental contamination with the elements platinum (Pt), rhodium (Rh) and palladium (Pd) (11). Whether this also means human exposure is not yet clear. All three elements are present in blood, which can potentially be used for biomonitoring.

This study continues the work of Wennberg et al. (10), of human exposure to heavy metals in the population of northern Sweden, adding 10 more years, resulting in a time trend study of a total period of 20 years. Also, levels in urine of Cd and alpha-1-microglobuline (A1M), a potential biomarker of tubular dysfunction presumed to be effected by body burdens of Cd, are monitored in samples from 2004 and 2009. The elements Pt, Rh and Pd were measured in samples from 2009.

Materials and Methods

Study population

An invitation to participate in this study was sent to randomly selected women and men from the counties Norrbotten and Västerbotten in Northern Sweden within the population based survey of the general population: WHO MONICA Project (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease). The participants filled in a questionnaire regarding medical history, socioeconomic condition and life style factors such as smoking, drinking and food habits. More information concerning the Monica study is available elsewhere (12). Total participation rate 1990, 1994 and 1999 was 79.2, 76.8 and 72.9%, respectively. The participation rate was 76.2% in 2004 and 69.2% in 2009 (13). In this study, the study population was divided in sub groups of gender and two age groups; "younger" (25-35 years in 1990-2004 and 25-29 in 2009) and "older" (50-60 years in 1990-2004 and 50-59 in 2009). In 2004, only women were studied. In this study, only those in ages 25-35 and 50-60 from the 1990-1999 study (10) were included, to make data comparable with the study persons from 2004 and 2009. The elements Pt, Pd and Rh were analysed in blood in 26 women in ages 55-59 years sampled in 2009. This study was approved by the ethics committee at Umeå University.

Sampling of blood and urine

Blood samples were obtained by venipuncture into Venoject tubes (Terumo, Leuven, Belgium) with lithium-heparin. Erythrocytes and plasma were separated into aliquots and kept

at -80° C in the biobank in Umeå, after centrifugation at 1500g. The tubes were tested for contamination of Cd, Pb and Hg.

Samples of morning urine were collected in paper cups and transferred to acid washed tubes in the surveys conducted in 2004 and 2009. The samples were sent to Lund University for analysis.

Pt, Rh and Pd in blood were analyzed at ALS Scandinavia AB, Luleå, Sweden.

Chemical analysis

Cd, Pb and Hg

All samples from 1990 to 1999 were analysed in one campaign in erythrocytes (Ery-) and presented in a time trend study by Wennberg et al. (10). In the current study the erythrocyte levels have been recalculated to B-Cd and B-Pb using the formula; B-Cd=Ery-Cd×EVF and B-Pb= Ery-Pb×EVF where EVF=42% (0.42) median value (n=295; 2004).

In 2004 and 2009, cadmium, lead and mercury were analysed in whole blood (B-Cd, B-Pb and B-Hg tot). Cd and Pb were analysed using a inductively coupled plasma-mass spectrometer (ICP-MS) (14). The detection limits (LOD), calculated as three times the standard deviation (SD) of the blank for B-Cd, were 0.02 µg/L in 2004 and 0.06 µg/L in 2009. Corresponding levels for B-Pb were 0.04 µg/L and 0.09 µg/L, respectively. LOD in urinary Cd was 0.01 µg/L in both 2004 and 2009. B-Hg was analysed in acid digested samples by cold vapour atomic fluorescence spectrometry (15). The detection limits were 0.07 µg/L and 0.09 µg/L in the samples from 2004 and 2009, respectively. LOD was 0.20 µg/L in the samples from 1990-1999.

For urine samples, density and creatinine were analysed immediately when the samples arrived to Lund, and the samples were then stored frozen until analysis of heavy metals.

A1M

Urine was analysed for alpha-1-microglobulin using the Mancini radial immunodiffusion technique with polyclonal antibodies (DAKO A7S, Glostrup, Denmark) (16). Calibration

curves were established and the limit of detection was 0.9 mg/L in 2004 and 1.2 mg/L in 2009.

Pt, Rh and Pd in blood

Sample preparation consisted of microwave-assisted closed vessel digestion (1mL blood + 1mL sub boiled concentrated nitric acid) at 600W effect for 1 h. At least two method blank samples were prepared with each batch of 38 samples using 1 ml de-ionized water instead of blood. Digests were diluted to 10 mL using distilled, de-ionized water and spiked with internal standard (In) at 2 ppb.

Determination was made by high resolution inductively coupled plasma mass spectrometry [ICP-MS; ELEMENT2 ICP-SFMS equipped with high sensitivity introduction system (X skimmer cone, shielded torch, APEX desolvation nebulizer)]. All measurements were performed in high resolution mode (R=13000), using 80% acquisition window and 40% integration window. Apart from isotopes of analyte elements, potential interfering elements (Cu, Sr, Mo, Ru, Cd) were monitored as well. In order to decrease oxide formation, addition of methane to the ICP was used (17). Instrumental parameters were optimized daily using digested blood matrix. Sensitivity for ^{103}Rh was above 120 counts s^{-1} per ppt and urane oxide formation <5%. For reproducibility assessment, eleven samples were analysed in duplicate.

Accuracy

Cd, Pb and Hg

The analytical accuracy in blood was verified towards certified reference material; Seronorm Trace elements whole blood (SERO AS, Billingstad, Norway) and human blood reference samples from Centre de Toxicologie du Quebec, Canada, International Comparison Programme. Imprecision was calculated as the coefficient of variation for duplicate sample analysis. To check accuracy for B-Cd and B-Pb Seronorm batches; MR4206 (in 2004 and 2009) and 503109 (in 2009) were used and from centre de Toxocologie batch C05-15 (2004 and 2009) and C0912 in 2009. B-Hg was tested towards MR 4206 and 512627 (2004 and 2009)(SERO A/S) and to M0408 (2009) (Quebec). Similarly, for Cd in urine, analytical accuracy was verified towards Seronorm, batch OK4636 (2004 and 2009) and OK0511545 (2009). Further, U-Cd was also verified towards urine samples from Centre de Toxicologie du

Quebec, batch TD0514 (2004 and 2009). All accuracy tests were determined acceptable and within (or slightly below) the recommended range.

B-Cd 2004; imprecision 4.3%. Batch MR4206 and batch C05-15. For Cd, the results (mean± SD) were 0.67±0.03 µg/L (n=17) and 0.73±0.05 µg/L, (n=12), recommended 0.68–0.8l and 0.79±0.23 µg/L, respectively. B-Cd 2009; imprecision 5.4%. Batch MR4206, 503109: 0.70±0.08 µg/L (n=30) and 6.3±0.26 µg/L, (n=27), recommended 0.68–0.8 and 5.6–6.4 µg/L, respectively.

B-Pb 2004; imprecision 2.2%. Batch MR4206: For Pb the result was 26±0.89 µg/L (n=17), recommended 26–29 µg/L. Toxicologie du Quebec (batch QMEAQAS06-08); 103± 2.4 µg/L (n=19), recommended 100± 5.4 µg/L. B-Pb 2009: imprecision 5.8%. Batch MR4206 and 503109: 29.4±3.1 µg/L (n=27) and 408±13 µg/L (n=27), recommended 26–29 and 372–414 µg/L. The results of the human reference samples from Quebec were (batch L0909 and L0807) 24.7±1.02 and 118±2.9 µg/L (n=28), recommended 22.8±1.1 and 110±9.9 µg/L, respectively.

B-Hg 2004; imprecision 8.3%. Batch MR4206 and 512627: 1.9±0.13 µg/L (n=12) and 16±1.4 µg/L (n=14), recommended 2.0–2.4 and 16–20 µg/L. B-Hg 2009; imprecision 5.8%. Batch MR4206 and 512627: 2.2±0.17 µg/L (n=106) and 15.2±1.1 µg/L (n=103), recommended 2.0-2.4 and 16-20 µg/L. Batch M0408: 2.0±0.16 µg/L (n=28), recommended 2.2±0.68 µg/L.

U-Cd 2004; imprecision 5.1%, Batch OK4636; 0.27±0.01 µg/L (n=22), recommended 0.26-0.36 µg/L and batch D0514 0.97±0.08 µg/L, (n=9), recommended 1.1±0.10 µg/L. U-Cd 2009; imprecision 6.12%. Batch OK4636 and 0511545: 0.24±0.02 µg/L (n=19) and 4.0±0.11 µg/L (n=19), recommended 0.26–0.36 and 3.8–5.4 µg/L, respectively.

Concentrations of cadmium and protein A1M in urine was density adjusted to a specific gravity (SG) of 1.015 Kg/L. Creatinine adjustments are commonly used, but creatinine levels in urine have been shown to be more affected by diurnal variation and factors such as age, gender, body size, meat intake than urine density (18, 19).

Pt, Rh and Pd

Data for method blanks were used to calculate limit of detection (LOD; 3 sigma approach)

and limit of quantification (LOQ; 10 sigma approach) (Table 7). It should be stressed that for isotopes severely affected by spectral interferences unresolved in high resolution mode, this may result in overly optimistic assessment of detection capabilities (20). Actual LOD/LOQ will depend on concentrations of interfering elements in the particular sample and on the formation rate of interfering species in the ICP. The use of ICP-SFMS operated in high resolution mode allows interference-free determination of Sr, Mo and Pt isotopes. For Pd and Rh isotopes a significant part of interferences cannot be completely resolved from the analyte signals even in high resolution mode, making thorough mathematical corrections mandatory. Formation rates for interfering signals were determined during each measurement session using digested bovine blood spiked with potentially interfering elements at different levels. Both uncorrected and corrected concentrations were calculated for Pd and Rh isotopes. When the degree of mathematical correction exceeds 50% of the uncorrected value, the accuracy of results can be affected, though one can assume that the actual concentration in a sample is not above the uncorrected concentration (regardless of which isotope gives this lowest value). The uncertainty of low Pd concentrations (<5 ng/L) may be very high which is confirmed by poor reproducibility of duplicate analyses, and data are therefore not included in the present report.

External quality assurance was accompanied by regular participation in Inter-laboratory Comparison Program for trace metals in biological materials (managed by Le Centre de Toxicologie du Quebec, Canada) that includes Mo and Pt determination in whole blood. The majority of ICP-SFMS results reported during the last 8 years were within ±10% of the assigned concentrations. It should be stressed though that Pt concentrations in the test specimens were at least one order of magnitude higher than in the blood samples from the present study. For internal quality control, bovine blood CRM A-13 (IAEA) was used. The material was spiked with Rh, Pd and Pt at two levels in order to provide 5 ng L-1 and 10 ng L-1 concentrations. Spike recoveries were in 98%-102% range for Pt, 92%-98% for Rh and 85-94% for Pd at both concentration levels. Sr and Mo concentrations were in agreement with previously published data for this CRM (21).

Results

For all three heavy metals the older age group had higher levels all over the time series, except for B-Pb in 1990, where younger men had higher levels than older ones. As expected, women were higher in B-Cd and U-Cd and men higher in B-Pb, while there was no clear sex

difference in the levels of mercury (B-Hg or Ery-Hg) (Table 1-3 and Figure 1-2). Smokers were higher in B-Cd, U-Cd and B-Pb, but not in B-Hg (data not shown).

Cadmium

For B-Cd, there were no evident changes over time in any age-group over the time interval 1990-2009 (Table 1 and Figure 1). Interestingly, there was a decrease in U-Cd for women between 2004 and 2009, for the younger women also in never-smokers (Table 1). From 1999 to 2009 the only evident change was an increase in B-Cd in young male never-smokers.

Lead

There was a decrease in B-Pb from 1990 to 2009 in both men and women (Table 2 and Figure 2), and the decrease was also evident from 1999 to 2009. The decrease in B-Pb was present in both age-groups and all smoking-classes, except for in young male current smokers (explained by few smokers in this age-group) (data not shown).

Mercury

Because Ery-Hg cannot be reliably transformed to B-Hg it was not possible to make comparisons over the whole time interval. In women comparisons of B-Hg between 2004 and 2009 was possible. There was a decrease in B-Hg 2004-2009 in women in the older age-group, but not in younger women (Table 3).

A1M

In data from 2009, the older age-group had higher levels of A1M in both men and women, and men had a higher median level compared to women, but only in the older age-group (Table 5).

Pt, Rh and Pd

Median and highest levels of Pt and Rh in 26 females sampled in 2009 are presented in Table 4. Levels of Pd was measured, but are not presented; because it is hard to find interference free isotopes we cannot interpret the data.

Discussion

The evident decrease in body burdens of lead over time, previously shown 1990-1999 in northern Sweden (10), was continued during the first decade of the 21th century. The continuing decrease is probably still an effect of the ban of lead as an additive in petrol 1994.

No decrease in B-Cd was found over time. The main sources of cadmium for the non-smoking, non-occupationally exposed population are vegetable food, which are estimated to contribute to 83% of the total intake of Cd via food (bread 36%, potatoes and roots 24% and vegetables 8.4% (22), that is foods that are healthy to eat for other reasons.

Comparing women in Northern Sweden with the women in southern Sweden, the levels of Cd in both blood and urine are lower in Northern Sweden (23). Yet, there are health effects also at these levels found in northern Sweden. This emphasizes the importance of efforts to decrease the smoking rate in the population to improve human health, and also of efforts to decrease the pollution with cadmium ending up in otherwise healthy foods.

For body burdens of mercury, it is not possible to follow a time serie from 1990-2009, because of measurements in erythrocytes 1990-99 and whole-blood 2004-2009. An evident decrease in Ery-Hg was previously shown in northern Sweden 1990-99 (10). However, in older women there was a decrease in B-Hg also between 2004 and 2009.

Due to a change in the analytical method for U-A1M between the sampled years, the U-A1M levels in women sampled 2004 cannot be directly compared to levels in samples from 2009.

In conclusion, there is a continuing decrease in Pb levels in northern Sweden whilst we cannot for sure say that there has been a decrease in levels of Hg since 1999. The levels of cadmium in the general population do not seem to have decreased since 1990. The levels of Pb and Hg in the studied population are regarded as safe, but for Cd, there are indications of risk of effects on kidney, bone and oestrogen related cancer at present levels (1, 24). Hence, it is of importance that efforts to reduce exposure to heavy metals of the general population are continued, especially for cadmium. Levels of Pt and Rh cannot be compared over time, because measurements over the LOD were only achieved in samples from 2009. However, the levels are in ng/L; that is about one thousandth of the heavy metal levels. As for A1M, the levels were higher in the older age-group, and in the older age-group men had higher levels than women.

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Table 1. Median levels of cadmium in blood and urine (density adjusted to a specific gravity) in men and women in age-group 25-35 years or 50-60 years in 1990-2009. Data are presented for all participants and for never-smokers.

	Men						Women				
	1990 (min-max)	1994 (min-max)	1999 (min-max)	2004	2009 (min-max)		1990 (min-max)	1994 (min-max)	1999 (min-max)	2004 (min-max)	2009 (min-max)
B-Cd (µg/L)											
25-35 years											
All	0.130 (0.02-2.87) N=26	0.078 (0.02-2.21) N=24	0.084 (0.02-0.67) N=25	-	0.110 (0.04-1.77) N=68		0.206 (0.07-2.97) N=25	0.143 (0-1.73) N=25	0.116 (0.06-1.60) N=24	0.156 (0.07-2.95) N=164	0.135 (0.05-3.39) N=91
Never-smokers	0.103 (0.02-0.24) N=16	0.069 (0.02-0.16) N=20	0.076 (0.02-0.12) N=17	-	0.105 (0.04-0.41) N=57		0.134 (0.07-0.26) N=12	0.122 (0-0.29) N=15	0.097 (0.06-0.22) N=13	0.136 (0.07-0.42) N=111	0.121 (0.05-0.42) N=64
50-60 years											
All	0.172 (0.05-3.08) N=25	0.218 (0.08-2.13) N=15	0.214 (0.04-0.74) N=25	-	0.162 (0.05-4.32) N=82		0.244 (0.06-2.69) N=29	0.248 (0.15-1.47) N=24	0.384 (0.09-1.85) N=24	0.263 (0.09-1.97) N=123	0.244 (0.08-2.59) N=86
Never-smokers	0.103 (0.05-0.21) N=8	0.189 (0.14-0.66) N=3	0.160 (0.04-0.24) N=7	-	0.122 (0.05-0.43) N=32		0.231 (0.10-0.45) N=15	0.195 (0.15-0.33) N=8	0.227 (0.09-0.64) N=12	0.227 (0.09-0.67) N=54	0.199 (0.08-0.54) N=35
U-Cd SG (g/ml)†											
25-35 years											
All	-	-	-	-	0.064 (0.01-0.44) N=64		-	-	-	0.113 (0.03-0.53) N=158	0.091 (0.03-0.41) N=87
Never-smokers	-	-	-	-	0.064 (0.01-0.34) N=54		-	-	-	0.098 (0.03-0.41) N=108	0.088 (0.03-0.41) N=61
50-60 years											
All	-	-	-	-	0.130 (0.03-1.09) N=84		-	-	-	0.218 (0.06-1.22) N=121	0.189 (0.03-0.84) N=85
Never-smokers	-	-	-	-	0.097 (0.03-0.46) N=33		-	-	-	0.181 (0.06-0.78) N=52	0.114 (0.03-0.55) N=35

† Density adjusted to a specific gravity (SG) of 1.015 Kg/L

Table 2. Median levels of lead in blood in men and women in age-group 25-35 or 50-60 years in 1990-2009. Data are presented for all participants and for never-smokers.

	Men						Women				
	1990 (min-max)	1994 (min-max)	1999 (min-max)	2004	2009 (min-max)		1990 (min-max)	1994 (min-max)	1999 (min-max)	2004 (min-max)	2009 (min-max)
B-Pb (µg/L)											
25-35 years											
All	38.1 (15.5-112) N=26	23.9 (6.14-56.3) N=25	17.6 (8.89-190) N=25	-	11.0 (3.49-35.6) N=68		20.0 (10.3-48.2) N=25	14.9 (7.90-37.0) N=25	12.8 (6.67-315) N=24	10.5 (4.85-70.0) N=164	7.66 (3.29-88.2) N=91
Never-smokers	38.1 (15.5-112) N=16	25.1 (6.14-56.3) N=20	15.7 (8.92-82.5) N=17	-	10.8 (3.49-35.6) N=57		19.6 (10.5-36.4) N=12	16.4 (9.69-37.0) N=15	11.2 (6.67-18.1) N=13	10.8 (4.85-70.0) N=111	7.45 (3.29-25.4) N=64
50-60 years											
All	31.1 (16.2-68.6) N=25	39.8 (11.3-98.4) N=15	24.1 (12.6-48.1) N=25	-	13.3 (4.78-42.0) N=82		24.4 (5.47-47.9) N=29	22.5 (8.95-48.8) N=24	17.0 (4.44-49.4) N=24	14.8 (5.95-60.2) N=123	12.8 (5.45-61.0) N=86
Never-smokers	30.4 (16.2-62.8) N=8	16.1 (11.3-39.8) N=3	20.8 (13.0-41.6) N=7	-	11.6 (6.04-35.2) N=32		20.1 (5.47-47.9) N=15	16.9 (12.0-48.8) N=8	16.6 (4.44-49.4) N=12	14.4 (5.95-44.6) N=54	11.8 (5.90-32.5) N=35

Table 3. Median levels of mercury in blood in men and women in age-group 25-35 or 50-60 years in 2004 (women only) and 2009. Data are presented for all participants and for never-smokers.

	Men						Women				
	1990 (min-max)	1994 (min-max)	1999 (min-max)	2004	2009 (min-max)		1990 (min-max)	1994 (min-max)	1999 (min-max)	2004 (min-max)	2009 (min-max)
B-Hg (µg/L)											
25-35 years											
All	-	-	-	-	0.624 (0.06-3.61) N=68		-	-	-	0.778 (0.04-2.70) N=164	0.754 (0.06-4.14) N=91
Never-smokers	-	-	-	-	0.625 (0.06-3.61) N=57		-	-	-	0.755 (0.04-2.70) N=111	0.826 (0.06-4.14) N=64
50-60 years											
All	-	-	-	-	1.14 (0.12-5.35) N=82		-	-	-	1.45 (0.04-7.12) N=123	1.29 (0.21-6.35) N=86
Never-smokers	-	-	-	-	1.55 (0.35-5.35) N=32		-	-	-	1.63 (0.28-7.12) N=54	1.25 (0.43-3.04) N=35

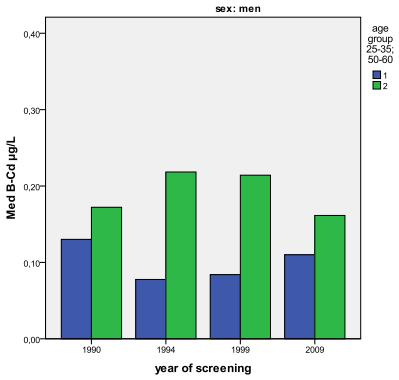
Table 4. Median blood levels of rhodium (Rh) and platinum (Pt) in 26 women 55-59 years in northern Sweden, sampled in 2009.

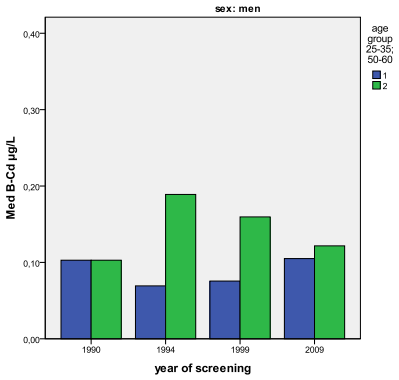
	Median (min-max)
Rhodium (ng/L)	0.650 (<0.4-2.20)
Platinum (ng/L)	1.35 (<0.6-5.20)

Table 5. Median levels (mg/L) of alpha-1-microglobulin (density adjusted to a specific gravity) in men and women sampled in 2004 or 2009*

	Men		Women	
	2004 Median (min-max)	2009 Median (min-max)	2004 Median (min-max)	2009 Median (min-max)
25-35 years				
All	-	1.99 (0.41-5.00) N=64	1.03 (0.24-7.08) N=157	1.92 (0.27-7.50) N=89
Never-smokers	-	2.00 (0.41-5.00) N=54	1.03 (0.28-7.08) N=107	1.93 (0.27-7.50) N=63
50-60 years				
All	-	3.23 (0.88-9.24) N=84	1.10 (0.24-7.95) N=121	2.29 (0.39-15.6) N=87
Never-smokers	-	2.95 (1.04-5.40) N=33	1.09 (0.43-2.94) N=52	2.10 (0.39-4.15) N=36

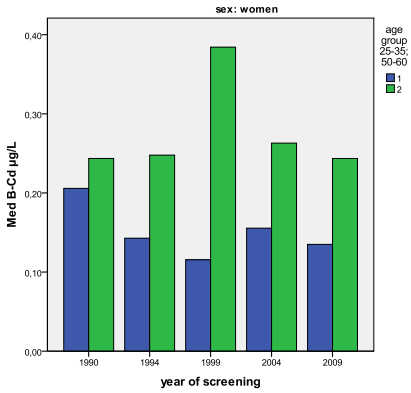
* Due to a change in the analytical method for U-A1M between the sampled years, the U-A1M levels in women sampled 2004 cannot be directly compared to levels in samples from 2009.

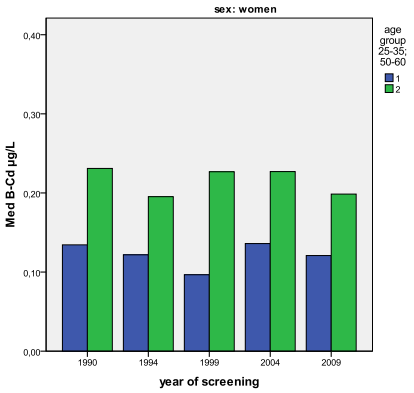




All Never-smokers

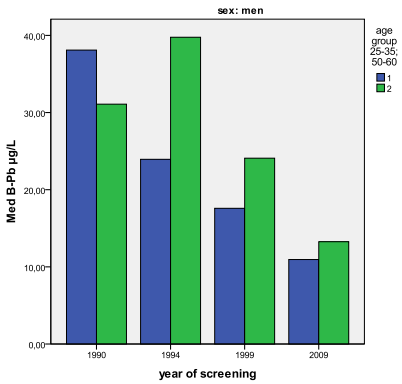
Figure 1a. Time trends in levels of cadmium in blood in men in age-group 25-35 years and 50-60 years, in all subjects and never-smokers

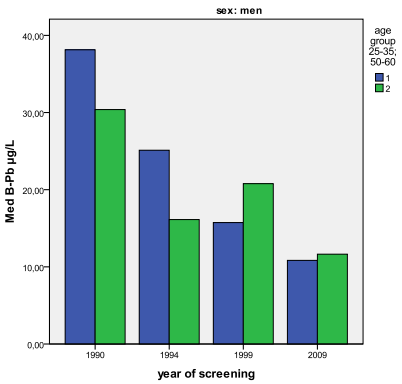




All Never-smokers

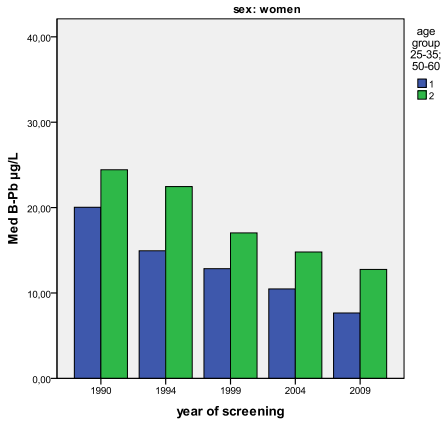
Figure 1b. Time trends in levels of cadmium in blood in women in age-group 25-35 years and 50-60 years, in all subjects and never-smokers

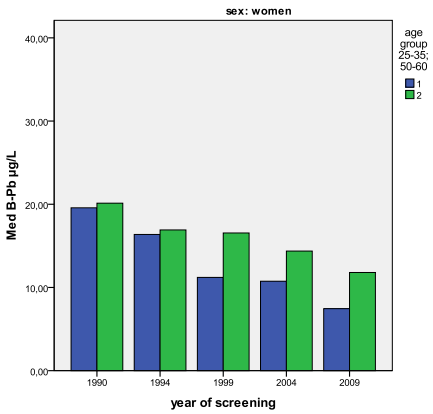




All Never-smokers

Figure 2a. Time trends in levels of lead in blood in men in age-group 25-35 years and 50-60 years, in all subjects and never-smokers





All Never-smokers

Figure 2b. Time trends in levels of lead in blood in women in age-group 25-35 years and 50-60 years, in all subjects and never-smokers