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Assessment of dietary cadmium exposure in Sweden and population health concern including scenario analysis

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ABSTRACT

The median dietary cadmium exposure for adults in Sweden is around 1 μg/kg/week and the upper 95th and 99th percentiles are 1.6–1.8 and 1.9–2.2 μg/kg/week, respectively. Potatoes and wheat flour were the most important food categories, contributing with 40–50% to the exposure. Differences in dietary patterns between high and low exposed individuals were observed; for high exposed individuals, seafood and spinach contributed with an exposure similar to that low exposed individuals received from potatoes and wheat flour. Consequences of differences in methodology used for exposure assessment are discussed. The median exposure is a factor 2 lower compared to that estimated by the European Food Safety Authority (EFSA). It is also a factor 1.4 lower compared to that of the assessment used for development of the EFSA tolerable weekly intake (TWI). The potential importance of this latter fact was addressed by adjusting the present assessment to that used for TWI derivation. While the percentage of the population exceeding the TWI was <1% for the present data, it was around 3% for adjusted data, which is more in line with observations at the level of urinary cadmium. Scenario analysis was also performed to addresses the consequence of increasing/decreasing cadmium occurrence levels.

1. Introduction

Cadmium is a heavy metal found in the environment, both through natural occurrence and from industrial and agricultural sources. Non-ferrous metal mining and refining, manufacture and application of phosphate fertilizers, fossil fuel combustion, and waste incineration and disposal are the main anthropogenic sources of cadmium in the environment (ATSDR, 2008). Food is the major source of cadmium exposure for non-smokers (WHO/IPCS, 1992). High cadmium concentrations can e.g. be found in offal products such as liver and kidney, certain wild mushrooms, and shellfish (Jorhem et al., 1994, 1984). Foods from plants generally contain higher concentrations of cadmium than meat, egg, milk and dairy products, and fish muscle (Järup and Åkesson, 2009). He and Singh (1994) reported that, for plants grown in the same soil, accumulation of cadmium decreased in the order: leafy vegetables > root vegetables > grain crops. According to Swedish data, cadmium concentrations in ambient air are generally low and contribute, on average, to only about 1% of the total absorbed dose of cadmium (Vahter et al., 1991).

Cadmium accumulates mainly in the kidneys with a biological half-life of around 10–30 years (Järup and Åkesson, 2009). The cadmium concentration in the kidney is reflected in the urine. Because of this, the urinary cadmium concentration can be used as a marker of long-term exposure (Nordberg et al., 2007). In 2009, the European Food Safety Authority (EFSA) performed a risk assessment of cadmium (EFSA, 2009), and they established a tolerable weekly intake (TWI) of 2.5 μg cadmium per kilo bodyweight. A tolerable intake is the estimated maximum amount of an agent, expressed on a body mass basis, to which each individual in a (sub)population may be exposed over a specified period (weekly in this case) without appreciable risk. The term "tolerable" is used for agents that or not deliberately added (e.g. contaminants like cadmium) while the term "acceptable intake", which has the same interpretation, is typically used for food additives and pesticides (WHO/IPCS, 2004).

An increased excretion of the kidney marker, beta-2-microglobulin was used as the critical endpoint in the EFSA cadmium risk assessment. Based on a meta-analysis of epidemiological data using the benchmark dose approach, a critical cadmium concentration in urine of 1 μg/g creatinine was established as the reference point. The TWI was then developed by toxicokinetic modelling using data on 680 Swedish never-smoking women (56–70 years of age) living in the town of Uppsala and part of the Swedish Mammography Cohort (Amzal et al., 2009). The urinary cadmium concentration resulting from a long-term dietary cadmium intake

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of 2.5 μg/kg b.w. per week (the TWI), was estimated to be lower than the critical concentration of 1 μg/g for 95% of the population.

Using the same epidemiological dataset, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) established a provisional tolerable monthly intake of 25 μg/kg b.w. (FAO/WHO, 2010). If expressed on a weekly basis, this value is about twice as high compared to the EFSA TWI. As a consequence, EFSA was asked by the European Commission to confirm their TWI. A number of methodological differences in the derivation of the respective guidance values were identified. Following this evaluation, the EFSA concluded that the approach they had adopted was appropriate and their TWI (2.5 μg/kg b.w./week) was maintained in order to ensure a high level of protection of consumers (EFSA, 2011).

EFSA has also conducted dietary exposure assessments based on consumption data in the EFSA's Concise European Food Consumption Database and occurrence data (from 2003–2007) reported by the Member States (EFSA, 2009). The mean exposure to cadmium in food was estimated to be 1.89–2.96 μg/kg b.w./week for the different Member States, and "high exposure" was estimated to be 2.54–3.91 μg/kg b.w./week. These estimates are in the range of, or slightly exceeding, the TWI. The EFSA estimated that subgroups such as vegetarians, children, smokers, and people living in highly contaminated areas may exceed the TWI by about 2-fold. They suggested that the risk for adverse effects on the kidney function at an individual level, associated with the dietary exposures across Europe, is very low, but concluded that the current exposure to cadmium at the population level should be reduced (EFSA, 2009).

In this paper, a detailed dietary exposure assessment for cadmium is performed for the Swedish adult population. The objectives were (1) to provide a refined exposure assessment at national level including analysis of the level of population health concern associated with dietary cadmium, (2) perform detailed analysis of the contribution of different food categories to the total dietary cadmium exposure, (3) compare the results to other exposure assessments directed toward analysis of similar populations, and (4) assess statistical uncertainties and perform scenario analysis for illustrating the consequences of increasing or decreasing cadmium occurrence levels in foods.

2. Materials and methods

2.1. Consumption and occurrence data

The data used as basis for this assessment are presented in Table 1. Data from the food consumption survey conducted by the National Food Agency in collaboration with the Swedish Statistical Agency on adults in 1997–1998 (Riksmaten 97–98) was used (Becker and Pearson, 2002). Riksmaten 97–98 is based on a 7-day dietary record, and consumption data is available for 1211 adult Swedish individuals between 17 and 80 years of age. The study population was systematically selected from the national population registry, which guarantees an even geographical distribution of the study population. Participants recorded their daily food consumption during seven consecutive days starting at different time points during a 12 month period. Food frequency questionnaire have also been used as a compliment for certain food products; e.g. to better facilitate stratification of total fish consumption with regard to different types of fish. The consumption data from Riksmaten 97–98 was herein stratified into 31 food categories with subgroups for certain categories (a total of 48 food groups).

Data from the National Food Agency was also used regarding the occurrence of cadmium in different food items. This data was collected as part of the Swedish national monitoring programs or Swedish market basket surveys between the years of 1999–2008. Parts of this data have been published in scientific literature (Becker et al., 2011). Since this assessment concerns chronic exposure, a mean cadmium occurrence level was established with regard to each food category (Table 1).

2.2. General exposure assessment

The body weight adjusted weekly dietary cadmium exposure for an individual, I_i (μg/kg b.w./week), is given by:

$$I_i = 7 \times \frac{\sum_{j=1}^{g} copt_{ij} \times conc_j}{bw_i}, \quad (1)$$

where g in the number of food categories; $copt_{ij}$ is the i'th individuals (average) consumption in grams per day of food category j; $conc_j$ is the mean cadmium occurrence level in mg/kg with regard food category j; and where bw_i is the reported body weight for the i'th individual. Individuals with missing values in any food category, or missing information regarding body weight, were excluded; I was thus calculated for a total of 1160 individuals. In the calculation of $conc_j$, concentration values below the limit of detection (LOD) for individual samples were set to half the LOD. A log-normal distribution was fitted to I and the median (geometric mean), 1st, 5th, 95th, and 99th percentiles were estimated.

The contribution of each food category (nr. 1–31 N, Table 1) to the total exposure (I) was also calculated. Three "exposure groups" were here defined; the 90–99th percentile ("high exposed group"), the 45–55th percentile ("moderate exposed group"), and the 1st–10th percentile ("low exposed group"). For each of the three "exposure groups" the mean percent contribution each food category had to the mean total exposure was calculated as well as the corresponding mean dietary exposure (μg/kg b.w./week).

2.2.1. Comparison with the EFSA exposure assessment

The discrepancy between the present exposure assessment and that conducted in 2009 by EFSA for Sweden was investigated. At the time of the EFSA assessment, data in the EFSA Concise European Food Consumption Database for Sweden corresponded to the data from Riksmaten 97–98, that was also used in this assessment. Cadmium (mean) concentrations used by EFSA (2009) for each food category in the Concise Database are based on a compilation of data reported from the Member States, taking into account the period from 2003 to 2007. EFSA reported a mean dietary exposure for Sweden of 2.3 μg/kg b.w./week (EFSA, 2009). This value was calculated using consumption data for consumers only in each food category, and assuming a standard body weight of 60 kg (Table 2).

In the Concise Database, data from Riksmaten 97–98 was aggregated into 15 broad food categories, compared to the 31 categories, with subgroups considered in this assessment. Besides different levels of stratification, there are also a few other discrepancies between the consumption datasets. The category "Cereals" in the Concise Database corresponds to the consumption of bread, porridge and gruel, breakfast cereals and muesli, buns, cakes and biscuits, pancakes, crepes, pie and pizza, pasta, and rice reported in Riksmaten 97–98. In the present assessment, rice as well as breakfast cereals and muesli, were separate categories, and data on the remaining products were divided into three categories and expressed in terms of wheat flour, rye flour, and rolled oats. The latter foods are expressed as raw ingredient, i.e. amount of flour/grain, whereas in the Concise Database they are expressed "as consumed", i.e. as prepared. Also, in the Concise Database the category "Miscellaneous" consists of spices, salt, vinegar, certain type of sauce, and sweet soups reported in Riksmaten 97–98. The consumption of these products was excluded in the present assessment since their contribution to the cadmium exposure was considered negligible.

Using the EFSA Concise Database, and considering consumers only in each food category, a comparison between the estimated exposure resulting from application of the EFSA occurrence levels and those used as a basis for the present assessment was conducted. Because this comparison was performed under the EFSA stratification of the consumption data, the occurrence means used in this assessment (Table 1) needed to be adjusted, since a given category in the Concise Database in several instances corresponded to the sum of several food categories as defined in this assessment. Occurrence means were adjusted, by considering the relative level of consumption of the food categories that added up to a single category in the Concise Database. For example, the category "Meat" in the Concise Database represents the sum of three categories in the present assessment; "meat, poultry and dishes", offal", and "sausage", and the relative consumption in Riksmaten 97–98 of these categories was, on average, 0.77, 0.03, and 0.20, respectively. The adjusted mean occurrence level for "Meat" was then calculated as $(0.77 \times 0.0024) + (0.03 \times 0.0181) + (0.20 \times 0.0015) = 0.0027$ mg/kg. Table 2 summarize the mean occurrence levels used in the EFSA assessment and those resulting for data used in the present assessment after adjustment.

2.3. Uncertainty and scenario analysis

An approach for uncertainty analysis was implemented in Matlab (version 7.4). This approach is described below and it was also used as part of the analysis described in Sections 2.3.1 and 2.3.2:

(1) A non-paramteric bootstrap sample was drawn with replacement from the consumption data matrix consisting of 1160 individuals.
(2) From the occurrence data matrix, a non-parametric bootstrap sample was drawn with replacement with regard to each food category. A mean cadmium concentration level was then calculated with regard to each food category. Concentration values below the LOD for individual samples were set to half the LOD, but the impact of setting these values to zero or the LOD, respectively, was also assessed.
(3) The total exposure, I_i, was calculated for all 1160 individuals according to equation (1). The median, the upper 95 and 99th percentiles, and the percent of the population exceeding the TWI of 2.5 μg/kg b.w. was estimated by a log-normal model .

Table 1
Summary of the different food categories and Cd occurrence data used for dietary exposure assessment.

Consumption data (Riksmaten 1997–1998)	Occurrence data			
	Description[a]	Year	Mean[b] (mg Cd/kg)	No. of samples
1: Fats	Market basket: butter, margarine, cooking oil, mayonnaise	1999	0.0015 (0–0.0031)	8
2: Cheese	Cheese Soft cheese Curd (cottage) cheese	2000 2005 2004	0.0015	3
3: Milk, soured milk, yoghurt	Full milk	2008	0.001 (0–0.002)	10
4: Potatoes	Potatoes 22 different brands	2007, 2008	0.017	52
5: Root vegetables and meals	Carrot	2007, 2008	0.019	48
6 A: Vegetables and meals	Market basket: vegetables and root vegetables; fresh, frozen, and canned products	1999	0.0073	8
6 B: Spinach	Spinach	2005	0.14	8
7: Fruit and berries	Market basket: fresh, frozen, and canned fruit products, juice, nuts, cordials, and jam	1999	0.0008 (0.0006–0.001)	8
8: Juice	Juice	2005	0.0011 (0.0009–0.0013)	5
9: Breakfast cereals, muesli	Cornflakes Rolled oats	2005	0.013	16
10: Rice	Rice Basmati rice Jasmine rice	2005, 2007, 2008	0.020	63
11: Wheat flour All wheat flour in Riksmaten	Wheat flour	2005, 2006, 2007	0.028	21
12: Rye flour All rye flour in Riksmaten	Rye flour	2005, 2006, 2007	0.014	18
13: Rolled oats All porridge oat in Riksmaten, mainly from porridge	Rolled oats	2005	0.024	8
14: Legumes and meals	Yellow peas	2005	0.0051	8
15: Meat, poultry, and meals	Market basket: beef, pork, lamb, poultry, cured/processed meat	1999	0.0024	8
16: Eggs	Eggs conventional/ecological	2007	0.0002 (0–0.0004)	8
17: Offal	Liver paste	2004	0.018	1
18: Sausage	Sausage 6 different types	2004–2005	0.0015 (0.0015–0.0016)	8
19: Snacks Potato crisps, cheese doodles, nuts	Potato crisps flavoured, light	2002	0.036	2
20: Popcorn	Popcorn, popped	2002	0.011	1
21: Ice cream	Market basket: Ice cream, frozen	1999	0.0018 (0.0015–0.002)	2
22: Cream	Cream Whipped cream Creme fraich	2005	0.0012 (0.0012–0.0013)	3
23: Soft drinks, fruit syrup, table drinks	Market basket: Soft drinks, mineral water, light lager, medium-strong beer (2.1–3,5% alcohol)	1999	0.0002 (0–0.0004)	8
24 A: Chocolate	Milk chocolate Dark chocolate Filled chocolate	2005	0.039	4
24 B: Chocolate cracker	Chocolate cracker	2002	0.01	1
24 C: Caramel	Chocolate caramel		0.017	1
24 D: Chocolate drink (milk based)	Chocolate powder	2005	0.0011[c]	8
25: Sugar, honey, syrup	Honey	2003	0.0011 (0.0008–0.0014)	20
26: Alcohol	Red wine White wine Strong beer Vodka Gin Whiskey	2004	0.0005 (0–0.0009)	10
27: Coffee	Coffee powder	2003–2007	0.0004[d]	544
28: Tea	Tea powder	2003–2007	0.0003[e]	816
29: Tap water	Tap water	2003–2007	0.0004[f]	19000
30: Mineral water	Bottled water	2003–2007	0.0004[f]	2448

Table 1 (*continued*)

Consumption data (Riksmaten 1997–1998)	Occurrence data			
	Description[a]	Year	Mean[b] (mg Cd/kg)	No. of samples
31 A: Cod etc. cod, coalfish, haddock, whiting, hake (fresh, frozen)	Cod (muscle) Haddock (muscle) Atlantic halibut (muscle)	2005	0.0045	19
31 B: Other Atlantic fish e.g. plaice, mackerel, turbot, common sole	Plaice (muscle) Mackerel (muscle)	2001	0.0021	39
31 C: Canned fish e.g. tuna, pickled herring, pilchard, mackerel	Canned tuna (muscle)	2005	0.023	8
31 D: Fish meals fish fingers, fish buns, fish au gratin	Cod (muscle)	2005	0.0068	8
31 E: Herring, buckling Smoked herring from Baltic Sea, and the west cost	Herring (muscle)	2001	0.0029	20
31 F: Atlantic salmon and trout from Baltic Sea, Pacific Ocean	Salmon (muscle)	2001	0.0006 (0.0005–0.0007)	24
31 G: Other salmon farmed salmon, trout, rainbow trout, char, whitefish	Farmed salmon (muscle)	2001	0.0008 (0.0007–0.0008)	10
31 H: Lean fish pike, perch, pike-perch, burbot	Pike (muscle) Perch (muscle) Pike-perch (muscle)	2005	0.010	7
31 I: Eel cocked, fried, smoked	Eel (muscle)	2001	0.0012	14
31 J: Caviar caviar, roe	Caviar (lean)	2004	0.0042	1
31 K: Fish liver from cod or burbot	Herring liver	2001	0.66	20
31 L: Seafood mainly shrimp, mussel, and crab	Shrimp (muscle) Mussel (fresh/canned) Crab (claw)	2001 2005 2009	0.14	3 9 10
31 M: Seafood from salad	Shrimp (muscle) Mussel (fresh/canned) Crab (claw)	2001 2005 2009	0.17	3 9 10
31 N: Shrimp In addition to that in 31 L and 31 M	Shrimp (muscle)	2001	0.008	3

[a] Market basket mean occurrence levels are the mean of concentrations resulting for a weighted mixture consisting of the products mostly consumed in the food category. When two or more specific food items instead have been used as basis for the reported mean occurrence level for the whole food category, they have each been given the same weight, with the following exceptions: For category 31 L and 31 M, different scenarios (case A, B, and C below) regarding the relative consumption of shrimp, mussel, and crab has been used to derive weighted mean occurrence levels. Case A is based on data from the Swedish Board of Agriculture and Case B and C is based on recipes for sea food salad from the Swedish National Food Agency. Case A: 77% shrimps, 15% mussel, 8% crab. Case B: 60% shrimps, 20% mussel, 20% crab. Case C: 50% shrimps, 30% mussel, 20% crab. For category 31L, all three cases were used in the uncertainty analysis. The mean of Case A, B, and C is given in Table 1, which was used for the general exposure assessment. For category 31 M, Case B and C were used in the uncertainty analysis. The mean of Case B and C is given in Table 1, which was used for the general exposure assessment.

[b] Mean occurrence levels have been calculated by setting concentration values (for individual samples) that are below the limit of detection (LOD) equal to 0.5 * LOD. A range for the mean occurrence is also given when the mean, obtained by setting the individual values below the LOD equal to zero, differed to the mean obtained by setting the same values equal to the LOD.

[c] The occurrence level in chocolate powder has been re-calculated to liquid product: 13.5 g powder per 0.2 L chocolate drink.

[d] The occurrence level in coffee powder has been re-calculated to liquid product: 7 g powder per 0.15 L coffee. Mean occurrence for powder is taken from EFSA (2009).

[e] The occurrence level in tea powder has been re-calculated to liquid product: 2 g powder per 0.2 L tea. Mean occurrence for powder is taken from EFSA (2009).

[f] Mean occurrence is taken from EFSA (2009).

(4) The process described under bullets 1–3 was repeated 1000 times.
(5) A 90% confidence interval was calculated for the median, the upper 95th and 99th percentiles, and the percent of the population exceeding the TWI.

2.3.1. Extended comparison between estimated exposures and the EFSA TWI

Besides directly comparing exposure estimates resulting from the present assessment with the EFSA TWI, such comparison were also performed after that exposure estimates had been adjusted with respect to those used in the process of TWI development. EFSA determined the critical level in urine to 1 μg/g creatinine, and the TWI was then established by toxicokinetic modelling. Estimates of dietary exposure in Amzal et al. (2009) were used in this process, and these estimates differ from the results in this assessment. Differences in estimates of dietary exposure between assessments will, considering all else equal, impact on the TWI development performed by EFSA.

In Amzal et al. (2009), the median dietary cadmium exposure for Swedish never-smoking women (56–70 years of age) was estimated to 1.4 μg/kg/week. According to the present assessment, the median dietary cadmium exposure for adults (males and females, 17–80 years of age) in Sweden is in the range of 1 μg/kg/week (Fig. 1); results were similar for both males and females (data not shown). The variability in exposure appeared to be similar between this and the Amzal et al. (2009) assessments; in each assessment the ratio between the 95 and 5th percentiles of exposure was approximately a factor 3, and the ratio between the 99th and 1st percentiles of exposure was approximately a factor 5 (Fig. 1, Amzal et al., 2009); and personal communication with Agneta Åkesson). Thus, it seems mainly to be a systematic difference between the two assessments (i.e. approximately difference of a factor 1.4).

An extended comparison with the EFSA TWI was performed after adjusting the present assessment by multiplying estimated exposures with a factor 1.4. Observe that this analysis focuses only on the potential consequence of a systematic and methodologically related difference in estimated dietary exposure with respect to the margin to the TWI. The analysis does not consider other parameters that may influence the TWI estimate itself and/or the margin to the TWI, and which may also differ between the two populations discussed. For example, the participants in Riksmaten 1997–1998 are less homogenous compared to the group of women in Amzal et al. (2009), which in addition may influence the TWI development performed by EFSA.

2.3.2. Scenario analysis

The consequence of increasing and decreasing cadmium occurrence levels was also evaluated. Exposure estimates for the median and the 95th percentile was derived for changes in cadmium occurrence, in the range of 0.5 to 1.5 times the base line concentration. For a given scenario, all individual concentration values for a selected food group were adjusted with a factor in the range of 0.5–1.5. The relationship between the factor change of cadmium occurrence in selected food groups, and the dietary exposure, as well as the percent of population exceeding the TWI, was established.

Table 2
Mean cadmium occurrence levels based on European and Swedish data and the corresponding estimated dietary cadmium exposure.

Food category (Concise European Food Consumption Database)	EFSA occurrence means[a] (mg Cd/kg)	Swedish occurrence means[b] (mg Cd/kg)	Mean dietary cadmium exposure (μg/kg b.w./week) Using European occurrence data and a standard b.w. = 60 kg	Median dietary cadmium exposure (μg/kg b.w./week)	
				Using European occurrence data and reported b.w.	Using Swedish occurrence data and reported b.w.
1: Cereals	0.0163	–[c]	0.56	0.44	0.34
2: Sugar	0.0264	0.011	0.094	0.063	0.025
3: Fats	0.0062	0.0015	0.018	0.012	0.0029
4: Vegetables	0.0189	0.011	0.26	0.19	0.11
5: Potatoes	0.0209	0.017	0.35	0.26	0.22
6: Fruit	0.0039	0.0008	0.063	0.043	0.0088
7: Juice and soft drinks	0.001	0.0005	0.040	0.026	0.013
8: Coffee and tea	0.0018	0.0004	0.13	0.098	0.021
9: Alcohol	0.0042	0.0005	0.12	0.074	0.0088
10: Meat[e]	0.0165	0.0027	0.29	0.23	0.037
11: Fish and seafood	0.0268	0.027	0.12	0.084	0.085
12: Eggs	0.003	0.0002	0.0078	0.0051	0.00034
13: Milk and diary products	0.0039	0.0011	0.18	0.13	0.036
14: Miscellaneous	0.0244	-[d]	0.066	0.036	-
15: Tap water	0.0004	0.0004	0.027	0.018	0.018
Sum	–	–	2.3	1.7	0.93

Note: Estimated dietary exposures are based on consumption data from the Concise European Food Consumption Database (consumers only) combined with the European or Swedish occurrence means. An exception is the category, "Cereals", for which the median exposure resulting from the present assessment is given (0.34; the sum of flakes and muesli, rice, wheat flour, rye flour, and rolled oats), since the format of the consumption data for this group differed between the present assessment and that in the Concise Database.

[a] Data from EFSA (2009).

[b] Adjusted occurrence mean based on occurrence means used in the present assessment (see materials and methods for details). In the establishment of occurrence means, concentration values in individual samples below the limit of detection (LOD) were set equal to 0.5 * LOD.

[c] No (adjusted) occurrence mean was established for "Cereals", since the format of the consumption data for this group differed between the present assessment and that in the Concise Database.

[d] No (adjusted) occurrence mean was established for "Miscellaneous", since data from this group was excluded in the present assessment.

[e] For meat, the largest difference in median exposures was observed (≈0.2), as a result of using European or Swedish occurrence data.

3. Results

3.1. General exposure assessment

The distribution describing variability in dietary exposure is illustrated in Fig. 1. The median, and the upper 95 and 99th percentiles are 0.97, 1.7 and 2.1 μg/kg b.w./week, respectively (Fig. 1). No pronounced differences in cadmium exposure between males and females, and across different age groups (17–80 years of age) were observed (data not shown).

In Fig. 2, the 10 food categories that contribute most to the total exposure is presented for three different groups; the high exposed group (90–99th percentile), the moderate exposed group (45–55th percentile), and the low exposed group (1st–10th percentile). The number of males and females is evenly distributed in each of the three groups (Fig. 2). Consumption of potatoes and wheat flour (from cereal products) contribute most to the exposure; around 20–30% each (Fig. 2). For wheat flour, the percent contribution differs systematically between the groups; low exposed group > moderate exposed group > high exposed group (Fig. 2). Considering both potatoes and wheat flour the percent contribution is smaller for the high exposed group relative to the moderate and low exposed groups. In absolute terms, however, the high exposed group have an exposure from potatoes and wheat flour that is about 0.2 units (μg Cd/kg b.w./week) higher compared to that of the moderate exposed group and about 0.4 units higher compared to that of the low exposed group (Fig. 2).

For seafood and spinach the percent contribution also differs between the exposure groups, but in the opposite direction; high exposed group > moderate exposed group > low exposed group (Fig. 2). In absolute terms, the high exposed group has an exposure from seafood and spinach that is about 0.2 units (μg Cd/kg b.w./week) higher compared to that of the moderate exposed group and about 0.3 units higher relative to that of the low exposed group (Fig. 2). For vegetables, rice, rye flour, snacks, and milk (including sour milk) and yoghurt, the percent contribution is similar across the three groups, and the sum of the remaining 38 food categories contributes with 20–25% (individually, the remaining categories contributed very little to the total exposure).

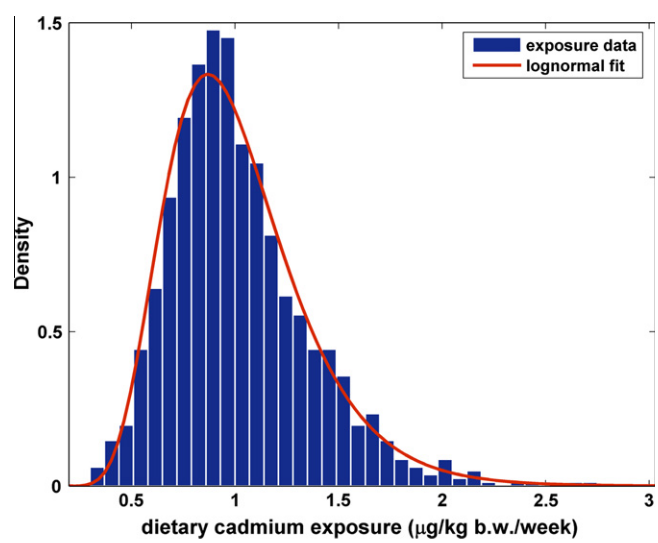

Fig. 1. Distribution describing the variability in dietary cadmium exposure. The log-normal probability density function (density) has been fitted to the exposure data. According to the log-normal model, the median is 0.97 μg/kg b.w./day, and the 1st 5th, 95th and 99th percentiles are 0.45, 0.57, 1.7 and 2.1 μg/kg b.w./week, respectively. No pronounced differences in cadmium exposure between males and females, and across different age groups (17–80 years of age) were observed (data not shown).

Results from the comparison to the EFSA exposure assessment are shown in Table 2. Using the Concise Database, the mean exposure estimated for Sweden is 2.3 μg/kg b.w./week using EFSA occurrence levels and assuming a standard body weight of 60 kg. If the reported body weights are used instead, and the median is used instead of the mean, the value becomes 1.7 μg/kg b.w./week. Use of the mean occurrence levels in the present assessment, after adjustment, results in a median exposure close to 1 μg/kg b.w./week (Table 2). This is similar to the present assessment discussed above that considers a more stratified version of the consumption data from Riksmaten 97–98. Apparently, the differences in occurrence data result in almost a factor 2 difference in estimates of the median exposure (Table 2; 1.7 vs. 0.93). The highest difference was observed for the category "Meat" in the Concise Database; the median exposure from this group differed by around 0.2 units depending on the use of Swedish or European occurrence data (Table 2).

3.2. Uncertainty and scenario analysis

Results from the uncertainty analysis are given in Table 3. For Case 1, the median exposure is in the range of 0.9–1 μg/kg b.w./week; the 95th percentile of exposure is in the range of 1.6–1.8; and the 99th percentile of exposure is in the range of 1.9–2.2 (Table 3). As shown in Table 3, setting concentration values below the limit of detection (LOD) equal to zero, or equal to the LOD, does not have a large impact on the estimated exposure. The estimated percent of the population exceeding the TWI (under Case 1) is also given in Table 3; the median percent exceeding the TWI is about 0.2% (90% confidence interval, CI, is about 0.1–0.4%). In the extended case of considering adjusted exposure estimates (see Section 2) the median percent exceeding the TWI becomes approximately 15 times higher; the median is about 3% (90% CI is about 2–5%).

In Figs. 3 and 4 results from scenario analysis are shown that illustrates how the dietary exposure (Fig. 3), and the percent of the population exceeding the TWI (Figs. 4), changes with increasing or decreasing cadmium occurrence levels in the most important food products (potatoes and wheat flour). For increases in occurrence levels up to 30% it may be excluded with high confidence that the percent exceeding the TWI is higher than about 1% (Fig. 4, part A). However, considering the adjusted exposure estimates, the percentage exceeding the TWI is about three at

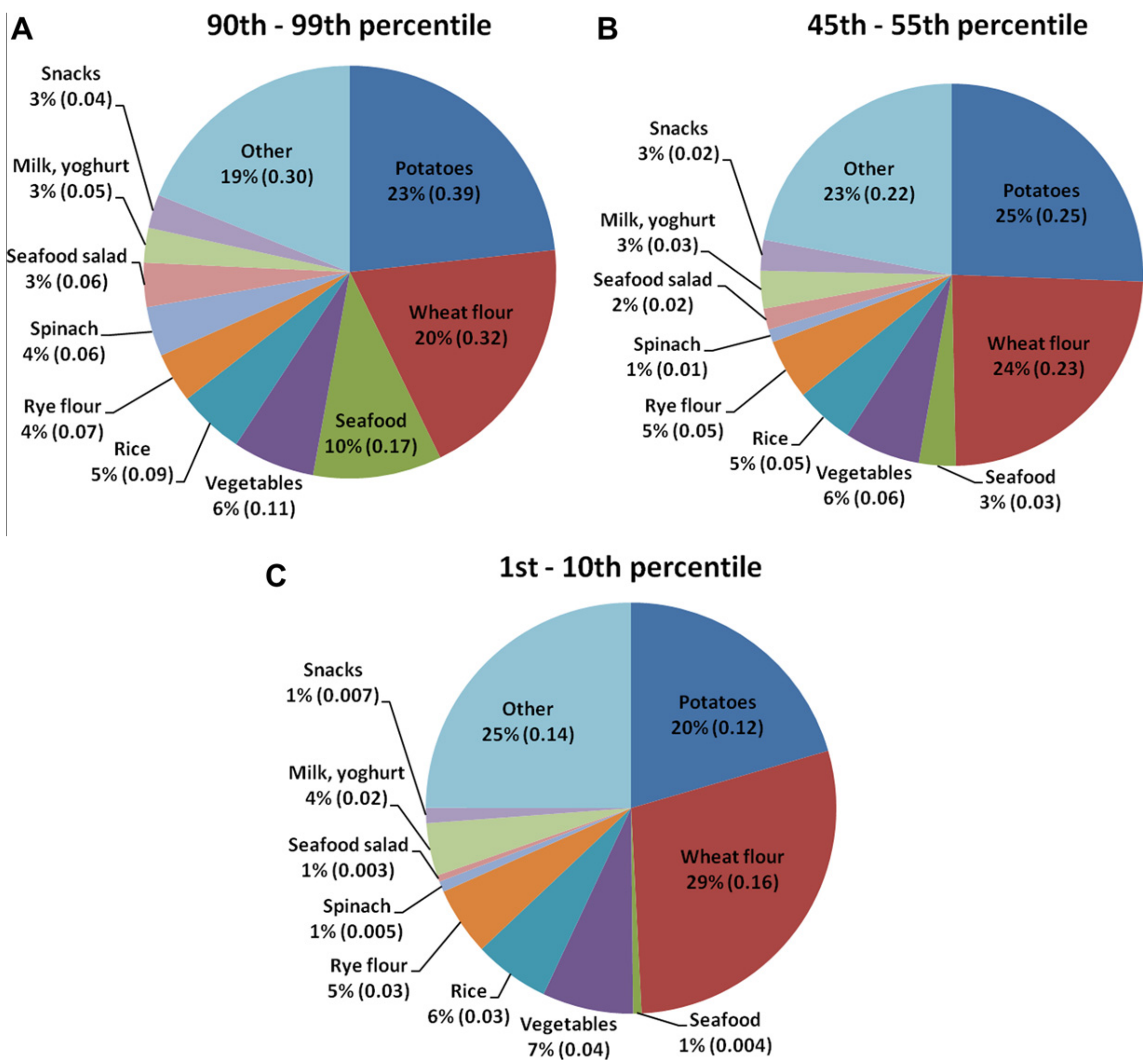

Fig. 2. Illustration of the 10 food groups that contributed most to the dietary cadmium exposure. For each of the three "exposure groups" (A–C) the average percent contribution each food group has the total exposure is given. Values within parenthesis are the corresponding average dietary exposures in terms of μg Cd/kg b.w./week. (A) The high exposed group (90–99th percentile) includes 52 men and 54 females. (B) The moderate exposed group (45–55th percentile) includes 64 men and 53 females. (C) The low exposed group (1st–10th percentile) includes 53 men and 52 females.

Table 3
Estimated dietary cadmium exposure in micrograms per kilo body weight and week, and the percent of individuals exceeding the TWI of 2.5 μg/kg b.w.

Case[a]	Median	95th percentile	99th percentile	Percent exceeding the TWI[d]	
				Un-adjusted	Adjusted
Case 1	0.97[b] (0.91–1.02)[c]	1.66 (1.55–1.76)	2.08 (1.93–2.21)	0.2 (0.08–0.4)	3.1 (1.9–4.6)
Case 2	0.91 (0.86–0.97)	1.59 (1.48–1.69)	1.99 (1.85–2.13)	0.1 (0.06–0.3)	–
Case 3	1.02 (0.97–1.07)	1.73 (1.63–1.83)	2.15 (2.02–2.29)	0.3 (0.1–0.5)	–

[a] Case 1: concentration values in individual samples below the limit of detection (LOD) set equal to 0.5*LOD. Case 2: concentration values in individual samples below the LOD set equal to zero. Case 3: concentration values in individual samples below the LOD set equal to the LOD.
[b] Median.
[c] 90% confidence interval.
[d] The proportion of the population exceeding the EFSA TWI of 2.5 μg/kg/week has been calculated using un-adjusted and adjusted exposure estimates. In the latter case, individual exposure estimates have been multiplied with a factor 1.4, which is approximately the difference between the median exposure in the assessment used in the process of TWI development (Amzal et al. 2009; median = 1.4 μg/kg/week) and the median exposure in this assessment (1.0 μg/kg/week) (see materials and methods).

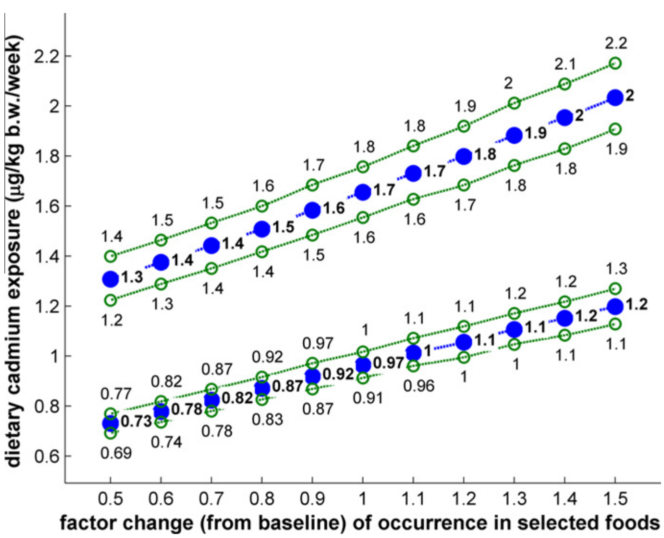

Fig. 3. The relationship between increases and decreases in cadmium occurrence, in potatoes and wheat flour, and estimated dietary cadmium exposure (uncertainty analysis; Case 1). The median and the 95th percentile are illustrated (medians with 90% confidence intervals). A factor change in occurrence = 1, corresponds to the baseline concentrations.

baseline (CI = 2–5%; Fig. 4, part B), and it increases to about seven (CI = 4.5–10%; Fig. 4, part B) after a 30% increase of the cadmium occurrence in the considered food products.

4. Discussion

A detailed assessment of the dietary cadmium exposure in the Swedish adult population was performed in this study. The percent of the population exceeding the EFSA TWI is estimated to be lower than 1% (Fig. 1, Table 3). Recent studies at the national level in Spain have also reported that estimated cadmium exposures are below the TWI (Martorell et al., 2011). In the present analysis, potatoes and wheat flour contributed most to the cadmium exposure (Fig. 2). It is well known that these food groups are important for the cadmium exposure at population level (Amzal et al., 2009; Olsson et al., 2002). In addition, the present analysis indicated differences in the dietary patterns between high and low exposed individuals with respect to consumption of seafood/spinach and also for potatoes/wheat flour to some extent. While potatoes and wheat flour were the most important Cd-contributors for both high and low exposed groups, seafood and spinach also contributed significantly for high exposed individuals; the high exposed group had an exposure from seafood and spinach (Fig. 2: 0.17 + 0.06 + 0.06 = 0.29 μg Cd/kg b.w./week,) which was similar to that the low exposed group received from the basic products, potatoes and wheat flour (Fig. 2: 0.12 + 0.16 = 0.28 μg Cd/kg b.w./week).

For Sweden three recent assessments have been made regarding dietary cadmium exposure, which all differs; the present exposure assessment (median exposure of 1.0 μg/kg/week), the exposure assessment used in the process of TWI development (Amzal et al., 2009; median exposure of 1.4 μg/kg/week), and the EFSA exposure assessment for Sweden (EFSA, 2009; median exposure of 1.7 μg/kg/week). In addition Cd exposure has been assessed by analysing market baskets comprising of foods purchased in supermarkets in four Swedish towns during 1999 (Becker et al., 2011). The baskets represent about 90% of the per capita supply. Average Cd content was 10 μg/person/day, corresponding to 1.2 μg/kg b.w./week (assuming a body weight of 60 kg). The somewhat higher estimate of exposure compared to Riksmaten 97–98 (1 μg/kg b.w./week) can be explained by the fact that food energy intake level is considerably higher, about 12.5 MJ/day compared to about 8.8 MJ/d in Riksmaten 97–98.

The discrepancy between this exposure assessment and that preformed by EFSA (median = 1 vs. 1.7 μg/kg/day) could be investigated in detail in this study. It was concluded, that the Swedish occurrence data on cadmium from the National Food Agency used herein differed from that applied by EFSA (Table 2); the consumption data used in the respective assessment was essentially the same. The differences in the occurrence data used as basis resulted in that estimates of the median exposure differed by almost a factor 2 (Table 2). Differences in occurrence data from different countries does not necessarily mean that the actual contaminant levels in food items are different. Factors such as sampling frame and strategy influence how analyzed foods mirror general food supply/consumption pattern. Discrepancies in the analytical quality control (AQC) between different surveys have been observed to affect cadmium occurrence measures (Jorhem et al., 2006). Since AQC may differ between different parts of Europe, pooling data from different regions may be problematic. Meat has for example been identified as a problem commodity in this regard (Jorhem et al., 2006); for this food category the largest difference in median exposures was observed, depending on the use of European or Swedish occurrence data (Table 2).

The discrepancy between the present assessment and that used for TWI development (Amzal et al., 2009) could potentially be explained by an actual difference in food consumption between the two populations being investigated. However, a higher cadmium exposure could not be observed for participants in Riksmaten 97–98 (men and women 17–80 years of age) that corresponds to

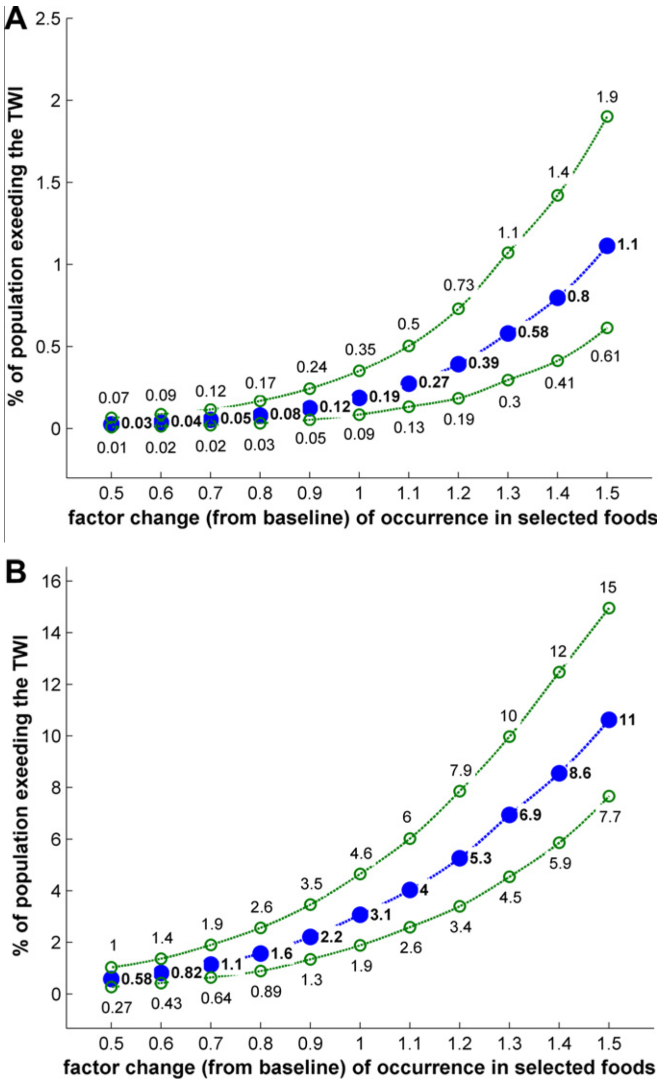

Fig. 4. The relationship between increases and decreases in cadmium occurrence, in potatoes and wheat flour, and the estimated percent of the population exceeding the EFSA TWI. A factor change in occurrence = 1, corresponds to the baseline concentrations. (A) The percent of the population exceeding the TWI (median with 90% confidence interval) calculated based on estimates of dietary exposures obtained in this study (uncertainty analysis; Case 1). (B) The percent of the population exceeding the TWI (median with 90% confidence interval) calculated after adjusting estimates of dietary exposures obtained in this study (uncertainty analysis; Case 1) by the multiplication of a factor 1.4; see materials and methods for details and assumptions made.

the target population considered in Amzal et al. (2009) (i.e. women 56–70 years of age) (data not shown). The body weight adjusted cadmium exposure was similar for males and females, and across different age groups (data not shown). Previous observations have also indicated no substantial difference across age groups in the adult population (Choudhury et al., 2001). The difference between the two assessments may alternatively be attributed to differences in the methodology applied for exposure assessment. In Amzal et al. (2009) consumption data is derived from food frequency questionnaires (covering 67, 96, and 123 food items for assessments based on data from 1987–1990, 1997, and 2004–2007, respectively, while the consumption data used in present assessment is based on a 7-day dietary record (covering about 1000 food items). The occurrence data used is in both instances from the National Food Agency, but it is derived from different time periods, and any differences in the matching of consumption and occurrence data may also impact on the estimates of dietary exposure.

Taken together, it appears unlikely that the difference between the present assessment and that in Amzal et al. (2009) result due to actual differences in the food consumption in the two populations that were studied. Based on this assumption, an extended analysis was also considered where, the present estimates of exposure were adjusted by a factor 1.4; see materials and methods for details. Under this case, the median adjusted percent of the population exceeding the EFSA TWI was then about 3% (CI = 2–5%; Table 3). As pointed out initially, a provisional tolerable monthly intake (PTMI) for cadmium of 25 μg/kg b.w. has been established by JECFA (FAO/WHO, 2010). If applying the JECFA PTMI as a reference instead of the EFSA TWI, a margin of exposure >1 will be observed for the present exposure data whether or not the type of adjustment discussed above is made, and a (very) low percent of the population will be estimated to exceed the JEFCA PTMI.

Additional scenario analysis was performed in this study to illustrate the consequences of increasing or decreasing cadmium occurrence in the most important food categories (potatoes and wheat flour). It may be discussed what increases (e.g. due to the use of cadmium containing fertilizer), or decreases (e.g. by interventions) that may be reasonable to expect over time, but the results (Figs. 3 and 4) provides a basis that describes the anticipated impact of such changes (in occurrence levels).

Changes in the kidney marker beta-2-microglobulin was regarded as the critical endpoint in the risk assessment of cadmium (EFSA, 2009; FAO/WHO, 2010), but there are ongoing discussions in the scientific literature concerning other potential critical effects, including bone effects and cancer (Suwazono et al., 2010; Åkesson et al., 2008; Åkesson et al., 2006). Investigations indicate that a critical concentration in urine similar to that established by EFSA, for beta-2-microglobulin, also apply for cadmium-induced osteoporosis (Suwazono et al., 2010). Thus, besides changes in kidney markers, a critical concentration of around 1 μg/g can also be linked to clinically relevant outcomes. In Amzal et al. (2009), the median urinary cadmium concentration in 680 Swedish never-smoking women was 0.31 μg/g; with a range of 0.09–1.23 μg/g. Other data, from the Swedish environmental monitoring programme, on never-smoking women (50–59 years of age) from four different regions indicate median values between 0.22–0.30 μg/g depending on region (N = 34–52 depending on region); the highest value observed in each region was 1 μg/g (Berglund and Åkesson, 2008). Thus, for never-smoking Swedish women a small group of individuals appear be above the critical concentration of 1 μg/g; using the data presented in Berglund and Åkesson (2008) the percent exceeding the critical concentration could roughly be approximated to 1/34–1/52, i.e. 2–3%. Data from the southern part of Sweden (the Lund area) on 807 women (54–63 years of age), including both smokers and non-smokers (about 54% never-smokers), have shown higher values; Åkesson et al. (2005) reports a median of 0.67 with a 90% confidence interval of 0.31–1.6. The adjusted percent of individuals above the TWI (i.e. 3%, Table 3) is in more resemblance with what is suggested from the Swedish environmental monitoring program, at the level of urinary cadmium concentrations, compared to the "unadjusted" percent of individuals above the TWI (i.e. <1%, Table 3).

All major food categories have been considered in the present exposure assessment, but particular food items, in some of the categories, that are rarely consumed and which could be of importance for the dietary exposure due to their relatively high cadmium content, are not covered. For example, this concerns parts of shellfish, particularly crab hepatopancreas, certain types of mushrooms, particularly the prince (Agaricus augustus), and offal products such as liver and kidney. If such products are additionally consumed it may significantly increase the individual's exposure. Regarding shellfish, however, certain studies have on the other hand suggested that the bioavailability of Cd is lower for a diet that includes shellfish once a week or more, compared to a diet low in shellfish (Vahter et al., 1996).

Uncertainties also exist at the level of what this assessment attempts to cover; i.e. the dietary exposure from all major food categories and items. The uncertainty analysis presented (Table 3) covers statistical uncertainties associated with the data, but there are also other uncertainties that may not be readily quantified:

(1) Response rate in the consumption survey; about a 60% response rate was obtained in Riksmaten 97–98. A reduction in response rate is a typical problem in consumption surveys.
(2) The consumption data used as basis is from 1997–1998; the dietary habits in Sweden may have changed somewhat since this period.
(3) The non-perfect matching between consumption data and occurrence data. Occurrence data is generally not available on all the individual food items covered in a dietary survey. For the most important products (Fig. 2), the matching between consumption an occurrence is very good, e.g. for wheat flour and rye flour, and the risk for underestimation of selected mean occurrence levels is considered low for the remaining food categories in Fig. 2. Seafood is potentially an exception.

5. Conclusions

This study estimates that the median dietary cadmium exposure for adults in Sweden is in the range of 1 μg/kg/week and the upper 95 and 99th percentiles of exposure are in the range of 1.6–1.8 and 1.9–2.2 μg/kg/week, respectively. For the present assessment, the percent of the population exceeding the TWI was lower than 1%. Potatoes and wheat flour were the most important food categories, contributing with 40–50% to the total exposure. Differences in dietary patterns between high and low exposed individuals were observed; for high exposed individuals, seafood and spinach contributed significantly with an exposure similar to that low exposed individuals received from the basic products, potatoes and wheat flour.

The consequence of differences related to methodology applied in exposure assessment were illustrated and discussed. Due to the use of different occurrence levels, the estimate of the median exposure was about a factor 2 lower in this study compared that presented for Sweden as part of the EFSA cadmium risk assessment. The potential importance of the fact that the present exposure estimates are systematically lower than those used in the process for TWI development was also addressed (considering all else equal). After adjusting to the higher dietary exposure reported in Amzal et al. (2009) the adjusted median fraction of the Swedish population exceeding the TWI was then about 3%, which is in line with observations at the level of urinary cadmium for never-smoking Swedish women.

Conflict of Interest

The authors declare that there are no conflicts of interest.

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