Published in final edited form as:

Sci Total Environ. 2011 April 1; 409(9): 1632–1637. doi:10.1016/j.scitotenv.2011.01.037.

Sources of Cadmium Exposure Among Healthy Premenopausal Women

Scott V. Adams[1,2], **Polly A. Newcomb**[1,2], **Martin M. Shafer**[3], **Charlotte Atkinson**[4], **Erin J. Aiello Bowles**[5], **Katherine M. Newton**[2,5], and **Johanna W. Lampe**[1,2]

[1] Fred Hutchinson Cancer Research Center, PO Box 19024, M4-B402, Seattle, WA 98109 USA

[2] Department of Epidemiology, University of Washington, Box 357236, Seattle, WA 98195 USA

[3] Environmental Chemistry and Technology Program, University of Wisconsin and Wisconsin State Laboratory of Hygiene, Madison, WI

[4] Department of Oral and Dental Science, Bristol Dental School, Bristol, UK

[5] Group Health Research Institute, Seattle, WA

Abstract

Background—Cadmium, a persistent and widespread environmental pollutant, has been associated with kidney function impairment and several diseases. Cigarettes are the dominant source of cadmium exposure among smokers; the primary source of cadmium in non-smokers is food. We investigated sources of cadmium exposure in a sample of healthy women.

Methods—In a cross-sectional study, 191 premenopausal women completed a health questionnaire and a food frequency questionnaire. The cadmium content of spot urine samples was measured with inductively-coupled plasma mass spectrometry and normalized to urine creatinine content. Multivariable linear regression was used to estimate the strength of association between smoking habits and, among non-smokers, usual foods consumed and urinary cadmium, adjusted for age, race, multivitamin and supplement use, education, estimated total energy intake, and parity.

Results—Geometric mean urine creatinine-normalized cadmium concentration (uCd) of women with any history of cigarette smoking was 0.43 μg/g (95% confidence interval (CI): 0.38–0.48 μg/g) and 0.30 μg/g (0.27–0.33 μg/g) among never-smokers, and increased with pack-years of smoking. Analysis of dietary data among women with no reported history of smoking suggested that regular consumption of eggs, hot cereals, organ meats, tofu, vegetable soups, leafy greens, green salad, and yams was associated with uCd. Consumption of tofu products showed the most robust association with uCd; each weekly serving of tofu was associated with a 22% (95% CI: 11–33%) increase in uCd. Thus, uCd was estimated to be 0.11 μg/g (95% CI: 0.06 – 0.15 μg/g) higher among women who consumed any tofu than among those who consumed none.

Corresponding Author: Scott V. Adams, Fred Hutchinson Cancer Research Center, 1100 Fairview Ave N, M4-B402, Seattle, WA 98109, sadams@fhcrc.org, Tel: (206)-667-6427, Fax: (206)-667-5977.

Conflicts of Interest: None.

Conclusions—Cigarette smoking is likely the most important source of cadmium exposure among smokers. Among non-smokers, consumption of specific foods, notably tofu, is associated with increased urine cadmium concentration.

Keywords

cadmium; tofu; soy; diet; smoking; soybean

1. Introduction

Cadmium is a heavy metal that has been widely dispersed in the environment as a result of industry and agriculture (Jarup and Akesson, 2009). Non-occupationally exposed persons are exposed to cadmium primarily by smoking tobacco or by eating foods containing cadmium (Jarup and Akesson, 2009). Once inhaled or ingested, cadmium is inefficiently excreted and accumulates primarily in the liver and kidneys (Jarup and Akesson, 2009). Long-term exposure at levels estimated to be achievable by non-occupationally exposed non-smokers can result in impaired kidney function (Jarup, 2003; Satarug et al., 2003). Urine cadmium levels have also been associated with several other health conditions, including osteoporosis(Jarup and Alfven, 2004; Jarup et al., 1998), hypertension(Gallagher and Meliker, 2010), peripheral artery disease(Tellez-Plaza et al., 2010), diabetes mellitus(Schwartz et al., 2003), and cancers including lung, breast and endometrial cancers (Akesson et al., 2008; McElroy et al., 2006; Nawrot et al., 2006).

Tobacco has been documented as the dominant source of cadmium exposure in smokers (McElroy et al., 2007a; McElroy et al., 2007b; Pappas et al., 2006; Richter et al., 2009). The tobacco plant readily accumulates cadmium from the soil, which is subsequently released by burning and absorbed through the lungs(Elinder et al., 1983; Pappas et al., 2006; Watanabe et al., 1987). Among non-smokers, direct measurements of cadmium in foods indicate that leafy green vegetables, grains, shellfish, root vegetables, legumes, seeds and nuts, and organ meats are typically considered to be the most significant dietary sources of cadmium (Egan et al., 2007; Egan et al., 2002). However, there is limited empiric data comparing measurement of urine cadmium (uCd) with reported routine consumption of potential dietary sources (Haswell-Elkins et al., 2007; Hellstrom et al., 2007; McElroy et al., 2007a; Satarug et al., 2010; Vahter et al., 1996).

In this study we combined measurement of urine cadmium with reported smoking habits and dietary data to assess sources of urine cadmium in a sample of healthy premenopausal women in Washington State. We hypothesized that cigarette smoking would be associated with higher urine cadmium in a dose-dependent manner; and that reported usual consumption of foods identified as containing cadmium, such as leafy green vegetables, grains, shellfish, root vegetables, legumes, seeds and nuts, and organ meats would also be associated with elevated urine cadmium.

2. Materials and Methods

2.1 Study population and recruitment

The recruitment, exclusion criteria, and clinical protocols of the Equol, Breast, and Bone (EBB) study have been detailed elsewhere (Atkinson et al., 2008a; Atkinson et al., 2008b). Briefly, premenopausal women aged 40–45 years were recruited from a mammographic screening program within Group Health (GH), an integrated healthcare system in Washington State. Based on self-report, peri- and postmenopausal women, women with a history of breast cancer, and women using hormone therapy or oral contraceptives were excluded from the study population; consistent with other goals of the EBB study, women with certain digestive conditions and women using antibiotics were also excluded (Atkinson et al., 2008a; Atkinson et al., 2008b). Study procedures were approved by the Fred Hutchinson Cancer Research Center (FHCRC) and GH Institutional Review Boards.

2.2 Data collection

Participants completed a health questionnaire, a food frequency questionnaire (FFQ) developed by the Nutrition Assessment Shared Resource of the FHCRC (Patterson et al., 1999), and a study clinic visit during which height and weight were measured. Spot urine samples were collected using standard "clean-catch" procedures. Urine samples were aliquoted and frozen at −70°C until analysis. Separate aliquots were assayed for creatinine and heavy metals.

2.3 Urine cadmium and creatinine measurement

A panel of 30 elements including cadmium was quantified by sector field inductively coupled plasma mass spectrometry (SF-ICPMS) on a Thermo-Finnigan Element 2 (Thermo Scientific, Waltham, MA) at the Wisconsin State Laboratory of Hygiene (Madison, WI), following quality control procedures similar to those previously described (McElroy et al., 2007a). Urine was diluted in 2% high purity nitric acid containing internal normalization standards, and introduced to the plasma with a low-flow Teflon nebulizer interfaced to an ESI FAST auto-sampler. Isotopes were acquired in peak jumping mode. A series of dedicated samples (molybdenum spiked reference materials and spiked samples) were positioned throughout the analytical sequence to address potential molybdenum oxide interference. A typical SF-ICPMS batch included 20 participant samples, 3 standard reference material aliquots (including National Institute of Standards of Technology 2670a), and multiple quality control samples (duplicates, spikes, check standards and blanks) (McElroy et al., 2007a). The mean of batch-specific reagent blanks was subtracted from the mean of triplicate sample measurements to arrive at the cadmium concentration used for statistical analysis. All participant samples were above the lower limit of quantification of cadmium (0.008 μg/L). Levels of extractable metals (0.5M nitric acid for 48 hours) in un-used urine collection containers and storage/transport vials were also quantified to assess potential contamination biases. Extractable concentrations of cadmium in the urine collection containers (0.0004 ± 0.0002 μg/L, n=4) and storage vials (0.0020 ± 0.0006 μg/L, n=9) were significantly below the method quantification limit of cadmium in urine and therefore judged to be an insignificant source of error.

Urine creatinine was assessed using a colorimetric assay (Atkinson et al., 2008a).

2.4 Smoking

Participants self-reported smoking history. Women who reported smoking less than 100 cigarettes in total were categorized as "never-smokers". Pack-years (py) of smoking was calculated among smokers by multiplying reported average number of cigarettes smoked per day and the reported number of years of smoking, and assuming 20 cigarettes per pack. Women were also categorized as never-, former or current smokers; and in a single combined variable: never-smokers; smoker with <10py; smoker with 10–20 py; or smoker with ≥20 py. Three women who indicated formerly smoking but indicated "social smoking" in place of an average daily number of cigarettes were categorized as former smokers with less than 10 py. No participating women without a personal history of smoking reported current exposure to secondhand smoke in the home.

2.5 Diet

The average weekly consumption of individual food items, total energy intake, and intake of specific nutrients were estimated from food frequency questionnaire (FFQ) responses using the Nutrient Data System for Research software and database developed by the Nutrition Coordinating Center, University of Minnesota, following methods previously reported (Schakel et al., 1997; Schakel, 1988). In summary, each participant indicated how often she consumed each food item, and a typical serving size (small, medium, or large). A reference measure for a “medium serving” for each food was given on the FFQ. Total medium servings per day of most individual foods items were directly estimated from the response to FFQ items. Consumption of some items (*e.g.*, cold cereals, crackers, popcorn) were estimated by combining two or more closely related FFQ items, for example, “low-fat” and “regular” items for the same basic food item, as indicated in footnotes to Table 2. Oils used in cooking or as food toppings, salad dressings, and dairy products added to cereals and coffee or tea were not considered as individual food items, but were included in estimation of nutrient and total energy intake (Schakel et al., 1997).

2.6 Statistical analysis

Potential confounding was evaluated for the following set of variables selected *a priori*: age, race, total energy intake, parity, body mass index (BMI), education, and use of mineral or multivitamin supplements. BMI was not included in final multivariable models because no association with urine cadmium was observed. Other potential confounders were included in the final models as parameterized in Table 1, with the exception that total energy intake and age were modeled as continuous variables.

Creatinine-corrected cadmium concentration for each spot urine sample, reported as μg cadmium per g creatinine, was calculated as the measured cadmium concentration divided by creatinine concentration. Creatinine-normalized urinary cadmium concentrations were log-transformed (base 2) to normalize the distribution. The logarithm of creatinine-corrected cadmium was the dependent variable in each multivariable linear regression model.

Linear regression was fit using ordinary least squares regression and robust standard error estimates. Following model fitting, estimates of urine creatinine-corrected cadmium were back-transformed from log-scale, yielding percentage change in uCd per unit change of each independent variable and corresponding 95% confidence interval (95% CI). Least-squares adjusted geometric means and 95% CIs were also estimated from the multivariable linear regression models. Modeling assumptions of homoscedasticity, normality of residuals, and linearity were checked graphically for each food, and no substantial violations were noted. Outliers were detected graphically and investigated for influence on regression estimates.

Smoking and diet were considered separately; diet was analyzed only among never-smokers. A single model was examined with smoking history categorized by pack-years as described above. Among never-smokers, each food item was entered individually in a separate multivariable model, estimating the association between average weekly servings of the individual food and uCd, adjusted for potential confounders (but not other foods). A final model including several foods, and the same potential confounders, was also examined.

Statistical analyses were completed with Stata version 11 (Stata Corp, College Station, TX).

3. Results

One hundred ninety one EBB study participants (Atkinson et al., 2008a; Atkinson et al., 2008b), completed a health questionnaire and FFQ, and provided a urine sample on which cadmium and creatinine analysis were completed. Of these women, 128 (63%) reported having smoked fewer than 100 cigarettes in their lifetime and were thus categorized as having no history of smoking (never-smokers; Table 1). Fourteen women (7%) self-identified as Asian, Native Hawaiian, or Pacific Islander (hereafter grouped together as Asian); the majority women self-identified as White. Nine women reported consuming meat (not including fish) never or less than once per month, and were categorized as vegetarians. Urine from smokers, Asians, and vegetarians contained higher levels of cadmium than urine from other women, with or without creatinine correction. Parous women, women using multivitamins or dietary supplements, and women without a college degree had slightly lower urine cadmium levels; higher total energy intake was also linked to somewhat lower urine cadmium.

Multivariable linear regression adjusted for age, multivitamin or supplement use, education, parity, and total energy intake showed that smoking was strongly and dose-dependently associated with uCd (Table 2). Each pack-year of smoking history was associated with a 2% increase in uCd (95% CI: 0.5 – 3%); thus, 20 or more pack-years of smoking was associated with uCd approximately 150% higher than among never-smokers. Geometric mean uCd was 0.30 μg/g (95% CI: 0.27–0.33 μg/g) and 0.43 (95% CI: 0.38–0.48 μg/g) among never- and ever-smokers, respectively. Among ever-smokers, samples from former and current smokers yielded nearly similar uCd, 0.42 μg/g (95% CI: 0.36–0.47 μg/g) and 0.43 μg/g (95% CI: 0.38–0.48 μg/g), respectively.

Multivariable linear regression, restricted to non-smokers and adjusted for age, multivitamin or supplement use, education, parity, race, and total energy intake showed that routine consumption of several foods were individually associated with uCd (Table 2). Direct associations approaching statistical significance ($p<0.05$) were observed between uCd and weekly servings of cooked cereals, eggs, liver and other organ meats, tofu and other tofu products, vegetable soups, cooked leafy green vegetables, green salad, and yams (Table 2). Weak inverse associations were observed between milk and soy milk, consumed as beverages, and uCd.

Regular consumption of liver and eggs were substantially correlated with one another (pairwise Pearson correlation coefficient, 0.66). Furthermore, only 6 women reported eating any liver, and a single participant with urine cadmium content in the upper 15% of all non-smokers reported consuming 5.2 servings of liver and 20 servings of eggs per week. Removing this one participant removed most evidence of association between liver or egg consumption and urine cadmium. The associations between uCd and consumption of vegetable soups was similarly strongly influenced by a single outlier.

In a statistical model including all of the potential confounders and the following food items: tofu, cooked cereals, vegetable soup, liver, eggs, cooked greens, green salad, yams, milk, and soy milk estimates in the same model, only tofu and cooked cereals remained virtually unchanged and associated with uCd. Overall, the linear regression model with only potential confounding variables explained 17% of the variability in uCd. With the addition of only tofu, this increased to 26%; including all foods individually associated with uCd resulted in a model accounting for 32% of variability in uCd.

Based upon the estimated relationship between tofu consumption and urine cadmium, least-square adjusted geometric mean urine creatinine-normalized cadmium levels were estimated to be 0.38 μg/g (95% CI: 0.33–42 μg/g) and 0.27 μg/g (95%CI: 0.24–0.30 μg/g) among women who reported any (N=46), or no (N=82), tofu product consumption, respectively. Similarly, urine cadmium was estimated to be 0.30 μg/g (0.15–0.45 μg/g) higher among the 11 women reporting an average of at least 1 serving of tofu products per week, compared to the 82 women reporting no consumption of tofu.

4. Discussion

This study utilized detailed dietary and health data, and highly sensitive measurement of urinary cadmium from a sample of healthy premenopausal women in Washington State to investigate sources of cadmium exposure. The urinary cadmium concentrations measured in this study are comparable to measurements in similar populations, including the National Health and Nutrition Examination Survey (NHANES) (Paschal et al., 2000) (McElroy et al., 2007a; McElroy et al., 2006). Although a 24-hour urine collection would be preferred to our use of a spot urine sample, 24-hour collection is impractical; therefore, spot urine samples are widely used in epidemiological studies, and creatinine normalization is applied to reduce intra-individual variability due, for example, to hydration (Lauwerys et al., 1994; Mason et al., 1998; Sorahan et al., 2008; Suwazono et al., 2005). The spot urine samples analyzed in this study were provided under controlled conditions in a research clinic, and the consistency of the urine cadmium concentrations with comparable cohorts, our assessment of container blanks and high accuracy of SF-ICPMS measurements on reference materials indicate that the urinary cadmium measurements appear to be both internally and externally valid.

As expected based on previously published research, we observed that smoking was associated with substantial dose-dependent increases in urine cadmium. Our estimate that ever-smoking is associated with an additional 0.13 μg/g uCd is consistent with the ~0.14 μg/g higher uCd in ever-smoking women than never-smoking women reported from the NHANES (Richter et al., 2009) and a previous study of Wisconsin women (McElroy et al., 2007b). Among 63 women in this study who reported any history of cigarette smoking, 55 were former smokers. Little difference in uCd between current and former smokers, or between former smokers who quit more or less recently (not shown), was observed, consistent with the reported persistence of cadmium in the human body.

Among non-smokers, food is widely believed to be the primary source of cadmium exposure (Jarup and Akesson, 2009; Satarug et al., 2003; Satarug et al., 2010). Different plant species and, within a single species, different cultivars, absorb cadmium and sequester it in edible tissues to differing degrees (Grant et al., 2008; Wolnik et al., 1983). Furthermore, food preparation may affect cadmium content of food ultimately consumed.

We observed associations between reported consumption of individual FFQ items and uCd that were generally consistent with our expectations based upon previously published research describing the cadmium content of commonly consumed foods (Egan et al., 2007; Egan et al., 2002). We found evidence suggesting that eating leafy greens, green salad, yams, cooked cereals, and vegetable soups was associated with uCd. However, we did not observe an association between uCd and “peanut butter, peanuts, and other nuts or seeds”, shellfish, potatoes, rice, or carrots, as might have been anticipated (Egan et al., 2007; Egan et al., 2002; Haswell-Elkins et al., 2007; Hellstrom et al., 2007; Vahter et al., 1996). Liver and other organ meats were not eaten regularly enough by study participants to draw reliable conclusions. Finally, previous research indicates that meats, fish, many vegetables such as broccoli, cauliflower, onions, squashes, and fruits, do not contain significant levels of cadmium, and these foods were observed to have no association with uCd in our study (Egan et al., 2007; Egan et al., 2002).

The observed association between reported consumption of “tofu, tempeh and products such as tofu hot dogs, soy burgers, and tofu cheese” and uCd was the strongest of all foods examined in this study. The association remained after further adjustment for other foods potentially associated with uCd, and was not the result of a few influential observations.

Furthermore, the association was not changed by adjustment for race or vegetarianism, and was of identical strength when analysis was restricted to non-Asian women.

Recent studies suggest uCd levels at ~1 μg/g can contribute to kidney dysfunction (Jarup et al., 2000; Olsson et al., 2005; Satarug et al., 2003). Our observation that creatinine-corrected mean uCd levels were 0.11 μg/g higher among tofu consumers—and 0.30 μg/g higher among women who ate more than one serving of tofu per week, on average-- is potentially relevant to health impacts of cadmium. Surprisingly, the additional uCd we observed associated with tofu consumption is comparable to estimates of elevated uCd we and others have observed associated with smoking.

Legumes, including soybeans, have generally been considered a minor source of dietary cadmium in the United States (Egan et al., 2007; Egan et al., 2002). In Asia, however, soybeans have been suggested to be an important source of dietary cadmium exposure (Arao et al., 2003; Zhang et al., 1998). To our knowledge, no published data exist on the cadmium content of commercially available solid soy products commonly consumed in the US; the Food and Drug Administration Total Diet Study, for example, does not include assay of tofu or similar products (Egan et al., 2007; Egan et al., 2002).

Nonetheless, soybeans have been demonstrated to absorb cadmium from the soil and retain it in seeds (Arao et al., 2003; Cataldo et al., 1981; Shute and Macfie, 2006; Wolnik et al., 1983), and some food products, such as soy-based infant formulas, have been found to be relatively high in cadmium (Dabeka, 1989; Eklund and Oskarsson, 1999). Although the amount of cadmium present in soybeans depends on several factors including soil conditions and plant cultivars (Cataldo and Wildung, 1978; Cataldo and Wildung, 1983; Grant et al., 2008), uptake and concentration of cadmium in seeds of high-protein soybean varieties used to produce tofu has been documented, even when soil cadmium concentrations are relatively low (Arao et al., 2003; Poysa and Buzzell, 2001; Shute and Macfie, 2006).

Our results are limited by the modest number of participants, and are based on self-reported smoking history and diet. Because of the design of the study, we did not obtain samples of food or cigarettes to test for cadmium concentration. We are unable to distinguish between different tofu products, or their sources (*e.g.*, imported or domestic), but the consistency of association among both Asian and non-Asians suggests that the source of the tofu product is not an important factor in this study population. The number of comparisons made in our analysis suggests that some of the results may be expected to be spuriously significant due to chance. We also used spot urine samples, corrected for urine creatinine, in place of 24-hour urine collection. Use of spot urine samples likely introduced additional variability into our results. In addition, urine creatinine is influenced by age, gender, body size, meat consumption, and kidney function, and therefore use of creatinine correction may pose a problem in some studies(Suwazono et al., 2005). However, the participants in this study are all women, within a narrow age range, and in good health without reported kidney disease; we found no evidence that BMI, reported usual total meat consumption, or total energy intake was correlated to urine creatinine in our data (not shown), and adjustment for BMI did not influence our results.

Finally, it is possible that an unidentified food, not listed on the FFQ but often consumed with tofu and other soy products, is the true source of cadmium. However, given the level of detail of the FFQ, few omitted foods appear to be likely candidates. We investigated every line-item of the FFQ, in addition to those listed in Table 2, and could not find any suggestion that the tofu-uCd association was confounded by consumption of another food or beverage. In addition, the homogeneity of the study sample—all participants were premenopausal women of similar age residing in the same geographical region, and were members of the same healthcare delivery organization—suggests the influence of other confounding factors is limited.

We can only speculate on the mechanisms underlying the tofu-uCd association. It could be that tofu products indeed contain high levels of cadmium. Most cadmium in soy plants is likely bound to phytochelatins or metallothionein (Kawashima et al., 1991; Steffens, 1990), and cadmium in food may not be highly bioavailable to humans once ingested (Vahter et al., 1996). Soy products could also be contaminated during processing to tofu, for example, by the addition of impure calcium and magnesium salts. However, it may also be that cadmium in soy products may be more highly bioavailable than that in other food sources, or consumption of tofu products could enhance cadmium absorption from other foods. Low physiological stores of iron—as might be experienced by premenopausal women—have been suggested to increase enteric cadmium absorption (Vahter et al., 2002; Vahter et al., 1996). It is also possible that consumption of soy increases excretion of cadmium in urine, perhaps due to enhanced mobilization of cadmium from body stores; to our knowledge, no studies to date appear to have addressed this possibility.

Our results are consistent with previous reports that cigarette smoking is an important source of cadmium. We also observed associations between uCd and routine consumption of food items that direct measurements of cadmium levels indicate could be dietary sources of cadmium. In particular, we observed that tofu products were strongly associated with uCd concentration, and this intriguing result calls for additional study of the cadmium content of tofu products commonly available in the United States.

Acknowledgments

This work supported by NIH R01 CA 097366 (Equol, Breast and Bone study), NIH U01 CA 63731 (Group Health Breast Cancer Screening Program), NIH National Cancer Institute Cancer Prevention Training Grant R25 CA094880 (to SVA), and the Breast Cancer Research Program at the Fred Hutchinson Cancer Research Center, through donation by Safeway, Inc. The funding agencies played no role in the design, execution, analysis, or interpretation of this study.

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Table 1

Personal characteristics and mean urine cadmium concentrations of participating women.

					Cadmium/creatinine (μg/g)[a]		Cadmium (μg/L)[b]	
	Mean	(SD)	N	%	Geometric Mean	± 1 SD	Geometric Mean	± 1 SD
Age[c]	42.4	1.3	191	100	0.33	(0.27 – 0.39)	0.14	(0.13 – 0.15)
Cigarettes (pack-years)								
Never			128	67	0.29	(0.23 – 0.36)	0.13	(0.11 – 0.14)
<10			42	22	0.39	(0.29 – 0.49)	0.17	(0.17 – 0.17)
10–20			15	8	0.41	(0.22 – 0.60)	0.15	(0.12 – 0.18)
≥20			6	3	0.68	(0.62 – 0.72)	0.22	(0.21 – 0.23)
Asian								
No[d]			177	93	0.31	(0.23 – 0.39)	0.13	(0.13 – 0.13)
Yes			14	7	0.62	(0.52 – 0.71)	0.31	(0.18 – 0.45)
Vegetarian								
No			182	95	0.32	(0.25 – 0.39)	0.25	(0.24 – 0.26)
Yes			9	5	0.51	(0.43 – 0.58)	0.41	(0.37 – 0.45)
Supplements [e]								
No			61	32	0.35	(0.24 – 0.46)	0.16	(0.16 – 0.16)
Yes			130	68	0.32	(0.27 – 0.36)	0.13	(0.11 – 0.15)
College Graduate								
No			62	32	0.32	(0.24 – 0.41)	0.11	(0.10 – 0.12)
Yes			129	68	0.33	(0.28 – 0.38)	0.15	(0.14 – 0.17)
BMI								
<25			98	51	0.34	(0.29 – 0.39)	0.15	(0.15 – 0.15)
25 to 30			57	30	0.32	(0.25 – 0.39)	0.13	(0.09 – 0.16)
≥30			36	19	0.32	(0.23 – 0.40)	0.15	(0.13 – 0.16)
Parity [f]								
Nulliparous			74	39	0.35	(0.30 – 0.40)	0.15	(0.12 – 0.17)
Parous			117	61	0.31	(0.24 – 0.39)	0.13	(0.13 – 0.14)
Total Energy Intake (kcal)								

					Cadmium/creatinine (µg/g)[a]		**Cadmium (µg/L)[b]**	
	Mean	**(SD)**	**N**	**%**	**Geometric Mean**	**± 1 SD**	**Geometric Mean**	**± 1 SD**
<1270			47	25	0.34	(0.20 – 0.47)	0.17	(0.17 – 0.17)
1270 – 1612			48	25	0.34	(0.28 – 0.40)	0.14	(0.11 – 0.17)
1612 – 2008			48	25	0.32	(0.27 – 0.37)	0.12	(0.11 – 0.13)
>2008			48	25	0.31	(0.29 – 0.33)	0.25	(0.23 – 0.27)

[a] Urine cadmium (µg) per gram urine creatinine; geometric mean and endpoint of values within ±1 geometric standard deviation.

[b] Urine cadmium (µg) per liter urine; geometric mean and endpoint of values within ±1 geometric standard deviation.

[c] Mean age and urine cadmium of all study participants.

[d] 114 White, 2 African-American or Black, 4 other

[e] Current use of multi-vitamins, mineral supplements, or any other dietary supplement

[f] Including all pregnancies that lasted at least 6 months.

Table 2

Estimated adjusted[a] percentage change and 95% confidence interval (95% CI) in urine creatinine-corrected cadmium (uCd) associated with smoking and, among never-smokers, weekly servings of selected food frequency items.

Smoking			**% change uCd**	**95% CI**
Never			Ref.	
<10 pack-years			37	14 to 63
10–20 pack-years			45	17 to 81
20+ pack-years			149	59 to 291
per pack-year (among smokers)			2	0.5 to 3
FFQ Items[b]	Mean weekly servings[c]	SD	% change uCd[d]	95% CI
Cereals, Breads, Snacks				
Bread*	3.5	3.9	1	−1 to 4
Rice, noodles, and other grains (as a side dish)	2.3	2.5	2	−2 to 7
Cold cereals	2.1	2.6	−1	−4 to 2
Cooked cereals and grits	0.7	1.4	**8**	**2 to 14**
Popcorn*	0.7	1.3	2	−5 to 10
Peanut butter, peanuts, and other nuts and seeds	2.0	2.6	2	−1 to 6
Meat, Fish, and Eggs				
Eggs	1.4	2.4	**4**	**2 to 7**
Liver, chicken liver, and organ meats	0.1	0.5	**18**	**4 to 33**
Ground beef*	0.7	0.7	−3	−17 to 13
Shellfish, not fried (shrimp, lobster, crab and oysters)	0.2	0.3	−23	−48 to 14
Fish*	0.8	0.8	5	−6 to 17
Chicken and turkey (roasted, stewed, grilled, and broiled)	0.9	1.2	0	−7 to 8
Mixed Dishes				
Asian-style (stir-fried) noodles and rice such as chow mein, fried rice, and Pad Thai	0.4	0.5	1	−22 to 30
Miso soup	0.1	0.5	23	−10 to 70
Tofu, tempeh and products such as tofu hot dogs, soy burgers, and tofu cheese	0.4	0.9	**22**	**11 to 33**
Ramen noodle soup	0.1	0.3	6	−16 to 33
Vegetable soups	0.5	1.3	**6**	**1 to 12**
Bean soups	0.2	0.4	12	−13 to 45
Vegetables and Grains				
Cauliflower, cabbage, and Brussels sprouts	0.9	1.5	0	−6 to 6
Cooked greens such as spinach, mustard greens, and collards	0.9	1.5	**5**	**0 to 11**
Green salad (lettuce or spinach)	4.0	3.7	**2**	**0 to 4**
Carrots	2.4	2.7	−1	−4 to 2
Potatoes (boiled, baked, or mashed)	0.8	0.9	−4	−11 to 4
Yams and sweet potatoes	0.2	0.5	**23**	**1 to 49**
Onions and leeks	1.6	1.7	0	−6 to 7

Smoking			**% change uCd**	**95% CI**
Fresh tomatoes	1.9	2.0	3	−1 to 8
Broccoli	2.3	2.5	1	−3 to 5
Peppers	1.2	1.9	2	−3 to 7
Green or string beans	1.3	1.9	0	−4 to 4
Green peas	0.6	0.8	−4	−18 to 13
Squashes*	1.1	1.7	1	−3 to 6
All other beans (baked, lima, or chili without meat)	0.4	0.7	14	−2 to 32
Fruit				
Peaches, nectarines, and plums	0.7	1.0	8	−1 to 19
Oranges, grapefruit, and tangerines (not juice)	1.0	1.7	3	−1 to 7
Dried fruit (other than apricots) such as raisins and prunes	0.7	1.3	2	−4 to 7
Apples, applesauce, and pears	2.5	3.1	−2	−5 to 2
Bananas	2.1	2.7	2	−1 to 6
Beverages				
Coffee (not lattes or mochas)	5.6	9.2	0	−1 to 1
Tea (all types)	7.4	11.0	0	−1 to 1
Milk (all types) as a beverage **	4.1	6.4	−2	−3 to 0
Soy milk **	0.2	1.1	−4	−8 to 0
Soda*	3.3	5.7	0	−2 to 1

[a] adjusted for age, race, parity, total energy intake, multivitamin/supplement use, and education.

[b] Among participants reporting no personal history of cigarette smoking (N=128).

[c] medium serving as defined for each food item on the FFQ

[d] per weekly medium serving

* Combines two or more closely related FFQ items.

** Soy milk and milk derived from the combination of FFQ food items assessing milk consumption, and the type(s) of milk most frequently consumed.