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Variation in Rice Cadmium Related to Human Exposure

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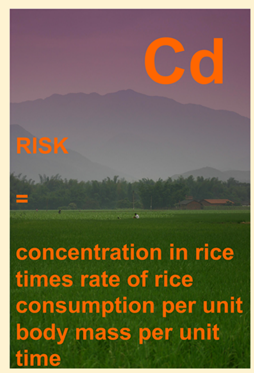
Supporting Information

ABSTRACT: Cereal grains are the dominant source of cadmium in the human diet, with rice being to the fore. Here we explore the effect of geographic, genetic, and processing (milling) factors on rice grain cadmium and rice consumption rates that lead to dietary variance in cadmium intake. From a survey of 12 countries on four continents, cadmium levels in rice grain were the highest in Bangladesh and Sri Lanka, with both these countries also having high *per capita* rice intakes. For Bangladesh and Sri Lanka, there was high weekly intake of cadmium from rice, leading to intakes deemed unsafe by international and national regulators. While genetic variance, and to a lesser extent milling, provide strategies for reducing cadmium in rice, caution has to be used, as there is environmental regulation as well as genetic regulation of cadmium accumulation within rice grains. For countries that import rice, grain cadmium can be controlled by where that rice is sourced, but for countries with subsistence rice economies that have high levels of cadmium in rice grain, agronomic and breeding strategies are required to lower grain cadmium.



■ INTRODUCTION

Cadmium is a chronic potent nephrotoxin, as well as a class one carcinogen, and is associated with a range of other severe diseases, where human exposure is primarily, for nonsmokers, through food, with cereal grains contributing a large portion to dietary consumption.[1,2] Rice grain can be particularly elevated in cadmium.[3] Any food associated health risk is governed not just by the concentrations of a particular toxin in dietary items, but also by the rate of consumption of those items. Rice is, therefore, of particular concern in regions where it is the dietary staple.[2,3] Furthermore, particular subpopulations, such as babies and toddlers, have higher food consumption rates per unit body mass; and vegetarians, who have an enhanced dependence on grain and vegetables, tend to have higher rates of cadmium exposure from foods.[1,2]

Cadmium sources to paddy soils can be natural[4] or by contamination from base-metal mining,[5−7] industrial discharge,[3] or phosphate fertilizers.[8] Accumulation of cadmium in rice is also dependent on edaphic factors in paddy fields that regulate cadmium mobilization from soil minerals,[9] as well as levels of micronutrients, mainly manganese and zinc, for which cadmium is an analogue.[10] Also, irrigation practices are very important, because they influence the redox status of paddy soil, with more aerobic cultivation conditions favoring cadmium uptake;[11,12] but anaerobic conditions decreasing uptake, as cadmium readily precipitates as sulfides.[13] Rice is also known to

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have inherent genetic variation in uptake and translocation of cadmium into grain, which could potentially be used to breed cultivars low in cadmium.[14−16] It is also important to consider localization of cadmium within grain, to see how polishing to produce white rice, the normal practice throughout the globe, affects cadmium content of the consumed product.[14]

Here, extensive measurements of cadmium in rice with respect to regional sourcing and genetic diversity are reported in order to explore inherent variation of rice grain cadmium in the global food supply chain. Rice data from 12 countries in four continents is reported. To complement this, grain cadmium concentrations are reported from field experiments from two locations each in Bangladesh, China, and India where common cultivars, locally important improved cultivars as well as local land races, could be compared. Additionally, the consequences of milling were identified. These data sets were then considered with respect to strategies for reducing cadmium in the global diet.

■ MATERIALS AND METHODS

Grain Sourcing. Rice was collected from a range of geographic market basket and field surveys throughout 12 countries, as listed in Table 1. Market basket survey data include samples imported to other countries with clear labeling of country of origin, or collected by sourcing rice at different markets within the country of origin. The sourcing and geographic distribution of the samples for each individual country is discussed in the Results and Discussion sections.

Table 1. Descriptive Statistics for Cadmium (mg/kg) in Grain by Country Surveyed

country	*N*	mean	median	minimum	maximum
Bangladesh	260	0.099	0.057	<0.0005	1.31
Cambodia	14	0.006	0.001	0.0010	0.03
France	37	0.010	0.006	0.0030	0.10
Ghana	428	0.020	0.013	<0.005	0.27
India	58	0.078	0.028	0.0020	1.00
Italy	114	0.038	0.027	0.0030	0.16
Japan	18	0.059	0.050	0.0101	0.14
Nepal	12	0.050	0.048	0.0139	0.08
Spain	92	0.024	0.016	0.0008	0.14
Sri Lanka	75	0.081	0.024	<0.0005	0.80
Thailand	18	0.027	0.020	0.0057	0.07
USA	21	0.018	0.017	0.0095	0.04

Furthermore, we include rice from field experiments designed to study variation in grain trace element status between cultivars at six field sites—2 in Bangladesh, 2 in China, and 2 in India—that used the same experimental design described in Norton et al.[17] Cultivars included a diverse panel of varieties reflecting parents used in genetic mapping populations, local improved cultivars, and land races. The number of cultivars was between 72 and 81 cultivars at each field site, with the same cultivars grown at the two filed sites within countries. From these cultivars a total of 13 were the same across all the six field sites. For the Chinese samples, milling was undertaken to allow comparison of milled and unmilled samples.

Preparation and Analysis. All reagents used were of trace element grade. Grain samples were oven-dried at 70 °C for 24 h. Samples were then ball-milled to a fine powder and ~0.1 g accurately weighed into 50 mL polypropylene tubes, to which 2 mL of concentrated nitric acid was added and left to stand overnight, and then a further 2 mL of concentrated hydrogen peroxide was added just before the samples were microwave digested (CEM Technologies, U.K.) for 30 min at 90 °C. On cooling, samples were made up to 50 mL with double deionized water (18.2 ΩM cm^{-1}). With each batch of 40 samples, a reagent blank and rice flour CRM NIST-1568a were included. Digested samples were analyzed on an Agilent Technologies 7500 series Inductively Coupled Plasma − Mass Spectrometer (ICP-MS). Rhodium was used as an internal standard.

■ RESULTS AND DISCUSSION

Limits of detection (LOD) for grain cadmium were <0.0005 mg/kg. Where a sample was below LOD, it was allocated a value of half-LOD for subsequent interpretation. Rice flour CRM recovery (N = 12) was 85% ± standard error of 2.8%.

Field Experiments. For all six-field sites there was significant genetic variation for brown rice grain cadmium (Table 2).

A total of 13 cultivars were in common across the six-field sites (all diverse cultivars previously used in genetic mapping) (Supporting Information Table 1). Analysis of variance of the 13 genotypes at the six field sites indicated that the site (P < 0.001, F = 100.6), genotype (P < 0.001, F = 17.9), and site by genotype interaction (P < 0.001, F = 8.8) had a significant effect on grain cadmium. When the variance was partitioned, 15% of the variation was explained by genotype, 42% was by site, and 31% was the genotype by site interaction. When cadmium concentrations between different cultivars were compared between the two sites for each of the three countries studied, there was a strong correlation for cultivars grown at the Bangladesh sites (P < 0.001) and for Indian sites (P = 0.002), but not for the cultivars grown at the Chinese sites (P = 0.513, Figure 1). The Indian and Bangladeshi sites have a history of tubewell irrigation, with arsenic being the sole contaminant for these sites, while the Chinese sites were impacted by mining.[17] Mining-impacted sites appear inherently more variable, probably due to complex mineralogies and trace element availabilities,[17] which may explain the considerable between-site

Table 2. Descriptive Statistics and One-Way ANOVA for the Effect of All Cultivars Grown at the 6 Field Sites

			grain cadmium for cultivars (mg/kg)			ANOVA	
country	site	*N*	mean	minimum	maximum	*F*	*P*
Bangladesh	Sonargaon	76	0.019	0.009	0.078	9.4	<0.001
Bangladesh	Faridpur	72	0.005	0.001	0.025	2.6	<0.001
India	Nonaghata	80	0.028	0.008	0.060	13.1	<0.001
India	DeGanga	80	0.013	0.0005	0.045	13.3	<0.001
China	Chenzhou	81	0.017	0.006	0.063	2.0	<0.001
China	Qiyang	77	0.015	0.008	0.025	7.1	<0.001

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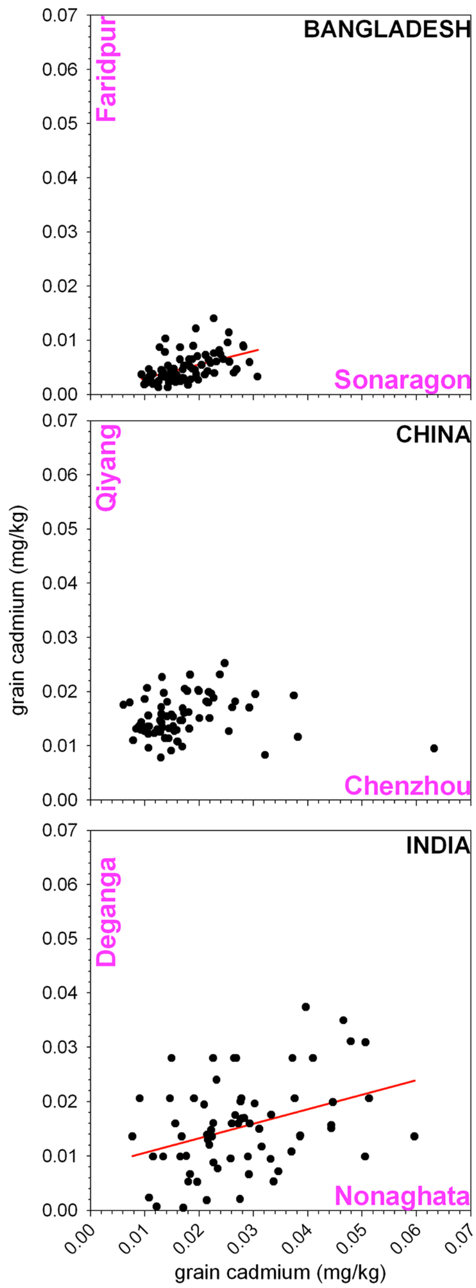

Figure 1. Correlation of grain cadmium concentration in unmilled rice for each cultivar at the two fields sites within Bangladesh, China, and India.

differences in cultivar behavior in the Chinese sites. This must be borne in mind when breeding rice for low cadmium uptake for base- and precious-metal mining polluted sites, where elevated cadmium in rice is often of concern,[7] as it appears from this study to be difficult to predict how cultivars are going to perform on any given soil. There were large differences in the overall range of grain cadmium for all the sites, by ~2-fold for each pairwise comparison. Cultivation practices (irrigation patterns, organic manuring), edaphic factors, and field drainage will greatly affect redox cycling within any given paddy field, as cadmium mobilization into soil solution is redox sensitive, with cadmium being mobilized under less reduced conditions,[9,12] and these will all impact grain cadmium concentrations.

The observed genetic variation could be exploited to breed low grain cadmium cultivars, or at least to select low grain cadmium cultivars suitable for particular environments. However, given the strong effect of environment and the genotype by environment interaction, the same cultivars will respond differently and accumulate different concentrations of cadmium within the grain in different conditions. When comparing the minimum and maximum grain cadmium values for each field site the range in grain cadmium for cultivars grown within field sites was greater than 5-fold for all sites (Table 2). It is known from previous studies that Quantitative Trait Loci (QTLs) exist for grain cadmium,[16,18,19] that specific genes can down-regulate cadmium assimilation and reduce grain cadmium content,[20] and that rice can be genetically modified to reduce cadmium in the grain.[10,16]

For the field experiments at Chenzou and Qiyang in China, both white and brown rice grains were analyzed; this enabled these two types of rice to be directly compared (Figure 2).

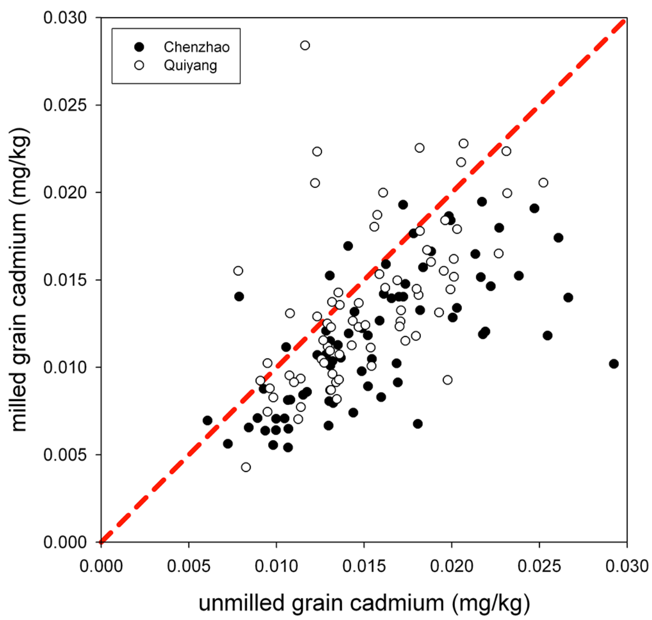

Figure 2. Correlation between unmilled grain cadmium and milled grain cadmium for two Chinese sites for a range of cultivars.

Regression analysis between Cd concentrations in brown and white rice were highly significant ($P < 0.001$) for both Chinese sites, with the slope of the regression (with intercept set at zero) being 0.622 for Chenzhou and 0.803 for Qiyang, showing that Cd concentration is decreased by 20−40% by milling. Other studies that compared brown versus white rice found similar results.[14]

Geographical Variation in Grain Cadmium and Subsequent Human Exposure. From the preceding description of the field studies, it was observed that milling (Figure 2), interfield variation, and intercultivar variation (Figure 1) all have a large role to play in determining grain cadmium concentration, and thus, any wide survey of cadmium in grain should reflect this. Figure 3 presents the range of grain cadmium found for rice surveyed from either field or market basket surveys for 12 countries. Although it was shown in Figure 1 that milling reduces grain cadmium, both brown and white rice are important commodities in Western diets, and in the poorest of Asian diets, as subsistence farmers can rely on wholegrain rice;[21] thus, brown and white rice was considered together with respect to human exposure. While milling only

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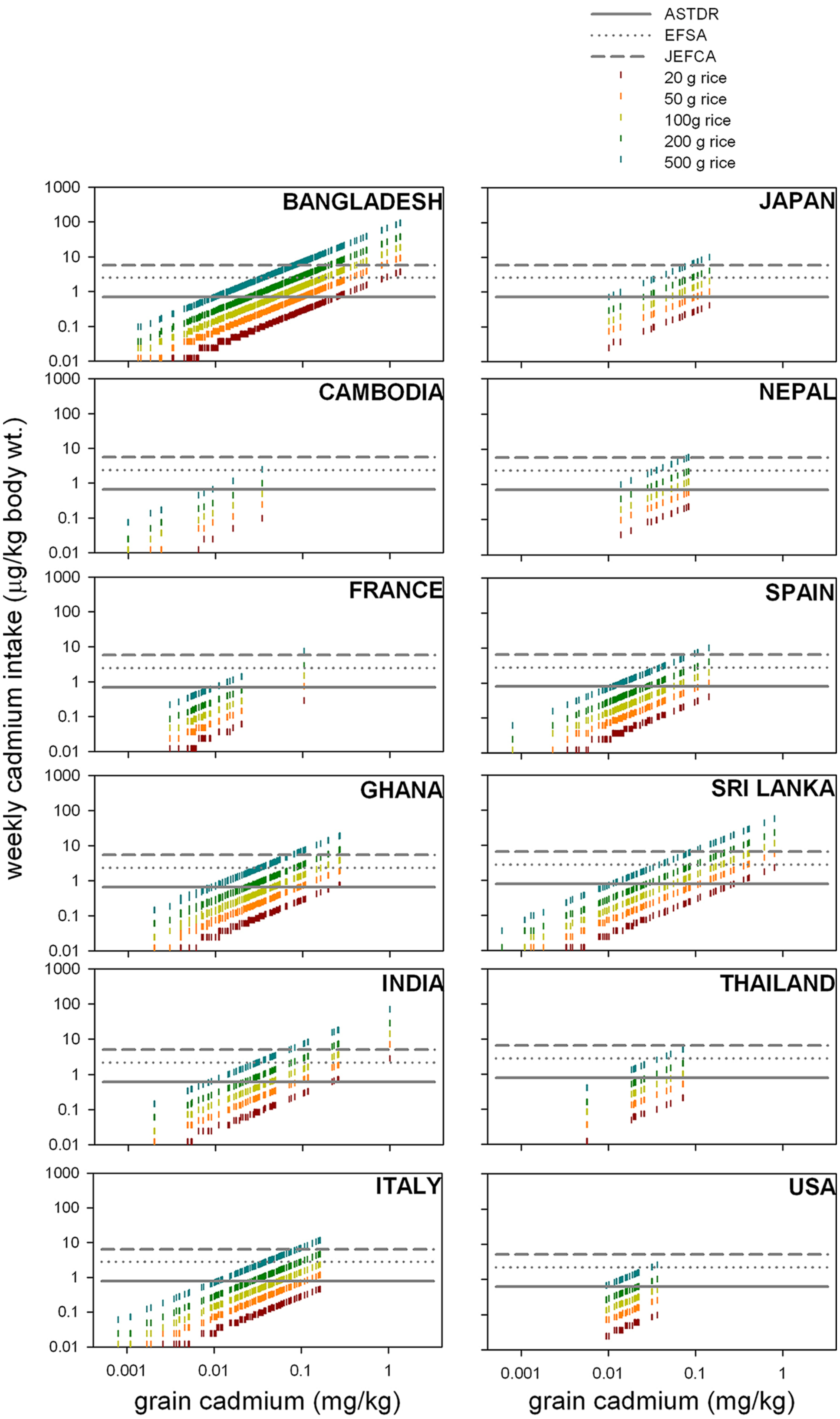

Figure 3. Grain cadmium in market basket and field surveyed samples with weekly intakes (concentration in rice * intake of rice per week/body mass of consumer) calculated for different rates of rice ingestion (rates given in legend) assuming a 60 kg body mass of the consumer. International thresholds for cadmium in rice (ATSDR, JECFA, EFSA) were as reported in Clemens et al.[2]

resulted in a 20−40% decrease in grain cadmium, the measured range of grain cadmium concentrations for the entire data set (>1600 samples) was 3 orders of magnitude, from 0.01 to 1 mg/kg (Figure 3), and thus any subtle differences observed when directly comparing paired milled and unmilled samples (Figure 1) will be subsumed by the considerable variance

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observed within and between countries (Figure 3). One-way analysis of variance, comparing the distribution of grain cadmium between different countries, was highly significant ($P < 0.001$). This survey represents the first large-scale survey of cadmium in rice from Bangladesh, with 260 samples from 12 of Bangladesh's 64 districts. Many samples had above 0.1 mg/kg cadmium, yet Bangladesh has little industrial pollution of paddies. This suggests that the cadmium assimilated by rice is from natural sources and/or that Bangladeshi rice cultivars are efficient at assimilating cadmium, possibly due to genetic variance, edaphic factors, or management practice.

Behind Bangladesh with respect to cadmium levels in rice was Sri Lanka (Figure 3). Concerns regarding elevated cadmium in the Sri Lankan diet, specifically rice, were raised by Bandara et al.[4] They found that, in some irrigation command areas, rice cadmium concentrations could reach ∼0.1 mg/kg, equating to weekly ingestion rates of ∼10 μg/kg body weight per week, within the ranges found for this current study. Renal failure was prevalent in residents of these high cadmium areas, with this disease linked to this elevated cadmium in the diet.[4]

French and Cambodian rice had the lowest grain cadmium, followed by Ghana. Italy, Japan, Nepal, Spain, India, Thailand, and the U.S. could all be considered as having intermediate grain cadmium. Note that Ghana has some rice samples relatively high in cadmium, reflecting mining contamination of paddies that this country is known to suffer from.[22]

Human ingestion of rice-derived cadmium is dependent on three factors: the concentration of cadmium in grain consumed; the rate of rice ingestion; and body mass of the consuming individual. It is noted that, although rice is the primary exposure path to cadmium in Japan, rice consumption rates there are falling and thus exposure to cadmium is falling.[3] Such temporal trends in rice consumption patterns also have to be borne in mind. As rice grain consumption rates vary from country to country by nearly 3 orders of magnitude,[23] this is a greater determinant of exposure from rice than body weight for adults. Infants and toddlers are exceptions, as they have typically 3-fold greater food consumption rates per body weight compared to adults,[23] and this must be borne in mind when considering the risk posed by cadmium in rice, as exemplified by studies on cadmium exposure to infants from baby foods.[24] Considering adults, where a 60 kg body mass was used to model the data, rice grain cadmium exposure in different regions of the globe can be considered at different rates of rice consumption and placed in context of different thresholds derived for "safe" exposure (Figure 3). These thresholds are as follows: 0.7 μg/kg/week, US Agency for Toxic Substances and Diseases Registry (ATSDR); 2.5 μg/kg/week, European Food Safety Authority (EFSA); and 5.8 μg/kg/week, Joint FAO/WHO Expert Committee on Food Additives (JECFA);[2] noting that ATSDR is most stringent, an order of magnitude lower than JECFA (Figure 3). The range of rice consumption rates considered varies: from 20 g, which is roughly representative of the average European or U.S. rice consumption patterns; 100 g is representative of Asians living in Europe or the U.S.; 200 g is typical of many SE Asian rice consumption rates; while 500 g is typical of consumption rates of some of the poorest countries in Asia such as Bangladesh, Burma, and Laos.[23] These plots of weekly cadmium consumption rates versus grain cadmium concentration at different rice consumption rates enable the risk from cadmium in rice to be placed in context for each country (Figure 3). There is little or no risk of cadmium for those consuming rice from Cambodia, France, and Ghana across all potential consumption rates. While for Italy, Spain, and the U.S., even though grain cadmium concentration is intermediate in a global context, the risk to the "average" consumer is small, given that even at the highest grain cadmium recorded those consuming 20 g of rice per day do not exceed the most stringent of international thresholds, the ATSDR. For a high rice consuming country such as Cambodia, given that the number of samples analyzed from this country is relatively small ($N = 14$), very few of the samples exceed "safe" thresholds, even at the highest rates of consumption. Results presented here from Japan, Nepal, and the U.S. suggest there may be concerns at high rates of rice consumption, but again it is only the most stringent ATSDR safety value that, in the main, is exceeded. For Sri Lanka, Bangladesh, and, to a lesser extent, India (the high samples here came almost exclusively from Assam), the situation is much more worrying, with many samples exceeding the threshold with the lowest stringency, JECFA. While overall cadmium levels are lower in Bangladeshi rice, rice consumption rates are high. At 500 g of rice consumption per day, Bangladesh is one of the highest per capita rice consumers globally.[23] Those most likely to be at severest risk of cadmium exposure to rice are farmers living in high grain cadmium areas who consume their own produce, as typified from a Japanese study that found high levels of renal damage in 70-year-old-plus female farmers.[3] The results presented here suggest that cadmium is too high in the Bangladeshi diet, and it is a priority to identify what the edaphic factors are that govern high cadmium in rice, as well as assessing the impact of cadmium on the health of this nation.

The study presented here cannot be described as being descriptive of global exposures to cadmium in rice, as this would be a monumental task involving a detailed survey on a fine geographic scale, covering all rice producers; and similarly for a detailed basket survey, as rice is widely exported within and between countries.[25] This is illustrated by the Thai data set presented in Figure 3 which shows low grain cadmium, although specific studies targeted with *a priori* knowledge of where contamination may be present have found highly elevated grain cadmium, up to 1.75 mg/kg, in Thailand.[5] Similar extremes in cadmium in rice, comparing mine-impacted and nonimpacted regions in China, have also been illustrated,[7,26,27] and thus cadmium-impacted soils need special attention when trying to lower cadmium intakes by local communities.

The current study clearly points out that elevation of cadmium concentration in rice is a widespread problem, and we have identified, for the first time, that Bangladeshi populations are exposed to excessively high levels of cadmium in their diet. Widening and deepening the global survey of cadmium in rice grain will help to further define the problem, and better characterize cadmium exposure. Breeding low-cadmium rice[15] and improved cultivation practices offer hope for lowering cadmium in the global food-chain. Unfortunately, the conditions that favor low cadmium uptake in rice, i.e., more prolonged periods of anaerobism, lead to greatly enhanced uptake of inorganic arsenic,[11] a class one, nonthreshold carcinogen,[25] and it is already known that arsenic contamination of soils and rice is a major problem in Bangladesh and some other rice-growing countries of South and Southeast Asia. Thus, care must be taken that, in solving the cadmium problem, it is not exchanged for high arsenic in rice.

ASSOCIATED CONTENT

Supporting Information

Mean grain cadmium concentrations of the 13 cultivars common across the six field sites. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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