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ORIGINAL PAPER

Assessment of Cadmium Concentrations in Foodstuffs and Dietary Exposure Risk Across China: A Metadata Analysis

Ying Qing[1,2] · Yongzhen Li[3] · Xinyi Cai[2] · Wenting He[2] · Shishi Liu[2] · Yunhe Ji[2] · Meng Jiang[2] · Linjing Yang[2] · Jutao Wang[2] · Siyuan Ping[2] · Yu Chen[2] · Yingyi Luo[2] · Yanfei Li[1]

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Abstract
Cadmium (Cd) is a persistent and toxic heavy metal widely present in the environment and can cause damage to a variety of human organs and systems. Based on published studies from 2000 to 2021, this study established a comprehensive database of Cd concentrations in Chinese foods, and described the spatial and temporal trends of Cd concentrations in foods across China. The average Cd concentration in total foodstuff was 0.078 mg/kg, with edible fungi and algae having the highest concentrations, followed by aquatic foods, nuts, cereals, beans, vegetables, meats, eggs, milk, and fruits. The average dietary Cd exposure of Chinese residents was 34.3 µg/day (varying from 22.6 to 54.5 µg/day across regions), with the highest exposures in South China. Cereals (46.2%), vegetables (19.2%), and aquatic food (18.4%) contributed the most to the dietary Cd exposure of Chinese residents. According to Monte Carlo simulations of the risk assessment of dietary exposure to Cd, approximately, 15.4% of the Chinese population exceeded the Joint FAO/WHO Expert Committee on Food Additives health-based guidance value. The hazard quotient and excess lifetime cancer risk indices of dietary Cd exposure indicated that the Chinese residents would not be at significant non-cancer and carcinogenic risk. In summary, this study obtained comprehensive and reliable results on Cd concentrations in Chinese food and dietary Cd exposure risk of Chinese residents, which can provide a data base for the development of dietary Cd exposure limits in China.

Keywords Cadmium · Concentration · Foodstuffs · Dietary exposure · Risk assessment · China

Introduction

Cadmium (Cd) is a widespread toxic heavy metal that can enter the soil, air, and water through phosphate fertilizer, garbage incineration, ore mining, and smelting, causing persistent pollution of the environment and crops (Jarup 2003; Xu et al. 2018). Studies indicate that at least one-fifth of China's farmland is contaminated with Cd and other heavy metals, and farmland soils near mining and industrial areas are contaminated with higher levels of heavy metal (Li et al. 2020; Yang et al. 2018). According to the World Health Organization (WHO), the Chinese have a high level of dietary Cd exposure, second only to Japan, but higher than Europe, the United States, Australia, and other countries (WHO 2011; Yu et al. 2017).

Cadmium can bioaccumulate through the food chain and participate in human metabolism with a biological half-life of more than 10-years (ATSDR 2012). Cereals, vegetables, aquatic products, and other food categories are contaminated with Cd to varying degrees through environmental transport. Therefore, apart from occupational exposure and smokers, dietary intake is the most important route of Cd exposure in the general population (Satarug et al. 2017b; Song et al. 2017). Several studies have confirmed that long-term exposure to low doses of dietary Cd in the general population can cause damage to the nervous system, cardiovascular system, genitourinary system, kidney function, and bones (Buha et al. 2019; Chouit et al. 2021; Obeng-Gyasi 2020; Qing et al. 2021b; Zeng et al. 2021). In addition, the carcinogenic effects of lung, breast, and prostate cancers caused by long-term Cd exposure, and the teratogenic effects of growth retardation and mental

✉ Yanfei Li
liyf@sumhs.edu.cn

1 Shanghai University of Medicine & Health Sciences Affiliated Zhoupu Hospital, 201300 Shanghai, China

2 Shanghai University of Medicine & Health Sciences, 201318 Shanghai, China

3 Children's Hospital of Fudan University, 201107 Shanghai, China

retardation in offspring caused by disruption of the endocrine system have also been demonstrated (Eriksen et al. 2017; Gari et al. 2022; Pietrzak et al. 2021; Rapisarda et al. 2018). Due to the damage caused by Cd to human health, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) established a provisional tolerable monthly intake (PTMI) of 25 µg/kg BW (FAO/WHO 2011). Many Chinese dietary Cd exposure risk assessment studies often use the above limit as the assessment criteria (Chen et al. 2021; He et al. 2013; Song et al. 2017). However, Chinese dietary patterns are quite different from those of Europe, the United States, and other countries. Judging the risk of Cd exposure in the Chinese based on international standards may inevitably increase uncertainty (Kant and Graubard 2018; Martinez-Gonzalez and Martin-Calvo 2013; Wu et al. 2018). China has not issued the health guidance value for dietary Cd exposure in the population, and understanding the regional and species distribution characteristics of Cd concentrations in Chinese foods is the first step in developing relevant standards.

With the rapid development of economy and industrialization, environmental heavy metal pollution is becoming more and more prominent. A large number of heavy metals are released into the ecosystem, causing pollution and economic losses in agriculture, husbandry, and aquaculture (Liu et al. 2018; Peng et al. 2022). With the increasing concern for food safety in China, a large number of studies on monitoring Cd concentrations in food have been published. However, due to the complex of food types, insufficient sample size, different detection methods, and limited sampling areas, research results are difficult to be directly used as data support to establish the dietary Cd exposure limits in China. Therefore, in this study, a database of Cd concentrations in Chinese foods was established based on published studies. By collating and analyzing the database, we described the spatial and temporal trends of Cd concentrations in Chinese foods. Based on the dietary patterns of residents in different regions of China, the risk of dietary Cd exposure was assessed. For now, the big data meta-analysis of lead and mercury concentrations in foods has been completed (Qing et al. 2022; Zhang et al., 2021b), but database establishment and categorical assessment of Cd concentrations in foods across China are still lacking. This study will fill this gap and provide a data basis for the development of dietary Cd exposure limits and related control measures in China.

Data sources and Methods

Literature Search

The concentrations of Cd in foods were assessed by the following food categories: plant-based foods (cereals, vegetables, fruits, beans, nuts, edible fungi, and algae) and animal source foods (meats, aquatic foods, eggs, and milk). Six databases were consulted to obtain data on Cd concentrations in food published between 2000 and 2021 (Web of Science, PubMed, Medline, Chinese Medical Journal Database (CMJD), China National Knowledge Infrastructure (CNKI), and WANFANG Database). The databases were searched using the following keywords: cadmium, Cd, food, cereals, vegetables, meat, mushroom, poultry, eggs, milk, fruit, fish, crustacea, seafood, concentration, level, and content.

Papers were screened for inclusion in the comprehensive database based on the following criteria: (1) All food products were sampled within China; (2) The detection methods of Cd in foods conformed to the national standards or industry standards. (3) The methods section contained clear sampling information: food category, sampling site, quantity, average Cd concentrations, detection method. (4) Excluding studies that developed new methods for Cd concentrations in food. (5) Excluding studies on Cd concentrations in health care products, infant food, spices, tea, beverages, and alcohol. The search process is shown in Figure S1.

Cadmium Concentrations in FOODS ACROSS CHINA

To avoid the effect of individual studies on Cd concentrations in foods, the weighted average of Cd concentration in each food category was calculated using the sample size as the weight. The sample size-weighted average Cd concentrations in food categories were calculated by the following formula (Zhang et al. 2021b):

$$Cd_{i,j} = \sum_{n=1}^{N}(Cd_{i,j,n} \times m_{i,j,n}) / \sum_{n=1}^{N} m_{i,j,n}, \tag{1}$$

where $Cd_{i,j}$ is the average sample size-weighted concentration of Cd in food category i from region j (mg/kg); $m_{i,j,n}$ is the sample size for food category i from region j in the nth data record; N is the number of included data records.

The exceedance rate (ER) of Cd in food categories was calculated following the equation of the number of samples with Cd concentrations higher than the maximum allowable concentration (MAC) in China (GB 2762-2017) accounting for the total number of collected samples (Zhang et al. 2021b):

$$ER_i = \sum_{m=1}^{M} N_{i,m} / \sum_{m=1}^{T} N_{i,m}, \tag{2}$$

where ER_i is the exceedance rate in food category i (%); m is the number of samples; M is the number of records for Cd concentrations higher than the MAC; and T is the total number of samples for Cd concentrations in food i.

Dietary Exposure Assessment of Cadmium

Estimation of Dietary Cd Exposure Risk

The provinces with food consumption data were divided into seven regions according to geographic location (Northeast China: Heilongjiang, Liaoning, Jilin; East China: Shanghai, Jiangsu, Zhejiang, Anhui, Fujian, Jiangxi, Shandong, Taiwan; North China: Beijing, Tianjin, Shanxi, Hebei, Inner Mongolia; Central China: Hubei, Hunan, Henan; South China: Guangdong, Guangxi, Hainan, Hongkong, Macao; Southwest China: Chongqing, Sichuan, Guizhou, Yunnan, Tibet; Northwest China: Shaanxi, Gansu, Xinjiang, Qinghai, Ningxia). The average dietary consumption of residents in the seven regions was calculated based on the food consumption survey data published by the Centers for Disease Control and Prevention in each province. Details are found in Table S1. The dietary Cd exposure and contribution ratio of different food categories were calculated based on food consumption in each region and the average Cd concentrations in each food category (Wei et al. 2019; Zhang et al. 2021b):

$$Cd_{intake,j} = \sum_{i=1}^{10} (Cd_{i,j} \times C_{i,j}) \tag{3}$$

$$CR_{i,j} = \frac{Cd_{i,j} \times C_{i,j}}{Cd_{intake,j}} \times 100\%, \tag{4}$$

where $Cd_{intake,j}$ is the dietary Cd intake from the ten food categories in region j (μg/day), $C_{i,j}$ is the consumption (g/day) of food category i at region j. $CR_{i,j}$ is the contribution rate of food category i to dietary Cd exposure (%).

To reduce uncertainty and the influence of individual data on the results, a probabilistic estimation was applied to calculate the health risk associated with dietary Cd exposure for each region. The distribution of Cd concentrations in each food category was fitted using @Risk 7.6 (Palisade Software, USA). An assessment model based on Monte Carlo simulation (iteration = 100,000) was developed to estimate the cumulative population distribution of dietary Cd exposure according to Eq. (3). The provisional tolerable monthly intake (PTMI = 25 μg/kg BW) set by JECFA for dietary Cd exposure was used as a criterion to assess the potential exposure risk (FAO/WHO 2011).

Non-carcinogenic Risk Assessment

The hazard quotient (HQ) was adopted to assess the potential non-cancer risk of dietary exposure to Cd. The calculation formula is as follows (Qing et al. 2020; Wang et al. 2020; Yuan et al. 2014):

$$\mathrm{ADD} = \frac{Cd_{intake,j} \times EF \times ED}{\mathrm{BW} \times \mathrm{AT}} \tag{5}$$

$$HQ = \frac{ADD}{RfD}, \tag{6}$$

where ADD is the average daily intake of Cd per day per kg of body weight (mg/kg/day); EF is the exposure frequency (365 days/years); ED is the exposure duration (76.34 years, according to the life expectancy of China Statistical Yearbook 2015) (NBS, 2015); BW is body weight (60.6 kg, the average weight of Chinese adults) (Duan 2015); AT is the exposure period (days) within the life expectancy; and RFD is reference dose, referring to the kidney injury under dietary Cd exposure (1×10^{-3} mg/kg/day) (IRIS 2013). If the HQ is below 1, the risk of Cd exposure is at an acceptable level. If the HQ exceeds 1, adverse health effects may occur.

Cancer Risk Assessment

The excess lifetime cancer risk (ELCR) defines carcinogenic risk as the excess probability of developing cancer over a lifetime after being exposed to a contaminant. The ELCR was estimated as follows (Mirzabeygi et al. 2017; USEPA 2001):

$$ELCR = ADD \times CSF, \tag{7}$$

where CSF is cancer slope factor, which is defined as a plausible upper-bound estimate of the probability of a response per unit intake of the chemical over a lifetime (Cd: 0.38 mg/kg/day) (USEPA 2004). The ELCR above 10^{-4} is considered to require mediation; below 10^{-6} implied no obvious hazard; between 10^{-6} and 10^{-4} is acceptable (USEPA 2004).

Internal Exposure Risk Assessment of Cd by TK Model

A toxicokinetic model (TK model) is a mathematical model capable of quantitatively assessing the level of chemical exposure in the organism (Dixit et al. 2003). In this study, a TK model that fits the metabolic profile of Cd in Chinese was used to simulate the distribution of urinary cadmium (UCd) in Chinese and to assess the potential risk of renal injury:

$$Cd_{urine} = \frac{f_u \times f_k}{\log(2)} \times d \times t_{1/2} \frac{\left[1 - exp\left(-\frac{\log(2) \times age}{t_{1/2}}\right)\right]}{\left[1 - exp\left(-\frac{\log(2)}{t_{1/2}}\right)\right]} \tag{8}$$

The parameters were derived from Qing's study (Qing et al. 2021a), where Cd_{urine} is the UCd (μg/g creatinine); $t_{1/2}$ is the half-life (log-normal distribution, mean: 12.7 years, standard deviation: 7.4 years); d is average daily dietary Cd exposure (μg/kg bw/day); $f_k \times f_u$ refers to the absorption rate of the gastrointestinal tract and renal cortex (log-normal distribution, mean: 0.0076, standard deviation: 0.0062); The "*age*" is set at 50-year-olds according to the European Food Safety Authority (EFSA) (EFSA, 2011). The probability density distribution of UCd was assessed using dietary Cd exposure in different regions. The @Risk software was used to simulate sampling with 100,000 iterations. The safety limit for UCd (5.24 μg/g creatinine) established by JECFA was used to assess the risks of Cd exposure to the Chinese residents.

Results and Discussion

Cadmium Concentrations in Foodstuffs

A total of 701 studies on Cd concentrations in Chinese foods were included in this study. The database contained 4682 data records with a total sample size of 566,646. All included studies are detailed in Table S4. A total of 33 provinces (municipalities or autonomous regions, except Macau) in China were covered. The sample sizes of cereals, vegetables, meats, aquatic foods, beans, eggs, nuts, edible fungi and algae, milk, and fruits accounted for 22.2%, 25.6%, 4.8%, 25.4%, 1.0%, 2.7%, 3.7%, 5.2%, 3.0%, and 6.4%, respectively.

The sample size-weighted average Cd concentration in total foodstuffs was 0.078 mg/kg, with the highest concentration in edible fungi and algae (0.336 mg/kg), followed by aquatic foods (0.157 mg/kg), nuts (0.110 mg/kg), cereals (0.041 mg/kg), beans (0.024 mg/kg), vegetables (0.021 mg/kg), meats (0.020 mg/kg), eggs (0.011 mg/kg), milk (0.007 mg/kg), and fruits (0.007 mg/kg) (Fig. 1A). Based on the MACs of Cd in China (GB2762-2017), we compared the Cd concentration of each subcategory (Fig. 1B) and calculated the exceedance rate (Table S2). The Cd concentration of algae was much higher than that of edible fungi, but there were no MACs for algae, and the exceedance rate of edible fungi was 7.7%. The adsorption of heavy metals by edible fungi was much greater than that of other plant foods. This is due to their mycelia colonize mineral soils and produces enzymes and various organic acids that play an important role in humus formation and metal mineralization and mobilization (Siric et al. 2016). In addition, metallothionein in edible fungi cells can specifically bind heavy metals to form chelates, thus facilitating their absorption, transfer, and storage (Liu et al. 2019).

With the exception of edible fungi, Cd concentrations in aquatic foods were higher than those in other foods. Bivalves (0.454 mg/kg), cephalopods (0.368 mg/kg), and crustaceans (0.160 mg/kg) had higher Cd concentrations than fish (0.027 mg/kg). Numerous studies have pointed out that the enrichment of Cd in crustaceans and bivalves was higher than that in fish (Lu et al. 2021; Wang et al. 2020; Yu et al. 2017; Zhang et al. 2016). This is due to the significant positive correlation between heavy metal concentrations in marine organisms and the surrounding environment

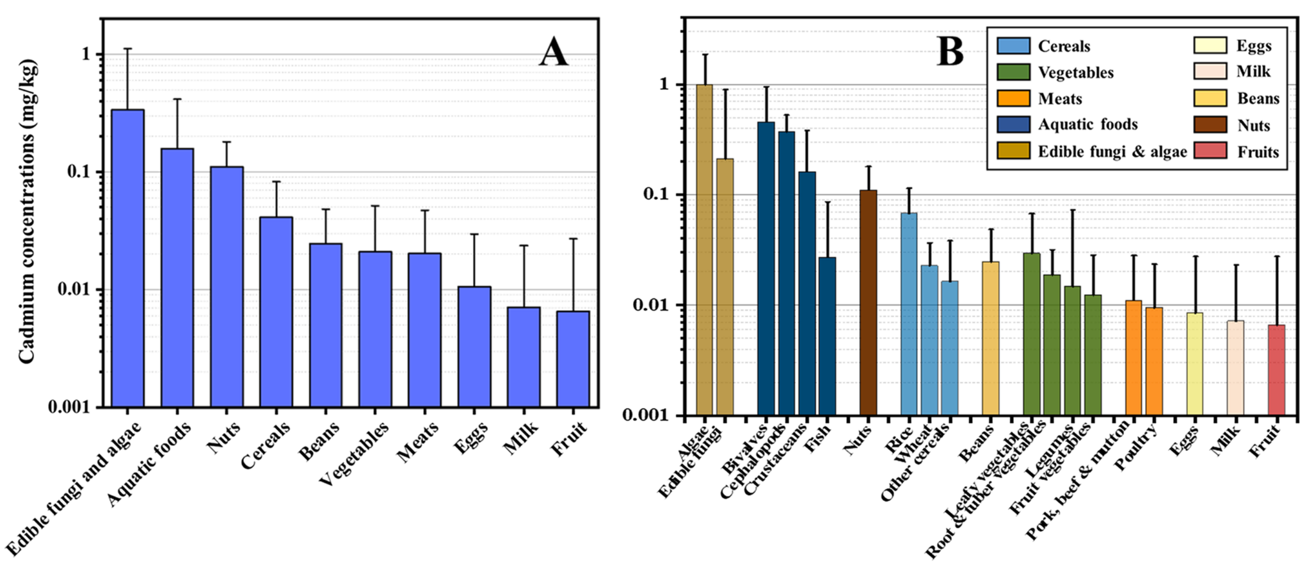

Fig. 1 Cadmium concentrations in food items across China based on published studies between 2000 and 2021. Panel **A** indicates the sample size-weighted average Cd concentrations of ten food items. Panel **B** indicates the Cd concentrations in each food subcategories. (The error bars represent the standard deviation of Cd concentrations in foods)

(water/sediment) (Wang et al. 2010). The coastal waters are severely affected by land-based pollution, which exacerbates heavy metals pollution of water and sediments, and leads to the deterioration of the farming environment (Lu et al. 2021). Bivalves and most crustaceans are benthic organisms with weak migration ability and small activity range. Therefore, they lack the ability to avoid regional environmental pollution and are the most vulnerable aquatic animals to heavy metal pollution (Lin et al. 2021).

As a staple food of Chinese residents, rice had an average Cd concentration of 0.067 mg/kg, higher than wheat and other cereals, with an exceedance rate of 3.2%. This result was the same as that of China National Center for Food Safety Risk Assessment, which found that rice had the highest mean Cd concentrations (0.062 mg/kg) among cereals (Song et al. 2017). After rice absorbs Cd from the soil, it will be rapidly transported from the roots to the plumule, resulting in a large accumulation of Cd in the grains (Tanaka et al. 2007). The bioavailability of Cd in rice depends largely on the physicochemical properties of the soil and the physiological characteristics of rice. Soil redox potential, soil pH, organic matter content, and essential trace element status in the soil affect bioavailability of Cd. These elements affect the solubility of Cd, which further affects the uptake of Cd by rice (Li et al. 2017; Sebastian and Prasad 2013).

For the vegetables, the mean Cd concentration in leafy vegetables (0.029 mg/kg) was higher than in the other three vegetables and about twice as high as in legumes and fruit vegetables. The accumulation of Cd in different vegetables varies greatly. Different organs of the same plant have different enrichment coefficients for Cd, generally: roots > stems and leaves > fruits. Cadmium is mainly concentrated in the roots of plants. After entering the root cortex cells, Cd forms stable macromolecular complexes or insoluble organic macromolecules by combing with proteins, polysaccharides, ribose, and nucleic acids in the roots (Li et al. 2008). In addition, the concentrations of Cd in leafy vegetables increased due to deposition and adhesion of atmospheric particulate pollutants on the leaf surface (Xu et al. 2022). Song et al. studied Cd concentrations in vegetables from 31 provinces in China, and the results showed that the order of Cd concentration was leafy vegetables > root and stalk vegetables > fruit vegetables (Song et al. 2017). Yang et al. investigated Cd accumulation in different vegetable species. The results showed that the order of Cd accumulation in vegetables was leaves > roots > melons > beans (Yang et al. 2010).

The average concentrations of Cd in foods from different regions are shown in Fig. 2. The highest Cd concentrations in cereals and aquatic foods were found in south China, while the highest Cd concentrations in vegetables and edible fungi were found in southwest China. The geographical distribution of Cd concentrations in foods was influenced not only by the Cd absorption capacity of plants and the accumulation capacity of animals to the environment, but also by the local environment pollution. In fact, numerous studies have identified three main sources of Cd contamination in Chinese cropland: mining and smelting activities, wastewater irrigation, and urban activities (Liu et al. 2016; Lu et al. 2015; Zhang et al. 2015). Among them, soils polluted by mining and smelting industries had higher Cd concentrations than soils polluted by other sources (Cheng and Nathanail 2021). Cadmium minerals were mainly found in southwest, central, and east China, and these regions account for 88% of the country's proven Cd deposits (Yuan et al. 2012). In addition, south China is a developed region for electronics, chemical, and other light industries in China. Wastewater discharged from pyrite ore for sulfuric acid production and phosphate ore for phosphate fertilizer production is an important source of heavy metals pollution (Luo et al.

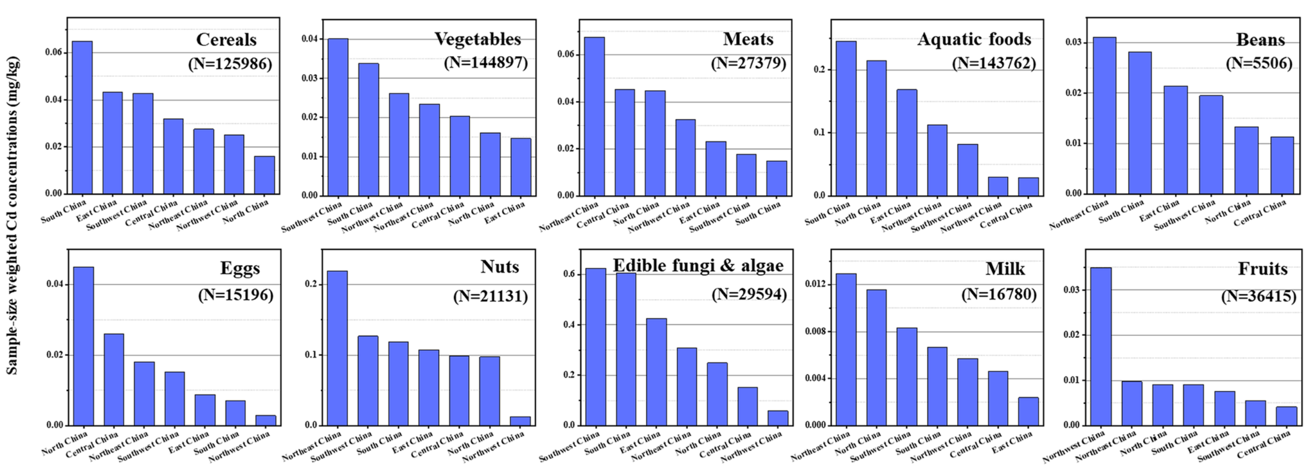

Fig. 2 The cadmium concentrations in each food items in different regions

2020). E-waste recycling is another source of heavy metals pollution. Heavy metal pollution is present in air, surface water, groundwater, soil, and river sediments at e-waste disposal site (Zheng et al. 2013). Most of the crops in the vicinity of the electronics factory had Cd concentrations that seriously exceeded the Chinese MACs (Zhang et al. 2021a).

The temporal analysis showed an increasing trend in the sample size-weighted average Cd concentration for the total food category from 2011 to 2021 (Fig. S2). During this period, Cd concentrations in cereals and vegetables showed a decreasing trend, while Cd concentrations in aquatic foods showed an increasing trend (Fig. S2). However, there was no statistically significant relationship between changes in Cd concentrations and temporal changes ($p > 0.05$). The concentration of Cd in food may be influenced by a variety of factors, including the promulgation of the MACs in China and environmental contamination. In 1994, China introduced the first permissible limit for Cd in foods, stipulating that the MAC of Cd in rice was 0.2 mg/kg, which was the same as European standard and stricter than the international standards (WHO: 0.4 mg/kg) (CAC, 2006; EFSA, 2009). The MACs for Cd in rice have not changed so far, but the MACs for Cd in vegetables, aquatic foods, and other foods have changed. In 1994, the MACs for Cd in vegetables, meats, and aquatic foods were 0.05, 0.1, and 0.1 mg/kg, respectively (GB 15201-1994). After continuous revision of standards and subdivision of food categories, the MACs introduced have been revised to 0.05–0.2 mg/kg for vegetables, 0.1–1.0 mg/kg for meats in 2005 (GB 2762-2005), and 0.1–2.0 mg/kg for aquatic foods in 2012 (GB 2762-2012). The MACs of Cd in these food categories were more lenient than in the past after 2012.

On the other hand, the temporal changes of Cd in atmosphere, agricultural soils, and water across China also have a potential impact on the Cd concentration in foods. Shi et al. assessed the status of Cd accumulation in agricultural soils across China and noted a gradual increase in Cd concentration from 1981 to 2016 (Shi et al. 2019). Soil contamination surveys in China have shown that Cd concentrations in north, northeast, and west China have increased by an average of 10–40% since the 1980s. In coastal regions and south China, the increase was more than 50% (MEE and MNR 2014). Another reason is soil acidification. About 80–90% of paddy fields in China are located in red soil region (Yu et al. 2016). Soils in red soil regions are naturally acidic, but artificial acidification is occurring due to overuse of nitrogen fertilizers and the intensification of agricultural production (Wang et al. 2019b). Over the past 30 years, the pH of agricultural soils in China has decreased by nearly 1 unit (Zhu et al. 2016). Soil acidification has significantly increased the solubility of Cd in the soil (Wang et al. 2019a).

Dietary Exposure Assessment of Cd Across China

The average daily intake of Cd for the Chinese residents was 34.3 μg/day (approximately 0.57 μg/kg BW/day). A total of 74.1% of dietary Cd exposure came from plant-based foods, while 25.9% came from animal-based foods (Fig. 3A). Cereals (46.2%), vegetables (19.2%), and aquatic foods (18.4%) were the three food categories that contributed the most to dietary Cd exposure, with a total contribution of 83.8%. This result was similar to that of China National Center for Food Safety Risk Assessment. The exposure of the general Chinese residents to Cd through dietary sources was 30.6 μg/day. Cereals accounted for more than 55.8% of Cd exposure, followed by vegetables (15.8%) and aquatic foods (10.7%) (Song et al. 2017). Dietary Cd exposure in European was generally lower than in China. EFSA estimated that the Cd exposure of European population was 0.25 μg/kg BW/day (EFSA 2012). The dietary Cd exposure of Austrian adults

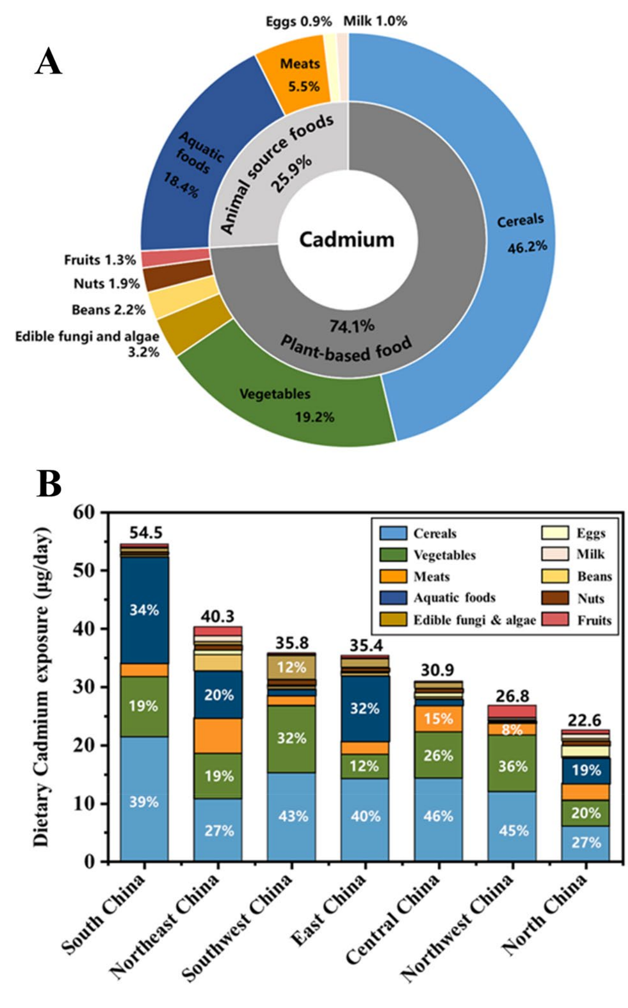

Fig. 3 **A** The contribution ratio of ten food items to dietary Cd intake in China. **B** Dietary Cd exposure and contribution ratio of ten food items in regions

was 0.17 μg/kg BW/day, with the highest exposure (29.2%) for "grains and grain-based products" (including bread, pasta and rice), followed by "potatoes" (14.2%) and "leafy vegetables" (12.2%) (Vlachou et al. 2021). The average exposure of the French population to Cd was estimated at 0.16 μg/kg BW/day. The main causes of Cd exposure were "bread and dried bread products" (22%) and "potatoes and potato products" (12%) (Arnich et al. 2012). Compared with other Asian countries, Cd exposure among Chinese was lower than that in Thailand (50 μg/day), but higher than Japan (22.8 μg/day) and South Korea (14.5 μg/day) (Kim and Wolt 2011; Ohno et al. 2010; Satarug et al. 2013). As a staple food in these countries, rice is the most important source of dietary Cd exposure (Chunhabundit 2016; Marcussen et al. 2013).

The spatial distribution of dietary Cd exposure in seven regions of China is shown in Fig. 3B. The dietary Cd exposures ranged from 22.6 to 54.5 μg/day in different regions, with higher exposures in southern regions than that in northern regions. Due to the great differences in dietary patterns, the dietary Cd exposure of southern residents was generally significantly higher than that of northern residents (Cheng and Nathanail 2021; Song et al. 2017; Yuan et al. 2014). A risk assessment study of Cd concentrations in farmland across 19 provinces/cities in China showed that farmland posing a high risk to human health was located in south China, while farmland posing a low risk was located in north China (Cheng and Nathanail 2021). The National Center for Food Safety Risk Assessment also found that the dietary Cd exposure of the southern population was significantly higher than that of the northern population, with a 1.5–1.8-fold difference between different age and sex groups (Song et al. 2017). As for the food contribution, consistent with the national Cd exposure profile, cereals were the largest source of dietary Cd exposure in all regions. In South, Northeast, and East China, aquatic foods ranked second in terms of contribution to Cd exposure. In the remaining regions, vegetables were the second largest source of dietary Cd exposure for the local residents. This is due to the food choices of local residents are influenced by local food production, food processing and trade practices, purchase levels, and dietary habits (Yin et al. 2020). The higher Cd contribution of edible fungi and algae in southwestern China was attributed to the abundance of edible fungi in Yunnan and Guizhou provinces and the high consumption of edible fungi by local residents (Fu et al. 2020).

Risk Assessment of Dietary Cd Exposure in Chinese

The cumulative population frequency distribution of daily dietary Cd exposure is shown in Fig. 4A. Approximately, 15.4% of Chinese residents exceeded the health-based guideline value set by JECFA, indicating a risk of kidney damage. Among the seven regions, south China had the highest proportion of the population exceeding the guideline value (37.2%).

The cumulative probability distribution of Chinese UCd simulated by the toxicokinetic model based on dietary Cd exposure nationwide and regions is shown in Fig. 4B. The mean and median UCd in Chinese residents were 1.62 and 0.60 μg/g creatinine, respectively. The cumulative probability density distribution showed that 6.6% of Chinese residents exceeded the JECFA safety threshold. Residents of south China were at relatively higher risk, with 11.7% of residents exceeding the safety threshold. Compared to the results from the Chinese Center for Disease Control and Prevention, the geometric mean UCd for 9,821 Chinese adults

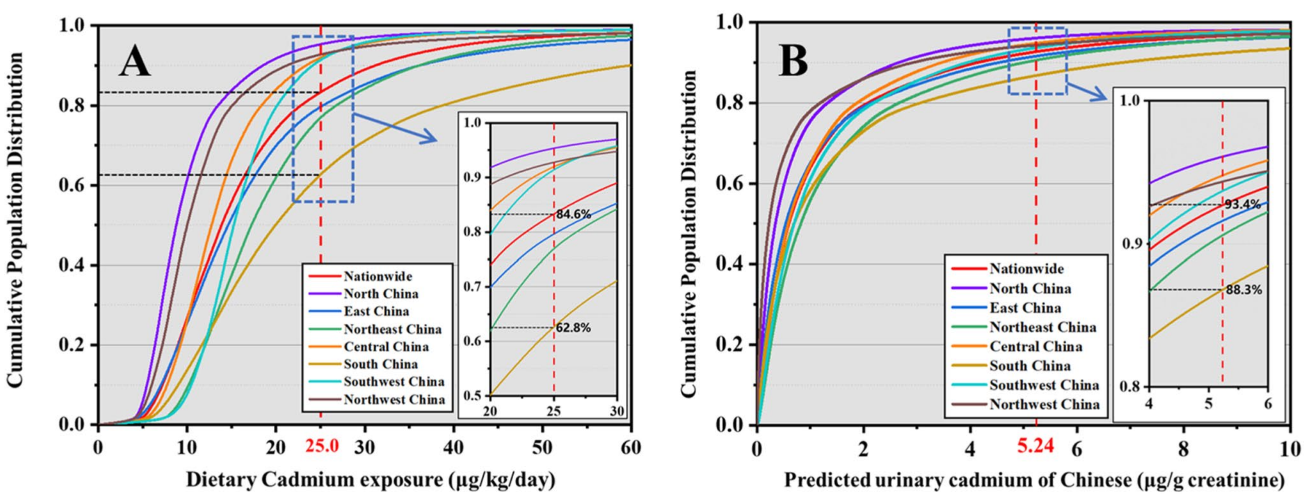

Fig. 4 The cumulative population frequency distribution of **A** daily dietary Cd exposure simulated by probabilistic estimation in different regions. **B** Urinary Cd concentrations simulated by toxicokinetic model in different regions. (The sub-figure is the enlargement of the dashed boxes)

in 2017–2018 was 0.58 μg/g creatinine (Lv et al. 2021). In comparison, the UCd of residents from Korea and Japan were 1.81 and 3.03 μg/g creatinine, respectively, which was higher than that of this study (Horiguchi et al. 2013; Moon et al. 2014). The Canadian Health Measures Survey showed that the UCd of Canadian residents was 0.41 μg/g creatinine from 2009 to 2011 (Garner and Levallois 2016). In countries such as Australia, Norway, Italy, and Sweden, residents generally have lower UCd concentrations. Residents of these countries rely mainly on potatoes, cereals, aquatic products, and beans, and the diet structure was quite different from that of Chinese (Satarug et al. 2017a). Kidney is the main accumulation site and target organ for Cd exposure. Cadmium can exert toxic effects through oxidative stress, apoptosis, calcium imbalance, and other mechanisms (Jin et al. 2018). It leads to congestion and edema in the early stage, and persistent toxic effects such as apoptosis in the later stage, ultimately affecting glomerular and tubular reabsorption (Jain 2020). Qing et al. established an overall association between UCd and renal injury biomarkers in Chinese residents, and explored a benchmark dose of UCd at 2.98 μg/g creatinine (Qing et al. 2021b).

The estimated HQ and ELCR indices for dietary Cd exposure in China and each region are summarized in Table S3. The national HQ index was 0.57, with all regions below 1, indicating that the Chinese population has no significant non-cancer health risks. In addition, the ELCR for each region ranged from 1.41 to 3.42×10^{-4}, which is within the acceptable range of health risks for carcinogenic chemicals recommended by the USEPA. The nationwide ELCR index was 2.17×10^{-4}, indicating that the lifetime probability of a person developing cancer through dietary exposure to Cd was 1/4608. Similar conclusions were derived in another risk assessment that the current risk of dietary Cd exposure in the Chinese population does not require additional attention, and that the risk of Cd carcinogenesis was higher in the south China than in the north China (Yuan et al. 2014).

Uncertainty and Limitations

The sensitivity of Cd concentration in foodstuffs to dietary Cd exposure of Chinese residents is shown in Fig S3. Spearman correlation coefficients were used to represent the sensitivity of each input variable, and the @Risk was used to fit the distribution characteristics of each input variable. The rank correlation coefficients between all input variables and the outcome were calculated using a linear model. The concentration of Cd in cereals, aquatic foods, and vegetables had the greatest effect on dietary exposure to Cd. The Spearman's rank correlation coefficients were 0.71, 0.40, and 0.30, respectively. This implies that the most effective way to reduce Cd exposure in the Chinese population may be to control or reduce the Cd concentrations in these foods.

The risk assessment process is inevitably subject to uncertainties and limitations, especially when the data come from different studies. Although this study applied the sample size weighting to calculate Cd concentrations in foods as well as Monte Carlo simulations to assess dietary Cd exposure risk to reduce the uncertainty of the results. However, there were still some inevitable uncertainties: 1. There might be systematic errors in the detection of Cd concentration in foods because the data came from different institutions and the detection methods were inconsistent. 2. The uneven distribution of sample size in time, space, and food categories increased the uncertainty of the results. Fig. S4 shows the frequency distributions of sample sizes across time, region, and food category for the included studies. Most of the sample sizes were derived from studies published in the last 5 years. Among the regions, East and South China had larger sample size than other regions. Among the food categories, the sample sizes of Cd concentrations in vegetables, cereals, and aquatic foods were higher than those of other foodstuffs. Foodstuffs or regions with unequal amount of data may increase the uncertainty in the assessment of Cd concentrations.

Conclusions

This study was the first large-scale metadata analysis of Cd concentrations in Chinese foods and assessed the dietary Cd exposure risk of the Chinese residents. The Cd concentrations in different food categories and regions showed strong variations and plant-based foods being the main source of dietary Cd exposure for Chinese residents. Due to the comprehensive effect of environmental pollution and dietary habits in various regions, the dietary Cd exposure of Chinese residents was 34.3 μg/day, varying from 22.6 to 54.5 μg/day in seven regions. The risk of renal injury from dietary Cd exposure in South China deserves further attention. The distribution characteristics of Cd concentrations in regions and foodstuffs obtained in this study can be used as a reference for Cd exposure risk assessment and provide database support for the formulation of dietary exposure standards in China.

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Author Contributions YQ contributed toward conceptualization, methodology, data curation, writing-original draft, and writing-review& editing. YL contributed toward methodology and data curation. XC contributed toward literature screening, database construction, and writing-original draft. WH contributed toward literature screening and database construction. SL contributed toward literature screening and database construction. YJ contributed toward literature screening and database construction. MJ contributed toward literature screening and database construction. LY contributed toward database check. JW contributed toward database check. SP contributed toward database check. YC contributed toward database check. YL contributed toward methodology. YL contributed toward validation and, supervision.

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Data Availability Data will be made available on request.

Declarations

Competing Interests The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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