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Joint effects between cadmium exposure and dietary antioxidant quality score on osteoporosis and bone mineral density

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Abstract

To explore the relationship between dietary antioxidant quality score (DAQS) and Cd exposure both alone and in combination with osteoporosis and bone mineral density (BMD) among postmenopausal women. In total, 4920 postmenopausal women from the National Health and Nutrition Examination Survey were included in this cross-sectional study. Weighted univariate and multivariate logistic regression analyses to assess the association between DAQS and Cd exposure with femur neck BMD, total femur BMD, osteoporosis among postmenopausal women, respectively, and the coexistence effect of DAQS and Cd exposure. Four hundred and ninety-nine had osteoporosis. DAQS (OR = 0·86, 95 % CI 0·77, 0·97) and high DAQS (OR = 0·60, 95 % CI 0·36, 0·99) were found to be associated with decreased odds of osteoporosis, while Cd exposure (OR = 1·34, 95 % CI 1·04, 1·72) and high Cd exposure (OR = 1·45, 95 % CI 1·02, 2·06) were related to increased odds of osteoporosis. A positive correlation was observed between high DAQS and both total femur BMD and femur neck BMD. Conversely, Cd exposure was found to be negatively correlated with total femur BMD and femur neck BMD. Additionally, taking low-Cd and high-quality DAQS group as reference, the joint effect of Cd exposure and DAQS showed greater increased odds of osteoporosis and decreased total femur BMD and femur neck BMD as Cd level and DAQS combinations worsened. There may be an interaction between Cd exposure and DAQS for femur neck BMD, total femur BMD, and osteoporosis in postmenopausal women.

Keywords: **Dietary antioxidant quality score: Cadmium exposure: Bone mineral density: Osteoporosis: Postmenopausal women**

Osteoporosis, the most prevalent bone disease worldwide, is characterised by reduced bone mineral density (BMD) and deterioration of microstructure, resulting in fragility fractures that significantly impair patients' quality of life and increase their risk of mortality and disability[1,2]. It is estimated that osteoporosis affects over 50 billion individuals globally[3]. Previous studies have indicated that females are at a higher risk of developing osteoporosis and associated fractures compared with males[4], with the likelihood of developing this condition increasing during menopause[5,6]. Identifying modifiable factors associated with osteoporosis may help mitigate the risk of developing this condition.

Cd is a heavy metal that occurs naturally[7]. Due to the extensive use of Cd in industry and agriculture, as well as other anthropogenic activities, the levels of Cd in soil, water and air have increased, thereby elevating general human exposure to Cd[7]. Certain subgroups, including vegetarians, children, smokers, and individuals residing in heavily contaminated areas, may encounter elevated levels of Cd exposure[8]. Cd exposure has been considered as an important risk factor for osteoporosis in numerous studies[9]. A systematic review and meta-analysis have indicated that environmental exposure to Cd was linked with an increased risk of osteoporosis in post-menopausal women[9]. On the other hand, it has been suggested that the risk of osteoporosis may be associated with the consumption of various dietary antioxidants, such as vitamins A, C, and E, Zn, Mg and Se[10,11]. Antioxidants have the ability to inhibit oxidative stress, which in turn can prevent or delay the risk of osteoporosis[12]. Interestingly, a cross-sectional study based on the National Health and Nutrition Examination Survey (NHANES) revealed that intake of dietary antioxidant was able to modify the effects of Cd exposure on markers of inflammation and oxidative stress[13]. Additionally, animal experiments have demonstrated that α-tocopherol can reduce Cd-induced oxidative stress[14]. A study conducted by Li et al. revealed that a higher intake of α-tocopherol may potentially improve the Cd-related osteoporosis and mitigate the loss of BMD in individuals aged 50 years or older[15]. These findings suggested that dietary

Abbreviations: BMD, bone mineral density; DAQS, dietary antioxidant quality score; NHANES, National Health and Nutrition Examination Survey.

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antioxidants may ameliorate the effect of Cd exposure on the risk of osteoporosis. Previous research has primarily focused on the effects of individual antioxidants on bone health. However, it is important to note that multiple dietary nutrients are often present simultaneously and the impact of diet on an individual's health may be influenced by complex interactions between these nutrients[16]. Therefore, investigating the overall consumption of multiple dietary antioxidants is more valuable than examining a single antioxidant. Dietary antioxidant quality score (DAQS) represents a composite score of six dietary antioxidant combinations. To our knowledge, limited studies are available on the combined effect of Cd exposure and DAQS on orthopaedic disorders for postmenopausal women.

In this study, we hypothesised that there was an interaction between Cd exposure and DAQS on BMD and osteoporosis in postmenopausal women.

Methods

Study population

This cross-sectional study utilised data from the NHANES database 2005–2010 and 2013–2014 (BMD data were not available in the NHANES database 2011–2012). The NHANES database is an ongoing cross-sectional survey of the non-institutionalised civilian population in the USA, utilising a stratified multi-stage probability sampling design[13]. The collection of participants' information involved interviews and physical examinations. We included 7608 postmenopausal women. Postmenopausal women with missing data on serum Cd level (n 965), DAQS (n 259), femur neck and total femur BMD (n 1464) were excluded from analysis. Finally, 4920 postmenopausal women were included in the final analysis (Fig. 1). The requirement of ethical approval for this was waived by the Institutional Review Board of Affiliated Hospital of Nantong University, because the data were accessed from NHANES (a publicly available database). The need for written informed consent was waived by the Institutional Review Board of Affiliated Hospital of Nantong University due to the retrospective nature of the study. All methods were performed in accordance with the relevant guidelines and regulations.

Definition of menopausal status

Menopausal status was determined based on a self-reported reproductive health questionnaire[17]. Females were asked to answer 'Have you had at least once menstrual period in the past 12 months?' If the answer was 'no', she was then asked, 'What is the reason that you have not had a period in the past 12 months?' She was considered as postmenopausal if she answered menopause or hysterectomy.

Outcome variable

The outcome variable was femur neck BMD level, total femur BMD level and osteoporosis risk. For participants from NHANES database, dual-energy X-ray absorptiometry examinations were utilised to quantify BMD. The examination was conducted by a certified radiology technician utilising the Hologic QDR-4500A fan-beam densitometer (Hologic, Inc.) (https://wwwn.cdc.gov/Nchs/Nhanes/2013–2014/DXXFEM_H.htm). Femoral neck and total femur BMD were transformed into T-scores using the following formula: $\text{T-score} = (\text{BMD}_{\text{respondent}} - \text{mean BMD}_{\text{reference}})/\text{SD}_{\text{reference}}$. Osteoporosis was defined as femur neck or total femur BMD T-score $\leq -2{\cdot}5$[18].

Explanatory variables

Blood samples were collected and stored under appropriate freezing conditions (–30°C) before being shipped to the Laboratory Science Department, National Center for Environmental Health, and Centers for Disease Control and Prevention for analysis. The Cd level in whole blood was measured using inductively coupled plasma-mass spectrometry (ICP-MS). In this study, Cd exposure levels were stratified into two groups based on the upper quartile, namely low and high Cd levels.

The DAQS is composed of six essential dietary antioxidant micronutrients, namely vitamins A, C, E, Se, Zn and Mg[19]. Each of the six nutrient/mineral intakes was compared with the respective recommended daily intake for US adults. DAQS of 0 is assigned when antioxidant vitamin/mineral intake < 2/3 of the RDA, while a score of 1 is given when the intake ≥ 2/3 of the recommended daily intake. The total DAQS ranges from 0 to 6. In this study, the intake of each nutrient/mineral was calculated using the average of two 24-h dietary reviews. The first 24-h recall was collected face to face at the Mobile Examination Center (MEC) examination, and the second 24-h recall was collected by a phone call at least 3–10 d later. This method involves documenting all food and beverage items consumed by individuals within 24 h. Trained technicians collect and analyse the dietary data to determine nutrient composition. Each nutrient/mineral content in food is determined by the US Department of Agriculture's National Nutrient Database. In addition, NHANES also collected information about dietary supplement. Total intakes of each nutrient/mineral were calculated by summing from total daily intake from diet and supplemental intake. DAQS was categorised as three groups: low quality (1–2 score), medium quality (3–4 score) and high quality (5–6 score)[19].

Possible confounding variables

The potential confounding variables in this study were collected[10,12,15]: age, race/ethnicity, education, marital status, family poverty-to-income ratio, BMI (kg/m^2), smoking status, physical activity, history of fracture, history of diabetes and hypertension, parental history of fracture, cotinine (ng/ml), Pb (μg/dl), Fe (μmol/l), serum 25-hydroxyvitamin D (25(OH)D, nmol/l), Ca (mg/d), using of female hormone, glucocorticoid, anti-osteoporosis therapy, energy (kcal/d), protein (g/d), carbohydrate (g/d), fat (g/d), vegetable intake (cups/d) and grain intake (cups/d). Smoking is defined as a lifetime history of having smoked at least 100 cigarettes. Participants' parental history of fractures was ascertained via a questionnaire.

Statistical analysis

This study used three weighted variables: the mobile examination centre exam weight was used for weighting (WTMEC2YR) and study design variables (SDMVPSU and SDMVSTRA). The

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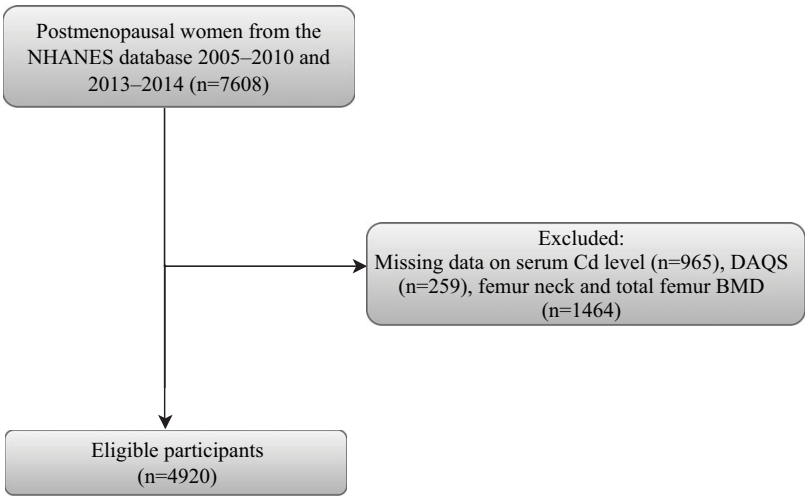

Fig. 1. Flow chart for screening the participants. NHANES, National Health and Nutrition Examination Survey; DAQS, dietary antioxidant quality score; BMD, bone mineral density.

baseline characteristics of participants were presented by the weighted mean and standard error (continuous variables) and weighted percentages and frequencies (*n* (%)) (categorical variables). Additionally, we performed a multiple imputation method to fill the missing variables and conducted sensitivity analysis before and after interpolation (online Supplementary Table 1). SAS 9.4 software (SAS Institute Inc.) software was used for data extraction and cleaning, and R 4.2.2 software was used for statistical analyses.

First, weighted univariate logistic regression analysis was employed to identify potential confounding factors associated with each outcome variable (namely femur neck BMD, total femur BMD and osteoporosis). $P < 0{\cdot}05$ was considered statistically significant. Then, we adopted weighted univariate and multivariate logistic regression analyses to assess the association between DAQS and Cd exposure with femur neck BMD, total femur BMD and osteoporosis among postmenopausal women, respectively. OR, β coefficients and 95 % CI were calculated. In addition, we categorised Cd exposure and DAQS into six distinct groups based on varying levels: low-Cd and low-quality DAQS group, low-Cd and medium-quality DAQS group, low-Cd and high-quality DAQS group, high-Cd and low-quality DAQS group, high-Cd and medium-quality DAQS group, and high-Cd and high-quality DAQS group. The coexistence effect of DAQS and Cd exposure for femur neck BMD, total femur BMD and osteoporosis risk was assessed by weighted univariate and multivariate logistic regression analyses. The R package 'visreg' was utilised to visually represent the interaction.

Results

Characteristics of study population

A total of 4920 postmenopausal women were included for further analysis. The characteristics of the study population are presented in Table 1. The mean age was 61·71 years (SE = 0·25 years), with a mean BMI of 28·59 kg/m^2 (SE = 0·12 kg/m^2). 83·00 % of participants had not a history of diabetes. The majority of participants had a history of hypertension. Overall, the mean Cd level was 0·56 ug/l, and the mean DAQS was 4·09. Importantly, of these 4920 postmenopausal women, 499 had osteoporosis. Table 1 also shows a comparison of characteristics between osteoporosis and non-osteoporosis groups. The osteoporosis group exhibited significantly higher values in age (71·01 (0·56) *v.* 60·72 (0·24) years), Cd level (0·73 (0·04) *v.* 0·54 (0·02) ug/l), cotinine level (63·82 (7·24) *v.* 41·40 (2·61) ng/ml) and Pb level (1·71 (0·05) *v.* 1·60 (0·02) ug/dl) compared with the non-osteoporosis group, while their DADS score (3·84 (0·08) *v.* 4·11 (0·04)), total femur BMD (0·63 *v.* 0·88 gm/cm^2) and femoral neck BMD (0·52 *v.* 0·75 gm/cm^2) were significantly lower ($P < 0{\cdot}05$).

Independent association of cadmium exposure and dietary antioxidant quality score on femur neck bone mineral density, total femur bone mineral density and osteoporosis risk

The univariate logistic regression analysis revealed confounding factors ($P < 0{\cdot}05$) associated with femoral neck BMD, total femoral BMD and osteoporosis, respectively (online Supplementary Table 2). As shown in Table 2, the independent association of Cd exposure and DAQS on femur neck BMD, total femur BMD and osteoporosis risk was explored. After adjusting age, race/ethnicity, education level, marital status, family poverty-to-income ratio, BMI, history of fracture, history of hypertension, cotinine, Pb, using of female hormone, anti-osteoporosis therapy, energy, protein and fat, DAQS (OR = 0·86, 95 % CI 0·77, 0·97; $P = 0{\cdot}013$) and high DAQS (OR = 0·60, 95 % CI 0·36, 0·99; $P = 0{\cdot}044$) were found to be associated with decreased odds of osteoporosis, while serum Cd level (OR = 1·34, 95 % CI 1·04, 1·72; $P = 0{\cdot}022$) and high serum Cd level (OR = 1·45, 95 % CI 1·02, 2·06; $P = 0{\cdot}038$) were related to increased odds of osteoporosis. In the fully adjusted model, a positive correlation was observed between high DAQS and both total femur BMD (β = 0·12, 95 % CI 0·01, 0·23, $P = 0{\cdot}040$) and femur neck BMD (β = 0·12, 95 % CI 0·01, 0·24; $P = 0{\cdot}039$). Conversely, Cd exposure was found to be negatively correlated

Table 1. Characteristics of the study population and comparison between osteoporosis and non-osteoporosis groups

	Total (*n* 4920)		Non-osteoporosis group (*n* 4421)		Osteoporosis group (*n* 499)		
Variables	*n*	%	*n*	%	*n*	%	*P*
Age (years)							
Mean	61·71		60·72		71·01		< 0·001
SE	0·25		0·24		0·56		
Race/ethnicity							< 0·001
Mexican American	669	4·91	629	5·18	40	2·37	
Other Hispanic	466	4·04	425	4·11	41	3·35	
Non-Hispanic White	2466	76·14	2144	75·40	322	83·15	
Non-Hispanic Black	969	9·14	919	9·66	50	4·29	
Other Race including Multi-Racial	350	5·77	304	5·65	46	6·85	
Education level							0·010
Less than 9th grade	573	5·59	499	5·26	74	8·67	
9–11th grade	648	10·58	568	10·07	80	15·37	
High school grade/GED or equivalent	1266	28·23	1127	28·20	139	28·57	
Some college or AA degree	1467	30·45	1345	30·92	122	26·00	
College graduate or above	966	25·15	882	25·55	84	21·39	
Marital status							< 0·001
Married	2445	57·39	2259	58·79	186	44·24	
Widowed	1337	21·44	1122	19·46	215	40·02	
Divorced	690	13·60	625	13·81	65	11·67	
Separated	106	1·38	99	1·46	7	0·65	
Never married	243	4·17	220	4·29	23	3·03	
Living with partner	99	2·02	96	2·20	3	0·38	
	Mean	SE	Mean	SE	Mean	SE	
Family PIR	3·13	0·04	3·18	0·04	2·62	0·12	< 0·001
BMI (kg/m^2)	28·59	0·12	29·01	0·13	24·64	0·29	< 0·001
Physical activity, MET/min	743·30	59·33	761·13	57·93	575·56	99·74	0·012
	n	%	*n*	%	*n*	%	
Smoking status							0·159
Yes	1957	44·03	1743	43·63	214	47·89	
No	2963	55·97	2678	56·37	285	52·11	
History of fracture							< 0·001
Yes	89	1·68	59	1·18	30	6·45	
No	4831	98·32	4362	98·82	469	93·55	
History of diabetes							0·503
No	3803	83·00	3399	82·86	404	84·33	
Yes	1117	17·00	1022	17·14	95	15·67	
History of hypertension							< 0·001
No	1287	30·21	1204	31·68	83	16·33	
Yes	3633	69·79	3217	68·32	416	83·67	
Parental history of fracture							0·285
No	4362	88·19	3932	88·37	430	86·57	
Yes	558	11·81	489	11·63	69	13·43	
	Mean	SE	Mean	SE	Mean	SE	
Cotinine (ng/ml)	43·55	2·48	41·40	2·61	63·82	7·24	0·004
Cd (μg/l)	0·56	0·01	0·54	0·02	0·73	0·04	< 0·001
Pb (μg/dl)	1·61	0·02	1·60	0·02	1·71	0·05	0·023
Fe (μmol/l)	14·78	0·12	14·77	0·12	14·90	0·28	0·641
25(OH)D (nmol/l)	7·95	0·24	8·15	0·26	6·05	0·51	< 0·001
Ca (mg/d)	1099·08	15·64	1098·86	16·02	1101·17	35·46	0·948
	n	%	*n*	%	*n*	%	
Using of female hormone							< 0·001
No	4596	90·15	4108	89·41	488	97·05	
Yes	324	9·85	313	10·59	11	2·95	
Glucocorticoid							0·743
No	4487	90·56	4032	90·50	455	91·13	
Yes	433	9·44	389	9·50	44	8·87	
Anti-osteoporosis therapy							< 0·001
No	4624	94·18	4189	94·91	435	87·33	
Yes	296	5·82	232	5·09	64	12·67	
	Mean	SE	Mean	SE	Mean	SE	
Energy (kcal/d)	1697·06	13·58	1709·32	13·83	1581·74	30·53	< 0·001
Protein (g/d)	66·07	0·53	66·77	0·57	59·45	1·36	< 0·001
Carbohydrate (g/d)	205·00	1·49	205·44	1·57	200·84	4·92	0·378
Fat (g/d)	66·29	0·58	66·72	0·62	62·23	1·62	0·012
DAQS	4·09	0·04	4·11	0·04	3·84	0·08	0·002
	n	%	*n*	%	*n*	%	

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Table 1. (*Continued*)

Variables	Total (*n* 4920)		Non-osteoporosis group (*n* 4421)		Osteoporosis group (*n* 499)		*P*
	n	%	*n*	%	*n*	%	
DAQS							0·021
Low quality	2137	41·61	734	13·59	111	18·88	
Medium quality	1938	44·29	1927	41·45	210	43·11	
High quality	845	14·10	1760	44·95	178	38·01	
	Mean	SE	Mean	SE	Mean	SE	
Total femur BMD (gm/cm^2)	0·85	0·00	0·88	0·00	0·63	0·00	< 0·001
Femoral neck BMD (gm/cm^2)	0·73	0·00	0·75	0·00	0·52	0·00	< 0·001

GED, general educational development; AA, associate of arts; PIR, poverty to income ratio; MET, metabolic equivalent; 25(OH)D, 25-hydroxyvitamin D; DAQS, dietary antioxidant quality score; BMD, bone mineral density.

Table 2. Independent association of Cd exposure and DAQS on femur neck BMD/total femur BMD/osteoporosis risk

Variables	Osteoporosis*			Total femur BMD*			Femur neck BMD†		
	OR	95 % CI	*P*	β	95 % CI	*P*	β	95 % CI	*P*
Model 1									
DAQS	0·87	0·80, 0·95	0·002	0·02	0·01, 0·04	0·030	0·01	−0·02, 0·03	0·683
DAQS levels									
Low quality	Ref			Ref			Ref		
Medium quality	0·75	0·51, 1·11	0·145	0·12	0·02, 0·22	0·019	0·10	−0·00, 0·21	0·052
High quality	0·61	0·42, 0·88	0·010	0·10	0·02, 0·19	0·019	0·05	−0·05, 0·15	0·303
Cd	1·53	1·28, 1·82	< 0·001	−0·20	−0·28, −0·13	< 0·001	−0·15	−0·21, −0·09	< 0·001
Cd									
Low level	Ref			Ref			Ref		
High level	1·87	1·48, 2·37	< 0·001	−0·26	−0·33, −0·19	< 0·001	−0·15	−0·23, −0·08	< 0·001
Model 2									
DAQs	0·86	0·77, 0·97	0·013	0·03	0·01, 0·06	0·034	0·02	−0·01, 0·05	0·080
DAQs levels									
Low quality	Ref			Ref			Ref		
Medium quality	0·88	0·54, 1·44	0·604	0·08	−0·01, 0·18	0·093	0·09	−0·01, 0·20	0·073
High quality	0·60	0·36, 0·99	0·044	0·12	0·01, 0·23	0·040	0·12	0·01, 0·24	0·039
Cd	1·34	1·04, 1·72	0·022	−0·08	−0·14, −0·01	0·021	−0·07	−0·13, −0·00	0·038
Cd									
Low level	Ref			Ref			Ref		
High level	1·45	1·02, 2·06	0·038	−0·08	−0·17, −0·00	0·046	−0·02	−0·10, 0·06	0·667

DAQS, dietary antioxidant quality score; BMD, bone mineral density.
Model 1: univariate logistic regression analysis.
* Model 2: I/II: adjusted age, race/ethnicity, education level, marital status, family poverty-to-income ratio (PIR), BMI, history of fracture, history of diabetes, parental history of fracture, cotinine, Ca, Pb, Fe, 25-hydroxyvitamin D (25(OH)D), using of female hormone, anti-osteoporosis therapy, energy, protein, fat and vegetable intake.
† III: adjusted age, race/ethnicity, education level, marital status, family PIR, BMI, history of fracture, history of hypertension, cotinine, Pb, using of female hormone, anti-osteoporosis therapy, energy, protein and fat.

with total femur BMD (β = −0·08, 95 % CI −0·14, −0·01; *P* = 0·021) and femur neck BMD (β = −0·07, 95 % CI 0·13, 0·00; *P* = 0·038).

Joint effects of cadmium exposure and dietary antioxidant quality score on femur neck bone mineral density, total femur BMD and osteoporosis

As presented in Fig. 2, taking low-Cd and high-quality DAQS group as reference, the joint effect of Cd exposure and DAQS showed greater increased odds of osteoporosis, decreased total femur BMD and femur neck BMD as Cd level and DAQS combinations worsened. Additionally, Fig. 3(a)–(c) also showed varying levels of Cd exposure and different quality of DAQS had joint effects on osteoporosis, total femur BMD and femur neck BMD. These results demonstrated that there may be an interaction of Cd exposure and DAQS on osteoporosis risk, total femur BMD and femur neck BMD.

Discussion

In this cross-sectional study, we found that Cd exposure and DAQS were significantly associated with osteoporosis risk, total femur BMD and femur neck BMD, respectively. In addition, we observed the potential interaction of Cd exposure and DAQS on osteoporosis risk, total femur BMD and femur neck BMD in postmenopausal women.

Many studies have provided evidence that dietary antioxidant micronutrients play a crucial role in the development of bone health[20,21]. The Mendelian randomisation study has proposed that α-tocopherol, the most potent form of vitamin E, was believed to have a positive correlation with increased BMD[21]. In a study of 280 healthy Spanish women, there was an observed association between DAQS and BMD[22]. As numerous studies have indicated, oxidative stress plays a pivotal role in the pathogenesis of osteoporosis. The consumption of antioxidants

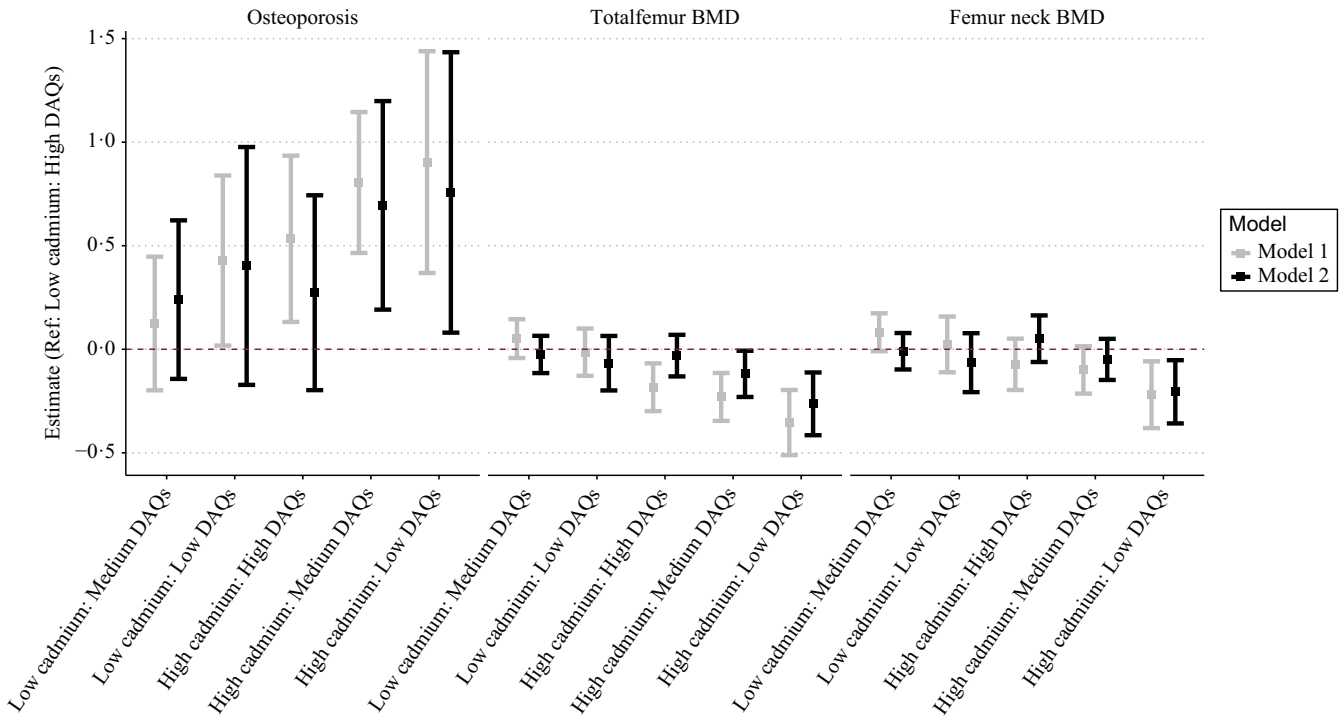

Fig. 2. Effect size for the combination of different quality of DAQS and different serum Cd levels on osteoporosis, total femur BMD and femur neck BMD. DAQS, dietary antioxidant quality score; BMD, bone mineral density.

may impact BMD by mitigating free radical production and preventing oxidation-induced damage to bone cells[21–23]. However, there is still uncertainty about the relationship between DAQS and BMD in postmenopausal women. Our study has demonstrated that a higher-quality DAQS diet may significantly increase BMD in postmenopausal women and effectively reduce the risk of developing osteoporosis.

Consistent with prior research, exposure to Cd was a risk factor for osteoporosis in postmenopausal women[8]. This may be attributed to the direct osteotoxic effect of Cd, which can impede osteoblast differentiation and metabolism, stimulate osteoclast formation and activity, and hasten bone remodelling[9]. It is worth noting that an interaction between Cd exposure and DAQS on the femur neck BMD, total femur BMD and osteoporosis in postmenopausal women was found in this study after adjusting all confounding factors, which meant that the combined effect of the higher Cd exposure and lower DAQS may lead to increased risk of osteoporosis and decreased femur neck BMD and total femur BMD. The mechanisms underlying the interaction between Cd exposure and DAQS on the BMD and osteoporosis remain incompletely understood. This may still be associated with inflammation and oxidative stress[24,25]. Exposure to Cd induces both inflammatory levels and oxidative stress. Dietary intake with antioxidant properties may regulate inflammation and oxidative stress[13,26]. In addition, as shown in online Supplementary Table 3, the proportion of participants in the high-Cd group who had a history of smoking was higher compared with that in the low-Cd group (79·54 % *v.* 32·21 %, $P < 0·001$), indicating smokers may encounter elevated levels of Cd exposure. The Ca level in the high-Cd group was lower than that in the low-Cd group (online Supplementary Table 3, 987·65 mg/d *v.* 1136·40 mg/d, $P < 0·001$). Based on our findings, promoting a high intake of DAQS may potentially mitigate the risk of osteoporosis and enhance BMD in postmenopausal women, particularly those with high Cd exposure (such as smokers), as long as Ca intakes remain adequate. Cd may disrupt the biological functions of Ca^{2+} ions[27]. Higher serum Cd may reflect a higher intake of dietary Cd, and/or be a marker for low dietary Ca, and/or be a marker for vegetarian type of diet. However, the data utilised in this study originated from the NHANES public database, which unfortunately lacked information on vegetarian type of diet. We only obtained participants' data on intake of vegetables and grains. In this study, the data showed no significant evidence (online Supplementary Table 3, $P = 0·360$) that higher Cd intakes were linked with more dietary grain consumption, but an equivocal finding that on average, the high-Cd group showed lower vegetable consumption ($P = 0·024$). This is a little contrary to expectations as vegetarian diets are expected to provide more Cd but may reflect the characteristics of the US population in the NHANES study group.

Furthermore, urinary Cd was also used to assess the level of Cd exposure in this study. Due to a high number of missing urinary Cd data among participants, only 1795 individuals had available urinary Cd data. Urine specimens are processed, stored and shipped to the Division of Environmental Health Laboratory Sciences, National Center for Environmental Health, and Centers for Disease Control and Prevention for analysis (https://wwwn.cdc.gov/Nchs/Nhanes/2007–2008/UHM_E.htm). The urinary Cd level was measured using ICP-MS. Urinary Cd concentrations were standardised by urine creatinine. As displayed in online Supplementary Fig. 1 and Fig. 2, there was a joint effect of urinary Cd level and DAQS on BMD and osteoporosis.

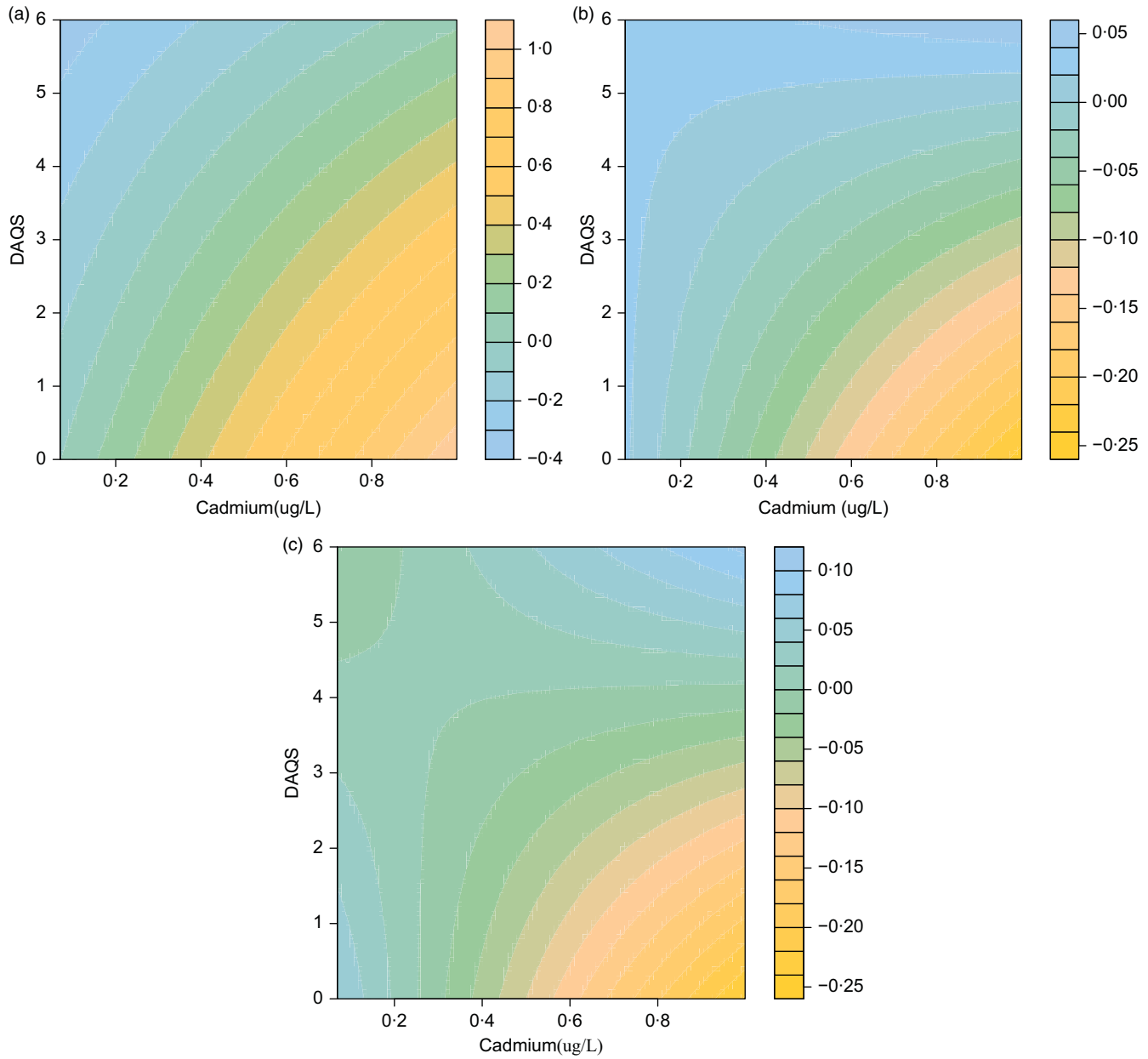

Fig. 3. Joint effects of different quality of DAQS and varying levels of serum Cd exposure on (a) osteoporosis, (b) total femur BMD and (c) femur neck BMD. DAQS, dietary antioxidant quality score; BMD, bone mineral density.

The findings of our study could offer novel evidence of bone health, aiming to enhance control and prevention measures against bone diseases. Nonetheless, our study has also a few limitations. First, the cross-sectional design of this study makes it difficult to determine the causal relationship between DAQS, Cd exposure, BMD and osteoporosis. Second, the DAQS was calculated from the mean intake by using two the 24-h dietary recall method, which may only reflect the dietary antioxidant micronutrients intake at the time of survey, but not the long-term dietary intake. The data collected from questionnaires and interviews may lead to recall bias. Lastly, in the NHANES study, BMD was measured at various sites. However, in the present study, femur BMD was chosen as a standard indicator for assessing osteoporosis; it is possible that this approach may underestimate the current prevalence of osteoporosis. In summary, it is imperative to conduct prospective studies in order to thoroughly validate the findings of this study.

Conclusion

In this study, we found that DAQS may be associated with decreased odds of osteoporosis, increased femur neck BMD and total femur BMD in postmenopausal women. Importantly, the interaction between Cd exposure and DAQS may influence femur neck BMD, total femur BMD and osteoporosis in postmenopausal women. Our findings provide evidence of

the association between Cd exposure and DAQS with bone health in postmenopausal women in the USA.

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H. L. designed the study and wrote the manuscript. H. L., A. Z. and N. L. collected, analysed and interpreted the data. H. L. critically reviewed, edited and approved the manuscript. All authors read and approved the final manuscript.

There are no conflicts of interest.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114523002477

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