British Journal of Nutrition (2024), 131, 123–133 doi:10.1017/S0007114523001435

Association between plasma and dietary trace elements and obesity in a rural Chinese population

Yufu Lu[1]†, Qiumei Liu[1]†, Chuwu Huang[1]†, Xu Tang[1], Yanfei Wei[1], Xiaoting Mo[1], Shenxiang Huang[1], Yinxia Lin[1], Tingyu Luo[2], Ruoyu Gou[2], Zhiyong Zhang[3], Jian Qin[5,6,7]* and Jiansheng Cai[2,4]

[1]*School of Public Health, Guangxi Medical University, Shuangyong Road No.22, Nanning 530021, Guangxi, People's Republic of China*

[2]*School of Public Health, Guilin Medical University, 20 Lequn Road, Guilin, Guangxi, People's Republic of China*

[3]*Guangxi Key Laboratory of Environmental Exposomics and Entire Lifecycle Health, Guilin Medical University, Guilin, Guangxi, People's Republic of China*

[4]*Guangxi Key Laboratory of Tumor Immunology and Microenvironmental Regulation, Guilin Medical University, Guilin, Guangxi, People's Republic of China*

[5]*Key Laboratory of Longevity and Aging-related Diseases of Chinese Ministry of Education, Guangxi Medical University, Nanning 530021, People's Republic of China*

[6]*Guangxi Colleges and Universities Key Laboratory of Prevention and Control of Highly Prevalent Diseases, School of Public Health, Guangxi Medical University, Nanning 530021, People's Republic of China*

[7]*Guangxi Key Laboratory of Environment and Health Research, Guangxi Medical University, Nanning 530021, People's Republic of China*

(Submitted 22 February 2023 – Final revision received 18 June 2023 – Accepted 23 June 2023 – First published online 13 July 2023)

Abstract

Trace elements may play an important role in obesity. This study aimed to assess the plasma and dietary intake levels of four trace elements, Mn, Cu, Zn and Se in a rural Chinese population, and analyse the relationship between trace elements and obesity. A cross-sectional study involving 2587 participants was conducted. Logistic regression models were used to analyse the association between trace elements and obesity; restricted cubic spline (RCS) models were used to assess the dose–response relationship between trace elements and obesity; the weighted quantile sum (WQS) model was used to examine the potential interaction of four plasma trace elements on obesity. Logistic regression analysis showed that plasma Se concentrations in the fourth quartile (Q4) exhibited a lower risk of developing obesity than the first quartile (Q1) (central obesity: OR = 0·634, P = 0·002; general obesity: OR = 0·525, P = 0·005). Plasma Zn concentration in the third quartile (Q3) showed a lower risk of developing obesity in general obesity compared with the first quartile (Q1) (OR = 0·625, P = 0·036). In general obesity, the risk of morbidity was 1·727 and 1·923 times higher for the second and third (Q2, Q3) quartiles of dietary Mn intake than for Q1, respectively. RCS indicated an inverse U-shaped correlation between plasma Se and obesity. WQS revealed the combined effects of four trace elements were negatively associated with central obesity. Plasma Zn and Se were negatively associated with obesity, and dietary Mn was positively associated with obesity. The combined action of the four plasma trace elements had a negative effect on obesity.

Key words: Obesity: Rural population: Diet: Trace elements

The prevalence of obesity is increasing at an alarming rate worldwide today, with more than one billion people worldwide suffering from obesity according to the latest figures from the WHO[1]. Obesity directly or indirectly increases the risk of many chronic diseases, such as type 2 diabetes mellitus, hyperlipidaemia, hypertension, neurological diseases and even cancer[2]. Studies have found that overweight and obesity are important causes of increased all-cause mortality[3]. In 2017 alone, overweight and obesity caused more than 4 million deaths and 148 million disability-adjusted life years globally[4]. Obesity has become one of the most serious global public health problems and seriously threatens human life and health.

Abbreviations: RCS, restricted cubic spline; WQS, weighted quantile sum.

* **Corresponding author:** Jian Qin, email qinjian@gxmu.edu.cn

† These authors contributed equally to this work

Understanding the pathogenesis of obesity and its factors is of great importance for public health. In recent years, as research progressed, the important role of trace elements in the development of obesity, including their role in the development of various diseases, has been gradually recognised. For example, Cu, Zn and Se play an essential role in cardiovascular protection; Mn is involved in lipid metabolism and is a component of many enzymes including arginase, glutamine synthetase, phosphoenolpyruvate decarboxylase and Mn superoxide dismutase[5,6]. In addition, these trace elements are cofactors of many enzymes involved in the antioxidant defence system and are associated with changes in the body's homoeostatic mechanisms, particularly inflammation and oxidative stress, which are important in the prevention of obesity[7,8]. Studies have found that the prevalence of obesity is significantly higher in areas with a high prevalence of certain micronutrient deficiencies[9,10]. Several other studies have also found that overweight or obese individuals are more likely to have micronutrient deficiencies relative to normal-weight individuals[11,12]. These findings suggest a possible association between increased obesity prevalence and micronutrients.

The impact of micronutrients on the development of obesity in the population is complex and variable in terms of daily dietary intake and potential mechanisms of action. A study by Major *et al*. found that trace elements may play an important role in central nervous system function and food intake control through synthesising and regulating neurotransmitters[13]. However, several inconsistencies were noted regarding the association between obesity and micronutrients[14,15]. For example, data on the relationship between obesity and Se were contradictory[16], and the reasons for these contradictory results are still unknown.

The control and management of obesity require the identification of its potential factors. Therefore, this study aimed to analyse the relationship between plasma and dietary trace element (Mn, Cu, Zn and Se) intake with obesity and to provide a scientific basis for scientific diet and health promotion for obese people in rural China. The results of this study will help raise public health awareness and reduce the risk of trace element deficiency-related diseases.

Materials and methods

Study population

The study participants were from the towns of Lianhua and Limu in the Hongshui River Basin in Gongcheng Yao Autonomous County, Guangxi, China. The cross-sectional survey was conducted from December 2018 to November 2019. A total of 4356 residents aged 30 years or older participated in the study. Participants met the following criteria: (a) they had lived in the study area for more than 5 years and (b) they were at least 30 years old at the time of enrolment. Individuals were excluded if: (a) recently taken diet pills, (b) those with abnormal plasma metal concentration (higher than three times the 99th percentile), (c) participants with abnormal waist circumference and BMI levels (defined as below mean waist circumference minus three standard deviations or above mean waist circumference plus three standard deviations) and (d) participants with unreasonable energy intake (greater than 16736 KJ (4000 Kcal) or less than 2510 KJ (600 Kcal)). With the exclusion of participants who failed to complete the required examination and whose questionnaire data were missing, a total of 2587 participants were enrolled in the final study. The currently expected prevalence of general obesity is approximately 18 %[17] and the expected prevalence of central obesity is 44 %[18]. The estimated sample size for this study was 1749 according to the cross-sectional sampling survey sample size formula, so this study increased the sample by 30–35 %. The study procedures were approved by the Medical Ethics Committee of Guilin Medical College (No: 20180702–3) and were conducted by the principles of the Declaration of Helsinki. Written informed consent was provided by each participant.

Biochemical analyses

After fasting for at least 12 h, venous blood was drawn by a professional nurse on the morning of the physical examination and transferred to the Laboratory Department of Gongcheng Yao Autonomous County People's Hospital via cold chain. After centrifugation at 3000 rpm for 5 min, biochemical parameters such as total serum cholesterol, TAG, LDL-cholesterol and HDL-cholesterol and fasting blood glucose were measured using a chemical auto-analyser (Hitachi 7600–020), and the remaining blood samples were stored at −80°C for subsequent testing.

Plasma trace element assessment

The method of detection of plasma trace element concentrations was mentioned in our previously published article[19]. Inductively coupled plasma MS (Thermo Fisher Scientific iCAPRQ01408) was used to measure the plasma trace element concentrations. In summary, according to the instructions, plasma samples were transferred from –80°C ambient to room temperature for dissolution before testing and later diluted 20 times with a concentration of 1 % HNO3. The standard solution consisted of a mixed standard solution composed of forty-three elements and a single standard solution composed of six elements including Cu, Zn, Fe, Mg and Ca. Based on the results of the pre-experiments, we established standard curves in the range of 5·05 ~ 1010 ppb and required a correlation coefficient $R^2 \geq 0·999$ to ensure that 80 % of the samples were within the concentration range of the standard curve. Quality control was performed by ClinChek® (Level I: No. 8883; Level II: No. 8884; Recipe Chemicals) for the samples tested, and the quality control solution was measured every twenty-five samples. In addition, the spiked recoveries of the four trace elements measured were in the range of 80–120 %. If any was below the limit of detection, it was replaced with (limit of detection)/$\sqrt{2}$[20]. All trace elements in this study were above the limit of detection. According to Berger *et al*., Mn deficiency is rare in humans and Cu deficiency may be present in plasma Cu concentrations < 0·08 μg/l[21]. In addition, a study by Gać *et al*. pointed out that the reference ranges for plasma Zn and Se deficiency in adults are < 660 μg/l and < 70 μg/l, respectively[22].

https://doi.org/10.1017/S0007114523001435 Published online by Cambridge University Press

British Journal of Nutrition

https://doi.org/10.1017/S0007114523001435 Published online by Cambridge University Press

Dietary micronutrient intake assessment

Diet was assessed using a FFQ in reference to the questionnaire designed by Liu *et al.*[23]. Several previous studies confirmed the rationality, validity and reliability of the FFQ in assessing long-term average dietary intake[24,25]. The FFQ is one of the most commonly used dietary questionnaire tools, with the following main components: cereals (9 items) and tuber crops (2 items), processed vegetables (2 items), fresh vegetables (22 items), fruits (14 items), processed meat (1 item), fresh meat (6 items), fresh eggs (3 items), processed eggs (3 items), beans and products (7 items), nuts and seeds (4 items), alcohol (2 items), and tea a total of 12 groups and 76 items, including intake of tea (1 item). During the survey, the researchers asked participants to recall the frequency and average consumption of 109 food items in the previous year through a food album aid (including diet items, measurement tools and weight of each portion) accompanying the FFQ. The energy and nutrient contents of these foods were referenced from the Chinese Food Composition Table (2018/2019 edition). The daily intakes of four micronutrients and total energy were obtained by calculation.

Anthropometric measurements

Height (accurate to 0·1 cm) and weight (accurate to 0·1 kg) were measured on an electronic digital scale (BODIVIS, MYBODY1) by trained staff with the participant wearing minimal clothing and no shoes, and BMI was calculated from the weight and height data as weight (kg)/height^2 (m^2). The participants stood naturally and our staff placed a non-elastic tape at the midpoint of the line between the upper edge of the participant's hip bone and the lower edge of the rib cage, parallel to the floor, around the abdomen, tightly but without squeezing and measured waist circumference (accurate to 0·1 cm) at the end of a normal exhalation. Based on the consensus of Chinese experts on obesity management[26], waist circumference greater than or equal to 90 cm for men and greater than or equal to 85 cm for women was defined as central obesity; according to some previous studies, BMI ≥ 27·5 kg/m^2 was considered generally obese[27,28].

Blood pressure measurements

Blood pressure was measured by staff using an electronic sphygmomanometer (OMRON, U724J), with participants sitting still for at least 15 min before measurement, and measured thrice on different days and averaged.

Data collection

On the morning of the examination, participants were interviewed face-to-face by professional investigators using standardised and structured questionnaires to obtain baseline information on sex, age, ethnicity (Yao or other), smoking (yes or no), alcohol consumption (yes or no) and agricultural physical activity (yes or no).

Statistical analysis

Continuous information was described by mean values and standard deviation or median and interquartile range, and comparisons between groups were made using the independence *t* test or Wilcoxon, Kruskal–Wallis rank sum test. Frequencies (*n*%) describe categorical information, and comparisons between groups were performed by the χ^2 test or Fisher exact probability method. Plasma and dietary trace elements were transformed log10 in the logarithmic form to reduce bias.

First, trace elements were divided into four groups according to quartiles (Q1, Q2, Q3 and Q4), and the association between plasma and dietary trace element intake and the risk of obesity development was assessed by logistic regression models using Q1 as a reference. Our sample gave us 93·10 % power to detect the OR of 0·634 for the association of plasma Se with central obesity risk at $P < 0·05$ (two-tailed). Subsequently, the dose–response relationship between micronutrients and obesity was evaluated using a restricted cubic spline (RCS) model with three cross-sections of the RCS located at 25 %, 50 % and 75 % of the micronutrient concentration range. All multivariate analyses were adjusted separately for sex, age, ethnicity, smoking (defined as ≥ 1 cigarette/d), alcohol consumption (defined as ≥ 50 g of alcohol per month), physical activity in agriculture (engaged in farming, planting and weeding), diabetes (defined as fasting blood glucose ≥ 7·0 mmol/l or taking glucose-lowering medication or doctor-diagnosed diabetes or self-reported history of diabetes), hypertension (defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or taking anti-hypertensive medication or doctor's diagnosis of hypertension or self-reported history of hypertension) and hyperlipidaemia (defined as total cholesterol > 5·72 mmol/l, TAG > 1·70 mmol/l or taking lipid-lowering medication).

Second, the overall effect of the four plasma micronutrients on obesity was assessed utilising a weighted quantile sum (WQS) regression model. The WQS regression model can combine linear or logistic regression, which combines multiple variables into a single score, thus avoiding any over-fitting and collinearity problems[29]. The model combines highly correlated variables in an efficiently supervised manner to construct a weighted index to assess the overall effect of multiple variables and the contribution of each of these components to the overall effect. In brief, each study factor was divided into four equal parts, and after adjusting for covariates, the WQS regression outputs an empirically weighted sum of the quartiles of the study factors. The weights of each study factor were constrained to be between 0 and 1, with a sum of 1. The weights were assessed based on the effect of each component on the outcome, the greater the effect is, the higher the weight. Another feature of the WQS regression model is that it constrains all components to be associated in the same direction (positive or negative) as the outcome[30]. According to Czarnota *et al.*, if the trace elements associated with obesity are misclassified in the WQS model, they would have negligible weight in terms of WQS index weight assignment and present the opposite result[31,32]. Therefore, we performed two analyses in different directions.

All statistical analyses described above were performed with SPSS version 26.0, R language (4.2.1) (GWAS), (RMS) package, and $P < 0·05$ (two-tailed) was considered statistically significant.

Results

Demographic characteristics

General demographic characteristics are shown in Table 1, and 2587 participants were included in the analysis. Of these, 203

Table 1. Descriptive characteristics of the subjects (Numbers and percentages; mean values and standard deviations)

	Total		No obesity		Central obesity		*P*	No obesity		General obesity		*P*
	n 2587		*n* 2061		*n* 526			*n* 2384		*n* 203		
	n	%	*n*	%	*n*	%		*n*	%	*n*	%	
Age												
Mean	57·68		57·68		57·65		0·848	57·99		54·01		< 0·001
SD	11·94		12·23		10·74			11·98		10·79		
Sex							0·002					0·925
Male	986	38·1	816	39·6	170	32·3		908	38·1	78	38·4	
Female	1601	61·9	1245	60·4	356	67·7		1476	61·9	125	61·6	
Ethnicity							0·531					0·009
Yao	1930	74·6	1532	74·3	398	75·7		1763	74·0	16 782·3)		
Other	657	25·4	529	25·7	128	24·3		621	26·0	36	17·7	
Smoking status							< 0·001					0·013
Yes	474	18·3	412	20·0	62	11·8		450	18·9	24	11·8	
No	2113	81·7	1649	80·0	464	88·2		1934	81·1	179	88·2	
Drinking status							0·196					0·072
Yes	848	32·8	688	33·4	160	30·4		793	33·3	55	27·1	
No	1739	67·2	1373	66·6	366	69·6		1591	66·7	148	72·9	
Agricultural activities							0·001					0·750
Yes	1694	65·5	1381	67·0	313	59·5		1559	65·4	135	66·5	
No	893	34·5	680	33·0	213	40·5		825	34·6	68	33·5	
Hypertension							< 0·001					< 0·001
Yes	1193	46·1	868	42·1	325	61·8		1069	44·8	124	61·1	
No	1394	53·9	1193	57·9	201	38·2		1315	55·2	79	38·9	
Hyperlipidaemia							< 0·001					< 0·001
Yes	1269	49·1	925	44·9	344	65·4		1136	47·7	133	65·5	
No	1318	50·9	1136	55·1	182	34·6		1248	52·3	70	34·5	
Diabetes							< 0·001					< 0·001
Yes	315	12·2	201	9·8	114	21·7		274	11·5	41	20·2	
No	2272	87·8	1860	90·2	412	78·3		2110	88·5	162	79·8	
	Median	Interquartile range	Median	Interquartile range	Median	Interquartile range		Median	Interquartile range	Median	Interquartile range	
Plasma Mn (μg/l)	2·14	1·55, 3·03	2·12	1·54, 3·00	2·21	1·57, 3·15	0·162	2·13	1·54, 3·02	2·24	1·61, 3·10	0·140
Plasma Cu (μg/l)	919·36	804·20, 1039·58	917·13	799·44, 1038·22	929·81	823·74, 1047·40	0·071	919·12	802·12, 1038·53	926·57	821·03, 1055·27	0·455
Plasma Zn (μg/l)	1067·24	762·02, 4793·93	1078·60	761·37, 4830·75	1030·03	763·49, 4084·60	0·411	1073·85	762·06, 4753·07	993·15	761·43, 5321·49	0·813
Plasma se (μg/l)	109·22	94·59, 123·32	109·64	94·89, 123·89	107·78	93·39, 120·97	0·042	109·29	94·88, 123·60	107·87	92·06, 118·17	0·053
Dietary Mn (mg/d)	3·90	2·79, 5·42	3·89	2·77, 5·41	3·96	2·82, 5·49	0·381	3·87	2·75, 5·38	4·35	3·22, 6·20	< 0·001
Dietary Cu (mg/d)	0·99	0·66, 1·49	0·98	0·65, 1·49	1·00	0·68, 1·49	0·526	0·98	0·64, 1·48	1·07	0·74 1·65	0·014
Dietary Zn (mg/d)	6·74	4·72, 9·54	6·76	4·71, 9·56	6·67	4·77, 9·45	0·866	6·70	4·67, 9·548	7·16	5·27, 10·31	0·018
Dietary se (mg/d)	17·61	11·08, 28·21	17·62	11·03, 28·16	17·49	11·35, 28·38	0·722	17·50	10·98, 28·00	19·67	12·65, 29·65	0·064

Table 2. The logistic regression model for the association between plasma trace elements and obesity (Odds ratios and 95 % confidence intervals)

	Q1	Q2			Q3			Q4		
		OR	95 % CI	*P*	OR	95 % CI	*P*	OR	95 % CI	*P*
Central obesity										
Mn (μg/l)	1·00 (Ref)	1·037	0·776, 1·387	0·805	1·059	0·790, 1·420	0·703	1·168	0·874, 1·560	0·294
Cu (μg/l)	1·00 (Ref)	1·142	0·853, 1·529	0·373	1·093	0·814, 1·467	0·554	0·962	0·712, 1·301	0·802
Zn (μg/l)	1·00 (Ref)	1·044	0·788, 1·382	0·765	0·837	0·628, 1·115	0·224	0·865	0·643, 1·164	0·338
se (μg/l)	1·00 (Ref)	0·995	0·754, 1·313	0·972	0·814	0·614, 1·079	0·152	0·634	0·472, 0·852	0·002
General obesity										
Mn (μg/l)	1·00 (Ref)	1·022	0·658, 1·588	0·922	1·015	0·655, 1·572	0·947	0·979	0·633, 1·515	0·926
Cu (μg/l)	1·00 (Ref)	1·312	0·851, 2·021	0·218	1·036	0·657, 1·633	0·880	1·427	0·913, 2·231	0·119
Zn (μg/l)	1·00 (Ref)	0·939	0·623, 1·416	0·764	0·625	0·403, 0·970	0·036	0·743	0·485, 1·138	0·171
se (μg/l)	1·00 (Ref)	0·838	0·558, 1·257	0·393	0·816	0·547, 1·218	0·319	0·525	0·335, 0·822	0·005

Adjusted for age, sex, ethnicity (Yao or other), agricultural activities (yes or no), type 2 diabetes (yes or no), hyperlipidaemia (yes or no), hypertension (yes or no), smoking (yes or no), alcohol consumption (yes or no) and total energy intake (continuous variable).

(7·85 %) were generally obese and 526 (20·33 %) were centrally obese. In the total population, the median plasma levels of the four trace elements Mn, Cu, Zn and Se were 2·14, 919·36, 1067·24 and 109·22 (μg/l), respectively, with 272 (10·51 %) Zn-deficient and 90 (3·48 %) Se-deficient individuals; the median intakes of the four trace elements were 3·90, 0·99, 6·74 and 17·61 (mg/d). In the comparison between groups, there were significant differences between the two obese phenotypes and non-obese in smoking, hypertension, hyperlipidaemia and diabetes mellitus; there were significant differences between the general obese and non-obese groups in age, ethnicity and intake of Mn, Cu and Zn.

Logistic regression analysis of micronutrients and obesity

After adjusting for ethnicity, smoking, alcohol consumption, sex, age, physical labour, hypertension, hyperlipidaemia, diabetes and total energy intake as covariates, the results of logistic regression analysis of plasma trace elements and obesity are shown in Table 2. Compared with Q1, Q4 plasma Se concentrations exhibited a lower risk of obesity development (central obesity: OR = 0·634, $P = 0·002$; general obesity: OR = 0·525, $P = 0·005$). Compared with Q1, Q3 plasma Zn concentrations showed a lower risk of developing general obesity (OR = 0·625, $P = 0·036$).

The results of the logistic regression analysis of dietary micronutrients and obesity are shown in Table 3. In general obesity, the risk of Mn intake was 1·727 ($P = 0·024$) and 1·923 ($P = 0·009$) times higher in Q2 and Q3 than in Q1, respectively.

Restricted cubic spline model analysis of micronutrients and obesity

The dose–response relationship between micronutrients and the risk of obesity development was assessed by the RCS model; after adjusting for ethnicity, smoking, alcohol consumption, sex, age, physical labour, hypertension, hyperlipidaemia, diabetes and total energy intake as covariates, the results of the analysis are shown in Fig. 1. Plasma Se concentration (Fig. 1(d)) was associated with obesity in an inverted U-shape (central obesity: P-overall ≤ 0·001, P-nonlinear = 0·004, general obesity: P-overall = 0·004, P-nonlinear = 0·015).

Weighted quantile sum regression model to assess the association between plasma trace elements and obesity

The results of the WQS regression model for plasma micronutrients and obesity are shown in Table 4. The estimated weights for each wq index are shown in Fig. 2; the highest weights of the four plasma trace elements for obesity were Mn and Cu, respectively (central obesity: Mn – 0·689, Cu – 0·228; general obesity: Cu – 0·674, Mn – 0·200). To further analyse the changes in the effects of mixtures on body indices, for continuous outcome waist circumference and BMI, a WQS model was installed to assess the influences of exposure to the four trace elements on obesity indices. As shown in Table 4, the wq index was significantly negatively associated with BMI ($\beta = -0·264$, 95 % CI −0·479, −0·050). Regarding the weighted estimation of wq index weight, Fig. 2(d) shows that Mn and Se contributed the largest weight to BMI, whereas waist circumference was the largest contribution of Mn and Cu.

We also analysed whether there was a negative association between micronutrients and obesity. The results are shown in Table 5; wq index was significantly negatively associated with central obesity, waist circumference and BMI (central obesity: $\beta = -0·174$, 95 % CI −0·342, −0·006; waist circumference: $\beta = -1·170$, 95 % CI −1·769, −0·567; BMI: $\beta = -0·250$, 95 % CI −0·442, −0·059), and the estimated weight of wq index is shown in Fig. 3, where Zn was the largest contributor to this negative association.

Discussion

As essential trace elements for life activities, whether deficient or excessive, they may lead to physiological dysfunction, decreased resistance and immunity and cause a variety of diseases. In the present study, we assessed the plasma and dietary intake levels of four trace elements in the rural Chinese population and evaluated their association with obesity based on logistic regression model. Then we analysed the potential interactions of the four plasma trace elements through the WQS model. Logistic regression analysis revealed that plasma Zn and Se reduced the risk of obesity and dietary Mn increased the risk of obesity. RCS analysis also showed an inverse U-shaped association between plasma Se and the risk of obesity. WQS

Table 3. The logistic regression model for the association between dietary trace elements and obesity (Odds ratios and 95 % confidence intervals)

	Q1	Q2			Q3			Q4		
		OR	95 % CI	*P*	OR	95 % CI	*P*	OR	95 % CI	*P*
Central obesity										
Mn (mg/d)	1·00 (Ref)	1·126	0·841, 1·507	0·426	1·146	0·839, 1·565	0·392	1·079	0·739, 1·577	0·694
Cu (mg/d)	1·00 (Ref)	1·066	0·791, 1·435	0·676	1·308	0·950, 1·801	0·100	1·078	0·711, 1·634	0·722
Zn (mg/d)	1·00 (Ref)	1·224	0·914, 1·640	0·175	1·125	0·817, 1·550	0·471	0·932	0·610, 1·425	0·745
se (mg/d)	1·00 (Ref)	1·221	0·914, 1·631	0·176	1·131	0·829, 1·543	0·437	0·997	0·680, 1·463	0·989
General obesity										
Mn (mg/d)	1·00 (Ref)	1·727	1·076, 2·771	0·024	1·923	1·178, 3·140	0·009	1·755	0·971, 3·172	0·062
Cu (mg/d)	1·00 (Ref)	1·290	0·815, 2·043	0·277	1·477	0·904, 2·412	0·119	1·266	0·678, 2·365	0·459
Zn (mg/d)	1·00 (Ref)	1·578	0·997, 2·497	0·051	1·442	0·876, 2·375	0·150	1·482	0·779, 2·817	0·230
se (mg/d)	1·00 (Ref)	1·469	0·940, 2·295	0·091	1·367	0·851, 2·196	0·196	1·134	0·636, 2·021	0·670

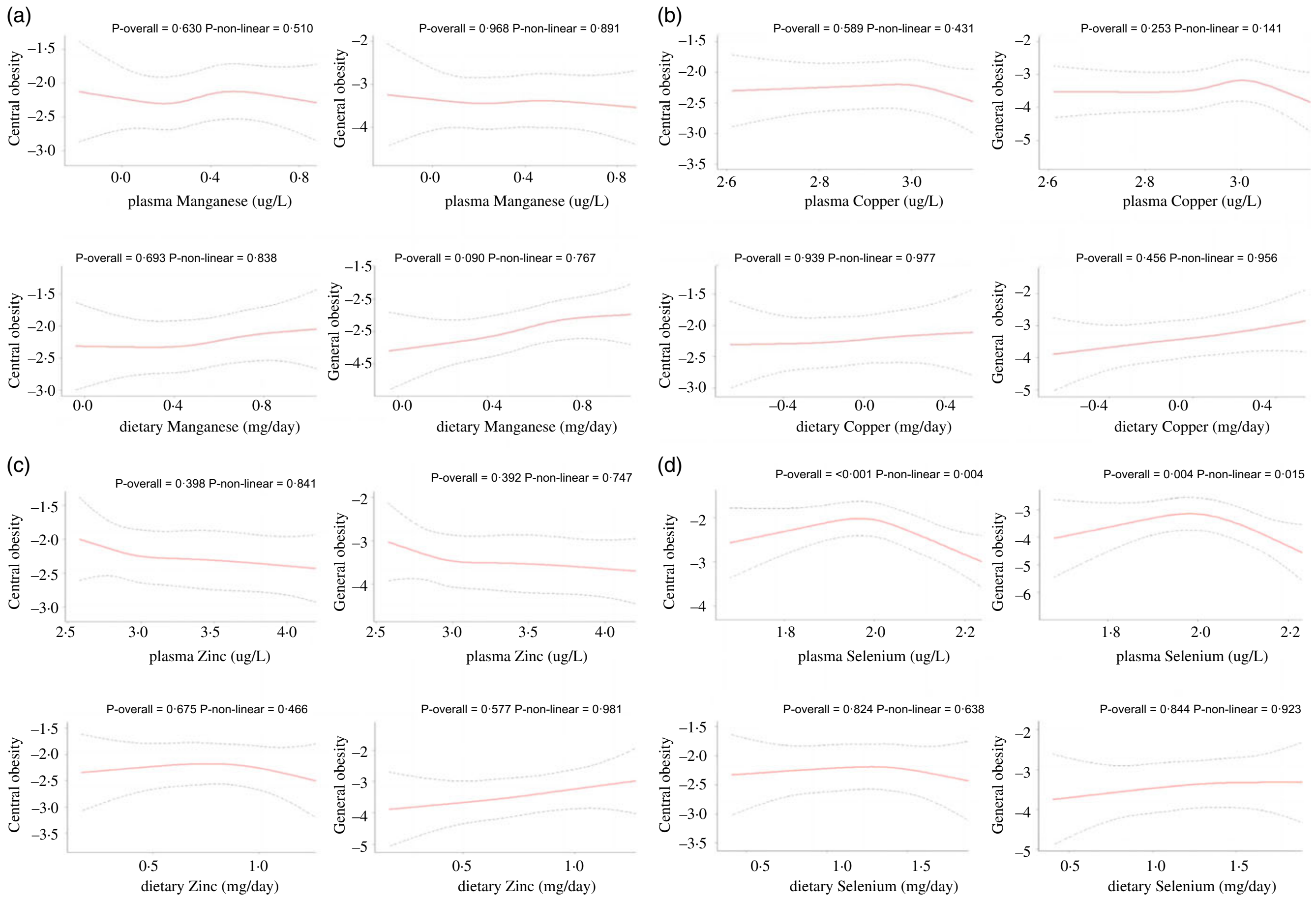

Fig. 1. Dose-response relationship between log10-transformed trace elements and obesity. The solid and dotted lines represent the fitting curves and 95 % CI, respectively. Adjusted for age, sex, ethnicity (Yao or other), agricultural activities (yes or no), type 2 diabetes (yes or no), hyperlipidaemia (yes or no), hypertension (yes or no), smoking (yes or no), alcohol consumption (yes or no) and total energy intake (continuous variable).

model analysis revealed a negative joint effect of combined exposure of the four trace elements on obesity.

Mn is the 12th most abundant element in the earth's crust[33] and is widely present in soil, water and food. Our study found that increased intake of Mn resulted in a higher risk of developing general obesity. According to the appropriate standard of Mn intake for healthy individuals described in the US Food and Drug Administration 1991–1997 Total Diet Study, the daily intakes for adult males and females are 2·3 and 1·8 mg/d, respectively[34]. The median intake of Mn in our study population was 3·9 mg/d, which was higher than the above-mentioned standard. The study by Lv *et al.* also confirmed that excess Mn induced lipogenesis and accumulation in the intestine through deacetylation of the oxidative stress-SIRT 1-PPAR*γ* pathway[35]. In addition, recent experimental studies found that Mn levels dys-regulated TFEB, Beclin 1, Bcl-2 and mTOR proteins and induce dys-regulation of autophagy, another potentially relevant pathway for Mn and central obesity[36,37].

Table 4. WQS model to estimate the associations between WQS index and obesity (95 % confidence intervals)

Outcomes	β	95 % CI of β	P
Central obesity			
Model 1	0·083	−0·074, 0·240	0·302
Model 2	−0·018	−0·176, 0·141	0·828
General obesity			
Model 1	0·047	−0·211, 0·305	0·720
Model 2	−0·033	−0·278, 0·213	0·795
Waist circumference			
Model 1	0·191	−0·457, 0·839	0·564
Model 2	0·067	−0·523, 0·657	0·825
BMI			
Model 1	0·032	−0·235, 0·172	0·763
Model 2	−0·264	−0·479, −0·050	0·002

WQS, weighted quantile sum.
β estimates represent the OR of obesity when the WQS index was increased by one quartile. Model 1: adjusted for crude. Model 2: adjusted for age, sex, ethnicity (Yao or other), agricultural activities (yes or no), type 2 diabetes (yes or no), hyperlipidaemia (yes or no), hypertension (yes or no), smoking (yes or no), alcohol consumption (yes or no) and total energy intake (continuous variable).

However, contradictory results on the effects of Mn intake on obesity remain. Data from a Chinese National Nutrition and Health Survey showed that higher Mn intake was negatively associated with central obesity in men[38]. In addition, unlike the findings below, we did not find an association between plasma Mn and obesity. A cross-sectional study in Poland found that serum Mn concentration was significantly and positively associated with BMI, waist circumference and waist-to-hip ratio[39]. A national nutrition and health survey of children and adolescents in the USA showed that Mn increases the risk of obesity[40]. It may be influenced by factors such as age, sex or exposure, as in the study by Tao *et al.* who observed significant sex differences in the relationship between blood Mn levels and visceral adipose tissue accumulation[41]. The current inadequate biological evidence on Mn and the many conflicting results of cross-sectional studies require more large cohort studies similar to long-term follow-up or with full consideration of various confounding factors (sex, age) to further reveal the association between Mn and obesity.

Cu is the third most essential trace element and one of the components of antioxidant enzymes. Cu can affect oxidative stress, which is a fundamental mechanism in the development of obesity and its associated complications, through a variety of mechanisms[42]. First, glutathione is a powerful cellular antioxidant and high levels of Cu can decrease glutathione levels in the body, thereby increasing oxidative stress[43]. Second, Cu can promote oxidative stress through the up-regulation of several cytokines including activator protein-1, hypoxia-inducible factor 1-α, IL-6, IL-1β, TNF and IL-8[44]. A cross-sectional study found that elevated serum Cu levels were associated with a high ratio of overweight/overall obesity and central obesity in children and adolescents[45]. Several other studies have also shown that serum Cu levels were significantly higher in overweight and obese patients than in those of normal weight[46,47]. Unexpectedly, we did not observe an association between Cu and obesity, perhaps influenced by population characteristics such as age and sex. Previous studies reported significant differences in plasma Cu concentrations across sex and age groups, with females being significantly higher than males and plasma Cu/Zn increasing significantly with ageing[48]. In addition, Koppel *et al.* found an antagonistic effect between Zn and Cu[49], an important factor that we must consider.

Zn is an essential trace element for balancing the body's diet and vital activities. Studies have found that Zn deficiency or inadequate intake can lead to elevated circulating TNF-α and increase the release of reactive oxygen species in tissues, which can cause oxidative stress leading to obesity[50,51]. In addition, Xiao *et al.* found that Zn-α2-glycoprotein, an adipokine, can reduce lipid accumulation by up-regulating lipocalin and lipolytic genes (FXR, PPARα, etc.) and inhibit NF-κB/JNK signalling, thereby suppressing obesity and related inflammatory responses[52]. Liu *et al.* also found that overexpression of the Zn-α2-glycoprotein gene significantly reduced mice's body weight and adipose tissue mass[53]. In a study about Mexican adults, Héctor Hernández-Mendoza *et al.* found a negative association between plasma Zn levels and obesity[54]. Several other studies similarly found a negative association between plasma Zn levels and waist circumference and/or BMI[55–57], which is consistent with our findings that plasma Zn was negatively associated with general obesity. In our study, the median dietary Zn intake of the total population was 6·74 mg/d, which was lower than the study by Ju *et al.* (8·5 mg/d), who found that Zn intake was a protective factor for overweight/obesity in women[58]. Perhaps due to the influence of sex, we did not find an association between dietary Zn intake and obesity, and a larger sample size prospective study is needed.

Se, a vital micronutrient, was first discovered in 1817. Adequate intake of Se has been found to maintain tissue Se concentrations and selenoprotein activity, which is important in preventing the development of obesity and its associated metabolic disorders[59,60]. Nada *et al.* found that Se can inhibit fat formation by regulating selenoprotein gene expression and oxidative stress-related genes[61]. In addition, a study by Hossain *et al.* observed that Se regulated lipid metabolism in humans and rodents and increasing dietary Se intake has an important role in the prevention of obesity and diabetes[62]. Wang *et al.* found that Se methionine could reduce obesity by promoting the leukocyte formation in white adipose tissue[63]. A negative association between serum Se and obesity was also observed in a study of adolescent children[64]. In a cross-sectional study on National Health and Nutrition Examination Survey, a negative association between Se levels and systemic and central obesity was observed[65]. Consistent with these findings, our study found that plasma Se was negatively associated with central obesity. Given the pathogenic role played by oxidative stress and inflammation in the development of obesity, that Se had a beneficial role in preventing and managing obesity was not unexpected. We did not observe a correlation between dietary Se and obesity, and perhaps micronutrient intakes showed large differences between studies and practice, with medians or mean not reflecting the true picture. Our results were supported by a meta-analysis that showed that dietary Se levels did not differ significantly between overweight/obese and malnourished groups at all ages[66].

The mechanisms of single metal effects on obesity are well understood, but research on the overall effects of multiple trace

British Journal of Nutrition

https://doi.org/10.1017/S0007114523001435 Published online by Cambridge University Press

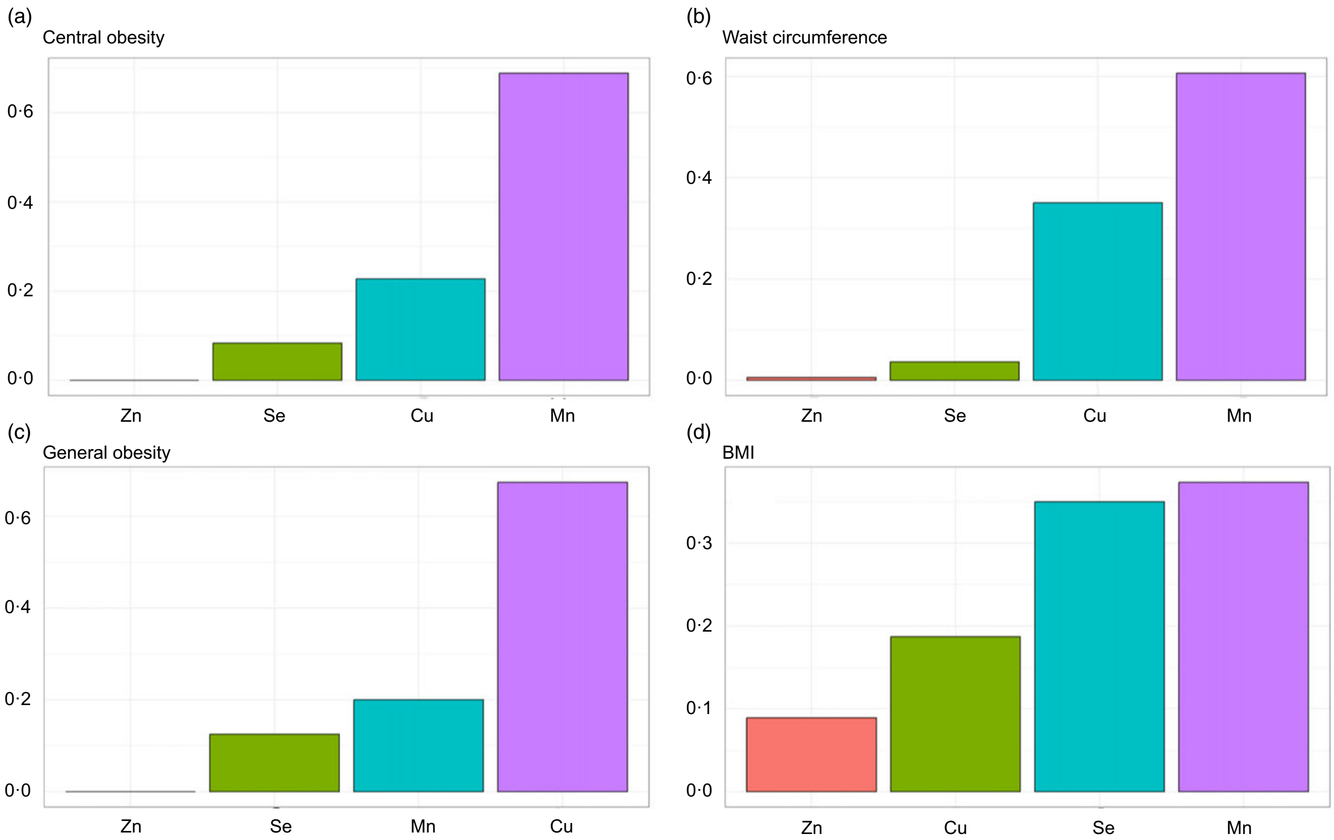

Fig. 2. WQS model regression index weights for central obesity (a) and waist circumference (b); general obesity (c) and BMI (d). Models were adjusted for age, sex, ethnicity (Yao, or other), agricultural activities (yes or no), type 2 diabetes (yes or no), hyperlipidaemia (yes or no), hypertension (yes or no), smoking (yes or no), alcohol consumption (yes or no) and total energy intake (continuous variable). The horizontal axis represents the exposure and the vertical axis represents the weighting coefficient. WQS, weighted quantile sum.

Table 5. WQS model to estimate the associations between WQS index and obesity (95 % confidence intervals)

Outcomes	β	95 % CI of β	P
Central obesity			
Model 1	–0·095	–0·245, 0·056	0·215
Model 2	–0·174	–0·342, –0·006	0·042
General obesity			
Model 1	–0·006	–0·211, 0·200	0·958
Model 2	–0·118	–0·324, 0·089	0·264
Waist circumference			
Model 1	–0·576	–1·205, 0·053	0·073
Model 2	–1·170	–1·769, –0·567	< 0·001
BMI			
Model 1	–0·051	–0·205, 0·102	0·512
Model 2	–0·250	–0·442, –0·059	0·011

WQS, weighted quantile sum.
β estimates represent the OR of obesity when the WQS index was increased by one quartile. Model 1: adjusted for crude. Model 2: adjusted for age, sex, ethnicity (Yao or other), agricultural activities (yes or no), type 2 diabetes (yes or no), hyperlipidaemia (yes or no), hypertension (yes or no), smoking (yes or no), alcohol consumption (yes or no) and total energy intake (continuous variable).

metals on obesity is quite scarce. Compared with single metal elements, the mixture of metals reflects real-life metal exposure scenarios. WQS is a model developed to assess the health effects of mixture exposures compared with single metal studies, which are more realistic in real-life scenarios. The current study was able to assess the overall effect of four trace element exposures on obesity and the contribution of each component to the overall effect. Several previous studies have noted that the WQS regression model had higher sensitivity than other single analyses in assessing important influences[67]. Our study found that in the positive analysis, the four micronutrients had a negative effect on BMI, with Mn and Cu accounting for the highest weighting. In the negative analysis, the combined effect of the four micronutrients was significantly and negatively associated with central obesity, waist circumference and BMI with Zn as the largest contributor. This result is consistent with the results of the single-metal analysis. However, more studies are needed to predict the interaction between trace elements (e.g. Cu and Zn) and to determine the mechanisms involved.

This study combined plasma and diet to analyse the relationship between multiple micronutrients and obesity to increase the reliability of the results. It has to be discussed here that the present study also had some limitations. First, because of the nature of cross-sectional studies, we were unable to assess the causal relationship between micronutrients and obesity. Second, we only analysed plasma and dietary trace elements and did not take urine into account, so more evidence on urinary trace elements is needed to support our conclusions. In addition, although this study adjusted for some potential confounders as much as possible, information on life circumstances, economic

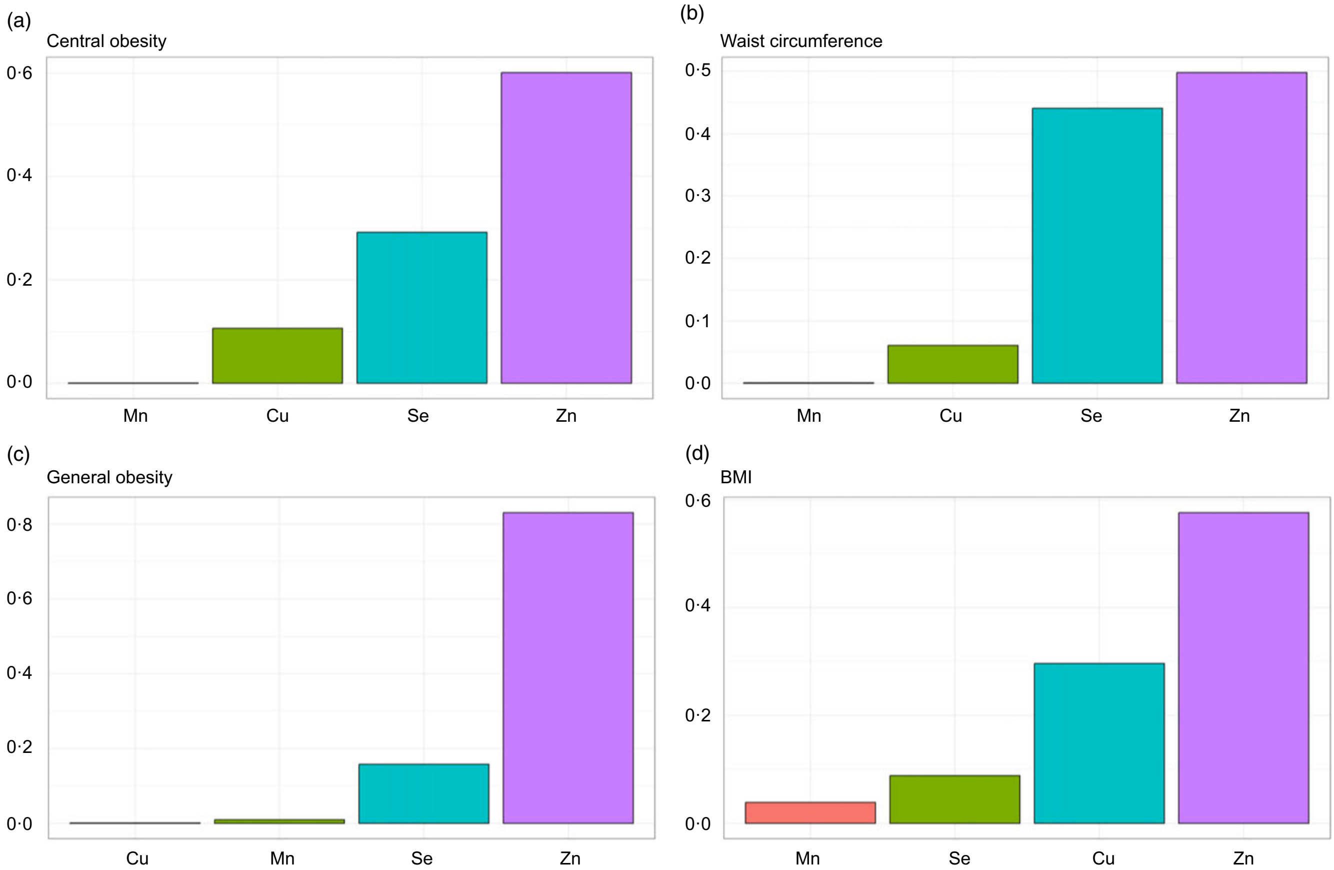

Fig. 3. WQS model regression index weights for central obesity (a) and waist circumference (b); general obesity (c) and BMI (d). Models were adjusted for age, sex, ethnicity (Yao or other), agricultural activities (yes or no), type 2 diabetes (yes or no), hyperlipidaemia (yes or no), hypertension (yes or no), smoking (yes or no), alcohol consumption (yes or no) and total energy intake (continuous variable). The horizontal axis represents the exposure and the vertical axis represents the weighting coefficient. WQS, weighted quantile sum.

conditions, family history and genetic characteristics was not taken into account, and the effect of residual confounders was still unavoidable.

Conclusion

In conclusion, our results suggest that plasma Zn and Se are negatively associated with obesity, dietary Mn intake is positively associated with obesity and the combined action of the four trace elements has a negative effect on obesity. Selective increase of micronutrients while maintaining safe levels may be a potential strategy to prevent and treat obesity.

Acknowledgements

We would like to thank all the participants of the study. We thank the doctors and nurses of Gongcheng County People's Hospital for their contributions to blood collection and examination. We thank Editage (https://www.kdocs.cn/l/ctoY3NJGDnJ8) for English language editing.

Y. L., Writing – original draft, Writing – review & editing. Q. L., Writing – review & editing. C. H., Writing – review & editing. T. X., Investigation. Y. W., Methodology. X. M., Software. S. H., Investigation, Data curation. Y. L., Investigation, Data curation. T. L., Investigation. R. G., Investigation. Z. Z., Funding acquisition. J. C., Writing – review & editing, Supervision. J. Q., Supervision, Project administration.

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.

References

1. https://news.un.org/zh/story/2022/03/1100142
2. Bendor CD, Bardugo A, Pinhas-Hamiel O, *et al.* (2020) Cardiovascular morbidity, diabetes and cancer risk among children and adolescents with severe obesity. *Cardiovasc Diabetol* **19**, 79.
3. Santamaría-Ulloa C, Chinnock A & Montero-López M (2022) Association between obesity and mortality in the Costa Rican elderly: a cohort study. *BMC Public Health* **22**, 1007.
4. Stanaway JD, Afshin A, Gakidou E, *et al.* (2018) Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* **392**, 1923–1994.
5. Mohammadifard N, Humphries KH, Gotay C, *et al.* (2019) Trace minerals intake: risks and benefits for cardiovascular health. *Crit Rev Food Sci Nutr* **59**, 1334–1346.

6. Li L & Yang X (2018) The essential element manganese, oxidative stress, and metabolic diseases: links and interactions. *Oxid Med Cell Longevity* **2018**, 7580707.
7. Basu A, Alman AC & Snell-Bergeon JK (2022) Associations of dietary antioxidants with glycated hemoglobin and insulin sensitivity in adults with and without type 1 diabetes. *J Diabetes Res* **2022**, 4747573.
8. Wong MMH, Chan KY & Lo K (2022) Manganese exposure and metabolic syndrome: a systematic review and meta-analysis. *Nutrients* **14**, 825.
9. Monteiro CA, Moura EC, Conde WL, *et al.* (2004) Socioeconomic status and obesity in adult populations of developing countries: a review. *Bull World Health Organ* **82**, 940–946.
10. Monteiro CA, Conde WL & Popkin BM (2007) Income-specific trends in obesity in Brazil: 1975–2003. *Am J Public Health* **97**, 1808–1812.
11. Skalnaya MG, Skalny AV, Grabeklis AR, *et al.* (2018) Hair trace elements in overweight and obese adults in association with metabolic parameters. *Biol Trace Elem Res* **186**, 12–20.
12. Tinkov AA, Bogdański P, Skrypnik D, *et al.* (2021) Trace element and mineral levels in serum, hair, and urine of obese women in relation to body composition, blood pressure, lipid profile, and insulin resistance. *Biomolecules* **11**, 689.
13. Major GC, Doucet E, Jacqmain M, *et al.* (2008) Multivitamin and dietary supplements, body weight and appetite: results from a cross-sectional and a randomised double-blind placebo-controlled study. *Br J Nutr* **99**, 1157–1167.
14. Błażewicz A, Klatka M, Astel A, *et al.* (2013) Differences in trace metal concentrations (Co, Cu, Fe, Mn, Zn, Cd, And Ni) in whole blood, plasma, and urine of obese and nonobese children. *Biol Trace Elem Res* **155**, 190–200.
15. Yerlikaya FH, Toker A & Arıbaş A (2013) Serum trace elements in obese women with or without diabetes. *Indian J Med Res* **137**, 339–345.
16. Tinkov AA, Ajsuvakova OP, Filippini T, *et al.* (2020) Selenium and selenoproteins in adipose tissue physiology and obesity. *Biomolecules* **10**, 658.
17. Chooi YC, Ding C & Magkos F (2019) The epidemiology of obesity. *Metab Clin Exp* **92**, 6–10.
18. Du P, Wang HJ, Zhang B, *et al.* (2017) Prevalence of abdominal obesity among Chinese adults in 2011. J Epidemiol 27, 282–286.
19. Zhang J, Liu Q, Xu M, *et al.* (2022) Associations between plasma metals and cognitive function in people aged 60 and above. *Biol Trace Elem Res* **200**, 3126–3137.
20. Feng X, Li L, Huang L, *et al.* (2021) Associations between serum multiple metals exposures and metabolic syndrome: a longitudinal cohort study. *Biol Trace Elem Res* **199**, 2444–2455.
21. Berger MM, Shenkin A, Schweinlin A, *et al.* (2022) ESPEN micronutrient guideline. *Clin Nutr* **41**, 1357–1424.
22. Gać P, Czerwińska K, Macek P, *et al.* (2021) The importance of selenium and zinc deficiency in cardiovascular disorders. *Environ Toxicol Pharmacol* **82**, 103553.
23. Liu X, Wang X, Lin S, *et al.* (2015) Reproducibility and validity of a food frequency questionnaire for assessing dietary consumption via the dietary pattern method in a Chinese rural population. *PLoS One* **10**, e0134627.
24. Barak F, Falahi E, Keshteli AH, *et al.* (2015) Red meat intake, insulin resistance, and markers of endothelial function among Iranian women. *Mol Nutr Food Res* **59**, 315–322.
25. Esfahani FH, Asghari G, Mirmiran P, *et al.* (2010) Reproducibility and relative validity of food group intake in a food frequency questionnaire developed for the Tehran Lipid and Glucose Study. *J Epidemiol* **20**, 150–158.
26. Mu L, Liu J, Zhou G, *et al.* (2021) Obesity prevalence and risks among Chinese adults: findings from the China PEACE million persons project, 2014–2018. *Circ Cardiovasc Quality Outcome* **14**, e007292.
27. Hu L, Ma L, Xia X, *et al.* (2022) Efficacy of bariatric surgery in the treatment of women with obesity and polycystic ovary syndrome. *J Clin Endocrinol Metab* **107**, e3217–e3229.
28. Li P, Ji G, Li W, *et al.* (2020) The relationship between BMI, body composition, and fat mass distribution in Rou-en-Y gastric bypass patients. *Obes Surg* **30**, 1385–1391.
29. Bellavia A, James-Todd T & Williams PL (2019) Approaches for incorporating environmental mixtures as mediators in mediation analysis. *Environ Int* **123**, 368–374.
30. Wheeler DC, Rustom S, Carli M, *et al.* (2021) Assessment of grouped weighted quantile sum regression for modeling chemical mixtures and cancer risk. *Int J Environ Res Public Health* **18**, 504.
31. Czarnota J, Gennings C, Colt JS, *et al.* (2015) Analysis of environmental chemical mixtures and non-Hodgkin lymphoma risk in the NCI-SEER NHL study. *Environ Health Perspect* **123**, 965–970.
32. Czarnota J, Gennings C & Wheeler DC (2015) Assessment of weighted quantile sum regression for modeling chemical mixtures and cancer risk. *Cancer Inf* **14**, 159–171.
33. Nadaska G, Lesny J & Michalik I (2010) Environmental aspect of manganese chemistry. *Chemistry* 1–16. http://heja.szif.hu/ENV/ENV-100702-A/env100702a.pdf
34. Martins AC, Krum BN, Queirós L, *et al.* (2020) Manganese in the diet: bioaccessibility, adequate intake, and neurotoxicological effects. *J Agric Food Chem* **68**, 12893–12903.
35. Lv WH, Zhao T, Pantopoulos K, *et al.* (2022) Manganese-induced oxidative stress contributes to intestinal lipid deposition via the deacetylation of PPARγ at K339 by SIRT1. *Antioxid Redox Signaling* **37**, 417–436.
36. Ma Z, Wang C, Liu C, *et al.* (2020) Manganese induces autophagy dysregulation: the role of S-nitrosylation in regulating autophagy related proteins *in vivo* and *in vitro*. *Sci Total Environ* **698**, 134294.
37. Zhang Z, Yan J, Bowman AB, *et al.* (2020) Dysregulation of TFEB contributes to manganese-induced autophagic failure and mitochondrial dysfunction in astrocytes. *Autophagy* **16**, 1506–1523.
38. Zhou B, Su X, Su D, *et al.* (2016) Dietary intake of manganese and the risk of the metabolic syndrome in a Chinese population. *Br J Nutr* **116**, 853–863.
39. Rotter I, Kosik-Bogacka D, Dołęgowska B, *et al.* (2015) Relationship between the concentrations of heavy metals and bioelements in aging men with metabolic syndrome. *Int J Environ Res Public Health* **12**, 3944–3961.
40. Fan Y, Zhang C & Bu J (2017) Relationship between selected serum metallic elements and obesity in children and adolescent in the U.S. *Nutrients* **9**, 104.
41. Tao C, Huang Y, Huang X, *et al.* (2022) Association between blood manganese levels and visceral adipose tissue in the United States: a population-based study. *Nutrients* **14**, 4770.
42. Pérez-Torres I, Castrejón-Téllez V, Soto ME, *et al.* (2021) Plant natural antioxidants, and obesity. *Int J Mol Sci* **22**, 1786.
43. Liu H, Guo H, Jian Z, *et al.* (2020) Copper induces oxidative stress and apoptosis in the mouse liver. *Oxid Med Cell Longevity* **2020**, 1359164.
44. Gu K, Li X, Xiang W, *et al.* (2020) The relationship between serum copper and overweight/obesity: a meta-analysis. *Biol Trace Elem Res* **194**, 336–347.
45. Ge W, Liu W & Liu G (2020) The relationships between serum copper levels and overweight/total obesity and central obesity in children and adolescents aged 6–18 years. J Trace Elements Med Biol: Organ Soc Minerals Trace Elements (GMS) 61, 126557.

https://doi.org/10.1017/S0007114523001435 Published online by Cambridge University Press

46. Vazquez-Moreno M, Sandoval-Castillo M, Rios-Lugo MJ, *et al.* (2022) Overweight and obesity are positively associated with serum copper levels in Mexican schoolchildren. Biol Trace Element Res 201, 2744–2749.
47. Yang H, Liu CN, Wolf RM, *et al.* (2019) Obesity is associated with copper elevation in serum and tissues. *Metallomics: Integrated Biometal Sci* **11**, 1363–1371.
48. Piacenza F, Giacconi R, Costarelli L, *et al.* (2021) Age, sex, and BMI influence on copper, zinc, and their major serum carrier proteins in a large European population including nonagenarian offspring from MARK-AGE study. *J Gerontol Ser A, Biol Sci Med Sci* **76**, 2097–2106.
49. Koppel DJ, Adams MS, King CK, *et al.* (2019) Preliminary study of cellular metal accumulation in two Antarctic marine microalgae - implications for mixture interactivity and dietary risk. *Environ Pollut* **252**, 1582–1592.
50. Zavala G, Long KZ, García OP, *et al.* (2013) Specific micronutrient concentrations are associated with inflammatory cytokines in a rural population of Mexican women with a high prevalence of obesity. *Br J Nutr* **109**, 686–694.
51. Cayir Y, Cayir A, Turan MI, *et al.* (2014) Antioxidant status in blood of obese children: the relation between trace elements, paraoxonase, and arylesterase values. *Biol Trace Elem Res* **160**, 155–160.
52. Xiao XH, Wang YD, Qi XY, *et al.* (2018) Zinc alpha2 glycoprotein protects against obesity-induced hepatic steatosis. *Int J Obes* **42**, 1418–1430.
53. Liu M, Zhu H, Dai Y, *et al.* (2018) Zinc-α2-glycoprotein is associated with obesity in Chinese people and HFD-induced obese mice. *Front Physiol* **9**, 62.
54. Hernández-Mendoza H, Martínez-Navarro I, Hernández-Ochoa E, *et al.* (2022) Serum zinc levels are associated with obesity and low-density lipoprotein cholesterol in Mexican adults. J Trace Elements Med Biol: Organ Soc Minerals Trace Elements (GMS) 73, 127002.
55. Jiang S, Ma X, Li M, Yan S, Zhao H, Pan Y, *et al.* (2020) Association between dietary mineral nutrient intake, body mass index, and waist circumference in U.S. adults using quantile regression analysis NHANES 2007–2014. Peer J 8, e9127.
56. Tinkov AA, Skalnaya MG, Ajsuvakova OP, *et al.* (2021) Selenium, zinc, chromium, and vanadium levels in serum, hair, and urine samples of obese adults assessed by inductively coupled plasma mass spectrometry. *Biol Trace Elem Res* **199**, 490–499.
57. Kerkadi A, Alkudsi DS, Hamad S, *et al.* (2021) The association between zinc and copper circulating levels and cardiometabolic risk factors in adults: a study of Qatar Biobank Data. *Nutrients* **13**, 2729.
58. Ju L, Wei X, Yu D, *et al.* (2022) Dietary micronutrient status and relation between micronutrient intakes and overweight and obesity among non-pregnant and non-lactating women aged 18–49 in China. *Nutrients* **14**, 1895.
59. Burk RF & Hill KE (2015) Regulation of selenium metabolism and transport. *Annu Rev Nutr* **35**, 109–134.
60. Duntas LH & Benvenga S (2015) Selenium: an element for life. *Endocrine* **48**, 756–775.
61. Abo El-Magd NF, Barbosa PO, Nick J, *et al.* (2022) As selenite, prevents adipogenesis by modulating selenoproteins gene expression and oxidative stress-related genes. *Nutrition* **93**, 111424.
62. Hossain A, Skalicky M, Brestic M, *et al.* (2021) Selenium biofortification: roles, mechanisms, responses and prospects. *Molecule* **26**, 881.
63. Wang X, Wu B, Sun G, *et al.* (2022) Dietary selenomethionine attenuates obesity by enhancing beiging process in white adipose tissue. *J Nutr Biochem* **113**, 109230.
64. Błażewicz A, Klatka M, Astel A, *et al.* (2015) Serum and urinary selenium levels in obese children: a cross-sectional study. J Trace Elements Med Biol: Organ Soc Minerals Trace Elements (GMS) 29, 116–122.
65. Zhong Q, Lin R & Nong Q (2018) Adiposity and serum selenium in U.S. Adults. *Nutrients* **10**
66. Fontenelle LC, Cardoso de Araújo DS, da Cunha Soares T, *et al.* (2022) Nutritional status of selenium in overweight and obesity: a systematic review and meta-analysis. *Clin Nutr* **41**, 862–884.
67. Artacho-Cordón F, León J, Sáenz JM, *et al.* (2016) Contribution of persistent organic pollutant exposure to the adipose tissue oxidative microenvironment in an adult cohort: a multipollutant approach. *Environ Sci Technol* **50**, 13529–13538.