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Dietary Selenium Intake and Mortality in two Population-based Cohort Studies of 133957 Chinese Men and Women

Jiang-Wei Sun[1,2], **Xiao-Ou Shu**[3], **Hong-Lan Li**[2], **Wei Zhang**[2], **Jing Gao**[2], **Long-Gang Zhao**[2], **Wei Zheng**[3], and **Yong-Bing Xiang**[2]

[1]School of Public Health, Fudan University, Shanghai, China

[2]Shanghai Cancer Institute, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai 200032, China

[3]Division of Epidemiology, Department of Medicine, Vanderbilt Epidemiology Center, Vanderbilt-Ingram Cancer Center, Vanderbilt University School of Medicine, Nashville, USA

Abstract

Objective—To investigate the potential influence of dietary Se intake on mortality among Chinese populations.

Design—We prospectively evaluated all-cause, CVD, and cancer mortality risks associated with dietary Se intake in participants of the Shanghai Women's Health Study (SWHS) and the Shanghai Men's Health study (SMHS). Dietary Se intake was assessed by validated food-frequency questionnaires during in-person interviews. Cox proportional hazards models were used to calculate hazard ratios (HR) and 95% CI.

Setting—Urban city in China.

Subjects—Chinese adults (*n* 133957).

Results—During an average follow-up of 13.90 years in the SWHS and 8.37 years in the SMHS, 5749 women and 4217 men died. The mean estimated dietary Se intake was 45.48 μg/day for women and 51.34 μg/day for men, respectively. Dietary Se intake was inversely associated with all-cause mortality and CVD mortality in both women and men, with respective HR for the highest compared with the lowest quintile being 0.79 (95% CI 0.71, 0.88; P_{trend}<0.0001) and 0.80 (95% CI 0.66, 0.98; P_{trend} =0.0268) for women, and 0.79 (95% CI 0.70, 0.89; P_{trend} =0.0001) and 0.66 (95% CI 0.54, 0.82; P_{trend} =0.0002) for men. No significant associations were observed for cancer mortality in both women and men. Results were similar in subgroup and sensitivity analyses.

Conclusions—Dietary Se intake was inversely associated with all-cause and cardiovascular mortality in both sexes, but not cancer mortality.

Conflict of interest: None.

Authorship: Y.B.X. conceived and designed the study, and is responsible for final editing and approval of the manuscript; J.W.S., H.L.L., W. Zhang, L.G.Z. analyzed the data. J.W.S. wrote the first draft. All authors critically reviewed manuscript and approved the final version.

Ethical Standards Disclosure: This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the all relevant Institutional Review Boards. Written informed consent was obtained from all participants.

Keywords

Dietary; Selenium intake; mortality; prospective study; China

Se, which is an essential trace element to maintain optimal human health, is incorporated into selenoproteins that have a wide variety of effects, ranging from antioxidant and anti-inflammatory effects to the production of active thyroid hormone [(1)]. Low Se status has been associated with increased mortality from cancer, poor immune function, male infertility and cognitive decline [(1,2)]. Meta-analysis of observational studies have provided some evidence for a beneficial effect of Se levels and bladder cancer [(3)], prostate cancer [(4)], lung cancer[(5)] and CHD[(6)], but findings from randomized trials have been mixed. Besides, randomized trials assessing use of supplements for primary prevention usually need long periods to affect health outcomes significantly and thus observational studies, such as cohort study, may facilitate the assessment of the association between long-term nutritional status and health outcomes.

Although several prospective studies have explored the association between Se levels and all-cause mortality, their findings have been mixed with some studies showing an effect of increasing Se on decreasing risk [(7–10)] and some not[(11)]. Researchers often focused on the association between all-cause mortality and the Se concentration in serum or plasma. Few studies exist in the literature examining the association between dietary Se intake and all-cause and cause-specific mortality. Moreover, dietary intake of Se varies widely worldwide owing to the variability of the Se content of soil and hence of plant foods and animal forage [(12)]. In China, the level of Se intake exhibited huge variation ranging from toxic (approximately 5 mg/d in areas of Enshi County) or adequate-marginally adequate (approximately 30–90 μg/d) to low or deficient intake (Heilongjiang Province: 7–11 μg/d)[(12,13)].

Therefore, using data collected in the Shanghai Women's Health Study (SWHS) and the Shanghai Men's Health Study (SMHS), we assessed the average level of dietary Se intake in Shanghai and prospectively investigated the potential long-term associations of dietary Se intake with all-cause, cardiovascular, and cancer mortality risks in middle-aged and older Chinese adults.

Methods

Study population

Participants from the SWHS and the SMHS were included in the analysis. Details regarding the designs and methods used in these studies have been described elsewhere [(14,15)]. Briefly, between March 1997 to May 2000, a total of 74941women aged 40 to 70 years were recruited for the SWHS (participation rate: 92.7%), and between April 2002 to June 2006, a total of 61480 men aged 40–74 years with no previous history of cancer were recruited for the SMHS (participation rate: 74.1%). In-person interviews were conducted to obtain information on socio-demographic factors, dietary and lifestyle habits, physical activity and

medical history using structured questionnaires. Anthropometrics measurements including weight, height, and waist and hip circumferences were also measured at baseline.

We excluded participants from the analysis who immediately lost to follow-up after study enrollment (5 women and 14 men), had missing data for any of covariates of interest (957 women and 1135 men), and 125 women and 228 men with extreme energy intake (<3347 or >17573 kj/d (<800 or >4200 kcal/d) for men; <2092 or >14644 kj/d (<500 or >3500 kcal/d) for women). The resulting analytic cohort included 73854 women and 60103 men.

Dietary assessment

In both the SWHS and the SMHS, usual dietary intakes were assessed using semi-quantitative FFQ. The FFQ used in the SWHS included seventy-seven items that covered 85.6% of foods commonly consumed in urban Shanghai in 1996[16]. A similar but extended FFQ with eighty-one items was used in the SMHS which captured 88.8% of commonly consumed foods[17]. During the in-person interviews, participants were asked about how frequently they consumed the food or food group during the preceding year (5 categories: daily, weekly, monthly, yearly or never) and then followed by a question on the amount of food consumed each time, in liangs (1 liang=50g). Each participant was also asked about whether he or she had taken supplements (vitamin A, B, C or E; a multivitamin; or calcium) at least three times per week continuously for more than 2 months.

The Chinese Food Composition Tables [18] was used to calculate daily intakes of total energy and nutrients. The reproducibility and validity of FFQs in the SMHS/SWHS were determined using monthly (SMHS; n=12) or biweekly (SWHS; n=24) 24-hour dietary recall evaluation over a 1-year period. The correlation coefficients for micronutrients ranged from 0.33 to 0.58 in the SMHS [17], and 0.41–0.59 in the SWHS [16].

Follow-up and Outcome ascertainment

Study participants were followed up by in-person survey every two to three years and annual record linkage with the Shanghai Vital Statistics Registry. For the SWHS, the response rates for the first, second, third, and fourth surveys were 99.8%, 98.7%, 96.7% and 92.3%, respectively. For the SMHS, the response rates for the first and second surveys were 97.6% and 93.7%, respectively. All possible matches identified through the linkage were verified by home visits. The underlying cause of death was determined primarily on the basis of death certificate data from the Shanghai Vital Statistics Unit and coded according to the *International Classification of Diseases, the Ninth Revision* (ICD-9). Our primary end point was death from any cause. We also examined deaths from CVD (ICD-9 codes 390–459) and cancer (ICD-9 codes:140–208).

Statistical analysis

Dietary Se intake was adjusted for total energy using the nutrient density method[19], and then categorized by quintile distribution, with the lowest quintile serving as the reference group. We used Cox proportional hazards regression models to determine the association of dietary Se intake with total and cause-specific mortality, with person-years as the underlying time metric. The proportional hazards assumption was evaluated using Schoenfeld residual

plots, and no evidence of violation was observed. Tests for linear trend across quintiles were estimated by assigning the median intake value for the quartile to each person and including this as a continuous variable in the regression model. Person-years of follow-up were calculated as the interval between baseline recruitment to the date of death, loss to follow-up or December 31, 2012, whichever was earlier.

We present risk estimates separately for men and women. In minimally adjusted models, we included age and energy intake as covariates. In multivariable-adjusted models, we further adjusted the following baseline factors: birth cohort (1920s, 1930s, 1940s, 1950s, 1960s), level of education (four categories: elementary school or less, middle school, high school and college or above), income (four categories: low, low to middle, middle to high and high), marital status (four categories), occupation (housewife(women only), manual, clerical and professional), BMI (four categories: <18.5kg/m^2, 18.5–24 kg/m^2, 24–28 kg/m^2, ≥28 kg/m^2), physical activity (quartiles of MET-h/week per year, where MET=metabolic equivalent of task), energy-adjusted fat intake (g/4184kj (1000kcal) per d, continues), use of any vitamin supplement (yes/no), smoking status (for men: never, ever and current; for women: never and ever), drinking status(for men: never, ever and current; for women: never and ever), status with regard to a history of hypertension (yes/no), diabetes (yes/no), CHD (yes/no), stroke (yes/no), and family history of cancer (yes/no). For women, menopausal status (yes/no) was also included in multivariate models.

To minimize the influence of possible reverse causation owing to the presence of chronic diseases at baseline, sensitivity analyses were conducted by excluding the first 2 years of follow-up and restricting the analyses to participants who did not have a history of hypertension, diabetes, CHD, stroke at baseline, or family history of cancer. We also restricted the analysis among lifetime nonsmokers to eliminate the potential confounding effect of cigarette smoking on the association between dietary Se intake and death. In secondary analyses, we examined associations among pre-specified baseline subgroups based on the following: body mass index, drinking status, use of any supplement; and in women, menopausal status.

Analyses were performed with the statistical package SAS version 9.2. Statistical tests were two-sided, and *P* values of less than 0.05 were considered statistically significant.

Results

Se intake and dietary, lifestyle factors

The average estimated dietary Se intake were 45.48 μg/day for women and 51.34 μg/day for men, respectively, which is close to the recommended nutrient intake level of 50μg/d for the Chinese population[18]. Compared with participants in the lowest quintile of Se density intake, those in the highest quintile were younger, lower BMI and less likely to exercise, but had higher total energy and fat intake, family income and educational levels. They were also more likely to use multivitamin supplements, but less likely to have history of hypertension, CHD and stroke. Men in the highest quintile were also more likely to smoke and consume alcoholic drinks (Table 1).

Dietary Se intake and total mortality

During an average follow-up of 13.90 years in the SWHS and 8.37 years in the SMHS, we documented 9966 deaths from all causes (4217 men and 5749 women), including 3154 deaths from CVD (1402 men and 1752 women) and 4352 deaths from cancer (1798 men and 2554 women).

Age- and energy-adjusted and multivariate-adjusted analyses showed a significant inverse association between dietary Se intake and total mortality among both men and women (Table 2). Multivariate adjusted hazard ratios (HR) for total death among women across the lowest to the highest quintiles of Se intake were 1.00 (reference), 0.96(95%CI 0.89, 1.03), 0.92(95%CI 0.84, 1.00), 0.90(95%CI 0.82, 0.99) and 0.79(95%CI 0.71, 0.88), respectively (P <0.0001 for trend across categories). The corresponding HR among men were 1.00 (reference), 0.91(95%CI 0.83, 0.99), 0.86(95%CI 0.78, 0.95), 0.82(95%CI 0.73, 0.91), and 0.79(95%CI 0.70,0.89), respectively (P =0.0001 for trend across categories).

Dietary Se intake and CVD and cancer mortality

In multivariate analyses, Se intake was inversely associated with CVD mortality in both men and women. The HR for the highest versus lowest quintile were 0.80 (95%CI 0.66, 0.98; *P* for trend=0.0268) among women, and 0.66 (95%CI 0.54, 0.82; *P* for trend=0.0002) among men, respectively. In contrast, no significant associations between Se intake and deaths from cancer were observed in both women and men.

Sensitivity and subgroup analysis

The significant inverse association between Se intake and all-causes mortality remained largely unchanged when we excluded the first 2 years of follow-up (628 men and 441 women, see online supplementary material, Table S1); excluded participants with hypertension (17940 men and 17544women), diabetes (3767 men and 3216women), CHD (3069 men and 5411women), stroke at baseline (2265men and 853 women), or family history of cancer(17062 men and 19710 women); excluded participants who had ever smoked(41900 men and 2059 women); excluded participants who had ever drunk (20231 men); and excluded participants who reported use of any supplement at baseline survey (10480 men and 22940 women; Table S2).

In stratified analyses, we found similar inverse associations between dietary Se intake and all-cause mortality across subgroups defined by menopause status (*P*=0.6543 for interaction) and BMI (*P*=0.8968 for interaction in men, and *P*=0.8259 for interaction in women). We noted significant interactions between waist-hip-ratio and Se intake with respect to the total death (*P*=0.0399 for interaction in men, and *P*<0.0001 for interaction in women), stronger associations were observed among men and women who had lower waist-hip-ratio (≤0.90 for men, HR=0.71 (95%CI 0.60, 0.84); and ≤0.85 for women, HR=0.76 (95%CI 0.67, 0.87)) than among those who had high waist-hip-ratio (HR=0.87 (95%CI 0.73,1.03) for men, and HR=0.83 (95%CI 0.69,1.00) for women; see online supplementary material, Table S3).

Discussion

In the current analysis of two large population-based cohorts involving 133957 participants living in Shanghai, China, we found a significant inverse association between dietary Se intake and all-cause and CVD mortality, after adjusting for potential confounders. Compared with the lowest quintile, women in the highest quintile of Se intake had a 21% lower risk of all-cause mortality and a 20% of CVD mortality, whereas men in this category of consumption had a 21% and a 34% lower risk, respectively. No association was found between Se intake and cancer mortality for either men or women.

Our finding of significant inversed association of dietary Se intake and all-cause mortality is generally consistent with findings from most previous prospective studies on plasma or serum Se level and mortality. In an analysis of 1389 elderly French participants in the Etude du Vieillissement Arteriel (EVA), low plasma Se at baseline was positively associated with all-cause mortality (relative risk (RR)=1.54 (95%CI 1.25, 1.88))[9]. In the Invecchiare in Chianti, adults in the lowest quartile of plasma Se had higher mortality risk compared with those in the highest quartile (RR=1.60 (95%CI 1.04, 2.47))[7]. A non-linear association between Se level and all-cause mortality was observed in 13887 US adult participants followed up for up to 12 years in the Third National Health and Nutrition Examination Survey [10]. By contrast, in a cohort analysis of 1103 participants in LinXian[11], China, no association was noted between baseline serum Se (mean 73μg/L) and all-cause mortality(RR=0.93 (95% CI 0.72–1.19)). Moreover, in a meta-analysis of randomized controlled trials, Se given alone or in combination with other supplements had no significant effect on mortality in 17 trials (RR=0.97, (95% CI 0.91, 1.03) [20], such as the Nutritional Prevention of Cancer (NPC) trial (median baseline plasma Se: 114 ng/ml) [21] and the Selenium and Vitamin E Cancer Prevention Trial (SELECT) (median baseline serum Se: 136 μg/L) [22].

Se may protect against CVD by preventing oxidative modification of lipids, inhibiting platelet aggregation, reducing inflammation[1,23], and improving functional capillary recruitment[24]. Although a meta-analysis of observational studies showed a significant inverse association between Se concentration and risk of CHD[6], randomized trials using Se in combination with other antioxidants have not shown a significant protective effect on CVD or mortality[6,22]. However, most of these large prevention trials did not consider baseline nutrition level in their inclusion criteria and Se was given in combination with other vitamins and minerals in all but two trials [25,26].

In contrast with previous prospective studies, our analysis of the SWHS and the SMHS data found no association between dietary Se intake and cancer mortality. In meta-analysis of observational studies, the pooled RR comparing the highest with the lowest category of Se levels was 0.61 (95% CI, 0.32, 0.95) for bladder cancer [3] and 0.74 (95%CI 0.57, 0.97)[5] for lung cancer. For prostate cancer, a more significant protective association was detected between Se and risk of advanced, rather than localized or low-grade, prostate cancer [27]. However, results from the recent randomized controlled trials have failed to provide evidence of beneficial effect of Se supplementation on risk of all cancers, prostate cancer or other site-specific cancers [28]. In NPC trial, Se supplementation was associated with a

statistically significant decrease in total cancer mortality, total cancer incidence, and incidence of lung, colorectal and prostate cancers [29]. However, with longer follow up time, the differences in lung and colorectal cancer became statistically non-significant. Another randomized controlled trail, SELECT found no evidence of effects of on the incidence of prostate, lung or any cancer overall at or beyond 5 years of follow-up with Se supplementation [22].

Differences in baseline Se plasma or serum levels of the populations studied might account for the observed differences. Beyond a specific Se concentration, additional Se intake dose not result in additional reduction of mortality and human studies have provided evidence of a U-shaped association between intake or status and health outcomes [10,29]. Moreover, because published randomized trials used a wide variety of supplements, in different doses, with different objectives and populations, and with short duration of follow-up time and small sample size, the power to detect the health effects of Se was slightly limited.

The underlying biological mechanism by which low dietary Se intake contribute to an increased mortality risk may be related to the increased oxidative stress and inflammation effects [8]. Higher Se levels may potentially protect against oxidative stress and reduce pro-inflammation cytokines and other markers of inflammation including C-reactive protein by incorporating into selenoprotein, such as glutathione peroxidase and seleneprotein S (SEPS 1)[30]. Low Se may compromise health by decreasing the synthesis and activity of deiodinase, the enzyme that transforms thyroxine into the biologically active triiodothyronine[31]. Moreover, low Se status may be implicated in the pathogenesis of atherosclerosis through its effects on regulating the cyclo-oxygenase and lipoxygrnase pathways of the arachidonic acid cascade in endothelial cells[23]. In the Uppsala Longitudinal Study of Adult Men, high concentrations of serum Se predicted reduced levels of urinary F_2 isoprostane, a biomarker of lipid peroxidation and oxidative stress[32].

Strength of our study includes the population-based, prospective design with high participation and retention rates and detailed information on diet. The extensive data on possible risk factors for mortality allowed comprehensive adjustments of confounders. Results from the various sensitivity and subgroup analyses we carried out yielded similar results throughout, which suggests that our findings are fairly robust. However, several limitations of our study also merit consideration. First, as with any nutritional epidemiological study, measurement errors in self-reported dietary data introduced by FFQ, which are most likely non-differential, may have attenuated estimates for the associations. Second, because dietary and lifestyle factors interact in complex ways with each other, we cannot entirely separate the effect of dietary Se from those of other nutrients, and foods, thus we cannot completely rule out the possibility that some unmeasured confounders or residual confounding accounted for the observed associations. Third, Se intake from supplements was not taken into account in our analysis. However, the associations between Se intake and mortality did not change substantially after exclusion of supplement users. Fourth, dietary intake assessed at baseline may have been affected by preclinical conditions. Nevertheless, excluding the first 2 years of follow-up and participants with chronic diseases at baseline did not alter the results. Fifth, since Se levels in foods may vary between geographic regions due to the Se content of the soil where the food was produced, serum or plasma Se levels would

have been preferable to estimate Se exposure. However, owing to constraint of resources, serum or plasma Se levels were not measured for the participants in our study. We expect that the errors in dietary Se assessment would be random and likely lead to an attenuation of the true effect rather than create an artificial effect when none existed. Sixth, it is not known whether participants' diet during the baseline year reflected their diet during the biologically relevant period. Thus, although an inverse association between Se exposure and mortality was found in some observational studies, including our study, this cannot be taken as evidence of a causal relation, and our results should be interpreted with caution.

Conclusion

In conclusion, we found that increased dietary Se intake was associated with lower all-cause and CVD mortality risk among Chinese men and women, consistent with previous observational studies, suggesting individuals in the lower categories of Se exposure may benefit from increased Se intake.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline Characteristics by Energy-adjusted Quintile of selenium intake in the Shanghai Women's Health Study (SWHS; 1997–2000) and the Shanghai Men's Health Study (SMHS; 2002–2006)

	Energy-adjusted Quintile of selenium intake										
	1		2		3		4		5		
	Mean/%	SD	Mean/%	SD	Mean/%	SD	Mean/%	SD	Mean/%	SD	*P* value
SWHS											
Number of participants	14771	-	14771	-	14769	-	14771	-	14772		
Age (years)	56.72	9.14	53.4	8.97	51.94	8.64	51.03	8.42	49.77	8.03	<0.0001
High educational level (%)†	2.07	-	4.08	-	5.5	-	6.06	-	5.89	-	<0.0001
High income (%)‡	10.02	-	14.95	-	18.43	-	20.7	-	23.78	-	<0.0001
Currently married (%)	83.83	-	89.22	-	90.07	-	91.04	-	90.29	-	<0.0001
Body mass index, kg/m2	24.87	3.69	24.13	3.44	23.82	3.38	23.73	3.25	23.56	3.22	<0.0001
Waist-to-hip ratio	0.82	0.06	0.81	0.05	0.81	0.05	0.81	0.05	0.80	0.05	<0.0001
Physical activity, MET-h/w/y§	109.42	45.69	107.98	45.72	105.86	44.61	105.26	44.48	103.71	44.56	<0.0001
Total energy intake, kcal/day	1580.99	396.44	1656.97	381.32	1687.19	377.31	1708.87	383.92	1739.03	411.1	<0.0001
Total fat, g/day	19.47	9.42	26.55	10.23	30.48	11.39	33.48	12.32	37.01	13.9	<0.0001
Ever smoker (%)	4.64	-	2.83	-	2.28	-	2	-	2.19	-	<0.0001
Alcohol drinking (ever) (%)	1.81	-	1.9	-	1.97	-	2.15	-	3.33	-	<0.0001
History of hypertension (%)	31.52	-	25.84	-	22.09	-	21.07	-	18.25	-	<0.0001
History of Coronary heart disease (%)	9.46	-	8.22	-	6.93	-	6.61	-	5.42	-	<0.0001
History of stroke (%)	2.15	-	1.37	-	0.99	-	0.69	-	0.58	-	<0.0001
Family history of cancer (%)	23.33	-	26.63	-	27.77	-	27.81	-	27.9	-	<0.0001
History of diabetes (%)	4.85	-	4.89	-	4.24	-	4.16	-	3.63	-	<0.0001
Supplement use (%)//	24.15	-	29.19	-	31.61	-	34.75	-	35.6	-	<0.0001
Postmenopausal (%)	67.48	-	53.73	-	46.88	-	42.33	-	36.98	-	<0.0001
SMHS											
Number of subjects	12021	-	12022	-	12022	-	12016	-	12022	-	
Age (years)	57.1	10.06	56.11	9.78	55.6	9.64	54.88	9.53	53.11	9.23	<0.0001
High educational level (%)†	6.77	-	10.44	-	12.63	-	13.71	-	13.89	-	<0.0001

	Energy-adjusted Quintile of selenium intake										
	1		2		3		4		5		
	Mean/%	SD	Mean/%	SD	Mean/%	SD	Mean/%	SD	Mean/%	SD	*P* value
High income (%)‡	4.77	-	7.62	-	9.87	-	11.79	-	14.37	-	<0.0001
Currently married (%)	82.41	-	85.15	-	85.67	-	85.49	-	83.7	-	<0.0001
Body mass index, kg/m2	23.79	3.12	23.75	3.09	23.7	3.07	23.74	3.07	23.63	3.04	0.001
Waist-to-hip ratio	0.90	0.06	0.90	0.06	0.90	0.06	0.90	0.06	0.90	0.06	<0.0001
Physical activity, MET-h/w/y§	62.79	35.28	60.8	33.73	59.87	34.26	58.55	33.25	56.41	34.06	<0.0001
Total energy intake, kcal/day	1892.54	476.06	1906.29	463.51	1914.39	463.84	1915.61	466.66	1921.87	502.04	<0.0001
Total fat, g/day	24.34	11.13	31.25	11.99	35.28	13.72	38.71	14.75	43.25	17.87	<0.0001
Current Smoking (%)	56.89	-	55.97	-	57.54	-	58.82	-	64.38	-	<0.0001
Current alcohol consumption (%)	19.03	-	23.32	-	28.89	-	32.08	-	42.8	-	<0.0001
History of hypertension (%)	32.93	-	31.52	-	29.75	-	29.21	-	25.83	-	<0.0001
History of Coronary heart disease (%)	5.76	-	5.4	-	5.32	-	5.06	-	3.99	-	<0.0001
History of diabetes (%)	4.67	-	5.8	-	6.39	-	7.5	-	6.99	-	<0.0001
History of stroke (%)	5.53	-	4.3	-	3.7	-	3.01	-	2.3	-	<0.0001
Family history of cancer (%)	26.65	-	28.32	-	29.35	-	28.86	-	28.76	-	<0.0001
Supplement use (%)//	11.72	-	16.49	-	18.47	-	20.02	-	20.48	-	<0.0001

The median and cut points for the quintile of Se intake in the SWHS were 15.86 (7.19–19.04), 21.16 (19.05–23.15), 25.18 (23.16–27.31), 30.02 (27.32–33.35) and 42.22 (33.36–124.64) μg/4184KJ (1000kcal) per d and in the SMHS were 16.46 (7.43–19.36), 21.33 (19.37–23.20), 25.09 (23.21–27.11), 29.72 (27.12–32.91), 41.70 (32.92–165.38) μg/4184KJ (1000kcal) per d.

†High educational level was defined as having a college degree or above.

‡High income was defined as a family income greater than 30,000 Yuan per year for women or a personal income greater than 2,000 Yuan per month for men.

§Physical activity: metabolic equivalent (MET)-hours per week per year (1 MET h=15 min of moderate intensity activity).

//Use of any vitamin A, B, C, or E supplements, multivitamins or calcium.

Table 2

Association of dietary selenium intake with total and cause-specific mortality in the Shanghai Women's Health Study (SWHS; 1997–2000) and the Shanghai Men's Health Study (SMHS; 2002–2006)

	Quintile category					
Cause of Death	**1**	**2**	**3**	**4**	**5**	***P* for trend** *
			Shanghai Women's Health Study			
All causes						
Median(ug/4184KJ (1000kcal) per d) †	15.86	21.16	25.18	30.02	42.22	
No. of deaths/person-years	1863/199978	1285/203892	1033/204976	892/205253	676/205437	
Model 1‡	1.00(reference)	0.94(0.88–1.01)	0.89(0.82–0.96)	0.85(0.79–0.93)	0.76(0.69–0.83)	<.0001
Model 2§	1.00(reference)	0.96(0.89–1.03)	0.92(0.84–1.00)	0.90(0.82–0.99)	0.79(0.71–0.88)	<.0001
CVD						
No. of deaths/person-years	648/199978	390/203892	303/204976	235/205253	176/205437	
Model 1‡	1.00(reference)	0.90(0.79–1.02)	0.85(0.74–0.97)	0.76(0.65–0.89)	0.71(0.60–0.84)	<.0001
Model 2§	1.00(reference)	0.94(0.82–1.07)	0.93(0.80–1.08)	0.87(0.73–1.03)	0.80(0.66–0.98)	0.0268
Cancer						
No. of deaths/person-years	708/199978	559/203892	482/204976	451/205253	354/205437	
Model 1‡	1.00(reference)	1.00(0.89–1.12)	0.97(0.86–1.09)	0.98(0.87–1.11)	0.87(0.76–0.99)	0.0326
Model 2§	1.00(reference)	1.02(0.90–1.14)	1.00(0.87–1.14)	1.02(0.89–1.17)	0.90(0.77–1.05)	0.1539
			Shanghai Men's Health Study			
All causes						
Median(ug/4184KJ (1000kcal) per d) †	16.46	21.33	25.09	29.72	41.7	
No. of deaths/person-years	1136/98122	885/98995	819/99583	745/100137	632/101936	
Model 1‡	1.00(reference)	0.86(0.78–0.93)	0.82(0.75–0.90)	0.79(0.72–0.87)	0.77(0.70–0.85)	<.0001
Model 2§	1.00(reference)	0.91(0.83–0.99)	0.86(0.78–0.95)	0.82(0.73–0.91)	0.79(0.70–0.89)	0.0001
CVD						
No. of deaths/person-years	433/98122	302/98995	253/99583	235/100137	179/101936	
Model 1‡	1.00(reference)	0.78(0.67–0.90)	0.68(0.58–0.80)	0.68(0.58–0.80)	0.61(0.51–0.72)	<.0001
Model 2§	1.00(reference)	0.85(0.73–1.00)	0.75(0.63–0.89)	0.73(0.61–0.88)	0.66(0.54–0.82)	0.0002

Cause of Death	Quintile category 1	2	3	4	5	*P* for trend *
Cancer						
No. of deaths/person-years	432/98122	366/98995	356/99583	325/100137	319/101936	
Model 1‡	1.00(reference)	0.92(0.80–1.05)	0.92(0.80–1.05)	0.88(0.76–1.02)	0.98(0.85–1.13)	0.8311
Model 2§	1.00(reference)	0.95(0.82–1.10)	0.94(0.81–1.10)	0.90(0.76–1.06)	0.97(0.81–1.15)	0.7802

HR, hazard ratio.

**P* values for trend were estimated by assigning the median intake value for the quartile to each person and including this as a continuous variable in the model.

†Dietary intakes were adjusted for energy intake using nutrient density method, and expressed as per ug/4184KJ (1000kcal) per d.

‡Adjusted for age and total energy intake.

§Adjusted for age, birth cohort, education, income, marital status, occupation, body mass index, physical activity, total energy intake, dietary fat intake, vitamin supplement use, smoking status, drinking status, status with regard to a history of hypertension, diabetes, coronary heart disease or stroke, family history of cancer and menopausal status (women only).