Cruciferous vegetable consumption is associated with a reduced risk of total and cardiovascular disease mortality[1–4]

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ABSTRACT

Background: Asian populations habitually consume a large amount of cruciferous vegetables and other plant-based foods. Few epidemiologic investigations have evaluated the potential health effects of these foods in Asian populations.

Objective: We aimed to examine the associations of cruciferous vegetables, noncruciferous vegetables, total vegetables, and total fruit intake with risk of all-cause and cause-specific mortality.

Design: The analysis included 134,796 Chinese adults who participated in 2 population-based, prospective cohort studies: the Shanghai Women's Health Study and the Shanghai Men's Health Study. Dietary intakes were assessed at baseline through in-person interviews by using validated food-frequency questionnaires. Deaths were ascertained by biennial home visits and linkage with vital statistics registries.

Results: We identified 3442 deaths among women during a mean follow-up of 10.2 y and 1951 deaths among men during a mean follow-up of 4.6 y. Overall, fruit and vegetable intake was inversely associated with risk of total mortality in both women and men, and a dose-response pattern was particularly evident for cruciferous vegetable intake. The pooled multivariate hazard ratios (95% CIs) for total mortality across increasing quintiles of intake were 1 (reference), 0.91 (0.84, 0.98), 0.88 (0.77, 1.00), 0.85 (0.76, 0.96), and 0.78 (0.71, 0.85) for cruciferous vegetables ($P < 0.0001$ for trend) and 0.88 (0.79, 0.97), 0.88 (0.79, 0.98), 0.76 (0.62, 0.92), and 0.84 (0.69, 1.00) for total vegetables ($P = 0.03$ for trend). The inverse associations were primarily related to cardiovascular disease mortality but not to cancer mortality.

Conclusion: Our findings support recommendations to increase consumption of vegetables, particularly cruciferous vegetables, and fruit to promote cardiovascular health and overall longevity. *Am J Clin Nutr* 2011;94:240–6.

INTRODUCTION

Increasing fruit and vegetable consumption has been widely recommended as a key component of a healthy diet to reduce the risk of major chronic diseases such as cancer and cardiovascular disease (CVD), the leading causes of death worldwide (1, 2). Recent large prospective studies, however, have found no or minimal effects of fruit and vegetable consumption on overall cancer risk, which casts doubt on this dietary recommendation (3–6). Questions have also arisen as to whether certain groups of fruit or vegetables may be more beneficial than others. Specifically, cruciferous vegetables have attracted considerable attention in recent years. Several prospective studies focusing on specific cancers have shown a null association for total vegetable consumption, but a significant inverse association for cruciferous vegetable consumption (7, 8). Relatively few studies have examined the association between cruciferous vegetable consumption and CVD risk or mortality. Currently, data are insufficient to support specific recommendations for cruciferous vegetable intake.

Asian populations are known to regularly consume a large amount of cruciferous vegetables and other plant-based foods, which provides a unique opportunity to address hypotheses related to the potential role of these foods in disease prevention. Few large-scale epidemiologic studies, however, have been conducted in Asian populations, and data on the potential health effects of fruit and vegetable consumption have been derived predominantly from Western populations. We analyzed data from 2 prospective cohort studies conducted in China—the Shanghai Women's Health Study (SWHS) and the Shanghai Men's Health Study (SMHS)—to evaluate the associations of cruciferous vegetable, noncruciferous vegetable, total vegetable, and total fruit intakes with the risk of all-cause and cause-specific mortality.

SUBJECTS AND METHODS

The SWHS and the SMHS are population-based, prospective cohort studies conducted in urban Shanghai, China. Both studies were approved by the Institutional Review Boards of all institutes involved, and informed consent was obtained from all participants. Similar designs and methods have been used in the 2 studies and have been described in detail previously (9, 10). Briefly, from 1996 to 2000, the SWHS recruited 74 942 women aged 40–70 y from 7 typical urban communities of Shanghai (participation rate: 92.7%). From 2002 to 2006, the SMHS

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recruited 61 500 men aged 40–74 y from the same communities (participation rate: 74.1%). In both studies, trained interviewers conducted baseline surveys and anthropometric measurements at participants' homes. Structured questionnaires were used during the surveys to obtain information on demographics, diet and other lifestyle habits, medical history, and other characteristics.

Dietary assessment

In both the SWHS and the SMHS, usual dietary intakes were assessed through in-person interviews using validated food-frequency questionnaires (FFQs) (11, 12). The FFQ used in the SWHS captured 86% of the foods consumed by the study population. It included 33 vegetable items and 8 fruit items. A similar, but expanded, FFQ was used in the SMHS. It covered 89% of commonly consumed foods and included 38 vegetable items and 8 fruit items. Vegetable groups included mainly cruciferous vegetables (bok choy, cabbage, napa cabbage, cauliflower, and turnip), green leafy vegetables (bok choy and spinach), allium vegetables (garlic, garlic sprouts, onions, green onions, and Chinese chives), and legumes (soybeans, peas, broad beans, Chinese long beans, green beans, hyacinth beans, and snow peas). During the in-person interview, each participant was first asked how often, on average, during the previous year that he or she had consumed a specific food or food group (the possible responses were daily, weekly, monthly, yearly, or never), followed by a question on the amount consumed in grams per unit of time. The average daily intake of total vegetables, total fruit, and other food groups was estimated by summing the intake of each of these food items. The intake of nutrients was calculated by multiplying the amount of food consumed by the nutrient contents per gram of food obtained from the Chinese Food Composition Tables (13).

The validity and reproducibility of the SWHS and SMHS FFQs for assessing usual dietary intake were described elsewhere (11, 12). Overall, the estimates of nutrient and food intakes derived from the FFQs and from multiple 24-h dietary recalls correlated reasonably well. The correlation coefficients for total fruit were 0.55 in the SWHS and 0.72 in the SMHS. The correlations for total vegetables were 0.41 and 0.42 in the SWHS and SMHS, respectively.

Outcome ascertainment

The participants were followed through biennial home visits and record linkage to the Shanghai Cancer Registry and the Shanghai Vital Statistics Registry. The primary endpoint for the current analysis was death from all causes that occurred after the baseline survey, with follow-up through November 2009 for the SWHS and through December 2009 for the SMHS. In both cohorts, follow-up for the vital status of participants was >99.9% complete. The underlying cause of death was determined primarily on the basis of death certificates and coded according to the codes of the *International Classification of Diseases, Ninth Revision* (ICD-9). In particular, we examined deaths from CVD (ICD-9 codes 390–459) and cancer (ICD-9 codes 140–208). Validation studies of cause-of-death statistics in urban China, including Shanghai, have shown that information on the death certificates was reasonably accurate for major causes of death, such as CVD and cancer (14).

Statistical analysis

A history of cancer was an exclusion criterion for enrollment in the SMHS, but not for enrollment in the SWHS. To be consistent, we excluded from the analyses women with a history of cancer at baseline. We also excluded participants with extreme total energy intake (<500 or >3500 kcal/d for women and <500 or >4200 kcal/d for men) and those lost to follow-up shortly after enrollment. After these exclusions, 73,360 women and 61,436 men remained for the analyses.

We first conducted analyses separately for each cohort. The participants were classified into 5 categories according to quintiles of fruit and vegetable intake, with the lowest quintile serving as the reference category. Cox proportional hazards models were used, with age as the time scale, to estimate hazard ratios (HRs) for death associated with fruit and vegetable intake and 95% CIs and to adjust for potential confounders. Entry time was defined as age at enrollment, and exit time was defined as age at death or censoring. Covariates included age (continuous), education level (4 categories), occupation (3 categories), family income (4 categories), cigarette smoking (never, past, or current: 1–9, 10–19, or ≥20 cigarettes/d), alcohol consumption (3 categories in women, 5 categories in men), body mass index (quintiles), amount of regular exercise (4 categories), multivitamin supplement use (yes or no), total energy intake (continuous), saturated fat intake (quintiles), menopausal status and hormone therapy use (yes or no; for women only), and history of coronary heart disease, stroke, hypertension, or diabetes (yes or no). Tests for linear trend in risk across categories of fruit and vegetable intake were performed by using the median value for each intake category and modeling them as continuous variables. We also conducted pooled analyses using a random-effects model to obtain summary estimates for both women and men. In addition, we conducted sensitivity analyses, excluding the first 2 y of follow-up, to assess the potential influence of baseline illness. Finally, we evaluated the proportional hazards assumption using the Schoenfeld residuals and found no significant violation of the assumption. Statistical analyses were performed by using SAS statistical software (version 9.2; SAS Institute Inc, Cary, NC). All statistical tests were based on 2-sided probability.

RESULTS

The mean ages of the participants at enrollment were 53 y in the SWHS and 55 y in the SMHS. For women, the median intakes (interquartile ranges) of total vegetables, cruciferous vegetables, and total fruit were 261 (179–373), 83 (51–129), and 238 (134–358) g/d, respectively; for men, the respective median intakes were 307 (213–429), 94 (59–145), and 129 (57–126) g/d. The baseline characteristics of the study participants by quintiles of total fruit and vegetable intake are shown in **Table 1**. In both women and men, individuals with a higher total fruit and vegetable intake compared with those with a lower intake tended to be younger and have higher levels of education, occupational status, and family income. They exercised more and were more likely to take multivitamin supplements and less likely to smoke cigarettes. Total fruit and vegetable intake also appeared to be positively associated with level of BMI and intake of total energy and saturated fat.

TABLE 1
Characteristics of study participants by quintile of total fruit and vegetable intake[1]

	Quintile of total fruit and vegetable intake				
	1	2	3	4	5
Women (SWHS)					
Median intake (g/d)	239	387	514	664	930
No. of subjects	14,672	14,672	14,672	14,672	14,672
Age (y)	55.5 ± 9.7[2]	52.9 ± 9.2	52.0 ± 8.8	51.4 ± 8.6	50.8 ± 8.2
Educational level (%)					
≤Elementary school	38.0	23.0	18.1	15.2	12.7
Middle school	33.9	37.8	37.8	37.8	38.6
High school	19.4	26.7	29.2	31.5	32.9
≥College	8.6	12.5	15.0	15.6	15.9
Occupation (%)					
Manufacturing and agricultural workers	58.5	51.5	48.8	47.8	46.7
Clerical and service workers	20.8	20.8	20.8	20.2	21.5
Professionals, administrators	20.7	27.7	30.5	32.0	31.8
Annual family income (%)					
<10,000 yuan	21.6	16.5	14.0	14.0	14.4
10,000–19,999 yuan	40.5	39.2	38.4	36.8	36.3
20,000–29,999 yuan	25.3	28.1	29.1	29.5	28.5
≥30,000 yuan	12.5	16.3	18.5	19.7	20.8
Cigarette smoking (%)	5.2	2.7	2.2	1.8	2.1
Alcohol consumption (%)	2.5	2.1	2.0	2.1	2.6
Multivitamin supplement use (%)	4.5	6.5	7.5	8.0	9.1
Hormone therapy (%)	1.3	1.8	2.1	2.4	2.6
BMI (kg/m^2)	24.0 ± 3.6	23.9 ± 3.5	23.9 ± 3.4	24.0 ± 3.3	24.3 ± 3.3
Regular exercise (h/wk)	1.7 ± 3.4	1.8 ± 3.4	2.0 ± 3.6	2.1 ± 3.7	2.4 ± 4.2
Total energy intake (kcal/d)	1450 ± 340	1578 ± 339	1657 ± 338	1751 ± 360	1932 ± 413
Saturated fat intake (g/d)	6.5 ± 3.5	7.8 ± 3.6	8.6 ± 3.8	9.4 ± 4.1	10.6 ± 4.7
Men (SMHS)					
Median intake (g/d)	214	340	450	582	827
No. of subjects	12,287	12,288	12,286	12,288	12,287
Age (y)	56.0 ± 10.3	55.5 ± 9.8	55.4 ± 9.6	55.1 ± 9.5	54.9 ± 6.4
Educational level (%)					
≤Elementary school	11.8	7.3	5.9	5.1	3.5
Middle school	38.2	35.4	33.7	31.1	29.3
High school	34.6	35.9	36.6	36.5	36.8
≥College	15.4	21.5	23.8	27.4	30.3
Occupation (%)					
Manufacturing and agricultural workers	58.6	53.1	51.2	48.3	46.3
Clerical and service workers	21.2	22.0	21.7	22.3	22.5
Professionals, administrators	20.2	24.9	27.1	29.5	31.3
Annual per capita family income (%)					
<6000 yuan	17.4	12.9	12.0	10.3	10.3
6000–11,999 yuan	47.1	44.2	42.4	41.2	38.0
12,000–23,999 yuan	29.5	34.5	36.0	37.4	38.3
≥24,000 yuan	6.0	8.4	9.6	11.1	13.4
Cigarette smoking (%)	78.9	71.9	69.0	65.5	62.7
Alcohol consumption (%)	40.0	35.3	32.4	30.3	30.6
Multivitamin supplement use (%)	5.1	6.6	7.2	8.9	10.0
BMI (kg/m^2)	23.2 ± 3.1	23.6 ± 3.1	23.7 ± 3.1	23.9 ± 3.0	24.2 ± 3.0
Regular exercise (h/wk)	1.7 ± 3.7	1.9 ± 3.7	2.1 ± 3.9	2.4 ± 4.2	2.8 ± 4.5
Total energy intake (kcal/d)	1650 ± 428	1791 ± 417	1894 ± 422	1996 ± 439	2204 ± 491
Saturated fat intake (g/d)	8.2 ± 4.5	9.3 ± 4.4	10.1 ± 4.5	11.1 ± 4.9	12.7 ± 5.7

[1] SWHS, Shanghai Women's Health Study; SMHS, Shanghai Men's Health Study. All P for trend values <0.05, except for alcohol consumption in women (P = 0.47); the Cochran-Mantel-Haenszel test was used for categorical variables, and the general linear model was used for continuous variables.
[2] Mean ± SD (all such values).

In the SWHS cohort, we identified 3442 deaths, including 1023 from CVD (55.3% stroke, 22.0% coronary heart disease, and 22.7% other circulatory diseases) and 1485 from cancer (20.3% lung cancer, 13.9% colorectal cancer, 13.1% stomach cancer, 8.1% liver cancer, 6.8% breast cancer, and 37.8% other cancers) during a mean follow-up of 10.2 y. In the SMHS cohort, we identified 1951 deaths, including 635 from CVD (49.1% stroke, 33.7% coronary heart disease, and 17.2% other circulatory diseases) and 853 from cancer (31.8% lung cancer, 14.5% liver cancer, 13.0% stomach cancer, 7.4% colorectal cancer, and 33.3% other cancers) during a mean follow-up of 4.6 y. The HRs and 95% CIs of total mortality according to quintiles of total vegetable intake, cruciferous vegetable intake, noncruciferous vegetable intake, and total fruit intake in women and men are shown in **Table 2**. Overall, fruit and vegetable intake was inversely associated with risk of total mortality, and a dose-response pattern was particularly evident for cruciferous vegetable intake. The results were generally consistent across both cohorts. The pooled multivariate HRs (95% CIs) for total mortality across increasing quintiles of intake were 1 (reference), 0.88 (0.79, 0.97), 0.88 (0.79, 0.98), 0.76 (0.62, 0.92), and 0.84 (0.69, 1.00) for total vegetable intake (*P* = 0.03 for trend) and

TABLE 2
Hazard ratios (HRs) for total mortality by quintile of fruit and vegetable intake

	Quintile of intake					
	1	2	3	4	5	*P* for trend
Total vegetables						
Women						
Median intake (g/d)	124	196	261	345	506	
No. of deaths	961	698	646	556	581	
Age-adjusted HR	1.00	0.87 (0.79, 0.96)	0.87 (0.78, 0.96)	0.76 (0.69, 0.85)	0.84 (0.75, 0.93)	0.0001
Multivariate HR[1]	1.00	0.92 (0.83, 1.01)	0.92 (0.83, 1.02)	0.83 (0.74, 0.93)	0.91 (0.81, 1.03)	0.07
Men						
Median intake (g/d)	144	232	307	398	583	
No. of deaths	602	398	359	286	306	
Age-adjusted HR	1.00	0.74 (0.65, 0.84)	0.71 (0.62, 0.80)	0.56 (0.48, 0.64)	0.60 (0.52, 0.68)	<0.0001
Multivariate HR[1]	1.00	0.83 (0.73, 0.94)	0.82 (0.72, 0.94)	0.68 (0.59, 0.79)	0.75 (0.65, 0.88)	<0.0001
Pooled multivariate HR	1.00	0.88 (0.79, 0.97)	0.88 (0.79, 0.98)	0.76 (0.62, 0.92)	0.84 (0.69, 1.00)	0.03
Cruciferous vegetables						
Women						
Median intake (g/d)	28	57	83	114	166	
No. of deaths	824	675	666	656	621	
Age-adjusted HR	1.00	0.87 (0.78, 0.96)	0.89 (0.81, 0.99)	0.88 (0.79, 0.97)	0.79 (0.72, 0.88)	<0.0001
Multivariate HR[1]	1.00	0.90 (0.82, 1.00)	0.93 (0.84, 1.04)	0.90 (0.81, 1.00)	0.80 (0.72, 0.89)	0.0002
Men						
Median intake (g/d)	34	66	94	133	208	
No. of deaths	544	410	342	333	322	
Age-adjusted HR	1.00	0.83 (0.73, 0.94)	0.70 (0.61, 0.80)	0.67 (0.58, 0.77)	0.62 (0.54, 0.71)	<0.0001
Multivariate HR[1]	1.00	0.91 (0.80, 1.04)	0.82 (0.71, 0.94)	0.79 (0.69, 0.91)	0.73 (0.64, 0.85)	<0.0001
Pooled multivariate HR	1.00	0.91 (0.84, 0.98)	0.88 (0.77, 1.00)	0.85 (0.76, 0.96)	0.78 (0.71, 0.85)	<0.0001
Noncruciferous vegetables						
Women						
Median intake (g/d)	73	124	173	236	362	
No. of deaths	998	720	600	588	536	
Age-adjusted HR	1.00	0.91 (0.83, 1.00)	0.81 (0.73, 0.90)	0.84 (0.76, 0.93)	0.82 (0.73, 0.91)	<0.0001
Multivariate HR[1]	1.00	0.98 (0.88, 1.08)	0.88 (0.79, 0.98)	0.95 (0.85, 1.06)	0.95 (0.84, 1.06)	0.38
Men						
Median intake (g/d)	89	148	201	269	413	
No. of deaths	600	416	343	299	293	
Age-adjusted HR	1.00	0.78 (0.69, 0.88)	0.68 (0.59, 0.77)	0.62 (0.54, 0.71)	0.59 (0.51, 0.68)	<0.0001
Multivariate HR[1]	1.00	0.89 (0.78, 1.01)	0.81 (0.70, 0.93)	0.78 (0.67, 0.90)	0.75 (0.64, 0.87)	0.0001
Pooled multivariate HR	1.00	0.94 (0.86, 1.03)	0.85 (0.78, 0.93)	0.87 (0.71, 1.06)	0.85 (0.67, 1.06)	0.15
Total fruit						
Women						
Median intake (g/d)	62	155	238	330	489	
No. of deaths	1254	697	575	499	417	
Age-adjusted HR	1.00	0.71 (0.65, 0.78)	0.65 (0.59, 0.72)	0.62 (0.56, 0.69)	0.59 (0.53, 0.66)	<0.0001
Multivariate HR[1]	1.00	0.87 (0.79, 0.96)	0.85 (0.77, 0.94)	0.84 (0.75, 0.94)	0.81 (0.72, 0.92)	0.0004
Men						
Median intake (g/d)	14	71	129	196	308	
No. of deaths	541	451	362	291	306	
Age-adjusted HR	1.00	0.75 (0.66, 0.85)	0.61 (0.53, 0.69)	0.50 (0.43, 0.57)	0.51 (0.44, 0.59)	<0.0001
Multivariate HR[1]	1.00	0.97 (0.86, 1.11)	0.88 (0.77, 1.02)	0.79 (0.68, 0.93)	0.88 (0.75, 1.02)	0.02
Pooled multivariate HR	1.00	0.91 (0.82, 1.02)	0.86 (0.79, 0.94)	0.82 (0.75, 0.90)	0.83 (0.76, 0.92)	<0.0001

[1] Cox proportional hazards model adjusted for age, education, occupation, family income, cigarette smoking, alcohol consumption, BMI, amount of regular exercise, multivitamin supplement use, intakes of total energy and saturated fat, menopausal status and hormone therapy use (for women only), and history of coronary heart disease, stroke, hypertension, or diabetes.

0.91 (0.82, 1.02), 0.86 (0.79, 0.94), 0.82 (0.75, 0.90), and 0.83 (0.76, 0.92) for total fruit intake ($P < 0.0001$ for trend). The corresponding HRs (95% CIs) for cruciferous vegetable intake were 0.91 (0.84, 0.98), 0.88 (0.77, 1.00), 0.85 (0.76, 0.96), and 0.78 (0.71, 0.85) ($P < 0.0001$ for trend).

The multivariate HRs of CVD-related and cancer-related mortality associated with fruit and vegetable intake in women and men are summarized in **Tables 3** and **4**. Consistent with the results for total mortality, intakes of total vegetables, particularly cruciferous vegetables, and total fruit were also inversely associated with risk of CVD mortality in both women and men. The inverse associations appeared to be somewhat stronger for CVD mortality than for total mortality. No significant association, however, was found between intake of total vegetables, cruciferous vegetables, or total fruit and cancer mortality in either women or men.

Similar results were found in analyses that excluded the first 2 y of follow-up. The pooled multivariate HRs (95% CIs) for CVD mortality across increasing quintiles of total vegetable intake were 1 (reference), 0.90 (0.73, 1.11), 0.86 (0.73, 1.01), 0.65 (0.38, 1.13), and 0.74 (0.59, 0.92), ($P = 0.004$ for trend). The corresponding HRs for CVD mortality (95% CIs) for cruciferous vegetables were 1.03 (0.88, 1.20), 0.85 (0.66, 1.11), 0.83 (0.70, 0.99), and 0.76 (0.64, 0.91) ($P = 0.0004$ for trend). No association was found for cancer mortality.

DISCUSSION

In these 2 large prospective cohort studies of Chinese women and men, we found that high intakes of total vegetables, particularly cruciferous vegetables, and total fruit were associated with a significantly reduced risk of overall mortality. The reduced mortality risk was primarily related to death from CVD. We found no significant association between intake of total vegetables, cruciferous vegetables, or total fruit and cancer mortality.

Our findings on fruit and vegetable consumption and death from CVD and cancer are supported by several previous large cohort studies that have evaluated the contribution of fruit and vegetable consumption to CVD and cancer incidence or mortality (3–5, 15–19). In combined analyses of the Nurses' Health Study and the Health Professionals Follow-Up Study, fruit and vegetable consumption was found to be inversely associated with risk

TABLE 3
Multivariate hazard ratios (HRs) for cardiovascular disease mortality by quintile of fruit and vegetable intake

	Quintile of intake					
	1	2	3	4	5	*P* for trend
Total vegetables						
Women						
No. of deaths	303	225	173	169	153	
Multivariate HR[1]	1.00	0.99 (0.83, 1.18)	0.84 (0.69, 1.02)	0.86 (0.71, 1.05)	0.84 (0.67, 1.04)	0.06
Men						
No. of deaths	220	139	112	69	95	
Multivariate HR[1]	1.00	0.79 (0.64, 0.98)	0.70 (0.55, 0.89)	0.45 (0.34, 0.60)	0.64 (0.49, 0.83)	<0.0001
Pooled multivariate HR	1.00	0.89 (0.71, 1.11)	0.78 (0.65, 0.92)	0.63 (0.33, 1.19)	0.74 (0.57, 0.96)	0.02
Cruciferous vegetables						
Women						
No. of deaths	255	205	202	181	180	
Multivariate HR[1]	1.00	0.91 (0.76, 1.09)	0.94 (0.78, 1.13)	0.82 (0.68, 1.00)	0.76 (0.62, 0.92)	0.004
Men						
No. of deaths	196	144	100	98	97	
Multivariate HR[1]	1.00	0.90 (0.73, 1.12)	0.68 (0.53, 0.87)	0.66 (0.52, 0.85)	0.61 (0.47, 0.78)	<0.0001
Pooled multivariate HR	1.00	0.91 (0.79, 1.04)	0.81 (0.59, 1.11)	0.75 (0.61, 0.92)	0.69 (0.56, 0.85)	<0.0001
Noncruciferous vegetables						
Women						
No. of deaths	323	206	182	175	137	
Multivariate HR[1]	1.00	0.93 (0.78, 1.11)	0.90 (0.74, 1.08)	0.98 (0.81, 1.20)	0.85 (0.68, 1.06)	0.26
Men						
No. of deaths	217	148	99	79	92	
Multivariate HR[1]	1.00	0.88 (0.71, 1.09)	0.66 (0.52, 0.84)	0.59 (0.45, 0.78)	0.66 (0.50, 0.86)	0.0004
Pooled multivariate HR	1.00	0.91 (0.79, 1.04)	0.78 (0.57, 1.05)	0.77 (0.47, 1.27)	0.76 (0.59, 0.97)	0.09
Total fruit						
Women						
No. of deaths	419	192	174	125	113	
Multivariate HR[1]	1.00	0.76 (0.64, 0.91)	0.86 (0.72, 1.04)	0.72 (0.58, 0.89)	0.78 (0.62, 0.98)	0.01
Men						
No. of deaths	189	153	114	99	80	
Multivariate HR[1]	1.00	0.94 (0.76, 1.18)	0.79 (0.61, 1.01)	0.77 (0.59, 1.00)	0.63 (0.48, 0.85)	0.0008
Pooled multivariate HR	1.00	0.84 (0.68, 1.03)	0.83 (0.72, 0.97)	0.74 (0.63, 0.87)	0.72 (0.59, 0.87)	0.02

[1] Cox proportional hazards model adjusted for age, education, occupation, family income, cigarette smoking, alcohol consumption, BMI, amount of regular exercise, multivitamin supplement use, intakes of total energy and saturated fat, menopausal status and hormone therapy use (for women only), and history of coronary heart disease, stroke, hypertension, or diabetes.

TABLE 4
Multivariate hazard ratios (HRs) for cancer mortality by quintile of fruit and vegetable intake

	Quintile of intake					
	1	2	3	4	5	*P* for trend
Total vegetables						
Women						
No. of deaths	358	291	292	254	290	
Multivariate HR[1]	1.00	0.97 (0.83, 1.14)	1.03 (0.88, 1.21)	0.93 (0.78, 1.10)	1.11 (0.93, 1.32)	0.30
Men						
No. of deaths	228	164	168	147	146	
Multivariate HR[1]	1.00	0.90 (0.73, 1.10)	1.02 (0.83, 1.25)	0.91 (0.73, 1.14)	0.95 (0.75, 1.20)	0.73
Pooled multivariate HR	1.00	0.94 (0.83, 1.07)	1.03 (0.91, 1.17)	0.92 (0.81, 1.06)	1.05 (0.90, 1.21)	0.58
Cruciferous vegetables						
Women						
No. of deaths	325	279	300	296	285	
Multivariate HR[1]	1.00	0.91 (0.77, 1.06)	1.01 (0.86, 1.18)	0.99 (0.84, 1.16)	0.91 (0.77, 1.08)	0.52
Men						
No. of deaths	213	180	157	150	153	
Multivariate HR[1]	1.00	1.02 (0.83, 1.24)	0.94 (0.76, 1.16)	0.89 (0.72, 1.11)	0.89 (0.72, 1.11)	0.18
Pooled multivariate HR	1.00	0.95 (0.84, 1.07)	0.98 (0.87, 1.12)	0.95 (0.84, 1.08)	0.90 (0.79, 1.03)	0.16
Noncruciferous vegetables						
Women						
No. of deaths	362	303	289	261	270	
Multivariate HR[1]	1.00	1.05 (0.90, 1.23)	1.07 (0.91, 1.25)	1.02 (0.86, 1.21)	1.12 (0.94, 1.34)	0.27
Men						
No. of deaths	230	171	161	147	144	
Multivariate HR[1]	1.00	0.94 (0.77, 1.15)	0.97 (0.79, 1.20)	0.98 (0.78, 1.22)	0.95 (0.75, 1.20)	0.76
Pooled multivariate HR	1.00	1.01 (0.89, 1.14)	1.03 (0.91, 1.17)	1.01 (0.88, 1.15)	1.05 (0.89, 1.24)	0.52
Total fruit						
Women						
No. of deaths	416	324	273	257	215	
Multivariate HR[1]	1.00	1.03 (0.89, 1.20)	0.97 (0.82, 1.14)	0.99 (0.83, 1.17)	0.91 (0.76, 1.09)	0.28
Men						
No. of deaths	210	195	169	126	153	
Multivariate HR[1]	1.00	1.04 (0.85, 1.27)	1.00 (0.81, 1.24)	0.82 (0.65, 1.04)	1.03 (0.82, 1.30)	0.69
Pooled multivariate HR	1.00	1.03 (0.92, 1.17)	0.98 (0.86, 1.11)	0.92 (0.77, 1.09)	0.96 (0.83, 1.10)	0.25

[1] Cox proportional hazards model adjusted for age, education, occupation, family income, cigarette smoking, alcohol consumption, BMI, amount of regular exercise, multivitamin supplement use, intakes of total energy and saturated fat, menopausal status and hormone therapy use (for women only), and history of coronary heart disease, stroke, hypertension, or diabetes.

of ischemic stroke and coronary heart disease, but unrelated to overall cancer incidence or cancer mortality (3, 15, 16). Similarly, in an analysis of data from the first National Health and Nutrition Examination Survey Epidemiologic Follow-up Study, frequent intake of fruit and vegetables was linked to reduced CVD mortality, but not to non-CVD mortality, for which cancer was likely to be the main cause (18). A lower risk of CVD, but not cancer, mortality with higher intake of fruit and vegetables was also observed in a cohort study of diabetic populations in Europe (19). In contrast, a small cohort study involving only 910 total deaths suggested an inverse association for both CVD and cancer mortality (20).

Fruit and vegetables are rich in antioxidant vitamins, folate, potassium, fiber, and various phytochemicals and may affect health through multiple biological pathways (21). Fruit and vegetables have been shown to lower levels of blood pressure, homocysteine, oxidative stress, and inflammation, all of which may contribute to their cardiovascular protective effects (22–24). There is growing evidence that certain groups of fruit and vegetables, such as cruciferous vegetables, may be particularly beneficial. A unique feature of cruciferous vegetables is their high content of sulfur-containing compounds, known as glucosinolates (25). It has been suggested that some breakdown products of glucosinolates may confer protection against certain cancers by modulating the activity of enzymes involved in detoxifying carcinogens and metabolizing sex hormones (25). Although our study and several other prospective studies failed to provide support for a protective effect of cruciferous vegetables on overall cancer risk (3), some studies have found an inverse association of cruciferous vegetable intake with risk of individual cancers, including bladder and prostate cancer (7, 8). Most research on cruciferous vegetables has focused on cancer prevention. In recent years, however, evidence has emerged suggesting a potential role for cruciferous vegetables in preventing CVD (15, 26). One particular glucosinolate breakdown product, sulforaphane, has been shown to reduce oxidative stress and inflammation in the cardiovascular system by activating transcription factor Nrf2 (27, 28). It has also been suggested that sulforaphane and other isothiocyanates may exert antiinflammatory effects through modulation of toll-like receptor 4 signaling and modification of proinflammatory cytokine macrophage migration inhibitory factor (29, 30). These findings provide possible explanations for the inverse associations between intake of cruciferous vegetables and risk of CVD and related mortality observed in previous studies and in ours (15, 26). In addition, several reports have suggested that the associations of cruciferous vegetables with cancer and CVD risk may be modified by genetic variations that affect the activity of glutathione *S*-transferases–enzymes involved in the metabolism and elimination of isothiocyanates and other compounds (26, 31). Failure to account for the potential interaction between cruciferous vegetable intake and glutathione *S*-transferase gene variants may have contributed to some of the inconsistent findings for cruciferous vegetable intake and disease risk.

Our study had several limitations that need to be considered when interpreting the results. The follow-up time, particularly for the men's cohort, is relatively short, which raises concern about the potential influence of baseline illness on the results. However, we found no material change in the risk estimates in sensitivity analyses that excluded early years of follow-up. Another concern was related to potential random errors in dietary assessment that might have attenuated the true associations between fruit and vegetable intake and risk of total and CVD mortality and might have contributed to the apparent null associations for cancer mortality in our study. Given the observational nature of the study, there is also concern about the potential for confounding. We conducted analyses adjusted for age only and analyses that accounted for a range of potential confounders, including socioeconomic status, other lifestyle factors, and major baseline comorbidities, and found no substantial change in our main results. Of particular note, however, are the consistent findings seen in both women and men, in whom there were marked differences in lifestyle habits such as smoking and alcohol consumption. These observations argue against the possible presence of substantial confounding. Nevertheless, we could not completely exclude the possibility of residual confounding by unmeasured covariates. In conclusion, our findings based on 2 large cohorts of Chinese women and men support the recommendation to increase consumption of fruit and vegetables, particularly cruciferous vegetables, to promote cardiovascular health and overall longevity.

The authors' responsibilities were as follows—XZ, X-OS, Y-BX, GY, Y-TG, and WZ: designed the research; X-OS, Y-BX, GY, HL, JG, Y-TG, and WZ: contributed to the data collection; XZ and HC: conducted the statistical analysis; and XZ: drafted the manuscript. All authors contributed to the revision of the manuscript and read and approved the final manuscript. None of the authors had any conflicts of interest to declare.

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