Cruciferous and Allium Vegetable Intakes are Inversely Associated With 15-Year Atherosclerotic Vascular Disease Deaths in Older Adult Women

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Background—Higher vegetable intake is consistently associated with lower atherosclerotic vascular disease (ASVD) events. However, the components responsible and mechanisms involved are uncertain. Nonnutritive phytochemicals may be involved. The objective of this study was to investigate the associations of total vegetable intake and types of vegetables grouped according to phytochemical constituents with ASVD mortality.

Methods and Results—The cohort consisted of 1226 Australian women aged 70 years and older without clinical ASVD or diabetes mellitus at baseline (1998). Vegetable intakes were calculated per serving (75 g/d) and were also classified into prespecified types relating to phytochemical constituents. ASVD-related deaths were ascertained from linked mortality data. During 15 years (15 947 person-years) of follow-up, 238 ASVD-related deaths occurred. A 1-serving increment of vegetable intake was associated with a 20% lower hazard of ASVD-related death (multivariable-adjusted hazard ratio, 0.80; 95% confidence interval, 0.69–0.94 [$P=0.005$]). In multivariable-adjusted models for vegetable types, cruciferous (per 10-g/d increase: hazard ratio, 0.87; 95% confidence interval, 0.81–0.94 [$P<0.001$]) and allium (per 5-g/d increase: hazard ratio, 0.82; 95% confidence interval, 0.73–0.94 [$P=0.003$]) vegetables were inversely associated with ASVD-related deaths. The inclusion of other vegetable types, as well as lifestyle and cardiovascular risk factors, did not alter these associations. Yellow/orange/red ($P=0.463$), leafy green ($P=0.063$), and legume ($P=0.379$) vegetables were not significant.

Conclusions—Consistent with current evidence, higher cruciferous and allium vegetable intakes were associated with a lower risk of ASVD mortality. In addition, cruciferous and allium vegetables are recognized to be a good source of several nonnutritive phytochemicals such as organosulfur compounds.

Clinical Trial Registration—URL: http://www.anzctr.org.au. Unique identifier: ACTRN12617000640303. (*J Am Heart Assoc*. 2017;6:e006558. DOI: 10.1161/JAHA.117.006558.)

Key Words: allium • atherosclerosis • atherosclerotic vascular disease • cardiovascular events • cruciferous • diet • follow-up study • observational studies • vegetables

Atherosclerotic vascular disease (ASVD) is the most common cause of death worldwide.[1] Higher vegetable intake has been consistently associated with lower risk of ASVD.[2] Results from these studies have provided the basis for guideline recommendations around the world to increase vegetable intake.[3–5] In recent years, further analysis of the role of specific vegetable and fruit species has been undertaken to identify potentially beneficial varieties and thus to allow consideration of the potential nutrient and phytochemical effects on health outcomes. A recent report of

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Clinical Perspective

What Is New?

- In a cohort of older Australian women, higher intakes of cruciferous and allium vegetables were independently associated with lower risk of atherosclerotic vascular disease mortality.

What Are the Clinical Implications?

- Cruciferous and allium vegetables are recognized to be a good source of several nonnutritive phytochemicals such as organosulfur compounds.
- If future studies support our findings, dietary guidelines promoting increased vegetable intake could highlight the importance of cruciferous and allium vegetables for vascular health.

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the beneficial effects of certain vegetables and fruits on the risks of developing hypertension is an excellent example of the approach required to advance our knowledge of the role of specific vegetable and fruit species on preventing disease.[6]

Vegetables contain many important nutrients and phytochemicals that may be cardioprotective.[7] For example, recent meta-analyses have identified the beneficial effects on health outcomes of dietary fiber[8] and the micronutrients potassium[9] and magnesium.[10] In addition, specific groups of phytochemicals such as organosulfur compounds, carotenoids, nitrogen-containing compounds, and polyphenols have been postulated to have additional benefits towards cardiovascular health.[11–14] Thus, the aim of this study was to investigate the associations of total vegetable intake as well as types of vegetables grouped according to phytochemical constituents with ASVD mortality over 15 years of follow-up in a cohort of older adult women.

Methods

Ethics Statement

The PLSAW (Perth Longitudinal Study of Aging in Women) was approved by the University of Western Australia's human ethics committee and complied with the Declaration of Helsinki. Written informed consents were obtained from all participants. Human ethics approval for the use of linked data for the project was provided by the Western Australian Department of Health Human Research Ethics Committee (project #2009/24).

Study Population

The population of this prospective cohort study consisted of participants in the PLSAW. This study originated in 1998 as the CAIFOS (Calcium Intake Fracture Outcome Study). The CAIFOS was a 5-year, double-blind, randomized, placebo-controlled trial of daily calcium supplementation (1.2 g calcium carbonate) to prevent fractures.[15] Women aged 70 years and older (n=1500) were recruited from the Western Australian general population by mail using the Electoral Roll, which is maintained for all Australian citizens enrolled to vote in Western Australia. After the completion of the CAIFOS, participants were enrolled in a 10-year extension follow-up study. In total, there were 15 years of follow-up (PLSAW).

Eligibility criteria included available data on all exposure and outcome variables. Dietary data were available for 1485 of 1500 (99.0%) participants at baseline. Participants (17 of 1485 [1.1%]) with implausible energy intakes (<2100 kJ [500 kcal] or >14 700 kJ [3500 kcal]) were excluded. Further exclusion of participants with prevalent ASVD (n=152), diabetes mellitus (n=69), or both (n=21) at baseline resulted in 1226 of 1500 (81.7%) participants being included for the analysis of this study. Prevalent ASVD and/or diabetes mellitus at baseline was an a priori exclusion criteria because participants with a clinical diagnosis of ASVD or diabetes mellitus may have resulted in altered dietary intake and thereby attenuated the association of interest.

History of ASVD at baseline (1998) was determined from principal hospital discharge diagnosis codes from 1980 to 1998 using the Hospital Morbidity Data Collection, linked via the Western Australian Data Linkage System. Diagnosis codes were defined using the *Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death, 9th Revision* (*ICD-9*)[16] and the Australian version of the *International Classification of Diseases, 9th Revision, Clinical Modification* (*ICD-9-CM*).[17] ASVD diagnosis codes included ischemic heart disease (*ICD-9/ICD-9-CM* codes 410–414); heart failure (*ICD-9/ICD-9-CM* code 428); cerebrovascular disease, excluding hemorrhage (*ICD-9/ICD-9-CM* codes 433–438); and peripheral arterial disease (*ICD-9/ICD-9-CM* codes 440–444). Baseline history of diabetes mellitus was determined from medication use, which was coded (T89001–T90009) using the International Classification of Primary Care—Plus (ICPC-Plus) method.[18] This coding methodology allows aggregation of different terms for similar pathologic entities as defined by the *ICD-10* coding system.

ASVD Mortality Assessment

Any death relating to ASVD was the primary outcome of the study. Coded multiple causes of death data over a 15-year period were retrieved from linked mortality data via the Western Australian Data Linkage System. Multiple causes of death data included the underlying cause of death and all associated causes of death listed on the death certificate. The causes of death were obtained from the coded death certificate using

information in parts 1 and 2 of the death certificate or all diagnosis text fields from the death certificate when coded deaths were not yet available. ASVD deaths were defined using diagnosis codes from the *ICD-9-CM*[16] and the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Australian Modification (ICD-10-AM)*.[19] ASVD-related death diagnosis codes included deaths attributed to ischemic heart disease (*ICD-9-CM* codes 410–414 and *ICD-10-AM* codes I20–I25); heart failure (*ICD-9-CM* code 428 and *ICD-10-AM* code I50); cerebrovascular disease, excluding hemorrhage (*ICD-9-CM* codes 433–438 and *ICD-10-AM* codes I63–I69, G45.9); and peripheral arterial disease (*ICD-9-CM* codes 440–444 and *ICD-10-AM* codes I70–I74).

Dietary Intake Assessment

A self-administered, semiquantitative food frequency questionnaire developed by the Cancer Council of Victoria was used to assess dietary intake at baseline (1998), 5 years (2003), and 7 years (2005).[20] This questionnaire was designed to assess the usual frequency of dietary intakes over a 12-month period with 10 frequency response options ranging from "never" to "3 or more times per day" and has been validated using 7-day weighed food records.[21] Portion size was calculated using photographs of scaled portions of different food types. Energy (kJ/d) and nutrient intakes were calculated by the Cancer Council of Victoria using the NUTTAB 95 food composition database[22] and were supplemented by other data where necessary. Individual food items were calculated in grams per day by the Cancer Council of Victoria. Participants were supervised by a research assistant while completing the food frequency questionnaire. Food models and food charts as well as measuring cups and measuring spoons were provided to ensure the accuracy of reported food consumption.

Total vegetable intake

Total vegetable intake was calculated in servings per day. Vegetable servings were based on the 2013 Australian Dietary Guidelines of 1 serving of vegetables being equivalent to 75 g.[4] Servings per day were calculated as a continuous variable and then categorized as a discrete variable (<2 servings, 2 to <3 servings, ≥3 servings). Vegetable intake was assessed using 24 vegetable items and did not include "potatoes, roasted or fried, including hot chips" as hot chips are not recommended as part of a healthy diet.[4] "Potatoes cooked without fat" were included.

Vegetable type

Classification of vegetable types were based on the 2013 Australian Dietary Guidelines[4] and modified to include the following subgroups of vegetables relating to phytochemical

profiles: cruciferous vegetables (cabbage, brussels sprouts, cauliflower, and broccoli)—source of organosulfur compounds[11]; allium vegetables (onion, leek, and garlic)—source of organosulfur compounds[11]; yellow/orange/red vegetables (tomato, capsicum, beetroot, carrot, and pumpkin)—source of carotenoids such as lycopene and beta carotene[12]; leafy green vegetables (lettuce and other salad greens, celery, silver beet, and spinach)—source of nitrogen-containing compounds such as nitrate[13]; and legumes (peas, greens beans, bean sprouts and alfalfa sprouts, baked beans, soy beans, soy bean curd and tofu, and other beans)—source of polyphenolic compounds such as isoflavonoids and saponins.[14]

Nutrient-Rich Foods Index

We assessed overall diet quality using the Nutrient-Rich Foods Index.[23] This index was calculated using the Nutrient Reference Values for Australia and New Zealand based on adult women older than 70 years[24] and has been previously described.[25]

Baseline Demographic and Clinical Assessment

Body mass index (BMI) (kg/m^2) was calculated using body weight (kg) and height (m), which were assessed while participants were wearing light clothes without socks and shoes. Body weight was measured using digital scales to the nearest 0.1 kg and height was assessed using a wall-mounted stadiometer to the nearest 0.1 cm. Physical activity was assessed by asking participants about participation in sport, recreation, and/or regular physical activities undertaken in the past 3 months before their baseline visit.[26] The level of activity (kJ/d) was calculated using a validated method applying the type of activity, time engaged in the activity, and body weight.[27,28] Alcohol (g/d) intake was assessed along with other dietary intakes using the validated food frequency questionnaire developed by the Cancer Council of Victoria as described above. Smoking history was collected using a questionnaire and was coded as nonsmoker or ex-smoker/current smoker if they had smoked >1 cigarette per day for longer than 3 months at any time in their life. Socioeconomic status was calculated using the Socioeconomic Indexes for Areas developed by the Australian Bureau of Statistics.[29] The index ranked residential postcodes according to relative socioeconomic advantage and disadvantage. Participants were coded into 6 groups from the top 10% most highly disadvantaged to the top 10% least disadvantaged.[29]

 Participants were asked to provide a detailed medical history and list of medications, which were verified by their general practitioner where possible. The ICPC-Plus method was used to code medication use.[18] Medication use included antihypertensive, statin, and low-dose aspirin medications. These medications were used to adjust for ASVD risk factors such as

hypertension and dyslipidemia. Baseline serum creatinine was analyzed in 1106 of 1226 (90.2%) participants using an isotope dilution mass spectrometry traceable Jaffe kinetic assay for creatinine on a Hitachi 917 analyzer (Roche Diagnostics GmbH). Estimated glomerular filtration rate was then calculated using the Chronic Kidney Disease Epidemiology Collaboration equation[30] and was added to the multivariable-adjusted models, as this has been shown to predict ASVD in this cohort.[31] Total cholesterol, high-density lipoprotein cholesterol, and triglyceride concentrations were analyzed in 895 of 1226 (73.0%) participants using a Hitachi 917 auto analyzer (Roche Diagnostics). Low-density lipoprotein cholesterol was calculated in 888 of 1226 (72.4%) participants using the Friedewald method.[32]

Framingham 10-Year General Cardiovascular Risk Scores

The Framingham risk score (FRS) was calculated using BMI data in 1188 participants. The FRS included age, sex, previous diabetes mellitus, BMI, current smoking status, and treated (prescribed antihypertensive medications) or untreated systolic blood pressure using the equation and estimated regression coefficients developed by D'Agostino and others.[33]

$$FRS = 1 - 0.94833^{\exp(2.72107 \times \ln(Age) + 0.51125 \times \ln(BMI)} $$
$$+2.81291 \times \ln(SBP) + 0.61868 \times (Current\, smoker) + $$
$$0.77763 \times (Diabetes) - 26.0145)$$

These scores were confirmed using the online calculator developed by D'Agostino and Pencina based on the publication by D'Agostino and others.[33]

Statistical Analysis

An analytical protocol was produced before analysis began. Statistical significance was set at a 2-sided type 1 error rate of $P < 0.05$. All data were analyzed using IBM SPSS Statistics for Windows, version 21.0 (IBM Corporation) and SAS software, version 9.4 (SAS Institute Inc). Descriptive statistics of normally distributed continuous variables were expressed as mean±SD; non-normally distributed continuous variables (physical activity, alcohol intake, allium vegetable intake, nut intake, fish intake, processed meat intake, and red meat intake) were expressed as median and interquartile range; and categorical variables were expressed as number and proportion (percentage). Differences in baseline characteristics among vegetable serving categories were tested using 1-way ANOVA for normally distributed continuous variables and the Kruskal–Wallis test for non-normally distributed continuous variables. Chi-square test for independence was used to test for differences in baseline characteristics among vegetable serving categories for categorical variables.

The primary outcome of the study was any death relating to ASVD. Complete follow-up of death records was available for all participants who remained in Western Australia, which was likely to be almost all participants given their age. The follow-up period for each participant was calculated in days from their baseline visit until their last day of follow-up, which was their date of death or 15 years of complete follow-up. Cox proportional hazards modeling was used to analyze the associations between vegetable variables and ASVD mortality. Total vegetable intake was analyzed per serving (75 g/d) and then further categorized into 3 groups (<2 servings, 2 to <3 servings, and ≥3 servings). For vegetable types, intakes of cruciferous, yellow/orange/red, leafy green, and legumes varieties were analyzed per 10 g/d. Intakes of allium were analyzed per 5 g/d. Three models of adjustment were used for the Cox proportional hazards modeling. These models included unadjusted, age- and energy-adjusted, and multivariable-adjusted models. The multivariable-adjusted models included age, BMI, level of physical activity, alcohol intake, energy intake, Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate (entered as continuous variables), smoking history, socioeconomic status, the CAIFOS supplementation group of calcium versus placebo, antihypertensive medication, statin medication, and low-dose aspirin (entered as categorical variables). Covariates were selected on an a priori basis as these covariates are known risk factors for ASVD. We also tested for evidence of linear trends across categories of vegetable servings using the median value for each category as a continuous variable in separate Cox proportional hazards models. Cox proportional hazards assumptions were tested using log-log plots, which were shown to be parallel, indicating that proportional hazards assumptions were not violated.

Sensitivity analyses

Reverse causality bias was explored in multivariable-adjusted analyses, excluding all-cause deaths occurring within the first 24 months, for total vegetable intake (per 75 g/d) and intakes of cruciferous (per 10 g/d), allium (per 5 g/d), and leafy green (per 10 g/d) vegetables.

Since higher vegetable intake may be considered a surrogate marker of a healthier diet, we further adjusted for diet quality using the Nutrient-Rich Foods Index in multivariable-adjusted models for total vegetable intake (per 75 g/d) and intakes of cruciferous (per 10 g/d) and allium (per 5 g/d) vegetables. We also considered the impact of possible dietary confounders by including the estimated daily intakes of total fruit (g/d), fish (g/d), nuts (g/d), fiber (g/d), potassium (mg/d), magnesium (mg/d), beta carotene (µg/d), and saturated fat (g/d).[34] These dietary confounders were entered

separately as continuous variables in multivariable-adjusted Cox proportional hazards models on a variable-by-variable basis for total vegetable intake (per 75 g/d) and intakes of cruciferous (per 10 g/d) and allium (per 5 g/d) vegetables.

Subgroups of ASVD-related mortality, including ischemic heart disease and ischemic cerebrovascular disease mortality, were investigated in multivariable-adjusted models for total vegetable intake and intakes of cruciferous (per 10 g/d) and allium (per 5 g/d) vegetables. The FRS was used in multivariable-adjusted models to adjust for the estimated 10-year risk of developing cardiovascular disease for total vegetable intake (per 75 g/d) and intakes of cruciferous (per 10 g/d) and allium (per 5 g/d) vegetables. The multivariable-adjusted models included level of physical activity, alcohol intake, socioeconomic status, the CAIFOS supplementation group of calcium versus placebo, statin use, low-dose aspirin use, Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate, and energy intake. Age, BMI, antihypertensive medication, and smoking history were not included in this model because the FRS takes into account the participants' age, BMI, untreated systolic blood pressure, and current smoking status.

The relationship between cruciferous, allium, and total vegetables were investigated using Spearman rank order correlation (ρ). To examine whether the individual associations of cruciferous and allium vegetables were not caused by collinearity and were independent of total vegetable intake, a forward stepwise Cox proportional hazards model with all multivariable-adjusted variables as well as total vegetable intake and intakes of cruciferous (per 10 g/d) and allium (per 5 g/d) vegetables was tested.

One-way repeated measures ANOVA was used to test for differences between intakes of cruciferous, allium, and total vegetables at baseline (1998), 5 years (2003), and 7 years (2005). The average of the 3 time points (baseline and 5 and 7 years) for cruciferous, allium, and total vegetables were used separately in multivariable-adjusted Cox proportional hazards models to account for the change in intake.

Results

Participants and Their Characteristics

The flow diagram for participant selection is shown in Figure 1. In the 15 947 person-years of follow-up, there were 238 of 1226 (19.4%) ASVD-related deaths, of which 128 of 1226 (10.4%) were caused by ischemic heart disease and 92 of 1226 (7.5%) were caused by ischemic cerebrovascular disease. Participant demographics, medication use, and biochemical analyses presented according to all 1226 study participants and by categories of vegetable
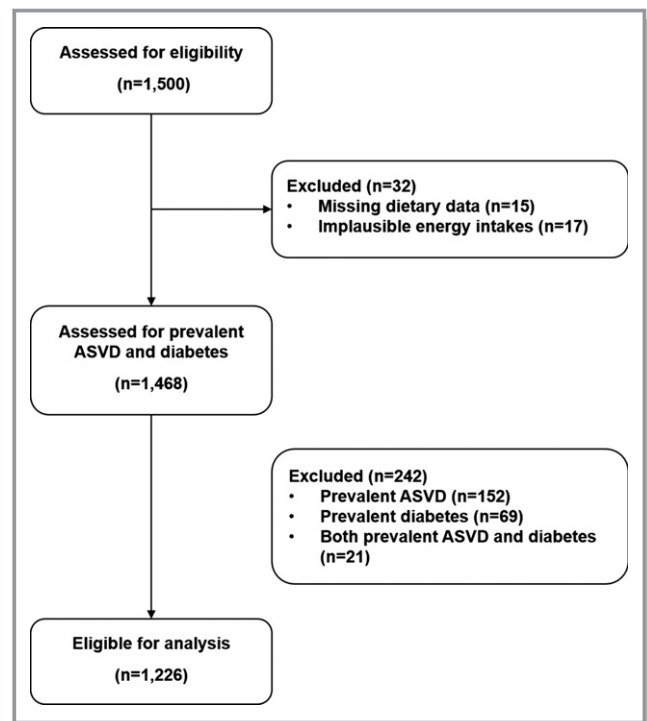

Figure 1. Participant flow diagram. ASVD indicates atherosclerotic vascular disease.

servings are presented in Table 1. Nutrient and food intakes are presented in Table 2. Body weight (kg) (Table 1) and all dietary intakes (Table 2) were significantly different among vegetable serving categories ($P<0.05$ for all). Participants who consumed more vegetable servings also consumed more of each vegetable type ($P<0.001$) (Table 2). The mean vegetable intake was 196.5 (SD, 78.8) g/d and vegetable servings was 2.6 (SD, 1.0) for all participants. The mean intake (from highest to lowest) of vegetable types was: yellow/orange/red vegetables 52.4 (SD, 27.6) g/d; cruciferous vegetables 32.3 (SD, 22.0) g/d; legumes 27.0 (SD, 18.7) g/d; and leafy green vegetables 18.8 (SD, 12.1) g/d. The median intake for allium vegetables was 6.2 (interquartile range, 2.9–10.6) g/d (Table 2). The percentage contribution of vegetable types, including potatoes, from all vegetables consumed (g/d) are presented in Figure 2.

Total Vegetable Intake and ASVD Mortality

The association of total vegetable intake with ASVD mortality was statistically significant in unadjusted, age- and energy-adjusted, and multivariable-adjusted models ($P<0.01$ for all models) (Table 3). Multivariable-adjusted cumulative survival curves for ASVD mortality according to vegetable servings are presented in Figure 3. The survival benefit of higher vegetable intakes diverged after 60 months.

Table 1. Baseline Characteristics of All Study Participants and by Categories of Vegetable Servings*

Participant Demographics	All Participants (N=1226)	<2 Servings (n=355)	2 to <3 Servings (n=486)	≥3 Servings (n=385)	P Value
Age, y	75.1±2.7	75.2±2.7	75.0±2.6	75.0±2.6	0.636
BMI, kg/m^2	27.0±4.6	26.7±4.7	27.0±4.3	27.2±4.8	0.334
Body weight, kg	68.1±12.1	66.8±11.8	68.2±11.9	69.2±12.5	0.029
Physical activity, median (IQR), kJ/d	460.5 (101.7–860.8)	419.9 (0.0–860.9)	472.7 (163.7–884.0)	491.3 (187.1–854.6)	0.248
Alcohol intake, median (IQR), g/d,	2.1 (0.3–10.4)	2.0 (0.3–9.8)	2.0 (0.3–10.1)	2.3 (0.3–11.3)	0.929
Smoking history, No. (%)[†]	441 (36.0)	125 (35.3)	186 (38.7)	130 (33.9)	0.327
Socioeconomic status[‡]					0.789
Top 10% most highly disadvantaged, No. (%)	41 (3.3)	11 (3.1)	17 (3.5)	13 (3.4)	
Highly disadvantaged, No. (%)	146 (11.9)	45 (12.7)	54 (11.2)	47 (12.4)	
Moderate-highly disadvantaged, No. (%)	194 (15.8)	54 (15.3)	81 (16.8)	59 (15.6)	
Low-moderately disadvantaged, No. (%)	185 (15.1)	59 (16.7)	63 (13.0)	63 (16.6)	
Low disadvantage, No. (%)	255 (20.8)	69 (19.5)	100 (20.7)	86 (22.7)	
Top 10% least disadvantaged, No. (%)	394 (32.1)	115 (32.6)	168 (34.8)	111 (29.3)	
Treatment with calcium supplements, No. (%)	641 (52.3)	167 (47.0)	261 (53.8)	213 (55.3)	0.055
Framingham risk score, %[§]	20.6±9.1	20.2±9.1	20.7±9.2	20.9±9.0	0.561
Medication use					
Antihypertensive medication, No. (%)	493 (40.2)	135 (38.0)	195 (40.1)	163 (42.3)	0.489
Statin medication, No. (%)	184 (15.0)	53 (14.9)	73 (15.0)	58 (15.1)	0.999
Low-dose aspirin, No. (%)	193 (15.7)	66 (18.6)	78 (16.0)	49 (12.7)	0.089
Biochemical analyses					
CKD-EPI eGFR, mL/min per 1.73 m^2[‖]	67.6±13.0	67.4±13.3	67.2±12.3	68.1±13.5	0.677
Total cholesterol, mmol/L[¶]	5.9±1.1	6.0±1.1	6.0±1.0	5.8±1.1	0.265
HDL cholesterol, mmol/L[¶]	1.5±0.4	1.5±0.4	1.5±0.4	1.4±0.4	0.125
LDL cholesterol, mmol/L[#]	3.7±1.0	3.8±1.0	3.8±0.9	3.7±1.0	0.425
Triglycerides, mmol/L[¶]	1.5±0.7	1.5±0.7	1.5±0.7	1.6±0.7	0.511

BMI indicates body mass index; CKD-EPI eGFR, Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein.

*Vegetable servings were calculated based on the 2013 Australian Dietary Guidelines of a vegetable serving equal to 75 g/d. P values are a comparison between groups using ANOVA, Kruskal–Wallis test, and chi-square test where appropriate. Values are presented as mean±SD unless otherwise indicated.

[†]Measured in 1218 participants.

[‡]Measured in 1215 participants.

[§]Measured in 1188 participants.

[‖]Measured in 1106 participants.

[¶]Measured in 895 participants.

[#]Measured in 888 participants.

To avoid the potential of reverse causality, participants who died in the first 24 months were excluded. Total vegetable intake remained a statistically significant predictor of ASVD death (per 75-g/d increase: hazard ratio [HR], 0.81; 95% confidence interval [CI], 0.70–0.95 [P=0.008]).

Additional adjustment for the Nutrient-Rich Foods Index attenuated the association of total vegetable intake (per 75-g/d increase: HR, 0.86; 95% CI, 0.73–1.02 [P=0.076]). Separate analyses that adjusted for the individual dietary factors, total fruit, fish, nuts, and beta carotene, did not change the association between total vegetable intake and ASVD mortality (Table 4). Adjustment for potassium, magnesium, fiber, and saturated fat attenuated the association (Table 4).

Total vegetable intake was inversely associated with ischemic heart disease mortality with borderline significance (P=0.050). Ischemic cerebrovascular disease mortality did not reach significance (P=0.074) (Table 5).

Vegetable Types and ASVD Mortality

The associations between intakes of vegetable types and ASVD mortality are presented in Table 6. Higher intakes of cruciferous and allium vegetables were associated with lower

Table 2. Dietary Intakes of All Study Participants and by Categories of Vegetable Servings*

	All Participants (N=1226)	<2 Servings (n=355)	2 to <3 Servings (n=486)	≥3 Servings (n=385)	P Value
Dietary intakes					
Vegetable servings, g/d	2.6±1.0	1.5±0.4	2.5±0.3	3.8±0.8	
Vegetables, g/d	196.5±78.8	111.7±29.4	186.2±21.3	287.5±58.2	<0.001
Cruciferous vegetables, g/d	32.3±22.0	18.9±12.8	31.2±18.1	46.0±25.1	<0.001
Allium vegetables, median (IQR), g/d	6.2 (2.9–10.6)	3.5 (1.7–6.2)	6.2 (3.4–10.1)	10.0 (5.9–15.5)	<0.001
Yellow/orange/red vegetables, g/d	52.4±27.6	30.1±14.7	50.9±18.3	74.8±29.2	<0.001
Leafy green vegetables, g/d	18.8±12.1	13.3±9.4	19.2±11.1	23.4±13.4	<0.001
Legumes, g/d	27.0±18.7	16.5±9.9	26.2±14.8	37.6±23.2	<0.001
Nutrient-Rich Foods Index	75.2±24.4	78.7±22.4	77.9±24.3	68.4±24.8	<0.001
Energy, kJ/d	7146.5±2091.9	6225.9±1757.7	7021.0±1949.9	8153.7±2118.6	<0.001
Total fat, g/d	64.7±23.3	57.4±20.5	63.9±22.6	72.4±24.4	<0.001
Saturated fat, g/d	25.8±11.2	23.9±10.5	25.3±10.9	28.1±11.8	<0.001
Monounsaturated fat, g/d	22.5±8.7	19.4±7.2	22.3±8.3	25.6±9.3	<0.001
Polyunsaturated fat, g/d	10.6±4.8	9.2±4.2	10.6±4.6	12.0±5.1	<0.001
Omega 3 fatty acids, g/d	1.3±0.6	1.1±0.5	1.3±0.6	1.6±0.7	<0.001
Dietary cholesterol, mg/d	238.6±99.6	214.7±90.4	236.0±94.8	264.0±107.6	<0.001
Protein, g/d	79.5±26.4	66.8±20.8	78.3±25.0	92.6±26.6	<0.001
Carbohydrate, g/d	191.1±58.1	165.1±48.6	186.6±52.5	220.7±59.8	<0.001
Sugar, g/d	92.1±31.9	81.1±28.3	89.6±28.8	105.4±34.1	<0.001
Fiber, g/d	22.8±7.8	17.7±5.3	22.4±6.3	28.0±8.1	<0.001
Potassium, mg/d	2948.9±844.9	2368.6±625.1	2882.7±674.2	3567.6±801.3	<0.001
Magnesium, mg/d	298.9±93.0	247.9±70.3	293.7±81.9	352.5±96.1	<0.001
Beta carotene, μg/d	2747.9±1260.0	1676.3±578.9	2682.9±847.1	3818.2±1278.2	<0.001
Fruit, g/d	256.1±131.5	206.3±111.4	255.6±116.5	302.7±148.8	<0.001
Nuts, median (IQR), g/d	0.6 (0.2–2.7)	0.3 (0.1–2.0)	0.5 (0.2–2.2)	1.1 (0.3–4.5)	<0.001
Fish, median (IQR), g/d	19.3 (9.3–35.7)	14.5 (6.8–27.0)	19.3 (8.7–35.0)	25.4 (13.4–49.3)	<0.001
Red meat intake, median (IQR), g/d	42.2 (23.6–69.5)	31.3 (16.4–48.3)	42.5 (25.3–65.2)	58.3 (33.1–92.4)	<0.001
Processed meat intake, median (IQR), g/d	10.4 (4.9–20.6)	9.6 (3.8–18.2)	11.2 (5.0–21.7)	10.8 (5.1–22.4)	0.011

IQR indicates interquartile range.

*Vegetable servings were calculated based on the 2013 Australian Dietary Guidelines of a vegetable serving equal to 75 g/d. P values are a comparison between groups using ANOVA and Kruskal–Wallis test where appropriate. Values are presented as mean±SD unless otherwise indicated. Cruciferous vegetables included cabbage, brussels sprouts, cauliflower, and broccoli. Allium vegetables included onion, leek, and garlic. Yellow/orange/red vegetables included tomato, capsicum, beetroot, carrot, and pumpkin. Leafy green vegetables included lettuce and other salad greens, celery, silver beet, and spinach. Legumes included peas, greens beans, bean sprouts and alfalfa sprouts, baked beans, soy beans, soy bean curd and tofu, and other beans.

ASVD mortality in unadjusted, age- and energy-adjusted, and multivariable-adjusted models (*P*<0.01 for all). These associations were also independent of other vegetable intakes (*P*<0.05 for both cruciferous and allium). Higher intakes of leafy green vegetables were associated with lower ASVD mortality in the unadjusted model (*P*=0.048) but not in the age- and energy-adjusted (*P*=0.055) and multivariable-adjusted (*P*=0.063) models. Likewise, higher intakes of yellow/orange/red vegetables were associated with lower ASVD mortality in the unadjusted model (*P*=0.040) but not in

the adjusted models (*P*>0.05). Lastly, intakes of legumes were not associated with ASVD mortality in any models (*P*>0.05).

When excluding participants who died in the first 24 months of the study, cruciferous (per 10 g/d) and allium (per 5 g/d) vegetables remained inversely associated with ASVD mortality, with a multivariable-adjusted HR of 0.87 (95% CI, 0.80–0.93) and 0.83 (95% CI, 0.73–0.94) (*P*<0.01 for both). Although not significant in the initial multivariable-adjusted analysis, intakes of leafy green vegetables (per 10 g/d) were significant after excluding all deaths that
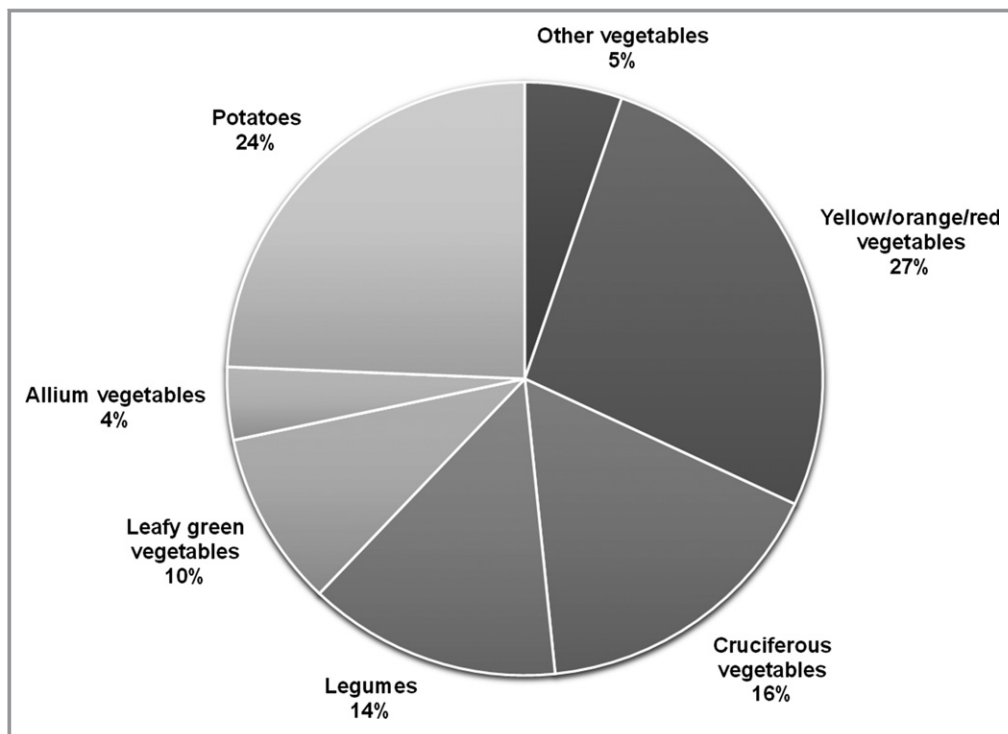
Figure 2. Percentage contribution of vegetable types from total vegetables (g/d) consumed. Cruciferous vegetables included cabbage, brussels sprouts, cauliflower, and broccoli. Allium vegetables included onion, leek, and garlic. Yellow/orange/red vegetables included tomato, capsicum, beetroot, carrot, and pumpkin. Leafy green vegetables included lettuce and other salad greens, celery, silver beet, and spinach. Legumes included peas, greens beans, bean sprouts and alfalfa sprouts, baked beans, soy beans, soy bean curd and tofu, and other beans.

occurred in the first 24 months (multivariable-adjusted HR, 0.88; 95% CI, 0.78–1.00 [P=0.047]). The median intake for leafy green vegetables for participants excluded in the first 24 months was 12.1 (interquartile range, 3.9–25.8) g/d, whereas for the cohort excluding these participants it was 17.1 (interquartile range, 9.8–25.8) g/d.

Additional adjustment for the Nutrient-Rich Foods Index did not alter the significant associations of cruciferous (per 10-g/d increase: HR, 0.89; 95% CI, 0.82–0.95 [P=0.002]) and allium (per 5-g/d increase: HR, 0.84; 95% CI, 0.74–0.95 [P=0.006]) vegetable intakes. Separate analyses that adjusted for individual dietary factors (total fruit, fish, nuts, fiber, potassium, magnesium, beta carotene, and saturated fat) did not change the associations of both cruciferous and allium vegetable intakes with ASVD mortality (Table 4).

Table 3. Association of Total Vegetable Intake and by Serving Categories With ASVD Mortality*

	All Participants (N=1226)	P Value[†]	<2 Servings (n=355)	2 to <3 Servings (n=486)	≥3 Servings (n=385)	P for Trend[‡]
Median vegetable servings, No.			1.5	2.5	3.6	
ASVD						
Deaths, No. (%)	238 (19.4)		83 (23.4)	98 (20.2)	57 (14.8)	
Unadjusted	0.80 (0.70–0.92)	0.001	1.00 (Referent)	0.80 (0.60–1.08)	0.58 (0.42–0.82)	0.002
Age- and energy-adjusted	0.82 (0.71–0.94)	0.005	1.00 (Referent)	0.84 (0.62–1.13)	0.61 (0.43–0.87)	0.007
Multivariable-adjusted[§]	0.80 (0.69–0.94)	0.005	1.00 (Referent)	0.78 (0.57–1.08)	0.57 (0.38–0.83)	0.004

ASVD indicates atherosclerotic vascular disease.

*Results are presented as hazard ratios (95% confidence intervals) using Cox proportional hazards modeling. Vegetable servings were calculated based on the 2013 Australian Dietary Guidelines of a vegetable serving equal to 75 g/d.

[†]P values are for vegetable servings (per 75 g/d) entered as a continuous variable.

[‡]P values are a trend test using the median values of each vegetable serving category in Cox proportional hazards models.

[§]Multivariable-adjusted model included age, body mass index, physical activity, alcohol intake, smoking history, socioeconomic status, calcium supplementation group, antihypertensive medication, statin medication, low-dose aspirin, Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate, and energy intake.

Figure 3. Multivariable-adjusted cumulative survival curves for atherosclerotic vascular disease (ASVD) mortality according to vegetable serving categories. The multivariable-adjusted model included age, body mass index, physical activity, alcohol intake, smoking history, socioeconomic status, calcium supplementation group, antihypertensive medication, statin medication, low-dose aspirin, Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate, and energy intake. CI indicates confidence interval; HR, hazard ratio.
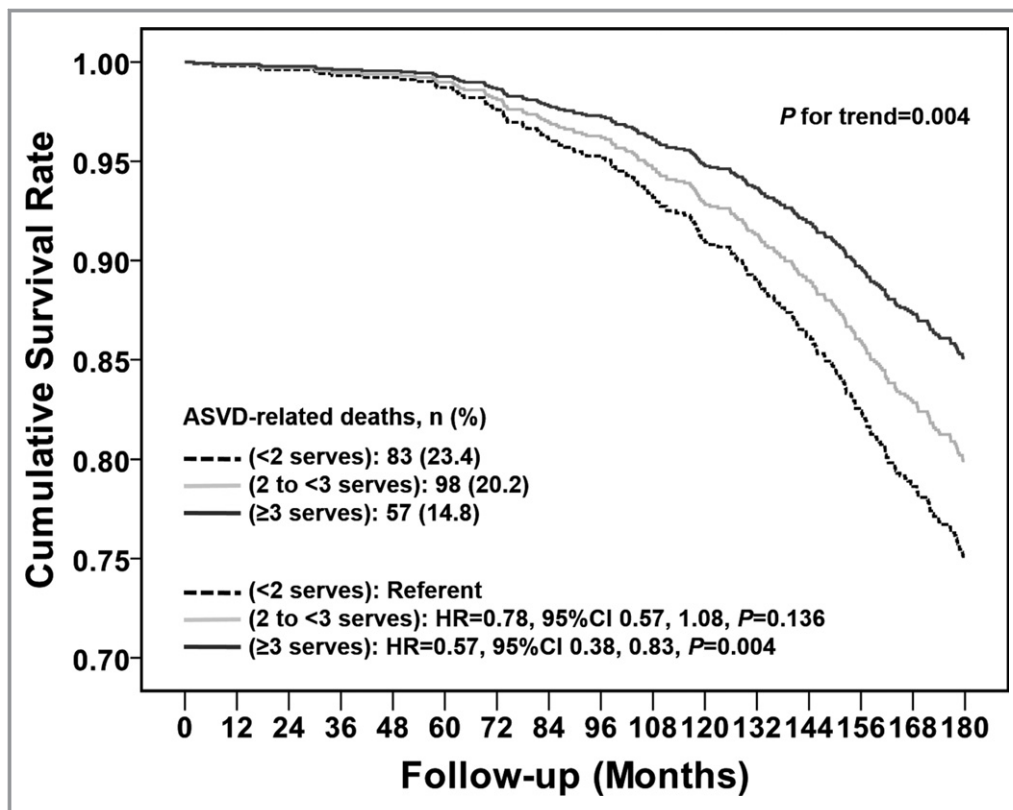
Cruciferous and allium vegetable intakes were inversely associated with ischemic heart disease mortality ($P<0.05$ for both), and allium vegetable intake was inversely associated with ischemic cerebrovascular disease mortality ($P=0.011$) (Table 5).

Additional Sensitivity Analyses

Separate analyses that adjusted for FRS did not change the interpretation of the associations between cruciferous (per 10-g/d increase: HR, 0.88; 95% CI, 0.82–0.95 [$P=0.001$]), allium (per 5-g/d increase: HR, 0.81; 95% CI, 0.71–0.92 [$P=0.001$]), and total vegetables (per 75-g/d increase: HR, 0.81; 95% CI, 0.69–0.94 [$P=0.006$]) and ASVD mortality.

There was a weak positive correlation between intakes of cruciferous and allium vegetables (Spearman's $\rho=0.12$, $P<0.001$) and a moderate positive correlation between intakes of allium and total vegetables (Spearman's $\rho=0.44$,

$P<0.001$) and intakes of cruciferous and total vegetables (Spearman's $\rho=0.51$, $P<0.001$). In a forward stepwise Cox proportional hazards model, which included all multivariable-adjusted variables and intakes of cruciferous, allium, and total vegetables, age ($P<0.001$), BMI ($P=0.016$), antihypertensive medication ($P<0.001$), cruciferous vegetables ($P<0.001$), and allium vegetables ($P=0.014$) were independent predictors of ASVD mortality (Table 7).

The mean (SD) of cruciferous, allium, and total vegetables at baseline (1998) and 5 years (2003), and 7 years (2005) are presented in Table 8. A significant effect for time was observed for intakes of cruciferous, allium, and total vegetables using 1-way repeated measures ANOVA (Wilks Λ $P<0.01$ for all). To account for this change, the average was individually calculated across all 3 time points (baseline and 5 and 7 years) for cruciferous, allium, and total vegetable intakes. These average values were then entered separately in multivariable-adjusted Cox proportional hazards models for ASVD mortality. This did not substantively alter the

Table 4. Multivariable-Adjusted Hazard Ratios and 95% Confidence Intervals for ASVD-Related Mortality for Cruciferous and Total Vegetable Intake With Additional Adjustments for Individual Dietary Confounders*

	All Participants (N=1226)	P Value
Cruciferous vegetables		
Multivariable-adjusted[†] plus total fruit, g/d	0.87 (0.81–0.94)	<0.001
Multivariable-adjusted plus fish, g/d	0.87 (0.81–0.94)	<0.001
Multivariable-adjusted plus nuts, g/d	0.87 (0.81–0.94)	<0.001
Multivariable-adjusted plus fiber, g/d	0.88 (0.82–0.95)	0.001
Multivariable-adjusted plus potassium, mg/d	0.89 (0.83–0.96)	0.003
Multivariable-adjusted plus magnesium, mg/d	0.89 (0.82–0.96)	0.002
Multivariable-adjusted plus beta carotene, μg/d	0.87 (0.81–0.94)	0.001
Multivariable-adjusted plus saturated fat, g/d	0.89 (0.82–0.96)	0.002
Allium vegetables		
Multivariable-adjusted plus total fruit, g/d	0.83 (0.73–0.94)	0.003
Multivariable-adjusted plus fish, g/d	0.82 (0.73–0.94)	0.003
Multivariable-adjusted plus nuts, g/d	0.83 (0.73–0.94)	0.004
Multivariable-adjusted plus fiber, g/d	0.84 (0.74–0.96)	0.010
Multivariable-adjusted plus potassium, mg/d	0.85 (0.75–0.96)	0.011
Multivariable-adjusted plus magnesium, mg/d	0.84 (0.74–0.95)	0.006
Multivariable-adjusted plus beta carotene, μg/d	0.83 (0.73–0.95)	0.007
Multivariable-adjusted plus saturated fat, g/d	0.85 (0.75–0.96)	0.009
Total vegetables		
Multivariable-adjusted plus total fruit, g/d	0.81 (0.67–0.94)	0.006
Multivariable-adjusted plus fish, g/d	0.81 (0.69–0.94)	0.006
Multivariable-adjusted plus nuts, g/d	0.81 (0.70–0.94)	0.006
Multivariable-adjusted plus fiber, g/d	0.84 (0.71–1.00)	0.051
Multivariable-adjusted plus potassium, mg/d	0.88 (0.74–1.06)	0.183
Multivariable-adjusted plus magnesium, mg/d	0.86 (0.73–1.01)	0.059
Multivariable-adjusted plus beta carotene, μg/d	0.78 (0.63–0.95)	0.015
Multivariable-adjusted plus saturated fat, g/d	0.86 (0.73–1.01)	0.057

*Results are presented as hazard ratios (95% confidence intervals) using multivariable-adjusted Cox proportional hazards modeling with additional adjustment for dietary confounders per 10 g/d for cruciferous vegetables, per 5 g/d for allium vegetables, and per 75 g/d for total vegetables.

[†]The multivariable-adjusted model included age, body mass index, physical activity, alcohol intake, smoking history, socioeconomic status, calcium supplementation group, antihypertensive medication, statin medication, low-dose aspirin, Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate, and energy intake. Cruciferous vegetables included cabbage, brussels sprouts, cauliflower, and broccoli. Allium vegetables included onion, leek, and garlic.

interpretation of the associations between baseline values and ASVD-related mortality (Table 9).

Discussion

This study demonstrates that total vegetable intake was inversely associated with ASVD mortality, supporting current guideline recommendations to increase vegetable consumption.[3–5] The major new finding is that both cruciferous and allium vegetables were inversely associated with ASVD mortality. These associations remained after extensive adjustment for other vegetable intakes as well as lifestyle and cardiovascular risk factors. In a forward stepwise model with cruciferous, allium, and total vegetable intake, cruciferous and allium vegetables were both independent predictors of ASVD mortality. Total vegetable intake was not considered an independent predictor possibly because of the moderate correlations of allium and cruciferous vegetables with total vegetable intakes. This should not be misinterpreted to indicate a lack of importance for total vegetable intake. If replicated in other studies, these data further emphasize the importance of cruciferous and allium vegetable intakes in reducing ASVD.

Emerging evidence suggests a protective role for cruciferous vegetables in cardiovascular health.[35–38] Evidence also

Table 5. Multivariable-Adjusted Hazard Ratios and 95% Confidence Intervals for the Association of Intakes of Cruciferous, Allium, and Total Vegetables With Ischemic Heart Disease Mortality and Ischemic Cerebrovascular Disease Mortality*

	All Participants (N=1226)	P Value
Ischemic heart disease mortality, No. (%)	128 (10.4)	
Cruciferous vegetables	0.83 (0.75–0.92)	<0.001
Allium vegetables	0.82 (0.70–0.97)	0.022
Total vegetables	0.82 (0.67–1.00)	0.050
Ischemic cerebrovascular disease mortality, No. (%)	92 (7.5)	
Cruciferous vegetables	0.94 (0.84–1.05)	0.299
Allium vegetables	0.75 (0.60–0.93)	0.011
Total vegetables	0.80 (0.62–1.02)	0.074

*Results are presented as hazard ratios (95% confidence intervals) using multivariable-adjusted Cox proportional hazards modeling per 10 g/d for cruciferous vegetables, per 5 g/d for allium vegetables, and per 75 g/d for total vegetables. Cruciferous vegetables included cabbage, brussels sprouts, cauliflower, and broccoli. Allium vegetables included onion, leek, and garlic. The multivariable-adjusted model included age, body mass index, physical activity, alcohol intake, smoking history, socioeconomic status, calcium supplementation group, antihypertensive medication, statin medication, low-dose aspirin, Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate, and energy intake.

suggests allium vegetables such as onions to be protective.[39,40] However, this relationship is inconsistent for garlic.[40] The results of some population studies and associated meta-analyses reporting cruciferous and allium vegetable consumption have not always identified an association, possibly because of type II error.[41] Cruciferous and allium vegetables contain a variety of nutritive and nonnutritive components that may benefit cardiovascular health. We studied the potential effects of nutritive components such as potassium[9] and magnesium[10] on the relationships between cruciferous and allium vegetables and ASVD mortality. We found no evidence of change in efficacy. Organosulfur compounds, a nonnutritive component of both cruciferous and allium vegetables, may have benefits.[11]

Organosulfur compounds are organic sulfur-containing compounds that have the ability to be hydrogen sulfide (H_2S) donors.[42] H_2S is a gasotransmitter that plays an important role in the regulation of vasodilation, angiogenesis, inflammation, oxidative stress, and apoptosis.[43] Organosulfur compounds found abundantly in cruciferous vegetables are glucosinolates, which are a precursor for isothiocyanates. Isothiocyanates have been widely researched because of their anticancer properties.[44–46] Isothiocyanates also have antioxidant and anti-inflammatory effects, both of which may prevent the progression of atherosclerosis.[11,47,48] The inflammatory properties of isothiocyanates can be supported by a study demonstrating an inverse association between cruciferous vegetables and proinflammatory cytokines.[49]

Organosulfur compounds found in allium vegetables have been studied in more depth. Although intake of allium vegetables was 6.2 g/d compared with 196.5 g/d in total vegetable intake, the association of allium vegetables and ASVD mortality was strong. There is evidence that organosulfur compounds found in allium vegetables may have the ability to prevent the production of reactive oxygen species, prevent vascular inflammation, inhibit platelet aggregation, and increase the bioavailability of NO.[11] Recent evidence also suggests that allicin, an organosulfur compound found in garlic, is readily degraded into organic polysulfides and the subsequent interactions with thiol groups result in the generation of H_2S.[50] Preclinical studies have demonstrated possible cardioprotective effects of H_2S, and cross talk between H_2S and NO signaling may explain these cardioprotective effects.[50]

Leafy green vegetables are a rich source of dietary nitrate that can be reduced to NO via the entero-salivary nitrate–nitrite–NO pathway.[51] Although significant in the unadjusted analysis, after adjustment for covariates and especially after further adjustment of intake of nonleafy green vegetables, which included allium and cruciferous vegetables, the beneficial effect disappeared. This result differs from other studies.[41] It should be noted that after excluding all deaths that occurred in the first 24 months, intake of leafy green vegetables became significant after adjustment for multiple covariates. While not consistently significant, leafy green vegetables had a consistent suggestive relationship warranting more research (HR between 0.88 and 0.91 and CI between 0.78 and 1.01). This suggests that leafy green vegetables may still be an important contributor to the benefits seen with ASVD mortality.

Study Strengths

Strengths of this prospective population-based cohort study were that participants were representative of older adult women from the Australian population. The average vegetable intake of participants in this study was 2.6 servings per day, the same for Australian adult women 75 years and older.[52] Food intake was also assessed at 3 different time points during the 15 years of follow-up, thus reducing measurement error. Given the participants' age at baseline and the long follow-up period of 15 years, the ASVD death rate was also increased, giving the study further power to detect an association. Lastly, loss to follow-up bias was likely minimized, having a complete follow-up of death records for all participants who remained in Western Australia, which was likely to be the majority of women given their age.

Study Limitations

Our findings need to be interpreted carefully in the context of limitations applicable to prospective cohort studies.

Table 6. The Association Between Intakes of Specific Types of Vegetables and ASVD*

	All Participants (N=1226)	P Value
Cruciferous vegetables		
Unadjusted	0.88 (0.83–0.94)	<0.001
Age- and energy-adjusted	0.88 (0.82–0.94)	<0.001
Multivariable-adjusted†	0.87 (0.81–0.94)	<0.001
Multivariable-adjusted plus noncruciferous vegetables	0.88 (0.81–0.95)	0.001
Allium vegetables		
Unadjusted	0.82 (0.74–0.92)	0.001
Age- and energy-adjusted	0.84 (0.75–0.95)	0.005
Multivariable-adjusted	0.82 (0.73–0.94)	0.003
Multivariable-adjusted plus nonallium vegetables	0.85 (0.75–0.97)	0.017
Yellow/orange/red vegetables		
Unadjusted	0.95 (0.90–1.00)	0.040
Age- and energy-adjusted	0.96 (0.91–1.01)	0.114
Multivariable-adjusted	0.98 (0.93–1.04)	0.463
Multivariable-adjusted plus non-yellow/orang/red vegetables	1.02 (0.96–1.08)	0.511
Leafy green vegetables		
Unadjusted	0.89 (0.80–1.00)	0.048
Age and energy-adjusted	0.90 (0.80–1.00)	0.055
Multivariable-adjusted	0.89 (0.79–1.01)	0.063
Multivariable-adjusted plus nonleafy green vegetables	0.91 (0.80–1.03)	0.127
Legumes		
Unadjusted	0.97 (0.90–1.04)	0.394
Age- and energy-adjusted	0.98 (0.91–1.05)	0.511
Multivariable-adjusted	0.97 (0.90–1.04)	0.379
Multivariable-adjusted plus nonlegumes	0.99 (0.92–1.07)	0.793

ASVD indicates atherosclerotic vascular disease.

*Results are presented as hazard ratios (95% confidence intervals) using Cox proportional hazards modeling per 5 g/d for allium vegetables and per 10 g/d for all other vegetable types. Cruciferous vegetables included cabbage, brussels sprouts, cauliflower, and broccoli. Allium vegetables included onion, leek, and garlic. Yellow/orange/red vegetables included tomato, capsicum, beetroot, carrot, and pumpkin. Leafy green vegetables included lettuce and other salad greens, celery, silver beet, and spinach. Legumes included peas, greens beans, bean sprouts and alfalfa sprouts, baked beans, soy beans, soy bean curd and tofu, and other beans.

†Multivariable-adjusted models included age, body mass index, physical activity, alcohol intake, smoking history, socioeconomic status, calcium supplementation group, antihypertensive medication, statin medication, low-dose aspirin, Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate, and energy intake.

Classification by one characteristic results in many other differences in other characteristics such as food and nutrients intakes, energy intake, and physical activity, which may have a substantial effect on the outcome of interest. This problem was addressed by the use of multivariable adjustments that may not have correctly allowed for residual or unknown confounders. For example, it should be noted that the group with the highest versus the lowest intake of vegetable servings reported an ≈30% higher energy intake and higher proportions of most nutrients and food types despite similar BMI values, suggesting that they were correspondingly more active. An important consideration to be noted is that physical activity has been shown to be a strong predictor of cardiovascular health.[53,54] To address this concern, both total energy intake and self-reported physical activity were included as covariates without affecting the outcome of interest. The self-reported physical activity used in this study has been shown to be related to bone mineral density in the same cohort of older adult women.[55] Higher intakes of nonvegetable foods such as fish and nuts, which have been shown in other studies to have cardiovascular health benefits,[56,57] were observed in participants who consumed higher vegetable servings. Individual adjustments for these foods did not alter the interpretation between cruciferous, allium, and total vegetable intakes and ASVD mortality. Dietary intakes in this study were self-reported and, therefore, measurement

Table 7. Hazard Ratios and 95% Confidence Intervals for the Best Predictive Model for ASVD Mortality Including Multivariable-Adjusted Variables and Intakes of Cruciferous, Allium, and Total Vegetables*

	All Participants (N=1226)	P Value
Age, y	1.17 (1.11–1.23)	<0.001
BMI, kg/m^2	1.04 (1.01–1.07)	0.016
Antihypertensive medication (yes/no)	1.64 (1.24–2.16)	<0.001
Cruciferous vegetable intake, per 10 g/d	0.88 (0.82–0.94)	<0.001
Allium vegetable intake, per 5 g/d	0.86 (0.76–0.97)	0.014

ASVD indicates atherosclerotic vascular disease.
*Results are presented as hazard ratios (95% confidence interval) using forward stepwise Cox proportional hazards modeling. Cruciferous vegetables included cabbage, brussels sprouts, cauliflower, and broccoli. Allium vegetables included onion, leek, and garlic. Forward stepwise Cox proportional hazards model included age, body mass index (BMI), physical activity, alcohol intake, smoking history, socioeconomic status, calcium supplementation group, antihypertensive medication, statin medication, low-dose aspirin, Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate, and energy intake, and intakes of cruciferous, allium, and total vegetables.

error and misclassification are possible. We attempted to address measurement error by averaging the intakes of cruciferous, allium and total vegetables across baseline, 5 years (2003) and 7 years (2005), and entering these values individually in multivariable-adjusted Cox proportional hazards models for ASVD mortality. This did not substantively alter the interpretation between baseline values and ASVD-related mortality. Lastly, given the observational nature of this study,

Table 8. Mean (SD) for Intakes of Cruciferous, Allium, and Total Vegetables at Baseline and at 5 Years (2003) and 7 Years (2005)*

	Mean	SD
Cruciferous vegetables, g/d		
Baseline[†]	32.3	22.0
5 y (2003)[‡]	32.2	23.0
7 y (2005)[§]	30.0	21.3
Allium vegetables, g/d		
Baseline	7.8	6.7
5 y (2003)	6.5	5.5
7 y (2005)	6.0	5.5
Total vegetables, g/d		
Baseline	196.5	78.9
5 y (2003)	176.3	73.6
7 y (2005)	169.3	68.6

*Cruciferous vegetables included cabbage, brussels sprouts, cauliflower, and broccoli. Allium vegetables included onion, leek, and garlic.
[†]N=1226
[‡]N=1023
[§]N=852

Table 9. Multivariable-Adjusted Hazard Ratios and 95% Confidence Intervals for ASVD-Related Mortality for Intakes of Cruciferous, Allium, and Total Vegetables Averaged Across Baseline, 5 Years (2003) and 7 Years (2005)*

	All Participants (N=1226)	P Value
Cruciferous vegetables	0.83 (0.76–0.91)	<0.001
Allium vegetables	0.83 (0.71–0.97)	0.017
Total vegetables	0.74 (0.61–0.89)	0.002

ASVD indicates atherosclerotic vascular disease.
*Results are presented as hazard ratios (95% confidence intervals) using multivariable-adjusted Cox proportional hazards modeling per 10 g/d for cruciferous vegetables, per 5 g/d for allium vegetables, and per 75 g/d for total vegetables. The multivariable-adjusted model included age, body mass index, physical activity, alcohol intake, smoking history, socioeconomic status, calcium supplementation group, antihypertensive medication, statin medication, low-dose aspirin, Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate, and energy intake. Cruciferous vegetables included cabbage, brussels sprouts, cauliflower, and broccoli. Allium vegetables included onion, leek, and garlic.

a causal relationship between the exposure and ASVD mortality remains uncertain.

Conclusions

Intakes of cruciferous and allium vegetables were inversely associated with ASVD mortality in this cohort of women aged 70 years and older. These findings support a focus on studying the effects of increased intake of cruciferous and allium vegetables on cardiovascular disease risk. They may precipitate greater study of the role and potential mechanisms of organosulfur compounds on ASVD outcomes. If supported by other studies, efforts to increase cruciferous and allium vegetables within the diet may lead to an achievable and cost-effective approach to reduce worldwide cardiovascular morbidity and mortality.

Author Contributions

Ms Blekkenhorst and Drs Lewis, Devine, Prince, and Hodgson designed the research; Ms Blekkenhorst and Dr Hodgson conducted the research; Drs Lewis, Zhu, Lim, Devine, and Prince provided the essential materials; Ms Blekkenhorst, and Drs Woodman and Hodgson analyzed the data; Ms Blekkenhorst and Drs Prince and Hodgson wrote the article; Ms Blekkenhorst had primary responsibility for the final content; and all authors critically revised the article for important intellectual content. All authors read and approved the final article.

Acknowledgments

Births, Deaths and Marriages for their work on providing the data for this study.

Sources of Funding

Disclosures

None.

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