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Fruit and vegetable intake and the risk of hypertension in middle-aged and older women

Lu Wang, MD, PhD, **JoAnn E. Manson, MD, DrPH**, **J. Michael Gaziano, MD, MPH**, **Julie E. Buring, ScD**, and **Howard D. Sesso, ScD, MPH**
Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, MA (LW, JEM, JMG, JEB, HDS); Department of Epidemiology, Harvard School of Public Health, Boston, MA (JEM, JEB, HDS); Division of Aging, Department of Medicine, Brigham and Women's Hospital, Boston, MA (JMG, JEB, HDS); Massachusetts Veterans Epidemiology Research and Information Center and Geriatric Research, Education, and Clinical Center, Boston Veterans Affairs Healthcare System, Boston, MA (JMG)

Abstract

Background—Despite the promising findings from short-term intervention trials, the long-term effect of habitual fruit and vegetable intake on blood pressure (BP) remains uncertain. We therefore assessed the prospective association between baseline intake of fruits and vegetables and the risk of hypertension in a large cohort of middle-aged and older women.

Methods—We conducted analyses among 28,082 US female health professionals aged ≥39 years, free of cardiovascular disease, cancer, and hypertension at baseline. Baseline intake of fruits and vegetables was assessed using semi-quantitative food frequency questionnaires. Incident hypertension was identified from annual follow-up questionnaires.

Results—During 12.9 years of follow-up, 13,633 women developed incident hypertension. After basic adjustment including age, race, and total energy intake, the hazard ratio and 95% CI of hypertension was 0.97 (0.89-1.05), 0.93 (0.85-1.01), 0.89 (0.82-0.97), and 0.86 (0.78-0.94) comparing women who consumed 2-<4, 4-<6, 6-<8, and ≥8 servings/day of total fruits and vegetables with those consuming <2 servings/day. These associations did not change after additionally adjusting for lifestyle factors but were attenuated after further adjustment for other dietary factors. When fruits and vegetables were analyzed separately, higher intake of all fruits but not all vegetables remained significantly associated with reduced risk of hypertension after adjustment for lifestyle and dietary factors. Adding body mass index to the models eliminated all associations.

Conclusions—Higher intake of fruits and vegetables, as part of a healthy dietary pattern, may only contribute a modest beneficial effect to hypertension prevention, possibly through improvement in body weight regulation.

Keywords

fruits; vegetables; diet; hypertension; prospective; women

Corresponding author and reprints: Lu Wang, 900 Commonwealth Avenue East, Division of Preventive Medicine, Brigham and Women's Hospital, Boston MA 02215; phone: (617) 278-0802; Fax: (617) 731-3843; luwang@rics.bwh.harvard.edu.

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Introduction

Hypertension remains the most common chronic disease in the U.S.,[1] affecting more than 74.5 million adults in 2003-2006.[2] As a major risk factor for cardiovascular disease, renal disease, and other morbidities, hypertension is the largest contributor to deaths in the US and world-wide.[3,4] Among many known modifiable risk factors, diet plays a prominent role in the development of hypertension. Dietary change can lower blood pressure (BP), prevent the onset of hypertension, and reduce the risk of hypertension related clinical complications.[5]

Individuals whose diets are based on vegetable products have lower BP levels and lower incidence of hypertension than those who consume regular western diets.[6] Small feeding trial showed that changing from an omnivorous to a vegetarian diet can lower BP in hypertensive[7] individuals with no change in body weight. In the Dietary Approaches to stop Hypertension (DASH) trial, the diet emphasizing fruit and vegetable intake significantly reduced BP during an 8-week intervention, albeit to a smaller magnitude than the combination DASH diet rich in fruits, vegetables, and low-fat dairy foods, and reduced in total fat, saturated fat, and cholesterol.[8-10] A more recent trial among healthy volunteers recruited from a primary-care health center, the Oxford Fruit and Vegetable Study, also found that after a 6-month intervention that encouraged increases in fruit and vegetable consumption to at least 5 servings/d, both systolic and diastolic BP were substantially reduced compared with the control group that continued their usual diet without receiving specific advice.[11] These trials have provided solid evidence for the benefits of fruit and vegetable intake on lowering BP in select participants during short-term intervention.

Several epidemiologic studies also examined the association between habitual fruit and vegetable intake and BP change as well as risk of elevated BP or hypertension during long-term follow-up.[12-17] The findings have generally shown an association between high fruit and vegetable consumption and low risk of hypertension, but the magnitude of association varied by participants' characteristics, methods of diet assessment and outcome ascertainment, and duration of cohort follow-up. In the current study, we investigated the prospective association between intake of total, subgroup, and individual items of fruits and vegetables and the subsequent risk of hypertension over an average of 12.9 years follow-up in a large cohort of middle-aged and older US women.

Methods

Study Population

The Women's Health Study (WHS) was a randomized, double-blind, placebo-controlled, 2×2 factorial trial evaluating the risks and benefits of low-dose aspirin and vitamin E in the primary prevention of cardiovascular disease and cancer.[18,19] A third component, β-carotene, was initially included in the WHS but terminated after a median treatment of 2.1 years.[20] Written informed consent was obtained from all participants. During the WHS, participants received study agents and follow-up questionnaires by mail and reported the occurrence of major morbidities and risk factor information every 6 months for the first year and annually thereafter. The trial and ongoing cohort follow-up was approved by the institutional review board of Brigham and Women's Hospital, Boston, MA.

From September 1992 to May 1995, a total of 39,876 female US health professionals, aged 39 to 89 years and free from cardiovascular disease and cancer (except non-melanoma skin cancer), were randomized into the WHS. Of those randomized, 39,310 (98.6%) completed a 131-item validated semiquantitative food frequency questionnaire (FFQ). For this study, we excluded 10,751 women with hypertension at baseline, defined as having a self-reported physician diagnosis of hypertension, self-reported systolic BP ≥140 mmHg or diastolic BP

≥90 mmHg, or any history of antihypertensive treatment. Baseline systolic BP was reported as 1 of 9 ordinal categories in 10 mmHg increment from <110 to ≥180 mmHg, and diastolic BP was reported as 1 of 7 ordinal categories in 5 or 10 mmHg increment from <65 to ≥105 mmHg. We also excluded 829 women who reported implausible total daily energy intake (≤600 or ≥3,500 kcal/d), 41 women who had pre-randomization cardiovascular disease or cancer, 21 women who had >70 items left blank on the FFQ, and 109 women who provided incomplete information for assessment of fruit and vegetable intake. After all the exclusions, a baseline population of 28,082 women remained for analyses.

Assessment of Fruit and Vegetable Intake

On the baseline FFQ, a commonly used unit or portion size was specified for each food item. Participants were asked how often they had consumed that amount, on average, during the previous year. Nine possible responses ranging from "never or less than once per month" to "6+ per day" were reported. The FFQ included 28 vegetable items and 16 fruit items. The average daily intake of individual fruit and vegetable items was converted from the responses and summed to compute total fruit, total vegetable, and total fruit and vegetable intake. We also *a priori* combined specific vegetables into subgroups of green leafy vegetables (spinach, kale, and lettuce), cruciferous vegetables (broccoli, cabbage, cauliflower, and Brussels sprouts), and dark and yellow vegetables (carrots, yellow squash, yams, and sweet potatoes), established by Smith et al.[21] In similar populations of female health professionals, the FFQ has demonstrated high validity as a measure of long-term average dietary intake.[22-24] In the Nurses' Health Study, Pearson correlation coefficients comparing responses from the FFQ with those from four 1-week detailed dietary records spaced over a year were 0.80 for apples, 0.84 for grapefruit, 0.74 for tomatoes, and 0.50 for yellow squash.[22]

Ascertainment of Incident Hypertension

Incident hypertension was ascertained from annual follow-up questionnaires by meeting at least 1 of 4 criteria: a new physician diagnosis of hypertension; newly initiated antihypertensive treatment; self-reported systolic BP elevated to ≥140 mmHg; or self-reported diastolic BP elevated to ≥90 mmHg. Women reported the month and year of hypertension diagnosis. For missing dates of physician diagnosis or hypertension defined by other criteria, time of event was assigned by randomly selecting a date between questionnaires without and with hypertension. Individuals who developed cardiovascular disease during follow-up, for which the management may affect BP, were censored on the date of cardiovascular disease diagnosis. In health professionals, self-reported BP correlates well with measured systolic BP (r=0.72) and diastolic BP (r=0.60),[25] and the validity of self-reported hypertension is high.[12,26] In the Nurses' Health Study, all women in a sub-sample who reported hypertension were confirmed by medical record review with documented systolic and diastolic BP ≥140/90 mmHg;[26] in the Health Professionals' Follow-up Study, all men in a sub-sample who reported hypertension were confirmed by medical record review with physician diagnosis.[12] In a random sample of WHS participants, self-reported incident hypertension was confirmed in 48 of 50 (96%) women and absence of hypertension was confirmed in 45 of 50 (90%) women through telephone interviews.

Other Baseline Variables

On the baseline questionnaire, women provided self-reports of age, weight and height, smoking status, alcohol use, physical activity, postmenopausal status, postmenopausal hormone use, multivitamin supplement use, history of physician diagnosed diabetes, and history of hypercholesterolemia. Body mass index (BMI) was computed as body weight (in kg) divided by square of height (in m). Total alcohol intake was calculated by summing alcohol content from beer, wine, and liquor consumed. Physical activity was assessed from self-reported frequency, intensity, and duration of walking and recreational activities, and expressed as energy expenditure in kcal/week. Hypercholesterolemia was defined as having a physician diagnosis of high cholesterol, self-reported total cholesterol concentration ≥240 mg/dL, or past or current treatment for high cholesterol.

Data Analyses

Statistical analyses were performed using SAS software (SAS Institute, Cary, NC, USA) version 9.1. We divided intake of fruits and vegetables into pre-determined categories that reflect current public health recommendations.[27,28] Distribution of hypertension risk factors was compared across categories of fruit and vegetable intake to identify potential confounding factors. Person-years of follow-up were calculated for each participant from randomization to the date of incident hypertension, the last day in the study, or [29] February 2007, whichever came first. After verifying the assumption of proportional hazards over time (p>0.05), we used Cox models to estimate the hazard ratio (HR) and 95% confidence interval (CI) of hypertension across levels of fruit and vegetable intake. Models first adjusted for age, race, total energy intake, and randomized treatment assignment; then additionally adjusted for lifestyle factors including smoking status, alcohol use, physical activity, postmenopausal status, postmenopausal hormone use, multivitamin supplement use, history of diabetes, and history of hypercholesterolemia (multivariable model 1); and finally adjusted for other dietary risk factors for hypertension including the intake of whole grains, red meats, low-fat dairy products, and nuts (multivariable model 2). Because the potential effect of fruit and vegetable intake on BP may be mediated by body weight regulation, we also evaluated the extent to which the adjustment for BMI might affect the association of fruit and vegetable intake with hypertension risk. Analyses were further stratified by known hypertension risk factors including age (<55, ≥55 years), BMI (<25, ≥25 kg/m^2), smoking status (current, non-current), and baseline systolic/diastolic BP (<120/80, ≥120/80 mmHg). Multiplicative interactions were tested using Wald χ^2 tests. Sensitivity analyses that considered alternative definitions for incident hypertension (e.g. self-reported elevated BP only, physician diagnosis or antihypertensive treatment only) and treated intermediate cardiovascular disease as diagnosed hypertension yielded similar results (data not shown).

Results

Among 28,082 women free of hypertension at baseline, the mean ± SD intake of total fruits and vegetables was 6.1 ± 3.6 servings/d, including 2.2 ± 1.6 servings/d of total fruits and 3.9 ± 2.6 servings/d of total vegetables. The proportion of women that consumed ≥5 servings/day of total fruits and vegetables, as recommended by US Centers for Disease Control and Prevention,[28] was 31.6%. Women with higher fruit and vegetable intake were older, less likely to be current smokers, exercised more, and more likely to use postmenopausal hormones (Table 1). Women with higher fruit intake had lower baseline BMI, consumed less alcohol, were more likely to take multivitamin supplements and to have history of hypercholesterolemia, while women with greater vegetable intake had similar baseline BMI and consumed more alcohol. Greater fruit and vegetable intake was also associated with higher total energy intake and higher consumption of whole grains and low-fat dairy products. Baseline diastolic, but not systolic, BP decreased with increasing fruit and vegetable intake.

During a mean of 12.9 years of follow-up, 13,633 women developed incident hypertension. After adjusting for age, race, total energy intake, and randomized treatment, there was a significant, inverse association between baseline total fruit and vegetable intake and subsequent risk of hypertension (Table 2): the HRs and 95% CIs of hypertension were 0.97 (0.89-1.05), 0.93 (0.85-1.01), 0.89 (0.92-0.97), and 0.86 (0.78-0.94) (p, trend: < 0.0001) comparing women who consumed 2-<4, 4-<6, 6-<8, and ≥8 servings/day with those who

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consumed <2 servings/day. This association was slightly attenuated after adjustment for lifestyle factors and further attenuated after adjustment for intake of other foods. When total fruits and total vegetables were analyzed separately, an inverse association was observed for both in the basic model while the magnitude of association appeared stronger for total fruits. After adjusting for lifestyle factors and other food intake, total fruits (HR in the highest category: 0.89, 95%CI: 0.81-0.96, p, trend: 0.0005) but not total vegetables (HR in the highest category: 0.99, 95%CI: 0.92-1.06, p, trend: 0.54) remained significantly and inversely associated with risk of hypertension. Adding BMI eliminated the associations in all multivariable models.

We further examined the consumption of subgroups and individual fruit and vegetable in association with the risk of hypertension. After adjusting for lifestyle and other dietary factors, a reduced risk of hypertension with higher fruit intake was observed mainly for apples, oranges, and raisins (Table 3). Compared with women who consumed respective fruit item rarely, the multivariable model 2 adjusted HRs of hypertension were 0.91 (95%CI: 0.84-0.98) for those consuming apples or oranges >4 servings/d and 0.90 (95%CI: 0.84-0.95) for those consuming raisins >1 serving/week. In parallel, the reduced risk of hypertension with higher vegetable intake was observed mainly for green-leafy vegetables and dark-yellow vegetables (Table 4). Compared with women who consumed <0.2 servings/d of respective vegetable subgroups, the multivariable model 2 adjusted HRs of hypertension were 0.94 (95%CI: 0.88-1.01) for those consuming ≥1.0 servings/d of green-leafy vegetables and 0.88 (95%CI: 0.82-0.95) for those consuming ≥1.0 servings/d of dark-yellow vegetables.

When we stratified analyses by participant baseline characteristics,(Table 5) the associations between fruit and vegetable intake and risk of hypertension were generally similar by subgroups of baseline age, BMI, smoking status, and BP, with a borderline significant interaction (p = 0.02) with baseline BP. The magnitude of association was stronger for total fruits than for total vegetables in all subgroups.

Discussion

In this large-scale prospective cohort of middle-aged and older women, we found an inverse association between total fruit and vegetable intake and risk of hypertension. The association remained significant after adjustment for lifestyle factors, but was no longer significant after adjustment for other dietary factors. When fruit and vegetable intake was examined separately, fruit intake was more strongly and significantly associated with risk of hypertension than vegetable intake, but all associations were eliminated after adding BMI into the model.

Dietary intervention trials,[8,11] including the DASH trial,[8] have demonstrated a short-term BP-lowering effect of increased fruit and vegetable consumption. Of prospective observational studies, the Health Professionals Follow-up Study[12] and the Nurses' Health Study[13] previously reported that high baseline intake of fruits and vegetables was associated with lower BP as well as lower risk of hypertension after 4 years of follow-up. The CARDIA study found that baseline fruit and vegetable intake was inversely related to 15-year incidence of elevated BP among young adults.[14] In the Chicago Western Electric Study, baseline fruit and vegetable intake was inversely related to 7-year BP change among middle-aged men.[15] Among Spanish participants in the Seguimiento University of Navarra (SUN) Project, an inverse association between fruit and vegetable intake and risk of hypertension was found particularly for those who consumed low levels of olive oil.[16] In a recent Japanese study, high intake of fruit, but not vegetable, was associated with a lower risk of future hypertension among subjects without baseline hypertension.[17] In line with these findings, our study results strengthen evidence for a long-term benefit of fruit and vegetable consumption in prevention of hypertension among free-living individuals. These results also corroborate our earlier findings in the same cohort that higher intake of fruits and vegetables was associated with a lower risk of CVD, and the association was partly explained by other heart-healthy lifestyle factors and traditional CVD risk factors.[29]

In the present study, an inverse association with hypertension risk appeared to be stronger for intake of fruits than for vegetables. After adjustment for intake of other foods, a tendency towards reduced risk of hypertension with high vegetable intake did not reach the conventional significance level at $\alpha=0.05$. Although similar weak associations with vegetable intake have been also noted in other studies,[12,14,17] in the context of a totality of existing literature, our study findings cannot rule out the possibility that vegetable intake contributes to lower risk of hypertension. One possible explanation for this weak association is the complicated processing of vegetable while consumed. The added fats and seasonings and the method of cooking may have offset part of the beneficial effect of fresh vegetables, though additional adjustment for sodium and total fat intake only marginally changed our observed association (data not shown). Moreover, because vegetable intake is inherently integrated into the overall lifestyle, it is not surprising to observe only a modest effect remaining for vegetables alone when many other behavioral and dietary factors are simultaneously considered.

Many known nutrients rich in fruits and vegetables, such as fiber, potassium, magnesium, folate, and vitamin C, are postulated to lower BP. Trials that tested the BP-lowering effects of these nutrients in the form of dietary supplements have shown inconsistent results,[30,31] suggesting that other components in fruits and vegetables or potential interactions among multiple nutrients may be responsible for the benefits. When we examined individual and subgroups of fruit and vegetable, a stronger inverse association was observed for green-leafy vegetables, dark-yellow vegetables, apples, oranges, and raisins. Dark-green and orange vegetables have been emphasized in the dietary recommendations by the US Department of Agriculture (USDA)[27] and Harvard healthy eating guidelines.[32] It is possible that the nutrient components in these food subgroups have particularly strong effects on BP, but this hypothesis needs to be further investigated. Elimination of the associations after adjustment for BMI supports a concept that maintaining normal body weight could be one important pathway through which fruit and vegetable consumption may contribute to BP regulation.[33]

The 5-A-Day for Better Health program since 1991 has substantially increased public awareness on the importance of fruit and vegetable intake.[28] However, data from the 2005 Behavior Risk Factor Surveillance System (BRFSS) showed that average fruit intake among Americans aged ≥2 years remained the same (1.6 servings/d) from 1994-1996 to 1999-2002 and that average vegetable intake declined from 3.4 to 3.2 servings/d during the same period.[34] Data from NHANES 1999-2002 showed that only 28% of US adults consumed fruits ≥2 servings/d and 32% adults consumed vegetables ≥3 servings/d.[35] These data underscore the need for continued intervention that encourages greater fruit and vegetable consumption among US adults. Our study offers additional support to the current USDA[27] and American Heart Association[5] dietary guidelines, which emphasizes a DASH-type dietary pattern rich in fruits and vegetables, rich in low-fat dairy products, and low in saturated fat and cholesterol. The modest magnitude of association in our study indicated that fruits and vegetables alone may contribute only a small proportion of the BP-lowering effect of the DASH diet. Of note, adherence to low-risk dietary, including DASH diet, and lifestyle factors has been associated with a substantially lower incidence of hypertension during long-term follow-up.[36]

Our study has several strengths, including a large sample size, the prospective study design, close cohort follow-up, standardized ascertainment of endpoint, and comprehensive assessment of covariates. Nevertheless, limitations of this study also deserve comments. First, because fruit and vegetable intake was assessed from a single baseline FFQ, measurement error is of concern. However, such measurement error is unlikely to be prospectively associated with the endpoint, and thus the non-differential misclassification would tend to bias observed association towards a more conservative estimate. Second, the current study is a secondary analysis of the WHS cohort and incident hypertension is a post-hoc, self-reported endpoint also subject to misclassification. Whereas the high accuracy of self-reported hypertension among health professionals has been consistently demonstrated,[25,26] and sensitivity analyses using alternative definitions for incident hypertension yielded similar results. Third, despite comprehensive adjustment for multiple lifestyle, clinical, and dietary factors, residual confounding by unmeasured or imprecisely measured hypertension risk factors may persist. Finally, the relative homogeneity of the WHS cohort in terms of race/ethnicity, education, and socioeconomic status may have limited study generalizability. Yet similar associations reported in other study populations[14-17] suggest that our results may indeed be applicable to the general population.

In conclusion, in this large-scale prospective cohort of middle-aged and older women, higher intake of fruits and vegetables was associated with a lower risk of hypertension in minimally adjusted models, but these associations were attenuated and no longer statistically significant upon adjustment for other dietary factors and BMI. High intake of fruits and vegetables, as part of an overall healthy dietary pattern, may only contribute a modest beneficial effect to hypertension prevention, possibly through improvement in body weight regulation.

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Authorship: LW and HDS designed and conducted research; LW analyzed data and wrote the paper; JEM, JMG and JEB provided critical editorial comments to the paper; LW had primary responsibility for final content. All authors read and approved the final manuscript.

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Table 1

Baseline characteristics of 28,082 women free of hypertension according to fruit and vegetable intake[1]

Characteristics	Total fruit intake				Total vegetable intake			
	Lowest	Medium	Highest	P, trend[2]	Lowest	Medium	Highest	P, trend[2]
N	2091	4708	5802		2873	8927	6679	
Median intake (servings/d)	0.3	1.8	3.8		1.2	3.2	6.4	
Age (y)	52.1±5.7	53.7±6.4	55.1±7.2	< 0.0001	52.7±6.3	53.8±6.5	54.4±6.8	< 0.0001
Body mass index (Kg/m^2)	25.6±5.0	25.2±4.4	24.8±4.3	< 0.0001	25.3±4.6	25.1±4.4	25.1±4.4	0.33
Race of white (%)	95.4	96.5	94.4	0.01	95.3	96.6	94.7	0.05
Current smoking (%)	30.9	12.4	7.0	< 0.0001	19.6	13.0	10.3	< 0.0001
Alcohol intake (g/day)	5.2±11.3	4.1±7.5	3.7±7.0	0.02	3.3±8.6	4.2±7.8	4.6±8.3	< 0.0001
Exercise (Kcal/week)	622±1044	929±1067	1340±1471	< 0.0001	674±1013	921±1083	1323±1510	< 0.0001
Postmenopausal (%)	42.4	51.0	56.5	< 0.0001	44.5	50.5	54.3	< 0.0001
Postmenopausal hormone use (%)	34.6	41.1	42.4	< 0.0001	36.8	41.1	42.3	< 0.0001
Multivitamin supplement use (%)	24.3	29.3	32.9	< 0.0001	29.5	29.8	30.1	0.57
History of diabetes (%)	1.24	1.15	1.69	0.09	1.22	1.12	1.54	0.18
History of hypercholesterolemia (%)	23.7	24.5	26.0	0.002	24.4	24.7	25.2	0.37
Dietary factors								
Total energy intake (Kcal/d)	1333±462	1674±461	2081±514	< 0.0001	1303±433	1684±456	2065±529	< 0.0001
Whole grain intake (servings/d)	0.81±0.92	1.37±1.13	1.88±1.39	< 0.0001	0.95±1.03	1.36±1.11	1.85±1.38	< 0.0001
Low-fat dairy intake (servings/d)	0.66±0.81	1.19±1.01	1.54±1.13	< 0.0001	0.90±0.96	1.19±1.02	1.41±1.11	< 0.0001
Red meat intake (servings/d)	0.75±0.58	0.70±0.50	0.66±0.53	< 0.0001	0.61±0.50	0.71±0.52	0.72±0.59	< 0.0001
Systolic BP at baseline (%)				0.11				0.81
< 110 mmHg	20.0	19.8	21.5		21.6	19.7	21.2	
110 – 119 mmHg	39.4	37.6	36.4		37.2	37.7	38.0	
120 – 129 mmHg	28.2	29.7	28.2		28.3	29.5	27.1	
130 – 139 mmHg	12.4	12.9	13.9		12.9	13.1	13.8	
Diastolic BP at baseline (%)				0.003				0.003
< 65 mmHg	10.8	12.3	13.4		12.0	11.8	12.9	
65 – 74 mmHg	40.8	40.2	42.3		40.3	40.9	42.3	
75 – 84 mmHg	40.6	39.3	36.4		39.9	39.4	36.6	

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Characteristics	Total fruit intake				Total vegetable intake			
	Lowest	Medium	Highest	P, trend[2]	Lowest	Medium	Highest	P, trend[2]
85 – 89 mmHg	7.8	8.2	7.8		7.8	7.9	8.2	

[1]Values are mean ± SD for continuous variables and % for categorical variables.

[2]Linear trends across increasing fruit and vegetable intake were tested using Jonckheere-Terpstra test for continuous variables and Cochrane-Armitage test for categorical variables.

Table 2

Hazard ratios of hypertension according to baseline fruit and vegetable intake

	Categories of intake					
	Lowest	**2 nd**	**3 rd**	**4 th**	**Highest**	**P, trend[1]**
Total fruits and vegetables						
Range (servings/d)	<2	2-<4	4-<6	6-<8	≥8	
Median (servings/d)	1.6	3.2	5.0	6.9	9.8	
N, cases/total	685 / 1468	3128 / 6429	4050 / 8386	2881 / 5898	2880 / 5901	
Basic model[2]	1.00 (reference)	0.97 (0.89-1.05)	0.93 (0.85-1.01)	0.89 (0.82-0.97)	0.86 (0.78-0.94)	< 0.0001
Multivariable model 1[3]	1.00 (reference)	0.99 (0.91-1.08)	0.95 (0.88-1.04)	0.94 (0.86-1.03)	0.90 (0.82-0.99)	0.001
Multivariable model 2[4]	1.00 (reference)	1.00 (0.92-1.09)	0.98 (0.90-1.07)	0.98 (0.90-1.08)	0.96 (0.88-1.06)	0.31
Multivariable 2+BMI	1.00 (reference)	1.03 (0.95-1.12)	1.02 (0.94-1.11)	1.04 (0.95-1.14)	1.03 (0.93-1.13)	0.80
Total fruits						
Range (servings/d)	<0.5	0.5-<1.5	1.5-<2	2-<3	≥3	
Median (servings/d)	0.3	1.1	1.8	2.4	3.8	
N, cases/total	1017 / 2091	4013 / 8254	2285 / 4708	3538 / 7220	2770 / 5802	
Basic model[2]	1.00 (reference)	0.93 (0.87-1.00)	0.88 (0.81-0.95)	0.85 (0.79-0.92)	0.78 (0.73-0.85)	< 0.0001
Multivariable model 1[3]	1.00 (reference)	0.95 (0.88-1.02)	0.90 (0.83-0.97)	0.88 (0.82-0.95)	0.82 (0.75-0.89)	< 0.0001
Multivariable model 2[4,5]	1.00 (reference)	0.98 (0.91-1.05)	0.94 (0.87-1.02)	0.93 (0.86-1.01)	0.89 (0.81-0.96)	0.0004
Multivariable 2+BMI	1.00 (reference)	0.99 (0.92-1.06)	0.98 (0.90-1.06)	0.98 (0.91-1.06)	0.95 (0.88-1.04)	0.19
Total vegetables						
Range (servings/d)	<1.5	1.5 - <2.5	2.5 - <4	4 - <5	≥5	
Median (servings/d)	1.2	2.0	3.2	4.5	6.4	
N, cases/total	1387 / 2873	2679 / 5650	4375 / 8927	1919 / 3952	3263 / 6679	
Basic model[2]	1.00 (reference)	0.93 (0.87-0.99)	0.94 (0.88-1.00)	0.92 (0.86-0.99)	0.89 (0.83-0.96)	0.008
Multivariable model 1[3]	1.00 (reference)	0.94 (0.88-1.00)	0.96 (0.90-1.02)	0.95 (0.88-1.02)	0.93 (0.86-0.99)	0.13
Multivariable model 2[4,5]	1.00 (reference)	0.94 (0.88-1.01)	0.98 (0.92-1.05)	0.98 (0.91-1.06)	0.99 (0.92-1.06)	0.56
Multivariable 2+BMI	1.00 (reference)	0.95 (0.89-1.01)	0.99 (0.93-1.05)	0.99 (0.92-1.07)	0.98 (0.91-1.06)	0.63

[1] Linear trend was tested using the median value in each intake category as an ordinal variable.

[2]Basic model adjusted for age (continuous), race (white, non-white), total energy intake (continuous), and randomized treatment (vitamin E, aspirin, β-carotene, or placebo).

[3]Multivariable model 1 additionally adjusted for smoking (never, former, current), daily alcohol intake (continuous), exercise (continuous), postmenopausal status (yes, no, uncertain), postmenopausal hormone use (never, former, current), multivitamin supplement use (never, former, current), history of diabetes (yes, no), history of hypercholesterolemia (yes, no).

[4]Multivariable model 2 adjusted for all covariates in multivariate model 1 plus intake of whole grains, red meats, low-fat dairy products, and nuts (all in quintiles).

[5]Multivariable model 2 for fruit intake also adjusted for vegetable intake and vice versa.

Table 3

Hazard ratios of hypertension according to individual fruit intake

	Categories of intake					
	Lowest	**2 nd**	**3 rd**	**4 th**	**Highest**	**P, trend[1]**
Apples						
Range	None / rarely	1-3 sv / month	1 sv / week	2-4 sv / week	>4 sv / week	
N, cases / total	1274 / 2509	3245 / 6583	3061 / 6341	3849 / 8092	2076 / 4323	
Multivariable model 1[2]	1.00 (reference)	0.94 (0.88-1.00)	0.89 (0.83-0.95)	0.85 (0.80-0.91)	0.85 (0.79-0.91)	< 0.0001
Multivariable model 2[3]	1.00 (reference)	0.95 (0.89-1.02)	0.93 (0.86-0.99)	0.90 (0.84-0.96)	0.91 (0.85-0.99)	0.03
Bananas						
Range	None / rarely	1-3 sv / month	1 sv / week	2-4 sv / week	>4 sv / week	
N, cases / total	1286 / 2730	3241 / 6686	3033 / 6252	4045 / 8252	1857 / 3822	
Multivariable model 1[2]	1.00 (reference)	1.03 (0.97-1.10)	1.01 (0.95-1.08)	1.00 (0.93-1.06)	0.97 (0.90-1.05)	0.07
Multivariable model 2[3]	1.00 (reference)	1.02 (0.96-1.09)	1.02 (0.96-1.10)	1.02 (0.96-1.09)	1.02 (0.95-1.10)	0.88
Oranges						
Range	None / rarely	1-3 sv / month	1 sv / week	2-4 sv / week	>4 sv / week	
N, cases / total	2680 / 5431	3952 / 8045	2968 / 6227	2739 / 5686	1132 / 2388	
Multivariable model 1[2]	1.00 (reference)	0.97 (0.92-1.02)	0.93 (0.88-0.98)	0.91 (0.86-0.97)	0.86 (0.80-0.92)	< 0.0001
Multivariable model 2[3]	1.00 (reference)	0.98 (0.94-1.03)	0.96 (0.90-1.01)	0.95 (0.90-1.00)	0.91 (0.85-0.98)	0.01
Raisins						
Range	None / rarely	1-3 sv / month	1 sv / week	> 1 sv / week		
N, cases / total	4629 / 9389	5101 / 10456	2153 / 4527	1665 / 3557		
Multivariable model 1[2]	1.00 (reference)	0.96 (0.92-1.00)	0.90 (0.85-0.95)	0.85 (0.80-0.90)		< 0.0001
Multivariable model 2[3]	1.00 (reference)	0.98 (0.94-1.02)	0.93 (0.88-0.98)	0.90 (0.85-0.96)		0.0004
Strawberries						
Range	None / rarely	1-3 sv / month	1 sv / week	> 1 sv / week		
N, cases / total	3393 / 7042	5723 / 11876	3376 / 6899	1042 / 2103		
Multivariable model 1[2]	1.00 (reference)	0.98 (0.94-1.03)	1.00 (0.95-1.05)	1.02 (0.94-1.09)		0.58
Multivariable model 2[3]	1.00 (reference)	1.00 (0.96-1.04)	1.03 (0.97-1.08)	1.07 (0.99-1.15)		0.04

	Categories of intake					
	Lowest	**2 nd**	**3 rd**	**4 th**	**Highest**	**P, trend[1]**
Apples						
Blueberries						
Range	None / rarely	1-3 sv / month		≥1 sv / week		
N, cases / total	8740 / 17867	3326 / 7028		1441 / 2959		
Multivariable model 1[2]	1.00 (reference)	0.95 (0.91-0.99)		0.98 (0.92-1.03)		0.08
Multivariable model 2[3]	1.00 (reference)	0.97 (0.93-1.01)		1.02 (0.96-1.08)		0.93

[1] Linear trend was tested using the median value in each intake category as an ordinal variable.

[2] Multivariable model 1 adjusted for age (continuous), race (white, non-white), total energy intake (continuous), randomized treatment (vitamin E, aspirin, β-carotene, or placebo), smoking (never, former, current), daily alcohol intake (continuous), exercise (continuous), postmenopausal status (yes, no, uncertain), postmenopausal hormone use (never, former, current), history of diabetes (yes, no), and history of hypercholesterolemia (yes, no).

[3] Multivariable model 2 adjusted for all covariates in multivariable model 1 plus intake of whole grains, red meats, low-fat dairy products, and nuts (all in quintiles), intake of vegetables (categories as defined in Table 2) and other fruits (continuous).

Table 4

Hazard ratios of hypertension according to subgroup and individual vegetable intake

	Categories of intake					
	Lowest	**2 nd**	**3 rd**	**4 th**	**Highest**	**P, trend[1]**
Green-leafy vegetables						
Range (servings/d)	<0.2	0.2 - <0.4	0.4 - < 0.6	0.6 - <1.0	≥1.0	
N, cases / total	1858 / 3771	2317 / 4718	3097 / 6294	3228 / 6745	3117 / 6542	
Multivariable model 1[2]	1.00 (reference)	0.97 (0.91-1.04)	0.97 (0.92-1.03)	0.94 (0.88-1.00)	0.92 (0.86-0.98)	0.05
Multivariable model 2[3]	1.00 (reference)	0.99 (0.93-1.05)	0.98 (0.93-1.04)	0.96 (0.90-1.02)	0.94 (0.88-1.01)	0.26
Cruciferous vegetables						
Range (servings/d)	<0.2	0.2 - <0.4	0.4 - < 0.6	0.6 - <1.0	≥1.0	
N, cases / total	2372 / 5105	4730 / 9674	2649 / 5535	2375 / 4833	1496 / 2933	
Multivariable model 1[2]	1.00 (reference)	1.05 (1.00-1.10)	1.01 (0.96-1.07)	1.03 (0.97-1.10)	1.07 (1.00-1.15)	0.20
Multivariable model 2[3]	1.00 (reference)	1.06 (1.01-1.12)	1.05 (0.99-1.11)	1.09 (1.02-1.16)	1.14 (1.06-1.23)	0.002
Dark-yellow vegetables						
Range (servings/d)	<0.2	0.2 - <0.4	0.4 - < 0.6	0.6 - <1.0	≥1.0	
N, cases / total	3422 / 6994	4075 / 8332	2466 / 5023	2198 / 4607	1460 / 3120	
Multivariable model 1[2]	1.00 (reference)	0.95 (0.90-0.99)	0.96 (0.91-1.01)	0.90 (0.85-0.95)	0.84 (0.79-0.90)	< 0.0001
Multivariable model 2[3]	1.00 (reference)	0.96 (0.91-1.01)	0.99 (0.93-1.05)	0.93 (0.87-0.99)	0.88 (0.82-0.95)	0.005
Legumes						
Range (servings/d)	<0.2	0.2 - <0.4	0.4 - < 0.6	0.6 - <1.0	≥1.0	
N, cases / total	2536 / 5332	5562 / 11672	2310 / 4622	2195 / 4468	1020 / 1987	
Multivariable model 1[2]	1.00 (reference)	0.96 (0.91-1.01)	1.02 (0.96-1.08)	0.99 (0.93-1.05)	1.03 (0.95-1.12)	0.12
Multivariable model 2[3]	1.00 (reference)	0.96 (0.92-1.01)	1.02 (0.97-1.09)	1.00 (0.94-1.07)	1.08 (0.99-1.17)	0.01
Onions						
Range (servings/d)	<0.1	0.1 - <0.3	0.3 - < 0.5	0.5 - <1.0	≥1.0	
N, cases / total	3101 / 6664	4243 / 8667	2352 / 4887	2486 / 4976	1424 / 2852	
Multivariable model 1[2]	1.00 (reference)	1.06 (1.01-1.11)	1.04 (0.99-1.10)	1.08 (1.02-1.14)	1.06 (0.99-1.13)	0.02
Multivariable model 2[3]	1.00 (reference)	1.06 (1.01-1.11)	1.04 (0.99-1.10)	1.09 (1.03-1.15)	1.07 (1.00-1.15)	0.01

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	Categories of intake					
	Lowest	**2 nd**	**3 rd**	**4 th**	**Highest**	**P, trend[1]**
Tomatoes						
Range (servings/d)	<0.1	0.1 - <0.3	0.3 - < 0.5	0.5 - <1.0	≥1.0	
N, cases / total	689 / 1441	5008 / 10353	1992 / 4078	4309 / 8933	1619 / 3265	
Multivariable model 1[2]	1.00 (reference)	1.03 (0.94-1.11)	1.00 (0.92-1.10)	1.01 (0.93-1.10)	1.03 (0.94-1.13)	0.80
Multivariable model 2[3]	1.00 (reference)	1.02 (0.94-1.11)	1.01 (0.93-1.11)	1.02 (0.93-1.11)	1.05 (0.95-1.16)	0.83

[1] Linear trend was tested using the median value in each intake category as an ordinal variable.

[2] Multivariable model 1 adjusted for age (continuous), race (white, non-white), total energy intake (continuous), randomized treatment (vitamin E, aspirin, β-carotene, or placebo), smoking (never, former, current), daily alcohol intake (continuous), exercise (continuous), postmenopausal status (yes, no, uncertain), postmenopausal hormone use (never, former, current), history of diabetes (yes, no), and history of hypercholesterolemia (yes, no).

[3] Multivariable model 2 adjusted for all covariates in multivariable model 1 plus intake of whole grains, red meats, low-fat dairy products, and nuts (all in quintiles), intake of fruits (categories as defined in Table 2) and other vegetables (continuous).

Table 5

Hazard ratios of hypertension according to fruit and vegetable intake in subgroups of women

	Categories of intake						
	1st	2nd	3rd	4th	5th	P, trend[1]	P, interaction[2]
Total Fruits (servings/d)	<0.5	0.5 - <1.5	1.5 - <2	2 - <3	≥3		
Baseline age							0.19
<55 y							
N, cases / total	754 / 1586	2667 / 5899	1363 / 3089	1938 / 4432	1411 / 3350		
Multivariable model 2[3,4]	1.00 (reference)	0.93 (0.85-1.01)	0.89 (0.81-0.98)	0.88 (0.80-0.97)	0.83 (0.75-0.93)	0.0006	
≥55 y							
N, cases / total	263 / 505	1346 / 2355	922 / 1619	1600 / 2788	1359 / 2452		
Multivariable model 2[3,4]	1.00 (reference)	1.11 (0.97-1.28)	1.08 (0.93-1.25)	1.08 (0.93-1.25)	1.02 (0.88-1.19)	0.17	
Body mass index							0.50
<25 kg/m^2							
N, cases / total	448 / 1133	1795 / 4481	1068 / 2609	1696 / 4145	1425 / 3504		
Multivariable model 2[3,4]	1.00 (reference)	1.03 (0.93-1.15)	1.04 (0.92-1.17)	1.02 (0.90-1.14)	1.01 (0.89-1.14)	0.69	
≥25 kg/m^2							
N, cases / total	554 / 920	2125 / 3598	1169 / 2011	1771 / 2943	1296 / 2197		
Multivariable model 2[3,4]	1.00 (reference)	0.93 (0.85-1.03)	0.88 (0.79-0.99)	0.91 (0.82-1.01)	0.86 (0.76-0.96)	0.02	
Smoking							0.14
Never							
N, cases / total	636 / 1318	2176 / 4417	1174 / 2317	1650 / 3347	1197 / 2405		
Multivariable model 2[3,4]	1.00 (reference)	1.00 (0.91-1.10)	0.99 (0.89-1.10)	0.95 (0.85-1.05)	0.94 (0.84-1.05)	0.09	
Ever							
N, cases / total	381 / 773	1830 / 3825	1110 / 2388	1884 / 3867	1573 / 3396		
Multivariable model 2[3,4]	1.00 (reference)	0.92 (0.82-1.03)	0.87 (0.76-0.98)	0.89 (0.79-1.01)	0.81 (0.71-0.92)	0.001	
Baseline systolic/diastolic BP							0.02
<120/80 mmHg							
N, cases / total	274 / 872	1175 / 3550	617 / 2007	956 / 3068	770 / 2581		
Multivariable model 2[3,4]	1.00 (reference)	1.06 (0.92-1.22)	0.93 (0.80-1.09)	0.94 (0.81-1.09)	0.88 (0.75-1.04)	0.003	

	Categories of intake						
	1st	2nd	3rd	4th	5th	P, trend[1]	P, interaction[2]
≥120/80 mmHg							
N, cases / total	722 / 1176	2773 / 4565	1634 / 2638	2531 / 4049	1966 / 3140		
Multivariable model 2[3,4]	1.00 (reference)	0.95 (0.87-1.03)	0.96 (0.87-1.06)	0.95 (0.86-1.04)	0.94 (0.85-1.04)	0.48	
Total Vegetables (servings/d)	<1.5	1.5-<2.5	2.5-<4	4-<5	≥5		
Baseline Age							0.97
<55 y							
N, cases / total	934 / 2063	1682 / 3862	2601 / 5785	1117 / 2553	1798 / 4096		
Multivariable model 2[3,4]	1.00 (reference)	0.95 (0.87-1.03)	1.01 (0.93-1.09)	1.00 (0.91-1.10)	1.02 (0.93-1.12)	0.22	
≥55 y							
N, cases / total	453 / 810	997 / 1788	1774 / 3142	802 / 1399	1465 / 2583		
Multivariable model 2[3,4]	1.00 (reference)	0.93 (0.83-1.05)	0.94 (0.84-1.05)	0.95 (0.84-1.08)	0.93 (0.82-1.05)	0.60	
Body mass index							0.44
<25 kg/m^2							
N, cases / total	620 / 1592	1270 / 3181	2083 / 5079	913 / 2224	1545 / 3800		
Multivariable model 2[3,4]	1.00 (reference)	0.99 (0.90-1.10)	1.01 (0.91-1.11)	1.03 (0.92-1.15)	1.01 (0.90-1.12)	0.71	
≥25 kg/m^2							
N, cases / total	733 / 1220	1366 / 2377	2203 / 3679	962 / 1649	1652 / 2746		
Multivariable model 2[3,4]	1.00 (reference)	0.91 (0.83-1.00)	0.98 (0.90-1.07)	0.95 (0.85-1.05)	0.98 (0.89-1.09)	0.43	
Smoking							0.58
Never							
N, cases / total	713 / 1462	1320 / 2774	2191 / 4343	947 / 1924	1662 / 3302		
Multivariable model 2[3,4]	1.00 (reference)	0.94 (0.85-1.03)	1.01 (0.92-1.10)	1.00 (0.90-1.11)	1.01 (0.91-1.12)	0.27	
Ever							
N, cases / total	671 / 1408	1357 / 2871	2180 / 4578	971 / 2026	1599 / 3371		
Multivariable model 2[3,4]	1.00 (reference)	0.95 (0.86-1.05)	0.96 (0.88-1.06)	0.97 (0.87-1.09)	0.97 (0.87-1.08)	0.97	
Baseline systolic/diastolic BP							0.92
<120/80 mmHg							
N, cases / total	381 / 1217	735 / 2395	1190 / 3776	525 / 1681	961 / 3013		

	Categories of intake						
	1st	**2nd**	**3rd**	**4th**	**5th**	**P, trend[1]**	**P, interaction[2]**
Multivariable model 2[3,4]	1.00 (reference)	0.97 (0.86-1.11)	0.99 (0.87-1.12)	1.01 (0.88-1.17)	1.05 (0.91-1.21)	0.19	
≥120/80 mmHg							
N, cases / total	979 / 1591	1907 / 3156	3112 / 5022	1372 / 2224	2256 / 3577		
Multivariable model 2[3,4]	1.00 (reference)	0.94 (0.86-1.01)	0.99 (0.91-1.07)	0.99 (0.90-1.08)	1.02 (0.93-1.11)	0.10	

[1] Linear trend was tested using the median value in each intake category as an ordinal variable.

[2] Interaction was tested using Wald χ^2 tests.

[3] Multivariable model adjusted for age (continuous), race (white, non-white), total energy intake (continuous), randomized treatment (vitamin E, aspirin, β-carotene, or placebo), smoking (never, former, current), daily alcohol intake (continuous), exercise (continuous), postmenopausal status (yes, no, uncertain), postmenopausal hormone use (never, former, current), history of diabetes (yes, no), history of hypercholesterolemia (yes, no), intake of whole grains, red meats, low-fat dairy products, and nuts (all in quintiles).

[4] Model for fruit intake also adjusted for vegetable intake and vice versa.