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Associations of vegetable and fruit consumption with age-related cognitive change

M.C. Morris, ScD; D.A. Evans, MD; C.C. Tangney, PhD; J.L. Bienias, ScD; and R.S. Wilson, PhD

Abstract—Objective: To examine the association between rates of cognitive change and dietary consumption of fruits and vegetables among older persons. **Methods:** The authors conducted a prospective cohort study of 3,718 participants, aged 65 years and older of the Chicago Health and Aging Project. Participants completed a food frequency questionnaire and were administered at least two of three cognitive assessments at baseline, 3-year, and 6-year follow-ups. Cognitive function was measured using the average z-score of four tests: the East Boston Tests of immediate memory and delayed recall, the Mini-Mental State Examination, and the Symbol Digit Modalities Test. **Results:** The mean cognitive score at baseline for the analyzed cohort was 0.18 (range: -3.5 to 1.6), and the overall mean change in score per year was a decline of 0.04 standardized units. In mixed effects models adjusted for age, sex, race, and education, compared with the rate of cognitive decline among persons in the lowest quintile of vegetable intake (median of 0.9 servings/day), the rate for persons in the fourth quintile (median, 2.8 servings/day) was slower by 0.019 standardized units per year ($p = 0.01$), a 40% decrease, and by 0.018 standardized units per year ($p = 0.02$) for the fifth quintile (median, 4.1 servings/day), or a 38% decrease in rates. The association remained significant (p for linear trend = 0.02) with further control of cardiovascular-related conditions and risk factors. Fruit consumption was not associated with cognitive change. **Conclusion:** High vegetable but not fruit consumption may be associated with slower rate of cognitive decline with older age.

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A number of prospective epidemiologic studies and animal models have found associations between individual dietary components and age-related cognitive change and dementia, including antioxidant nutrients, B-vitamins, and dietary fats. Where it is useful to examine individual dietary components to better understand the biochemical mechanisms underlying disease processes and to identify potential therapeutic agents, it is also helpful, especially from a public health perspective, to understand associations at the level of food groups. The message to consume more or less of a food group is much simpler than the message to consume more or less of individual nutrients, which vary from food to food.

Previously, we found associations of a number of food components with age-related cognitive decline, including tocopherols (vitamin E), niacin, folate, vitamin B-12, and fat composition. In this study, we focus on fruits and vegetables, as they are rich sources of antioxidant nutrients and bioactive compounds (e.g., vitamin E, vitamin C, carotenoids, and flavonoids) and also low in saturated fats. In animal models, diets supplemented with fruit and vegetable extracts protected against cognitive behavioral changes and brain neuropathology. We examined

fruit and vegetable consumption in relation to 6-year cognitive change in a large, biracial population of older Chicago residents.

Methods. Population. Study subjects were participants in the Chicago Health and Aging Project (CHAP), a 1993–2002 cohort study of older residents from a geographically defined population of the south side of Chicago that is 62% black and 38% white.¹ A door-to-door census identified 8,501 residents aged 65 years and older, of whom 439 died and 249 moved before participation could be secured. Of the remaining 7,813 surviving residents, 6,158 agreed to participate in 90-minute in-home interviews that included the administration of four cognitive tests (79% participation overall; 81% among African Americans, 75% among whites). All study participants were contacted for 3-year and 6-year follow-up interviews. A total of 4,930 participants survived to the 3-year follow-up of which 4,398 (88%) black and white participants completed at least one follow-up interview for the analysis of change in cognitive function. The Institutional Review Board of Rush University Medical Center approved the study, and all participants gave written informed consent.

Dietary assessments. We assessed diet using a modified version of the Harvard semi-quantitative food frequency questionnaire (FFQ) that included 139 food items and vitamin supplements.^{2,3} The FFQ was shown to be a valid and reproducible measure of dietary intake in the CHAP study population.^{4,5} The FFQs were optically scanned at Harvard University and daily nutrient intake was computed using the Harvard nutrient database which is based on the USDA nutrient composition of foods⁶ along with supplementary data from scientific publications and

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Table 1 Comparison of baseline characteristics of the analyzed cohort ($n = 3,718$) to the entire CHAP study population ($n = 6,158$)

Characteristic	Analyzed cohort	CHAP study population
Age, y, mean	73.6	75.0
Male, %	38.0	39.3
Black, %	60.4	61.6
Education, y, mean	12.2	11.8
Global Cognitive Score,* mean	21.1	-2.2
MMSE score, mean	26.7	25.3

* Global cognitive scores are multiplied by a factor of 100.

CHAP = Chicago Health and Aging Project; MMSE = Mini-Mental State Examination.

other sources.⁷ Participants reported their usual frequency of intake of a specified portion size for each food over the past year. Each fruit and vegetable item had up to six response categories ranging from never/less than one per month to one or more per day. Responses to the individual items were converted to average daily intake and summed into composite groups of vegetable and fruit intake. Total vegetable consumption represented servings per day of 19 items listing 28 different vegetables, excluding potatoes. Total fruit consumption represented servings per day of 14 items listing 21 different fruits. Subgroups of vegetables and fruits were based on similar groupings used by others,^{8,9} and included green leafy vegetables (lettuce/tossed salad, spinach, and greens/kale/collards), cruciferous vegetables (broccoli and coleslaw), legumes (peas/lima beans and beans/lentils/soybeans), yellow vegetables (cooked carrots, raw carrots, yams/sweet potatoes, zucchini/summer squash/eggplant, and beets), and citrus fruits (orange/grapefruits, orange juice, apple juice/other fruit juices). To allow for secondary analyses of the contributions of individual nutrients to fruit and vegetable associations, we computed the estimated daily nutrient intakes by multiplying the nutrient composition of each food item by the frequency of intake and summing over all food items. Information provided by participants on brand names of multivitamins and dosage levels of individual supplements was used to compute daily nutrient intake from vitamin supplements.

Participants. In this study, we were interested in the effects of vegetable and fruit consumption on within person change in cognitive function. Therefore, we only analyzed participants who had at least two cognitive assessments. Persons who had baseline scores only would contribute to the estimates of association with the intercept, but not to the estimated effects on rate of change.

Of the 4,390 persons who completed at least two of the three cognitive assessments and a food frequency questionnaire during the 6-year follow-up, we eliminated 217 because of potentially invalid FFQ data (e.g., implausible energy intake, more than half of the items missing). We eliminated an additional 455 persons who completed the FFQ more than 2.5 years after the baseline interview and had only two cognitive assessments. This left 3,718 persons for analysis with a median follow-up of 5.5 years. Of these, 1,946 persons had three cognitive assessments with a median follow-up of 6.3 years. The self-administered FFQs were completed by the analyzed participants a mean of 1.2 years ($SD \pm 0.8$) after the initial cognitive test. The analyzed cohort had higher global cognitive scores and slightly higher Mini-Mental State Examination (MMSE) scores than the entire study population at baseline. There were also small differences in demographic characteristics in the two groups (table 1).

We conducted a study of the validity (using multiple 24-hour recall interviews as the comparison) and 1-year reproducibility of the FFQ among 232 randomly selected CHAP participants.^{4,5} The FFQ was shown to produce valid estimates of nutrient intake, unbiased by age, race, education, and cognitive ability.⁴

Cognitive function assessment. Interviewers administered four cognitive tests during in-home interviews conducted at baseline, and 3-year and 6-year follow-ups. The tests included the East

Boston tests of immediate and delayed recall (each with possible scores of 0 to 12 story ideas recalled),^{10,11} the MMSE (score range: 0 to 30 correct items),¹² and the Symbol Digit Modalities Test,¹³ a timed test of perceptual speed and attention (score range: 0 to 96 items correctly identified). Scores on each of the four tests were expressed as z-scores and then averaged to provide a global measure of cognitive function that was approximately normally distributed, and reduced the floor and ceiling effects and other measurement errors of the individual tests. In a previous factor analysis, all four tests loaded on a single factor that accounted for 74% of the variance.¹⁴ The percentage of interviewed participants that completed all four tests was high: 98.4% at the baseline, 92.2% at the first follow-up, and 89.8% at the second follow-up. A global score was computed only for participants who completed at least two of the four tests.

Other covariates. Sex and race were obtained at the time of the census and verified at the baseline interview. Race was determined by questions and categories of the 1990 US census. Information on non-dietary variables was collected at participants' baseline interview. Age was computed from self-reported birth date and date of baseline cognitive assessment. Education was computed from self-reported highest grade or years of formal education. Frequency of participation in cognitive activities was based on the average response, ranging from one (once a year or less) to five (everyday), for each of eight different activities, such as reading newspapers, books, or magazines, listening to the radio, playing games/crossword puzzles, watching TV, and going to religious services and the museum.^{14,15} Physical activity was computed as the total number of hours per week of participation in nine activities (walking, biking, calisthenics, gardening, swimming, jogging, golfing, bowling, dancing, and other). Questions on cigarette smoking allowed for the computation of an indicator variable for ever smoked and number of pack years. Daily consumption of alcohol (g/day) was based on three questions from the FFQ about usual consumption during the past year of beer, wine, and liquor. Heart disease was determined by self-reported history of myocardial infarction or use of digitalis. Hypertension history was based on self-reported history or measured blood pressure ≥ 160 mm Hg systolic or ≥ 95 mm Hg diastolic. Stroke history was determined through self-report. Diabetes mellitus was determined either by self-report or use of anti-diabetic medication. Information on medication use was based on interviewer inspection of all medications taken within the previous 2 weeks.

Statistical analysis. We used linear mixed effects models¹⁶ fitted in SAS¹⁷ to test the hypotheses that fruit and vegetable consumption would slow the rate of within-person decline in cognitive score over 6 years. Linear mixed effects models allow one to model the variables of interest (fixed effects) while simultaneously partitioning the variability into between-person and within-person components. In our model, the fixed effects included terms for time since baseline of the study, the main effect term for each variable (e.g., age, fruit consumption), and interactions between time and each variable. The main effect for a given variable represented its effect at baseline (i.e., at time = 0). The interaction between a given variable and time represented the effect of that variable on change in cognitive score over time. In addition to these main effects, we included two primary random effects: one for initial level (intercept) and one for rate of change (slope). These random effects were person-specific. That is, the fixed effects part of the model captures the overall behavior of the group, and the random effects represent the average deviation of each individual person from the overall behavior of the group, conditional on all of the fixed covariates in the model. One can think of this as fitting a separate straight line for each person's trajectory over time. In addition, we included a third random effect that captured the covariance between the two (intercept and slope) random effects. Finally, we have a random error term, which represents the deviation within a given person from their predicted path, modeled as a straight line, and the actual observed data for that person. Partitioning the total variability in this manner allows for more precise tests of our hypotheses than would be obtainable from a fixed-effects-only model.

We first determined the best model of the important confounding variables by considering non-linear and interaction associations with both initial cognitive score and rate of change. All interaction terms between demographic variables were significant at $p < 0.05$. Fruit and vegetable intakes were modeled in quintiles

using the lowest quintiles as the referent categories. All models were adjusted for total calorie intake to control for potential confounding and measurement error by this variable. The *p* value for trend was based on modeling fruit/vegetable intake as a continuous variable with persons in each quintile assigned the median value of the quintile. Effect modification was examined by including terms in the model for all two-way and three-way interaction terms among the covariate, quintile of fruit/vegetable intake, and time.

Results. The analyzed cohort of 3,718 community residents was 60% black and 62% female, and had a mean age of 74.3 years (range: 65 to 102) at baseline and a mean educational level of 12.2 years (SD: ± 3.7).

Persons with high intakes of fruits and vegetables tended to have a favorable risk profile for health and cognition (table 2). They were more likely to be female, to be white, to have more years of education, and to have higher levels of physical activity. The high fruit consumers, but not high vegetable consumers, were also somewhat more likely to have a cardiovascular-related condition, including myocardial infarction, hypertension, and diabetes.

The mean cognitive score at baseline for the cohort of 3,718 persons was 0.18 (range: -3.5 to 1.6). The overall mean change in cognitive score was a decline of 0.04 standardized units per year (SU/y).

The average total daily intake of both fruits and vegetables combined was 4.5 servings per day (range, 0 to 14.4). There was no association between combined fruit and vegetable intake and 6-year change in cognitive score in models that adjusted for age and total energy intake (*p* for trend = 0.28), or with additional control for sex, race, education, cognitive activity, physical activity, and alcohol consumption, although the differences in rates for upper quintiles compared with the first were in the positive direction indicating slower rates of decline (data not shown).

We next examined the rates of change in cognitive score by quintiles of vegetable intake. The average number of vegetable servings per day was 2.3, with a range of 0 to 8.2. When we adjusted for age and total energy intake, we observed a marginally significant association of slower cognitive decline with higher intake (*p* for linear trend = 0.06) (figure). The association became stronger when we added control for sex, race, education, cognitive activity, physical activity, and alcohol consumption (*p* for trend = 0.04). Compared with a cognitive decline rate of -0.046 SU/y for persons in the first quintile of vegetable intake (median of 0.9 servings/day), the rates were -0.030 SU/y for persons in the fourth quintile (median, 2.8 servings/day), and -0.032 SU/y for persons in the fifth quintile (median 4.1 servings/day). The difference of 0.016 between the fourth and first quintiles represented a 35% reduction in annual rate of cognitive decline. The difference of 0.014 with the fifth quintile represented a 30% reduction, although the difference was marginally significant.

In separate analyses we added terms for cardiovascular-related conditions, including history of stroke, heart disease, hypertension, and diabetes, as these conditions may serve as confounders or as the intermediate mechanisms through which vegetable consumption is associated with slower cognitive decline. However, the rate differences were not materially changed (rate differences were 0.015 [*p* = 0.04] for the fourth quintile and 0.014 [*p* = 0.09] for the fifth quintile, compared with the first; *p* for linear trend = 0.05).

Daily servings of fruit intake for the cohort ranged from 0 to 8.5 servings per day, with an average of 2.2. There was no evidence of association between fruit intake and cognitive change in either the age- or the multiple-adjusted models (figure). The rate differences between upper quintiles of intake compared with the first fluctuated around zero, and became even smaller with further control for all other potential confounding variables.

We investigated in two ways whether the fact that some persons completed the FFQ after the baseline interview had any effect on our findings. First, we repeated the analyses with the addition of a variable that represented the number of days the FFQ was completed after the baseline, but there was virtually no change in the rate differences or *p* values for significance. Second, we created an indicator variable to identify persons who completed the FFQ within 1 year after baseline cognitive testing and re-analyzed the multiple-adjusted models with multiplicative terms between the indicator variable and quintiles of vegetable and fruit intakes. There were no significant differences in the rates of change for vegetable intake among persons who completed the FFQ within 1 year after baseline and those who completed it more than 1 year after baseline. However, persons who completed their FFQ close to baseline and who had high fruit intake (fourth and fifth quintiles) had significantly greater rates of decline than persons who had high fruit intake and completed their FFQ later than 1 year after baseline.

We next repeated the analyses after excluding persons whose baseline cognitive scores were in the bottom 10% of the distribution. The multiple-adjusted rate differences for persons in the fourth and fifth quintiles of vegetable intake changed little ($\beta = 0.015$; *p* = 0.05 and $\beta = 0.014$; *p* = 0.10) and the test for trend was marginally significant. There were no material changes in the rate differences of cognitive decline by quintile of fruit consumption, which remained non-significant.

We also examined the data for modifications in the rate differences by the demographic variables, age, sex, race, and education in separate multiple-adjusted models for both fruit and vegetable intake. The only evidence of effect modification was between vegetable intake and age, such that the association of slower decline with higher vegetable intake was stronger among persons of older age. In each of the third through fifth quintiles of vegetable intake, for each additional year of age, there was a reduction in the rates of cognitive decline by more than 0.002 SU/y (all *p* values < 0.03). The observed inverse association of cognitive decline with vegetable consumption and the absence of association with fruit consumption were not modified according to whether persons consumed a vitamin supplement (43% were taking a multivitamin or vitamin E or vitamin C supplement), currently smoked (15%), or reported a history of stroke (9%), or any cardiovascular-related condition (64%).

In previous studies, we found associations between cognitive change and individual dietary components, including vitamin E intake from foods, total vitamin C, niacin, folate, fish, and fat composition. When we adjusted for each of these dietary components in separate multiple-adjusted models, there was little difference in the effect estimates except for the models that included terms for vitamin E in food and different types of fat intake. In the

Table 2 Baseline characteristics* of 3,718 participants of the Chicago Health and Aging Project (CHAP)

	Quintiles of total vegetable intake				
	1	2	3	4	5
N	752	750	726	761	729
Total vegetable intake, range, servings/d	0–1.1	1.2–1.7	1.8–2.4	2.5–3.3	3.4–8.2
Age, y, mean	73.8	74.0	74.5	74.5	74.7
Male, %	43.0	39.0	36.9	37.4	32.8
Black, %	75.1	66.3	57.3	51.1	52.5
Education, y, mean	11.3	11.9	12.3	12.5	13.1
Baseline Cognitive Score, mean	0.02	0.14	0.19	0.27	0.29
Cognitive activities, mean frequency	3.0	3.1	3.2	3.3	3.3
Total energy intake, kcal/d	1,300	1,590	1,752	1,903	2,184
Fruit intake, mean servings/d	1.4	1.7	2.2	2.5	3.1
Vitamin E food intake, mean mg/d	5.6	6.1	6.2	6.8	6.8
Vitamin C total intake, mean mg/d	224	226	259	277	293
Saturated fat intake, mean g/d	19.0	19.2	18.8	17.7	16.1
Transunsaturated fat intake, mean g/d	3.6	3.6	3.5	3.3	3.0
Polyunsaturated fat intake, mean g/d	11.0	11.5	11.5	11.5	10.9
Niacin intake, mean mg/d	23.6	27.5	26.3	26.8	27.4
Fish meals per week, mean	1.0	1.3	1.3	1.6	1.9
Physical activity, h/wk	3.0	3.4	3.6	3.8	4.2
Ever smoked, %	54.4	55.0	52.2	54.2	49.9
Stroke, %	9.5	10.0	8.0	7.7	9.6
Myocardial infarction, %	16.0	16.4	16.3	17.6	18.0
Hypertension, %	55.6	56.1	51.5	58.0	54.5
Diabetes, %	17.4	16.1	18.1	15.6	18.4

	Quintiles of fruit intake				
	1	2	3	4	5
N	737	765	751	701	764
Total fruit intake, range, servings/d	0–1.0	1.1–1.6	1.7–2.3	2.4–3.1	3.2–8.5
Age, y, mean	73.5	74.3	74.6	74.6	74.5
Male, %	41.1	40.8	37.6	37.9	31.9
Black, %	71.6	56.8	55.1	54.0	64.4
Education, y, mean	11.3	12.4	12.6	12.6	12.3
Baseline Cognitive Score, mean	0.09	0.22	0.21	0.22	0.17
Cognitive activities, mean frequency	3.0	3.1	3.2	3.2	3.2
Total energy intake, kcal/d	1,402	1,583	1,736	1,899	2,100
Vegetable consumption, mean servings/d	1.5	1.9	2.2	2.7	3.2
Vitamin E food intake, mean mg/d	5.8	6.1	6.5	6.6	6.6
Vitamin C total intake, mean mg/d	178	225	270	278	326
Saturated fat intake, mean g/d	20.1	19.4	18.4	17.3	15.5
Transunsaturated fat intake, mean g/d	3.7	3.7	3.4	3.3	2.9
Polyunsaturated fat intake, mean g/d	11.9	11.8	11.3	11.3	10.2
Niacin intake, mean mg/d	23.1	25.9	26.9	29.5	26.5
Fish meals per week, mean	1.1	1.2	1.4	1.5	1.8
Physical activity, h/wk	3.1	3.3	3.7	3.8	4.2
Ever smoked, %	57.2	56.7	57.2	49.0	45.8
Stroke, %	9.7	8.9	8.4	9.9	8.3
Myocardial infarction, %	13.3	16.3	18.6	17.4	18.6
Hypertension, %	51.6	51.5	55.8	56.3	60.6
Diabetes, %	14.0	17.2	15.8	19.6	19.1

*All variables (except age) are age standardized to the age distribution of the total CHAP population at baseline.

		Quintile of Intake					P-Value
		1	2	3	4	5	for Trend
Vegetable Servings	Median per day	0.8	1.5	2.1	2.8	4.1	
Age-Adjusted Annual Change ^a		-0.043	-0.040	-0.037	-0.029	-0.031	
Difference in Annual Change (p-value)		0 (Referent)	0.003 (.70)	0.006 (.34)	0.014 (.05)	0.012 (.13)	.06
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Multiple-Adjusted Annual Change ^b		-0.046	-0.043	-0.036	-0.030	-0.032	
Difference in Annual Change (p-value)		0 (Referent)	0.003 (.61)	0.010 (.18)	0.016 (.03)	0.014 (.08)	.04
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Fruit Servings	Median per day	0.6	1.4	2.0	2.7	3.9	
Age-Adjusted Annual Change ^a		-0.034	-0.039	-0.038	-0.036	-0.031	
Difference in Annual Change (p-value)		0 (Referent)	-0.004 (.52)	-0.004 (.57)	-0.002 (.81)	0.003 (.68)	.50
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Multiple-Adjusted Annual Change ^b		-0.036	-0.040	-0.041	-0.037	-0.033	
Difference in Annual Change (p-value)		0 (Referent)	-0.004 (.59)	-0.005 (.52)	-0.001 (.87)	0.003 (.70)	.55
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Figure. Annual rates of change and differences in the rates (p value) by quintile of fruit and vegetable intake based on random effects models of 3,718 persons with cognition measured at three time points over 6 years, Chicago Health and Aging Project, 1993–2002. (A) The age-adjusted model includes terms for age, age², total energy intake (linear, squared, and cubic terms), quintiles of fruit/vegetable intake, time, and the interaction between time and each of age, total energy intake (all terms), and quintiles of fruit/vegetable intake. (B) The multiple-adjusted model included terms from the age-adjusted model plus sex, race (black/white), education (years), participation in cognitive activities, physical activity, alcohol consumption (linear and squared terms), interaction terms between sex and age, sex and education, and race and education, two-way interaction terms between time and each covariate, and a three-way interaction term between time, race, and education.

model adjusted for vitamin E, the rate difference for the fifth vs first quintile of vegetable intake was modified to 0.12 and no longer significant. When we adjusted for dietary intakes of saturated (g/day), transunsaturated (g/day), and polyunsaturated fats (g/day) the difference in rate for the fifth quintile of vegetable intake was 0.014 ($p = 0.10$).

We next investigated cognitive decline according to intake of specific types of vegetables and citrus fruits in multiple-adjusted models (table 3). All types of vegetables, except legumes, were inversely associated with cognitive decline. Green leafy vegetables had the highest consumption of all vegetable categories, and also had the strongest linear association (p for linear trend = 0.03). Analyses of each individual fruit and vegetable food item in separate multiple-adjusted models revealed a number of individual foods with statistically significant inverse associations, including zucchini/summer squash/eggplant, broccoli, lettuce/tossed salad, and greens/kale/collards (data not shown).

Discussion. Greater consumption of vegetables was associated with slower rate of cognitive decline over 6 years in this large community-based popula-

tion of older persons. The decrease in rate for persons who consumed greater than two vegetable servings per day was equivalent to about 5 years of younger age. Of the different types of vegetables, green leafy vegetables had the strongest association. Fruit consumption was not associated with cognitive change.

That the relation observed between vegetable consumption and cognitive decline differed markedly from that found for fruit consumption was unanticipated and raises several questions. Probably the most important is whether the data collected are meaningful in addressing this issue. Several considerations provide assurance that they are. The outcome of interest, change in cognitive function, was measured using a global measure of multiple tests administered at multiple time points, thus minimizing bias due to random and non-random error. Vegetable consumption and fruit consumption were well measured as they were each based on reported intake of over 20 different food items. The food frequency questionnaire overall was shown to be a valid measure of intake among CHAP participants, unbiased by age, education, or cognitive ability.⁴ We also

Table 3 Multiple-adjusted differences in the rates of cognitive change (*p* value) by quintile of fruit and vegetable intake based on multiple-adjusted random effects models of 3,718 persons with cognition measured at three time points over 6 years, Chicago Health and Aging Project, 1993–2002

Model	Quintile of intake					<i>p</i> Value trend
	1	2	3	4	5	
Green leafy vegetables						
Servings per day	0.08	0.22	0.36	0.65	1.08	0.03
N	843	873	754	739	709	
Difference in annual change	0	0.009	0.014	0.016	0.018	
<i>p</i> Value	(referent)	(0.19)	(0.04)	(0.03)	(0.02)	
Yellow vegetables						
Servings per day	0.08	0.16	0.28	0.42	0.79	0.34
N	759	800	724	691	744	
Difference in annual change	0	0.012	0.015	0.025	0.011	
<i>p</i> Value	(referent)	(0.08)	(0.04)	(0.0006)	(0.15)	
Cruciferous vegetables						
Servings per day	0	0.08	0.16	0.22	0.43	0.09
N	556	926	1,008	461	777	
Difference in annual change	0	0.004	0.002	0.022	0.12	
<i>p</i> Value	(referent)	(0.56)	(0.76)	(0.01)	(0.14)	
Legumes						
Servings per day	0	0.08	0.16	—	0.22	0.39
N	488	931	1,267		1,032	
Difference in annual change	0	−0.001	0.008	—	0.005	
<i>p</i> Value	(referent)	(0.87)	(0.91)		(0.48)	
Citrus fruits & fruit juices						
Servings per day	0.14	0.65	1.08	1.28	2.08	0.92
N	785	740	693	705	815	
Difference in annual change	0	−0.00	−0.003	0.001	0.001	
<i>p</i> Value	(referent)	(0.98)	(0.67)	(0.93)	(0.82)	

The multiple-adjusted models are described in the figure.

considered the possibility of confounding by some other dietary or lifestyle behavior. This explanation appears unlikely because both fruit and vegetable consumption were associated with factors related to a healthy lifestyle, yet the observed protection against cognitive decline was specific to vegetable and not to fruit consumption. In addition, there was no evidence of modification in the vegetable effect by sex, race, or educational level. It should also be noted that the protective association in the age-adjusted model became stronger with further adjustment for the known important confounders, thus the potential for residual confounding is in the opposite direction of the vegetable association.

A limitation of the study is that a number of participants were not included in the analysis because their dietary questionnaires were obtained midway into the study, or were invalid. Participants who were included in the analyses were somewhat younger and their baseline cognitive scores were somewhat higher than the entire cohort. The fact

that the vegetable association was stronger among the oldest old suggests that this limitation may have resulted in an underestimation of the vegetable effect. A second limitation of the study is that the dietary assessments were not obtained at the baseline for a number of the analyzed participants. Concern that this may have biased the study findings is tempered by the fact that cognitive decline was measured over a 6-year period, and by the fact that there was no change in the estimated effects after control for the date that the dietary assessments were completed. Another limitation of the study is the absence of information on apolipoprotein E (APOE) genotype on the entire cohort for analysis. Some previous studies have found that dietary associations with cognitive conditions vary by APOE status.^{18–20}

Our findings are consistent with those of the Nurses' Health Study,²¹ which found that higher vegetable consumption, but not higher fruit consumption, was associated with significantly less decline in cognitive score over 2 years. However, because these

studies are observational in design, it is always possible that the observed associations are due to residual or unmeasured confounding.

Thus, the observed associations appear to be valid, and possible explanations for these apparently paradoxical results must be considered. Vegetables contain more of vitamin E than do fruits, and this antioxidant nutrient was previously shown to be inversely related to risk of cognitive decline in the CHAP study population.²² This explanation of the findings is supported by the fact that green leafy vegetables (which generally contain more vitamin E than other vegetable types) had the strongest inverse relation with cognitive decline. Vegetables, but not fruits, are also typically consumed with added fats (e.g., salad dressings, mayonnaise, margarine or butter), and fats increase the absorption of vitamin E and other fat soluble antioxidant nutrients, such as carotenoids and flavonoids. Notably, the inverse vegetable association was attenuated and no longer statistically significant when we controlled for intakes of vitamin E in food or different types of fat. And finally, it is possible that some unknown dietary component that is present in fruit may offset the protective effects of antioxidant nutrients.

Fruits and vegetables are rich sources of antioxidant nutrients and bioactive compounds, such as flavonoids, that are thought to be involved in neurodegenerative processes. In a previous study of the CHAP participants, intakes of vitamin E in food and total vitamin C, but not β -carotene,²³ were associated with slower cognitive decline over 3 years. Vitamin E levels in food^{19,24} and plasma²⁵ were found to decrease the risk of incident AD in three prospective studies. The Rotterdam Study found evidence of inverse associations between food intakes of vitamin C, carotenoids, and flavonoids²⁴; however, no such associations were observed in the CHAP study¹⁹ and a study of New York residents.²⁶ Dietary intake of flavonoids was also associated with 50% reduction in risk of 5-year incidence of dementia²⁷ in a French study.

The CHAP study findings are promising that consumption of vegetables including green leafy, yellow, and cruciferous types may protect against age-related cognitive decline. Further study is required to understand the absence of association with fruit consumption, and should include investigation of specific dietary components that are high in citrus and many other fruits.

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