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Colors of Fruit and Vegetables and 10-Year Incidence of Stroke

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Background and Purpose—The color of the edible portion of fruits and vegetables reflects the presence of pigmented bioactive compounds, (eg, carotenoids, anthocyanidins, and flavonoids). Which fruit and vegetable color groups contribute most to the beneficial association of fruit and vegetables with stroke incidence is unknown. Therefore, we examined associations between consumption of fruit and vegetable color groups with 10-year stroke incidence.

Methods—This was a prospective, population-based cohort study, including 20 069 men and women age 20 to 65 years and free of cardiovascular diseases at baseline. Participants completed a validated, 178-item food frequency questionnaire. Hazard ratios (HR) were calculated for stroke incidence using multivariate Cox proportional hazards models adjusting for age, sex, lifestyle, and dietary factors.

Results—During 10 years of follow-up, 233 incident cases of stroke were documented. Fruits and vegetables were classified into 4 color groups. Medians of green, orange/yellow, red/purple, and white fruit and vegetable consumption were 62, 87, 57, and 118 g/d, respectively. Green, orange/yellow, and red/purple fruits and vegetables were not related to incident stroke. Higher intake of white fruits and vegetables was inversely associated with incident stroke (Q4, >171 g/d, versus Q1, ≤78 g/d; HR, 0.48; 95% CI, 0.29–0.77). Each 25-g/d increase in white fruit and vegetable consumption was associated with a 9% lower risk of stroke (HR, 0.91; 95% CI, 0.85–0.97). Apples and pears were the most commonly consumed white fruit and vegetables (55%).

Conclusions—High intake of white fruits and vegetables may protect against stroke. **(*Stroke*. 2011;42:3190-3195.)**

Key Words: fruit ■ vegetables ■ stroke ■ prospective cohort studies ■ epidemiology

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Prospective cohort studies have consistently shown that high consumption of fruits and vegetables lowers risk of stroke.[1,2] Various subgroups of fruits and vegetables contain different micronutrients and phytochemicals.[3] However, which subgroups of fruits and vegetables contribute most to this inverse association remains unclear. Inconsistent results were found for citrus fruit juice,[4,5] berries,[6–8] cruciferous vegetables,[4,8,9] leafy vegetables,[4,9] and root vegetables.[8,9] However, 5 prospective cohort studies found that the intake of citrus fruit was inversely associated with incident stroke.[4,8–11] Apples and pears were inversely, but not significantly, related to incident stroke,[5,10–12] and onions were not associated with stroke incidence.[9,12]

Previous prospective cohort studies used different characteristics to categorize fruits and vegetables, eg, botanical family or part of the plant. However, the beneficial effect of fruits and vegetables may also be caused by combined, or even synergistic, effects of these different components in their natural food matrix.[13] Recently, Pennington and Fisher defined 10 fruit and vegetable subgroups in a novel way based on a combination of their unique nutritional value and characteristics, eg, edible part of the plant, color, botanical family, and total antioxidant capacity.[3,14]

The color of the edible portion of fruits and vegetables reflects the presence of pigmented phytochemicals, eg, carotenoids and flavonoids. Their color could, therefore, be an indicator of their nutrient profile and could be used to group various fruits and vegetables.[3,15] Heber has suggested using fruit and vegetable colors as a tool to translate the science of phytochemical nutrition into dietary guidelines for the public.[16] This has also been acknowledged in the 2010 Dietary Guidelines for Americans, which advises selecting vegetables from 5 subgroups (dark green, red-orange, legumes, starchy, and other vegetables) to reach the recommendation.[17] However, to the best of our knowledge, no prospective studies have yet investigated fruit and vegetable color groups in relation to stroke incidence. In the present study, we investigated the associations of fruit and vegetable color groups with 10-year stroke incidence in a population-based, follow-up study in the Netherlands.

Subjects and Methods

Study Population

The present study was conducted in a Dutch population-based cohort, the Monitoring Project on Risk Factors and Chronic Diseases in the Netherlands (MORGEN Study). Baseline measurements, including dietary assessment, were carried out between 1993 and

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Table 1. Classification of Fruits and Vegetables According to Color Groups*

Color Group	Fruit and Vegetable Subgroup	Proportion of Subgroups to Color Group	Fruit and Vegetable
Green	Cabbages	18%	Broccoli, brussels sprouts, and green cabbages (Chinese, green, oxhear, sauerkraut, savoy, white)
	Dark green leafy vegetables	15%	Kale and spinach
	Lettuces	13%	Endive and lettuce
	Other green fruits and vegetables	54%	French beans, green sweet pepper, honeydew melon, and kiwi fruit
Orange/yellow	Citrus fruits	78%	Citrus fruit juices, grapefruit, orange, and tangerine
	Deep orange fruits and vegetables	22%	Cantaloupe, carrot, carrot juice, and peach
Red/purple	Berries	41%	Cherries, grapes, grape and berry juices, and strawberries
	Red vegetables	59%	Red beet, red beet juice, red cabbage, red sweet pepper, tomato, tomato juice, and tomato sauce
White	Allium family bulbs	10%	Garlic, leek, and onion
	Hard fruits	55%	Apples and pears, apple juice, apple sauce
	Other white fruits and vegetables	35%	Banana, cauliflower, chicory, cucumber, and mushroom

*Fruit and vegetables were classified into subgroups as recently proposed by Pennington and Fisher.[3,14]

1997.[18] The Medical Ethics Committee of the Netherlands Organization for Applied Scientific Research approved the study protocol, and all participants signed informed consent. Of 22 654 participants, we excluded: respondents without informed consent for vital status follow-up (n=701), those who did not fill out a food frequency questionnaire (FFQ; n=72), those with reported total energy intake <500 or >4500 kcal per day for women or <800 or >5000 kcal per day for men (n=97), those with prevalent myocardial infarction or stroke (n=442) and self-reported diabetes, and those using lipid-lowering or antihypertensive drugs (n=1273). This resulted in a study population of 20 069 participants, comprising 8988 men and 11 081 women.

Dietary Assessment

Information on habitual food consumption of 178 food items, covering the previous year, was collected using a validated, self-administered, and semiquantitative FFQ developed for the Dutch cohorts of the European Prospective Investigation into Cancer (EPIC) Study.[19] Participants indicated their consumption as absolute frequencies in times per day, per week, per month, or per year; or as never. For several food items, additional questions were included about consumption frequency of different subitems or preparation method using the following categories: always/mostly, often, sometimes, and seldom/never. Consumed amounts were calculated using standard household measures, natural units, or indicated portion sizes by colored photographs. The photographs showed different portion sizes to assess consumed quantities of 21 food items, mainly vegetables. Frequencies per day and portion sizes were multiplied to obtain grams per day for each food item. The Dutch food composition database of 1996 was used to calculate values for energy.[20]

The FFQ assessed habitual intake of commonly consumed fruits and vegetables, including juices and sauces. Fruit and vegetable consumption during winter and summer was assessed separately to take seasonal variation into account. We did not consider potatoes and legumes to be vegetables, because their nutritional value differs significantly from that of true vegetables.[20]

Reproducibility of the FFQ after 12 months and relative validity of the FFQ against 12 repeated 24-hour recalls for food group and nutrient intake were tested in 63 men and 58 women.[19,21] Reproducibility of the FFQ after 12 months expressed as Spearman correlation coefficients for vegetables was 0.76 in men and 0.65 in women. Reproducibility for fruit intake was 0.61 in men and 0.77 in women. The validity against 12 repeated 24-hour recalls was 0.31 in women and 0.38 in men for vegetables, and 0.56 in women and 0.68 in men for fruit consumption.

In 284 men and 287 women of the MORGEN Study, Jansen et al validated fruit and vegetable intake using plasma carotenoids; they found that intake of several specific fruits and vegetables was associated with plasma levels of specific carotenoids.[22] Participants in the highest quartile of carrot intake showed a 31% higher plasma α-carotene level compared with participants in the lowest quartile. For tomatoes, 26% higher plasma β-carotene and 21% higher plasma lycopene levels were observed. For cabbages, plasma β-carotene levels were 17% higher and plasma lutein levels were 13% higher.

Classification of Fruits and Vegetables

Fruits and vegetables were classified into 4 color groups (Table 1). These were made according to the color of the primarily edible portion; green, orange/yellow, red/purple, and white. The color groups comprised 9 fruit and vegetable subgroups and 2 rest groups as recently proposed by Pennington and Fisher.[3,14] We made small adjustments in the classification of subgroups to make it more compatible with our FFQ. Cabbages were classified according their color as green, red/purple, and white cabbages. Apples and pears are commonly consumed in the Netherlands and are an important source of flavonoids.[23] Therefore, we created the specific subgroup of hard fruits. Several green and white fruits and vegetables that are unique in their micronutrient composition could not be classified into neat groups and were classified into 2 heterogeneous rest groups.

Risk Factors

Baseline measurements were previously described by Verschuren et al.[18] Body weight, height, and blood pressure of the participants were measured by trained research assistants during a physical examination at a municipal health service site. Nonfasting venous blood samples were collected, and serum total and high-density lipoprotein cholesterol concentrations were determined using an enzymatic method. Data on cigarette smoking, educational level, physical activity, use of antihypertensive and lipid-lowering drugs, ever-use of hormone replacement therapy, and both participants' and their parents' history of acute myocardial infarction were obtained by a self-administered questionnaire. Dietary supplement use (yes/no) and alcohol intake were obtained from the FFQ. Alcohol intake was expressed as number of glasses of beer, wine, port wines, and strong liquor consumed per week. Beginning in 1994, physical activity was assessed using a validated questionnaire that was developed for the

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EPIC Study.[24] Physical activity was defined as engaging in at least 5 days per week and ≥30 minutes in activities with an intensity of ≥4 metabolic equivalents.

Ascertainment of Fatal and Nonfatal Events

Data on participants' vital status up to January 1, 2006 was monitored using the municipal population register. Information on the primary cause of death was obtained from Statistics Netherlands. The hospital discharge register provided clinically diagnosed stroke admissions. According to the Dutch guideline for the diagnosis of stroke subtypes,[25] brain imaging (computed tomography or magnetic resonance imaging) is used in Dutch hospitals to identify stroke and its subtypes in 98% of admitted patients.[26] Stroke incidence was defined as the first nonfatal or fatal stroke event, not preceded by any other nonfatal stroke event. Stroke included codes I60–I67, I69, as well as G45 (Transient Ischemic Attack) of the 10th revision of the International Classification of Diseases (ICD-10). For hospital admission data, corresponding ICD-9 codes were used. If the dates of hospital admission and death coincided, the event was considered fatal.

Statistical Analysis

For each participant, we calculated time from date of enrollment until the first event (nonfatal or fatal stroke), date of emigration (n=693), date of death, or censoring date (January 1, 2006), whichever occurred first. We calculated the average consumption of fruits and vegetables that were consumed during summer and winter in grams per day. Quartiles of intake were computed for each fruit and vegetable color group. Hazard ratios (HR) for each category of fruits and vegetables using the lowest category as reference and per 25 grams per day increase in intake were estimated using Cox proportional hazards models. We repeated the analyses for ischemic stroke, but not for hemorrhagic stroke because of the small number of cases. In addition, we analyzed the most commonly consumed white fruits and vegetables (hard fruits) separately. The Cox proportional hazards assumption was fulfilled in all models according to the graphical approach and Schoenfeld residuals. To test P for trend across increasing categories of intake, median values of intake were assigned to each quartile and used as a continuous variable in the Cox models.

Besides an age- (continuous) and sex-adjusted model, we used a multivariate model that included total energy intake (kcal), smoking status (never; former; current smoker of <10, 10–20, or ≥20 cigarettes/d), alcohol intake (never, moderate, or high consumption of >1 glass/d in women and >2 glasses/d in men), educational level (4 categories), dietary supplement use (yes/no), past or present use of hormone replacement therapy (yes/no), family history of acute myocardial infarction before age 55 years of the father or before age 65 years of the mother (yes/no), and body mass index (kg/m^2). In addition, we extended the model with dietary covariates, including intake of whole grain foods (g/d), processed meat (g/d), and fish (quartiles), and mutually for the sum of intake of the other fruit and vegetable color groups or subgroups. Within the subsample of participants enrolled since 1994, we evaluated whether physical activity was a potential confounder (active being defined as engagement in cycling or sports) by comparing HR with and without physical activity in the multivariate model.

Stratified analyses and the log-likelihood test using cross-product terms into the multivariate model showed no evidence for potential effect modification by age (<50 years versus ≥50 years), sex, or smoking status (never versus current). Two-tailed probability values <0.05 were considered statistically significant. Analyses were performed using SAS version 9.1 (SAS Institute).

Results

Participants were, on average, age 42±11 years, and 45% of the population were men. Women had lower educational level, consumed less alcohol, and used dietary supplements more often than did men (Table 2). Women had higher total fruit and vegetable consumption, and lower intake of energy, whole grain foods, and processed meat than did men.

Table 2. Demographic and Lifestyle Characteristics for Men and Women Separately

Characteristic	Men	Women
N	8 988	11 081
Age, y	42.0 (11.0)	41.1 (11.2)
Low educational level*, %	42.0	50.9
Current smokers, %	36.4	36.7
Moderate alcohol consumption†, %	55.6	57.8
High alcohol consumption‡, %	36.1	26.7
Any dietary supplement use, %	23.6	36.7
Physically active§, %	31.9	31.8
Body Mass Index, kg/m^2	25.3 (3.4)	24.5 (4.1)
Serum total cholesterol, mmol/L	5.3 (1.1)	5.2 (1.0)
Serum HDL cholesterol, mmol/L	1.2 (0.3)	1.5 (0.4)
Systolic blood pressure, mm Hg	124 (15)	117 (15)
Family history of AMI‖, %	9.0	9.1
Hormone replacement therapy, %	. . .	8.9
Total energy intake, Kcal/d	2,614 (673)	1,993 (516)
Whole grain foods, g/d	71 (84)	56 (59)
Processed meat, g/d	56 (38)	34 (25)
Fish consumers¶, %	24.7	25.1
Total fruit and vegetables, g/d	341 (185)	393 (184)
Green, g/d	62 (31)	72 (34)
Orange/yellow, g/d	94 (80)	115 (81)
Red/purple, g/d	57 (34)	68 (36)
White, g/d	128 (82)	138 (75)

HDL indicates high-density lipoprotein; AMI, acute myocardial infarction.

*Low educational level is defined as primary school and lower, intermediate general education.

†Moderate alcohol consumption is defined as 0<glass/d≤1 in women and as 0<glass/d≤2 in men.

‡High alcohol consumption is defined as >1 glass/d in women and >2 glasses/d in men.

§Physically active is defined as engagement in cycling or sports of ≥4 metabolic equivalents. In sub sample of participants enrolled from 1994 onwards (n=15,433).

‖Family history of AMI is defined as occurrence of AMI before 55 y of the father or before 65 y of the mother.

¶Fish consumption is defined as the highest quartile of fish intake (median: 17 g/d, i.e. approximately 1 portion of fish per wk).

Participants had an average daily fruit and vegetable intake of 378±193 g/d. The largest contributors to total fruit and vegetable consumption were white (36%) and orange/yellow (29%) fruits and vegetables (Table 1). The most commonly consumed white fruits and vegetables were hard fruits (55%). Orange/yellow fruits and vegetables comprised mainly citrus fruits (78%). Many different fruits and vegetables contributed to green fruits and vegetables, and included cabbages (18%), dark leafy vegetables (15%), and lettuces (13%) as defined subgroups. Red/purple fruits and vegetables comprised mostly red vegetables (59%). Spearman correlation coefficients ranged from 0.42 for white with green fruits and vegetables to 0.60 for white with orange/yellow fruits and vegetables.

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Table 3. Hazard Ratios and 95% Confidence Intervals of Stroke Incidence by Quartiles and per 25-g/d Increase of Fruit and Vegetable Color Group Intake of 20 069 Dutch Participants*

	Quartiles of Fruit and Vegetable Color Group Intake					
Characteristic	Q1†	Q2	Q3	Q4	*P* for Trend	Per 25 g/d Increase
Green						
Median, g/d	34	54	72	105		
Cases, n	48	61	62	62		233
Model 1	1.00	1.19 (0.81–1.73)	1.12 (0.77–1.63)	1.04 (0.71–1.52)	0.93	1.01 (0.92–1.11)
Model 2	1.00	1.26 (0.86–1.85)	1.20 (0.81–1.76)	1.12 (0.76–1.66)	0.79	1.02 (0.93–1.12)
Model 3	1.00	1.30 (0.89–1.91)	1.28 (0.86–1.90)	1.25 (0.83–1.90)	0.41	1.06 (0.95–1.18)
Orange/yellow						
Median, g/d	30	66	110	193		
Cases, n	69	49	58	57		233
Model 1	1.00	0.73 (0.51–1.06)	0.88 (0.62–1.25)	0.84 (0.58–1.19)	0.58	0.99 (0.95–1.03)
Model 2	1.00	0.84 (0.58–1.22)	1.01 (0.70–1.45)	0.99 (0.68–1.44)	0.77	1.01 (0.96–1.05)
Model 3	1.00	0.94 (0.64–1.38)	1.25 (0.84–1.85)	1.37 (0.87–2.14)	0.10	1.04 (0.99–1.10)
Red/purple						
Median, g/d	29	48	67	100		
Cases, n	92	43	45	53		233
Model 1	1.00	0.51 (0.35–0.73)	0.57 (0.40–0.82)	0.70 (0.50–0.99)	0.09	0.93 (0.84–1.03)
Model 2	1.00	0.53 (0.37–0.77)	0.64 (0.44–0.93)	0.80 (0.55–1.15)	0.37	0.97 (0.88–1.08)
Model 3	1.00	0.56 (0.38–0.82)	0.69 (0.46–1.04)	0.90 (0.56–1.45)	0.88	1.02 (0.89–1.17)
White						
Median, g/d	57	98	142	216		
Cases, n	75	62	54	42		233
Model 1	1.00	0.81 (0.58–1.13)	0.71 (0.50–1.00)	0.54 (0.37–0.79)	0.001	0.93 (0.89–0.98)
Model 2	1.00	0.88 (0.62–1.23)	0.78 (0.54–1.13)	0.60 (0.40–0.91)	0.01	0.95 (0.90–0.99)
Model 3	1.00	0.83 (0.59–1.18)	0.70 (0.48–1.04)	0.48 (0.29–0.77)	0.002	0.91 (0.85–0.97)

CI indicates confidence interval; AMI, acute myocardial infarction; BMI, body mass index.

*Hazard ratios (95% CI) were obtained from Cox proportional hazards models. Model 1 was adjusted for age and sex (n=20 069). Model 2 was the same as model 1 with additional adjustments for energy intake (kcal), alcohol intake (3 categories), smoking status (5 categories), educational level (4 categories), dietary supplement use (yes/no), use of hormone replacement therapy (yes/no), family history of AMI (yes/no), body mass index (kg/m^2), (n=19 819). Model 3 was the same as model 2 with additional adjustment for intake of whole grain foods (g/d), processed meat (g/d), fish (quartiles), and mutually for intake of the sum of the other fruit and vegetable color groups (g/d), (n=19 819).

†Reference group.

During an average follow-up period of 10.3 years, 19 fatal and 226 nonfatal stroke cases occurred; of the 19 fatal cases, 12 patients had a nonfatal stroke previously. Two hundred thirty-three first-ever incident strokes remained for the present analysis (139 ischemic, 45 hemorrhagic, and 49 other or unspecified strokes). Green, orange/yellow, and red/purple fruits and vegetables were not related to incident stroke (Table 3). After adjustment for lifestyle and dietary factors, higher consumption of white fruits and vegetables was inversely associated with incident stroke (Q4, >171 g/d; HR, 0.48; 95% CI, 0.29–0.77) compared with participants with low consumption (Q1, ≤78 g/d). We found for each 25-g/d increase of white fruit and vegetable consumption a 9% lower risk of stroke (HR, 0.91; 95% CI, 0.85–0.97). Similar results were found when we repeated the analysis for ischemic stroke, as well as when we stratified by age, sex, or smoking status. In addition, we analyzed apples and pears (55%), the largest contributors of white fruits and vegetables, separately. Each 25-g/d increase in intake of apples and pears was inversely associated with stroke (HR, 0.93; 95% CI, 0.86–1.00).

We evaluated whether physical activity was a potential confounder for white fruits and vegetables with incident stroke within participants enrolled since 1994 (n=15 433). HRs for each 25-g/d increase of white fruit and vegetable consumption was 0.90 (95% CI, 0.84–0.98) and remained similar when physical activity was added to the model (HR, 0.91; 95% CI, 0.84–0.98).

Discussion

In this prospective cohort of healthy Dutch men and women, we found that a higher consumption of white fruits and vegetables was inversely associated with total stroke incidence. Green, orange/yellow, and red/purple fruits and vegetables were not related to incident stroke.

Major strengths of this study include its prospective and population-based study design and large sample size. With respect to nonfatal events, it was shown on the national level

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that data from the Dutch hospital discharge register can be uniquely matched to an individual for at least 88% of hospital admissions.[27] We expect possible misclassification to be random and not to be related to fruit and vegetable consumption. Therefore, the strengths of the associations may have been underestimated. Our findings are based on the combined end point of total stroke. We were unable to perform separate analyses for subtypes of stroke, because of the rather small number of stroke cases. Results of other prospective cohort studies with larger numbers of cases are needed to distinguish between different types of stroke.

We used a detailed FFQ that was primarily designed to measure the consumption of different types of fruits and vegetables. This enabled us to classify fruits and vegetables according to their color. The relative validity of the FFQ for vegetable intake, however, remains of concern.[19] Possible reasons may be the narrower range of vegetable intake or measurement errors in the portion size estimation of vegetables. However, correlation coefficients for vegetable intake were in the same range as those in other studies.[19,28] In addition, Jansen et al found positive associations between plasma concentrations of carotenoids and individual vegetables, eg, α-carotene with carrot intake that added additional strength to the relative validity of our FFQ.[22] Furthermore, some vegetables, eg, onions and cabbages, are commonly used in mixed dishes. This complicates the estimation of intake using a FFQ, and may have led to underestimation of the intake of these vegetables.

We adjusted for potential risk factors as well as for important food groups; nevertheless, we cannot rule out the possibility of residual confounding. However, after adjustment for these confounders, we found similar results in both men and women. This argues against residual confounding, because in men, fruit and vegetable intake is less strongly related to healthy behavior.

Apples and pears were the most commonly consumed white fruits and vegetables, and were inversely associated with incident stroke. This is in line with 4 previous prospective cohort studies that found that apples and pears were inversely related to incident stroke, although not statistically significantly.[5,10–12] Apples are a rich source of dietary fiber ($\approx$2.3 g/100 g) and the flavonol quercetin (3.6 mg/100 g).[20,23] Two meta-analyses of randomized, placebo-controlled intervention studies showed that dietary fiber had a small blood-pressure-lowering effect.[29,30] With regard to flavonols, Hollman et al found in a meta-analysis of 6 prospective cohort studies that high intake of flavonols was associated with a 20% lower risk of incident stroke.[31] Another important contributor to white fruit and vegetable consumption was bananas. To our knowledge, no previous prospective cohort studies have investigated the association between bananas and incident stroke.

The results of the present study suggest that high consumption of white fruit and vegetables, comprising mainly apples and pears, may protect against incident stroke. This is the first prospective cohort study to our knowledge that examined consumption of fruit and vegetable color groups in relation to stroke incidence. However, our findings need to be confirmed in other prospective cohorts studies before recommendations for the consumption of white fruits and vegetables can be made.

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Disclosures

None.

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