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Colours of fruit and vegetables and 10-year incidence of CHD

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Abstract

The colours of the edible part of fruit and vegetables indicate the presence of specific micronutrients and phytochemicals. The extent to which fruit and vegetable colour groups contribute to CHD protection is unknown. We therefore examined the associations between fruit and vegetables of different colours and their subgroups and 10-year CHD incidence. We used data from a prospective population-based cohort including 20 069 men and women aged 20–65 years who were enrolled between 1993 and 1997. Participants were free of CVD at baseline and completed a validated 178-item FFQ. Hazard ratios (HR) for the association between green, orange/yellow, red/purple, white fruit and vegetables and their subgroups with CHD were calculated using multivariable Cox proportional hazards models. During 10 years of follow-up, 245 incident cases of CHD were documented. For each 25 g/d increase in the intake of the sum of all four colours of fruit and vegetables, a borderline significant association with incident CHD was found (HR 0·98; 95 % CI 0·97, 1·01). No clear associations were found for the colour groups separately. However, each 25 g/d increase in the intake of deep orange fruit and vegetables was inversely associated with CHD (HR 0·74; 95 % CI 0·55, 1·00). Carrots, their largest contributor (60 %), were associated with a 32 % lower risk of CHD (HR 0·68; 95 % CI 0·48, 0·98). In conclusion, though no clear associations were found for the four colour groups with CHD, a higher intake of deep orange fruit and vegetables and especially carrots may protect against CHD.

Key words: Fruit: Vegetables: Myocardial infarction: CHD: Prospective cohort studies: Epidemiology

Prospective cohort studies have shown that a high consumption of fruit and vegetables lowers the risk of CHD[1,2]. Various subgroups of fruit and vegetables provide a different array of micronutrients and phytochemicals[3], which may underlie the observed association with CHD. Consistent evidence for subgroups of fruit and vegetables in relation to CHD is lacking since prospective cohort studies have focused on only a limited number of fruit and vegetables that were selected on the basis of their botanical family, content of one specific micronutrient or bioactive compound.

Previous cohort studies have shown inconsistent results for specific fruit and vegetables. Thus, two prospective cohort studies have observed inverse associations between intake of citrus fruit and incident CHD[4,5], while two other studies have not found an association with fatal CHD[6,7]. Intake of berries was found to lower the risk of fatal CVD[7–9], but not the risk of incident CHD in male smokers[10]. Also, two prospective cohort studies have found that apples were not significantly inversely related to fatal CHD[11–13]. Vegetables rich in carotenoids[14], tomatoes and tomato-based products, however, were inversely related to fatal CVD[15] as well as to incident CVD[16]. Carrots were inversely associated with both fatal CHD[17] and fatal CVD[6,15,18]. Cruciferous vegetables were inversely related to incident CHD[4], and broccoli to fatal CHD[13]. With regard to incident CHD only, inverse relationships were observed for intake of green leafy and vitamin C-rich vegetables[4].

Randomised trials focusing on antioxidant supplements have failed to demonstrate a beneficial effect on CVD[19,20]. Although this could be explained by methodological issues, such as a relatively brief follow-up period or the use of high doses of antioxidants, this could also indicate that the protective effect of fruit and vegetables may be due to the combined or even synergistic effects of the various components in their natural food matrix and not to one particular antioxidant[21]. Fruit and vegetable subgroups, therefore, need to be classified according to similarities in micronutrient and phytochemical content. Pennington & Fisher[3,22] defined ten fruit and vegetable subgroups based on their unique nutritional value and characteristics, e.g. edible part of the plant, colour, botanical family or total antioxidant capacity.

Abbreviations: AMI, acute myocardial infarction; HR, hazard ratio.

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The colour of the edible part of fruit and vegetables reflects the presence of pigmented phytochemicals, e.g. carotenoids and flavonoids, and therefore indicates their nutritional value[23]. Drewnowski[24] found that consumers perceive the most colourful vegetables as the most nutritious and suggested that fruit and vegetable colours may be an important factor in food selection. Heber & Bowerman[25] has suggested using fruit and vegetable colours as a tool to translate the science of phytochemical nutrition into dietary guidelines for the public. The 2010 Dietary Guidelines for Americans recommend selecting vegetables from five subgroups, i.e. dark green, red–orange, legumes, starchy and other vegetables to reach the recommendation[26]. However, there have been no prospective cohort studies to date that focus on fruit and vegetable colour groups in relation to incident CHD.

Our investigation, therefore, focuses on the associations of fruit and vegetable colour groups and their subgroups with 10-year CHD incidence in a population-based follow-up study in The Netherlands.

Methods

Population

We used data from the Monitoring Project on Risk Factors and Chronic Diseases in The Netherlands (MORGEN Study), a Dutch population-based cohort[27,28]. The baseline measurements were carried out between 1993 and 1997. The present study was conducted in accordance with the guidelines laid down in the declaration of Helsinki and all procedures involving human subjects were approved by the Medical Ethics Committee of The Netherlands Organisation for Applied Scientific Research. Written informed consent was obtained from all participants. Of the total 22 654 participants, we excluded respondents without informed consent for vital status follow-up (*n* 701), with incomplete dietary assessment (*n* 72), with reported extreme total energy intakes of <2094 or $>18\,844$ kJ/d for women or <3350 or $>20\,938$ kJ/d for men (*n* 97), with a history of myocardial infarction or stroke at baseline (*n* 442) and with self-reported diabetes or use of lipid-lowering or anti-hypertensive drugs (*n* 1273). This resulted in a study population of 20 069 participants, including 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, semi-quantitative FFQ developed for the Dutch cohorts of the European Prospective Investigation into Cancer Study[29]. Participants indicated their consumption as absolute frequencies in times per d, per week, per month, per year or as never. For several food items, additional questions were included about consumption frequency of different sub-items or preparation methods using the following categories: always/mostly, often, sometimes and seldom/never. Consumed amounts were calculated using standard household measures, natural units or portion sizes indicated by coloured photographs. Frequencies per d and portion sizes were multiplied to obtain g/d for each food item. The Dutch food composition database of 1996 was used to calculate values for energy and nutrient intakes[30]. To calculate the intake of carotenoids and flavonoids from fruit and vegetables, the Dutch food composition database of 2001 was used[31].

The FFQ was designed to assess habitual intake during summer and winter of thirty-five commonly used fruit and vegetables in The Netherlands, including juices and sauces. Potatoes and legumes were not included, because their nutritional value differs significantly from that of vegetables[30]. The reproducibility of the FFQ after 12 months and relative validity against twelve repeated 24 h recalls for food group and nutrient intake were tested in sixty-three males and fifty-eight females[29,32]. Reproducibility of the FFQ after 12 months expressed as Spearman's correlation coefficients for vegetables was 0·76 in men and 0·65 in women; for fruit intake, it was 0·61 in men and 0·77 in women. The validity against twelve repeated 24 h recalls over a period of 1 year varied between 0·31 and 0·38 for vegetables, and between 0·56 and 0·68 for fruit.

In 284 men and 287 women of the MORGEN Study, Jansen *et al.*[33] validated fruit and vegetable intake using plasma carotenoids and found that intake of several fruit and vegetable subgroups was positively associated with plasma levels of specific carotenoids. Participants in the highest quartile of carrot intake showed a 31 % higher α-carotene level compared with participants in the lowest quartile. For tomatoes, 26 % higher β-carotene and 21 % higher lycopene levels were observed. For cabbages, β-carotene levels were 17 % higher and lutein levels were 13 % higher.

Classification of fruit and vegetables

Fruit and vegetables were classified into colour groups and subgroups (Table 1). First, we categorised fruit and vegetables into four fruit and vegetable colour groups according to the colour of the primarily edible part: green, orange/yellow, red/purple and white. Second, we subdivided fruit and vegetables within these colour groups, resulting in nine fruit and vegetable subgroups and two groups with 'other' fruit and vegetables, as recently proposed by Pennington & Fisher[3,22]. We made small adjustments in the classification of subgroups to make it more compatible with our FFQ and the Dutch situation. Cabbages were classified according to their colour as green, red/purple and white cabbages. As apples and pears are commonly consumed in The Netherlands and are an important source of flavonoids[34], we created the specific subgroup of hard fruits. Several green and white fruit and vegetables that could not be classified because of their unique micronutrient composition were allocated to an 'other' group.

Risk factors

The baseline measurements were previously described in detail by Verschuren *et al.*[27]. Body weight, height and blood pressure of the participants were measured by trained

Table 1. Classification of fruit and vegetables according to type and colour group*

Colour group	Fruit and vegetable type	Fruit and vegetable items
Green	Cabbages (18 %)	Broccoli, Brussels sprouts and green cabbages (Chinese, green, oxheart, sauerkraut, savoy and white)
	Dark green leafy vegetables (15 %)	Kale and spinach
	Lettuces (13 %)	Endive and lettuce
	Other green fruit 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 fruit 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	Hard fruits (55 %)	Apple, apple juice, apple sauce and pear
	Allium family bulbs (10 %)	Garlic, leek and onion
	Other white fruit and vegetables (35 %)	Banana, cauliflower, chicory, cucumber and mushroom

* Fruit and vegetables were classified into subgroups as proposed by Pennington & Fisher[3,22].

research assistants during a physical examination at a municipal health service site. Non-fasting venous blood samples were collected, and serum total and HDL-cholesterol concentrations were determined using an enzymatic method. Information on cigarette smoking, educational level, physical activity, use of anti-hypertensive and lipid-lowering drugs, past or present use of hormone replacement therapy and the history of acute myocardial infarction (AMI) of the participants' parents were obtained through a self-administered questionnaire. Dietary supplement use (yes/no) and alcohol intake were obtained from the FFQ. Alcohol intake was expressed as the number of glasses of beer, wine, port wines and strong liquor consumed per week. From 1994 onwards, physical activity was assessed using a validated questionnaire that was developed for the European Prospective Investigation into Cancer Study[35]. Physical activity was defined as engaging in cycling and/or sports on at least 5 d/week during ≥30 min with an intensity of ≥4 metabolic equivalents. In this subsample, both cycling and sports were related to CVD[36].

Ascertainment of fatal and non-fatal events

After enrolment, the participants' vital status up to 1 January 2006 was monitored using the municipal population register. For participants who died, information on cause of death was obtained from Statistics Netherlands. The hospital discharge register provided information on clinically diagnosed AMI discharges. CHD incidence was defined as the first non-fatal AMI or fatal CHD event that was not preceded by any other CHD event. Non-fatal AMI comprised code 410 of the 9th revision of the International Classification of Diseases[37]. Fatal CHD included ICD-10 codes I20–I25 as the primary cause of death[38]. Where the dates of hospital admission and death coincided, the event was considered fatal.

Statistical analysis

For each participant, we calculated person time from date of enrolment until the first event (non-fatal AMI or fatal CHD), date of emigration (n 693), date of death or censoring date (1 January 2006), whichever occurred first. The intake of the total of fruit and vegetable colour groups was calculated by summing the intake of fruit and vegetable colour groups. Quartiles of intake were computed for each fruit and vegetable colour group. Tertiles of intake were calculated for each fruit and vegetable type. Hazard ratios (HR) for each category of fruit and vegetables compared with the lowest category and per 25 g/d increase in intake were estimated using Cox proportional hazards models. 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 category and used as a continuous variable in the Cox model.

Besides an age- (continuous) and sex-adjusted model, we used a multivariable model that included total energy intake (continuous), smoking status (never, former, current smoker of <10, 10–20, ≥20 cigarettes/d), alcohol intake (never, moderate and high consumption of more than one glass/d in women and two glasses/d in men), educational level (four categories), dietary supplement use (yes/no), past or present hormone replacement therapy (yes/no), family history of AMI before 55 years of the father or before 65 years of the mother (yes/no) and BMI (kg/m^2). In addition, we extended the model with dietary covariates, including intake of whole-grain foods and processed meat (g/d), fish (quartiles) and mutually for the sum of the intake of the other fruit and vegetable colour groups or subgroups. With regard to the participants enrolled from 1994 onwards, we evaluated whether physical activity was a potential confounder ('active' being defined as engagement in cycling or sports of ≥4 metabolic equivalents). We calculated the HR with and without physical activity in the multivariable model.

According to stratified analyses and the log-likelihood test using cross-product terms in the multivariable model, no evidence was observed for potential effect modification by age (<50 *v.* ≥50 years), sex or smoking status (never *v.* current). P values <0·05 (two-tailed) were considered statistically significant. Analyses were performed using the Statistical Analysis System (version 9.1; SAS Institute, Inc., Cary, NC, USA).

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Results

Participants were 42 (SD 11) years old at baseline and 45 % were male. Women had a higher fruit and vegetable consumption, had a lower educational level, used alcohol less often and used dietary supplements more often than men (Table 2). Women had a lower intake of energy and dietary fibre, but a higher intake of vitamin C and flavonoids than men.

Participants had an average daily fruit and vegetable intake of 378 (SD 193) g/d. The largest contributors to total fruit and vegetable consumption were white (36 %) and orange/yellow (29 %) fruit and vegetables (Table 1). The most commonly consumed items in the white fruit and vegetable range were hard fruits (55 %). Orange/yellow fruit and vegetables comprised citrus fruits (78 %) and deep orange fruit and vegetables (22 %). Green fruit and vegetables consisted of several vegetable subgroups, e.g. cabbages (18 %), dark leafy vegetables (15 %) and lettuces (13 %), and other green fruit and vegetables (54 %). Red/purple fruit and vegetables comprised red vegetables (59 %) and berries (41 %). Spearman's correlation coefficients between fruit and vegetable colour groups ranged from 0·38 for green *v.* orange/yellow fruit and vegetables to 0·60 for orange/yellow *v.* white fruit and vegetables.

After a median follow-up of 10·5 (interquartile range 9·2–11·8) years, we documented 245 incident CHD events, which comprised 211 non-fatal cases of AMI and thirty-four fatal cases of CHD. After adjustment for lifestyle and dietary factors, we observed for each 25 g/d increase in the intake of the sum of green, orange/yellow, red/purple and white fruit and vegetables a borderline significant association with incident CHD (HR 0·98; 95 % CI 0·97, 1·01; Table 3). No clear associations were found between intake of the four fruit and vegetable colour groups separately and incident CHD.

In addition, we analysed the subgroups of fruit and vegetables as proposed by Pennington & Fisher[22]. After adjustment for lifestyle and dietary factors, continuous analysis per 25 g/d increase in the intake of deep orange fruit and vegetables was inversely associated with CHD (HR 0·74; 95 % CI 0·55, 1·00; Table 4). Carrots were the largest contributor to deep orange fruit and vegetables (60 %). Each 25 g/d increase in the intake of carrots was associated with a 32 % lower risk of CHD (HR 0·68; 95 % CI 0·48, 0·98), whereas each 25 g/d increase in the intake of the sum of the other fruit and vegetable subgroups was weakly associated (HR 0·99; 95 % CI 0·97, 1·01). The consumption of the other fruit and vegetable subgroups was not associated with CHD (Table 4).

Table 2. Baseline characteristics of 20 069 Dutch men and women for high and low fruit and vegetable intake
(Mean values and standard deviations or percentages)

	Men				Women			
	Low (*n* 5177)		High (*n* 3811)		Low (*n* 4857)		High (*n* 6224)	
Characteristics	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	42·0	10·8	41·9	11·1	40·7	10·9	41·4	11·4
Low educational level (%)*	44·6		38·5		57·4		45·8	
Current smoking (%)	40·1		36·4		44·0		31·0	
High alcohol consumption (%)†	39·6		31·4		27·0		26·5	
Physically active (%)‡	28·3		36·7		27·3		35·3	
Dietary supplement use (%)	21·6		26·4		33·8		39·0	
Fish consumers (%)§	21·5		29·1		19·8		29·3	
BMI (kg/m^2)	25·3	3·5	25·2	3·3	24·5	4·3	24·5	4·0
Serum total cholesterol (mmol/l)	5·3	1·1	5·2	1·1	5·2	1·0	5·2	1·0
Serum HDL-cholesterol (mmol/l)	1·2	0·3	1·2	0·3	1·5	0·4	1·5	0·4
Systolic blood pressure (mmHg)	124	15	124	15	117	16	117	15
Family history of AMI (%)‖	9·2		9·0		9·3		9·1	
Nutrient intake								
Total energy intake (kJ)	10 559	2696	11 471	2898	7950	2037	8656	2204
SFA (%)	15	3	14	2	15	3	14	2
Dietary fibre (g/d)	25	7	31	8	20	5	25	6
Vitamin C (mg/d)	75	21	138	42	75	20	139	41
Carotenoids (mg/d)	8·1	3·2	11·0	4·4	8·0	3·0	10·9	4·2
Flavonoids (mg/d)	41·9	37·5	57·7	41·3	50·2	43·5	67·0	44·8
Fruit and vegetable intake (g/d)								
Total	225	72	516	176	244	67	525	162
Green	50	23	78	33	54	23	86	34
Orange/yellow	51	31	154	86	57	32	160	79
Red	40	18	80	36	44	18	87	36
White	81	37	191	84	84	34	180	71

AMI, acute myocardial infarction.
* Low educational level is defined as primary school and lower, intermediate general education.
† 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 a subsample of participants enrolled from 1994 onwards (*n* 15 433).
§ Fish consumption is defined as the highest quartile of fish intake (median 17 g/d, i.e. approximately one portion of fish/week).
‖ Family history of AMI is defined as occurrence of AMI before 55 years of the father or before 65 years of the mother.

Table 3. Associations between quartiles (Q) and per 25 g/d increase in fruit and vegetable colour group intake and incident CHD of 20 069 Dutch participants*

(Hazard ratios (HR), 95 % confidence intervals and medians)

	Quartiles of fruit and vegetable colour group intake									
	Q1†	Q2		Q3		Q4			Per 25 g increase	
	HR	HR	95 % CI	HR	95 % CI	HR	95 % CI	*P* for trend	HR	95 % CI
Green										
Median (g/d)	34		54		72		105			
No. of cases	65		60		71		49		245	
Model 1	1·00	0·89	0·63, 1·27	1·02	0·73, 1·44	0·69	0·47, 1·01	0·08	0·91	0·82, 1·01
Model 2	1·00	0·93	0·65, 1·33	1·08	0·76, 1·52	0·74	0·51, 1·09	0·18	0·93	0·84, 1·03
Model 3	1·00	0·95	0·66, 1·37	1·14	0·80, 1·62	0·83	0·55, 1·24	0·47	0·95	0·85, 1·07
Orange/yellow										
Median (g/d)	30		66		110		193			
No. of cases	91		55		58		41		245	
Model 1	1·00	0·66	0·48, 0·93	0·75	0·54, 1·04	0·54	0·37, 0·78	0·003	0·93	0·89, 0·98
Model 2	1·00	0·80	0·56, 1·12	0·88	0·62, 1·24	0·65	0·44, 0·96	0·05	0·95	0·91, 1·00
Model 3	1·00	0·82	0·58, 1·17	0·93	0·63, 1·36	0·70	0·44, 1·12	0·19	0·96	0·91, 1·02
Red/purple										
Median (g/d)	29		48		67		100			
No. of cases	90		62		58		35		245	
Model 1	1·00	0·80	0·58, 1·11	0·85	0·61, 1·18	0·58	0·39, 0·86	0·01	0·86	0·77, 0·95
Model 2	1·00	0·83	0·59, 1·15	0·93	0·66, 1·32	0·63	0·41, 0·96	0·05	0·88	0·78, 0·98
Model 3	1·00	0·86	0·61, 1·21	1·00	0·68, 1·47	0·70	0·41, 1·19	0·29	0·89	0·76, 1·03
White										
Median (g/d)	57		98		142		216			
No. of cases	81		60		48		56		245	
Model 1	1·00	0·77	0·55, 1·08	0·64	0·45, 0·91	0·74	0·52, 1·04	0·07	0·98	0·94, 1·02
Model 2	1·00	0·84	0·59, 1·18	0·73	0·50, 1·06	0·82	0·57, 1·18	0·27	0·99	0·95, 1·03
Model 3	1·00	0·92	0·65, 1·31	0·88	0·59, 1·31	1·11	0·71, 1·74	0·67	1·04	0·99, 1·09
Total of fruit and vegetable colour groups										
Median (g/d)	182		286		395		572			
No. of cases	88		62		51		44		245	
Model 1	1·00	0·79	0·57, 1·09	0·65	0·46, 0·92	0·59	0·41, 0·86	0·003	0·98	0·96, 1·00
Model 2	1·00	0·89	0·64, 1·24	0·77	0·54, 1·11	0·66	0·44, 0·98	0·03	0·98	0·96, 1·00
Model 3	1·00	0·92	0·66, 1·28	0·81	0·56, 1·16	0·70	0·47, 1·04	0·06	0·98	0·97, 1·01

*HR (95 % CI) 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, alcohol intake, smoking status, educational level, dietary supplement use, use of hormone replacement therapy, family history of acute myocardial infarction and BMI (*n* 19 819). Model 3 was the same as model 2 with additional adjustment for intake of whole-grain foods, processed meat, fish and mutually for the sum of the other fruit and vegetable colour groups.

† Reference group.

We evaluated whether physical activity was a potential confounder for the sum of green, orange/yellow, red/purple and white fruit and vegetables with incident CHD for participants enrolled from 1994 onwards (*n* 15 433). HR for each 25 g increase of all fruit and vegetable colour groups was 0·97 (95 % CI 0·95, 0·99) and remained similar when physical activity was added to the model (HR 0·97; 95 % CI 0·95, 1·00).

Discussion

In the present study, we observed that consumption of the four fruit and vegetable colour groups together was weakly related to a lower risk of CHD. A more detailed analysis of fruit and vegetable subgroups, as defined by Pennington & Fisher[3,22], showed that deep orange fruit and vegetables and their largest contributor, carrots, were strongly associated with a lower risk of incident CHD. The inverse relationship of consumption of fruit and vegetable colour groups with incident CHD was attenuated after adjustment for potential confounders.

A major strength of the present study is the almost complete follow-up for CHD mortality. With respect to non-fatal events, it was shown on the national level that data from the Dutch hospital discharge register can be uniquely matched to an individual for at least 88 % of the hospital admissions[39]. In a validation study, 84 % of the AMI cases in the cardiology information system of the University Hospital Maastricht corresponded with AMI cases identified in the hospital discharge register[40]. Mild AMI cases where hospitalisation was not necessary may have been missed, but we expect this to be random and not to be related to fruit and vegetable intake. It is unlikely, therefore, that this has influenced the relationship of fruit and vegetable colour groups with CHD incidence.

A potential limitation of the present study was that some vegetables, such as onions and cabbages, are commonly used in mixed dishes which complicates the estimation of intake using an FFQ. Furthermore, fruit and vegetable intake is part of a healthy lifestyle and diet. Although we adjusted for potential risk factors as well as important food groups in relation to CHD, we cannot rule out residual confounding. In addition, comparing studies on subgroups of fruit and

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Table 4. Associations between tertiles (T) and per 25 g/d increase in fruit and vegetable subgroup intake and incident CHD of 20 069 Dutch participants* (Hazard ratios (HR), 95 % confidence intervals and medians)†

	Tertiles of intake							
	T1‡	T2		T3			Per 25 g increase	
	HR	HR	95 % CI	HR	95 % CI	*P* for trend	HR	95 % CI
Green cabbage family vegetables								
Median (g/d)	5		10		19			
No. of cases	76		84		85		245	
Model 1	1·00	1·08	0·79, 1·48	1·14	0·84, 1·55	0·43	0·96	0·67, 1·39
Model 2	1·00	1·16	0·85, 1·60	1·23	0·90, 1·69	0·22	1·04	0·72, 1·50
Model 3	1·00	1·18	0·86, 1·63	1·26	0·91, 1·73	0·19	1·13	0·78, 1·64
Dark green leafy vegetables								
Median (g/d)	2		8		18			
No. of cases	84		80		81		245	
Model 1	1·00	0·96	0·71, 1·30	1·01	0·75, 1·38	0·89	1·00	0·70, 1·42
Model 2	1·00	0·97	0·71, 1·32	0·93	0·68, 1·27	0·64	0·88	0·62, 1·26
Model 3	1·00	0·97	0·71, 1·33	0·94	0·68, 1·28	0·68	0·89	0·62, 1·27
Lettuce								
Median (g/d)	2		6		16			
No. of cases	77		69		99		245	
Model 1	1·00	0·80	0·58, 1·11	0·96	0·71, 1·30	0·88	0·94	0·68, 1·31
Model 2	1·00	0·84	0·60, 1·17	0·93	0·68, 1·27	0·88	0·87	0·62, 1·21
Model 3	1·00	0·84	0·60, 1·17	0·93	0·68, 1·27	0·89	0·87	0·63, 1·22
Other green fruit and vegetables								
Median (g/d)	17		31		55			
No. of cases	103		78		64		245	
Model 1	1·00	0·71	0·53, 0·96	0·59	0·43, 0·82	0·002	0·82	0·70, 0·97
Model 2	1·00	0·78	0·58, 1·05	0·67	0·48, 0·93	0·02	0·88	0·75, 1·03
Model 3	1·00	0·80	0·59, 1·09	0·73	0·50, 1·06	0·10	0·94	0·78, 1·13
Citrus fruits								
Median (g/d)	21		64		142			
No. of cases	108		74		63		245	
Model 1	1·00	0·79	0·59, 1·07	0·69	0·50, 0·94	0·02	0·94	0·89, 0·99
Model 2	1·00	0·94	0·69, 1·27	0·82	0·59, 1·14	0·24	0·96	0·91, 1·01
Model 3	1·00	1·01	0·73, 1·39	0·94	0·65, 1·37	0·73	0·98	0·92, 1·03
Deep orange fruit and vegetables								
Median (g/d)	9		20		36			
No. of cases	105		77		63		245	
Model 1	1·00	0·73	0·55, 0·99	0·61	0·45, 0·84	0·003	0·65	0·51, 0·83
Model 2	1·00	0·80	0·59, 1·08	0·69	0·50, 0·96	0·03	0·72	0·56, 0·92
Model 3	1·00	0·82	0·60, 1·12	0·75	0·51, 1·09	0·13	0·74	0·55, 1·00
Berries								
Median (g/d)	7		20		44			
No. of cases	105		80		60		245	
Model 1	1·00	0·77	0·58, 1·04	0·61	0·44, 0·84	0·003	0·77	0·65, 0·92
Model 2	1·00	0·84	0·62, 1·13	0·72	0·52, 1·01	0·06	0·84	0·70, 1·00
Model 3	1·00	0·88	0·64, 1·21	0·80	0·53, 1·22	0·32	0·87	0·69, 1·09
Red vegetables								
Median (g/d)	19		33		54			
No. of cases	112		73		60		245	
Model 1	1·00	0·86	0·64, 1·16	0·89	0·64, 1·22	0·44	0·88	0·74, 1·05
Model 2	1·00	0·89	0·65, 1·20	0·91	0·65, 1·27	0·56	0·87	0·73, 1·05
Model 3	1·00	0·95	0·70, 1·30	1·03	0·72, 1·47	0·89	0·93	0·77, 1·12
Allium family bulbs								
Median (g/d)	2		9		21			
No. of cases	94		73		78		245	
Model 1	1·00	0·84	0·62, 1·14	0·93	0·69, 1·26	0·76	0·99	0·78, 1·25
Model 2	1·00	0·90	0·66, 1·23	0·94	0·69, 1·28	0·75	0·89	0·68, 1·16
Model 3	1·00	0·91	0·67, 1·24	0·94	0·69, 1·29	0·77	0·91	0·70, 1·19
Hard fruits								
Median (g/d)	24		60		120			
No. of cases	93		74		78		245	
Model 1	1·00	0·84	0·62, 1·15	0·85	0·63, 1·15	0·34	0·99	0·94, 1·05
Model 2	1·00	0·92	0·67, 1·26	0·96	0·70, 1·33	0·86	1·00	0·95, 1·06
Model 3	1·00	1·03	0·74, 1·42	1·24	0·86, 1·79	0·24	1·05	0·99, 1·11
Other white fruit and vegetables								
Median (g/d)	22		40		70			
No. of cases	101		79		65		245	
Model 1	1·00	0·86	0·64, 1·16	0·73	0·54, 1·00	0·05	0·89	0·78, 1·00
Model 2	1·00	0·94	0·70, 1·28	0·85	0·61, 1·17	0·31	0·93	0·82, 1·05
Model 3	1·00	1·02	0·75, 1·39	0·99	0·68, 1·44	0·95	0·99	0·86, 1·14

* Fruit and vegetables were classified into subgroups as proposed by Pennington & Fisher[3,22].

† HR (95 % CI) 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, alcohol intake, smoking status, educational level, dietary supplement use, use of hormone replacement therapy, family history of acute myocardial infarction and BMI (*n* 19 819). Model 3 was the same as model 2 with additional adjustment for intake of whole-grain foods, processed meat, fish and mutually for the sum of the other fruit and vegetable subgroups.

‡ Reference group.

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vegetables is challenging, since the availability and range of intake of commonly consumed fruit and vegetables differ between countries[41].

In the present study, we found that consumption of the four fruit and vegetable colour groups combined was weakly inversely related to incident CHD. Mixed fruit juices that could not be classified into colour groups were not included in the present analysis. However, we reported previously that the intake of total fruit and vegetables, including mixed fruit juices, was associated with a 6% lower risk of incident CHD in the same population[42]. This finding confirms the results of previous meta-analyses that showed a 4–11% lower risk of CHD for each approximately 100 g/d increase in fruit and vegetable intake[1,2].

After adjustment for lifestyle and dietary factors, we did not observe significant associations of the sum of fruit and vegetable colour groups as well as with the four colour groups separately, with incident CHD. In this respect, the present study may have had insufficient power to detect statistically significant associations. Results of further prospective cohort studies with larger numbers of cases are therefore needed to investigate these associations.

A more detailed analysis of fruit and vegetable colour groups defined by Pennington & Fisher[3,22] showed that intake of deep orange fruit and vegetables was associated with a lower risk of incident CHD. Carrots, the primary source of deep orange fruit and vegetables (60%), were inversely associated with incident CHD, while the intake of the remaining fruit and vegetables was not related. This suggests that the lower CHD risk of total fruit and vegetable intake could be driven by the strong inverse association of carrots, which, is consistent with findings of previous studies with fatal CHD[17] and fatal CVD[6,15,18] as endpoints. Carrots are a rich source of carotenoids[3,30]. Recently, it has been found that serum α-carotene concentrations were inversely associated with IHD mortality among US adults[43]. Circulating carotenoids were also inversely associated with markers of inflammation, oxidative stress and endothelial dysfunction[44] and may protect against early atherosclerosis[45,46]. This suggests that carotenoids may lower CHD risk through different pathways.

In conclusion, we found that consumption of the sum of all four fruit and vegetable colour groups was weakly inversely related to CHD. A more detailed analysis of different colour groups showed that a higher intake of deep orange fruit and vegetables, especially carrots, may protect against incident CHD. Prospective cohort studies with a larger number of cases are needed to replicate these findings.

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References

1. Dauchet L, Amouyel P, Hercberg S, *et al.* (2006) Fruit and vegetable consumption and risk of coronary heart disease: a meta-analysis of cohort studies. *J Nutr* **136**, 2588–2593.
2. He FJ, Nowson CA, Lucas M, *et al.* (2007) Increased consumption of fruit and vegetables is related to a reduced risk of coronary heart disease: meta-analysis of cohort studies. *J Hum Hypertens* **21**, 717–728.
3. Pennington JAT & Fisher RA (2010) Food component profiles for fruit and vegetable subgroups. *J Food Compost Anal* **23**, 411–418.
4. Joshipura KJ, Hu FB, Manson JE, *et al.* (2001) The effect of fruit and vegetable intake on risk for coronary heart disease. *Ann Intern Med* **134**, 1106–1114.
5. Dauchet L, Ferrieres J, Arveiler D, *et al.* (2004) Frequency of fruit and vegetable consumption and coronary heart disease in France and Northern Ireland: the PRIME study. *Br J Nutr* **92**, 963–972.
6. Sahyoun NR, Jacques PF & Russell RM (1996) Carotenoids, vitamins C and E, and mortality in an elderly population. *Am J Epidemiol* **144**, 501–511.
7. Mink PJ, Scrafford CG, Barraj LM, *et al.* (2007) Flavonoid intake and cardiovascular disease mortality: a prospective study in postmenopausal women. *Am J Clin Nutr* **85**, 895–909.
8. Rissanen TH, Voutilainen S, Virtanen JK, *et al.* (2003) Low intake of fruits, berries and vegetables is associated with excess mortality in men: the Kuopio Ischaemic Heart Disease Risk Factor (KIHD) Study. *J Nutr* **133**, 199–204.
9. Sesso HD, Gaziano JM, Jenkins DJA, *et al.* (2007) Strawberry intake, lipids, C-reactive protein, and the risk of cardiovascular disease in women. *J Am Coll Nutr* **26**, 303–310.
10. Hirvonen T, Pietinen P, Virtanen M, *et al.* (2001) Intake of flavonols and flavones and risk of coronary heart disease in male smokers. *Epidemiology* **12**, 62–67.
11. Hertog MG, Feskens EJ, Hollman PC, *et al.* (1993) Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study. *Lancet* **342**, 1007–1011.
12. Knekt P, Järvinen R, Reunanen A, *et al.* (1996) Flavonoid intake and coronary mortality in Finland: a cohort study. *BMJ* **312**, 478–481.

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13. Yochum L, Kushi LH, Meyer K, *et al.* (1999) Dietary flavonoid intake and risk of cardiovascular disease in postmenopausal women. *Am J Epidemiol* **149**, 943–949.
14. Liu S, Lee IM, Ajani U, *et al.* (2001) Intake of vegetables rich in carotenoids and risk of coronary heart disease in men: The Physicians' Health Study. *Int J Epidemiol* **30**, 130–135.
15. Gaziano JM, Manson JE, Branch LG, *et al.* (1995) A prospective study of consumption of carotenoids in fruits and vegetables and decreased cardiovascular mortality in the elderly. *Ann Epidemiol* **5**, 255–260.
16. Sesso HD, Liu S, Gaziano JM, *et al.* (2003) Dietary lycopene, tomato-based food products and cardiovascular disease in women. *J Nutr* **133**, 2336–2341.
17. Mann JI, Appleby PN, Key TJ, *et al.* (1997) Dietary determinants of ischaemic heart disease in health conscious individuals. *Heart* **78**, 450–455.
18. Buijsse B, Feskens EJ, Kwape L, *et al.* (2008) Both alpha- and beta-carotene, but not tocopherols and vitamin C, are inversely related to 15-year cardiovascular mortality in Dutch elderly men. *J Nutr* **138**, 344–350.
19. Vivekananthan DP, Penn MS, Sapp SK, *et al.* (2003) Use of antioxidant vitamins for the prevention of cardiovascular disease: meta-analysis of randomised trials. *Lancet* **361**, 2017–2023.
20. Sesso HD, Buring JE, Christen WG, *et al.* (2008) Vitamins E and C in the prevention of cardiovascular disease in men: the Physicians' Health Study II randomized controlled trial. *JAMA* **300**, 2123–2133.
21. Jacobs DR Jr, Gross MD & Tapsell LC (2009) Food synergy: an operational concept for understanding nutrition. *Am J Clin Nutr* **89**, 1543S–1548S.
22. Pennington JAT & Fisher RA (2009) Classification of fruits and vegetables. *J Food Compost Anal* **22**, S23–S31.
23. Simon PW (1997) Plant pigments for color and nutrition. *HortScience* **32**, 12–13.
24. Drewnowski A (1996) From asparagus to zucchini: mapping cognitive space for vegetable names. *J Am Coll Nutr* **15**, 147–153.
25. Heber D & Bowerman S (2001) Applying science to changing dietary patterns. *J Nutr* **131**, 3078S–3081S.
26. U.S. Department of Health and Human Services & U.S. Department of Agriculture (2010) *Dietary Guidelines for Americans*, 7th ed. Washington, DC: U.S. Government Printing Office.
27. Verschuren WMM, Blokstra A, Picavet HS, *et al.* (2008) Cohort profile: the Doetinchem Cohort Study. *Int J Epidemiol* **37**, 1236–1241.
28. Van Loon AJ, Tijhuis M, Picavet HS, *et al.* (2003) Survey non-response in the Netherlands: effects on prevalence estimates and associations. *Ann Epidemiol* **13**, 105–110.
29. Ocké MC, Bueno-de-Mesquita HB, Goddijn HE, *et al.* (1997) The Dutch EPIC food frequency questionnaire. I. Description of the questionnaire, and relative validity and reproducibility for food groups. *Int J Epidemiol* **26**, Suppl. 1, S37–S48.
30. Dutch food composition database (1996) The Hague. The Netherlands: Netherlands Nutrition Centre (in Dutch).
31. Dutch food composition database (2001) The Hague. The Netherlands: Netherlands Nutrition Centre (in Dutch).
32. Ocké MC, Bueno-de-Mesquita HB, Pols MA, *et al.* (1997) The Dutch EPIC food frequency questionnaire. II. Relative validity and reproducibility for nutrients. *Int J Epidemiol* **26**, Suppl. 1, S49–S58.
33. Jansen MC, Van Kappel AL, Ocké MC, *et al.* (2004) Plasma carotenoid levels in Dutch men and women, and the relation with vegetable and fruit consumption. *Eur J Clin Nutr* **58**, 1386–1395.
34. Hertog MGL, Hollman PC & Katan MB (1992) Content of potentially anticarcinogenic flavonoids of 28 vegetables and 9 fruits commonly consumed in the Netherlands. *J Agric Food Chem* **40**, 2379–2383.
35. Pols MA, Peeters PH, Ocké MC, *et al.* (1997) Estimation of reproducibility and relative validity of the questions included in the EPIC Physical Activity Questionnaire. *Int J Epidemiol* **26**, Suppl. 1, S181–S189.
36. Hoevenaar-Blom MP, Wanda Wendel-Vos GC, Spijkerman AM, *et al.* (2011) Cycling and sports, but not walking, are associated with 10-year cardiovascular disease incidence: the MORGEN Study. *Eur J Cardiovasc Prev Rehabil* **18**, 41–47.
37. World Health Organization (WHO) (1977) *International Classification of Diseases*, 9th revision. Geneva: WHO.
38. World Health Organization (WHO) (1992) *International Classification of Diseases*, 10th revision. Geneva: WHO.
39. De Bruin A, De Bruin EL, Gast A, *et al.* (2003) *Linking data of national ambulant register and GBA data: methods, results and quality research* (in Dutch). Voorburg: Statistics Netherlands.
40. Merry AH, Boer JM, Schouten LJ, *et al.* (2009) Validity of coronary heart diseases and heart failure based on hospital discharge and mortality data in the Netherlands using the cardiovascular registry Maastricht cohort study. *Eur J Epidemiol* **24**, 237–247.
41. Agudo A, Slimani N, Ocké MC, *et al.* (2002) Consumption of vegetables, fruit and other plant foods in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohorts from 10 European countries. *Public Health Nutr* **5**, 1179–1196.
42. Oude Griep LM, Geleijnse JM, Kromhout D, *et al.* (2010) Raw and processed fruit and vegetable consumption and 10-year coronary heart disease incidence in a population-based cohort study in the Netherlands. *PLoS One* **5**, e13609.
43. Li C, Ford ES, Zhao G, *et al.* (2011) Serum α-carotene concentrations and risk of death among US adults: The Third National Health and Nutrition Examination Survey Follow-up Study. *Arch Intern Med* **171**, 507–515.
44. Hozawa A, Jacobs DR Jr, Steffes MW, *et al.* (2007) Relationships of circulating carotenoid concentrations with several markers of inflammation, oxidative stress, and endothelial dysfunction: The Coronary Artery Risk Development in Young Adults (CARDIA)/Young Adult Longitudinal Trends in Antioxidants (YALTA) study. *Clin Chem* **53**, 447–455.
45. Dwyer JH, Navab M, Dwyer KM, *et al.* (2001) Oxygenated carotenoid lutein and progression of early atherosclerosis: the Los Angeles atherosclerosis study. *Circulation* **103**, 2922–2927.
46. Dwyer JH, Paul-Labrador MJ, Fan J, *et al.* (2004) Progression of carotid intima-media thickness and plasma antioxidants: the Los Angeles Atherosclerosis Study. *Arterioscler Thromb Vasc Biol* **24**, 313–319.

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