

## Dietary patterns and CVD: a systematic review and meta-analysis of observational studies

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### Abstract

Epidemiological studies show that diet is linked to the risk of developing CVD. The objective of this meta-analysis was to estimate the association between empirically derived dietary patterns and CVD. PubMed was searched for observational studies of data-driven dietary patterns that reported outcomes of cardiovascular events. The association between dietary patterns and CVD was estimated using a random-effects meta-analysis with 95% CI. Totally, twenty-two observational studies met the inclusion criteria. The pooled relative risk (RR) for CVD, CHD and stroke in a comparison of the highest to the lowest category of prudent/healthy dietary patterns in cohort studies was 0.69 (95% CI 0.60, 0.78;  $I^2 = 0\%$ ), 0.83 (95% CI 0.75, 0.92;  $I^2 = 44.6\%$ ) and 0.86 (95% CI 0.74, 1.01;  $I^2 = 59.5\%$ ), respectively. The pooled RR of CHD in a case-control comparison of the highest to the lowest category of prudent/healthy dietary patterns was 0.71 (95% CI 0.63, 0.80;  $I^2 = 0\%$ ). The pooled RR for CVD, CHD and stroke in a comparison of the highest to the lowest category of western dietary patterns in cohort studies was 1.14 (95% CI 0.92, 1.42;  $I^2 = 56.9\%$ ), 1.03 (95% CI 0.90, 1.17;  $I^2 = 59.4\%$ ) and 1.05 (95% CI 0.91, 1.22;  $I^2 = 27.6\%$ ), respectively; in case-control studies, there was evidence of increased CHD risk. Our results support the evidence of the prudent/healthy pattern as a protective factor for CVD.

**Key words:** Dietary patterns: CVD: Systematic reviews: Meta-analyses

CVD is the world's leading cause of morbidity and mortality, affecting millions of people in developed and developing countries<sup>(1,2)</sup>. In Europe, a decline in CVD deaths has been observed, particularly in affluent countries<sup>(3)</sup>. Analysis from the WHO MONICA (Multinational MONitoring of trends and determinants in Cardiovascular disease) project attributed this lower CVD incidence and more than two-thirds of the decline in CHD deaths to a reduced exposure to risk factors, such as smoking or high blood cholesterol levels<sup>(4)</sup>. Nevertheless, CVD remains the major cause of overall death and premature deaths in Europe, especially in people younger than 75 years, accounting for 42 and 38% of all deaths in women and men, respectively. In addition to 4.3 million deaths every year, there is an enormous individual and societal burden of cardiovascular ill-health<sup>(5)</sup>. Similarly, some studies have found that a large proportion of the decline in mortality – from approximately 44% in the USA, Italy, England and Spain, for example, to as much as 72% in Finland – can be attributed to reduced exposure to risk factors<sup>(6–9)</sup>. The interrelationship between many chronic conditions and their risk factors also means that targeting key CVD risk factors may help prevent cancer and diabetes<sup>(10)</sup>.

Multiple risk factors for CVD, such as family history, obesity, diabetes, hypertension and hypercholesterolaemia, are well established<sup>(11)</sup>. Furthermore, the evolution of the disease depends on how many factors can be modified throughout life. The existing research shows the importance of dietary and lifestyle changes in the prevention of CVD<sup>(12,13)</sup>.

The multiple ways of studying relationships between CVD and diet, specific nutrients, food groups or dietary patterns offer the possibility to study the association of foods and nutrients of a specific type of diet with the risk of disease. The link between diet and the risk of a specific disease can be analysed by evaluating dietary patterns. A technique known as dietary pattern analysis has evolved in nutritional epidemiology as a complementary approach to the study of individual foods. Furthermore, there are two different ways to define dietary patterns: '*a priori*', focusing on the construction of patterns that reflect hypothesis-oriented combinations of foods and nutrients, and '*a posteriori*', which builds on exploratory statistical methods and uses the observed dietary data in order to extract dietary patterns. Both ways show positive and negative aspects; '*a priori*'

**Abbreviation:** RR, relative risk.

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methods are based on predefined diet quality indices, using current nutrition knowledge, and identify a desirable pattern adherence to which could maximise health benefits. On the contrary, ‘*a posteriori*’ methods use dietary data in-hand but might be debatable in relating diet and disease; the extracted dietary patterns may have little relation to morbidity and mortality when nutrients or foods relevant to the aetiology of diseases are not included in their definition. However, focus on ‘*a posteriori*’ dietary patterns helps avoid increased heterogeneity<sup>(14,15)</sup>. Diverse classifications have been used to group the different dietary patterns, primarily categorising them as healthy or prudent *v.* unhealthy or western<sup>(16,17)</sup>. The Mediterranean dietary pattern approach, classified as a prudent or healthy dietary pattern, is one of the best established<sup>(18–21)</sup>. Several studies have reported a weak association between dietary patterns and CVD risk, especially those dietary patterns with high fat, dairy products, fried foods and meat intake classified as western or unhealthy. Our systematic review and meta-analysis complements the latest meta-analysis on this topic by analysing a larger population (610 691 participants), adding studies that identified dietary patterns by cluster analysis and considering not only CVD or stroke mortality but also CVD outcomes such as clinical CVD, CHD, stroke and overall CVD<sup>(22–32)</sup>.

The objective of this study was to systematically review and synthesise the results from observational studies and to clarify

the association between empirically defined (*a posteriori*) dietary patterns and CVD outcomes.

## Methods

### Search strategy

We searched PubMed for relevant studies published through September 2014 using the following combination of Medical Subject Heading (MeSH) terms and text words, with no language limitations: (‘dietary patterns’[All Fields] OR ‘dietary intake’[All Fields]) AND ((‘mortality’[Subheading] OR ‘mortality’[All Fields] OR ‘mortality’[MeSH Terms]) OR (‘myocardial infarction’[MeSH Terms] OR ‘myocardial’[All Fields] AND ‘infarction’[All Fields]) OR ‘myocardial infarction’[All Fields]) OR (‘stroke’[MeSH Terms] OR ‘stroke’[All Fields]) OR (‘peripheral vascular diseases’[MeSH Terms] OR ‘peripheral’[All Fields] AND ‘vascular’[All Fields] AND ‘diseases’[All Fields]) OR ‘peripheral vascular diseases’[All Fields] OR (‘peripheral’[All Fields] AND ‘arterial’[All Fields] AND ‘disease’[All Fields]) OR ‘peripheral arterial disease’[All Fields]) OR ((‘hypertension’[MeSH Terms] OR ‘hypertension’[All Fields]) OR ‘elevated blood pressure’[All Fields]). The search strategy retrieved 1578 citations (Fig. 1). We included all observational studies that assessed the association of dietary patterns analysed by cluster analysis, factor analysis or principal component

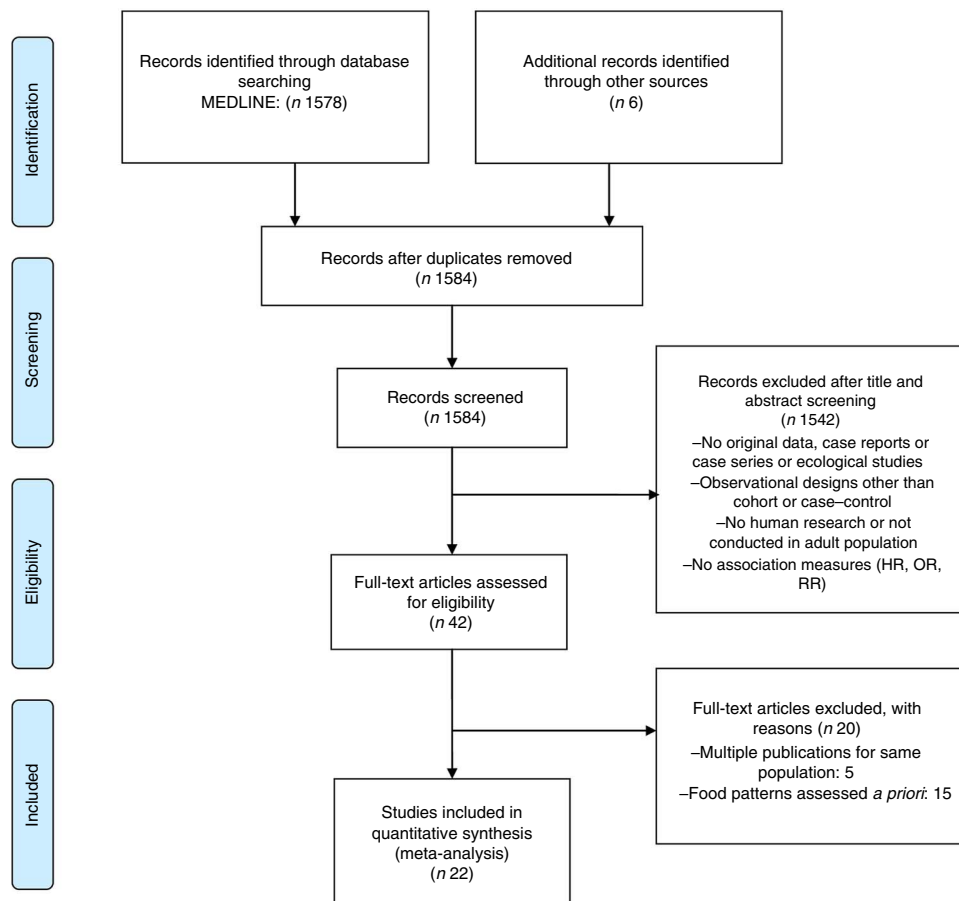


Fig. 1. Flow diagram of the study selection process. HR, hazard ratio; OR, odds ratio; RR, relative risk.

analysis (PCA) with CVD outcomes. We limited the search to clinical CVD, defined *a priori* as CHD (including myocardial infarction and ischaemic heart disease), stroke (cerebrovascular disease and ischaemic stroke) and overall CVD.

Two investigators (M. R.-M and G. F.-M.) independently reviewed each of the 1578 papers identified and applied the following exclusion criteria: (a) no original research (i.e. reviews, editorials, non-research letters); (b) case reports or case series; (c) ecological studies; (d) lack of data on dietary patterns; (e) studies without CVD, cardiovascular death or cardiovascular events as the end point; (f) studies not conducted in humans or adult population; (g) studies without measures of association (hazard ratios, OR, relative risks (RR)); and (h) observational designs other than cohort or case–control. Fig. 1 summarises the study selection process. Any discrepancies were resolved by consensus.

After retrieval of articles from the search, the reference lists of all selected articles were checked for other potentially relevant articles; six additional papers were identified.

### Data extraction and quality assessment

Two investigators (M. R.-M. and G. F.-M.) independently abstracted the articles that met the selection criteria. They resolved discrepancies by consensus. The investigators of the original studies were contacted if relevant information on eligibility or key study data were not available in the published report. The following information was recorded from all studies: study design, geographic region, sex, sample size, dietary assessment method, dietary patterns identified and by which *a posteriori* method, factors adjusted for in each study, outcome and outcome assessment, population age range and follow-up time (cohort studies), naming of patterns, factor loadings per pattern and total variance (Tables 1 and 2, and see online Supplementary Material). Measures of association (OR, RR, hazard ratios) and their 95% CI were abstracted.

We defined those patterns having generally healthy characteristics as prudent/healthy and those patterns having generally less-healthy characteristics as unhealthy/western, on the basis of the food loading reported within individual studies. The prudent/healthy pattern tended to have high-factor loading for food such as fruit, vegetables, whole grains, fish and poultry. The unhealthy/western pattern was characterised by high-factor loadings for foods such as meat, processed meat, refined grains, sweets, sugar drinks and fried foods. When several healthy and unhealthy patterns were reported, we first selected the pattern that explained the maximum of variation in food groups<sup>(25,26,28,31,39)</sup> and then the pattern that fulfilled the most healthy or unhealthy criteria, determined by the highest factor loadings<sup>(30,37,43,44,47)</sup>.

As the studies were observational, the quality assessment was based on the Newcastle–Ottawa Assessment Scale (NOS), using a star system for cohort and case–control studies. The NOS is one of the more comprehensive instruments for assessing the quality of non-randomised studies in meta-analyses. The eight-item instrument consists of three subscales: selection of subjects (four items), comparability of subjects (one item) and assessment of outcome/exposure (three items). High-quality

responses earn a star and the comparability question earns up to two stars, yielding a maximum total of nine stars. The present study dichotomised the NOS scores, considering  $\geq 7$  points an indication of high methodological quality<sup>(33)</sup> (Appendices 1 and 2).

### Statistical analysis

Cohort studies and case–control studies were analysed separately. The results of dietary patterns were variously reported as quintiles, quartiles or dietary factor scores and CVD risk or outcomes. A meta-analysis was conducted to combine the results and evaluate the risk of CVD in the highest compared with the lowest categories of prudent/healthy and western/unhealthy dietary patterns. Heterogeneity was quantified using the  $I^2$  statistic, which describes the proportion of total variation in study estimates that is due to heterogeneity<sup>(34)</sup>. Each study's estimate and SE was used to produce a forest plot that yielded a pooled estimate.

To explore sources of heterogeneity, we performed a subgroup analysis to evaluate whether results differed depending on the number of FFQ items (categorised as median number of <101 or  $\geq 101$  FFQ items or other information source), geographic area (Asia or other countries), *a posteriori* approach (PCA, factor analysis or cluster analysis), sex (men, women or both), sample size (categorised as >40 011 or  $\geq 40 011$  participants, according to median sample size in the meta-analysis), adjustment or non-adjustment for all key confounders (considering as key confounders age, sex, family history of CVD, CHD or stroke, diabetes, hypertension and BMI) and incidence or mortality outcomes. We did not perform subgroup analysis of case–control studies because of the limited number of such studies that reported an association between dietary patterns and CVD outcomes.

Assessment of the relative influence of each study was based on pooled estimates, omitting one study at a time (sensitivity analysis). Finally, publication bias was assessed using the Egger test and funnel plots. Statistical analyses were conducted using the Stata software (version 11; StataCorp LP).

## Results

### Study selection

The search strategy retrieved 1578 articles in the PubMed index. Of these citations, 1542 publications were excluded on the basis of title and abstract and twenty were excluded after full-text review. The remaining twenty-two observational studies, all published between 2000 and 2014, were included in the meta-analysis<sup>(23–31,35–47)</sup> (Fig. 1). The studies were conducted in Europe<sup>(23,26,28,31,38,39,41)</sup>, America<sup>(35,36,40,44,45)</sup>, Asia<sup>(25,27,30,37,43,47)</sup> and Australia<sup>(24)</sup>. There were nineteen cohort studies<sup>(23–31,35–44)</sup> (Table 1) and three case–control studies<sup>(45–47)</sup> (Table 2). The number of cases ranged from 449<sup>(29)</sup> to 74 942<sup>(37)</sup>. All the selected studies assessed total CVD, CVD mortality, CHD and stroke as the end point; Nettleton *et al.*<sup>(42)</sup> also assessed revascularisation. All of these papers met most of the present study's quality criteria (Tables 1 and 2).



**Table 1.** Prospective cohort studies of dietary patterns and CVD (Hazard ratios, risk ratios and 95 % confidence intervals)

References, country	Population	Sample size (sex)	Age range (years)	Outcome ascertainment	Diet-assessment method (items)	Follow-up (years)	Outcome	Hazard ratio/ risk ratio	95 % CI	Dietary pattern identified and method used	Factors adjusted for in analyses	NOS quality score/number of stars/9*
Hu <i>et al.</i> <sup>(35)</sup> , USA	US health professionals	44 875 (men)	40–75	Medical records	FFQ (131)	8	CHD incidence	Prudent Q1:1.0 Q2:0.90 Q3:0.83 Q4:0.79 Q5:0.75 Western Q1:1.0 Q2:1.21 Q3:1.27 Q4:1.27 Q5:1.43	0.74, 1.08 0.68, 1.01 0.64, 0.98 0.59, 0.95 0.98, 1.50 0.99, 1.63 0.99, 1.69 1.01, 2.01	Prudent/ healthy, western/ unhealthy FA	Age, BMI, smoking alcohol consumption, physical activity, parental history of AMI before 60 years, multivitamin and vitamin E supplements use, BP, diabetes, hypercholesterolaemia, total energy and nutrient intake	8
Osler <i>et al.</i> <sup>(23)</sup> , Denmark	Copenhagen county	7316 (both)	30–60	Medical records and National Board of Health Interview, medical records or/and National Death Index	FFQ (26)	1	CHD incidence	–	–	Western-unhealthy FA	Age, sex, BMI, smoking, alcohol consumption, physical activity, education	8
Fung <i>et al.</i> <sup>(36)</sup> , USA	Boston, Nurses' Health Study	71 768 (women)	38–63	Medical records and National Death Index	FFQ (116)	14	Stroke incidence	Prudent Q1:1.0 Q2:0.89 Q3:1.02 Q4:0.85 Q5:0.74 Western Q1:1.0 Q2:1.16 Q3:1.30 Q4:1.26 Q5:1.56 Prudent CHD Q1:1.0 Q2:0.51 Q3:0.91 Q4:1.10 Western CHD Q1:1.0 Q2:0.99 Q3:1.14 Q4:1.58 Prudent stroke Q1:1.0 Q2:1.20 Q3:1.09 Q4:1.35 Western stroke Q1:1.0 Q2:1.03 Q3:0.94 Q4:0.76	0.54, 1.02 1.05, 2.33 0.25, 1.02 0.50, 1.65 0.61, 1.99 0.56, 1.78 0.61, 2.14 0.81, 3.08 0.83, 1.75 0.74, 1.61 0.92, 1.97 0.75, 1.43 0.65, 1.35 0.48, 1.19	Prudent/ healthy, western/ unhealthy FA	Age, BMI, alcohol consumption, smoking, physical activity, family history of AMI, BP, hypercholesterolaemia, diabetes, menopausal status, aspirin use, multivitamin use, food and nutrient intake	8
Cai <i>et al.</i> <sup>(37)</sup> , China	Shanghai Women's Health Study	74 942 (women)	40–70	Medical records and National Death Index	FFQ (71)	5.7	CHD and stroke mortality	Prudent CHD Q1:1.0 Q2:0.51 Q3:0.91 Q4:1.10 Western CHD Q1:1.0 Q2:0.99 Q3:1.14 Q4:1.58 Prudent stroke Q1:1.0 Q2:1.20 Q3:1.09 Q4:1.35 Western stroke Q1:1.0 Q2:1.03 Q3:0.94 Q4:0.76	0.25, 1.02 0.50, 1.65 0.61, 1.99 0.56, 1.78 0.61, 2.14 0.81, 3.08 0.83, 1.75 0.74, 1.61 0.92, 1.97 0.75, 1.43 0.65, 1.35 0.48, 1.19	Prudent/ healthy, western/ unhealthy FA	Age, BMI, smoking, alcohol consumption, physical activity, WHR, education, marital status, income, tea consumption, ginseng intake	8
Harriss <i>et al.</i> <sup>(24)</sup> , Australia	Melbourne Collaborative study	40 653 (both)	40–69	Medical records or/and National Death Index	FFQ (121)	10.4	CVD mortality	Prudent Q1:1.0 Q2:0.92 Q3:0.89 Q4:0.70 Western Q1:1.0 Q2:0.84 Q3:0.99 Q4:0.91	0.75, 1.14 0.69, 1.14 0.51, 0.96 0.67, 1.06 0.79, 1.24 0.70, 1.18	Prudent/ healthy, western/ unhealthy FA	Age, sex, BMI, smoking, physical activity, country of birth, family history of CVD, diabetes and BP, education, social isolation, WHR, energy intake	8

Table 1. Continued

References, country	Population	Sample size (sex)	Age range (years)	Outcome ascertainment	Diet-assessment method (items)	Follow-up (years)	Outcome	Hazard ratio/ risk ratio	95 % CI	Dietary pattern identified and method used	Factors adjusted for in analyses	NOS quality score/number of stars/9*
Shimazu <i>et al.</i> <sup>(24)</sup> , Japan	Ohsaki National Health Insurance study	40 547 (both)	40–79	Death certificates filed	FFQ (40)	7	Stroke and CHD mortality	Prudent CHD Q1:1.0 Q2:0.86 Q3:0.71 Q4:0.82	0.57, 1.29 0.46, 1.11 0.52, 1.29	Prudent/ healthy, western/ unhealthy FA	Age, sex, BMI, smoking, alcohol consumption, walking duration, energy intake, BP, education	9
								Western CHD Q1:1.0 Q2:1.10 Q3:1.39 Q4:1.50	0.72, 1.70 0.89, 2.16 0.95, 2.37			
								Prudent stroke Q1:1.0 Q2:0.71 Q3:0.67 Q4:0.64	0.54, 0.92 0.51, 0.88 0.48, 0.86			
								Western stroke Q1:1.0 Q2:0.89 Q3:1.11 Q4:1.00	0.69, 1.15 0.85, 1.45 0.74, 1.35			
Akesson <i>et al.</i> <sup>(38)</sup> , Sweden	Swedish mammo-graphy cohort	24 444 (women)	43–83	Medical records or/and National Death Index	FFQ (96)	6.2	CHD incidence	Prudent Q1:1.71 Q2:1.50 Q3:1.28 Q4:1.22 Q5:1.0	1.14, 2.55 1.00, 2.25 0.85, 1.94 0.80, 1.84	Prudent/ healthy FA	Age, smoking, alcohol consumption, physical activity, family history of AMI, hypercholesterolaemia, hypertension, hormone therapy use, aspirin use, WHR, energy and nutrient intake, education	8
Brunner <i>et al.</i> <sup>(41)</sup> , UK	Whitehall II study	7731 (both)	50	Medical records or/and National Death Index	FFQ (127)	15	CHD incidence	–	–	Prudent/ healthy CA	Sex, BMI, smoking, physical activity, waist circumference, systolic BP, cholesterol, TAG, employment grade	9
Heidemann <i>et al.</i> <sup>(40)</sup> , USA	Nurses' Health Study	72 113 (women)	30–55	Family reports or/and National Death Index	FFQ (116)	18	CVD mortality	Prudent Q1:1.0 Q2:0.78 Q3:0.85 Q4:0.69 Q5:0.72	0.65, 0.93 0.71, 1.01 0.57, 0.83 0.60, 0.87	Prudent/ healthy, western/ unhealthy FA	Age, BMI, smoking, physical activity, hormone therapy, BP, multivitamin supplement, dietary intake	9
								Western Q1:1.0 Q2:0.98 Q3:1.13 Q4:1.20 Q5:1.22	0.81, 1.19 0.93, 1.36 0.99, 1.45 1.01, 1.48			
Panagiotakos <i>et al.</i> <sup>(39)</sup> , Greece	ATTICA study	3042 (both)	18–89	Medical records	FFQ (156)	5	CVD incidence	–	–	Prudent/ healthy, western/ unhealthy PCA	Age, sex, years of school, physical activity, BP, cholesterol, fasting glucose, diabetes, family history of CHD, BMI, obesity, abnormal waist	9
Nettleton <i>et al.</i> <sup>(42)</sup> , USA	MESA study	5316 (both)	45–84	Medical records and/or National Death Index	FFQ (120)	7	CVD incidence	Prudent Q1:1.0 Q2:0.81 Q3:0.82 Q4:0.67 Q5:0.54	0.52, 1.27 0.52, 1.30 0.41, 1.08 0.33, 0.91	Prudent/ healthy PCA	Age, sex, BMI, smoking, physical activity, ethnicity, supplement use, waist circumference, BP, CRP, IL-6, fibrinogen, homocysteine, HDL, LDL, energy intake, education	8

Table 1. Continued

References, country	Population	Sample size (sex)	Age range (years)	Outcome ascertainment	Diet-assessment method (items)	Follow-up (years)	Outcome	Hazard ratio/risk ratio	95 % CI	Dietary pattern identified and method used	Factors adjusted for in analyses	NOS quality score/number of stars/9*
Guallar-Castillon <i>et al.</i> <sup>(26)</sup> , Spain	EPIC study	40 757 (both)	29–69	Medical records, population-based AMI registries and National Death Index	Interview	11	CHD incidence	Prudent Q1:1.0 Q2:0.77 Q3:0.64 Q4:0.56 Q5:0.73 Western Q1:1.0 Q2:0.96 Q3:0.81 Q4:0.98 Q5:0.86	0.61, 0.98 0.50, 0.83 0.43, 0.73 0.57, 0.94 0.75, 1.24 0.61, 1.09 0.72, 1.34 0.60, 1.24	Prudent/ healthy, western/ unhealthy FA	Age, sex, BMI, smoking, physical activity, diabetes, hypertension, hypercholesterolaemia, cancer, waist circumference, oral contraceptives, menopausal status, hormone therapy, energy and nutrient intake, education	9
Maruyama <i>et al.</i> <sup>(27)</sup> , Japan	JACC study	64 037 (both)	40–79	Medical records and/or National Death Index	FFQ (40)	12.6	Stroke and CHD mortality	Prudent CHD men Q1:1.0 Q2:0.81 Q3:0.77 Q4:0.79 Q5:0.73 Western CHD men Q1:1.0 Q2:0.73 Q3:0.89 Q4:0.72 Q5:0.72 Prudent stroke men Q1:1.0 Q2:1.11 Q3:1.07 Q4:1.19 Q5:1.13 Western stroke men Q1:1.0 Q2:0.79 Q3:0.84 Q4:0.93 Q5:0.97 Prudent CHD women Q1:1.0 Q2:0.87 Q3:0.88 Q4:0.66 Q5:0.67 Western CHD women Q1:1.0 Q2:0.85 Q3:0.93 Q4:0.96 Q5:0.73 Prudent stroke women Q1:1.0 Q2:0.93 Q3:0.80 Q4:0.89 Q5:0.91 Western stroke women Q1:1.0 Q2:0.91 Q3:0.98 Q4:0.87 Q5:1.03	0.56, 1.19 0.53, 1.14 0.54, 1.16 0.49, 1.08 0.51, 1.06 0.63, 1.27 0.49, 1.06 0.48, 1.08 0.83, 1.49 0.80, 1.43 0.90, 1.58 0.85, 1.51 0.61, 1.03 0.65, 1.09 0.71, 1.21 0.74, 1.27 0.57, 1.43 0.57, 1.33 0.42, 1.05 0.43, 1.06 0.57, 1.26 0.61, 1.41 0.61, 1.50 0.42, 1.26 0.70, 1.24 0.59, 1.08 0.66, 1.19 0.68, 1.22 0.70, 1.18 0.75, 1.30 0.64, 1.18 0.75, 1.41	Prudent/ healthy, western- unhealthy FA	Age, sex, BMI, current smoker, physical activity, mental stress, sleep duration, total energy intake, BP and diabetes, education	8

Table 1. Continued

References, country	Population	Sample size (sex)	Age range (years)	Outcome ascertainment	Diet-assessment method (items)	Follow-up (years)	Outcome	Hazard ratio/ risk ratio	95 % CI	Dietary pattern identified and method used	Factors adjusted for in analyses	NOS quality score/number of stars/9*
Stricker <i>et al.</i> <sup>(28)</sup> , The Netherlands	EPIC study	35 910 (both)	20–69	Medical records and/or National Death Index	FFQ (79)	13	Stroke and CHD incidence	Prudent CHD Q1:1.0 Q2:0.99 0.87, 1.12 Q3:0.96 0.85, 1.10 Q4:0.87 0.75, 1.00 Western CHD Q1:1.0 Q2:0.89 0.78, 1.01 Q3:0.94 0.81, 1.09 Q4:0.91 0.76, 1.08 Prudent stroke Q1:1.0 Q2:0.85 0.69, 1.05 Q3:0.78 0.62, 0.98 Q4:0.69 0.53, 0.88 Western stroke Q1:1.0 Q2:0.81 0.65, 1.01 Q3:0.94 0.73, 1.52 Q4:1.11 1.81, 1.52	Prudent/ healthy, western/ unhealthy PCA	Age, sex, BMI smoking, physical activity, energy intake, diabetes, WHR, BP, education	8	
Chen <i>et al.</i> <sup>(43)</sup> , India	HEALS	11 116 (both)	18–75	Proxy reports, medical records,	FFQ (39)	6.6	Stroke and CHD mortality	Prudent CHD Q1:1.0 Q2:1.01 0.57, 1.80 Q3:1.06 0.61, 1.85 Q4:0.79 0.44, 1.40 Western CHD Q1:1.0 Q2:1.38 0.63, 3.04 Q3:1.76 0.84, 3.71 Q4:1.94 0.95, 4.00 Prudent stroke Q1:1.0 Q2:1.88 1.03, 3.46 Q3:0.87 0.43, 1.75 Q4:1.05 0.56, 1.99 Western stroke Q1:1.0 Q2:0.80 0.41, 1.56 Q3:0.69 0.36, 1.36 Q4:0.74 0.39, 1.41	Prudent/ healthy, western/ unhealthy PCA	Age, sex, BMI, current smoker, BP, education, energy intake, own a land, own a television	8	
Judd <i>et al.</i> <sup>(44)</sup> , USA	REGARDS	28 151 (both)	>65	Telephone contact, medical records, National Death Index	FFQ (107)	5.7	Stroke incidence	Prudent Q1:1.0 Q2:0.80 0.62, 1.02 Q3:0.74 0.57, 0.96 Q4:0.85 0.65, 1.12 Western Q1:1.0 Q2:0.93 0.71, 1.22 Q3:1.12 0.86, 1.47 Q4:1.30 0.97, 1.76	Prudent/ healthy, western/ unhealthy PCA	Age, sex, BMI, smoking, sedentary, race, residence, education, income	9	

Table 1. Continued

References, country	Population	Sample size (sex)	Age range (years)	Outcome ascertainment	Diet-assessment method (items)	Follow-up (years)	Outcome	Hazard ratio/ risk ratio	95 % CI	Dietary pattern identified and method used	Factors adjusted for in analyses	NOS quality score/number of stars/9*
Hsiao <i>et al.</i> <sup>(29)</sup> , USA	GRAS	449 (both)	>75	Medical records	Dietary recalls	5	CVD incidence	–		Western-unhealthy CA	Age, sex, BMI, smoking, waist circumference, PASE, prescribed medication, MMSE, GDS, marital status, education	7
Chan <i>et al.</i> <sup>(30)</sup> , China	Osteoporosis Hong Kong	2735 (both)	>65	Medical records	FFQ (280)	2	Stroke incidence	Prudent men		Prudent/healthy, western/unhealthy FA	Age, BMI, smoking, current drinker, PASE, BP, education, energy intake, community ladder	9
								Q2:0.63	0.36, 1.09			
								Q3:0.41	0.22, 0.76			
								Q4:0.70	0.71, 1.20			
								Western men				
								Q1:1.0				
								Q2:0.87	0.49, 1.56			
								Q3:0.86	0.48, 1.55			
								Q4:1.05	0.59, 1.88			
								Prudent women				
								Q1:1.0				
								Q2:0.61	0.28, 1.31			
Q3:0.66	0.30, 1.45											
Q4:0.88	0.43, 1.82											
Western women												
Q1:1.0												
Q2:0.59	0.29, 1.65											
Q3:1.39	0.66, 2.92											
Q4:0.99	0.44, 2.23											
Zazpe <i>et al.</i> <sup>(31)</sup> , Spain	SUN project	16 008 (both)	>18	Medical records and/or National Death Index	FFQ (136)	7	CVD mortality	–		Prudent/healthy, western/unhealthy PCA	Age, sex, current smoker, alcohol consumption, BMI, physical activity, BP, self-report depression, hypercholesterolaemia, special diet, energy and nutrient intake, profession	9

NOS, Newcastle–Ottawa Scale; AMI, acute myocardial infarction; FA, factor analyses; BP, blood pressure; WHR, waist:hip ratio; CA, cluster analyses; MMSE, Mini-Mental State Examination; GDS, Geriatric Depression Scale; PASE, activity score for the elderly; PCA, principal component analyses. Currently, mortality is included; MESA, Multi-Ethnic Study of Atherosclerosis; CRP, C-reactive protein; EPIC, European Prospective Investigation into Cancer and Nutrition; JACC, Japan Collaborative Cohort Study; HEALS, Health Effects of Arsenic Longitudinal Study; REGARDS, Reasons for Geographic and Racial Differences in Stroke; GRAS, Geisinger Rural Aging Study; SUN, Seguimiento Universidad de Navarra.

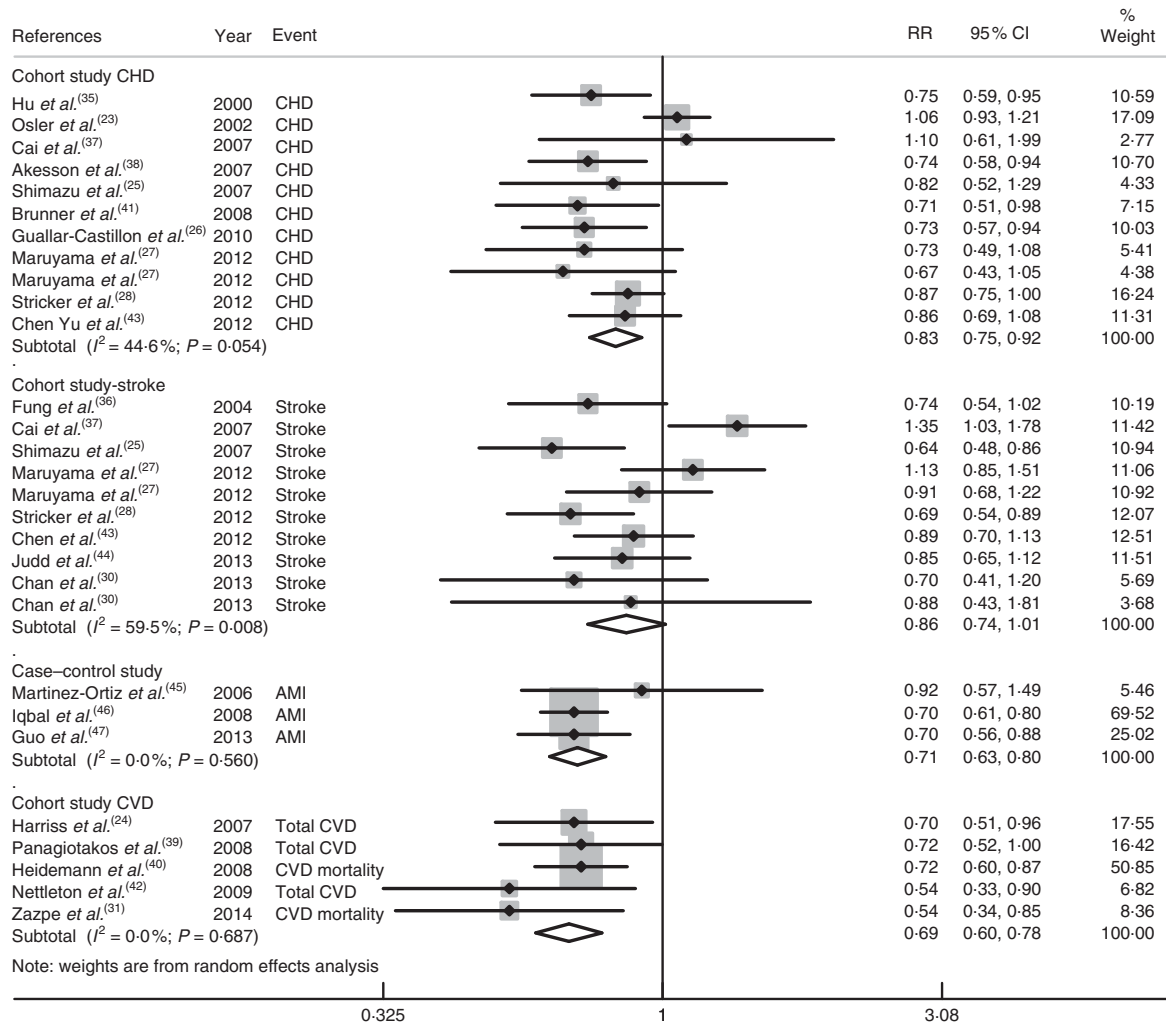
\* Quality assessment of cohort studies with the NOS. The full NOS score is 9 points. Scores  $\geq 7$  were considered high-quality.



**Table 2.** Case-control studies of dietary patterns and CVD (Hazard ratios, risk ratios and 95 % confidence intervals)

References, country	Population (sex)	Age range (years)	Type of controls	Source of cases	Outcome	Number of cases/non-cases	Dietary pattern and method used	Dietary pattern categorisation		Factors adjusted for in analyses	NOS quality score/number of stars (9)*
								Hazard ratio/risk ratio	95 % CI		
Martinez-Ortiz <i>et al.</i> <sup>(45)</sup> , Costa Rica	1062 (both)	≥75	Survivors of a first AMI between 1994 and 1998	Hospital	CHD incidence (AMI)	496/518	Prudent/healthy, western/unhealthy FA	Prudent		Age, sex, current smoker, physical activity, WHR, self-reported history of diabetes, self-reported history of BP, income	7
								Q1:1.0			
								Q2:0.89	0.58, 1.37		
								Q3:1.08	0.69, 1.70		
								Q4:1.17	0.72, 1.92		
								Q5:0.92	0.57, 1.50		
								Western			
								Q1:1.0			
								Q2:2.42	1.44, 4.08		
								Q3:3.55	2.05, 6.15		
Q4:3.21	1.85, 5.57										
Q5:3.53	1.98, 6.31										
Iqbal <i>et al.</i> <sup>(46)</sup> , 52 countries worldwide	16 407 (both)	53–57	General population	Hospital	CHD incidence (AMI)	5761/10 646	Prudent/healthy, western/unhealthy FA	–		Age, sex, BMI, current smoker, alcohol consumption, physical activity, psychosocial factors, education, household income, region, ApoB/ApoA1 tertiles	9
Guo <i>et al.</i> <sup>(47)</sup> , China	1312 (both)	≥18	Survivors of a first AMI	Hospital	CHD incidence (AMI)	1312/2235	Prudent/healthy, western/unhealthy FA	Prudent		Age, sex, BMI, current smoker, alcohol consumption, physical activity, WHR, educational level, marital status, general stress, depression region	7
								Q1:1.0			
								Q2:0.81	0.66, 1.00		
								Q3:0.67	0.54, 0.82		
								Q4:0.70	0.56, 0.88		
								Western			
								Q1:1.0			
								Q2:0.96	0.78, 1.19		
								Q3:0.94	0.75, 1.17		
								Q4:1.36	1.09, 1.69		

NOS, Newcastle–Ottawa Scale; AMI, acute myocardial infarction; FA, factor analyses; WHR, waist:hip ratio; BP, blood pressure.  
 \* Quality assessment of case-control studies with the NOS. The full NOS score is 9 points. Scores ≥7 were considered with high-quality.



**Fig. 2.** Meta-analysis of prudent/healthy dietary pattern and CVD in observational studies. Relative risks (RR) correspond to comparisons of extreme categories of exposure within each study. The area of each square is proportional to the inverse of the variance of the log RR. Horizontal lines represent 95 % confidence intervals. Diamonds represent pooled estimates from inverse-variance-weighted random-effects models. AMI, acute myocardial infarction.

### Meta-analysis of prudent/healthy dietary pattern

Totally, eighteen cohort studies<sup>(23–28,29,31,35–44)</sup> and three case-control studies<sup>(45–47)</sup> were included in the meta-analysis of prudent/healthy dietary pattern and CVD outcomes. Ten cohort studies analysed the association between the prudent/healthy dietary pattern and CHD risk<sup>(23,25–28,35,37,38,41,43)</sup>. Five studies also analysed the association between a prudent/healthy dietary pattern and total CVD risk and CVD mortality<sup>(24,31,39,40,42)</sup>. Eight cohort studies<sup>(25,27,28,30,36,37,43,44)</sup> described the relationship between prudent/healthy dietary pattern and the risk of stroke.

The association between dietary pattern and CVD was estimated using a random-effects meta-analysis with 95 % CI. In all, twenty-one observational studies met the inclusion criteria. Overall, in a comparison of the highest to the lowest category of prudent/healthy dietary patterns in cohort studies, the pooled RR for CVD, CHD and stroke was 0.69 (95 % CI 0.60, 0.78;  $P_{\text{heterogeneity}} = 0.687$ ; and  $I^2 = 0\%$ ), 0.83 (95 % CI 0.75, 0.92;

$P_{\text{heterogeneity}} = 0.054$ ; and  $I^2 = 44.6\%$ ) and 0.86 (95 % CI 0.74, 1.01;  $P_{\text{heterogeneity}} = 0.008$ ;  $I^2 = 59.5\%$ ), respectively. In case-control studies, the pooled RR for CHD was 0.71 (95 % CI 0.63, 0.80;  $P_{\text{heterogeneity}} = 0.560$ ;  $I^2 = 0\%$ ) (Fig. 2).

To further explore the reasons for heterogeneity, we performed subgroup analysis according to sex, geographic area, sample size, number of FFQ items, incidence or mortality outcomes, *a posteriori* approach and adjustments for confounders (Table 3). As shown in Table 4, most subgroups showed no significant association with heterogeneity between dietary patterns and CVD outcomes.

In sensitivity analyses, exclusion of individual studies did not modify the estimates substantially, with pooled RR of CVD, CHD and stroke in cohort studies ranging from 0.65 to 0.70, 0.80 to 0.84 and 0.82 to 0.89, respectively. In case-control studies, the pooled RR of CHD in case-control studies ranged from 0.70 to 0.73. The funnel plot showed reasonable symmetry and a non-significant Egger test for publication bias ( $P = 0.278$ ) (Appendix 3).

**Table 3.** Subgroup analyses for prudent/healthy dietary pattern  
(Pooled relative risk values and 95 % confidence intervals)

	Cohort studies CHD					Cohort studies stroke					Cohort studies CVD				
	Number of studies	Relative risk	95 % CI	Heterogeneity $I^2$ (%) $P$		Number of studies	Relative risk	95 % CI	Heterogeneity $I^2$ (%) $P$		Number of studies	Relative risk	95 % CI	Heterogeneity $I^2$ (%) $P$	
Geographic area															
Other countries	6	0.82	0.71, 0.95	67.3	0.009	3	0.75	0.64, 0.88	0.0	0.541	5	0.69	0.60, 0.78	0.0	0.687
Asia	4	0.82	0.70, 0.96	0.0	0.694	7	0.92	0.75, 1.12	63.3	0.012	–	–	–	–	–
Sample size															
$\geq 40\ 011$	6	0.81	0.73, 0.89	0.0	0.015	5	0.87	0.68, 1.11	76.8	0.069	2	0.71	0.61, 0.84	0.0	0.880
$< 40\ 011$	4	0.85	0.69, 1.04	71.4	0.029	3	0.85	0.72, 1.00	0.0	0.000	3	0.63	0.50, 0.79	0.0	0.489
Incidence or mortality outcome															
Mortality	4	0.82	0.71, 0.96	0.0	0.694	4	0.95	0.75, 1.21	73.5	0.005	3	0.69	0.60, 0.81	0.0	0.521
Incidence	6	0.82	0.71, 0.95	67.3	0.009	4	0.75	0.65, 0.87	0.0	0.831	2	0.66	0.50, 0.87	0.0	0.350
FFQ items															
$\geq 101$ items	3	0.73	0.63, 0.85	0.0	0.964	3	0.79	0.65, 0.95	0.0	0.869	5	0.68	0.60, 0.78	0.0	0.687
$< 101$ items	7	0.87	0.77, 0.98	42.9	0.092	5	0.90	0.72, 1.12	75.3	0.001	–	–	–	–	–
Sex															
Men	2	0.74	0.61, 0.91	0.0	0.909	2	0.94	0.59, 1.48	57.9	0.123	–	–	–	–	–
Women	2	0.81	0.58, 1.15	32.9	0.222	4	0.96	0.71, 1.3	64.8	0.036	2	0.71	0.60, 0.84	0.0	0.772
Both	6	0.86	0.75, 0.98	55.2	0.048	4	0.76	0.65, 0.89	28.2	0.243	4	0.65	0.54, 0.78	0.0	0.631
A posteriori approach															
PCA	3	0.82	0.70, 0.96	57.6	0.021	3	0.80	0.69, 0.94	11.0	0.325	3	0.63	0.50, 0.79	0.0	0.489
FA	6	0.84	0.70, 1.00	64.6	0.015	5	0.89	0.71, 1.12	67.0	0.006	2	0.71	0.61, 0.84	0.0	0.880
CA	1	0.71	0.51, 0.98	–	–	–	–	–	–	–	–	–	–	–	–
Adjustment for key confounding factors*															
Adjusted for all	2	0.74	0.63, 0.88	0.0	0.937	1	0.74	0.53, 1.01	–	–	1	0.72	0.51, 0.99	–	–
Not adjusted	8	0.85	0.76, 0.96	44.1	0.074	7	0.88	0.74, 1.04	62.2	0.007	4	0.68	0.59, 0.79	0.0	0.539

PCA, principal component analysis; FA, factor analysis; CA, cluster analysis.

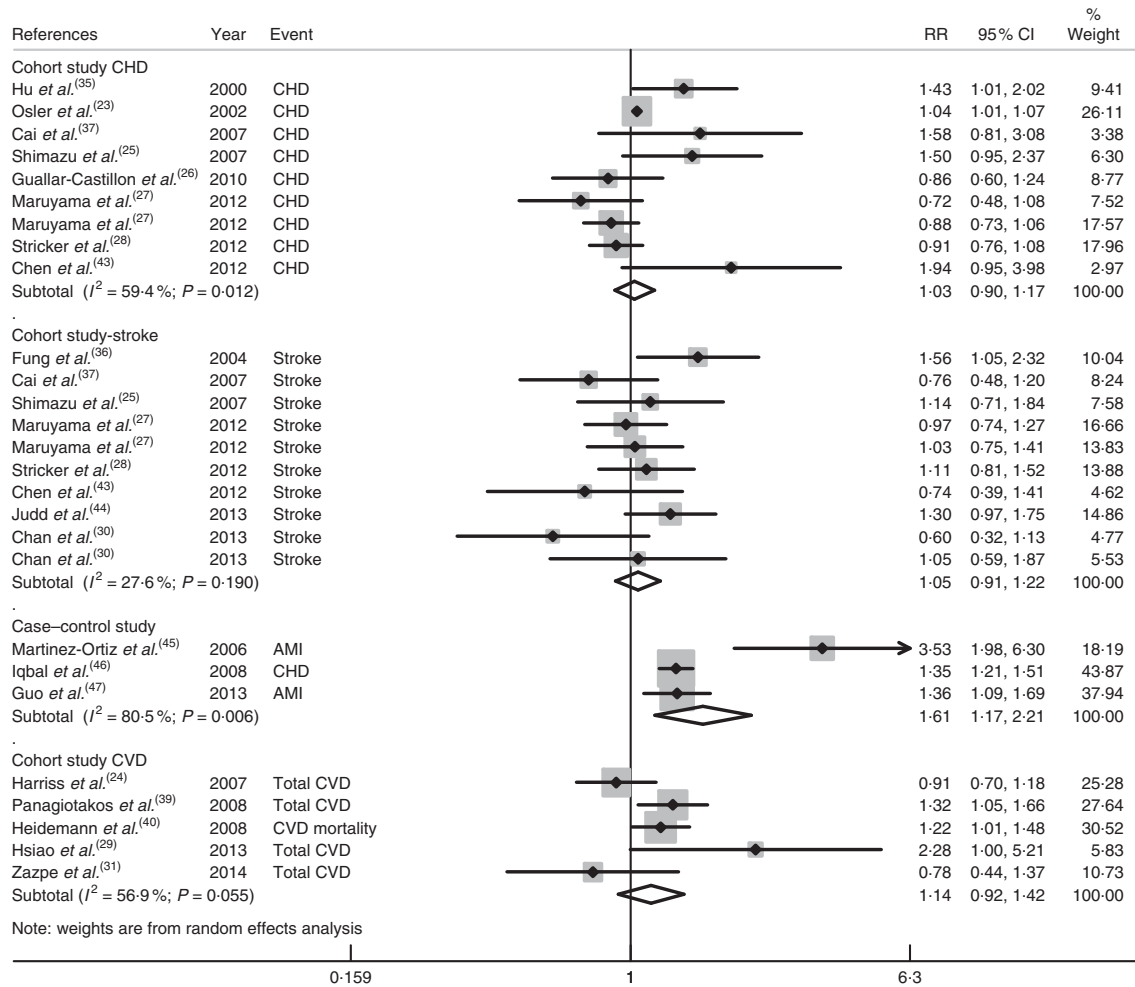
\* Key confounding factors are age, sex, family history of CVD, CHD or stroke, diabetes, hypertension and BMI.

**Table 4.** Subgroup analyses for western/unhealthy dietary pattern (Pooled relative risk values and 95 % confidence intervals)

	Cohort studies CHD					Cohort studies stroke					Cohort studies CVD				
	Number of studies	Relative risk	95 % CI	Heterogeneity <i>I</i> <sup>2</sup> (%) <i>P</i>		Number of studies	Relative risk	95 % CI	Heterogeneity <i>I</i> <sup>2</sup> (%) <i>P</i>		Number of studies	Relative risk	95 % CI	Heterogeneity <i>I</i> <sup>2</sup> (%) <i>P</i>	
Geographic area															
Other countries	4	1.02	0.89, 1.59	54.1	0.088	3	1.28	1.06, 1.55	0.0	0.418	5	1.14	0.92, 1.42	56.9	0.055
Asia	4	1.13	0.81, 1.59	67.5	0.015	5	0.93	0.80, 1.09	0.0	0.616	–	–	–	–	–
Sample size															
≥40 011	6	1.14	0.88, 1.48	62.0	0.032	4	1.05	0.87, 1.27	31.2	0.201	2	1.06	0.80, 1.42	68.3	0.076
<40 011	2	1.27	0.71, 2.26	65.3	0.089	1	1.30	0.96, 1.75	–	–	3	1.25	0.79, 1.98	59.2	0.086
Incidence or mortality outcome															
Mortality	4	1.13	0.80, 1.59	54.1	0.088	4	0.95	0.80, 1.13	0.0	0.674	3	1.01	0.78, 1.31	55.5	0.106
Incidence	4	1.02	0.88, 1.17	67.5	0.015	4	1.15	0.90, 1.47	42.9	0.136	2	1.49	0.95, 2.33	35.8	0.212
FFQ items															
≥101 items	1	1.43	1.01, 2.01	–	–	3	1.14	0.81, 1.60	55.6	0.080	4	1.10	0.90, 1.35	54.9	0.084
<101 items	6	1.00	0.87, 1.16	60.8	0.018	5	0.98	0.85, 1.14	0.0	0.698	–	–	–	–	–
Other information sources	1	0.86	0.59, 1.23	–	–	–	–	–	–	–	1	2.28	0.99, 5.21	–	–
Sex															
Men	2	1.02	0.52, 2.00	84.4	0.011	2	0.91	0.72, 1.17	5.2	0.348	–	–	–	–	–
Women	2	1.07	0.62, 1.85	63.6	0.097	3	1.07	0.74, 1.57	64.6	0.059	1	1.22	1.00, 1.47	–	–
Both	5	1.03	0.88, 1.20	53.5	0.072	4	1.14	0.95, 1.38	0.0	0.474	4	1.12	0.80, 1.56	66.0	0.032
A <i>posteriori</i> approach															
PCA	2	1.22	0.59, 2.52	75.1	0.045	3	1.13	0.89, 1.43	20.2	0.285	3	1.03	0.75, 1.41	69.5	0.053
Factor analysis	6	1.03	0.88, 1.20	59.1	0.023	5	1.01	0.83, 1.22	33.7	0.171	1	1.22	1.00, 1.47	–	–
Cluster analysis	–	–	–	–	–	–	–	–	–	–	1	2.28	0.99, 5.21	–	–
Adjustment for key confounding factors*															
Adjusted for all	1	1.43	1.01, 2.01	–	–	1	1.59	1.04, 2.32	–	–	1	1.32	1.05, 1.66	–	–
Not adjusted	7	0.99	0.86, 1.13	57.0	0.023	7	1.01	0.89, 1.16	5.5	0.389	4	1.08	0.81, 1.45	60.3	0.056

PCA, principal component analysis.

\* Key confounding are age, sex, family history of CVD, CHD or stroke, diabetes, hypertension and BMI.



**Fig. 3.** Meta-analysis of western/unhealthy dietary pattern and CVD in observational studies. Relative risks (RR) correspond to comparisons of extreme categories of exposure within each study. The area of each square is proportional to the inverse of the variance of the log RR. Horizontal lines represent 95% confidence intervals. Diamonds represent pooled estimates from inverse-variance-weighted random-effects models. AMI, acute myocardial infarction.

### Meta-analysis of western/unhealthy dietary pattern

In all, sixteen cohort studies<sup>(23–31,35–37,39,40,43,44)</sup> were included in the meta-analysis of western/unhealthy dietary pattern and CVD. Eight studies<sup>(23,25–28,35,37,43)</sup> analysed the relationship between a western/unhealthy dietary pattern and CHD incidence. Five studies<sup>(24,29,31,39,40)</sup> analysed the relationship between a western/unhealthy dietary pattern and CVD and CVD mortality risk. Eight studies<sup>(25,27,28,30,36,37,43,44)</sup> also analysed the relationship between a western/unhealthy dietary pattern and the risk of stroke. Three case-control studies<sup>(45–47)</sup> were also included.

Totally, nineteen observational studies met the inclusion criteria. Overall, the pooled RR for CVD, CHD and stroke in a comparison of the highest to the lowest category of western/unhealthy dietary patterns in cohort studies was 1.14 (95% CI 0.92, 1.42;  $P_{\text{heterogeneity}} = 0.055$ ; and  $I^2 = 56.9\%$ ), 1.03 (95% CI 0.90, 1.17;  $P_{\text{heterogeneity}} = 0.012$ ; and  $I^2 = 59.4\%$ ) and 1.05 (95% CI 0.91, 1.22;  $P_{\text{heterogeneity}} = 0.190$ ;  $I^2 = 27.6\%$ ), respectively (Fig. 3).

The pooled RR for CHD in case-control studies was 1.61 (95% CI 1.17, 2.21), with statistically significant heterogeneity

between studies ( $P_{\text{heterogeneity}} = 0.006$ ;  $I^2 = 80.5\%$ ). The sensitivity analysis indicates that a single study was the main origin of heterogeneity among studies (forty-five). The heterogeneity decreased ( $I^2 = 0\%$ ;  $P = 0.953$ ) after Martinez study was excluded; however, the association remained was significant (the pooled RR was 1.35 (95% CI 1.22, 1.49)). Other sources of heterogeneity produced only non-significant differences (Table 4).

In sensitivity analyses, exclusion of individual studies did not modify pooled RR substantially: CHD risk ranged from 0.99 to 1.06, stroke risk from 1.01 to 1.08 and CVD risk from 1.08 to 1.23 in cohort studies, and CVD risk ranged from 1.35 to 2.10 in case-control studies. The funnel plot was reasonably symmetric and the Egger test for publication bias did not reach statistical significance ( $P = 0.219$ ) (Appendix 4).

### Discussion

Our meta-analysis evaluated the results from published cohort and case-control studies involving approximately 610 691 participants,

all of which investigated the association between *a posteriori* dietary patterns and CVD. The findings indicated that healthier patterns are associated with a lower risk for all clinical cardiovascular end points, except for stroke. When we pooled the results of cohort or case-control studies, the association between unhealthy/western dietary patterns and an increased risk of CHD, CVD mortality and stroke was not clearly established. Because there was significant heterogeneity among case-control studies, a sensitivity analysis was conducted to explore possible explanations for heterogeneity. After deleting the study that was the main origin of the heterogeneity, the summary ranged from 1.61 (95% CI 1.7, 2.21) to 1.21 (95% CI 1.22, 1.49), which suggested that the association remained significant and our findings were reliable and robust.

Despite a statistically significant association between unhealthy dietary patterns and CVD risk in some studies, the pooled estimation was non-significant. According to our findings, following an unhealthy pattern is not always synonymous with developing CVD. There are several reasons why the unhealthy/western pattern may not necessarily represent the food choices that pose the highest CVD risk. Maruyama *et al.*<sup>(27)</sup> studied an unhealthy pattern defined by milk and dairy products, butter, margarine, fruits, coffee and tea that was protective against stroke risk. Judd *et al.*<sup>(44)</sup> also included a pattern defined by high intake of sweets and saturated fats that was associated with a reduction in stroke risk. In both cases, adherence to that pattern could be associated with a higher risk of cancer or some kind of CHD that might lead to death before a stroke could occur.

The adjusted confounding factors differed in the included studies. All of the studies were adjusted for age and sex. Most of them also were adjusted for BMI, diabetes or hypertension<sup>(24,25,27,28,30,31,38,39,41–43,45,46)</sup>. However, family history as a non-modifiable risk factor for CVD and high cholesterol levels as a modifiable risk factor for CVD<sup>(48)</sup> were not considered<sup>(23,25,27,29–31,37,41–47)</sup>, and it should be taken into account in future research. Only four studies adjusted for all key confounding factors<sup>(35,36,38,39)</sup>. The subgroup analysis by adjusted confounders in CHD cohort studies showed low heterogeneity, but the association remained significant, which confirmed our findings.

We identified two prominent general dietary patterns: a healthy/prudent and an unhealthy/western pattern. Following a healthy or unhealthy dietary pattern is also culturally and socially mediated. The factor loadings per pattern analysis reflected the foods most commonly consumed within the healthy dietary patterns, considering cultural differences. Authors from Asian countries study dietary patterns very divergent from those of Europe or America<sup>(25,27,30,35–37,40,43–45,47)</sup>. In the subgroup analysis by country, the studies conducted in Europe and America showed that the unhealthy/western dietary pattern was a risk factor for stroke but was not associated with CHD, and the pooled results from studies of Asian countries showed a non-significant association. The studies from China or Japan defined other dietary patterns as normal for the general population; for example, Chen *et al.*<sup>(43)</sup> includes a pattern named 'gourd and root vegetable' in China and Shimazu *et al.*<sup>(25)</sup> includes a Japanese dietary pattern represented

by high intake of soyabean products, fish, seaweed, vegetables and green tea.

Many reports have shown that the association of diet with CVD is plausible<sup>(12,49,50)</sup>. One of the most representative examples is the association with cardiovascular risk prevention linked to the Mediterranean dietary pattern, based on fish and plant foods such as fruits, vegetables, cereals, legumes, wholegrain products, nuts and olive oil and the moderate consumption of red wine, along with low consumption of red meat, dairy products and SFA<sup>(19–21)</sup>.

Different biological mechanisms might explain the results of the meta-analysis regarding the effect on CVD outcome of following a healthy or an unhealthy dietary pattern. The prudent/healthy dietary pattern included high-factor loadings for vegetables, fruit, legumes, whole grains, fish and poultry, whereas the western/unhealthy pattern included high-factor loadings for red and processed meat, refined grains, French fries, sweets, desserts, high-fat dairy products and alcohol. The consumption of vegetables and fruits is protective: the more the better, and no upper limit has been found. The higher proposed population goal of 600 g/d is in line with the most recent global population goal proposed by the World Cancer Research Fund in 2009<sup>(51,52)</sup>. Several systematic reviews on this subject<sup>(53,54)</sup> have shown that the consumption of fruit (>2 servings/d, 200 g) and vegetables (>2 servings/d, 200 g) significantly reduces the risk of CHD and stroke. Furthermore, the intake of fruit, vegetables, whole grains and legumes increases the amount of fibre, which can have protective value against CVD<sup>(55,56)</sup>. Antioxidants – such as vitamin C, flavonoids, K and folates – that can be found in fruits and vegetables also might influence the decrease in CVD risk<sup>(50)</sup>.

In addition, oily fish and nuts contain PUFA (*n*-3 fatty acid), which reduce the risk of CHD<sup>(57)</sup>. Some studies have provided evidence that a modest increase (1–2 servings/week) in fish consumption reduces CHD mortality by 36%<sup>(58,59)</sup>, and that 2–4 servings/week can decrease the risk of stroke by 18%<sup>(60)</sup>. Nevertheless, fish was included as a component in the unhealthy pattern in some studies, and related to an increased acute myocardial infarction, stroke and CVD risk<sup>(26,29,43,44,47)</sup>.

On the other hand, the intake of refined grains, deep-fried potatoes, sweets (especially sugar-sweetened soft drinks), desserts and high-fat dairy products increases the amount of saturated and *trans*-saturated fat, dietary sugars and salt consumed. These three dietary components have been shown to directly or indirectly increase CVD risk<sup>(61–63)</sup>. Moderate alcohol consumption might be protective against CVD according to different epidemiological studies because of the content of polyphenols. However, increasing the intake above 10 g/d for women and 20 g/d for men may increase the risk of CVD<sup>(64)</sup>.

According to our results, alcohol seems to have an important role in the studies included in the unhealthy pattern, especially in European and American cultures. According to Zazpe *et al.*<sup>(31)</sup> and Judd *et al.*<sup>(44)</sup>, it was considered a negative predisposing factor.

The main limitation of our study is that factor loadings for individual foods in the different dietary patterns were not identical between the included studies, which may result in a misclassification bias. Descriptions of the factor loadings for

individual food items for the dietary patterns analysed in our meta-analysis were not exactly equal between studies, and included different food items. Despite this, there were similarities in the type of foods that generally featured within the healthy patterns (fruit, vegetables, whole grains, fish and poultry) and the western patterns (meat, processed meat, refined grains, sweets, sugar drinks and fried foods) (see online Supplementary Material)<sup>(32)</sup>. Depending on the predominant factor loadings per food in each pattern, the influence of that pattern would generally be considered healthy or unhealthy. This means that, commonly, dietary patterns mix different kinds of foods, but the ones that are more predominant will define the final influence of that pattern.

Another limitation could be the inclusion of *a posteriori* dietary patterns, which can vary depending on the population and are more complex to standardise and compare across cohorts and population groups.

Confounding factors within the different studies also had an important role in the final results.

Another limitation of this meta-analysis is related to the heterogeneity found. However, this heterogeneity was not explained by the study design, number of FFQ items, geographic area, type of *a posteriori* approach, quality assessment, sex or sample size. Our study population was rather heterogeneous, which can increase residual confounding, biasing the estimate to the null, but it leads to generalisability<sup>(40)</sup>.

Finally, dietary patterns may represent a lifestyle in general and, even the adjustment for known and suspected confounders, residual confounding cannot be ruled out because of the observational nature of the studies included<sup>(65,66)</sup>.

To the best of our knowledge, this is the first meta-analysis of empirically derived dietary patterns to relate dietary patterns and CVD outcomes. Dietary patterns are becoming an essential approach to discovering the association of diet with the risk of a specific pathology. These patterns may be a consequence of cultural and ethnic heritage and of many environmental factors, including the availability of foods, the ability to purchase and prepare foods, the numerous advertisements for foods and the efforts of the government and the nutrition community to foster healthy diets<sup>(16)</sup>.

Four meta-analyses relating dietary patterns to different CVD events are also in line with our results and conclude that, despite a need for further studies to confirm the findings, adherence to a prudent/healthy dietary pattern is associated with a lower risk of CVD mortality but not significantly associated with stroke mortality or CHD risk and, furthermore, that a western/unhealthy dietary pattern is not associated with CHD or stroke mortality<sup>(22,32,67,68)</sup>. Our meta-analysis adds to these findings a similar conclusion about other outcomes such as CVD or stroke incidence and mortality in cohort and case-control studies.

In summary, this meta-analysis strengthens the evidence in support of a prudent/healthy dietary pattern as a protective factor for CVD, especially CHD, but it fails to demonstrate a direct association between adherence to unhealthy dietary patterns and CVD incidence. These results may help reaffirm the clinical advice from health professionals such as physicians, nurses or dietitians in this field.

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M. R.-M. and G. F.-M. formulated the research question, designed the study, carried it out and analysed the data. M. R.-M. and E. S. discussed the results and wrote the paper. All authors contributed to the revision of the manuscript, and read and approved the final version.

There are no conflicts of interest.

## Supplementary material

For supplementary material/s referred to in this article, please visit <http://dx.doi.org/doi:10.1017/S0007114515003177>

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Appendix 1. Quality assessment scheme for cohort studies (Newcastle–Ottawa Scale (NOS))

Study (author and year)							
Selection			Comparability		Outcome		
Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow-up cohorts
★ (a) Truly representative of the average of CVD events in the community	★ (a) Drawn from the same community as the exposed cohort	★ (a) Secure record (e.g. clinical records)	★ (a) Yes	★ (a) Most important adjustment factors (age, sex, BMI, diabetes mellitus, hypertension) ★ (b) Any additional factor (family history, cholesterol levels)	★ (a) Independent blind assessment	★ (a) Yes (minimum of 1 year of follow-up)	★ (a) Complete follow-up – all subjects accounted for
★ (b) Somewhat representative of the average of CVD events in the community	(b) Drawn from a different source	★ (b) Structured interview or questionnaire	(b) No		★ (b) Record linkage	(b) No (<1 year of follow-up)	★ (b) Subjects lost to follow-up unlikely to introduce bias (lost to follow-up ≤5%)
(c) Selected group of users	(c) No description of the derivation of the non-exposed cohort	(c) Written self-report			(c) Self-report		(c) Subjects lost to follow-up >5% and description provided of those lost
(d) No description of the derivation of the cohort		(d) No description			(d) No description		(d) No statement

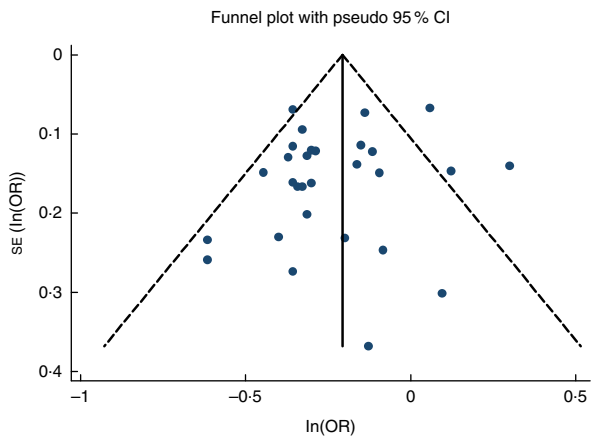
A study can be awarded a maximum of one star for each numbered item within the selection and outcome categories. A maximum of two stars can be given for comparability.

Appendix 2. Quality assessment scheme for case–control studies (Newcastle–Ottawa Scale (NOS))

Study (author and year)							
Selection			Comparability		Exposure		
Is the case definition adequate?	Representativeness of cases	Selection of controls	Definition of controls	Comparability of cohorts on the basis of the design or analysis	Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-response rate
★ (a) Yes, with independent validation	★ (a) Consecutive or obviously representative series of cases	★ (a) Community controls	★ (a) No history of CVD	★ (a) Most important adjustment factors (age, sex, BMI, diabetes mellitus, hypertension) ★ (b) Any additional factor (family history, cholesterol levels)	★ (a) Secure record (e.g. clinical records)	★ (a) Yes	★ (a) Same rate for both groups
(b) Yes, for example, record linkage	(b) Potential for selection biases or not stated	★ (b) Hospital controls	(b) No description of source		★ (b) Structured interview or questionnaire where blind to case–control status	(b) No	(b) Non-respondents described
(c) No description		(c) No description			(c) Interview not blinded to case/control status (d) No description		(c) Rate different and no designation

A study can be awarded a maximum of one star for each numbered item within the selection and outcome categories. A maximum of two stars can be given for comparability.

Appendix 3. Publication bias, prudent/healthy dietary pattern.



Appendix 4. Publication bias, western/unhealthy dietary pattern.

