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Special Article

Dietary pattern analysis and biomarkers of low-grade inflammation: a systematic literature review

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The purpose of the present literature review was to investigate and summarize the current evidence on associations between dietary patterns and biomarkers of inflammation, as derived from epidemiological studies. A systematic literature search was conducted using PubMed, Web of Science, and EMBASE, and a total of 46 studies were included in the review. These studies predominantly applied principal component analysis, factor analysis, reduced rank regression analysis, the Healthy Eating Index, or the Mediterranean Diet Score. No prospective observational study was found. Patterns identified by reduced rank regression as being statistically significantly associated with biomarkers of inflammation were almost all meat-based or "Western" patterns. Studies using principal component analysis or a priori*-defined diet scores found that meat-based or "Western-like" patterns tended to be positively associated with biomarkers of inflammation, predominantly C-reactive protein, while vegetable- and fruit-based or "healthy" patterns tended to be inversely associated. While results of the studies were inconsistent, interventions with presumed healthy diets resulted in reductions of almost all investigated inflammatory biomarkers. In conclusion, prospective studies are warranted to confirm the reported findings and further analyze associations, particularly by investigating dietary patterns as risk factors for changes in inflammatory markers over time.*

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INTRODUCTION

Chronic low-grade inflammation has been hypothesized as an underlying pathophysiological mechanism linking behavioral factors and obesity to chronic disease risk.[1,2] Elevated levels of inflammatory biomarkers such as C-reactive protein (CRP), interleukin (IL) 6 and 18, fibrinogen, and adhesion molecules (e.g., E-selectin, intercellular adhesion molecule 1 [ICAM-1], and vascular cell adhesion protein 1 [VCAM-1]) have been shown to predict type 2 diabetes,[3,4] cardiovascular disease (CVD),[5] and cancer.[6,7] In contrast, concentrations of the anti-inflammatory hormone adiponectin were inversely associated with CVD,[8] type 2 diabetes,[9] and obesity-related cancer.[10]

Dietary intake in relation to low-grade inflammation has been investigated in a number of studies exploring nutrients, foods, or dietary patterns.[11,12] The latter integrate dietary behaviors and have a number of advantages over the single-nutrient or food approach. Taking into account that nutrients or foods are rarely eaten in isolation, dietary patterns consider synergistic or antagonistic biochemical interactions among nutrients as well as different food sources of the same nutrient.[13] To investigate

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dietary patterns, two general approaches have been established in nutritional epidemiology.[13,14] First, the *a priori* or hypothesis-oriented approach, which determines diet scores or indices (e.g., Healthy Eating Index [HEI], Mediterranean Diet Score [MDS]) based on *a priori* assumptions, like dietary recommendations, which could also be applied in interventional studies. Second, the *a posteriori* or exploratory approach, which is a data-driven method identifying dietary patterns through consideration of dietary behaviors in specific study populations. The most commonly applied *a posteriori* approaches are principal component analysis (PCA) and factor analysis (FA), both of which generate results by combining foods that maximally explain the variance in food intake among participants.[15] In contrast, cluster analysis, as a further exploratory method, identifies dietary patterns by grouping individuals according to similarities in their dietary behavior.[13] Reduced rank regression (RRR) analysis presents a statistical data reduction method that combines the *a priori* and *a posteriori* approaches by exploring the dietary data of the study and applying prior knowledge by selecting disease-related response variables (e.g., biomarkers). The dietary patterns identified explain as much variance as possible in the distribution of response variables, e.g., levels of biomarkers.[14]

The aim of the present systematic literature review was to investigate and summarize the current evidence on associations between dietary patterns identified using *a posteriori* and *a priori* approaches and biomarkers of inflammation, as derived from epidemiological studies. Particular emphasis is placed on dietary patterns predicting change in physiological biomarker levels.

METHODS

A systematic literature search was conducted using the databases PubMed, Web of Science, and EMBASE using the following search terms: "dietary pattern," "dietary patterns," "food pattern," "food patterns," "diet score," "diet scores," "diet index," "diet indices," "eating index," "eating indices," "dietary habit," or "dietary habits" in combination with "inflammat*," "C-reactive protein," "CRP," "interleukin," "IL-6," "tumor necrosis factor," "TNF," "adiponectin," "fibrinogen," "E-selectin," "serum amyloid A," "ICAM-1," "intercellular adhesion molecule 1," "VCAM-1," or "vascular cell adhesion protein 1" in all fields.

The titles and abstracts of identified articles were screened by two authors (J.B. and M.K.) to identify the studies meeting the following inclusion criteria: 1) studies describing the association between blood biomarker(s) of chronic inflammation and *a priori* or *a posteriori* dietary pattern(s); 2) observational epidemiological studies or intervention studies based on *a priori*-defined dietary patterns; 3) studies in humans; 4) publication in scientific journals (conference abstracts were excluded); and 5) articles published from January 2000 to January 2012. The full-text articles were retrieved for all eligible studies. The following exclusion criteria were additionally applied: 1) studies based on children, adolescents, or pregnant women (examination of the effects of maternal diet only); 2) studies containing less than 50 participants or an intervention group of less than 50 participants; 3) dietary assessment not based on an FFQ, dietary record, dietary history, or 24-h recall; 4) repeated publication of the same study. In the latter case, the study with the larger sample size or the one providing more information on biomarkers was included. No limitations on the language of the publication were applied. The reference lists of the selected studies were manually reviewed to identify additional articles meeting the eligibility criteria.

The following details were extracted from each study: first author and year of publication; study design; participant characteristics (age, disease status); dietary assessment method; dietary pattern approach; dietary patterns identified or diet scores/indices investigated; associations among dietary patterns; and inflammatory biomarkers in the fully adjusted model.

Dietary habits differ across cultures, and *a posteriori* dietary patterns vary in their compositions and descriptive terms as a result, e.g., "Japanese pattern"[16] or "traditional English pattern."[17] Thus, the compositions of dietary patterns are additionally presented in tables.

Studies restricted to participants with CVD, type 2 diabetes, or other chronic diseases are listed separately because of the generally higher levels of inflammatory biomarkers in participants.

RESULTS

After duplicates were removed, 647 potentially relevant articles were identified (Figure 1). Review of the titles and abstracts revealed 66 publications that met the inclusion criteria. After reading the full texts of articles, 19 studies were removed for meeting one or more of the exclusion criteria. Additionally, three articles used population data previously presented and provided no additional information. From two reports,[18,19] only additional data were extracted, which supplemented previously reported studies. Screening of reference lists led to the inclusion of two additional studies.[20,21] In total, 46 studies were included in the present review.[16–61]

None of the studies applied a prospective observational design to investigate associations between food patterns and changes in biomarker profiles.

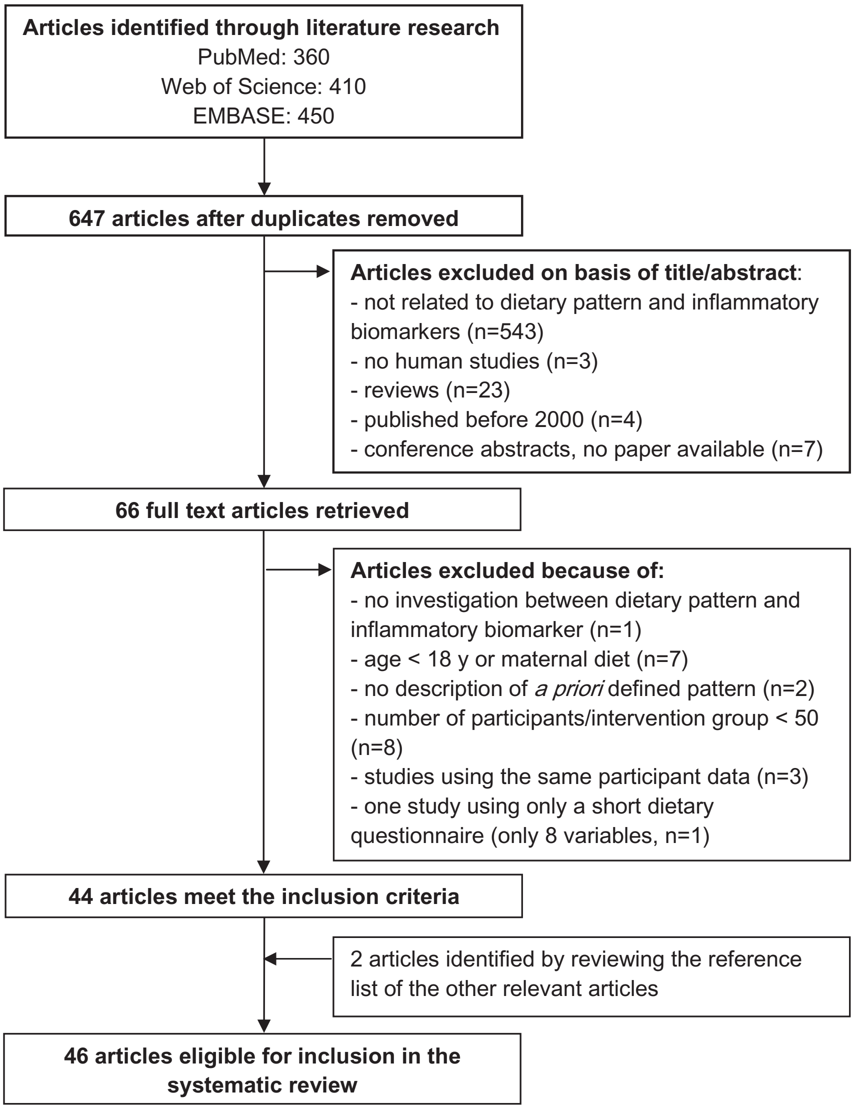

Figure 1 **Flow chart illustrating the literature search and study selection process.**

Dietary patterns identified by reduced rank regression analysis

Seven studies[18,22–27] used RRR analysis to identify food patterns predictive for individual sets of biomarkers; some of these included inflammatory markers only and some additionally examined metabolic markers like high-density lipoprotein or blood glucose (Table 1). CRP, as the most frequently investigated marker of chronic inflammation, was included in six of these studies.[18,22,23,25–27] Explained variation for single biomarkers (where provided) ranged from below 1% (IL-18)[22] to 15% (plasminogen activator inhibitor 1)[24]; for combined markers, the range was from 5.01%[22] to 8%.[24] All but one of the food patterns were positively associated with the biomarkers, and almost all of the associations were statistically significant. These patterns collectively included meat (red meat or processed meat), low-fiber foods (e.g., refined grains), and often alcohol.[18,22–24,26,27] The pattern inversely associated with biomarkers also fit this picture, since it included negative loadings of red meat, beer, and bread, with the exception of whole-grain bread[25]; levels of the anti-inflammatory biomarker adiponectin were positively associated with this food pattern, but CRP was not.[25]

Dietary patterns identified by principal component analysis or factor analysis

Seventeen studies (Table 2) investigated *a posteriori*-defined dietary patterns using PCA or factor analysis.[16,17,20,22,23,28–39] One study additionally applied partial least square analysis.[22] Fourteen of these studies, reported statistically significant findings for at least one pattern.[16,17,22,23,28–35,38,39] Most of the associations were

Table 1 **Summary of studies investigating the associations between inflammatory biomarkers and dietary patterns identified by reduced rank regression analysis.**

Reference	Country	No. and age of participants	Dietary assessment method	Components of the dietary pattern	Response variables	Proportion of explained variance in distribution of biomarkers	Positive (↑), inverse (↓), and no (↔) statistically significanto associations (r)
Meyer et al. (2011)[22]	Germany	981 men 45–64 years	7-day dietary record	Positive factor loadings for beer, meat (except poultry); negative loadings for sweet bread spread, fresh fruit, cake and pastries, whole-meal bread, condensed milk and cream, fresh vegetables, curd, chocolates, cereals and muesli, butter, nuts, tea, cooked vegetables, cheese	IL-6, IL-18, CRP	Total: 5.01% IL-6: 3.86% IL-18: 0.06% CRP: 11.11%	IL-6↑ (0.27[a]) IL-18↑ (0.08[a]) CRP↑ (0.33[a])
Centritto et al. (2009)[23]	Italy	7,646 participants ≥35 years	FFQ	Positive loadings for wine, pasta/other grains, bread, animal fat, beer, red meat; negative loadings for breakfast cereals, yogurt, sugar and sweets	HDL, triglycerides, SBP, blood glucose, CRP	Total: 6%	CRP↑ (n.a.)
Liese et al. (2009)[24]	USA	880 participants 40–69 years	FFQ	Positive loadings for red meats, low-fiber bread and cereal, dried beans, fried potatoes, tomato vegetables, eggs, cheese, cottage cheese; negative loadings for wine	PAI-1, fibrinogen	Total: 8% PAI-1: 15% fibrinogen: 1%	PAI-1↑ (n.a.) Fibrinogen↔ (n.a.)
Nettleton et al. (2007)[18]	USA	5,089 participants 45–84 years	FFQ	Positive loadings for fats and oils, processed meats, nondiet soda, potatoes, sweet breads, cheeses/cheese and cream sauce, sweet extras, beans, poultry, meal-replacement drinks, desserts; negative loadings for cruciferous vegetables, dark-yellow vegetables, soy foods and beverages, fish, other alcohol, other vegetables	CRP, fibrinogen, IL-6, homocysteine	CRP: 5.3% IL-6: 4% fibrinogen: 2.4%	CRP↑ (0.228[b]) IL-6↑ (0.199[b]) fibrinogen↑ (0.153[b])
Heidemann et al. (2005)[25]	Germany	574 participants 35–65 years	FFQ	Positive loadings for fresh fruit; negative loadings for red meat, beer, poultry, legumes, high-caloric soft drinks, processed meat, and bread (except whole-grain bread)	HbA_1c, HDL cholesterol, CRP, adiponectin	CRP: 1.1% adiponectin: 10.2%	Adiponectin↑ (n.a.) CRP↔ (n.a.)
Schulze et al. (2005)[26]	USA	1,350 women 43–69 years	FFQ	Positive loadings for sugar-sweetened soft drinks, refined grains, processed meat, diet soft drinks; negative loadings for wine, coffee, cruciferous vegetables, yellow vegetables	sTNFR2, IL-6, CRP, E-selectin, sICAM-1, sVCAM-1	n.a.	CRP↑ (0.23[b]) sTNFR2↑ (0.12[b]) IL-6↑ (0.21[b]) E-selectin↑ (0.26[b]) sICAM-1↑ (0.18[b]) sVCAM-1↑ (0.14[b])
Cross-sectional analysis of patients with coronary artery disease							
Hoffmann et al. (2004)[27]	Germany	455 women (200 cases, 255 controls) 30–80 years	FFQ	Positive loadings for margarine, meat (except poultry), other vegetable fats and oils (except margarine and olive oil); negative loadings for vegetarian dishes, wine	HDL and LDL cholesterol, C-peptide, CRP, Lipoprotein(a)	CRP: 5.9%	CRP↑ (n.a.)

[a] Spearman correlation coefficients.
[b] Pearson correlation coefficients.
Abbreviations: CRP, C-reactive protein; FFQ, food frequency questionnaire; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; IL, interleukin; LDL, low-density lipoprotein; PAI-1, plasminogen activator inhibitor 1; SBP, systolic blood pressure; sICAM-1, soluble intercellular adhesion molecule 1; sTNFR2, soluble tumor necrosis factor α receptor 2; sVCAM-1, soluble vascular cell adhesion molecule 1.

Table 2 **Summary of cross-sectional studies investigating the associations between inflammatory biomarkers and *a posteriori*-defined dietary patterns.**

Reference	Country	No. and age of participants	Dietary assessment method	Dietary patterns identified	Dietary pattern components	Positive(↑), inverse(↓), and no (↔) statistically significant associations
PCA/FA or PLS						
Guo et al. (2012)[16]	Japan	702 men 44.5 y (median)	BDHQ	"Japanese"	Green-leaf vegetables, cabbage, Japanese white radish, turnips, other root vegetables, carrot, pumpkin, seaweeds, potatoes, vegetable salad, mushrooms, soybean, pickled vegetables, tomato, pickles, fish, fermented soybeans, fruits, mayonnaise, miso soup, chicken egg, green tea, rice, squid, octopus, lobster, shellfish, citrus fruits	Adiponectin↑
				"Sweets-fruits"	Ice cream, Western-style cake, cookie, biscuit, Japanese cake, rice cracker, rice cake, okonomiyaki, fruits, bread, citrus fruits, fruits, dairy products, 100% fruits or vegetables juice, cola; low in alcohol	Adiponectin↔
				"Izakaya"	Squid, octopus, lobster, shellfish, noodles, buckwheat noodles, fish, pork, beef, ham, sausage, bacon and liver, fruits, noodles, Japanese cake, alcohol, citrus fruits, rice cracker, rice cake, okonomiyaki, mushrooms, black or oolong tea, chicken egg; low in rice	Adiponectin↓
Villegas et al. (2012)[31]	China	3,646 men 40–74 y	FFQ	"Vegetable-based"	Green beans, yard long bean, wax gourd, cucumber, tomatoes, Chinese celery, wild rice stems, amaranth, Chinese chives, eggplant, potatoes, baby soya beans, garlic and garlic shoots, Chinese cabbage/bok choi cabbage, cauliflower, hyacinth beans/snow peas, garland chrysanthemum, asparagus lettuce, fresh red and green peppers, white turnips, luffa, clover, fresh mushrooms/ fresh xianggu mushrooms, spinach, greens/Chinese greens, green cabbage, bamboo shoots, shepherd's purse, onions, snow pea shoots, fresh peas, fried bean curd/vegetarian chicken/bean curd cake and other kinds of bean products, lotus roots, carrots, bean curd, soybean sprouts, fresh broad beans, mung bean sprouts, head of garlic, green onions	CRP↔
				"Fruit-based"	Tangerines/oranges/ grapefruits, apples, watermelon, pears, grapes, peaches, bananas, other fruits, fresh milk, bread, shrimp/crab etc., tomatoes, all kind of desserts, mung bean/red beans and other dried beans, fresh mushrooms/fresh xianggu mushrooms, preserved fruits	CRP↓
				"Meat-based"	Chicken, pig's feet, duck/goose, beef/lamb, organ meat, pig's ham hock, rice field eel or river eel, pork ribs, salt water fish, shrimp/crab etc., fried bean curd/vegetarian chicken/ bean curd cake and other kinds of bean products, soybean sprouts, fresh pork, pig liver, mung bean sprouts, pork chops, conch, bean curd, fresh water fish	CRP↔
Heidemann et al. (2011)[28]	Germany	4,025 participants 18–79 y	Dietary history instrument	"Processed foods"	Refined grains, processed meat, red meat, high-sugar beverages, eggs, potatoes, beer, sweets and cakes, snacks, butter, other animal fats; low in fruits, whole grains, tea	Fibrinogen↔
				"Health-conscious"	Cruciferous vegetables, fruity and root vegetables, other vegetables, leafy vegetables, vegetable oils, legumes, fruits, fish, red meat, potatoes, whole grains, other animal fats, poultry, eggs	Fibrinogen↓
Meyer et al. (2011)[22]	Germany	981 men 45–64 y	7-day dietary record	PCA pattern	Beer, cooked sausage, meat (except poultry); low in fresh fruit, whole-meal bread, cooked vegetables, cheese, curd, sweet bread spread, fresh vegetables, tea, cereals and muesli, nuts, rice, potatoes, condensed milk and cream, vegetable oil	CRP↑, IL-6↑, IL-18↑
				PLS pattern	Beer, meat (except poultry), cooked sausage; low in fresh fruit, sweet bread spread, whole-meal bread, cooked vegetables, curd, cheese, fresh vegetables, tea, cereals and muesli, condensed milk and cream, cake and pastries, butter, nuts, chocolates, fruit and vegetable juice, potatoes	CRP↑, IL-6↑, IL-18↑

Table 2 **Continued**

Reference	Country	No. and age of participants	Dietary assessment method	Dietary patterns identified	Dietary pattern components	Positive(↑), inverse(↓), and no (↔) statistically significant associations
Nanri et al. (2011)[29]	Japan	9,545 participants 40–69 y	Short FFQ	"Healthy"	Carrots, green leafy vegetables, other green/yellow vegetables, other vegetables, mushrooms, daikon, cabbage, potatoes, seaweed, pumpkin, burdock/bamboo shoot, broccoli, other fruit, citrus fruit, fish, bone-edible small fish, tofu products, tofu, fermented and unfermented soybean, miso soup, kiriboshi-daikon, stir-fried foods, yogurt, green tea	CRP↓ (in men only)
				"Western"	Deep-fried foods, stir-fried foods, mayonnaise, beef/pork, ham/sausage/salami/bacon, chicken, eggs, other vegetables, fish paste products, cabbage, coffee, liver, canned tuna, fish roe, carrots, other green/yellow vegetables, western confections, squid/octopus/shrimp/crab, mushrooms; low in yogurt, other fruit	CRP↔
				"Seafood"	Shellfish, squid/octopus/shrimp/crab, fish roe, bone-edible small fish, fermented and unfermented soybean, liver, fish, fish paste products, tofu products, noodles, pumpkin, yogurt, broccoli, miso soup, potatoes, canned tuna, tofu, chicken, kiriboshi-daikon, daikon, burdock/ bamboo shoot	CRP↑ (in men only)
				"Bread"	Bread, margarine, noodles, coffee, milk, yogurt, butter; low in rice, miso soup, green tea	CRP↔
				"Dessert"	Japanese confections, Western confections, citrus fruit, other fruit, peanuts, milk, butter, bread, green tea, shellfish, squid/octopus/shrimp/crab, fish roe, fish paste products, tofu products, deep-fried foods; low in noodles	CRP↓ (in men only)
Nettleton et al. (2010)[30]	USA	1,101 participants men: 71.8 y (mean) women: 70.7 y (mean)	FFQ	"Healthy"	Dark yellow vegetables, other vegetables, cruciferous vegetables, green leafy vegetables, fruit, legumes, fin fish, tomatoes, whole grains, poultry, nuts and peanut butter, seafood, low-fat dairy, eggs, oils, white potatoes	CRP↓
				"Western"	Processed meat, red meat, fried potatoes, refined grains, high-fat dairy, desserts, sugar-sweetened beverages, candy and added sweets, white potatoes, eggs, pizza, butter, regular coffee, nuts and peanut butter, added oils, fried fish, tomatoes	CRP↔
Cassidy et al. (2009)[17]	UK	1,754 women 18–80 y	FFQ	"Fruit and vegetable"	Green leafy vegetables, other vegetables, yellow vegetables, other fruit, vegetables & allium, cruciferous vegetables; low in fried potatoes	Adiponectin↔
				"Traditional English"	Cruciferous vegetables, meat, processed meats, legumes, savory pies, fried potatoes, fried fish	Adiponectin↓
				"Dieting"	Low-sugar soda, low-fat dairy products, lasagna; low in butter, sweets and sweet condiments, tea, sweet baked products	Adiponectin↑
Centritto et al. (2009)[23]	Italy	7,646 participants ≥35 y	FFQ	"Olive oil and vegetables"	Olive oil, cooked vegetables, raw vegetables, legumes, soups, fish, potatoes, fruits, bouillon, fresh cheese, white meat	CRP↓
				"Pasta and meat"	Pasta/other grains, cooked tomatoes, red meat, animal fats, other sauces, wine, processed meat, bread, olive oil, beer; low in yogurt	CRP↑
				"Eggs and sweets"	Eggs, margarines, processed meat, sugar and sweets, vegetable oils, snacks, mayonnaises, butter, seasoned cheese, olive oil, fresh cheese, pizza, canned fish	CRP↑

Eilat-Adar et al. (2009)[32]	USA	1,066 participants 18–92 y	FFQ	"Traditional foods"	Fish, native sea and land mammals, stew, mostly meat and stew mostly rice/noodles, native birds, wild greens, wild berries and native berry agutuk, native sea and land animal fats; low in candy bars and sugar syrup, store-bought non-hydrogenated vegetable fats, milk, cheese, ice cream and non-dairy creamer	CRP↔, fibrinogen↔
				"Western foods"	Store-bought meats and chicken, fatty meats, snack chips, pizza, French fries or fried potatoes, soda pop, stew with mostly meat, stew with mostly rice/noodles, milk, cheese, ice cream, nondairy creamer; low in evaporated milk, store-bought hydrogenated vegetable fats, native sea and land animal fats, store-bought animal fats, pancakes, hot cereal	CRP↔, fibrinogen↔
				"Purchased healthy foods"	Beans dry, dark bread, store-bought non-hydrogenated vegetable fats, peanut butter, store-bought fruits, vegetables and lettuce salad, hot cereal, milk, cheese, ice cream, non-dairy creamer; low in flavored drinks, soda pop, snack chips, pizza	CRP↔, fibrinogen↓
				"Beverages and sweets"	Coffee and tea, candy bars, sugar syrup, eggs, pancakes, native birds, stew with mostly meat, stew with mostly rice/noodles; low in store-bought fruits, vegetables and lettuce salad, white bread, pasta, rice, cold cereal, pilot bread, lower fat milk	CRP↓, fibrinogen↔
Nanri et al. (2008)[33]	Japan	7,802 participants 50–74 y	FFQ	"Healthy"	Green leafy vegetables, mushrooms, carrots, other green and yellow vegetables, other vegetables, seaweed, daikon, potatoes, other fruit, pumpkin, cabbage, citrus fruit, broccoli, burdock or bamboo shoot, bone-edible small fish, natto and soybean, tofu products, yogurt, fish, kiriboshi-daikon, tofu, Japanese confectioneries, miso soup, stir-fried foods	CRP↓
				"High-fat"	Deep-fried food, beef or pork, stir-fried foods, mayonnaise, chicken, ham/sausage/bacon, cabbage, egg, other vegetables, fish-paste products, carrots, potatoes, other green and yellow vegetables, coffee, daikon, burdock or bamboo shoot, tofu products	CRP↔
				"Seafood"	Squid or octopus and shrimp or crab, shellfish, fish roe, salted fish guts, tsukudani, fish-paste products, bone-edible small fish, fish, deep-fried foods, egg, tofu	CRP↔
				"Westernized breakfast"	Bread, margarine, coffee, yogurt, ham/sausage/bacon, other fruit, Japanese confectioneries; low in rice, miso soup	CRP↔
Yannakoulia et al. (2008)[34]	Greece	196 women 18–84 y	3-day food records	PC1	Whole-grain cereals, low-fat dairy; low in refined cereals	Adiponectin↑
				(PC2-PC10)	(Only one or a few food groups included[a])	(Adiponectin↔)
Esmaillzadeh et al. (2007)[35]	Iran	486 women 40–60 y	FFQ	"Healthy"	Fruits, other vegetables, tomatoes, poultry, legumes, cruciferous and green leafy vegetables, tea, fruit juices, whole grains, potatoes, low-fat dairy products, fish, yellow vegetables; low in butter, high-fat dairy products, hydrogenated fats	CRP↓, VCAM-1↓, IL-6↔, E-selcetin↔, ICAM-1↔, TNF-α↔, SAA↔
				"Western"	Refined grains, red meat, butter, high-fat dairy products, processed meat, sweets and desserts, pizza, eggs, potatoes, hydrogenated fats, soft drinks, snacks, French fries, coffee, mayonnaise, fruit juices, vegetable oils; low in low-fat-dairy products, other vegetables, fruits, fish	IL-6↑, SAA↑, CRP↔, VCAM-1↔, E-selcetin↔, ICAM-1↔, TNF-α↔
				"Traditional"	Refined grains, potatoes, tea, whole grains, hydrogenated fats, legumes, casserole	IL-6↑, CRP↔, SAA↔, VCAM-1↔, ICAM-1↔, E-selcetin↔, TNF-α↔

Table 2 **Continued**

Reference	Country	No. and age of participants	Dietary assessment method	Dietary patterns identified	Dietary pattern components	Positive(↑), inverse(↓), and no (↔) statistically significant associations
Mikkilä et al. (2007)[36]	Finland	1,037 participants 24–39 y	48-h recall	"Traditional"	Rye, butter, milk, coffee, sausages, margarines and oil, potatoes, wheat, eggs, pork, other meat, alcoholic beverages; low in tea, other dairy products, fruit and berries, legumes and nuts, sugars and confectionery, other vegetables	CRP↔
				"Health-conscious"	Other vegetables, tea, cheese, alcoholic beverages, fruit and berries, rye, fish and shellfish, legumes and nuts, root vegetables; low in milk, coffee, potatoes, sugars and confectionery	CRP↔
Pierce[b] et al. (2007)[37]	USA	219 Nisei 69.8 y (mean)	Short FFQ	"Japanese food factor"	Fish, rice, Tsukemono, tofu, soy sauce	CRP↔
		277 Sansei 41.8 y (mean)		"Western food factor"	Cheese, meat (beef or pork and poultry), snacks, soda	CRP↔
Nettleton et al. (2006)[38]	USA	5,089 participants 45–84 y	FFQ	"Fats and processed meats"	Fats and oils, high-fat and processed meats, fried potatoes, salty snacks, desserts, high-fat cheeses/cheese and cream sauces, red meat, pizza, pasta and potato salads, sweet breads, ice cream, vegetables/potatoes, poultry, nondiet soft drinks, sweet extras, eggs and omelets, chicken/tuna/egg salads, coffee, cream soups/chowders, refined grain bread/ rice/pasta, coffee and tea creamer	CRP↑, IL-6↔, E-selectin↔, ICAM-1↔
				"Vegetables and fish"	Dark-yellow vegetables, cruciferous vegetables, other vegetables, fish, other soups, red meat, high-fat Chinese dishes, poultry, soy foods and beverages, refined-grain bread/ rice/pasta, tea; low in coffee	CRP↔, IL-6↔, E-selectin↔, ICAM-1↔
				"Beans, tomatoes and refined grains"	Beans, tomatoes, refined-grain bread/rice/pasta, high-fat cheeses/cheese/cream sauces, avocados and guacamole, red meat, poultry, high-fat Chinese dishes, whole milk	ICAM-1↑, CRP↔, IL-6↔, E-selectin↔
				"Whole grains and fruit"	Whole-grain bread/rice/pasta, fruit, seeds/nuts/peanut butter, green leafy vegetables, low-fat milk, cottage and ricotta cheese, pasta and potato salads, chicken/tuna/egg salads, low-fat dairy desserts, other vegetables, tomatoes, fruit juices, yogurt, dark-yellow vegetables	CRP↓, IL-6↔, E-selectin↔, ICAM-1↔
Lopez-Garcia et al. (2004)[39]	USA	732 women 43–69 y	FFQ	"Prudent"	Other vegetables, green, leafy vegetables, dark-yellow vegetables, cruciferous vegetables, fruit, tomatoes, legumes, fish and other seafood, poultry, whole grains, salad dressings, low-fat dairy products, fruit juices	CRP↓, E-selectin↓, IL-6↔, ICAM-1↔, VCAM-1↔
				"Western"	Red meats, processed meats, refined grains, sweets and desserts, French fries, high-fat dairy products, potatoes, condiments, eggs, pizza, sugar-containing beverages, mayonnaise and other creamy salad dressings, margarine, cream soup, snacks, butter, nuts	CRP↑, E-selectin↑, ICAM-1↑, VCAM-1↑, IL-6↔

Fung et al. (2001)[20]	USA	466 men 40–75 y	FFQ	"Prudent"	Other vegetables, leafy vegetables, yellow and orange vegetables, cruciferous vegetables, legumes, tomatoes, fruit, fish, olive oil, garlic, fruit juices, poultry, water, refined grains, salad dressings	CRP↔, fibrinogen↔
				"Western"	Red meats, processed meats, French fries, eggs, high-fat dairy products, butter, coffee, beer, added salt, mayonnaise, refined grains, cream soups, desserts, liquor, pizza; low in fruits, breakfast cereals, whole grains	CRP↔, fibrinogen↔
Cluster analysis						
Anderson et al. (2011)[40]	USA	1,751 participants 70–79 y	FFQ	"Healthy foods"	Low-fat dairy products, fruit, whole grains, rice, pasta and mixed dishes, poultry, fish and other seafood, other vegetables, dark yellow vegetables, dark green vegetables; lowest intakes of beer, fried poultry, high-calorie drinks, processed meat, meat, high-fat dairy products, miscellaneous fats	Reference pattern
				"Breakfast cereal"	Other cold breakfast cereal, cold breakfast cereal-fiber/bran; lowest intakes of snacks, rice, pasta and mixed dishes, refined grains	CRP↔, IL-6↔, TNF-α↔
				"Meat and alcohol"	Beer, meat, processed meat, liquor, fried poultry; lowest intakes of dark yellow vegetables, cold breakfast cereal-fiber/bran, other vegetables, fish and other seafood, poultry, whole grains, nuts, fruit, other cold breakfast cereal, sweets and desserts	CRP↔, IL-6↔, TNF-α↔
				"Sweets and dessert"	Sweets and desserts; lowest intakes of dark green vegetables, liquor	IL-6↑, CRP↔, TNF-α↔
				"Refined grains"	Refined grains; lowest intakes of mayonnaise and salad dressing	CRP↔, IL-6↔, TNF-α↔
				"High-fat dairy products"	High-fat dairy products, miscellaneous fats, mayonnaise and salad dressing, nuts, high-calorie drinks, snacks; lowest intakes of low-fat dairy products	IL-6↑, CRP↔, TNF-α↔
Hlebowicz et al. (2011)[41]	Sweden	4,999 participants 45–73 y	7-day menu book, diet history questionnaire and 1-h interview	"Many foods and drinks"	Cheese, high-fat meats, cake/pastry, fruits, white bread, sweets, low-fat meats, boiled potatoes, medium-fat spread, low-fat milk, whole milk, low-fat spread, fiber bread	CRP↔
				"Fiber bread"	Fiber-rich bread, high-fat meats, sweets, fruits, low-fat meats, low-fat spread, cheese, boiled potatoes, low-fat milk, cake/pastry, vegetables	CRP↔
				"Low fat and high fiber"	Fruits, low-fat milk, high-fat meats, low-fat meats, sweets, vegetables, boiled potatoes, cake/pastry, fiber bread, white bread, fiber crisp-bread, low-fat spread, cereals, cheese	CRP↔
				"White bread"	White bread, high-fat meats, sweets, low-fat spread, low-fat meats, cheese, fruits, boiled potatoes, cake/pastry, low-fat milk, whole milk, medium-fat spread	CRP↔
				"Milk fat"	Bregott spread, sweets, white bread, high-fat meats, cheese, whole milk, low-fat meats, cake/pastry, fruits, boiled potatoes, fiber bread	CRP↔
				"Sweets and cakes"	Sweets, high-fat meats, white bread, fruits, cake/pastry, cheese, low-fat meats, whole milk, low-fat milk, low-fat spread, boiled potatoes, fiber bread	CRP↔

Table 2 **Continued**

Reference	Country	No. and age of participants	Dietary assessment method	Dietary patterns identified	Dietary pattern components	Positive(↑), inverse(↓), and no (↔) statistically significant associations
Multivariate finite mixture model						
Oliveira et al. (2011)[42]	Portugal	925 participants ≥18 y	FFQ	Women		
				"Healthy"	Highest consumption of vegetables, vegetable soup, fruits, dairy products; lowest consumption of red meat, fast foods, soft drinks	Reference pattern
				"Low fruit and vegetable"	Lowest intake of fruit and vegetables	CRP↔
				"Red meat and alcohol"	Highest intake of red meat and alcoholic beverages; lowest intake of dairy products, vegetable soup	CRP↔
				"In transition to fast food"	Highest intake of white meat, sweets, fast foods	CRP↔
				Men		
				"Healthy"	Highest consumption of vegetable soup, fruits, dairy products, cereals; lowest intake of red meat, fast food, alcoholic beverages	Reference pattern
				"Fish"	Highest intake of fish	CRP↔
				"Red meat and alcohol"	Highest consumption of red meat, alcoholic beverages, fast foods, lowest intake of fruits, vegetable soup, dairy products, cereals	CRP↑
				"Intermediate intake"	Intermediate consumption of most food groups; lowest consumption of white meat	CRP↔

[a] PC2: high in vegetables, fruit, and olive oil; PC3: high in coffee and low-fat dairy; PC4: high in full-fat dairy products; PC5: high in poultry and low in red meat and its products; PC6: high in fish and low in red meat and its products; PC7: high consumption of alcoholic beverages; PC8: high in nuts and low in fruits; PC9: high in legumes; PC10: high in potatoes.

[b] Confirmatory factor analysis, the authors hypothesized two dietary patterns based on studies of Japanese Americans and native Japanese persons living in Japan, CFA was used to test the hypothesis.

Abbreviations: BDHQ, brief, self-administered diet history questionnaire; CRP, C-reactive protein; FA, factor analysis; FFQ, food frequency questionnaire; ICAM-1, intercellular adhesion molecule 1; IL, interleukin; PC, principal component; PCA, principal component analysis; PLS, partial least squares; SAA, serum amyloid A; TNF-α, tumor necrosis factor α; VCAM-1, vascular cell adhesion molecule 1.

linked with CRP. Positive factor loadings revealed food groups that were positively associated with the identified pattern. Dietary patterns positively associated with biomarker levels were largely characterized by positive loadings of red meat, processed meat, and beer[22,23,38,39]; one of these patterns also showed negative loadings of fruit, vegetables, and whole-grain products.[22] Patterns inversely associated with CRP concentrations were characterized by high loadings of fruit and vegetables, whole grains, or fish.[23,29–31,33,35,38,39] However, one study[29] performed in Japan found a pattern characterized by high loadings of fish and fish products that was positively associated with CRP levels in men. Two other studies, by Eilat-Adar et al.[32] and Nanri et al.,[29] found that high loadings of sweets, desserts, and refined grains were inversely associated with CRP. Four studies additionally reported on IL-6[22,35,38,39] or IL-18,[22] and two of these found positive associations with patterns high in red and processed meat and low in vegetables and fruits.[22,35] No inverse associations were observed. Fibrinogen[20,28,32] and adhesion molecules (such as E-selectin, ICAM-1, or VCAM-1)[35,38,39] were rarely investigated, but when they were, patterns high in vegetables, fruits, and whole grains showed inverse associations[28,32] and no positive associations were found. Regarding the anti-inflammatory biomarker adiponectin, positive associations were found for vegetable-, fruit-, and fish-based patterns,[16] low-sugar and low-fat dairy diets,[17] and whole-grain-based diets.[34] Inverse associations were reported for patterns somewhat more meat/processed meat- and (fried) fish-based.[16,17]

Of three analyses applying cluster analysis[40,41] or the similar multivariate finite mixture model[42] (Table 2), two found positive associations between "sweet and dessert" dietary patterns, a "high-fat dairy product" pattern, and a "red meat and alcohol" pattern and IL-6[40] or CRP levels.[42]

Dietary indices and scores

Studies of the associations between *a priori* dietary patterns and inflammatory biomarkers are summarized in Table 3. Three intervention studies applied the Mediterranean diet,[21,43,44] and almost all biomarkers of inflammation, especially CRP, were lower and adiponectin concentrations were higher after those interventions.

Among the cross-sectional studies investigating *a priori* dietary patterns (Table 3),[19,45–61] 10 used the Mediterranean Diet Score (MDS),[19,45,46,48,49,53,57,59–61] one used an alternative to the original MDS score,[55] seven investigated the Healthy Eating Index (HEI)[47,52,54–56,58] or an alternative HEI,[50,55] and five used other indices. Seventeen studies reported statistically significant associations with biomarkers of low-grade chronic inflammation. Positive associations were reported between the different healthy *a priori* patterns and the anti-inflammatory markers adiponectin[19,50] and IL-10.[45] Ten studies reported inverse associations for CRP levels and dietary indices that were almost all MDS/alternative MDS or HEI/alternative HEI.[46,50,51,53–59] Inverse associations were also reported for several interleukins,[48,49,51,55,57,59] fibrinogen,[46,51,53,56,57] E-selectin,[50,55] ICAM-1 and VCAM-1,[55] and TNF-α.[45]

DISCUSSION

This is believed to be the first systematic review of the associations between dietary patterns and biomarkers of inflammation. While numerous studies were identified, no prospective observational study investigating dietary patterns and changes in biomarkers of inflammation was found. Overall, the dietary patterns identified by RRR were almost all meat-based patterns and nearly all of them were statistically significantly associated with biomarkers such as CRP, IL-6, and fibrinogen. After taking into account the inconsistencies of results, which were generated using different methods of identifying dietary patterns, the current work showed some evidence to support the hypothesis that Western-like or meat-based patterns are positively associated with low-grade inflammation. Additionally, vegetable- and fruit-based patterns and *a priori* healthy dietary patterns appeared to be inversely related to inflammatory biomarkers; this was particularly well supported by intervention studies investigating the Mediterranean diet.

A posteriori dietary patterns analysis

The inconsistency of the statistically significant associations across studies could be due to the data-driven nature of *a posteriori* dietary pattern analysis, which depends strongly on the dietary behavior and the culture of the study population.[15] Thus, dietary patterns across populations differ in their compositions and in the weightings of food groups. In addition, the method used to identify the dietary patterns may affect the magnitude of outcomes. For example, RRR analysis creates combinations of food groups that maximize the variance in the selected biomarkers.[14] Consequently, the dietary patterns generated with RRR were statistically significantly associated with almost all biomarkers of inflammation.[18,22–26] In one study that did not report statistically significant associations, the authors chose hemoglobin A1c, high-density lipoprotein cholesterol, CRP, and adiponectin as response variables, which resulted in a pattern that did not explain much variance in CRP concentrations (1.1%).[25] This could explain the lack of statistical significance in that study.

Where provided, the Pearson correlation coefficients for CRP were 0.228[18] and 0.23,[26] and the Spearman

Table 3 **Summary of studies investigating the associations between inflammatory biomarkers and dietary scores or indices.**

Reference	Country	No. and age of participants	Dietary assessment method	Dietary score/index	Positive (↑), inverse (↓), and no (↔) statistically significant associations
Interventional studies					
Blüher et al. (2012)[43]	Israel	109 participants 40–65 y	FFQ, 24-h dietary recall (subgroup)	Mediterranean Diet (2-y intervention)	Adiponectin↑ CRP↓ MCP-1↓[a]
Konstantinidou et al. (2010)[44]	Spain	60 participants 20–50 y	FFQ	Mediterranean Diet (3-mo. intervention)	P-selectin↓ CRP↓ MCP-1↔
Interventional studies investigating patients with metabolic syndrome					
Esposito et al. (2004)[21]	Italy	90 patients 44.3 y (mean)	3-day food record	Mediterranean-Style Diet (2-y intervention)	CRP↓ IL-6↓ IL-7↓ IL-18↓
Cross-sectional studies					
Azzini et al. (2011)[45]	Italy	131 participants 20–40 y	Dietary diary (4 days including the weekend)	Mediterranean Diet Score	IL-10↑ TNF-α↓
Carter et al. (2010)[46]	USA	13,197 participants 18–90 y	FFQ, 24-h dietary recall	Mediterranean Diet Score	CRP↓[b] Fibrinogen↓[b]
Fragopoulou et al. (2010)[19]	Greece	3,042 participants 18–89 y	FFQ	Mediterranean Diet Score	Adiponectin↑
Shahar et al. (2009)[47]	USA	298 participants 70–79 y	FFQ	Healthy Eating Index	CRP↔ IL-6↔
Dai et al. (2008)[48]	Vietnam	345 men about 54 y (mean)	FFQ	Mediterranean Diet Score	IL-6↓ CRP↔
Dedoussis et al. (2008)[49]	France, Greece, Italy, Poland, Germany	957 participants >60 y	FFQ	Mediterranean Diet Score	IL-8↓[c] IL-6↔ TNF-α↔ MCP-1↔
Fargnoli et al. (2008)[50]	USA	1,922 women 30–55 y	FFQ	Alternate Healthy Eating Index	Adiponectin↑ CRP↓ E-selectin↓ IL-6↔ ICAM-1↔ VCAM-1↔ TNF-α↔
Nettleton et al. (2008)[51]	USA	5,042 participants 45–84 y	FFQ	Comprehensive Healthy Dietary Pattern (47 food groups)	CRP↓ IL-6↓ Fibrinogen↓
				Simplified Healthy Dietary Pattern (6 food groups)	CRP↓ IL-6↔ Fibrinogen↔

Boynton et al. (2007)[52]	USA	110 women 51–75 y	FFQ	Diet Quality Index	CRP↔ IL-6↔ SAA↔
				Diet Quality Index with calcium from supplements	CRP↔ IL-6↔ SAA↔
				Healthy Eating Index	CRP↔ IL-6↔ SAA↔
Panagiotakos et al. (2006)[53]	Greece	3,042 participants >18 y	FFQ	Mediterranean Diet Score	CRP↓ Fibrinogen↓
Ford et al. (2005)[54]	USA	13,811 participants ≥20 y	Single 24-h recall, FFQ	Healthy Eating Index	CRP↓ CRP↓ (women only) CRP↔ (men only)
Fung et al. (2005)[55]	USA	660 women 43–69 y	FFQ	Healthy Eating Index	CRP↔ IL-6↔ E-selectin↔ ICAM-1↔ VCAM-1↔
				Alternate Healthy Eating Index	CRP↓ IL-6↓ E-selectin↓ ICAM-1↓ VCAM-1↔
				Diet Quality Index Revised	CRP↔ IL-6↔ E-selectin↔ ICAM-1↔ VCAM-1↔
				Recommended Food Score	E-selectin↓ CRP↔ IL-6↔ ICAM-1↔ VCAM-1↔
				Alternate Mediterranean Diet Score	CRP↓ IL-6↓ E-selectin↓ VCAM-1↓ ICAM-1↔

Table 3 **Continued**

Reference	Country	No. and age of participants	Dietary assessment method	Dietary score/index	Positive (↑), inverse (↓), and no (↔) statistically significant associations
Kant et al. (2005)[56]	USA	8,719 participants ≥20 y	24-h recall	Healthy Eating Index	CRP↓ Fibrinogen↔
				Recommended Foods Score	CRP↓ Fibrinogen↓
				Dietary Diversity Score for Recommended Foods	CRP↓ Fibrinogen↔
Chrysohoou et al. (2004)[57]	Greece	3,042 participants 18–89 y	FFQ	Mediterranean Diet Scores	CRP↓ IL-6↓ Fibrinogen↓ TNF-α↔ SAA↔
Cross-sectional studies investigating patients with CVD or cancer					
George et al. (2010)[58]	USA	746 breast cancer survivors >18 y	FFQ	Healthy Eating Index (2005)	CRP↓ SAA↔ Adiponectin↔
Panagiotakos et al. (2009)[59]	Europe	1,003 myocardial infarction survivors 35–80 y	FFQ	Mediterranean dietary pattern	CRP↓ IL-6↓ Fibrinogen↔
Salas-Salvadó et al. (2008)[60]	Spain	772 participants at high risk for CVD[d] 55–80 y	FFQ, 14-item questionnaire	Mediterranean-type food pattern	CRP↔ IL-6↔ ICAM-1↔ VCAM-1↔
Mantzoros et al. (2006)[61]	USA	987 diabetic women 30–55 y	FFQ	Mediterranean dietary pattern score	Adiponectin↔

[a] MCP-1 concentration decreased only after 6-month intervention; after 24-month intervention, MCP-1 level returned to baseline concentration.
[b] Significant association found only in males aged ≥45 years.
[c] Significant association found only in male participants and in Greek participants.
[d] Inclusion criteria: type 2 diabetes or three or more CHD risk factors. Exclusion criteria: previous history of CVD, any severe chronic illness, drug or alcohol abuse, history of allergy or intolerance to olive oil or nuts.
Abbreviations: CRP, C-reactive protein; FFQ, food frequency questionnaire; ICAM-1, intercellular adhesion molecule 1; IL, interleukin; MCP-1, monocyte chemoattractant protein-1; SAA, serum amyloid A; VCAM-1, vascular cell adhesion molecule 1.

correlation coefficient was 0.33.[22] The mean differences between the highest and lowest quintiles of dietary patterns ranged from 0.09 mg/L in a large study population of 7,646[23] to 1.31 mg/L in a study sample of 5,089 participants.[18] Although not statistically significant, Heidemann et al.[25] found a meaningful difference of 0.96 mg/L in a smaller study population of 574 participants.

In contrast to RRR, PCA identifies dietary patterns that explain as much variance as possible in the food groups.[13] Nevertheless, PCA has some limitations related to subjectivity at several steps of the analysis, which may influence the structure of the dietary patterns identified.[62] For example, the choice and the number of food groups may affect the composition of the generated patterns.[15] This was demonstrated by McCann et al.,[63] who investigated the effect of food classification on PCA-generated dietary patterns and ascertained that the misclassification of participants between patterns generated on the basis of 36 and 168 food groups was relatively high (41% of participants were misclassified as having a healthy pattern score). Thus, as the number of food items included in an analysis decreases, the explained variance in food intake increases, and the estimation of disease risk may decrease as well. Therefore, the number of food groups should not be set too low. The method of food grouping may also influence the dietary patterns identified for a population,[15] so reducing the number of food items and limiting the other food groups included in the analysis may result in less differentiated dietary patterns. For example, if white bread, pasta, rice, cold cereal, and bread are categorized as one broad food group, it will be unclear which of those foods mainly contributes to an identified dietary pattern.[32]

The rarely applied cluster analysis (or multivariate finite mixture model) was found to identify dietary patterns that predominantly showed no associations with higher or lower CRP levels.[40–42] These methods group individuals according to similarities in their dietary behavior. Within each cluster, intake levels of all investigated food groups and biomarker levels are reported as arithmetic means.[13] These results probably have less power to ascertain associations with health outcomes compared to continuous score variables, as calculated with PCA and RRR.[15]

Dietary indices and scores

Following this review's initial assumption that *a posteriori* patterns are difficult to compare, using indices or scores should be advantageous. Regarding CRP, nearly three-quarters of the studies using healthy dietary indices or scores found inverse associations and the MDS seemed to be more strongly inversely associated with CRP levels than the HEI. The latter is based on the Dietary Guidelines for Americans and the Food Guide Pyramid, which both recommend high consumption of fruits, vegetables, dairy, and grains but also meat.[64] In contrast, the MDS includes high intakes of whole grains, fruits, vegetables, olive oil, low-fat dairy products, fish, poultry, pulses, and nuts. Red meat consumption is assessed as negative within the MDS, but this is not the case with the HEI.[65]

When using diet indices or scores, investigators must additionally pay attention to the food intake levels of the study population and should, thus, define cut-off values to allow discrimination among individuals.[65]

Intervention studies with the Mediterranean diet found statistically significant inverse associations with almost all inflammatory biomarkers, thus providing more evidence that this dietary pattern may help lower low-grade inflammation.

General methodological aspects

The heterogeneity of results across studies can be explained by the use of different inflammatory markers in the investigations. As metabolite markers, some have previously been associated with disease risks; for example, CRP was found to be a strong predictor of type 2 diabetes[3] or cancer[7] after adjustment for potential confounders, whereas IL-6 showed weaker associations with disease risks, which were not statistically significant.[3,7] Different pathological mechanisms may also explain, to some extent, the heterogeneity among the reported associations with diet, while different physiological pathways involving the biomarkers may account for differences among the dietary patterns associated with inflammatory markers. On the other hand, since inflammatory markers are largely correlated, e.g., IL-6 and CRP, similarities are also possible. For example, while IL-6 induces the production of CRP, at certain concentrations, CRP may stimulate the production of adhesion molecules.[66]

Most of the studies adjusted their analysis for potential confounders such as age, body mass index, total energy intake, physical activity, and medications, but whether the associations in the unadjusted analyses of some studies could be explained by adiposity or other confounders remains uncertain.[18,21,22,24,27,30,43,45] While many studies found statistically significant associations between some dietary patterns and levels of inflammatory biomarkers after adjustment for potential confounders,[16,17,19,23,26,29,31–35,38,39,46,48–50,54–59] the process by which potential confounders were selected was not reported. No evidence was found to indicate that those analyses adjusting for fewer potential confounders showed different results than those investigating more.

The results of this review indicate that the dietary assessment method applied may influence the dietary patterns identified and the classification of individuals on the pattern score. Using a simple 24-h dietary recall, for example, disregards the day-to-day variation in dietary choices and may result in the identification of dietary patterns that are not typical for the study population.[15] As an example, Kant et al.[56] found statistically significant associations between diet scores or indices and CRP by applying single 24-h recalls in a large population; in contrast, a study utilizing PCA and 48-h recalls in a smaller population found no associations with inflammatory markers.[36] This review shows that the study characteristics and the types of analyses applied, including adjustment factors, differ across studies, making it difficult to draw further conclusions.

All of the observational studies published to date used cross-sectional designs to elucidate associations between dietary patterns and markers of chronic inflammation. Using a prospective design would allow dietary factors to be analyzed as predictors of change in inflammatory markers. While intervention studies provide some information in this respect, in the current context, they are limited to *a priori* dietary patterns and, thus, do not necessarily reflect usual dietary intake. Prospective observational studies are consequently warranted.

CONCLUSION

The present systematic literature review investigated whether specific dietary patterns are associated with biomarkers of low-grade inflammation. The results show that only observational studies have been reported on to date, and they all examined the association in a cross-sectional manner. The presently available findings support the notion that a positive association exists between Western-type and meat-based diets and low-grade chronic inflammation while an inverse association exists for vegetable- and fruit-based patterns. In order to confirm these associations, it is suggested that prospective studies are strongly needed to investigate dietary patterns as risk factors for changes in biomarkers of inflammation over time.

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