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A posteriori dietary patterns are related to C-reactive protein levels: results from a systematic review and meta-analysis

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ABSTRACT

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Given the small effects of single nutrients, evaluating the relationships between cardiovascular disease risk factors and dietary patterns may be particularly useful. An increasing number of studies in recent years are investigating the association of dietary patterns with C-reactive protein (CRP) levels. This systematic review and meta-analysis examined the association between a posterioriderived dietary patterns and CRP levels in adults. PubMed and Scopus were searched for articles published up to March 2015 that examined the association of total diet and CRP levels among adults. Two independent reviewers performed the study selection, quality rating, and data extraction process. Effect sizes of eligible studies were pooled by using random-effects models. Heterogeneity was tested using I^2 statistic. Overall, 16 cross-sectional and 4 case-control studies that used a posteriori approach were considered for the meta-analysis and were eligible for inclusion. The comparison of the highest and lowest categories of healthy/prudent patterns revealed a significant decrease in CRP (mean difference (MD): -0.23; 95% CI: -0.40 to -0.056; p = 0.006) when other lifestyle factors were controlled for, although there was heterogeneity in the studies. Pooled results indicated higher levels of CRP (MD: 0.16; 95% CI: 0.15 to 0.23; p < 0.001) in the highest category of unhealthy/Western pattern compared with those in the lowest category, though there was significant heterogeneity. The results of the present meta-analysis provide evidence that a healthy/prudent pattern decreases CRP level, while adherence to unhealthy/Western pattern leads to higher level of CRP in adults.

Introduction

C-reactive protein (CRP) is an inflammatory biomarker and acute phase protein synthesized primarily by the liver in response to proinflammatory cytokines like interleukin 6 [1]. Recent evidence indicates that an elevated CRP level is a predictor of numerous conditions, including cardiovascular disease [2], type 2 diabetes [3], metabolic syndrome [4], and breast cancer [5].

There are several genetic and environmental determinants of inflammatory cytokines [6-9]; however, the association between diet and markers of systemic inflammation have not been studied in depth [10-12]. Nutrition plays a crucial role in maintaining health and preventing diseases. A

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healthy diet can decrease the risk of progressive diseases such as cardiovascular disease, cancers, and diabetes [13]. So far, most of the nutritional studies have focused on foods [14, 15] and nutrients or supplements [16, 17]. For example, dietary interventions involving supplementation with single nutrients, such as omega-3 fatty acids, folic acid, or antioxidants, may be effective in reducing systemic inflammation and reversing endothelial dysfunction [18].

However, the last decade has seen a shift in attention towards assessing dietary patterns because it is more reflective of real intakes. Individuals typically consume meals containing a variety of foods and nutrients, instead of just a single nutrient [19]. Since there are likely important interactions and synergy among and within foods, the combined effect of the diet's constituent parts is greater than the individual effects of single foods and nutrients [20]. Considering the small effects of single nutrients, evaluating the relationship between cardiovascular disease (CVD) risk factors and dietary patterns may be particularly useful. Accumulating evidence suggests that there is a relationship between healthy dietary patterns and low levels of serum CRP [21, 22]. Furthermore, some studies have shown the association between unhealthy dietary patterns and elevated serum CRP [21, 23]. Nevertheless, several published studies did not confirm these findings [24]. Therefore, this systematic review aimed to investigate and abstract more comprehensively the association between dietary patterns and CRP levels. Our study aimed to answer the following question: Is there any association between dietary patterns and circulating high-sensitivity (hs)-CRP levels in adults in higher compared with lower intakes of dietary patterns?

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement was used for writing up this systematic review [25].

Search strategy

A systematic search was performed using PubMed and Scopus databases to identify the related observational studies (cross-sectional, case-control, and cohort) from the earliest available time up to January 2015. The reference list of a relevant systematic review was also reviewed [26]. Literature searches were downloaded into EndNote (version X7, Thomson Reuters, Philadelphia, PA, USA) to merge the retrieved records, eliminate duplications, and facilitate the review process. Search terms included (dietary pattern* OR eating pattern* OR food* pattern* OR dietary habit OR diet OR dietary) AND (factor analysis OR principal component analysis) AND (C-reactive protein OR CRP OR high-sensitivity C-reactive protein OR high-sensitive C-reactive protein OR hs-CRP).

Study selection

Titles and abstracts of all articles retrieved in the initial search were evaluated independently by 2 reviewers (MH and SS). Articles not meeting the eligibility criteria were excluded by using a screen form with a hierarchical approach based on the study design, population, exposure, and outcome. The reference lists of relevant review articles identified during this process were also examined to include additional studies. Full-text articles were retrieved if the citation was considered eligible, and subjected to a second evaluation for relevance by the same reviewers. Any disagreements were discussed and resolved by consensus.

Eligibility criteria

Articles were obtained and included in this review if they (1) examined the whole diet and included measurements of all dietary components by using a 24-h dietary recall, food record, food frequency questionnaire (FFQ), or similar instruments; (2) included hs-CRP measures; and (3) enrolled adults. Articles were excluded if they (1) examined only individual nutrients or did not examine all dietary components; (2) did not report hs-CRP data in a format that can be extracted; (3) comprised study samples that were not population-based or only focused on a subgroup of individuals with nutritional needs that are different from the general population; (4) were non-human studies; (5) were reviews, case reports, conference papers, and letters; (6) were studies focused on pregnant or lactating women; (7) were non–English language papers; (8) were studies conducted on infants, children, and adolescents; (9) did not report serum concentrations of CRP; (10) did not assess dietary intakes using FFQ, 24-h recall, or 3-day recall; (11) were abstracts with no more information ; (12) were dissertations.

Data extraction

The following information were extracted: first author, publication year and country, study design, sample size, number of cases and controls (if available), dietary assessment tool and validation method (if applicable), method of identifying dietary patterns, dietary patterns identified, confounders adjusted for in analysis, and main findings, including the estimates of association. When a study provided several estimates with adjustment for different confounders, results were reported for the one adjusting for the largest number of factors. Two reviewers independently performed the data extraction and settled differences by consensus. Where further detail was required, we contacted study authors for additional information.

Data synthesis

Only the most common patterns of dietary intake were considered for meta-analysis. Because the labeling of dietary patterns varied across studies, as long as the selected patterns were similar with regard to the most frequently consumed foods, these studies were grouped and analyzed together regardless of their original label. For example, most studies examined dietary patterns with a high intake of fruit and vegetables, fish, and whole grains. These studies were pooled and analyzed together and the corresponding dietary pattern was labeled "healthy."

Statistical analysis

To combine the results, a meta-analysis was conducted in which we evaluated CRP levels for the highest versus the lowest categories of dietary pattern. To estimate the overall effect size, we calculated the weighted mean difference (WMD) between the highest and the lowest categories of adherence to each dietary pattern and then pooled them using the generic inverse variance method by the user-written "metan" command in Stata (version 11) software [27]. A random-effects model (DerSimonian–Laird) was used for the analysis. We assessed heterogeneity using Cochran's Q test, and the I2 statistic provided the relative amount of variance of the summary effect [28]. Sensitivity analyses were carried out by disaggregating results with the user-written "metan" command ("by option") in Stata (version 11) software [27]. We also carried out formal statistical tests for funnel plot asymmetry with the user-written "metabias" command in Stata (version 11) software [27]. All statistical analyses were conducted by using Stata version 11 (StataCorp, College Station, Texas, USA).

Results

Search results

We identified 824 records in PubMed and 2482 in Scopus database. After removing 735 duplicates, 2571 abstracts remained. Of these, 2510 were excluded after the screening of titles and abstracts. Full texts of the remaining 61 articles were obtained. By reviewing the reference list of a relevant systematic review [26], 4 additional articles were included [10, 15, 23, 29]. Separate screening forms were used to summarize and examine the full-text articles. Finally, 15 papers were identified for inclusion in the meta-analysis. The flow diagram of studies identified for review is shown in detail in Figure 1.

Description of studies

The characteristics of the studies included in this review are presented in Table 1. Five studies were conducted in European countries [30-33]{Oliveira, 2011 #118}, 10 in the US [29, 34-42], 2 in Canada and Portugal [43, 44], 3 in Japan and Korea [22, 45, 46], and one in Iran [21]. The number of participants in each study ranged from 38 to 9545. Participants' ages ranged from 10 to 84 years. Four studies were restricted to female subjects [21, 29, 32, 39], and 1 included only male subjects [42]. All studies were done in healthy populations except 5 studies that were conducted on subjects with type 2 diabetes [29, 31], myocardial infarction [43], and coronary artery disease [32].

Fifteen studies examined both sexes, with 3 examining men and women separately [22, 33, 45] and 12 in combination. All of the studies were observational, of which 16 were cross-sectional and the remaining were case-control studies [29, 31, 32, 43].

Dietary variables were measured using a variety of instruments. Except for one study [33], all studies used validated FFQs (n = 19). We identified two major dietary patterns across studies: a healthy dietary pattern characterized by high intakes of fruits, vegetables, fish, and whole grains; and a Western diet, consisting of refined grains, processed meat foods or snacks, and high-sugar and high-fat products, which was identified in studies using the a posteriori method.

	Example search strategy: Source: PubMed
1.	Dietary pattern*
2.	Eating pattern*
3.	Food*Pattern*
4.	Dietary habit*
5.	1 OR 2 OR 3 OR 4
6.	Factor analysis
7.	Principal component analysis
8.	6 OR 7
9.	C-reactive protein
10.	CRP
11.	high-sensitivity C-reactive protein
12.	highly-sensitive C-reactive protein
13.	hs-CRP
14.	9 OR 10 OR 11 OR 12 OR 13
15.	5 AND 8 AND 14
16.	Limit 15 to English language

Figure 1. PubMed search strategy for a systematic review and meta-analysis examining a posteriori dietary patterns and CRPa levels
[a] CRP: C-reactive protein

Table 1. Summary of cross-sectional and case-control studies (n = 15) examining a posteriori dietary patterns and serum C-reactive protein (CRP) levels in adults

Author	Country	Design	Study population	Sex/ Age	Sample size	Method of identifying dietary patterns	Dietary intake assessment	Type of Dietary pattern	CRP Mean or Median(mg/L)	Factors adjusted for in analyses
Lee, Y. /2014	Korea	Cross-sectional	Middle-aged Koreans	Ma/Fb 40-69*	7574	factor analysis	FFQc	Fruit pattern	Q[d]1:0.2±0.6 Q4:0.2±0.4	
								Vegetable pattern	Q1:0.2±0.6 Q4:0.2±0.3	
								meat pattern	Q1:0.3±0.7 Q4:0.2±0.4	
								coffee pattern	Q1:0.2±0.5 Q4:0.2±0.4	
Labonte, M. 2014	Canada	Cross-sectional	Inuit population	M/F ≥18 y	666	principal component analysis	FFQ	“Traditional”	Q1:1.38±1.1 Q4:1.18±1.1	Age and waist circumference
								"Western"	Q1:1.12±1.1 Q4:1.15±1.1	
								"Nutrient-poor food"	Q1:1.58±1.1 Q4:0.94±1.1	
								"Healthy"	Q1:1.25±1.1 Q4:1.22±1.1	
Oliveira, A. 2011	Portugal	Case-control study	General Population	M/F ≥18 y	925	Multivariate finite mixture model	FFQ			Age, education, smoking status regular physical activity, total energy intake, and a family history of acute myocardial infarction.
				Women	147			“Healthy”	2.27	
					43			“Low fruit and vegetable”	2.66	
					134			“Red meat and alcohol”	2.72	
					271			“In transition to fast food”	2.67	
				Men	66			“Healthy”	1.68	
					136			“Fish”	1.96	
					90			“Red meat and alcohol”	2.64	
					38			“Intermediate intake”	1.95	
								“Western”	Q1:1.7±0.3 Q3:1.9±0.3 Q5:2.5±0.3	
Nanri, H. 2011	Japan	Cross-sectional study	Middle-aged Japanese population	M 40-69* y	9545	Factor analysis	Short FFQ	Healthy	Q1:0.425 Q2:0.423 Q3:0.423 Q4:0.412 Q5:0.402	Age, alcohol, smoking, and physical activity level and body mass index
								Western	Q1:0.408 Q2:0.439 Q3:0.419 Q4:0.411 Q5:0.433	

Author	Country	Design	Study population	Sex/ Age	Sample size	Method of identifying dietary patterns	Dietary intake assessment	Type of Dietary pattern	CRP Mean or Median(mg/L)	Factors adjusted for in analyses
								Seafood	Q1:0.390 Q2:0.432 Q3:0.420 Q4:0.427 Q5:0.441	
								Bread	Q1:0.447 Q2:0.413 Q3:0.420 Q4:0.428 Q5:0.403	
								Dessert	Q1:0.451 Q2:0.450 Q3:0.410 Q4:0.403 Q5:0.400	
Nanri, H. 2011	Japan	Cross-sectional study	Middle-aged Japanese popuation	F 40-69* y	9545	Factor analysis	Short FFQ	Healthy	Q1:0.296 Q2:0.308 Q3:0.313 Q4:0.289 Q5:0.285	Age, alcohol consumption, smoking, and physical activity level and body mass index
								Western	Q1:0.280 Q2:0.311 Q3:0.291 Q4:0.301 Q5:0.309	
								Seafood	Q1:0.302 Q2:0.302 Q3:0.283 Q4:0.305 Q5:0.300	
								Bread	Q1:0.303 Q2:0.301 Q3:0.292 Q4:0.304 Q5:0.290	
								Dessert	Q1:0.303 Q2:0.303 Q3:0.291 Q4:0.295 Q5:0.300	
Nettleton, J. A. 2010	USA	Cross-sectional study	Adults	M/F M:71.8[s] F:70.7[s]	1101	PCAe	FFQ	Healthy	Q1:3.43±0.3 Q2:3.96±0.5 Q3:3.23±0.6 Q4:2.52±0.2	
								Western	Q1:3.19±0.3 Q2:3.62±0.4 Q3:3.08±0.3 Q4:3.14±0.2	
Centritto, F. 2009	Italy	Cross-sectional study	Healthy Italian population	M/F ≥35 years	7243	PFA[f]	FFQ	Olive Oil and Vegetables	Q1:1.26±1.09 Q2:1.27±1.09 Q3:1.24±1.09 Q4:1.24±1.09 Q5:1.17±0.99	Age, sex, BMI[g], daily energy intake, socioeconomic status, smoking, total physical activity, and triglycerides

Author	Country	Design	Study population	Sex/ Age	Sample size	Method of identifying dietary patterns	Dietary intake assessment	Type of Dietary pattern	CRP Mean or Median(mg/L)	Factors adjusted for in analyses
								Pasta and Meat	Q1:1.16±1.09 Q2:1.16±1.09 Q3:1.26±1.09 Q4:1.29±1.05 Q5:1.30±1.29	
								Eggs and Sweets	Q1:1.16±0.99 Q2:1.20±1.09 Q3:1.22±1.09 Q4:1.27±1.09 Q5:1.33±1.29	
Eilat-Adar, S. 2009	USA	Cross-sectional study	Inupiat Eskimos	M/F 41.7[$]y	1066	PCA	FFQ	Traditional diet	Q1:0.849 Q3:0.849 Q5:0.8	Age, gender, BMI, MET[h], smoking and drinking status, education level, total energy intake, cancer status, baseline CVD[i], hypertension, and cholesterol medication use.
								Western diet	Q1:0.87 Q3:0.91 Q5:0.899	
								Purchased healthy diet pattern	Q1:0.809 Q3:0.78 Q5:0.99	
								Beverages and sweets diet	Q1:1.01 Q3:0.809 Q5:0.749	
Nettleton, J. 2009	USA	Cross-sectional study	White, black, Hispanic, and Chinese adults free of CVD and diabetes	M/F 45–84* y	5316	PCA	FFQ	Fats and Processed Meat pattern	Q1:1.34 Q3:1.86 Q5:2.32	Sex and age.
								Whole Grains and Fruit pattern	Q1:1.82 Q3:1.87 Q5:1.66	
Nanri, A. 2008	Japan	Cross-sectional study	Adults	M 50-74*	7802	PCA	FFQ	"Healthy"	Q1:0.479 Q2:0.44 Q3:0.42 Q4:0.427 Q5:0.397	Age , BMI, smoking, alcohol, and physical activity
								"High-fat"	Q1:0.466 Q2:0.428 Q3: 0.436 Q4:0.436 Q5:0.452	
								"Seafood"	Q1:0.417 Q2:0.436 Q3:0.445 Q4:0.457 Q5:0.45	
								"Westernized breakfast"	Q1:0.448 Q2:0.451 Q3:0.448 Q4:0.422 Q5:0.44	

Author	Country	Design	Study population	Sex/ Age	Sample size	Method of identifying dietary patterns	Dietary intake assessment	Type of Dietary pattern	CRP Mean or Median(mg/L)	Factors adjusted for in analyses
Nanri, A. 2008	Japan	Cross-sectional	Adults	F 50-74* y	7802	PCA	FFQ	"Healthy"	Q1:0.387 Q2:0.38 Q3:0.373 Q4:0.353 Q5:0.338	Age, BMI, smoking, alcohol, and physical activity
								"High-fat"	Q1:0.356 Q2:0.342 Q3: 0.359 Q4:0.384 Q5:0.363	
								"Seafood"	Q1:0.333 Q2:0.376 Q3:0.367 Q4:0.364 Q5:0.368	
								"Westernized breakfast"	Q1:0.361 Q2:0.365 Q3:0.354 Q4:0.366 Q5:0.357	
Pierce, B. L. 2007	USA	Cross-sectional	A sample of Nisei	M/F Nisei=69.8[$]	209	Confirmatory factor analysis	Short FFQ	Western food factor	Q1:1.61±1.54 Q2:1.31±1.19 Q3:2.03±2.14 Q4:1.76±2.38 Q5:1.76±1.81	
				Sansei= 41.8[$]	259 Sansei	Confirmatory factor analysis	Short FFQ	Western food factor	Q1:0.6±0.64 Q2:1.21±0.95 Q3:1.1±1.22 Q4:1.13±1.61 Q5:1.15±1.4	
					219 Nise, 277 Sansei	Confirmatory factor analysis	Short FFQ	Japanese food factor	Data not shown	
Nettleton, J. 2007	USA	Cross-sectional	Participants with no CVD	M/F 45-84*y	5089	PCA 1	FFQ	"fats and processed meats"	Q1:1.44 Q3:1.86 Q5:2.10	
Mikkilä, V. 2007[a]	Finland	Cross-sectional	Young adults	M/F 24-39* y Male	1037	PCA	48-h recall	"Traditional"	Q1:1 Q2-Q4:2.1 Q5:2.7	Age
								"Health-conscious"	Q1:1.91 Q2-Q4:2.01 Q5:2.19	
Mikkilä, V. 2007[b]	Finland	Cross-sectional	Young adults	M/F 24-39* y Female	1037	PCA	48-h recall	"Traditional"	Q1:2.1 Q2-Q4:1.9 Q5:1.7	Age
								"Health-conscious"	Q1:2.3 Q2-Q4:1.9 Q5:1.53	
Esmaillzadeh, A. 2007	Iran	Cross-sectional	Healthy women	F 40-60* y	486	Factor analysis	FFQ	"Healthy"	Q1:2.2±1.2 Q3:1.8±1.8 Q5:1.9±1.3	Age, smoking, physical activity, current estrogen use, menopausal status, family history of diabetes and stroke, and energy intake, BMI and WCj.

Author	Country	Design	Study population	Sex/ Age	Sample size	Method of identifying dietary patterns	Dietary intake assessment	Type of Dietary pattern	CRP Mean or Median(mg/L)	Factors adjusted for in analyses
								"Western"	Q1:2±2.2 Q3:2±2.3 Q5:2.3±2	
								"Traditional"	Q1:2.1±2.4 Q3:2.3±2.2 Q5:2.2±2.2	
Nettleton, J. A. 2006	USA	Cross- sectional	non-Diabetic population	M/F 45-84*y	5089	PCA	FFQ	Fats and processed meats	Q1:1.52±1.04 Q2:1.71±1.04 Q3:1.81±1.04 Q4:1.99±1.04 Q5:2.02±1.05	Study center , age , education, energy , active leisure activity, inactive leisure activity , smoking, and supplement use
								Vegetables and fish	Q1:1.75±1.04 Q2:1.9±1.04 Q3:1.82±1.04 Q4:1.81±1.04 Q5:1.73±1.04	
								Beans, tomatoes and refined grains	Q1:1.7±1.04 Q2:1.74±1.04 Q3:1.8±1.04 Q4:1.93±1.04 Q5:1.84±1.04	Age, BMI, physical activity, smoking, and average alcohol consumption
								Whole grains and fruit	Q1:1.96±1.04 Q2:1.99±1.04 Q3:1.8±1.04 Q4:1.74±1.04 Q5:1.55±1.04	
Lopez-Garcia, E. 2004	USA	Cross-sectional	Women	F 43-69* y	732	PCA	FFQ	Prudent	Q1:0.15 Q2:0.17 Q3:0.16 Q4:0.14 Q5:0.13	
								Western	Q1:0.12 Q2:0.15 Q3:0.15 Q4:0.16 Q5:0.17	
Fung, T. T. 2001	USA		A subsample of men from the Health Professionals Follow-up Study	M 40-75* y	466	factor analysis	FFQ	Prudent	Q1:2.4±0.3 Q3:1.6±0.3 Q5:1.8±0.3	
								Western	Q1:1.7±0.3 Q3:1.9±0.3 Q5:2.5±0.3	

*[a] M: male, [b] F: female, [c] FFQ: food frequency questionnaire, [d] Q: quartile/quintile, [e] PCA: principal component analysis, [f] PFA: principal factor analysis, [g] BMI: body mass index, [h] MET: metabolic equivalent, [i] CVD: cardiovascular disease, [j] WC: waist circumferences. *represent range, [$] represent mean.*

Healthy diets

The results of all studies that examined the association between the healthy diet consumption and change of hs-CRP are shown in Figure 2. Subjects with higher consumption of the healthy diet were shown to have lower levels of hs-CRP (WMD: -0.23; 95% CI: -0.40 to -0.056; p = 0.006). There was evidence of heterogeneity (I2 = 99.8%, p < 0.001).

Western/unhealthy diets

Results from the meta-analysis of the Western diet are presented in Figure 3. A significant positive association between consumption of the Western/unhealthy diets and levels of hs-CRP was observed (WMD: 0.19; 95% CI: 0.15 to 0.23; p < 0.001), although there was significant heterogeneity (I2 = 99.8%, p < 0.001).

Sensitivity analysis

There were not much changes in the mean difference in Western/unhealthy pattern after the exclusion of Hoffman et al [32] (WMD = 0.18, 95% CI: 0.15 to 0.23; p < 0.001, I2 = 99.8%). Excluding Mikka's study [35] resulted in a WMD of 0.14 (95% CI: 0.10 to 0.18; p < 0.001, I2 = 99.7%). When we excluded Nettelton's study [35], subjects with higher consumption of the healthy diet were shown to have a lower change of hs-CRP (WMD: -0.17; 95% CI: -0.26 to -0.08; p = 0.001) and there was no evidence of heterogeneity (I2 = 16.0% and p = 0.23).

Publication bias

The funnel plot for the Western/unhealthy pattern and healthy/prudent patterns gave evidence of asymmetry and small-study effects (Figure 4). However, it was not confirmed by Egger's test (p = 0.64 for healthy/prudent dietary patterns and p = 0.93 for unhealthy/Western patterns).

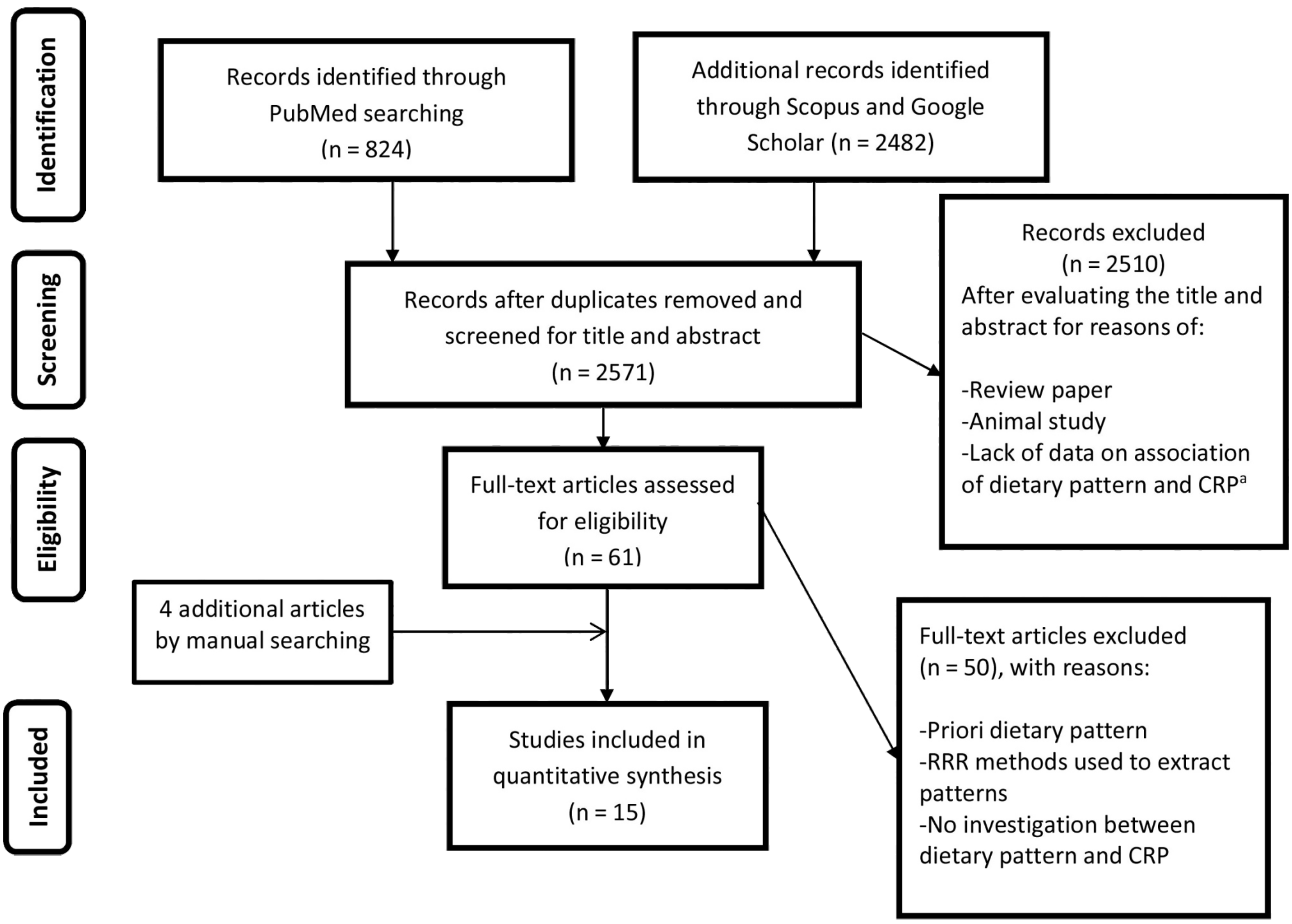

Figure 2. Summary of the study methodology, processes of review, and outcomes of inclusion and exclusion criteria
[a] C-reactive protein

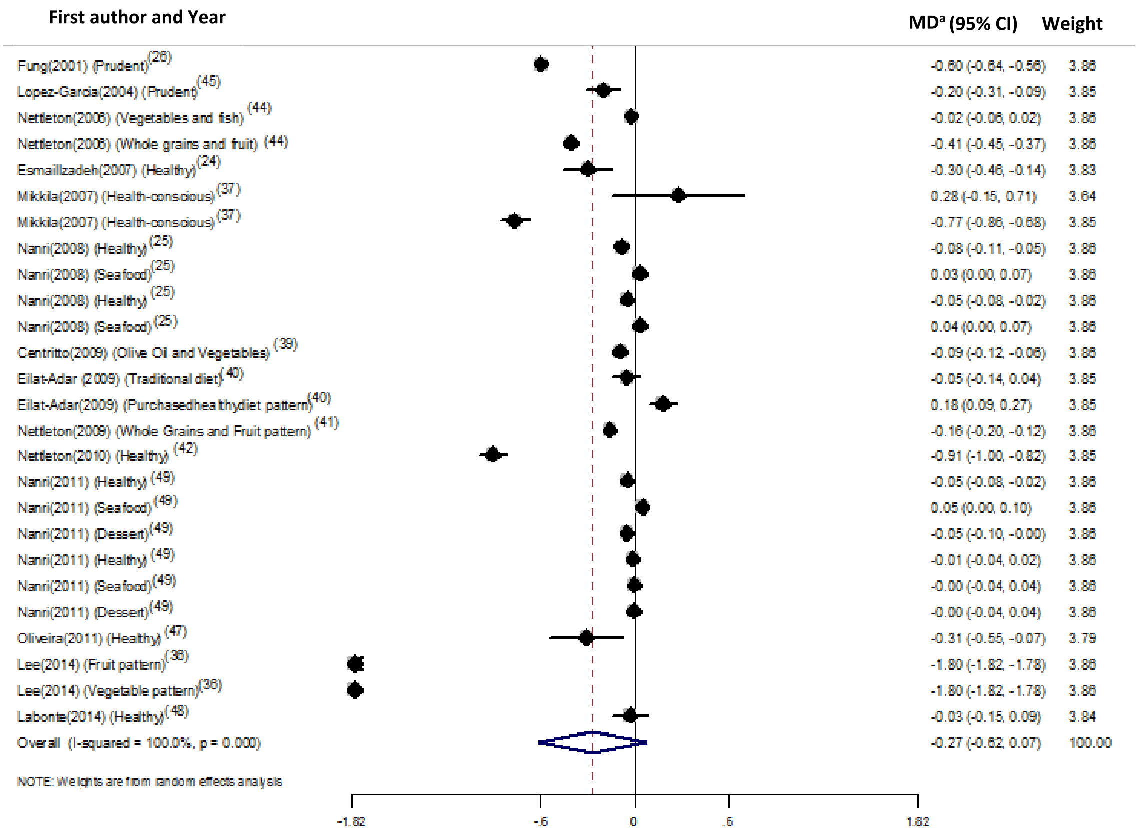

Figure 3. Forest plot of Healthy/Prudent pattern and CRPb level
a MD: mean difference, b C-Reactive Protein, Values are mg/L.

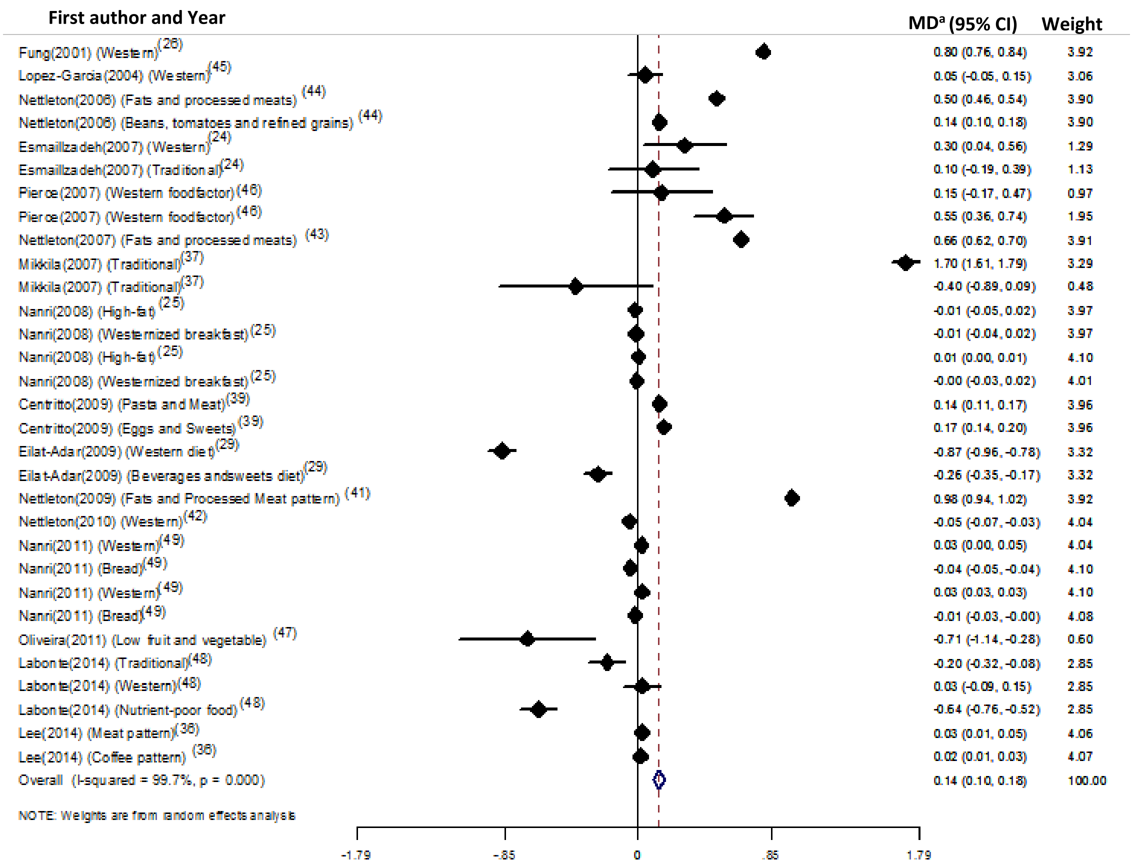

Figure 4. Forest plot of unhealthy/Western pattern and CRP[b] level
a MD: mean difference, b C-Reactive Protein, Values are mg/L.

Discussion

The existing evidence indicates that adherence to healthy/prudent dietary patterns is associated with reduced hs-CRP levels, while unhealthy/Western dietary patterns are associated with increased hs-CRP levels in adults.

Healthy dietary patterns have been proven to prevent subclinical inflammation [47]. Although it is difficult to compare the results of dietary pattern studies because the derived patterns are unique to each study population, healthy/prudent patterns share certain food groups with similar factor loadings. Healthy/prudent patterns are rich in whole grains, vegetables, fruits, poultry, fish, and low-fat dairy products and low in refined grains, red meat, sweetened beverages, added fats, sweets, and high-fat dairy products. It has been reported that this dietary pattern is linked to lower systemic inflammation. These dietary patterns are high in specific protective nutrients, some perhaps not yet identified, but the current study was not intended to investigate the effects of individual nutrients [48]. Higher vitamin C [49, 50] and fiber [51] content of these foods may mediate their beneficial effects on the risk markers. However, the inverse relation of the healthy/prudent pattern to inflammatory markers may not be confined to its fruit and vegetable content; other foods such as tea [15], fish [52], and whole grains [14] in this pattern may contribute to the associations.

In our analyses, an increase in hs-CRP levels with the unhealthy/Western dietary pattern was observed when the results of all studies were pooled. This finding is not surprising because the Western dietary pattern includes a collection of unhealthy foods such as high-fat dairy, butter, red meat, and other sources of cholesterol and saturated and trans fatty acids, all of which are suggested to have a potential positive association with hs-CRP [16, 53]. This association may be to some extent explained by increasing body mass index (BMI) and accumulating body fat. Adipose tissue secretes proinflammatory cytokines such as tumor necrosis factor α and interleukin 6. These cytokines stimulate the production of inflammatory markers such as CRP, which suggests the effect of the Western /unhealthy dietary pattern on the development of several diseases.

This systematic review was performed with an assumption of methodological homogeneity across articles in population characteristics, study design, and methods used for measuring exposure and for characterizing dietary patterns. All included articles adopted a cross-sectional design to explore the association of potential dietary patterns with CRP level. In addition, the two patterns under study were selected from the included articles with similar higher factor loadings in target components. However, we had heterogeneity among studies in both patterns in term of association with circulating hs-CRP, which partially contributed to the variation in FFQs used for measuring dietary intakes. Variation in FFQs could influence the selection of foods loading on the dietary patterns. Moreover, the heterogeneity of reported results may be explained by the number of confounders controlled for in the studies, which could pose challenges to interpretation of the diet-disease relationship. However, the effect size in most of the studies was adjusted for major potential confounding variables, including age, sex, BMI, education, energy intake, and physical activity.

To minimize the risk of bias, we matched factor loadings as closely as possible between studies. The actual factor loading for the same food within the same dietary pattern was never identical between studies. Additionally, it is possible that intercultural variations in such factors as cooking methods or food grouping, which could not be accounted for, may have contributed to inter-study heterogeneity. Moreover, the principal component factor analysis used for deriving the dietary patterns in the included articles is a subjective technique and may increase variation at almost every step, such as a variation in the number, type of dietary patterns derived within each study, and categories of dietary patterns score [54].

Our review indicates that healthy/prudent patterns are associated with a reduction in hs-CRP levels, while an unhealthy/Western one is associated with a substantial increase in levels of hs-CRP in adults. Although dietary patterns are diverse across different populations, the general recommendation of increasing the intake of fruits, vegetables, and complex carbohydrates and reducing the intake of refined carbohydrate, meat, processed meat, and fried foods may improve circulating levels of hs-CRP. Further well-designed clinical trials are needed to test the efficacy of compliance with dietary patterns in reducing circulating levels of hs-CRP.

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Author disclosure statement

There is no conflict of interest to declare.

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