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Association of dietary inflammatory potential with cardiometabolic risk factors and diseases: a systematic review and dose–response meta-analysis of observational studies

Zahra Aslani1,2, Omid Sadeghi1,2, Motahar Heidari-Beni3, Hoda Zahedi4, Fereshteh Baygi5, Nitin Shivappa6,7,8, James R. Hébert6,7,8, Sajjad Moradi9,10, Gity Sotoudeh1, Hamid Asayesh11, Shirin Djalalinia12,13 and Mostafa Qorbani14,15*

Abstract

Context: The association of dietary inflammatory index (DII®), as an index of inflammatory quality of diet, with cardiometabolic diseases (CMDs) and risk factors (CMRFs) has been inconsistent in previous studies.

Objective: The current systematic review and dose–response meta-analysis was performed to investigate the association of the DII score with CMDs and CMRFs.

Data Sources: All published observational studies (cohort, case–control and cross-sectional) using PubMed/Medline, Scopus, ISI Web of Science, and Google Scholar databases were retrieved from inception through November 2019.

Data extraction: Two reviewers independently extracted the data from included studies.

Data analysis: Pooled hazard ratio (HR) or odds ratio (OR) were calculated by using a random-effects model.

Results: Ten prospective cohort studies (total n = 291,968) with 31,069 CMDs-specific mortality, six prospective cohort studies (total n = 43,340) with 1311 CMDs-specific morbidity, two case–control studies with 2140 cases and 6246 controls and one cross-sectional study (total n = 15,613) with 1734 CMDs-specific morbidity were identified for CMDs. Meta-analyses of published observational studies demonstrated that the highest DII score category versus the lowest DII score category was associated with 29% increased risk of CMDs mortality (HR = 1.29; 95% confidence interval (CI) 1.18, 1.41). Moreover, there was a significant association between the DII score and risk of CMDs in cohort studies (HR = 1.35; 95% CI 1.13, 1.61) and non-cohort study (HR = 1.36; 95% CI 1.18, 1.57). We found a significant association between the DII score and metabolic syndrome (MetS) (OR: 1.13; 95% CI 1.03, 1.25), hyperglycemia and hypertension. None-linear dose response meta-analysis showed that there was a significant association between the DII score and risk of CMDs mortality (Pnonlinearity < 0.001). Moreover, evidence of none-linear association between the DII score and risk of CMDs was not observed (p-value = 0.1).

Conclusions: Adherence to pro-inflammatory diet was associated with increased risk of CMDs, mortality and MetS.

Keywords: Diet, Inflammation, Cardiovascular diseases, Dietary inflammatory index

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including high sensitivity C-reactive protein (hs-CRP), interleukin (IL)-6, and tumor necrosis factor-α (TNF-α). This situation is associated with chronic outcomes including cardiovascular diseases (CVDs) [2], type 2 diabetes mellitus [3], cancer [4], obesity [5], and metabolic syndrome (MetS) and its components [6]. The association of diet with inflammation and CVDs is well demonstrated in previous studies. Adherence to Mediterranean diet, which is characterized by high intake of fruits and vegetables, whole grains, legumes, nuts, fish, and olive oil, decreases chronic inflammation and is associated with lower risk of CVDs [7–11], whereas intake of foods with high amount of sugar, refined grains, red and processed meat, foods with high saturated and trans fatty acids, and sodium (Western diet) is associated with higher levels of chronic inflammation and intermediate markers of CVDs [12].

The dietary inflammatory index (DII) is a novel and validated tool designed in 2009 [13] and updated in 2014 to estimate the inflammatory potential of an individual's diet [14]. According to this index, the food items, macronutrients, and micronutrients (45 food parameters) based on their effect on inflammatory biomarkers (IL-1β, IL-4, IL-6, IL-10, TNF-α, and CRP) were classified into pro-inflammatory, anti-inflammatory, and inflammatory neutral [14].

Multiple studies have assessed the association of the DII score with different chronic diseases [15–18] and their risk factors [19–23]; however, findings are conflicting. Various studies showed the association between the DII score and cardiometabolic risk factors (CMRFs) such as MetS [23], hypertension (HTN) [17, 24], and serum glucose levels [20], while other studies did not show this association [25–28]. Several observational reports have demonstrated the obvious association of the DII score with cardiometabolic diseases (CMDs)-specific morbidity and mortality [15, 19, 29, 30], whereas other studies failed to find any association [31, 32].

Given the inconsistent findings, this meta-analysis was conducted to summarize the association of DII with CMRFs and CMDs in observational studies.

Although recently some systematic reviews and meta-analyses have addressed the association between the DII score and CVDs morbidity and mortality [33–35] and MetS [34], none of them has evaluated the association of DII score with cardio-metabolic risk factors (e.g. lipid profile, glycemic indices, and anthropometric measures). Moreover, there is no comprehensive systematic review of estimating the association of both continuous and categorical DII score variables with CMRFs (e.g. lipid profile, glycemic indices, anthropometric measures, blood pressure (BP), and metabolic syndrome) and CMDs-specific morbidity and mortality. Therefore, the aim of this systematic review and meta-analysis study was to assess the association of both continuous and categorical DII score variables with risk of CMRFs and risk of CMDs and mortality.

**Methods**

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for reporting in the current systematic review and meta-analysis study (Additional file 1: Appendix S1).

**Search strategy**

Published reports with the aim of studying the association of DII score with CMRFs (e.g. glycemic indices, lipid profiles, anthropometric measures, MetS and its components) and CMDs (like MI, IHD, stroke, congestive heart failure, and coronary heart disease (CHD) according to the International Classification of Diseases (ICD)-9-390-465) were included through comprehensive searches on PubMed and the NLM Gateway (for MEDLINE), Scopus, and Institute of Scientific Information (ISI) electronic databases up to February 2020. The appropriate medical subject headings, Entry Terms, and Enttree options were applied to carry out the most sensitive search operations. The search strategy is presented in Additional file 2: Appendix S2. A manual search was performed on Google Scholar database and the references listed in relevant reviews.

**Inclusion criteria**

Two reviewers (ZA and HA) independently reviewed and screened the appropriate published papers based on title, abstract, and full text. The third reviewer (MQ) resolved any discrepancy in choosing eligible records. All observational studies (cross-sectional, case–control, and cohort) on human subjects without restriction of age group, gender, year of publication, and language examining the association between the DII score with CMRFs (e.g. glycemic indices, lipid profiles, anthropometric measures, MetS and its components) and CMDs were included in the current study.

**Exclusion criteria**

The papers with the following conditions were excluded: (1) studies that considered the DII as a dependent variable, (2) letters, abstracts and reviews, and (3) duplicated publications. For multiple publications of the same population, only the article with the largest sample size was included.

The participants, intervention, comparators, outcomes, study design criteria are listed in Table 1.
Table 1 Participants, intervention, comparators, outcomes, study design (PICOS) criteria for inclusion of studies

| Population        | All population   |
|-------------------|------------------|
| Intervention      | The DII score    |
| Comparison        | The higher DII score vs. the lower DII score |
| Outcome           | Risk of cardiometabolic diseases and mortality |
| Study design      | Observational studies |

Data extraction
Two investigators (ZA and SD) independently extracted the following information from each qualified study: first author, year of publication, study design, country, age range/mean age, gender, sample size, diet assessment tool, the number of subjects with abnormal CMRFs/CMRs, the number of subjects with CMDs, follow-up duration, exposure variable (DII/E-DII), and the number of food items used to calculate it, the type and definition of outcome, outcome assessment method, the type of DII score variable (categorical/continuous), and effect size, study quality, and confounders. Any disagreements were removed by the third author (MQ). Studies which reported correlation or beta coefficient, were included in the systematic review and they were not entered the meta-analyses.

Quality assessment
The quality assessment of included studies was performed by two independent reviewer using Newcastle–Ottawa Scale (NOS) [36]. This scale consists of three portions of the selection, comparability and outcomes/exposures, and the studies earned maximum nine points. In the present study, the reports with seven or more stars were assumed to have high quality. Any discrepancy between reviewers was resolved by the third reviewer (MQ).

Statistical analysis
All observational studies with any reported effect size (odds ratio (OR), hazard ratio (HR), correlation, or Beta coefficient) were included in qualitative synthesis. Meta-analysis was performed only for studies which reported OR and HR.

In meta-analysis, we examined association of all types of DII [continuous (per one-unit increment), categorical (highest/lowest level) and dose–response association] with CMRFs and CMDs. Meta-analyses were performed separately for CMRFs morbidity, CMDs morbidity, and CMDs related mortality.

We performed random/fixed effects meta-analysis using maximally adjusted OR/HR with 95% confidence interval (CI). Heterogeneity among studies was assessed by $I^2$ [37–39]. There was between-study heterogeneity if $I^2 > 50\%$ and $p < 0.1$ for the result of Q test. If the results showed the heterogeneity, a random-effects model (the DerSimonian–Laird estimator) was applied to assess the pooled OR/HR. The results of the meta-analyses were schematically presented by forest plots.

Dose–response meta-analysis was performed using a method suggested by Greenland and Orsini [40] to assess the dose–response association between DII score and CMDs related morbidity and mortality. The natural logs of the HRs and their CIs across categories of the DII score were used to compute study-specific slopes (linear trends). In this method, the distribution of cases and the HRs with the variance estimates for $\geq 3$ quantitative categories of exposure were required. We considered the median or mean values of the DII scores in each category to the corresponding HR for each study. For studies that reported the scores as ranges, the midpoint was estimated in each category by calculating the mean of the lower and upper bound. When the highest and lowest categories were open-ended, the length of these open-ended intervals was assumed to be the same as that of the adjacent intervals. Restricted cubic splines (three knots at fixed percentiles of 10%, 50%, and 90% of the distribution [41]) was used to examine potential nonlinear dose–response associations of the DII score with risk of CMDs and mortality.

Publication bias was examined using Egger test and funnel plots. Subgroup analysis according to the type of study design was used to examine the association between the DII score with risk of CMDs and mortality. Sensitivity analysis was performed to assess the effect of removing any of the studies or group of studies on CMDs and CMRFs. All statistical analyses were performed using Stata software version 12 (Stata Corp, College Station, Texas, USA) and $p$-value < 0.05 was considered statistically significant.

Results
Search results and study selection
A flow diagram for the process of study selection is shown in Fig. 1. The initial search recognized 1,535 papers, and 708 of them remained after duplicate exclusion. Then 653 papers were removed after examining title/abstract and full text of records. The papers were investigated according to the inclusion and exclusion criteria. Eventually, 55 studies were included in the systematic review [15–17, 19–32, 42–79] and 32 records (16 records for CMRFs [17, 19, 20, 23–26, 28, 58, 61, 62, 68, 70, 72, 73, 76] and 18 records for CMDs [15–17, 19, 29–32, 51–57, 77–79]) were selected for meta-analysis. Two studies addressed the association between the DII score and both CMRFs and CMDs outcomes [17, 19].
Fig. 1  Flow chart of study selection process
various outcomes of CMRFs, we considered only studies reporting OR along with 95% confidence interval (CI) for MetS or its components in the meta-analysis.

Study characteristics
Overall, 55 eligible publications were included in the study. Tables 2 and 3 show the general characteristics of included studies. In general, nine and 10 surveys had considered the morbidity [15–17, 19, 30, 32, 52, 53, 57] (the range of HR was 0.98 [32] to 2.03 [17]) and mortality [29–31, 51, 54–56, 77–79] (the range of HR was 0.98 [51] to 2.50 [78]) of CMDs as outcome, respectively. In addition, 39 studies addressed the association between the DII score and CMRFs [17, 19–28, 42–50, 58–76]. Four case–control studies [15, 21, 57, 74], 23 cohort studies [16, 17, 22–24, 27, 29–32, 44, 45, 48, 51–56, 59, 77–79], and 28 cross-sectional studies [19, 20, 25, 26, 28, 42, 43, 46, 47, 49, 50, 58, 60–73, 75, 76] were included. The number of subjects included in the studies ranged from 90 [48] to 83,054 [79]. The age range of participants was 3–97 years. All records were published between 2014 and 2019. The included studies were conducted in Sweden [15, 45, 55], Australia [24, 29, 32, 53, 77], USA [19, 20, 27, 44, 46, 50, 51, 54, 56, 70, 78, 79], France [23, 52], Spain [16, 17, 22, 47, 49, 63, 69], Germany [31], Italy [57], England [30] Luxembourg [26, 42], Iran [21, 43, 58, 60, 65, 71, 73, 74], Lebanon [68, 75], Poland [28], Myanmar [72], Ireland [62], China [76], Mexico [64], Indonesia [66], Pakistan [67], Brazil [59, 61], and Colombia [48]. The maximum duration of follow up in cohort studies was 25.8 years [31]. Of total included studies, eleven studies were performed on women [24, 27, 29, 32, 50, 54, 55, 59, 72, 74, 75] three on men [31, 53, 67] and 41 reports contained both men and women [15–17, 19–25, 28, 30, 42–49, 51, 52, 56–58, 60–66, 68–71, 73, 76–79]. Validated food frequency questionnaire (FFQ) was applied to assess dietary intakes in 36 studies [15–17, 20–22, 24–30, 32, 42–45, 47, 49, 50, 53–55, 57, 58, 60–62, 64–66, 71, 73, 74, 77, 79], 24-h recall in 13 surveys [16, 19, 46, 51, 56, 59, 67–70, 75, 76, 78], 72- hour recall in one study [63], 24-h recall and FFQ in one report [72] and record in four studies [23, 31, 48, 52]. The exposure variable was considered categorical in 42 studies [15–17, 19–26, 28–32, 43, 46, 48, 51–58, 60, 62, 64, 65, 67, 68, 70, 72–79] and continuous in 32 studies [16, 19, 21, 28–32, 42–45, 47, 49, 50, 52, 54–61, 63, 66, 69, 71, 74, 76, 78, 79].

Results of qualitative synthesis

**Association between the DII score with risk of CMDs and mortality**
The positive association between the DII score (as a continuous variable) and risk of CMDs and mortality was observed in three [16, 19, 57] and six [29, 30, 54, 56, 78, 79] studies, respectively. Moreover, three records did not indicate the significant association between the DII score and risk of CMDs [31, 32, 52]. In addition, two studies failed to find any significant association between the DII score and risk of CMDs mortality [31, 55].

The DII score (as a categorical variable) was associated significantly with the risk of CMDs in six studies [15–17, 19, 30, 57] and seven reports showed the positive association between the index and risk of CMDs mortality [29, 51, 54, 56, 77–79]. Furthermore, three studies did not demonstrate any significant association between the DII score and risk of CMDs [31, 32, 52]. Moreover, three studies reported no significant association between this index and risk of CMDs mortality [30, 31, 55]. In one study, a significant association was observed between the DII score and risk of CMDs mortality only in normal and pre-diabetic participants [51].

**Association between DII with CMRFs**
Totally, 39 studies (28 cross-sectional study [19, 20, 25, 26, 28, 42, 43, 46, 47, 49, 50, 58, 60–73, 75, 76], nine cohort study [17, 22–24, 27, 44, 45, 48, 59] and two case–control studies [21, 74]) had assessed CMRFs as an outcome [17, 19–28, 42–50, 58–76]. The lowest and highest reported ORs were observed for the association between the DII score and abdominal obesity [OR: 0.58 (95% CI 0.16, 2.05)] [58] and morbidity of pre-diabetes [OR: 18.88 (95% CI 7.02, 50.82)] [21], respectively. Nine studies reported no association between the DII score and abdominal obesity [20, 25, 26, 28, 58, 68, 72, 73, 76]. Two reports illustrated a significant association between the DII score and low level of high-density lipoprotein cholesterol (HDL-C) [26, 28], whereas six studies failed to find this association [20, 25, 58, 68, 73, 76]. With respect to hypertriglyceridemia, eight studies reported no association between this score and hypertriglyceridemia [20, 25, 26, 28, 58, 68, 73, 76]. The DII score was associated with HTN in five studies [17, 19, 24, 70, 76] and eight studies did not show any significant association [20, 25–28, 58, 68, 73]. Moreover, one study reported no association between the DII score and gestational HTN [27]. Six studies reported no association between the DII score and hyperglycemia [25–28, 58, 76], whereas two studies revealed this association [20, 73]. Another study indicated a positive association between this score and hyperglycemia only in men [68]. Also, four studies reported a positive association between the DII score and MetS [23, 62, 70, 73]; six studies reported no association in this regard [20, 25, 26, 28, 61, 76]. Moreover, one study demonstrated a significant association between this score and MetS only in men [68]. In terms of body mass index (BMI), four studies showed no association between the
| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | Number of subjects with CMDs (years) | Duration of follow-up (years) | Number of used dietary factors in DII calculation | Outcome Measure of outcome | Type of DII variable (categorical/measure continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|-------------------|--------|-------------|----------------------|-------------------------------------|-------------------------------|---------------------------------|-----------------------------|-------------------------------|--------------------------|--------------------------|-------------|------------|
| 15        | Bodén et al 2017    | Case–control | Sweden  | 30–73             | F/M    | 6944        | FFQ                  | 1389                                | 6.4                           | 30                              | Morbidity                   | Quartile-4 (NR) vs. Quartile-1 (NR) | Categorical OR            | 1.37 (1.07, 1.73)          | 8           | 1, 2, 3, 4, 5, 6, 7, 8 |
| 29        | Bondonno et al. 2017 | Cohort      | Australia | ≥ 70               | F      | 1304        | FFQ                  | 269                                 | 15                            | 31                              | Mortality                  | Quartile-4 (1.72, 5.80) vs. Quartile-1 (−6.14, −1.37) | Categorical HR              | 2.02 (1.30, 3.13)          | 8           | 1, 2, 7, 9, 10, 11, 12, 13, 14, 15, 16 |
|           |                     |              |         |                   |        |             |                      |                                     |                               |                                 | Ischaemic cerebrovascular disease | Quartile-4 (1.72, 5.80) vs. Quartile-1 (−6.14, −1.37) | Categorical               | 1.36 (1.15, 1.66)          | 4           | 2, 7, 9, 10, 11, 12, 13, 14, 15, 16 |
| 51        | Deng et al. 2017    | Cohort      | USA     | 20–90             | F/M    | 9631        | 24-h dietary recall | 676                                 | 18                            | 27                              | Mortality                   | Quartile-3 (>2.0) vs. Quartile-1 (<−0.20) | Categorical HR              | 1.52 (1.18, 1.96)          | 9           | 2, 3, 4, 7, 9, 17, 18, 19 |
| 16        | Garcia-Arellano et al. 2015 | Cohort | Spain  | 67.0              | F/M    | 7216        | FFQ                  | 277                                 | Median follow-up of 4.8         | 32                              | Morbidity                   | Quartile-4 (median = 1.17) vs. Quartile-1 (median = −2.46) | Categorical HR              | 1.73 (1.15, 2.60)          | 7           | 1, 3, 4, 6, 7, 9, 17, 20, 21, 22, 23, 24, 25, 26 |
| 52        | Neufcourt et al. 2016 | Cohort     | France  | 35–60             | F/M    | 7743        | At least 3 valid 24-h dietary records | 292                                 | 13                            | 36                              | Morbidity                   | Quartile-4 (mean (Q4) vs. Quartile-1 (−1.7) (Q1)) | Categorical HR              | 1.16 (0.79, 1.69)          | 7           | 1, 2, 3, 7, 9, 17, 25, 27, 28, 29, 30 |
|           |                     |              |         |                   |        |             |                      |                                     |                               |                                 | Overall CVD                  | Quartile-4 (median = 1.17) vs. Quartile-1 (−1.7) | Categorical               | 1.03 (0.96, 1.11)          | 7           | 1, 3, 4, 6, 7, 9, 17, 20, 21, 22, 23, 24, 25, 26 |
Table 2 (continued)

| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | Number of subjects with CMDs (years) | Duration of follow-up (years) | Number of used dietary factors in DII calculation | Outcome Measure of outcome | Comparison | Type of DII variable (categorical/measure continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|--------------------|--------|-------------|---------------------|-------------------------------------|-----------------------------|---------------------------------|-----------------------------|-------------|-----------------------------------------------|-----------------------------|-----------------------------|--------------|-------------|
| 93        | MI                  |              |         |                    |        |             |                     |                                     |                             |                                 | Quartile 4 (mean(IQR) (3.1 (1.3)) vs. Quartile 1 (−1.7 (1.1))) | Categorical              | 2.26 (1.08, 4.71) | 7 1, 3, 4, 6, 7, 9, 31, 32 |                   |             |
| 58        | Stroke              |              |         |                    |        |             |                     |                                     |                             |                                 | Quartile 4 (mean(IQR) (3.1 (1.3)) vs. Quartile 1 (−1.7 (1.1))) | Categorical              | 1.22 (0.56, 2.65) | 7 1, 2, 3, 6, 7, 9, 17, 22, 23, 24, 25, 33, 34, 35, 36 |                   |             |
| 128       | AP/RI               |              |         |                    |        |             |                     |                                     |                             |                                 | Quartile 4 (mean(IQR) (3.1 (1.3)) vs. Quartile 1 (−1.7 (1.1))) | Categorical              | 0.73 (0.41, 1.30) | 7 1, 2, 3, 6, 7, 9, 17, 22, 23, 24, 25, 33, 34, 35, 36 |                   |             |
| 13        | Sudden deaths       |              |         |                    |        |             |                     |                                     |                             |                                 | Quartile 4 (mean(IQR) (3.1 (1.3)) vs. Quartile 1 (−1.7 (1.1))) | Categorical              | NR           | NR                                             |                   |             |
| 53        | O’Neil et al. 2015  | Cohort       | Australia | 20–97              | M      | 1363        | FFQ                 | 76                                  | 5                           | 22                              | Pre-inflammatory (positive DII) vs. anti-inflammatory (negative DII) | Categorical | OR 2.00 (1.01, 3.96) | 7 1, 3, 4, 6, 7, 9, 31, 32 |                   |             |
| 17        | Ramalal et al. 2015 | Cohort       | Spain    | 38                 | F/M    | 18,4794     | FFQ                 | 117                                | Median (89)                 | 28                              | Quartile 4 (−0.74, 3.97) vs. Quartile 1 (−5.14, 2.68) | Categorical | HR 2.03 (1.06, 3.88) | 7 1, 2, 3, 6, 7, 9, 17, 22, 23, 24, 25, 33, 34, 35, 36 |                   |             |
| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | Number of subjects with CMDs | Duration of follow-up (years) | Number of used dietary factors in DII calculation | Study quality | Confounders |
|-----------|---------------------|--------------|---------|-------------------|--------|-------------|---------------------|-----------------------------|-----------------------------|--------------------------------|--------------|-------------|
| 54        | Shivappa et al. 2016| Cohort       | USA     | 55--69 F          | 286.77 | FFQ         | 6528                | NR                          | CVD                         | Mortality                      | Categorical | 1.09 (1.01, 1.18) | 8            | 1, 2, 6, 7, 9, 22, 25, 33, 37, 38 |
|           |                     |              |         |                   |        |             |                     |                             |                             |                                |              |             |
| 3381      |                     |              |         |                   |        |             |                     |                             |                             |                                | Categorical | 1.17 (1.05, 1.30) | 1            | 33, 37, 38 |
| 1439      |                     |              |         |                   |        |             |                     |                             |                             |                                | Categorical | 1.04 (1.08, 1.22) | 1            | 37, 38 |
| 417       |                     |              |         |                   |        |             |                     |                             |                             |                                | Continuous (per one unit) | 1.01 (0.95, 1.08) | 1            |             |
| 736       |                     |              |         |                   |        |             |                     |                             |                             |                                | Continuous (per one unit) | 1.06 (0.95, 1.19) | 1            |             |
| 1177      |                     |              |         |                   |        |             |                     |                             |                             |                                | Continuous (per one unit) | 1.14 (1.05, 1.24) | 1            |             |
| 1825      |                     |              |         |                   |        |             |                     |                             |                             |                                | Continuous (per one unit) | 1.07 (1.01, 1.13) | 1            |             |
| 2373      |                     |              |         |                   |        |             |                     |                             |                             |                                | Continuous (per one unit) | 1.00 (0.96, 1.02) | 1            |             |
| 260       |                     |              |         |                   |        |             |                     |                             |                             |                                | Continuous (per one unit) | 1.13 (0.68, 1.31) | 1            |             |
| 447       |                     |              |         |                   |        |             |                     |                             |                             |                                | Continuous (per one unit) | 1.15 (1.03, 1.28) | 1            |             |
| 681       |                     |              |         |                   |        |             |                     |                             |                             |                                | Continuous (per one unit) | 0.98 (0.90, 1.07) | 1            |             |
| 918       |                     |              |         |                   |        |             |                     |                             |                             |                                | Continuous (per one unit) | 1.12 (1.04–1.20) | 1            |             |
| 1075      |                     |              |         |                   |        |             |                     |                             |                             |                                | Continuous (per one unit) | 1.03 (0.96, 1.11) | 1            |             |
| 54        |                     |              |         |                   |        |             |                     |                             |                             |                                | Continuous (per one unit) | 1.05 (0.77, 1.42) | 1            |             |
| Reference | First author (year) | Study design | Country | Age range/ mean age | Gender | Sample size | Diet assessment tool | Number of subjects with CMDs | Duration of follow-up (years) | Number of used dietary factors in DII calculation | Outcome Measure of outcome | Comparison | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|---------------------|--------|-------------|----------------------|----------------------------|----------------------------|--------------------------------|---------------------------|------------|-----------------------------------------------|-----------------------------|---------------------------|----------------|-------------|
| 129       |                     |              |         |                     |        | 129         |                      | 5–9.99                    |                            |                                | CVD Mortality              | Quintile 5 (≥ 1.91) vs. Quintile 1 (≤ -0.67) | Categorical HR           | 1.07 (0.87, 1.32)               | 8            | 1, 2, 3, 7, 9, 25, 39 |
| 2.33      |                     |              |         |                     |        | 2.33        |                      | 10.00–14.99               |                            |                                | CVD Mortality              | –                        | Continues (per one unit)             | 1.06 (0.92, 1.23)               | 8            | 1, 2, 3, 7, 9, 25, 39 |
| 4.41      |                     |              |         |                     |        | 4.41        |                      | 15.00–19.99               |                            |                                | CVD Mortality              | –                        | Continues (per one unit)             | 1.04 (0.93, 1.16)               | 8            | 1, 2, 3, 7, 9, 25, 39 |
| 5.82      |                     |              |         |                     |        | 5.82        |                      | 20.00–25.00               |                            |                                | CVD Mortality              | –                        | Continues (per one unit)             | 0.90 (0.87, 1.00)               | 8            | 1, 2, 3, 7, 9, 25, 39 |
| 55        | Shivappa et al. 2016| Cohort       | Sweden  | NR                  | F      | 33,747      | FFQ                  | 2.399                      | 15                         | 27                            | CVD Mortality              | Quartile 5 (median = 2.507) vs. Quartile 1 (median = -0.803) | Categorical HR           | 1.26 (0.93, 1.70)               | 8            | 1, 3, 7, 9, 25, 39 |
| 30        | Shivappa et al. 2017| Cohort       | Germany | 45–64               | M      | 1297        | 7-day dietary record | Survey 1: median follow-up = 25.8 |                     |                                | CHD Mortality               | Quartile 4 (median = 2.507) vs. Quartile 1 (median = -0.803) | Categorical HR           | 1.19 (0.76, 1.86)               | 7            | 1, 3, 6, 7, 9, 22, 25, 40, 41, 42 |
|           |                     |              |         |                     |        |             |                      | Survey 3: median follow-up = 16.7 |                     |                                | –                        | Continues (per one unit)             | 1.05 (0.92, 1.20)               | 1, 2, 3, 7, 9, 25, 39 |
|           |                     |              |         |                     |        |             |                      |                            |                                |                                | CHD Morbidity              | Quartile 4 (median = 2.507) vs. Quartile 1 (median = -0.803) | Categorical HR           | 1.02 (0.57, 1.82)               | 8            | 1, 2, 3, 7, 9, 25, 39 |
|           |                     |              |         |                     |        |             |                      |                            |                                |                                | –                        | Continues (per one unit)             | 1.01 (0.86, 1.18)               | 8            | 1, 2, 3, 7, 9, 25, 39 |
| 1252      |                     |              |         |                     |        | 155         |                      |                            |                                |                                | CHD Morbidity              | Quartile 4 (median = 2.507) vs. Quartile 1 (median = -0.803) | Categorical HR           | 1.53 (0.93, 2.53)               | 8            | 1, 2, 3, 7, 9, 25, 39 |
|           |                     |              |         |                     |        |             |                      |                            |                                |                                | –                        | Continues (per one unit)             | 1.11 (0.97, 1.27)               | 8            | 1, 2, 3, 7, 9, 25, 39 |
| 56        | Shivappa et al. 2017| Cohort       | USA     | > 19                | F/M    | 12,366      | One-in-person 24-h dietary recall | 1235                      | Mean ± SD (13.5 ± 4.0)    | 27                            | CVD Mortality              | Tertile 3 (2.03, 4.83) vs. Tertile 1 (−5.60, −0.22) | Categorical HR           | 1.46 (1.18, 1.81)               | 8            | 2, 3, 6, 7, 9, 17, 18, 22, 33, 43 |
| Reference | First author (year) | Study design | Country | Age range/mean age | Gender Sample size | Diet assessment tool | Number of subjects with CMDs | Duration of follow-up (years) | Number of used dietary factors in DII calculation | Outcome Measure of outcome | Comparison | Type of DII variable (categorical/measure continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|---------------------|-------------------|---------------------|-------------------------|-----------------------------|--------------------------------------------------|-------------------------|------------|----------------------------------|-----------------------------|--------------------------|--------------|------------|
| 57        | Shivappa et al. 2017 | Case–control | Italy   | Case (19–79) Control (16–79) | F/M 1442 (423) M (1019) | FFQ 760 – 30 | AMI Morbidity | Quartile 4 (1.10, 5.45) vs. Quartile 1 (−4.46, −1.38) | Continuous (1-unit increment in DII (corresponding to 0.5 standard deviation increase)) | Categorical OR | 1.60 (1.06, 2.41) | 7 | 1, 2, 3, 6, 7, 9, 17, 22, 23, 24, 25, 44 |
| 31        | Vissers et al. Cohort 2016 | Australia | 52 (1) F | 6/972 | FFQ 335 | Mean ± SD (11 ± 1.6) | CVD Morbidity | (DII ≥ 0) vs. (DII < 0) Categorical HR | 1.03 (0.76, 1.42) | 8 | 1, 2, 3, 6, 7, 9, 22, 23, 37, 39, 45 |
| 191       | IHD                 | (DII ≥ 0) vs. (DII < 0) Categorical | 1.33 (0.98, 1.86) | 1, 6, 7, 9, 22 |
| 69        | MI                  | (DII ≥ 0) vs. (DII < 0) Categorical | 1.59 (0.72, 3.52) | 1, 6, 7, 9, 22 |
| 59        | Cerebrovascular disease | (DII ≥ 0) vs. (DII < 0) Categorical | 0.57 (0.29, 1.15) | 1, 6, 7, 9, 22 |
| 40        | Stroke              | (DII ≥ 0) vs. (DII < 0) Categorical | 0.55 (0.24, 1.26) | 1, 6, 7, 9, 22 |
| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | Number of subjects with CMDs (years) | Duration of follow-up (years) | Number of used dietary factors in DII calculation | Outcome Measure of outcome | Comparison | Type of DII variable (categorical/measure continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|-------------------|--------|-------------|---------------------|------------------------------------|-----------------------------|---------------------------------|-----------------------------|-------------|---------------------------------|-----------------------------|----------------------------|-------------------------|-------------|
| 19        | Wirth et al. 2016   | Cross‑ sectional | USA     | 20–80             | F/M    | 15,613 F (8047) M (7566) | 24-h dietary recall | 1734                              | 27                          | Combined circulatory disorders | Morbidity                  | Quartile 4 (194, 483) vs. Quartile 1 (−5.81, −0.81) | Categorical                | POR                     | 1.30 (1.06, 1.58) | 5           | 2, 7, 9, 46                  |
| 15.622    |                     |              |         |                   |        | 501          | Congestive heart failure |                                  |                             |                                 |                             |                                  | Continuous (per one unit) | 1.05 (1.01, 1.08) |
| 15.623    |                     |              |         |                   |        | 634          | CHD                 |                                    |                             |                                 |                             |                                  | Categorical                | 1.38 (1.09, 1.74) |
| 15.643    |                     |              |         |                   |        | 423          | AP                  |                                    |                             |                                 |                             |                                  | Continuous (per one unit) | 1.06 (1.02, 1.10) |
| 15.664    |                     |              |         |                   |        | 685          | Heart attack       |                                    |                             |                                 |                             |                                  | Categorical                | 0.96 (1.72, 1.28) |
| 15.666    |                     |              |         |                   |        | 604          | Stroke             |                                    |                             |                                 |                             |                                  | Continuous (per one unit) | 0.99 (0.94, 1.05) |
| 32        | Shivappa et al. 2017| Cohort      | England | 35–55             | F/M    | 7627 F (2319) M (5308) | FFQ     | 264 22 27         | CVD Mortality                  | Tertile 3 (0.74–3.82) vs. Tertile 1 (−3.08–0.39) | Categorical                | HR                      | 1.46 (1.00, 2.13) | 7           | 1, 2, 3, 6, 9, 7, 17, 18, 22, 29, 33, 39, 47, 48, 49, 50 |
Table 2 (continued)

| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | Number of subjects with CMDs | Duration of follow-up (years) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|-------------------|--------|-------------|---------------------|-----------------------------|-----------------------------|--------------|-------------|
| 77        | Hodge et al. 2018   | Cohort       | Australia | 40–69 F/M         | 3.95   | FFQ         | 2.081               | 19                          | 29                          | CVD Mortality     | 1.23 (1.04, 1.47) | 6, 17, 24, 33, 39, 51, 52 |
| 78        | Mark Park et al. 2018 | Cohort | USA      | 20–90 F/M         | 2.37   | 24-h dietary recall | 2.52               | 18.5                        | 27                          | CVD Mortality     | 1.16 (1.01, 1.33) | 8, 2, 3, 7, 9, 17, 18, 25, 53 |
| 79        | Park et al. 2018    | Cohort       | USA      | 45–75 F/M         | 6.83   | FFQ         | 7.811               | 18.2 ± 4.9                   | 28                          | CVD Mortality     | 1.29 (1.17–1.42) | 1, 2, 3, 6, 7, 9, 18, 25, 29, 37, 39 |
|           |                     |              |          |                   |        | M           | 67,551              | 8401                         |                             |               |             |

1—total energy intake, 2—body mass index, 3—physical activity, 4—systolic blood pressure, 5—total cholesterol, 6—diabetes, 7—smoking, 8—postsecondary academic education, 9—age, 10—energy expended in physical activity, 11—socioeconomic status, 12—use of low-dose aspirin, 13—use of antihypertensive medication, 14—use of statins, 15—prevalent atherosclerotic vascular disease, 16—treatment code, 17—sex, 18—race, 19—HbA1c, 20—overweight/obesity, 21—waist to height ratio, 22—hypertension, 23—dyslipidemia, 24—family history of premature cardiovascular disease, 25—educational level, 26—stratified by intervention group and center, 27—supplementation, 28—number of 24-h records, 29—marital status, 30—treatment allocation group (placebo or active), 31—diastolic blood pressure, 32—waist circumference, 33—previous history of other cardiovascular diseases, 34—following a special diet, 35—hours spent sitting down, 36—hours spent watching television, 37—hormone replacement therapy use, 38—prevalent cancer (yes/no), 39—alcohol intake, 40—survey number, 41—place of residence, 42—ratio of total cholesterol and high density lipoprotein cholesterol, 43—poverty index, 44—coffee consumption, 45—menopausal status, 46—family member, 47—occupational grade, 48—use of lipid-lowering drugs, 49—high density lipoprotein cholesterol, 50—longstanding illness, 51—country of birth, 52—socio-economic indexes for areas quintile, 53—income

F female, M male, FFQ food frequency questionnaire, MI myocardial infarction, AMI acute myocardial infarction, ASVD atherosclerotic vascular disease, IHD ischaemic heart disease, CVD cardiovascular diseases, AP/RI angina pectoris/revascularization intervention, CHD coronary heart disease, OR odds ratio, POR prevalence odds ratio, HR hazard ratio, NR not reported

1 Participants included three groups of normal, pre-diabetic and diabetic adults
| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|--------------------|--------|-------------|---------------------|-------------------------------|---------------------------|-----------------------------------|----------------|-----------------|-----------|------------------------------------------|-----------------|-----------------|--------------|-----------|
| 24        | Alkerwi et al. 2014 | Cross-sectional | Luxembourg | 18–69 | F/M | 1552 F (693) M (857) | FFQ | 430 | – | 24 | Abdominal obesity | Morbidity | DII > 1 vs DII ≤ 1 | Categorical | OR | 1.12 (0.81, 1.56) | 7 | 3, 7, 9, 11, 17, 25 |
| 24        | Alkerwi et al. 2014 | Cross-sectional | Luxembourg | 18–69 | F/M | 249 | – | 24 | | | Low HDL-C | | | | | | 1.46 (1.00, 2.13) | 1.17 (0.82, 1.67) | |
| 24        | Alkerwi et al. 2014 | Cross-sectional | Luxembourg | 18–69 | F/M | 351 | – | 24 | | | Hyper-triglyceridemia | | | | | | 0.85 (0.61, 1.18) | 1.30 (0.90, 1.89) | |
| 24        | Alkerwi et al. 2014 | Cross-sectional | Luxembourg | 18–69 | F/M | 741 | – | 24 | | | HTN | | | | | | 1.18 (0.81, 1.71) | |
| 24        | Alkerwi et al. 2014 | Cross-sectional | Luxembourg | 18–69 | F/M | 307 | – | 24 | | | Hyperglycemia | | | | | | | |
| 24        | Alkerwi et al. 2014 | Cross-sectional | Luxembourg | 18–69 | F/M | 346 | – | 24 | | | MetS | | | | | | | |
| 42        | Alkerwi et al. 2015 | Cross-sectional | Luxembourg | 18–69 | F/M | 1040 F (NR) M (NR) | FFQ | 1040 | – | NR | HDL-C (mmol/l) | Morbidity | – | Continuous (each 1-z score difference across the DII) | β-Coefficient | 0 | 8 | 3, 7, 9, 17, 25 |
| 42        | Alkerwi et al. 2015 | Cross-sectional | Luxembourg | 18–69 | F/M | 1106 F (NR) M (NR) | | | | | TC (mmol/l) | | | | | 0.0409 | |
| 42        | Alkerwi et al. 2015 | Cross-sectional | Luxembourg | 18–69 | F/M | 1,106 | | | | | TG (mmol/l) | | | | | – 0.00003 | |
| 42        | Alkerwi et al. 2015 | Cross-sectional | Luxembourg | 18–69 | F/M | 1153 F (NR) M (NR) | | | | | LDL-C (mmol/l) | | | | | 0.0003 | |
| 42        | Alkerwi et al. 2015 | Cross-sectional | Luxembourg | 18–69 | F/M | 1153 | | | | | ApoA1 (mg/l) | | | | | 0.02 | |
| 42        | Alkerwi et al. 2015 | Cross-sectional | Luxembourg | 18–69 | F/M | 1153 | | | | | Apo B (mg/l) | | | | | 0.13 | |
| 42        | Alkerwi et al. 2015 | Cross-sectional | Luxembourg | 18–69 | F/M | 1106 | | | | | FBS (mmol/l) | | | | | – 0.0002 | |
| 42        | Alkerwi et al. 2015 | Cross-sectional | Luxembourg | 18–69 | F/M | 1106 | | | | | Hba1c (%) | | | | | – 0.0001 | |
| 42        | Alkerwi et al. 2015 | Cross-sectional | Luxembourg | 18–69 | F/M | 1106 | | | | | HOMA-IR | | | | | – 0.0017 | |
| 42        | Alkerwi et al. 2015 | Cross-sectional | Luxembourg | 18–69 | F/M | 1106 | | | | | Insulin (mg/l) | | | | | 0.22 | |
| 42        | Alkerwi et al. 2015 | Cross-sectional | Luxembourg | 18–69 | F/M | 1106 | | | | | BMI (kg/m²) | | | | | 0.003 | |
| 42        | Alkerwi et al. 2015 | Cross-sectional | Luxembourg | 18–69 | F/M | 1007 F (NR) M (NR) | | | | | WC (cm) | | | | | 0.002 | |
| 42        | Alkerwi et al. 2015 | Cross-sectional | Luxembourg | 18–69 | F/M | 1007 | | | | | SBP (mmHg) | | | | | – 0.001 | |
| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/ continuous) | Type of effect size measure | Effect size measure (95% CI) | Confounders | Study quality |
|-----------|---------------------|-------------|---------|-------------------|--------|-------------|---------------------|----------------------------------|---------------------------|-----------------------------------------------|----------------|----------------|-----------|------------------------------------------|--------------------------|------------------------|------------|-------------|
| 43 | Moslehi et al. 2016 | Cross-sectional | Iran | 19–75 | F/M | 2975 | FFQ | F (1641) M (1304) | 1007 | – | 37 | Glucose tolerance abnormality | Quartile 4 (0.29, 5.23) vs. Quartile 1 (−5.82, −2.67) | Categorical OR | 1.15 (0.90, 1.48) | 8 | 2, 3, 6, 7, 9, 17, 22, 48 |
| | | | | | | | | | | | | IFG | 1.09 (0.83, 1.44) | 259 | | |
| | | | | | | | | | | | IGT | 1.24 (0.84, 1.81) | 286 | | |
| | | | | | | | | | | | Type 2 diabetes | 0.98 (0.66, 1.47) | 1923 | | |
| | | | | | | | | | | | Insulin resistance | 1.18 (0.91, 1.51) | 2975 | | |
| | | | | | | | | | | | FBS levels (mmol/L) | - | Continuous β-Coefficient | 0.01 | | |
| | | | | | | | | | | | Postload glucose levels (mmol/L) | | | | |
| | | | | | | | | | | | Fasting insulin (U/mL) | | | | |
| | | | | | | | | | | | HOMA-IR | | | | |
| | | | | | | | | | | | HOMA-B | | | | |
| | | | | | | | | | | | QUICKI | | | | |
| 25 | Naja et al. 2017 | Cross-sectional | Lebanon > 18 | | F/M | 330 | FFQ | F (NR) M (NR) | 171 | – | 25 | Abdominal obesity | Quartile 5 (NR) vs. Quartile Categorical 1 (NR) | OR | 0.66 (0.29, 1.48) | 7 | 3, 7, 9, 17, 25, 29, 35 |
| | | | | | | | | | | | Low HDL-C | 0.74 (0.31, 1.75) | 105 | | |
| | | | | | | | | | | | Hyper-triglyceridemia | 0.84 (0.35, 1.03) | 103 | | |
| | | | | | | | | | | | HTN | 0.40 (0.23, 1.04) | 329 | | |
| | | | | | | | | | | | Hyperglycemia | 1.80 (0.80, 4.01) | 331 | | |
| | | | | | | | | | | | MetS | 0.72 (0.31, 1.67) | 328 | | |
| 23 | Neufcourt et al. 2015 | Cohort | France | 35–60 | | 3726 | At least 3 valid 24-h dietary records | 524 | 13 | 36 | MetS | Morbidity | Quartile 4 (mean (QR) 2.97 (1.27)) vs. Quartile 1 (−1.76 (1.07)) | Categorical OR | 1.39 (1.0, 1.92) | 7 | 1, 3, 7, 9, 17, 25, 56 |
| | | | | | | | | | | | Obesity | | | | |
| 22 | Ramalal et al. 2017 | Cohort | Spain | 37.4 | | 7027 | FFQ | F (4355) M (2492) | 1433 overweight (1409) Obese (24) | 10 | 28 | Overweight/Obesity | Morbidity | Quartile 4 (−0.59, 4) vs. Quartile 1 (−5.1, −2.5) | Categorical HR | 1.32 (1.08, 1.60) | 8 | 1, 2, 3, 7, 9, 17, 34, 35, 36, 39, 57, 58, 59, 60 |
| Reference First author (year) | Study design | Country Age range/mean age | Gender Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|------------------------------|-------------|-----------------------------|--------------------|---------------------|----------------------------------|---------------------------|---------------------|-------------------|----------------|------------------------------------------|--------------------------|---------------------------|----------------|------------|
| 17 Ramallal et al. 2015 | Cohort Spain 38 | F/M | FFQ NR 2 | 28 | HTN | Morbidity | Quartile 4 (−0.74, 3.97) vs. Quartile 1 (−5.14, −2.68) | Categorical | OR | 1.71 (1.11, 2.64) | 7 | 1, 2, 3, 7, 9, 17, 24, 25, 35, 36, 39, 57 |
| 44 Sen et al. 2018 | Cohort USA 2.8-4.9 | F/M | FFQ 775 4.5 | NR | BMI z-score | Morbidity | Continue (β-Coefficient (per 1 point increment in pregnancy DII)) | Categorical | OR | 1.04 (0.69, 1.57) | 8 | 9, 17, 25, 18, 53 |
| 481 481 | 481 | 481 | Mid-childhood metabolic risk score | | | | | | | | | | | |
| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|--------------------|--------|-------------|---------------------|-------------------------------|-----------------------------|--------------------------------|-----------------|-----------------|------------|-------------------------------|------------------------|-----------------------------|----------------|-----------|
| 28 Sokol et al. 2016 | Cross-sectional | Poland | 45–64 | F/M | 3862 | FFQ | 1759 | - | 22 | Abdominal obesity | Quartile 4 (−0.75, 4.00) vs. Quartile 1 (−4.56, −2.62) | Categorical | OR | 0.79 (0.61, 1.03) | 7 | 2, 9 | |
| | | | | | | | | | | | | | | | | | | |
| 615 | | | | | | | | | | | | | | | | | |
| 815 | | | | | | | | | | | | | | | | | |
| 2590 | | | | | | | | | | | | | | | | | |
| 1402 | | | | | | | | | | | | | | | | | |
| 1159 | | | | | | | | | | | | | | | | | |
| 21 Vahid et al. 2016 | Case–control | Iran | 31–67 | F/M | 414 | FFQ | 214 | - | 27 | Pre-diabetes | Morbidity | Tertile 3 (≥−0.54) vs. Tertile 1 (<−1.21) | Categorical | OR | 18.88 (7.02, 50.82) | 7 | 1, 2, 3, 7, 9, 17, 25 | |
| | | | | | | | | | | | | | | | | | |
| 414 | | | | | | | | | | | | | | | | | |
| 414 | | | | | | | | | | | | | | | | | |
| 414 | | | | | | | | | | | | | | | | | |
Table 3 (continued)

| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|-------------------|--------|-------------|----------------------|--------------------------------|-----------------------------|---------------------------------|------------------|-----------------|------------|---------------------------------|---------------------------|-------------------------|-----------------|-----------|
| 414       | Vissers et al. 2017 | Cohort       | Australia | 52                | F      | 7,169       | FFQ                  | 1680                          | 12                          | 25                              | DII ≥ 0 vs. DII < 0 | Categorical     | OR          | 1.24 (1.06, 1.45)                      | 7                         | 1, 2, 3, 6, 7, 9, 25, 40, 45 |                |           |
|           |                     |               |          |                   |        |             |                      |                               |                             |                                 |                  |                 |            |                                  |                           |                        |                 |           |
Table 3 (continued)

| Reference | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|--------------|---------|--------------------|--------|-------------|---------------------|---------------------------------|-------------------------------|--------------------------------|------------------|-----------------|------------|----------------------------------------|-------------------|----------------------|---------------|------------|
| Michael D. Wirth et al. 2014 | Cross-sectional | United States of America | 42.4 ± 8.5 | F/M | 447 F (112) M (335) | FFQ | 125 | - | DI (36 food items) | Morbidity | Presence of at least three of the five components: WC of ≥102 cm for males or ≥88 for females; BP ≥ 130 for systolic or ≥85 for diastolic or reported diagnosis of hypertension; HDL-C of < 40 mg/dL in men and < 50 in women; TG ≥ 150 mg/dL and glucose ≥ 100 mg/dL or reported treatment for diabetes | Categorical | OR | 0.87 (0.46–1.63) | Age, sex |
| Wirth et al. 2014 | Cross-sectional | USA | 42.4 | F/M | 447 F (112) M (335) | FFQ | 150 | - | 36 | Abdominal obesity | Morbidity | Quartile 4 (2.64, 5.89) vs. Quartile 1 (−6.27, −1.26) | Categorical | OR | 0.93 (0.52, 1.67) | Age, sex |

1. Quartile 4: Presence of at least three of the five components: WC of ≥102 cm for males or ≥88 for females; BP ≥ 130 for systolic or ≥85 for diastolic or reported diagnosis of hypertension; HDL-C of < 40 mg/dL in men and < 50 in women; TG ≥ 150 mg/dL and glucose ≥ 100 mg/dL or reported treatment for diabetes.

2. Quartile 1: Lower quartile of the DII distribution.

3. OR: Odds Ratio.
| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|--------------------|--------|-------------|---------------------|-------------------------------|-------------------------------|----------------------------------|----------------|------------------|------------|----------------------------|-------------------|------------------------|--------------|------------|
| 46        | Tyrovolas et al. 2017 | Cross-sectional | USA     | ≥ 20               | F/M    | 7880        | F (NR) M (NR)     | 24-h dietary recall          | NR                            | NR – 27                        | CVD-RF morbidity index (included obesity, diabetes, hypertension, and hypercholesterolemia. The total number of these risk factors was calculated (range 0–4) for each individual and used as the outcome) | Quartile 4 (NR) vs. Quartile 1 (NR) | OR               | 1.39 (1.15, 1.67) | 8                 | 3, 7, 9, 17, 18, 25, 29, 33, 59 |
| 19        | Wirth et al. 2016    | Cross-sectional | USA     | 20–80              | F/M    | 15666       | F (NR) M (NR)     | 24-dietary recall            | 5408                          | Quartile 4 (1.94, 4.83) vs. Quartile 1 (-5.81, -0.81) | HTN Morbidity | Categorical OR | 1.19 (1.05, 1.34) | 5                 | 2, 7, 9, 46 |
| 27        | Sen et al. 2015      | Cohort       | USA     | 32.2               | F      | 1779        | FFQ 160           | 6 months                      | 28                            | Isolated hyperglycemia          | -                | Continuous OR | 0.94 (0.82, 1.07) | 7                 | 2, 7, 9, 18, 25, 53 |

| 58        | Impaired glucose tolerance |
| 96        | GDM                      |
| 1775      | Inadequate pregnancy weight gain |
| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects (years) | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|-------------------|--------|-------------|---------------------|-------------------------------|--------------------------|------------------------------------------|----------------|----------------|-------------------------------------------------|----------------|----------------|----------------|----------|
| 47        | Ruiz-Canela et al. 2015 | Cross-sectional | Spain | 56–80 F | 4145 FFQ | 4145 | – | 33 | BMI (kg/m²) | Morbidity | Continuous | Pearson coefficient (r) | Anti-inflammatory diet = −0.122, pro-inflammatory diet = 0.111 | 0.06 (0.03, 0.09) | 1, 3, 6, 7, 9, 22, 25, 29 |
|           |                     |              |         |       |             |           |             |       | WC (cm) |                       |                       | 0.05 (0.02, 0.08) | | |
|           |                     |              |         |       |             |           |             |       | WHR (%) |                       |                       | 0.06 (0.03, 0.09) | | |
|           |                     |              |         |       |             |           |             |       | BMI (kg/m²) |                       |                       | 0.05 (0.01, 0.09) | | |
|           |                     |              |         |       |             |           |             |       | WC (cm) |                       |                       | 0.08 (0.05, 0.20) | | |
|           |                     |              |         |       |             |           |             |       | WHR (%) |                       |                       | 0.09 (0.06, 0.13) | | |
| 48        | Camargo-Ramos et al. 2017 | Cohort | Colombia | 39.7 F/M | 90 F (NR) M (NR) | 24-dietary record | 90 NR | 28 | DXA total tissue (% fat) | Morbidity | Categorical | Pearson coefficient (r) | Anti-inflammatory diet = −0.122, pro-inflammatory diet = 0.111 | 7 | 9, 17 |
|           |                     |              |         |       |             |           |             |       | TC (mg/dL) |                       |                       | Anti-inflammatory diet = −0.210, pro-inflammatory diet = 0.010 | | |
|           |                     |              |         |       |             |           |             |       | TG (mg/dL) |                       |                       | Anti-inflammatory diet = −0.354, pro-inflammatory diet = −0.009 | | |
Table 3 (continued)

| Reference First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-------------------------------|-------------|---------|-------------------|--------|-------------|---------------------|-----------------------------|-----------------------------|-----------------------------------------------|-----------------|-------------------|-----------|---------------------------------------------|-----------|------------------|-------------|------------|
|                              |             |         |                   |        |             |                     |                             |                             |                                | HDL-C (mg/dL)     | Anti-inflamatory diet = -0.100, Pro-inflammatory diet = 0.028 |            |                                |             |            |             |
|                              |             |         |                   |        |             |                     |                             |                             |                                | LDL-C (mg/dL)     | Anti-Inflammatory Diet = 0.350, Pro-Inflammatory Diet = -0.084 |            |                                |             |            |             |
|                              |             |         |                   |        |             |                     |                             |                             |                                | FBS (mg/dL)       | Anti-inflammatory diet = -0.422, pro-inflammatory diet = -0.228 |            |                                |             |            |             |
|                              |             |         |                   |        |             |                     |                             |                             |                                | MetScore          | Anti-inflammatory diet = -0.292, pro-inflammatory diet = 0.410 |            |                                |             |            |             |
|                              |             |         |                   |        |             |                     |                             |                             |                                | HbA1c (%)         | Anti-inflammatory diet = 0.004, pro-inflammatory diet = 0.090 |            |                                |             |            |             |
|                              |             |         |                   |        |             |                     |                             |                             |                                | FMD (%)            | Anti-inflammatory diet = 0.261, pro-inflammatory diet = -0.233 |            |                                |             |            |             |
|                              |             |         |                   |        |             |                     |                             |                             |                                | PWV (m/s)          | Anti-inflammatory diet = -0.437, pro-inflammatory diet = 0.014 |            |                                |             |            |             |
| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Study quality | Confounders | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Outcome variable | Measure of outcome | Comparison Type of DII variable (categorical/continuous) | Effect size measure (95% CI) | Outcomes |
|-----------|---------------------|--------------|---------|-------------------|--------|-------------|---------------------|---------------------------------|------------------------|-----------------------------------|--------------|------------|------------------------------------------|--------------------------|--------------------------|----------------|----------------|------------------------------------------|--------------------------|-----------|
| 49        | Cantero et al. 2017 | Cross-sectional | Spain   | 55–80 F/M         | F/M    | 794         | FFQ                 | 794                         | –                      | NR                                |              |            | Anti-inflammatory diet = –0.271           | Pro-inflammatory diet = –0.126 | Anti-inflammatory diet = –0.300 | Aortic SBP (mm Hg) | Anti-inflammatory diet = –0.271           | Pro-inflammatory diet = –0.126 |
| 50        | Tabung et al. 2017  | Cross-sectional | USA     | 25–42 F           | F      | 3985        | FFQ                 | 3985                         | –                      | 38                                |              |            | Anti-inflammatory diet = –0.299           | Pro-inflammatory diet = –0.064 | Anti-inflammatory diet = –0.011 | Aortic pulse pressure (mm Hg) | Anti-inflammatory diet = –0.299           | Pro-inflammatory diet = –0.064 |
| 58        | Abdurahman et al. 2018 | Cross-sectional | Iran    | 19–59 M/F         | M/F    | 277         | FFQ                 | 176                         | –                      | 32                                |              |            | Categorical OR = 2.58 (1.19, 5.59)       | –0.05                  | Categorical OR = 2.58 (1.19, 5.59)       | Brachial augmentation index (%) | Categorical OR = 2.58 (1.19, 5.59)       | –0.05                             |
| Reference   | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-------------|---------------------|--------------|---------|-------------------|--------|-------------|----------------------|-------------------------------|--------------------------|--------------------------------------------|----------------|----------------|------------|-----------------------------------------------|----------------------------|--------------------------|----------------|-------------|
| NR          | Abdominal obesity   | Quartile 4 (7.98) vs. Quartile 1 (−8.87) | Categorical | Continues (per one quartile) | 1.18 (1.01, 1.39) |
| NR          | Low HDL-C           | Quartile 4 (7.98) vs. Quartile 1 (−8.87) | Categorical | Continues (per one quartile) | 0.91 (0.73, 1.14) |
| NR          | Hyper-triglyceridemia | Quartile 4 (7.98) vs. Quartile 1 (−8.87) | Categorical | Continues (per one quartile) | 1.11 (0.95, 1.33) |
| NR          | HTN                 | Quartile 4 (7.98) vs. Quartile 1 (−8.87) | Categorical | Continues (per one quartile) | 1.11 (0.96, 1.29) |
| NR          | Hyperglycemia       | Quartile 4 (7.98) vs. Quartile 1 (−8.87) | Categorical | Continues (per one quartile) | 1.13 (0.97, 1.32) |
| 59          | Andrade et al. 2018 | Cohort Brazil | 43.0    | F                  | 132    | 24-h dietary recall | 132 0.5 21 | Postoperative weight (kg) | Morbidity | Continues (per one unit) | β-coefficient | 2.02 (0.33, 3.70) | 7 1, 9 |
| 60          | Aslani et al. Cross-sec-tional 2018 | 6–18 | F/M | 5427 | FFQ, FFQ (2541) M(2,886) | 5427 – 25 | BMI z-score | Morbidity | Quartile 4 (1.50 to 4.26) vs. Quartile 1 (−4.42 to −1.63) | Categorical | β-coefficient | 0.07 (0.01, 0.14) | 8 2, 9, 11, 17, 36, 41 |
| Reference First author (year) | Study design | Country Age range/ mean age | Gender Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/ continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|---------------------------------|--------------|-----------------------------|--------------------|---------------------|---------------------------------|-----------------------------|-------------------------------|-----------------|-----------------|------------|-----------------------------------------------|--------------------------|----------------------------|----------------|-------------|
| -                               |              |                             |                    |                     | Continue                        |                             |                               |                 |                 |            | (per one quartile)                            |                          | 0.01 (0.002, 0.04)               |               |             |
| Wrist Circumference (cm) Quartile 4 (1.50 to 4.26) vs. Quartile 1 (−4.42 to −1.63) | Categorical |                             |                    |                     | Continue                        |                             |                               |                 |                 |            | (per one quartile)                            |                          | 0.06 (−0.09, 0.21)               |               |             |
| NC (cm) Quartile 4 (1.50 to 4.26) vs. Quartile 1 (−4.42 to −1.63) | Categorical |                             |                    |                     | Continue                        |                             |                               |                 |                 |            | (per one quartile)                            |                          | 0.03 (−0.01, 0.08)               |               |             |
| WC (cm) Quartile 4 (1.50 to 4.26) vs. Quartile 1 (−4.42 to −1.63) | Categorical |                             |                    |                     | Continue                        |                             |                               |                 |                 |            | (per one quartile)                            |                          | 0.00 (−0.11, 0.11)               |               |             |
| HC (cm) Quartile 4 (1.50 to 4.26) vs. Quartile 1 (−4.42 to −1.63) | Categorical |                             |                    |                     | Continue                        |                             |                               |                 |                 |            | (per one quartile)                            |                          | 0.89 (0.07, 1.70)                |               |             |
| WHR Quartile 4 (1.50 to 4.26) vs. Quartile 1 (−4.42 to −1.63) | Categorical |                             |                    |                     | Continue                        |                             |                               |                 |                 |            | (per one quartile)                            |                          | 1.13 (0.29, 1.96)                |               |             |
| WHtR Quartile 4 (1.50 to 4.26) vs. Quartile 1 (−4.42 to −1.63) | Categorical |                             |                    |                     | Continue                        |                             |                               |                 |                 |            | (per one quartile)                            |                          | − 0.001 (−0.04, 0.002)           |               |             |
| Parental BMI (kg/m²) Quartile 4 (1.50 to 4.26) vs. Quartile 1 (−4.42 to −1.63) | Categorical |                             |                    |                     | Continue                        |                             |                               |                 |                 |            | (per one quartile)                            |                          | 1.05 (0.61, 1.49)                |               |             |
Table 3 (continued)

| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|--------------------|--------|-------------|---------------------|----------------------------------|------------------------|-----------------------------------------------|----------------|----------------|------------|----------------------------------------|----------------------|----------------------|--------------|------------|
| 61        | Carvalho et al. 2018 | Cross-sectional | Brazil | 23–25 F 1,034 FFQ | 110   | – 35        | Insulin resistance   | Morbidity                        | –                     | Continues (per one quartile)                | PR               | Continues (per one unit)             | 0.96 (0.87, 1.07) | 9 53                          |              |            |
|           |                     |              |         | M 942 67 134       | 180   |             | MetS               | Insulin resistance     |                        |                                 | MetS             |                            | 1.05 (0.91, 1.20) |              |              |            |
|           |                     |              |         |                    |       |             | MetS               | MetS                |                        |                                 | MetS             |                            | 0.98 (0.91, 1.07) |              |              |            |
| 62        | Phillips et al. 2018 | Cross-sectional | Ireland | 50–69 F/M 1,992 F (1,016) M (976) | NR | – 26        | MetS               | Morbidity             | < Median DII (−5.10 to −1.28) vs > Median DII (−1.28 to 3.68) | Categorical OR | 1.37 (1.01, 1.86) | 8 2, 9, 17, 66 |              |            |
|           |                     |              |         |                   |       |             | large VLDL particles (nmol/L) |                      |                                 |                                 |                                 | 1.28 (1.07, 1.54) |              |              |            |
|           |                     |              |         |                   |       |             | small HDL particle size (nmol/L) |                      |                                 |                                 |                                 | 1.45 (1.21, 1.74) |              |              |            |
|           |                     |              |         |                   |       |             | small LDL particle size (nmol/L) |                      |                                 |                                 |                                 | 1.54 (1.28, 1.84) |              |              |            |
|           |                     |              |         |                   |       |             | Lipoprotein Insulin Resistance score |                      |                                 |                                 |                                 | 1.24 (1.10, 1.50) |              |              |            |
| 63        | Correa-Rodríguez et al. 2018 | Cross-sectional | Spain | 18–25 F/M 599 F (141) M (185) | 72-h dietary recall 599 | – 25        | BMI (kg/m²) | Morbidity | Continues (per one coefficient) | β-coefficient | –0.0073 (−0.0487, 0.0026) | 1, 9, 17 |              |            |
|           |                     |              |         |                   |       |             | FM (kg) |                      |                                 |                                 | –0.0074 (−1.052, 0.005) |              |            |
|           |                     |              |         |                   |       |             | PFM (%) |                      |                                 |                                 | –0.0047 (0.945, 0.170) |              |            |
|           |                     |              |         |                   |       |             | FFM (kg) |                      |                                 |                                 | –0.0059 (−0.842, −0.107) |              |            |
|           |                     |              |         |                   |       |             | VFR |                      |                                 |                                 | –0.0017 (−0.217, 0.142) |              |            |
| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|-------------------|--------|-------------|----------------------|-------------------------------|--------------------------|---------------------------------------------|----------------|----------------|-----------|---------------------------------------------|------------------|----------------------|----------------|-----------|
| 64        | Denova-Gutiérrez et al. 2018 | Cross-sectional | Mexico | 20–69 | F/M | 1174 F (515) M (659) | Semi-quantitative FFQ | 201 | – | 27 | TZDM | Morbidity | Quintile 5 (NR) vs. Quintile 1 (NR) | OR | 3.02 (1.39, 6.58) | 8 | 2, 3, 6, 9, 11, 17, 22, 25, 27, 36, 39, 66, 69 |
| 65        | Abbasalizad Farhangi et al. 2018 | Cross-sectional | Iran | 35–80 | F | 120 | FFQ | 120 | – | 28 | HbA1C (%) | Morbidity | Quartile 4 (≤ 5.6) vs. Quartile 1(> 7.0) | Categorical | β-coefficient | 0.88 (0.55, 1.31) | 6 | 2, 6, 9, 17, 25, 67 |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | TC (mg/dl) |                | 0.67 (0.34, 1.37) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | TG (mg/dl) |                | 1.08 (0.94, 1.25) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | LDL-C (mg/dl) |            | 1.46 (0.72, 2.97) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | HDL-C (mg/dl) |            | 1.42 (0.70, 2.88) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | Lipoprotein (a) (mg/dl) | | 0.98 (0.96, 1.00) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | HbA1C (%) |                | 0.89 (0.71, 1.12) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | TC (mg/dl) |                | 1.02 (0.99–1.04) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | TG (mg/dl) |                | 0.99 (0.98–0.99) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | LDL-C (mg/dl) |            | 1.01 (0.96–1.06) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | HDL-C (mg/dl) |            | – 0.95 (0.91–1.00) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | Lipoprotein (a) (mg/dl) | | 1.01 (0.99–1.02) |                      |                     |
| 66        | Luglio Muhammad et al. 2018 | Cross-sectional | Indonesia | 19–56 | F/M | 503 | FFQ | 503 | – | 30 | BMI (kg/m2) | Morbidity | Continues (per one unit) | β-coefficient (SE) | 0.08 (0.036) | 6 | 1, 2, 3, 9, 17 |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | Body weight (kg) |                | – 0.03 (0.09) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | Body fat (%) |                | – 0.04 (0.04) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | WC (cm) |                | – 0.04 (0.09) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | HC (cm) |                | – 0.04 (0.07) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | SBP (mmHg) |            | 0.03 (0.16) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | DBP (mmHg) |            | 0.04 (0.10) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | TG (mmol/L) |            | 0.04 (0.06) |                      |                     |
|           |                     |              |        |       |    |   |      |                          |                              |                          |                             | HDL-C (mmol/L) |            | – 0.04 (0.04) |                      |                     |
| Reference First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/ continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-------------------------------|--------------|---------|--------------------|--------|-------------|---------------------|-----------------------------------|-----------------------------|------------------------------------------|----------------|----------------|------------|---------------------------------------------|----------------------------|--------------------------|---------------|--------|
| 67 Alam et al. 2018           | Cross-sectional | Pakistan | 54–95              | M      | 651         | 24-dietary recall   | 651                              | –                           | NW                        | Body weight (kg) | Morbidity       | Categorical | Tertile 3 (Mean±SD)                        | 69.05±10.2               | 8                         | -             | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | BMI (kg/m²)     | WC (cm)         | WHR        | 24±18                                      | 85.5±7.4                 | 0.99±0.11                |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | WC (cm)         | WHR            | WHR        | 1.22 (1.09, 1.64)                              |                          | 1.22 (1.09, 1.64) |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | Low HDL-C       | Hyper-triglyceridemia | Hyper-triglyceridemia | 1.07 (0.84, 1.38)                              |                          | 1.07 (0.84, 1.38) |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | Abdominal obesity | Morbidity       | Quartile 4 (≥1.28) vs. Quartile 1 (<0.85) | 1.35 (0.94, 1.94)               | 8                         | 1,2, 3, 7, 9, 25, 39 |              | -      |
| 68 Kim et al. 2018            | Cross-sectional | Korea | 19–65              | F      | 5609        | 24-h dietary recall | 1044                             | –                           | 23                       | Abdominal obesity | Morbidity       | Categorical | OR                        | 1.07 (0.72, 1.61)               | 1.07 (0.72, 1.61) | 1,2, 3, 7, 9, 25, 39 |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | Low HDL-C       | Hyper-triglyceridemia | Hyper-triglyceridemia | 0.85 (0.71, 1.04)                             |                          | 0.85 (0.71, 1.04) |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | WC (cm)         | WHR            | WHR        | 1.10 (0.87, 1.38)                              |                          | 1.10 (0.87, 1.38) |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | Low HDL-C       | Hyper-triglyceridemia | Hyper-triglyceridemia | 0.95 (0.77, 1.18)                             |                          | 0.95 (0.77, 1.18) |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | BMI z-score     | Morbidity       | Q4 (≥1.89) vs Q1 (<0.16) | 1.35 (0.94, 1.94)               | 1.35 (0.94, 1.94) | 1,2, 3, 7, 9, 25, 39 |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | Abdominal obesity | Morbidity       | Q4 (≥1.89) vs Q1 (<0.16) | 1.35 (0.94, 1.94)               | 1.35 (0.94, 1.94) | 1,2, 3, 7, 9, 25, 39 |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | Low HDL-C       | Hyper-triglyceridemia | Hyper-triglyceridemia | 0.93 (0.71, 1.21)                             |                          | 0.93 (0.71, 1.21) |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | WC (cm)         | WHR            | WHR        | 1.14 (0.88, 1.46)                              |                          | 1.14 (0.88, 1.46) |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | Low HDL-C       | Hyper-triglyceridemia | Hyper-triglyceridemia | 1.22 (1.09, 1.64)                             |                          | 1.22 (1.09, 1.64) |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | WC (cm)         | WHR            | WHR        | 1.30 (1.02, 1.65)                              |                          | 1.30 (1.02, 1.65) |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | Low HDL-C       | Hyper-triglyceridemia | Hyper-triglyceridemia | 1.40 (1.06, 1.85)                             |                          | 1.40 (1.06, 1.85) |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | WC (cm)         | WHR            | WHR        | 1.07 (0.87, 1.38)                              |                          | 1.07 (0.87, 1.38) |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | Low HDL-C       | Hyper-triglyceridemia | Hyper-triglyceridemia | 1.10 (0.87, 1.38)                             |                          | 1.10 (0.87, 1.38) |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | WC (cm)         | WHR            | WHR        | 0.95 (0.77, 1.18)                             |                          | 0.95 (0.77, 1.18) |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | Abdominal obesity | Morbidity       | Quartile 4 (≥1.28) vs. Quartile 1 (<0.85) | 1.35 (0.94, 1.94)               | 1.35 (0.94, 1.94) | 1,2, 3, 7, 9, 25, 39 |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | Abdominal obesity | Morbidity       | Quartile 4 (≥1.28) vs. Quartile 1 (<0.85) | 1.35 (0.94, 1.94)               | 1.35 (0.94, 1.94) | 1,2, 3, 7, 9, 25, 39 |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | Abdominal obesity | Morbidity       | Quartile 4 (≥1.28) vs. Quartile 1 (<0.85) | 1.35 (0.94, 1.94)               | 1.35 (0.94, 1.94) | 1,2, 3, 7, 9, 25, 39 |              | -      |
|                               |              |         |                    |        |             |                     |                                   |                            |                           | Abdominal obesity | Morbidity       | Quartile 4 (≥1.28) vs. Quartile 1 (<0.85) | 1.35 (0.94, 1.94)               | 1.35 (0.94, 1.94) | 1,2, 3, 7, 9, 25, 39 |              | -      |
| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|-------------------|--------|-------------|---------------------|-----------------------------|--------------------------|---------------------------------|-----------------|-----------------|------------|----------------------------|----------------------|------------------------|----------------|------------|
| 70 Mazidi et al. 2018 | Cross-sectional | USA | ≥ 18 | F/M | 17689 | F (9082) M (8,607) | 24-h dietary recall NR | - | 18 | - | MetS | Morbidity | Q4 (16.2 to 4.24) vs. Q1 (5.66 to -104) | Categorical OR | 1.23 (1.07, 1.41) | 8 | 1, 2, 7, 9, 17, 18, 25, 29 |
| 71 Mirmajidi et al. 2018 | Cross-sectional | Iran | 18–60 | F/M | 150 | F (74) M (76) | FFQ | 150 | 34 | BMI (kg/m²) | Morbidity | - | Continuous (per one unit) | β-coefficient | 0.351 (0.258, 1.247) | 6 | 1, 3, 17 |
| 72 Moe San et al. 2018 | Cross-sectional | Myanmar | 25–60 | F | 244 | | 24-h dietary recall and Semi-quantitative FFQ | 91 | 31 | - | High BMI | Morbidity | Higher DII (> 1.07) vs. lower DII (< 1.07) | Categorical OR | 1.40 (0.80, 2.30) | 6 | 2, 9, 29, 68 |

**Outcome variable**
- FFM (kg)
- SBP (mmHg)
- DBP (mmHg)
- MetS
- Obesity
- HTN
- FBS (mg/dl)
- Insulin (mg/dl)
- HOMA-IR (mg/dl)
- HOMA-B (mg/dl)
- QUICKI
- Chemerin (ng/mL)
- Omentin (ng/mL)
- LBP (mg/ml)
- Abdominal obesity
- Body fat mass
| Reference | First author (year) | Study design | Country | Age range/mean age | Gender | Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison | Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-----------|---------------------|--------------|---------|-------------------|--------|-------------|---------------------|-------------------------------|-----------------------------|-----------------------------------------------|-----------------|-------------------|-----------|---------------------------------------------|-------------------|----------------------|---------------|-------------|
| 73        | Nikniaz et al. 2018 | Cross-sectional | Iran    | 18–64 F/M          |       | 606 F (324) M (282) | FFQ     | NR              |                             | 30                            |                               | Abdominal obesity | Quartile 4 (NR) vs. Quartile 1 (NR) | OR                | 0.86 (0.39, 1.91) | 7              | 2, 3, 7, 9, 17 |
| 75        | Park et al. 2018    | Cross-sectional | Korea   | ≥ 50 F             |       | 1344        | 24-h dietary recall | 334              | -                           | 42                            |                               | Osteopenic obesity | Higher DII (> −0.07) vs. lower DII (≤ − 0.07) | OR                | 2.757 (1.398, 5.438) | 8              | 2, 7, 9, 25, 37, 53 |
| 74        | Shivappa et al. 2018| Case–control  | Iran     | 18–40 F            |       | 388         | FFQ     | 122             | -                           | 32                            |                               | GDM              | Tertile 3 (> −0.38) vs. tertile 1 (≤ −1.32) | OR                | 2.10 (1.02, 4.34) | 7              | 1, 2, 3, 6, 7, 9, 27 |
| 45        | Winkvist et al. 2018| Cohort       | Sweden   | 30–60 F/M          |       | 8345        | FFQ     | NR              | 10                           | 30                            |                               | BMI (kg/m²)     | -                             | Continuous (per one unit) | 1.20 (0.94, 1.54) | 8              | 3, 7, 9, 25, 63 |
| 76        | Ren et al. 2018     | Cross-sectional | China   | 18–75 F/M          |       | 1712 F (1130) M (582) | 24-h dietary recall | NR               | -                           | 21                            |                               | Abdominal obesity | Tertile 3 (1.12 to 3.49) vs. tertile 1 (2.50 to 0.04) | OR                | 0.86 (0.59–1.24) | 8              | 2, 7, 9, 17, 25 |

## Table 3 (continued)

| Reference First author (year) | Study design | Country Age range/mean age | Gender Sample size | Diet assessment tool | The number of subjects with CMRFs | Duration follow-up (years) | Number of used dietary factors in DII calculation | Outcome variable | Measure of outcome | Comparison Type of DII variable (categorical/continuous) | Type of effect size measure | Effect size measure (95% CI) | Study quality | Confounders |
|-------------------------------|-------------|-----------------------------|--------------------|---------------------|----------------------------------|---------------------------|-----------------------------|-----------------|-----------------|---------------------|--------------------------|---------------------------|--------------|------------|
| Low HDL-C                    | Tertile 3 (1.12 to 3.49) vs. tertile 1 -3.50 to 0.04 | Categorical        |                      |                     |                                  |                           |                             |                 |                 | Categorical         | Continuous (per one unit) | 1.17 (0.88–1.50) | 1            | 11-19      |
| Hyper-triglyceridemia        | Tertile 3 (1.12 to 3.49) vs. tertile 1 -3.50 to 0.04 | Categorical        |                      |                     |                                  |                           |                             |                 |                 | Categorical         | Continuous (per one unit) | 1.03 (0.78–1.37) | 2            | 11-19      |
| HTN                          | Tertile 3 (1.12 to 3.49) vs. tertile 1 -3.50 to 0.04 | Categorical        |                      |                     |                                  |                           |                             |                 |                 | Categorical         | Continuous (per one unit) | 1.40 (1.03–1.89) | 3            | 11-19      |
| Hyperglycemia                | Tertile 3 (1.12 to 3.49) vs. tertile 1 -3.50 to 0.04 | Categorical        |                      |                     |                                  |                           |                             |                 |                 | Categorical         | Continuous (per one unit) | 0.85 (0.64–1.14) | 4            | 11-19      |
| MetS                         | Tertile 3 (1.12 to 3.49) vs. tertile 1 -3.50 to 0.04 | Categorical        |                      |                     |                                  |                           |                             |                 |                 | Categorical         | Continuous (per one unit) | 1.02 (0.75–1.40) | 5            | 11-19      |

1—total energy intake, 2—body mass index, 3—physical activity, 4—systolic blood pressure, 5—total cholesterol, 6—diabetes, 7—smoking, 8—postsecondary academic education, 9—age, 10—energy expended in physical activity, 11—socioeconomic status, 12—use of low-dose aspirin, 13—use of antihypertensive medication, 14—use of statins, 15—prevalent atherosclerotic vascular disease, 16—treatment code, 17—sex, 18—race, 19—HbA1c, 20—overweight/obesity, 21—waist to height ratio, 22—hypertension, 23—dyslipidemia, 24—family history of premature cardiovascular disease, 25—educational level, 26—stratified by inter vention group and center, 27—supplementation, 28—number of 24-h records, 29—marital status, 30—treatment allocation group (placebo or active), 31—diastolic blood pressure, 32—waist circumference, 33—previous history of other cardiovascular diseases, 34—following a special diet, 35—hours spent sitting down, 36—hours spent watching television, 37—hormone replacement therapy use, 38—prevalent cancer (yes/no), 39—alcohol intake, 40—survey number, 41—place of residence, 42—ratio of total cholesterol and high density lipoprotein cholesterol, 43—poverty index, 44—coffee consumption, 45—menopausal status, 46—family member, 47—occupational grade, 48—use of lipid-lowering drugs, 49—high density lipoprotein cholesterol, 50—longstanding illness, 51—country of birth, 52—socio-economic indexes for areas quintile, 53—income, 54—glucose lowering medication, 55—cigarette index, 56—number of available dietary records, 57—snacking between meals, 58—parental history of obesity, 59—depression (previous or incident), 60—analgesic use, 61—triglyceride, 62—low density lipoprotein cholesterol, 63—year of study participation, 64—years of police work, 65—history of chronic diseases, 66—medication use, 67—myocardial infarction, 68—use of contraceptives, 69—tobacco use

CMRFs: cardio-metabolic risk factors
DII: dietary inflammatory index
F: female
M: male
FFQ: food frequency questionnaire
HDL-C: high density lipoprotein-cholesterol
LDL-C: low density lipoprotein-cholesterol
VLDL: very low density lipoprotein
HbA1c: glycosylated hemoglobin
LBP: lipopolysaccharide-binding protein
TC: total cholesterol
TG: triglyceride
SBP: systolic blood pressure
DBP: diastolic blood pressure
MetS: metabolic syndrome
OR: odds ratio
HOMA-IR: homeostasis model assessment of insulin resistance
HOMA-B: homeostatic model assessment of β-cell function
QUICKI: quantitative insulin-sensitivity check index
FPG: fasting plasma glucose
IGT: impaired glucose tolerance
OGTT: oral glucose tolerance test
GDM: gestational diabetes mellitus
BMI: body mass index
WC: waist circumference
HC: hip circumference
VFR: visceral fat ratio
SS+Tr: subscapular + triceps skinfold thickness
LBM: lean body mass
DXA: Dual energy X-ray absorptiometry
FMD: flow-mediated vasodilation
PWV: pulse wave velocity
MAP: mean arterial pressure
MUO: metabolically unhealthy obese
NR: not reported
DII score and BMI [42, 45, 63, 66], whereas two studies indicated a significant association [49, 71]. Another report found a significant association between the DII score and BMI only in women [47]. One cohort study showed a significant association between the DII score and BMI z-score in boys [44]; another study failed to find any association between the DII score and BMI z-score [69]. Moreover, another study indicated this association in all students [60]. A significant association between the DII score and low density lipoprotein cholesterol (LDL-C) levels was observed in two studies [21, 65] and three studies failed to find any association [42, 44, 48]. The DII score was associated with total cholesterol (TC) levels only in one study [65], whereas three studies did not show this association [42, 45, 48]; another study reported no association between the DII score and hypercholesterolemia [17].

Quality assessment
According to NOS, 49 studies had high quality (NOS ≥ 7) [15–17, 21–32, 42–64, 67–70, 73–79], and four studies obtained 6 stars [65, 66, 71, 72]. Only, two reports achieved NOS = 5 [19, 20].

Results of meta-analysis

\[ \text{DII score and risk of CMDs and mortality} \]

Thirteen studies that investigated the association between the DII score (as a continuous variable) and risk of CMDs and mortality were included in this meta-analysis [16, 19, 29–32, 52, 54–57, 78, 79] (Figs. 2 and 3). Subgroup analysis was performed according to the type of outcome (morbidity/mortality) and study design (cohort/non-cohort) (Table 4). Results of fixed effect meta-analysis showed that per one-unit increment in the DII score the risk of CMDs mortality increased significantly by 4% (HR = 1.04; 95% CI 1.03, 1.05). Also, a significant association was observed between the continuous DII and risk of CMDs in cohort (HR = 1.06; 95% CI 1.03, 1.09) and non-cohort studies (HR = 1.06; 95% CI 1.03, 1.10).

We also assessed the association between the categorical DII score and risk of CMDs and mortality using 18 observational studies [15–17, 19, 29–32, 51–57, 77–79]. Meta-analysis of cohort studies showed that the most pro-inflammatory diet category (the highest DII score group) compared to the most anti-inflammatory diet category (the lowest DII score group), increases the risk of CMDs mortality by 29% (HR = 1.29; 95% CI 1.18, 1.41) (Fig. 4).
Also, the association between the DII and risk of CMDs was statistically significant in cohort (HR = 1.35; 95% CI 1.13, 1.61) and non-cohort studies (HR = 1.36; 95% CI 1.18, 1.57) (Fig. 5).

**DII score and CMRFs**

Of 39 publications, 16 studies had assessed the association between the DII score and MetS or at least one of its components and had reported measure of association (OR) included in the meta-analysis [17, 19, 20, 23–26, 28, 58, 61, 62, 68, 70, 72, 73, 76] (Table 5). Results of meta-analysis indicated a significant association between the DII score and MetS (OR: 1.13; 95% CI 1.03–1.25) (Fig. 6), hyperglycemia (OR: 1.21; 95% CI 1.01–1.44) and HTN (OR: 1.17; 95% CI 1.10–1.25). We failed to find any significant association between the DII score and other components of MetS (abdominal obesity, low HDL-C and hyper-triglyceridemia).

**Results of dose–response meta-analysis**

In the terms of risk of CMDs mortality in relation to the DII score, nine cohort studies [29, 31, 51, 54–56, 77–79] were included in dose–response analysis. A significant non-linear positive association was found between the DII score and CMDs mortality (P_{nonlinearity} < 0.001). Unlike the overall association, the DII score was inversely associated with CMDs mortality from score of −5 to −2 (P_{nonlinearity} = 0.01). However, the risk was significantly increased when increasing the score of DII from −2 to 1.5 (P_{nonlinearity} < 0.001). The slope was slightly flattening from DII score of 1.5 to upper levels (Additional file 3: Figure S1).

Six studies (four cohorts [16, 17, 31, 52], one case–control [57] and one cross-sectional study [19]) were included in dose–response analysis assessing the association between the DII score and risk of CMDs (Additional file 4: Figure S2). No significant non-linear association was found in this regard (p-value = 0.1). Such non-significant association was also seen after considering only cohort studies and excluding case–control and cross-sectional studies (p-value = 0.2) (Additional file 5: Figure S3).

**Publication bias**

No publication bias was observed between studies of MetS according to Egger test results (p-value = 0.323). Moreover, the results of Egger test for studies evaluated the association between the continuous DII score and risk of CMDs and mortality showed that there was no evidence of publication bias between studies (p-value = 0.114, p-value = 0.745, respectively).
| Type of the DII measurement | Type of outcome | Type of study | Number of studies | Sample size | Number of events | Type of effect size measures | Test of association | Test of heterogeneity | Effect size measure | 95% CI | Model | I² | p-value |
|-----------------------------|----------------|---------------|-------------------|-------------|-----------------|---------------------------|-------------------|-------------------|-------------------|-------|-------|-----|--------|
| Continuous (per one unit increment) | Mortality | Cohort | 8 | 239,156 | 27,403 | HR<sup>a</sup> | 1.04 | 1.03–1.05 | Fixed | 38.7 | 0.12 |
| | Morbidity | Cohort | 4 | 23,183 | 1117 | HR | 1.06 | 1.03–1.09 | Fixed | 22.3 | 0.27 |
| | | Non-cohort<sup>b</sup> | 2 | 17,055 | 2494 | OR<sup>a,b</sup> | 1.06 | 1.03–1.10 | Random | 69.1 | 0.07 |
| Categorical (highest DII/lowest DII) | Mortality | Cohort | 10 | 291,968 | 30,813 | HR | 1.29 | 1.18–1.41 | Random | 65.9 | < 0.001 |
| | Morbidity | Cohort | 6 | 43,340 | 1310 | HR | 1.35 | 1.13–1.61 | Fixed | 37.0 | 0.16 |
| | | Non-cohort<sup>b</sup> | 3 | 23,999 | 3883 | OR<sup>b</sup> | 1.36 | 1.18–1.57 | Fixed | 0.0 | 0.67 |

OR odds ratio, HR hazard ratio, CI confidence interval

<sup>a</sup> HR, Hazard ratio; OR, Odds ratio; Q test, Cochran test

<sup>b</sup> Case–control or cross-sectional study
When we considered studies with the categorical DII score, the publication bias was observed in our analysis ($P_{Egger} = 0.001$ for risk of CMDs and $P_{Egger} = 0.04$ for risk of CMDs mortality) (Additional file 8: Figure S6 and Additional file 9: Figure S7).

Sensitivity analysis
Sensitivity analysis showed that removing any of the studies or a group of studies could not significantly change the effect of DII score (as a continuous or categorical variable) on risk of CMDs and mortality. In terms of MetS and its components, the results of sensitivity analysis demonstrated that neither an individual study nor group of studies had a remarkable effect on our results.

Discussion
The present meta-analysis showed evidences of the association between increasing the inflammatory potential of diet and risk of CMDs and mortality. Also, individuals with the highest pro-inflammatory diet had 13%, 21%, and 17% higher risk for MetS, hyperglycemia and HTN than those with the lowest pro-inflammatory diet.

Subgroup analysis showed that the association of DII (as continuous and categorical variable) with risk of CMDs did not change appreciably in the cohort and non-cohort studies. One important issue in studies on the association of the dietary indices and chronic diseases is the sample size. We can find more precise results using larger sample sizes. Similar findings in the cohort and non-cohort studies can be probably explained by the larger sample size of non-cohort studies.

In the current study, there was a significant association between the DII score and risk of CMDs and mortality. There are some theories that explain the relationship between the DII score and risk of CVDs. Findings of studies showed that higher consumption of pro-inflammatory foods such as red and processed meat, sugar, and refined grains increases level of IL-6, TNF-a, and hs-CRP [12]. Higher levels of these inflammatory biomarkers is the main etiologic factor in CMDs development [80–84]. Since the DII score was calculated using dietary factors (nutrients and specific food items) which show the diet-associated inflammation [14], it was anticipated to observe an association between the DII score and risk of CMDs.
Fig. 5 Association of dietary inflammatory index (DII) (as a categorical variable) with risk of cardiometabolic diseases

Table 5 Meta-analysis of association between dietary inflammatory index (DII) (as a categorical index) and cardiometabolic risk factors

| Outcome variable       | Number of studies | Sample size | Number of events | Test of association | Test of heterogeneity |
|------------------------|-------------------|-------------|------------------|---------------------|-----------------------|
| Abdominal obesity      | 9                 | 18,121      | 4655ab           | 1.00                | 0.88–1.12             | Fixed                |
| Low HDL-C              | 8                 | 17,874      | 4148ab           | 0.94                | 0.78–1.14             | Random               |
| Hyper-triglyceridemia  | 8                 | 17,874      | 3954ab           | 1.09                | 0.98–1.22             | Fixed                |
| HTN                    | 12                | 77,194      | 13,496c          | 1.17                | 1.10–1.25             | Fixed                |
| Hyperglycemia          | 8                 | 17,876      | 4651b            | 1.21                | 1.01–1.44             | Random               |
| MetS                   | 11                | 42,978      | 4524ab           | 1.13                | 1.03–1.25             | Random               |

HDL-C high density lipoprotein-cholesterol, HTN hypertension, MetS metabolic syndrome, OR odds ratio, CI confidence interval

1 HR; Hazard ratio; OR; Odds ratio; Q test, Cochran test
2 Cohort or cross-sectional study
3 Participants with abdominal obesity, low-HDL-C, hyper-triglyceridemia, hyperglycemia and MetS had not been stated in three studies
4 Participants with HTN had not been stated in five studies
5 The odds ratio is for the highest pro-inflammatory diet (the highest DII) versus the highest anti-inflammatory diet (the lowest DII)
6 Case–control or cross-sectional study
A population-based study including 1,363 men aged 18 years and older (the Geelong osteoporosis study) showed that the adjusted OR (95% CI) for CVDs was 2 (1.01–3.96) for those with pro-inflammatory diet compared with anti-inflammatory diet [53]. The PREDIMED study investigated 7,216 men aged 55–80 years and women aged 60–80 years at high risk of CVDs. A total of 277 CVDs events were considered. The adjusted hazard ratio (95% CI) for CVDs was 1.73 (1.15–2.60) for participants with pro-inflammatory diet. A stronger relationship was showed when cases occurring during the first year of follow-up were excluded from the analysis [16]. Moreover, the SU.VI.MAX study included 7743 women aged 35–60 years and men aged 45–60 years with 11.4 years follow-up, no statistically significant association was found between the DII score and the composite CVDs outcome. However, a significant relationship was shown for MI when the highest quartile of the DII score was compared with the lowest quartile of the DII score [52]. Moreover, another cross-sectional study carried out on Sweden men and women aged 30–73 years showed a positive association between the DII score and risk of CMDs [15]. A cohort study on a large sample size of Sweden women indicated that there is not association between the DII score and risk of CVDs mortality [55]. This finding may related to the low number of used dietary factors in DII calculation. In another cohort study on diabetic patients, results showed that there is not any association between the DII score and risk of CVDs mortality that it is not in line our study. This finding can be related to the low sample size and dietary factors used for DII calculation [51].

This meta-analysis of 16 studies examining the association between the DII score and MetS or at least one of its components [17, 19, 20, 23–26, 28, 58, 61, 62, 68, 70, 72, 73, 76], showed a significant association between the DII score and MetS, hyperglycemia and HTN. Several population-based studies carried out in France, Ireland, USA and Iran demonstrated the significant association between the DII score and MetS [23, 62, 70, 73]. However, other studies failed to find this association [20, 25, 26, 28, 61, 76]. Ramallal et al. [17] in a cohort study on 18,794 Spanish men and women showed the higher DII score is associated with greater incidence of HTN. Also, other studies indicated this significant association [19, 24, 70, 73]. In the regard of hyperglycemia, studies carried out in USA and Iran indicated a positive association between the DII score and hyperglycemia [20, 73]. However, some studies did not demonstrate this association [25, 26, 28, 58].

The meta-analysis of 14 studies revealed that subjects in the highest versus the lowest DII score category showed 36% increased risk of CVDs incidence and
mortality [33]. Another meta-analysis found that participants with higher DII score had a higher risk of cardiovascular and cancer mortality [30]. The strengths of our study against the other two meta-analyses include the evaluation of the association between the DII score and CMRFs and the dose–response association between the DII score and risk of CMDs and mortality. In addition, we assessed the risk of CMDs separately in all cohort and non-cohort studies.

The current study had several limitations. Absence of a specific cut-off point for the association of the DII score and occurrence of morbidity or mortality of CMDs is the first limitation. Most of studies included in the MetS and its components analyses had a cross-sectional design, so the limitations of this type of study should be considered and the results should be interpreted with cautious. Other limitations include different numbers of dietary factors used in the DII score calculation and applying different adjustment models in the analyses. Evidence of publication bias, the other limitation, was observed when the DII score was considered as a categorical variable in the analyses.

Conclusion
The current meta-analysis study showed a positive association between the DII score and risk of CMDs and mortality. Also, we find a significant association between adherence to pro-inflammatory diet and MetS, hyperglycemia, and HTN. More studies with prospective designs and in different societies are needed to confirm the findings.

Supplementary information
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Disclosure
Dr. James R. Hébert owns controlling interest in Connecting Health Innovations LLC (CHI), a company planning to license the right to his invention of the dietary inflammatory index (DII) from the University of South Carolina in order to develop computer and smart phone applications for patient counselling and dietary intervention in clinical settings. Dr. Nitin Shivappa is an employee of CHI.

Authors’ contributions
The contribution of authors was as follows: 2A: conducted systematic search on electronic databases, screened the papers, extracted the data and wrote the manuscript; OS: analyzed the data and wrote the manuscript; MH-B: wrote the manuscript; HZ: wrote the manuscript; FB: wrote the manuscript; NS: wrote the manuscript; JRH: wrote the manuscript; SM: analyzed the data, GS: wrote the manuscript; HA: conducted systematic search on electronic databases, and screened the papers; SD: extracted the data; MQ: designed the study, analyzed the data and is the responsible for the final content. All authors read and approved the final manuscript.

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Author details
1 Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran. 2 Students’ Scientific Research Center, Tehran University of Medical Sciences, Tehran, Iran. 3 Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of Southern Denmark, Esbjerg, Denmark. 4 Cancer Prevention and Control Program, University of South Carolina, Columbia, SC 29208, USA. 5 Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC 29208, USA. 6 Connecting Health Innovations LLC, Columbia, SC 29201, USA. 7 Halal Research Center of IRI, FDA, Tehran, Iran. 8 Department of Clinical Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran. 9 Hematopoietic Stem Cell Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. 10 Center of Maritime Health and Society, Department of Public Health, University of Southern Denmark, Esbjerg, Denmark. 11 Department of Medical Emergencies, Qom University of Medical Sciences, Qom, Iran. 12 Development of Research & Technology Center, Ministry of Health and Medical Education, Tehran, Iran. 13 Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran. 14 Non-Communicable Diseases Research Center, Alborz University of Medical Sciences, Karaj, Iran. 15 Chronic Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

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Author details
1 Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran. 2 Students’ Scientific Research Center, Tehran University of Medical Sciences, Tehran, Iran. 3 Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of Southern Denmark, Esbjerg, Denmark. 4 Cancer Prevention and Control Program, University of South Carolina, Columbia, SC 29208, USA. 5 Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC 29208, USA. 6 Connecting Health Innovations LLC, Columbia, SC 29201, USA. 7 Halal Research Center of IRI, FDA, Tehran, Iran. 8 Department of Clinical Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran. 9 Hematopoietic Stem Cell Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. 10 Center of Maritime Health and Society, Department of Public Health, University of Southern Denmark, Esbjerg, Denmark. 11 Department of Medical Emergencies, Qom University of Medical Sciences, Qom, Iran. 12 Development of Research & Technology Center, Ministry of Health and Medical Education, Tehran, Iran. 13 Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran. 14 Non-Communicable Diseases Research Center, Alborz University of Medical Sciences, Karaj, Iran. 15 Chronic Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

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