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Review article

Pistachios and cardiometabolic risk factors: a systematic review and meta-analysis of randomized controlled clinical trials

Matin Ghanavati[1, 2], Jamal Rahmani[1], Cain C. T. Clark[3], Susan Mohammadi Hosseinabadi[1], Mehran Rahimlou[4*]

[1] Student Research Committee, (Department and Faculty of Nutrition Sciences and Food Technology), Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[2] Department of Clinical Nutrition and Dietetics, Faculty of Nutrition Sciences and Food Technology, National Nutrition and Food Technology, Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[3] Centre for Intelligent Healthcare, Coventry University, Coventry, CV15FB, United Kingdom.

[4] Nutrition and Metabolic Disease Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Correspondence: Mehran Rahimlou. Nutrition and Metabolic Disease Research Center, Ahvaz. Jundishapur University of Medical Sciences, Ahvaz, Iran. Email: Rahimlum@gmail.com. Fax: Fax: (9861)33738253. Tel: (061) 33738252, Orchid number: 0000-0002-7861-8287

Abstract

Background: Previous experimental studies have reported that pistachios can elicit positive effects on lipid profile, blood pressure, and inflammation; however, a meta-analysis of the available evidence has yet to be performed. *Objective*: the aim of this study was to conduct systematic review and meta-analysis of the effect of pistachio enriched diets on cardiometabolic risk factors, such as weight, BMI, blood pressure, serum lipids, blood glucose, and inflammatory biomarkers. *Design*: A literature search was carried out for RCTs in medical databases, including PubMed/MEDLINE, Scopus, and Cochrane databases, with no time limitation up to August 2019, and conducted in accordance with the Preferred Reporting Items of Systematic Reviews and Meta-Analysis guidelines. *Results*: 11 RCTs, with 506 participants, that reported the effect of pistachios consumption on cardiometabolic risk factors were included in this systematic review and meta-analysis. Our findings indicated that pistachios consumption significantly reduced FBS (WMD: -3.73, 95% CI: -6.99, -0.46, I^2=99%), TC/HDL (WMD: -0.46, 95% CI: -0.76, -0.15, I^2=95%), LDL/HDL (WMD: -0.24, 95% CI: -0.38, -0.11, I^2=96%), HbA1C (WMD: -0.14, 95% CI: -0.26, -0.02, I^2=60%), Insulin (WMD: -2.43, 95% CI: -4.85, -0.001, I^2=58%), SBP (WMD: -3.10, 95% CI: -5.35, -0.85, I^2=63%), and MDA (WMD: -0.36, 95% CI: -0.49, -0.23, I^2=0%). Importantly, we did not observe adverse effects of pistachios consumption on BMI or blood pressure. *Conclusion*: This systematic review and meta-analysis demonstrates that pistachios consumption can elicit a beneficial effect on some cardiometabolic risk factors. Further examination is required to determine the effect of pistachios consumption on further metabolic risk factors.
Keywords: pistachios, cardiometabolic risk factors, meta-analysis.

Introduction:

Cardio metabolic risk factors, such as raised blood sugar, blood pressure, blood lipids, obesity, and inflammation are well established precursors to CVD (1). There is a considerable body of evidence that has shown consuming nuts, in particular tree nuts, may yield beneficial effects on cardio metabolic risk factors (2-9). The results of a previous systematic review and meta-analysis of 18 cohort studies highlighted that the consumption of nuts, seven times per week, was associated with a decrease in the incidence of ischemic heart disease and CVD (10). Moreover, a recent pooled analysis of 25 clinical studies on the consumption of various types of nut, with an average daily intake of 67 g, reported a dose-mediated response in reducing cholesterol levels (11). The United States food and drug administration (FDA) has approved health claims that consuming 1.5g, once per day, of macadamia nuts, walnuts, or tree nuts can help reduce the risk of coronary heart disease (www.fda.gov). The apparent beneficial effects of nuts consumption on lipid profile could be manifest from their unsaturated fats, phytostrols, and fiber content, respectively, in addition to the lysine to arginine ratio of nuts (12, 13). Relative to other tree nuts, pistachios contain fewer calories, higher essential amino acids, and, according US department of agriculture database, possess the highest phytosterols and potassium content; contextually, 100 g of pistachios contains 560 kcal, 20.16 g protein, 45.32 g fats, 1025 mg potassium and approximately 214 mg phytosterols (12). Recently, it was demonstrated that pistachios contain the highest concentration of B-carotene, Ύ-tocopherol, and lutein/zeaxanthin among nuts (14).

The potential for pistachio enriched diets to positively influence blood pressure may be attributed to their potassium, magnesium, arginine, and polyphenol content (15). Given that pistachios contain phytosterols, such as B-sitosterol, and high amounts of polyphenols, such as lutein/zeaxanthin, they may promote an inflammatory and oxidative state, leading to a reduction in oxidized LDL cholesterol, and vascular inflammation, that are key events in atherosclerosis and CVD development (16-18). Previous experimental studies have reported that pistachios can elicit a wide range of effects on lipid profile, blood pressure, and inflammation; however, a meta-analysis of the available evidence has yet to be performed. We hypothesized that regular consumption of the pistachios in a healthy diet would improve cardiovascular risk factors and vascular function. Thus, the aim of this study was to conduct systematic review and meta-analysis of the effect of pistachio enriched diets on cardiometabolic risk factors.

Methods

The Preferred Reporting Items of Systematic Reviews and Meta-Analysis guidelines (PRISMA)(19) were followed in the conducting of this meta-analysis. (Supplemental table and figure)

Search strategy

A literature search was carried out by two independent reviewers (JR) and (MGH) in medical databases, including PubMed/MEDLINE, Scopus, and Cochrane databases, with no time limitation up to August 2019. The following Medical Subject Headings (MeSH) terms were selected to search the databases, keyword group 1: “pistachio”; “pistacia nut tree”, “pistachios nut tree”; keyword group 2: “blood pressure”, “serum lipids”, “blood glucose”, “CVD”, “cholesterol”, “lipoproteins, HDL”, “lipoproteins, LDL”, “triglyceride”, “glucose tolerance test”, “insulin”, “blood glucose”, “insulin resistance”, “low density lipoprotein”, “high density lipoprotein”, “TG”, “TC”, “GTT”, “FBS”, “FBG”, “FPG”, “CRP”, “IL-6”, “FMD”, “TNF-alpha”, “ICAM-1”, “VCAM-1”, “fasting insulin”, “fasting blood sugar”, “fasting blood glucose”, “inflammation”, “fasting plasma glucose”, “insulin sensitivity”, “blood sugar”, “lipid profile”, “serum lipid”, “blood pressure”, “hypertension”, “cardiovascular disease”, “coronary disease”, “coronary artery disease”, “CVD”, coronary artery disease (“CAD”), “obesity”, and “weight”, ; and keyword group 3: “randomized”, “intervention”, “controlled trial”, “random”, and “placebo”. We searched keyword group 1 in combination with both keyword groups 2 and 3. The search strategy can be found in Supplementary figure 1. In primary screening, the abstracts and titles of selected studies were read to identify relevant information. Following this, 25 articles remained , and were assessed for eligibility, where the full-text of each article was read by 2 independent reviewers (MGH and SM). Finally, 11 articles were included in the meta-analysis. In order to identify additional studies, all reference lists of eligible articles, reviews, and meta-analyses were scrutinized. Unpublished articles, conference papers, and theses were not included in this study. To identify new articles that may have been published after our search, the PubMed’s email alert service was created.

Eligibility criteria

The PICOS (patients, intervention, comparator, outcome, study design) criteria was used to establish study eligibility. All clinical trials were included in this meta-analysis if they fulfilled the following criteria: 1) the study design was RCT, 2) the intervention was pistachios consumption, 3) conducted among adults (age $\geq$ 18 years), 4) assessed lipid profile, blood pressure, and inflammation biomarkers as outcome, 5) were published in English. Studies were excluded if they had the following exclusion criteria: 1) non-RCTs studies, 2) conducted on non-humans, 3) conducted on children, 4) studies without a placebo group, 5) examined the effect of other interventions along with pistachios in cases but not in placebo group, 6) lipid profile or blood pressure or inflammation biomarkers were not reported at baseline and end of the intervention, 7) uncontrolled RCTs.

Data extraction

Data scanning and extraction were performed by two independent researchers (JR and MGH) and discrepancies were discussed and eventually resolved by a senior author (MR). The following information was extracted: first author's last name, year of publication, type of study population, number of cases and controls, participants' gender, geographic location, study design, intervention duration, type and dose of intervention and placebo, and Mean and SD of outcome (BMI, FBS, LDL-C, HDL-C, TG, TC, TC/HDL, LDL/HDL, INSULIN, HBA1C, HOMA-IR, SBP,DBP, FMD) in baseline study and post-intervention. Some ratios which include in this meta-analysis such as TC/HDL and LDL/HDL were obtained from the included studies.

Statistical analysis

Stata software (version 14) was used to perform all statistical analyses. The following formula: $SD^2_{\text{baseline}} + SD^2_{\text{final}} - (2 R^* SD_{\text{baseline}} + SD_{\text{final}})$ (20) was used to calculate the SD change for mean difference in studies that did not report such data. DerSimonian and Laird random-effects model was utilized to calculate weighted mean difference (WMD). The I^2 index and Q test were calculated to evaluate heterogeneity across included studies (21). Meta regression analysis, based on duration of intervention, was used to identify the source of heterogeneity among included trials. The funnel plot, Egger's weighted regression tests, and Begg's rank correlation were conducted to evaluation publication bias between studies. Statistical significance was accepted at $P < 0.05$. Sensitivity analysis was conducted to evaluate the effect of each study on combined results.

Results:

In our initial search of PubMed, Scopus, and Cochrane Library, 327 articles were identified (Supplementary Figure 1). After removing duplicates, 280 articles remained. Based on initial title and abstract inspection, 255 articles were excluded, and 25 articles were retained for more detailed evaluation. Fourteen articles were excluded based on the following reason: 1) included pistachios oil or extract (n=2), 2) In Vitro trial (n=2), 3) study intervention combined with other foods and supplements (n=3), 4) No SE/SD/CI reported (n=4) and 5) Not reporting outcomes of interest (n=3). Finally, 11 articles with 506 participants were included in this systematic review and meta-analysis(6, 22-31).

Study characteristics

Studies included in this meta-analysis were published between 2006 and 2015, with sample sizes ranging from 28 to 90, with an average of 46 participants in each study. General characteristics of the included studies are presented in Table 1. Two of included studies were conducted in Turkey (6, 23), four in the USA (22, 25, 29, 31), one in China (24), two in India (26, 30), one in Iran (28), and one in Spain (28). The mean age of participants was 45 years, with a mean duration of the interventions of 9.7 weeks, ranging from 3 to 24 weeks. Table 2 details the quality assessment of the studies. Quality assessment of the included studies was performed using the Cochrane Collaboration's tool for assessing risk of bias (32). Seven items were scored with 3 rating categories for each item, including low risk of bias, unclear risk of bias, and high risk of bias. An item was scored as high risk, unless there was sufficient information on it. Overall quality was obtained by summing the scores for each study. Two authors (JR and SM) scored the articles, and all of the included studies were regarded as possessing 'fair' or 'good' overall quality.

Meta-analysis results

Combined analysis of the effect of pistachio consumption on BMI, weight, WC, FBS, LDL, HDL, TG, TC, TC/HDL, LDL/HDL, HbA1C, Insulin, HOMA-IR, systolic blood pressure, diastolic blood pressure, CRP, FMD, and MDA are presented in figure 1. Following pistachio consumption there was: An increasing effect on weight (WMD: 0.19 kg, 95% CI: 0.12, 0.26, I^2=0%); whist there was no overall effect on BMI (WMD: -0.21 kg/m2, 95% CI: -0.77, 0.34, I^2=65%), WC (WMD: 0.67 cm, 95% CI: -0.27, 1.61, I^2=42%), LDL (WMD: -2.40 mg/dl, 95% CI: -5.70, 0.90, I^2=92%), HDL (WMD: 2.34 mg/dl, 95% CI: -3.76, 8.44, I^2=99%), TG (WMD: -8.62 mg/dl, 95% CI: -20.11, 2.86, I^2=93%), TC (WMD: -6.03 mg/dl, 95% CI: -12.38, 0.31, I^2=95%), HOMA-IR (WMD: -0.73, 95% CI: -1.97, 0.51, I^2=94%), DBP (WMD: -0.83 mmHg, 95% CI: -2.75, 1.09, I^2=63%), CRP (WMD: -0.04 mg/dl, 95% CI: -0.43, 0.36, I^2=42%), and FMD (WMD: 0.94%, 95% CI: -0.99, 2.86, I^2=83%).

Furthermore, we found that there was a lowering effect on FBS (WMD: -3.73 mg/dl, 95% CI: -6.99, -0.46, I^2=99%), TC/HDL (WMD: -0.46, 95% CI: -0.76, -0.15, I^2=95%), LDL/HDL (WMD: -0.24, 95% CI: -0.38, -0.11, I^2=96%), HbA1C (WMD: -0.14%, 95% CI: -0.26, -0.02, I^2=60%), Insulin (WMD: -2.43 mLU/mL, 95% CI: -4.85, -0.001, I^2=58%), SBP (WMD: -3.10 mmHg, 95% CI: -5.35, -0.85, I^2=63%), and MDA (WMD: -0.36 nmol/l, 95% CI: -0.49, -0.23, I^2=0%). Meta-regression analysis, based on duration of intervention, was only significant for BMI (coef=0.18, p=0.01) and FMD (coef=0.69, p=0.05) (Supplemental Fig 2). Sensitivity analysis demonstrated no significant differences were evident beyond the limit of the 95% CI

Publication bias

Although the funnel plots highlighted some visual asymmetry between included studies in some outcomes (Supplemental Fig 3), the Egger's and Begg's tests did not show any publication bias for BMI (p=0.13, p=0.49, asymmetry), WC (p=0.44, p=0.49, symmetry), FBS (p=0.45, p=0.53, symmetry), LDL (p=0.54, p=0.67, asymmetry), HDL (p=0.28, p=0.45, asymmetry), TG (p=0.84, p=0.21, asymmetry), TC (p=0.70, p=0.99, asymmetry), TC-HDL (p=0.14, p=0.62, asymmetry), LDL-HDL (p=0.80, p=0.60, asymmetry), HbA1C (p=0.13, p=0.17, asymmetry), Insulin (p=0.08, p=0.85, asymmetry), HOMA-IR (p=0.30, p=0.60, asymmetry), SBP (p=0.43, p=0.05, asymmetry), DBP (p=0.21, p=0.49, asymmetry), CRP (p=0.21, p=0.62, asymmetry), and FMD (p=0.26, p=0.07, asymmetry), respectively. Because of the significant Egger's test for weight (p=0.01, asymmetry), Trim and filled analysis was conducted to detect for potential publication bias. Accordingly, the test did not highlight any publication bias (Effect size: 0.19, CI: 0.12-0.26).

Discussion

To our knowledge, this is the first study to systematically review and meta-analyze the effects of pistachios consumption on the cardio metabolic risk factors.

Our findings indicated that pistachios consumption significantly reduced FBS, TC/HDL, LDL/HDL, HbA1C, insulin, SBP, and MDA levels. Importantly, we did not observe any adverse effects of pistachios consumption on BMI or blood pressure. However, pistachios consumption did result in a significant increase in weight. Nuts, especially pistachios, contain a variety of micronutrients that can exert a protective effect against chronic diseases. Indeed, consistent with our findings, several previous studies have also reported the cardio metabolic protective effects of the nuts (33, 34).

Body composition

The results of the current meta-analysis indicated that pistachios intake has no significant effects on BMI and WC, however, may increase weight significantly; although this change is not clinically significant. Interestingly, studies that reported weight and body mass index differed in sample sizes, potentially explaining why weight, but not BMI, was significantly altered. Moreover, in a previous study, it was reported that a decrease in WC and BMI without significant reduction body weight may indicate preferential loss of abdominal fat as shown by trend toward decrease in subcutaneous abdominal adipose tissue (SCAT) (26). It is widely accepted that nut intake, due to its high fat content, can lead to weight gain in the general population, especially in obese subjects and those with metabolic syndrome (24). However, in the present study, changes were only significant in weight, and no significant change was observed in BMI and WC. Nuts, especially pistachios, are high energy-dense foods and over-consumption can, therefore, lead to weight gain. Previous research has shown that the energy density of pistachios is 23.7 kJ/g, as calculated using the Atwater general factors (35). However, pistachios have a low glycemic index score and it has been shown that concomitant consumption of pistachio with high carbohydrate diets can partially inhibit carbohydrate absorption (36).

Glycaemia control

Our results revealed that pistachios consumption may improve glycaemia. Indeed, in our study, pistachios consumption led to a significant improvement in most of the reported glycemic control markers, except for HOMA-IR. However, the heterogeneity was high in FBS (99.5%), insulin (58%), and HbA1c (60.6%), and subgroup analysis did not reveal the source of the heterogeneity; conceivably impacting the accuracy of the results. Nuts. such as pistachios, are a rich source of magnesium and monounsaturated and polyunsaturated fatty acids, which can reduce insulin resistance, and improve carbohydrate metabolisms and insulin homeostasis (37). On the other hand, some of the positive effects of pistachios on glycemic control are mediated through the effect on the mRNA regulation. Previous research has shown that some mRNA may be involved in protein cascades, especially in in the insulin signaling pathway. Some of the mRNA can reportedly regulate the expression of insulin receptors, insulin secretion, also in addition to regulating some proteins, such as Insulin Receptor Substrate 1 (IRS-1) and Phosphoinositide 3-Kinases (PI3Ks)(38). Pistachios are dense foods and possess many nutrients and bioactive compounds, for instance, omega-3 fatty acids found in pistachios have anti-inflammatory properties and can help to reduce insulin resistance (39). Moreover, pistachios are a rich source of polyphenols, which can improve glycaemia control and insulin sensitivity(40).

Lipid Profile

Results of the present study showed that pistachios consumption yielded beneficial effects on TC/HDL and LDL/HDL ratios. However, there was a higher heterogeneity for TC/HDL and LDL/HDL ratios (95.3% and 96.3%, respectively). While measurement of serum lipids is a recommended part of cardiovascular risk detection, the predictive value of specific lipid measures remains controversial. Several studies have shown that changes in ratios of TC/HDL-C and LDL-C/HDL-C are better predictors of CVD and Coronary Heart Disease (CHD) than individual markers (41-43). There are some reasonable, putative, biological mechanisms for these effects; indeed, pistachio nuts contain good levels of dietary fiber, which has inhibitory effects on cholesterol absorption. Also, pistachios contain a higher amounts of phytosterols (up to 289 mg per 100 g of edible fruit). The amount of phytoestrol in pistachios is more than three times that of other nuts, such as walnuts or almonds (44). Phytosterols are one of the most potent plant bioactive compounds in reducing total cholesterol and LDL cholesterol, and can also increase HDL cholesterol levels by binding to estrogen receptors (45).

Blood pressure

According to our research, pistachios consumption can elicit significant effects on SBP, but not DBP. Although elevated arterial resistance is a characteristic of mixed systolic and diastolic hypertension in young people, raised arterial stiffness is the dominant hemodynamic factor and overrides resistance in elderly hypertensive patients, leading to a decrease in DBP, a rise in pulse pressure, and, therefore, independent systolic hypertension (46). Thus, pistachios consumption appears capable of maximizing the decrease in SBP and minimizing the reduction in DBP in direct proportion to the age-related stiffening of large arteries. The main fatty acids in pistachios include; palmitic, stearic, oleic, linoleic, and linolenic acids. Pistachio contains lower amounts of saturated fatty acids, such as palmitic acid, which play an important role in the incidence of cardiovascular disease. Additionally, pistachios contain higher amounts of arginine that can be converted into other bioactive products, such as nitric oxide, which acts as a vasodilator and an antiplatelet agen t(47). Moreover, the antioxidants in pistachios can reduce oxidative stress and formation of reactive oxygen species (ROS), which are both known to play an important role in the pathogenesis of cardiovascular disease and hypertension (48).

Other factors

We did not find any significant effect of pistachios consumption on FMD and MDA. Concordantly, previous studies to have evaluated the effects of nuts on endothelial function have reported mixed results (49). Indeed, some of these studies reported positive effects (50) and some have reported null effects (48, 51). In line with our findings, Neale et al., in a systematic review and meta-analysis, evaluated the effects of nuts on endothelial function; accordingly, subgroup analyses revealed significant improvements in FMD, but only in those studies using walnuts (52). Finally, we also showed no significant effects of pistachios intake on CRP.

Strengths and Limitations

The present study had a number of strengths, including the use of the industry standard systematic methodology (PRISMA). Importantly, endothelial function was evaluated for the first time in this study, whilst we also considered a range of biomarkers that are associated with metabolic, inflammation, and endothelial function. These biomarkers are a good indicator of the progression of cardiovascular disease and metabolic syndrome. However, despite the strengths evident in the present study, there were some limitations that must be considered, including; higher heterogeneity in some biomarkers, lack of adequate studies to perform the meta-analysis in all areas regards the endothelial function, and differing sample sizes, populations, and health statuses. Additionally, this systematic review and meta-analysis did not perform a dose-response analysis, risk of bias for individual studies, and did not evaluate the strength of the evidence, which may represent viable opportunities for further investigation.

Conclusion

In conclusion, the current systematic review and meta-analysis suggests that a balanced consumption of pistachios nuts may be beneficial for lowering some cardio metabolic risk factors. Furthermore, the authors suggest that further studies, aimed to identifying the exact mechanisms involved in these beneficial effects, be conducted.

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No funding to declare.

Author's contribution

M.G, S.M and J.R designed the study and analyzed the data. M.G and C.C wrote the manuscript in consultation with M.R. all authors discussed the results, commented on the manuscript and approved the final manuscript.

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https://www.fda.gov/food/food-labeling-nutrition/qualified-health-claims-letters-enforcement-discretion

Abbreviations

WC- waist circumstance
FBS-fasting blood sugar
TC-total cholesterol
TG- triacylglycerol

LDL-C- low density lipoproteins
HDL-C- high density lipoproteins
HOMA-IR- homeostatic model assessment for insulin resistance)
HbA1c-hemoglobin A1c
FMD- flow mediated dilation
MDA- malondialdehyde

Supplemental Fig. 1. Flow chart of included studies.

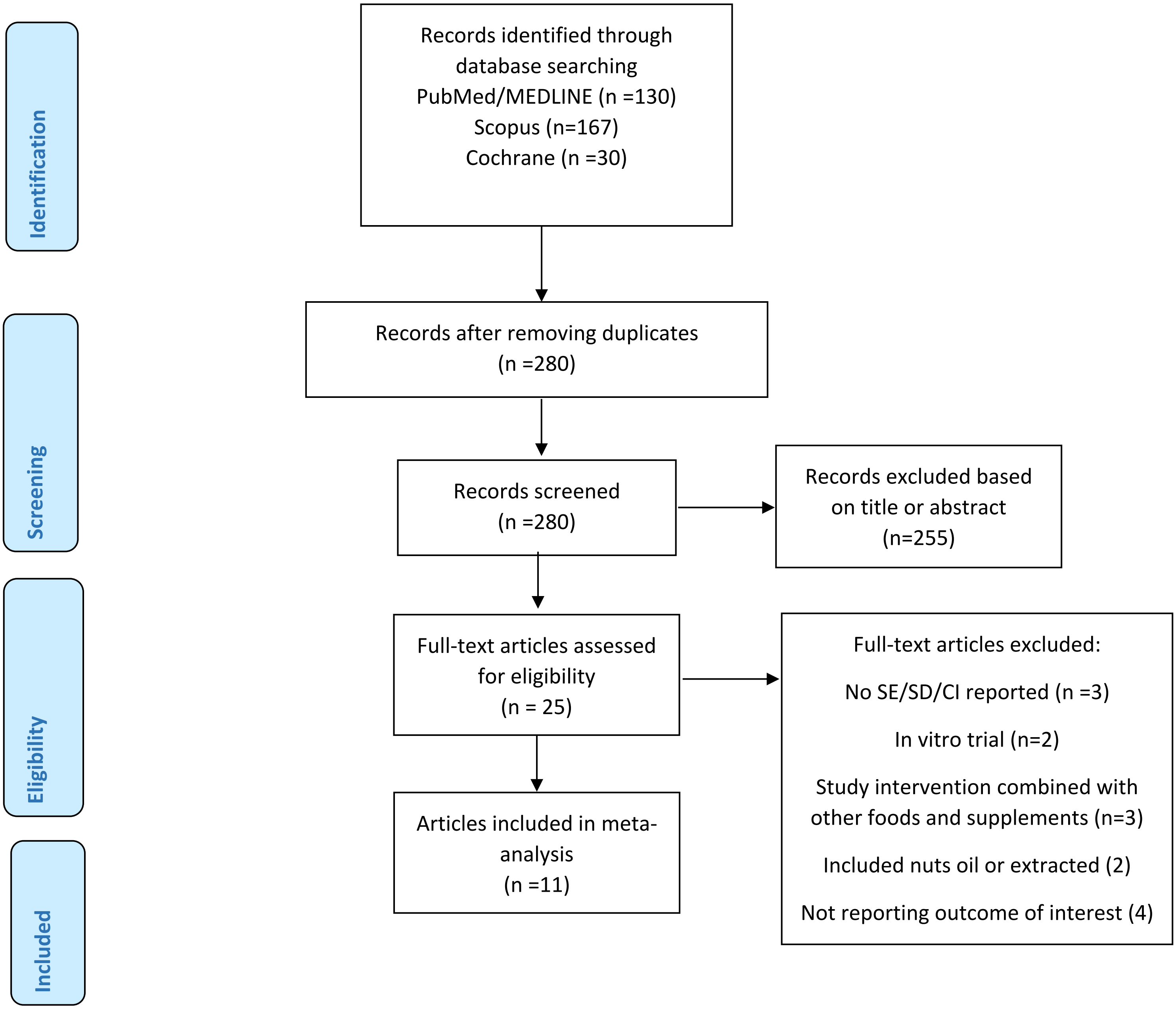

Table 1. Baseline Characteristics of Included Studies in the Meta-analysis

Table 1. Baseline Characteristics of Included Studies in the Meta-analysis

Studies	Author	Country	Year	Follow- up, (W)	Gender	Patients (n)	Mean age(y)	Diet type		Blinding	Type of population	Outcomes
								Intervention	Control			
1	S. Gulati	India	2014	24	Women/men	60	42.5	Standard diet + 20% daily caloric intake from pistachios per day	Standard diet	no	MS	Weight, WC, FBS, LDL-C, HDL-C, TG, TC, HBA1C, Insulin, HS-CRP
2	Kasliwal, R. R.	India	2015	12	Women/men	42	39	Life style modifications(LSM) + 80 gr pistachios per day	LSM	no	mild dyslipidemia	BMI, Weight, WC, FBS, LDL-C, HDL-C, TC/HDL, SBP, DBP, HS-CRP, FMD
3	Kocyigit, A.	Turkey	2006	3	Women/men	44	33.1	Normal diet+ 20% daily caloric intake from pistachios	Normal diet	no	healthy	LDL-C, HDL-C, TG, TC, LDL/HDL, TC/HDL, MDA
4	Li, Z.	USA	2010	12	Women/men	52	46.35	Weight reduction diet + 53gr pistachios per day	Weight reduction diet+ 56 gr of salted pretzels per day	no	obese	BMI, Weight, FBS, LDL-C, HDL-C, TG, TC, Insulin
5	Parham, M.	Iran	2014	12	Women/men	44	51.5	Previous diet+ 2 snacks of 25 gr pistachios per day	Previous diet	yes	diabetics	BMI, FBS, HBA1C, HOMA-IR, SBP, DBP, HS-CRP,
6	Sari, I.	Turkey	2010	4	men	32	22	Mediterranean diet + pistachios replacing MUFA content constituting 20 % daily caloric intake	Mediterranean diet	no	healthy	Weight, FBS, LDL-C, HDL-C, TG, TC, LDL/HDL, TC/HDL, SBP, DBP, HS-CRP, MDA
7	Sauder, K. A.	USA	2014	4	Women/men	30	56.1	American Heart Association's Therapeutic Lifestyle Changes diet + 20% daily caloric intake from pistachios	American Heart Association's Therapeutic Lifestyle Changes diet	no	diabetics	FMD
8	Sauder, K. A.	USA	2015	4	Women/men	30	56.1	American Heart Association's Therapeutic	American Heart Association's Therapeutic	no	diabetics	FBS, LDL-C, HDL-C, TG, TC, TC/HDL, HBA1C, Insulin, HOMA-IR, HS-CRP

								Lifestyle Changes diet + 20% daily caloric intake from pistachios	Lifestyle Changes diet			
9	Wang, X.	china	2012	12	Women/men	90	51.46	received dietary counseling according to the guidelines of the American Heart Association + 42or 70 gr pistachios per day	received dietary counseling according to the guidelines of the American Heart Association	no	MS	FBS, LDL-C, TG, TC, Insulin,
10	West, S. G.	USA	2012	4	Women/men	28	-	10% (30% total fat) or 20% (34%total fat) daily caloric intake from pistachios	Low-fat control diet (25% total fat)	no	dyslipidemi a	FMD
11	Hernandez-Alonso, P.	Spain	2014	16	Women/men	54	55	Normo-caloric diet + 57gr pistachios per day	Normo-caloric diet	no	healthy	BMI, Weight, WC, FBS, LDL-C, HDL-C, TG, TC, LDL/HDL, TC/HDL, HBA1C, Insulin, HOMA-IR, SBP, DBP

Table 2: quality assessment of included studies

Table 2. quality of the studies								
Study name	**Selection bias** Random sequence generation	**Selection bias** Allocation concealment	**Reportin g bias** Selective reporting	**Other bias** Other sources of bias	**Performance bias** Blinding	**Detection bias** Blinding	**Attrition bias** Incomplete outcome data	**Overall quality**
S. Gulati 2014	LOW	UNCLEAR	LOW	LOW	HIGH	HIGH	LOW	Good
Kasliwal, R. R.2015	LOW	UNCLEAR	LOW	LOW	HIGH	HIGH	LOW	Good
Kocyigit, A.2006	LOW	UNCLEAR	LOW	LOW	HIGH	HIGH	LOW	Good
Li, Z. 2010	LOW	LOW	LOW	LOW	HIGH	HIGH	LOW	Good
Parham, M.2014	LOW	UNCLEAR	LOW	LOW	LOW	LOW	LOW	Good
Sari, I.2010	UNCLEAR	UNCLEAR	LOW	LOW	HIGH	HIGH	LOW	Fair
Sauder, K. A.2014	LOW	LOW	LOW	LOW	HIGH	HIGH	LOW	Good
Sauder, K. A.2015	LOW	LOW	LOW	LOW	HIGH	HIGH	LOW	Good
Wang, X.2012	LOW	UNCLEAR	LOW	LOW	HIGH	HIGH	LOW	Good
West, S. G.2012	LOW	UNCLEAR	LOW	LOW	HIGH	HIGH	LOW	Good
Hernandez-Alonso, P.2014	LOW	LOW	LOW	LOW	HIGH	HIGH	LOW	Good