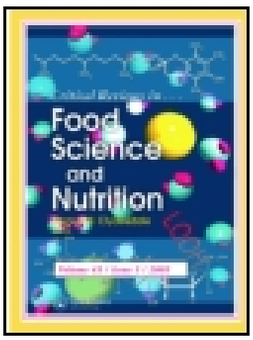

Taylor & Francis
Taylor & Francis Group

Critical Reviews in Food Science and Nutrition

ISSN: 1040-8398 (Print) 1549-7852 (Online) Journal homepage: http://www.tandfonline.com/loi/bfsn20

Peanut and cardiovascular disease risk factors: A systematic review and meta-analysis

Banafsheh Jafari Azad, Elnaz Daneshzad & Leila Azadbakht

To cite this article: Banafsheh Jafari Azad, Elnaz Daneshzad & Leila Azadbakht (2019): Peanut and cardiovascular disease risk factors: A systematic review and meta-analysis, Critical Reviews in Food Science and Nutrition, DOI: 10.1080/10408398.2018.1558395

To link to this article: https://doi.org/10.1080/10408398.2018.1558395

View supplementary material

Published online: 13 Jan 2019.

Submit your article to this journal

View Crossmark data

Full Terms & Conditions of access and use can be found at
http://www.tandfonline.com/action/journalInformation?journalCode=bfsn20

CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
https://doi.org/10.1080/10408398.2018.1558395

Taylor & Francis
Taylor & Francis Group

REVIEW

Check for updates

Peanut and cardiovascular disease risk factors: A systematic review and meta-analysis

Banafsheh Jafari Azad[a], Elnaz Daneshzad[a], and Leila Azadbakht[a,b]

[a]Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran; [b]Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

ABSTRACT

Several studies have been conducted on the effects of peanut consumption on cardiovascular diseases (CVD) risk factors. However, the findings are conflicting and appear inconsistent. The aim of this review is to summarize the findings on the effect of peanut consumption on the risk factors of CVDs. We used relevant keywords and searched through PubMed, Scopus and Web of Science for articles published studies up to November 2018. Randomized controlled trials (RCTs) were included in this meta-analysis. Random or fixed-effects meta-analysis method depending on the results of heterogeneity tests was used to estimate the effect size. Between-study heterogeneity was assessed by Q test and I^2 index. Subgroup analysis was conducted to find any excess relationship. Publication bias was checked by Egger's test and funnel plot. Quality of studies was assessed by the Cochrane criteria. According to the results of 13 RCTs, peanuts has no significant effect on weight (WMD: −0.11 kg, P = 0.773), waist circumference (WMD: −1.41 cm, P = 0.139), body mass index (WMD: −0.14 kg/m^2, P = 0.428), systolic and diastolic blood pressure (WMD: −0.09 mmHg, P = 0.939 and WMD: 0.60 mmHg, P = 0.652, respectively), low-density lipoprotein cholesterol (WMD: −3.31 mg/dl, P = 0.472), triglyceride (WMD: −7.59 mg/dl, P = 0.180), total cholesterol (WMD: 3.15 mg/dl, P = 0.171), fasting blood sugar (WMD: 0.57 mg/dl, P = 0.604) and serum insulin (WMD: −0.40, P = 0.582). Also, this meta-analysis showed that peanut had a positive significant effect on high-density lipoprotein cholesterol (HDL) (WMD: 2.72 mg/dl, P = 0.001). Peanuts consumption has a positive significant effect on HDL especially at the type of peanut oil, high-oleic peanut and peanut sprout and in healthy subjects and for consumption more than 12 weeks, while has no significant effect on other CVD risk factors.

KEYWORDS

Peanut; cardiovascular risk factors; lipid profile; meta-analysis

Introduction

Cardiovascular diseases (CVDs), as a class of diseases that involve the heart or blood vessels, meaninga series of related diseases, including coronary artery disease, atherosclerosis, hypertension and heart failure (Ros et al. 2014). Cardiovascular disease is the most common cause of death in the world (Widmer et al. 2015). Generally, CVDs cause morbidity, disability, and mortality in patients. According to international statistics, annual mortality rates of 15–25% in the West Asian region are due to CVDs (Mohammadi et al. 2002). Many factors including high blood pressure, hyperlipidemia, overweight, obesity, diabetes, inflammation, inappropriate diet, and several uncontrollable factors such as age, sex, and family history lead to CVDs (Micha et al. 2017). Studies have shown that controlling these risk factors can decrease or prevent the cardiovascular diseases (McGill, McMahan, and Gidding 2008; Kim, Keogh, and Clifton 2017).

Diet is a well-known factor which can impact on health status. Foods rich in bioactive nutrients, antioxidants, fiber, and polyunsaturated fatty acid (PUFAs) has the most impact on the cardiovascular risk factors (Funtikova et al. 2015). Nuts contain these beneficial nutrients such as monounsaturated fatty acids (MUFAs), PUFAs, fiber, lignanes, vitamins, minerals and phytochemicals including phenolic acids, phytosterols and flavonoids, which have anti-oxidative, anti-inflammatory, and antiproliferative properties (Schwingshackl et al. 2017; Bolling et al. 2011). Nut intake has been associated with reduced risk of non-communicable diseases such as cardiovascular diseases and diabetes (Hernández-Alonso et al. 2017; Asghari et al. 2017). Studies have shown that regular nut consumption has a beneficial impact on control and modify overweight, lipid profiles, blood glucose, and blood pressure (Barbour et al. 2015; de Souza et al. 2017).

Peanut Consumption as a desirable nut is consumed 4.2 million ton in the world (Dineshkumar et al. 2009). Peanut contains nutritious components such as protein, fiber, folate, niacin, magnesium, selenium, manganese, MUFAs, antioxidants, and other bioactive nutrients (Reis et al. 2013; Alves et al. 2014). Peanuts are a source of phenolic compounds that have the high antioxidant capacity, which may prevent

CONTACT Leila Azadbakht azadbakhtleila@gmail.com Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, P. O. Box: 1416643931, Tehran, Iran.
Banafsheh Jafari Azad and Elnaz Daneshzad are co-first author.

Supplemental data for this article can be accessed here.

© 2019 Taylor & Francis Group, LLC

endothelial damage and contribute to an anti-inflammatory postprandial response (Singh, Devaraj, and Jialal 2005). Postprandial inflammation and oxidative stress can exaggerate postprandial lipemia, which leads to vascular dysfunction (Moreira et al. 2016).

Peanuts also include arginine which probably mediates the cardioprotective effects (Liu et al. 2017). Peanut consumption may induce satiety and moderate weight, glycemic control, insulin resistance, lipids profile and blood pressure and has been negatively associated with cardiovascular risk factors (de Souza et al. 2017; Lokko et al. 2007; Mukuddem-Petersen, Oosthuizen, and Jerling 2005; Ros 2010; Hargrove et al. 2001; Ha et al. 2015). However, there are several studies that have shown peanut has no effect on weight and waist circumference (WC) (Barbour et al. 2015). Also, some others reported that peanut consumption can increase weight and body mass index (BMI) (Barbour et al. 2015; Akuamoah-Boateng et al. 2007). Peanut may be effective on body weight control through different mechanisms (Hou et al. 2018; Alper and Mattes 2002). The first is via increasing energy expenditure and resting metabolic rate which could be attributed to both the high unsaturated fat and protein in nuts (Coelho et al. 2006). The second is peanut energy is not completely available because incomplete digestion that is may be due to the properties of cell walls and fiber-rich skins in nuts (Barbour et al. 2015; Ellis et al. 2004). The third is satietogenic effect that may be attributed to its peculiar lipid, fiber, and protein composition (Sabaté 2003). The fourth is via suppression of appetite by reduced leptin and increased Glucagon-like peptide release, an incretin hormone that contributes to the suppression of appetite (Kim, Keogh, and Clifton 2017). In addition via the production of butyrate nut may be an effective on body weight control. Butyrate is a short chain fatty acid that can stimulate the expression of peptide YY, Which has an inhibitory effect on appetite (Kim, Keogh, and Clifton 2017). One animal study postulate that the presence of trypsin inhibitors in peanuts through increase the concentration of cholecystokinin, which has a satietogenic effect, may lead to a reduction in weight gain (Serquiz et al. 2016). Some studies also failed to report significant changes in total cholesterol, low-density lipoprotein cholesterol (LDL-C),triglyceride (TG),fasting serum glucose and insulin concentrations following a peanut intervention trial (Barbour et al. 2015; Alper and Mattes 2003; Jones et al. 2014; Ghadimi Nouran et al. 2010).

Regarding controversial results of the studies, the present study conducted a meta-analysis to find a comprehensive result which can helpful for prevention and management of cardiovascular disease. The current study is the first meta-analysis to assess the effects of peanut consumption on cardiovascular risk factors.

Methods

Search strategy

This study was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) protocol (Moher et al. 2009). To ensure a comprehensive assessment of all available evidence and publications on the effects of peanuts on CVD risk factors, we simultaneously searched the main international electronic data sources including PubMed, Scopus and Web of Science up to November 2018.

We used the following keywords to search the databases: (peanut OR Arachis[MeSH] OR Arachis[tiab] OR nut[tiab] OR Groundnut OR "Ground Nut"[tiab] OR "peanut oil"[tiab] OR "peanut butter"[tiab]) AND (Glycosylated Hemoglobin A[tiab] OR "Hemoglobin A, Glycosylated"[Mesh] OR "Insulin Resistance"[tiab] OR "Insulin Resistance"[MeSH] OR Insulin[tiab] OR Insulin [Mesh] OR Glucose[tiab] OR "Glucose Intolerance"[tiab] OR Glucose[Mesh] OR "Glucose Intolerance"[Mesh] OR "Waist Circumference"[tiab] OR "Waist Circumference"[Mesh] OR "Body Mass Index"[tiab] OR "Body Mass Index"[Mesh] OR Triglycerides[tiab] OR Triglycerides[Mesh] OR "Cholesterol, HDL"[tiab] OR "HDL Cholesterol"[Mesh] OR "Cholesterol, LDL"[tiab] OR "LDL Cholesterol"[Mesh] OR "Blood Pressure"[tiab] OR "Arterial Pressure"[tiab] OR "Hypertension"[tiab] OR "Blood Pressure"[Mesh] OR "Arterial Pressure"[Mesh] OR "total cholesterol" OR "Hypertension"[Mesh]).

Moreover, to prevent missing related papers, we checked the references of the included articles.

Inclusion and exclusion criteria

Clinical trials that evaluated the effect of different forms of peanut on CVD risk factors were included in this systematic review and meta-analysis. Studies were included if they have the following criteria: the study design was a controlledtrial and reported mean and standard derivation (SD) of factors at the baseline and final or mean changes for peanut and the placebo group. Only English language articles were included in the present study.

Animal studies, books, letters, comments, conference papers, observational studies, non-interventional studies, and reviews were excluded.

Data extraction

Two investigators (BJA and ED) separately reviewed the articles by title and abstract. Any non-agreement between these two authors was resolved by a third researcher (LA). In this study intervention was defined as any different peanut forms. Moreover, the mean and standard derivation of cardiovascular risk factors was considered as outcomes. We extracted the following characteristics from each included study: first author, year of publication, type of study, population, number of intervention and ontrol groups, participants' gender, participants' age, study location, study design, intervention duration and dosage, means and standard deviations of weight, WC, BMI, fasting blood sugar (FBS), serum insulin, glycated hemoglobinA1c (HbA1c), systolic and diastolic blood pressure (SBP and DBP, respectively), LDL-C, high density lipoprotein cholesterol

(HDL-C), total cholesterol (TC) and TG, before and after intervention.

Assessment of study quality

A systematic assessment of bias in the included studies was performed based on the Cochrane criteria (Higgins and Green 2011). Two authors (B.J.A. and E.D.) independently evaluated the quality of the studies by following criteria: random sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other possible sources of bias. According to Cochrane Handbook recommendation, studies were stratified as low risk of bias, high risk of bias or unclear regarding each domain (Table 2).

Table 1. Clinical trial studies in meta-analysis of the effect of peanut on cardiovascular risk factors.

First author, (year), country	Study design	Population, gender, age (year)	Participant (intervention/ control)	Duration (week)	Type, dose (g/d)	Control group	Quality score	Outcome
Akuamoah-Boateng et al. (2007), United States	Parallel	Healthy subjects/ both (18–50)	(32/32)	8	Peanut oil + milk-shake /(33)	Peanut oil free-milkshake	4	WT
Alves et al. (2014), Brazil*	Parallel	Overweight and obese /male/(18–50)	(21/22)	4	High oleic pea-nut + hypocal-oric-diet/(56)	Hypocaloric-diet	2	WT, WC, BMI
Alves et al. (2014), Brazil*a	Parallel	Overweight and obese/ male/(18–50)	(22/22)	4	Conventional pea-nuts + hypoca-loric diet/(56)	Hypocaloric-diet	2	WT, WC, BMI
Barbour et al. (2015), Australia	Crossover	Healthy subjects/ both (50–75)	(34/35)	12	High oleic pea-nut/(70)	Not Peanut	2	WC, LDL, HDL, TG, TC, FBS, Ins, BMI
Ghadimi Nouran et al. (2010), Iran	Crossover	Hypercholesterol-emia/ male (25–65)	(30/30)	4	Peanuts + habitu-al diet/(77)	Not peanut	2	HDL, WT, SBP, DBP, TC, TG, LDL
Ha et al. (2015), Korea*	Parallel	Overweight and obese/ female/(20–55)	(15/15)	4	Peanut sprout capsules/(5.8)	Pelacebo capsules	4	WC, LDL, WT, BMI, SBP, DBP, TC, HDL, TG
Ha et al. (2015). Korea*	Parallel	Overweight and obese/ female/(20–55)	(15/15)	4	Peanut sprout/(2.6)	Pelacebo capsules	4	WC, SBP, TG, WT, BM, TC, HDL, LDL
Alves et al. (2014), Brazil*	Parallel	Overweight and obese/ male/(18–50)	(21/22)	4	High oleic pea-nut + hypocal-oric diet/(56)	Hypocaloric diet	2	FBS, SBP, DBP, Ins, TC, LDL WT, BMI, TG, HDL
Alves et al. (2014), Brazil*	Parallel	Overweight and obese/ male/(18–50)	(22/22)	4	Peanuts + hypoc-aloric diet/(56)	Hypocaloric diet	2	LDL, SBP, DBP, Ins, TCWT, BMI, TG, HDL
O'Byrne, Knauft, and Shireman (1997), United States	Parallel	Hypercholesterol-emic female (50–65)	(12/13)	24	High oleic pea-nut + low fat diet/(51.5)	Low fat diet	1	WT, BMI, HDL, TC, LDL, TG
Pelkman et al. (2004), United States	Parallel	Overweight and obese/ both/(20–67)	(27/25)	6	Peanut oil + low fat diet, weight loss diet/(88.3)	Low fat diet, weight loss diet	3	TC, TG, LDL, HDL, WT
Sales et al. (2008), United States	Parallel	Healthy subjects/ both (18–50)	(32/32)	8	Peanut oil + milk-shake/(80)	Not peanut	2	WT, SBP, DBP, TC, TG, HDL, LDL
Sankar et al. (2005), India	Parallel	HTN/both/(50)	(47/40)	8	Peanut oil + Nifedipin-e/(35)	Nifedipine	2	TC, LDL, SBP, DBP, HDL, TG
Wien, Oda, and Sabaté (2014), United States●	Parallel	T2DM/ both/(34–84)	(30/30)	24	Peanuts + ADA# plan/(46)	Peanut free-ADA plan	2	WT, WC, BMI, FBS, HbA1C , LDL, HDL, TG, TC
Barbour et al. (2017), Australia	Crossover	Overweight and obese/ both/(50–75)	(34/35)	12	High oleic pea-nut/(70)	Not peanut	3	BMI
Rao, Rao, and Srikantia (1981), India●	Parallel	HTN/both/(46)	(8/8)	6	Peanut oil/(10)	Not peanut	3	SBP, DBP

WT, weight; WC, waist circumference; BMI, body mass index; LDL, low density lipoprotein; HDL, high density lipoprotein; TC, total cholesterol; TG, Triglyceride; FBS, fasting blood sugar; Ins, insulin; HbA1C, hemoglobin A1c; SBP, systolic blood pressure; DBP, diastolic blood pressure.

*The papers Alves et al. (a, b) and Ha et al. were analyzed as two studies, due to the difference in the type and amount of peanuts consumption, respectively.

#ADA = American Diabetes Association meal plan.

●All outcome variables in this intent-to-treat analysis were adjusted for their baseline values in the models.

Data synthesis and statistical analysis

Mean change of above-mentioned variables and the relevant standard deviations (SD) were extracted. In those studies which did not report the mean change, mean of variables before and after intervention were extracted. Regarding those studies that reported standard error (SE) we calculated SD according to this formula: (SD = SE * $\sqrt{N}$). For cross-over studies, we extracted mean changes and relevant SDs for the first step of the studies. The reported concentration of lipid profile and glucose in all studies were converted into the usual unit (mg/dl). We contacted the authors of published papers, whenever some data were non-available. At first, a fixed-effect model was performed to determine the relationship with a forest plot. If there was a high heterogeneity ($P < 0.10$ for Q test), a random-effect model (the Dersimonian–Laird method) was performed to calculate the pooled effect size. Subgroup analysis was conducted to find any excess relationship. Publication bias was checked by Egger's test.

Results

Systematic review

Study selection

Overall, 5051 potential records were identified after searching the databases, and 1067 articles were removed because of duplication. After screening the titles and abstracts and removing irrelevant studies, 33 articles were selected for detailed assessment. twenty studies were removed for the following reasons: were done on infants (n = 1) (Hariharan, Kurien, and Rao 1995), lack of the control group (n = 14) (Dineshkumar et al. 2009; Lokko et al. 2007; Hou et al. 2018; Alper and Mattes 2003; Jones et al. 2014; Bell et al. 2014; Claesson et al. 2009; Johnston, Trier, and Fleming 2013; Kris-Etherton et al. 1999; McKiernan et al. 2010; Zhang et al. 1997; Reddy and Sesikaran 1995; Nagashree et al. 2017; Vijayakumar et al. 2018), postprandial study (n = 5) (Reis et al. 2013; Moreira et al. 2016; Liu et al. 2017; Reis et al. 2011; Lilly et al. 2018). Also there were two articles that we did not have access to their full text (Vigne 1974; Lin, Lin, and Shen 2017). Ultimately, 13 studies fulfilled our inclusion criteria, including 10 parallel clinical trials (Alves et al. 2014; Ha et al. 2015; Akuamoah-Boateng et al. 2007; Moreira Alves et al. 2014; O'Byrne, Knauft, and Shireman 1997; Pelkman et al. 2004; Sales et al. 2008; Sankar et al. 2005; Wien, Oda, and Sabaté 2014; Rao, Rao, and Srikantia 1981) and 3 crossover studies (Barbour et al. 2015; Ghadimi Nouran et al. 2010; Barbour et al. 2017). The flowchart for study selection is presented in Figure 1.

Study characteristics

Data were pooled from 13 eligible studies including 800 subjects, 402 subjects in the intervention group and 398 subjects in the control group. The amount of different kinds of peanut consumption was 33 to 88 g/d except two of them which consumed less than 10 g/d (Ha et al. 2015; Rao, Rao, and Srikantia 1981). The participants were between 18 and 75 years old. The duration of intervention in these studies varied from 4 to 24 weeks. These studies examined the effects of four forms of peanut (peanuts, peanut oil, high oleic peanut and peanut sprout) on CVD risk factors. The selected articles were published between 1981 and 2017. Seven studies were carried out in the United States (Alves et al. 2014; Akuamoah-Boateng et al. 2007; Moreira Alves et al. 2014; O'Byrne, Knauft, and Shireman 1997; Pelkman et al. 2004; Sales et al. 2008, Wien, Oda, and Sabaté 2014), four in Asia countries (Ha et al. 2015; Ghadimi Nouran et al. 2010; Sankar et al. 2005; Rao, Rao, and Srikantia 1981) and 2 in Australia (Barbour et al. 2015; Barbour et al. 2017). Participants in 3 articles were healthy subjects (Barbour et al. 2015; Akuamoah-Boateng et al. 2007; Sales et al. 2008), in 5 articles were obese (Alves et al. 2014; Ha et al. 2015; Ghadimi Nouran et al. 2010; Moreira Alves et al. 2014; Pelkman et al. 2004), in 2 articles hypertensive subjects (Sankar et al. 2005; Rao, Rao, and Srikantia 1981), in 2

Table 2. Cochrane risk of bias assessment.

Study	Random sequence generation	Allocation concealment	Blinding of participants, personnel and outcome assessors	Incomplete outcome data	Selective outcome reporting	Other bias
Akuamoah-Boateng et al. (2007)	U	L	L	U	L	L
Alves et al. (2014)	U	U	L	L	U	L
Barbour.et al. (2015)	L	U	L	L	L	U
Ghadimi Nouran et al (2009)	U	U	L	L	L	U
Ha et al. (2015)	U	L	L	U	L	U
Alves et al. (2014)	U	U	L	L	L	U
O'Byrne, Knauft, and Shireman (1997)	H	U	H	L	L	U
Pelkmn et al. (2004)	U	H	U	L	L	U
Sales et al. (2008)	U	L	L	U	L	U
Sankar et al. (2005)	U	U	U	L	L	U
Wien, Oda, and Sabaté (2014)	U	U	L	L	L	L
Barbour et al. (2017)	L	U	L	L	L	U
Rao, Rao, and Srikantia (1981)	L	L	L	L	L	U

L, low risk of bias; H, high risk of bias; U, unclear risk of bias.

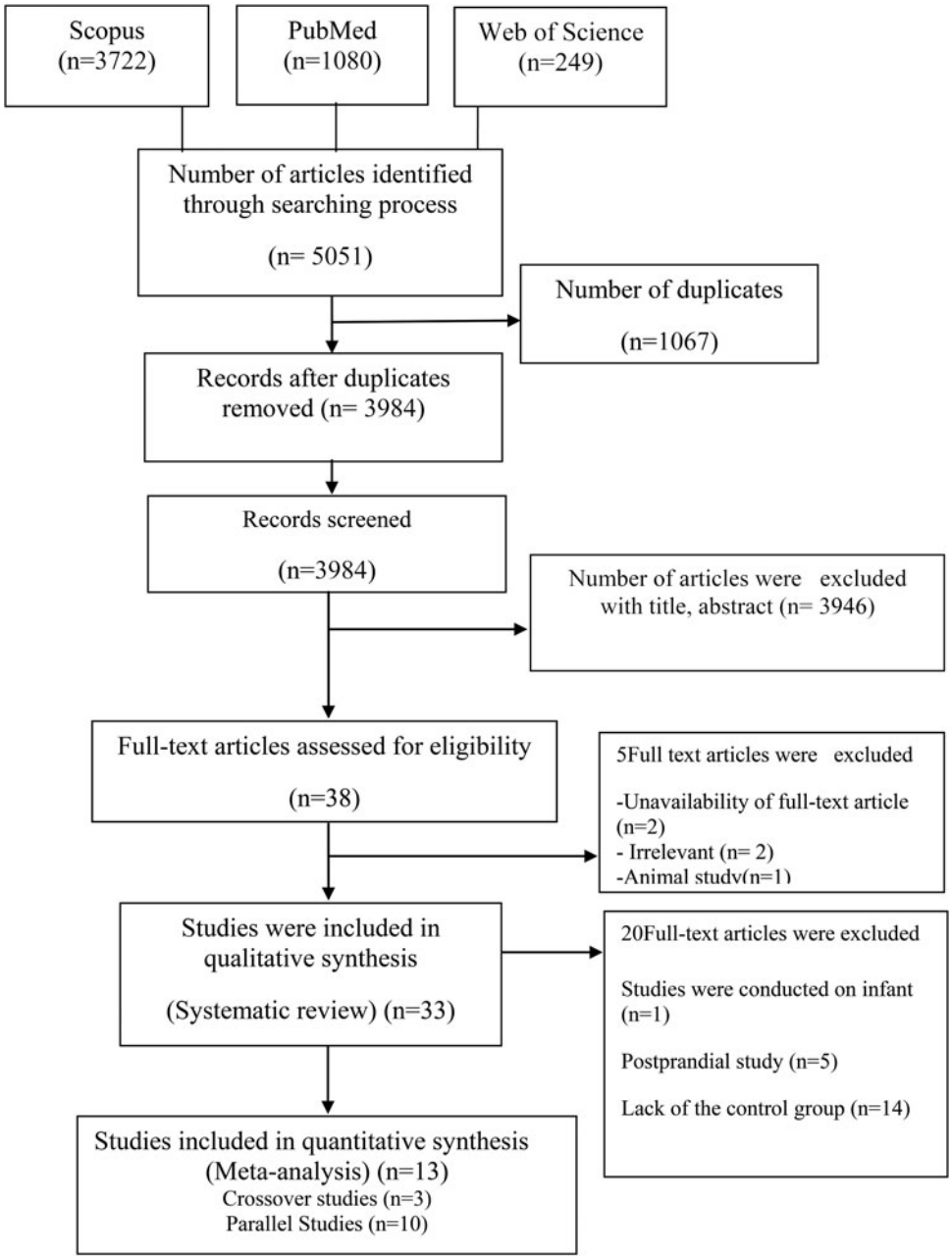

Figure 1. Flowchart for study selection.

articles were subjects with Hypercholesterolemia (Ghadimi Nouran et al. 2010; O'Byrne, Knauft, and Shireman 1997) and in one article were subjects with type 2 diabetes (Wien, Oda, and Sabaté 2014).

The intervention was investigated in two articles along with a hypocaloric diet (Alves et al. 2014; Sales et al. 2008) and in one study with nifedipine (Sankar et al. 2005). Only one of the included studies reported effects peanuts on the infant (Hariharan, Kurien, and Rao 1995). In addition one of these studies reported the effects of peanut sprout on CVD risk factors in two different quantities and therefore was considered as 2 studies in our analysis (Ha et al. 2015).

Main results of 33 included studies in this present systematic review are as follows:

Peanut and anthropometric indices

Nine studies did not find any significant effect on weight (Ha et al. 2015; Akuamoah-Boateng et al. 2007; Ghadimi Nouran et al. 2010; Hariharan, Kurien, and Rao 1995; Claesson et al. 2009; McKiernan et al. 2010; Nagashree et al. 2017; Vijayakumar et al. 2018; Pelkman et al. 2004), 5 articles indicated a significant reduction in weight (Alves et al. 2014; Johnston, Trier, and Fleming 2013; Moreira Alves et al. 2014; O'Byrne, Knauft, and Shireman 1997; Wien, Oda, and Sabaté 2014) and 2 studies revealed a positive effect on weight (Jones et al. 2014; Sales et al. 2008). Four studies did not reportthe significant effect on WC (Barbour et al. 2015; Claesson et al. 2009; Johnston, Trier, and Fleming 2013; Vijayakumar et al. 2018) and in 3 articles

negative effect have reported (Alves et al. 2014; Ha et al. 2015; Wien, Oda, and Sabaté 2014). Seven studies did not report the significant effect on BMI (Barbour et al. 2015; Ha et al. 2015; Hou et al. 2018; Claesson et al. 2009; McKiernan et al. 2010; Nagashree et al. 2017; Vijayakumar et al. 2018),5 articles indicated a significantreduction in BMI (Alves et al. 2014; Moreira Alves et al. 2014; O'Byrne, Knauft, and Shireman 1997; Wien, Oda, and Sabaté 2014; Barbour et al. 2017) and just one studies revealed a positive effect on BMI [33].

Peanut and lipid profile

Eighteen studies did not find any significant changes in serum LDL concentration (Barbour et al. 2015; Dineshkumar et al. 2009; Liu et al. 2017; Lokko et al. 2007; Hou et al. 2018; Jones et al. 2014; Ghadimi Nouran et al. 2010; Hariharan, Kurien, and Rao 1995; Claesson et al. 2009; McKiernan et al. 2010; Zhang et al. 1997; Reddy and Sesikaran 1995; Nagashree et al. 2017, Moreira Alves et al. 2014; Sales et al. 2008; Sankar et al. 2005; Wien, Oda, and Sabaté 2014, Flores-Mateo et al. 2013),however, 5 articles indicated significant reduction (Ha et al. 2015; Kris-Etherton et al. 1999; McKiernan et al. 2010; O'Byrne, Knauft, and Shireman 1997; Pelkman et al. 2004) and just one studies revealed positive effect on LDL (Moreira Alves et al. 2014). Sixteen studies did not find any significant effect on serum HDL concentration (Barbour et al. 2015; Dineshkumar et al. 2009; Liu et al. 2017; Lokko et al. 2007; Ha et al. 2015; Hou et al. 2018; Jones et al. 2014; Hariharan, Kurien, and Rao 1995; Claesson et al. 2009; Kris-Etherton et al. 1999; Zhang et al. 1997; Reddy and Sesikaran 1995; Pelkman et al. 2004; Sales et al. 2008; Wien, Oda, and Sabaté 2014; Flores-Mateo et al. 2013), 4 articles indicated significant reduction (Zhang et al. 1997; Nagashree et al. 2017; Moreira Alves et al. 2014; O'Byrne, Knauft, and Shireman 1997) and 3 studies revealed positive effect on HDL (Ghadimi Nouran et al. 2010; McKiernan et al. 2010; Sankar et al. 2005). Thirteen studies did not find any significant effect on serum TG concentration (Barbour et al. 2015; Ha et al. 2015; Hou et al. 2018; Jones et al. 2014; Ghadimi Nouran et al. 2010; Hariharan, Kurien, and Rao 1995; McKiernan et al. 2010; Zhang et al. 1997; Reddy and Sesikaran 1995; Nagashree et al. 2017, O'Byrne, Knauft, and Shireman 1997; Sales et al. 2008; Wien, Oda, and Sabaté 2014), while 7 articles indicated significant reduction (Lokko et al. 2007; Ha et al. 2015; Alper and Mattes 2003; Kris-Etherton et al. 1999; McKiernan et al. 2010; Moreira Alves et al. 2014; Pelkman et al. 2004) and 3 studies revealed positive effect on TG concentration (Moreira et al. 2016; Liu et al. 2017; Sankar et al. 2005). seventeen studies did not find any significant effect on serum TC concentration (Barbour et al. 2015; Dineshkumar et al. 2009; Liu et al. 2017; Ha et al. 2015; Hou et al. 2018; Alper and Mattes 2003; Jones et al. 2014; Ghadimi Nouran et al. 2010, Hariharan, Kurien, and Rao 1995; Claesson et al. 2009; McKiernan et al. 2010; Zhang et al. 1997; Reddy and Sesikaran 1995, Moreira Alves et al. 2014; Sales et al. 2008; Sankar et al. 2005; Wien, Oda, and Sabaté 2014), 5 articles indicated significant reduction in TC level (Lokko et al. 2007; Kris-Etherton et al. 1999; McKiernan et al. 2010; Nagashree et al. 2017; O'Byrne, Knauft, and Shireman 1997). In a study in newborn infants, peanut oil consumption for 24 weeks did not have a significant effect on blood lipid profile (TC, TG, LDL, HDL) (Hariharan, Kurien, and Rao 1995).

Peanut and glycemic factors

Nine studies did not find any significant effect on FBS (Barbour et al. 2015; Reis et al. 2013; Moreira et al. 2016; Liu et al. 2017; Jones et al. 2014; Ghadimi Nouran et al. 2010; Claesson et al. 2009; Johnston, Trier, and Fleming 2013; Wien, Oda, and Sabaté 2014), 5 articles indicated significant reduction (Hou et al. 2018; Johnston, Trier, and Fleming 2013; Vijayakumar et al. 2018; Reis et al. 2011; Lilly et al. 2018) and just one study revealed a positive effect on FBS (Moreira Alves et al. 2014). Eight studies did not observe a significant effect on serum insulin (Barbour et al. 2015; Reis et al. 2013; Liu et al. 2017; Jones et al. 2014; Claesson et al. 2009; Johnston, Trier, and Fleming 2013; Vijayakumar et al. 2018; Moreira Alves et al. 2014), and just one article indicated a significant increase in serum insulin level (Moreira et al. 2016). two study did not find any significant effect on HbA1C (Hou et al. 2018; Wien, Oda, and Sabaté 2014) and one article indicated a significant reduction inHbA1C [42].

Peanut and blood pressure

Eight studies did not find any significant effect on SBP (Ha et al. 2015; Jones et al. 2014; Ghadimi Nouran et al. 2010; Reddy and Sesikaran 1995; Vijayakumar et al. 2018; Moreira Alves et al. 2014; Rao, Rao, and Srikantia 1981; Barbour et al. 2017) and 3 articles indicated a significantreduction in SBP (Ha et al. 2015; Sales et al. 2008; Sankar et al. 2005). Five studies did not find any significant effect on DBP (Ha et al. 2015; Ghadimi Nouran et al. 2010; Reddy and Sesikaran 1995; Moreira Alves et al. 2014; Barbour et al. 2017), 4 articles indicated significant reduction (Jones et al. 2014; Sales et al. 2008; Sankar et al. 2005; Rao, Rao, and Srikantia 1981) and just one study revealed positive effect on DBP (Vijayakumar et al. 2018).

Peanut and postprandial measures

Among 5 postprandial studies, one study showed that after consuming 85 g of peanut for 240 minutes in overweight men, TG levels in the intervention group significantly increased, while they did not have a significant effect on FBS, insulin, LDL, HDL, and TC [19]. Also, one study indicated that after consuming 56 g of high oleic peanut for 180 minutes, TG levels in the intervention group significantly increased but did not have a significant effect on glucose and insulin levels (Moreira et al. 2016). One of these studies demonstrated that after eating 45 g of peanut for 490 minutes in overweight women with type 2 diabetes,

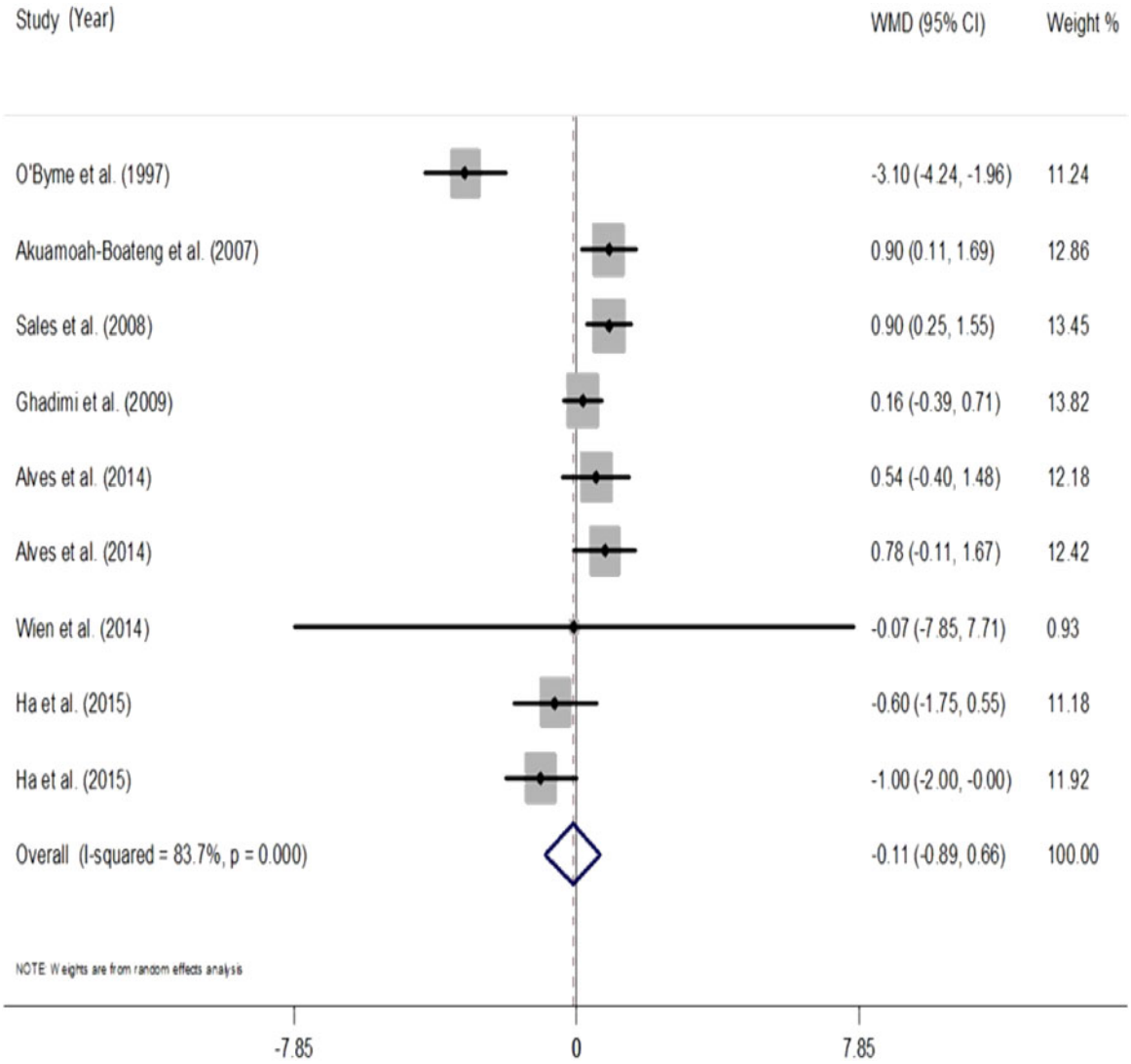

Figure 2. Forest plot of the effect of peanut consumption on weight.

there was no significant effect on glucose and insulin levels (Reis et al. 2013). However, one study indicated that after consumption 63 g of ground roasted peanut for 120 minutes, significant reduction occurs in the glucose level (Reis et al. 2011). Also, in one study has been reported that after consumption 32 g of peanut butter along with a high–glycemic index meal, the spike of blood glucose and FBG level after 60 minutes decrease significantly Compared to a group that just received a high–glycemic index meal (Lilly et al. 2018).

Meta-analysis

The characteristics of the clinical trial studies are presented in Table 1.

Peanut consumption and weight

The pooled estimate from the random-effect model that performed on 9 studies including 209 cases and 211 controls, showed that peanut had no significant effect on weight (WMD: −0.11 kg; 95% CI: −0.89 to 0.66, p = 0.773) (I^2 = 83.7%, p < 0.0001) (Figure 2). Even, after exclusion of two studies Wien et al. (Wien, Oda, and Sabaté 2014) and O'Byrne et al. (O'Byrne, Knauft, and Shireman 1997) peanut did not have a significant effect on weight (WMD: 0.31 kg; 95% CI: −0.19 to 0.81, p = 0.227) (I^2 = 61.8%, p = 0.015). The subgroup analysis showed that sex, duration of the intervention, type of peanut intervention, the populations based on health status were the potential sources of heterogeneity (Supplemental Table 1 in supplementary information). According to subgroup analysis based on population health status, peanut have shown positive effect on weight gain in healthy people (P < 0.0001). Assessment of publication bias by visual inspection of a funnel plot indicated no evidence of publication bias (Supplemental Figure 1 in supplementary information). Also, Egger's test affirmed the same result (p = 0.351)

Peanut consumption and waist circumference

The pooled estimate from the random-effect model that performed on 6 studies including 137 cases and 139 controls, showed that peanut had no significant effect on WC (WMD: −1.41 cm; 95% CI: −3.27 to 0.46, p = 0.139) (I^2 =

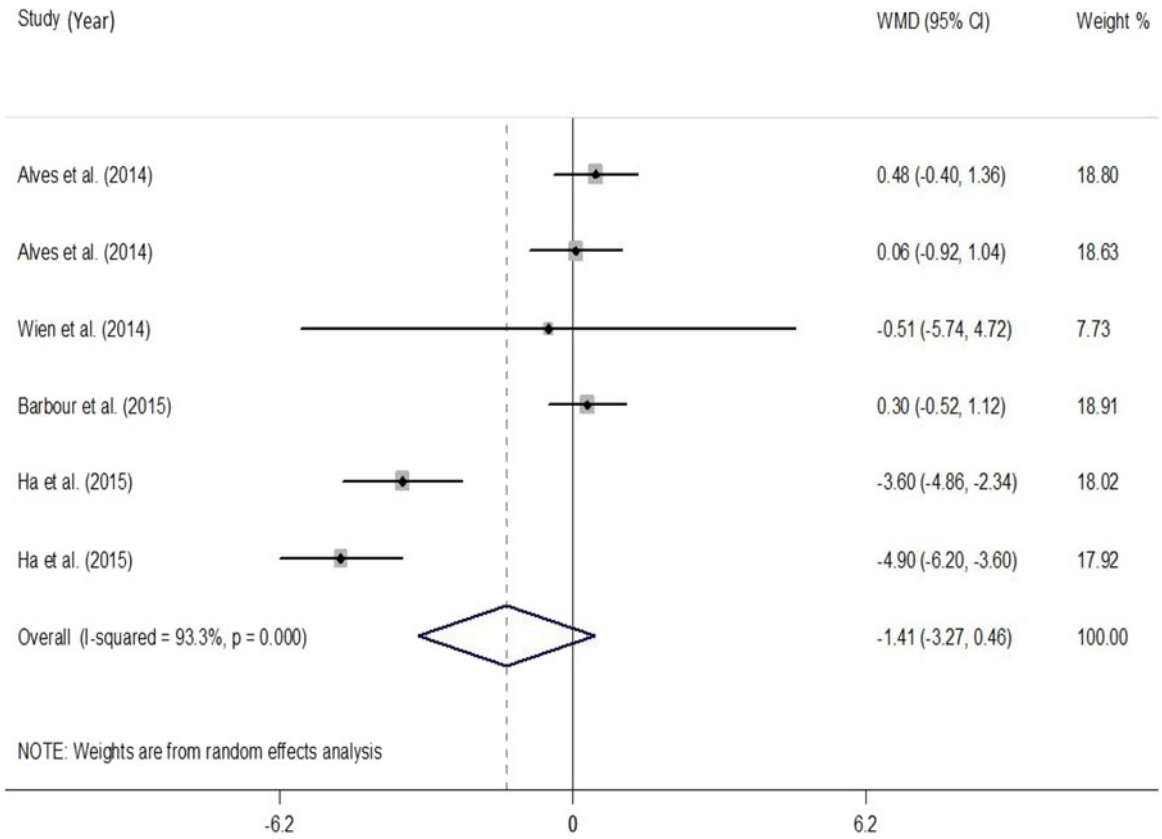

Figure 3. Forest plot of the effect of peanut consumption on WC.

93.3%,P < 0.0001) (Figure 3). Even, after exclusion of two studies (Ha et al. 2015; Wien, Oda, and Sabaté 2014) peanut did not have a significant effect on WC (WMD: 0.294; 95% CI: −0.218 to 0.807, p = 0.260) (I^2 = 0%p = 0.822). The subgroup analysis showed that sex, type of peanut, duration and dose were the potential sources of heterogeneity (Supplemental Table 2 in supplementary information). The population health status was not the source of heterogeneity. Assessment of publication bias by visual inspection of a funnel plot indicated no evidence of publication bias (Supplemental Figure 2 in supplementary information). Moreover, Egger's test showed the same result (p = 0.417).

Peanut consumption and BMI

The pooled estimate from the random-effect model that performed on 8 studies including 182 cases and 187 controls, showed that peanut had no significant effect on BMI (WMD: −0.14 kg/m^2; 95% CI: −0.48 to 0.20, p = 0.428) (I^2 = 88.5%, p < 0.0001) (Figure 4). Even, after exclusion of two studies (O'Byrne, Knauft, and Shireman 1997; Wien, Oda, and Sabaté 2014) peanut had no significant effect on BMI (WMD: 0.03 kg/m^2; 95% CI: −0.22 to 0.29, p = 0.788) (I^2 = 80.2%, P < 0.0001). The subgroup analysis showed that sex, type of peanut, and dose were the potential sources of heterogeneity (Supplemental Table 3 in supplementary information). The population health status was not the source of heterogeneity. Assessment of publication bias by visual inspection of funnel plot indicated no evidence of publication bias (Supplemental Figure 3 in supplementary information) and also, Egger's test affirmed the same result (p = 0.114).

Peanut consumption and SBP

The pooled estimate from the fix-effect model that performed on 6 studies including 147 cases and 140 controls, showed that peanut had no significant effect on SBP (WMD: −0.09 mmHg; 95% CI: −2.51 to 2.32, p = 0.939) (I^2 = 40.2%, p < 0.137) (Figure 5). Assessment of publication bias by visual inspection of a funnel plot indicated no evidence of publication bias (Supplemental Figure 4 in supplementary information). Egger's test also showed the same result (p = 0.326).

Peanut consumption and DBP

The pooled estimate from the random-effect model that performed on 6 studies including 147 cases and 140 controls, showed that peanut had no significant effect on DBP (WMD: 0.60 mmHg; 95% CI: −2.00 to 3.20, p = 0.652) (I^2 = 55.3%, p < 0.048) (Figure 6). The subgroup analysis showed that sex, population based on health status, type of peanut, and dose were the potential sources of heterogeneity (Supplemental Table 4 in supplementary information). According to subgroup analysis based on population health status, peanut have shown positive effect on DBP in overweight participants (P < 0.047). Assessment of publication bias by visual inspection of a funnel plot indicated no evidence of publication bias (Supplemental Figure 5 in

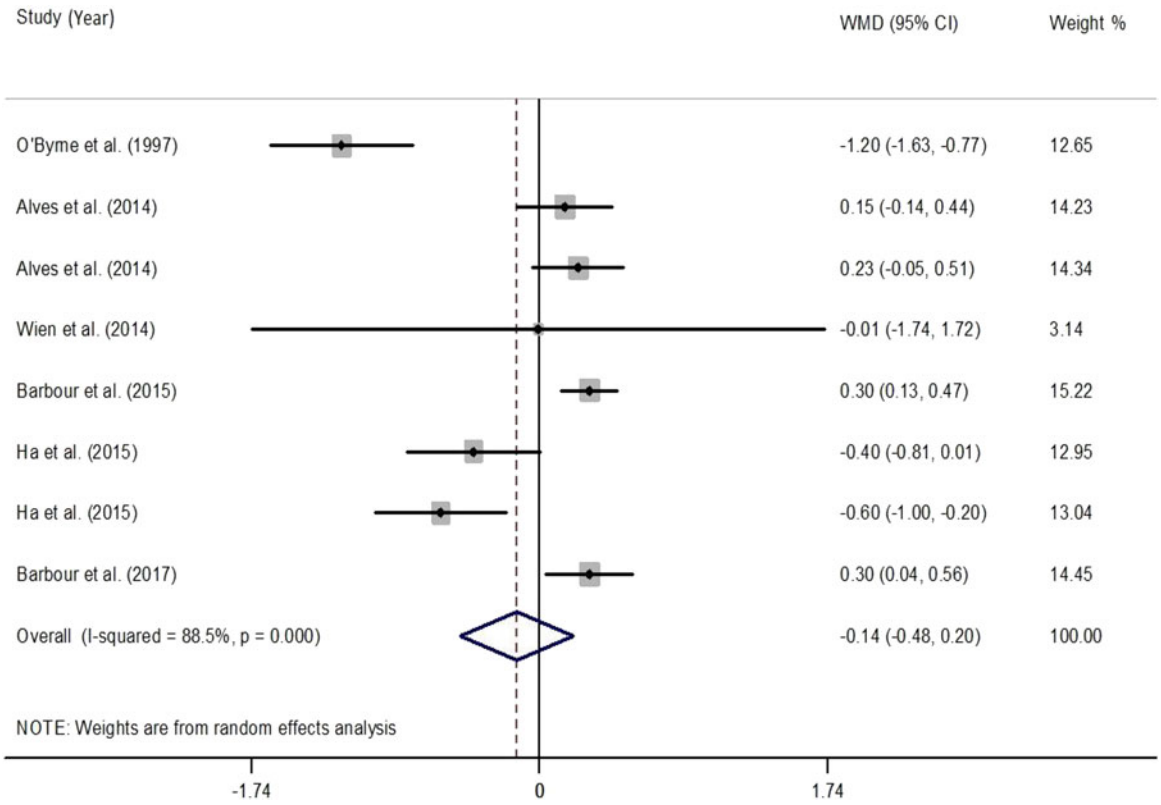

Figure 4. Forest plot of the effect of peanut consumption on BMI.

supplementary information). Egger's linear regression test also showed the same result (p = 0.845).

Peanut consumption and LDL

The pooled estimate from the random-effect model that performed on 11 studies including 285 cases and 279 controls, showed that peanut had no significant effect on LDL (WMD: −3.31 mg/dl; 95% CI: −12.32 to 5.71, p = 0.472) (I^2 = 82.3%, p < 0.001) (Figure 7). After exclusion of one study (Wien, Oda, and Sabaté 2014), peanut had no significant effect on LDL (WMD: 0.83 mg/dl; 95% CI: −3.95 to 5.60, p = 0.734) (I^2 = 28.5, P = 0.182). The subgroup analysis showed that gender, dose, population based on health status, type of peanut and duration were the potential sources of heterogeneity (Supplemental Table 5 in supplementary information). According to subgroup analysis based on population health status, peanut have not significant effect on LDL in overweight and Healthy participants (P < 0.594 and P < 0.885, respectively). Assessment of publication bias by visual inspection of a funnel plot indicated no evidence of publication bias (Supplemental Figure 6 in supplementary information). Egger's linear regression test also showed the same result (P = 0.951).

Peanut consumption and HDL

The pooled estimate from the random-effect model that performed on 10 studies including 255 cases and 249 controls, showed that peanut had a positive significant effect on HDL (WMD: 2.72 mg/dl; 95% CI: 1.10 to 4.35, P = 0.001) (I^2 = 66.3%, P = 0.002) (Figure 8). The subgroup analysis showed that population based on health status, sex, type of peanut and duration were the potential sources of heterogeneity (Supplemental Table 6 in supplementary information). According to subgroup analysis based on population health status, peanut have shown no significant effect on HDL in healthy subjects participants (P < 0.629). Assessment of publication bias by visual inspection of a funnel plot indicated no evidence of publication bias (Supplemental Figure 7 in supplementary information). Egger's linear regression test also showed the same result (P = 0.999). After analysis of dose-response, we did not observe a significant relationship between peanuts and HDL concentration (P = 0.344) (Supplemental Figure 8 in supplementary information).

Peanut consumption and TG

The pooled estimate from the fix-effect model that performed on 10 studies including 255 cases and 249 controls, showed that peanut had no significant effect on TG (WMD:−7.59 mg/dl; 95% CI: −18.68 to3.50, P = 0.180) (I^2 = 0.0%, P = 0.566) (Figure 9). Assessment of publication bias by visual inspection of a funnel plot indicated no evidence of publication bias (Supplemental Figure 9 in supplementary information). Egger's linear regression test also showed the same result (P = 0.064).

Peanut consumption and TC

The pooled estimate from the fix-effect model that performed on 10 studies including 255 cases and 249 controls,

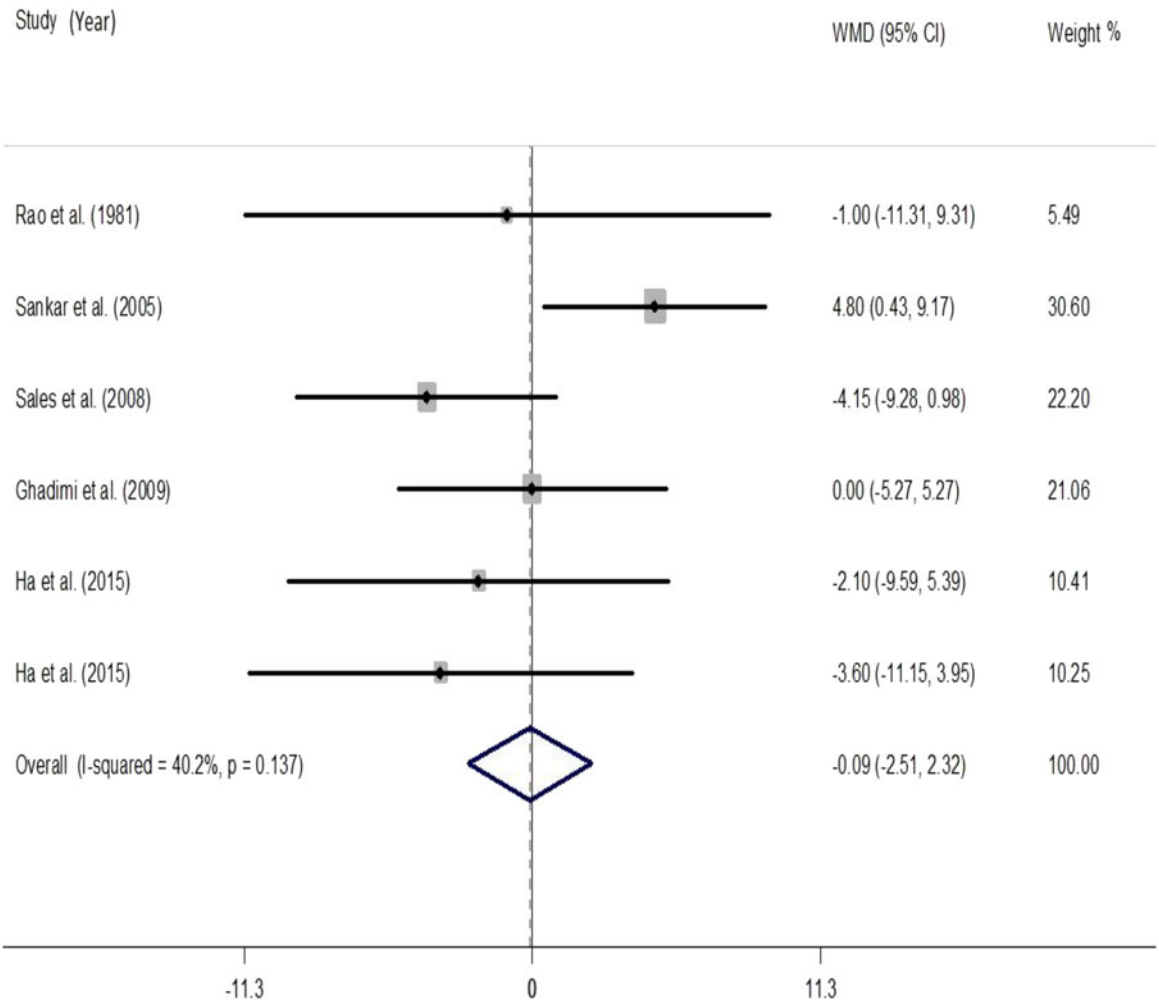

Figure 5. Forest plot of the effect of peanut consumption on SBP.

showed that peanut had no significant effect on TC (WMD: 3.15 mg/dl; 95% CI: −1.36 to7.66, P = 0.171) (I^2 = 10.2%, P = 0.349) (Figure 10). Even, after exclusion of one study (Wien, Oda, and Sabaté 2014) peanut had no significant effect on TC (WMD: 4.44 mg/dl; 95% CI: −0.189 to9.07, P = 0.06) (I^2 = 0.0%, P = 0.823). Assessment of publication bias by visual inspection of funnel plot indicated no evidence of publication bias (Supplemental Figure 10 in supplementary information). Egger's linear regression test also showed the same result (P = 0.434).

Peanut consumption and FBS

The pooled estimate from the fix-effect model that performed on 5 studies including 107 cases and 109 controls, showed that peanut had no significant effect on FBS (WMD: 0.57 mg/dl; 95% CI: −1.58 to2.72, P = 0.604) (I^2 = 0.0%, P = 0.922) (Figure 11). Assessment of publication bias by visual inspection of a funnel plot indicated no evidence of publication bias (Supplemental Figure 11 in supplementary information). Egger's linear regression test also showed the same result (P = 0.779).

Peanut consumption and serum insulin

The pooled estimate from the fix-effect model that performed on 3 studies including 77 cases and 79 controls, showed that peanut had no significant effect on serum insulin (WMD: −0.40; 95% CI: −1.84 to1.03, P = 0.582) (I^2 = 0.0%, P = 0.750) (Figure 12). Assessment of publication bias by visual inspection of a funnel plot indicated no evidence of publication bias (Supplemental Figure 12 in supplementary information). Egger's linear regression test also showed the same result (P = 0.494).

Discussion

This is the first study that summarizing the effect of peanut on CVD risk factors from earlier clinical results. In the current study, we proved a significant positive association between peanut consumption and plasma HDL concentrations in adult populations. This analysis also revealed markedly between-study heterogeneity and we found intervention dosage, study quality, and participants' health status were the potential sources of heterogeneity. Peanut consumption did not indicate any significant effect on other CVD risk factor. Peanuts are rich sources of nutritious components

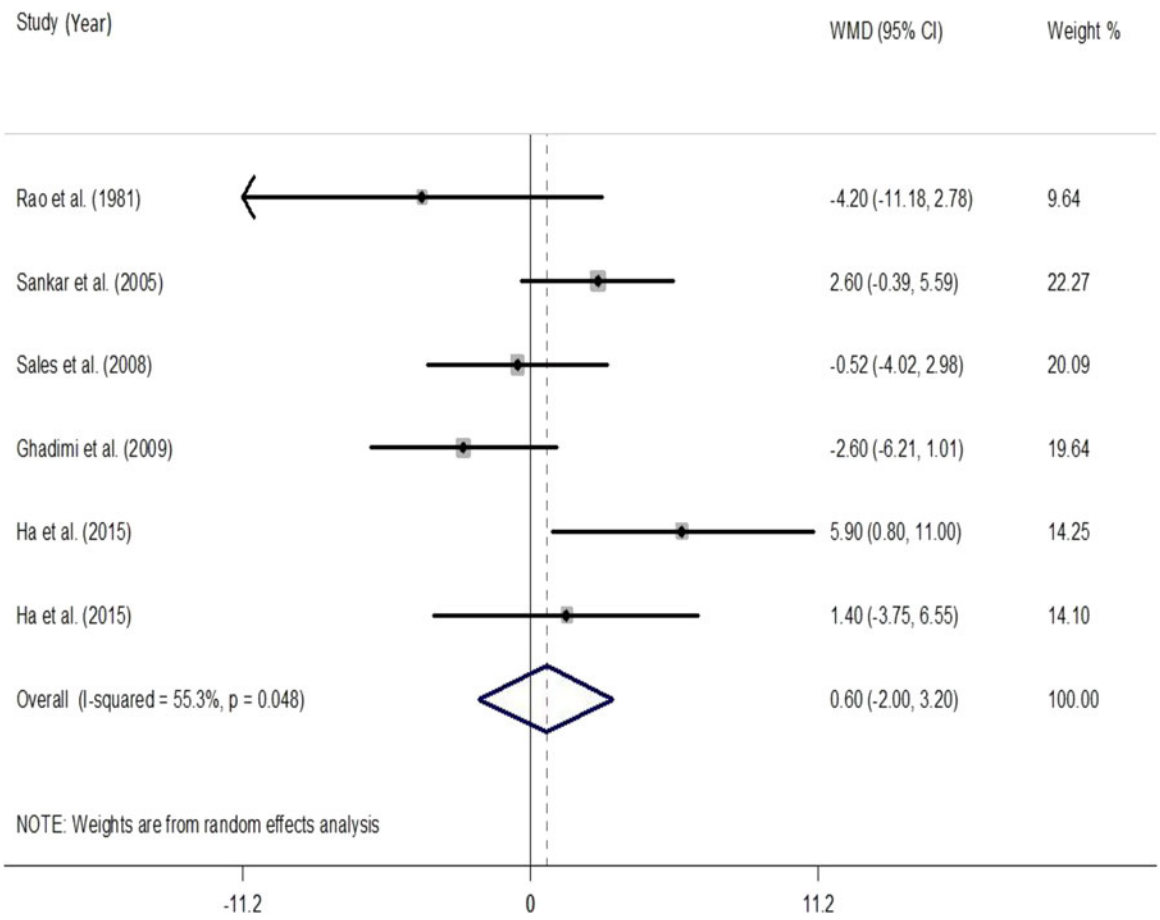

Figure 6. Forest plot of the effect of peanut consumption on DBP.

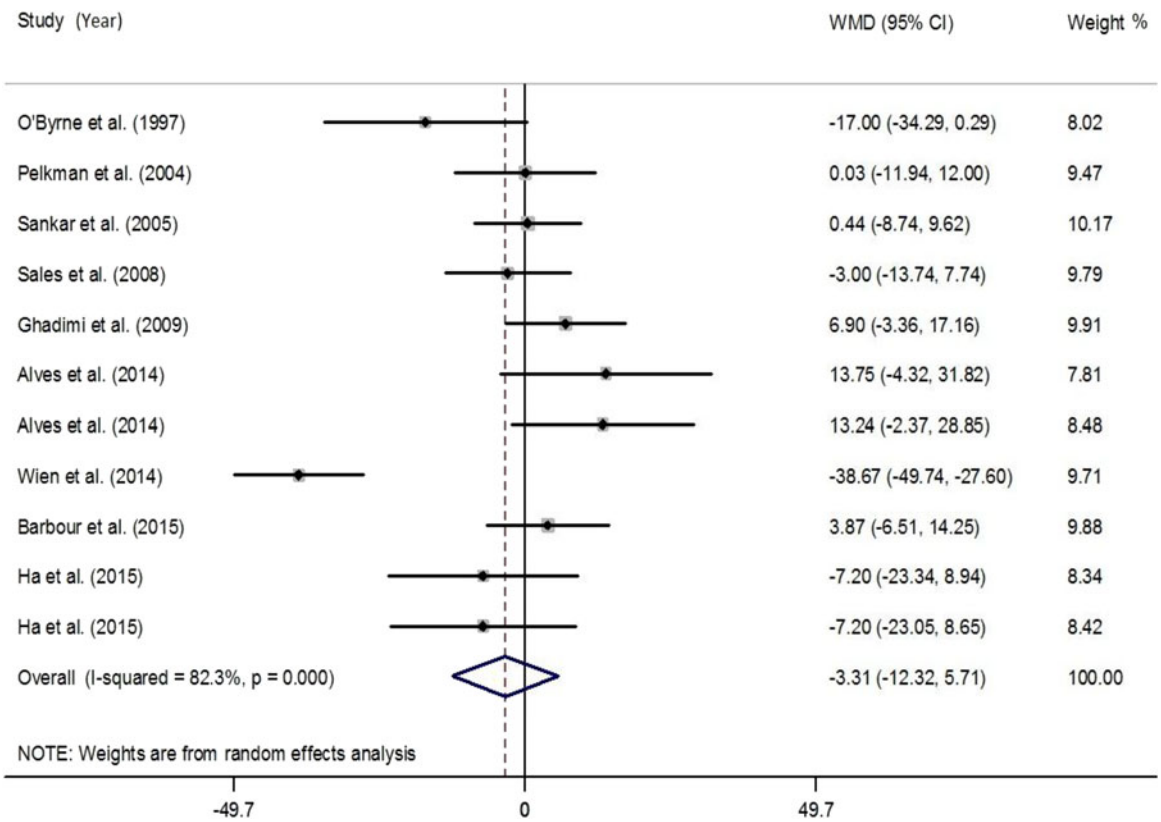

Figure 7. Forest plot of the effect of peanut consumption on LDL.

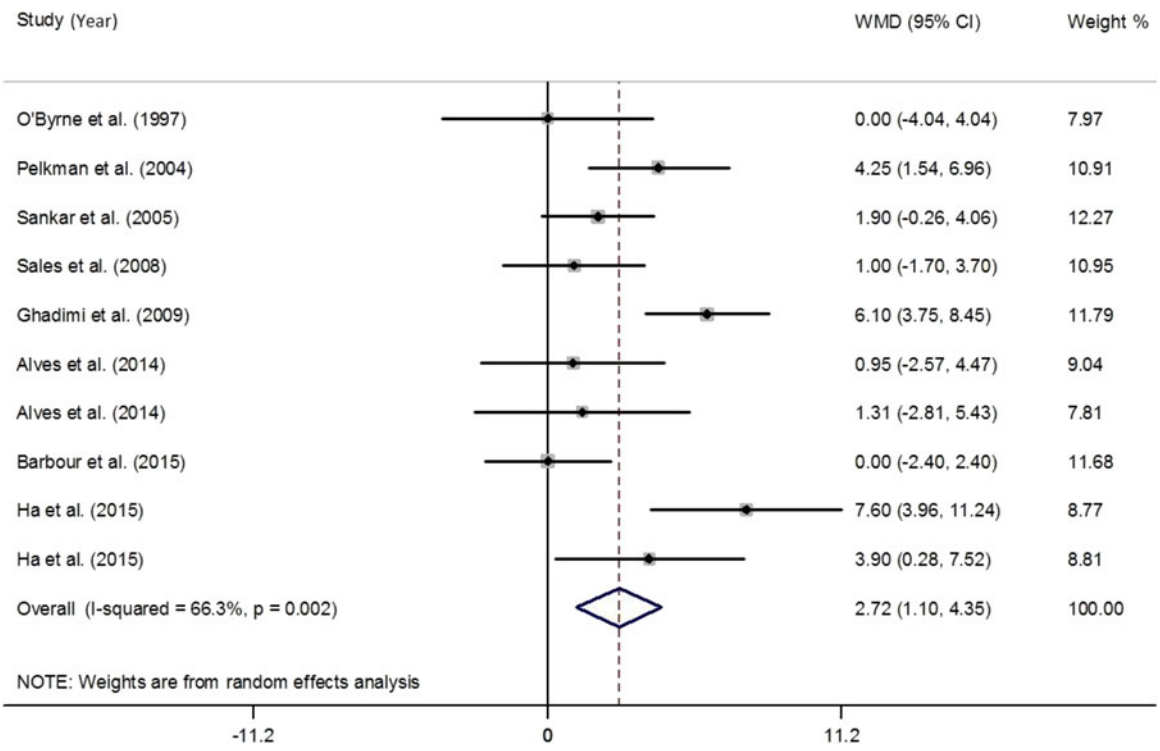

Figure 8. Forest plot of the effect of peanut consumption on HDL.

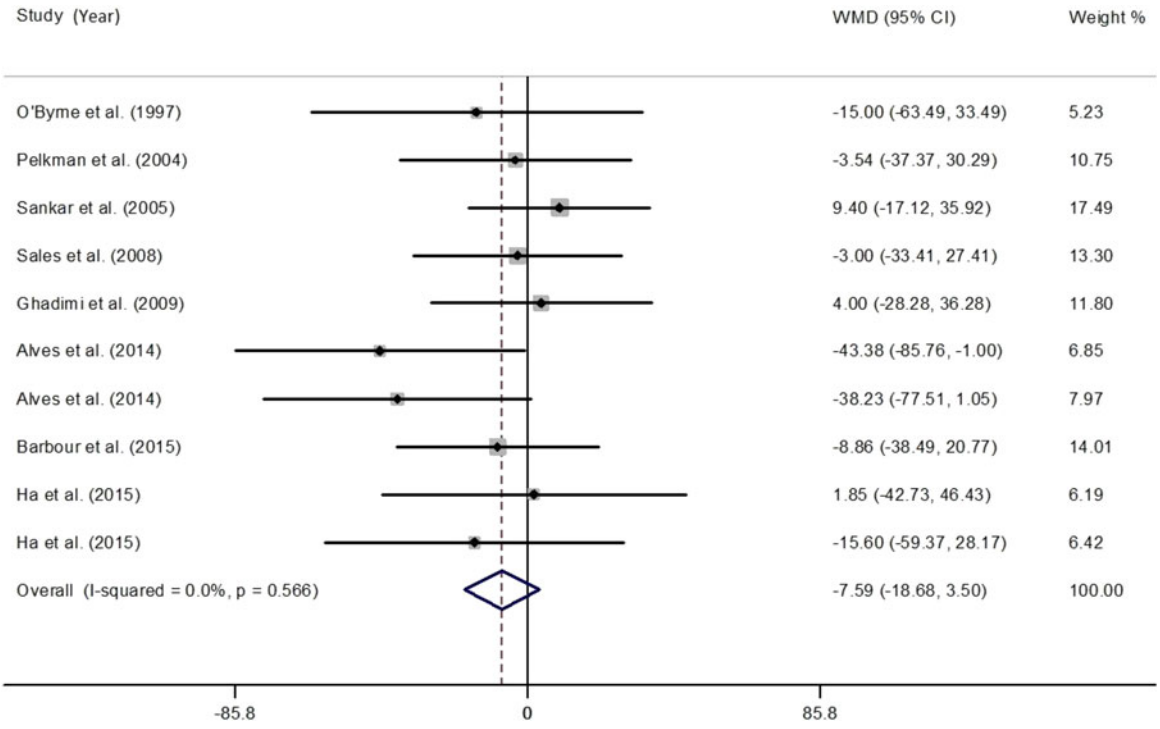

Figure 9. Forest plot of the effect of peanut consumption on TG.

such as protein, fiber, folate, niacin, magnesium, selenium, arginine, α-tocopherol, phenol compounds, resveratrol, manganese, Cu, MUFA, antioxidants, and other bioactive nutrients. All of these compounds have been shown to reduce CVDs risk in various ways (Reis et al. 2013; Alves et al. 2014; Singh, Devaraj, and Jialal 2005, Good, Lavie, and Ventura 2009), and this suggests that peanut consumption might be beneficial for decreasing the risk of CVDs (de Souza et al. 2017; Lokko et al. 2007; Mukuddem-Petersen, Oosthuizen, and Jerling 2005; Ros 2010; Hargrove et al. 2001; Ha et al. 2015).

The findings from this study showed that peanuts intervention had no significant effect on weight, BMI and WC. In line with our findings, some studies have shown that peanut consumption has no significant effect on weight, BMI and WC (Claesson et al. 2009; Johnston, Trier, and Fleming

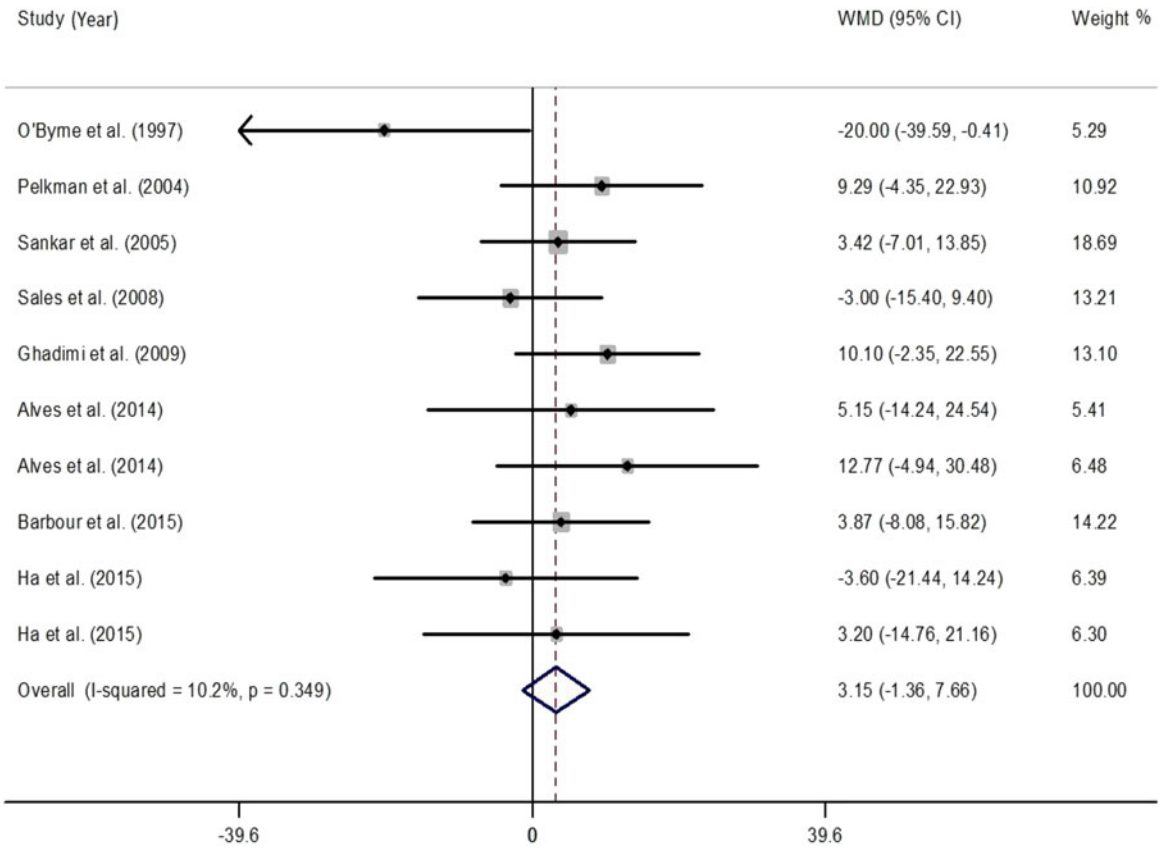

Figure 10. Forest plot of the effect of peanut consumption on TC.

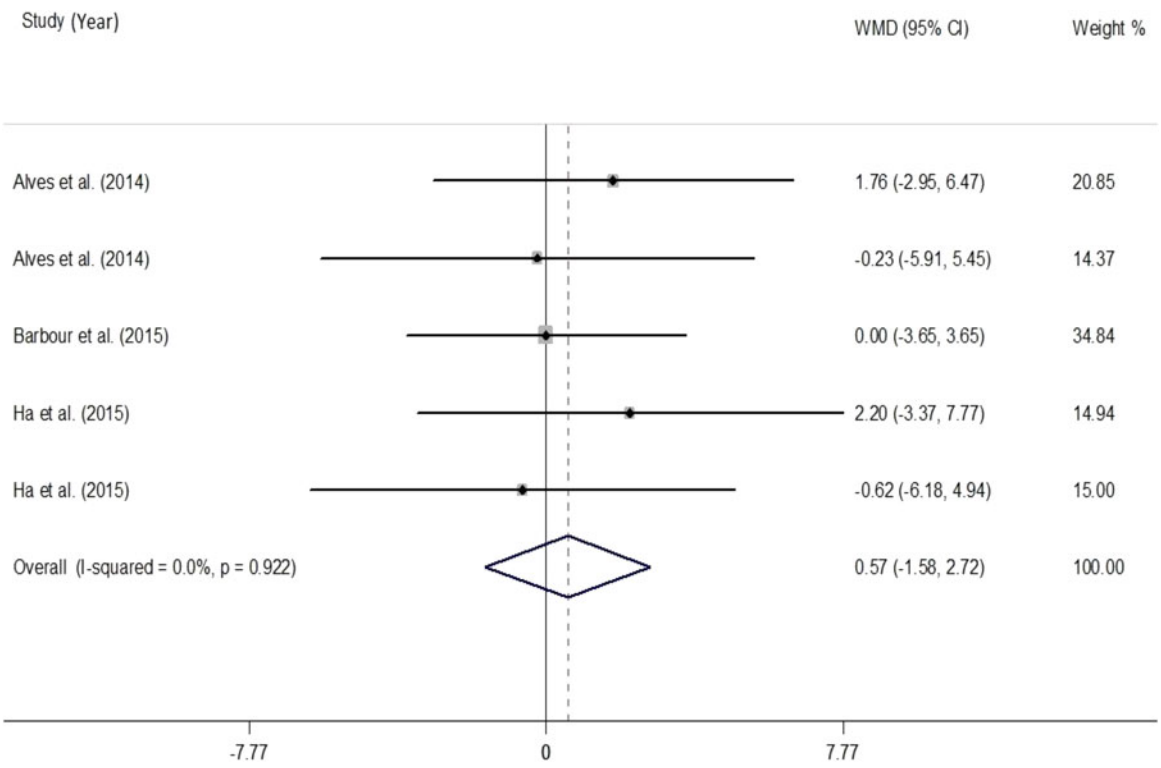

Figure 11. Forest plot of the effect of peanut consumption on FBS.

2013; McKiernan et al. 2010; Vijayakumar et al. 2018). As well as consistent with our results in one meta-analysis of a clinical trial that compared nut-enriched diets with the control group, the nut diet indicated no significant effect on WC (Flores-Mateo et al. 2013). The possible mechanism may be due to incomplete fat absorption from the peanuts because peanut lipid contained within walled cellular structures of nuts that has been found to be incompletely

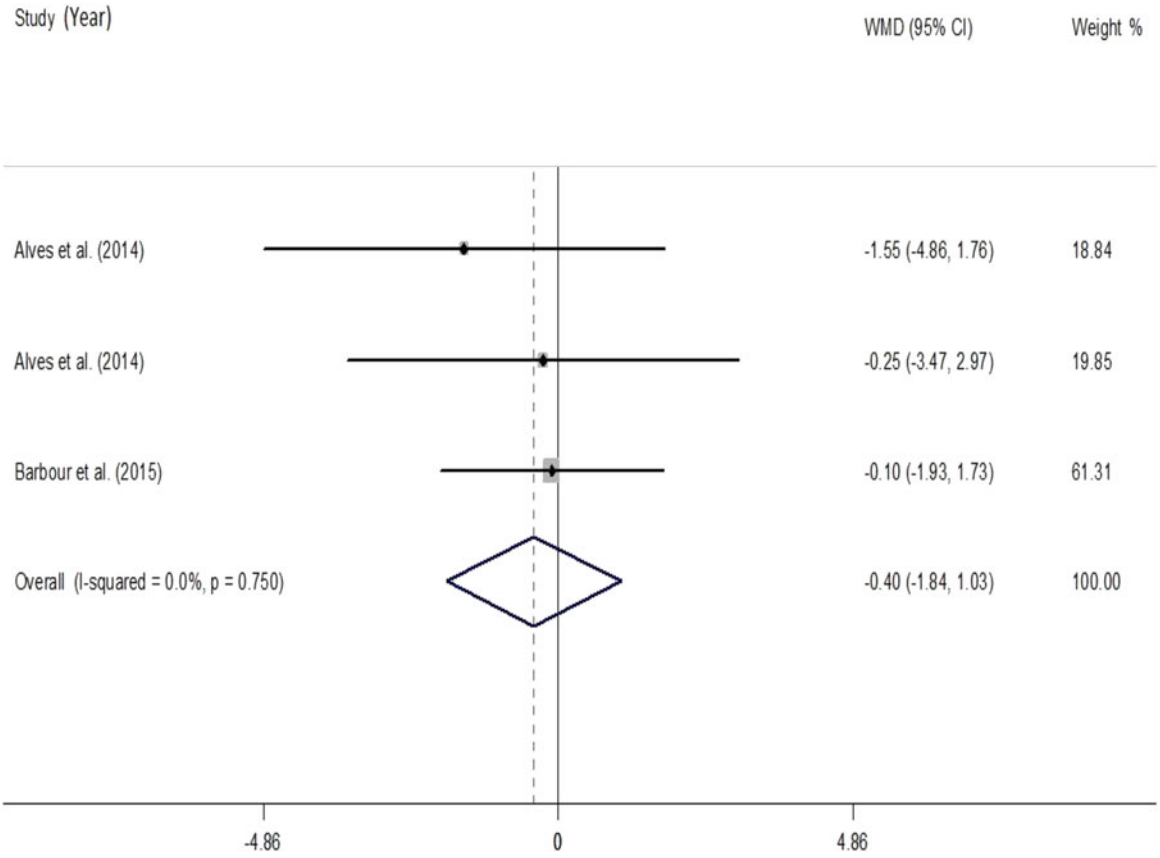

Figure 12. Forest plot of the effect of peanut consumption on serum insulin.

digested in the gut and so peanut energy is not completely available (Barbour et al. 2015). Fecal fat and energy loss is great with consumption of whole peanuts, therefore the process of digestion and absorption will be incomplete and this seems to be the reason for not affecting on weight despite have high fat content (Traoret et al. 2008). Hence daily consumption of nuts did not effect on 24-hours energy intakes or body weight, WC and BMI. Obesity is growing in many regions of the world and is one of the most important causes of CVD (Poirier and Eckel 2002). In the treatment of obesity, factors such as the high cost of drugs and its side effects have increased the demand by the population for natural products using plants with slimming actions. Oilseeds intake, regardless their high fat composition, have shown beneficial effects on health (Serquiz et al. 2016). The present study revealed that peanut as good sources of fat and protein can have a control effect on weight gain. In summary, it would appear that peanut can be added to a diet for treatment and prevention of obesity. During peanut consumption, energy expenditure is increased and it has been reported that subjects feel satiated for a long time may be due to peanuts are rich source of fiber and protein and MUFA (Alper and Mattes 2002; Sabaté 2003). In this regard, studies reported that MUFA than other fatty acids has a higher potential for stimulation of the sympathetic nervous system (Moussavi, Gavino, and Receveur 2008). In contrast, there are reports that indicate high oleic peanut intake can decrease weight, BMI and WC significantly when combined with a hypo-caloric diet in overweight men (Alves et al. 2014). Based on subgroup analysis, high oleic peanut and peanut sprout had a negative significant effect on weight. Also, peanut sprout had a reverse significant effect on WC and BMI. Peanuts sprout contain plenty of resveratrol, polyphenols, essential amino acids, fatty acids, and antioxidants than in peanuts (Wang et al. 2005; Kang et al. 2010; Lin et al. 2008). One in vivo study indicated that anti-obesity activity by peanut sprout may be due to improve adiponectin secretion in adipose tissues that play important roles in thermogenesis (Kang et al. 2014). Although, there are some reports that indicate BMI and weight increase significantly after long-term peanut consumption (Jones et al. 2014; Sales et al. 2008). Based on subgroup analysis in the present study, peanut intervention showed a significant positive effect on weight and BMI in healthy subjects.

The current meta-analysis showed that peanuts intervention can increase serum HDL concentrations. In this regard, some reports have shown that peanuts and peanut oil consumption has a positive effect on HDL concentration (Coelho et al. 2006; Ghadimi Nouran et al. 2010; McKiernan et al. 2010; Xu et al. 2004). Mediterranean diets enriched with nuts after 1 year showed an increase in the large size HDL-C particles (Hernáez et al. 2017). Nuts contain (MUFA and PUFA) with a low amount of saturated fatty acids (SFA). Oleic acid is the major MUFA in all nuts (Venkatachalam and Sathe 2006; Laaksonen et al. 2005), therefore may be related to the positive effect on HDL level. Based on subgroup analysis, HDL concentration increased through peanut consumption in overweight and

hypercholesterolemia individuals. Our overall finding showed that peanuts intervention had no significant effect on serum LDL, TC and TG concentrations. In line with our finding, several studies have shown that peanuts consumption for over 4 weeks does not have a significant effect on LDL,TG, TC levels on healthy subjects or on patients with hypercholesterolemia or T2DM (Jones et al. 2014; Ghadimi Nouran et al. 2010; Wien, Oda, and Sabaté 2014). There are reports that indicate serum TG,TC and LDL concentration decrease significantly after peanuts consumption in individuals classified as having elevated fasting plasma lipid (Kris-Etherton et al. 1999; McKiernan et al. 2010). In contrast, some postprandial studies reported that peanut increased significantly TG level in obese participants while this increase was delayed (Liu et al. 2017). The LDL-C lowering effect that has been reported in some studies may regard to the change in SFA intake. When SFA intake is sustained at low levels and MUFA intake increase to very high levels, nuts can reduce LDL concentration (Spiller et al. 1992). One study indicated that replacement of a diet containing SFA as 16% of energy and MUFA as 11% of energy with a diet with peanuts containing as 7% SFA and MUFA as 17% of energy could significantly reduce TC level (Kris-Etherton et al. 1999). The possible mechanism for lack of impact seen in our results may be due to increase in of MUFA and PUFA intake from peanut without decreasing SFA that is not sufficient to decrease LDL and total cholesterol (Laaksonen et al. 2005). Also researchers demonstrated that a simultaneous increase in MUFA and reduction in SFA may be needs to changes in plasma lipids in normolipidemic individuals with peanut consumption (McKiernan et al. 2010). This finding shows that dietary lipid interventions are more effective for normal lipidemic participants than those who are hyperlipidemic (Kris-Etherton et al. 1999). Also, obesity and insulin-resistant states are associated with reduced intestinal cholesterol absorption, so when cholesterol absorption rates are reduced the cholesterol-lowering effects from the plant sterols in nuts will be blunted (Simonen et al. 2000). Although peanut is a rich source of phytosterol and fiber, but some studies have shown that high-dose (500–3400 mg/d of phytosterol) and (49 g/d of fiber) is necessary for exerting a lowering effect on cholesterol (Ling and Jones 1995; Lairon 1996). Lipid-lowering effects of nuts appear when their intake is substituted for SFA in the diet rather than being added to the diet (Barbour et al. 2015). Also, the high MUFA content of the peanut prevent an increase in serum triglycerides when total dietary fat and SFA were reduced (O'Byrne, Knauft, and Shireman 1997).

The findings from this study showed that peanuts intervention had no significant effect on serum insulin, FBS, and HbA1C. According to this finding, some studies have shown that peanut consumption has no significant effect on serum insulin (Liu et al. 2017; Vijayakumar et al. 2018), FBS and HbA1C (Liu et al. 2017; Jones et al. 2014; Claesson et al. 2009; Johnston, Trier, and Fleming 2013; Reis et al. 2011). In contrast, some studies have shown that peanut consumption significantly decrease serum insulin, FBS and HbA1C (Johnston, Trier, and Fleming 2013; Vijayakumar et al. 2018; Reis et al. 2011; Moreira Alves et al. 2014). Peanuts contain high concentrations of arginine and protein, Zn, MUFA that each one has a role in glycemic response: arginine for insulin secretion (O'Neil et al. 2010), Zn for improving insulin sensitivity by the impact on tyrosine kinase receptor (Jansen, Karges, and Rink 2009). But peanut fat is enclosed in the cell wall, which is resistant to enzymatic digestion in the gastrointestinal tract (Higgs 2005). Therefore, bioavailability fat peanut depends on the degree of mastication and depend on peanut form. So the serum glucose and insulin are under the influence of some factors: reducing the gastric emptying, digestion and absorption rates (Barbour et al. 2015). Moreover, alpha-Amylase inhibitory activity by the higher polyphenol content of the peanuts may be is account for slow carbohydrate digestion (Tsujita, Shintani, and Sato 2013). Some studies indicated that the effects of nuts on insulin sensitivity are depended on changes in body weight (Barbour et al. 2015). As there were no changes in body weight, WC and BMI in this study, improvement in serum glucose is less likely.

The findings from this study showed that peanuts intervention had no significant effect on SBP and DBP. Some studies have shown that peanut consumption has no significant effect on SBP and DBP (Ha et al. 2015; Jones et al. 2014; Reddy and Sesikaran 1995; Vijayakumar et al. 2018). In contrast, one study has shown that a low dose of peanut sprouts have a negative effect on SBP in overweight/obese women (Ha et al. 2015). In addition, Interventions have shown a beneficial effect on blood pressure nut consumption for periods of 12 weeks up to 2 years (Barbour et al. 2017). As well as some studies showed that 12 weeks of intervention with peanut leads to negative effect on DBP in participants with elevated blood pressure at baseline (Jones et al. 2014). Peanut is rich source of polyphenol compounds, fiber, magnesium and potassium arginine (which promotes the production of nitric oxide), MUFA and oleic acid that each one can effect on blood pressure, however, meta analysis of included studies did not shown an significant relationship between peanut consumption and blood pressure.

Limitations

The present study is the first meta-analysis to assess the effects of peanut consumption on (CVDs) risk factors. In the current study, subgroup analyses were conducted to identify sources of heterogeneity. Also, a comprehensive systematic literature search was performed to find all relevant publication. Moreover, considering different types of peanuts is one of strengths of the present study. However, this meta-analysis has some limitations. First, the number of peanuts consumed in two studies was less than 10 g/d, contrary to other studies resulted in statistically less meaningful and increased risk of report greater effect sizes [24, 39]. Second, the populations' health status of included studies was not homogeneous (including patients with HTN, T2DM, hypercholesterolemia, overweight and healthy subjects). Therefore, the different baseline levels of weight, glucose, SBP, DBP, lipid profile, serum insulin, were observed; however, we

performed a subgroup analysis. Third, since differences in body fat distribution may have different impacts on metabolic parameters, information on body composition has not been reported in most of the included studies. Besides in most studies, participants was reported food intake through a 24-hour recall, as well; subjects that were overweight reported their condition healthy by self-report, Hence; self-reporting errors may influence on results. Moreover, the most of the studies were performed in USA and obesity and metabolic pattern of other countries are not mainly considered

Conclusion

In the present study, combined findings from 13 eligible clinical trials showed peanut had no significant effect on most of the variables which are CVD risk factors (WT, WC, BMI, glucose, serum insulin, SBP, DBP, LDL-C, TC, TG). However, HDL-C increased significantly. Additional studies with larger sample sizes should be performed to approve our findings.

Disclosure statement

The authors declare that they have no conflict of interest.

Funding

The present systematic review and meta-analysis was supported by Tehran University of Medical Sciences (grant number: 97-03-161-40425)

References

Akuamoah-Boateng, L., S. S. Iyer, R. L. Sales, P. Lokko, A. Lartey, J. B. Monteiro, and R. D. Mattes. 2007. Effect of peanut oil consumption on energy balance. *Journal of Applied Research* 7 (2):185–96.

Alper, C. M., and R. D. Mattes. 2003. Peanut consumption improves indices of cardiovascular disease risk in healthy adults. *Journal of the American College of Nutrition* 22 (2):133–41. doi:10.1080/07315724.2003.10719286.

Alper, C., and R. Mattes. 2002. Effects of chronic peanut consumption on energy balance and hedonics. *International Journal of Obesity* 26 (8):1129. doi:10.1038/sj.ijo.0802050.

Alves, R. D. M., A. P. B. Moreira, V. S. Macedo, R. de Cássia Gonçalves Alfenas, J. Bressan, R. Mattes, and N. M. B. Costa. 2014. Regular intake of high-oleic peanuts improves fat oxidation and body composition in overweight/obese men pursuing a energy-restricted diet. *Obesity (Silver Spring, MD)* 22 (6):1422–9.

Asghari, G., Z. Ghorbani, P. Mirmiran, and F. Azizi. 2017. Nut consumption is associated with lower incidence of type 2 diabetes: The Tehran lipid and glucose study. *Diabetes & Metabolism* 43 (1):18–24.

Barbour, J. A., P. R. C. Howe, J. D. Buckley, J. Bryan, and A. M. Coates. 2015. Effect of 12 weeks high oleic peanut consumption on cardio-metabolic risk factors and body composition. *Nutrients* 7 (9):7381–98.

Barbour, J. A., P. R. C. Howe, J. D. Buckley, J. Bryan, and A. M. Coates. 2017. Cerebrovascular and cognitive benefits of high-oleic peanut consumption in healthy overweight middle-aged adults. *Nutritional Neuroscience* 20 (10):555–62. doi:10.1080/1028415X.2016.1204744.

Bell, K. J., R. Gray, D. Munns, P. Petocz, G. Howard, S. Colagiuri, and J. C. Brand-Miller. 2014. Estimating insulin demand for protein-containing foods using the food insulin index. *European Journal of Clinical Nutrition* 68 (9):1055. doi:10.1038/ejcn.2014.126.

Bolling, B. W., C.-Y. O. Chen, D. L. McKay, and J. B. Blumberg. 2011. Tree nut phytochemicals: Composition, antioxidant capacity, bioactivity, impact factors. A systematic review of almonds, Brazils, cashews, hazelnuts, macadamias, pecans, pine nuts, pistachios and walnuts. *Nutrition Research Reviews* 24 (02):244–75. doi:10.1017/S095442241100014X.

Claesson, A.-L., G. Holm, Å. Ernersson, T. Lindström, and F. H. Nystrom. 2009. Two weeks of overfeeding with candy, but not peanuts, increases insulin levels and body weight. *Scandinavian Journal of Clinical and Laboratory Investigation* 69 (5):598–605. doi:10.1080/00365510902912754.

Coelho, S. B., R. L. de Sales, S. S. Iyer, J. Bressan, N. M. B. Costa, P. Lokko, and R. Mattes. 2006. Effects of peanut oil load on energy expenditure, body composition, lipid profile, and appetite in lean and overweight adults. *Nutrition* 22 (6):585–92. doi:10.1016/j.nut.2006.03.012.

de Souza, R. G. M., R. Schincaglia, G. Pimentel, and J. Mota. 2017. Nuts and human health outcomes: A systematic review. *Nutrients* 9 (12):1311.

Dineshkumar, B., S. Mukherjee, R. Pradhan, A. Mitra, and C. Chakraborty. 2009. Effects of edible oils in type 2 diabetes mellitus. *Journal of Clinical and Diagnostic Research* 3:1389–94.

Ellis, P. R., C. W. C. Kendall, Y. Ren, C. Parker, J. F. Pacy, K. W. Waldron, and D. J. A. Jenkins. 2004. Role of cell walls in the bioaccessibility of lipids in almond seeds. *The American Journal of Clinical Nutrition* 80 (3):604–13.

Flores-Mateo, G., D. Rojas-Rueda, J. Basora, E. Ros, and J. Salas-Salvadó. 2013. Nut intake and adiposity: Meta-analysis of clinical trials. *The American Journal of Clinical Nutrition* 97 (6):1346–55. doi:10.3945/ajcn.111.031484.

Funtikova, A. N., E. Navarro, R. A. Bawaked, M. Fíto, and H. Schröder. 2015. Impact of diet on cardiometabolic health in children and adolescents. *Nutrition Journal* 14 (1):118

Ghadimi Nouran, M., M. Kimiagar, A. Abadi, M. Mirzazadeh, and G. Harrison. 2010. Peanut consumption and cardiovascular risk. *Public Health Nutrition* 13 (10):1581–6.

Good, D., C. J. Lavie, and H. O. Ventura. 2009. Dietary intake of nuts and cardiovascular prognosis. *The Ochsner Journal* 9 (1):32–6.

Ha, A. W., W. K. Kim, J. H. Kim, and N. E. Kang. 2015. The supplementation effects of peanut sprout on reduction of abdominal fat and health indices in overweight and obese women. *Nutrition Research and Practice* 9 (3):249–55. doi:10.4162/nrp.2015.9.3.249.

Hargrove, R. L., T. D. Etherton, T. A. Pearson, E. H. Harrison, and P. M. Kris-Etherton. 2001. Low fat and high monounsaturated fat diets decrease human low density lipoprotein oxidative susceptibility in vitro. *The Journal of Nutrition* 131 (6):1758–63. doi:10.1093/jn/131.6.1758.

Hariharan, K., S. Kurien, and S. V. Rao. 1995. Effect of supplementation of milk fat with peanut oil on blood lipids and lipoproteins in infants. *International Journal of Food Sciences and Nutrition* 46 (4):309–17.

Hernáez, Á., O. Castañer, R. Elosua, X. Pintó, R. Estruch, J. Salas-Salvadó, D. Corella, F. Arós, L. Serra-Majem, M. Fiol, et al. 2017. Mediterranean diet improves high-density lipoprotein function in high-cardiovascular-risk individuals: A randomized controlled trial. *Circulation* 135 (7):633–43.

Hernández-Alonso, P., L. Camacho-Barcia, M. Bulló, and J. Salas-Salvadó. 2017. Nuts and dried fruits: An update of their beneficial effects on type 2 diabetes. *Nutrients* 9 (7):673.

Higgins, J. P., and S. Green. 2011. Cochrane handbook for systematic reviews of interventions 5.1. 0. *The Cochrane Collaboration* :33–49.

Higgs, J. 2005. The potential role of peanuts in the prevention of obesity. *Nutrition & Food Science* 35 (5):353–8. doi:10.1108/00346650510625566.

Hou, Y.-Y., O. Ojo, L.-L. Wang, Q. Wang, Q. Jiang, X.-Y. Shao, and X.-H. Wang. 2018. A randomized controlled trial to compare the

effect of peanuts and almonds on the cardio-metabolic and inflammatory parameters in patients with type 2 diabetes mellitus. *Nutrients* 10 (11):1565. doi:10.3390/nu10111565.

Jansen, J., W. Karges, and L. Rink. 2009. Zinc and diabetes—Clinical links and molecular mechanisms. *The Journal of Nutritional Biochemistry* 20 (6):399–417. doi:10.1016/j.jnutbio.2009.01.009.

Johnston, C. S., C. M. Trier, and K. R. Fleming. 2013. The effect of peanut and grain bar preloads on postmeal satiety, glycemia, and weight loss in healthy individuals: An acute and a chronic randomized intervention trial. *Nutrition Journal* 12 (1):35.

Jones, J. B., M. Provost, L. Keaver, C. Breen, M.-J. Ludy, and R. D. Mattes. 2014. A randomized trial on the effects of flavorings on the health benefits of daily peanut consumption. *The American Journal of Clinical Nutrition* 99 (3):490–6. doi:10.3945/ajcn.113.069401.

Kang, H.-I., J. Y. Kim, K. W. Park, J. S. Kang, M. R. Choi, K. D. Moon, and K. I. Seo. 2010. Resveratrol content and nutritional components in peanut sprouts. *Korean Journal of Food Preservation* 17 (3):384–90.

Kang, N. E., A. W. Ha, H. W. Woo, and W. K. Kim. 2014. Peanut sprouts extract (*Arachis hypogaea* L.) has anti-obesity effects by controlling the protein expressions of PPARγ and adiponectin of adipose tissue in rats fed high-fat diet. *Nutrition Research and Practice* 8 (2):158–64. doi:10.4162/nrp.2014.8.2.158.

Kim, Y., J. B. Keogh, and P. M. Clifton. 2017. Benefits of nut consumption on insulin resistance and cardiovascular risk factors: Multiple potential mechanisms of actions. *Nutrients* 9 (11):1271. doi:10.3390/nu9111271.

Kris-Etherton, P. M., T. A. Pearson, Y. Wan, R. L. Hargrove, K. Moriarty, V. Fishell, and T. D. Etherton. 1999. High-monounsaturated fatty acid diets lower both plasma cholesterol and triacylglycerol concentrations. *The American Journal of Clinical Nutrition* 70 (6):1009–15. doi:10.1093/ajcn/70.6.1009.

Laaksonen, D. E., K. Nyyssönen, L. Niskanen, T. H. Rissanen, and J. T. Salonen. 2005. Prediction of cardiovascular mortality in middle-aged men by dietary and serum linoleic and polyunsaturated fatty acids. *Archives of Internal Medicine* 165 (2):193–9. doi:10.1001/archinte.165.2.193.

Lairon, D. 1996. Dietary fibres: Effects on lipid metabolism and mechanisms of action. *European Journal of Clinical Nutrition* 50:125–33

Lilly, L. N., C. J. Heiss, S. F. Maragoudakis, K. L. Braden, and S. E. Smith. 2018. The effect of added peanut butter on the glycemic response to a high–Glycemic index meal: A pilot study. *Journal of the American College of Nutrition* 5:1–7. doi:10.1080/07315724.2018.1519404. doi:10.1080/07315724.2018.1519404.

Lin, B.-S., T.-F. Lien, M.-R. Chao, T.-Y. Lai, J.-C. Chang, S.-J. Chou, H.-F. Liao, and R. Y.-Y. Chiou. 2008. Toxicological and nutraceutical assessments of peanut sprouts as daily supplements to feed Sprague-Dawley rats for 18 weeks. *Journal of the Science of Food and Agriculture* 88 (12):2201–7. doi:10.1002/jsfa.3335.

Lin, Y.-H., Y.-K. Lin, and Y.-C. Shen. 2017. Evaluation effects of peanut skin extract on blood glucose regulation and body fat reduction. *Journal of Biobased Materials and Bioenergy* 11 (3):242–7. doi:10.1166/jbmb.2017.1666.

Ling, W., and P. Jones. 1995. Dietary phytosterols: A review of metabolism, benefits and side effects. *Life Sciences* 57 (3):195–206.

Liu, X., A. M. Hill, S. G. West, R. M. Gabauer, C. E. McCrea, J. A. Fleming, and P. M. Kris-Etherton. 2017. Acute peanut consumption alters postprandial lipids and vascular responses in healthy overweight or obese men. *The Journal of Nutrition* 147 (5):835–40.

Lokko, P., A. Lartey, M. Armar-Klemesu, and R. D. Mattes. 2007. Regular peanut consumption improves plasma lipid levels in healthy Ghanaians. *International Journal of Food Sciences and Nutrition* 58 (3):190–200. doi:10.1080/09637480701198067.

McGill, H. C., C. A. McMahan, and S. S. Gidding. 2008. Preventing heart disease in the 21st century: Implications of the pathobiological determinants of atherosclerosis in youth (PDAY) study. *Circulation* 117 (9):1216–27. doi:10.1161/CIRCULATIONAHA.107.717033.

McKiernan, F., P. Lokko, A. Kuevi, R. L. Sales, N. M. B. Costa, J. Bressan, R. C. G. Alfenas, and R. D. Mattes. 2010. Effects of peanut processing on body weight and fasting plasma lipids. *The British Journal of Nutrition* 104 (3):418–26.

Micha, R., M. L. Shulkin, J. L. Peñalvo, S. Khatibzadeh, G. M. Singh, M. Rao, S. Fahimi, J. Powles, and D. Mozaffarian. 2017. Etiologic effects and optimal intakes of foods and nutrients for risk of cardiovascular diseases and diabetes: Systematic reviews and meta-analyses from the nutrition and chronic diseases expert group (NutriCoDE). *PLoS ONE* 12 (4):e0175149. doi:10.1371/journal.pone.0175149.

Mohammadi, M., H. Doostkami, B. Dadkhah, and S. Sezavar. 2002. Survey of knowledge, attitude and practice of Ardabil citizens about risk factors of coronary artery disease, 2001. *Journal of Ardabil University of Medical Sciences* 2 (2):42–8.

Moher, D., A. Liberati, J. Tetzlaff, and D. G. Altman. 2009. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Annals of Internal Medicine* 151 (4):264–9. doi:10.7326/0003-4819-151-4-200908180-00135.

Moreira Alves, R. D., A. P. Boroni Moreira, V. S. Macedo, J. Bressan, R. de Cássia Gonçalves Alfenas, R. Mattes, and N. M. Brunoro Costa. 2014. High-oleic peanuts: New perspective to attenuate glucose homeostasis disruption and inflammation related obesity. *Obesity (Silver Spring)* 22 (9):1981–8. doi:10.1002/oby.20825.

Moreira, A. P. B., T. F. S. Teixeira, R. D. M. Alves, M. C. G. Peluzio, N. M. B. Costa, J. Bressan, R. Mattes, and R. C. G. Alfenas. 2016. Effect of a high-fat meal containing conventional or high-oleic peanuts on post-prandial lipopolysaccharide concentrations in overweight/obese men. *Journal of Human Nutrition and Dietetics* 29 (1):95–104. doi:10.1111/jhn.12284.

Moussavi, N., V. Gavino, and O. Receveur. 2008. Could the quality of dietary fat, and not just its quantity, be related to risk of obesity? *Obesity (Silver Spring, MD)* 16 (1):7–15.

Mukuddem-Petersen, J., W. Oosthuizen, and J. C. Jerling. 2005. A systematic review of the effects of nuts on blood lipid profiles in humans. *The Journal of Nutrition* 135 (9):2082–9. doi:10.1093/jn/135.9.2082.

Nagashree, R. S., N. K. Manjunath, M. Indu, M. Ramesh, V. Venugopal, P. Sreedhar, N. Pavithra, and H. R. Nagendra. 2017. Effect of a diet enriched with fresh coconut saturated fats on plasma lipids and erythrocyte fatty acid composition in normal adults. *Journal of the American College of Nutrition* 36 (5):330–4. doi:10.1080/07315724.2017.1280713.

O'Byrne, D. J., D. A. Knauft, and R. B. Shireman. 1997. Low fat-monounsaturated rich diets containing high-oleic peanuts improve serum lipoprotein profiles. *Lipids* 32 (7):687–95. doi:10.1007/s11745-997-0088-y.

O'Neil, C. E., D. R. Keast, V. L. Fulgoni, and T. A. Nicklas. 2010. Tree nut consumption improves nutrient intake and diet quality in US adults: An analysis of national health and nutrition examination survey (NHANES) 1999–2004. *Asia Pacific Journal of Clinical Nutrition* 19 (1):142.

Pelkman, C. L., V. K. Fishell, D. H. Maddox, T. A. Pearson, D. T. Mauger, and P. M. Kris-Etherton. 2004. Effects of moderate-fat (from monounsaturated fat) and low-fat weight-loss diets on the serum lipid profile in overweight and obese men and women. *The American Journal of Clinical Nutrition* 79 (2):204–12.

Poirier, P., and R. H. Eckel. 2002. Obesity and cardiovascular disease. *Current Atherosclerosis Reports* 4 (6):448–53. doi:10.1007/s11883-002-0049-8.

Rao, R. H., U. B. Rao, and S. Srikantia. 1981. Effect of polyunsaturate-rich vegetable oils on blood pressure in essential hypertension. *Clinical and Experimental Hypertension* 3 (1):27–38. doi:10.3109/10641968109037166.

Reddy, V., and B. Sesikaran. 1995. Palmolein and groundnut oil have comparable effects on blood lipids and platelet aggregation in healthy Indian subjects. *Lipids* 30 (12):1163–9.

Reis, C., L. A. Bordalo, A. L. Rocha, D. M. Freitas, M. V. Da Silva, V. C. De Faria, H. S. Martino, N. M. Costa, R. C. Alfenas. 2011. Ground roasted peanuts leads to a lower post-prandial glycemic response than raw peanuts. *Nutricion Hospitalaria* 26 (4):745–51.

Reis, C. E. G., D. N. Ribeiro, N. M. B. Costa, J. Bressan, R. C. G. Alfenas, and R. D. Mattes. 2013. Acute and second-meal effects of

peanuts on glycaemic response and appetite in obese women with high type 2 diabetes risk: A randomised cross-over clinical trial. *British Journal of Nutrition* 109 (11):2015–23. doi:10.1017/S0007114512004217.

Ros, E. 2010. Health benefits of nut consumption. *Nutrients* 2 (7): 652–82.

Ros, E., M. A. Martínez-González, R. Estruch, J. Salas-Salvadó, M. Fitó, J. A. Martínez, and D. Corella. 2014. Mediterranean diet and cardiovascular health: Teachings of the PREDIMED study. *Advances in Nutrition (Bethesda, MD)* 5 (3):330S–6S.

Sabaté, J. 2003. Nut consumption and body weight. *The American Journal of Clinical Nutrition* 78 (3 Suppl):647S–50S.

Sales, R. L., S. B. Coelho, N. M. B. Costa, J. Bressan, S. Iyer, L. A. Boateng, P. Lokko, and R. D. Mattes. 2008. The effects of peanut oil on lipid profile of normolipidemic adults: A three-country collaborative study. *Journal of Applied Research* 8 (3):216–25.

Sankar, D., G. Sambandam, M. Ramakrishna Rao, and K. V. Pugalendi. 2005. Modulation of blood pressure, lipid profiles and redox status in hypertensive patients taking different edible oils. *Clinica Chimica Acta* 355 (1–2):97–104. doi:10.1016/j.cccn.2004.12.009.

Schwingshackl, L., G. Hoffmann, B. Missbach, M. Stelmach-Mardas, and H. Boeing. 2017. An umbrella review of nuts intake and risk of cardiovascular disease. *Current Pharmaceutical Design* 23 (7): 1016–27. doi:10.2174/1381612822666161010121356.

Serquiz, A. C., R. J. A. Machado, R. P. Serquiz, V. C. O. Lima, F. M. C. de Carvalho, M. A. A. Carneiro, B. L. L. Maciel, A. F. Uchôa, E. A. Santos, A. H. A. Morais, et al. 2016. Supplementation with a new trypsin inhibitor from peanut is associated with reduced fasting glucose, weight control, and increased plasma CCK secretion in an animal model. *Journal of Enzyme Inhibition and Medicinal Chemistry* 31 (6):1261–9. doi:10.3109/14756366.2015.1103236.

Simonen, P., H. Gylling, A. N. Howard, and T. A. Miettinen. 2000. Introducing a new component of the metabolic syndrome: Low cholesterol absorption. *The American Journal of Clinical Nutrition* 72 (1):82–8.

Singh, U., S. Devaraj, and I. Jialal. 2005. Vitamin E, oxidative stress, and inflammation. *Annual Review of Nutrition* 25:151–74.

Spiller, G. A., D. J. Jenkins, L. N. Cragen, J. E. Gates, O. Bosello, K. Berra, C. Rudd, M. Stevenson, and R. Superko. 1992. Effect of a diet high in monounsaturated fat from almonds on plasma cholesterol and lipoproteins. *Journal of the American College of Nutrition* 11 (2):126–30.

Traoret, C. J., P. Lokko, A. C. R. F. Cruz, C. G. Oliveira, N. M. B. Costa, J. Bressan, R. C. G. Alfenas, and R. D. Mattes. 2008. Peanut digestion and energy balance. *International Journal of Obesity* 32 (2):322.

Tsujita, T., T. Shintani, and H. Sato. 2013. α-Amylase inhibitory activity from nut seed skin polyphenols. 1. Purification and characterization of almond seed skin polyphenols. *Journal of Agricultural and Food Chemistry* 61 (19):4570–6. doi:10.1021/jf400691q.

Venkatachalam, M., and S. K. Sathe. 2006. Chemical composition of selected edible nut seeds. *Journal of Agricultural and Food Chemistry* 54 (13):4705–14.

Vigne, J. 1974. Possible effects of peanut oil on human atherosclerosis. *Annals Hygiene Lang Franc* 10 (4):351–9.

Vijayakumar, V., N. R. Shankar, R. Mavathur, A. Mooventhan, S. Anju, and N. K. Manjunath. 2018. Diet enriched with fresh coconut decreases blood glucose levels and body weight in normal adults. *Journal of Complementary and Integrative Medicine* 15 (3). doi: 10.1515/jcim-2017-0097.

Wang, K.-H., Y.-H. Lai, J.-C. Chang, T.-F. Ko, S.-L. Shyu, and R. Y.-Y. Chiou. 2005. Germination of peanut kernels to enhance resveratrol biosynthesis and prepare sprouts as a functional vegetable. *Journal of Agricultural and Food Chemistry* 53 (2):242–6. doi:10.1021/jf048804b.

Widmer, R. J., A. J. Flammer, L. O. Lerman, and A. Lerman. 2015. The Mediterranean diet, its components, and cardiovascular disease. *The American Journal of Medicine* 128 (3):229–38.

Wien, M., K. Oda, and J. Sabaté. 2014. A randomized controlled trial to evaluate the effect of incorporating peanuts into an American diabetes association meal plan on the nutrient profile of the total diet and cardiometabolic parameters of adults with type 2 diabetes. *Nutrition Journal* 13 (1):10.

Xu, G., H. Guo, H. Zhu, M. Cao, J. Xu, and W. Mao. 2004. The protective effect of peanut oil on risk of cadiovascular disease. [ying yang xue bao]. *Acta Nutrimenta Sinica* 26 (4):249–52.

Zhang, J., W. Ping, W. Chunrong, C. X. Shou, and G. Keyou. 1997. Nonhypercholesterolemic effects of a palm oil diet in Chinese adults. *The Journal of Nutrition* 127 (3):509S–13S.