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Review

The effect of almonds consumption on blood pressure: A systematic review and dose-response meta-analysis of randomized control trials

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ABSTRACT

Almond is rich in antioxidants and phytochemicals such as methylquercetin, protocatechuic acid, catechin, flavonoids, p-hydroxybenzoic acid, resveratrol, vanillic acid, and kaempferol. The aim of the present study was to systematically review and dose-response meta-analyses the effects of almond consumption on systolic and diastolic blood pressure (SBP/DBP), respectively, in Randomized Controlled Trials (RCTs). A systematic search was performed in PubMed/MEDLINE, web of sciences and SCOPUS by 2 researchers, independently to identify randomised controlled trials up to July 2019. There were no time or language restrictions. PRISMA guidelines were followed in conducting this meta-analysis. Fifteen studies with 21 arms, containing 853 participants, reported SBP as an outcome measure. Pooled results showed significant reduction in SBP (WMD: −0.90 mmHg, 95% CI: −1.74, −0.06, $P_{heterogeneity}$ = 0.94) by almond intervention. There is no significant effect from almond consumption on DBP (WMD: 0.67 mmHg, 95% CI: −1.93, 0.60, $P_{heterogeneity}$ = 0.001). Meta-regression analysis showed dose of used almond (g/d) as source of heterogeneity between results of DBP. In conclusion results of this meta-analysis showed reduce effect of Almonds on systolic blood pressure.

Contents

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; RCT, Randomized Controlled Trials; WMD, weighted mean diffrence.

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1. Introduction

Hypertension is one of the important causes of mortality in worldwide (Mills et al., 2016). Its prevalence is increasing dramatically; there was a 10.5% increase of the death rate attributed to high blood pressure in the US from 2005 to 2015 (Benjamin et al., 2018). Worldwide, 1.3 billion hypertensive people have been diagnosed in 2010. According to WHO, the number 1 cause of death in 2016 is the ischemic heart disease and the stroke, a main complication of this silent killer. Eleven percent of children and young adolescents in the US were prone to this non-communicable disease in 2012 according to the American Heart Association (Mills et al., 2016).

Nutrition, in conjunction with pharmacotherapy, plays an important role in either increasing or managing the high blood pressure; high sodium chloride intake increases the incidence and alcohol consumption may cause an acute elevation in blood pressure. In contrast, high intake of potassium, polyunsaturated fatty acids, and protein may help in lowering blood pressure (Savica et al., 2010).

Almonds, a type of tree nut, are rich in vitamins, minerals, mono-saturated and polyunsaturated fatty acid (Jaceldo-Siegl et al., 2004). Recently, almonds have been advocated as a promising part of a healthy diet improving the blood pressure, weight, and the lipid profile (O'Neil et al., 2016). Many studies reported almond's role in reducing serum levels of triglycerides, low-density lipoprotein, and total cholesterol (Griel and Kris-Etherton, 2006; Sabaté et al., 2010). In addition, almonds affect the appetite and the post-ingestive metabolism positively without increasing the body mass index (Tan and Mattes, 2013).

While some studies have shown almond to have a potential reducing effect on SBP and DBP (Choudhury et al., 2014; Dhillon et al., 2016), other studies have not shown significant effects (Chen et al., 2015; de Souza et al., 2018; Foster et al., 2012; Liu et al., 2018). The aim of present dose-response meta-analysis was to determine the effect of almonds consumption on blood pressure in adults.

2. Methods

2.1. Literature search

For conducting the present systematic review and dose-response meta-analysis, the Preferred Reporting Items of Systematic Reviews and Meta-Analysis (PRISMA) statement guideline was followed (23). Two authors (MB and CC) independently conducted a search of the databases MEDLINE/PubMed, Web of sciences, and Scopus up to July 2019. Medical subject headings (MeSH) and non-MeSH (title and/or abstract) terms were used for searching (Supplemental Table 1) and reference lists of included studies were searched manually, too. No date or language or grey literature restrictions were applied. Any disagreements between authors were resolved by way of cooperative triangulation with the senior author. Data from articles were extracted by two authors, independently.

2.2. Study selection

Studies screened based on title and abstract in first step of screening. In second step, we evaluate studies based on our inclusion criteria in full text of them. Studies that met inclusion criteria included in analysis.

2.3. Eligibility criteria

Studies were included if they involved: a) Parallel or cross over randomized clinical trial (RCT) designs, b) consumption of Almond as intervention c) reported blood pressure as outcome measure. d) adults Animal, in-vitro, studies without control group, and review papers were excluded. PICOS for this study was: P – public population, I – intervention with Almond, C – placebo group, O – blood pressure, and S – RCTs.

2.4. Statistical analyses

Effect sizes and 95% confidence intervals were reported for each study.SD change of the mean difference was calculated using the $SD^2 = [(SD\ baseline^2 + SD\ final^2) - (2 \times r \times SD\ baseline \times SD\ final)]$ formula (Higgins and Green, 2011) if the studies did not report, it. Included studies results combined by random effect model. Meta-regression analysis based on used dose of almond conducted to find source of heterogeneity. Heterogeneity among the studies was assessment using the I-squared (I^2) statistics. Funnel plots, Begg's and Egger's weighted regression tests were used to assessment publication bias (2); the trim and fill approach was used to adjust for publication bias (Duval and Tweedie, 2000). Sensitivity analysis was additionally conducted to investigate the individual effect of each study on the overall analysis. Cochrane collaboration's Risk of Bias tool was used to assess included studies (4). STATA software version 12 (STATA Corp, College119 station, Texas) was used in all analyses.

3. Results

In our initial comprehensive systematic search from PubMed, Scopus, and web of sciences, 104 papers were located. Fig. 1 depicts a flow diagram of the search strategy. After removing duplicates, 66 articles were identified for title and/or abstract screening. Screening led to the removal of 39 articles Subsequently, 11 additional articles were removed because they did not meet the inclusion criteria during afull text screening. Finally, 15 articles with 21 arms were included for meta-analysis (Abazarfard et al., 2014; Chen et al., 2015, 2017; Choudhury et al., 2014; de Souza et al., 2018; Dhillon et al., 2016, 2018; Foster et al., 2012;

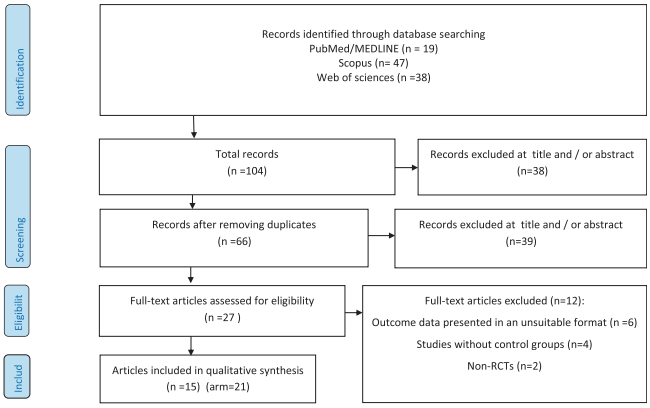

Fig. 1. Flow chart of included studies.

Jamshed et al., 2015; Jenkins et al., 2002; Johnston et al., 2017; Liu et al., 2018; Richmond et al., 2013; Sweazea et al., 2014; Tan and Mattes, 2013; Wien et al., 2010).

3.1. Study characteristics

Characteristics of the eligible studies are detailed in Table 1. Studies were published from 2002 to 2018. Sample sizes ranged from 6 to 137. Seven studies were conducted in the USA (Chen et al., 2015; Dhillon et al., 2016, 2018; Foster et al., 2012; Johnston et al., 2017; Sweazea et al., 2014; Wien et al., 2010), 1 in New Zealand (Richmond et al., 2013), 1 in Canada (Jenkins et al., 2002), 1 in Taipei (Chen et al., 2017), Brazil (de Souza et al., 2018), UK (Choudhury et al., 2014), Korea (Liu et al., 2018), Pakistan (Jamshed et al., 2015), and Australia (Tan and Mattes, 2013). Length of follow up ranged from 3 to 78 weeks. The quality of eligible studies was evaluated using the Cochrane collaboration's Risk of Bias tool for quality assessment of RCT's, where the majority studies were assigned low risk (Fig. 2).

3.2. Meta-analysis results

Sixteen studies, with 21 arms, containing 853 participants, reported SBP as an outcome measure. Pooled results did not show any significant reductive effect from almonds on SBP (WMD: −0.90 mmHg, 95% CI: −1.74, −0.06, I2 = 00%, $P_{heterogeneity}$ = 0.94) (Fig. 3).

Almond consumption did not show any significant effect on DBP (WMD: 0.67 mmHg, 95% CI: −1.93, 0.60, I2 = 52%, $P_{heterogeneity}$ = 0.001). Meta-regression analysis based on used dose of almond was performed and showed dose of almond as a source of heterogeneity (I2 = 0%). There was inverse relation between dose of almond and blood pressure (Coef = −0.0097) but this relation was not statistically significant (p = 0.72) (Supplemental Fig. 1).

3.3. Publication bias and sensitivity analysis

There is not any asymmetry in the funnel plot of included studies for SBP (Fig. 4), but there was an asymmetry between included studies for DBP. The Egger's and Begg's tests for SBP were p = 0.63 and p = 0.80, respectively, and p = 0.01 and p = 0.09 for DBP, respectively. A Trim and fill method was used to adjust for publication bias for DBP; results showed 32 papers and a significant reduction in DBP (WMD: −2.91 mmHg, 95% CI: −4.11, −1.71). The sensitivity analysis showed no significant differences beyond the 95% CI of calculated combined results for each of included studies (Supplemental Fig. 2).

4. Discussion

Whilst consumption of almonds has been shown to elicit improvements in triglycerides, total cholesterol (Sabaté et al., 2010), low density lipoprotein-cholesterol, and various cardiovascular disease risk factors (Griel and Kris-Etherton, 2006; Li et al., 2010); its' widescale recommendation and uptake remains inconsistent. Observational studies have reported that almond consumption is associated with a reduced risk of developing various non-communicable diseases, including; elevated blood pressure (hypertension), coronary artery disease, and type 2 diabetes (Jiang et al., 2002; Kris-Etherton et al., 2001). However, despite numerous reports suggesting almond consumption may elicit positive effects on vascular health, there still exists some equivocality, particularly when considered concurrently with weight-loss and blood lipid markers (Foster et al., 2012). Moreover, to date, no systematic compilation of relevant data has taken place; thus, we sought to conduct a systematic review and dose-response meta-analysis of the effect of almond consumption on blood pressure. In accord with the aim of this study, we found that, overall, almond consumption had significant reduction in SBP but on DBP. However, following meta-regression analyses, we found that a reduction in DBP by higher dose of Almond.

Lifestyle modifications consisting of regular adherence to physical activity guidelines, reduced consumption of fat, increased consumption of plant-based foods and smoking cessation are recommended to complement pharmacological regimens in the management and prevention of hypertension, and related comorbidities (Booth et al., 2014). However, a recent meta-analysis investigating dietary-based almond interventions asserted that the current evidence base does not support almond consumption specifically for lipid altering effects (Phung et al., 2009), whilst dietary intervention with almonds demonstrably improves biomarkers of insulin sensitivity in prediabetic adults (Wien et al., 2010). Almond consumption has been shown to positively impact markers of inflammation and hemostasis, respectively, independent of dose (Rajaram et al., 2010). Furthermore, almonds represent major dietary sources of α-tocopherol and mono-unsaturated fatty acids and regular consumption evidently diminishes the risk of early mortality attributed to coronary heart disease, myocardial infarction (Hu et al., 1997), and sudden cardiac death (Albert et al., 2002). Moreover, nutrients constituent within almonds are associated with beneficial cardiovascular outcomes, such as antioxidant flavonoids and L-arginine, which is key for the synthesis of the vasodilatory molecule, nitric oxide. The precise nutrient composition of almonds differs dependent on the cultivar (Barreira et al., 2008), and the overall positive effects of almonds may conceivably be attributable to the milieu of nutrients.

Some studies, such as Dhillon et al., have reported that almond consumption results in greater proportional reductions of trunk and total body fat as well as DBP, and thus may help to lower metabolic disease risk in obesity (Dhillon et al., 2016); however, in such examples, participants were concurrently following an energy restriction protocol and were overweight or obese at study commencement. Thus, whilst consuming almonds, alongside calorie-restriction, was more beneficial than calorie restriction alone.

Epidemiological and clinical evidence demonstrates that adherence to a diet enriched in mono-unsaturated fatty acids and tocopherols from nuts, can reduce blood pressure (SBP and DBP) and blood lipid levels (Einarsson et al., 1985). Indeed, regular nut consumption, demarcated by 1–4 times per week, has been reported to diminish the risk of early mortality attributed to cardiovascular disease by, roughly, one-quarter (Dreher et al., 1996). Indeed, mechanistically, muscle relaxation is putatively mediated by the availability of nitric oxide (Hijmering et al., 2002). Almonds are

Table 1
Characteristics of included studies.

First Author	Country	Year	Study Population (n)	Age	Sex (1. male 2. female 3. both)	Dose of Almond	basic participant disease	type of Almond	Duration of treatment (week)
Chen	USA	2015	45	61.8	3	85 g/d	CAD patients	Raw whole almonds	2 × 6 wk intervention phases
Chen	USA-collected in Taipe	2017	33	54.9	3	60 g/d	T2DM	Roasted almonds	12 wk × 2 phases (CO)
Choudhury	UK	2014	60	Middle age 56y; young male 22.1y; young male with risk factors 27.3y; CL gp allocated from the above 3 groups	1	50 g/d	healthy middle-aged (MA); Healthy yound (HY); "young, at risk (YR); Habitual (control)	not specified-2 bags	4wk
Dhillon	USA	2016	50	18–60	3	providing 15% of Energy	Overweight and obese individuals	Dry roasted, lightly salted	12 wks
Foster	USA	2012	123	46.8	3	two 28-g packages of almonds (24) Over the first 5 wk of treatment, participants received whole, raw almonds only. At week 6, roasted almonds were introduced and, over time, a variety of isocaloric, flavored almonds were used.	Overweight and obese individuals	first 5 wk – whole, raw almonds only.At week 6, roasted almonds were introduced over time:over time,a variety of isocaloric, flavored almonds were used.	18 months
Jaapna Dhillon	USA	2018	73	18	3	56.7 g/day	–	dry roasted almonds	12 wks
Jamshed	Pakistan	2015	113	32–86	3	10 g/d PA: Pakinstan almonds AA: american almonds	Included CAD patients with optimal LDL cholesterol and low HDL cholesterol	Pakistan almonds (Talwar (sword shape) & American almonds (Carmel variety, California Shelled. Soak overnight and eat after removing the skin, before breakfast	12 wk
Jenkins	Canada	2002	27	64	3	73.3 g/d	hyperlipidemic subjects	whole raw unblanched almonds	3 phases 1 month each
Johnston	USA	2017	12	45–60	3	2.5 oz/d	sedentary older adults	raw, whole	8 wks (wk 1–5 walking) but group comparisons with almonds vs cookie butter were on wk 6–8
Lui	Rep Korea	2018	85	26	3	56 g/d	Healthy adults	whole	20wks
Richmond	New Zealand	2018	22	62	2	30 g/d	postmenopausal women with type 2 diabetes	whole nature almonds	3wk x2 (CO)
Souza	Brazil	2018	46	20–59	2	20 g	Adult women , overweight or obese	roasted Baru almonds	8 wks
Sweazea	USA	2014	21	55	3	1.5 oz/5–7 days a wk	Health adults with T2D	skins	12 wk
Tan	Australia	2013	137	31	3	43 g/d in 4 conditions	Risk of T2D	Dry roasted, lightly salted	4 wks 5 groups
Wien,	USA	2010	6	53	3	Participants consumed an ADA diet with 20% from almonds and avoided other tree nuts and peanuts (intervention) energy from almonds	Prediabetes	no mentioned	16 wks

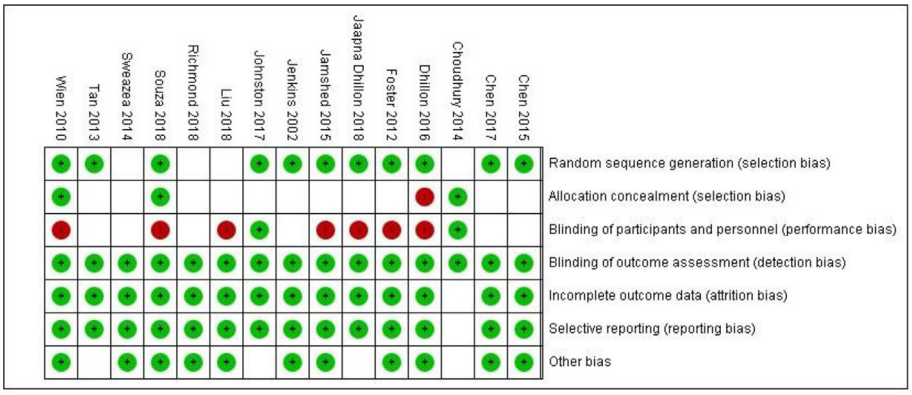

Fig. 2. Cochrane risk of bias assessment.

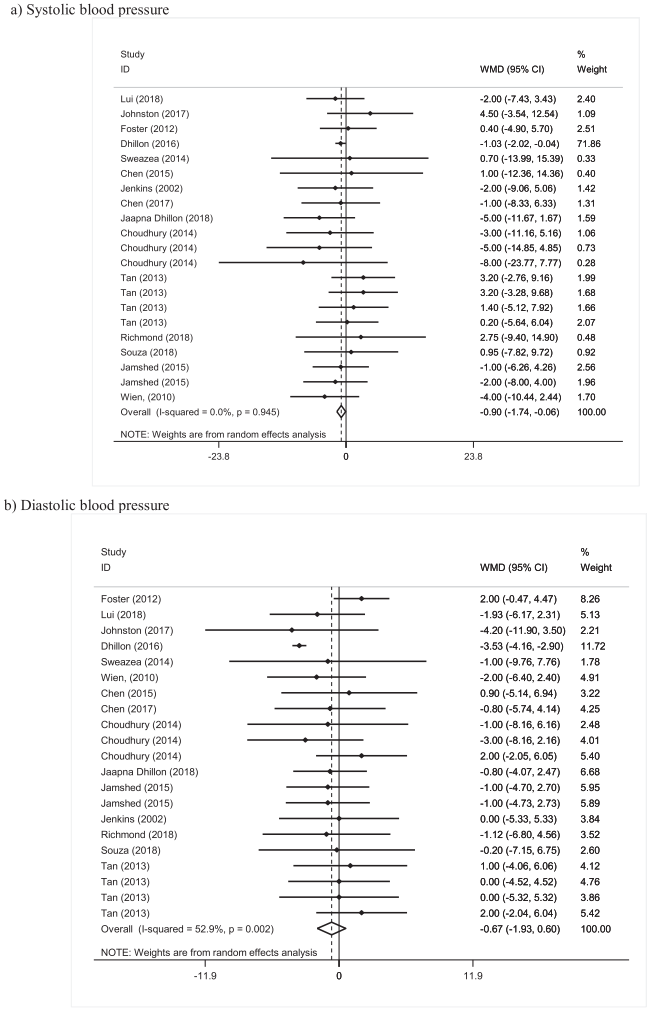

Fig. 3. Meta-analysis of effect of Almond consumption on:

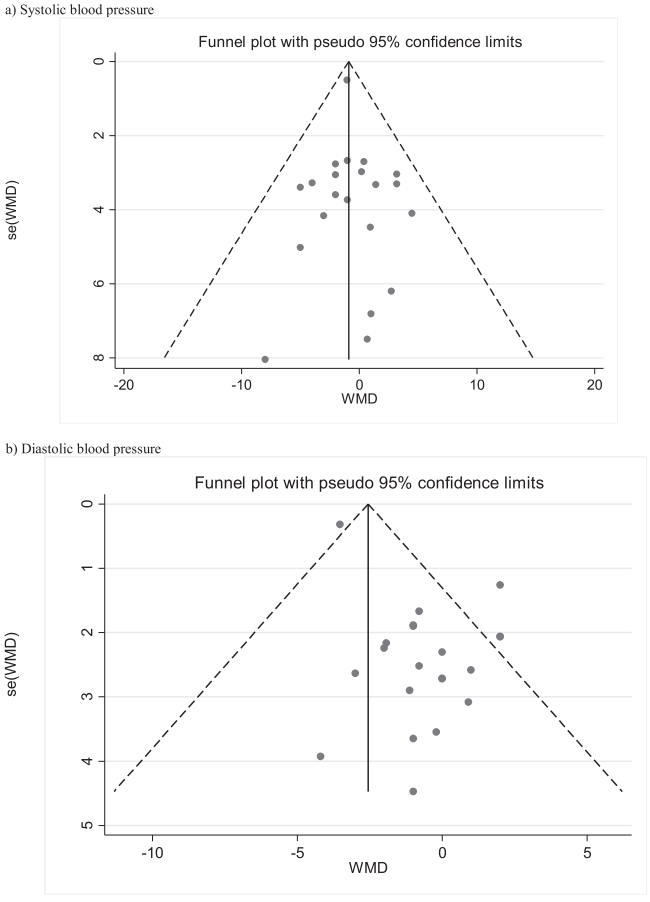

Fig. 4. Funnel plot to assess publication bias.

abundant in L-arginine, which is a rate-limiting substrate for the production of endothelial nitric oxide and in the synthesis of vitamin E, and acts as a scavenger of free radicals; in combination, this is asserted to increase bioavailable nitric oxide. Age-dependent vascular stiffness might also be a mitigating factor, where, although the mechanism by which baroreceptor control is mediated via nutrients is not well defined, some empirical evidence suggests that redox imbalances might precipitate high blood pressure and baroreflex responses, whilst tocopherol can modulate vascular responses (El-Mas et al., 2012; Wu et al., 2011). Furthermore, lipid dysfunction may intermediate this effect, where hyperlipidemia in hypertensive and obese patients has been attributed to baroreceptor reflex impairment, resulting in hypertension (SBP and DBP) (Gadegbeku et al., 2002).

5. Strengths and limitations

The primary strength of the present study was that we assessed the impact of almond consumption on blood pressure, which has not previously been reported; and given the potential influence on clinical and holistic practice, this represents an important addition to the literature. The evidence base, prior to this investigation,

was far from consensual, and thus necessitated a meta-analytical evaluation, which we have provided. An additional strength of the current meta-analysis is the heterogeneous sample assimilated, with a range of demographics, ethnicities, and ages. Moreover, we were also able to stratify our analyses based upon dosage of supplementation. However, there are some limitations that need to be appreciated within this meta-analysis. Varying diets, ad libitum or prescribed, may elicit different magnitudes of weight change during trials, possibly confounding the results of the meta-analysis; moreover, it should be considered that control group diets designed to mimic the overall energy content of almonds may also represent a confounding variable. Bias associated with attrition may be a concern in the present meta-analysis, however, the compliance of participants to study diets was scarcely reported; consequently, we were unable to assess attrition bias in the included studies and their consequential impact on the overall results of the meta-analysis.

6. Conclusion

The current body of evidence supports the ingestion of almonds for their beneficial effect on blood pressure. However, both the vascular moderating effects and the safety and acceptability of almond consumption should be further investigated in large, randomized, double-blind, placebo-controlled trials of longer duration, across age groups.

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Declaration of Competing Interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jksus.2020.01.013.

References

Abazarfard, Z., Salehi, M., Keshavarzi, S., 2014. The effect of almonds on anthropometric measurements and lipid profile in overweight and obese females in a weight reduction program: a randomized controlled clinical trial. J. Res. Med. Sci. 19 (5), 457–464.

Albert, C.M., Gaziano, J.M., Willett, W.C., Manson, J.E., 2002. Nut consumption and decreased risk of sudden cardiac death in the Physicians' Health Study. Arch. Intern. Med. 162 (12), 1382–1387.

Barreira, J.C., Ferreira, I.C., Oliveira, M.B.P., Pereira, J.A., 2008. Antioxidant activity and bioactive compounds of ten Portuguese regional and commercial almond cultivars. Food Chem. Toxicol. 46 (6), 2230–2235.

Benjamin, E.J., Virani, S.S., Callaway, C.W., Chamberlain, A.M., Chang, A.R., Cheng, S., Deo, R., 2018. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. Circulation 137, (12) e67.

Booth III, J.N., Levitan, E.B., Brown, T.M., Farkouh, M.E., Safford, M.M., Muntner, P., 2014. Effect of sustaining lifestyle modifications (nonsmoking, weight reduction, physical activity, and mediterranean diet) after healing of myocardial infarction, percutaneous intervention, or coronary bypass (from the REasons for Geographic and Racial Differences in Stroke Study). Am. J. Cardiol. 113 (12), 1933–1940.

Chen, C.Y., Holbrook, M., Duess, M.A., Dohadwala, M.M., Hamburg, N.M., Asztalos, B. F., Vita, J.A., 2015. Effect of almond consumption on vascular function in patients with coronary artery disease: a randomized, controlled, cross-over trial. Nutr. J. 14 (1). https://doi.org/10.1186/s12937-015-0049-5.

Chen, C.M., Liu, J.F., Li, S.C., Huang, C.L., Hsirh, A.T., Weng, S.F., Chen, C.O., 2017. Almonds ameliorate glycemic control in Chinese patients with better controlled type 2 diabetes: a randomized, crossover, controlled feeding trial. Nutr. Metab. (Lond.) 14, 51.

Choudhury, K., Clark, J., Griffiths, H.R., 2014. An almond-enriched diet increases plasma alpha-tocopherol and improves vascular function but does not affect oxidative stress markers or lipid levels. Free Radic. Res. 48 (5), 599–606.

de Souza, R.G.M., Gomes, A.C., de Castro, I.A., Mota, J.F., 2018. A baru almond-enriched diet reduces abdominal adiposity and improves high-density lipoprotein concentrations: a randomized, placebo-controlled trial. Nutrition 55, 154–160.

Dhillon, J., Tan, S.-Y., Mattes, R.D., 2016. Almond consumption during energy restriction lowers truncal fat and blood pressure in compliant overweight or obese adults. J. Nutr. 146 (12), 2513–2519.

Dhillon, J., Thorwald, M., De La Cruz, N., Vu, E., Asghar, S.A., Kuse, Q., Ortiz, R.M., 2018. Glucoregulatory and cardiometabolic profiles of almond vs. cracker snacking for 8 weeks in young adults: a randomized controlled trial. Nutrients 10 (8).

Dreher, M.L., Maher, C.V., Kearney, P., 1996. The traditional and emerging role of nuts in healthful diets. Nutr. Rev. 54 (8), 241–245.

Duval, S., Tweedie, R., 2000. Trim and fill: a simple funnel-plot–based method of testing and adjusting for publication bias in meta-analysis. Biometrics 56 (2), 455–463.

Einarsson, K., Nilsell, K., Leijd, B., Angelin, B., 1985. Influence of age on secretion of cholesterol and synthesis of bile acids by the liver. N. Engl. J. Med. 313 (5), 277–282.

El-Mas, M.M., El-Din, M.M.M., Helmy, M.M., Omar, A.G., 2012. Redox imbalances incite the hypertensive, baroreflex, and autonomic effects of cyclosporine in rats. Eur. J. Pharmacol. 694 (1–3), 82–88.

Foster, G.D., Shantz, K.L., er Veur, S.S., Oliver, T.L., Lent, M.R., Virus, A., Gilden-Tsai, A., 2012. A randomized trial of the effects of an almond-enriched, hypocaloric diet in the treatment of obesity. Am. J. Clin. Nutr. 96 (2), 249–254.

Gadegbeku, C.A., Dhandayuthapani, A., Sadler, Z.E., Egan, B.M., 2002. Raising lipids acutely reduces baroreflex sensitivity. Am. J. Hypertens. 15 (6), 479–485.

Griel, A.E., Kris-Etherton, P.M., 2006. Tree nuts and the lipid profile: a review of clinical studies. Br. J. Nutr. 96 (S2), S68–S78.

Higgins, J.P., Green, S., 2011. Cochrane Handbook for Systematic Reviews of Interventions. John Wiley & Sons.

Hijmering, M.L., Stroes, E.S., Olijhoek, J., Hutten, B.A., Blankestijn, P.J., Rabelink, T.J., 2002. Sympathetic activation markedly reduces endothelium-dependent, flow-mediated vasodilation. J. Am. Coll. Cardiol. 39 (4), 683–688.

Hu, F.B., Stampfer, M.J., Manson, J.E., Rimm, E., Colditz, G.A., Rosner, B.A., Willett, W. C., 1997. Dietary fat intake and the risk of coronary heart disease in women. N. Engl. J. Med. 337 (21), 1491–1499.

Jaceldo-Siegl, K., Sabaté, J., Rajaram, S., Fraser, G.E., 2004. Long-term almond supplementation without advice on food replacement induces favourable nutrient modifications to the habitual diets of free-living individuals. Br. J. Nutr. 92 (3), 533–540.

Jamshed, H., Sultan, F.A., Iqbal, R., Gilani, A.H., 2015. Dietary almonds increase serum HDL cholesterol in coronary artery disease patients in a randomized controlled trial. J. Nutr. 145 (10), 2287–2292.

Jenkins, D.J., Kendall, C.W., Marchie, A., Parker, T.L., Connelly, P.W., Qian, W., Spiller, G.A., 2002. Dose response of almonds on coronary heart disease risk factors: blood lipids, oxidized low-density lipoproteins, lipoprotein(a), homocysteine, and pulmonary nitric oxide: a randomized, controlled, crossover trial. Circulation 106 (11), 1327–1332.

Jiang, R., Manson, J.E., Stampfer, M.J., Liu, S., Willett, W.C., Hu, F.B., 2002. Nut and peanut butter consumption and risk of type 2 diabetes in women. JAMA 288 (20), 2554–2560.

Johnston, C.S., Sweazea, K.L., Schwab, E., McElaney, E.A., 2017. Almond ingestion contributes to improved cardiovascular health in sedentary older adults participating in a walking intervention: a pilot study. J. Funct. Foods 39, 58–62.

Kris-Etherton, P.M., Zhao, G., Binkoski, A.E., Coval, S.M., Etherton, T.D., 2001. The effects of nuts on coronary heart disease risk. Nutr. Rev. 59 (4), 103–111.

Li, Z., Song, R., Nguyen, C., Zerlin, A., Karp, H., Naowamondhol, K., Tseng, C.-H., 2010. Pistachio nuts reduce triglycerides and body weight by comparison to refined carbohydrate snack in obese subjects on a 12-week weight loss program. J. Am. Coll. Nutr. 29 (3), 198–203.

Liu, Y., Hwang, H.J., Kim, H.S., Park, H., 2018. Time and intervention effects of daily almond intake on the changes of lipid profile and body composition among free-living healthy adults. J. Med. Food 21 (4), 340–347.

Mills, K.T., Bundy, J.D., Kelly, T.N., Reed, J.E., Kearney, P.M., Reynolds, K., He, J., 2016. Global disparities of hypertension prevalence and control: a systematic analysis of population-based studies from 90 countries. Circulation 134 (6), 441–450.

O'Neil, C.E., Nicklas, T.A., Fulgoni III, V.L., 2016. Almond consumption is associated with better nutrient intake, nutrient adequacy, and diet quality in adults: national health and nutrition examination survey 2001–2010. Food Nutr. Sci. 7 (07), 504.

Phung, O.J., Makanji, S.S., White, C.M., Coleman, C.I., 2009. Almonds have a neutral effect on serum lipid profiles: a meta-analysis of randomized trials. J. Am. Diet. Assoc. 109 (5), 865–873.

Rajaram, S., Connell, K.M., Sabaté, J., 2010. Effect of almond-enriched high-monounsaturated fat diet on selected markers of inflammation: a randomised, controlled, crossover study. Br. J. Nutr. 103 (6), 907–912.

Richmond, K., Williams, S., Mann, J., Brown, R., Chisholm, A., 2013. Markers of cardiovascular risk in postmenopausal women with type 2 diabetes are improved by the daily consumption of almonds or sunflower kernels: a feeding study. ISRN Nutr. 2013, 626414.

Sabaté, J., Oda, K., Ros, E., 2010. Nut consumption and blood lipid levels: a pooled analysis of 25 intervention trials. Arch. Intern. Med. 170 (9), 821–827.

Savica, V., Bellinghieri, G., Kopple, J.D., 2010. The effect of nutrition on blood pressure. Annu. Rev. Nutr. 30, 365–401.
Sweazea, K.L., Johnston, C.S., Ricklefs, K.D., Petersen, K.N., 2014. Almond supplementation in the absence of dietary advice significantly reduces C-reactive protein in subjects with type 2 diabetes. J. Funct. Foods 10, 252–259.
Tan, S.Y., Mattes, R., 2013. Appetitive, dietary and health effects of almonds consumed with meals or as snacks: a randomized, controlled trial. Eur. J. Clin. Nutr. 67 (11), 1205–1214.
Wien, M., Bleich, D., Raghuwanshi, M., Gould-Forgerite, S., Gomes, J., Monahan-Couch, L., Oda, K., 2010. Almond consumption and cardiovascular risk factors in adults with prediabetes. J. Am. Coll. Nutr. 29 (3), 189–197.
Wu, Y.-C., Wang, Y.-J., Tseng, G.-F., 2011. Ascorbic acid and α-tocopherol supplement starting prenatally enhances the resistance of nucleus tractus solitarius neurons to hypobaric hypoxic challenge. Brain Struct. Funct. 216 (2), 105–122.