

What are the health effects related to consumption of nuts?

Conclusion

There is moderate evidence that consumption of unsalted peanuts and tree nuts, specifically walnuts, almonds and pistachios, in the context of a nutritionally adequate diet and when total calorie intake is held constant, has a favorable impact on cardiovascular disease risk factors, particularly serum lipid levels.

Grade: Moderate

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades, [click here](#).

Evidence Summary Overview

Review of seventeen studies [five cohort (positive quality), nine randomized controlled trials (RCTs) (five positive, four neutral quality) and three positive quality reviews (two systematic reviews and one meta-analysis)] provided evidence that consumption of nuts collectively and walnuts, almonds and pistachio nuts individually, in the context of a healthy diet when total calorie intake is held constant, has a favorable impact on cardiovascular risk factors, particularly serum lipid levels. The evidence was strongest for walnuts. Insufficient evidence was available to address the health effects of macadamia nuts.

Nuts (Including Peanuts) and Health Effects

Seven studies were reviewed to determine the health benefits related to consumption of nuts, five prospective cohort studies (all positive), one randomized crossover trial (positive) and one systematic review (positive quality).

One systematic review, Mukuddem-Petersen et al, 2005 (positive quality), investigated the effect of nuts on lipid profiles in 185 men and women (23 studies) and reported results of three almond (50 to 100g per day), two peanut (35 to 68g per day), one pecan nut (72g per day) and four walnut (40 to 84g per day) studies showing decreases in total cholesterol (TC) between 2% and 16%, low-density lipoprotein cholesterol (LDL-C) between 2% and 19% compared with subjects consuming control diets, and not so convincing results for studies consuming macadamia nuts (50 to 100g per day).

Two positive quality prospective cohort studies (Bes-Rastrollo et al, 2007; Bes-Rastrollo et al, 2009) assessed the associations between nut (including peanut butter) consumption and changes in body weight in cohorts of free-living adults (SUN study), the Nurses' Health study and in the Physician Health Study I and body mass index (BMI), reporting that increased frequency of nut consumption (two or more times per week) is associated with lower risk of weight gain or obesity. Djousse et al, 2009 (positive quality), as part of the Physician Health Study I (N=15,966) found an inverse relationship between nut intake and hypertension (HTN) in lean subjects, but not in overweight or obese subjects.

Two positive quality cohort studies assessed the association of nut consumption with cardiac-related outcomes in high-risk populations. Li et al, 2009, in a positive quality prospective cohort study (N=6,309 diabetic women), found consumption of at least five servings a week of nuts or peanut butter [serving size, 28g (1oz) for nuts and 16g (one tablespoon) for peanut butter] was significantly associated with a lower risk of cardiovascular disease (CVD) (RR=0.56; 95% CI: 0.36 to 0.89). Increasing nut consumption was significantly associated with a more favorable plasma lipid profile, including lower LDL-C, non-high density lipoprotein cholesterol (non-HDL-C), TC and apolipoprotein-B-100 concentrations. Salas-Salvado et al, 2008 (positive quality), in a three-arm randomized controlled trial (RCT) conducted in among 1,224 Spanish subjects with type 2 diabetes (T2D) or three or more CVD risk factors, assessed the effect of a Mediterranean diet high in olive oil (MedDiet + VOO) or nuts (MedDiet + 30g per day of mixed nuts) and a low-fat diet (control diet) and found one-year prevalence of metabolic syndrome was reduced by 6.7% (MedDiet + VOO), 13.7% (MedDiet + nuts) and 2.0% (control diet), respectively (MedDiet + nuts vs. control groups, P=0.01; MedDiet + VOO vs. control group, P=0.18). This researcher also found diets high in nuts and virgin olive oil was associated with lower serum concentrations of inflammatory markers, especially those related to endothelial function.

Almonds and Health Effects

To assess the health benefits related to consumption of almonds, the US Department of Agriculture Nutrition Evidence Library (USDA-NEL) updated the American Dietetic Association (ADA) reviews, pulling in two small RCTs [Kurlandsky S, Stote K. 2006 (neutral quality); Wien et al, 2003 (positive quality)] and reviewed one meta-analysis [Phung et al, 2009 (positive quality)].

Phung et al, 2009 analyzed five RCTs totaling 142 participants and reported that consumption of almonds (25 to 168g per day) decreases TC, does not affect LDL-C or HDL-C, triglycerides (TG), or the LDL:HDL ratio, concluding that the current body of randomized trials does not support the ingestion of almonds solely for their lipid-modifying effects.

One neutral quality study (Kurlandsky S, Stote K, 2006) assessed the effect of combining chocolate and almonds as part of the Therapeutic Lifestyle Changes (TLC) diet in 47 normolipidemic women and reported that intake of almonds reduced serum TG by 13% but had no effect on serum cholesterol level.

Wien et al, 2003 reported that HDL-C decreased with consumption of 85g per day of almonds (-6%, P=0.05) compared to complex carbohydrates (CHO) (provided as a part of a formula diet), but TC, TG, LDL-C and LDL-C:HDL-C ratio decreased significantly to a similar extent in both almond and complex CHO interventions. There was a significantly greater percent change in body weight among the almond group (-18% vs. -11%).

Walnuts and Health Effects

Four studies evaluated the effects of walnuts on health outcomes, one positive quality systematic review and meta-analysis and three RCTs (one positive and two neutral quality).

In one systematic review and meta-analysis, Banel and Hu, 2009 (positive quality), reviewed 13 studies (12 RCTs) with walnuts providing 10% to 24% of calories, representing 365 participants and found that compared with control diets, diets supplemented with walnuts resulted in a significantly greater decrease in TC and LDL-C. Triglycerides and HDL-C were not affected by walnuts.

Two small RCTs (both neutral), reported that a walnut diet containing 42.5g (1.5oz) walnuts per 10.1mJ (2,400kcal) (Rajaram et al, 2009), or consumption of a meat product with walnuts (19.4g per day) five times per week for five weeks (Olmedilla-Alonso et al, 2008) resulted in a

decrease in TC at four weeks when compared to baseline ($P<0.002$) and at five weeks compared to four weeks ($P=0.027$). LDL-cholesterol was also decreased at four weeks when compared to baseline ($P<0.007$), but no further changes occurred by five weeks compared to four weeks ($P=0.303$). Rajaram et al, 2009 found that the ratios of TC:HDL-C, LDL-C:HDL-C and apoB:apoA-I were lower in those who followed the walnut diet. Olmedilla-Alonso et al, 2008, found that compared to baseline, meat products with walnuts decreased body weight.

One randomized crossover trial, Sabate et al, 2005 (positive-quality), found that a walnut-supplemented diet (28 to 56g per day, 12% energy from walnuts) provided approximately 133 more calories per day than the control diet and increased the weight, BMI, fat mass and lean mass of the subjects. Energy-adjusted results were not significant, indicating that care must be taken to accommodate the caloric content of nuts in the diet.

Macadamia and Health Effects

One RCT was reviewed for macadamia nuts. Griel et al, 2008 (neutral quality), report that serum concentrations of TC and LDL-C were lower after consumption of macadamia nut-rich diet than the average American diet. Serum TG and serum non-HDL-C concentrations were not affected.

Pistachios and Health Effects

Two studies (Sheridan et al, 2007; Gebauer et al, 2008) assessed the effects of pistachio nuts on serum lipid response. Sheridan et al, 2007, in a randomized crossover trial, found two to three ounces a day of pistachio nuts (15% of daily calorie intake), when substituted for high-fat snacks by free living subjects over a four-week period, significantly decreased saturated fatty acid (SFA) intake and increased polyunsaturated fatty acid (PUFA) and fiber intake, resulting in a significant reduction in TC/HDL-C, LDL-C/HDL-C and HDL-C. The pistachio diet had no effect on blood pressure (BP) in the 15 subjects. Gebauer et al, 2008, in a four-week randomized crossover trial, found a dose-dependent response ($P<0.05$) on TC, HDL-C, LDL-C:HDL-C and non-HDL-C:HDL-C in 28 hyperlipidemic adults consuming an isocaloric diet (SFA and cholesterol-controlled) with either 10% or 20% of total energy (from 32 to 63g per day and from 63 to 126g per day, respectively) from pistachio nuts.

Evidence Summary Paragraphs

Nuts and Health (Including Peanuts)

Bes-Rastrollo et al, 2007 (positive quality), a prospective cohort study conducted in Spain, assessed the association between nut consumption and risk of weight gain or the risk of becoming overweight or obese in the Mediterranean dynamic Seguimiento Universidad de Navarra (SUN) cohort of free-living adults. Of 11,714 eligible adults, a total of 8,865 adults completed a follow-up questionnaire after a median of 28 months and were included in the analysis. Participants were classified based on their baseline frequency of nut consumption (in 50g servings): Never/almost never (33.1% male, mean age 35.6 years); one to three times per month (40.8% male, mean age 36.7 years); once per week (46.9% male, mean age 37.6 years); or at least twice per week (51.0% male, mean age 41.5 years). Walnuts were found to be the most frequently consumed nut, followed by hazelnuts, almonds and peanuts, respectively. At the 28-month follow-up, 937 participants reported a weight gain of at least 5kg. After adjustment for confounding variables, participants who ate nuts two or more times per week had a significantly lower risk of weight gain (OR=0.69, 95% CI: 0.53 to 0.90, $P=0.006$) than those who never or almost never ate nuts; participants who never or almost never consumed nuts gained an average of 424g (95% CI: 102 to 746) more than frequent nut consumers. Nut consumption was not significantly associated with incident overweight or obesity. Authors note that the participants were not representative of the general population; in addition, dietary habits were only measured at baseline and body weight was based on self-report.

Bes-Rastrollo et al, 2009 (positive quality), a prospective cohort study conducted in the US, assessed the long-term relation between nut or peanut butter consumption and weight change in participants of the Nurses' Health Study II. Of 116,671 female nurses aged 24 to 44 years at baseline in 1989, 51,188 were included in the 1991 to 1999 analysis. A semi-quantitative food frequency questionnaire (FFQ) was administered originally in 1991 that included 133 items to obtain dietary information about their average consumption of a commonly used unit or portion size of each food during the previous year. Similar questionnaires were used to update information on the subject's diet in 1995 and 1999. Participants were asked about their average consumption of peanut butter [one tablespoon equivalent to 1oz of peanuts (1oz=28.35g)], peanuts [1oz (28.35g) of peanuts] and tree nuts [1oz (28.35g) of nuts] during the previous year. In 1999 "tree nuts" was subdivided into two separate items, walnuts and other nuts. Over eight years of follow-up, women who reported eating nuts more than two times per week had slightly less mean weight gain than women who rarely ate nuts (5.04±0.12kg vs. 5.55±0.04kg, $P<0.001$); the results were similar when total nut consumption was subdivided by peanuts and tree nuts and when subjects were subdivided by normal weight, overweight and obese. After adjustment for confounding variables, greater nut consumption (more than two times per week) was associated with a slightly lower risk of obesity compared with never/almost never consuming nuts (HR=0.77, 95% CI: 0.57 to 1.02, $P=0.003$). Authors note that there were a small percentage of women in the cohort with high levels of nut consumption. In addition, weight was based on self-report.

Djousse et al, 2009 (positive quality), a prospective cohort study conducted in the US, examined the association between nut consumption and lower risk of incident HTN in participants of the Physician's Health Study I. Of 22,071 male physicians aged 40 to 84 years (mean age 52.3±8.9 years) at baseline in 1981, 15,966 were included in the analysis. During the 237,585 person-years of follow-up, there were 8,423 new cases of HTN. Compared to subjects who did not consume nuts, multivariable adjusted hazard ratios (HR) for HTN were 0.97 (95% CI: 0.91 to 1.03) for nut consumption of one to two times per month, 0.98 (95% CI: 0.92 to 1.05) for nut consumption of once per week, 0.96 (95% CI: 0.89 to 1.03) for nut consumption of two to six times per week, and 0.82 (95% CI: 0.71 to 0.94) for nut consumption of seven or more times per week. In analyses stratified by BMI, there was an inverse relation between nut intake and HTN in lean subjects ($P=0.0019$) but not in overweight or obese subjects (P for interaction = 0.0037). Authors note that participants were male physicians who may have different behaviors or lifestyles than the general population, limiting the generalizability of findings; in addition, incidence of HTN was based on self-report.

Li et al 2009 (positive quality), a prospective cohort study, assessed the association between intake of nuts and incident CVD in a cohort of women with T2D. For the primary analysis, there were 6,309 women with T2D who completed a validated FFQ every two to four years between 1980 and 2002 and were without CVD or cancer at study entry. Major CVD events included incident myocardial infarction (MI), revascularization and stroke. During 54,656 person-years of follow-up, there were 452 coronary heart disease (CHD) events (including MI and revascularization) and 182 incident stroke cases. Frequent nut and peanut butter consumption was inversely associated with total CVD (P -trend = 0.015) and MI (P -trend = 0.05) risk in age-adjusted analyses. After adjustment for conventional CVD risk factors, consumption of at least five servings a week of nuts or peanut butter [serving size, 28 g (1oz) for nuts and 16g (one tablespoon) for peanut butter] was significantly associated with a lower risk of CVD (RR=0.56; 95% CI: 0.36 to 0.89). Increasing nut consumption was significantly associated with a more favorable plasma lipid profile, including lower LDL-C ($P=0.008$), non-HDL cholesterol ($P=0.014$), TC ($P=0.007$), and apolipoprotein-B-100 concentrations ($P=0.016$). No significant (NS) associations for HDL-C or inflammatory markers were observed. Authors conclude that frequent nut and peanut butter consumption is associated with a significantly lower CVD risk in women with T2D.

Salas-Salvadó J et al, 2008 (positive quality), a cross-sectional study of subjects within cohort previously subjected to a randomized controlled study (Estruch et al 2006) in Spain. The study assessed the associations between components of the Mediterranean diet and circulating markers of inflammation in a large cohort of asymptomatic subjects, 339 men and 433 women aged between 55 and 80 years at high cardiovascular risk

because of the presence of diabetes, or at least three classical cardiovascular risk factors at high risk for CVD. Food consumption was determined by a semi-quantitative FFQ. Serum concentrations of high-sensitivity C-reactive protein (CRP) were measured by immunonephelometry and those of interleukin-6 (IL-6), intracellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1). After adjusting for age, gender, BMI, diabetes, smoking, use of statins, non-steroidal anti-inflammatory drugs and aspirin, a higher consumption of fruits and cereals was associated with lower concentrations of IL-6 (P for trend = 0.005). Subjects with the highest consumption of nuts and virgin olive oil showed the lowest concentrations of VCAM-1, ICAM-1, IL-6 and CRP; albeit only for ICAM-1 was this difference statistically significant in the case of nuts (P for trend = 0.003) and for VCAM-1 in the case of virgin olive oil (P for trend = 0.02). Participants with higher adherence to the Mediterranean-type diet did not show significantly lower concentrations of inflammatory markers ($P < 0.1$ for VCAM-1 and ICAM-1). Authors conclude that consumption of some typical Mediterranean foods (fruits, cereals, virgin olive oil and nuts) was associated with lower serum concentrations of inflammatory markers, especially those related to endothelial function, in subjects with high cardiovascular risk living in a Mediterranean country.

Salas-Salvadó J et al, 2008 (positive study), a multicenter, three-arm, RCT conducted in Spain. The study compared the one-year effect of two behavioral interventions to implement the Mediterranean diet (MedDiet) vs. advice on a low-fat diet on metabolic syndrome (MetS) status. One thousand two hundred twenty-four participants (presence of T2D mellitus and three or more CVD risk factors) recruited from the PREDIMED (Prevención con Dieta Mediterránea) Study to determine the efficacy of the MedDiet on the primary prevention of CVD. Participants were older subjects (55 and 80 years) at high risk for CVD. Interventions included: 1) Quarterly education about the MedDiet; 2) Provision of either 1L per week of virgin olive oil (MedDiet + VOO); or 3) 30g per day of mixed nuts (MedDiet + nuts), and advice on a low-fat diet (control diet ad libitum). and there was no increase in physical activity for any of the interventions. Lifestyle variables and MetS features as defined by the National Cholesterol Education Program Adult Treatment Panel III criteria were assessed. 61.4% of participants met criteria for the MetS at baseline. One-year prevalence of MetS was reduced by 6.7% (MedDiet + VOO), 13.7% (MedDiet + nuts) and 2.0% (control diet), respectively (MedDiet + nuts vs. control groups, $P = 0.01$; MedDiet + VOO vs. control group, $P = 0.18$). Incident rates of the MetS were not different among groups (22.9%, 17.9% and 23.4%, respectively). After adjustment for sex, age, baseline obesity status and weight changes, the odds ratios for reversion of MetS were 1.3 (95% CI, 0.8 to 2.1) for the MedDiet + VOO group and 1.7 (1.1 to 2.6) for the MedDiet + nuts group compared with the control diet group. Authors conclude that a traditional MedDiet enriched with nuts could be a useful tool in the management of the MetS. The authors also made note of the age of the participants.

Mukudde-Petersen et al, 2005 (positive quality) conducted a systematic review to investigate the effects of nuts on the lipid profile searching the MEDLINE and Web of Science databases from the start of the database to August 2004. Four-hundred fifteen publications were screened and 23 intervention studies (16 RCTs and seven non-RCTs) were included. Dietary intervention studies with 186 healthy or diseased (216 hypercholesterolemic, 66 hyperlipidemic, 30 T2D) or mixed (95) subjects (312 men and 281 women) were included in this systematic review. The results of three almond (50 to 100g per day), two peanut (35 to 68g per day), one pecan nut (72g per day), and four walnut (40 to 84g per day) studies showed decreases in TC between 2% and 16% and LDL-C between 2% and 19% compared with subjects consuming control diets. Consumption of macadamia nuts (50 to 100g per day) produced less convincing results. The authors concluded that, consumption of 50 to 100g (1.5 to 3.5 servings) of nuts five times a week as part of a heart-healthy diet with total fat content (high in mono- or polyunsaturated fatty acids) of 35% of energy may significantly decrease TC and LDL-C in normo- and hyperlipidemic individuals.

Almonds (including ADA update)

Kurlandsky S, Stote K. 2006 (neutral quality), in a six week four-armed randomized parallel trial assessed the effect on selected CVD factors of combining chocolate and almonds as part of a low-fat diet on circulating levels of serum lipids and inflammatory markers: Intercellular adhesion molecule (ICAM), vascular adhesion molecule, and high-sensitivity CRP in 47 normolipidemic women. All subjects followed the NCEP Lifestyle Changes diet. The intervention involved four diets: 1) 60g almonds with a self-selected diet; 2) 41g dark chocolate with a self-selected diet; 3) Almonds (60g) and chocolate (41g) with a self-selected diet; 4) Control diet which was a self-selected diet avoiding nuts and chocolate. All subjects improved dietary intakes in accordance with guidelines, and no subjects gained or lost weight. Serum cholesterol concentrations showed no changes after six weeks; however, triacylglycerol levels were reduced by approximately 21%, 13%, 19% and 11% ($P < 0.05$), in the chocolate, almond, chocolate and almond and control groups, respectively. Circulating ICAM levels decreased significantly by 10% in the treatment group consuming chocolate only ($P = 0.027$). No significant changes were observed for vascular adhesion molecule and high-sensitivity CRP levels in any treatment group. No synergistic or additive effects were observed when both products were consumed. In conclusion, consumption of chocolate and almonds as part of the TLC diet for six weeks showed no harmful effects in healthy women; all dietary modifications improved serum triacylglycerol levels and consumption of chocolate reduced levels of circulating ICAM.

Phung et al, 2009 (positive quality), a meta-analysis of five international RCTs totaling 142 participants, evaluated the influence of almonds on lipid parameters. Almond consumption ranging from 25 to 168g per day significantly lowered TC [weighted mean difference = -6.95mg per dL (95% CI: -13.12 to -0.772mg per dL)] and showed a strong trend toward reducing LDL-C [weighted mean difference = -5.79mg per dL (95% CI: -11.2 to 0.00)]. There were no significant effects on HDL-C, TG, or LDL:HDL ratio. Authors note that the meta-analysis may have been underpowered to demonstrate statistical significance for some endpoints or subgroups. In addition, different background diets may have resulted in weight loss, potentially confounding the results.

Wien et al, 2003 (positive quality), in a randomized, prospective 24-week trial evaluated the effect of an almond-enriched or complex carbohydrate-enriched formula-based low-calorie diet on anthropometric, body composition and metabolic parameters in 65 overweight or obese subjects (age: 27 to 79 years, BMI: 27 to 55kg/m²) enrolled in a weight-reduction program. The intervention involved a formula-based LCD enriched with 84g per day of almonds (almond-LCD; 39% total fat, 25% MUFA and 32% carbohydrate as percent of dietary energy) or self-selected complex carbohydrates (CHO-LCD; 18% total fat, 5% MUFA and 53% CHO as percent of dietary energy) featuring equivalent calories and protein. Intake of almonds in the LCD, in contrast to complex CHO, was associated with greater reductions in weight/BMI (-18 vs. -11%), waist circumference (WC) (-14 vs. -9%), fat mass (FM) (-30 vs. -20%), total body water (-8 vs. -1%) and systolic blood pressure (SBP) (-11 vs. 0%), $P = 0.0001-0.05$. A 62% greater reduction in weight/BMI, 50% greater reduction in WC and 56% greater reduction in fat mass were observed in the almond-LCD as compared to the CHO-LCD intervention. Ketone levels increased only in the almond-LCD group (+260 vs. 0%, $P < 0.02$). Baseline TC level in the almond vs. CHO group was close to normal (198±8 and 216±7mg per dL). HDL-cholesterol increased in the CHO group and decreased in the almond groups (+15% vs. -6%, $P = 0.05$). Glucose, insulin, diastolic blood pressure (DBP), TC, TG, LDL-C and LDL-C to HDL-C ratio decreased significantly to a similar extent in both dietary interventions. Homeostasis model analysis of insulin resistance (HOMA-IR) decreased in both study groups over time (almond-LCD: -66% and CHO-LCD: -35%, $P < 0.0001$). Homeostasis model analysis of insulin resistance (HOMA-IR) decreased in both study groups over time (almond-LCD: -66% and CHO-LCD: -35%, $P < 0.0001$). Among subjects with T2D, diabetes medication reductions were sustained or further reduced in a greater proportion of almond-LCD as compared to CHO-LCD subjects (96 vs. 50%, respectively). Intake of almonds was associated with greater reduction in weight/BMI (-18% vs. -11%, $P < 0.0001$), WC (-14% vs. -9%, $P < 0.05$), fat mass (-30% vs. -20%, $P < 0.05$). Subjects self-reported evaluation of almond and complex CHO diet acceptability, satiety, palatability and texture did not differ over time or between groups. Both dietary interventions were effective in decreasing body weight beyond the weight loss recorded during long-term pharmacological interventions, but the almond-LCD group experienced a sustained and greater weight reduction during the 24 weeks of intervention. Authors conclude that an almond-enriched LCD improves a preponderance of the abnormalities associated with the metabolic syndrome.

Walnuts and Health Effects

Banel and Hu, 2009 (positive quality), in a systematic review and meta-analysis of 13 international studies, examined the changes in lipid concentrations induced by a walnut-enhanced diet. Of the 13 studies, 12 were randomized trials, 10 of which had a crossover design; 365 participants were included in the analysis. When compared with control diets, diets supplemented with walnuts (10% to 24% of total calories) resulted in a significantly greater decrease in TC (weighted mean difference = -10.3mg per dL, $P<0.001$) and LDL-C (weighted mean difference = -9.2mg per dL, $P<0.001$) concentrations, while HDL-C concentrations, TG levels and body weight were not significantly affected. Some trials reported that walnuts provided significant benefits for antioxidant capacity and inflammatory markers. Authors noted that studies had relatively small sample sizes and short durations of follow-up; the longest follow-up time was six months.

Olmedilla-Alonso et al, 2008 (neutral quality), a randomized crossover trial conducted in Spain, assessed the potential effect of regular consumption of walnut-enriched restructured meat products on biomarkers of coronary heart disease in subjects at risk for CVD. Subjects consumed a meat product, with or without walnuts, five times per week for five weeks with a one-month washout period in between diets. From 144 respondents, 25 were selected to participate and all completed the study (15 men, 10 women, mean age 54.4 ± 8.1 years). Compared to the meat products without walnuts, consumption of the meat products with walnuts resulted in a decrease in TC of 6.8mg per dL (95% CI: -12.8 to -0.85mg per dL), $P=0.02$. Compared to baseline, consumption of the meat products with walnuts resulted in a decrease in TC of -10.7mg per dL (95% CI: -17.1 to -4.2mg per dL) $P=0.002$, LDL-C of -7.6mg per dL (95% CI: -2.2 to -13.0mg per dL), $P=0.007$ and body weight of -0.5 kg (95% CI: -0.1 to -0.9kg), $P=0.032$, as well as an increase in α -tocopherol of 8.9mg per dL (95% CI: 1.0 to 16.8mg per dL), $P=0.029$. Enrollment of subjects may have led to selection bias, and certain factors were not controlled for in the analysis.

Rajaram et al, 2009 (neutral quality), a randomized crossover trial conducted in the US, investigated whether walnuts and fatty fish have similar effects on serum lipid markers. Subjects consumed three isoenergetic diets (30% total fat, less than 10% saturated fat) for four weeks each, with a weekend break between diets: A control diet containing no nuts or fish, a walnut diet containing 42.5g walnuts per 10.1mJ and a fish diet containing 113g salmon twice per week. Of 27 subjects initially enrolled, 25 completed the study (14 males, 11 females, aged 23 to 65 years). Serum total cholesterol and LDL-C concentrations were lower when following the walnut diet (4.87 ± 0.18 and 2.77 ± 0.15 mmol per L, respectively, $P<0.0001$) than when following the control diet (5.14 ± 0.18 and 3.06 ± 0.15 mmol per L, respectively) and the fish diet (5.33 ± 0.18 and 3.2 ± 0.15 mmol per L, respectively). However, the fish diet resulted in decreased serum TG ($P<0.05$) and increased HDL-C concentrations ($P<0.001$) compared with the control diet and walnut diet. In addition, the ratios of TC:HDL-C, LDL-C:HDL-C, and apolipoprotein B:apolipoprotein A-I were lower ($P<0.05$) in those after consumption of the walnut diet compared with the control and fish diets. Authors note that the sample was relatively small in size, and that the washout period between treatments was short.

Sabate et al, 2005 (positive quality), a randomized crossover trial conducted in the US, determined the potential changes in body weight and body composition related to walnut consumption. Subjects were randomly assigned to two diets for six months: A walnut-supplemented diet (28 to 56 g per day, 12% of energy) and a control diet, then switched diets for another six months. Of 94 subjects randomized, 90 completed the trial, 50 females and 40 males aged 30 to 72 years (mean 54.3; SD, 10.6) years. The walnut supplementation resulted in greater daily energy intake of 133kcal. For all participants, walnut supplementation increased weight (0.4 ± 0.1 kg, $P<0.01$), BMI (0.2 ± 0.1 kg/m², $P<0.05$), fat mass (0.2 ± 0.1 kg, $P<0.05$) and lean mass (0.2 ± 0.1 kg, $P<0.05$); however, after adjusting for energy differences between diets, no significant differences were observed in body weight or body composition parameters except for BMI (0.1 ± 0.1 kg/m², $P<0.05$). Authors conclude that regular walnut intake results in weight gain much lower than expected was not significant after adjustment for differences in energy intake. No limitations were noted.

Macadamia Nuts and Health Effects

Griell et al, 2008 (neutral quality), a randomized crossover trial conducted in the US, evaluated the lipid and lipoprotein responses of a blood cholesterol-lowering diet that contained macadamia (MAC) nuts when substituted for saturated fat content of the average American diet. Subjects were randomly assigned to two diets for five weeks each: A macadamia nut-rich diet (1.5oz per 2,100kcal, 33% total fat, 7% SFA) and the average American diet (13% SFA and matched for total fat, protein and carbohydrate). Of 25 mildly hypercholesterolemic subjects randomized (10 men and 15 women, mean age 50.2 ± 8.4 years), 24 completed the trial. Compliance was confirmed by serum fatty acid analysis, serum MUFA increased while SFA decreased with intake of MAC ($P<0.05$). Serum concentrations of TC and LDL-C were lower following the macadamia nut-rich diet than the average American diet (4.94 ± 0.17 mmol per L vs. 5.45 ± 0.17 mmol per L for TC, 3.14 ± 0.14 mmol per L vs. 3.44 ± 0.14 mmol per L for LDL-C, both $P<0.05$). While there was no change in serum TG concentrations, the serum non-HDL cholesterol concentration was reduced following consumption of the macadamia nut-rich diet compared to the average American diet ($P<0.05$). The study was based on relatively small sample size; difficult to define the average American diet.

Pistachios Nuts and Health Effects

Gebauer et al, 2008 (neutral quality), a randomized crossover trial conducted in the US, assessed potential mechanisms that may account for the lipid and lipoprotein responses to a cholesterol-lowering diet with varying levels of pistachios. After a two-week run-in period, subjects were randomly assigned to three treatment diets for four weeks each, with two-week compliance breaks between diets: A lower-fat control diet with no pistachios (25% total fat), one serving per day of pistachios (10% of energy from pistachios, 30% total fat) and two servings per day of pistachios (20% of energy from pistachios, 34% total fat). Twenty-eight subjects completed the trial (10 men, 18 women, mean age 48 ± 1.5 years). Compared with the control diet, the diet with two servings per day of pistachios decreased TC (-8%), LDL-C (-11.6%), non-HDL cholesterol (-11%), apo B (-4%), apo B/apo A-I (-4%) and plasma stearoyl-CoA desaturase activity (-1%, all $P<0.05$). Both pistachio-based diets elicited a dose-dependent lowering of TC/HDL-C, LDL-C/HDL-C, and non-HDL cholesterol/HDL-C (all $P<0.05$). Recruitment methods were not described and the original number of subjects enrolled was unclear; each dietary period only lasted four weeks.

Sheridan et al, 2007 (neutral quality), a prospective randomized cross-over trial, investigated the effects of consuming 15% of the daily caloric intake in the form of pistachio nuts on the lipid profiles of 15 free-living subjects, average (mean \pm SEM) age of 60 ± 3 years with primary, moderate hypercholesterolemia (serum cholesterol higher than 210mg per dL) in the US. The intervention involved consumption of two to three ounces per day of Pistachio nut over a four-week period. Seven subjects were randomized to the pistachio diet for four weeks followed by four weeks on their regular diet, while eight subjects followed these diets in reverse order. The control diet was not defined. Outpatient dietary counseling and blood analysis were conducted and no differences were observed for total energy or percent of energy from protein, carbohydrate or fat. A significant decrease in percent energy from saturated fat was observed (mean difference, -2.7%; 95% CI: -5.4% to -0.08%; $P=0.04$) on the pistachio nut diet. Significant increases were seen for percent energy from polyunsaturated fat (mean difference, 6.5%; 95% CI: 4.2% to 8.9%; $P<0.0001$) and fiber intake (mean difference, 15g; 95% CI, 8.4g to 22g; $P=0.0003$) on the pistachio nut diet. There was a significant reduction in TC/HDL-C (mean difference, -0.38; 95% CI: -0.57 to -0.19; $P=0.001$), LDL-C/HDL-C (mean difference, -0.40; 95% CI: -0.66 to -0.15; $P=0.004$), B-100/A-1 (mean difference, -0.11; 95% CI: -0.19 to -0.03; $P=0.009$) and a significant increase in HDL-C (mean difference, 2.3; 95% CI: 0.48 to 4.0; $P=0.02$) on the pistachio diet. Total cholesterol, triglycerides, LDL-C, VLDL-C, apolipoprotein A-1 or apolipoprotein B-100 were not different. Body mass index or blood pressure did not change. Authors conclude that a diet consisting of 15% of calories as pistachio nuts can favorably improve some lipid profiles in subjects with moderate hypercholesterolemia and may reduce risk of coronary disease. Note that the study had design flaws such as a lack of proper controls, and used the experimental diet (pistachio nut) as a source of fat calories for subjects not

used to high fat snacks. There was also no definitive compliance measure of pistachio consumption. The study was industry funded.

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| Author, Year, Study Design, Class, Rating | Study Duration | Study Population/Location | Intervention Protocol/Exposure levels | Significant Results | Limitations; Funding Source |
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| <p>Banel DK and Hu FB 2009</p> <p>Study Design: Systematic Review/Meta-analysis</p> <p>Class: M</p> <p>Rating: </p> | <p>Minimum four to 24 weeks.</p> | <p>N=365 participants.</p> <p>13 international studies.</p> <p>12 were RCTs (10 crossover design).</p> <p>Location: International.</p> | <p>Walnuts and Blood Lipid</p> <p>Literature data bases.</p> <p>Diets lasting four to 24 weeks.</p> <p>Walnut providing 10% to 24% of calories.</p> <p>Jadad rating used to score RCTs (one to five points).</p> | <p>Compared with control diets, diets supplemented with walnuts (10% to 24% of total calories) resulted in a significantly greater ↓ in TC (weighted mean difference = -10.3mg per dL, P<0.001) and LDL-C (weighted mean difference = -9.2mg per dL, P<0.001) concentrations.</p> <p>HDL-C, TG levels and body weight were NS affected.</p> <p>Some trials reported that walnuts provided significant benefits for antioxidant capacity and inflammatory markers.</p> | <p>Authors noted that studies had relatively small sample sizes and short durations of follow-up; the longest follow-up time was six months.</p> |
| <p>Bes-Rastrollo M et al 2007</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p> | <p>28 months follow-up.</p> | <p>N=8,865 of 11,714 participants of the Mediterranean dynamic Seguimiento Universidad de Navarra (SUN) cohort of free-living adults.</p> <p>Age based on frequency of nut consumption (mean and SD):</p> <p>Never/almost never: 35.6 (11.9) years.</p> <p>One to three times a month: 36.7 (11.8) years.</p> <p>Once a week: 37.6 (12.0) years.</p> <p>At least two times per week: 41.5 (13.1) years.</p> <p>Location: Spain.</p> | <p>Nut Consumption and Risk of Weight Gain</p> <p>Follow-up questionnaire after a median of 28 months.</p> <p>Participants were grouped based on baseline frequency of nut consumption (50g servings):</p> <p>Never/almost never (33.1% male, mean age 35.6 years)</p> <p>One to three times a month (40.8% male, mean age 36.7 years)</p> <p>One time a week (46.9% male, mean age 37.6 years)</p> <p>At least twice per week (51.0% male, mean age 41.5 years).</p> | <p>At the 28-month follow-up, 937 participants reported a weight gain of at least 5kg.</p> <p>After adjustment for confounding variables, participants who ate nuts two or more times a week had a ↓ risk of weight gain (OR=0.69, 95% CI: 0.53 to 0.90, P=0.006), than those who never or almost never ate nuts.</p> <p>Participants who never or almost never consumed nuts gained an average of 424g (95% CI: 102 to 746) more than frequent nut consumers.</p> <p>Nut consumption was not associated with incident overweight or obesity.</p> | <p>Authors note that the participants were not representative of the general population.</p> <p>Dietary habits were only measured at baseline.</p> <p>Body weight based on self-report.</p> |

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| <p>Bes-Rastrollo M et al 2009</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p> | <p>Eight years of follow-up.</p> | <p>Participants of the Nurses' Health Study II.</p> <p>Of 116,671 female nurses aged 24 to 44 years at baseline in 1989, 51,188 were included in the 1991 to 1999 analysis.</p> <p>Location: United States.</p> | <p>Long-term Relation Between Nut or Peanut Butter Intake and Weight Δ</p> <p>Semi-quantitative FFQ at baseline (1991) included 133 items to obtain dietary information. Participants asked to report their average consumption of a commonly used unit or portion size of each food during the previous year. Nine possible responses, ranging from never to more than six times a day.</p> <p>Average intake of peanut butter [one Tbsp equivalent to one ounce of peanuts (28.35g)], peanuts [1oz (28.35g) of peanuts] and tree nuts [1oz (28.35g) of nuts] during the previous year.</p> | <p>Women who ate nuts more than two times a week had slightly less mean weight gain than women who rarely ate nuts (5.04±0.12kg vs. 5.55±0.04kg, P<0.001).</p> <p>Results were similar when total nut intake was subdivided by peanuts and tree nuts and when subjects were subdivided by normal weight, overweight and obese.</p> <p>After adjustment for confounding variables, greater nut consumption (more than two times a week) was associated with a slightly ↓ risk of obesity compared with never or almost never consuming nuts (HR = 0.77, 95% CI: 0.57 to 1.02, P=0.003).</p> | <p>Authors note that there were a small percentage of women in the cohort with high levels of nut consumption, in addition.</p> <p>Weight was self-reported.</p> |
| <p>Djousse L, Rudich T and Gaziano JM 2009</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p> | <p>237,585 person-years follow-up.</p> | <p>Participants of the Physician's Health Study I.</p> <p>Of 22,071 male physicians aged 40 to 84 years (mean age 52.3±8.9 years) at baseline in 1981, 15,966 were included in the analysis.</p> <p>Location: United States.</p> | <p>Nut Intake and Risk of Incident HTN</p> <p>Nut consumption was self-reported on a simple abbreviated semi-quantitative FFQ at 12 months post-randomization (1983–1985).</p> <p>Possible response categories were: "Rarely/never," "one to three times a month," "once a week," "two to four times a week," "five to six times a week," "daily," and "two times a day."</p> <p>Diagnosis of hypertension was made based on self-reported treatment.</p> | <p>During 237,585 person-years of follow-up, there were 8,423 new cases of hypertension.</p> <p>Compared to subjects who did not consume nuts, multivariable adjusted HR for hypertension were 0.97 (95% CI: 0.91 to 1.03) for nut consumption of one to times a month; HR=0.98 (95% CI: 0.92 to 1.05) for nut consumption of once a week; HR=0.96 (95% CI: 0.89 to 1.03) for nut consumption of two to six times a week; and HR= 0.82 (95% CI: 0.71 to 0.94, for nut consumption seven or more times per week.</p> <p>In analyses stratified by BMI, there was an inverse relation between nut intake and hypertension in lean subjects (P for trend = 0.0019) but not in overweight or obese subjects (P for interaction = 0.0037).</p> | <p>Authors note that participants were male physicians who may have different behaviors or lifestyle habits than the general population, limiting the generalizability of findings.</p> <p>Incidence of hypertension was based on self-reports.</p> |

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| <p>Gebauer SK et al 2008</p> <p>Study Design: Randomized Crossover Trial</p> <p>Class: A</p> <p>Rating: </p> | <p>Four weeks.</p> | <p>N=28 (10 men, 18 women) with hyperlipidemia.</p> <p>Mean age: 48±1.5 years.</p> <p>Location: United States.</p> | <p>Pistachios and Lipid- and Lipoproteins-lowering</p> <p>Two-week run-in period.</p> <p>Three diets for four weeks each, with two-week compliance breaks between diets:</p> <ol style="list-style-type: none"> 1. Lower-fat control diet with no pistachios (25% total fat) 2. One serving per day of pistachios (10% of energy from pistachios, 30% total fat). 3. Two servings per day of pistachios (20% of energy from pistachios, 34% total fat). | <p>Compared with the control diet, diet with two servings per day of pistachios lowered TC (-8%), LDL-C (-11.6%), non-HDL-C (-11%), apo B (-4%), apo B/apo A-I (-4%) and plasma stearoyl-CoA desaturase activity (-1%, all P<0.05).</p> <p>Both pistachio-based diets elicited dose-dependent lowering TC/HDL-C, LDL-C/HDL-C, and non-HDL-C/HDL-C (all P<0.05).</p> | <p>Recruitment methods were not described.</p> <p>The original number of subjects enrolled was unclear.</p> <p>Each dietary period only lasted four weeks.</p> |
| <p>Griel AE, Cao Y et al, 2008</p> <p>Study Design: Randomized crossover trial</p> <p>Class: A</p> <p>Rating: </p> | <p>Five weeks.</p> | <p>N=24 (10 men and 15 women), mildly hypercholesterolemic.</p> <p>Attrition: 0.4%.</p> <p>Mean age: 50.2±8.4 years.</p> <p>Location: United States.</p> | <p>Macadamia Nuts and Lipid and Lipoprotein Responses</p> <p>Two diets for five weeks each: Macadamia (MAC) nut-rich diet [1.5oz per 2,100kcal, 33% total fat (7% SFA, 18% MUFA, 5% PUFA), 17% protein and 52% CHO].</p> <p>The average American diet (AAD) [matched for total fat, 33% (13% SFA, 11% MUFA, 5% PUFA), 19% protein and 50% CHO].</p> | <p>Serum SFA lowered and MUFA rose after MAC diet compared to AAD (P<0.05) and no Δs in PUFA, indicating compliance.</p> <p>Serum TC and LDL-C lowered following MAC nut-rich diet than the AAD (4.94±0.17mmol per L vs. 5.45±0.17mmol per L for TC, 3.14±0.14mmol per L vs. 3.44±0.14mmol per L for LDL-C, both P<0.05).</p> <p>Serum TG remained unchanged.</p> <p>Serum non-HDL-C concentration lowered following the MAC nut-rich diet (3.83±0.14mmol per L vs. 4.60±0.24mmol per L for TC, 2.91±0.17mmol per L compared to the AAD (4.26±0.17mmol per L vs. 4.89±0.24mmol per L for TC, 3.09±0.18mmol per L (P<0.05).</p> | <p>Study based on relatively small sample size.</p> <p>Supported by The Hershey Company.</p> |
| <p>Kurlandsky and Stote, 2006</p> <p>Study Design: Randomized controlled parallel trial.</p> <p>Class: A</p> | <p>Six weeks.</p> | <p>N=47 normolipidemic women.</p> <p>Mean age: 36.5 years.</p> <p>Location: United States.</p> | <p>Almonds and Cholesterol</p> <p>Diets: 1) 60g almonds with a self-selected diet; 2) 41g dark chocolate with a self-selected diet; 3) Chocolate (41g) and almonds (60g) with a self-selected diet; and 4) A self-selected diet avoiding nuts and chocolate</p> | <p>NS Δ in cholesterol level over the six-week trial.</p> <p>TG levels ↓ in all treatment groups, and by 21 % with chocolate, 13% with almonds, 19% with almonds and chocolate combined and 11% in controls.</p> | <p>Small sample size.</p> <p>Limiting to measures of markers of inflammation due to loss of sample.</p> <p>Bias in the recruitment of only healthy subjects with good blood</p> |

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| Rating:  | | | (Control). Self-selected diet was based on the NCEP ATP III TLC diet. | | lipid. |
| Li TY, Brennan AM et al, 2009 Study Design: Prospective cohort study. Class: B Rating:  | | N=6309 women with T2D, without CVD or cancer at study entry. Location: United States. | Nuts, Peanut Butter and Incidents of CVD. Frequency of nut intake. Validated FFQ every two to four years between 1980 and 2002. A semi-quantitative FFQ included 61 foods in 1980. Later revised and expanded. Participants report their average frequency of consumption of selected foods and beverages with a specified commonly used unit or portion size . In 1980 and 1984 dietary questionnaires, participants were asked how often, on average, they consumed nuts [serving size, 28g (1oz)] according to categories: never/ almost never, one to three servings a month, one serving a week, two to four servings a week, five to six servings a week, one serving a day, two to three servings a day, four to six servings a day or six servings a day. In the 1986, 1990, 1994, and 1998 dietary questionnaires, the question for nuts was divided into two separate questions: peanuts and other nuts. | During 54,656 person-years of follow-up: 452 CHD events (MI and revascularization) 182 incident stroke cases. Intake of at least five servings a week of nuts or peanut butter [28g (1oz.) for nuts and 16g (one tablespoon) for peanut butter]: Significantly associated with ↓ risk of CVD (RR=0.56; 95% CI: 0.36 to 0.89) and more favorable plasma lipid profile, lower LDL, non-HDL-C, TC and apo-B100 conc. NS associations for HDL-C or inflammatory markers were observed. | Very well conducted prospective cohort study. Authors note the small sample size effect on power to conduct detailed analyses for biomarker. Method of handling withdrawals was not described. Authors presented results based on the total initial sample size. Characteristics of withdrawals, if any, were not described. Power calculation and intent to treat analysis were not described. |
| Mukuddem-Petersen J, Oosthuizen W et al, 2005 Study Design: Narrative Review Class: R Rating:  | Minimum four to 24 weeks of intake. | N=186 healthy or diseased (216 hypercholesterolemic, 66 hyperlipidemic, 30 T2D) or mixed (95) subjects (312 men and 281 women). 23 international studies. Location: International. | Nuts and Blood Lipid Studies were included if objective was to investigate the independent effect of nuts on lipid concentrations and study was conducted among humans. Trials were excluded when these independent effects could not be assessed and had incomplete or missing data. 23 original research papers were identified that were suitable for inclusion. Main outcome measures percentage differences between treatment and control for blood TC, LDL-C, HDL-C, and TG. | Most of the studies (12 of 16) included more than 20 subjects per group. Three almond (50 to 100g per day), two peanut (35 to 68g per day), one pecan nut (72g per day) and four walnut (40 to 84g per day) studies showed ↓ in TC between 2% and 16% and LDL-C between 2% and 19%, compared with subjects consuming control diets. Consumption of macadamia nuts (50 to 100g per day) produced less convincing results. | Did not conduct a meta-analysis. Authors noted that studies had large differences in study designs of the dietary intervention trials. University. |

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| <p>Olmedilla-Alonso et al 2008</p> <p>Study Design: Randomized Crossover Trial</p> <p>Class: A</p> <p>Rating: </p> | <p>Five weeks.</p> | <p>N=25 (15 men, 10 women). Mean age: 54.4±8.1 years.</p> | <p>Walnut-enriched Restructured Meat and Biomarkers of CHD</p> <p>Consumed a meat product, with or without walnuts, five times a week.</p> <p>Five weeks.</p> <p>One-month washout period between diets.</p> | <p>Compared to the meat products without walnuts, intake of the meat products with walnuts resulted in TC of 6.8mg per dL (95% CI: -12.8 to -0.85mg per dL); P=0.027.</p> <p>Compared to baseline, consumption of the meat products with walnuts resulted in a ↓ in TC of -10.7mg per dL (95% CI: -17.1 to -4.2mg per dL) P=0.002; LDL-C of -7.6mg per dL (95% CI: -2.2 to -13.0mg per dL), P=0.007; and body weight of -0.5kg (95% CI: -0.1 to -0.9kg), P=0.032; and an increase in g-tocopherol of 8.9mg per dL (95% CI: 1.0 to 16.8mg per dL), P=0.029.</p> | <p>Enrollment of subjects may have led to selection bias, and confounding factors were not controlled for in the analysis.</p> |
| <p>Phung OJ et al 2009</p> <p>Study Design: Meta-analysis</p> <p>Class: M</p> <p>Rating: </p> | | <p>N=142 participants. 40% hyperlipidemic; 21% T2D.</p> <p>Location: Five International RCTs.</p> | <p>Almonds Intake and Lipid Profiles</p> | <p>Almond consumption ranging from 25 to 168g per day significantly TC [weighted mean difference = -6.95mg per dL (95% CI: -13.12 to -0.772mg per dL)].</p> <p>NS effects on HDL-C, TG or LDL:HDL ratio.</p> | <p>Authors note that the meta-analysis may be underpowered to demonstrate statistical significance for some endpoints or subgroups.</p> <p>Different background diets may have resulted in weight loss, potentially confounding the results.</p> <p>Four of five trials funded by Almond Board.</p> |
| <p>Rajaram S et al 2009</p> <p>Study Design: Randomized Crossover Trial</p> <p>Class: A</p> <p>Rating: </p> | <p>Four weeks.</p> | <p>N=25 (14 males, 11 females). Attrition: 7.4%. Age: 23 to 65 years. Location: United States.</p> | <p>Walnuts vs. Fatty Fish and Serum Lipid Markers</p> <p>Three isoenergetic diets (30% total fat, less than 10% saturated fat):</p> <ol style="list-style-type: none"> 1) Control diet with no nuts or fish 2) Walnut diet containing 42.5g (1.5oz) walnuts per 10.1mJ (2,400kcal) 3) Fish diet containing 113g (4oz raw) salmon twice per week. <p>Four weeks each, with a weekend break between diets.</p> | <p>Serum TC and LDL-C concentrations were lower on the walnut diet (4.87±0.18 and 2.77±0.15mmol per L, respectively, P<0.0001) than on the control diet (5.14±0.18 and 3.06±0.15mmol per L, respectively) and the fish diet (5.33±0.18 and 3.2±0.15mmol per L, respectively).</p> <p>The fish diet resulted in lower serum TG (P<0.05), higher HDL-C (P<0.001), compared with the control</p> | <p>Authors noted the relatively small sample size.</p> <p>Short washout period between treatments.</p> |

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| | | | | and walnut diet. Ratios: TC:HDL-C, LDL-C:HDL-C and apo B:apo A-I were lower (P<0.05) after intake of the walnut diet compared with the control and fish diets. | |
| Sabate J, Corder-Macintyre Z et al, 2005 Study Design: Randomized crossover trial Class: A Rating:  | Six months. | N=90, relatively healthy subjects (less than 1kg weight Δ in the last six months; BMI less than 35kg/m ² . Attrition: 5.23%. Location: United States. | Walnuts, Body Weight and Body Composition Two diets for six months each: A walnut-supplemented diet (28 to 56g per day, 12% of energy) and a control diet. | Walnut diet resulted in greater daily energy intake of 133kcal. Walnut intake group gained weight (0.4±0.1kg), BMI (0.2±0.1kg/m ²), both P<0.01. Fat mass (0.2±0.1kg) and lean mass (0.2±0.1kg), both P<0.05. After adjusting for energy no differences were observed in body weight or body composition parameters, except for BMI (0.1±0.1kg/m ²) P<0.05. | No limitations were noted. |
| Salas-Salvado et al 2008 Study Design: Randomized Controlled Trial Class: A Rating:  | Cross-sectional study of a cohort subjected to RCT (Estruch et al, 2006). | N=772 (339 men and 433 women), asymptomatic. Age: 55 and 80 years. Location: United States. Length of time not clear. | Mediterranean Diet (Nuts and Circulating Markers of Inflammation). Food intake by a semi-quantitative FFQ. Measured Serum concentrations of high-sensitive CRP, interleukin-6 (IL-6), intracellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1). Adjusted for age, gender, BMI, diabetes, smoking, and use of statins, non-steroidal anti-inflammatory drugs and aspirin. | ↑ consumption of nuts and virgin olive oil showed the lowest concentrations of VCAM-1, ICAM-1, IL-6 and CRP; only in ICAM-1 was this significantly different in the case of nuts (P for trend = 0.003) and for VCAM-1 in the case of virgin olive oil (P for trend = 0.02). ↑ consumption of fruits and cereals was associated with ↓ concentrations of IL-6 (P for trend = 0.005). ↑ adherence to the Mediterranean-type diet did not show significantly ↓ concentration of inflammatory markers (P<0.1 for VCAM-1 and ICAM-1). | Authors note the possibility of measurement error in FFQ. Some associations may be overlooked. Score used may not be discriminatory enough of adherence to the Mediterranean dietary pattern. Study design may not have been the right choice to achieve their objective. |

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| <p>Salas-Salvadó J, Garcia-Arellano A et al, 2008</p> <p>Study Design: Prospective cohort study</p> <p>Class: B</p> <p>Rating: </p> | <p>Three-arm, randomized clinical trial.</p> | <p>N=1,224.</p> <p>Presence of T2D or three or more CVD risk factors:</p> <ul style="list-style-type: none"> • Current smoker • BP 140/90mmHg or treatment with antihypertensive drugs • LDL-C of 160mg per dL or higher or treatment with hypolipidemic drugs • HDL-C level of 40mg per dL or lower • BMI of 25kg/m² or higher • Family history of premature CVD. <p>Recruited from the PREDIMED (Prevención con DietaMediterránea) Study.</p> <p>Attrition: 4%.</p> <p>Age: 55 and 80 years.</p> <p>Location: United States.</p> | <p>Mediterranean Diet + Mixed Nuts and Incidence of MetS</p> <p>Multicenter recruiting.</p> <p>Food intake by a semi-quantitative FFQ.</p> <p>14-item questionnaire: Individual adherence to the MedDiet, dietitians gave personalized dietary advice to participants in both MedDiet groups during a 30-minute session.</p> <p>Dietitians delivered a separate 60-minute group session for each MedDiet group.</p> <p>Given written material with descriptions of typical Mediterranean foods, seasonal shopping lists, meal plans and recipes. Participants assigned to the MedDiet groups were given either free VOO (15L for three months) or packets of mixed nuts [1,350g of walnuts (15g per day), 675g of hazelnuts (7.5g per day) and 675g of almonds (7.5g per day) every three months].</p> | <p>One-year prevalence of high WC, elevated TG level and high BP significantly ↓ in the MedDiet + nuts group compared with the control group (P<0.05).</p> <p>One-year prevalence of MetS was ↓ by 6.7% (MedDiet + VOO), 13.7% (MedDiet + nuts) and 2.0% (control diet), respectively (MedDiet + nuts vs. control groups, P=0.01; MedDiet + VOO vs. control group, P=0.18).</p> <p>No differences among groups in the incidence or reversion of high fasting glucose or low HDL-C levels.</p> <p>MedDiet + nuts was associated with MetS reversion among individuals who had the syndrome at baseline.</p> | <p>Participants were older subjects at high risk for CVD.</p> <p>Nearly 45% had diabetes mellitus and 61.4% had MetS; results cannot be extrapolated to the general population.</p> <p>Nutritional education for the low-fat diet group was less intense than the behavioral intervention in the MedDiet groups.</p> <p>Study duration was too short to address clinical outcomes.</p> |
| <p>Sheridan MJ, Cooper JN et al, 2007</p> <p>Study Design: Randomized crossover (time series) trial</p> <p>Class: A</p> <p>Rating: </p> | | <p>N=15 (11 males, 4 females) free-living subjects, with primary, moderate hypercholesterolemia (serum cholesterol greater than 210mg per dL).</p> <p>Average (mean ± SEM) age: 60±3 years.</p> <p>Attrition: 25%.</p> <p>Location: United States.</p> | <p>Pistachio Nut Intake, Blood Lipids, BMI and BP</p> <p>Outpatient dietary counseling and blood analysis.</p> <p>Four weeks of dietary modification with 15% caloric intake from pistachio nuts.</p> <p>Measures of outcome: Serum lipid levels of TC, HDL-C, LDL-C, VLDL-C, TGs, apo A-1 and B-100. BMI, BP, and nutrient intake (total energy, fat, protein and fiber).</p> <p>All outcomes measured at baseline, during and after dietary intervention.</p> | <p>Total energy or percent of energy from protein, CHO or fat not different.</p> <p>On pistachios diet: Significant ↓ was seen for percent energy from saturated fat (mean difference, -2.7%; 95% CI: -5.4% to -0.08%; P=0.04).</p> <p>Significant rise for percent energy from PUFA fat (mean difference, 6.5%; 95% CI: 4.2% to 8.9%; P<0.0001).</p> <p>Rise in fiber intake (mean difference, 15g; 95% CI: 8.4g to 22g; P=0.0003).</p> <p>Significant ↓ in TC/HDL-C (mean difference, -0.38; 95% CI: -0.57 to -0.19; p = 0.001), LDL-C/HDL-C (mean difference, -0.40; 95% CI: -0.66 to -0.15; P=0.004), B-100/A-1</p> | <p>Small number of random sample, all above middle age.</p> <p>Short study duration does not allow for inferences on sustainability or outcomes.</p> <p>Design flaws and lack of proper controls, not described.</p> <p>Meets exclusion criteria.</p> <p>Not possible to assess whether the eating of pistachios as a snack food is sustainable over time as a healthy dietary behavior.</p> <p>Difficult to assess how the inclusion of this single food source might alter other aspects of the diet, perhaps</p> |

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| | | | | (mean difference, -0.11; 95% CI: -0.19 to -0.03; P=0.009). Significant ↑ in HDL-C (mean difference, 2.3; 95% CI: 0.48 to 4.0; P=0.02). No differences for TC, TG, LDL-C, VLDL-C, apo A-1 or apo B-100. No Δs observed in BMI or BP. | unfavorably. Not possible to assess biases as clinical setting, environment, socioeconomic status and co-morbidity. Supported by California Pistachio Commission. |
| Wien, Sabate et al, 2004 Study Design: Randomized trial Class: A Rating:  | Four weeks. | N=65 overweight or obese adults. Age: 27 to 79 years. BMI: 27 to 55kg/m ² . Almond diet: N=32; mean LDL-C, 99±5mg per dL. CHO diet: N=33; mean HDL-C, 108±5mg per dL. Attrition: 20%. Location: United States. | Formula-based LCD enriched with 84g per day of almonds or self-selected complex CHOs of equivalent calorie content. | HDL-C ↑ in the CHO group and ↓ in the almond groups (+15 vs. -6%, P=0.05). TC, TG, LDL-C and LDL-C to HDL-C ratio ↓ significantly to a similar extent in both dietary interventions. | |

Research Design and Implementation Rating Summary

For a summary of the Research Design and Implementation Rating results, [click here](#).

Worksheets

-  [Banel DK, Hu FB. Effects of walnut consumption on blood lipids and other cardiovascular risk factors: a meta-analysis and systematic review. *Am J Clin Nutr*. 2009;90\(1\):56-63.](#)
-  [Bes-Rastrollo M, Sabaté J, Gómez-Gracia E, Alonso A, Martínez JA, Martínez-González MA. Nut consumption and weight gain in a Mediterranean cohort: The SUN study. *Obesity \(Silver Spring\)*. 2007;15\(1\):107-116.](#)
-  [Bes-Rastrollo M, Wedick NM, Martinez-Gonzalez MA, Li TY, Sampson L, Hu FB. Prospective study of nut consumption, long-term weight change, and obesity risk in women. *Am J Clin Nutr*. 2009 Jun;89\(6\):1913-9. Epub 2009 Apr 29.](#)
-  [Djoussé L, Rudich T, Gaziano JM. Nut consumption and risk of hypertension in US male physicians. *Clin Nutr*. 2009 Feb;28\(1\):10-4.](#)
-  [Gebauer SK, West SG, Kay CD, Alaupovic P, Bagshaw D, Kris-Etherton PM. Effects of pistachios on cardiovascular disease risk factors and potential mechanisms of action: a dose-response study. *Am J Clin Nutr*. 2008 Sep;88\(3\):651-9.](#)
-  [Griel AE, Cao Y, Bagshaw DD, Cifelli AM, Holub B, Kris-Etherton PM. A macadamia nut-rich diet reduces total and LDL-cholesterol in mildly hypercholesterolemic men and women. *J Nutr*. 2008 Apr; 138 \(4\): 761-767.](#)
-  [Kurlandsky S, Stote K. Cardioprotective effects of chocolate and almond consumption in healthy women. *Nutrition Research*. 2006; 26\(10\): 509-516.](#)
-  [Li TY, Brennan AM, Wedick NM, Mantzoros C, Rifai N, Hu FB. Regular consumption of nuts is associated with a lower risk of cardiovascular disease in women with type 2 diabetes. *J Nutr*. Jul 2009; 139\(7\): 1,333-1,338.](#)
-  [Mukuddem-Petersen J, Oosthuizen W, Jerling JC. A systematic review of the effects of nuts on blood lipid profiles in humans. *J Nutr*. 2005 Sept; 135: 2,082-2,089. PMID: 16140880](#)
-  [Olmedilla-Alonso B, Granado-Lorenzo F, Herrero-Barbudo C, Blanco-Navarro I, Blázquez-García S, Pérez-Sacristán B. Consumption of restructured meat products with added walnuts has a cholesterol-lowering effect in subjects at high cardiovascular risk: a randomised, crossover, placebo-controlled study. *J Am Coll Nutr*. 2008 Apr;27\(2\):342-8.](#)
-  [Phung OJ, Makanji SS, White CM, Coleman CI. Almonds have a neutral effect on serum lipid profiles: a meta-analysis of randomized trials. *J Am Diet Assoc*. 2009 May;109\(5\):865-73.](#)

-  [Rajaram S, Haddad EH, Mejia A, Sabaté J. Walnuts and fatty fish influence different serum lipid fractions in normal to mildly hyperlipidemic individuals: a randomized controlled study. *Am J Clin Nutr*. 2009 May;89\(5\):1657S-1663S.](#)
-  [Sabaté J, Cordero-Macintyre Z, Siapco G, Torabian S, Haddad E. Does regular walnut consumption lead to weight gain? *Br J Nutr*. 2005 Nov; 94 \(5\): 859-864.](#)
-  [Salas-Salvado J, Fernandez-Ballart J, Ros E, Martinez-Gonzalez MA, Fito M, Estruch R, Corella D, Fiol D, Gomez-Gracia E, Aros F, Flores G, Lapetra J, Lamuela-Raventos R, Ruiz-Gutierrez V, Bullo M, Basora J, Covas M. Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status: one-year results of the PREDIMED randomized trial. *Arch Intern Med*. 2008; 168\(22\):2449-2458.](#)
-  [Salas-Salvado J, Garcia-Arellano A, Estruch R, Marquez-Sandoval F, Corella D, Fiol M, Gómez-Gracia E, Viñoles E, Arós F, Herrera C, Lahoz C, Lapetra J, Perona JS, Muñoz-Aguado D, Martínez-González MA, Ros E; PREDIMED Investigators. Components of the Mediterranean-type food pattern and serum inflammatory markers among patients at high risk for cardiovascular disease. *Eur J Clin Nutr*. May 2008; 62 \(5\): 651-659.](#)
-  [Sheridan MJ, Cooper JN, Erario M, Cheifetz CE. Pistachio nut consumption and serum lipid levels. *J Am Coll Nutr*. 2007 Apr; 26 \(2\): 141-148.](#)
-  [Wien MA, Sabate JM, Ikle DN, Cole SE, Kandeel FR. Almonds vs. complex carbohydrates in a weight reduction program. *Int J Obes Relat Metab Disord*. 2003; 27\(11\): 1,365-1,372. Erratum in: *Int J Obes Relat Metab Disord*. 2004 Mar; 28 \(3\): 459.](#)