

CALIFORNIA WALNUTS NUTRITION & SCIENTIFIC RESEARCH REVIEW







TABLE OF CONTENTS

Why Walnuts? | 4

Essential Omega-3s | 6

Health Research on Walnuts

For more than 30 years, the California Walnut Commission has supported scientific research on consumption of walnuts and outcomes in the following areas:

Gut Health | **8**

Cognitive Health | **10**

Weight | **12**

Heart Health | **14**

Cancer | **16**

Diabetes and Metabolic Syndrome | **18**

Reproductive Health | **20**

Mediterranean Diet and Health | 22

WHY WALNUTS?

WALNUTS ARE THE ONLY NUT to contain a significant amount of the plant-based omega-3 alpha-linolenic acid (2.5 grams/ounce). One ounce of walnuts also offers four grams of protein, two grams of fiber, and is a good source of magnesium (10% DV).

Walnuts' unique nutrient profile also makes meeting the 2020-2025 Dietary Guidelines for Americans easy and delicious. The Dietary Guidelines encourage a healthy eating pattern that emphasizes nutrient-dense, plant-based foods and includes a variety of protein sources, including nuts and seeds, seafood, lean meats and poultry, eggs, legumes and soy products.¹

There is also an emphasis on reducing saturated fat intake to less than 10 percent of calories per day and shifting food choices from those that contain saturated fats to those with polyunsaturated fats. Walnuts are predominantly composed of polyunsaturated fat (13 out of 18 grams of total fat per 1 ounce serving).

A STUDY FROM THE HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH suggests people who replace saturated fats with polyunsaturated fats in their diet may have a lower risk of heart disease.² The study analyzed the diets of nearly 85,000 nurses and 43,000 doctors every four years over 30 years. After calculating the percentage of calories the participants received from polyunsaturated fatty acids (PUFAs), monounsaturated fatty acids (MUFAs), whole grain carbohydrates and refined carbohydrates, the study found that substituting five percent of the calories from saturated fat with the same amount of energy from PUFAs was associated with a 25 percent lower risk of coronary heart disease (CHD). Replacing saturated fats with equivalent energy intake from MUFAs or whole grain carbohydrates was associated with a 15 percent and nine percent lower risk of CHD, respectively. Given this was an observational study, the findings cannot prove causality and additional research is needed to determine how these results apply to more diverse populations. Furthermore, residual confounding cannot be ruled out.

RESEARCHERS ARE INVESTIGATING ways to identify more precisely the components in walnuts that may be associated with beneficial health outcomes. A study used a novel machine learning model to identify 19 markers in the body that were associated with walnut consumption - a "walnut signature."³ The body forms specific metabolites based on what food is consumed. Researchers examined data from 1,833 participants from the PREvención con Dieta MEDiterránea (PREDIMED) study, who were at high cardiovascular risk, and found the "walnut signature" was associated with a 17% lower risk of type 2 diabetes and 29% lower risk of cardiovascular disease. Though the results do not prove cause and effect, new tools as used in this epidemiological study will help identify links between diet and disease.

¹U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025. 9th Edition. December 2020. Available at [DietaryGuidelines.gov](https://www.dietaryguidelines.gov).

²Li Y, Hruby A, Bernstein AM, et al. Saturated fats compared with unsaturated fats and sources of carbohydrates in relation to risk of coronary heart disease. *J Am Coll Cardiol*. 2015;66(14):1538-48.

³Guasch-Ferré M, Hernández-Alonso P, Drouin-Chartier JP, et al. Walnut Consumption, Plasma Metabolomics, and Risk of Type 2 Diabetes and Cardiovascular Disease. *J Nutr*. 2021;151(2):303-311.



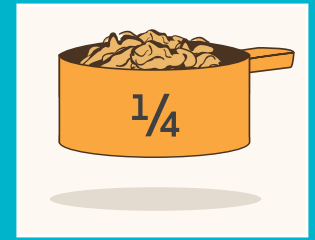


A DAILY SERVING

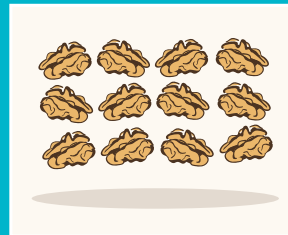
OF WALNUTS IS:



1 OUNCE



1/4 CUP



12-14 HALVES



1 HANDFUL

NUTRITION FACTS FOR WALNUTS

Nutrition Facts

Serving Size 1oz. (28g / about 1/4 cup)

Amount Per Serving
Calories 190

% Daily Value*

Total Fat 18g 23%

Saturated Fat 1.5g 8%

Trans Fat 0g

Polyunsaturated Fat 13g

Monounsaturated Fat 2.5g

Cholesterol 0mg 0%

Sodium 0mg 0%

Total Carbohydrate 4g 1%

Dietary Fiber 2g 7%

Total Sugars 1g

Incl. 0g Added Sugars 0%

Protein 4g

Vitamin D 0mcg 0%

Calcium 30mg 2%

Iron 0.8mg 4%

Potassium 130mg 2%

*The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

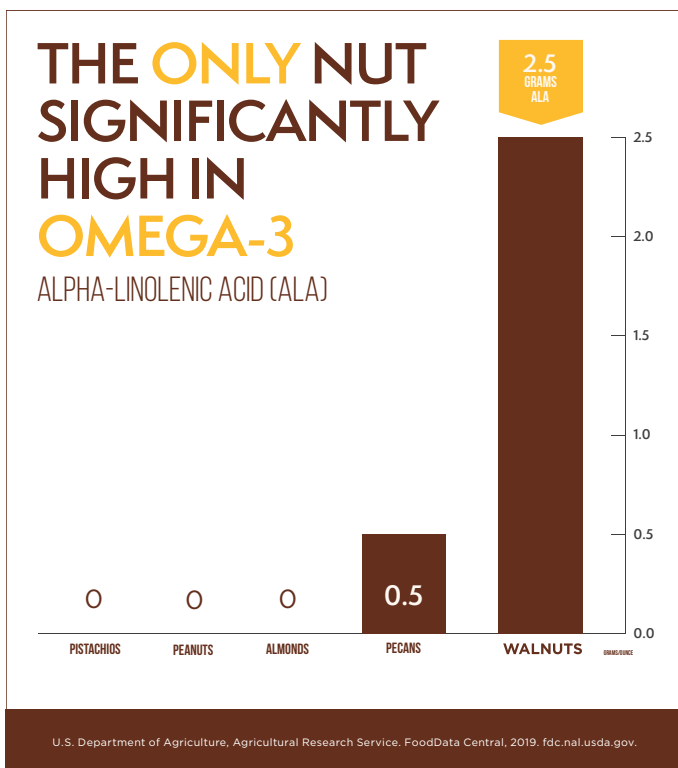
See page 17 for more information about the calorie count of walnuts.

ESSENTIAL OMEGA-3s

WALNUTS ARE UNIQUE AMONG NUTS

because they are primarily comprised of polyunsaturated fatty acids, or PUFAs, with 13 out of 18 grams of total fat per one ounce serving. Many other nuts contain mostly monounsaturated fatty acids (MUFAs). As a result, walnuts are the only nut that offer an excellent source of the plant-based omega-3 alpha-linolenic acid or ALA (2.5 grams per 1 ounce serving). Research specific to ALA and its contribution to health benefits continues to evolve.

Based on findings from a literature review, ALA may be as effective in reducing the risk of cardiovascular disease (CVD) as marine-derived omega-3s, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have been shown to be.¹ This review presented evidence for a beneficial role of ALA in the primary and secondary prevention of CVD.

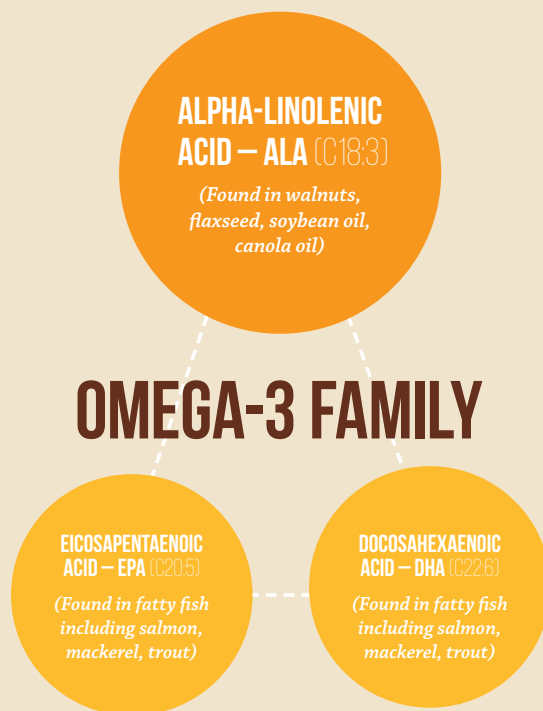


OMEGA-3 OVERVIEW

The predominant essential fatty acids in the human diet are alpha-linolenic acid (ALA, an omega-3 fatty acid) and linoleic acid (LA, an omega-6 fatty acid). ALA is the precursor or “parent” to two important long-chain omega-3 fatty acids: eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).²

In recent years, the number of studies describing the health-promoting benefits of omega-3 fatty acids has increased substantially, primarily in the area of heart health.¹

The role of ALA in the body relates to structural membrane lipids and a lack of ALA can result in a deficiency. The Dietary Reference Intake report that includes fatty acids set an adequate intake (AI) for ALA at 1.6 and 1.1 grams per day for men and women, respectively. While deficiency is rare, meeting the AI for ALA can provide the beneficial health effects associated with consumption of omega-3 fatty acids.²



AN OBSERVATION STUDY found that regular consumption of foods rich in omega-3 eicosapentaenoic acid (EPA), found in marine foods like fatty fish, and alpha-linolenic acid (ALA), found in plant foods like walnuts, was associated with improved outcomes in individuals who suffered a heart attack, including decreased risk of death.³

The study included 944 participants (mean age of 61) who experienced a ST-segment elevation myocardial infarction (STEMI). Researchers found that those who showed higher blood levels of ALA were at decreased risk of three-year all-cause mortality, and those with higher levels of EPA were at decreased risk of death or needing hospital readmission for cardiovascular reasons.

RESEARCH IN HEALTHY ADULTS (ages 18-35) exhibited that regularly eating foods that contain PUFAs, including walnuts, salmon, tuna, flaxseed oil, grapeseed oil, canola oil and fish oil supplements, may significantly improve fat metabolism and protect against the negative effects of saturated fats such as high cholesterol levels.⁴ For the study, researchers placed 26 healthy adults (13 men and 13 women) on a diet rich in polyunsaturated fats (21% polyunsaturated fat, 9% monounsaturated fat, and 5% saturated fat) or a control diet that was a typical American pattern (7% of polyunsaturated fat, 15% monounsaturated fat and 13% saturated fat) for seven days and had them consume a meal high in saturated fat (7% of polyunsaturated fat, 16% monounsaturated fat and 47% saturated fat) before and after the seven day diet. The diet rich in PUFAs was achieved by participants' consuming the whole foods described above in conjunction with fish oil supplements. Researchers observed significant decreases in total cholesterol (TC) and low-density lipoprotein (LDL) levels in the study participants who followed an eating plan rich in PUFAs, even though they were young, healthy and didn't have high cholesterol levels when the study began.

Though the findings cannot prove causality, the research demonstrates that consumption of both ALA and EPA provided the greatest benefit, suggesting a synergistic effect and unique protective qualities when both types of omega-3 are consumed.

Larger and longer-term studies, as well as studies in diverse populations, are needed to clarify population-wide effects.^{3,4} Additionally, more clinical trials are needed to evaluate the effects of ALA intake on cardiovascular disease risk as well as determine the optimal quantity of all dietary omega-3 PUFAs to offer the greatest health benefit.^{1,3,4}

¹Fleming JA, Kris-Etherton PM. The evidence for α -linolenic acid and cardiovascular disease benefits: comparisons with eicosapentaenoic acid and docosahexaenoic acid. *Adv Nutr.* 2014;5(6):863S-76S. ²Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids (Macronutrients) (2005) NAS. IOM. Food and Nutrition Board. ³Lázaro I, Rueda F, Cediel G, et al. Circulating Omega-3 Fatty Acids and Incident Adverse Events in Patients With Acute Myocardial Infarction. *J Am Coll Cardiol.* 2020; 76 (18) 2089-2097. ⁴Stevenson JL, Miller MK, Skillman HE, et al. A PUFA rich diet improves fat oxidation following saturated fat rich meal. *Eur J Nutr.* 2017;56(5):1845-1857.



WALNUTS & GUT HEALTH

EMERGING RESEARCH ON THE GUT MICROBIOME suggests walnuts may be one food to consider for gut health due to their prebiotic potential and possible role in providing a variety of associated health benefits.

A STUDY FROM THE USDA AND UNIVERSITY OF ILLINOIS found that walnut consumption was associated with positive changes to the gut microbiome.¹ A small sample of 18 healthy adults (ages 35-68) who ate 42 grams (about 1.5 ounces) of walnuts each day for three weeks experienced a decrease in secondary bile acids, which may play a role in colon cancer, inflammation, and gastrointestinal diseases. The study also found that eating walnuts resulted in an increase in gut bacteria that is thought to be beneficial for health.



CONSUMING A WALNUT-ENRICHED DIET POSITIVELY IMPACTED THE GUT MICROBIOME

by enhancing good probiotic- and butyric acid-producing bacteria in another study.² Butyric acid is thought to be useful for digestive health by helping to maintain the health of the colon. The study included 194 healthy German adults (mean age of 63 years old) randomized into two different diet phases, each lasting for eight weeks. One group ate 43 grams (about 1.5 ounces) of walnuts per day and then switched to a nut-free diet. The other group followed the diets in reverse order. During the walnut diet, participants were also randomized to reduce their intake of carbohydrates, fat, or both under the advisory of a nutritionist.

A CLINICAL TRIAL REVEALED THERE MAY BE A CONNECTION BETWEEN HEART AND GUT HEALTH

aided by the consumption of walnuts.³ Findings showed that consuming walnuts may enrich certain gut bacteria in the digestive system that are associated with improvements in blood pressure and cholesterol. Study participants included 42 overweight or obese (BMI: 25.0 – 39.9 kg/m²) individuals aged 30-65 and at risk for heart disease. All participants first followed an average American diet and then they were randomly assigned to a diet that replaced some saturated fat with either walnuts, a vegetable oil blend that included the same fatty acids as walnuts (including omega-3 ALA, a type of polyunsaturated fat), or a vegetable oil blend higher in monounsaturated fat. Individuals who consumed walnuts and the vegetable oil with the same fatty acid profile as walnuts had favorable changes in gut bacteria, suggesting a positive impact of omega-3 ALA. Those following the walnut diet only, had a unique enrichment of bacteria – one that plays an important role in metabolizing ellagitannins, a bioactive component of walnuts that may be associated with cardiovascular benefits.

Larger and longer-term studies are needed to clarify these effects in broader populations, and more research is needed to understand how specific bacterial species may be associated with favorable health effects, such as heart health.

WALNUT CONSUMPTION MAY BE BENEFICIAL FOR DIGESTIVE HEALTH

by increasing the amount of probiotic-type bacteria in the gut, as evidenced in an animal study.⁴ In this study, rats were randomly assigned an isocaloric and isonutrient diet containing ground walnuts (equivalent to about 2 ounces per day in humans) or a diet without walnuts for up to ten weeks. Calorie and nutrient intake were similar

between the two groups. Compared to those that did not consume walnuts, rats that ate a walnut-enriched diet saw an increase in beneficial bacteria including *Lactobacillus*, *Roseburia*, and *Ruminococcaceae*.

WALNUTS CAN PLAY A ROLE IN LIMITING GASTROINTESTINAL DAMAGE,

like stomach ulcers, caused by commonly consumed non-steroidal anti-inflammatory drugs (NSAIDs), according to a study.⁵ These animal study findings set the stage for future studies to explore the role of walnuts as a functional food for gut health in humans.

ANOTHER STUDY SUGGESTS regular walnut consumption may be a promising intervention for reducing negative outcomes associated with *Helicobacter pylori* (*H. pylori*) infection, a widespread bacterial infection that affects more than half of the world's population.⁶ Using mice models, researchers from the CHA Cancer Prevention Research Center in Korea found preliminary evidence that eating a diet rich in walnuts may help protect against negative outcomes associated with *H. pylori* infection. Specifically, the research found that walnut extracts, formed from whole walnuts, may help create protective proteins and anti-inflammatory actions in the gut that may safeguard against *H. pylori* infection and resulting cancer in mice.

Animal studies provide background that can be used to inform future studies needed to understand the effect on humans.^{4,5,6} Researchers studied mice that had colon cancer, which may have altered the normal function of the gut microbiome.⁴ Mice have different microbiota than humans, so further research is needed to determine how observed results may translate.^{4,5,6}

¹Holscher HD, Guetterman HM, Swanson KS, et al. Walnut Consumption Alters the Gastrointestinal Microbiota, Microbially Derived Secondary Bile Acids, and Health Markers in Healthy Adults: A Randomized Controlled Trial. *J Nutr*. 2018; 148, 861. ²Bamberger C, Rossmeier A, Lechner K, et al. A Walnut-Enriched Diet Affects Gut Microbiome in Healthy Caucasian Subjects: A Randomized, Controlled Trial. *Nutrients*. 2018; 10, 244. ³Tindall AM, McLimans CJ, Petersen KS, et al. Walnuts and Vegetable Oils Containing Oleic Acid Differentially Affect the Gut Microbiota and Associations with Cardiovascular Risk Factors: Follow-up of a Randomized, Controlled, Feeding Trial in Adults at Risk for Cardiovascular Disease [published online ahead of print December 18, 2019] *J Nutr*. ⁴Byerley LO, Samuelson D, Blanchard E, et al. Changes in the Gut Microbial Communities Following Addition of Walnuts to the Diet. *J Nutr Biochem*. 2017; 48, 94. ⁵An JM, Kim EH, Lee H, Lee HJ, Hahm KB. Dietary walnut as food factor to rescue from NSAID-induced gastrointestinal mucosal damages. *Archives of Biochemistry and Biophysics*. 2020; 687:108466. ⁶Park JM, Han YM, Park YJ, et al. Dietary intake of walnut prevented *Helicobacter pylori*-associated gastric cancer through rejuvenation of chronic atrophic gastritis. *J Clin Biochem Nutr*. 2021;68(1):37-50.

WALNUTS & COGNITIVE HEALTH

RESEARCH SUGGESTS walnut consumption may be associated with improved cognitive function.¹ Nutrients in walnuts, including polyphenols (69.3 ± 16.5 μmol catechin equivalents/g), tocopherols (5.91mg/oz) and polyunsaturated fatty acids (13g/oz) may play an important role.² Additionally, substantial research supports the inclusion of walnuts for cardiovascular health, which has been linked to brain health.

AGE-RELATED COGNITIVE DECLINE

A RANDOMIZED CLINICAL TRIAL found that eating a Mediterranean diet supplemented with olive oil or nuts (primarily walnuts) was correlated with reduced age-related decline in cognitive function in an older Spanish population (ages 55-80) at high cardiovascular risk.³ This clinical trial was conducted in a subcohort of the PREvención con Dieta MEDiterránea (PREDIMED) trial. Participants (447 total) were randomly assigned to a Mediterranean diet supplemented with either mixed nuts (15g walnuts, or about 0.5 ounces, 7.5g almonds and 7.5g hazelnuts per day) or extra virgin olive oil (at least 50 grams or 4 tablespoons per day), or a low-fat diet (control group). The study found participants who consumed a Mediterranean diet with nuts, including walnuts, showed improvements in memory compared to a low-fat diet.

RESEARCHERS FROM NYS INSTITUTE FOR BASIC RESEARCH IN DEVELOPMENTAL DISABILITIES

demonstrated that a diet including walnuts may have a beneficial effect in reducing the risk, delaying the onset or slowing the progression of Alzheimer's disease in an animal model.⁴ Researchers examined the effects of dietary supplementation with six percent or nine percent walnuts in mice (equivalent to 1 ounce and 1.5 ounces of walnuts per day in humans) compared to a control diet with no walnuts. The study found significant improvement in learning skills, memory, anxiety reduction and motor development in mice fed a walnut-enriched diet. This research stemmed from a cell culture study that highlighted the protective effects of walnut extract against the oxidative damage caused by amyloid beta protein, the major component of amyloid plaques that form as a result of Alzheimer's disease.⁵ Findings from animal and cell studies are provided as background and used to formulate hypotheses for additional research needed to determine the effects on humans.

COGNITIVE FUNCTION & MENTAL HEALTH

ACCORDING TO AN EPIDEMIOLOGICAL STUDY, eating walnuts may improve performance on cognitive function tests for memory, concentration and information processing speed in adults (ages 20-59 and 60 and older).⁶ This was seen even after adjusting for age, gender, race, education, BMI, smoking, alcohol consumption and physical activity. Analyses were based on single, 24-hour recalls, which reflect one day of intake. This retrospective cross-sectional study included cognitive data across multiple National Health and Nutrition Examination (NHANES) surveys, representing over 10,000 individuals in the U.S.

ANOTHER EPIDEMIOLOGICAL STUDY suggests consuming walnuts may be associated with lower depression symptoms in American adults.⁷ Based on NHANES data, adults (average age 46) who ate walnuts (just under 1 ounce per day) were more likely to have greater interest in activities, higher energy levels, less hopelessness (for women), better concentration and greater optimism, compared to those not consuming nuts - even after controlling for age, sex, race, BMI, smoking, alcohol consumption and marital status. This association appeared to be strongest in women, who are more likely to report greater depression symptoms and use of antidepressants.

A STUDY IN NUTRIENTS found that walnut consumption may help improve mood in men.⁸ Maintaining their typical diet and lifestyle habits, 64 college-age men and women ate about two ounces of walnuts daily for eight weeks. Mood was assessed using a common questionnaire (Profiles of Mood States) addressing tension, depression, anger, vigor, fatigue and confusion. Non-depressed healthy, young males (ages 18-25) showed a 27 percent reduction in overall mood disturbances. No significant changes in mood were observed in females or when data included both genders.

WALNUTS & HEALTHY AGING

IN ADDITION TO COGNITIVE HEALTH, maintaining and improving physical function and lowering the risk for chronic diseases are factors that can influence independence and quality of life as people age. Research demonstrated that eating a healthy diet that includes foods like walnuts was associated with reduced likelihood of developing physical impairment in older adults.^{9,10} Investigators examined data from 12,658 men from the Health Professionals Follow-Up Study and 54,762 women in the prospective Nurses' Health Study. An overall healthy diet pattern was more strongly associated with better physical function than an individual food. Greater intake of vegetables, legumes and nuts, including walnuts, polyunsaturated fats, and lower intake of red or processed meats and sugar-sweetened beverages each modestly lowered risk of impairment.

ANOTHER STUDY FOUND that women who consumed at least two servings of walnuts per week during their late 50s and early 60s were more likely to age healthfully compared to those who did not eat nuts.¹¹ In this study, "healthy aging" was defined as having no chronic diseases, reported memory impairment or physical disabilities as well as having intact mental health after the age of 65. Researchers looked at data from 33,931 women in the Nurses' Health Study to evaluate the association between nut consumption and overall health and well-being in aging. After accounting for various factors that could impact health in older adults such as age, education, income, BMI, calorie intake, smoking, physical activity and diet quality, researchers found a significant association between total nut intake (including peanuts, walnuts and other nuts) and higher odds of healthy aging. When looking at the impact of specific types of nuts, only walnuts were associated with significantly better odds of healthy aging.

For epidemiological studies, residual confounding cannot be ruled out (i.e., other lifestyle habits which are more common in adults who eat walnuts could contribute to the study results) and findings cannot

prove causality.^{6,7,8,9,10,11} More research is needed to clarify how the health benefits apply to other populations, as well as to determine the optimal quantity of walnuts needed to confer associated benefits.^{1,6,7,8,9,10} In the context of a Mediterranean diet, it is difficult to define what part of the diet is associated with cognitive health.¹

¹Poulose SM, Miller MG, Shukitt-Hale B. Role of walnuts in maintaining brain health with age. *J Nutr.* 2014, 144, 561S. ²The data for antioxidant capacity of foods generated by test-tube methods cannot be extrapolated to human effects. Clinical trials to test benefits of dietary antioxidants have produced mixed results. ³Valls-Pedret C, Sala-Vila A, Serra-Mir M, et al. Mediterranean diet and age-related cognitive decline: a randomized clinical trial. *JAMA Intern Med.* 2015, 175, 1094. ⁴Muthaiyah B, Essa MM, Lee M, et al. Dietary supplementation of walnuts improves memory deficits and learning skills in transgenic mouse model of Alzheimer's disease. *J Alzheimers Dis.* 2014, 42, 1397. ⁵Chauhan N, Wang KC, Wegiel J, et al. Walnut extract inhibits the fibrillization of amyloid beta-protein, and also defibrillizes its preformed fibrils. *Curr Alzheimer Res.* 2004, 1, 183. ⁶Arab L, Ang A. A cross sectional study of the association between walnut consumption and cognitive function among adult US populations represented in NHANES. *J Nutr Health Aging.* 2015, 19, 284. ⁷Arab L, Guo R, Elashoff D. Lower Depression Scores among Walnut Consumers in NHANES. *Nutrients.* 2019, 11, 275. ⁸Pribis P. Effects of Walnut Consumption on Mood in Young Adults – A Randomized Controlled Trial. *Nutrients.* 2016, 8, 668. ⁹Hagan KA, Grodstein F. The Alternative Healthy Eating Index and Physical Function Impairment in Men. *J Nutr Health Aging.* 2019, 23, 459. ¹⁰Hagan KA, Chiuve SE, Stampfer MJ, et al. Greater adherence to the alternative healthy eating index is associated with lower incidence of physical function impairment in the nurses' health study. *J Nutr.* 2016, 146, 1341. ¹¹Freitas-Simoes TM, Wagner M, Samieri C, et al. Consumption of Nuts at Midlife and Healthy Aging in Women [published online ahead of print January 17, 2020] *J Aging Res.*



WALNUTS & WEIGHT

Walnuts can be eaten as part of a healthy diet that won't contribute to weight gain or hinder weight loss goals.

APPETITE CONTROL

A RANDOMIZED TRIAL SHOWED that healthy adults (ages 18-35) who regularly consumed foods containing PUFAs experienced favorable changes in appetite hormones associated with hunger and satiety.¹ Twenty-six participants consumed meals high in saturated fat at the beginning of the study and then were placed on a seven-day control diet consisting of a typical American eating pattern or a diet high in PUFAs (included foods such as walnuts, Alaska salmon, tuna, canola oil, and fish oil supplements). After the seven-day diet, participants consumed meals high in saturated fat, again. Participants who consumed a PUFA-rich diet had a significant decrease

in fasting ghrelin, a hormone that increases hunger, and a significant increase in peptide YY (PYY), a hormone that increases fullness or satiety. Participants saw increases in PYY while fasting and after consuming a meal. These hormone changes could help with better appetite control although it is difficult to know if the changes are due to a specific type of PUFA, food, or a combination of overall dietary factors.

RESEARCHERS FOUND WALNUTS MAY INCREASE SATIETY and sense of fullness in a short-term study at Beth Israel Deaconess Medical Center and Harvard Medical School.² Twenty men and women (ages 57-61) with metabolic syndrome participated in this randomized, double blind, cross-over study. For four days, subjects consumed isocaloric diets including a liquid meal with either 48 grams of walnuts (approximately 1.7 ounces) or no walnuts. The walnut meal was rich in PUFAs whereas the placebo was rich in monounsaturated fats (MUFAs). By the third day of the study, subjects on the walnut-containing diet reported feeling more satiated and had a significantly higher rate of feeling full compared to those on the placebo diet.

RESEARCHERS HAVE ALSO USED MAGNETIC RESONANCE IMAGING (MRI) to explore possible connections between walnut consumption and important functions in the body. Investigators from the Beth Israel Deaconess Medical Center found that eating walnuts may activate an area of the brain associated with hunger and cravings.³ Ten obese adult participants (ages 48-54) lived at the medical center for two five-day sessions and were closely monitored for food intake and appetite. Participants reported feeling fuller when they consumed a daily smoothie with 48 grams of walnuts (approximately 1.7 ounces), compared to when they consumed a placebo smoothie with the same macronutrient content but with safflower oil instead of walnuts. Researchers saw increased activity in a part of the brain that is thought to be involved in cognitive control and salience, suggesting participants paid more attention to food choices after eating walnuts.

CALORIE CONTENT

A STUDY FROM THE UNITED STATES DEPARTMENT OF AGRICULTURE (USDA) found that one serving of walnuts (1 ounce) may provide 146 calories, which is 39 calories less, or 21 percent fewer, than the 185 calories listed in the USDA FoodData Central.⁹ Eighteen healthy adults were randomly assigned to a sequence of two isocaloric diets: A controlled American diet without walnuts for a three-week period, and a controlled diet with 1.5 servings of walnuts (1.5 ounces) for another three-week period. Bomb calorimetry was used to measure calories and then the data was used to calculate the metabolizable energy of the walnuts. The study took into account the digestibility of walnut pieces and halves and further research is needed to better understand the results of the study and how this technique for calculating calories could potentially affect the calorie count of other foods.

BODY WEIGHT & COMPOSITION

A STUDY USED IMAGING TECHNOLOGY to map body organ fat storage pools in 278 participants (ages 28-69; mostly male and obese) following two types of diet: a Mediterranean, low-carbohydrate diet that included one ounce of walnuts per day and a low-fat diet, with and without moderate exercise.⁴ After following the diets for 18 months, the Mediterranean, low-carbohydrate diet with walnuts was found to be most effective in reducing fat deposits around the liver, abdomen, and heart. Adding exercise provided additional benefit for visceral fat loss in all groups.

Total lean body mass or fat mass measurements were not available from the MRI analysis. Since this intervention involved dietary and physical activity changes, it is difficult to identify the exact factors responsible for the effects.

RESEARCH FOUND that a diet containing unsaturated fats, such as those found in walnuts and olive oil, may have similar effects on weight loss as compared to a lower fat, higher carbohydrate diet among overweight and obese women.^{5,6} Two hundred forty-five women (ages 22-72) were enrolled in a one-year behavioral weight loss intervention and randomly assigned to three different diets: 1) a lower fat, higher carbohydrate diet (excluded nuts), 2) a lower carbohydrate, higher fat diet (excluded nuts), or 3) a walnut-rich (1.5 ounces per day), higher fat, lower carbohydrate diet. Participants reduced their intake by 500-1000 calories per day under dietary guidance from a dietitian and were encouraged to exercise at moderate intensity for at least 60 minutes per day. Another study with a similar design found a walnut-enriched (1-1.5 ounces per day), reduced-calorie diet had similar effects on weight loss compared to a standard reduced-calorie diet.⁷ One-hundred overweight and obese adults (average age 52-53) followed a behavioral weight loss intervention for six months instead of one year. In these studies, weight loss was similar across all diet groups, demonstrating that walnuts may play a role in achieving ideal body weight, when consumed as part of an overall healthy diet.

AN OBSERVATIONAL STUDY found that increasing daily nut consumption by just half a serving (1/2 ounce) was linked to less weight gain and lower risk



*Toasted Walnut,
Black Bean, Corn
and Tomato Salad*

of obesity.⁸ Researchers investigated the association between nut consumption and weight change by analyzing more than 20 years of data from the Health Professionals Follow-Up Study, Nurses' Health Study and Nurses' Health Study II. In total, these cohorts included 289,915 men and women ages 24-75. An increase in consumption of walnuts and other tree nuts by half a serving per day was associated with a 15 percent and 11 percent lower risk of developing obesity and lesser weight gain of -0.37 and -0.36 kilograms (-0.82 and -0.79 pounds), respectively.

Information on dietary intake and diet adherence may have been limited in studies where participants were free-living and data was self-reported.^{1,2,3,5} Larger and longer-term studies, as well as studies in more diverse populations, are needed to understand population-wide effects.^{1,2,3}

¹Stevenson JL, Paton CM, Cooper JA. Hunger and satiety responses to high-fat meals after high polyunsaturated fat diet: a randomized trial. *Nutrition*. 2017, 41, 14. ²Brennan AM, Sweeney LL, Liu X, et al. Walnut consumption increases satiation but has no effect on insulin resistance or the metabolic profile over a 4-day period. *Obesity (Silver Spring)*. 2010, 18, 1176. ³Farr OM, Tuccinardi D, Upadhyay J, et al. Walnut consumption increases activation of the insula to highly desirable food cues: A randomized, double-blind, placebo-controlled, cross-over fMRI study. *Diabetes Obes Metab*. 2018, 20, 173. ⁴Gepner Y, Shelef I, Schwarzfuchs D, et al. Effect of Distinct Lifestyle Interventions on Mobilization of Fat Storage Pools: CENTRAL Magnetic Resonance Imaging Randomized Controlled Trial. *Circulation*. 2018, 137, 1143. ⁵Rock CL, Flatt SW, Pakiz B, et al. Effects of diet composition on weight loss, metabolic factors and biomarkers in a 1-year weight loss intervention in obese women examined by baseline insulin resistance status. *Metabolism*. 2016, 65, 1605. ⁶Le T, Flatt SW, Natarajan L, et al. Effects of diet composition and insulin resistance status on plasma lipid levels in a weight loss intervention in women. *J Am Heart Assoc*. 2016, 25. ⁷Rock CL, Flatt SW, and Barkai HS. Walnut consumption in a weight reduction intervention: effects on body weight, biological measures, blood pressure and satiety. *Nutr J*. 2017, 16, 76. ⁸Liu X, Li Y, Guasch-Ferré M, et al. Changes in nut consumption influence long-term weight change in US men and women. *BMJ NPH*. 2019, 0, 1. ⁹Baer DJ, Gebauer SK, Novotny JA. Walnuts consumed by healthy adults provide fewer available calories than predicted by the atwater factors. *J Nutr*. 2016, 146, 9.

WALNUTS & HEART HEALTH

SINCE 1993, published research has been investigating how eating walnuts affects various heart health biomarkers and risk markers including:

- LDL and HDL cholesterol
- Apolipoprotein B and non-HDL cholesterol
- Blood pressure
- Inflammation
- Endothelial function
- Plaque formation

WALNUTS ARE CERTIFIED BY THE AMERICAN HEART ASSOCIATION WITH THE HEART-CHECK MARK



**PER 1 OZ.
SERVING**

Please note that the Heart-Check Food Certification does not apply to scientific research by an organization other than the AHA unless expressly stated. For more information, see the AHA nutrition guidelines at: heartcheckmark.org/guidelines.

Butternut Squash, Quinoa, Pear and Walnut Bowl





A RANDOMIZED CONTROLLED TRIAL FOUND that people in their 60s and 70s who regularly consume walnuts may have reduced inflammation, a factor associated with a lower risk of heart disease, compared to those who do not eat walnuts.¹ The research was part of the Walnuts and Healthy Aging (WAHA) study – the largest and longest trial to date exploring the benefits of daily walnut consumption.

In the study, more than 600 healthy older adults consumed 30 to 60 grams of walnuts per day as part of their typical diet or followed their standard diet (without walnuts) for two years. Those who consumed walnuts had a significant reduction in inflammation, measured by the concentration of known inflammatory markers in the blood, which were reduced by up to 11.5%. The study's conclusion is that the anti-inflammatory effects of walnuts provide a mechanistic explanation for cardiovascular disease reduction beyond cholesterol lowering.

RESEARCH FROM THE PREVENCIÓN CON DIETA MEDITERRÁNEA (PREDIMED) study further demonstrated the potential heart health benefits of walnuts. The study was conducted among more than 7,000 Spanish individuals (ages 55-80) at high risk for cardiovascular disease and found that a Mediterranean diet supplemented with mixed tree nuts (primarily walnuts), was associated with a lower risk of cardiovascular events, including cardiovascular death, myocardial infarction (heart attack), and stroke, when compared to a low-fat control diet.²

Larger and longer-term studies, as well as studies in more diverse populations, are needed to clarify population-wide effects.^{1,2} In the PREDIMED study, it is difficult to precisely define what part of the Mediterranean diet was associated with cardiovascular benefits.²

Due to the evidence supporting the cardiovascular benefits of walnuts, the U.S. Food and Drug Administration approved one of the first qualified health claims for a whole food in March of 2004: “Supportive but not conclusive research shows that eating 1.5 ounces of walnuts per day, as part of a low saturated fat and low cholesterol diet, and not resulting in increased caloric intake may reduce the risk of coronary heart disease.”³

¹Cofán M, Rajaram S, Sala-Vila A, et al. Effects of 2-Year Walnut-Supplemented Diet on Inflammatory Biomarkers. *J Am Coll Cardiol*. 2020 Nov, 76 (19) 2282-2284. ²Estruch R, Ros E, Salas-Salvadó J, et al. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. *N Engl J Med*. 2018;378(25):e34. ³One ounce of walnuts provides 18g of total fat, 2.5g of monounsaturated fat, 13g of polyunsaturated fat, including 2.5g of alpha-linolenic acid, the plant-based omega-3.

WALNUTS & CANCER

A healthy eating pattern that includes a variety of plant-forward foods such as vegetables, fruits, grains, oils, nuts and seeds, as well as protein and fat-free or low-fat dairy, is associated with a reduced risk of certain types of cancers, according to the Dietary Guidelines for Americans.¹ Walnuts offer a variety of important nutrients, including good fats (13g/oz polyunsaturated fat), making them an ideal ingredient for plant-forward meals.

A pilot clinical trial and preliminarily animal and cell model research have investigated the potential benefit walnuts may have on cancer. A review of animal research pointed toward multiple nutrients in walnuts that may act in various ways to help decrease risk of cancer development.² Animal and cell studies are provided as background and used to formulate hypotheses for additional research needed to determine the effects on humans.

BREAST CANCER

INFORMATION ABOUT WALNUT CONSUMPTION AND BREAST CANCER was revealed in a pilot clinical trial.³ This small study of ten women (ages 45-67) found those with breast cancer who consumed two

ounces of walnuts per day for about two weeks experienced beneficial genetic changes related to cancer development and growth. This is encouraging, but much larger and longer-term studies are needed before any conclusions can be made based on these findings.

A STUDY LOOKED AT the role of walnut consumption on potential breast cancer protection in maternal mice and their offspring. Researchers found that a diet including a modest amount of walnuts (equivalent to 2 ounces per day in humans) was associated with a decreased risk of breast cancer in mice.⁴ Maternal mice were randomized to a control diet with corn oil or a diet containing walnuts, and both diets were designed to be isocaloric and isonutrient. The maternal mice were then bred, and the offspring were randomized to the same two diets after weaning. The findings showed a significant reduction in tumor incidence, number and size in maternal and offspring mice that consumed walnuts compared to mice that did not consume walnuts.

Researchers have found that a diet including a modest amount of walnuts (equivalent to 2 ounces per day in humans) may be associated with a lower risk of breast, colorectal, and prostate cancer in mice.



COLORECTAL CANCER

A STUDY FOUND that eating walnuts may modify gut bacteria to promote colon health including colon tumor suppression.⁵ In the study, researchers incorporated walnuts into two different diets, a standard mouse diet supplemented with 0, 15, 22.5, or 30.2 percent of calories from walnuts and a typical Western diet supplemented with 0, 5.2, 10.5, or 21.4 percent of calories from walnuts. Calories from fat were proportionally lowered in each diet to compensate for the addition of walnuts. Male mice fed the Western diet with 10.5 percent of total calories from walnuts (equivalent to just over 1 ounce of walnuts in humans), showed a significant reduction in the number and size of tumors.

ANOTHER STUDY DEMONSTRATED that walnuts in the diet may inhibit colorectal cancer growth in mice by suppressing angiogenesis.⁶ In this study, mice with human colon cancer cells were randomized to diets containing approximately 19 percent of total energy from corn oil (control diet), flaxseed oil, or ground walnuts (equivalent to approximately 2 ounces of walnuts in humans). Compared with the corn oil diet, mice fed the walnut diet or flaxseed diet exhibited significantly slower tumor growth rates and lower tumor weights. Differences between the walnut and flaxseed diets were not statistically significant, but compared to control-fed mice, those consuming walnuts experienced significantly decreased angiogenesis which may help inhibit the progression of colorectal cancer.

PROSTATE CANCER

WALNUTS CONTAIN SEVERAL BIOACTIVE compounds including ellagitannins (ETs), a type of polyphenol. After consumption, ETs are metabolized to release ellagic acid (EA), which is further metabolized by gut microbiota to form urolithins, such as A (UA) and B (UB). A cell study looked at gene expression in prostate cancer cells and found that UA, the main human metabolite of walnut polyphenols, may help to inhibit or reduce the risk of prostate cancer development.⁷ Another cell study showed that a diet rich in ET-containing foods, like walnuts, could reduce the risk of prostate cancer by influencing regulatory mechanisms involved.⁸

EXPERIMENTAL RESEARCH SHOWED that walnuts may help reduce prostate cancer risk in mice.⁹ Researchers found the final average tumor size in mice fed a diet enriched with walnuts (equivalent to 2 ounces of walnuts per day in humans) to be approximately 25 percent of the average size of the prostate tumors in the mice that consumed a non-walnut control diet.

¹U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025. 9th Edition. December 2020. Available at [DietaryGuidelines.gov](https://www.dietaryguidelines.gov). ²Hardman, WE. Walnuts have potential for cancer prevention and treatment in mice. *J Nutr*. 2014, 144, 555S. ³Hardman WE, Primerano DA, Legenza MT, et al. Dietary walnut altered gene expressions related to tumor growth, survival, and metastasis in breast Cancer patients: A pilot clinical trial. *Nutr Research*. 2019, 66, 82. ⁴Hardman WE, Ion G, Akinsete JA, et al. Dietary walnut suppressed mammary gland tumorigenesis in the C(3)1 Tag mouse. *Nutr Cancer*. 2011, 63, 960. ⁵Nakanishi M, Chen Y, Qendro V, et al. Effects of walnut consumption on colon carcinogenesis and microbial community structure. *Cancer Prev Res (Phila)*. 2016, 9, 692. ⁶Nagel JM, Brinkoetter M, Magkos F, et al. Dietary walnuts inhibit colorectal cancer growth in mice by suppressing angiogenesis. *Nutrition*. 2012, 28, 67. ⁷Sánchez-González C, Ciudad CJ, Izquierdo-Pulido M, et al. Urolithin A causes p21 up-regulation in prostate cancer cells. *Eur J Nutr*. 2016, 55, 1099. ⁸Sánchez-González C, Ciudad CJ, Noé V, et al. Walnut polyphenol metabolites, urolithins A and B, inhibit the expression of the prostate-specific antigen and the androgen receptor in prostate cancer cells. *Food Funct*. 2014, 5, 2922. ⁹Reiter RJ, Tan DX, Manchester LC, et al. A walnut-enriched diet reduces the growth of LNCaP human prostate cancer xenografts in nude mice. *Cancer Invest*. 2013, 31, 365.



WALNUTS & DIABETES AND METABOLIC SYNDROME

INDIVIDUALS WITH DIABETES OR METABOLIC SYNDROME often have conditions such as elevated blood pressure, cholesterol, or triglycerides, which can increase the risk for heart disease and stroke. Research on the association between walnut consumption and these conditions demonstrate the importance of walnuts as part of a healthy diet to help manage complications associated with diabetes and metabolic syndrome.

DIABETES

IN A NOVEL RESEARCH APPROACH, investigators from the Harvard T.H. Chan School of Public Health in collaboration with investigators from Rovira i Virgili University and the University of Navarra, Spain, used machine learning models, a subset of artificial intelligence, to identify more precisely the components in walnuts that may be responsible for potentially reducing the risk of type 2 diabetes and cardiovascular diseases.¹

The study used a novel machine learning model to identify 19 markers in the body that were associated with walnut consumption - a "walnut signature." The body forms specific metabolites based on what food is consumed. Researchers examined data from 1,833 participants from the PREvención con Dieta MEDiterránea (PREDIMED) study, who were at high cardiovascular risk, and found the "walnut signature" was associated with a 17% lower risk of type 2 diabetes and 29% lower risk of cardiovascular disease.

Though findings do not prove causality, new tools as used in this epidemiological study will help identify links between diet and disease.

AN EPIDEMIOLOGICAL STUDY representing more than 34,000 American adults suggests that those who consume walnuts may have about half the risk of developing type 2 diabetes compared to adults who do not eat nuts.² Researchers from the University of California Los Angeles looked at data from the National Health and Nutrition Examination Survey (NHANES), in which adults (ages 18-85) were asked about their dietary intake over the course of one to two days and assessed for diabetes. According to the study, the average intake among walnut consumers was approximately one and a half tablespoons per

day. Doubling walnut consumption (eating three tablespoons) was associated with a 47 percent lower prevalence of type 2 diabetes. The study did not look at the impact of increasing walnut consumption beyond doubled intake.

RESEARCHERS FROM HARVARD found that walnut consumption was associated with a significantly lower risk of type 2 diabetes in women who regularly consumed walnuts compared with women who never/rarely consumed walnuts.³ The study looked at two large prospective cohorts of U.S. women: The Nurses' Health Study (NHS) and NHS II, which followed 58,063 women (ages 52-77) in NHS (1998-2008) and 79,893 women (ages 35-52) in NHS II (1999-2009) without diabetes, cardiovascular disease or cancer at baseline. They found two or more servings (1 serving is equivalent to 1 ounce) of walnuts per week, as part of a healthy diet, was associated with a 21 percent and 15 percent lower risk of incident type 2 diabetes before and after adjusting for body mass index (BMI), respectively.

Research has found that including the right type of fats, like those found in walnuts, can be beneficial to people with diabetes.



METABOLIC SYNDROME

A STUDY found that short-term consumption of walnuts may improve blood lipids, by increasing apolipoprotein A concentration.⁴ Apolipoprotein A is the primary protein component of HDL, and is one of many factors that may be considered in a complete lipid profile when estimating cardiovascular disease risk. For this study, 15 obese subjects (ages 56-61) with metabolic syndrome were enrolled in a randomized, double-blinded, placebo-controlled crossover study in which they consumed two different isocaloric diets, one with 48 grams of walnuts daily (approximately 1.7 ounces) and one without walnuts for four days each. The results suggest that eating walnuts may have a beneficial effect on lipid metabolism even within short-term consumption.

Larger and longer-term studies, as well as studies in more diverse populations, are needed to clarify population-wide effects. In some cases, residual confounding cannot be ruled out (i.e., other lifestyle factors which are more common in adults who eat walnuts could contribute to the study results).^{1,2,4}

¹Guasch-Ferré M, Hernández-Alonso P, Drouin-Chartier JP, et al. Walnut Consumption, Plasma Metabolomics, and Risk of Type 2 Diabetes and Cardiovascular Disease. *J Nutr.* 2021;151(2):303-311. ²Arab L, Dhaliwal SK, Martin CJ, et al. Association between walnut consumption and diabetes risk in NHANES [published online ahead of print June 21, 2018]. *Diabetes Metab Res Rev.* doi.org/10.1002/dmrr.3031. ³Pan A, Sun Q, Manson JE, et al. Walnut consumption is associated with lower risk of type 2 diabetes in women. *J Nutr.* 2013;143(4):512-8. ⁴Aronis KN, Vamvini MT, Chamberland JP, et al. Short-term walnut consumption increases circulating total adiponectin and apolipoprotein A concentrations, but does not affect markers of inflammation or vascular injury in obese humans with the metabolic syndrome: data from a double-blinded, randomized, placebo-controlled study. *Metabolism.* 2012;61(4):577-82.



Thai Walnut BBQ Chicken Bowl



WALNUTS & REPRODUCTIVE HEALTH

THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE has found evidence that infertility affects men and women equally. Twenty-five percent of infertile couples have more than one factor that contributes to their infertility.¹

Walnut health studies have provided encouraging results regarding the role of walnuts in reproductive health.

A STUDY found healthy young men (ages 21-35) who ate 75 grams (approximately 2.5 ounces) of walnuts per day experienced positive shifts in sperm quality factors, including sperm vitality, motility (movement) and morphology (form).² Sperm quality is an indicator of male fertility.³ This randomized, parallel two-group dietary intervention trial included 117 participants who routinely ate a Western-style diet. Approximately half were assigned to consume 75 grams of walnuts per day for 12 weeks as part of their usual diet, while the remaining half followed their typical diet but avoided consumption of tree nuts.

Consuming walnuts may have contributed to shifts in certain sperm quality factors in these healthy young men, but more research is needed to understand how these findings impact the broader male population, including men in fertility clinics. This study also reported higher amounts of alpha-linolenic acid (ALA), provided by walnuts, correlated with less frequent sperm aneuploidy (abnormal cell chromosome numbers), which can result in genetic abnormalities such as Down syndrome. Walnuts are the only nut with an excellent source of ALA, the plant-based omega-3 fatty acid (2.5g/oz).

ANOTHER STUDY explored possible mechanistic reasons for the results seen in the clinical trial. Mice fed a walnut-rich diet showed a reduction in lipid peroxidation, a process that can damage sperm cells.⁴ This form of cell damage harms sperm membranes, which are primarily made up of polyunsaturated fatty acids (PUFAs). Previous studies have shown that PUFAs may play a role in sperm health and membrane function. Walnuts are the only tree nut that are predominantly comprised of PUFAs (1 ounce

contains 13 grams of PUFAs out of 18 grams of total fat), which is why they were included in this study. This promising animal research provides important insight, but the results are inconclusive regarding the effects on humans and how PUFAs function to reduce lipid peroxidation. Future human clinical studies are needed.

A CLINICAL TRIAL that examined the impact of a Mediterranean diet on maternal and offspring outcomes showed encouraging results. The study examined 1,252 multi-ethnic inner-city pregnant women in England with metabolic risk factors, including obesity and chronic hypertension. Researchers found those who followed a Mediterranean-style diet with a daily portion of nuts (30g/day or just over 1 ounce of mixed nuts; 15g walnuts, 7.5g almonds, 7.5g hazelnuts) and extra virgin olive oil saw a 35 percent lower risk of gestational diabetes and on average, gained 2.75 pounds less, compared to women who received standard prenatal care.⁵

In these studies, information on dietary intake and diet adherence was limited since participants were free-living and data was self-reported.^{3,5} In the study on healthy young men, collection of blood specimens for hormone analysis occurred throughout the day to accommodate busy schedules of the subjects, but participants were asked to return at the same time of day for follow-up appointments to maintain consistency in the data collection.³ In the context of a whole food diet, it is difficult to discern whether changes can be attributed to one specific food source or a combination of factors.^{3,5}

¹American Society for Reproductive Medicine. (2016). Quick Facts About Infertility. Retrieved from www.reproductivefacts.org/faqs/quick-facts-about-infertility/ ²Robbins WA, Xun L, FitzGerald LZ, et al. Walnuts improve semen quality in men consuming a Western-style diet: randomized control dietary intervention trial. *Biol Reprod.* 2012, 87, 101. ³World Health Organization. Laboratory Manual for the Examination and Processing of Human Semen, 5th ed. Cambridge, UK: Cambridge University Press; 2010. ⁴Coffua LS, Martin-DeLeon PA. Effectiveness of a walnuts-enriched diet on murine sperm: involvement of reduced peroxidative damage. *Heliyon.* 2017, 3. ⁵H. Al Wattar B, Dodds J, Placzek A, Beresford L, Spyrelli E, Moore A, et al. Mediterranean-style diet in pregnant women with metabolic risk factors (ESTEEM): A pragmatic multicentre randomised trial. *PLoS Med* 2019, 16, e1002857.

MEDITERRANEAN DIET & HEALTH

THERE ARE VARIOUS FORMS of the Mediterranean diet, which emphasizes more fruits and vegetables, nuts and seeds (including walnuts), grains, olive oil, moderate amounts of fish, poultry, eggs and wine, and limits the amounts of red meat, processed meat, dairy and sweets.¹ The U.S. Dietary Guidelines for Americans recommends a Mediterranean-style eating pattern as one example of a healthy diet plan.²

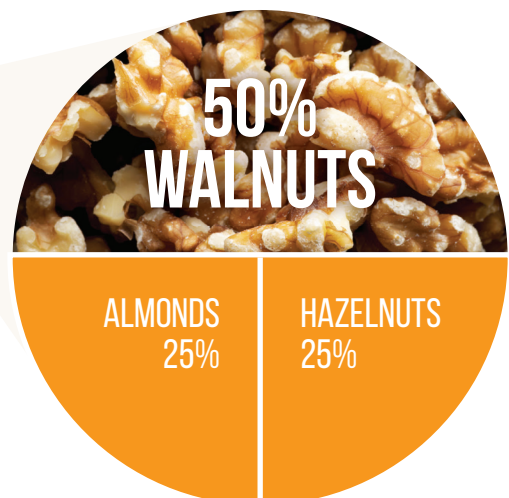
PREDIMED (PREvención con Dieta MEDiterránea = Prevention with Mediterranean Diet) was a landmark study aimed at assessing the efficacy of the Mediterranean diet in the primary prevention of cardiovascular disease.³ Researchers examined whether a Mediterranean diet supplemented with extra-virgin olive oil or mixed tree nuts (50% walnuts, 25% almonds, and 25% hazelnuts), compared to a low-fat diet, could help reduce the risk of major cardiovascular events, including cardiovascular death, myocardial infarction (heart attack) and stroke. The study was a parallel group, multi-center, single blind, randomized clinical trial that was conducted by 16 research groups and seven communities and

supported by the Spanish Health Ministry. Participants included 7,447 Spanish individuals (ages 55-80) at high risk of cardiovascular disease, but without symptoms at baseline, and were followed for a median of 4.8 years. Subjects were randomly assigned to one of three diet groups, content listed below, and were given dietetic support and educational sessions to ensure compliance. Energy intake was not specifically restricted in any intervention group.

A Mediterranean diet including tree nuts, primarily walnuts, was associated with a 30 percent lower risk of cardiovascular events (myocardial infarction, stroke or cardiovascular death) and specifically, a 46 percent lower risk of stroke, when compared to a low-fat diet.

PREDIMED DIET GROUPS

1. Mediterranean diet supplemented with **MIXED NUTS** (30 g per day; 15g walnuts (about 0.5 ounces), 7.5g almonds and 7.5g hazelnuts)
2. Mediterranean diet supplemented with **EXTRA VIRGIN OLIVE OIL** (at least 50g or 4 tablespoons per day)
3. **LOW-FAT DIET** (control group; American Heart Association guidelines)



The Mediterranean diet enriched with extra-virgin olive oil also reduced the risk of cardiovascular diseases by 30 percent. More than 300 additional publications have resulted from the PREDIMED research investigating outcomes such as cognitive function,⁴ blood pressure,⁵ total cholesterol,⁵ and fasting glucose.⁵

The study had some limitations including the fact that participants lived in a Mediterranean country and were at high risk for cardiovascular disease. More research is needed to clarify the health benefits in other populations. Additionally, it is difficult to precisely define what part of the Mediterranean diet was associated with cardiovascular benefits.

A few research papers have published exploring the various health benefits of a green Mediterranean diet, including 28 g/day walnuts, 3–4 cups/day of green tea and 100 g frozen cubes of *Wolffia globosa* duckweed (Mankai) among a study population of 294 participants with abdominal obesity/dyslipidemia.^{6,7,8} An 18-month randomized control trial found that those following a green Mediterranean diet showed beneficial changes in their gut microbiota and reduced risk of non-alcoholic fatty liver disease by half.⁶ Another study found that after 6 months, those who followed a green Mediterranean diet lost more weight and had a larger decrease in LDL cholesterol as well as insulin resistance than those following a traditional Mediterranean diet or healthy diet.⁷ Lastly, a study, explored fecal microbiota transplantation as a novel approach to understand the potential impact on lessening weight regain after being on a weight-loss diet, among individuals who were obese or had dyslipidemia.⁸ Individuals who followed a green Mediterranean diet, and consumed capsules of their

own fecal microbiome, had significantly limited weight regain between months 6-14, compared to those who followed the same green-Mediterranean diet but consumed the placebo capsules.

While researchers aren't sure why they see these results, what seems to be consistent is starting with a foundation of a healthy Mediterranean diet with fruits, vegetables, grains, olive oil, walnuts and seeds, and then adding a layer of tea and microgreens.

Larger and longer-term studies, as well as studies in more diverse populations, are needed to understand population-wide effects. Information on diet intake and adherence may have been limited because participants were free-living and data was self-reported.^{6,7,8}

¹Willett WC, Sacks F, Trichopoulos A, et al. Mediterranean diet pyramid: a cultural model for healthy eating. *Am J Clin Nutr* 1995;61(6 Suppl):1402S-1406S. ²U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025. 9th Edition. December 2020. Available at DietaryGuidelines.gov. ³Estruch R, Ros E, Salas-Salvadó J, et al. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. *N Engl J Med*. 2018;378(25):e34. ⁴Valls-Pedret C, Sala-Vila A, Serra-Mir M, et al. Mediterranean diet and age-related cognitive decline: a randomized clinical trial. *JAMA Intern Med*. 2015;175(7):1094-103. ⁵Doménech M, Roman P, Lapetra J, et al. Mediterranean diet reduces 24-hour ambulatory blood pressure, blood glucose, and lipids: one-year randomized, clinical trial. *Hypertension*. 2014 Jul;64(1):69-76. ⁶Yaskolka Meir A, Rinott E, Tsaban G, et al. Effect of green-Mediterranean diet on intrahepatic fat: the DIRECT PLUS randomised controlled trial. *Gut*. Epub ahead of print: [January 2018, 2021]. ⁷Tsaban G, Yaskolka Meir A, Rinott E, et al. The effect of green Mediterranean diet on cardiometabolic risk; a randomised controlled trial. *Heart* Published Online First: 23 November 2020. ⁸Rinott E, Youngster I, Meir AY, Tsaban G, Zelicha H, Kaplan A, Knights D, Tuohy K, Fava F, Scholz MU, Ziv O, Reuven E, Tirosh A, Rudich A, Blüher M, Stumvoll M, Ceglarek U, Clement K, Koren O, Wang DD, Hu FB, Stampfer MJ, Shai I, Effects of Diet-Modulated Autologous Fecal Microbiota Transplantation on Weight Regain, *Gastroenterology* (2020).





CALIFORNIA WALNUT BOARD & COMMISSION

101 Parkshore Drive, Suite 250
Folsom, CA 95630

info@walnuts.org
www.walnuts.org

Follow us @CAWalnuts

