



CALIFORNIA WALNUTS NUTRITION & SCIENTIFIC RESEARCH

A RESOURCE GUIDE
FOR HEALTH
PROFESSIONALS





TABLE OF CONTENTS

Why Walnuts? | **4**

Essential Omega-3s | **6**

Health Research on Walnuts | **9**

Heart Health | **10**

Healthy Aging | **12**

- Cognitive Health
- Physical Function

Cancer | **14**

- Breast Cancer
- Colorectal Cancer
- Prostate Cancer

Diabetes and Metabolic Syndrome | **16**

Weight | **18**

Mediterranean Diet | **20**

Male Reproductive Health | **23**

WHY WALNUTS?

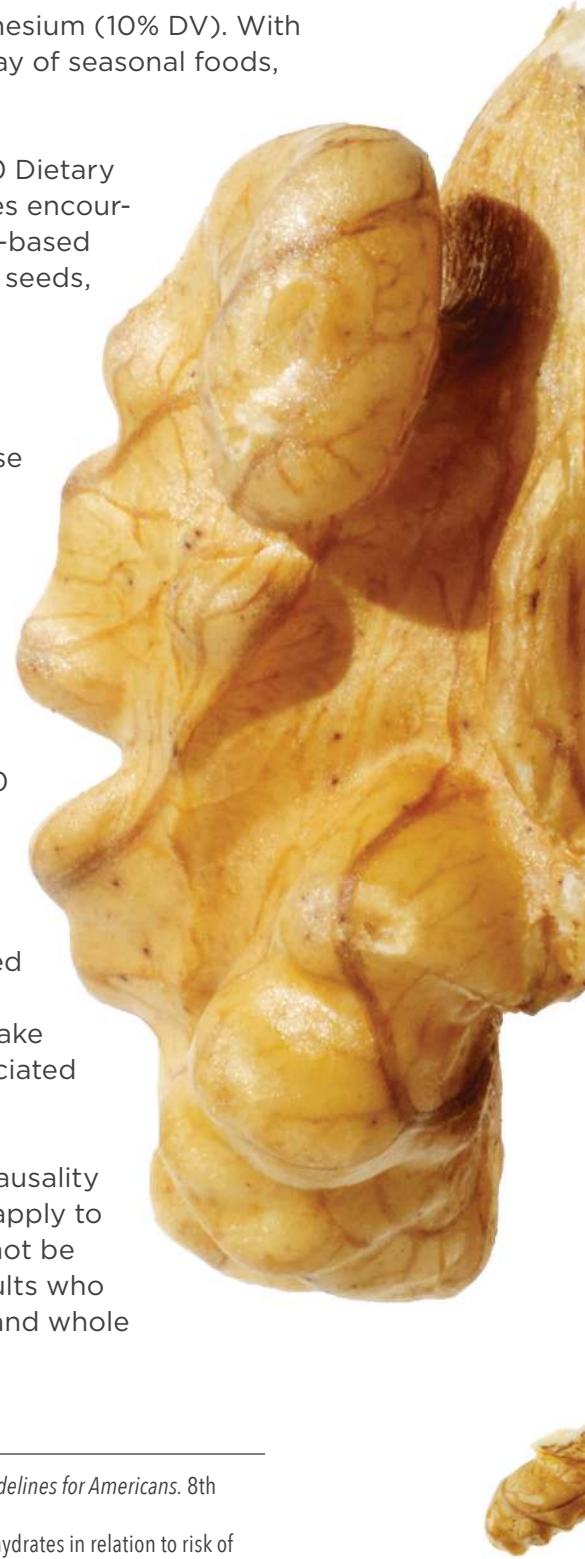
WALNUTS ARE THE ONLY NUT to contain a significant amount of the plant-based omega-3, alpha-linolenic acid (2.5 grams/ounce). One ounce of walnuts also offers four grams of protein, two grams of fiber, and is a good source of magnesium (10% DV). With a variety of nutrients and a flavor profile that pairs well with an array of seasonal foods, they are an ideal ingredient any time of the year.

Walnuts' unique nutrient profile also makes meeting the 2015-2020 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

The Dietary Guidelines also emphasize the importance of 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), making them an ideal food to help Americans meet this recommendation.

A STUDY FROM HARVARD suggests people who replace saturated fats with polyunsaturated fats in their diet may have a lowered 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, monounsaturated fatty acids, whole grain carbohydrates and refined carbohydrates, the study found that substituting 5 percent of the calories from saturated fat with the same amount of energy from polyunsaturated fats was associated with a 25 percent lower risk of coronary heart disease (CHD). Replacing saturated fats with equivalent energy intake from monounsaturated fat or whole grain carbohydrates was associated with a 15 percent and 9 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 (i.e., other lifestyle habits which are more common in adults who eat foods containing polyunsaturated fats, monounsaturated fats and whole grain carbohydrates could contribute to the study results).



¹U.S. Department of Health and Human Services and U.S. Department of Agriculture. *2015 - 2020 Dietary Guidelines for Americans*. 8th Edition. December 2015. Available at <http://health.gov/dietaryguidelines/2015/guidelines/>.

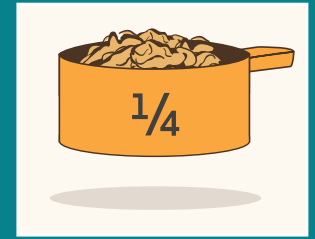
²Yanping L, Hruby A, Bernstein AM, et al. Saturated fats compared with unsaturated fats and sources of carbohydrates in relation to risk of coronary heart disease. *J Am Coll Cardiol*. 2015;66(14):1538-48.



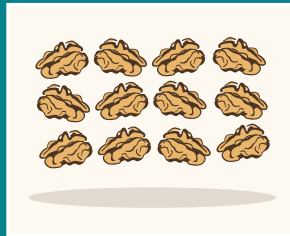
A DAILY SERVING OF WALNUTS IS:



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%**

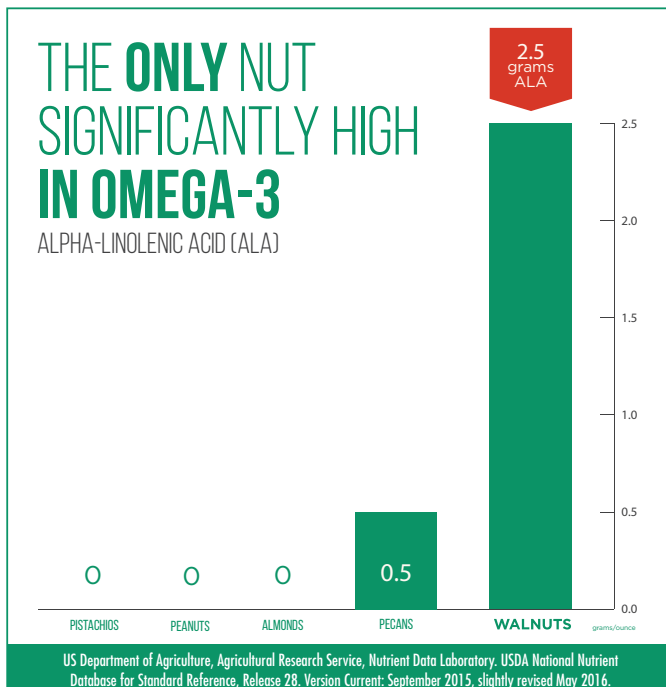
*The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

ESSENTIAL OMEGA-3s

WALNUTS ARE UNIQUE AMONG NUTS

for 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.

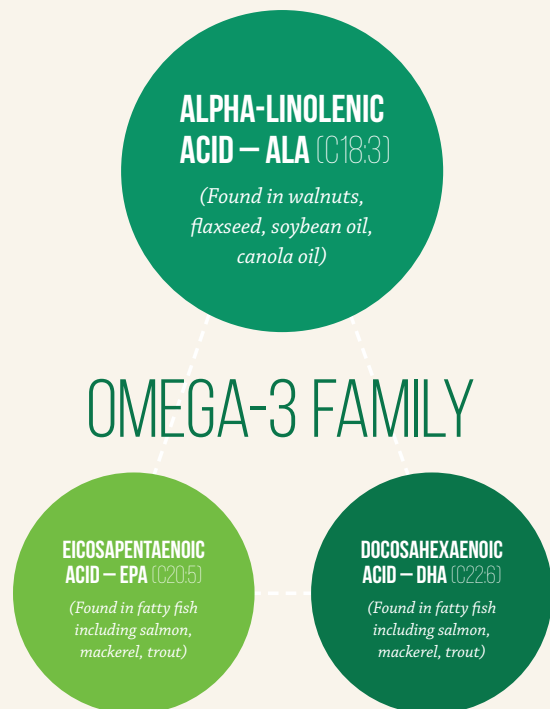


OMEGA-3 OVERVIEW

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



RESEARCH FROM THE LANDMARK PRE-
vención con Dieta MEDiterránea (PREDIMED)
study, one of the largest clinical trials, found
that both plant and marine-based sources
of omega-3s have complementary effects
against mortality in a population with high
seafood consumption.³ This secondary
analysis looked at data from participants in
the PREDIMED study. A total of 7,447 Spanish
subjects (ages 55-80) at high risk of cardio-
vascular disease, but with no symptoms at
baseline, were enrolled in the PREDIMED study
and followed for an average of 4.8 years. Sub-
jects were randomly assigned to a Mediterra-
nean diet supplemented with mixed nuts (15g
walnuts, or about 0.5 ounces, 7.5g almonds
and 7.5g hazelnuts per day), a Mediterranean
diet supplemented with extra virgin olive oil

(at least 50g or 4 tablespoons per day) or a
low-fat diet (control group). The study found
that consuming omega-3s from plant-based
sources, such as walnuts, may reduce risk of
all-cause mortality, whereas marine-derived
omega-3s, from fatty fish, may reduce the risk
of heart-related fatalities. The greatest protec-
tive effects from total mortality were observed
in diets that included both plant-based and
marine-derived omega-3s, as they appear to
act synergistically.

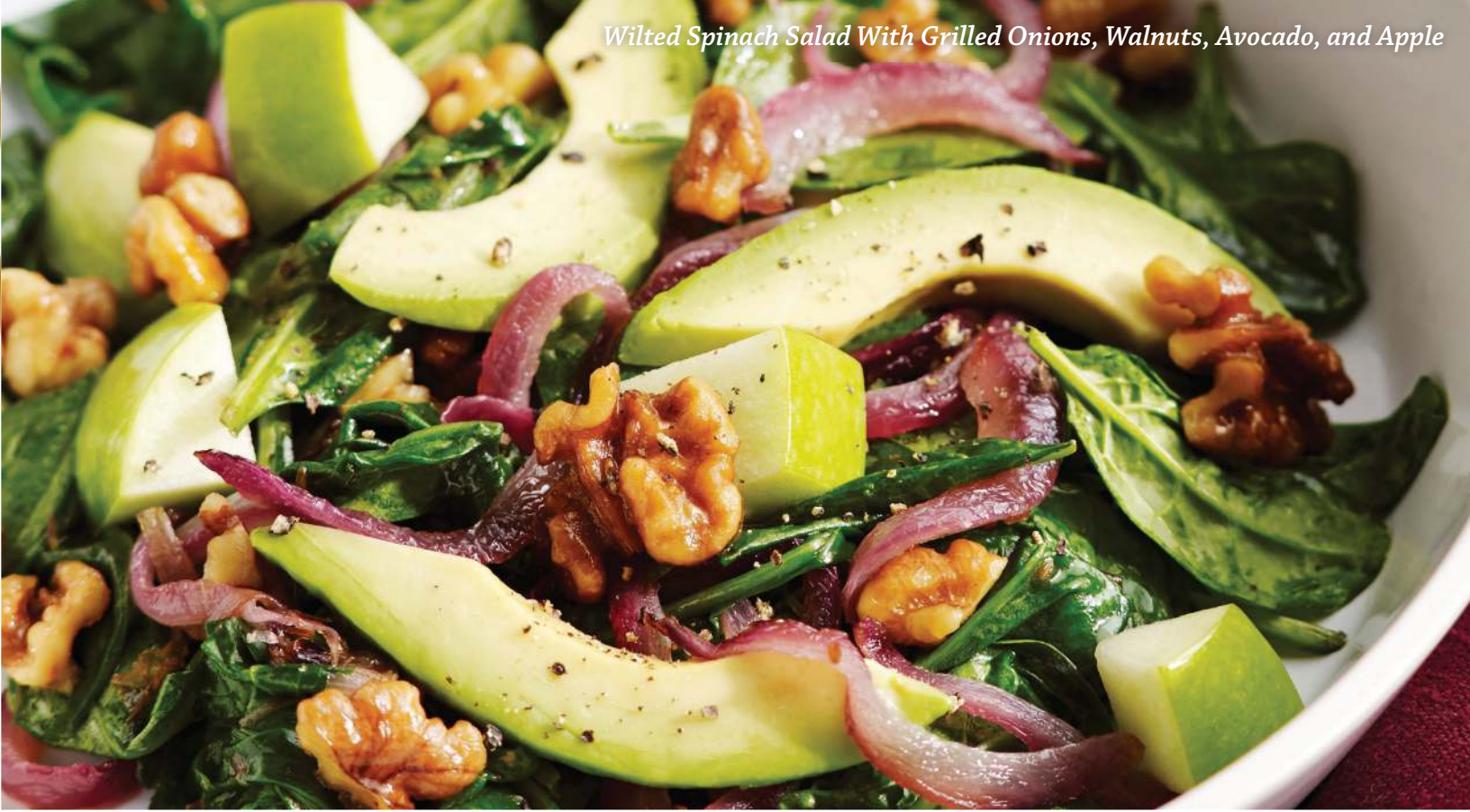
*Though the findings cannot prove causality,
the research demonstrates that ALA may
provide additional health benefits even in a
population with high consumption of EPA
and DHA from seafood.*

RESEARCH IN A MILLENNIAL population
(ages 18-35) exhibited regularly eating
foods that contain PUFAs, including wal-
nuts, 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% monounsatu-
rated 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 conjunc-
tion with fish oil supplements. Researchers
observed significant decreases in total
cholesterol (TC) and low-density lipopro-
tein (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.

Residual confounding cannot be ruled out in
observational studies (i.e., other lifestyle habits
which are more common in adults who eat
foods containing omega-3s could contribute
to the study results).³ Larger and longer-term
studies, as well as studies in diverse popula-
tions, 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} In the context of whole food diet,
it is difficult to discern whether changes seen
with the Mediterranean or PUFA-rich diet can
be attributed to one specific type of PUFA,
food source, or a combination of overall
dietary factors.^{3,4}

¹Fleming JA, Kris-Etherton PM. The evidence for α -linolenic acid and cardiovas-
cular disease benefits: comparisons with eicosapentaenoic acid and docosahex-
aenoic acid. *Adv Nutr*. 2014;5(6):863S-76S. ²Dietary reference intakes for energy,
carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids (Macro-
nutrients) (2005) NAS. IOM. Food and Nutrition Board. ³Sala-Vila A, Guasch-Ferré
M, Hu FB, et al. Dietary α -linolenic acid, marine ω -3 fatty acids, and mortality
in a population with high fish consumption: findings from the PREvención con
Dieta MEDiterránea (PREDIMED) study. *J Am Heart Assoc*. 2016;5(1):e002543.
⁴Stevenson JL, Miller MK, Skillman HE, et al. A PUFA rich diet improves fat
oxidation following saturated fat rich meal. *Eur J Nutr*. doi:10.1007/s00394-016-
1226-9.





HEALTH RESEARCH ON WALNUTS

FOR MORE THAN 25 YEARS, THE CALIFORNIA WALNUT COMMISSION HAS SUPPORTED SCIENTIFIC RESEARCH ON CONSUMPTION OF WALNUTS AND OUTCOMES IN THE FOLLOWING AREAS:

Heart Health

Healthy Aging

- Cognitive Health
- Physical Function

Cancer

- Breast Cancer
- Colorectal Cancer
- Prostate Cancer

Diabetes and Metabolic Syndrome

Weight

Mediterranean Diet

Male Reproductive Health

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.

Roasted Vegetables with Walnuts, Basil and Balsamic Vinaigrette





THE RESEARCH SUPPORTING the role that walnuts can play in heart health began with a Loma Linda University study, showing walnuts may lower total and LDL cholesterol in men by as much as 12 percent and 16 percent, respectively.¹ In this eight-week randomized, crossover trial, 18 healthy men (ages 21-43) were assigned to a cholesterol-lowering diet that did not include nuts or a cholesterol-lowering diet that included walnuts. All food was provided by the researchers and the walnut diet contained three servings (equivalent to 3 ounces) of walnuts per day.



A HARVARD UNIVERSITY META-ANALYSIS reviewed the heart health benefits of walnuts in 13 different trials. The trials represented 365 individuals, including those with a variety of characteristics such as high cholesterol, type 2 diabetes, metabolic syndrome and overweight or obesity, and those that were healthy.² When compared with control diets, such as a low-fat diet, Mediterranean-style diet or traditional American or Japanese diet, a diet supplemented with walnuts in amounts varying from 5-25 percent of total calories per day (equivalent to 1-3.9 ounces per day) resulted in a significantly greater decrease in total cholesterol (-10.29 mg/dL, -4.9%) and LDL cholesterol (-9.23 mg/dL, -6.7%). In addition, according to the studies in the analysis, walnuts provided significant benefits for certain antioxidant capacity and inflammatory markers and had no adverse effects on body weight.

RESEARCH FROM THE LANDMARK

PREvención con Dieta MEDiterránea (PREDIMED) study further demonstrated the potential heart health benefits that walnuts afford. 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), compared to a low-fat diet, may reduce the risk of major cardiovascular events, including cardiovascular death, myocardial infarction (heart attack), and stroke.³

Larger and longer-term studies, as well as studies in more diverse populations, are needed to clarify population-wide effects.^{1,2,3} In some cases, the amount of walnuts consumed in these trials was relatively large and might be difficult to maintain in a non-research setting.^{1,2} A meta-analysis offers a comprehensive look at findings among patients of various backgrounds, however, it can be limited by the methods, reported outcomes and quality of the individual studies involved.² In the PREDIMED study, it is difficult to precisely define what part of the Mediterranean diet was associated with cardiovascular benefits.³

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.”⁴

¹Sabaté J, Fraser GE, Burke K, et al. Effects of walnuts on serum lipid levels and blood pressure in normal men. *N Engl J Med.* 1993;328:603-607.

²Banel HK, 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. ³Estruch R, Ros E, Salas-Salvadó J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med.* 2013;368(14):1279-90. ⁴One 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 & HEALTHY AGING

SYNERGISTIC EFFECTS OF WALNUTS or their bioactive components may be contributing factors in protecting against the detrimental effects of aging. Research shows that nutrients found in walnuts, such as polyphenols, tocopherols and polyunsaturated fatty acids, may reduce oxidative stress and inflammation as well as help maintain neural membrane integrity and reduce protein aggregation involved in Alzheimer's disease.¹ Though more research is needed to confirm the benefits in humans, a review of animal studies suggests that the addition of walnuts (equivalent to a single serving or 1 ounce of walnuts for humans) is associated with improved motor and

cognitive behavior in aged animals. Additionally, human studies have shown that the inclusion of walnuts in the diet may improve cardiovascular health, which is a risk factor for neurodegenerative diseases and age-related cognitive decline.

Together, the evidence suggests that including walnuts as part of a healthy diet may play a role in helping to maintain and improve physical and cognitive health as people age.

COGNITIVE HEALTH

A STUDY PUBLISHED in the *Journal of the American Medical Association Internal Medicine* 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.² This clinical trial was conducted in a subcohort of the PREvención con Dieta MEDiterránea (PREDIMED) trial. Participants were randomly assigned to a Mediterranean diet supplemented with mixed nuts (15g walnuts, or about 0.5 ounces, 7.5g almonds and 7.5g hazelnuts per day), a Mediterranean diet supplemented with extra virgin olive oil (at least 50g or 4 tablespoons per day) or a low-fat diet (control group). The study found that participants who consumed a Mediterranean diet with nuts, including walnuts, showed improvements in memory compared to a low-fat diet.



ACCORDING TO A STUDY published in *The Journal of Nutrition, Health & Aging*, eating walnuts may improve performance on cognitive function tests, including those for memory, concentration and information processing speed in adults (ages 20-59 and 60 and older).³ In this retrospective study, cognitive function was consistently greater in adult participants who consumed walnuts, even after adjusting for age, gender, race, education, BMI, smoking, alcohol consumption and physical activity. Analyses are based on single,

24-hour recalls, which reflect one day of intake for the subjects. This cross-sectional study was the first large representative analysis of walnut intake and cognitive function, and the only study to include all available cognitive data across multiple National Health and Nutrition Examination (NHANES) surveys, representing over 10,000 individuals.



AN ANIMAL STUDY PUBLISHED in the *Journal of Alzheimer's Disease* 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.⁴ The research group examined the effects of dietary supplementation with 6 percent or 9 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 previous 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 in the brains of those with 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.

PHYSICAL FUNCTION

FINDINGS PUBLISHED in the *Journal of Nutrition* suggest that consumption of one to two servings of walnuts per week (1 ounce per serving) was associated with reduced risk of developing impairments in physical function in older women, which may help to maintain independence throughout the aging process.⁶ Researchers looked at data from 54,762 women in the prospective Nurses' Health Study, which tracked women for more than 30 years. This paper emphasized that overall diet quality, rather than individual foods, may have a greater impact on reducing risk of physical function impairments. Specifically, diet quality traits most associated with reduced rates of incident physical impairment were higher intake of fruits and vegetables; lower intake of sugar-sweetened beverages, trans fat, and sodium; and moderate alcohol intake. Among food components, the strongest relations were found for increased intakes of walnuts, oranges, orange juice, apples, pears and romaine or leaf lettuce.

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 in observational studies.^{2,6} More research is also needed to clarify how the health benefits apply to other populations.^{2,6} In the context of a Mediterranean diet, it is difficult to precisely define what part of the diet is associated with cognitive health.²

¹Poulose SM, Miller MG, Shukitt-Hale B. Role of walnuts in maintaining brain health with age. *J Nutr.* 2014;144(4 Suppl):561S-566S. ²Valls-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. ³Arab 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(3):284-90. 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(4):1397-405. 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(3):183-8. ⁶Hagan 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(7):1341-47.



Garden Salad with Walnut Vinaigrette

WALNUTS & CANCER

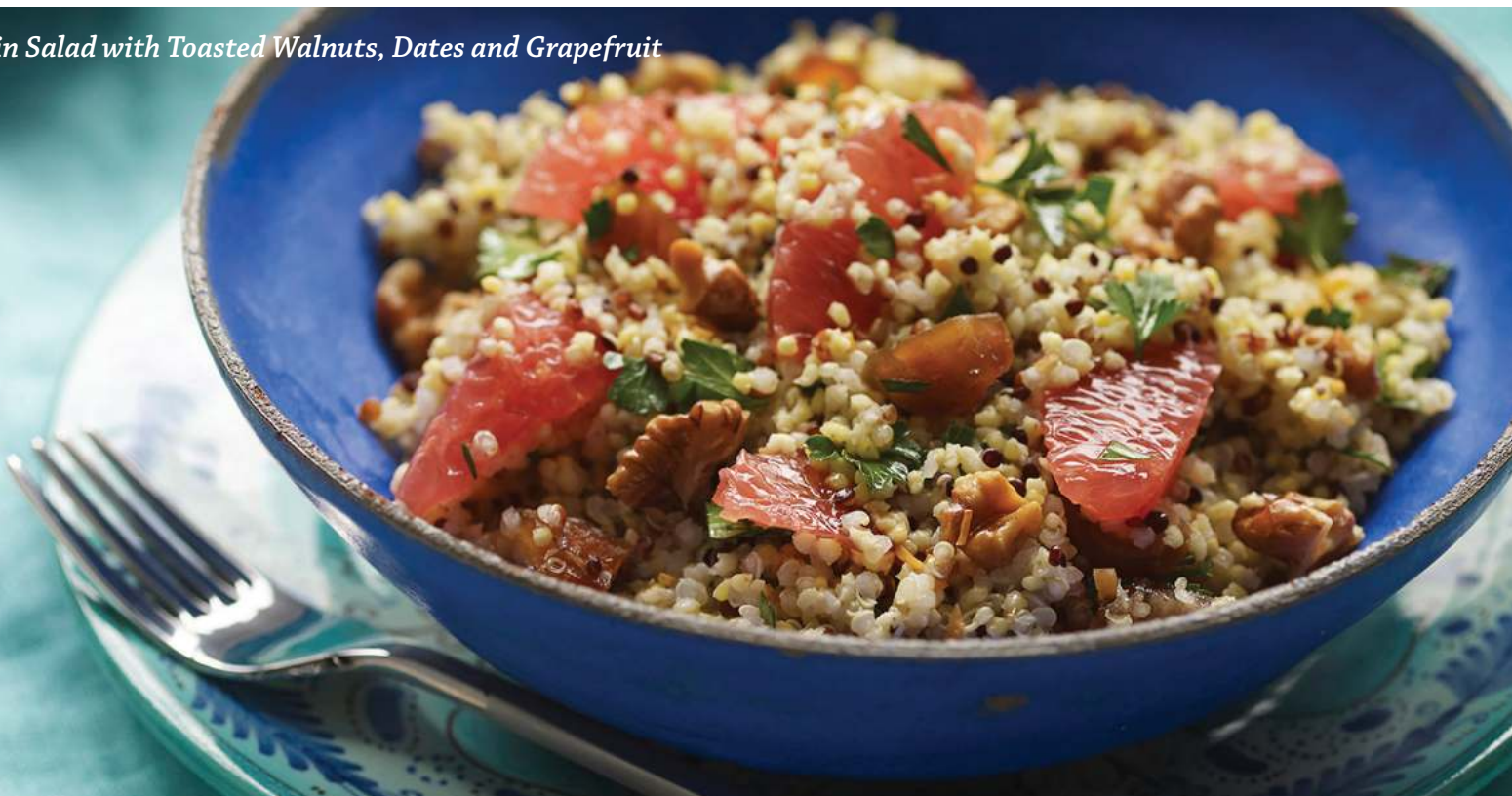
PRELIMINARY ANIMAL AND CELL model research has been investigating the potential benefit walnuts may have on a variety of cancers including breast, prostate and colorectal. Please note that the following animal and cell studies are provided as background and used to formulate hypotheses for additional research needed to determine the effects on humans.

A review of animal research published in *The Journal of Nutrition* demonstrates that walnuts may have multiple nutrients that could act in various ways to help decrease the risk of developing cancer. The studies reviewed suggest that these nutrients act together to provide more benefit than would be expected from the individual components.¹

BREAST CANCER

ANIMAL RESEARCH PUBLISHED in *Nutrition and Cancer* 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 for humans) was associated with a decreased risk of breast cancer in mice.² 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 with male mice 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. Although more research is needed to determine the specific components of walnuts and the mechanisms associated with tumor suppression, the findings demonstrate that walnuts may contribute to a healthy diet to reduce risk for breast cancer in mice.

Grain Salad with Toasted Walnuts, Dates and Grapefruit



COLORECTAL CANCER

AN ANIMAL STUDY PUBLISHED in *Cancer Prevention Research* found that eating walnuts could modify gut bacteria in a way that is beneficial to colon health, and may be associated with colon tumor suppression.³ 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 Western diet, representing typical American intake, supplemented with 0, 5.2, 10.5, or 21.4 percent of calories from walnuts. Calories from fat sources were proportionally lowered in each diet to compensate for the addition of walnuts. Male mice fed a Western diet with 10.5 percent of total calories from walnuts, which translates to just over one ounce of walnuts in a human diet, showed a significant reduction in the number and size of tumors.

Animal research conducted at the Beth Israel Deaconess Medical Center and Harvard Medical School demonstrated that walnuts in the diet may inhibit colorectal cancer growth in mice by suppressing angiogenesis.⁴ 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 (approximately 2 ounces of walnuts in a human diet). Compared with the corn oil diet, mice fed the walnut diet (equivalent to 2 servings of walnuts per day in humans) or flaxseed diet exhibited significantly slower tumor growth rates and lower tumor weights. The differences between walnut and flaxseed diets did not reach statistical significance. However, compared to the control-fed mice, consumption of walnuts significantly decreased angiogenesis which may be beneficial against 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 published in the *European Journal of Nutrition* 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 from developing.⁵ Similarly, another cell study showed that a diet rich in ET-containing foods, such as walnuts, could contribute to the prevention of prostate cancer by influencing the regulatory mechanisms in prostate cancer.⁶

Research published in *Cancer Investigation* showed that walnuts may help reduce prostate cancer risk in mice.⁷ In this experimental study,

mice were fed either a standard mouse diet (control diet) or a standard mouse diet enriched with walnuts (equivalent to 2 ounces of walnuts per day in humans). The final average tumor size in the walnut-fed mice was approximately 25 percent the average size of the prostate tumors that developed in the mice that consumed the non-walnut control diet.

¹Hardman, WE. Walnuts have potential for cancer prevention and treatment in mice. *J Nutr.* 2014;144(4 Suppl):555S-560S. ²Hardman WE, Ion G, Akinsete JA, et al. Dietary walnut suppressed mammary gland tumorigenesis in the C(3)1 TAg mouse. *Nutr Cancer.* 2011;63(6):960-70. ³Nakanishi M, Chen Y, Qendro V, et al. Effects of walnut consumption on colon carcinogenesis and microbial community structure. *Cancer Prev Res (Phila).* 2016;9(8):692-703. ⁴Nagel JM, Brinkoetter M, Magkos F, et al. Dietary walnuts inhibit colorectal cancer growth in mice by suppressing angiogenesis. *Nutrition.* 2012;28(1):67-75.

⁵Sánchez-González C, Ciudad CJ, Izquierdo-Pulido M, et al. Urolithin A causes p21 up-regulation in prostate cancer cells. *Eur J Nutr.* 2016;55(3):1099-112.

⁶Sánchez-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(11):2922-30. ⁷Reiter 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(6):365-73.

WALNUTS & DIABETES AND METABOLIC SYNDROME

INDIVIDUALS WITH DIABETES or metabolic syndrome often have conditions such as high blood pressure, abnormal cholesterol, high triglycerides and obesity. Together, these disorders 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.



RESEARCHERS FROM HARVARD found that walnut consumption was associated with a significantly lower risk of type 2 diabetes in women compared with women who never/rarely consumed walnuts.¹ 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.



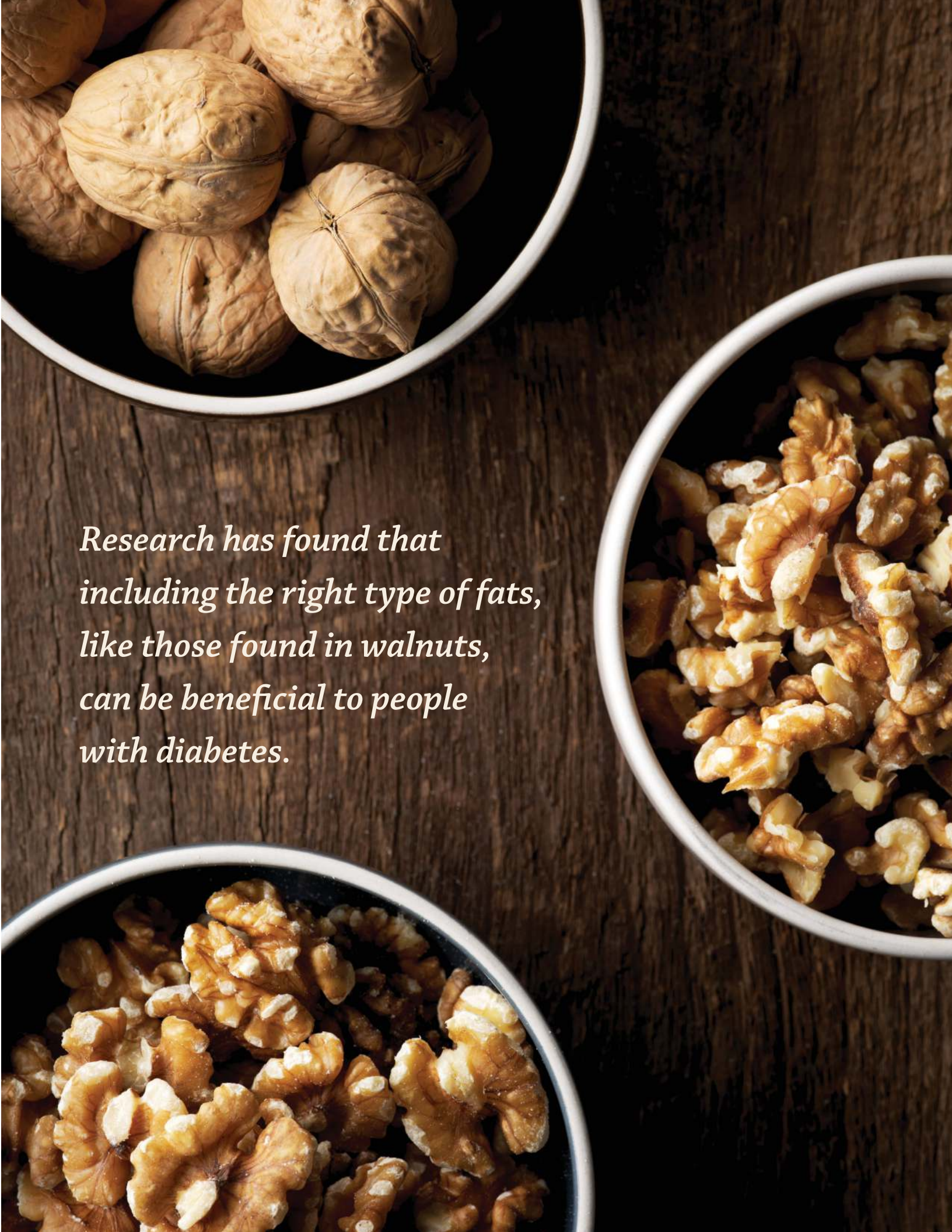
A STUDY PUBLISHED in *Metabolism* found that short-term consumption of walnuts may improve blood lipids, by increasing apolipoprotein A concentration.² Apolipoprotein A is the primary protein component of HDL, and is one of many factors that may be considered in a complete lipid profile when estimating 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 (approx-

mately 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.

FINDINGS FROM THE YALE-GRIFFIN PREVENTION RESEARCH CENTER demonstrated that consumption of a diet enriched with two ounces of walnuts per day for eight weeks significantly improved endothelial function in 24 adult participants (ages 49-67) with type 2 diabetes.³ Subjects were randomly assigned to an *ad libitum* diet enriched with 56 grams of walnuts per day or an *ad libitum* diet without walnuts. Researchers compared the dietary effects on endothelial function, a measure of how well blood vessels are able to dilate, resulting in increased blood flow, and a powerful predictor of overall cardiovascular risk. The same design was used in another study with 46 overweight adults with elevated waist circumference and one or more additional signs of metabolic syndrome. Findings showed that daily consumption of 56 grams of walnuts for eight weeks significantly improved endothelial function as compare with an *ad libitum* diet not supplemented with walnuts.⁴

Larger and longer-term studies, as well as studies in more diverse populations, are needed to clarify population-wide effects.^{1,2,3,4} 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).^{1,3,4}

¹Pan 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. ²Aronis 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. ³Ma Y, Njike VY, Millet J, et al. Effects of walnut consumption on endothelial function in type 2 diabetic subjects: a randomized controlled crossover trial. *Diabetes Care.* 2010;33(2):227-32. ⁴Katz DL, Davidhi A, Ma Y, et al. Effects of walnuts on endothelial function in overweight adults with visceral obesity: a randomized, controlled, crossover trial. *J Am Coll Nutr.* 2012 Dec;31(6):415-23.

The image features three white ceramic bowls filled with walnuts, arranged on a dark, textured wooden surface. The top-left bowl contains several whole, uncracked walnuts. The top-right bowl is filled with walnut halves. The bottom-left bowl contains walnut pieces, some of which appear to be roasted or glazed. The text is overlaid on the wooden background in the center-left area.

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

WALNUTS & WEIGHT

A SHORT-TERM STUDY from the Beth Israel Deaconess Medical Center and Harvard Medical School found that walnuts may increase satiety and sense of fullness.¹ Twenty men and women with metabolic syndrome participated in this randomized, double blind, cross-over study. For four days, subjects consumed isocaloric diets including a liquid meal containing either 48g of walnuts (approximately 1.7 ounces) or no walnuts. Both meals had similar macronutrient composition with the walnut meal being rich in polyunsaturated fats (walnuts are primarily comprised of polyunsaturated fats - 13 out of 18 grams of total fat per 1 ounce serving) and the placebo rich in monounsaturated fats. By day three 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.

In another study published in the *Journal of the American Heart Association and Metabolism*, researchers 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 245 overweight and obese women.^{2,3} Overweight and obese women 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, with guidance to reduce energy intake by 500-1000 calories per day. Participants on the lower fat diet were instructed to emphasize lean protein sources, reduced-fat dairy foods, vegetables, fruit and whole grains. Whereas participants on the lower carbohydrate diet were educated about lower carbohydrate choices and lean protein sources and were instructed to achieve a high monounsaturated fat intake. Weight loss was similar across the diet groups, demonstrating that walnuts can play a role in achieving ideal body weights, when consumed as part of an overall healthy diet.

Salmon with Stewed Chickpeas and Kale



A FRESH LOOK AT THE CALORIE CONTENT OF WALNUTS

A STUDY FROM THE 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 Nutrient Database.⁴ The research team studied 18 healthy adults. Each person was assigned randomly 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. Administered meals as well as walnut, fecal and urine samples were collected and subjected to bomb calorimetry to measure calories. The data from each 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.



IMPROVED DIET QUALITY

AS A NUTRIENT-DENSE FOOD, walnuts can be eaten in place of less healthy choices to improve overall diet quality. A study from Yale University found that including walnuts in a habitual diet, with or without dietary counseling to adjust calorie intake, significantly improved diet quality in adult men and women at high risk for diabetes.⁵ Diet quality was assessed using the Healthy Eating Index 2010 (HEI-2010). In this parallel design study, participants (31 men and 81 women ages 25–75) were assigned to a calorie adjusted diet or an *ad libitum* diet. The two diet groups were further randomized to one of two diet sequences to either include or exclude walnuts for 6 months, followed by a three month washout period consisting of an *ad libitum* diet without walnuts, and then to either exclude or include walnuts for another 6 months. During the walnut-included diet, participants were provided 392 grams of walnuts per week (2 ounces per day) to include in their diet. Subjects on the calorie adjusted diet met with a registered dietitian to maintain isocaloric conditions after incorporating walnuts in the diet whereas individuals on the *ad libitum* diet were not monitored or regulated.

Information on dietary intake and diet adherence may have been limited in studies where participants were free-living and data was self-reported.^{2,3,5} Although larger and longer-term studies, as well as studies in more diverse populations, are needed to understand population-wide effects,^{1,2,3,5} walnuts can play a role in optimal body weight and improving overall diet quality, when consumed as part of a healthy diet.

¹Brennan 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(6):1176-82. ²Rock 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(11):1605-13. ³Le 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;5(1):e002771. ⁴Baer DJ, Gebauer SK, Novotny JA. Walnuts consumed by healthy adults provide fewer available calories than predicted by the atwater factors. *J Nutr*. 2016;146(1):9-13. ⁵Njike VY, Ayettey R, Petraro P, et al. Walnut ingestion in adults at risk for diabetes: effects on body composition, diet quality, and cardiac risk measures. *BMJ Open Diabetes Res Care*. 2015;3(1):e000115.

WALNUTS & THE MEDITERRANEAN DIET

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. 2015-2020 Dietary Guidelines for Americans recommends a Mediterranean-style eating pattern as one example of a healthy diet plan.²

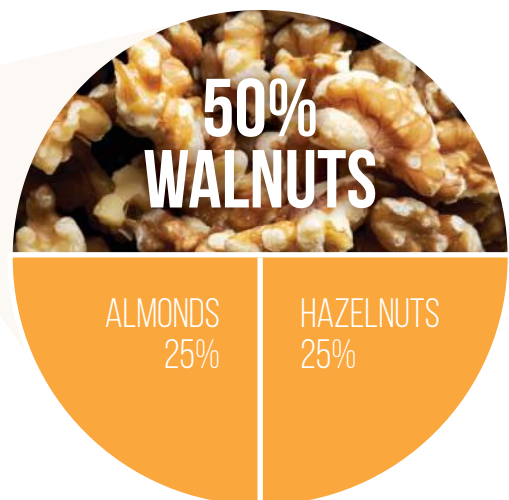
PREDIMED (PREvención con Dieta MEDiterránea = Prevention with Mediterranean Diet) is a landmark study aimed at assessing the efficacy of the Mediterranean diet in the primary prevention of cardiovascular diseases. The seminal paper, “Primary Prevention of Cardiovascular Disease with a Mediterranean Diet” was published in 2013 and more than 200 additional studies have resulted from the PREDIMED research.³

The aim of PREDIMED was to determine 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, can 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 an average 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.

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)



A Mediterranean diet including tree nuts, primarily walnuts, reduced the risk of cardiovascular diseases (myocardial infarction, stroke or cardiovascular death) by 30 percent and specifically reduced the risk of stroke by 46 percent when compared to the low-fat diet.

The Mediterranean diet enriched with extra-virgin olive oil also reduced the risk of cardiovascular diseases by 30 percent. Several studies have been published since the seminal paper investigating the Mediterranean diet on a number of outcomes including cognitive function,⁴ blood pressure,⁵ total cholesterol⁵ 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 studies are 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.

Interested in more resources? Oldways,⁶ a non-profit food and nutrition education organization, has created numerous helpful resources on the Mediterranean diet.

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 Health and Human Services and U.S. Department of Agriculture. *2015 - 2020 Dietary Guidelines for Americans*. 8th Edition. December 2015. Available at <http://health.gov/dietaryguidelines/2015/guidelines/>.

³Estruch R, Ros E, Salas-Salvadó J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med*. 2013;368(14):1279-90.

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.

⁶<http://www.oldwayspt.org/>



Beet, Goat Cheese and Walnut Salad



Toasted Walnut Hummus

WALNUTS & MALE REPRODUCTIVE HEALTH

ACCORDING TO THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE, infertility affects men and women equally with about one-third of infertility cases being attributed to male factors, and about one-third to factors that affect women.¹ Throughout history, food has been linked with human reproductive success, however most of the emphasis has been on the maternal diet and very little focus has been given to the paternal diet.

Research published in *Biology of Reproduction* reported that 75 grams (approximately 2.5 ounces) of walnuts consumed per day improved sperm vitality, motility and morphology (normal forms) in a group of healthy young men between 21-35 years of age.²

This randomized, parallel two-group dietary intervention trial included 117 healthy young men (ages 21-35) 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. After 12 weeks, compared to the control group, the walnut group experienced improvement in sperm vitality, motility and morphology - key components in male fertility.

Even though researchers controlled for education, race, BMI, weight and physical activity, additional research is needed to determine how these results apply to other male populations since participants were primarily white or Asian. Information on dietary intake and diet

adherence was limited since participants were free-living and data was self-reported. Additionally, collection of blood specimens for hormone analysis occurred throughout the day. Participants were asked to return at the same time of day for follow-up appointments to maintain consistency in the data collection.

This research suggests walnuts provide key nutrients that may be essential in male reproductive health.

Walnuts are the only nut with an excellent source of alpha-linolenic acid, or ALA, the plant-based omega-3 fatty acid (2.5 grams/ounce). This study reported higher amounts of ALA provided by walnuts correlated with less frequent aneuploidy, or abnormal cell chromosome numbers. Aneuploidy can result in genetic abnormalities such as Down syndrome.

¹American Society for Reproductive Medicine. (2016). *Quick Facts About Infertility*. Retrieved from www.reproductivefacts.org 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(4):101.





**CALIFORNIA WALNUT
BOARD & COMMISSION**

101 Parkshore Drive, Suite 250
Folsom, CA 95630

Email: info@walnuts.org
www.walnuts.org

Follow us @CAWalnuts

