



# The Mediterranean Diet: A Healthy Dietary Plan

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## Keywords

Healthy fat · Olive oil · Moderate alcohol intake · Fish and chicken

## Key Points

- The Mediterranean diet is a name encompassing foods that are typically eaten in countries surrounding the Mediterranean basin.
- Olive oil is the principal source of fat in this dietary pattern. This dietary pattern also includes generous amounts of nuts and legumes as well as fruits and vegetables. Moderate intake of red wine is characteristic, but not mandatory. Fish is a primary protein source.
- The Mediterranean diet significantly reduces the risk of cardiovascular disease as shown in the PREDIMED Trial (PREvencio'n con DIeta MEDiterra'nea).
- Substituting the Mediterranean diet for Western-diet foods reduces body weight gain.
- Individuals consuming the Mediterranean diet may also have a reduced risk of developing type 2 diabetes mellitus.
- The Mediterranean diet also improved components of the metabolic syndrome.

## Introduction

A separate chapter on the Mediterranean diet is included in this edition of *Nutrition Guide for Physicians and Related Healthcare Professionals*, along with chapters on the DASH diet and the vegetarian/flexitarian diet because these were the top-three-rated diets overall in the US News and World Report survey in 2019 and again in 2020 [1, 2].

Prior to the discovery of the “New World” by Christopher Columbus in 1492, European diets were very different than today. Important food components that are native to the Americas included tomatoes, squash, potato, avocado, the common bean, lima beans, and cacao. What an addition to the European diet! Can you imagine Italian food without tomatoes? The introduction of these foods led to a change in the dietary patterns in countries around the Mediterranean basin. But, even with these foods, there is considerable variation between the types of foods that are eaten in the eastern Mediterranean, in Greece,

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in Italy, in Spain, and in North Africa. Because of the variability in diet by country, there is no single Mediterranean diet, but rather a Mediterranean dietary pattern involving certain foods.

Ansel Keys played a major role in highlighting the importance of a healthy Mediterranean diet [3]. In his famous Seven Countries Study, he noted a lower incidence of heart disease in people living in Southern Europe [4]. In a review in 1995, Dr. Keys stated it this way: “My concern about diet as a public health problem began in the early 1950s in Naples, where we observed very low incidences of coronary heart disease associated with what we later came to call the ‘good Mediterranean diet’.” The heart of this diet is mainly vegetarian and differs from American and Northern European diets in that it is much lower in meat and dairy products and uses fruit for dessert. These observations led to our subsequent research in the Seven Countries Study, in which we demonstrated that saturated fat is the major dietary villain. Today, the healthy Mediterranean diet is changing, and coronary heart disease is no longer confined to medical textbooks. “Our challenge is to persuade children to tell their parents to eat as Mediterraneans do.” [3, 4]. Since these early reports, there have been many papers summarizing aspects of the Mediterranean diet, and a few recent reviews are listed here [5–8].

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## What Is a Mediterranean Diet?

As noted above, there is considerable variability in what we call the “Mediterranean diet.” Having said this, there are a few features that are common to most of them. These diets are generally not restricted in the amount of fat that is eaten, but emphasize healthy fats. In addition, a Mediterranean diet would generally contain two or more specific components. Olive oil is the main cooking oil as well as olive oil used on dressings for salads. There would be generous consumption of nuts and legumes as well as significant intakes of fruits and vegetables. Moderate intake of red wine is also a characteristic of this dietary plan, though not mandatory. Consumption of fish is a primary protein source, and consistent with this, there is limited consumption of red meat. Finally, there is limited consumption of dairy products. Panagiotakis et al. [9] included the following feature in their Mediterranean diet: 30–40% of total calories from fat using olive oil (and other monounsaturated fats such as canola oil). Also included are unrefined cereals and products with the emphasis on whole grain bread, whole grain pasta, and whole wheat. Vegetables at 2–3 servings/day and fruits at 4–6 servings/day were central elements of the diet. Fish as a major source of protein was included at 4–5 servings/week. Nuts at more than four servings/week were a second source of protein. Finally moderate consumption of wine was included in the diet.

The elements of this dietary plan can be used to assess the degree of adherence to the Mediterranean diet. A Mediterranean diet score can be calculated and used in evaluating the effect of this diet on markers of health. There are different ways the Mediterranean diet can be evaluated. This usually involves assigning points to whether a behavior was adhered to or not and sometimes, for example, red meat, when a behavior was avoided. The scores are then summed and a final score is derived. This often has a maximum point value of 9 with tertiles consisting of 0–2, 3–6, and 7–9 for poor, moderate, and good compliance with the diet. However, there are many other variants used to score adherence to a Mediterranean diet.

An example of the Mediterranean diet compared to the Western diet is the emphasis of fruits, vegetables, olive oil, nuts, and wine, being evident in one pattern with the ever-present “burger and fries” as one symbol of the Western diet. The concepts in the Mediterranean diet have also been presented by the Harvard School of Public Health in pyramid form which emphasizes the important foods by giving them larger areas at the bottom of the pyramid and putting at the top those foods that should be consumed less frequently. At the top are red meat and white rice and white bread, white pasta, soda, and desserts on the right. At the bottom are the preferred foods such as plant oils and whole grains along with exercise and weight control.

As noted at the beginning of this chapter, three diets are at the top of the US News and World Reports overall list for 2 years running.

## Effects of the Mediterranean Diet on Health Outcomes

In the remainder of this chapter, we will argue the case for using the Mediterranean diet based on its beneficial effects on body weight, diabetes, cardiovascular disease, and the metabolic syndrome. Since many of the important conclusions about the value of this diet have come from a single large study called PREDIMED (PREvencio'n con DIeta MEDiterra'nea), the interventions using in this diet will be described [10, 11]. This was a study from Spain involving 7557 individuals including men age 55–80 and women age 60–80 who were assigned to one of the 3 groups including a control diet group (N = 2450), a Mediterranean diet group supplemented with extra virgin olive oil (EVOO) (N = 2453), or a Mediterranean diet group supplemented with mixed nuts (N = 2454). In this trial, the Mediterranean diet consisted of more than three servings/d of fresh fruits; more than two servings/d of vegetables; more than three servings/week of legumes; more than three servings/week of fatty fish, white meat rather than red meat, wine with meals; and more than seven glasses/week for the extra virgin olive oil; and more than 1 L/week of olive oil and for the group with supplemental nuts, 30 g nuts/d. Items such as soft drinks, commercial bakery goods, spread fats, and processed and red meats were discouraged. The control diet in this study consisted of more than three servings/d of fresh fruits, more than two servings/d of vegetables, more than three servings/d of low-fat dairy products, more than three servings/week of lean fish, and more than  $\geq 3$  servings/d of bread/rice/potato/pasta. The following items were discouraged in the group on the Western/control diet: vegetable oils, commercial baked goods, nuts and fried snacks, red and processed meats, fatty fish, spread fats, and visible meat fat.

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### Body Weight

At baseline, the use of a Mediterranean-type diet was scored in the participants in the PREDIMED trial. Using a 14-point scale to rate adherence to the diet, Martinez-Gonzalez et al. [12] found that those with lower scores of 8 had more central obesity, as expressed as weight/height, compared to the groups with scores above 10. A score of 9 had no change in central obesity.

In the PREDIMED trial, dietary food intake was evaluated every year using a food frequency questionnaire [13]. The 6942 individuals included in this study were followed for a median of 4.8 years. When 5% of energy from saturated fatty acids (SFA) in the diet was replaced by equivalent amounts of monounsaturated fatty acids (MUFA), there was a weight loss of  $-0.38$  kg (95% CI:  $-0.69$ ,  $-0.07$  kg), and when replaced with polyunsaturated fatty acids (PUFA), there was a larger weight loss of  $-0.51$  kg (95% CI:  $-0.81$ ,  $-0.20$ ). Similarly, replacing equivalent amounts of energy from dietary proteins with MUFA or with PUFA decreased the odds of becoming obese. When a serving of red meat was replaced by white meat, oily fish, or white fish, weight losses of 0.64, 0.75, and 0.87 kg were observed, respectively. These data clearly show that increasing the intake of unsaturated fatty acids at the expense of SFA, proteins, and carbohydrates had beneficial effects on body weight and obesity. The effects of several of the substitutions evaluated in this paper are shown in Table 15.1.

### Diabetes

A number of studies have examined the relationship of the Mediterranean diet to the risk of developing diabetes or to the improvement in the control of this disease. Several of these trials are summarized in Table 15.2. It is clear that in most of these studies, the Mediterranean diet significantly reduced the risk of developing diabetes mellitus.

**Table 15.1** Estimated mean changes in body weight (kg) and 95 confidence interval<sup>a</sup> after substitution of one daily portion of high-fat food items in the Mediterranean diet for healthier options\*

Substitution	Mean body weight (kg) difference (95% CI)
White meat for red meat	-0.64 (-0.94, 0.35)*
Oily fish for red meat	-0.75 (-1.13, -0.38)*
White fish for red meat	-0.87 (-1.17, -0.56)*
Olive oil for butter	-0.25 (-0.56, 0.06)
Other vegetable oils for butter	-0.11 (-0.44, 0.22)
Olive oil for margarine	-0.04 (-0.18, 0.25)
Other vegetable oils for margarine	0.26 (0.02, 0.50)*
Walnuts for mixed nuts	-0.15 (-0.61, 0.32)

Adapted from Beulen et al. [13]

<sup>a</sup>Substitutions of a portion of 100, 10, and 30 g for meat/fish, butter/margarine/oils, and nuts, respectively. Adjusted for age, sex, baseline weight, recruitment center, intervention group, cumulative average of total energy intake, BMI, leisure-time physical activity (metabolic equivalent task in min/day), smoking status (never, former, current smoker), educational level (primary education, high school, university), working status (employed, unemployed, housewife, retired), and marital status (single, married). \*  $p < 0.05$

**Table 15.2** Trials on the relationship of the Mediterranean diet and the risk of developing diabetes mellitus

Author/year	Comments
Mozaffarian 2007 [15]	Top quintile had 35% lower risk of diabetes
Martinez-Gonzalez 2008 [16]	2 unit increase in Mediterranean diet score reduced risk of T2D by 35%
De Koning 2011 [17]	Top quintile, 25% reduced risk of diabetes
Romaguera 2011 [18]	High Mediterranean diet score, 12% reduced risk of diabetes
Tobias 2012a [19]	Women top quartile, 24% reduced gestational diabetes mellitus (GDM)
Tobias 2012b [20]	Women with top quartile of Mediterranean diet score has 40% reduced of T2D
Abiemo 2013 [21]	Higher adherence to Mediterranean diet did not reduce risk of diabetes
Rossi 2013 [22]	Top quartile of Mediterranean diet score had 12% reduced risk of T2D

Adapted from Georgoulis et al. [14]

Using a nine-point scale to evaluate adherence to the Mediterranean diet, Martinez-Gonzalez et al. [16] showed that those with a score of 3–6 or 7–9 score which indicates moderate to good adherence to the diet, respectively, had a significantly lower risk of developing diabetes over 2 years than those with poor adherence and a score of <3. In a meta-analysis, Esposito et al. [23] demonstrated that hemoglobin A1c was significantly lower in those using the Mediterranean diet (mean difference - 0.47 (95% CI -0.56 to -0.38)) compared with either a control or low-fat diet. Body weight was also significantly reduced. In the PREDIMED study, there was an interesting relationship between levels of branched chain amino acids and the risk of developing diabetes. At baseline each quartile of increasing concentration of leucine, isoleucine, and valine was associated with a greater risk of diabetes after 1 year [24]. This effect was attenuated in the Mediterranean diet with the extra virgin olive oil (EVOO), but not in the Mediterranean diet supplemented with nuts.

## Cardiovascular Effects

As with diabetes, the Mediterranean diet modulated the risk of cardiovascular disease. Most striking was the data from the PREDIMED trial where there was a 28–31% reduction in the composite end point of acute MI, stroke, and cardiovascular death [10]. However, total mortality was not reduced by this treatment. In addition to the effect on acute MI and stroke, there was a significant reduction in the incidence of atrial fibrillation over 4.7 years in the group receiving the Mediterranean diet + EVOO compared to the control group [25]. Supplementing the diet with nuts had no significant effect (Table 15.3).

Several meta-analyses have been done examining the relationship between the Mediterranean diet and cardiovascular disease [26, 31, 32]. In the first of these major adverse cardiovascular events (MACE), coronary events, heart failure, and stroke were all improved with the Mediterranean diet, but CVD mortality and all-cause mortality were not affected. In the second meta-analysis which included 38 cohort studies, CHD incidence, MI incidence, CHD incidence, and CVD mortality were significantly reduced along with stroke incidence and stroke mortality. In the third meta-analysis, all-cause mortality, CVD incidence, and mortality as well as cancer incidence and mortality were reduced, and there was less neurodegenerative disease [32]. Higher plasma concentrations of ceramides, a membrane lipid composed of sphingosine, and a long-chain fatty acid are associated in increased risk of cardiovascular disease. The effect of a Mediterranean diet on ceramides was undertaken in the PREDIMED study. The four principal fatty acids in the ceramides were hexadecanoate (C16:0), docosanoate (C22:0), tetracosanoate (24:0), and nervonate (C24:1). Higher levels of each of these ceramides were associated with a higher level of the composite end point in the PREDIMED study. The hazard ratio for highest vs. lowest quartile of MACE (nonfatal acute myocardial infarction, nonfatal stroke, or cardiovascular death) was HR = 2.39 (1.49–3.83, *P* trend <0.001) for hexadecanoate, HR = 1.91 (1.21–3.01, *P* trend = 0.003) for docosanoate, HR = 1.97 (1.21–3.20, *P* trend = 0.004) for tetracosanoate, and HR = 1.73 (1.09–2.74, *P* trend = 0.011) for nervonate [33]. For the individuals in the control/Western diet who had higher than the median ceramide levels at baseline, the Mediterranean diet + EVOO significantly reduced the effect of ceramides on major adverse cardiovascular events (MACE). It is interesting to note that for the effect on both atrial fibrillation and the adverse effects of ceramides, the extra virgin olive oil had more impact than the Mediterranean diet with nuts.

## The Metabolic Syndrome

The metabolic syndrome is associated with abnormal values in a group of cardiovascular risk factors that includes central obesity, abnormal blood glucose, high triglycerides, low HDL cholesterol, and high blood pressure. The main definition for the cut points are provided by the American Heart Association guidelines and when international criteria are considered by the modifications proposed by Alberti et al. [34].

**Table 15.3** Effect of the Mediterranean diet on cardiovascular risk in several studies

Author year	Title	MACE reduced	CVD mortality reduced	All-cause mortality reduced
de Lorgeril 1994 [27]	Lyon Ht study	Yes	Yes	Yes
Singh 2002 [28]	Indo-Mediterranean study	Yes	Yes	Yes
Burr 2003 [29]	The UK	–	No	No
Ng 2011 [30]	Hong Kong > 18 and HIV	–	–	Yes

Adapted from Liyanage et al. [26]

The Mediterranean diet has positive effects on the metabolic syndrome, just as it does on the risk for diabetes and obesity. In a study by Esposito et al. [35], 90 men and women with the metabolic syndrome were enrolled in an intervention group who were on average 44.3 years, and consumed a diet with a profile consistent with the Mediterranean diet. After 2 years, there were a number of statistically significant outcomes including decreased weight and waist circumference, increased HDL cholesterol, decreased triglycerides, decreased systolic and diastolic blood pressure, and improved glucose tolerance and insulin sensitivity, all of which are components of the metabolic syndrome. Pan et al. [36] similarly noted improvements in the components of the metabolic syndrome with the Mediterranean diet. HbA1c and fasting glucose were improved. There was weight loss and improvements in HDL-cholesterol, total cholesterol, and triglycerides.

Finally, using a Mediterranean diet as assessed by a modified Mediterranean diet score divided into quintiles, Steffen et al. [37] observed a graded decrease in the prevalence of the metabolic syndrome over a 25-year period. Thus not only are there acute effects on improving the short-term abnormalities in this syndrome, but there are long-term effects with predictive power out to 25 years.

In conclusion, it seems reasonable to give a high recommendation to the Mediterranean diet as a way to improve healthy living.

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## Suggested Further Readings

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- Keys A. Mediterranean diet and public health: personal reflections. *Am J Clin Nutr*. 1995;1(Suppl):1321S–3S. This paper provides insight into the man who was instrumental in initiating interest in this dietary pattern