The Mediterranean Diet and Your Health
Janet Bond Brill
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The evidence of a protective effect of the Mediterranean diet against the development of chronic disease and premature death is overwhelming.

The pioneering work of Ancel Keys and colleagues’ famed Seven Countries Study1 established a strong ecological correlation between serum cholesterol level and mortality from coronary heart disease (CHD) in 16 cohorts of participants from 7 countries. Keys’s concept that the blood cholesterol level and, consequently, risk of CHD were greatly influenced by what was served at mealtimes was such a radical idea at the time that it landed him on the cover of Time magazine on January 13, 1961. In his book How to Eat Well and Stay Well the Mediterranean Way,2 Keys first used the term good Mediterranean diet to describe the eating pattern of populations dwelling in southern Europe, especially the island of Crete in the late 1950s and early 1960s. During this period, Greece had the highest life expectancy in the world (and the lowest rate of CHD) despite consuming an unusually high amount of fat, suggesting that the eating habits of this population might be a model diet for promoting excellent health and longevity. Since then, both the scientific community and public alike have been captivated by the allure of the highly palatable and health-promoting nature of the Mediterranean style of eating. Described in the scientific literature as “very close to if not the ideal diet,”3 it is of interest to clarify what exactly defines the Mediterranean diet (MD) and to review selected older landmark studies as well as more recent scientific evidence, providing new insight linking this pattern of eating with the prevention of chronic degenerative diseases.
The purpose of this review is to examine the defining characteristics and the health benefits associated with consumption of the MD. Five sections follow. The first section highlights the myriad definitions of the MD that currently exist in the literature. In the second section, key components of the diet are addressed, and a consolidated global definition of the MD is given. The third section reviews the health benefits associated with the diet and summarizes the supporting scientific evidence. The fourth section presents the problematic trend of abandoning the traditional healthful diet of Mediterranean countries in favor of a more Westernized style of eating. In the final section, a summary of this article is provided along with practical applications of the MD as lifestyle medicine for the promotion of good health and longevity in the United States.

Defining the Mediterranean Diet

Defining the MD as a single entity is difficult because an assortment of Mediterranean-style eating patterns has emerged in the literature suggesting that there is “no single ideal Mediterranean diet” but rather a Mediterranean style of eating that shares several key dietary components. Furthermore, to use the term Mediterranean diet to describe the eating pattern of the people living around the Mediterranean basin would be a misnomer, as there are at least 18 countries with coastlines bordering the Mediterranean Sea, each with their own eating habits, religions, and ethnic and cultural customs. In fact, Ferro-Luzzi and Sette stated decades ago that “the all embracing term ‘Mediterranean diet,’ while very attractive, should not be used in the scientific literature until its composition, both in foods, nutrients and non-nutrients, is more clearly defined and the metabolic basis of its health-promoting virtues has been better explained.” Bach and colleagues addressed some of the problems with the concept of a single MD definition. They highlighted the debate over the type of fat (monounsaturated vs polyunsaturated), whether to include dairy products (amount and type), the inclusion of different types of meat, the inclusion and classification of refined cereals as protective or nonprotective, establishing a definition for moderate alcohol intake, and whether to include fish and nuts as independent components in the MD. The lack of a standard definition for use in experimental studies is not a minor issue, and according to Spanish researchers, applications of Mediterranean diets not fully in line with the traditional MD pattern have confounded the evidence. In contrast, Trichopoulou and Lagiou have stated that it is legitimate to consider all regional variations of the diet in the Mediterranean basin (Spain, France, Italy, Greece, etc) as variants of a single entity, the all-encompassing Mediterranean diet.

The Traditional Mediterranean Diet “Greek Style”

It was not until 1995, decades after Keys’s publication of the Seven Countries Study, that there was a resurgence of interest in the traditional MD as new scientific data began to emerge. The Mediterranean style of eating is based on centuries-old culinary traditions in countries around the Mediterranean Sea that have evolved over time and share several dietary traditions. It has been suggested that the archetypal diet be viewed as a “traditional Mediterranean diet” or as an amalgam of various elements of the eating habits of the people of Crete, parts of Greece, and southern Italy circa early 1960, a time when the rate of CHD in Crete was estimated to be 80% to 90% lower than in the United States. Willett and coworkers devised a food guide pyramid graphic, similar to the 1992 US Department of Agriculture food guide pyramid, to illustrate the key attributes of their definition of the traditional MD. Broad characteristics of this 1960s version of the traditional MD are presented in Table 1.

The original traditional Mediterranean diet score (tMED) was constructed by Trichopoulou et al. as a tool to assess adherence to the traditional MD in research. (Note that the original tMED was eventually revised to include fish.) The tMED involved 9 food components divided into “beneficial foods” (vegetables, legumes, fruit and nuts, cereal, fish) and “detrimental foods” (meat, poultry, dairy). One point was assigned for intake at or above the median of beneficial foods (and for moderate intake of wine) and 1 point given for less than the median intake of detrimental foods. The total tMED dietary score ranged from 0 (minimal adherence) to 9 (maximal adherence).

The Mediterranean Diet “Italian Style”

Further obscuring the notion of a single definition of the MD is that numerous studies have strayed from a unified categorization of the MD, using large variants in their own research. Italian researchers have, for example, laid claim to their own version of the MD, defined as “the dietary pattern followed by people living in southern Italy in the 1960s.” Here, the diet of the people living in Nicotera (the southern Italian cohort of the Seven Countries Study) is considered to be “the plant-based, low-fat, high-carbohydrate composition of the Mediterranean diet, Italian style.” The low-fat nature of this version of the MD differs markedly from the estimated 40% of total energy derived from fat in Crete in the early 1960s.

The Mediterranean Diet “American Style”

In the United States, an alternate MD index (aMED) was developed for use in clinical and epidemiologic investigations and more specifically for use with the Nurses’ Health Study and National Institutes of Health–AARP (NIH-AARP) Diet and Health Study. The aMED was formulated for use in conjunction with the tMED dietary scoring system discussed previously. The aMED was designed to better reflect the dietary habits of the American population as opposed to traditional Greek dietary habits. The aMED was derived from a 140-item food frequency questionnaire and based on the previously described 9-item scoring system used in the early Greek EPIC studies. The original scale was then updated and modified (Table 1) to reflect dietary patterns that have been consistently associated in the scientific literature with lower rates of chronic disease. Key differences included exclusion of

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### Table 1.
**Sampling of the Variability in the Mediterranean Diet (MD) Definition Drawn From Studies Investigating or Reviewing Mediterranean-Style Diets**

<table>
<thead>
<tr>
<th>Study</th>
<th>Review Article or Type of Study</th>
<th>Title of Diet</th>
<th>Description of MD and/or Characteristics</th>
</tr>
</thead>
</table>
| Trichopoulou28                                | Review article                  | Traditional Mediterranean diet          | 1. High ratio of monounsaturated to saturated dietary lipids (mainly olive oil)  
2. Moderate ethanol consumption  
3. High consumption of legumes  
4. High consumption of nonrefined cereals, including bread  
5. High consumption of fruits  
6. High consumption of vegetables  
7. Low consumption of meat and meat products  
8. Moderate consumption of milk and dairy products |
| Melbourne Collaborative Cohort Study18        | Large prospective cohort study  | The Mediterranean factor                | "The Mediterranean factor was characterized by frequent intake of items, including garlic, cucumber, olive oil, salad greens, capiscum, cooked dried legumes, legume soups, feta and ricotta cheeses, olives, steamed fish, and boiled chicken. This factor was also negatively associated with consumption of tea, margarine, sweet biscuits, and cake." |
| Prevención con dieta mediterránea (PREDIMED)58 | Large prospective cohort study  | Mediterranean-type food pattern         | "Beneficial foods’ (olive oil, vegetables, legumes, fruits, nuts, fish and seafood, white meats instead of red meats, home-made sauces, red wine). . . ’detrimental foods’ (red meats, fat-rich dairy products, commercial pastries and snacks, artificially sweetened beverages)." |
| Nurses’ Health Study16                        | Large prospective cohort study  | Alternate Mediterranean diet score (aMED) | "The original score (9,13) was based on the intake of 9 items: vegetables, legumes, fruit, nuts, dairy, cereals, meat and most products, fish, alcohol, and the ratio of monounsaturated to saturated fat. Intakes above the median of the study subjects received 1 point; all other intakes received 0 points. Meat and dairy product consumption less than the median received 1 point. We modified the original scale for this study by excluding potato products from the vegetable group, separating fruit and nuts into 2 groups, eliminating the dairy group, including whole-grain products only, including only red and processed meat for the meat group, and assigning alcohol intake between 5 and 15 g/d for 1 point." |
| Ambring et al46                               | Randomized clinical trial       | Mediterranean-inspired diet (MID)       | "The MID consisted of twice the amount of fiber in the ordinary Swedish diet, 3-4 times as many antioxidants, almost 3 times the amount of PUFA and twice the amount of n-3 fatty acids, one-half the amount of saturated fat, one-half the amount of cholesterol and a 35% reduction in the glycemic index. In addition, sterol esters were included as an ingredient in the margarine (2g/d) only during the MID." |
| Søndergaard et al61                           | Randomized clinical trial       | Mediterranean diet                      | "Eat at least 600 grams of fruits and vegetables daily, modify the intake of fat, especially saturated fat from meat and dairy, to eat fatty fish at least once a week and preferably several times a week, to eat plenty of bread and cereals, and to replace refined, hard, animal margarine products with vegetable oils, preferably canola oil." |
| Lyon Diet Heart Study48                       | Randomized clinical trial       | Cretan Mediterranean diet               | "The Six Dietary Commandments’: 1) more bread; 2) more vegetables and legumes; 3) more fish; 4) less meat (beef, lamb, pork), and replaced by poultry; 5) no day without fruit; 6) no more butter and cream, to be replaced by a special margarine. . . . Moderate alcohol consumption, mainly in the form of red wine, was allowed or recommended at meals." |
| Dalzeil et al19                               | Cost utility analysis          | Mediterranean diet                      | "Key elements of the Mediterranean diet are more whole-grain bread, more fruit and green vegetables, more fish, less red meat, no butter or cream, and oils/spreads restricted to olive oil. Moderate alcohol consumption (wine) is usually permitted." |

PUFAs, polyunsaturated fatty acids. This table provides a compilation of studies investigating the Mediterranean-style diet. It lists a variety of definitions of the MD and/or characteristics.
potatoes from the vegetable group, separation of fruit and nuts into 2 groups, elimination of dairy foods, inclusion of only whole grains, inclusion of only red and processed meats as a negative score, and use of the same alcohol range for both men and women (5-25 g/d). Final scores on the aMED retained the 0 to 9 range.16,17

Additional Variations of the Mediterranean Diet

Australian investigators studying dietary patterns and cardiovascular mortality among Mediterranean migrants to Melbourne18 used a 121-item food frequency questionnaire. A statistical factor analysis technique was then used to factor load food items into 4 main dietary factors. The “Mediterranean foods factor” was characterized by frequent intake of garlic, cucumber, olive oil, greens, capers, legumes, feta and ricotta cheese, fish, and chicken. In contrast, Australian and French researchers19 have published a shorter and more simplified description of the key elements of the MD (see Table 1).

Thus, a thorough review of the literature reveals as many different regional variations of the MD as there are countries that border the Mediterranean Sea. Table 1 includes a sampling of the variability in the MD definition drawn from a selection of studies investigating or reviewing Mediterranean-style diets. There are many existing models for a healthy Mediterranean way of eating. The MD definition should be consolidated so that more valid conclusions can be drawn from the literature regarding the health effects of a more global MD.

Key Components of the Mediterranean Diet

Several researchers have suggested that the health effects of the MD are due to a dietary pattern of eating, comprising a symphony of foods with the interaction of multiple synergistic protective factors as opposed to singling out individual nutrients or foods as the underlying protective mechanism. Quite possibly, it is the combined effect of many constituents of the Mediterranean pattern of eating that can explain the favorable effect on health and longevity that this lifestyle confers. That said, and before a global definition of the ideal MD can be proposed, several specific dietary factors merit discussion for the powerful role they play in the health-promoting actions of the MD.

Plant Foods and Antioxidants

Perhaps the most unifying theme of all the Mediterranean dietary patterns described in the literature is that they consist largely of foods from plant origin, with only modest amounts of animal food sources. A characteristic of the traditional MD is the unusually high intake of fruits, vegetables, nuts, legumes, whole-grain cereals, and olive oil,20 all of which are derived from the plant kingdom.

Plant foods are rich in dietary fiber, antioxidants, vitamins, minerals, and polyphenols, factors that confer numerous health benefits, most notably protection from cancer and CHD.21,22 Animal sources of protein such as beef, pork, and lamb—foods notoriously high in saturated fat and dietary cholesterol—are consumed relatively infrequently.23 In fact, low consumption of animal products in particular has been cited as a strong contributing factor for the excellent health of the Mediterranean people.24

The MD is renowned for its abundance of plant-based foods, filled with an extraordinary array of antioxidants. Antioxidants counter excessive production of reactive oxygen species (ROS), which include both free radicals and nonradicals. Pathologies arise in the body when the production of ROS exceeds the body’s antioxidant capacity.25 Thus, a large intake of antioxidants theoretically provides the underlying protective mechanism related to their ability to fight DNA damage and oxidative stress and therefore provides an explanation for the significant reduction in the incidence of chronic disease associated with the MD, rich in plant foods and their associated antioxidants.

Greek scientists of the epidemiological ATTICA study26 demonstrated that greater adherence to the MD in a large sample of healthy men and women is positively associated with an increase in a measurable level of total antioxidant capacity (TAC). TAC is a valid indicator of the cumulative action of all antioxidants in the plasma and tissues and is used as a tool to investigate the relationship between diet and oxidative stress.

What’s more, those participants reporting the greatest adherence to the MD (those in the highest tertile of the MD dietary score) exhibited, on average, a 19% lower concentration of oxidized low-density lipoprotein (LDL) cholesterol compared with those consuming a more Westernized pattern of eating (falling in the lowest tertile of the MD dietary score).

A review of the functional foods in the MD27 has shown that many of the plant-derived foods characteristic of the MD (nuts, fruits, vegetables, garlic, onions, herbs, and red wine) contain a vast number of bioactive compounds that collectively provide significant health benefits. Nuts, for example, are rich in phenols, flavonoids, and phytosterols. Fruits and vegetables contain flavonoids, carotenoids, folic acid, and fiber, all of which are instrumental in warding off CHD. Researchers in Australia28 identified a few of the typical Mediterranean foods eaten by the study participants that were thought to contribute to the elevated level of circulating carotenoids observed in Greek immigrants to Australia. Wild green leafy vegetables, figs, and extra virgin olive oil exhibited the highest concentration of carotenoids. In fact, it was noted that few foods on earth are known to contain the extraordinary range of carotenoids found in figs. Carotenoid-rich food intake has been inversely related to a reduced risk of death from cardiovascular disease (CVD). A recent 15-year prospective investigation of 559 men in the Netherlands’ Zutphen Elderly Study27 revealed that increased consumption of alpha- and beta-carotene was associated with a reduction in risk of CVD mortality by about 20%.

Wild greens are another Mediterranean dietary staple, typically consumed in large amounts in the traditional Greek MD. According to Trichopoulou,29 greens are routinely prepared with virgin olive oil, an additional source of antioxidants. Moreover, wild greens provide an appreciable amount of flavonoids, more than...
the amount found in an equal quantity of red wine. Keys30 described the abundance of green leafy vegetables at the heart of the MD simply as “leaves,” or verdure. He wrote of the principal role these vegetables play in the diet: “No main meal in the Mediterranean countries is replete without lots of verdure (greens).”

Alcohol, and more specifically red wine, is an important (albeit, optional) component of the Mediterranean pattern of eating and may be partially responsible for the lower rates of CVD among the peoples of the Mediterranean. The protective effect of alcohol consumption as it relates to the reduction of risk of CVD is well established.30 An estimated 2 drinks a day reduces risk of CHD by 30% to 40%.22 “Moderate” consumption of wine with meals is generally accepted as a component of the MD. Willett et al12 define a moderate amount of red wine as 1 to 2 glasses a day for men and 1 glass per day for women. The cardio-protective role of red wine has been linked to its polyphenol content (namely, resveratrol, a stilbene polyphenol) as well as its ability to positively affect endothelial function,25 reduce LDL oxidation, and raise serum level of high-density lipoprotein (HDL) cholesterol.30

Pitsavos et al24 make the case that it is the balance of food consumption and not the consumption of individual foods that affords the protection against chronic disease that this dietary pattern offers. It would therefore appear that each individual plant food may not work alone in its contribution to the health benefits of the whole dietary pattern. Consider that olive oil phenols, for example, work in conjunction with resveratrol, as well as with quercetin (a flavonoid found in high amounts in both fruit and wine), generating a collective arsenal of protection against disease. Hence, the dietary theme of the MD is largely vegetarian, providing a plethora of plant foods that guarantee a high intake of polyphenols, naturally occurring antioxidants that have proven to be highly instrumental in conferring protection against degenerative diseases.

Olive Oil

Another explanation for the health-promoting nature of this dietary pattern is that it is extremely high in monounsaturated fat, derived mainly from olive oil, a dietary strategy that, in combination with a low intake of animal products, virtually guarantees a low consumption of atherogenic saturated fat. Olive oil has been used for culinary purposes by the Mediterranean people for centuries. Some believe that the good health enjoyed by the Mediterranean people has been closely tied to the olive-growing areas in the Mediterranean region, suggesting that this component may be one of the key factors in providing the protection against chronic disease that this dietary pattern offers. In the 1950s and 1960s, Crete had an unusually high fat intake (primarily in the form of olive oil) estimated at or exceeding 40% of total dietary energy.30,31 Moreover, dairy fat and other animal fats such as butter and other shortenings were virtually unknown in the southern Mediterranean region in the early 1960s. Combine this information with the extremely low intake of saturated fat–rich meat, modest amounts of dairy (flavorful cheeses and yogurt), and the almost exclusive use of monounsaturated fat in the form of olive oil and you have a vivid account of how this population maintained such a low saturated fat intake and a clear explanation for the low serum cholesterol values that Keys described in his research.

One advantage of using olive oil in the kitchen is that it encourages the consumption of large amounts of vegetables and legumes, antioxidant and fiber-rich foods that many Americans find difficult to fit into their diet. According to Boskou,12 the protective nature of the MD is most likely due to 3 general factors: (1) consumption of a low amount of saturated fat; (2) intake of omega-3 fatty acids from fish, wild plants, nuts, and legumes; and (3) consumption of a large amount of olive oil. Hence, olive oil plays a central role in the MD, and so a discussion of its history, composition, and potential mechanism of action appears warranted.

Several of the foods commonly consumed in the traditional MD have a rich historical significance. Olives, figs, and grape vines, for example, were the type of tree crops capable of surviving the arid climate that pervades the Mediterranean basin. They were also plants that were hearty enough to thrive along hilly terrains amid largely unfertile soil. It was during the great Roman era—more than 750 years that the Mediterranean was under Roman rule—that most of the foods associated with the traditional MD (wheat, barley, figs, olives, grape vines, and a variety of fruits and vegetables) were established as part of the diet because of great demand from the population of Rome.35 It is for these reasons that olive oil became the principal source of fat in all Mediterranean-style diets.

The health benefits of olive oil have been attributed to 2 main constituents: the high oleic acid (a monounsaturated fatty acid, or MUFA) content and the large amount of antioxidant compounds. Olive oil contains a large proportion of monounsaturated fat in the form of oleic acid (55% to 85% of fatty acids)32 and antioxidants primarily in the form of the olive oil phenolics hydroxytyrosol and oleuropein.35 The high MUFA content of olive oil is highly cardioprotective, positively affecting numerous aspects of the lipid profile, including a reduction in total and LDL cholesterol, increased resistance of LDL to oxidation, and an increase in HDL.34 In fact, MUFAs from olive oil are more effective in raising HDL than polyunsaturated fat.30 In addition, the high polyphenol content of olive oil (specifically, hydroxytyrosol and oleuropein) provides potent free-radical scavenging activity, promotes resistance of LDL to oxidation,37 and has been shown to inhibit platelet aggregation36 as well as increase nitric oxide production38 and stimulate anti-inflammatory agents.39 Note that the extra-virgin type of olive oil, as opposed to the more refined olive oil, is highest in phenolic compounds and thus has the greatest free-radical scavenging potential.38

The health benefits of a high consumption of olive oil on reducing risk of myocardial infarction (MI)40 and attenuation of risk factors for CHD have been scientifically documented. Investigators from the Greek cohort of the EPIC study showed that olive oil intake was inversely associated with reduction of systolic and
Omega-3 Fatty Acids

Scientific data have begun to accumulate suggesting that an ideal MD should contain olive oil as the primary source of fat but also include a good amount of omega-3 polyunsaturated fatty acids (PUFAs) in the form of the long-chain omega-3 fatty acids eicosapentaenoic acid (EPA; 20:5n-3) and docosahexaenoic acid (DHA; 22:6n-3) and the short-chain omega-3 fatty acids, Swedish researchers, employing a 4-week crossover design, compared the effects of a typical Swedish diet with a Mediterranean-inspired diet on serum phospholipid fatty acid composition and markers of inflammation in 22 healthy individuals. The Mediterranean experimental diet was highly enriched with omega-3 fatty acids, including both forms of omega-3, fatty fish (high in DHA and EPA) and flaxseed (rich in ALA). Results showed a substantially lower plasma ratio of n-6:n-3 after the MD compared with the Swedish diet. What is more, the MD resulted in a significant reduction in serum markers of inflammation (reduction in total number of platelets, leukocytes, and vascular endothelial growth factors) in participants after 4 weeks on the omega-3-supplemented MD compared with 4 weeks on the Swedish diet.

Both the Indo-Mediterranean diet intervention trial and the Lyon Diet Heart Study provide evidence of the secondary protection that ALA confers against the risk of MI. In the Lyon Diet Heart Study, an intervention trial comparing an ALA-enriched MD with a “prudent” diet, the experimental group was advised to consume a MD with the addition of a specially formulated margarine, high in both ALA and MUFAs. Over several follow-up periods spanning 36 months, it was determined that the MD group was highly successful in favorably altering dietary habits from baseline, as they increased intake of oleic acid by 36% and ALA by 216% while decreasing saturated fat intake by 31%, cholesterol by 25%, and linoleic acid (LA; 18:2n-6) by 38%. Risk of recurrent cardiac events and mortality were reduced by more than 70% in the MD group compared with the control group. The authors concluded that although MUFAs are protective against LDL cholesterol oxidation, a reduction of dietary intake of LA and a concurrent increase in ALA use a separate set of cardioprotective mechanisms than MUFAs. Lowering dietary intake of LA while increasing intake of ALA gives ALA the competitive edge in competition for desaturase enzymes. Thus, production of EPA and DHA and subsequent conversion into the anti-inflammatory and antithrombotic family of n-3-derived eicosanoids are facilitated.

In summary, enriching the MD typically high in MUFAs with omega-3 PUFAs in the form of both ALA (from plants) and DHA/EPA (from fatty fish), in addition to including many of the functional foods reviewed above, is a dietary strategy that should be implemented when constructing the ideal MD.

A Unified Definition of the Mediterranean Style of Eating

A single, broad definition of the MD would be beneficial, as it would provide a more standardized reference diet. The ideal MD definition would stipulate general dietary intake suggestions as well as specify that the MD should restrict and omit unhealthful foods (such as saturated fat, cholesterol, trans fat, and refined, low-fiber carbohydrates). Furthermore, because additional healthful MD components have surfaced in the more recent literature, a broad and updated global definition of the MD including these foods would be helpful.

Drawing on this literature review, a uniting of the general characteristics that make up the ideal MD is as follows: a primarily plant-based, whole-foods diet filled with an abundance of healthful plant-derived bioactive compounds (such as polyphenols, phytosterols, vitamins, minerals, and fiber) and a diet that provides a low intake of atherogenic saturated fat, dietary cholesterol, and trans fat (via infrequent
consumption of animal protein sources such as red meat and meat products and processed foods).

More specifically, the necessary components of the unified MD that can be extracted from this review include the following:

1. daily consumption of several servings of whole grains (minimally processed);
2. daily consumption of a variety of vegetables (including root vegetables if desired), with an emphasis on daily intake of dark leafy greens (seasonally fresh);
3. daily consumption of fruit (seasonally fresh);
4. daily consumption of plant foods high in ALA such as flaxseeds and walnuts;
5. daily consumption of extra virgin olive oil (used as the main fat);
6. daily consumption of legumes;
7. daily consumption of red wine (1 to 2 glasses/d) with meals;
8. daily consumption of a small amount of nuts;
9. daily use of antioxidant-rich herbs and spices to flavor foods (such as garlic, onions, dill, oregano, and curry powder);
10. weekly consumption of omega-3-rich (EPA/DHA) fish, at least 2 servings per week;
11. weekly consumption of a small amount of low-fat or fat-free dairy (such as flavorful cheeses and yogurt), several servings per week;
12. moderate consumption of poultry and eggs (can be less than once per week if desired); and
13. occasional consumption of sweets containing refined sugars (can be less than once per week if desired).

Based on the collective scientific evidence to date, it appears that the ideal MD would contain these necessary components, in the amounts described above, ingested on a routine basis. A sample 1-day menu that reflects this global unified definition of the Mediterranean style of eating is presented in Table 2. This sample menu illustrates a Mediterranean style of eating, incorporating numerous aspects of the updated MD. This dietary pattern can be integrated into the lives of individuals from all nations with minor cultural modifications made, if desired. Regional foods (that fit within the cultural customs of the country of origin) could be substituted as long as those foods remain under the general designated component category.

### Health Benefits of the Mediterranean Diet

The evidence of a protective effect of the Mediterranean diet against the development of chronic disease and premature death is overwhelming. Since the mid-1990s, numerous well-designed scientific studies continue to add to the wealth of scientific data in support of the healthfulness of the Mediterranean pattern of eating. Variants of the MD have demonstrated protection against and improved prognosis for a wide range of diseases and disorders, including coronary heart disease, diabetes mellitus type 2, hypertension, embolisms, osteoporosis, and certain cancers such as breast, stomach, colorectal, and prostate. A review of all the health benefits associated with consumption of the MD is beyond the scope of this article. However, the bulk

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**Table 2.** Sample 1-Day Menu Reflecting the Unified Definition of a Mediterranean Style of Eating

<table>
<thead>
<tr>
<th>Meal</th>
<th>Food</th>
<th>MD Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast</td>
<td>Oatmeal, Ground flaxseeds, Soy milk, Mixed berries</td>
<td>Whole grain, Omega-3 ALA, Legume, Fresh fruit</td>
</tr>
<tr>
<td>Snack</td>
<td>Walnuts</td>
<td>Nuts, omega-3 ALA</td>
</tr>
<tr>
<td>Lunch</td>
<td>Greek salad: tomatoes, onions, cucumber, peppers, garlic, olives, a very small amount of low-fat feta cheese, and dressed with olive oil, vinegar, and fresh lemon juice</td>
<td>Vegetables, onions, Garlic, Olives, Low-fat dairy, EVOO, Fresh fruit</td>
</tr>
<tr>
<td>Snack</td>
<td>Apple</td>
<td>Fresh fruit</td>
</tr>
<tr>
<td>Dinner</td>
<td>Glass of red wine, Salmon seasoned with olive oil, garlic, dill, and lemon, Lentils served over brown rice, Spinach sautéed with garlic and olive oil, Figs for dessert</td>
<td>Wine with meal, Omega-3 EPA/DHA, EVOO, garlic, herbs, fruit, Legume, whole grain, Vegetable (dark leafy green), garlic, EVOO, Fruit</td>
</tr>
</tbody>
</table>

The menu can be culturally modified by incorporating regional foods that fit within the cultural customs of the country of origin. ALA, alpha-linolenic acid; EVOO, extra virgin olive oil; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; MD, Mediterranean diet.
of the scientific literature provides support of the impressive benefits of the MD in both the primary and secondary prevention of CVD in particular. Therefore, this article focuses on the MD with regard to protection from CVD as well as the association between the MD and a reduction in all-cause mortality.

Coronary Heart Disease

The popularity of the MD for its ability to grant protection against CHD is largely due to the work of Ancel Keys, so it is appropriate to begin this section with a discussion of Keys and his brilliant Seven Countries Study. In the late 1950s and early 1960s, was due to the work of Ancel Keys, so it is appropriate to begin this section with a discussion of Keys and his brilliant Seven Countries Study.10

Seven Countries Study

In the late 1950s, Keys and colleagues observed that the mortality rate from cardiovascular disease was significantly reduced in countries where the mean total blood cholesterol was lowest. Keys had a novel idea; he surmised that the remarkable immunity from coronary events and the long life expectancy of the Mediterranean population, particularly the people living on the isle of Crete in the late 1950s and early 1960s, was due to the impact of their diet on their health. Thus, the Seven Countries Study10 was begun in 1958 to examine the association among diet, cholesterol level, and rates of CHD in 16 cohorts of middle-aged men from Finland, Greece, Italy, Japan, the Netherlands, the United States, and Yugoslavia. Data were generated over several decades, providing evidence that a mainly plant-based diet, rich in vegetables, fruit, and olive oil and low in meat, eggs, and dairy—and combined with an active lifestyle—could significantly reduce mortality from CHD and promote longevity. The concept of the "good Mediterranean diet" was born.

Epidemiological Research

An ample amount of epidemiological evidence clearly shows that there is a positive relationship between consuming a Mediterranean pattern of eating and the primary and secondary prevention of CHD. In the Melbourne Collaborative Cohort Study,18 a prospective cohort study of 40,653 Australian volunteers (24% were migrants to Australia from Mediterranean countries) was followed for just over 10 years. A 121-item food frequency questionnaire was administered, and 4 main dietary factors or patterns of eating emerged from the data using statistical factor analysis. The 4 main dietary factors were identified as factor 1, high intake of Mediterranean foods; factor 2, high vegetable intake; factor 3, high meat intake; and factor 4, high fresh fruit intake. Results provided evidence of a strong inverse relationship between consumption of a factor of Mediterranean foods (a high intake of foods such as garlic, greens, legumes, fish, olives, and olive oil) and CVD mortality.

In the Greek cohort of the EPIC study,13 an inverse relationship was demonstrated between higher adherence to the MD and all-cause mortality and death from CHD. In fact, an increase of 2 units in the MD dietary score was associated with a 25% reduction in all-cause mortality and a 33% reduction in death from CHD. In the ATTICA study,49 a Framingham 10-year absolute risk score was statistically correlated with each participant’s level of MD adherence, assessed using a 0- to 55-point range. Results showed that individuals with the greatest adherence to the MD had a 43% lower likelihood of having a Framingham 10-year risk of CHD greater than 10%.

In Spain, a short questionnaire50 was devised to estimate consumption of cardioprotective elements that typically comprise the MD (olive oil, wine, fruits, vegetables, fish, legumes, and whole grains). The case control study of 171 MI survivors matched to 171 controls revealed that an increment of 1 point in the dietary score was correlated with a relative reduction in risk of a MI of 18%.

Regarding secondary prevention of CHD, a separate arm of the Greek EPIC cohort13 investigated the health benefits of the MD in 1302 men and women (of the original 22,000 who had been previously diagnosed with CHD at enrollment. After an approximate 4-year follow-up, those participants showing a higher adherence to the MD by 2 units demonstrated a reduction in all-cause mortality by 27% and, when only cardiac deaths were considered, a reduction in mortality by 31%.

Intervention Studies

Primary prevention. Several intervention studies have been published providing scientific evidence that Mediterranean-style diets have a causal role in the primary prevention of CHD. In Spain, the Prevención con dieta mediterránea (PREDIMED) study was a large-scale, 4-year, controlled multicenter clinical trial with approximately 9000 high-risk participants. The study was designed to assess the effect of the MD, enriched in either virgin olive oil or mixed nuts, on the primary prevention of CVD. In this subsection of the PREDIMED trial,52 the effect of 2 types of MDs on cardiovascular risk factors was examined. Study participants included 772 high-risk individuals randomly assigned to 1 of 3 diets (a low-fat diet, a MD supplemented with virgin olive oil, or a MD supplemented with mixed nuts) for 3 months. Results showed that both the MD groups had lower blood pressure, improved lipid profiles, decreased insulin resistance, and a reduction in markers of inflammation when compared with the low-fat diet group. Furthermore, the MD groups were more compliant with their diets when compared with the low-fat group, suggesting that the MD is superior to a low-fat diet in terms of reducing CVD risk factors and long-term dietary acceptability.

In France, the Mediterranean Diet, Cardiovascular Risks, and Gene Polymorphisms (Medi-RIVAGE) study,53 a clinical 3-month trial involving 212 men and women, compared the effects of 2 different diets on risk factors for CVD. Participants (moderate risk) were randomized to either a low-fat, low-cholesterol diet or a MD. Both diets resulted in statistically comparable reductions in CVD risk factors. However, upon additional statistical analyses of the serum cholesterol concentration, reductions based on Law’s concept54 of estimating the long-term size of CVD risk reduction, the authors predicted a greater reduction in CVD risk with the MD group, 15%, versus a 9% reduction in risk with the low-fat diet, respectively.
Furthermore, there was a 2-fold lower dropout rate in the MD group compared with the low-fat group, suggesting that the MD is superior to a low-fat diet in terms of both future CVD risk reduction and patient compliance.

Secondary prevention. Results of several randomized clinical trials provide sound scientific evidence supporting the protective effect of the MD in the secondary prevention of CHD. As noted previously, the Lyon Diet Heart Study provided striking evidence of the protective effect of the MD with regard to the recurrence of CHD in survivors of MI. The extraordinary results (a 50% to 70% reduction in risk of a recurrent MI in the MD group) warrant taking a closer look at the details of this particular study. The effectiveness of the MD versus a National Cholesterol Education Program (NCEP) Step I-type diet was tested on 423 MI survivors randomized to 1 of the 2 diets. The participants in the NCEP control diet group, however, failed to meet the dietary requirements and consumed a diet resembling that presently consumed in the United States (high in saturated fat and cholesterol). The MD contained more bread, root and green vegetables, fish, and daily fruit and less red meat than the prescribed NCEP diet. Furthermore, the MD group replaced butter and cream with a specially formulated margarine, high in ALA and olive oil, resulting in significantly higher plasma levels of oleic acid, ALA, and EPA compared with the control group. Recall that this particular version of the MD was unique regarding the enrichment of the diet with a large amount of ALA. Moreover, the fat composition of this version of the MD (30.5% of total calories) differed from the traditional Mediterranean dietary pattern, typically much higher in MUFA. The MUFA content of the Lyon diet trial contained just 12.9% MUFA, far less than the 15% to 20% characteristic of Mediterranean dietary patterns. Thus, despite the departure in fat makeup from the typical MD, the study results were truly remarkable. In conclusion, a MD, rich in ALA, is a valuable tool in the secondary prevention of CHD and appears to be more acceptable in terms of patient compliance than the archaic low-fat AHA Step I diet.

The Gruppo Italiano per lo Studio della Sopravvivenza Nell’Infarto Miocardico (GISSI) Prevention Trial for the secondary prevention of CHD was a large-scale (n = 11,246) intervention study designed to ascertain if consumption of the MD results in reduced mortality from CHD after a previous MI. A simple pamphlet describing suggested foods to include in the diet (fruits, vegetables, whole grains, olive oil, fish, legumes, fat-free dairy, poultry, and lean meats) was administered to study participants. A 5-food intake assessment (amounts of raw vegetables, cooked vegetables, fish, fruit, and olive oil) was calculated into a dietary score. Over the 6.5-year duration of the study, dietary assessments were taken 4 times. Results revealed that a 1-unit increase in the combined dietary score reduced the risk of death by 15%. Compared with participants in the lowest quarter, those with the highest dietary score exhibited an odds ratio for risk of death of 0.51. As a result, the authors concluded that uncomplicated dietary advice to increase consumption of a few foods characteristic of the MD can lead to a substantial reduction in risk of death in patients having a history of a previous MI.

The Indo-Mediterranean Diet Study was a randomized trial in the secondary prevention of CHD involving 1000 South Asian patients with a previous diagnosis of CHD or at high risk. Participants (most were vegetarians) were randomized to an experimental diet (a Mediterranean-style diet unusually high in ALA) or a control diet (similar to an NCEP Step I diet). This version of the MD included ample fruits, vegetables, nuts, whole grains, legumes, rice, maize, and wheat. A 52% relative reduction in cardiac endpoints was shown in those participants following the MD (supplemented with a high ALA fat source: mustard seed or soybean oil). It is of interest to note that this version of the MD contained a much lower percentage of MUFA (10%) than is typically characteristic of a traditional MD (15%-20%), providing further evidence of the cardioprotective value of supplementing the MD with omega-3 ALA. Therefore, the inclusion of a significant amount of both types of fatty acids (MUFA and ALA) in the MD appears to be a reasonable strategy for constructing an ideal MD.

Potential Mechanisms: Underlying the Protective Effect of the MD in CHD Prevention

Inflammation and endothelial dysfunction. It is well known that inflammation and endothelial dysfunction are involved in the etiology and progression of atherosclerosis. Markers of these disorders include a high concentration of high-sensitivity C-reactive protein (CRP), interleukin 6 (IL-6), E-selectin, soluble intercellular adhesion molecule–1 (ICAM-1), and vascular cell adhesion molecule–1 (VCAM-1). Data are beginning to emerge linking the MD with a reduction in these biomarkers, providing a biological pathway for the protective effect of the MD. US researchers generated data that support this notion. Fung et al correlated a higher aMED score with a significantly lower concentration of biomarkers for inflammation and endothelial dysfunction in the large-scale Nurses’ Health Study. More specifically, a higher adherence to the MD was associated with lower concentration of CRP, IL-6, E-selectin, and ICAM-1.

Concurrent with these findings is the reduction in serum inflammatory markers observed in the first cross-sectional analysis of a segment of 772 high-risk participants recruited for the PREDIMED study. Those individuals with the highest consumption of some of the foods typical of the MD (fruits, cereals, olive oil, and nuts) had the lowest serum concentrations of inflammatory markers CRP, IL-6, ICAM-1, and VCAM-1. Moreover, the large ATTICA study revealed that those participants demonstrating the highest adherence to the MD had significantly attenuated plasma levels of coagulation and inflammatory markers. On average, CRP was 20% lower, IL-6 was 17% lower, white blood cell count was 14% lower, fibrinogen was 6% lower, and homocysteine was 15% lower compared with those in the lowest tertile of dietary adherence.

Another intervention trial in Spain compared the effects of an NCEP Step I diet...
with the MD on endothelial function in hypercholesterolemic men and following an initial 28-day high saturated fat introductory diet. Both the NCEP diet group and the MD diet group showed significant improvements in LDL cholesterol, apolipoprotein B, and P-selectin. Compared with the saturated fat diet, however, only the MD increased flow-mediated vasodilation in the brachial artery.

Combining a statin treatment with the MD versus statin treatment alone has shown that the addition of the MD to a statin significantly improves endothelial function over and above medication alone. A clinical intervention trial\(^1\) recruited 131 hypercholesterolemic patients with previously diagnosed CHD and randomized them to the MD with 40 mg fluvastatin or 40 mg fluvastatin alone. After 12 months, the MD intervention group demonstrated a significant improvement in brachial flow-mediated vasodilation compared with the statin-only group, suggesting that combining the MD with statin therapy is a more beneficial therapeutic option than medication alone for the prevention of CHD.

Thus, a growing body of scientific evidence is emerging demonstrating the ameliorative effect that the MD has on biomarkers of inflammation and endothelial dysfunction, two processes strongly linked to atherosclerosis. This effect provides a potential mechanism for the reduction in risk of CVD associated with the MD.

**Oxidized LDL.** The role of oxidized LDL in the pathology of the atherosclerotic process has long been recognized. In a subsection of the PREDIMED trial\(^2\), 372 participants were randomly assigned to either a low-fat diet or 1 of 2 different versions of the traditional MD (virgin olive oil supplement or mixed nuts) for a 3-month period. Following the 3-month intervention, both the olive oil and the nut-supplemented MD had significantly reduced the concentration of oxidized LDL cholesterol compared with the low-fat diet. This study provides a key mechanism by which the MD may exert its protection against CHD.

**Metabolic syndrome.** The metabolic syndrome is a group of risk factors or metabolic disorders (abdominal obesity, insulin resistance, hypertension, and dyslipidemia) that, when clustered together in one individual, significantly increase the risk of atherosclerotic disease and type 2 diabetes mellitus.\(^3\) Recently, investigators in Italy\(^4\) randomized 180 men and women diagnosed with the metabolic syndrome to 1 of 2 dietary interventions: either the MD or a control “cardiac-prudent diet” with less than 30% of total calories from fat. After a 2-year period, and despite a similar increase in physical activity between the groups, the MD group lost more weight and exhibited a significant reduction in CRP and a reduction in insulin resistance compared with the prudent diet group. After 2 years, 40 of 90 participants in the intervention group still had metabolic syndrome versus 78 patients on the control diet. Thus, the MD lowered the prevalence of metabolic syndrome by 48%.

Concurring with these findings was the ATTICA study,\(^5\) where a 13% lower likelihood of having the metabolic syndrome was associated with adherence to a Mediterranean-style dietary pattern. The metabolic syndrome increases risk for the development of type 2 diabetes. A cross-sectional analysis of Greek adults in the large-scale ATTICA study\(^6\) revealed that consumption of the MD is associated with lower odds of having diabetes. A 10-unit increase in the MD score was linked with a 21% reduction in the risk of diabetes. Furthermore, if participants combined regular physical activity with high adherence to the MD, the risk of contracting diabetes was even less, with a 35% reduction in risk compared with sedentary participants.

In conclusion, the sum of the research provides powerful evidence that the MD is highly protective against CVD, the metabolic syndrome, and the development of type 2 diabetes. In fact, Willett\(^1\) has estimated that more than 80% of CHD, 70% of stroke, and 90% of type 2 diabetes can potentially be avoided with adherence to the traditional MD together with regular physical activity and not smoking.

**Longevity.** Considerable evidence exists that the MD increases longevity, particularly among the elderly population. Scientific data on the positive effect of the MD on longevity have been rapidly accumulating over the past decade. Perhaps the first study to credit the traditional MD as being responsible for the well-documented longevity of the rural Greek population was the investigation of the dietary patterns of elderly inhabitants of 3 Greek villages by Antonia Trichopoulou and associates.\(^7\) A 5-year follow-up of 182 elderly Greek participants provided evidence that individuals whose diets deviated from the traditional MD had a significant increase in probability of all-cause mortality compared with those following the traditional MD. A more recent study led by the same principal investigator\(^8\) assessed the effect of a traditional MD on survival rate of a large group of elderly men and women older than age 60 at baseline. The findings showed that greater adherence to the Mediterranean pattern of eating improved longevity in an older population. Using a dietary score (defined previously) from 0 (minimal adherence) to 9 (maximal adherence), data revealed that a 2-point increment in the MD score resulted in a 25% reduction in total mortality. Moreover, in the Danish cohort of the Euronut Survey in Europe on Nutrition and the Elderly via a Concerted Action (SENECA) study,\(^9\) researchers examined the effect of the MD on longevity in 202 elderly residents of a Danish municipality in 1988. After 6 years, a dietary assessment using 7 MD characteristics showed that a 1-unit increase in the diet score predicted a 21% reduction in mortality.

The HALE project, or Healthy Ageing: A Longitudinal Study in Europe,\(^10\) was a large-scale cohort study of healthy men (n = 1507) and women (n = 832) between the ages of 70 and 90 years, drawn from 11 European countries. The aim of the study was to investigate dietary and lifestyle factors associated with mortality from all causes, CHD, CVD, and cancer. Over the course of 10 years, individuals who adhered to a healthy lifestyle or a “low-risk pattern,” characterized by low-risk behaviors—adherence to the MD, moderate alcohol consumption, nonsmoking, and at least 30 minutes of physical
activity per day—exhibited a significant reduction in mortality. In fact, 60% to 64% of mortality was associated with lack of adherence to this low-risk pattern. The authors concluded that adherence to a Mediterranean lifestyle in a group of individuals aged 70 to 90 years was associated with a greater than 50% reduction in the rate of all-cause and cause-specific mortality.

The most recent publication on this topic outlines results from the first and largest US-based cohort evaluating the relationship between the MD and longevity.\(^7\) The NIH-AARP Diet and Health Study has provided strong evidence that adherence to a Mediterranean-style dietary pattern in an older American population is associated with a significant reduction in all-cause and cause-specific mortality.

Swedish investigators\(^6\) have provided data showing that the MD can reduce mortality even among young individuals. A cohort of 42,257 young women (aged 30-49 years) was followed for an average of 12 years. The MD 10-point assessment tool by Trichopoulou et al.\(^5\) was used. Among the subset of women aged 40 to 49 at enrollment, it was determined that closer adherence to the MD was inversely associated with deaths from cancer as well as all-cause mortality. A 2-point increase in the diet score was associated with a 13% reduction in all-cause mortality and a 16% reduction in cancer deaths. Hence, a large body of convincing scientific evidence continues to build suggesting that adherence to the MD favorably affects life expectancy in young and old as well as among people from different nations across the globe.

**The Shift Away From the Mediterranean Diet**

Unfortunately, new research is revealing that the traditional dietary patterns of countries lining the Mediterranean basin appear to be changing, with a rapid transition to a less healthful Western style of eating, high in saturated fat and refined carbohydrates and low in fiber. There is great concern regarding the deterioration in consumption of the traditional MD, a trend that is accompanying the industrialization and increase in prosperity of many southern Mediterranean countries. In reality, the healthy traditional MDs are being displaced not only by a Westernized pattern of eating but also with a highly sedentary lifestyle. This shift way from a healthier, largely plant-based traditional pattern of eating and active lifestyle is accompanied by undesirable effects on health status. An accelerated rise in CVD has been documented in addition to a significant increase in CVD risk factors such as diabetes, abdominal obesity, hypertension, and hypercholesterolemia.\(^7\)\(^6\)\(^7\)

Consequently, with the departure from traditional healthful eating habits in favor of a more Westernized diet higher in meat, full-fat dairy, and animal products, so too are the associated MD health benefits diminishing with the passage of time. Marion Nestle stated some time ago that given this alarming situation, “Mediterranean diets may well be considered to be endangered species.”\(^7\)\(^2\)

Scientists have put out a call to action in favor of large public health campaigns aimed at preserving the traditional MD in Mediterranean regions in an attempt to reverse the diet-related disease-promoting trend of changing to unhealthy dietary patterns and abandoning the customary traditional MD.\(^7\)\(^6\)\(^7\)

**Summary and Application**

The MD is a centuries-old style of eating that is a practical and highly enjoyable dietary pattern, comprising an abundance of whole nutrient-dense foods, including fruits and vegetables, grains, olive oil, fish, nuts, legumes, and moderate amounts of red wine. Consuming a Mediterranean dietary pattern has consistently been found to reduce CVD risk, protect against certain forms of cancer,\(^7\)\(^6\) and yield an overall protective effect for all-cause mortality. The widespread appeal of this style of eating and the worldwide awareness of the role diet plays in decreasing risk of chronic disease provide an enormous incentive for countries to consider promoting cultural modifications of the Mediterranean dietary pattern, a move that would benefit the health of people across all populations around the globe.

From a public health perspective, much work remains to be done to close the gap between knowledge and an actual change to more healthful dietary practices here in the United States. Given the extraordinary amount of scientific data backing the unquestionable health benefits of adhering to a Mediterranean dietary pattern of eating, as well as the fact that the public finds the MD attractive for its famous palatability and highly appealing aura, it would be prudent for health care practitioners to actively promote this “good Mediterranean diet” to the general public as the gold standard for the prevention and treatment of chronic disease and the promotion of a long and healthy life.

**References**


