The Effects of the Mediterranean Diet on the Risk for Cardiovascular Disease

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Abstract

Cardiovascular disease (CVD) is the leading cause of death in the United States and is largely due to poor diet and lifestyle choices. In general, the Western diet has shown a higher prevalence in CVD than those in the Mediterranean regions, and many theories attribute this to the differences in the Western diet from the Mediterranean diet. The Mediterranean diet is characterized as high intakes of plant foods (fruits, vegetables, cereals, potatoes, beans, nuts, seeds), seasonal and locally grown foods, minimal processed foods, the main source of fat as olive oil, low to moderate amounts of dairy and fish, moderate consumption of red wine, and low amounts of red meat. Research shows that overall mortality as well as mortality from CVD is lower in those who have a higher adherence to the Mediterranean diet, which is explained in depth by a higher consumption of olive oil, moderate consumption of red wine, and low consumption of red meat. Extra virgin olive oil contains complex phenolic compounds and monounsaturated fatty acids that lower LDL cholesterol. The antioxidants in olive oil and red wine prevent the oxidation of LDL. Higher consumption of red meat has shown to have a positive correlation with CVD and mortality rates. The exact mechanism for this is complex and more research needs to be done. Some explanations are that red meat raises LDL cholesterol and red meat consumption is also correlated with lower fruit, vegetable, and fiber intakes. Overall, adherence to a typical Mediterranean diet can lower the risk for CVD because of the components in olive oil and red wine as well as a decreased consumption of red meat.

Key words: Mediterranean Diet, CVD, saturated fat, polyphenols, olive oil

Introduction

The deadliest disease in the United States is also one that is largely exacerbated by a poor diet. In 2006, one in four Americans died of cardiovascular disease (CVD) and was the leading cause of death in both men and women (1). For such a common cause of mortality, this disease is not well-known or put into the public spotlight, which is why it is known as the "silent killer". From a global perspective, of the 58 million deaths that occurred in 2005, nearly 30% were caused by cardiovascular disease (2). A traditional Mediterranean diet is more beneficial in reducing the risk of cardiovascular disease than diets typical of the Western world. In fact, in an analysis of over 1.5 million individuals, those who had a higher adherence to the Mediterranean diet had a decreased incidence of overall mortality and cardiovascular mortality (3). Therefore, the Mediterranean diet is an effective lifestyle in improving overall health, especially for Americans who are at a high risk for CVD, because it contributes to a higher consumption of monounsaturated fat in olive oil, phytochemicals in red wine, and a low consumption of saturated fat from foods such as red meat, beef, and pork.

What is Cardiovascular Disease?

Cardiovascular disease is the overall term describing a group of various conditions that is associated with atherosclerosis, hypertension, and thrombosis. The Greek origins of atherosclerosis are the words, *athena*, meaning gruel, and *sclerosis*, meaning hardening. This suggests exactly what the condition does to the body, a fatty hardening and degeneration of the vascular wall (4). This buildup of plaque on the artery walls prevents an adequate amount of blood flow to the heart. Over time, this can cause the heart to weaken, prevent total blood flow to the heart, or cause heart failure (1). Risk factors for CVD include high levels of LDL and VLDL cholesterol, hypertension or high blood pressure, smoking, being overweight or obese,

diabetes, and a sedentary lifestyle. Another reason behind the development of the disease is a genetic component, where the disease poses a greater risk to individuals with a family history, as well as having a lifestyle and dietary component (4).

The origins of the disease can begin in childhood and worsen with time and aging as plaque buildup and arterial damage degenerates. Atherosclerosis begins when there is damage to the endothelial cells in the artery wall that are directly in contact with blood flow and act as a barrier to foreign cells and substances. LDL is the main transporter of cholesterol through the blood, but elevated levels of oxidative LDL could cause endothelial damage. This causes monocytes and T lymphocytes to rush to the affected area as well as platelets. The platelets release growth factor, which stimulate the smooth muscle cells to take up oxidized LDL by endocytosis, forming foam cells. Ultimately, the foam cells form a layer of plaque that, if continued over a long period of time, will cause atherosclerosis and restrict blood flow to the heart (5).

What is the Mediterranean Diet?

The Mediterranean diet is described as the diet consumed by the populations of Crete, Greece, as well as other olive growing areas of the Mediterranean region. Variations of the diet have been linked to France, Lebanon, Portugal, Turkey, Spain, and Morocco. A very broad spectrum of the components of the diet include high intakes of plant foods (fruits, vegetables, cereals, potatoes, beans, nuts, seeds), seasonal and locally grown foods, minimal processed foods, the main source of fat as olive oil, low to moderate amounts of dairy and fish, moderate consumption of red wine, and low amounts of red meat. Fat intake ranges from 25-35% of total calorie intake, with saturated fat contributing to less than 7% of total calories (6). The

Mediterranean diet is associated with a higher life expectancy than the western world. For example, in 1991 the life expectancy in Greece (77.5 years) was nearly two years higher than that in the United States (75.8 years) (7).

The Mediterranean diet can be traced back thousands of years owing to a vast amount of evidence through art, archaeological food debris, pottery, tools, and inscribed tablets dating back to the Neolithic and Bronze Ages.   The first study that attempted to investigate the exact dietary intake of the Mediterranean diet occurred in 1948. The Rockefeller Study was implemented in an effort to improve the social, economic, and health conditions on the island of Crete and Greece after WWII. The study consisted of weighed food inventories from 128 households, 7 day food intake questionnaires from over 500 individuals, and food frequency questionnaires of 765 households (7).

The results found that cereals contributed to 61% of the diet in Greece and 39% in Crete, compared to only 25% in the U.S. Meat, fish, dairy, and eggs accounted for 33% of the U.S. diet compared to 7% of the Greek diet.   The Cretan diet also had 29% of table oils and fats, but nearly 78% of those were olive oil. The Rockefeller Foundation concluded that "olives, cereal grains, pulses, wild greens and herbs, and fruits, together with limited quantities of goat meat and milk, game, and fish have remained the basic Cretan foods for forty centuries…no meal was complete without bread…olives and olive oil contributed heavily to energy intake" (7). This first analysis of the exact components of the Mediterranean diet holds to be extremely similar to the diet of the 21st century.

A Mediterranean diet "pyramid" was developed in 1994 in order to give a general and overall sense of the dietary patterns (See Figure 1). It is similar to the USDA food guide

pyramid in that it is representative of the healthy adult population (and may have to be adjusted for young children and pregnant women). However, the pyramid does not give exact definitions of weights and proportions of certain foods. The bottom of the pyramid represents the foods that are consumed most frequently which include breads, pasta, rice, couscous, polenta, and potatoes. The next level of the pyramid are foods that are consumed daily, which are mostly fruits and vegetables and to a lesser extent other legumes and beans. Olive oil is the next level followed by cheese and yogurt. Foods that should be eaten a few times a week are fish, poultry, eggs, and sweets. And at the peak of the pyramid is red meat, which is eaten a few times a month. The pyramid also includes wine drinking in moderation and the incorporation of regular physical activity (6).

Mediterranean Diet and Overall Health Benefits

This type of Mediterranean diet is believed to have several health benefits and is associated with a lower mortality rate. This is proven by a study that assessed 183 elderly individuals over the age of 70, equal numbers of men and women, in three villages in Greece. Food frequencies were recorded and then calculated in terms of specific quantities. These quantities were then used to assign a "Mediterranean Diet Score" for eight different categories. Each category was scored from 0 to 1, with 1 being associated with a higher adherence to a Mediterranean diet. The eight categories were: high monounsaturated to saturated fat ratio, moderate ethanol, high consumption of legumes, cereals, fruits, vegetables, and low consumption of meat and dairy/milk products. In general, the results of the study found that those individuals with a higher adherence and a higher score had a lower mortality rate than those with a lower score. The scores of each individual category had little statistical significance, whereas the overall score was a better determinant of mortality rate. With each one unit increase in diet score

there was a 17% decrease in mortality, and with a four unit increase there was a 50% decrease in mortality (8). From this data, it can be concluded that a higher adherence to an average Mediterranean diet lowers mortality and death rate.

One of the most striking studies that supports the evidence for the Mediterranean diet reducing the risk for CVD is the "Lyon Diet Heart Study". Individuals who had already suffered from a previous heart attack were assigned to one of two different groups. One group of 302 random individuals was asked to eat a Mediterranean diet and 303 individuals were asked to eat their normal diet and were given no dietary advice. The Mediterranean group's diet consisted of more bread, green leafy vegetables, fish, no day without some type of fruit, less beef, lamb, and pork, and butter and cream were replaced with margarine high in alpha linolenic acid. After one year, the study was stopped because of the Mediterranean group had significantly more benefits than the control group. The experiment group showed 50-70% lower risk of recurrent heart disease (19).

Effects of Increased Olive Oil Consumption

Olive oil is the principle source of fat in the Mediterranean regions and replaces the types of fats found in animal products. Olive trees are grown best in the regions from the 30 degree to 40 degree parallel, which is where the majority of the Mediterranean region lies. In fact, the Mediterranean region produces and supplies 95% of the world's olive oil (10). Olive oil is extracted from the olives by washing, crushing, kneading, and centrifugation of the olives. If the pH of the oil is below 3.3, it is then refined with chemicals to produce a common olive oil. Unrefined olive oil is known as extra virgin olive oil. Extra virgin olive oil retains the most nutrients because 80% of phenolic compounds are lost during the refining process (16). Olive oil

is most beneficial due to its high concentration in monounsaturated fats (MUFA's). Particularly, the MUFA's in olive oil are oleic acid (18:1) and linoleic acid (18:2). Olive oil has been shown to protect the oxidation of LDL (one of the initiating steps in atherosclerosis) (10).

The quality and type of fat, as opposed to the quantity, seems to have an effect on CVD risk. A study conducted by Penny Kris-Etheron, a professor at Penn State University, found a 25% decrease in CVD risk when consuming a diet where fat consists of 34% of total energy intake, with 21% of that coming from MUFA's in olive oil (4). In another study, Mensink and Katan suggest that saturated fat increases LDL levels, and monounsaturated and polyunsaturated fats reduce LDL concentrations. This is consistent with decreased cardiovascular rates in the Mediterranean region because olive oil is high in monounsaturated fats and low in saturated fats, thus lowering serum LDL cholesterol concentrations (9).

Higher HDL levels are also linked with a decreased risk in CVD. This is because HDL is responsible for reverse cholesterol transport, meaning HDL transports cholesterol from extrahepatic tissues to the liver, where it can then be eliminated from the body. This decreases overall cholesterol levels. In one study, supplementation with extra virgin olive oil improved the lipoprotein profile of elderly men by raising HDL levels and decreasing LDL levels (4).

Olive oil is also a rich source of vitamin E, also known as the antioxidant, alpha-tocopherol. There is evidence that higher levels of antioxidants (tocopherols, carotenoids, flavanoids, and polyphenols) are associated with lower levels of cardiovascular disease. This is because, extra virgin olive oil, not plain olive oil, contains 50-800 mg/kg of phenolic compounds which is what gives it it's attractive aroma and flavor. The amount of polyphenols in olive oil is dependent on the cultivar, the soil, the amount of ripeness, and the means by which the oil was

produced and stored. There are two types of polyphenols; simple and complex. Complex polyphenols include oleuropein and hydroxytyrosol, which has been shown to inhibit LDL oxidation. There is also evidence that the polyphenols limit platelet formation, scavenge reactive oxygen species, inhibit DNA damage, and inhibit bacterial growth (11). Therefore, the complex polyphenols in olive oil are associated with a decreased risk for the development of cardiovascular disease.

The polyphenols hydroxytyrosol and oleuropein have shown to prevent signs of CVD by preventing inflammation. In a study by Carluccio, hydroxytyrosol and oleuropein (as well as trans-reservatrol, which will be discussed later in the wine section) were incubated for thirty minutes with human umbilical vein endothelial cells. The researchers were investigating the effects of these antioxidants on leukocyte adhesion to the endothelial cells and leukocyte adhesion molecules, because this is one of the first signs of atherogenesis. The particular leukocyte adhesion molecule being assessed was vascular cell adhesion molecule-1 (VCAM-1) which is a protein that aids in the adhesion of leukocytes and monocytes to the endothelial wall. The results of the study found that the addition of hydroxytyrosol and oleuropein inhibited the action of VCAM-1 and reduced monocyte adhesion to endothelial cells (15). Therefore, the phytochemicals in olive oil, a main constituent of the Mediterranean diet, serve as antioxidants to protect the arteries of the heart from oxidative damage and thus prevent heart disease.

Some factors of olive oil that are not greatly focused on in research literature are the fact that olive oil has been consumed for thousands of years by people in the Mediterranean region with little to no negative impact. Butter and margarine in the Mediterranean region is almost nonexistent compared to its availability in the United States. Olive oil is also added to the preparation of many vegetable and legume dishes, thus increasing the intake of these beneficial

food groups as well. The phenolic compounds add to the characteristic taste and flavor of olive

oil that adds to the palatability of vegetables when cooked in the oil. Thus, this increases the

intake of the MUFA's in the oil as well as the nutrients in the vegetables (6).

Effects of Moderate Red Wine Consumption

People of the Mediterranean region have been drinking red wine in moderate amounts

during meals as a form of enjoyment and tradition for centuries. Moderate consumption is

assumed to be two glasses of wine per day for men and one glass of wine per day for women (6).

Moderate consumption of wine has been linked with decreased occurrence of CVD. The

antioxidant content in wine contributes to lowering oxidative stress and reactive oxygen species,

thus lowering the risk of CVD. Biologic activities of wine phenols include inhibition of LDL

oxidation, phytoestrogenic activity, inhibition of tumorigensis, vasorelaxation, inhibition of

platelet aggregation, and inhibition of human polymorphonuclear leukocytes (11). In fact, there

is data from an epidemiological study that concluded moderate wine drinking reduced the risk of

myocardial infarction (heart attack) by 30-40% (9).

The effects of red wine have shown to lower lipid levels, especially LDL. In one study,

45 postmenopausal women with moderate hypercholesterol ages 50-75 were given either 400 mL

of water, dealcholised wine, or full complement red wine for four weeks. During the four weeks

of red wine supplementation, all groups received standardized meals. At the end of the four

weeks followed a two week wash out period, which is when the lipid levels of the women were

taken. The consumption of full complement red wine lowered LDL levels by 8% and increased

HDL levels by 17% (17). The results would have been more significant if the researchers

measured LDL concentrations at the end of the four week intervention rather than after the

washout period. Nevertheless, these women were at a higher risk for CVD because of their original high lipid levels, but with the addition of red wine into the diet, "bad" cholesterol was lowered and "good" cholesterol was raised.

In a study by Leighton, 42 males ages 21-27 were split into two diet groups, receiving either a high fat diet or Mediterranean diet for three months. The first month consisted of wine alone. The second month consisted of the addition of 240 mL/day of red wine. And finally, during the third month no wine was distributed, serving as a "wash out" period. Blood samples and evaluations were performed at 0, 30, 60, and 90 days. The results showed that after the addition of red wine into the Mediterranean diet group, vitamin C levels increased 13.5% and total antioxidant capacity increased by 28%. Oxidative DNA damage was decreased by 50% in both the high fat diet and Mediterranean diet groups (as measured by 8-hydroxydeoxyguanosine levels). A peculiar finding in this study, however, was that vitamin E levels in the Mediterranean diet group decreased by 26% after the addition of wine (12). Overall, this study successfully demonstrated how the antioxidants in red wine contributed to a reduced incidence of oxidative stress, suggesting that moderate wine consumption reduces the risk for CVD.

An important biomolecule that aids in antioxidant activity is glutathione (GSH). The role of GSH in reducing oxidative stress is its ability to recycle oxidized alpha tocopherol and ascorbic acid (two other important antioxidants) in circulation. In one study conducted by Micallef, a younger (18-30 years) and older (over 50 years) group was either assigned to a control group that abstained from alcohol or a treatment group who received red wine. The treatment group received 400 mL. of Cabernet Sauvignon per day. The results of blood glutathione levels as well as total antioxidant status revealed that the groups who received red wine had elevated levels of GSH, with even more significant increases in the older group.

Malondialdehye (MDA) was measured as a marker of oxidative damage. Those individuals who consumed red wine had decreased levels of MDA, thus lower levels of oxidative damage compared to the control group (13). Therefore, moderate red wine consumption is beneficial to both young and older adults in terms of antioxidant status in the prevention of oxidative damage.

Another very important and effective phytochemical in red wine is trans-reservatrol. In the same study as described above, conducted by Carluccio, trans-reservatrol reduced monocyte cell adhesion to endothelial cells as well as VCAM-1 (15). Therefore trans-reservatrol in red wine acts as an antioxidant to protect the arteries of the heart from oxidative damage.

The type of alcoholic drink also seems to play a role in the effectiveness of cardiovascular function. The Kaiser Permanente Study found that middle-age British wine drinkers had the least coronary risk compared to those who were liquor, spirit, and beer drinkers. The wine drinkers also all had similar healthy lifestyle characteristics and tended to be lighter drinkers and less likely to drink heavily, they also had the least prevalence of smoking and obesity, while having a higher degree of physical activity (14).

This is not to say that excessive alcohol consumption does not have negative effects on the body. Chronic alcohol use has been linked with higher mortality from CVD, whereas moderate alcohol intake is protective against CVD. Chronic ethanol intake can cause hypertension, can damage the tissue of the heart, and cause a stroke. In alcoholics whose ethanol consumption counted for 50% of total energy, other nutrients are being replaced and can cause deficiencies in Thiamin, folate, and B vitamins (14). Therefore, alcohol consumption is all about maintaining a balance. And evidence shows that a moderate intake of alcohol in the form of red

wine increases the antioxidants glutathione and trans-resveratrol and thus reduces the risk of CVD.

Effects of Decreased Red Meat Consumption

A high intake of red meat tends to have a negative impact on heart health. In one instance, when red meat was added to a vegetarian diet, blood cholesterol, LDL, and blood pressure levels were elevated – which are all risk factors for cardiovascular disease (9). Ancel Keys was one of the first researchers to associate red meat consumption and cholesterol with CVD. In 1959, he published his study where he found that Italian diets were very low in fat (<20% of total kcals), which was nearly half of the fat intake of the American cohort. He found that the American diet was higher in red meat and dairy consumption and that its population also had higher blood cholesterol concentrations. Thus, Keys first associated red meat consumption with increased prevalence of CVD in America (7).

The western diet is characteristically associated with consuming high levels of meat products such as beef, pork and lamb and also has increased incidences of CVD. Carcinogens, which are cancer-causing agents, may form during the frying and cooking of meat. Meat contains no fiber and has few antioxidants, thus creating the perfect mixture for heart problems (6). Decreased dietary fiber is also a concern for CVD. The western diet appears to replace fruit and vegetable intake with red meat consumption. In a study following men and women in California, decreased fiber intake was associated with an increased incidence of CVD mortality. A study in Finland found that there was a slight inverse association between fiber and CVD mortality, but with no association in men. However, the study also found that there was an

inverse association between fruit and vegetable intake (which are food groups typically very high in fiber) in men and CVD mortality (9).

The Nurses' Health Study was a very large and successful investigation concerning long term consequences and chronic diseases in women. The participants included 122,000 female nurses', ages 30-55, who received questionnaires in the mail about risk factors for CVD every two years. Food intake questionnaires were included in 1980, 1986, 1994, 1998, and 2002. Women with high intakes of red meat, high red meat to poultry ratio, and high fat dairy also had an increased risk of CVD. Animal protein sources showed an increased risk whereas vegetable protein sources revealed a decreased risk. Individuals who consumed at least one serving per day of nuts showed a 30% lower risk of CVD compared to individuals who ate at least one serving of red meat per day (18). The Nurse's Health Study is a very reliable and valid study that strongly shows a relationship with red meat consumption and the risk of CVD.

Another interesting study was comprised of a special cohort of individuals known as Seventh Day Adventists. Seventh Day Adventists allow a unique situation for researchers to study the effects of diet on health. This is because, on the whole, Seventh Day Adventists do not drink alcohol or smoke cigarettes, and there is also a wide variety of diets within the population in terms of meat consumption. In 1976, a questionnaire was mailed to all Seventh-day Adventists in California, with 75% responding back (59,081 individuals). The participants were broken up into three separate categories: vegetarian (who ate no meat or fish), semivegetarian (who ate meat and fish less than one time per week), and nonvegetarian. Lifestyle factors of the three groups varied in that the nonvegetarian group ate am average of about 4.25 servings of meat per week (mostly beef) and also drank more alcoholic beverages. The results were striking. Nonvegetarian males weighed fourteen more pounds than vegetarians and nonvegetarian females

weighed twelve pounds more. Both males and female nonvegetarians, after adjusted for age, had twice the prevalence of hypertension and diabetes. Also, males who consumed beef three or more times per week had over two times a greater risk of suffering from fatal ischemic heart disease (however, no association was found in women). Overall, vegetarians lived 2.51 years longer than nonvegetarians. This study shows a correlation that as red meat consumption increases, so does the risk for hypertension, diabetes, colon cancer, prostate cancer, arthritis, fatal ischemic heart disease in males, and all causes of mortality (20).

Discussion

There may be a few confounding variables that could contribute to skewed results of the research studies that have been discussed. In general, nearly every study included dietary histories and questionnaires that were self-reported by the individual. This could have an effect on the outcome and results of the study because people tend to underreport how much or what type of foods they have eaten, they may forget what they ate, or inaccurately describe what they ate. Another factor that may prevent accurate results in these studies is that it is difficult to isolate or completely contribute one dietary source (such as olive oil, wine, or meat) to a disease that has so many factors that may cause it. Individuals who have a genetic disposition and a higher susceptibility for CVD could have taken part in some of these studies. Also, the Mediterranean diet is not about just these three types of foods that were discussed. Yes, olive oil, wine, and meat consumption are associated lowering CVD risk. But the Mediterranean diet is more about a type of lifestyle, suggesting that all of the food groups as a whole synergistically reduce the risk for CVD. Another negative aspect about these studies is that it is difficult to stereotype a particular diet when there is some variation from region to region and generation to generation. In general, the proportions of food groups of the Mediterranean diet is assumed in the

Mediterranean diet pyramid, but without specific weights and measures it is difficult to suggest "how many" servings of olive oil, for example, is considered healthy or reduces the risk of CVD.

Conclusions

Cardiovascular disease, also known as "the silent killer", is the deadliest disease in the United States. This may be attributed to the diet typical in the U.S. as well as the western world. In contrast, mortality from CVD and overall mortality is lower in those areas who consume a typical Mediterranean diet. The Mediterranean diet has been the traditional diet for thousands of years to those countries in the Mediterranean region such as Italy and Greece. From the vast amount of evidence discussed throughout this paper, it can be assumed that there is an association with a higher adherence to the Mediterranean diet and a reduced risk for cardiovascular disease. The Mediterranean diet is characterized as high intakes of plant foods (fruits, vegetables, cereals, potatoes, beans, nuts, seeds), seasonal and locally grown foods, minimal processed foods, the main source of fat as olive oil, low to moderate amounts of dairy and fish, moderate consumption of red wine, and low amounts of red meat.

Extra virgin olive oil is healthier than refined olive oil because the refining process loses vital phytochemicals and phenolic compounds. Complex phenols in olive oil, such as oleuropin and hydroxytrosol have shown to inhibit LDL oxidation and monocyte adhesion to endothelial cells. The monounsaturated fatty acids in olive oil are oleic and linoleic acid, which have been shown to lower LDL cholesterol levels and have been shown to decrease the risk for CVD.

Moderate consumption of red wine for men is considered to be two drinks per day and for women is considered one drink per day. The antioxidants in red wine, such as trans-resveratrol and glutathione, have shown to inhibit LDL oxidation. Red wine drinkers also tend to drink less

excessively and live a healthier lifestyle than beer, spirit, and liquor drinkers. Overall, moderate red wine consumption has shown to lower LDL levels and decrease the risk of CVD.

Low consumption of red meat also lowers the risk for CVD. Some of the mechanisms for this are unknown, but red meat is thought to have carcinogens, higher saturated fat content, and also replaces fruit, vegetable, and fiber intake in the diet.

In conclusion, a healthy lifestyle and diet is one of the simplest ways to prevent the risk for cardiovascular disease. Therefore, The Mediterranean diet is undoubtedly able to decrease the risk for CVD. This is largely due to consuming more olive oil, moderate amounts of red wine, and low amounts of red meat. The Mediterranean diet has been keeping the people of that particular region extremely "heart healthy" for thousands of years and should be adopted more by individuals in the western world and the United States.
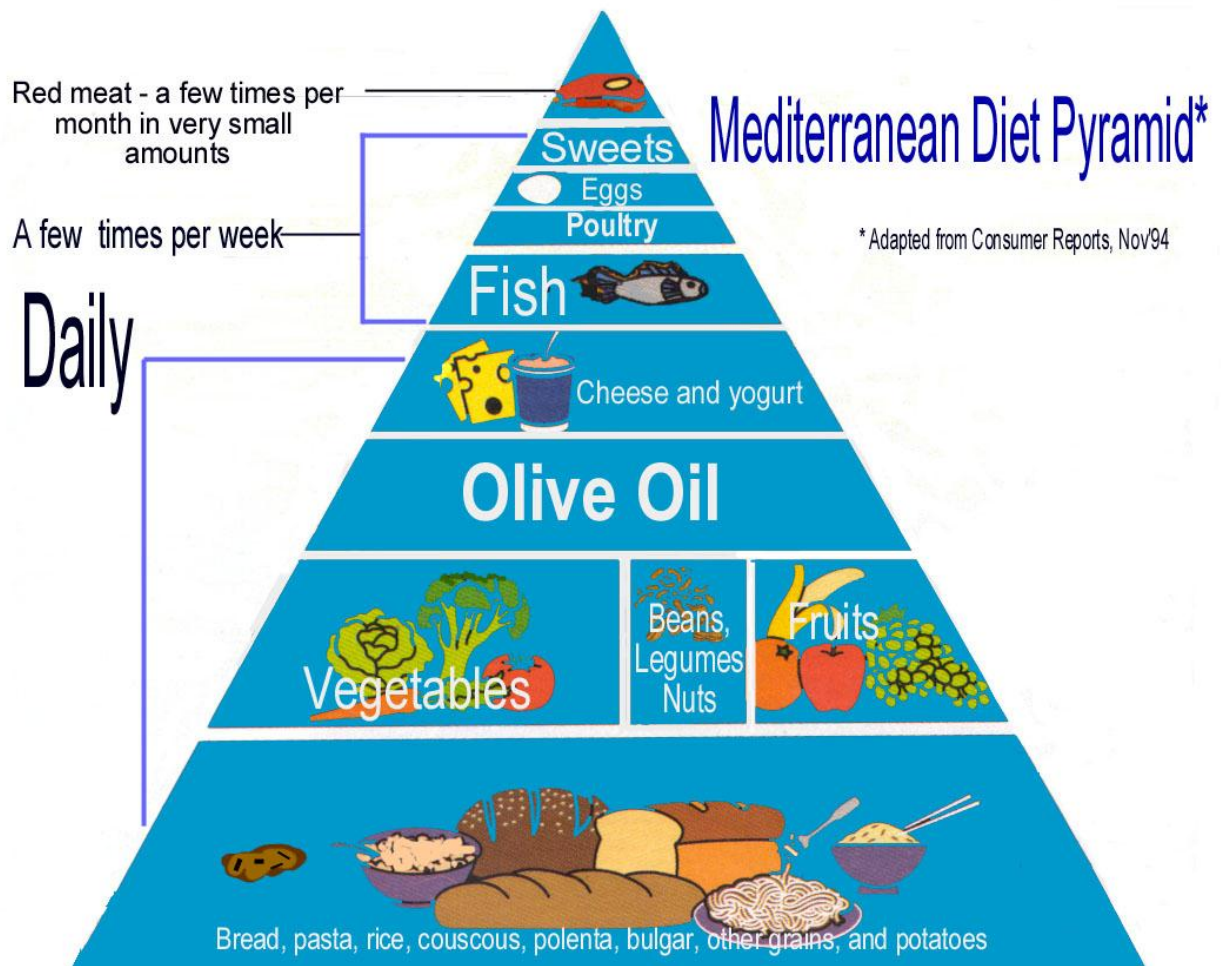
Figure 1: Mediterranean Diet Pyramid

Source: http://www.womensheart.org/images/Mediterranen_Pyramid.jpg

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