



# Mediterranean Diet and Its Effects on Preventing and Managing Type Two Diabetes: A Literature Review

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## Abstract

Diabetes has become a major epidemic in the United States. In 2012, 29.1 million Americans had type 2 diabetes and it is projected that there will be 1.4 million new cases each year. Having diabetes is a major risk factor for cardiovascular disease, renal disease, blindness and limb amputation. Due to the debilitating effects and complications diabetes can have on one's body, research has been conducted to find the best ways to prevent this chronic illness.

Diet tends to be a primary focus around diabetes prevention. A Mediterranean-style diet has been suggested as a good diet plan to prevent type 2 diabetes. A Mediterranean diet consists of high consumption of fruits and vegetables, whole grains, legumes and nuts, moderate intake of seafood and poultry with very minimal intake of red meat. Olive oil is the primary source of fat as well as a moderate intake of wine with meals. The diet suggests avoiding foods with added sugars, refined grains, Trans fats and anything highly processed. According to the literature, this diet can be used to prevent and also help control already diagnosed diabetics.

A review of the literature was performed to determine if there is enough evidence to support recommending a Mediterranean diet as a method of preventing and managing type 2 diabetes. The literature shows an overwhelming trend that following a Mediterranean diet can help lower the incidence of type 2 diabetes and reduce haemoglobin A1C in those already diagnosed.

**Keywords:** Type 2 diabetes; Prevent; Manage; Mediterranean diet

## Introduction

It is much easier and less expensive to prevent a disease than to treat an individual who has developed a chronic disease. In 2012, 29.1 million Americans had type 2 diabetes (T2DM); there are approximately 1.4 million new cases every year.

According to Salas-Salvado et al., diabetes is a potent risk factor for cardiovascular disease, renal failure, blindness, and amputation of lower limbs. Because of the detrimental effects of diabetes has on an individual, research has been done to find more effective ways to prevent the disease [1].

One important aspect of prevention is diet. T2DM can be managed and prevented by following a healthy diet. There are different recommendations for what diet is best. It has been discovered that following dietary patterns as opposed to focusing on single foods may be more effective in preventing T2DM [2]. Combinations of foods may have a synergistic or antagonistic effect together that may be too small to identify with single foods alone [2].

According to Eposito and Giugliano, a Mediterranean-style diet refers to a diet that is mostly plant-based. The consumption of this diet has been found to have a higher survival and a lower mortality rate [2]. A Mediterranean diet consists of high consumption of fruits and vegetables, whole grains, legumes, nuts, olive oil as the primary source of fat, moderate intake of wine with meals, lower amounts of fish, poultry, and red meat. Increased adherence to this diet led to lower hemoglobin A1C (HbA1c) results and 2 h post-prandial levels. These levels were independent of age, weight, physical activity and other variables [2].

A review of the literature shows several studies in favour of adherence to a Mediterranean-style diet and evidence of its positive effect on preventing or helping to control T2DM.

## Methods and Materials

Data for the literature review was obtained by researching electronic databases using keywords, including: type 2 diabetes, HbA1c, prevent,

manage, and Mediterranean diet. The results were further narrowed down to include only randomized controlled trials, prospective and retrospective cohort studies, literature reviews and meta-analysis in the years 1995 through 2016. Exclusion criteria included any study that used participants under the age of 18, recent cardiovascular history, stroke, and cancer. The results obtained from the electronic search were then further evaluated for relevance and inclusion criteria which included prevention of T2DM, Mediterranean diet intervention, measurable changes in diabetes outcomes, reproducible results and results from a reputable source.

## Literature review

**Incidence and prevention of type two diabetes with Mediterranean diet:** The first study reviewed was published by Salas-Salvado et al. [3]. The purpose of the study was to test the effects of two different Mediterranean diets (MedDiet) compared to a low-fat diet on the incidence of T2DM. A three-arm, randomized control trial was performed to test this intervention clinical question. A convenience sample of 418 non-diabetics participants was used with an age range of 55-80. Inclusion criteria included individuals without prior cardiovascular disease (CVD) but with risk factors such as smoking, hypertension, dyslipidemia, overweight and a family history of CVD. Exclusion criteria consisted of current diagnosis of diabetes, severe chronic illness, alcohol or drug abuse, body mass index (BMI) greater than 40 or a history of allergy to olive oil or nuts.

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These participants were divided into three random groups. The control group was educated on a low fat diet. The two intervention groups were educated on MedDiets, supplemented with free virgin olive oil (1 L/week) or nuts (30 g/day). The control group was not given any free food, but was given small gifts quarterly to encourage adherence, such as aprons, cookbooks, shopping bags, etc. Participants were given no advice on physical activity.

Questionnaires were administered at baseline and annually to assess lifestyle variables, medications, and medical conditions. Participants also had fasting blood glucose taken, given an oral glucose tolerance test (OGTT) and weighed annually. Statistically, a Cox regression was used for data with a confidence interval of 95%. P-values were two-tailed with a significance of <0.05.

After an average follow-up of 4 years, the incidence of diabetes was significantly lower in the MedDiets groups. The virgin olive oil group had an incidence of diabetes of 10.1% whereas the nut group's incidence rate was 11.0%. The control group's incidence was much higher eating only a low-fat diet at 17.9%. Combining the results of the two MedDiets created a risk reduction of 52% of T2DM. This study concluded that MedDiets without calorie restriction are effective in preventing T2DM in participants at high cardiovascular risk. This is due to the fact that chronic low grade inflammation is a factor in diabetes. A synergistic effect among the anti-inflammatory properties in the MedDiet, specifically olive oil and nuts, aid in diabetes reduction [1].

The study did list limitations. The cohort that was studied was an older population at high cardiovascular risk, so it is unclear on the generalizability with younger healthier individuals.

Some participants refused the OGTT, which limited the diagnosis of diabetes to a fasting glucose alone. Lastly, a larger sample size and longer follow-up would provide stronger evidence of diabetes prevention.

A study performed by Rossi et al., a general population, prospective cohort study that investigated the relation between adherence to a Mediterranean diet, glycemic load and the occurrence of diabetes [4]. Researchers followed a cohort of 22,295 participants for a median of 11.34 years in Greece during 1994 to 2009. Exclusion criteria included prevalent cancer, stroke, and cardiovascular disease. Participants were instructed to complete a semi-quantitative food questionnaire, administered by the interviewer at the beginning of the study. The information from the questionnaire allowed researchers to create a ten point Mediterranean diet score (MDS) that displayed the participant's adherence to the Mediterranean diet and glycemic load (GL). Over the course of the 11.34 years, incidents of type 2 diabetes through medical records and death certificates were recorded.

The results showed that of the 22,295 participants there were 2,330 cases of T2DM recorded. Overall, a significant inverse relation with adherence to the Mediterranean diet and incidence of T2DM diagnosis was derived from the study. The study also showed that both the Mediterranean diet and a diet with a low GL were associated with a lower diabetes risk.

Individuals with a high MDS and a low GL had the lowest diabetes risk. Unfortunately, a limitation of the study was that it is unclear exactly which component of the Mediterranean diet contributes the greatest effect on decreasing the odds of T2DM.

The results of this study are significant to the overall literature review due to its generalizability. The study used a large general

population based cohort, in a region where the Mediterranean diet is close to the standard of eating. The results provide substantial insight into the potential long term effects of the Mediterranean diet on the incidence of T2DM.

Koloverou et al., as part of the ATTICA cohort study 10 year follow-up, evaluated the adherence to a Mediterranean diet in healthy Greek adults and how it relates to the incidence of diabetes in this population [5]. The ATTICA study was a large epidemiological prospective study using random sampling from the Athens metropolitan area. The people living in the Mediterranean basin follow a traditional Mediterranean-style diet that has been recognized for its health benefits, particularly cardiovascular health. The ATTICA study revealed other health benefits of the Mediterranean diet, including primary prevention of T2DM. The relationships between inflammation, oxidative stress and coagulation and their role as potential mediators in protecting against the development of diabetes were also addressed as part of the study follow-up.

The study began in 2001-2002 with a random sample of 1514 men (ages 18-87) and 1528 women (ages 18-89), for a total of 3042 participants. Exclusion criteria included a history of cardiovascular disease (CVD) or other atherosclerotic disease, chronic viral infections, and being institutionalized. Baseline assessments and measurements were conducted and standard questionnaires were completed by trained personnel during interview sessions. Data were analyzed using ANOVA, Kruskal-Wallis test, or chi-square test, then with post hoc analyses, using the Bonferroni rule or the Mann-Whitney test. The MedDietScore was used to categorize adherence to the Mediterranean diet as being low, medium, or high through multiple logistic regression models. The protective effect of the Mediterranean diet as it relates to diabetes development was also tested using multiple logistic regression models.

A detailed 10 year follow-up evaluation was conducted during 2011-2012 on a working sample of 1485 participants who did not have diabetes at the beginning of the study. Of the working sample, 191 cases of diabetes were documented, which related to an incidence of 129 participants per 1000. The crude incidences were categorized to the appropriate level of adherence to the Mediterranean diet, with 21% having low adherence, 12% with medium adherence and 5% with a high level of adherence. The results showed a reduction in the 10 year diabetes risk of nearly 50% with medium adherence, and greater than 60% risk reduction with high adherence to the Mediterranean diet. Evaluation of the Mediterranean diet's protective effect on diabetes risk was found to be statistically significant only in those with increased abdominal fat as measured by waist circumference.

Study limitations listed for consideration included unknown exact time of diabetes onset in some cases, possibly affecting the estimate of relative risk. Also, possible changes in participants' dietary habits that may not have been reported in a timely fashion over the 10 years. Other limitations include diabetes incidence being underestimated through the exclusion of people with CVD and through the possibility of diabetes status being misclassified. The study results serve as evidence in support of following a Mediterranean-style diet for primary prevention of T2DM (Figure 1).

**The effects of a Mediterranean diet on HbA1c levels:** Another study reviewed was performed by Díez-Espino et al [6]. The purpose of the study was to determine if an association exists between glycemic control and adherence to the Mediterranean diet as assessed by HbA1c levels. A cross-sectional study was performed to answer this therapy clinical question. Purposive sampling technique was used in recruiting

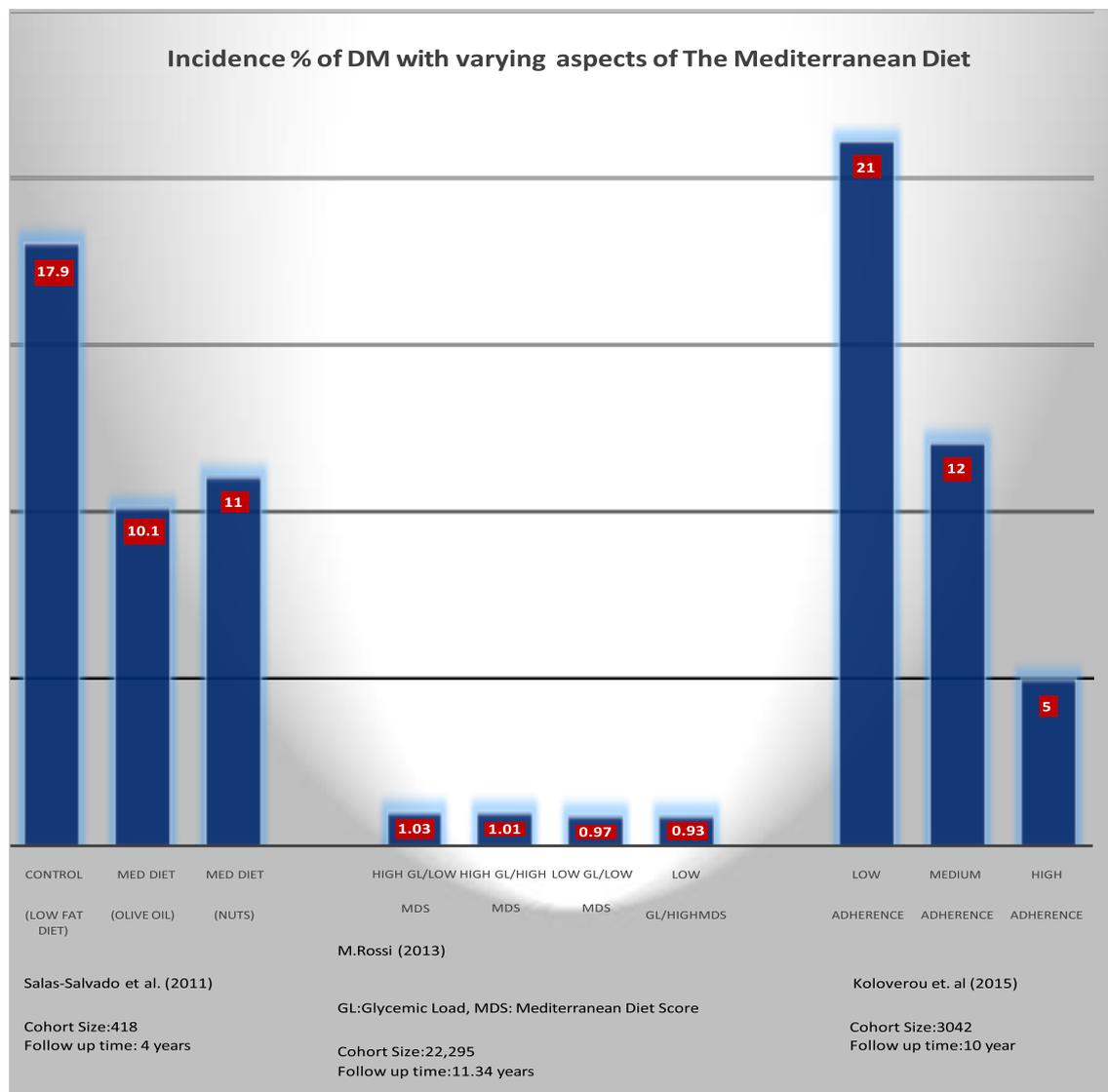


Figure 1: Shows the incidence percentage of DM as shown in the Sala-salvado et al., Rossi and Koloverou et al. studies. All three studies used varying aspects of the Mediterranean diet and measurement tools to display their results, as discussed previously [3,4].

383 participants with a diagnosis of T2DM from six primary health care centers in Pamplona, Spain that participated in the PREDIMED trial. These participants were aged 55-80. Exclusion criteria included a previous history of CVD, severe chronic illness, alcohol or drug abuse, history of allergies to olive oil or nuts and a low likelihood of changing dietary patterns according to the model.

To establish baseline, the participants were asked to fill out a 14-item questionnaire that assessed adherence to the traditional Mediterranean diet. The diet pattern is characterized by a large consumption of legumes, fruit, vegetables, cereals, fish, olive oil, low intake of saturated fats, low to moderate consumption of dairy products, low meat consumption, and regular to moderate consumption of alcohol, preferably wine [7]. HbA1c levels were available for 262 of the 383 participants. All samples were sent to the same laboratory.

Significant two-tailed p-values were used and set at 0.05. Logistic regression models were used to adjust for variables such as age, sex, smoking status, BMI or physical activity level. The average HbA1c was  $6.9 \pm 1.5\%$ .

The results of the study showed an inverse relationship between adherence to the Mediterranean diet and glycemic control. This meant the more an individual adhered to the diet, the lower their HbA1c. However, once confounding variables were accounted for, the association was not statistically significant. Although their data that showed an inverse association was consistent with other studies previously performed, the applicability is compromised since there was no statistical significance.

Ceriello et al. listed limitations to the study. It was acknowledged that the study sample was not a representative study of the general population of patients with T2DM. This limited the external validity of the study [7].

In a randomized cross-over study by Itsiopoulos et al., twenty-seven subjects (age 47-77) with type two diabetes were randomly assigned to consume either an intervention diet (Mediterranean diet) or their usual diet for 12 weeks and then cross over to the alternate diet [8].

The purpose of the study was to determine if diet had an overall effect on HbA1c levels. Prior to the start of the study and after the 12 weeks the participants' lipids, glycemic variables, blood pressure, homocysteine, C-reactive protein, plasma carotenoids, and body composition were assessed. To determine participants were adhering to their assigned diet, their plasma carotenoid and fatty acid composition were monitored throughout the course of the study.

Participants that had not previously been exposed to the Mediterranean diet were recruited for the study. Exclusion criteria included presence of disabling stroke, cancer not in remission, renal failure, or liver disease.

Participants were provided daily food for both the intervention diet and their usual diet. They were to record a daily diary of intake in addition to the blood serum monitoring. The intervention diet was based on the traditional Cretan (Mediterranean) diet and was created from the descriptive food data reported in the seven countries study. All participants met with a registered dietician prior to the start of the study for guidance on food preparation and daily intake.

The results showed that while on the intervention (Mediterranean) diet compared to the usual diet, HbA1c levels decreased from an average of 7.1% to 6.8%. Also, diet quality improved significantly among participants on the intervention diet, their plant to animal intake ratio increased from 1.3 to 5.4 g/day, plasma saturated fat and trans fatty acids decreased and mono unsaturated fatty acids increased (Figure 2).

The results of this study directly contribute to the overall literature review by providing significant results supporting the Mediterranean diet on several health related variables, mainly including the direct decrease of HbA1c levels. The diet also correlated with improved overall diet intake and lipid profile.

Esposito et al. performed a two-armed randomized controlled trial to assess the impact of dietary intervention, such as Mediterranean-style diets (Med diets), on the need for anti-hyperglycemic drug therapy and remission of T2DM in those newly diagnosed [9]. The study included 215 men and women who were middle-aged (mean age 52.2 years)

and overweight (mean BMI 29.6 kg/m<sup>2</sup>), were newly diagnosed with T2DM and had never received anti-hyperglycemic medications. The participants were randomized to either a low-carbohydrate MedDiet (LCMD) group or a low-fat diet group, with no significant difference between groups. At the beginning of the study the mean fasting plasma glucose was 160 mg/dL and mean HbA1c was 7.7%.

In both groups, women were restricted to 1,500 kcal/day and men restricted to 1,800 kcal/day. All participants were given detailed dietary advice and advised to increase their level of physical activity. Detailed assessments and measurements were conducted at regularly scheduled visits with a primary outcome measure of time to initiation of anti-hyperglycemic medications as determined by HbA1c and fasting plasma glucose levels. These measurements were also used for remission analysis. Secondary outcome measures included changes in weight, lipid levels and blood pressure, and meeting the American Diabetes Association (ADA) goals for coronary risk factors. At the end of 4 years, 44% of participants in the LCMD group had reached the primary end point of needing pharmacological treatment for hyperglycemia and 70% in the low-fat group. The primary end point was reached by all participants in the low-fat group after 6.1 years and after 8.1 years in the LCMD group. Rates for remission, weight reduction, improvement of HbA1c and other cardiovascular risk factors were greater overall in the LCMD group.

The authors recognize that through the study's unblinded nature, participants in the LCMD group may have been more encouraged to adhere to the diet over the low-fat group in order to obtain a lower HgA1c. This particular study is a post-core follow-up of the original study to determine long-term benefits of dietary intervention, such as a LCMD, and how it relates to remission of diabetes. The original trial was to be completed in 4 years after a follow-up at that time, but the authors decided to continue monitoring until all of the participants reached the primary end point, for a total post-core follow-up of 8.1 years. Statistical power may have been restricted due to the unknown post-core follow-up at the time of original sample size calculations.

It was concluded through the results of the study that a LCMD can have a greater impact on glycemic control, rates of diabetes remission,

### HBA1C AND HOMA SCORE AFTER THREE MONTH DIET INTERVENTION

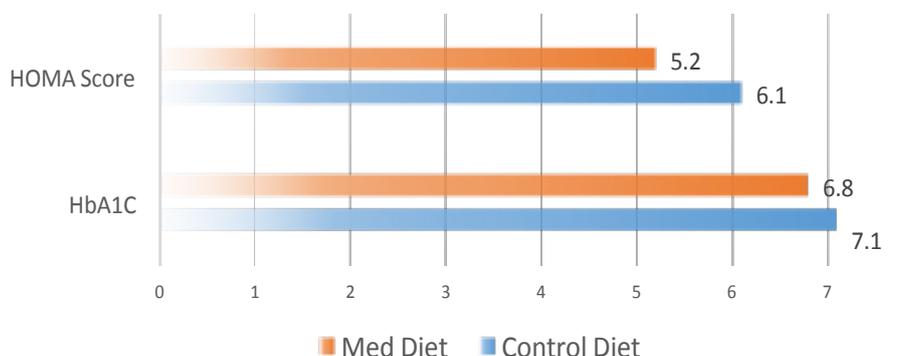


Figure 2: Displays the results of study regarding the change in HOMA score and HbA1c levels after 3 months of control diet and 3 months of intervention (Mediterranean) diet. The average baseline HbA1c score for all participants was 7.5+1.5, no baseline HOMA score was provided.

and the need for antihyperglycemic drug therapy in patients with newly diagnosed T2DM.

## Discussion

It is clear from the literature research that T2DM is a rampant disease that affects all populations across the globe and can result in serious complications or death if left untreated. Millions of Americans are affected by T2DM and failure to treat properly will lead to cardiovascular disease, amputations, or even blindness. The literature shows that following a Mediterranean diet can help prevent the development of T2DM and can help diabetics have better over the disease. These results were expected given the overall healthiness of the Mediterranean diet and the disease process of T2DM.

Implementing this diet in a patient with T2DM can allow them to go from uncontrolled blood sugar levels to a goal HbA1C. The RCT by Itsiopoulos et al. showed participants coming down from a 7.1% to 6.8% HbA1C on average [8]. The study completed by Espino et al. revealed an inverse relationship between adherence to the diet and HbA1C [6]. The higher the adherence to the Mediterranean diet the lower their HbA1C became. Providers need to be advocates for their patients and teach them the importance of diabetes maintenance on their overall health, and how diet plays a major role in this maintenance.

The articles in this review were from participants in European countries where a plant-based diet with minimal red meat and dairy is generally common. More research would need to be done to see how this diet would translate in the United States due to stark differences in diet choices. Although this diet may be challenging for some Americans due to lack of exposure, it is necessary to express to individuals the importance of trying new ways to manage disease based on evidence based practice.

Review of the literature shows that even minimal diet changes can result in a decrease in incidence and severity of the disease. The vast beneficial aspects of the Mediterranean diet, in congruence with physical activity, can help those with risk factors for the disease to decrease their odds of diagnoses, lower their HbA1c, decrease the need for pharmacological interventions and increase their odds of disease remission. Further research can be explored to investigate the generalizability of the study findings within the United States.

## Conclusion

In summary, the Mediterranean diet has been shown to reduce glycemic load, HbA1c and cardiovascular risk factors. Encouraging patients to adhere to a diet rich in fruits and vegetables, whole grains, legumes, nuts, olive oil, and decreased meat consumption may lead to a lower incidence of diabetes and help control T2DM in those already diagnosed. Although, more research needs to be done to apply these suggestions to patients in the United States. The results of the reviewed studies provide practitioners with statistically significant evidence to encourage educating at risk patients on instituting a Mediterranean diet to prevent further incidence of diagnoses and severity of T2DM.

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