Wine Information Council

Mediterranean diet – with or without wine?

TAKE HOME MESSAGES

1. Wine is an integral and indivisible component of the Mediterranean diet.
2. Wine significantly contributes to the overall beneficial effects of the Mediterranean diet.
3. Adherence to the Mediterranean drinking pattern of alcoholic beverages (particularly moderate total intake, consumption of wine with meals, avoidance of excess drinking occasions) maximizes benefits and minimizes alcohol-related health risks.
4. Wine in the context of Mediterranean diet may reduce the inflammatory potential of foods and favorably influence gut microbiota.
5. Benefits of the Mediterranean diet extend beyond the effects on individual health as it also promotes culture of moderation in every aspect of human life.
6. Enjoy wine knowledgably and in moderation following the published drinking guidelines.

1. Introduction

The term "Mediterranean Diet" (Med Diet) was created paradoxically by an American researcher in the early '60s. The physiologist Dr. Ancel Key first discovered the virtues of the Med Diet and communicated its beneficial and protective effects [1]. His large epidemiological study conducted among seven nations – "Seven Countries Study"- resulted in a high geographical variation concerning the rates for cardiovascular diseases. Mediterranean regions reported a lower incidence of cardiovascular disease (CVD) compared to Northern Europe and the USA [1]. Participants that followed the Mediterranean dietary pattern showed a 50% lower rate of cardiovascular mortality due to cardiovascular disease and had the highest life expectancy.

By now, the health benefits are supported by further scientific evidence: The Med Diet is associated with lower disease occurrence and all-cause mortality. The numerous health benefits linked to the Med Diet include a lower risk of cardiovascular disease [2], cognitive disease [3, 4] and cancer [5] as well as metabolic syndrome, obesity and type 2 diabetes [6-10].

UNESCO

In 2010, the UNESCO declared that these culinary practices and cooking culture in Croatia, Cyprus, Greece, Italy, Morocco, Portugal and Spain represent an "Intangible Cultural Heritage of Humanity" (on the United Nations Educational, Scientific and Cultural Organization's Representative List) [11]. This recognition by UNESCO values this eating pattern as part of a wider culture incorporating quality, simplicity, biodiversity and healthfulness of native food products as well as conviviality, socialization and respect the seasonality of foods [12]. Therefore, beyond the foods per se, other components of this lifestyle pattern may be important.

WORLD HEALTH ORGANISATION

The Med diet is considered one of the healthiest diets in the world. The World Health Organization (WHO) recognizes diet as a key risk factor for non-communicable diseases (NCD) that incur huge health and economic costs. They identified the Med diet as an effective dietary strategy to prevent NCDs, which are the leading cause of premature death globally (WHO 2018). The available literature overwhelmingly suggests that Mediterranean-like dietary patterns are beneficial in preventing and controlling diet-related NCDs [13].

Moderate consumption of wine with the meals is an important factor in the Med Diet and a positive item in the Med Diet score (*). However, some population studies suggested that ANY consumption of an alcoholic beverage is harmful to health, because of an increased cancer risk, regardless of the amount consumed and without assessing the pattern of consumption, the type of alcoholic beverage and other lifestyle factors [14, 15]. These authors concluded that it would be best for our overall health to avoid drinking at all, despite the fact that a reduced risk of myocardial infarction and of all-cause mortality was found, and that cardiovascular diseases are the number one cause of death globally (WHO 2017)[1].

[1] https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)

Thus, recommendations to adopt a Mediterranean diet but avoid any alcoholic beverage may be confusing. **Thus, can a Med Diet include a glass of wine with the meal?**

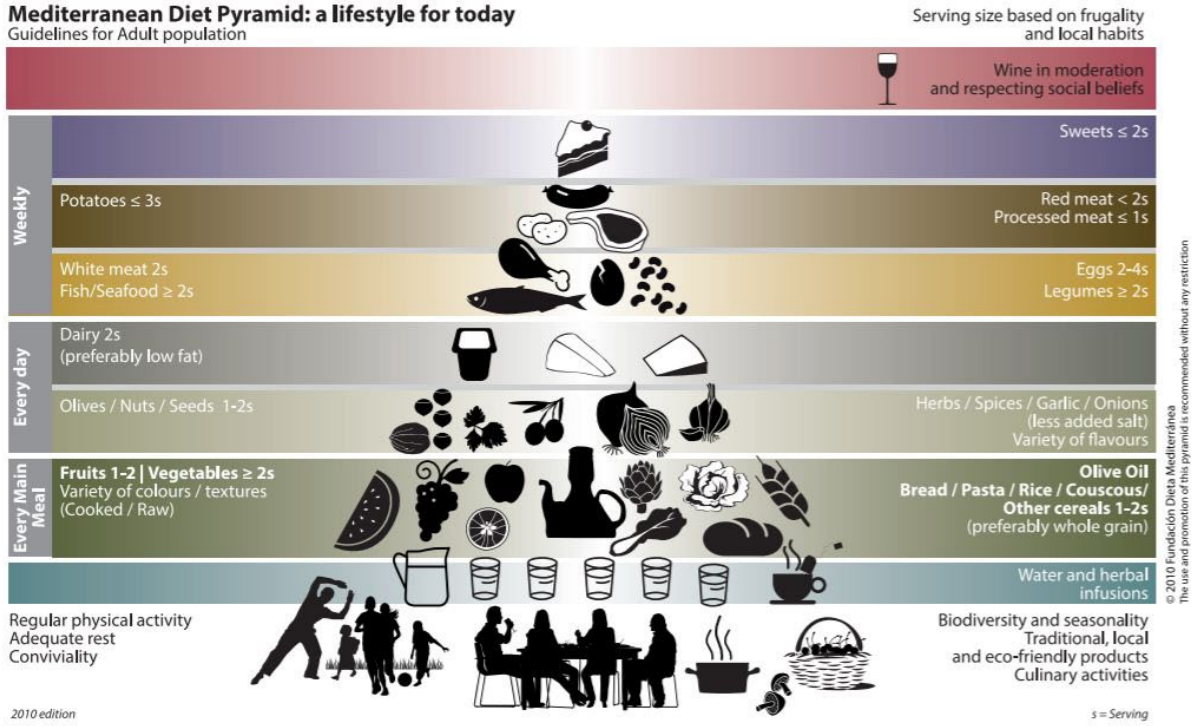
2. What is the Mediterranean diet?

The traditional Med Diet originated in the olive-growing areas of the Mediterranean region and has a strong cultural association with these areas. It is based on the traditional eating habits from the 1960's of individuals from countries surrounding the Mediterranean Sea (Greece, Italy, Spain) and encourages the intake of fresh, seasonal and local foods [16]. The Med Diet is not a single diet but a general eating pattern, which is marked by local and cultural differences throughout the Mediterranean region.
Thus, various definitions have developed as the MD has been adopted beyond the Mediterranean region. This dietary pattern has been increasingly described as both a treatment and a prevention intervention [17].

Social and cultural factors closely associated with the traditional Med Diet, including shared eating practices, post-meal siestas (afternoon naps) and lengthy mealtimes, are also thought to contribute to the attributed positive health effects recorded in the Mediterranean region [16]. The recommendation to practise conviviality (i.e. the quality of being friendly and lively) continues to form part of the modern day Med Diet pyramid (Mediterranean Diet Foundation) (Fig 1).

Of which foods is the Med Diet made up?

Figure 1



As illustrated in the Med Diet pyramid (recommended by the Mediterranean Diet Foundation; Fig. 1) [18], the Med Diet is generally characterised by a high intake of plant-based foods (fruit, vegetables, nuts and cereals) and olive oil; a moderate intake of fish and poultry; a low intake of dairy products (principally yoghurt and cheese), red meat, processed meats and sweets (for which fresh fruit is often substituted); and a moderate wine intake, normally consumed with meals [16] (WHO Europe 2018) .
Fat is predominately provided in the form of olive oil. Taken together, this results in a dietary pattern with a low content of saturated fatty acids (7–8% of daily total energy consumption) and a total percentage of fat of 30–40% or greater per day [5, 16, 19].

Mediterranean drinking pattern

The Med Diet also includes wine consumed the Mediterranean way:

- Moderately with the meals,
- Spread over the week instead of drinking at a single occasion,
- Avoiding binge drinking,
- Alternating with water.

Drinking patterns (frequency and the amount of wine consumed as well as drinking with or without a meal) are important influencing factors for the biological effects of an alcoholic beverage. Risky and harmful drinking patterns including the regular consumption of large amounts of wine, as well as consuming heavy and excessive amounts on a single occasion (binge drinking), should be discouraged. It is thus recommended that individuals drink wine as an accompaniment to food and alternate it with a non-alcoholic beverage such as water [20].

Spanish researchers examined the drinking patterns and concluded that the traditional Mediterranean drinking habits (such as moderate intake of alcoholic beverages, alcohol intake spread over the week, low spirit consumption, a preference for wine, wine consumed during meals, and avoidance of binge drinking) were also associated with a lower risk of all-cause mortality[21].

(*) Figure 2: Med Diet score

A Med Diet score is a reliable indicator of overall diet quality. One of these Mediterranean dietary indexes is the MEDAS score (Mediterranean Diet Adherence Screener) [22, 23] (Fig 2):

Table 1: Modified 14-item Mediterranean Diet Adherence Screener (MEDAS) [11].

	MEDAS Question	serving size [g]	Allocation criterion for 1 adherence point
1.	Do you use olive oil as the principal source of fat for cooking?		use of olive oil for the preparation of at least 2 of the following groceries: salad, vegetable, meat/fish
2.	How much olive oil do you consume per day (including that used in frying, salads, meals eaten away from home, etc.)?		>48 g vegetable oil
3.	How many servings of vegetables do you consume per day?	200	≥2 portions of vegetables per day (including salad, olives, mushrooms)
4.	How many pieces of fruit (including fresh-squeezed juice) do you consume per day?		≥3 portions of fruit (including mixed fruit, mixed stewed fruit and fruit juices)
5.	How many servings of red meat, hamburger, or sausages do you consume per day?	100-150	<100 g meat (beef, veal, pork, lamb) and processed meat Products
6.	How many servings of butter, margarine, or cream do you consume per day?	12	<1 portion butter, margarine and cream
7.	How many carbonated and/or sugar-sweetened beverages do you consume per day?		<1 portion sugar-sweetened beverages per day (including lemonade and colas)
8.	Do you drink wine? How much do you consume per week?		≥7 portions wine (red and white) per week *
9.	How many servings of pulses do you consume per week?	150	≥ 3 portions pulses per week
10.	How many servings of fish/seafood do you consume per week?		≥3 portions fish, fish products and seafood per week
11.	How many times do you consume commercial (not homemade) pastry such as cookies or cake per week?		<3 portions cakes, chocolate, cookies, sweets with and without chocolate per week
12.	How many times do you consume nuts per week?	30	≥3 portions nuts and seeds per week
13.	Do you prefer to eat chicken, turkey or rabbit instead of beef, pork, hamburgers, or sausages? **		g white meat (poultry, chicken, rabbit) > g red meat (beef, veal, pork, lamb, processed meat products)
14.	How many times per week do you consume boiled vegetables, pasta, rice, or other dishes with a sauce of tomato, garlic, onion, or leeks sautéed in olive oil?		> 1–2 times a week tomato sauce

Color code for MEDAS recommendation :	high consumption	moderate consumption	low consumption

12 questions relate to frequency of consumption and 2 questions (1,13) to specifics of the Mediterranean diet.
If the condition is not met, 0 points are recorded for the category. Adherence score ranges from 0 to 14 points. From 9 points upwards, high adherence is assumed.

*We prefer a modification of the Trichopoulou-definition of moderate wine consumption [7,12] because it is gender-specific and defines a range (women 5-20 g/day, men 10-40 g/day) representing the hormetic associations of wine with human health. In addition to the original scorecard, adherence point 8 should only be given if the following caveats are warranted allowing for responsible consumption.

- youth protection (complete abstinence in adolescents),
- sobriety in the workplace and traffic,
- deliberate and consistent approach to abstinence:
  - 1-2 abstinence days/week in general
  - complete abstinence for pregnant/lactating women
  - complete abstinence for subjects at increased risk of harm:
    - family history of alcohol abuse and dependence
    - mental health problems
    - diseases/conditions that can deteriorate or be affected by alcohol
    - use of certain over-the-counter or prescription medications, or recreational drugs

** 1 adherence point for vegetarians

From: [22, 23]

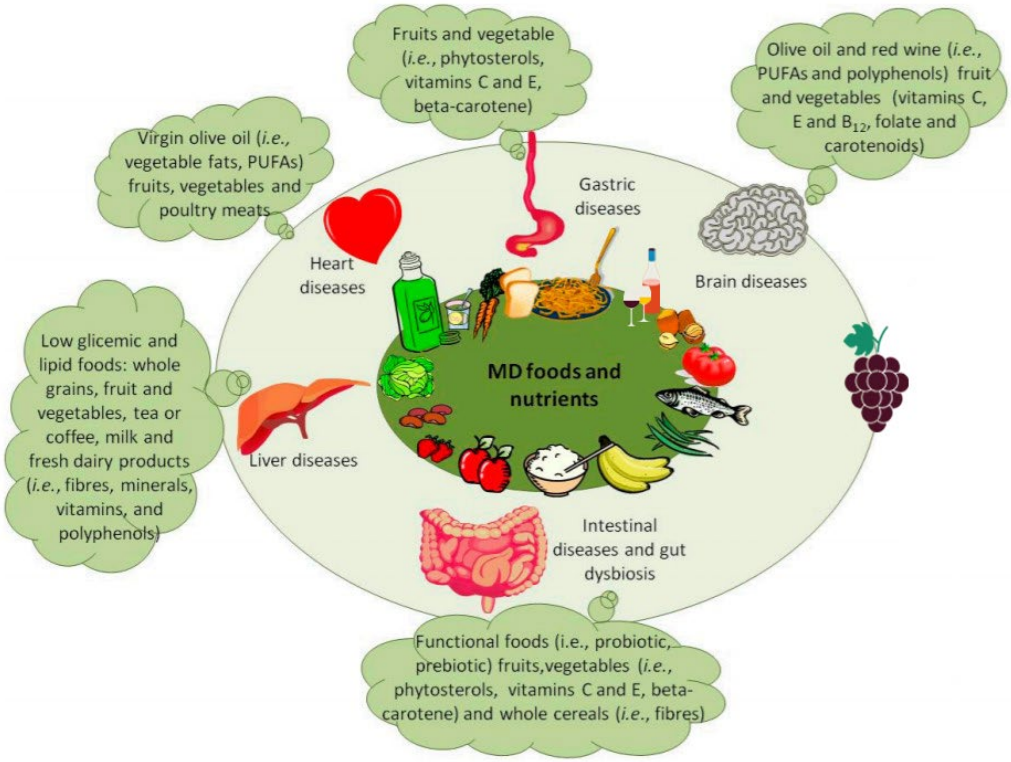
Med Diet and health

Consuming a Mediterranean diet rich in minimally processed plant foods has been associated with a reduced risk of developing multiple chronic diseases and increased life expectancy [24, 25] and these health benefits are supported by scientific evidence.

Dietary patterns rather than a single food or nutrient are more helpful to better understand the complex diet-disease associations. A large meta-analysis, including 636 studies (24 meta-analyses and nine systematic reviews), examined the relationship between the Med Diet and various chronic diseases and factors: adherence, all-cause mortality, asthma, cancer, cognitive functioning, cardiovascular disease, fractures, hypertension, metabolic syndrome, obesity, body weight and body mass index, rheumatoid arthritis, type 2 diabetes, and health-related quality of life. The results showed that the Med Diet is a healthy dietary pattern that can reduce the risk related to various NCDs. In addition, the effect was even greater when the dietary pattern was combined with physical activity and smoking, and excessive consumption of alcoholic beverages was avoided [26].

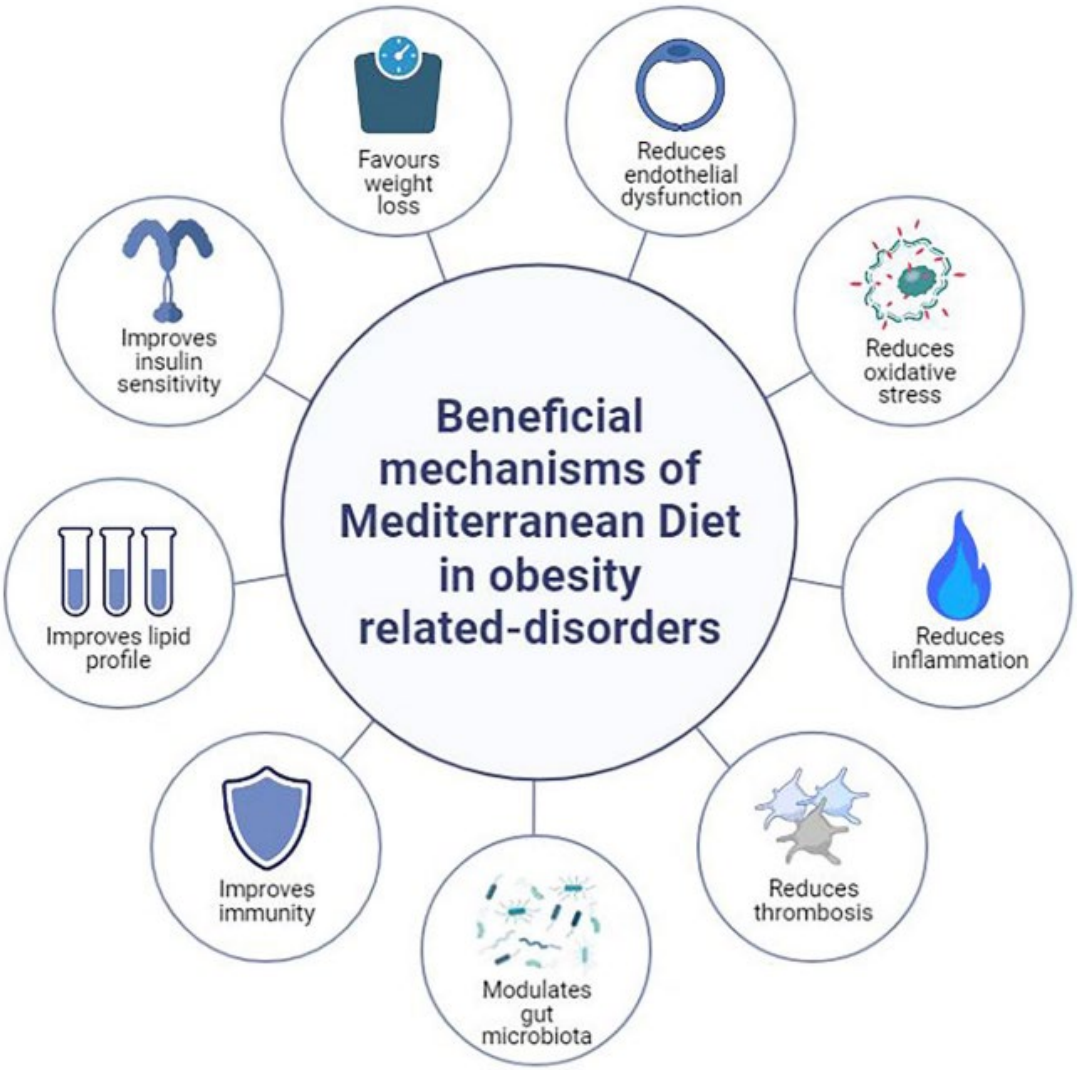
Following all-cause mortality, CVD, type 2 diabetes mellitus and dementia in the context of a Med Diet will be examined in more detail.

Figure 3: Med Diet-related positive effects on diseases



Adapted from: [27]

Figure 4



Adapted from: [28]

3. Med Diet can contribute to an increased life expectancy

Over the last two decades, several epidemiological studies have been carried out to identify the relationship between dietary pattern and survival rate. The Med Diet is one of the most widely evaluated dietary patterns for which a beneficial effect on lifespan [19, 29] was first suggested in the 1960s [1].

A large meta-analysis demonstrated that a higher adherence to a Mediterranean dietary pattern resulted not only in a reduced risk for cardiovascular diseases, coronary heart disease, stroke, overall cancer, type 2 diabetes, and neuro-degenerative diseases but also in a lower all-cause mortality[2] [30, 31]. A 2-point increase (*) in the adherence to a Med Diet was associated

[2] all-cause mortality refers to the risk of dying from any disease.

with a 10% lower risk of all-cause mortality. The reduced mortality risk was evident in both Mediterranean and non-Mediterranean regions. Similar findings were observed in a population of elderly individuals from a Mediterranean region: a close adherence to the Med Diet was associated with a 25% lower risk of all-cause mortality and an increased longevity [32].

Protective components of the Med Diet

Various prospective studies have consistently indicated that following a traditional Med Diet is associated with increased life expectancy/longevity. Researchers further examined the relative importance of the individual components of the Med Diet and those that predicted a lower mortality were:

- moderate consumption of wine/alcoholic beverages,
- low intake of meat and meat products and
- high consumption of vegetables, fruits and nuts, olive oil and legumes [33].

An updated meta-analysis quantified the adherence to the Med Diet and all its components with all-cause mortality [34]. When looking at the various Med Diet foods, an inverse association was highlighted for a moderate consumption of alcoholic beverages compared to abstinence or excessive consumption[3].

The combined effect of the Mediterranean dietary and drinking pattern was not significantly higher than their individual effects. However, a low adherence to both resulted in two-fold higher rates of all-cause mortality compared to individuals with a high adherence to both patterns [35].

4. Med Diet and better cardiovascular health

What is CVD?

Cardiovascular disease (CVD) is a general term for conditions affecting the heart, brain, or blood vessels. It is usually associated with a build-up of fatty deposits inside the arteries (atherosclerosis) and an increased risk of blood clots. It can also be associated with damage to arteries in organs such as the brain, heart, kidneys, and eyes.[4]

Cardiovascular diseases (CVDs) are considered to be the leading cause of mortality worldwide, accounting for 31% of all global deaths in 2015 [36]. CVDs are largely preventable by managing modifiable adverse behaviours such as an unhealthy diet, overweight, smoking or a sedentary lifestyle.

Diet has been traditionally considered as a main factor for cardiovascular health. In this context, the overall quality of whole food patterns may be more important than analysing single nutrients or foods. Studying food patterns is advantageous because it can capture the synergistic effects of individual foods and nutrients. The Med Diet represents such an overall dietary pattern that has been extensively studied. The pioneer epidemiological study

[3] Med diet score for alcoholic beverages = value of 1 for men who consumed quantities from 10 g /day to less than 50 g/day and a value of 0 otherwise; the corresponding cut-offs for women were 5 g/ day and 25 g/ day (Trichopoulou et al 2009)
[4] https://www.nhs.uk/conditions/cardiovascular-disease/#:~:text=Cardiovascular%20disease%20(CVD)%20is%20a,increased%20risk%20of%20blood%20clots

supporting the Med Diet for cardiovascular health was not conducted by anybody living in the Mediterranean area or with Mediterranean ancestry. The first evidence came from the Seven Countries Study where an American investigator (Ancel Keys) developed and promoted for the first time the concept of the cardio-protective Med Diet [1].

An increasing adherence to the Mediterranean diet has been consistently beneficial with respect to cardiovascular risk [37-39]. A systematic review ranked the Mediterranean diet as the best dietary pattern to provide protection against cardiovascular disease [40, 41].
To date, several comprehensive meta-analyses of observational studies
[2, 19, 42-45] and clinical trials [43, 46-48] analyzing the risk of mortality from different types of CVDs while consuming a Med Diet, support these beneficial effects.

5. Med Diet and improved cognitive function

What is dementia?
Dementia is a general term for loss of memory, language, problem-solving and other thinking abilities that are severe enough to interfere with daily life. Alzheimer disease is the most common cause of dementia. Dementia is not a single disease; it is an overall term — like heart disease — that covers a wide range of specific medical conditions, including Alzheimer's disease. Disorders grouped under the general term "dementia" are caused by abnormal brain changes. They also affect behavior, feelings, and relationships. Alzheimer's disease accounts for 60-80% of cases. Vascular dementia, which occurs because of microscopic bleeding and blood vessel blockage in the brain, is the second most common cause of dementia.[5]

With the increasing ageing of populations worldwide, cognitive impairment and Alzheimer disease/dementia are expected to increase and create serious challenges for healthcare providers. The global number of individuals with dementia is projected to triple, from approximately 50 million in 2018 to 152 million in 2050. Thus, it is very important to find ways of preventing and delaying the start of such cognitive decline [49]. Dementia not only affects individuals and their families, but it also exerts immense social and economic impacts. Most of the studies that examined the effectiveness of the Med Diet on non-communicable diseases, specifically in the older adult population, showed impressive results. Given that currently there is no treatment for dementia, it is crucial to find a way to delay its prognosis and reduce the risk of developing it. The Med Diet has been shown to aid in reducing this risk [50].

Figure 5: from [51]

[5] https://www.alz.org/alzheimers-dementia/what-is-dementia#:~:text=Dementia%20is%20a%20general%20term,most%20common%20cause%20of%20dementia

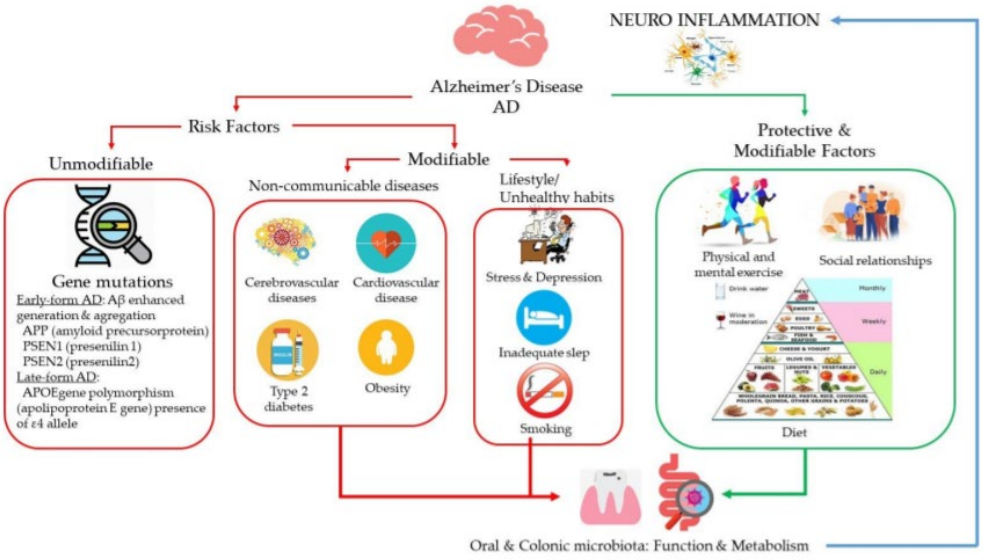


Figure 1. Genetic, environmental, and lifestyle factors known to determine brain functions and Alzheimer's disease (AD) onset. APOE: Apolipoprotein E.

What is good for the heart is also good for the brain. Prospective studies demonstrate that elderly individuals have fewer cardiovascular diseases and a better mental health when consuming a Med Diet including moderate wine consumption. Systematic reviews and meta-analyses indicate that adhering to a Mediterranean-style dietary pattern could play a protective role against cognitive decline and might also decrease the risk of developing Alzheimer Disease/dementia [3, 4, 52]. The biological activity of resveratrol, mainly in red wine, and its anti-inflammatory, anti-oxidative and anti-clotting characteristics, has been often associated with positive effects on neurodegenerative diseases [53].

Does nutrition in early adulthood play a role for cognitive functions at midlife?

Researchers further assessed which role nutrition in early adulthood plays with respect to the cognitive performance. During a period of 30 years, three heart-healthy dietary patterns (one of them the Med Diet) and cognitive performance in midlife was examined. At the beginning of the study, the 2600 healthy participants were 25 years old. Their eating patterns were assessed over a period of 20 years. The cognitive functions were evaluated after 25 and 30 years with validated neurological tests. The findings suggested that a greater long-term adherence to the Med Diet was related to less of a decline in general cognitive functions at midlife.

Med Diet in combination with other lifestyle behaviours

When in addition to a Mediterranean-style diet - other healthy lifestyle behaviors such as regular physical activities, not smoking and engaging in cognitive activities (reading, writing letters, playing games) were taken into account, older adults had up to a 60% lower risk of developing Alzheimer disease compared to individuals with none or only one of these behaviors [54].

6. Med Diet can decrease diabetes risk and improve blood glucose control in type 2 diabetics

What is diabetes mellitus?
Diabetes mellitus is a disease in which the body's ability to produce or respond to the hormone insulin is impaired, resulting in abnormal metabolism of carbohydrates and elevated levels of glucose in the blood. It occurs when the blood glucose or blood sugar, is too high. Blood glucose is the main source of energy and comes from the food eaten. The body breaks down the carbohydrates that we eat or drink, and this glucose is released into the blood. Insulin, a hormone made by the pancreas, allows the glucose in the blood enter the body cells to be used for energy. Individuals with **type 1 diabetes** do not produce insulin. Individuals with **type 2 diabetes** do not respond to insulin as well as they should and later in the disease, often don't make enough insulin.[6]

In the past few decades, the prevalence of diabetes mellitus has reached an epidemic level of 463 million people worldwide [55]. The prevalence of type 2 diabetes (T2D) is increasing and has become a public health challenge for many countries [55].
Increasing evidence has demonstrated that the combination of several unhealthy lifestyle factors, including a sedentary lifestyle, unhealthy, high-calorie diets, obesity, smoking, and excessive alcohol intake, were responsible for 90% of T2D cases [56]. For this reason, strategies focusing on lifestyle and the promotion of a healthy diet to prevent T2D have been identified by researchers and policymakers.

Can a healthy diet prevent the development of Type 2 diabetes?

Many dietary patterns have been suggested to prevent or manage diabetes. Data from several observational and clinical trials have demonstrated that eating a Med Diet can prevent the development of diabetes and lower the diabetes risk by approximately 20% [57, 58]. A systematic meta-analysis with more than 136,000 participants from various regions of the world showed that a higher adherence to the Med Diet was related to a 23% lower risk of becoming a type 2 diabetic compared to a minimum adherence. This beneficial effect was evident, irrespective of region of origin. The authors concluded that a Mediterranean dietary pattern could constitute a beneficial nutritional choice for the primary prevention of T2D [7].

In terms of data from clinical trials, the PREDIMED study, a one long-term, multi-center study, provided evidence that a Med Diet – compared to a low-fat diet- can reduce the risk of developing of type 2 diabetes by 52% in the elderly with a high cardiovascular risk [59].

Can diabetic individuals benefit from a Med Diet?

It seems that a Med Diet cannot only prevent becoming a type 2 diabetic, but also existing diabetics can benefit from this dietary pattern.
A comprehensive meta-analysis summarised the evidence about managing type 2 diabetes and pre-diabetic states with eating a Med Diet. T2D patients who consumed a Med Diet had a better long-term control of their blood sugar levels (lower HbA1c levels) and improved cardiovascular risk factors compared to other control diets [60].

[6] https://www.diabetes.org.uk/diabetes-the-basics

When looking at clinical trials, the researchers of the PREDIMED study - which compared a Mediterranean-style eating pattern with a low-fat eating pattern, reported that after 4 years, the management of blood sugar levels improved and the need for glucose-lowering medications was lower in the Mediterranean eating pattern group [48]. Similar results were observed in the CASCADE (= CArdiovaSCulAr Diabetes & Ethanol) study - the first large, long-term randomized controlled trial where specifically the effects of moderate wine consumption within a Med Diet among diabetics were examined. The findings suggested a better lipid and blood sugar control when alcohol-abstaining type 2 diabetics initiated moderate wine consumption combined with a Mediterranean-type diet [61] .

Long-term complications

However, it is not only important to prevent the development and management of type 2 diabetes but also to reduce the long-term health complications associated with it. A good control of the blood sugar can reduce the risk of diabetes complications in the short-, medium- and long-term [62]. Data from epidemiological studies suggest that diabetes is an important risk factor for CVD. In fact, a meta-analysis of 97 prospective studies revealed that individuals with diabetes had approximately a two-fold higher risk of coronary heart disease (CHD), stroke and vascular death, than their counterparts without the disease [9, 63].

Data from the PREDIMED trial showed that a Mediterranean-style eating pattern could significantly reduce the CVD incidence among individuals with and without diabetes [22]. A recent systematic review and meta-analysis obtained similar results and demonstrated that the Med Diet played a beneficial role in reducing the risk of developing and dying from various CVD outcomes, including individuals with diabetes [9].

Can it also work in non-Mediterranean countries?

A Mediterranean-style eating pattern is one of the eating patterns recommended by the American Heart Association, American College of Cardiology, and the Dietary Guidelines for Americans to reduce chronic disease risk. While there are cultural variations in the foods and beverages included in a Mediterranean pattern, overall, it is largely plant-based, relatively high in olive oil and seafood, but moderate to low in dairy, red meat, and refined grains. In Mediterranean and other European settings, adherence to a Mediterranean pattern is consistently associated with a reduced risk of diabetes. However, it is unclear, if a Mediterranean pattern, independent of a Mediterranean lifestyle, can reduce diabetes risk in US adult populations. The authors of the ARIC study explored whether potential benefits of a Mediterranean pattern are translatable to more heterogeneous populations. They investigated the association of a Mediterranean eating pattern and the diabetes risk among 12,000 US participants during a follow-up of 22 years. The results showed that higher Mediterranean-style eating pattern scores (*) were related to a significantly reduced risk of T2D. When the researchers examined which food factors were related to a reduced diabetes risk, they found that besides fish, vegetables and fruit, a higher nut and legume intake (8% respectively) and a moderate consumption of wine/alcoholic beverages (17%) were the main drivers of the reduced diabetes risk [64].

7. Role of wine

In a recent review, Spanish researchers evaluated the wine intake in the context of a Med Diet and the risk of chronic non-communicable diseases. They found that the several hundreds compounds – the wine polyphenols – play an important role in the protection against NCDs and describe the biological effects and mechanisms of action of the various polyphenolic compounds [25].
For example:

- Flavanols (mainly quercetin) with their anti-oxidant and anti-inflammatory properties
- Phenolic acids (gallic acid, caffeic acid) with their anti-mutagenic, anti-microbial, neuroprotective properties as well as
- Stilbenes (resveratrol) with their strong anti-fungal and anti-microbial capacities. Resveratrol presents anti-inflammatory, anti-oxidative and anti-clotting effects, as well as a high capacity for modulating lipoproteins and inhibit the initiation, promotion, and progression of tumors. Therefore, their biological activity has frequently been related to atherosclerosis, cancer, CVD, or neurodegenerative diseases [25, 53].

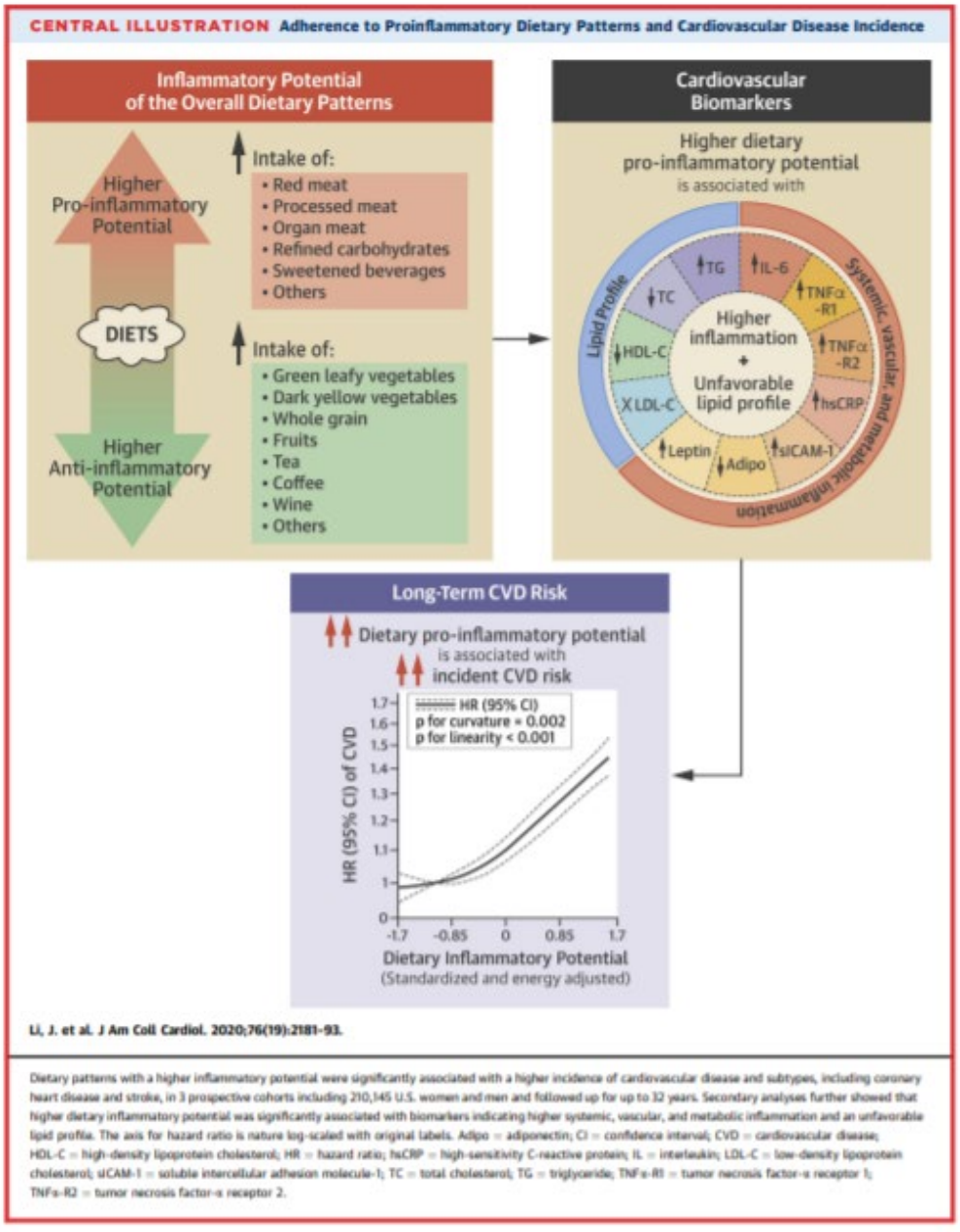
The researchers conclude that most of the scientific literature agrees that light to moderate wine intake seems to have beneficial effects to some extent in NCDs [25].

8. How does it work? Possible mechanisms

The exact mechanisms by which the traditional Med Diet exerts its favorable effects on health are not yet fully understood and various hypotheses have been proposed. The likely mechanisms involve oxidative stress, inflammatory and vascular disease pathways as well an influence of the Med Diet on the individual gut microbiome.

Inflammatory processes in the body are involved when chronic (non-communicable) diseases develop. The protective anti-oxidant and anti-inflammatory properties of foods typical of this dietary pattern but also vascular factors have been identified in possible mechanisms [65] in diseases where chronic inflammation plays a relevant role (CVD, diabetes, cancer, cognitive decline, Alzheimer Disease) [66].

Figure 6: from [67].



Bioactive compounds in the Med Diet - anti-oxidant and anti-inflammatory properties

Red wine, olive oil, nuts, fruits, and vegetables - key components of the Med Diet - are all foods rich in polyphenols and other bioactive compounds and can contribute to the protective effects through different synergistic mechanisms [68] and their anti-inflammatory and antioxidant properties [69, 70].

These polyphenols protect against oxidative damage with their capacity to delete reactive oxygen molecules (free radicals) caused by exercise, food metabolism and environmental factors such as exposure to air pollutants [25]. Such free radicals in the body are involved in the aging process as well as cardiovascular and neurodegenerative diseases and cancer.

Extra-virgin olive oil is probably one of the components that most differentiates the Med Diet from other dietary patterns. Phenolic components such as oleuropein and hydroxytyrosol, flavonoids, especially flavones, and lignans are abundant in extra-virgin olive oil.
Nuts, which are well-known for their unique nutritional composition (rich in unsaturated fatty acids, fiber, antioxidant vitamins, minerals, and other bioactive compounds), are also consumed in high amounts in the Med Diet.
In addition, scientific evidence has demonstrated a number of health benefits possibly associated with intake of mono-unsaturated fats which are abundant in extra-virgin olive oil and nuts [48, 71].

Special characteristics of wine

One of the main characteristics of the Med Diet is the **moderate intake of wine** consumed with meals and has been identified to have a higher protective effect compared to the other components of the Med Diet [5]. The reduced risk of all-cause mortality and cardiovascular disease has been associated with moderate intake of alcoholic beverages, mostly wine [44].

Besides ethanol, wine contains several hundred bioactive compounds (polyphenols) in very low concentrations, and they have been found to play an important role in the protection against various chronic diseases [72]. Particularly red wine is rich in phenolic compounds including flavonoids (anthocyanins, tannins, and catechin), stilbenes like resveratrol, tyrosol, and hydroxytyrosol. All these phenolic compounds present strong anti-oxidative, anti-inflammatory, and anti-blood clotting effects and seem to be beneficial for CVD, dementia as well as insulin resistance and T2D risk [65]. These bioactive compounds are involved in cardio-protective mechanisms that contribute to an improved blood sugar metabolism, a better functioning of the blood vessels, decreased inflammation and blood clotting (platelet aggregation) as well as exerting antioxidant effects [73, 74], the ethanol in wine is implicated in changing the blood lipids such as increasing the “good” HDL cholesterol.

It has been also demonstrated that individuals with a high adherence to the Med Diet, have a 40% lower rate of brain infarcts and 10% in fatal and non-fatal CVD risk [59]. Because polyphenols and unsaturated fatty acids exert an anti-inflammatory action on the brain [65], they seem to prevent inflammatory and neurodegenerative cascades, leading to Alzheimer disease and clinical dementia [66,67]. The results of the PREDIMED 67 study showed that some components of the Med Diet (i.e., total olive oil, walnuts and one glass of wine), with antioxidant properties or rich in polyphenols, were independently associated with better cognitive function and high plasma levels of omega-3 fatty acids [69].
This evidence suggests that the association between a Med Diet adherence and cognitive functions may be mediated by vascular factors, but also by non-vascular biological mechanisms, such as oxidative stress, inflammation, and metabolic disorders [70], supporting the importance of Med Diet in health, aging and lifestyle [71].

Microbiome

Recent scientific evidence further shows that diet has a major impact on the gut microbiota, its composition and function. It is suggested that the Med Diet promotes beneficial effects on the intestinal microbiota and can improve the immune system and several metabolic and inflammatory responses of the body [27, 75, 76].

9. Conclusions

Lifestyle habits are determining factors in the high prevalence of chronic diseases such as cardiovascular disease, diabetes, and dementia. Several studies have shown that non-smoking, being physical active, having a normal body weight and a healthy dietary pattern with moderate consumption of alcoholic beverages are related to a longer life expectancy and better health compared to an unhealthy lifestyle. The WHO recognizes diet as key risk factor for chronic diseases and the Med Diet was identified as an effective dietary strategy to prevent chronic diseases.
Even though some studies have reported a dose- response association between the consumption of alcoholic beverages and a higher risk of several chronic diseases, within the Med Diet, moderate wine consumption with the meals is considered a positive item in the Med Diet score.

According to the scientific evidence, consuming a Med Diet has been associated with a reduced risk of developing multiple chronic diseases and increased life expectancy [24]. It is inversely associated with all-cause mortality and has been linked to numerous health benefits, including a lower incidence of cognitive disease and CVD as well as for metabolic syndrome, obesity, and type 2 diabetes. The Med Diet has been associated with better long-term weight control, blood pressure, blood lipid profile, blood sugar metabolism and insulin resistance, inflammation, endothelial dysfunction and gut microbiome as well as a significant reduced all-cause mortality (8-10%) and risk of CVD (10%) and cancers (4%) for every 2-point increase in adhering to the Mediterranean diet pattern [31, 77].

Because the foods and wine of the Med Diet are rich in polyphenols and other bioactive compounds, their anti-inflammatory and antioxidant properties can act synergistically. These mechanisms together with its impact on the gut microbiome are though to be implicated in the health benefits of this dietary pattern.

It seems that wine within a Med Diet consumed moderately, with the meals and not in a binge drinking manner contributes to these beneficial effects on chronic diseases. However, high doses of any alcoholic beverages, including wine are harmful and should be avoided.

References

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