

KAPCIAK, Alicja, GÓRNY, Julia, KACZOROWSKI, Rafał, PELCZARSKA, Aleksandra, JANISZEWSKI, Michał, KOMOROWSKI, Marcin, FORENC, Tomasz, HUNIA, Jaromir and JUREK, Jonasz. The role of the Mediterranean Diet in preventing the development and complications of lifestyle diseases – a Review. *Quality in Sport*. 2024;33:55939. eISSN 2450-3118.
<https://dx.doi.org/10.12775/QS.2024.33.55939>
<https://apcz.umk.pl/QS/article/view/55939>

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.

Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).

Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.

Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

© The Authors 2024;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland

Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 03.10.2024. Revised: 13.11.2024. Accepted: 16.11.2024. Published: 16.11.2024.

The role of the Mediterranean Diet in preventing the development and complications of lifestyle diseases – a Review

Alicja Kapciak¹, Julia Górny², Rafał Kaczorowski³, Aleksandra Pelczarska⁴, Michał Janiszewski⁵, Marcin Komorowski⁶, Tomasz Forenc⁷, Jaromir Hunia⁸, Jonasz Jurek⁹

1. Alicja Kapciak [AK]
National Medical Institute of the Ministry of the Interior and Administration,
Wołoska 137, 02-507 Warsaw, Poland
<https://orcid.org/0009-0000-0655-8820>
E-mail: ala.kapciak@gmail.com
2. Julia Górny [JG]
Mazovian "Bródnowski" Hospital, Ludwika Kondratowicza 8, 03-242 Warsaw, Poland
<https://orcid.org/0009-0008-5363-1590>
E-mail: gornyjulia1@gmail.com
3. Rafał Kaczorowski [RK]
Mazovian "Bródnowski" Hospital, Ludwika Kondratowicza 8, 03-242 Warsaw, Poland
<https://orcid.org/0009-0004-7042-114X>
E-mail: rafal.kaczorowski1202@wp.pl
4. Aleksandra Pelczarska [AP]
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
<https://orcid.org/0009-0006-3505-1416>
E-mail: olapelczarska223@gmail.com
5. Michał Janiszewski [MJ]
Mazovian "Bródnowski" Hospital, Ludwika Kondratowicza 8, 03-242 Warsaw, Poland
<https://orcid.org/0009-0007-8932-3808>
E-mail: 1michal.janiszewski@gmail.com

6. Marcin Komorowski [MK]
Międzyzlesie Specialist Hospital, Bursztynowa 2, 04-749 Warsaw, Poland
<https://orcid.org/0009-0009-1423-7176>
E-mail: mkomorowski16@gmail.com
7. Tomasz Forenc [TF]
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
<https://orcid.org/0009-0007-9290-3571>
E-mail: forenctomasz@gmail.com
8. Jaromir Hunia [JH]
National Medical Institute of the Ministry of the Interior and Administration,
Wołoska 137, 02-507 Warsaw, Poland
<https://orcid.org/0000-0003-3596-0987>
E-mail: jaromirhunias@gmail.com
9. Jonasz Jurek [JJ]
National Medical Institute of the Ministry of the Interior and Administration,
Wołoska 137, 02-507 Warsaw, Poland
<https://orcid.org/0000-0001-9567-8663>
E-mail: jurekjonasz@gmail.com

Abstract

Introduction

The Mediterranean diet, inspired by traditional dietary habits of the Mediterranean region, exhibits anti-inflammatory and protective effects, reducing the risk of civilization diseases such as obesity, type 2 diabetes, and cardiovascular disorders. This diet is characterized by a high intake of plant-based foods, olive oil, and moderate consumption of fish and dairy products. These components provide unsaturated fatty acids, polyphenols, and antioxidants, which positively impact metabolic health and lower the risk of chronic diseases. In the face of the global obesity epidemic and an increasing number of individuals affected by lifestyle-related diseases, the Mediterranean diet offers a promising tool to support a healthy lifestyle.

Aim of study

This article aims to review current scientific studies evaluating the potential of the Mediterranean diet in preventing and managing civilization diseases. Particular attention is given to its effects on weight loss, improvements in glycemic markers, reductions in low density lipoproteins (LDL) cholesterol levels, and blood pressure control. The article also explores its benefits for athletes' health, as well as its potential to reduce oxidative stress and inflammatory states.

Material and methods

A literature review of the PubMed database was conducted, assessing relevant studies on the Mediterranean diet and its impact on lifestyle diseases.

Results and conclusions

The Mediterranean diet serves as a valuable dietary intervention, supporting metabolic health and significantly contributing to the reduction of body weight and abdominal obesity, especially when combined with physical activity and calorie reduction. Key active compounds, such as oleuropein and olive leaf extract, may support glycemic control and improve insulin sensitivity, which is crucial in managing type 2 diabetes. The diet's beneficial impact on cardiovascular health includes lowering LDL cholesterol, reducing oxidative stress and inflammation, and aiding in blood pressure management. Additionally, the Mediterranean diet supports athletes by enhancing endurance and recovery. In the context of preventing lifestyle diseases, the Mediterranean

diet proves to be an effective and accessible solution that can contribute to improving quality of life and health for the broader population.

Keywords: Mediterranean diet, lifestyle diseases, obesity, cardiovascular diseases, diabetes

1. Introduction

The Mediterranean Diet (MTD) was first widely described by Ancel Keys in the 1960s and is now recognized as a dietary standard that has gained popularity for its extensively documented health benefits (1). MTD is rooted in the traditional eating habits of communities in the Mediterranean region, particularly Crete, Greece, and southern Italy (2). It is characterized by a high intake of plant-based foods, such as vegetables, fruits, whole grains, and olive oil – the main fat source – as well as moderate amounts of fish, dairy, and red wine, while limiting meat and processed foods (3).

However, since the 1950s, the composition of the Mediterranean diet has changed significantly. The quality and quantity of foods consumed today in countries like Italy, Greece, and Spain differ from the traditional diet. Therefore, it is important to ensure that patients adhere to the original elements of this diet, which are responsible for its health-promoting effects, rather than modern, often less beneficial variations (4). The Mediterranean diet, now globally promoted as a healthy dietary model, is distinguished by its anti-inflammatory and antioxidant properties (5). Due to its unique health benefits, it has been included on The United Nations Educational, Scientific and Cultural Organization (UNESCO) list of Intangible Cultural Heritage (6).

Epidemiological studies confirm that the Mediterranean diet may play an important protective role against numerous lifestyle-related diseases. Following this dietary pattern is associated with a lower risk of cardiovascular diseases, stroke, obesity, type 2 diabetes, hypertension, and some cancers. Additionally, increasing evidence suggests potential benefits in preventing neurodegenerative diseases, such as Alzheimer's and Parkinson's (7-11). Studies have shown that individuals who follow the traditional Mediterranean diet have significantly lower all-cause mortality rates, including those related to cardiovascular disease and cancer (12). Moreover, analyses of European senior populations suggest that the Mediterranean diet may reduce all-cause mortality by 23% (13).

This review aims to discuss the current knowledge on the impact of the Mediterranean diet on key health indicators.

2. Characteristics and Components of the Mediterranean Diet

The Mediterranean diet, rooted in the traditional foods and beverages of countries bordering the Mediterranean Sea, is among the most renowned and extensively studied dietary patterns worldwide. Through a balanced intake of specific food groups combined with regular physical activity, Mediterranean-style nutrition plays a crucial role in preventing and delaying the onset of numerous diseases. Over the years, various forms of the Mediterranean diet have existed across the Mediterranean region; however, the common foundation has consistently included plant-based foods as the core of meals, with olive oil serving as the primary fat source.

2.1. Extra Virgin Olive Oil

The consumption of olive oil is often regarded as a key factor contributing to the longevity of Mediterranean populations (1). Extra virgin olive oil provides not only unsaturated fatty acids but also a range of nutrients, including fat-soluble vitamins, polyphenols, chlorophylls, and phytosterols (14). The polyphenols present in olive oil exhibit a variety of beneficial effects, such as anti-inflammatory, antioxidant, neuroprotective, cardioprotective, anti-cancer, anti-obesity, anti-diabetic, antibacterial, and anti-steatotic properties. These effects are primarily attributed to the presence of secoiridoid derivatives, as well as simple phenols (15-17).

2.2. Vegetables and Fruits

In the traditional variant of this dietary style, daily meals are based on a high intake of vegetables and fruits. Native vegetables characteristic of the Mediterranean region include radishes, artichokes, lettuce, and beets. Through contact with other regions, new varieties of fruits and vegetables were introduced. For instance, citrus fruits

and eggplants were brought from Northern Asia and India, while zucchini, tomatoes, potatoes, peppers, corn, and green beans arrived in the Mediterranean from the Americas (1). Fresh fruits are the primary dessert in this diet, while sweets containing sugar or honey are consumed sparingly- only a few times per week.

2.3. Legumes and Grains

Legumes are also a valuable source of nutrients, easy to prepare, and capable of being stored for extended periods. These attributes have undoubtedly contributed to their popularity and incorporation into traditional diets. In the Mediterranean diet, common legumes include beans, lentils, and chickpeas. Key components of these legumes are flavanols, which can help reduce endothelial dysfunction, lower cholesterol and blood pressure, and regulate energy metabolism (18). Additionally, residents of the Mediterranean region regularly consume grains such as rice and wheat in the form of pasta, bread, or couscous. These grains, along with potatoes, serve as the primary sources of energy and carbohydrates in the diet (1). This diet also includes moderate dairy intake, mainly in the form of cheeses and yogurts, and limited amounts of eggs, poultry, fish, and red meat (2).

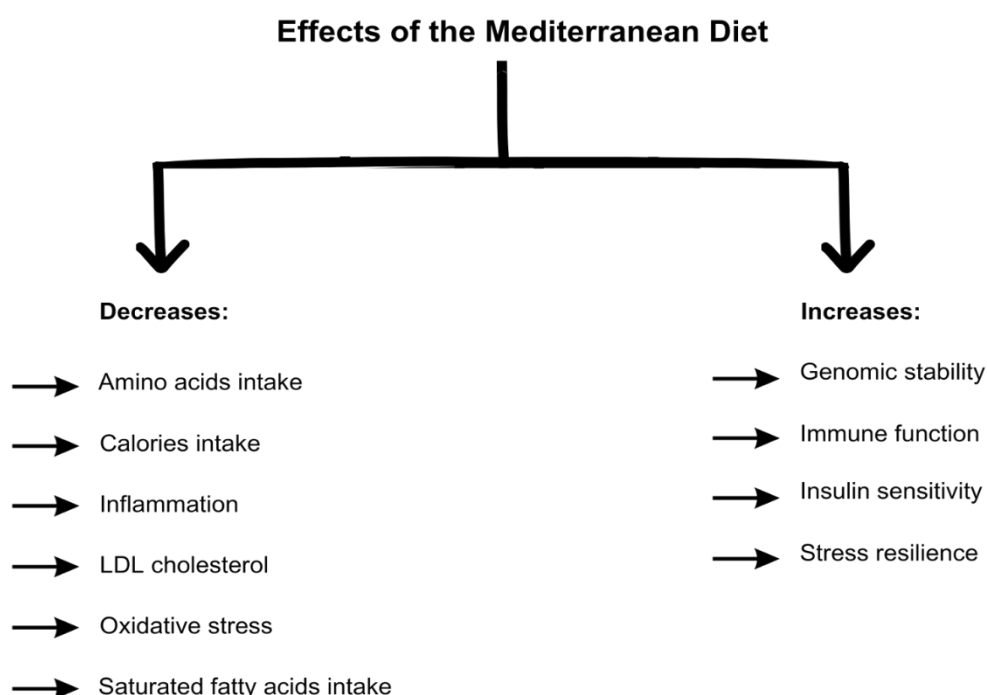
Due to its content of unsaturated fatty acids, polyphenols from olive oil, polyunsaturated fatty acids in fish, and various antioxidants from vegetables (19), fruits, and wine, the Mediterranean diet contributes to lowering the risk of chronic diseases (20). However, recent research focuses on the synergistic effects of the entire dietary model, which may have a more substantial impact on health than individual components (21).

3. Benefits of the Mediterranean Diet

The precise mechanism through which the Mediterranean diet exerts its beneficial effects on reducing disease risk is not fully understood. Key mechanisms that may mediate the health-promoting and life-prolonging effects of the traditional MTD include lipid-lowering actions, protection against oxidative stress, reduction of inflammation, inhibition of platelet aggregation, as well as modulation of hormones and growth factors involved in cancer development (22-24). Furthermore, this diet inhibits nutrient-sensing pathways through the restriction

of certain amino acids and supports the production of metabolites by the gut microbiota, which positively impacts metabolic health (25). The effects of the Mediterranean diet are illustrated in *Figure 1*.

Figure 1. Health Effects of the Mediterranean Diet [58,59,60,61]



*LDL- low density lipoproteins

4. The Mediterranean Diet and Obesity

Defined by the World Health Organization (WHO) as excessive fat accumulation that poses a health risk, obesity is now recognized as a global pandemic and one of the most pressing public health threats (26). The increasing prevalence of obesity across various demographic groups, regardless of age, gender, or socioeconomic status, is a concerning trend that places significant strain on healthcare systems (27). In 2022, there were 2.5 billion adults worldwide with overweight (43% of the population), of whom 890 million (16%) were obese, reflecting an increase from 1990, when only 25% of adults were overweight and the obesity rate was half of today's figures (28).

Excess body weight is associated with an increased risk of many chronic diseases, such as type 2 diabetes, hypertension, and dyslipidemia, which leads to a decline in quality of life and increased mortality (29). Interestingly, the adverse effects of obesity can be partially reversed through significant weight loss, highlighting the need for dietary interventions. The Mediterranean diet is currently one of the most promising approaches

in combating obesity (30). A meta-analysis of 16 studies found that the traditional Mediterranean diet supports weight loss and prevents weight regain, particularly when combined with calorie restriction and regular physical activity (31). Compared to other dietary models, adherence to MTD facilitates more sustainable weight loss, reinforcing its role in long-term weight management strategies (32).

Furthermore, MTD has the potential to reduce abdominal obesity, specifically the unhealthy visceral fat, independent of overall weight loss. Therefore, it is crucial to implement measures to control obesity, with the Mediterranean diet recommended as a healthy dietary choice for individuals with overweight and obesity (30).

5. The Mediterranean Diet and Diabetes

In recent years, research has increasingly focused on natural dietary components that may support the treatment of type 2 diabetes. In the Mediterranean diet, extra virgin olive oil, a primary fat source, contains oleuropein (OLE). Multiple studies on diabetic animal models have confirmed the beneficial effect of OLE or olive leaf extract rich in OLE on type 2 diabetes by reducing blood glucose levels (33, 34). In vivo studies suggest that olive leaf extract may alleviate insulin resistance by suppressing the messenger ribonucleic acid (mRNA) expression

of pro-inflammatory cytokines and enhancing the mRNA expression of insulin receptor substrate 1 (35). In a clinical study by Wainstein et al., which involved type 2 diabetes patients, treatment with olive leaf extract demonstrated significantly lower glycated haemoglobin (HbA1c) levels and fasting plasma insulin (36). Another study on middle-aged overweight men found that supplementation with olive leaf extract was associated with improved insulin sensitivity and pancreatic β -cell responsiveness (37). Research by Carnevale et al., involving healthy participants, showed a significant improvement in postprandial glycemia following OLE treatment (38). Meta-analyses of five studies have shown that the Mediterranean diet offers superior glycemic control for patients with type 2 diabetes and prediabetes compared to control diets (39). In summary, oleuropein and olive leaf extract present a promising therapeutic option for glycemic control, potentially improving insulin sensitivity and reducing the risk of complications associated with type 2 diabetes.

6. The Mediterranean Diet and Cardiovascular Diseases

The Mediterranean diet plays a significant role in the prevention of cardiovascular diseases. Studies show that phytosterols present in MTD products effectively reduce low density lipoproteins (LDL) cholesterol levels, a key factor in atherosclerosis development, by limiting intestinal absorption (40) and blocking the activity of proprotein convertase subtilisin/kexin type 9 (PCSK9) (41). The high content of healthy unsaturated fats and polyphenols supports lipid regulation, decreasing the risk of atherosclerosis and preventing the progression of cardiovascular diseases (42).

Additionally, randomized trials suggest that the consumption of soluble fiber, found in beans and fruits, significantly lowers LDL cholesterol levels; each additional gram of fiber reduces LDL by approximately 1.12 mg/L (43, 44). Soluble fiber limits cholesterol and bile acid reabsorption in the intestine, leading to increased hepatic LDL uptake (44). Moreover, MTD excludes foods high in partially hydrogenated trans fats, which

are associated with an increased risk of coronary artery disease (45).

Antioxidants and anti-inflammatory compounds present in fruits, vegetables, and nuts play a critical role in protecting the cardiovascular system (46). By reducing oxidative stress and inflammation, they lower the risk of plaque formation and endothelial damage, which are early stages of atherosclerosis (5, 46). The Mediterranean diet, rich in these components, helps reduce chronic inflammation, thereby decreasing the risk of myocardial infarction and stroke (7).

Another benefit of the Mediterranean diet is its effect on lowering blood pressure, which is crucial for preventing hypertension. A meta-analysis of six studies showed that following the Mediterranean diet for at least one year resulted in reduced systolic and diastolic blood pressure levels (47).

7. The Mediterranean Diet in Cancer

Observational studies indicate an association between adherence to the Mediterranean diet and reduced cancer incidence and lower cancer-related mortality, particularly for cancers of the breast, colon, head and neck, respiratory system, stomach, bladder, and liver (48). Fruits and vegetables within this diet are rich in various phytochemicals with anti-cancer properties that act synergistically, reducing oxidative cellular damage (49). Bioactive plant compounds have been shown to inhibit signal transduction pathways, cell proliferation, and oncogene expression while inducing cell cycle arrest (50).

Whole grains, legumes, fruits, and vegetables are also rich in dietary fiber, which provides a protective effect primarily against colorectal cancer (48). The metabolism of fiber by gut microbiota produces short-chain fatty acids, supporting intestinal epithelial health and reducing oncogenic potential by inducing cell apoptosis (51). Higher fiber intake is additionally associated with a decreased risk of other cancers, including breast, stomach and lung (52). Another crucial component of the MTD, particularly extra virgin olive oil, contains hydroxytyrosol, which demonstrates antioxidant, anti-proliferative, and pro-apoptotic properties. Hydroxytyrosol has been found to reduce androgen receptor expression and prostate-specific antigen (PSA) secretion in prostate cancer cells (53). In hepatocellular carcinoma, it inhibits proliferation, induces apoptosis, and arrests the cell cycle while also hindering angiogenesis and tumor growth (54).

Furthermore, the MTD decreases exposure to carcinogens by avoiding harmful foods such as red and processed meats, which are associated with increased cancer risk, especially colorectal and gastric cancers (55). Frequent consumption of whole grains, which contain alkylresorcinols, benzoxazinoids, and phytosterols, is correlated with a lower risk of cancer incidence and mortality (56, 57).

8. The Mediterranean Diet in Athletes

The Mediterranean diet is also recommended for athletes, as it provides nutritional support essential for achieving peak performance during competitions. It helps maintain optimal performance by offering an anti-inflammatory profile rich in antioxidants, as well as vital vitamins and minerals. The components of the diet, particularly plant-based foods, are high in carbohydrates, which effectively replenish glycogen stores. The antioxidants present help reduce inflammation and oxidative stress (58). Additionally, a high capacity for recovery is crucial for optimizing athletic performance. During exercise, lactate buildup leads to muscle fatigue and diminished training efficiency. Certain diet components, such as antioxidant vitamins and polyphenols abundant in the Mediterranean diet, can help reduce these levels (59). A study by Ficarra et al. on CrossFit athletes undergoing an 8-week Mediterranean diet intervention demonstrated a significant increase in squat jump performance, power, muscular endurance, and anaerobic capacity. Moreover, athletes showed improved performance in pull-up tests (60). Similar findings were observed in a study by Dorrell et al. involving kickboxers, who achieved a statistically significant increase in squat strength and sprinting ability (61).

9. Conclusion

The Mediterranean Diet is recognized as an effective tool in the prevention of lifestyle-related diseases, such as obesity, type 2 diabetes, and cardiovascular disease. This paper examines current evidence supporting its health-promoting effects, which stem from the anti-inflammatory, antioxidant, and metabolic properties of the diet's components, such as unsaturated fatty acids, fiber, and polyphenols. Studies indicate that the MTD effectively supports glycemic control, reduces LDL cholesterol levels, and minimizes oxidative stress and inflammation. In light of the global rise in obesity, the MTD demonstrates efficacy not only in prevention but also in sustainable weight reduction, particularly when combined with calorie restriction and physical activity. It is also notable for its ability to reduce visceral fat, which is crucial for metabolic health. Furthermore, thanks

to the synergy among its components, the MTD surpasses other diets in preventive efficacy and is easy to maintain over the long term. In conclusion, the Mediterranean Diet represents a valuable and well-tolerated dietary intervention, effective in both the prevention and management of lifestyle-related diseases. Its broader adoption

in daily dietary practice could significantly enhance population health and support a healthy lifestyle.

Disclosure

Author's contribution

Conceptualization: [AK], [RK], [MJ], [AP]

Methodology: [AK], [MJ], [MK]

Software: [AK], [JG], [RK]

Check: [AK], [JG], [MK]

Formal analysis: [JH], [JJ]

Investigation: [AK], [JG], [TF]

Resources: [AK], [RK], [JH]

Data curation: [AK], [AP], [JJ]

Writing - rough preparation: [AK], [JG], [RK], [MK]

Writing - review and editing: [MK], [TF], [JH], [JJ]

Visualization: [MJ], [JH], [JJ]

Supervision: [MJ], [TF], [AP]

Project administration: [AK], [AP], [TF]

All authors have read and agreed with the published version of the manuscript.

Funding Statement

No funding was sought or obtained in relation to this review article.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Not applicable.

Acknowledgments

The authors wish to emphasize that they do not express gratitude to any individuals or institutions.

Conflict of Interest Statement

The authors declare no conflicts of interest.

References:

1. Serra-Majem L, Roman-Vinas B, Sanchez-Villegas A, Guasch-Ferre M, Corella D, La Vecchia C. Benefits of the Mediterranean diet: Epidemiological and molecular aspects. *Mol Aspects Med.* 2019;67:1-55.
2. Willett WC, Sacks F, Trichopoulou A, Drescher G, Ferro-Luzzi A, Helsing E, et al. Mediterranean diet pyramid: a cultural model for healthy eating. *Am J Clin Nutr.* 1995;61(6 Suppl):1402S-6S.
3. Bach-Faig A, Berry EM, Lairon D, Reguant J, Trichopoulou A, Dernini S, et al. Mediterranean diet pyramid today. Science and cultural updates. *Public Health Nutr.* 2011;14(12A):2274-84.
4. Turrini A, Saba A, Perrone D, Cialfa E, D'Amicis A. Food consumption patterns in Italy: the INN-CA Study 1994-1996. *Eur J Clin Nutr.* 2001;55(7):571-88.
5. Tosti V, Bertozzi B, Fontana L. Health Benefits of the Mediterranean Diet: Metabolic and Molecular Mechanisms. *J Gerontol A Biol Sci Med Sci.* 2018;73(3):318-26.
6. Guasch-Ferre M, Willett WC. The Mediterranean diet and health: a comprehensive overview. *J Intern Med.* 2021;290(3):549-66.
7. Mazza E, Ferro Y, Pujia R, Mare R, Maurotti S, Montalcini T, et al. Mediterranean Diet In Healthy Aging. *J Nutr Health Aging.* 2021;25(9):1076-83.
8. Tektonidis TG, Akesson A, Gigante B, Wolk A, Larsson SC. A Mediterranean diet and risk of myocardial infarction, heart failure and stroke: A population-based cohort study. *Atherosclerosis.* 2015;243(1):93-8.
9. Schroder H, Marrugat J, Vila J, Covas MI, Elosua R. Adherence to the traditional mediterranean diet is inversely associated with body mass index and obesity in a spanish population. *J Nutr.* 2004;134(12):3355-61.
10. La Vecchia C. Association between Mediterranean dietary patterns and cancer risk. *Nutr Rev.* 2009;67 Suppl 1:S126-9.
11. Panagiotakos DB, Polystiopi A, Papairakleous N, Polychronopoulos E. Long-term adoption of a Mediterranean diet is associated with a better health status in elderly people; a cross-sectional survey in Cyprus. *Asia Pac J Clin Nutr.* 2007;16(2):331-7.
12. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med.* 2003;348(26):2599-608.
13. Knoops KT, de Groot LC, Kromhout D, Perrin AE, Moreiras-Varela O, Menotti A, et al. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. *JAMA.* 2004;292(12):1433-9.
14. Piroddi M, Albini A, Fabiani R, Giovannelli L, Luceri C, Natella F, et al. Nutrigenomics of extra-virgin olive oil: A review. *Biofactors.* 2017;43(1):17-41.

15. Fernandez-Prior A, Bermudez-Oria A, Millan-Linares MDC, Fernandez-Bolanos J, Espejo-Calvo JA, Rodriguez-Gutierrez G. Anti-Inflammatory and Antioxidant Activity of Hydroxytyrosol and 3,4-Dihydroxyphenylglycol Purified from Table Olive Effluents. *Foods*. 2021;10(2).
16. Bucciantini M, Leri M, Nardiello P, Casamenti F, Stefani M. Olive Polyphenols: Antioxidant and Anti-Inflammatory Properties. *Antioxidants (Basel)*. 2021;10(7).
17. Karkovic Markovic A, Toric J, Barbaric M, Jakobusic Brala C. Hydroxytyrosol, Tyrosol and Derivatives and Their Potential Effects on Human Health. *Molecules*. 2019;24(10).
18. Williamson G. The role of polyphenols in modern nutrition. *Nutr Bull*. 2017;42(3):226-35.
19. Grosso G, Marventano S, Yang J, Micek A, Pajak A, Scalfi L, et al. A comprehensive meta-analysis on evidence of Mediterranean diet and cardiovascular disease: Are individual components equal? *Crit Rev Food Sci Nutr*. 2017;57(15):3218-32.
20. Schwingshackl L, Hoffmann G. Adherence to Mediterranean diet and risk of cancer: a systematic review and meta-analysis of observational studies. *Int J Cancer*. 2014;135(8):1884-97.
21. Ros E. Health benefits of nut consumption. *Nutrients*. 2010;2(7):652-82.
22. Eisenberg T, Abdellatif M, Schroeder S, Primessnig U, Stekovic S, Pendl T, et al. Cardioprotection and lifespan extension by the natural polyamine spermidine. *Nat Med*. 2016;22(12):1428-38.
23. Calder PC, Ahluwalia N, Brouns F, Buetler T, Clement K, Cunningham K, et al. Dietary factors and low-grade inflammation in relation to overweight and obesity. *Br J Nutr*. 2011;106 Suppl 3:S5-78.
24. Longo VD, Fontana L. Calorie restriction and cancer prevention: metabolic and molecular mechanisms. *Trends Pharmacol Sci*. 2010;31(2):89-98.
25. Zhu W, Gregory JC, Org E, Buffa JA, Gupta N, Wang Z, et al. Gut Microbial Metabolite TMAO Enhances Platelet Hyperreactivity and Thrombosis Risk. *Cell*. 2016;165(1):111-24.
26. Collaborators GBD. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396(10258):1223-49.
27. Chooi YC, Ding C, Magkos F. The epidemiology of obesity. *Metabolism*. 2019;92:6-10.
28. Okunogbe A, Nugent R, Spencer G, Powis J, Ralston J, Wilding J. Economic impacts of overweight and obesity: current and future estimates for 161 countries. *BMJ Glob Health*. 2022;7(9).
29. Li Y, Pan A, Wang DD, Liu X, Dhana K, Franco OH, et al. Impact of Healthy Lifestyle Factors on Life Expectancies in the US Population. *Circulation*. 2018;138(4):345-55.
30. Muscogiuri G, Verde L, Sulu C, Katsiki N, Hassapidou M, Frias-Toral E, et al. Mediterranean Diet and Obesity-related Disorders: What is the Evidence? *Curr Obes Rep*. 2022;11(4):287-304.
31. Esposito K, Kastorini CM, Panagiotakos DB, Giugliano D. Mediterranean diet and weight loss: meta-analysis of randomized controlled trials. *Metab Syndr Relat Disord*. 2011;9(1):1-12.
32. Huo R, Du T, Xu Y, Xu W, Chen X, Sun K, et al. Effects of Mediterranean-style diet on glycemic control, weight loss and cardiovascular risk factors among type 2 diabetes individuals: a meta-analysis. *Eur J Clin Nutr*. 2015;69(11):1200-8.
33. Jemai H, El Feki A, Sayadi S. Antidiabetic and antioxidant effects of hydroxytyrosol and oleuropein from olive leaves in alloxan-diabetic rats. *J Agric Food Chem*. 2009;57(19):8798-804.
34. Murotomi K, Umeno A, Yasunaga M, Shichiri M, Ishida N, Koike T, et al. Oleuropein-Rich Diet Attenuates Hyperglycemia and Impaired Glucose Tolerance in Type 2 Diabetes Model Mouse. *J Agric Food Chem*. 2015;63(30):6715-22.

35. Liu YN, Jung JH, Park H, Kim H. Olive leaf extract suppresses messenger RNA expression of proinflammatory cytokines and enhances insulin receptor substrate 1 expression in the rats with streptozotocin and high-fat diet-induced diabetes. *Nutr Res.* 2014;34(5):450-7.
36. Wainstein J, Ganz T, Boaz M, Bar Dayan Y, Dolev E, Kerem Z, et al. Olive leaf extract as a hypoglycemic agent in both human diabetic subjects and in rats. *J Med Food.* 2012;15(7):605-10.
37. de Bock M, Derraik JG, Brennan CM, Biggs JB, Morgan PE, Hodgkinson SC, et al. Olive (*Olea europaea* L.) leaf polyphenols improve insulin sensitivity in middle-aged overweight men: a randomized, placebo-controlled, crossover trial. *PLoS One.* 2013;8(3):e57622.
38. Carnevale R, Silvestri R, Loffredo L, Novo M, Cammisotto V, Castellani V, et al. Oleuropein, a component of extra virgin olive oil, lowers postprandial glycaemia in healthy subjects. *Br J Clin Pharmacol.* 2018;84(7):1566-74.
39. Esposito K, Maiorino MI, Bellastella G, Chiodini P, Panagiotakos D, Giugliano D. A journey into a Mediterranean diet and type 2 diabetes: a systematic review with meta-analyses. *BMJ Open.* 2015;5(8):e008222.
40. Rudkowska I, Jones PJ. Functional foods for the prevention and treatment of cardiovascular diseases: cholesterol and beyond. *Expert Rev Cardiovasc Ther.* 2007;5(3):477-90.
41. Chan DC, Lambert G, Barrett PH, Rye KA, Ooi EM, Watts GF. Plasma proprotein convertase subtilisin/kexin type 9: a marker of LDL apolipoprotein B-100 catabolism? *Clin Chem.* 2009;55(11):2049-52.
42. Martinez-Gonzalez MA, Salas-Salvado J, Estruch R, Corella D, Fito M, Ros E, et al. Benefits of the Mediterranean Diet: Insights From the PREDIMED Study. *Prog Cardiovasc Dis.* 2015;58(1):50-60.
43. Salas-Salvado J, Farres X, Luque X, Narejos S, Borrell M, Basora J, et al. Effect of two doses of a mixture of soluble fibres on body weight and metabolic variables in overweight or obese patients: a randomised trial. *Br J Nutr.* 2008;99(6):1380-7.
44. Theuvsen E, Mensink RP. Water-soluble dietary fibers and cardiovascular disease. *Physiol Behav.* 2008;94(2):285-92.
45. Mozaffarian D, Clarke R. Quantitative effects on cardiovascular risk factors and coronary heart disease risk of replacing partially hydrogenated vegetable oils with other fats and oils. *Eur J Clin Nutr.* 2009;63 Suppl 2:S22-33.
46. Estruch R. Anti-inflammatory effects of the Mediterranean diet: the experience of the PREDIMED study. *Proc Nutr Soc.* 2010;69(3):333-40.
47. Nissensohn M, Roman-Vinas B, Sanchez-Villegas A, Piscopo S, Serra-Majem L. The Effect of the Mediterranean Diet on Hypertension: A Systematic Review and Meta-Analysis. *J Nutr Educ Behav.* 2016;48(1):42-53 e1.
48. Schwingshackl L, Schwedhelm C, Galbete C, Hoffmann G. Adherence to Mediterranean Diet and Risk of Cancer: An Updated Systematic Review and Meta-Analysis. *Nutrients.* 2017;9(10).
49. Phan MAT, Paterson J, Bucknall M, Arcot J. Interactions between phytochemicals from fruits and vegetables: Effects on bioactivities and bioavailability. *Crit Rev Food Sci Nutr.* 2018;58(8):1310-29.
50. Chen H, Liu RH. Potential Mechanisms of Action of Dietary Phytochemicals for Cancer Prevention by Targeting Cellular Signaling Transduction Pathways. *J Agric Food Chem.* 2018;66(13):3260-76.
51. Fung KY, Cosgrove L, Lockett T, Head R, Topping DL. A review of the potential mechanisms for the lowering of colorectal oncogenesis by butyrate. *Br J Nutr.* 2012;108(5):820-31.
52. Sun L, Brentnall A, Patel S, Buist DSM, Bowles EJA, Evans DGR, et al. A Cost-effectiveness Analysis of Multigene Testing for All Patients With Breast Cancer. *JAMA Oncol.* 2019;5(12):1718-30.

53. Zubair H, Bhardwaj A, Ahmad A, Srivastava SK, Khan MA, Patel GK, et al. Hydroxytyrosol Induces Apoptosis and Cell Cycle Arrest and Suppresses Multiple Oncogenic Signaling Pathways in Prostate Cancer Cells. *Nutr Cancer*. 2017;69(6):932-42.
54. Zhao B, Ma Y, Xu Z, Wang J, Wang F, Wang D, et al. Hydroxytyrosol, a natural molecule from olive oil, suppresses the growth of human hepatocellular carcinoma cells via inactivating AKT and nuclear factor-kappa B pathways. *Cancer Lett*. 2014;347(1):79-87.
55. Chiavarini M, Bertarelli G, Minelli L, Fabiani R. Dietary Intake of Meat Cooking-Related Mutagens (HCAs) and Risk of Colorectal Adenoma and Cancer: A Systematic Review and Meta-Analysis. *Nutrients*. 2017;9(5).
56. Schwingshackl L, Schwedhelm C, Hoffmann G, Knuppel S, Laure Preterre A, Iqbal K, et al. Food groups and risk of colorectal cancer. *Int J Cancer*. 2018;142(9):1748-58.
57. Xu Y, Yang J, Du L, Li K, Zhou Y. Association of whole grain, refined grain, and cereal consumption with gastric cancer risk: A meta-analysis of observational studies. *Food Sci Nutr*. 2019;7(1):256-65.
58. Barnard ND, Goldman DM, Loomis JF, Kahleova H, Levin SM, Neabore S, et al. Plant-Based Diets for Cardiovascular Safety and Performance in Endurance Sports. *Nutrients*. 2019;11(1).
59. Chang CC, Chen CW, Owaga E, Lee WT, Liu TN, Hsieh RH. Mangosteen Concentrate Drink Supplementation Promotes Antioxidant Status and Lactate Clearance in Rats after Exercise. *Nutrients*. 2020;12(5).
60. Ficarra S, Di Raimondo D, Navarra GA, Izadi M, Amato A, Macaluso FP, et al. Effects of Mediterranean Diet Combined with CrossFit Training on Trained Adults' Performance and Body Composition. *J Pers Med*. 2022;12(8).
61. Dorrell HF, Smith MF, Gee TI. Comparison of Velocity-Based and Traditional Percentage-Based Loading Methods on Maximal Strength and Power Adaptations. *J Strength Cond Res*. 2020;34(1):46-53.