Health Benefits of Vegetarian and Mediterranean Diets: Narrative Review

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Diet is an important lifestyle factor influencing disease risk. Vegetarian and Mediterranean diets have their proponents and are promoted for various potential health benefits. Over the years, numerous cross-sectional and cohort studies and randomized clinical trials have been conducted to elucidate the relationship between the Mediterranean and vegetarian diet and cardiovascular, cancer, diabetes, and other disease risks. More recently, research has been conducted to compare both diets directly. In this narrative review, we discuss the effects of vegetarian and Mediterranean diets on lipid profile, blood pressure, inflammation markers, body weight, risk of cardiovascular disease, cancer, diabetes mellitus, metabolic syndrome, and chronic kidney disease, as well as their associations with gut microbiota and mental health. The paper also discusses the studies comparing vegetarian and Mediterranean diets and their health effects. It provides further evidence that both diets can be beneficial and advocates their promotion, especially in Westernized populations plagued by various chronic lifestyle-associated diseases. At the same time, the Mediterranean dietary model may appear to be a superior public health strategy, less prone to the risk of nutritional deficiencies and less challenging in implantation on a broader scale. However, further studies based on cross-over design and long-term observations are recommended to thoroughly compare vegetarian and Mediterranean diets and draw more firm conclusions on their effects on health.

INTRODUCTION

Diet, among other lifestyle factors, is known to significantly influence disease risk, including cancer, metabolic disorders, and cardiovascular diseases. The awareness of this association leads to a growing interest in diets that offer specific health benefits. However, these benefits require scientific evaluation not only in observational research but also through clinical trials. The latter study design is considered the gold standard for evaluating particular treatments, including dietary interventions, and can provide a causal relationship between diet, health benefits, and disease risk in humans [Lucey et al., 2016; Mirmiran et al., 2021; Staudacher et al., 2022; Yao et al., 2013]. The number of such studies in recent years is growing, enabling meta-analyses and comparing different diet interventions [Ge et al., 2020]. However, similarly to the comparisons of the efficacy of various vaccines or other medical treatments, a direct comparison of health benefits related to particular diets should be made upon analyzing randomized controlled clinical trials involving the same group of volunteers. The number of such studies is still limited, although systematically increasing in recent years [Burrows et al., 2022; Mellor et al., 2022; Watson et al., 2015, 2018].

Particular attention is given to the health benefits of Mediterranean and vegetarian diets, which show some similarities but also distinctive differences (Table 1). The former dietary pattern is predominantly characterized by the consumption of plant-derived foods such as fruits, vegetables, beans, cereals, nuts, and seeds, with olive oil used as a primary source of fat, moderate amounts of dairy foodstuffs, principally cheese and yogurt, moderate consumption of fish and seafood, and low consumption of meat, with avoidance of notably low intake of red meat [Davis et al., 2015].

Traditionally embraced by the populations of Greece, Italy, and Spain, the Mediterranean diet pattern has also been promoted outside the Mediterranean region in the hope that it may benefit Westernized populations plagued by various chronic diseases, many of which are associated with lifestyle factors, including diets [Sotos-Prieto et al., 2022]. Despite these efforts, adherence to the Mediterranean diet in non-Mediterranean countries remains low [da Silva et al., 2009]. Moreover, recent studies show that adherence to this diet in the Mediterranean region is only moderate and has decreased...
over the decades [Obeid et al., 2022; Veronese et al., 2020]. Contrary to this, the interest in vegetarian diets appears to increase in high-income countries, as reflected by increasing interest in sales of plant-based alternatives to animal-derived products [Choudhury et al., 2020; Paslakis et al., 2020]. It is estimated that approximately 5% of Europeans may adopt vegetarian diets, compared to 8% of South Americans, over 15% of African and Middle East populations, and nearly 20% of Asians [Hargreaves et al., 2021].

On the other hand, India, often perceived as a household with the largest population of vegetarians (estimated at 30–40% of the population), is currently experiencing the highest growth rates for meat consumption in the world [Arora et al., 2020; Shridhar et al., 2014]. Vegetarianism is characterized by total abstention from consuming meat. There are different variations of this diet that include eggs (ovo-vegetarianism), dairy (lacto-vegetarianism), or both (lacto-ovo-vegetarianism), or exclude them and any other animal-derived products, e.g., honey (veganism) [Fontes et al., 2022]. A diet such as flexitarianism, which limits but does not entirely exclude meat, is regarded as semi-vegetarianism. In addition, some individuals adhere to pesco-vegetarianism, which excludes all meats except fish [Wozniak et al., 2020]. Although the motivations for transitioning to vegetarianism can be ethically- and environmentally driven, some individuals choose this dietary pattern for health-associated reasons [Dinu et al., 2017; Rosenfeld, 2019; Rosenfeld & Burrow, 2017]. However, ceasing meat consumption or switching to a diet low in meat appears to be a challenge for many people [Macdiarmid et al., 2016; O’Keefe et al., 2016; Tucker, 2014].

Considering that vegetarian and Mediterranean diets both focus on plant-based foods but take a different approach regarding meat products, it is pivotal to understand their effects, separately and jointly, on health outcomes. It is particularly important given that both diets are gaining attention in some regions and populations, leading to public discussion on the superiority of one diet over another. Considering the discussion on dietary interventions as a non-pharmaceutical approach to decrease the risk of disease, summarizing the health benefits of both diets and comparing them may be beneficial for dieters who work in the promotion of diets in various risk groups.

The objective of this narrative review was to present existing evidence on the potential associations between the Mediterranean and vegetarian diets and human health and to preliminary compare these diets. To this end, we have searched PubMed and Google Scholar databases using the following keywords: “Mediterranean diet”, “vegetarian diet”, “vegan diet”, “plant-based diet”, and “health”. Peer-reviewed papers related to the search terms were assessed by titles, abstracts, and article content. We have preferentially selected meta-analyses and systematic reviews, if available. If not, other types of papers (observational and interventional studies) were included. Only English-language articles published between 2012–2022 were chosen to elicit the latest trends. The selected papers were categorized to construct subsequent review sections discussing the established effects of each diet on the lipid profile, blood pressure, inflammation markers, overall cardiovascular risk, as well as the risk of cancer, diabetes mellitus, metabolic syndrome, and chronic kidney disease, and associations with gut microbiome and mental health. We have included these effects and health conditions as they are the most studied in relation to diet. At the same time, they pose significant challenges to public health, with a need to seek non-pharmaceutical interventions that could decrease the associated morbidity and mortality. Separately, we have also selected the available studies designed to compare both diets regarding cardiovascular parameters, kidney function, metabolic profile, gut microbiome, and pain in rheumatoid arthritis. The exact metabolic and molecular mechanisms of how these two diets can affect different aspects of human health are not fully elucidated and remain subject to study (e.g., see [Allen & Locasale, 2021; Tosti et al., 2018] for reviews on this matter). Based on the conducted review, the present paper provides a base for promoting Mediterranean and vegetarian diets in different populations and groups of patients to benefit their health.

### VEGETARIAN DIET AND HUMAN HEALTH

#### Vegetarian diet and lipid profile

The relationship between a vegetarian diet and lipid management has not been fully elucidated. Two meta-analyses

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**TABLE 1. Comparison of main characteristics of the vegetarian and Mediterranean diets.**

<table>
<thead>
<tr>
<th>Vegetarian diet</th>
<th>Mediterranean diet</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main protein sources</strong></td>
<td>Legumes, nuts; in some variations: fish, seafood, eggs, dairy</td>
</tr>
<tr>
<td><strong>Typical protein intake</strong></td>
<td>70 g/day (lacto-ovo-vegetarians)</td>
</tr>
<tr>
<td><strong>Main carbohydrates sources</strong></td>
<td>Cereals, fruits, vegetables, sweets</td>
</tr>
<tr>
<td><strong>Main fat sources</strong></td>
<td>Vegetable oils, nuts</td>
</tr>
<tr>
<td><strong>Excluded products</strong></td>
<td>Meat (and all animal-derived products in case of a vegan diet)</td>
</tr>
<tr>
<td><strong>Methods of thermal processing</strong></td>
<td>All; preferably raw fruits and vegetables</td>
</tr>
<tr>
<td><strong>Health risks</strong></td>
<td>Calcium, iron, vitamin D₃, and B₁₂ deficiencies</td>
</tr>
<tr>
<td><strong>Distinguishing features</strong></td>
<td>No meat consumption</td>
</tr>
</tbody>
</table>

Vegetarian diet and blood pressure

Two meta-analyses have confirmed the beneficial hypotensive properties of vegetarian diets. The first, published in 2014, included 39 publications [Yokoyama et al., 2014]. In six studies, a proportion of the participants were using antihypertensive medication; in twenty-two, the vegetarian dietary model was followed for more than one year. Seven of the works examined the impact of veganism, three focused on lacto-vegetarianism, fourteen on lacto-ovo-vegetarianism, and fifteen examined the diverse types (veganism, lacto-vegetarianism, lacto-ovo-vegetarianism, pesco-vegetarianism, and/or semi-vegetarianism). The analysis of 7 controlled clinical trials (311 subjects aged 38–54), with a duration of six weeks or more, revealed that in comparison with a traditional diet, vegetarian diet consumption was associated with a decrease in mean systolic blood pressure by 4.8 mmHg (–6.6 to –3.1 mmHg) and diastolic blood pressure by 2.2 mmHg (–3.5 to –1.0 mmHg). The analysis of 32 observational studies (21604 participants aged 28 to 68 years) indicated that compared to an omnivorous diet, mean systolic blood pressure in individuals on a vegetarian diet decreased by 6.9 mmHg (–9.1 to –4.7 mmHg) and diastolic blood pressure decreased by 4.7 mmHg (–6.3 to –3.1 mmHg) [Yokoyama et al., 2014].

The second meta-analysis, published six years later, including 15 randomized controlled trials with intervention periods ranging from 3 to 74 weeks, examined veganism (10 publications) and lacto-ovo-vegetarianism (5 papers) [Lee et al., 2020]. Adults were the participants in fourteen papers, and one paper involved children. Eight studies focused on diabetics, and seven on non-diabetics. Compared with an omnivorous diet, vegetarian diet consumption lowered systolic blood pressure by an average of 2.66 mmHg (–3.76 to –1.55) and diastolic blood pressure by 1.69 mmHg (–2.97 to –0.41). Subgroup analysis indicated that veganism reduced systolic blood pressure (–3.12 mmHg) more than lacto-ovo vegetarianism (–1.75 mmHg). A decrease in diastolic blood pressure was observed with the former diet (–1.92 mmHg), while no change was demonstrated for the latter. The authors reported the substantial heterogeneity of the studies used and noted that most were conducted in the USA. Despite the limitations, both meta-analyses suggest that vegetarian diets (mainly vegan diets) [Lee et al., 2020] may be an effective non-pharmacological strategy to lower blood pressure [Lee et al., 2020; Yokoyama et al., 2014].
Vegetarian diet and body weight

The meta-analysis on the impact of a vegetarian diet on weight loss confirms its effectiveness in this regard [Huang et al., 2016]. It included 12 randomized controlled trials involving 1,151 subjects from 18 to 82 years and examined the impact of a vegan diet (in 8 studies) and a lacto-ovo-vegetarian diet (in 4 studies). Obese or overweight participants were monitored for 8 weeks to 2 years. Subjects on vegetarian diets had significantly greater weight loss (2.02 kg on average) than those from the non-vegetarian groups. Compliance with the vegan diet resulted in more significant weight loss (–2.52 kg) than with the lacto-ovo-vegetarian diet (–1.47 kg). Furthermore, weight loss was greater in subjects with <1 year of intervention (–2.05 kg) than in those with ≥1 year of intervention (–1.13 kg) [Huang et al., 2016]. This indicates the beneficial effect of a vegetarian diet on weight reduction compared to non-vegetarian dietary practices. However, the attenuation observed after one year of adherence to a vegetarian diet requires further elucidation in future research and postulates a need to pursue more long-term studies.

Vegetarian diet and inflammation biomarkers

Three meta-analyses examining the effect of a vegetarian diet on inflammatory biomarkers confirm its key role in improving C-reactive protein (CRP) levels, whereas one of the analyses indicated a 2-year minimum intervention time [Craddock et al., 2019; Haghighatdoost et al., 2017; Menzel et al., 2020]. The meta-analysis of 30 (cross-sectional or cohort) observational studies aimed to determine the association between vegetarianism and inflammatory and immunological markers (CRP, tumor necrosis factor α, fibrinogen, natural killer (NK) cells, leukocytes, lymphocytes, thrombocytes, interleukins, and immunoglobulins) [Craddock et al., 2019]. The dietary models evaluated with an intervention period of 4 to 54 weeks involved lacto-ovo-vegetarianism (8 publications), lacto-vegetarianism (2), veganism (5), and a combination thereof. Participants included in two studies had chronic diseases: in one, patients were on dialysis; in the other, participants had cardiovascular disease and/or diabetes. Research on adult volunteers, with the exception of 1 study involving 2- to 18-year-old individuals, was conducted in Asia, Africa, North and South America, and Europe. As indicated, in comparison with the participants adhering to non-vegetarian dietary patterns, individuals on a vegetarian diet had lower levels of CRP (–0.61 mg/L), fibrinogen (–0.22 g/L), and a lower total leukocyte count (–0.62×10⁹/μL), thus suggesting a beneficial impact of vegetarianism on inflammation biomarkers [Craddock et al., 2019].

These conclusions contradict the results of a meta-analysis published two years earlier, which reported no differences in high-sensitivity CRP levels while maintaining a vegetarian and non-vegetarian diet for less than two years. In addition, when compared to an omnivorous diet, vegetarianism was associated with increased levels of interleukin-6 (0.21 pg/mL), which has a dual role: proinflammatory as cytokine and anti-inflammatory as myokine [Haghighatdoost et al., 2017]. As explained by Craddock et al. [2019], this is due to the inclusion of research on individuals treated with statins (reducing inflammation), which significantly altered the results. Moreover, the papers where participants consumed lesser amounts of meat in vegetarian groups, or the diet was not sufficiently described were also included in the meta-analysis conducted by Haghighatdoost et al. [2017]. Another meta-analysis (21 cross-sectional studies) evaluating the association of veganism and vegetarianism with biomarkers of inflammation was published in 2020 [Menzel et al., 2020]. The vegan diet adoption ranged from 1 year to 20 years and the vegetarian diet from 1 year to 25 years. Most studies (12) were conducted in Asia, followed by Europe (6) and South America (3). The research focused on the following biomarkers: CRP, tumor necrosis factor α, interleukin-6, interleukin-18, interleukin-1 receptor antagonist, selectin E, intercellular adhesion molecule, monocyte chemoattractant protein-1, adiponectin, omentin-1, and resistin. The meta-analysis indicated that veganism, compared to an omnivorous diet, reduced CRP levels (mean difference, MD=–0.54 mg/dL) more than vegetarianism (–0.25 mg/dL). It was observed that the association between the vegetarian pattern and CRP was significantly stronger in patients with renal impairment (–3.91 mg/L). However, no significant changes were observed for the other inflammatory biomarkers [Menzel et al., 2020].

Considering that inflammatory biomarkers, such as CRP, are associated with the pathogenicity of chronic diseases, such as type 2 diabetes and cardiovascular diseases, further investigations, including dietary interventional studies, are required to understand the effect of vegetarianism on reducing inflammation in specific groups of patients.

Vegetarian diet and cardiovascular disease

The impact of a vegetarian diet on cardiovascular disease (CVD) risk and mortality has been repeatedly examined [Matsumoto et al., 2019; Pawlak, 2015; Petermann-Rocha et al., 2021; Vahid et al., 2022]. According to the analysis of 10 prospective cohort studies, the risk of ischemic heart disease morbidity and/or mortality in participants on a plant-based diet was reduced by 25%, although not for all cerebrovascular and cardiovascular diseases [Dinu et al., 2017].

In 2021, two meta-analyses examining the impact of vegetarianism on CVD prevalence proved the key role of consumed plant-based food quality [Gan et al., 2021; Quek et al., 2021]. One analysis included 10 studies (9 cohorts) and a total of 698,707 participants, including 137,968 individuals with CVD, 41,162 with coronary heart disease (CHD), and 13,370 with stroke [Gan et al., 2021]. As revealed, the strictest adherence to vegetarian diets (as measured by the plant-based diet index, PDI) remained associated with a lower risk of CVD (relative risk, RR=0.84) and CHD (RR=0.88), although not with stroke (RR=0.87). Similarly, the meta-analysis of seven prospective cohort studies, encompassing 29,705 individuals adhering to a vegetarian diet, did not find an association with the risk of stroke compared to non-vegetarians [Lu et al., 2021].

It has also been reported that eating an unhealthy plant-based diet (rich in refined grains, sweets, and sweetened beverages) may increase CVD risk (RR=1.13) [Gan et al., 2021]. The second meta-analysis included thirteen prospective cohort studies (410,885 participants; 78,671 vegetarians and 332,214 non-vegetarians) and demonstrated that greater compliance with
a vegetarian diet appeared to be significantly associated with a lower risk of CVD morbidity (RR=0.90) and cardiovascular mortality (RR=0.92) [Quek et al., 2021]. Unhealthy plant-based diets (by PDI) increased the risk of cardiovascular mortality (RR=1.05) but did not affect the volume of CVD morbidity. A healthy vegetarian diet was associated with reduced CVD incidence (RR=0.87), although no association with mortality was demonstrated. Overall, vegetarians, compared with individuals following an omnivorous dietary pattern, had a significantly lower prevalence of CVD (RR=0.81) but with similar mortality rates from CVD [Quek et al., 2021].

The above-reviewed data confirm that a vegetarian diet may decrease cardiovascular risk; however, the quality of the plant-based products consumed is essential. It is also crucial for individuals adhering to vegetarian diets to improve their intake of B₉ vitamin since its deficiency has been associated with elevated plasma levels of homocysteine, an independent risk factor for CVD [Feng et al., 2020; Meleday & Graham, 1999; Obersby et al., 2013]. Such deficiency can be prevented by supplementation of B₉ vitamin or increased consumption of B₉-fortified foods [Damayanti et al., 2018].

**Vegetarian diet and cancer risk**

The results of three meta-analyses focused on assessing the impact of a vegetarian diet on cancer risk are inconclusive. The first analysis included seven papers in which lacto-ovo-vegetarianism or veganism was the considered dietary model [Huang et al., 2012]. A total of more than 124,000 participants from 10 to 90 years of age were under observation for 10 to 23 years. It has been reported that vegetarians had an 18% lower cancer morbidity than non-vegetarians [Huang et al., 2012]. The subsequent meta-analysis also demonstrated a positive impact of the discussed diet on cancer risk. It included 86 cross-sectional surveys and 10 prospective cohort trials [Dinu et al., 2017]. The analysis revealed a significant decrease in cancer risk compared to an omnivorous diet. Compliance with a vegetarian diet resulted in an 8% reduced risk and a 15% reduced risk with a vegan diet. However, no significant association was demonstrated for specific cancer types [Dinu et al., 2017]. Likewise, in a study focusing on breast, colorectal, and prostate cancers, vegetarian diets had no significant impact on reducing the risk of the variations mentioned above of oncological diseases compared to a non-vegetarian diet [Godos et al., 2017]. This meta-analysis included nine studies conducted on six cohorts. Among approximately 687,000 participants, there were 3,441 cases of breast cancer, 4,062 cases of colorectal cancer, and 1,935 cases of prostate cancer. However, during the analysis, a lower risk of colorectal cancer was noted with semi-vegetarian (~14%) and pesco-vegetarian (~33%) diets compared to a non-vegetarian pattern [Godos et al., 2017].

Although there is evidence that vegetarian diets may beneficially impact cancer risk, further studies, including long-term observations, are required to understand their association with specific cancer types.

**Vegetarian diet and type 2 diabetes mellitus risk**

A meta-analysis of two cohort studies and twelve cross-sectional studies on the impact of a vegetarian diet on type 2 diabetes risk was published in 2017 [Lee & Park, 2017]. The combined odds ratio for diabetes in vegetarians vs. nonvegetarians was 0.726. Subgroup analyses suggested vegetarians were less likely to suffer from diabetes than omnivores. It has been estimated that individuals on a vegetarian diet were 27% less likely to develop diabetes than those on a traditional diet. Compared to four studies conducted in Southeast Asia, lower risks were observed in three studies conducted in the Western Pacific region and seven in Europe and North America. The meta-analysis suggests that a vegetarian diet may protect against diabetes by, among other things, increasing insulin sensitivity (especially in vegans) and lowering intramuscular lipid levels, which affect insulin resistance. The authors confirm the need for further research on the type of vegetarianism and diet duration in relation to diabetes risk [Lee & Park, 2017].

Moreover, numerous research papers have confirmed the beneficial influence of vegetarianism on individuals with diabetes. In the meta-analysis involving nine clinical trials (a total of 664 subjects), an association has been observed between vegetarian diet consumption (for at least three weeks) and glycemic control, along with other cardiometabolic risk factors [Viguiliouk et al., 2019]. As demonstrated, this diet significantly reduced HbA1c (MD=−0.29%), fasting blood glucose (MD=−0.56 mmol/L), LDL cholesterol (MD=−0.12 mmol/L), non-HDL cholesterol (MD=−0.13 mmol/L), body weight (MD=−2.15 kg), body mass index (BMI) (MD=−0.74 kg/m²), and waist circumference (MD=−2.86 cm) [Viguiliouk et al., 2019]. The last three parameters were also analyzed in the 2021 meta-analysis of seven studies that examined the impact of plant-based diets on body weight in adults with type 2 diabetes and compared it to a regular meat diet [Austin et al., 2021]. Studies included a vegan diet and one considered a lacto-vegetarian diet. Body weight, BMI, and waist circumference were measured in a total of 353 participants. Significant reductions in average differences in body weight, BMI, and waist circumference were found for plant-based diets vs. regular meat diet. Plant-based diet adoption by individuals with type 2 diabetes resulted in a 5.1% reduction in average body weight, a 5.4% reduction in BMI, and a 4.3% reduction in waist circumference. Dietary interventions without restricting energy intake also resulted in a significant reduction in body weight. Regardless of caloric content, plant-based diets have proved to be effective in reducing central adiposity in individuals with type 2 diabetes mellitus [Austin et al., 2021]. Furthermore, adherence to a vegetarian diet was beneficial for diabetic patients to lower LDL cholesterol and non-HDL cholesterol, and also to ensure glycemic control [Viguiliouk et al., 2019]. The existing evidence indicates that implementation of vegetarian diet can potentially represent cost-effective and low-risk interventions in type 2 diabetes mellitus.

**Vegetarian diet and chronic kidney disease**

To the best of our knowledge, there is no meta-analysis testing the effect of a plant-based diet on chronic kidney disease (CKD). Only one meta-analysis focused on selected biomarkers associated with kidney impairment. It was demonstrated, considering four available studies, that compared to
an omnivorous diet, adherence to vegetarianism was associated with lower CRP levels (~3.9 mg/L) [Menzel et al., 2020].

In addition to this meta-analysis, there is one randomized controlled trial, two cross-over studies, and one cross-sectional study that tested vegetarianism’s effect in the groups of non-dialyzed patients with CKD [Valim et al., 2022]. A prospective, randomized, controlled trial of 207 participants showed that a very-low-protein vegetarian diet (VLPD; 0.4 g/kg/day) combined with amino acid ketoanalogues supplementation was more beneficial than a traditional low-protein diet (LPD; 0.6 g protein/kg/day) [Garneata et al., 2016]. After 15 months of complying with dietary recommendations, 42% of patients in the LPD group reached the endpoint (initiation of renal replacement therapy or a >50% reduction in initial estimated glomerular filtration rate, eGFR), while in the vegetarian group, 13% patients did. Initiation of renal replacement therapy was more required in the first group (30%) than in the second group (11%). After adjusting for relevant variables (eGFR, body mass index, CPR, and angiotensin-converting enzyme inhibitor), a VLPD combined with amino acid ketoanalogues supplementation appeared to be associated with a lower probability of reaching the endpoint [Garneata et al., 2016].

The other three studies (one cross-sectional study and two cross-over trials) did not show differences in renal function (measured parameters: eGFR or creatinine clearance) with vegan and meat-based diets [Chang et al., 2018; Moe et al., 2011; Soroka et al., 1998]. However, two of these studies (both cross-over design studies) included a very small sample size of only 8–9 participants; therefore, the meaning results may be limited [Moe et al., 2011; Soroka et al., 1998; Valim et al., 2022].

In summary, more studies on larger sample sizes and prolonged observation periods are required to draw final conclusions on vegetarian diets’ role in CKD.

**Vegetarian diet and gut microbiome**

Research shows that the composition of the gut microbiota is different in individuals on a plant-based and omnivorous (meat-containing) diet. In one study, 268 non-diabetic volunteers (41 to 58 years old) were assessed for the effect of practicing vegetarianism for at least one year (66 people in the vegetarian group, 102 in the lacto-ovo vegetarian group and 100 in the omnivorous group) on gut bacteria counts [Franco-de-Moraes et al., 2017]. Most of the studied population were women (54.2%) and 41.4% of the participants were over 60 years old in the vegetarian group, 102 in the lacto-ovo vegetarian group and 100 in the omnivorous group) on gut bacteria counts [Franco-de-Moraes et al., 2017]. Most of the studied population were women (54.2%) and 41.4% of the participants were over 60 years old in the vegetarian group, 102 in the lacto-ovo vegetarian group and 100 in the omnivorous group) on gut bacteria counts [Franco-de-Moraes et al., 2017]. Most of the studied population were women (54.2%) and 41.4% of the participants were over 60 years old in the vegetarian group, 102 in the lacto-ovo vegetarian group and 100 in the omnivorous group) on gut bacteria counts [Franco-de-Moraes et al., 2017].

The taxonomic composition and phylogenetic structure of the microbiota were obtained through the analysis of the 16S rRNA gene. Clinical, biochemical, and circulating inflammatory markers were compared. **Firmicutes and Bacteroidetes** were the most abundant bacterial types, with no differences in abundance between normal-weight and overweight subjects. Strict vegetarians had lower percentages of **Firmicutes and Bacteroidetes** than lacto-ovo vegetarians and omnivores.

Furthermore, a higher **Prevotella** abundance and **Prevotella/Bacteroides** ratio were noted in subjects on vegetarian diets than in the other groups. Both strict vegetarians and lacto-ovo vegetarians had a higher percentage of **Faecalibacterium** compared to omnivores, where excessive amounts of **Succinivibrio** and **Halomonas** from the Proteobacteria cluster were noted. Compared to the vegetarian groups, the latter group showed higher values of anthropometric data, insulin, insulin resistance index, and a worse lipid profile. Inflammatory markers exhibited a successive increase. Such findings suggest that the consumption of animal foods may trigger systemic inflammation and insulin resistance-dependent metabolic disorders [Franco-de-Moraes et al., 2017].

A randomized cross-over study examining the effects of a vegetarian diet on, among other things, microbiota composition in individuals with ischemic heart disease was published in 2020 [Djekic et al., 2020]. Participants (31 subjects; 29 men 63 to 70 years old), divided into two groups (vegetarian diet and omnivore diet), underwent a 4-week intervention. After a washout period (4 weeks), the groups swapped the isocaloric diets. Analysis showed that none of the dietary models affected the abundance or composition of the gut microbiota at the cluster level, while changes occurred in the abundance of several types of bacteria from the **Ruminococcaceae**, **Lachnospiraceae**, and **Eggerthellaceae** families. In vegetarian diet participants, the predominant **Ruminococcaceae** bacterial genera were associated with reduced oxidized LDL cholesterol levels and, subsequently, lower cardiometabolic risk. In addition, compared to the meat-eaters, the vegetarian group exhibited reduced fecal microbial taxa and plasma metabolites, associated with a lower risk of metabolic diseases, including cardiovascular diseases [Djekic et al., 2020].

Differences in gut microbiota composition between vegetarians and omnivores were also demonstrated in a 4-week randomized controlled trial including healthy individuals (53 subjects; 33 women, 20 men), 18 to 60 years of age. The participants were divided into two groups: vegan and omnivore. As in other publications, stool samples were analyzed using 16S rRNA gene amplicon sequencing. It was shown that, in contrast to the omnivore group, the vegetarian group had a decrease in **Roseburia** and **Faecalibacterium** abundance and an increase in **Coprococcus**. These three types of bacteria may be associated with mental and physical health; hence, further research is recommended [Kohnert et al., 2021]. The available data clearly show that different subtypes of vegetarian diets affect the abundance of other bacteria in the gut microbiota, resulting in improved physical and mental health.

**Vegetarian diet and mental health**

The effects of a vegetarian diet on mental health and the risk of depression have been analyzed numerous times in various populations, but the results of existing studies are inconsistent [Bègue & Shankland, 2022; Hopwood, 2022; Jin et al., 2021; Lee et al., 2021; Shen et al., 2021]. The meta-analysis of thirteen observational or interventional studies (17,809 individuals) evaluated the association of vegetarianism and veganism with mental health and cognitive functions [Iguacel et al., 2021]. It was demonstrated that vegans/vegetarians were more likely to suffer from depression (odds ratio, OR=2.1) but had lower anxiety levels (MD=−0.85) than those on a traditional diet. Subgroup analyses of anxiety showed higher risk in participants younger than 26 years and studies of higher quality. However, the heterogeneity of
the studies was considerable, although subgroup analyses showed numerous differences. The meta-analysis found no significant association between diet and depression, stress, mood, or cognitive impairment [Iguacel et al., 2021].

Another meta-analysis of 13 studies (43,728 participants; 5,436 vegetarians and 38,292 non-vegetarians) found that vegetarians had higher depression scores (according to the PHQ-9 patient health questionnaire) than non-vegetarians [Ocklenburg & Borawski, 2021]. However, the authors stated that due to the considerable heterogeneity of publications, further empirical studies are needed before any definitive conclusions can be formed. Another meta-analysis (thirteen papers, including four cohort studies and nine cross-sectional studies) published in 2022 examined the association of vegetarianism with depression, anxiety, and stress symptoms in adults [Askari et al., 2022]. Ten studies indicated no association of the dietary model in question with the incidence of depression. Four publications have suggested that adherence to a vegetarian diet is not associated with anxiety. Due to insufficient data, the authors could not collect stress scores; thus, the main conclusion of the meta-analysis was an indifferent effect of a vegetarian diet on depression and anxiety [Askari et al., 2022].

Given the conclusions of the above-discussed link between a vegetarian diet and mental health, there is a need to pursue further studies. Importantly, there is a need to conduct studies on different populations before a generalization of the effect can be outlined. Moreover, some authors suggest that future research should also consider the effect of experimental diet manipulation on mental health outcomes [Lavallee et al., 2019]. Last but not least, there are numerous confounding factors when testing the effect of any diet on mental health that need to be taken into account, e.g., age, gender, socioeconomic status, education, physical activity, genetic predisposition, smoking, chronic health issues, environmental background (e.g., trauma levels) [Alzahrani et al., 2022; Sheldon et al., 2021]. Controlling them all may be highly challenging when testing the effect of a particular diet.

MEDITERRANEAN DIET AND HUMAN HEALTH

Mediterranean diet and lipid profile

A cohort study of 4,740 participants 35–70 years of age examining the association between the Mediterranean diet and blood lipid levels in Iranian adults was published in 2021 [Panbehkar-Jouybari et al., 2021]. After a four-year observation, the HDL cholesterol level in these subjects significantly increased (52.8±12.3 for the third vs. 51.6±11.6, first tertile). Furthermore, strict compliance with Mediterranean diet was associated with decreased LDL to HDL cholesterol ratio (OR=0.85), which promoted proper lipid metabolism. However, no alterations were observed in total cholesterol, LDL fraction, or triglyceride levels [Panbehkar-Jouybari et al., 2021]. In the same year, a randomized cross-over study was published. It aimed to evaluate the effects of short-term (4-week) use of a caloric-restricted Mediterranean diet vs. a traditional caloric-restricted diet on lipid profile and other metabolic parameters in South Koreans with hypercholesterolemia [Son et al., 2021]. After a two-week washout period, participants, randomly assigned to the caloric-restricted Mediterranean diet group or the control diet group (92 subjects), exchanged diets. It was shown that even after accounting for age, gender, changes in total energy intake, alcohol intake, smoking, and changes in physical activity; the caloric-restricted Mediterranean diet group significantly decreased total cholesterol levels and LDL and HDL cholesterol levels, thereby supporting the treatment of dyslipidemia. In addition, it has also been shown that the diet used had a beneficial effect on reducing the risk of cardiovascular diseases by decreasing anthropometric parameters, decreasing levels of white blood cells, fasting glucose, fasting insulin, homeostatic model assessment for insulin resistance (HOMA-IR) index, and hepatic steatosis index (FLI), regardless of energy intake, physical activity, and changes in body weight reduction [Son et al., 2021].

Another cross-sectional study on the effect of the Mediterranean diet on lipid metabolism in subjects with familial hypercholesterolemia was conducted on Brazilian residents (n=92) and Spanish residents (n=98) [Antoniazzi et al., 2021]. As shown, the majority of Brazilian residents (83.7%) had low adherence to the Mediterranean diet, which was associated with their higher LDL cholesterol levels than in the Spanish group: 179 (135–250) and 161 (133–193) mg/dL. After adjusting for socioeconomic parameters, caloric and fatty acid intake, and lipid-lowering pharmacological therapies, a significant association was reported between high adherence to the Mediterranean diet and lowering of LDL cholesterol, thus a beneficial effect on familial hypercholesterolemia [Antoniazzi et al., 2021].

One multi-ethnic cohort study also examined the effects of the Mediterranean diet on the lipid profile of individuals from less-developed ethnic minorities [Zhang et al., 2022]. As demonstrated, adherence to the Mediterranean diet (as measured by the alternative Mediterranean diet scale – AMED) was negatively associated with total cholesterol, LDL, and HDL fraction levels. Comparing the highest quintiles with the lowest AMED scores, total cholesterol levels decreased by 0.082 (–0.092 to –0.049) mmol/L, LDL cholesterol by 0.030 (–0.048 to -0.012) mmol/L, and HDL cholesterol by 0.0275 (–0.036 to –0.019) mmol/L. Despite the absence of changes in triglyceride levels, the Mediterranean diet was found to effectively improve lipid metabolism in underdeveloped ethnic minorities [Zhang et al., 2022].

Mediterranean diet and blood pressure

Many studies have demonstrated that the Mediterranean diet lowers blood pressure [Ahmed et al., 2020; Dai et al., 2022; Jennings et al., 2019; Magrplis et al., 2020; Septiadi et al., 2021]. The meta-analysis encompassing six randomized controlled trials compared the Mediterranean diet with low-fat diets [Nissensohn et al., 2016]. As shown, adherence to the Mediterranean diet for at least one year resulted in reduced systolic (~1.44 mm Hg) and diastolic (~0.70 mm Hg) blood pressure. However, due to the small number of studies included in the meta-analysis and their large heterogeneity, the authors did not have sufficient evidence to support the blood-pressure-lowering effects of the Mediterranean diet [Nissensohn et al., 2016]. As many as three meta-analyses...
(evaluating the association between the Mediterranean diet and blood pressure) were published in 2021 [Bakaloudi et al., 2021; Cowell et al., 2021; Filippou et al., 2021]. One of these analyses, involving 19 randomized controlled trials (4,137 participants), showed that Mediterranean diet interventions reduced systolic and diastolic blood pressure by an average of 1.4 mmHg and 1.5 mmHg, respectively, compared with the control group [Cowell et al., 2021]. As shown in the meta-regression, longer study duration and higher baseline systolic blood pressure were associated with more significant decreases in response to the Mediterranean diet. In the same publication, the meta-analysis of 16 observational studies (59,001 participants) showed that with higher adherence to the Mediterranean diet, the probability of developing hypertension was 13% less than at a lower [Cowell et al., 2021].

Another meta-analysis of 54 observational studies noted that compared with the low adherence to the Mediterranean diet, greater adherence lowered systolic blood pressure (SMD=–0.08; –0.15 to –0.02) but did not significantly affect diastolic blood pressure (SMD=–0.07; –0.13 to 0.00) [Bakaloudi et al., 2021]. These findings may be related to normal levels (<90 mmHg) of mean diastolic pressure in all study participants.

The other meta-analysis encompassed 35 randomized controlled trials (13,943 participants). It demonstrated that, compared with the usual diet and other intervention diets, the Mediterranean diet reduced systolic blood pressure by 1.5 mmHg and diastolic blood pressure by 0.9 mmHg [Filippou et al., 2021]. Compared with the usual diet alone, the Mediterranean diet still caused both blood pressures to fall. However, the association disappeared when comparing the Mediterranean diet to all other intervention diets or a low-fat diet alone. Additionally, more significant reductions in diastolic blood pressure were observed in subjects with mean baseline systolic blood pressure ≥130 mmHg. It was noted that both systolic and diastolic blood pressure were lowered more in interventions with a mean follow-up period of ≥16 weeks [Filippou et al., 2021].

**Mediterranean diet and body weight**

Two meta-analyses have shown that following a Mediterranean diet may support weight loss [Esposito et al., 2011; Lotfi et al., 2022]. The first analysis included 16 randomized controlled trials and 3,436 participants (1,848 with a Mediterranean diet and 1,588 with a control diet – in most studies, represented by a low-fat diet, but also high-carbohydrate, prudent or high-saturated fat diets) [Esposito et al., 2011].

As shown, Mediterranean diet subjects had greater weight loss (–1.75 kg; –2.86 to –0.64 kg) and BMI (–0.57 kg/m²; –0.93 to –0.21 kg/m²), compared with the control group. Moreover, the weight loss was greater when following the Mediterranean diet with energy restriction (3.88 kg; –6.54 to –1.21 kg), increased physical activity (–4.01 kg; –2.59 to –2.23 kg), and intervention longer than 6 months (–2.69 kg; –3.99 to –1.38 kg). What is important, none of the studies showed significant weight gain when following the Mediterranean diet, thus confirming the lack of negative effects of the substantial amounts of olive oil used in the Mediterranean diet [Esposito et al., 2011].

The second meta-analysis included seven prospective cohort studies with a total of several hundred thousand participants [Lotfi et al., 2022]. As shown, adherence to the Mediterranean diet was strongly associated with a 9% reduced risk of overweight and/or obesity (RR=0.91) only for studies on overweight and obesity (RR=0.92) and not for articles focusing only on obesity (RR=0.68). In addition, the analysis of 6 publications proved a risk reduction (RR=0.98) of overweight and/or obesity of 2% per 1 Mediterranean Diet Score (MDS). Each unit increase in the MDS was associated with a reduction in weight gain of 0.04 kg over five years [Lotfi et al., 2022]. In summary, available meta-analyses suggest that the Mediterranean diet may support weight loss in adults.

**Mediterranean diet and inflammation biomarkers**

A meta-analysis of seventeen (lasting at least 12 weeks) randomized controlled trials on a total of 2,300 subjects evaluated the association of the Mediterranean diet with inflammation in adults [Schwingshackl & Hoffmann, 2014a]. Adherence to Mediterranean diet was shown to significantly increase adiponectin levels (weighted mean difference =1.69 μg/mL) and decrease high-sensitivity C-reactive protein (hs-CRP; –0.98 mg/L), interleukin-6 (–0.42 pg/mL), and intercellular adhesion molecule-1 (–23.73 ng/mL). The analysis results prove that adherence to the Mediterranean diet decreases inflammation and improves endothelial function [Schwingshackl & Hoffmann, 2014a].

The more recent meta-analysis, encompassing 13 publications (eight cross-sectional studies, three randomized clinical trials, 1 quasi-experiment, and 1 cohort study), examined the effect of the Mediterranean diet on inflammation in older people (≥65 years) [Wu et al., 2021]. Two randomized controlled trials demonstrated that greater adherence to the Mediterranean diet among the elderly was associated with a decrease in CRP (–0.54 and –0.34 mg/dL) and interleukin 6 (–1.6 and –0.2 pg/mL). In contrast, in a 3-year cohort study, only a decrease in CRP values was noted (–0.10 pg/mL).

The meta-analysis of 5 cross-sectional studies also demonstrated that the Mediterranean diet significantly decreased CRP levels (SMD=–0.26). Data on other inflammatory markers varied in the included publications; thus, no significant correlations were found [Wu et al., 2021].

**Mediterranean diet and cardiovascular disease**

The impact of the Mediterranean diet on cardiovascular risk and mortality associated with lipid and blood pressure was examined in five major meta-analyses. One of them included six studies and a total of 10,950 participants (477 major cardiovascular events, 693 deaths, 315 cardiovascular deaths) [Bloomfield et al., 2016; Chen et al., 2019; Liyanage et al., 2016; Mayr et al., 2018; Tang et al., 2021]. As shown, adherence to the Mediterranean diet decreased the risk of major cardiovascular events (RR=0.63), coronary events (RR=0.65), stroke (RR=0.65), and cardiac failure (RR=0.30) but was not associated with mortality from cardiovascular causes (RR=0.90) or any causes (RR=1.00). After excluding a large (1,000 participants) study with non-integral data, there was still evidence of a significant association of the Mediterranean diet with cardiovascular events.
(RR=0.69) and stroke (RR=0.66), although positive effects for coronary events (RR=0.73) and heart failure (RR=0.25) disappeared [Liyanage et al., 2016].

In the second meta-analysis, two publications on primary prevention demonstrated no difference in mortality from any cause between subjects using the Mediterranean diet and other groups. At the same time, one study showed that the Mediterranean diet decreased the incidence of major cardiovascular events (hazard ratio=0.71) [Bloomfield et al., 2016]. In one of the three publications on secondary prevention, adherence to the Mediterranean diet without fat intake restrictions appeared to decrease the risk of recurrent myocardial infarction and cardiovascular death [Bloomfield et al., 2016].

The third meta-analysis, focusing on stroke-related data, included twenty prospective cohort studies encompassing 682,149 participants (16,739 stroke cases) [Chen et al., 2019]. The RR for each 4-point increase in the MDS was 0.84 for all studies, 0.76 for studies on Mediterranean populations, and 0.86 for those on other populations. Adherence to the Mediterranean diet was associated with a lower risk of ischemic stroke (RR=0.86) and hemorrhagic stroke (RR=0.83).

The data suggest that regardless of residence, the Mediterranean diet reduced the risk of both strokes [Chen et al., 2019]. The most recent meta-analysis, including 7 cohort studies (37,879 participants with a history of CVD), found that the pooled RR for each 2-unit increment of the MDS was 0.85 for all-cause mortality and 0.91 for cardiovascular mortality [Tang et al., 2021]. Moreover, according to the subgroup analysis for all-cause mortality, the association was stronger in trials of shorter duration (RR=0.75) and Mediterranean regions (RR=0.76) than in non-Mediterranean areas (RR=0.95). Thus, the meta-analysis proved that adherence to a Mediterranean diet improved survival in people with a history of CVD [Tang et al., 2021].

The 2018 meta-analysis, including 11 studies, examined the effects of an olive oil-rich Mediterranean diet on inflammation in patients with coronary heart disease (CHD) [Mannisto et al., 2021; Montano et al., 2022; Schulpen & van den Brandt, 2021; Tayyem et al., 2022]. In a pooled analysis of 3 Italian case-control studies, including 5,079 women (1,411 diagnosed with endometrial cancer and 3,668 in the control group) the 9-item MDS used showed that high adherence to this diet vs. low adherence was associated with a 57% reduction in endometrial cancer risk (OR=0.43) [Filomeno et al., 2015]. The OR for an increment of one MDS unit, or one Mediterranean diet component, was 0.84. The findings suggest that a Mediterranean diet has a beneficial role in preventing endometrial cancer [Filomeno et al., 2015]. The meta-analysis encompassing six studies (3,986 women; 2,321 with diagnosed breast cancer and 1,665 in the control group) evaluated the association between the Mediterranean diet and breast cancer (estrogen/progesterone receptor subtypes: ER/PR) in postmenopausal women [van den Brandt & Schulpen, 2017]. As shown, high adherence to the Mediterranean diet was associated with a 23% reduction in ER–PR– and ER– breast cancer risk by 27%, whereas for ER+, this relationship was not statistically significant, indicating a positive effect of the Mediterranean diet on specific breast cancer subtypes only [van den Brandt & Schulpen, 2017].

Another meta-analysis of 10 observational studies (33,451 prostate cancer cases) examined the effect of the Mediterranean diet on prostate cancer risk [Cheng et al., 2019]. The RR was 0.95 in general for prostate cancer, 0.93 for advanced stage, and 0.92 for its lethal form. The results suggest that the Mediterranean diet is not associated with prostate cancer risk [Cheng et al., 2019].

The meta-analysis of 21 cohort studies and 12 case-control studies (just under 1.5 million participants) evaluating the impact of the Mediterranean diet on various cancers was published in 2014 [Schwingshackl & Hoffmann, 2014b]. As shown, the highest adherence to the Mediterranean diet resulted in a 4% reduction in prostate cancer risk, a 14% reduction in colorectal cancer risk, a 56% reduction in laryngeal cancer risk, and a 10% reduction in cancer mortality risk. An association of the Mediterranean diet with breast, stomach, and pancreatic cancer was not observed [Schwingshackl & Hoffmann, 2014b].

**Mediterranean diet and cancer risk**

According to research, the Mediterranean diet may reduce the risk of selected cancers [Gioxari et al., 2021; Mannisto et al., 2021; Montano et al., 2022; Schulpen & van den Brandt, 2021; Tayyem et al., 2022].
Conversely, a recent meta-analysis of 117 studies (encompassing a total of over 3 million participants) showed that the highest adherence to the Mediterranean diet reduced cancer mortality by 13% (based on eighteen cohort studies) and mortality from any cause among cancer survivors by 25% (based on eight cohort studies) [Morze et al., 2021]. Furthermore, higher adherence to the Mediterranean diet resulted in a lower risk of breast cancer (by 6%; twenty-three observational studies), bladder cancer (by 13%; four observational studies), respiratory cancer (by 16%; five cohort studies), colorectal cancer (by 17%; seventeen observational studies), stomach cancer (by 30%; 7 observational studies), liver cancer (by 36%; four observational studies), and head and neck cancer (by 54%; nine observational studies). The association between the Mediterranean diet and the incidence of blood, esophageal, pancreatic, and prostate cancers was not observed, which is a finding consistent with the results of previous publications [Morze et al., 2021].

**Mediterranean diet and type 2 diabetes mellitus**

In 2015, a large meta-analysis was published, including five randomized controlled clinical trials (lasting at least six months) and eight meta-analyses [Esposito et al., 2015]. Meta-analyses showed that higher adherence to the Mediterranean diet was associated with a 19% [Schwingshackl et al., 2015] and 23% reduction in type 2 diabetes risk, thus recommending the Mediterranean diet for the prevention of type 2 diabetes [Esposito et al., 2015; Koloverou et al., 2014]. The meta-analysis of 3 long-term clinical trials showed that the overall effect for HbA1c was -0.47% (-0.56 to -0.38), confirming the beneficial effect of the Mediterranean diet on glycemic control compared with traditional or low-fat diets. In addition, four other meta-analyses of randomized clinical trials also demonstrated lower HbA1c levels (-0.3% to -0.47%) in type 2 diabetes patients using the Mediterranean diet [Esposito et al., 2015].

The meta-analysis published five years later included as many as 41 articles (3 randomized clinical trials and 38 prospective cohort studies) [Becerra-Tomás et al., 2020]. The analysis of randomized controlled trials showed a beneficial effect of the Mediterranean diet on the prevalence of cardiovascular disease (RR=0.62) and myocardial infarction (MI; RR=0.65), whereas prospective cohort studies comparing the highest and lowest adherence to the Mediterranean diet proved an inverse association with CVD mortality (RR=0.79), coronary heart disease (RR=0.73), CHD mortality (RR=0.83) stroke incidence (RR=0.80), stroke mortality (RR=0.87), and MI incidence (RR=0.73). The above data suggest that the Mediterranean diet is highly beneficial in preventing CVD in individuals with type 2 diabetes [Becerra-Tomás et al., 2020].

**Mediterranean diet and chronic kidney disease**

A meta-analysis of four studies (8,467 participants) which was published in 2020, assessed the association between adherence to the Mediterranean diet (assessed by standardized food frequency questionnaires) and prevention of chronic kidney disease [Hansrivijit et al., 2020]. In all included articles, an index of the adopted diet’s similarity to the Mediterranean diet was used (mean MDS=3.8±0.3). With the mean follow-up duration of 20.6±7.0 years, the pooled OR for CKD was 0.901 for each 1-point increment of MDS. The incidence of CKD equaled 0.026 events per person-year. Furthermore, the male sex was associated with the incidence of chronic kidney disease in an adjusted meta-regression analysis. However, there was no significant association between chronic kidney disease incidence and age, ethnicity, smoking, comorbidities, kidney function, and total daily energy intake. Adherence to the Mediterranean diet with a 1-point increase in MDS was associated with a 10% lower risk of chronic kidney disease. However, there were insufficient data for patients on dialysis or with preexisting chronic kidney disease [Hansrivijit et al., 2020].

**Mediterranean diet and gut microbiome**

Mediterranean diet is characterized by high fiber intake, which is known to shift *Bacteroidetes* populations and maintain a reduced *Firmicutes* population, overall resulting in higher levels of short-chain fatty acids (SCFAs) in the gut [Haro et al., 2017; Nagpal et al., 2019]. A meta-analysis of seventeen studies was published in 2021 to determine whether the Mediterranean diet can prevent cancer and inflammatory bowel disease by modulating gut microflora [Illescas et al., 2021]. The Mediterranean diet was compared with different dietary models, including the Paleolithic diet and the Western diet. Analysis of 1,563 stool samples showed that the microbiota of patients following the Mediterranean diet was enriched with beneficial bacteria promoting an anti-inflammatory environment (*Verrucomicrobia, Bacteroidetes, Actinobacteria*), whereas the bacterial community was reduced in those with inflammatory bowel disease, colonic adenocarcinoma, and colorectal cancer. An inverse relationship was also observed, with a decrease in the abundance of bacteria with pro-inflammatory properties (*Proteobacteria, Euryarchaeota, Fusobacteria*) in the Mediterranean diet and an increase in inflammatory bowel disease, colonic adenocarcinoma, and colorectal cancer. Moreover, subjects on the Mediterranean diet increased the abundance of *Akkermansia*, regarded as a marker of a healthy gut, and decreased that of *Fusobacterium*, a pathogenic bacterium associated with colorectal cancer and inflammatory bowel disease (IBD) [Illescas et al., 2021]. Thus, the findings suggest that incorporating Mediterranean diet principles into lifestyle may prevent intestinal cancer.

**Mediterranean diet and mental health**

Of the twenty-two studies included in the 2013 meta-analysis, nine examined the effect of the Mediterranean diet on the risk of depression [Psaltopoulou et al., 2013]. As shown, high and moderate adherence to the Mediterranean diet was significantly associated with a reduced risk (RR=0.68; 0.54–0.86). The protective effects of high adherence seemed independent of age, whereas the beneficial effects of moderate adherence to the Mediterranean diet reducing the risk of depression seemed to disappear with age [Psaltopoulou et al., 2013]. A meta-analysis, published six years later, included a total of fourteen observational studies (four cohort and nine clinical-control studies) on a total of 56,043 participants [Shafiei et al., 2019]. Analysis of the cohort studies, despite
the lack of heterogeneity, showed no significant association between adherence to a Mediterranean diet and risk of depression (RR=0.95; 0.79–1.16), whereas the cross-sectional studies found a 28% reduction in the risk (RR=0.72; 0.60–0.87). Given the use of food frequency questionnaires, the above differences in findings may be due to the misclassification of participants in some studies [Sofi et al., 2019]. Similarly as in the “Vegetarian diet and mental health” subsection, discussing the potential association between a vegetarian diet with mental health, one should note that there are numerous confounding factors and controlling them all, when testing the effect of diet [Alzahrani et al., 2022; Sheldon et al., 2021].

**COMPARISON OF HEALTH BENEFITS OF VEGETARIAN AND MEDITERRANEAN DIETS**

This section discusses the research allowing for direct comparison of the vegetarian and Mediterranean diets. It should be highlighted that the number of such investigations is limited. Therefore, more research, preferably based on randomized cross-over studies in various populations, is encouraged in the future. The comparison of both diets discussed in subsequent subsections is summarized in Table 2.

**Cardiovascular disease prevention**

A randomized cross-over study performed as a part of the CARDIVEG Study examined the effect of the lacto-ovo vegetarian and Mediterranean diet on cardiovascular disease prevention [Sofi et al., 2018]. Participants included overweight omnivores, at low or intermediate cardiovascular risk, with at least one additional risk factor (i.e., abdominal obesity, high total cholesterol, high LDL cholesterol, high triglycerides, fasting glucose), and not on medications [Sofi et al., 2016]. Subjects (118 individuals) were randomly divided into two groups (vegetarian diet \(n=60\); Mediterranean diet \(n=58\)). Each dietary intervention phase lasted three months. After phase 1, the groups exchanged diets. Both low-calorie diets resulted in significant reductions in cardiovascular risk. A total of 81 subjects achieved the target values recommended by the European Society of Cardiology. Among them, 16 subjects in the lacto-ovo vegetarian group achieved target values for total cholesterol, 17 for LDL cholesterol, 6 for triglycerides, and 14 for BMI (body mass index). Meanwhile, from the Mediterranean diet group, target values for total cholesterol were achieved only by 7 participants, 6 for LDL cholesterol, 8 for triglycerides, and 10 for BMI. A low-calorie vegetarian diet was more effective in lowering total cholesterol and low-density lipoprotein levels, while a low-calorie Mediterranean diet led to greater reductions in triglyceride levels in overweight individuals [Sofi et al., 2018].

**Blood pressure in hypertension**

The meta-analysis, involving 67 randomized trials and over 17,000 participants, estimated the effects of thirteen different (lasting at least 12 weeks) dietary interventions (including the Mediterranean and vegetarian diets) on blood pressure in individuals with hypertension and prehypertension [Schwingshackl et al., 2019]. The Mediterranean diet ranked third as one of the most effective diets in reducing systolic and diastolic blood pressure. Although the vegetarian diet has not been distinguished in any way, the authors have found that an effective way to control blood pressure in populations with hypertension and prehypertension is to consume plenty of vegetables, fruits, grains, legumes, nuts, seeds, dairy products, and to follow a low intake of red meat, sugar-sweetened beverages, and sodium [Schwingshackl et al., 2019]. This dietary pattern, with the exception of meat consumption, is consistent with both types of the discussed diets.

**Cancer mortality**

A meta-analysis examining the effect of vegetarian and Mediterranean diets on cancer mortality was published in 2020 [Molina-Montes et al., 2020]. All papers included in the meta-analysis studied populations ranging from a few to several hundred thousand. Of the 13 articles, 5 focused on vegetarian/vegan diets and 8 on Mediterranean diets. The results indicated that the vegetarian/vegan diet did not exhibit significant preventative potential for overall cancer mortality compared with a non-vegetarian diet. However, the association between adherence to the Mediterranean dietary model and cancer mortality reached statistical significance. Nevertheless, none of the studies accounted for the influence of prognostic factors. Therefore, further analysis is needed to determine dietary guidelines for cancer survivors [Molina-Montes et al., 2020].

**Body weight control**

One study simultaneously evaluated the effect of low-calorie lacto-ovo vegetarian and Mediterranean diets on weight loss [Sofi et al., 2018]. A significant reduction occurred in both groups. The average weight reduction was –1.88 kg in the vegetarian group and –1.77 kg in the Mediterranean diet group. The decrease in BMI equaled –0.64 kg/m² in the vegetarian group and –0.67 kg/m² in the Mediterranean diet. In contrast, the reduction in fat mass reached –1.23 kg in the first group and –1.46 kg in the second group. The study confirms the beneficial effects of both vegetarian and Mediterranean diets in reducing body weight, BMI, and fat mass in overweight individuals. Given the comparable results, none of the diets could be determined as more effective [Sofi et al., 2018].

**Type 2 diabetes mellitus**

Type 2 diabetes mellitus is the most common type of diabetes worldwide and appears to increasingly affect also younger

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**TABLE 2. Comparison of health effects of vegetarian and Mediterranean diets emerging from comparative studies.**

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populations [Bellary et al., 2021; Lawrence et al., 2021]. Network meta-analysis was published in 2019, examining the effects of, among others, vegetarian and Mediterranean diets on blood lipid control in patients with type 2 diabetes [Neuenschwander et al., 2019]. Fifty-two randomized controlled trials on adults with type 2 diabetes, with an intervention period ≥12 weeks and comparing dietary approaches for LDL cholesterol, HDL cholesterol, or triglycerides were included. It was shown that of the nine dietary approaches, the vegetarian diet was most effective in lowering LDL cholesterol levels compared to the control diet. Conversely, the Mediterranean diet favorably raised HDL cholesterol and lowered triglyceride levels compared to the control diet [Neuenschwander et al., 2019]. Researchers assessing the effects of both diets on CVD prevention in overweight individuals reached similar conclusions [Sofi et al., 2018]. Therefore, this implies that the diets similarly affect the lipid profile in healthy individuals and those with type 2 diabetes. However, a 2019 meta-analysis recognized the Mediterranean dietary model as the most effective dietary approach for the full control of diabetic dyslipidemia (79% according to the surface under the cumulative ranking curve (SUCRA) score) [Neuenschwander et al., 2019].

Several studies have also reported the positive effects of Mediterranean and vegetarian diets on glycemic control in people with type 2 diabetes. A network meta-analysis of 56 studies comparing nine dietary approaches (including the two mentioned above) evaluated their effects on blood glucose levels in 500 people with type 2 diabetes [Schwingshackl et al., 2018]. Considering HbA1c lowering, the surface under the cumulative ranking (SUCRA) score ranked Mediterranean diet (80%) as the second-best diet compared to the control group, and vegetarianism (60%) ranked fourth. The network analysis also indicated that the Mediterranean diet was the best dietary approach to reduce fasting glucose levels compared to a control diet (88%), followed by a vegetarian diet in the third place (63%). The authors’ main conclusion is that the Mediterranean diet is the most effective dietary approach for improving glycemic control in patients with type 2 diabetes [Schwingshackl et al., 2018]. However, both dietary approaches are considered beneficial for diabetics since they feature an abundance of vegetables, fruits, grains, and cereals – and therefore fiber – which positively affects blood glucose levels [Benson & Hayes, 2020].

A randomized controlled cross-over study in overweight/obese individuals with type 2 diabetes examined the effects of the diets in question in terms of hunger and satiety perception [Di Mauro et al., 2021]. The Mediterranean and high-fiber vegetarian diets were compared. Participants (12 subjects; 5 women, 7 men) aged 54–72 years, consumed two types of isocaloric meals during two visits with trial investigators. Appetite, glucose, insulin, and gastrointestinal hormone levels were assessed during the appointments. Measurements were taken at fasting and every 30 min for 3.5 h after meal consumption. Glucagon-like peptide 1 and oxyntomodulin concentrations were significantly higher after the Mediterranean diet compared to the high-fiber vegetarian diet.

In addition, consumption of the Mediterranean meal was associated with a lower glycemic profile compared to a high-fiber vegetarian meal. However, there were no significant changes in self-reported scores on the visual analogue scale or insulin trend. In conclusion, in overweight/obese and type 2 diabetes participants, the Mediterranean diet was more effective than the high-fiber vegetarian diet in postprandial plasma glucose homeostasis and glucagon-like peptide 1 and oxyntomodulin release. However, the small number of participants must be considered [Di Mauro et al., 2021].

**Gut microbiome**

The cardiovascular prevention with vegetarian diet (CARDIVEG) study examined the effects of low-calorie Mediterranean and vegetarian diets on gut microbiome composition and SCFA production [Pagliai et al., 2020]. Omnivorous subjects (16 women and 7 men) with low to moderate cardiovascular risk were randomly assigned to the Mediterranean and vegetarian groups. After three months of dietary intervention, the groups exchanged. Next-generation 16S rRNA sequencing and SCFA analysis were performed on participants’ stool samples. As the analysis showed, adherence to the Mediterranean diet affected the abundance of Enterorhabdus, Lachnoclostridium, and Parabacteroides strains, while a vegetarian diet significantly affected the abundance of Anaerostipes, Streptococcus, Clostridium sensu stricto, and Odoribacter. However, microbiome composition did not change significantly in either of the groups. A comparison of the mean variation of each SCFA between Mediterranean and vegetarian diets showed an opposite and statistically significant trend for propionic acid (+10% vs –28%, respectively, p =0.034).

In addition, changes in SCFAs were negatively correlated with changes in some inflammatory cytokines (vascular endothelial growth factor, monocyte chemoattractant protein-1, interleukin-17, interferon gamma-induced protein-10 and interleukin-12) [Pagliai et al., 2020]. Correlation analyses showed a potential relationship between changes in strain types and changes in clinical and biological parameters. It was noted that with a Mediterranean diet, there were changes in the production of short-chain fatty acids, supporting their role in modulating the inflammatory response. However, short-term use of a Mediterranean or vegetarian diet did not result in major changes in the gut microbiota composition. It is suggested that such dietary interventions should last for more than three months, and it would be worthwhile to conduct the study on a greater sample size.

**Metabolic profile**

The recent study published in 2021 aimed to evaluate the effects of long-term vegetarian and Mediterranean dietary patterns on metabolic profile and salivary microbiota composition [Daniele et al., 2021]. Participants (42 subjects; 20 men, 22 women) approximately 38 years of age completed a questionnaire assessing dietary habits for at least two years. Information from medical history, saliva sample analysis, and basal metabolic rate and respiratory rate values were used to assess the metabolic profile. It was shown that individuals on the Mediterranean diet had a higher species diversity of oral bacteria and a better metabolic profile compared to the vegan diet. Participants in the Mediterranean dietary patterns group had higher percentages of Streptococcus and Prevotella species, lower carbohydrate consumption and higher lipid intake than
individuals on the vegetarian diet. Followers of the Mediterranean diet achieved higher basal metabolic and lower respiratory rates. It was observed that *Prevotella* abundance was inversely related to the respiration rate and carbohydrate consumption, whereas *Subtiliva* abundance was positively correlated with basal metabolic rate.

Furthermore, *Lactobacillus* abundance, inversely related to the presence of *Subtiliva* in the Mediterranean diet group, was associated with decreased basal metabolic rate. The study proved the association of macronutrient consumption with metabolic profile and oral microbiota. It also confirmed the positive effect of the Mediterranean diet on basal metabolic rate and the abundance of microbial species associated with better protein, carbohydrate, and lipid metabolism. The analysis suggests that long-term adherence to the Mediterranean diet, with high contents of protein and lipids, is associated with higher oral microbial diversity and, therefore, a better metabolic profile compared to veganism [Daniele et al., 2021].

Kidney function

In 2020–21, a randomized cross-over study was conducted as a part of the CARDIVEG Study to evaluate the effects of a lacto-ovo vegetarian diet versus the Mediterranean diet on kidney function in healthy individuals at medium to low cardiovascular risk [Dinu et al., 2021]. Participants (107 subjects; 82 women, 25 men) aged 21–75 years were assigned to a lacto-ovo vegetarian or Mediterranean diet group for three months, and then switched the diets. The analysis included confounding variables such as age, sex, weight, physical activity, alcohol consumption, smoking, hypertension, LDL cholesterol, and glucose levels. As shown, adherence to the lacto-ovo vegetarian diet decreased creatinine levels by 5.3%, blood urea nitrogen by 8.7%, and urea by 5.8%. In contrast, the eGFR increased by 3.5%. Clinically significant improvement in the above parameters may positively affect the protection of renal function, at least with a short-term vegetarian diet. In the Mediterranean diet group, no significant changes were observed in the parameters considered. However, the study covered a period of three months; thus, the effect of dietary intervention with this diet for a longer time was not evaluated [Dinu et al., 2021].

Pain in rheumatoid arthritis

A recent meta-analysis of seven randomized controlled trials (326 participants in total) was published to examine the effect of potentially anti-inflammatory diets (including, among others, vegetarian and Mediterranean) on pain in rheumatoid arthritis [Schönenberger et al., 2021]. Visual analogue scale (VAS), CRP level, erythrocyte sedimentation rate, health assessment questionnaire, disease activity score-28 for rheumatoid arthritis (DAS28), number of tender/swollen joints, body weight, and BMI were used for the assessment. It was noted that better outcomes were achieved in dietary interventions lasting more than three months. Subgroup analysis showed that the Mediterranean diet tended to have a greater effect on pain reduction than the vegetarian diet. However, the former dietary interventions were only evaluated in two papers. Nevertheless, the authors of the meta-analysis conclude that anti-inflammatory diets, including vegetarian and Mediterranean diets, decrease pain in rheumatoid arthritis compared to traditional diets [Schönenberger et al., 2021]. However, as indicated the risk of bias was high, while the evidence was very low, advocating further studies to understand the role of vegetarian and Mediterranean diets in rheumatoid arthritis and comparison of outcomes of their implementation.

FUTURE RESEARCH PROSPECTS AND CHALLENGES

Several gaps and challenges must be addressed in future assessments of the health benefits of vegetarian and Mediterranean diets, as well as their implementation as non-pharmacological methods of disease prevention.

1. As stated by the Academy of Nutrition and Dietetics, the vegetarian diet, including vegan, can provide health benefits if appropriately planned [Melina et al., 2016]. However, unbalanced plant-based diets can be harmful and lead to nutritional deficiencies, weight gain, increase in triglyceride and glucose levels [Sabaté, 2003]. Therefore, epidemiological studies should attempt to distinguish individuals adhering to a vegetarian diet based on how well it is planned. This is particularly important given the fact that some plant-based products fall into the category of ultra-processed food [Gehring et al., 2021; Ohlau et al., 2022].

2. There is a need to distinguish and define different types of vegetarianism when testing its health effect and comparing it to other diets, e.g., the Mediterranean diet. A vegetarian diet includes individuals restricting meat consumption but eating eggs (ovo-vegetarianism), dairy (lacto-vegetarianism), both (lacto-ovo-vegetarianism), and avoiding consumption of any animal-derived products (veganism). However, there appears to be an increased interest in flexitarianism, which assumes a primary focus on plant foods with the occasional inclusion of meat products (and can be regarded as semi-vegetarianism). The effects of this practice require further assessment [Derbyshire, 2017].

3. There are numerous confounding variables when addressing the health benefit of diet, encompassing age, BMI, physical activity, smoking, alcohol consumption, biochemical markers, clinical background, and genetic predispositions, while adjustment for all of them may often be a challenging or impossible task.

4. Some health effects of each diet are evidenced in a small sample size, advocating further research to provide additional data and improve the strength of evidence. Numerous studies include healthy subjects, and there remains a need to test whether specific diets can exert similar beneficial effects in individuals with active disease.

5. Pursuing cross-over interventional trials comparing the effects of vegetarian and Mediterranean diets in different groups is encouraged. This particularly concerns the studies designed to directly compare the effects of these diets on cardiovascular markers, gut microbiome, metabolic profile, kidney function, and course of autoimmune diseases.

6. Considering that a shift in diet may not produce immediate effects, there is a need to pursue long-term interventional trials for vegetarian and Mediterranean diets. This
is important to understand whether the effects evidenced so far are persistent or can attenuate over time (e.g., years of adherence to a specific diet).

7. Implementation of diets, such as vegetarian or Mediterranean, in selected populations may be faced with several obstacles that include economic factors, difficulties in the availability of certain food products, additional time and effort to prepare meals adhering to a particular diet [Bonaccio et al., 2016; Middleton et al., 2015]. The broader implementation of vegetarian or Mediterranean diets in some populations, e.g., the Western world, may also be challenging since both require limitation or complete abstinence from meat [Fehér et al., 2020].

CONCLUSIONS

Both vegetarian and Mediterranean diets exhibit various health-beneficial effects. Both diets are beneficial for lipid management, reduce cardiovascular risk, promote weight loss, and improve glycemic control in patients with type 2 diabetes. However, in most studies, the Mediterranean diet shows a higher health-promoting potential than the vegetarian diet, particularly regarding triglyceride levels, control of glycemia and blood pressure, and total cancer risk. Additionally, adherence to the Mediterranean diet is related to a lower risk of nutritional deficiencies than vegetarianism. At the same time, adherence to the Mediterranean diet or weight status in type 2 diabetes: A systematic review and meta-analysis of randomised controlled trials. Nutrients, 13(11), art. no. 4099.

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CONFLICT OF INTERESTS

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