The International Vegetarian Union’s

**Guide to VEGAN NUTRITION for adults**

*health professional edition*

[Image of various vegan dishes]
THE INTERNATIONAL VEGETARIAN UNION’S VEGAN NUTRITION GUIDE FOR ADULTS

VEGAN NUTRITION GUIDE FOR ADULTS OF THE INTERNATIONAL VEGETARIAN UNION (IVU)

VERSION FOR HEALTHCARE PROFESSIONALS

DEPARTMENT OF MEDICINE AND NUTRITION OF IVU
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Author's Note

This work has been improved with several explanatory videos to facilitate retention and deepening of the subjects.

In each QRCode there is a video. Point your cell phone camera (if it's in the print version) or click on the QRCode (if it is in the pdf version) to watch the video.

The Figures of this Guide can be downloaded by clicking on the link available in Part 10 (Appendix).

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This is just sample book. As such it’s provided with Chapter 2 only.
PART 2
EFFECTS ON HEALTH
The vegetarian diet is not a single diet model followed by people in an identical way. More or less healthy choices can be made, and this directly impacts the results obtained, either in terms of nutrient intake or disease prevention and treatment.

However, the choice of plant-based foods in their natural and whole form and the abstention or reduction in the consumption of animal foods have important metabolic impacts.

The focus of this guide is dietary planning, not examining the relationship between vegetarianism and disease prevention and treatment, as the latter is material for another work. Nevertheless, we briefly describe the main findings for different clinical conditions studied. In this part of the guide, we begin with a discussion of the potential effects of healthy eating and end by presenting important studies on the main chronic noncommunicable diseases.

1. POTENTIAL FOR DISEASE PREVENTION AND TREATMENT THROUGH A VEGETARIAN DIET

The use of whole, plant-based foods, as advocated by the IVU to obtain the greatest benefits from consuming a vegetarian diet, substantially increases the consumption of fiber and phytochemicals, positively modulates microbiota, and reduces the consumption of all negative elements present in animal products, which we will address later. Next, we will provide a brief synopsis of the action of these compounds.

1.1. Fiber

Fiber is nondigestible carbohydrates, usually derived from plant-derived polysaccharides, with several positive health benefits. A well-planned vegetarian diet contains a considerable amount of fiber, as such a diet will consist of natural and whole foods.

Fiber consumption by Americans and Europeans is approximately one-third lower than the recommended level [29]. It is also low worldwide, i.e., under 20 g per day, when the recommended intake is 25-29 g/day [30].

Fiber can act differently if it is soluble or insoluble, but in general, it decreases gastric emptying (increase satiety). Its viscosity (especially that of soluble fiber) slows the peristalsis of the small intestine.
(which favors the slower absorption of nutrients, including glucose, with a reduction in the glycemic index of the food) and leads to the formation of a more voluminous and softer fecal bolus. Its effect on glycemic control is remarkable, as indicated by a meta-analysis that showed improvements in insulin sensitivity, glycated hemoglobin, lipid profile, body weight and C-reactive protein level [31].

Due to its ability to bind with various intestinal compounds, fiber (especially soluble fiber) increases the fecal excretion of cholesterol and bile salts. It provides a substrate for bacterial fermentation and thus modulates the microbiota and generates several compounds beneficial to metabolism. Studies suggest that fiber has extraintestinal effects linked to a possible reduction in HMGCoA reductase activity (key enzyme in cholesterol synthesis), in addition to modulating LDLc (low-density lipoprotein), CYP7A1 and MAPK receptors, as well as other genes related to lipid metabolism [32].

A meta-analysis showed that for each 10 g increase in fiber intake per day (of any type), the risk of cardiovascular disease is reduced by 9%, that of coronary disease is reduced by 11% and that of all types of cancer is reduced by 6% [33]. The effect of fiber in the prevention of colorectal cancer (adenoma) is fully established, both in prevalence and incidence, and seems to be more closely associated with protecting males than females [34].

1.2. Gut microbiota

The microbiota has been the subject of many studies, from which there are important results that pertain to the vegetarian diet. A brief summary of these aspects is provided in the box below.
Brief summary of the gut microbiota

Use the subsequent passages to follow the figures (adapted from reference [35]).

The distal colon contains bacteria that ferment mostly peptides and proteins because fiber is less available at this site. **Proteolytic fermentation produces harmful substances** (ammonia, p-cresol, hydrogen sulfate, indole compounds and branched-chain fatty acids) that have a negative effect on liver function (reduced lipid oxidation capacity, increased lipogenesis, and inflammation), on adipose tissue (lipid storage capacity and inflammation) and on the integrity of the intestinal barrier, leading to endotoxemia. Carbohydrate fermentation has the opposite effect and improves pancreatic beta-cell function, insulin secretion capacity, muscle sensitivity and muscle lipid oxidation capacity [35].

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**Figure 2.1. Metabolic actions of carbohydrate and protein fermentation**

**Metabolic actions of carbohydrate and protein fermentation**

- **Pancreas**
  - Beta-cell function
  - Insulin secretion

- **Muscle**
  - Lipid oxidation capacity
  - Insulin sensitivity

- **Adipose tissue**
  - Lipid storage capacity
  - Inflammation

- **Liver**
  - Lipogenesis
  - Lipid oxidation capacity

**Enterocytes**

Intestinal barrier

Endotoxaemia

**Intestine**

Acetate
Propionate
Butyrate
Succinate

Carbohydrate fermentation

Ammonia
p-Cresol
Hydrogen sulfate
Indolic compounds
Branched-chain fatty acids

Protein fermentation

**Figure created by Professor Doctor Eric Slywitch**
Most studies indicate that protein intake is correlated with greater microbiota diversity. However, animal and plant proteins have different effects. Individuals who consume a high amount of meat (which contains a high amount of fat) show less abundance of bacteria such as *Roseburia*, *Eubacterium retale* and *Ruminococcus bromii* because they metabolize polysaccharides [36]. Bacterial populations that increase in response to increased meat consumption are tolerant to bile, for example, *Bacteroides* and *Clostridia*, and by increasing the amount of protein and fat in the diet, the amount of carbohydrate is automatically reduced, and the inflammatory response increases, as well as the risk of colorectal cancer [37]. Individuals who consume protein from *peas* exhibit increased *Bifidobacterium* and *Lactobacillus* proliferation and reduced pathogenic bacteria (e.g., *Bacteroides fragilis* and *Clostridium perfringens*) proliferation [38].

The change in the microbiota from proteolytic to saccharolytic (carbohydrate-based) fermentation plays a role in the prevention of metabolic diseases, such as type 2 diabetes and nonalcoholic fatty liver disease and produces the opposite effect to that caused by protein with fat. A more saccharolytic microbiota produces more acetate, butyrate, propionate, and succinate. Acetate, propionate, and butyrate (short-chain fatty acids – SCFAs) promote increased intestinal gluconeogenesis, with a beneficial effect on homeostatic energy regulation. Acetate and butyrate promote an increase in thermogenesis in adipose tissue and the liver and increase the amount of brown adipose tissue and the secretion of leptin (hormone produced by adipose tissue that plays a role in the control of food intake) and promote improvements in pancreatic function (optimization of beta-cell function and insulin secretion) and muscle function (greater fat oxidation capacity and greater insulin sensitivity). Additionally, acetate, propionate and butyrate stimulate the secretion of intestinal hormones with satietogenic action, for example GLP1 (glucagon-like peptide) and PYY (peptide YY). The vagus nerve has a direct influence on the feeling of satiety because after a vagotomy, GLP1 loses its satietogenic action. The action of SCFAs on afferent vagal stimulation and energy homeostasis is still the subject of investigations. In addition, increased intestinal gluconeogenesis results in reduced hepatic glucose production (hepatic gluconeogenesis) and improves energy homeostasis [35].
SCFAs are substrates for maintaining colonocyte health, play a role in the maintenance of the intestinal barrier and prevent endotoxemia and its secondary inflammatory effects. SCFAs play a protective role in type 2 diabetes, inflammatory bowel disease and autoimmune diseases, promote immunity against pathogens, and are important for microglia function and for the maturation and control of the integrity of the blood-brain barrier \[35\].

The consumption of plant-based foods with little or no cooking, with an intact cell wall, provides more substrate for use by intestinal bacteria. An ultra-processed diet with acellular nutrients is easily absorbed in the small intestine, depriving the colon of important nutrients and altering the composition and metabolism of the gut microbiota \[39\].

Regarding fat, both the quantity and quality affect the composition of the gut microbiota. A plant-based, low-fat diet increases the population of Bifidobacteria. With poly- and monounsaturated fats, the Bacteroidetes:Firmicutes ratio increases, as does the population of lactic acid-producing...
bacteria, bifidobacteria and Akkermansia muciniphila [38]. The consumption of nuts increases Ruminococceae and Bifidobacteria, in addition to reducing Clostridium sp.

Conversely, the consumption of saturated fat increases Bilophila and Faecalibacterium prausnitzii and reduces Bifidobacterium [38]. This change induces inflammation (production of cytokines such as IL-1, IL-6 and TNF-alpha) and metabolic disorders [40]. High intake of saturated and trans fat increases cardiovascular risk and reduces Bifidobacterium spp. and Bifidobacterium spp. and increases Firmicutes [41].

The adoption of plant-based eating has a positive effect on the gut microbiota, optimizing strain diversity, reducing the most pathogenic bacteria, reducing the level of inflammation and producing more SCFAs [42, 43].

From the cardiovascular perspective, in addition to the inflammatory effects previously mentioned, there are two other important points to consider: the effects on cholesterol and on trimethylamine N-oxide (TMAO) formation (which will be discussed in another section).

Several bacterial strains isolated from the gut or feces can convert cholesterol into coprostanol, which is weakly absorbed by the intestine and eliminated in the feces, disfavoring the cholesterol enterohepatic cycle and reducing serum cholesterol levels [44, 45]. Thus, a higher intake of carbohydrates with fiber and lower intake of animal protein with fat reduces the reabsorption of cholesterol by breaking its enterohepatic cycle.

In the context of cardiovascular risk, the Mediterranean (low consumption of animal products) and vegetarian diets show the best cardiovascular metabolic profile, represented by increased SCFA production and reduced TMAO and secondary bile acid production, because they lead to an increase in some bacterial strains (Prevotella, Candida albicans, Faecalibacterium prausnitzii, Clostridium cluster XIVa, Roseburia, Ruminococcus, and Parabacteroides distasonis) and a reduction in others (Bilophila wadsworthia, Alistipes putredinis, and Escherichia coli) [46].

1.3. Antioxidants, phytochemicals and phytosterols

Regarding the protective compounds present in a plant-based diet, a study analyzed the total antioxidants in more than 3,100 foods, beverages, spices, herbs, and supplements used worldwide. The mean antioxidant content in animal foods was 0.18 mmol/100 g, and in plant foods, it was 11.57 mmol/100 g. In other words, per the same unit weight, there is 64.27 times more antioxidants in foods originating from the plant kingdom than in foods originating from the animal kingdom [47].

A diet with one portion of meat and three portions of dairy products provides approximately 500-kcal from foods with a low antioxidant content (0.18 mmol/100 g). In a 1,500-kcal diet for women, this is equivalent to 33.3% of the diet consisting of foods with a low antioxidant content. The replacement of these animal products with vegetables (11.57 mmol/100 g of antioxidant content) substantially increases the intake of antioxidants.
More than a dozen previous studies have shown that vegetarians have higher serum levels of various antioxidants, higher SOD (superoxide dismutase) activity, greater protection against lipoprotein oxidation and greater genomic stability. Vegetarians who do not supplement vitamin B12 (we will discuss this further in the corresponding chapter) tend to have a higher homocysteine level, which increases free radical formation. However, even under these conditions, some researchers have shown a lower rate of atherogenicity, lipid peroxidation and oxidation. These findings reinforce the importance of the antioxidant system as an integrated system dependent on risk and protection variables [48-58]. Later, we will present meta-analyses that address this topic.

The effect of phytochemicals on health is remarkable. Containing an enormous amount of bioactive compounds, plant foods have the ability to influence various body systems, modulate anti-inflammatory action and the production of nitric oxide [59] and influence the fight against viruses [60, 61].

A study with 2,884 participants (94.8% physicians and 5.2% nurses and nursing assistants) who worked on the front line against COVID-19 in six countries (France, Germany, Italy, Spain, the United Kingdom and the United States) evaluated, based on the number of contaminations, the severity and duration of infection occurring between July 17 and September 25, 2020. The diets of the participants were classified into 11 established patterns, and a validated questionnaire was used to qualitatively assess the diets. At the end, the different diets were grouped as follows: plant-based diet, plant-based with fish diet and low-carbohydrate and high-fat diet). A total of 568 individuals with COVID-19 (half by serology and half by signs and symptoms because they could not undergo testing) and 2,316 controls were evaluated. The final analysis indicated that the group that consumed more vegetables and less meat (plant-based group) had a 73% lower chance of having moderate-to-severe COVID-19; the group who consumed fish had a 59% lower chance of developing moderate-to-severe COVID-19; and those who consumed a diet with a higher content of animal products had a 286% higher chance of developing moderate-to-severe COVID-19. Because the study was observational, with all the limitations inherent to that type of analysis, further studies are needed to validate the outcome, but the direction shows that a higher consumption of plant foods, compared to a higher consumption of animal foods, seems to reduce the manifestation of symptoms of COVID-19 [62]. Data such as these are not surprising in well-controlled studies of the antioxidant potential and improvements in metabolic conditions when adopting a well-planned vegetarian diet, as we will see later.

When plants are threatened by insects or predators, their secondary metabolism is activated and increases the production of phytochemicals, which protect the plant. Organic farming promotes plants with higher levels of polyphenols, silicic acid and vitamin C [63, 64].

Regarding protective compounds found in the plant kingdom, phytosterols deserve attention. Phytosterols are lipid compounds (steroids) derived from plants and represent the largest unsaponifiable lipid fraction in plants. Although found in all plants, most phytosterols are oils from unrefined plants, such as oilseeds (sesame, sunflower, soybean, macadamia, almond and olive). Oilseeds, whole grains and legumes are also good sources of phytosterols, and their best known representatives are beta-sitosterol, campesterol and stigmasterol [65].
The consumption of phytosterols has several health benefits, as these compounds modulate inflammatory and antioxidant responses and have antiulcer, immunomodulatory, antibacterial, and antifungal activities. They have a recognized cardiovascular effect due to the ability to inhibit platelet aggregation and reduce the levels of total cholesterol and LDLc by 7-12.5% at a dose of 1.5-3 g/day [65].

1.4. Exclusion of animal products

The exclusion of meat and animal products leads to a significant reduction in the consumption of saturated fat, heme iron, advanced glycation and lipoxidation end-products, carnitine, phosphatidylcholine and choline (precursors for the formation of trimethylamine N-oxide or TMAO), in addition to chemical compounds with carcinogenic action used in the preservation of these products, such as nitrites, which react with amines and amides in the gut and become N-nitrous compounds, nitrosamines and nitrosamides [66]. In addition, the exposure of meat to high temperatures leads to the formation of heterocyclic amines and polycyclic aromatic hydrocarbons, known to be carcinogenic. The presence of N-glycolylneuraminic acid in meat (especially red meat) increases the systemic inflammatory response. In addition, animal products are devoid of fiber and phytochemicals, in addition to having a macronutrient composition based on fats and proteins, with no or low carbohydrate content.

We must better understand the effect of these substances on the human body.

1.5. Saturated fat

The box below provides important information regarding the metabolic action of saturated fat.

Use the subsequent passages to follow Figure 2.3.
Figure 2.3. Action of saturated and trans fats and lipopolysaccharides (LPS) on insulin resistance.

Saturated fat, in addition to the already-mentioned negative effect on the gut microbiota, has a direct effect on the formation of compounds with inflammatory action (TNF-α) and negatively affects glycemic control.

The main mechanisms that lead saturated fat to affect insulin sensitivity are mediated by the stimulation of toll-like membrane receptors 2 and 4, present in the cell membrane. When saturated fat, trans fat and LPS (lipopolysaccharides from the outer membrane of gram-negative bacteria) come into contact with a toll-like receptor, a cascade reaction occurs via MDY-88 that leads to the production of NF-kappa B and, later, the expression of TNF-α (tumor necrosis factor alpha), causing insulin resistance by altering phosphorylation after the binding of insulin to its receptor. In physiological pathways, after insulin binds to its membrane receptors, tyrosine kinase activation triggers the phosphorylation of tyrosine residues on cellular substrates (IRS – insulin receptor substrate), resulting in the migration of glucose transporters (GLUT-4) to the cell membrane and favoring a reduction in blood glucose. The presence of TNF-α causes serine rather than tyrosine phosphorylation on insulin receptors, negatively affecting the intracellular response of GLUT-4 migration to the cell membrane. This slows the removal of serum glucose from insulin-dependent tissues [67].
In addition, higher fat intake, especially saturated fat, leads to adipocyte hypertrophy and macrophage infiltration, leading to the increased production of cytokines (such as TNF-α and IL-6) and negatively altering insulin sensitivity [67].

By dysbiosis, LPS stimulates toll-like receptor 4, causing stress in the endothelial reticulum, which leads to cell apoptosis (via caspase release) and insulin resistance via the formation of reactive oxygen species via JNK (Jun N-terminal kinase). It is worth mentioning that diets rich in fat reduce bifidobacteria, Eubacterium, Clostridium coccoides and Bacteroides, with an increase in serum LPS [67].

The metabolites derived from the oxidation of fatty acids (acylcarnitines, long-chain Acyl-CoAs, ceramides and diacylglycerols) promote insulin resistance [67].

The negative effect of saturated fat on insulin resistance is more evident when its intake exceeds 10% of the total caloric volume.

1.6. Advanced glycation and lipoxidation end-products

Advanced glycation end-products (AGEs) are proteins or lipids nonenzymatically glycated with glucose or other reducing sugars and their derivatives, such as glyceraldehyde, glycolaldehyde, methylglyoxal and acetaldehyde. This formation can occur through three different pathways: the Maillard reaction, the polyl pathway and lipid peroxidation. The formation of AGEs is directly linked to the mechanisms of various diseases, such as diabetes and its complications (retinopathy and neuropathy), neurological disorders (Parkinson’s and Alzheimer’s diseases), atherosclerosis, hypertension, nephropathy, rheumatoid arthritis, bone remodeling dysfunction, tumor growth, metastases, and other degenerative diseases. The endogenous formation of AGEs increases when there is hyperglycemia because there is more glucose to chemically react with the circulating products. The presence of AGEs results in altered chemotaxis, angiogenesis, oxidative stress, cell proliferation and apoptosis [68].

Glycation can also occur in products that are cooked, i.e., fried, roasted, or microwaved, especially during caramelization. The objective of these processes is to accentuate flavor and aroma. Acrylamide and the heterocyclic amines formed in this process can interfere with cell transduction signaling or in the expression of several genes, increasing oncological risk. Whether derived from endogenous or exogenous pathways, AGEs bind to receptors, cause oxidative stress and promote inflammatory processes [68].

Advanced glycation end-products and advanced lipoxidation end-products (ALEs) are found in large quantities in animal foods due to their high protein and fat contents. The higher the intake of animal foods, the greater is the absorption of these end-products [66].

The amount of AGEs or ALEs absorbed in the digestive tract is unclear, but studies estimate it to be 10% to 80%. Once absorbed, these end-products can biotransform, can be excreted or can accumulate in
various tissues. It is estimated that 30% of AGEs can be excreted in the urine of individuals with preserved renal function. The consumption of foods not subjected to high-temperature processes avoids the ingestion of AGEs and ALEs [68].

Insulin production is an energy (ATP)-dependent process. The transport of glucose into the pancreas (via GLUT-2, type 2 glucose transporter) promotes the production of ATP through the Krebs cycle in mitochondria. In the presence of ATP, potassium channels close, and calcium channels open; thus, as a second messenger, ATP causes insulin to be released into the bloodstream [69]. This is the process by which the pancreas releases insulin when there is an increase in serum glucose. AGEs inhibit ATP production in pancreatic beta cells and inhibit the release of insulin. The effect of this condition is glycemic increase [70].

The plant kingdom contains natural agents that inhibit glycation, such as anthocyanins and ellagic acid, which are present in fruits and vegetables. Active compounds are also found in green tea, garlic and wine and include resveratrol, curcumin, cinnamic acid derivatives (such as ferulic acid) and caffeic acid derived from mate tea. Reducing the consumption of AGEs can reduce the risk of diabetes, cardiovascular complications and other glycation-related diseases [68].

1.7. Trimethylamine N-oxide (TMAO)

Another point that currently stands out is the growing number of studies on TMAO formation by omnivorous gut microbiota. The box below summarizes the topic.
The formation of TMAO depends on several consecutive steps: substrate ingestion, metabolization by the gut microbiota, absorption, and hepatic production of TMAO, with subsequent metabolic effects.

1) Substrate ingestion

The substrates ingested and used for the production of TMAO are carnitine, phosphatidylcholine, and choline, betaine, dimethylglycine and ergothioneine [71].

Ergothioneine is found in meat derivatives (liver and kidneys), some beans and mushrooms. The major sources of phosphatidylcholine and, consequently, TMAO are eggs, liver, milk, meat (red and poultry) and fish [71].
Red meat is rich in carnitine (one of the main precursors of TMAO), while beef and other meats (such as poultry), liver, fish and egg yolk are rich in choline. Choline is also present in supplements and medications. Choline is less concentrated in the plant kingdom. Betaine is more present in plants [71].

2) Metabolization by the gut microbiota

The gut microbiota, through enzymes (trimethylamine-lyase, gamma-butyrobetaine, L-carnitine dehydrogenase, carnitine oxidoreductase and ergothionase), converts these substrates into TMA (trimethylamine). Meat consumption increases the proliferation of some species of Bacteroides, Alistipes, Ruminococcus, Clostridia and Bilophila and reduces Bifidobacterium, optimizing TMA production. The microbiome of vegetarians is different from that of omnivores, and the intake of carnitine and choline by vegetarians and vegans tends to be lower. Because of this, vegetarians have a reduced ability to produce TMA [71].

3) Absorption and hepatic production of TMAO

Approximately 95% of trimethylamine is converted by liver flavin monooxygenases (FMO1 and FMO3) into TMAO, transported to tissues or excreted by the kidneys [71]. Vegetarians have much lower serum levels of TMAO than do omnivores and produce significantly less TMAO after the ingestion of carnitine [72]. The plasma concentration of TMAO is similar in vegans and ovo-lacto vegetarians.

Eating two or more eggs per day is associated with high plasma and urine concentrations of TMAO [71].

4) Metabolic effects of TMAO

TMAO exerts deleterious effects on human metabolism and is associated with increased cardiovascular risk due to increased atherogenicity, heart failure, stroke, neurological disorders, intestinal inflammation, chronic kidney disease and mortality from all causes. TMAO reduces reverse cholesterol transport and deregulates proatherogenic scavenger receptors [72, 73]. An elevated TMAO level is also associated with Alzheimer’s disease [74], obesity [75] and mortality from type 2 diabetes [76].

The results of a three-year follow-up study with 4,007 individuals subjected to elective coronary angiography indicated that those who had an elevated TMAO level had a greater risk of adverse cardiovascular events (risk of 2.54 for highest vs lowest TMAO level) [77].

A study that compared eight vegetarians (vegans and ovo-lacto vegetarians) with ten omnivores showed that vegetarians have a lower plasma TMAO level. The presence of this substance in plasma increases the incidence of thrombotic events by increasing platelet responsiveness to multiple coagulation agonists because it increases the sensitization to calcium-dependent stimuli. After supplementation with 450 mg of choline per day for two months, both vegetarians and omnivores
exhibited increased TMAO levels; this increase was 10-fold in the vegetarian group and 14-fold in the omnivore group, when compared to the baseline values (lower in vegetarians and higher in omnivores). After using acetylsalicylic acid (81 mg/day) for one month with concomitant choline supplementation, TMAO increased the platelet aggregation capacity in omnivores [78].

A systematic review and meta-analysis of 11 prospective cohort studies published in 2018 indicated that an elevated TMAO level is associated with a **23% increase in cardiovascular events and a 55% higher risk of death from all causes** [79].

A systematic review and meta-analysis of 18 observational studies published in 2020 found a possible association with an increased risk of hypertension and other cardiometabolic disorders in adults. Individuals with the most elevated TMAO levels exhibited an 2.36 mmHg increase in systolic blood pressure when compared with the systolic pressure in those with lower TMAO levels, in addition to a reduction in the HDLc in apparently healthy individuals or with cardiovascular disease [80].

Another systematic review and meta-analysis with a dose-response analysis published in 2020 showed a 12% increase in the risk of **hypertension** in individuals with higher serum TMAO levels when evaluating eight studies with a total of 11,750 individuals and 6,176 cases of hypertension [81].

The last systematic review and meta-analysis published toward the end of the preparation of this guide, in 2021, supports the role of the plasma TMAO level as a predictor of cardiovascular events. An elevated TMAO level may be a **new cardiovascular risk factor** potentially useful for personalized planning as a strategy for the prevention of cardiovascular diseases [82].

The adoption of a Mediterranean diet, especially vegetarian, as well as increased consumption of plant-based foods, modifies the gut microbiota and, consequently, reduces TMAO levels. On average, 25% of plasma metabolites are different between vegetarians and nonvegetarians [46].

### 1.8. Action of heat on meat

The **heating of red meat** (meat from mammals) leads to the production of mutagenic substances that contribute to an increased risk of colorectal cancer. In some forms of preparation, the concentration of genotoxic agents can be altered by more than 100-fold. Table 2.1 explains each preparation [83, 84].
Table 2.1. Products present or formed in meat during heating

<table>
<thead>
<tr>
<th>Substance</th>
<th>Location where found</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-nitrous compounds (NOCs)</td>
<td>Cured* meats</td>
<td>Classified as group 1 mutagenic (carcinogenic). Their level in cured meat can vary from less than 1 ppb (part per billion) to more than 130 ppb. NOCs are activated by cytochrome P450 2E1 in the gastrointestinal tract. Their level in feces is ten times higher in omnivores than in vegetarians.</td>
</tr>
<tr>
<td>Heterocyclic aromatic amines (HCAs)</td>
<td>Well-done meats, including chicken</td>
<td>Formed when amino acids, sugars and creatine react at high temperature, and found in large quantities in meat cooked at high temperature.</td>
</tr>
<tr>
<td>Polycyclic aromatic hydrocarbons (PAHs)</td>
<td>Smoked meats and meats cooked over an open flame</td>
<td>Classified as group 1 mutagenic (carcinogenic). When they drip, the fat and juice of the meat grilled directly on an open fire creates a flame. This flame contains PAHs, which adhere to the surface of the meat. They are metabolized by cytochrome P450 and form genotoxic compounds, such as N-hydroxylated metabolites. PAHs are also present in tobacco and appear to contribute to lung cancer. They are also found in the smoke from vehicle exhaust.</td>
</tr>
<tr>
<td>Heme iron</td>
<td>Animal meats, especially red meat</td>
<td>Catalyzes the nitrosation of endogenous secondary amines and exerts a pro-oxidative effect by catalyzing lipid peroxidation in the gastrointestinal tract</td>
</tr>
</tbody>
</table>

*A meat preservation process achieved by adding salt, color fixing compounds (nitrates and/or nitrites), sugar and/or spices [83].

The formation of HCAs and PAHs varies based on the type of meat, the cooking method, and the cooking level (rare to well-done). Regardless of the type of cooked meat, the formation of HCAs and PAHs is accentuated when the temperature is higher than 149°C (300°F), and this occurs when grilling over an open flame or when pan frying. Meats cooked for longer periods tend to form more HCAs. As an example, well-done, grilled, or barbecued chicken and steak have high concentrations of HCAs. Cooking methods that expose meat to smoke or carbonization contribute to the formation of PAHs [84].

The role of these meats in cancer has been widely studied; we will discuss it later in the section on cancer.
1.9. N-glycolylneuraminic acid (Neu5Gc)

In addition to the aforementioned compounds, **N-glycolylneuraminic acid (Neu5Gc)**, which is abundant in red meat, is also noteworthy. Neu5Gc is not biosynthesized by humans but is bioavailable in ingested meat and is incorporated into human tissues, promoting the formation of anti-Neu5Gc antibodies, which cause **chronic inflammation** and lead to the formation of reactive oxygen species. This mechanism contributes to **carcinogenesis** and **tumor progression** [83].

1.10. Heme iron

**Heme iron** has several negative effects on metabolism, and we will present systematic reviews and meta-analyses of this compound in the chapter on iron.

2. PESTICIDES

The use of **pesticides in agriculture** began in the 1920s, and at that historical moment, they were little known from a toxicological standpoint. During World War II (1939–1945), pesticides were used as **chemical weapons**, and subsequently, their production was increased [85].

In Brazil, in 1975, the National Development Plan (Plano Nacional de Desenvolvimento-PND), responsible for opening the country to pesticide trade, instituted the inclusion of a defined pesticide quota for each loan needed and required farmers to purchase pesticides with farm credit resources. This requirement, added to manufacturers’ advertising, led to the increased and widespread use of pesticides in Brazil [85].

In the context of human health, exposure to pesticides, at any level, is harmful and is **associated with various diseases**, such as **hypersensitivity**, **cancer**, **asthma**, and **hormonal disorders**. It can also cause **congenital defects** and **low birth weight** and lead to **death** [86]. Organochlorine pesticides also appear to be associated with **Parkinson’s disease** [87].

In the food production process, plants use soil (including its nutrients, water, and microorganisms) and solar energy for development. Animals obtain their nutrients and energy from plants, other animals, or both. With population growth, **polyculture was replaced by monoculture**, and **synthetic chemical fertilizers and pesticides** were introduced; the use of **antibiotics**, **vitamins** and **minerals** became the **basis of global livestock farming**. **Confined animal farming requires large-scale planting**, usually in **monoculture**, for animal feeding. In the United States, the production of 1 kg of meat requires 10 kg of...
grains for animal feeding, more than 8,000 liters of water, approximately 8,000 kilojoules (1,910.7 kcal), 150 g of fertilizers, 7 g of pesticides and 21 square meters of land. As animals spend much of their energy for their own use, livestock is considered an inefficient form of resource use, with approximately 89% biomass loss over the life of the animal, as explained in the “Threat to planetary health” chapter. The resources needed for the production of 1 kg of kidney bean protein and 1 kg of beef protein is shown in Table 2.2 [7].

Table 2.2. Resource requirements to produce 1 kg of protein from kidney beans or beef.

<table>
<thead>
<tr>
<th>The production of 1 kg of beef protein compared to that of 1 kg of kidney bean protein requires:</th>
</tr>
</thead>
<tbody>
<tr>
<td>18× larger planting area</td>
</tr>
<tr>
<td>10× more water</td>
</tr>
<tr>
<td>12× more fertilizer</td>
</tr>
<tr>
<td>9× more fuel</td>
</tr>
<tr>
<td>10× more pesticide</td>
</tr>
</tbody>
</table>

Pesticides are used in the production of plant and animal foods. For plants, they are used to combat and prevent the multiplication of insects, a condition favored by large-scale monoculture. For animals, pesticides are used in the prevention and treatment of parasitic diseases. In addition, most crop production is used as animal feed, and pesticides present in plants are consumed by animals. Animals are primary or secondary consumers and due to their high body fat content, accumulate pesticide residues throughout their lifetime. As the top of this food chain, when humans consume animal fat, they ingest these xenobiotics in a concentrated form.

The use of pesticides was estimated at 3.5 million tons worldwide in 2020 [88].

The countries that used pesticides the most and their estimated consumption per kilogram per inhabitant in the period from 2010 to 2014 are shown in Table 2.3. [86, 88].

Table 2.3. Pesticide use by country

<table>
<thead>
<tr>
<th>Country</th>
<th>Pesticide use in kg/inhabitant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan</td>
<td>18.98</td>
</tr>
<tr>
<td>China</td>
<td>10.45</td>
</tr>
<tr>
<td>Mexico</td>
<td>7.87</td>
</tr>
<tr>
<td>Brazil</td>
<td>6.17</td>
</tr>
<tr>
<td>Germany</td>
<td>5.12</td>
</tr>
<tr>
<td>France</td>
<td>4.86</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>4.03</td>
</tr>
<tr>
<td>United States</td>
<td>3.89</td>
</tr>
<tr>
<td>India</td>
<td>0.26</td>
</tr>
</tbody>
</table>
These agents can remain active in the environment for long periods and affect the entire ecosystem, represent a major risk to public health and require monitoring and surveillance of water, soil, food and air [85].

Pesticides are classified as insecticides, herbicides and fungicides (Figure 2.5) [86].

Figure 2.5. Classification of pesticides

The compounds widely used in crop and livestock farming belong to four distinct groups: organophosphates, organochlorines, carbamates and pyrethroids. Their intake by humans occurs through the consumption of animal and plant foods [85].

**Organophosphates and carbamates** are cholinesterase-inhibiting insecticides that cause *acetylcholine accumulation* in nerve synapses. Carbamates are reversible and organophosphates are irreversible inhibitors of cholinesterase, but in the context of intoxication, both have the same degree of severity [85].

**Organochlorines** are widely used in crops and cattle to treat ectoparasites. These compounds are extremely *fat soluble* and exhibit slow degradation and accumulation capacities in the environment (they can remain *in the soil for more than 30 years*) and in living beings. Human contamination occurs directly (by respiratory, cutaneous, or digestive pathways) or through the food chain. However, the **main route of contamination** is the **consumption of foods that contain high amounts of fat** [85, 89]. The use of organochlorines in countries such as Brazil is restricted to combating ants (Aldrin) and to public health campaigns (DDT and BHC) [85].

A **review study** evaluated pesticide residues in cow milk from 1970 to 2002. According to the authors, the presence of such residues may occur through the consumption of contaminated pastures and feed or by ectoparasite treatment with pesticides, applied in noncompliance with good agricultural practices. The study showed that although their use is prohibited in several countries, **organochlorines** are still detected in milk, albeit in progressively smaller amounts across the years [90]. In almost all the countries studied, contamination reached **100% of the samples** at various times.
Table 2.4 shows the results of studies conducted in several countries that monitored pesticide residues in animal product samples (adapted from reference [85]).

Table 2.4. Pesticide residues animal product samples

<table>
<thead>
<tr>
<th>Product of animal origin</th>
<th>Pesticide found</th>
<th>Samples with detected residues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raw milk</td>
<td>Carbamates</td>
<td>93.8%</td>
</tr>
<tr>
<td></td>
<td>Organophosphates</td>
<td></td>
</tr>
<tr>
<td>Cheese</td>
<td>Organochlorines</td>
<td>100%</td>
</tr>
<tr>
<td>Pasteurized milk</td>
<td>Organochlorines</td>
<td>95%</td>
</tr>
<tr>
<td>Milk, cheese, butter and yogurt</td>
<td>Organochlorines</td>
<td>20.6%</td>
</tr>
<tr>
<td>Meat products under federal</td>
<td></td>
<td>96.9% in the raw material</td>
</tr>
<tr>
<td>inspection</td>
<td></td>
<td>97.7% in the processed product</td>
</tr>
<tr>
<td>Hot dog sausage</td>
<td>Organochlorines</td>
<td>Samples with a level below that</td>
</tr>
<tr>
<td></td>
<td>Polychlorinated biphenyls</td>
<td>established by the law</td>
</tr>
<tr>
<td>Eggs</td>
<td>Organochlorines</td>
<td>28%</td>
</tr>
<tr>
<td>Chicken</td>
<td></td>
<td>20%</td>
</tr>
<tr>
<td>Beef</td>
<td></td>
<td>49%</td>
</tr>
<tr>
<td>Fish</td>
<td>Organochlorines</td>
<td>100%</td>
</tr>
<tr>
<td>Mollusks</td>
<td>Polychlorinated biphenyls</td>
<td></td>
</tr>
<tr>
<td>Crustaceans</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In Brazil, several studies have identified many contaminated watersheds. More than ten years after the use of DDT was banned, contamination was still found in all broiler breeders in a region of Rio de Janeiro, along with the contamination of eggs destined for human consumption [89].

A study conducted between 1993 and 1995 in Hong Kong to evaluate the level of organochlorines in cow milk samples detected DDE and BHC at amounts that exceeded the maximum allowed by the Codex Committee on Food Additives of the Food and Agriculture Organization of the United Nations (FAO), even though China banned the use of these compounds in 1983, i.e., 10 years before the study [89].

An older study (published in 1983) evaluated breast milk samples from women who consumed a lactovegetarian diet (18 samples), an omnivorous mixed diet (20 samples) and a diet containing Baltic fatty fish (11 samples). The lowest levels of the various evaluated pesticides were found in the lactovegetarian group, whereas the highest were found in women who ate fatty fish [91].

In 1998, a study conducted in India (Punjab) evaluated food samples collected in markets every three months for a period of one year. The results showed contamination by DDT and BHC higher than that reported in industrialized countries. Fatty foods (milk and its derivatives, oils and fats, meats, eggs and cheeses) were responsible for 85% of the total DDT ingested, while BHC was found to be more distributed among the various analyzed foods [92].
The highest human contamination by organochlorines comes from the consumption of meat and animal-derived products [93, 94].

Another study evaluated the pesticide residues ingested by the general population of France in groups of omnivores, lactovegetarians, ovo-lacto vegetarians, pesco-lacto vegetarians and vegans. The maximum daily theoretical intake, based on the maximum residual level, was calculated as a percentage of the acceptable daily intake. Among the 421 pesticides studied, 48 were at a level above the acceptable level for at least one of the groups. Meat and eggs were the foods most responsible for the high ingestion of organochlorines, which, for Aldrin, reached 348% of the acceptable daily intake in the general population compared to 146% to 183% in the vegetarian group. The vegetarian diet left its practitioners more exposed to other pesticides [95].

A 2016 study from Israel evaluated the intake of pesticides (organophosphates and carbamates) in vegetarian and vegan diets in which foods produced in an organic or conventional system were consumed. The data were compared with the results of the Israel Biomonitoring Study (IBS). The evaluation was performed by identifying the urinary concentration of pesticide residues in 42 participants from a vegetarian community (Amirim), and 24-h recall dietary data were requested from the participants. Vegetarians exhibited higher urinary levels of pesticide residues than the previously evaluated population. Vegetarians whose diet consisted of more than 25% of organic products had significantly fewer pesticides measured in the urine. The authors concluded that the consumption of organic foods may offer some protection against increased exposure to organophosphate pesticides in vegetarians [96].

A study published in 2021 evaluated exposure to 25 pesticide residues in different diets, including omnivorous (n = 33,018), pesco-vegetarian (n = 555), ovo-lacto vegetarian (n = 501) and vegan (n = 368), that included organic or conventional plant-based foods. The evaluation was performed using the foods consumed. Two scenarios were evaluated: 100% conventional foods or 100% organic foods. The highest exposure found was to imazalil, a fungicide. In general, vegetarians were the least exposed to the pesticides studied. The consumption of products from conventional agriculture led to greater exposure to pesticides. The authors concluded that despite the high consumption of vegetables, vegetarians were less exposed to synthetic pesticides than were omnivores due to the greater propensity to consume organic products [97].

The IVU recommends the consumption of foods from organic production. In the absence of access to organic products, fruits, vegetables, and other plant foods should not be excluded from the diet because studies are consistent in showing positive effects on human health, even when these products are not derived from organic production.
3. CHRONIC NONCOMMUNICABLE DISEASES

Because this guide is focused on nutrition, we do not intend to delve into each disease in detail, but we want to provide an overview of the research on the subject. We will divide this chapter into systematic reviews/meta-analyses and controlled studies.

Although systematic reviews and meta-analyses are considered studies with the highest level of evidence from the scientific point of view, it is worth remembering that the origin and quality of the studies included in these analyses make a difference in the final conclusions of these publications. In the context of a vegetarian diet, some points should be noted regarding the conclusions drawn from these studies.

1) The term “vegetarian diet,” be it of any type, does not indicate what individuals eat but rather what they do not eat. Thus, when a review evaluates “vegetarians,” it often compares between eating or not eating meat, eggs, and dairy products in the case of vegans, without knowing whether the consumption of plant foods falls within a good standard of quality and quantity. The same occurs with the term “omnivore.” Thus, when a study is population-based and/or observational, the tendency is to draw conclusions about the effect of the presence or absence of meat, eggs, and dairy products on the outcome rather than on the intake of plant foods and plant groups, unless these evaluations were conducted in the studies of origin.

2) A vegetarian diet, of any type, has no rules on the proportion of food groups nor restricts the use of refined or processed foods. Thus, vegetarians with the same nomenclature (ovo-lacto, lacto, ovo or vegan) may show a totally different consumption of all micro- and macronutrients. The same is true for those who consume an omnivorous diet. Therefore, the evaluation of each individual profile may lead to different health outcomes and different nutritional analysis results regarding excess or deficiency.

3) The term plant-based technically refers to a vegan diet composed of natural and whole foods. However, it does not impose rules regarding the percentage amount of macronutrients or food groups consumed. Thus, this profile has great potential to distinguish between whole-food and processed-food vegan diets but does not necessarily show the prevalence of each food group consumed nor the amount of micronutrients or proportion of macronutrients consumed. This dietary composition usually consists of low-fat intake, and some authors modify the plant-based concept. Thus, depending on the analysis to be performed, the concept needs to be specified.

4) Considering the plant-based pattern, it is important to note the criteria used by different authors in the studies, as it may vary, in the same way that we find individuals who eat fish frequently being classified by some authors as vegetarians.
5) From the standpoint of the clinical details of the interventions, when the objective is to evaluate changes in parameters and outcomes between vegetarians and omnivores, the most reliable comparison is that between a well-planned vegetarian diet and a well-planned omnivorous diet.

3.1. SYSTEMATIC REVIEWS AND META-ANALYSES

We have compiled the latest published meta-analyses for a more comprehensive overview of the effects of diet on health. The studies are presented in chronological order of publication.

We chose not to report the p values and standard deviations (only the mean values), due to readers’ ease of access to all the articles presented and to make the text more fluid. When we presented differences, all were based on p < 0.05.

In 2013, a meta-analysis of 12 clinical studies with a control group (omnivores) compared the plasma triglyceride levels reported in 20 studies, totaling 1,300 individuals aged between 30 and 60 years. The diet was effective in reducing the level of triglycerides (-1.28 mmol/L or 113.4 mg/dL). In eight developed countries, the observed reduction was nonsignificant (-0.31 mmol/L or 27.5 mg/dL), but in four developing countries, the reduction was quite significant (-4.06 mmol/L or 359.6 mg/dL). The authors concluded that compared with an omnivorous diet, a vegetarian diet has health benefits, especially in developing countries, and that the effect occurs after a vegetarian diet has been consumed for at least 6 months [98].

In 2014, a systematic review and meta-analysis evaluated the effect of a vegetarian diet and the risk of cardiovascular mortality in Seventh-Day Adventists. Eight studies were included, totaling 183,321 participants. The authors concluded that there is a modest cardiovascular benefit in observational studies; however, the results are unclear in relation to overall mortality with the adoption of the diet. However, in all studies, Adventists had more protection. In this group, there was a 32% reduction in overall mortality, 40% reduction in ischemic cardiovascular disease and 29% reduction in cerebrovascular disease [99].

In 2015, a systematic review and meta-analysis of 11 randomized controlled trials showed that vegetarian diets significantly reduced the concentrations of total cholesterol (-0.36 mmol/L or 13.9 mg/dL), LDLc (-0.34 mmol/L or 13.1 mg/dL), HDLc (-0.10 mmol/L or 3.9 mg/dL) and non-HDLc (-0.30 mmol/L or 11.6 mg/dL) but not the concentration of triglycerides. The authors concluded that vegetarian diets effectively reduce cholesterol concentrations and can be used as a nonpharmacological option in the management of dyslipidemia, especially hypercholesterolemia [100].

A systematic review and meta-analysis of intervention trials published in 2016 analyzed the effect of a plant-based diet on the inflammatory profile associated with obesity. A total of 29 studies were evaluated, totaling 2,689 participants. The adoption of a plant-based diet resulted in significant reductions in the levels of C-reactive protein (CRP) (-0.55 mg/L), interleukin-6 (IL-6) (-0.25 ng/L) and, to a lesser extent, soluble intercellular adhesion molecule-1 (-25.07 ng/mL). There was no change in the levels of TNF-alpha, resistin, adiponectin or leptin. The authors concluded that a plant-based diet is associated with
improvements in obesity-related inflammatory profiles and may provide means for the prevention of chronic diseases [101].

In 2017, a systematic review and meta-analysis of cohort studies evaluated the effect of eating a vegetarian diet on breast, colorectal and prostate cancer. Nine studies were conducted in six cohorts, with a total of 686,629 individuals, with 3,441 cases of breast cancer, 4,065 cases of colorectal cancer and 1,935 cases of prostate cancer. None of these cancers were less prevalent in vegetarians, but a lower risk of colorectal cancer was found in semivegetarians and pesco-vegetarians than in omnivores. The authors concluded that the exclusion of any protein source from the diet is not associated with further benefits to human health [102].

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A systematic review and meta-analysis published in 2017 evaluated the effect of a plant-based diet on the lipid profile. Thirty observational studies and 19 controlled trials were selected, totaling 1,484 individuals (mean age of 48.6 years), with at least four weeks of adherence to a vegetarian diet. The vegetarian diet was significantly associated with lower total cholesterol (-29.2 and -12.5 mg/dL), LDLc (-22.9 to -12.2 μg/dL) and HDLc (-3.6 and -3.4 mg/dL) when comparing omnivores and vegetarians, respectively, in the observational studies and controlled trials. The authors concluded that a plant-based diet is associated with a reduction in LDLc and HDLc but not in triglycerides [103].

A systematic review and meta-analysis published in 2017 evaluated health outcomes (risk factors for chronic diseases, risk of all-cause mortality, incidence of and mortality from cardiocerebrovascular diseases, total cancer, and specific cancer subtype — colorectal, breast, prostate, and lung) with a vegetarian diet (ovo-lacto and vegan). A total of 86 cross-sectional studies and 10 prospective cohorts were included. The final result indicated a protective effect of the vegetarian diet with respect to the incidence of and/or mortality from ischemic heart disease (25% reduction) and the incidence of total cancer (15% reduction) [104].

Published in 2019, a meta-analysis evaluated the effect of a vegan diet by extracting data from 11 randomized controlled trials, totaling 983 participants. The results indicated nonsignificant differences in the blood pressure of normotensive individuals. However, in individuals with systolic blood pressure (SBP) > 130 mmHg, a vegan diet resulted in a significant decrease of 4.10 mmHg in SBP and of 4.01 mmHg in diastolic blood pressure. According to the authors, the change in blood pressure induced by a vegan diet without caloric restriction is comparable to those induced by dietary approaches recommended by medical societies and portion-controlled diets [105].

Published in 2019, a systematic review and meta-analysis evaluated the effect of a vegan diet on metabolic syndrome. A total of 71 studies (103,008 participants) from six randomized controlled trials, two cohort studies and 63 cross-sectional studies were evaluated. The analysis did not find a lower prevalence of metabolic syndrome in vegetarians. The results showed that when compared to omnivores, vegetarians had significantly lower systolic (reduction of 4.18 mmHg) and diastolic (reduction of 3.03 mmHg) blood pressure, fasting blood glucose (reduction of 0.26 mmol/L or 4.7 mg/dL), waist circumference (-1.63 cm) and HDLc (-0.05 mmol/L or 1.9 mg/dL). However, the authors considered that
due to the heterogeneity of the studies, the results are uncertain and further controlled studies are needed to evaluate the results [106].

A systematic review and meta-analysis of randomized controlled trials published in 2019 included nine studies, totaling 664 participants, and evaluated the effect of vegetarian dietary patterns on cardiometabolic risk factors in diabetic patients. The vegetarian diet was significantly more effective in glycemic control, in LDLc and non-HDLc reductions and in weight loss (adipose tissue). The authors suggest that further studies be conducted to improve confidence in the estimates [107].

In 2019, a systematic review and meta-analysis of prospective cohort studies evaluated the cardiovascular risk of a vegetarian diet in individuals with and without diabetes. Seven prospective studies were evaluated, totaling 197,737 patients and 8,430 events. The vegetarian dietary pattern was associated with a reduction of 22% in the incidence of and 28% in the mortality from coronary heart disease, but it was not associated with a reduction in mortality from stroke or from cardiovascular disease. However, the authors questioned the quality of the studies [108].

A systematic review and meta-analysis published in 2019 evaluated the effect of a vegetarian diet on inflammatory and immune biomarkers, i.e., CRP, tumor necrosis factor alpha, fibrinogen, natural killer cells, leukocytes, lymphocytes, thrombocytes, interleukins, and immunoglobulins. Thirty observational studies and 10 intervention studies were included in the evaluation. A vegetarian diet, compared to an omnivore diet, was associated with significantly lower concentrations of CRP (-0.61 mg/L), fibrinogen (-0.22 g/L) and total leukocytes (-0.62 x 10³/μL). The authors suggest that future studies focus on large-scale intervention studies comparing the differences in inflammation and immunological function between vegetarian and omnivorous populations [109].

Another systematic review and meta-analysis published in 2020 was conducted to evaluate inflammatory markers in ovo-lacto vegetarians and vegans, grouping the two together, without specifying dietary quality. A total of 21 cross-sectional studies were included for analysis, and the levels of CRP, IL-6, IL-18, IL-1 receptor antagonist, tumor necrosis factor alpha, E-selectin, intercellular adhesion molecule-1, chemotacttractant protein-1, adiponectin, omentin-1 and resistin in vegetarians were compared to those in omnivores. Of all inflammatory biomarkers, only CRP was significantly lower in vegetarians, with a reduction of 0.54 mg/L. This association was less pronounced in ovo-lacto vegetarians. In patients with impaired kidney function, a vegetarian diet provided an even more significant reduction in CRP, of 3.91 mg/L. According to the authors, despite the strong association between CRP levels and a vegetarian diet, further studies are needed because most of the inflammatory biomarkers have been investigated only in single studies thus far [110].

A systematic review and dose-response meta-analysis of prospective cohort studies published in 2020 evaluated the intake of total, animal and plant proteins and the risk of all-cause, cardiovascular, and cancer mortality in individuals older than 18 years. A total of 32 studies were included in the review and 31 in the meta-analysis, with follow-up periods ranging from 3.5 to 32 years and an evaluation of 113,039 deaths (16,429 due to cardiovascular disease and 22,303 due to cancer) among 715,128 participants. The intake of plant proteins was significantly associated with a lower risk of all-cause
mortality (8% reduction) and cardiovascular mortality (12% reduction) but was unrelated to cancer mortality. For each 3% increase in energy intake from plant proteins per day, there was a 5% lower risk of death from all causes [111].

In 2020, a rapid review and meta-analysis of cohort and case-control studies evaluated the impact of plant-based dietary patterns on cancer-related outcomes. Overall cancer mortality, cancer-specific mortality and cancer recurrence were the considered outcomes. A total of 26 studies that evaluated cancer outcomes and pre/postdiagnosis diets were selected, of which five investigated vegetarian diets, two investigated provegetarian diets, 13 investigated the Mediterranean diet and six evaluated cancer outcomes and postdiagnosis diets. The few studies available on vegetarian diets failed to show its potential preventive effect against overall cancer mortality when compared to a nonvegetarian diet. The few studies on provegetarian diets did not provide sufficient data for conclusions. The association between adherence to a Mediterranean diet and overall cancer mortality reached statistical significance, showing a reduction of 16% in the latter. The review points to a lack of studies on well-defined plant-based diets and notes that more research is needed to determine the effect of plant-based diets on cancer prevention and treatment so that dietary guidelines for cancer survivors can be defined [112].

A comprehensive review of the available systematic reviews and meta-analyses on the association between health outcomes of vegetarian diets was published in 2020. The review identified 20 meta-analyses of observational and intervention studies with 34 health outcomes, and 80% of the meta-analyses were classified as moderate to high quality. Compared with omnivorous diets, vegetarian diets resulted in significantly lower LDLc (-0.467 mmol/L or -18.1 mg/dL) and HDLc (-0.082 mmol/L or -3.12 mg/dL) levels and were associated with an 11% reduced risk of negative health outcomes. Among vegetarians, Seventh-Day Adventists had the best results in terms of health protection, with a 28% risk reduction. Conversely, vegetarians exhibited worse outcomes regarding one-carbon metabolism, which is the pathway associated with homocysteine metabolism, which was higher due to the lower level of vitamin B12. The authors concluded that a vegetarian diet is associated with a positive effect on the lipid profile and a reduction in the risk of negative health outcomes, such as diabetes, cardiovascular disease and cancer risk, and that vitamin B12 supplementation should be investigated [113].

In 2021, a systematic review and meta-analysis of cohort studies evaluated the association between risk of disease mortality and adherence to plant-based diets in the general population. Twelve prospective cohort studies with 42,697 deaths among 508,861 participants were evaluated. The plant-based profile included individuals who ate fish and were provegetarian; individuals with a true vegetarian profile had the lowest risk of cardiovascular mortality [114].

3.2. CONTROLLED STUDIES
As mentioned earlier, in terms of comparing the effects of vegetarian diets with omnivore diets, the most reliable comparison is made using a well-planned vegetarian diet and a well-planned omnivorous diet.

There are studies in the literature with this approach, and we describe some of them, in addition to delving deeper into some important aspects for each listed disease.

3.2.1. Diabetes

The effect of a vegan diet on glycemic control is well known.

A controlled study recruited 99 omnivorous individuals with type 2 diabetes and randomly allocated them to be followed up for 22 weeks, without practicing physical activity. Of these, 50 followed the omnivorous diet recommended by the American Diabetes Association (with caloric intake composed of 60–70% carbohydrates, 15–20% protein and 10–25% fat, with <7% saturated fat), and 49 followed a vegan diet with a low-fat content (75% carbohydrates, 15% protein and less than 15% fats). Only the vegetarian group could eat at will, without an amount restriction. At the end of the 22 weeks, both groups had positive outcomes, but the outcomes were significantly better in the vegan group. Comparatively, 43% of the individuals in the vegan group and 23% in the omnivore group were able to reduce the dose of drugs used. In individuals who maintained the use of drugs for glycemic control, glycated hemoglobin decreased by 1.23% in the vegan group and by 0.56% in the omnivore group, and weight decreased by 6.5 kg and 3.1 kg in the groups, respectively, contributing to the greater glycemic reduction in the vegan group. The LDLc levels in individuals who did not use oral lipid-lowering drugs decreased by 21.2 mg/dL and 10.7 mg/dL in the vegan and omnivorous groups, respectively. In addition, microalbuminuria was also more significantly reduced in the vegan group. The authors concluded that the diets benefited the diabetic patients but that the vegan diet provided better results [115].

With this same dietary profile model, but with 74 weeks (approximately one and a half years) of follow-up, the parameters were maintained, and the vegan group had better maintenance of their blood glucose level and lipid profile [116].

A 2011 study also stands out for its design and degree of control. The study was conducted in the Czech Republic and recruited 72 omnivorous individuals with type 2 diabetes (with overweight or obesity, without use of insulin, only oral hypoglycemic agents) to be followed up for 24 weeks. The participants were randomly allocated to follow one of two diets: vegan without fat reduction and omnivorous. The aim of the study was to evaluate insulin sensitivity. The vegan diet was structured with 60% of kilocalories as carbohydrates, 15% as protein and 25% as fat. The omnivorous diet was structured based on the recommendations of the European Association for Diabetes Studies, with a profile of 50% carbohydrates, 20% protein and up to 30% fat (<7% saturated fat). The diets were isocaloric, with a restriction of 500-kcal after individual indirect calorimetry. All meals were provided to the participants. Visceral fat was measured by nuclear magnetic resonance imaging, and oxidative stress was measured by the thiobarbituric acid reaction. Twelve weeks after the dietary change, physical activity was initiated, but only after undergoing a spiroergometric test. The activity was intended to be performed at 60% of
the maximal heart rate, twice a week with professional supervision and once a week without supervision, maintaining the same intensity. **Insulin sensitivity** was evaluated by **hyperinsulinemic-isoglycemic clamp** measured in the final 20 minutes of the three hours of examination after correction for changes in glucose pool size. The results of the intervention are shown in Table 2.5.

**Table 2.5. Results of dietary interventions with well-planned vegan and omnivorous diets**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Vegan group (n = 36)</th>
<th>Omnivorous group (n = 36)</th>
<th>Statistical analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced use of drugs for type 2 diabetes</td>
<td>-43%</td>
<td>-5%</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Weight loss</td>
<td>-6.2 kg</td>
<td>-3.2 kg</td>
<td>P = 0.001</td>
</tr>
<tr>
<td>Improved insulin sensitivity</td>
<td>+30%</td>
<td>+20%</td>
<td>P = 0.04</td>
</tr>
<tr>
<td>Glycated hemoglobin</td>
<td>Similar reduction</td>
<td>Similar reduction</td>
<td>Not significant</td>
</tr>
<tr>
<td>Glycated hemoglobin in patients who maintained the use of oral hypoglycemic agents</td>
<td>-0.9%</td>
<td>-0.2%</td>
<td>P = 0.08</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>-8.3 cm</td>
<td>-5.3 cm</td>
<td>P = 0.001</td>
</tr>
<tr>
<td>Subcutaneous visceral fat</td>
<td>Reduced with diet and another 4% with physical activity</td>
<td>Reduced with diet, similar to that of the vegetarian group; did not change with physical activity</td>
<td>P = 0.007</td>
</tr>
<tr>
<td>Adiponectin</td>
<td>+19%</td>
<td>No change</td>
<td>P = 0.02</td>
</tr>
<tr>
<td>Resistin</td>
<td>Decreased 19% after initiation of the diet (even without physical activity)</td>
<td>Increased 24% after start of physical activity</td>
<td>P = 0.05</td>
</tr>
<tr>
<td>Leptin</td>
<td>Decreased 35% throughout the study</td>
<td>Decreased after initiation of the diet but increased with the start of physical activity</td>
<td>P = 0.02</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>+16%</td>
<td>No change</td>
<td>P = 0.02</td>
</tr>
<tr>
<td>Superoxide dismutase</td>
<td>+49%</td>
<td>-30%</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Glutathione</td>
<td>+27%</td>
<td>-11%</td>
<td>P = 0.02</td>
</tr>
<tr>
<td>Quality of life</td>
<td>More significant improvement</td>
<td>Less significant improvement</td>
<td>P = 0.01</td>
</tr>
</tbody>
</table>

According to the authors, the vegan diet had a greater ability to improve insulin sensitivity. The reduction in visceral fat was an important factor that led to this improvement. The number of participants was not large enough to show a superior effect of the vegan diet on the reduction in glycated hemoglobin, as observed in other studies. A possible explanation for the less positive findings in the control group
( omnivorous diet) included lower adherence to physical activity and portion size restrictions, which caused more hunger, even during exercise [117].

Our focus, as stated above, is to address nutritional aspects of vegetarian diets; therefore, we will not perform an in-depth analysis of diseases by describing all studies here. There are approximately ten published studies that make this comparison between diets, and more positive outcomes associated with vegan diets are reported in all of them.

Due to the quality of what has already been published in this area, the Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the type 2 diabetes management algorithm, published in January 2020, recommends that nutrition for these patients should allow maintenance of their optimal weight, caloric reduction (in case of excess weight) and a plant-based diet with a predominance of polyunsaturated and monounsaturated fatty acids [118].

3.2.2. Cardiovascular diseases

Studies reporting the cardiovascular health of vegetarians have been published for many decades.

In addition to lower serum cholesterol levels in vegetarians, there is less lipid peroxidation secondary to a better antioxidant status [49, 119-126]. Vegans have a lower cholesterol level than do ovo-lacto vegetarians [127, 128].

In 1990, a study reported the remarkable results of an intervention with a plant-based diet in patients with coronary disease. The study was controlled, prospective and randomized and followed 28 individuals for one year to determine to what extent the intervention program affected coronary atherosclerosis in the period. The control group consisted of 20 individuals who followed the usual care recommended for heart disease patients. The intervention program, in addition to smoking cessation, stress management training and moderate physical activity, consumed a plant-based diet consisting of fruits, vegetables, whole grains, legumes and soybean products, without caloric restriction. No animal products were allowed, except egg whites and one cup of skim milk or yogurt per day. The final composition of the diet consisted of 70% to 75% predominantly complex carbohydrates, 15% to 20% protein and 19% fat (polyunsaturated/saturated fat ratio greater than 1). Cholesterol intake was limited to 5 mg/day or less. Sodium was restricted only in hypertensive patients. Coffee was eliminated, and alcohol was restricted to a maximum of two units per day. The diet was nutritionally adequate, and B12 was provided as a supplement. These individuals did not use any serum lipid-lowering drugs. A total of 195 coronary lesions were analyzed by angiography. The mean percent diameter stenosis regressed from 40% to 37.8% in the experimental group (plant-based diet) and progressed from 42.7% to 46.1% in the control group (omnivorous diet). When only lesions greater than 50% stenosed were analyzed, the mean regression was 61.1% to 55.8% in the experimental group, and there was progression in the control group, from 61.7% to 64.4%. Overall, 82% of patients in the experimental group had a mean change toward stenosis regression. The individuals with the highest adherence to the intervention had the highest percent diameter stenosis regression. The authors concluded that the applied lifestyle
interventions caused atherosclerosis to regress after one year, even in patients with severe coronary disease, without the use of lipid-lowering drugs [129].

In 1998, the same authors published another study showing the effect of this intervention at five years of follow-up, again with the individuals in the intervention group not using lipid-lowering drugs. The randomized controlled trial followed 48 patients with moderate-to-severe coronary heart disease, allocated to follow a plant-based diet (intervention group) or a healthy omnivorous diet and usual care (control group). The individuals were evaluated by coronary arteriography. The difference in the final outcome was significant between the two groups. In the experimental group, the mean percent diameter stenosis at the beginning of the study decreased by 1.75 percentage points after one year (4.5% improvement) and by 3.1 percentage points after five years (7.9% improvement). In contrast, the mean percent diameter stenosis in the control group increased by 2.3 percentage points after one year (5.4% progression) and by 11.8 percentage points after five years (27.7% progression). Over the five-year period, there were 25 cardiac events in the experimental group and 45 in the control group. The authors concluded that there was greater regression of coronary atherosclerosis after five years than after one year of follow-up in the intervention group. In contrast, atherosclerosis continued to progress in the control group [130].

A study published in 2009 reviewed 27 randomized controlled trials and observational studies and showed that a vegan or vegetarian diet combined with nuts, soybean and/or fiber led to a reduction in the LDLc of greater than 35%. Interventions that contained a small amount of lean meat led to a less pronounced reduction in total cholesterol and LDLc levels. The authors concluded that plant-based dietary interventions are effective in reducing cholesterol levels [131].

Among intervention studies, one randomly allocated 100 individuals with coronary artery disease to follow an omnivorous diet recommended by the American Heart Association or a vegan diet. The objective was to evaluate the level of high-sensitivity CRP (hsCRP). After eight weeks, the hsCRP level in the vegan group decreased 32% more than that in the omnivorous group [132].

The diets recommended by the American College of Cardiology and American Heart Association are the DASH (Dietary Approaches to Stop Hypertension) diet, Mediterranean diet and plant-based diet [133]. The common element of all these diets is more abundant consumption of whole plant foods and a reduction in dietary fat.

3.2.3. Cancer

The evaluation of the effect of diet on cancer is complex because different cancer types have different promoting factors and evolutionary patterns.

From the prevention standpoint, based on scientific evidence for each cancer type, it is important to apply precautionary principles. These include the behaviors described in Table 2.6 (taken from [134]).

Table 2.6. Precautionary principles in cancer prevention
Limit or avoid dairy products to reduce the risk of prostate cancer.

Limit or avoid alcohol to reduce the risk of cancers of the mouth, pharynx, larynx, esophagus, colon, rectum, and breast.

Avoid red and processed meats to reduce the risk of cancers of the colon and rectum.

Avoid grilled, fried and broiled meats to reduce the risk of cancers of the colon, rectum, breast, prostate, kidneys, and pancreas.

Consume soy products during adolescence to reduce the risk of breast cancer in adulthood and reduce the risk of recurrence and mortality for women previously treated for breast cancer.

Consume fruits and vegetables to reduce the risk of several common forms of cancer.

The consumption of plant-based foods has a protective effect in cancer prevention [135], and for plant-based foods to represent a higher proportion in meals, there must be a simultaneous reduction in animal product consumption.

On October 26, 2015, the International Agency for Research on Cancer, a sector of the World Health Organization, had 22 experts evaluate more than 800 studies that investigated the carcinogenic effect of processed and unprocessed meat consumption. Processed meat (meat subjected to salting, curing, fermentation, smoking and other processes to enhance flavor or improve preservation) was classified as Group 1, i.e., there is sufficient evidence to classify it as carcinogenic to humans. For every 50 g of processed meat consumed daily, the risk of colorectal cancer increases by 18%. Unprocessed red meat (defined as unprocessed mammalian meat, including beef, veal, pork, lamb, mutton, horse and goat) was classified as Group 2A (probably carcinogenic to humans) [136].

To illustrate the research on this subject in controlled trials, which is the focus of this part of the chapter, we will focus on prostate and breast cancer, the most common cancers in men and women, respectively. We begin with a brief review of these studies, followed by studies that applied a plant-based diet.

The consumption of milk and dairy products was the target of a systematic review and meta-analysis of cohort studies published in 2015, and the results showed a positive relationship between the consumption of these products and prostate cancer; notably, this association is not observed with calcium in the form of supplements. This review included 32 studies. The increased risk is 7% per 400 g of dairy products consumed per day, 3% per 200 g of milk consumed per day, 6% per 200 g of skimmed milk consumed per day and 9% per 50 g of cheese consumed per day [137].

In 2016, a meta-analysis of 11 cohort studies evaluated the relationship between dairy consumption and cancer mortality and concluded that the total intake of these products has no significant impact on increased mortality from all types of cancer but that the intake of whole milk by men contributed significantly to the high risk of mortality from prostate cancer. In addition, there is a linear dose-response relationship between whole milk consumption and an increased risk of mortality from prostate cancer [138].

In 2019, a literature review of dairy products and their impact on the promotion of prostate cancer concluded that it is possible to establish a relationship between the consumption of dairy products and...
the progression of prostate cancer. A possible association with the onset of prostate cancer was also found. The authors concluded that dairy product intake by men should be reduced or minimized [139].

3.2.3.1. Prostate cancer

A controlled study was conducted in 2005 with individuals with prostate cancer. The patients recruited had refused to undergo conventional treatment, which made it possible to randomize the groups without the bias of surgical interventions, androgen deprivation therapy or radiotherapy. A total of 93 volunteers with serum prostate specific antigen (PSA) levels between 4 and 10 ng/mL and Gleason cancer scores less than 7 (i.e., medium and low-grade tumors) were recruited, randomized and followed up for one year. A total of 44 individuals were included in the experimental group, and 49 were included in the control group. In addition to lifestyle changes, the experimental group adopted a vegan diet that included one tofu portion and 58 g of soy milk and supplementation with 400 IU of vitamin E, 200 μg of selenium, 2 g of vitamin C and 3 g of fish oil. The diet of this group contained up to 10% of kilocalories as fat, and whole foods were eaten; therefore, it was a plant-based diet. The control group was instructed to follow the diet recommended by the health professionals who treated them. In the experimental group, none of the patients underwent treatment because there was no increase in PSA or disease progression based on MRI, but treatment was necessary for six patients in the control group. The PSA level decreased significantly by 4% in the intervention group and increased significantly, i.e., 6%, in the control group. The growth of prostate cancer (LNCaP) cells was significantly inhibited almost eight times more in the control group than in the experimental group (70% versus 9%, respectively). As the PSA level increased and LNCaP cell growth significantly decreased in the control group, the authors concluded that the proposed lifestyle, which included a plant-based diet, may affect the progression of low-grade prostate cancer in men [140].

An intervention study published in 2006 with patients with recurrent prostate cancer implemented a six-month plant-based dietary intervention. The patients were asymptomatic, had not undergone previous hormonal treatment and had increased PSA levels as the first manifestation after surgery or radiotherapy. The control was each patient himself. The plant-based diet intervention was implemented by encouraging the consumption of plant-based and whole foods and avoiding the consumption of foods of animal origin and refined cereals. Ten individuals were included. Of those, four had an absolute reduction in PSA level across the six months. Nine of the ten individuals exhibited a reduction in the rate that PSA increased and an improvement in PSA level doubling time. The mean PSA doubling time increased from 11.9 months (preintervention) to 112.3 months (postintervention). In the periods with greater adherence to the diet, with greater consumption of whole foods, there was a greater reduction in the rate that PSA increased. The authors concluded that a plant-based diet can be adopted and maintained for several months in patients with recurrent prostate cancer and that this intervention has therapeutic potential for these patients [141].

3.2.3.2. Breast cancer
Regarding breast cancer, there is still controversial evidence among some studies regarding the effect of dairy consumption. However, in the context of the treatment of estrogen-dependent breast cancer, there are important considerations to be made.

Approximately 60% to 70% of the total animal-derived estrogen present in the human diet comes from the consumption of milk and dairy products. Cows produce milk up to 220 days of gestation, a period in which the increase in estrogen is 33 times the normal value. The free estrogen (estradiol) content in milk ranges from 1.0 to 2.4 pg/mL, and the serum estradiol found in women ranges from 2.0 to 266 pg/mL [142]. The amount of active estrogen absorbed via dairy consumption is uncertain. From the perspective of estrogen-dependent breast cancer, in which it is sought to reduce the amount of circulating estrogen, either by reducing ovarian production or inhibiting aromatase (reducing the conversion of testosterone into estrogen) or by blocking its receptor, milk consumption should be restricted until there are more studies on its safety.

In the context of breast cancer treatment, a critical review was published in 2017, providing guidelines for this condition. For animal products (meat, eggs, and low-fat dairy products), the recommendation is to restrict their consumption to once or twice a week [143].

A narrative review published in 2018 on advising women undergoing breast cancer treatment states that the evidence suggests following a plant-based diet for general health as a whole after diagnosis. In addition, as 35% of deaths in women with breast cancer result from cardiovascular disease, this approach has a protective effect [144].

In 2021, a case-control study was conducted with Iranian women with breast cancer (350 newly diagnosed women matched with 700 apparently healthy women (control group)). The association of the overall plant-based diet index with breast cancer was evaluated, with one group classified as following a healthy vegetarian diet and the other an unhealthy diet. After controlling for confounding factors, the participants with the best dietary pattern showed a 67% lower probability of breast cancer than those who had the worst dietary pattern. Women who had the worst dietary pattern were 2.23 times more likely to have breast cancer. Higher adherence to a healthy plant-based dietary pattern was inversely associated with breast cancer risk, while worse dietary patterns resulted in the highest risk [145].

### 3.2.4. Obesity

The results of population studies generally indicate that vegetarians, compared with omnivores, have a lower BMI throughout life [146-151]. An example of this finding is reported in the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford), in which 65,429 men and women aged 20 to 97 were evaluated, of whom 33,883 were omnivores, 10,110 were fish eaters, 18,840 were ovo-lacto vegetarians and 2,596 were vegan. The results showed that throughout life, both vegan men and women had a lower BMI (within normal weight) than omnivores (who were overweight in part of their lives). Ovo-lacto vegetarians and semivegetarians maintained an intermediate BMI between the two groups [146].
However, **body weight reacts to the energy intake and expenditure** of the individual, and dietary choices make a difference in the final caloric intake. A diet consisting of highly processed and low-fiber foods may lead to a higher BMI than an omnivorous diet consisting of unprocessed and fiber-rich foods. In addition, the increased consumption of industrialized products offered to the vegan public may contribute to the intake of foods with higher caloric density and favor weight gain if their consumption is not controlled.

Another factor to be considered is the **caloric density of foods**. With a caloric value of 4 kcal/g, carbohydrates and protein have a lower caloric density than fat (9 kcal/g). In addition, foods rich in carbohydrates, due to osmotic factors, have more added water, which makes them more voluminous. Foods rich in fat, which is hydrophobic, do not contain significant amounts water.

Due to these characteristics, fruits, leafy vegetables, starchy vegetables, other vegetables, legumes, and cereals are foods that require the intake of a larger volume to obtain more kilocalories. Conversely, oils, nuts, meats, eggs and dairy products provide high amounts of energy at a lower volume.

Based on this principle, **low-fat plant-based diets** (including those excluding oils, avocado and nuts), as designed in some studies, allow **free caloric intake and lead to significant weight loss** in individuals with overweight or obesity, even when compared to calorie-restricted omnivorous diets [115, 152].

A **randomized controlled trial** evaluated the effect of **plant-based diets without caloric restriction** on weight loss. The study followed adults with overweight and obesity randomized to a low-fat and low-glycemic index vegan (n = 12), vegetarian (n = 13), pesco-vegetarian (n = 13), semi-vegetarian (n = 13) or omnivorous (n = 12) diet. At the end of the study, **vegans exhibited more than twice the percentage weight loss** (7.5% weight loss) than the other groups. The authors concluded that a low-fat vegan diet results in greater weight loss [153].

A 16-week randomized clinical trial evaluated the effect of a **plant-based high-carbohydrate, low-fat diet** in overweight individuals. Of the 75 participants, 38 followed this plant-based diet, and 37 maintained their usual diet. Body composition was evaluated by whole-body dual-energy X-ray absorptiometry (DEXA). The intervention resulted in **significant weight loss** (-6.5 kg) and **adipose tissue loss** (-4.5 kg) with the adoption of a plant-based high-carbohydrate, low-fat diet. In addition, there was a significant reduction in **insulin resistance** [154].

Another study randomized 244 individuals with a BMI between 28 and 40 kg/m² to follow a **low-fat plant-based diet** (n = 122) or their usual diet (n = 122). The follow-up time was 16 weeks. In addition to body composition measured by DEXA, the thermic effect of food was also measured, and in 44 participants, hepatocellular and intramyocellular lipids were quantified by proton magnetic resonance spectroscopy. **Weight loss was significant** (-5.9 kg) and there were **reductions in insulin resistance** (-1.3 HOMA-IR units), hepatocellular lipids (-34.4%) and intramyocellular lipids (-10.4%) in the intervention group. The **thermic effect of food increased 14.1% in the intervention group**. In the control group, there was no change in any parameter. The authors concluded that a low-fat plant-based diet reduces body weight by reducing energy intake and increasing postprandial metabolism. The change was associated with reductions in hepatocellular and intramyocellular fat and increased insulin sensitivity [155].
A randomized intervention study (CARDIVEG – Cardiovascular Prevention with a Vegetarian Diet) evaluated the effect of a low-calorie ovo-lacto vegetarian diet versus a low-calorie Mediterranean diet on weight loss and the cardiovascular risk profile. The study followed 118 individuals with a low-to-moderate cardiovascular risk profile who consumed a ovo-lacto vegetarian or Mediterranean diet for three months and then switched to the other diet. At the end, the two diets led to an effective reduction in body weight, without significant differences between groups. However, the vegetarian diet was more effective in reducing LDLc, while the Mediterranean diet was more effective in reducing triglycerides [156].

A 2020 randomized crossover trial evaluated changes in body weight and cardiometabolic risk factors after the adoption of a low-fat vegan diet or a Mediterranean diet. The study followed 62 overweight individuals who followed one of the two diets for 16 weeks. In addition to body weight and body composition (analyzed by DEXA), plasma lipids, blood pressure, and glycemic control were measured. After consuming the diet for 16 weeks, the subjects returned to their usual previous diet and maintained it for 4 weeks and then began to follow the other diet (for 16 weeks). Weight loss was significant (6 kg) with the vegan diet, but there was no weight loss with the Mediterranean diet. The HOMA-IR index for participants consuming the vegan diet was significantly lower than that for participants consuming the Mediterranean diet. Among participants with no medication changes, LDLc significantly decreased when consuming the vegan diet and did not change when consuming the Mediterranean diet. Systolic and diastolic blood pressure decreased more significantly when consuming the Mediterranean diet, with decreases of 9.3 and 7.3 mmHg, respectively, with the Mediterranean diet and 3.4 and 4.1 mmHg, respectively, with the vegan diet. The authors concluded that a low-fat vegan diet optimizes weight loss, reduces serum lipids, and improves insulin sensitivity compared to baseline levels and more effectively than the Mediterranean diet. Blood pressure decreased with both diets but more significantly with the Mediterranean diet [157].

A vegetarian diet may lead to weight loss, weight maintenance or obesity. It all depends on food preparation, lifestyle, and an individual’s metabolic composition. Low-fat, high-carbohydrate vegan diets (consisting of whole foods), without calorie restriction, favor weight loss due to the lower caloric density intake.

### 3.2.5 Anorexia nervosa

Given questions regarding eating disorders with the adoption of a vegetarian diet, we included this topic in the chapter, even though it is not part of the evaluation of controlled studies.

Anorexia nervosa is a disease that has three essential characteristics: persistent restriction of caloric intake; intense fear of gaining weight or persistent behavior that prevents weight gain; and disturbance in perception of one’s own weight or shape. Its manifestation may involve only eating restrictions or binge eating followed by purging (autoinduced vomiting or the use of laxatives, diuretics or enemas) [158].
In 1987, a study evaluated 116 patients with anorexia nervosa and found discourse about vegetarianism in 54.3%. In only 6.3% of the assessed cases was the adoption of vegetarianism made before disease onset [159].

The greater concern with a healthy diet, which consequently brings health benefits, creates in some researchers the erroneous idea that vegetarians have eating disorders. This conceptual error is seen in studies in the peer reviewed literature [160, 161].

As meat is a caloric food with a high fat content, it is natural for individuals with anorexia nervosa, at some point, to avoid it, as well as various other caloric foods (pasta, yellow cheeses, and sweets). Vegetarianism is a consequence of choice in the disease and not a cause of it.

A study published in 2021 collected data on 124 patients (84.7% women with a mean age of 23.9 years) admitted to an intensive outpatient care program for patients with eating disorders. Of these individuals, 58.1% were omnivores, 27.2% were meat-reducers, 20.2% were vegetarians and 4.0% were vegans. Vegetarians had lower highest-ever BMI values than the others. The research data showed that meat restriction does not imply greater eating disorder severity [162].

Health professionals caring for patients with an altered body image should be aware of discourse that weight below adequate is achieved by adopting a vegetarian diet because this diet does not lead to excessive thinness, except when there is nutritional errors or when consuming diseases or anorexia nervosa is the primary cause [163].

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Eating a vegetarian diet does not lead to anorexia nervosa, but people with this condition can use discourse on the subject of vegetarianism to justify their low weight and hide the disease from others.
End of the Sample Book.