

Ultra-Processed Foods: Effects on Health

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Abstract

With industrialisation, food has become increasingly processed to reduce costs, improve sensory properties, etc. The NOVA classification system divides all nutrients into four groups according to the purpose and amount of processing to which they are subjected. According to the NOVA classification, the first group consists of unprocessed and minimally processed foods. The second group consists of processed culinary ingredients. The third group consists of processed foods and the fourth group consists of ultra-processed foods (UPF). Soft drinks, crisps, desserts, hamburgers and many other foods are among the UPFs. A diet high in UPFs is low in fiber, vitamins and minerals. It is thought to be detrimental to health due to high consumption of refined sugars, sodium and saturated fats. Compounds such as acrylamide and acrolein, formed as a result of heat treatment and food additives added to ultra-processed foods, are known to have adverse health effects. Examining ultra-processed foods as a group, rather than evaluating individual foods, can help us understand the effects of food processing on health, particularly obesity, type 2 diabetes, cardiovascular disease, cancer and gastrointestinal diseases. The aim of this study was to determine the possible effects of UPFs on health.

Keywords: Foods, Diabetes mellitus, Systemic diseases, Health

Introduction

NOVA Classification System and Ultra-Processed Foods

Technological developments, industrialisation and the globalisation of the food system have changed the purpose of food processing in recent years. Foods that are high in energy, low in nutritional value, have a long shelf life. These foods are cheap, easily accessible, consumable and are increasingly replacing traditional foods. As the production and consumption of processed foods increased. Their effects on health began to be discussed. Some classification systems have been developed to group these foods according to their level of processing. The NOVA classification system divides foods into four categories according to the extent and purpose of industrial processing: unprocessed and minimally processed foods, processed culinary ingredients, processed foods and ultra-processed foods (UPFs). The NOVA system recognises the role of food processing in maintaining food safety and providing convenience, and is not opposed to food processing (1). Unprocessed and minimally processed foods contain the edible parts of plants, animals or fungi without any processing. Foods are minimally processed to make them storable, edible and more palatable. This group includes fresh fruit and vegetables, cereals, pulses, meat and dairy products. The second group consists of processed culinary ingredients, which are substances derived from nature that are generally not consumed as such and are used

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in the kitchen to cook and flavour unprocessed foods. This group includes oils, salts, sugars and starches. Processed foods, which are created by adding processed culinary ingredients to unprocessed foods, are the third group. Pickled preserves, fruit jams, fermented foods such as cheese are processed foods. UPFs, which can be defined as formulations for industrial use, are the final group. Characteristic ingredients of UPFs are sugar, protein and fat derivatives (e.g. high fructose corn syrup, maltodextrin, protein isolates, hydrogenated oil) and food additives (emulsifiers, colourings and artificial sweeteners) (2). NOVA defines UPFs, which make up the fourth group, as a health risk. UPFs can be defined as formulations produced by industrial processes (1). A diet high in PUFAs is low in fiber, vitamins and minerals. It is thought to be detrimental to health due to high consumption of refined sugars, sodium and saturated fats. The aim of this review is to examine the effects of UPF consumption on cardiovascular health, diabetes, cancer and the gastrointestinal system in the light of the literature.

Unprocessed and minimally processed foods (group 1)

Unprocessed foods are the edible parts of plant and animal foods that can be eaten without processing after being separated from nature. Minimally processed foods are processed by drying, crushing, grinding, chopping, cooling, etc. It involves the removal of unwanted parts through processes (1). These processes are designed to extend the shelf life of natural foods and often make them easier to prepare. Sugar, salt, oils and other food additives are not added to the natural foods in this group. Examples of this group are plant seeds, stems, roots, edible parts of mushrooms, fruits, legumes, dairy products, tea, coffee, drinking water, eggs, etc. (3).

Processed culinary ingredients (group 2)

Foods in this group are substances such as oils, sugar and salt that are derived from foods in the first group or from nature. They are produced by industrial processes such as pressing, centrifuging, refining, clarifying and extraction. They are used in the preparation, seasoning and cooking of foods in the first group. Sugar, starch, salt, honey, vegetable oils, etc. belong to this group (1).

Processed foods (group 3)

Foods in this group are produced by adding nutrients from the second group to foods from the first group. Processes include fermentation methods used in the production of cheese and bread, and methods used in canning (1). The purpose of food processing is to extend the shelf life of foods in the first group and to make them more palatable by altering their sensory qualities. Canned foods, salted oilseeds, dried smoked meats, jams, pickled foods and cheeses are included in this group (4).

Ultra-processed foods (group 4)

UPFs are formulations that go through a series of industrial processes. The processes start with the breakdown of foods into substances that include sugars, oils, proteins, starches and fibers. These substances are usually derived from various high-yielding plant foods (maize, wheat, soya, sugar cane or beet) and from the pureeing or grinding of animal carcasses, usually from livestock farming. Some of these substances are hydrogenated or otherwise chemically modified. The food

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is then assembled using industrial techniques such as extrusion, moulding and deep-frying. Colours, artificial sweeteners, emulsifiers and other additives are added to make the product more palatable. Food additives can be used in all groups of foods to extend their shelf life, preserve their sensory properties and prevent the proliferation of micro-organisms. Finally, the products are packaged (5).

UPFs include carbonated soft drinks, sweet or savoury packaged snacks, chocolate, candy, ice cream, mass-produced packaged breads, buns, margarines, cookies, biscuits, pastries, cakes, breakfast cereals, ready-made pies, pizzas, sausages, hamburgers, processed meat products, instant soups and industrial desserts (1). They are convenient to eat, extremely tasty and cheap. They are easily accessible and can be eaten standing up. From the manufacturer's point of view, these foods are low cost, easy to promote and have a long shelf life. They contain more saturated fats, trans fats, sodium and refined sugars and less fiber, protein and potassium than other groups (6).

Health Effects of Ultra Processed Foods

Consumption of UPFs is associated with poor dietary quality and adverse health outcomes in different populations worldwide. The availability and consumption of UPFs has increased significantly in all countries, regardless of economic level, for reasons such as country food profiles, the globalising food system and industrial competition (7).

Many mechanisms need to be discussed to explain how UPF consumption may affect overall health. Some researchers attribute the observed associations between UPF consumption and adverse health outcomes to the high levels of saturated fat, sugar and salt, and the low levels of protein, fiber and unsaturated fat in these foods. In addition, the health effects of some harmful compounds and added food additives formed during food processing and found in high levels in UPFs are also being discussed. It is known that the risk of health problems such as obesity-related chronic diseases, diabetes, hypertension, metabolic syndrome, dyslipidaemia and cancer increases as the quality of the diet deteriorates.

Cardiovascular diseases

The biological pathways in the effects of UPFs on cardiovascular health may involve complex mechanisms. A number of factors such as metabolic, proinflammatory, prothrombotic, prooxidative and endothelial dysfunction co-exist and reinforce each other's effects. Many cardiovascular risk factors create a prothrombotic and proinflammatory environment and play a role in triggering endothelial dysfunction and damage (4). After 18 years of follow-up in the Framingham Offspring Study, additional daily servings of UPF were associated with a 7% increase in cardiovascular disease (CVD) risk and a 9% increase in CVD mortality in individuals who consumed 7.5 servings of UPF per day at baseline (8). A 10% increase in dietary UPF was associated with a 12% increase in CVD and a 13% increase in coronary heart disease (CHD) over a mean follow-up of 5.2 years in a French adult cohort (9). The relationship between UPF use and CVD has been attributed to several mechanisms.

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Plasma lipid profiles

Plasma lipid concentrations are influenced by the amount and quality of dietary fats and carbohydrates, which are influenced by food processing. There is a scientific consensus that trans-fatty acids in processed foods negatively affect the blood lipoprotein profile and increase the risk of CHD. Food sources of saturated fats include minimally processed foods such as full-fat dairy products, processed culinary ingredients such as cream and butter, and UPFs such as palm oil. The health effects of saturated fat in the diet are known to depend on the source of the food and the effects of compounds formed when fats are processed at high temperatures. For example, processed coconut oil, but not virgin coconut oil, has been shown to increase serum cholesterol concentrations in rats (10). Research shows that the effect of carbohydrates on serum lipid concentrations is also determined by the source of the carbohydrate and the degree of processing. Consumption of refined sugars increases serum triglycerides. Consumption of whole grain carbohydrates reduces total cholesterol and LDL cholesterol. Beta-glucans found in oats and barley reduce blood cholesterol. Consuming minimally processed whole grains, such as oatmeal, instead of ultra-processed, high-sugar and refined grain products may reduce CVD risk by increasing HDL cholesterol concentrations (11).

Weight gain and adiposity

In epidemiological and experimental studies, increased consumption of ultra-processed foods has been associated with obesity. One study showed that an ultra-processed diet increased ad libitum energy intake by an average of 500 kcal/day compared to a minimally processed diet, resulting in weight gain (12). Consumption of ultra-processed foods may increase energy intake by reducing consumption of minimally processed foods, which are low in energy. High levels of saturated fat, salt, sugar and sweeteners make UPFs very palatable. Because human satiety mechanisms are more sensitive to volume than energy content, foods with higher energy density may facilitate excess energy intake (13). The higher energy density and sensory properties of UPFs (soft, less fibrous and easy to chew) lead to excess energy intake in a short period of time, triggering obesity.

Experimental studies suggest that increased UPF intake may lead to increased energy intake due to a delay in satiety signals. In the study, the average eating rate, measured in grams per minute and kcal per minute, was reported to be significantly higher during the ultra-processed diet compared to the minimally processed diet. In addition, concentrations of the appetite-suppressing hormone peptide YY appeared to be higher during the minimally processed diet compared with the ultra-processed diet (12). The ease of consumption, ubiquity, affordability and persuasive marketing of UPFs may contribute to increased energy intake by encouraging poor eating habits, constant snacking and overeating.

A cross-sectional study used data from the 2008-2009 Brazilian Nutrition Survey to examine the association between UPF use and obesity in 30,243 adolescents and adults. Being in the highest quintile of UPF consumption compared to the lowest quintile was associated with higher body mass index (BMI) and obesity risk (14).

In obese individuals, adiponectin and insulin-mediated nitric oxide release are reduced, which is

International Journal of Basic and Clinical Studies, Bakkal LZ et al., 2024; 13(2): 1-17, 13201.

effective in increasing insulin sensitivity in peripheral tissues. The release of pro-inflammatory factors such as IL1-6, TNF- α , leptin and endothelin-1, which cause inflammation and disrupt the insulin signalling pathway, is increased. The decrease in insulin receptor expression and tyrosine kinase activity leads to hyperinsulinemia. The increase in abdominal obesity causes a deterioration in glucose homeostasis in the liver, resulting in an increase in the amount of free fatty acids released into the circulation. Free fatty acids increase insulin secretion by pancreatic beta cells. However, they cannot be effective because insulin resistance occurs and weight gain and obesity are considered important risk factors for cardiovascular disease. Leptin regulates energy metabolism under normal conditions and has anti-atherogenic, anti-inflammatory and anti-hypertrophic properties. However, in obese individuals it has negative effects such as increasing cellular immune response, blood pressure, sympathetic nervous system activation, reactive oxygen products, platelet aggregation, triggering arterial thrombosis, causing left ventricular hypertrophy and insulin resistance. It is therefore considered a risk factor for cardiovascular disease (15).

Glycemic response and insulin dysregulation

Excessive consumption of refined sugars is associated with many CVD risk factors, including obesity, hypertension, insulin resistance, type 2 diabetes, and dyslipidaemia. Diets with a high glycemic index and high glycemic load increase the risk of CVD and type 2 diabetes. Experimental evidence suggests that UPFs are on average more hyperglycemic than minimally processed and processed foods due to their low fiber and high simple sugar content. Postprandial hyperglycemia can increase food intake by increasing appetite and promoting fat deposition in adipose and non-adipose tissues. Increased fat storage in the liver and skeletal muscle is associated with insulin resistance (16). Hyperglycemia increases CVD risk by inducing weight gain, inflammation, oxidative stress and endothelial dysfunction (17). Experimental studies in animals and humans show that low-energy sweeteners such as sucralose, which is commonly found in UPFs, can alter glucose metabolism by acting on some centres in the brain and reduce insulin sensitivity by disrupting the gut-brain axis. In a study of seventeen obese individuals comparing the effect of sucralose and water consumption on the glycemic response before oral glucose consumption, 20% more insulin was required than normal insulin concentration to achieve the same glycemic response after sucralose consumption (18). Seven healthy individuals who had not previously used low-calorie sweeteners used sucralose for seven weeks. It was observed that the individuals' glycemic response decreased day by day with the consumption of 5 mg/kg of saccharin per day. It has been reported that the consumption of artificial sweeteners can negatively affect glucose intolerance and the gut microbiota in mice and humans (19).

The use of artificial sweeteners may increase the risk of CVD by causing insulin resistance, increased food intake and weight gain. Insulin resistance and the pathogenesis of CVD in diabetes are shown in Figure 1.

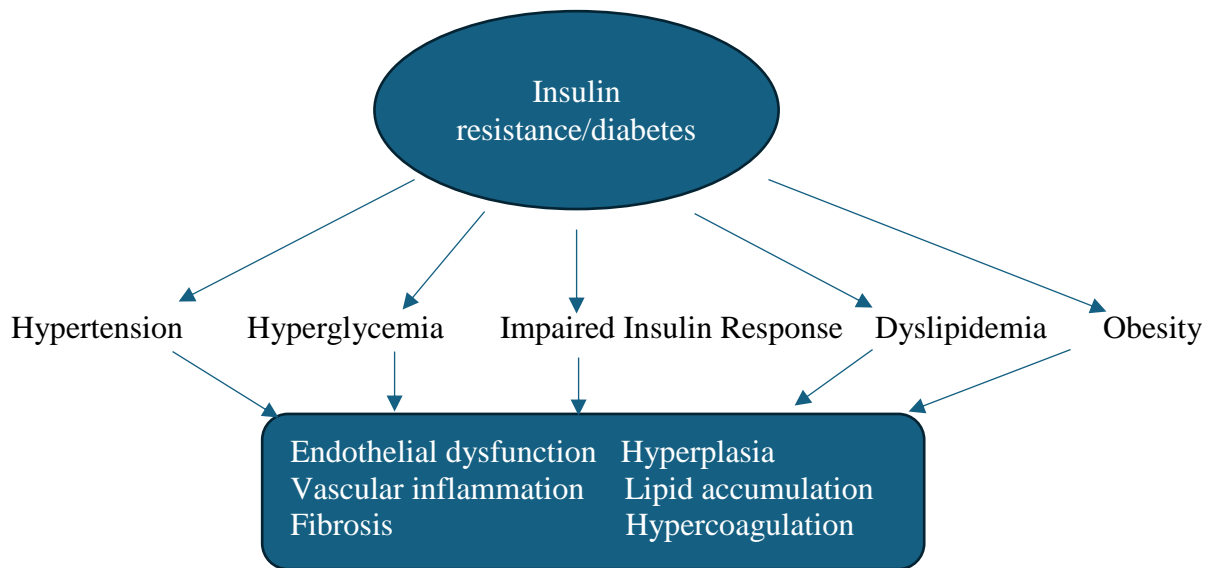


Figure 1. Insulin resistance and pathogenesis of cardiovascular disease in diabetes (20).

Diabetes

Many factors are known to contribute to the development of diabetes, particularly a poor diet characterized by low intake of fruits, vegetables, whole grains, oilseeds, and legumes. The low fiber content of UPFs may play a role in their association with type 2 diabetes. Mechanisms include fiber reducing postprandial hyperglycemia, delaying the digestion and absorption of carbohydrates, and increasing satiety by improving blood lipids, body weight and inflammation (21). Fiber may also increase peripheral insulin sensitivity via short-chain fatty acids produced by the gut microbiota (22). Therefore, consumption of low-fiber products increases the risk of diabetes. The pathophysiology of diabetes is shown in Figure 2.

Another factor is the refined sugar content of UPFs. Excessive sugar consumption is known to increase body weight, which increases insulin resistance and the risk of diabetes. Monosaccharides commonly found in UPFs, such as fructose and sucrose, can also be difficult for the liver to metabolise, leading to increased lipid accumulation in the liver and decreased insulin sensitivity. Excess fructose may increase inflammatory responses in the setting of impaired hepatic insulin signaling (23).

Although nutritional research has focused on energy intake and the role of macro/micronutrients in type 2 diabetes, the importance of the NOVA classification is highlighted when non-nutritional factors related to food processing are considered. Factors such as food additives, chemical compounds formed during production processes and packaging with synthetic materials may also influence the development of type 2 diabetes. UPFs are packaged with synthetic materials that may be sources of endocrine disrupting chemicals, including bisphenol A (BPA) and phthalates, which have been linked to diabetes (24). BPA may promote the development of type 2 diabetes through several mechanisms, including increased body weight, insulin resistance, inflammation, and oxidative stress, as well as impaired glucose homeostasis and beta-cell

International Journal of Basic and Clinical Studies, Bakkal LZ et al., 2024; 13(2): 1-17, 13201.

function. Exposure to PAH can cause oxidative stress and inflammation, which are involved in the pathogenesis of insulin resistance and beta-cell dysfunction (25). Monosodium glutamate, used as a flavour enhancer, has been suggested as a potential factor in the development of obesity and diabetes, as well as side effects such as hepatotoxic, neurotoxic, and genotoxic effects (26).

The study, based on dietary data from the Canadian Community Health Survey, found a strong association between high UPF consumption and the development of obesity and diabetes. Those who consumed high levels of UPF (73% of total energy) had a 37% increased risk of developing diabetes compared to those who consumed the lowest levels of UPF (24% of total energy). For every 10% increase in energy from UPF, there was a 6% increase in the risk of both obesity and diabetes (27). The study, which followed 104,707 participants without type 1 or type 2 diabetes for six years, reported that the risk of type 2 diabetes increased with increasing UPF consumption. A 10% increase in dietary UPF was associated with a 15% increase in the risk of type 2 diabetes (9). Two cohort studies conducted in the Netherlands and Brazil reported that a 10% increase in UPF consumption increased the risk of developing type 2 diabetes by 33% and 13%, respectively (28, 29). In a cohort study investigating the effect of UPF use on glycemic control in pregnant women with pregestational diabetes, each kcal increase in UPF use during the third trimester was associated with a 0.007% increase in glycemic hemoglobin, a 0.14 mg/dL increase in one-hour postprandial glucose, and a 0.11 kg increase in total gestational weight (30).

Studies have shown a strong association between UPF use and the incidence of diabetes.

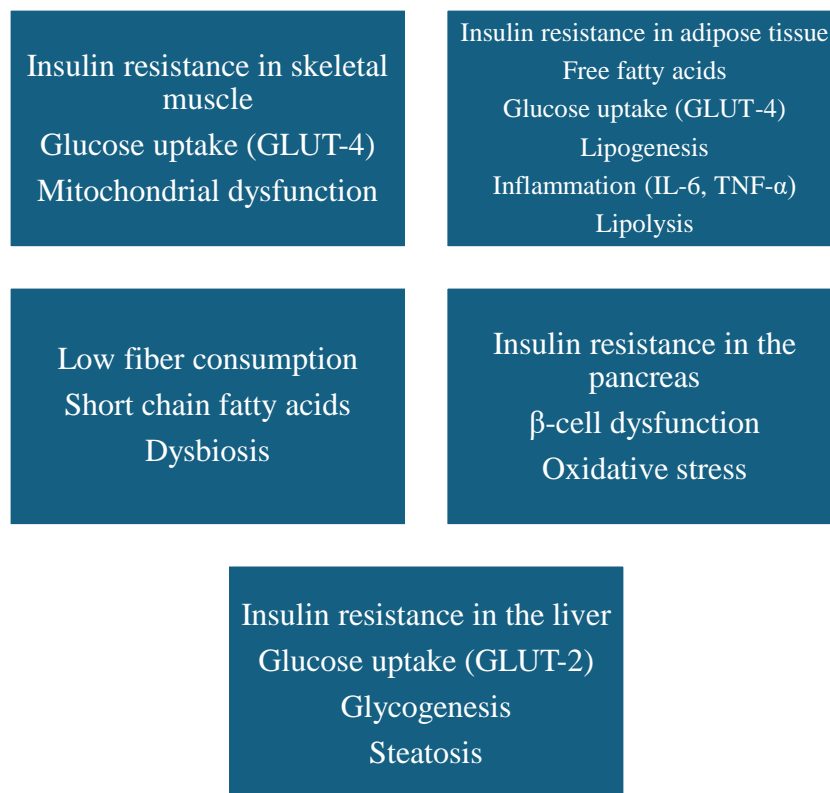


Figure 2. The pathophysiology of diabetes (31).

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Hypertension

Excessive dietary sodium intake is associated with increased hypertension, a major risk factor for CVD and stroke (32). Metabolic, hemodynamic and inflammatory changes lead to volume expansion, water retention, endothelial stiffening, increased peripheral resistance and subsequent elevation of blood pressure. Epidemiological studies support that a higher sodium/potassium ratio (≥ 1.0) is associated with an increased risk of CVD mortality, whereas a higher potassium intake is associated with a lower risk. Salt, the main source of sodium, is found in processed foods and convenience foods in many countries. Most processed foods are high in sodium. While UPFs are the main source of sodium, minimally processed foods such as fruits, vegetables, milk, and dairy products are the main dietary sources of potassium. Therefore, increased consumption of UPFs and decreased consumption of potassium-rich, minimally processed foods may affect CVD risk by increasing sodium intake and altering the sodium/potassium ratio of the diet (33).

The renin-angiotensin system is the hormonal system that regulates blood pressure and fluid balance. When blood pressure falls, renin is secreted from the juxtaglomerular cells, stimulating the formation of angiotensin I from angiotensinogen. Angiotensin I is converted to angiotensin II by angiotensin converting enzyme (ACE). Angiotensin II increases vascular blood pressure. Angiotensin II also stimulates the release of the hormone aldosterone from the adrenal cortex. Aldosterone increases the reuptake of water and sodium from the kidney tubules into the blood. Excessive activation of this system causes hypertrophy and fibrosis in the heart, vasoconstriction, inflammation, and thrombosis due to reduced nitric oxide production in the vessels. It also retains water in the body and increases the amount of sodium ions, causing endothelial dysfunction and ultimately cardiovascular disease (34). Another hypothesis to explain the relationship between UPF and hypertension risk could be weight gain due to UPF consumption. An unprocessed diet rich in fruits and vegetables helps to control body weight. It is associated with lower blood pressure by promoting adequate fiber, vitamin, and mineral intake. In a prospective study of 14,790 Spanish adults with a mean follow-up of 9.1 years, participants with the highest UPF consumption were reported to have the highest risk of developing hypertension (35). In studies conducted in Chile and the Americas, consumption of more than one serving of sugar-sweetened beverages per day was directly associated with hypertension (36, 37).

Gut microbiome

Diet is an important modulator of gut microbiota composition and activity. Alterations in the gut microbial ecosystem and intestinal barrier dysfunction are associated with excess adiposity, insulin resistance, type 2 diabetes, and CVD. Underlying mechanisms include increased bacterial production of atherogenic metabolites such as choline, trimethylamine N-oxide and betaine; low-grade systemic inflammation caused by endotoxemia; modulation of the host immune system and weight gain. Other mechanisms may include increased energy intake by the host, changes in energy homeostasis and hepatic lipid accumulation (38).

Altering the fat and fiber content of foods and incorporating certain food additives during processing can affect the composition, function, and bacteria-host interactions of the gut microbiota. Dietary fibers, which are abundant in unrefined plant foods, provide substrates for microbial fermentation. They are associated with increased microbial gene richness and the

International Journal of Basic and Clinical Studies, Bakkal LZ et al., 2024; 13(2): 1-17, 13201.

production of short-chain fatty acids, which have key functions in regulating host metabolism. Western dietary patterns, characterized by low intakes of dietary fiber and high intakes of sugar, saturated fat and animal protein, reduce the diversity of the microbiota. Low-fiber diets result in the depletion of host proteins and mucins, leading to dysbiosis and increased susceptibility to chronic inflammatory diseases. Compared with diets based on unprocessed whole grains, high-fiber diets based on processed grains reduced bacterial diversity and led to a reduction in beneficial butyrate-producing bacteria in animal models (39). Evidence from animal and human studies suggests that high-fat diets may induce low-grade systemic inflammation and metabolic disorders by increasing circulating concentrations of lipopolysaccharide produced by gut bacteria (metabolic endotoxemia) (40). Animal studies also support that diets high in glucose or fructose can reduce gut microbiota diversity and increase gut permeability (41). Excessive sugar consumption is known to cause changes in the gut microbiota, weight gain and metabolic disorders. One study reported that high doses of fructose were digested by the microbiota and the liver, and one of the possible mechanisms of fatty liver was the conversion of fructose to a hepatotoxic metabolite. It is thought that monosaccharides consumed in high doses are not cleared from the small intestine, thus altering the gut microbiota and triggering metabolic diseases.

Evidence from animal and human studies suggests that the consumption of low-calorie sweeteners may disrupt the diversity and balance of the gut microbiota, increasing metabolic disorders and insulin resistance (42). A study in mice found that commonly used artificial sweeteners such as aspartame, saccharin, sucralose and acesulfame potassium affected glucose metabolism. When mice were given water containing artificial sweeteners, their glucose tolerance was impaired and glucose levels increased. The use of artificial sweeteners suppressed some types of bacteria and increased others. In particular, some types of bacteria that are important for a healthy gut microbiota were found to be reduced, which can affect glucose metabolism. In addition, the study found that the use of artificial sweeteners caused inflammation in the intestinal wall of mice. This suggests that it may contribute to the deterioration of gut health and the development of glucose intolerance (19).

Other mechanisms

Intensive heat treatment during processing and cooking leads to increased oxidative stress and the formation of advanced glycation end products (AGEs), which are associated with inflammation and may play a role in the aetiology of CVD. AGE formation is particularly prevalent in foods of animal origin that are high in protein and fat, and increases with higher temperatures, longer cooking times and lack of moisture. Dry heat treatment and deep-frying of carbohydrate-rich foods (e.g. crackers, crisps, biscuits, and French fries) also accelerate the formation of AGEs. The mechanisms of action of dietary AGEs in the development of CVD are not fully understood (43). Acrylamide, acrolein, polycyclic aromatic hydrocarbons (PAHs) and furan are compounds associated with UPF. Acrylamide is an organic compound formed when starchy foods are cooked at high temperatures. French fries, chips and breakfast cereals are examples of foods that can contain high levels of acrylamide. Acrylamide exposure, as assessed by haemoglobin biomarkers, was shown to be significantly associated with all-cause mortality in the NHANES 2003-2006 cohort (44).

International Journal of Basic and Clinical Studies, Bakkal LZ et al., 2024; 13(2): 1-17, 13201.

The relationship between UPF consumption and acrylamide exposure was investigated in the study, which was conducted in America between 2013 and 2016 and included 4,418 participants. The percentage of daily energy intake from UPF was calculated and acrylamide exposure was assessed using the biomarkers acrylamide (HbAA) and glycidamide hemoglobin (HbGA). Compared to the lowest percentile, the highest percentile had 9.1% higher HbAA and HbGA levels. Both acrylamide and UPF have been associated with cardiovascular disease (45). Acrolein is an unsaturated aldehyde formed when oils are exposed to high temperatures and is found in high levels in UPFs. The Louisville Healthy Heart Study measured levels of the acrolein metabolite 3-hydroxy-2-propenal (3-HPMA) in urine samples from participants. The results showed that 3-HPMA levels were elevated in people with high acrolein exposure, which may increase the risk of cardiovascular disease. In addition, an association was found between acrolein exposure and cardiovascular disease mechanisms such as oxidative stress and inflammation. Adverse effects of acrolein on the cardiovascular system may include mechanisms such as endothelial dysfunction, oxidative stress, inflammation, thrombosis, and atherosclerosis (46). Food processing breaks down the cellular structures in food and produces cell-free food. Destruction of the cell wall accelerates digestion and can lead to bacterial growth in the small intestine. High proliferation of gut bacteria can cause low-grade inflammation in the host, and systemic circulation may be affected. This may increase the risk of CVD (47).

Cancer

Current evidence suggests that UPFs may increase cancer risk by increasing obesogenic properties, exposure to certain food additives and various compounds that are potentially carcinogenic. Results from the French NutriNet-Santé cohort support the association between high UPF consumption and the risk of developing total cancer and breast cancer (48). The potential mechanisms between diet and cancer are shown in Figure 3.

Higher dietary UPFs in postmenopausal women are associated with an increased risk of breast, stomach, liver, oesophageal, pancreatic and kidney cancer (49). According to data from 104,980 adult participants in the French NutriNet-Santé cohort, who were followed for an average of 5 years and had a 24-hour food consumption record, a 10% increase in energy from dietary PUFAs resulted in a 12% increase in all cancers and an 11% increase in breast cancer. Changes in carbohydrates, fat and sodium were not reported to have any effect on cancer development. This finding suggests that other bioactive compounds are involved in the consumption of UPFs (48).

Increased consumption of UPFs may increase the risk of exposure to potentially carcinogenic ingredients, including certain additives such as titanium dioxide, which are commonly used in UPFs and are not considered safe for humans. When food is processed, several reactions take place and the chemical structure of the food changes. This leads to the formation of compounds such as trans fats and acrylamide. Recent evidence has shown a positive association between trans-fat consumption and cancer risk. The relationship between industrial trans-fat consumption and breast cancer was investigated using data from 318,607 women who participated in the European Prospective Study on Cancer and Nutrition. After an average follow-up of eight years, higher consumption of industrial trans fatty acids was associated with breast cancer risk. Trans fatty acids increase adiposity, insulin resistance and systemic inflammation. Elaidic acid has

International Journal of Basic and Clinical Studies, Bakkal LZ et al., 2024; 13(2): 1-17, 13201.
been reported to modulate hepatic lipogenesis (50, 51).

Other compounds such as heterocyclic amines, PAHs, oxyhalides and haloacetic acids, which are also associated with cancer risk, are also formed in foods during processing. Urinary concentrations of di(ethylhexyl) phthalate, an endocrine disrupting chemical, have been associated with UPF consumption (52). Both human and animal studies have shown that exposure to di(ethylhexyl)phthalate can cause cancer through multiple molecular signals, including DNA damage. Exposure to BPA, an endocrine disrupting chemical used in various food packaging, has been reported to increase the risk of cancer. Exposure to BPA has been shown to deregulate signalling pathways involved in head and neck cancer (53). The International Agency for Research on Cancer added aspartame, an artificial sweetener commonly used in UPFs, to the group of probable carcinogens in 2023 (54). The study, which included 102,865 participants in the NutriNet-Santé cohort, showed an increased risk of all cancers at low levels of aspartame consumption (<5.06 mg/day in men and <15.39 mg/day in women). Mechanisms reported include weight gain, inflammation, angiogenesis, DNA damage and inhibition of apoptosis (55). Alcoholic beverages are considered ultra-processed beverages and have been linked to the development of cancer. Experimental evidence suggests that acetaldehyde, a toxic metabolite of alcohol, has carcinogenic properties by disrupting DNA synthesis and repair. Other possible underlying mechanisms include oxidative stress caused by ethanol consumption, which facilitates the entry of carcinogens into the cell. There is an association between chronic alcohol consumption and the risk of developing cancers of the upper gastrointestinal tract, liver, rectum, and breast. Smoking, malnutrition, and other factors increase the risk of cancer in addition to alcohol consumption (56).

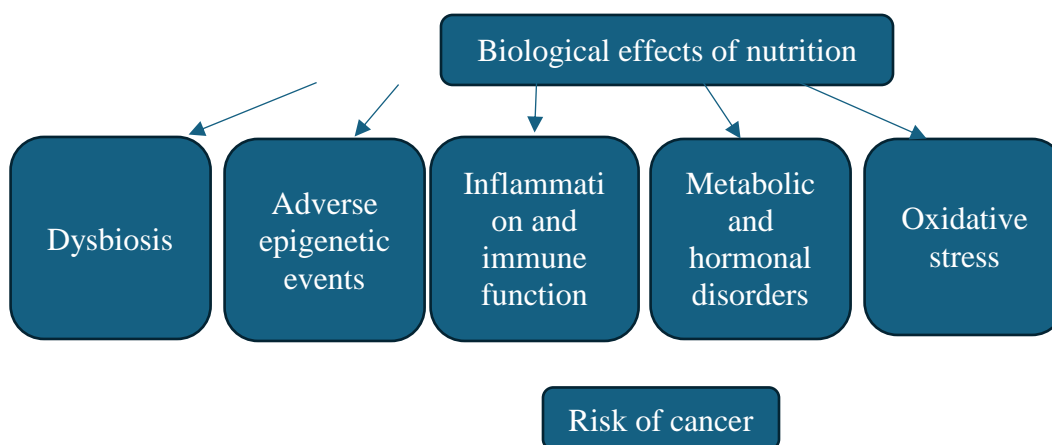


Figure 3. The potential mechanisms between nutrition and cancer (57).

Gastrointestinal system diseases

Diet may play a role in the pathogenesis of inflammatory gastrointestinal diseases by altering the microbiome. As UPF consumption increases, so does the incidence of inflammatory gastrointestinal diseases. Reasons such as consumption of refined sugars, increased consumption of omega-6 fatty acids, high sodium and low fiber consumption are potential risk factors. UPFs often contain additives such as artificial sweeteners, stabilisers, emulsifiers, and preservatives,

International Journal of Basic and Clinical Studies, Bakkal LZ et al., 2024; 13(2): 1-17, 13201.

which can have a detrimental effect on the intestinal barrier (58). In experimental models, higher levels of sodium chloride increased the production of inflammatory cytokines and exacerbated ulcerative colitis. Dietary sodium triggered intestinal inflammation by increasing intestinal permeability and decreasing short-chain fatty acid production (59). In the NutriNet-Sante cohort study, which investigated the relationship between UPF consumption and irritable bowel syndrome, a common gastrointestinal disorder, the percentage of daily energy from UPF was calculated for 33,343 participants. The group that consumed the most UPF was found to be the most likely to suffer from functional bowel disease (60).

Conclusion

The NOVA food classification system divides food into four categories according to the extent and purpose of industrial processing. In this classification, the fourth group consists of UPFs and beverages. They contain high levels of refined sugars, sodium, saturated fats and food additives. Soft drinks, crisps, sweets, desserts, doughnuts, burgers, etc. are examples of UPFs.

With globalisation and industrialisation, the production and consumption of low cost, high energy density, quick and easy to consume UPFs are replacing traditional foods. These foods contain higher amounts of refined sugars, trans fats, saturated fats, sodium and less fiber than unprocessed foods. They are risky for human health due to food additives added during processing and harmful substances that can be formed during food processing. UPFs, which provide high energy in small amounts, are low cost, have a long shelf life and are easy to consume.

It is known that the risk of obesity-related chronic diseases, cardiovascular diseases, gastrointestinal diseases and cancer may increase with the consumption of UPF. It is recommended that taxes be imposed on UPF, that it not be sold in institutions such as hospitals, schools, etc., that advertising in media communication tools be restricted, and that policies be developed on this issue.

Compliance with Ethical Standard

Conflict of interests: The author declares that for this article they have no actual, potential, or perceived conflict of interests.

Ethics committee approval: The author declares that this study does not include any experiments with human or animal subjects; therefore, no ethics committee approval is needed.

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References

1. Monteiro CA, Cannon G, Levy RB, Moubarac J-C, Louzada ML, Rauber F, et al. Ultra-processed foods: what they are and how to identify them. *Public health nutrition*. 2019;22(5):936-41.
2. Elizabeth L, Machado P, Zinöcker M, Baker P, Lawrence M. Ultra-processed foods and health outcomes: a narrative review. *Nutrients*. 2020;12(7):1955.
3. Gibney MJ. Ultra-processed foods: definitions and policy issues. *Current developments in nutrition*. 2019;3(2):nzy077.
4. Juul F, Vaidean G, Parekh N. Ultra-processed foods and cardiovascular diseases: potential mechanisms of action. *Advances in Nutrition*. 2021;12(5):1673-80.
5. Monteiro CA, Levy RB, Claro RM, Castro IRRd, Cannon G. A new classification of foods based on the extent and purpose of their processing. *Cadernos de saude publica*. 2010;26:2039-49.
6. Louzada MLdC, Martins APB, Canella DS, Baraldi LG, Levy RB, Claro RM, et al. Ultra-processed foods and the nutritional dietary profile in Brazil. *Revista de saude publica*. 2015;49.
7. Moodie R, Stuckler D, Monteiro C, Sheron N, Neal B, Thamarangsi T, et al. Profits and pandemics: prevention of harmful effects of tobacco, alcohol, and ultra-processed food and drink industries. *The lancet*. 2013;381(9867):670-9.
8. Juul F, Vaidean G, Lin Y, Deierlein AL, Parekh N. Ultra-processed foods and incident cardiovascular disease in the Framingham Offspring Study. *Journal of the American College of Cardiology*. 2021;77(12):1520-31.
9. Srour B, Fezeu LK, Kesse-Guyot E, Allès B, Méjean C, Andrianasolo RM, et al. Ultra-processed food intake and risk of cardiovascular disease: prospective cohort study (NutriNet-Santé). *bmj*. 2019;365.
10. Arunima S, Rajamohan T. Influence of virgin coconut oil-enriched diet on the transcriptional regulation of fatty acid synthesis and oxidation in rats—a comparative study. *British Journal of Nutrition*. 2014;111(10):1782-90.
11. Hollænder PL, Ross AB, Kristensen M. Whole-grain and blood lipid changes in apparently healthy adults: a systematic review and meta-analysis of randomized controlled studies. *The American journal of clinical nutrition*. 2015;102(3):556-72.
12. Hall KD, Ayuketah A, Brychta R, Cai H, Cassimatis T, Chen KY, et al. Ultra-processed diets cause excess calorie intake and weight gain: an inpatient randomized controlled trial

International Journal of Basic and Clinical Studies, Bakkal LZ et al., 2024; 13(2): 1-17, 13201.

- of ad libitum food intake. *Cell metabolism*. 2019;30(1):67-77. e3.
13. Rolls BJ. Dietary energy density: applying behavioural science to weight management. *Nutrition bulletin*. 2017;42(3):246-53.
 14. da Costa Louzada ML, Baraldi LG, Steele EM, Martins APB, Canella DS, Moubarac J-C, et al. Consumption of ultra-processed foods and obesity in Brazilian adolescents and adults. *Preventive medicine*. 2015;81:9-15.
 15. Solmaz H, Akbulut M. Obezite ve Kalp.
 16. Frayn KN, Arner P, Yki-Järvinen H. Fatty acid metabolism in adipose tissue, muscle and liver in health and disease. *Essays in biochemistry*. 2006;42:89-103.
 17. Fardet A. Minimally processed foods are more satiating and less hyperglycemic than ultra-processed foods: a preliminary study with 98 ready-to-eat foods. *Food & function*. 2016;7(5):2338-46.
 18. Pepino MY, Tiemann CD, Patterson BW, Wice BM, Klein S. Sucralose affects glycemic and hormonal responses to an oral glucose load. *Diabetes care*. 2013;36(9):2530-5.
 19. Suez J, Korem T, Zeevi D, Zilberman-Schapira G, Thaiss CA, Maza O, et al. Artificial sweeteners induce glucose intolerance by altering the gut microbiota. *Nature*. 2014;514(7521):181-6.
 20. Haas AV, McDonnell ME. Pathogenesis of cardiovascular disease in diabetes. *Endocrinology and Metabolism Clinics*. 2018;47(1):51-63.
 21. Reynolds AN, Akerman AP, Mann J. Dietary fibre and whole grains in diabetes management: Systematic review and meta-analyses. *PLOS Medicine*. 2020;17(3):e1003053.
 22. Robert EP, Arch GM, III, Dana EK, Kit NS. Dietary Fiber for the Treatment of Type 2 Diabetes Mellitus: A Meta-Analysis. *The Journal of the American Board of Family Medicine*. 2012;25(1):16.
 23. Stanhope KL. Sugar consumption, metabolic disease and obesity: The state of the controversy. *Crit Rev Clin Lab Sci*. 2016;53(1):52-67.
 24. Martínez Steele E, Khandpur N, da Costa Louzada ML, Monteiro CA. Association between dietary contribution of ultra-processed foods and urinary concentrations of phthalates and bisphenol in a nationally representative sample of the US population aged 6 years and older. *PLOS ONE*. 2020;15(7):e0236738.
 25. Guo H, Huang K, Zhang X, Zhang W, Guan L, Kuang D, et al. Women are more susceptible than men to oxidative stress and chromosome damage caused by polycyclic aromatic hydrocarbons exposure. *Environ Mol Mutagen*. 2014;55(6):472-81.

International Journal of Basic and Clinical Studies, Bakkal LZ et al., 2024; 13(2): 1-17, 13201.

26. Malik S, Kazmi Z, Fatima I. Monosodium glutamate: Review on clinical reports. *International Journal of Food Properties*. 2017;20.
27. Nardocci M, Polsky JY, Moubarac J-C. Consumption of ultra-processed foods is associated with obesity, diabetes and hypertension in Canadian adults. *Canadian Journal of Public Health*. 2021;112(3):421-9.
28. Levy RB, Rauber F, Chang K, Louzada M, Monteiro CA, Millett C, et al. Ultra-processed food consumption and type 2 diabetes incidence: A prospective cohort study. *Clin Nutr*. 2021;40(5):3608-14.
29. Llaveró-Valero M, Escalada-San Martín J, Martínez-González MA, Basterra-Gortari FJ, de la Fuente-Arrillaga C, Bes-Rastrollo M. Ultra-processed foods and type-2 diabetes risk in the SUN project: A prospective cohort study. *Clin Nutr*. 2021;40(5):2817-24.
30. Silva CFM, Saunders C, Peres W, Folino B, Kamel T, Dos Santos MS, et al. Effect of ultra-processed foods consumption on glycemic control and gestational weight gain in pregnant with pregestational diabetes mellitus using carbohydrate counting. *PeerJ*. 2021;9:e10514.
31. Bocanegra A, Macho-González A, Garcimartín A, Benedí J, Sánchez-Muniz FJ. Whole Alga, Algal Extracts, and Compounds as Ingredients of Functional Foods: Composition and Action Mechanism Relationships in the Prevention and Treatment of Type-2 Diabetes Mellitus. *Int J Mol Sci*. 2021;22(8).
32. He FJ, Tan M, Ma Y, MacGregor GA. Salt reduction to prevent hypertension and cardiovascular disease: JACC state-of-the-art review. *Journal of the American College of Cardiology*. 2020;75(6):632-47.
33. Woodruff RC. Top food category contributors to sodium and potassium intake—United States, 2015–2016. *MMWR Morbidity and mortality weekly report*. 2020;69.
34. SERBETCI T, Berfu B. Renin-Anjiyotensin-Aldosteron Sistemine Etkili Tıbbi Bitkilerin Potansiyel Kullanımı. *KTO Karatay Üniversitesi Sağlık Bilimleri Dergisi*. 2022;3(1):105-18.
35. Mendonça RdD, Lopes ACS, Pimenta AM, Gea A, Martinez-Gonzalez MA, Bes-Rastrollo M. Ultra-processed food consumption and the incidence of hypertension in a Mediterranean cohort: the Seguimiento Universidad de Navarra Project. *American journal of hypertension*. 2017;30(4):358-66.
36. Crovetto M, Uauy R, Martins AP, Moubarac JC, Monteiro C. Household availability of ready-to-consume food and drink products in Chile: impact on nutritional quality of the diet. *Revista médica de Chile*. 2014;142(7):850-8.
37. Moubarac J-C. Ultra-processed food and drink products in Latin America: trends, impact on obesity, policy implications. *Pan American Health Organization World Health*

International Journal of Basic and Clinical Studies, Bakkal LZ et al., 2024; 13(2): 1-17, 13201.

Organization: Washington, DC, USA. 2015:1-58.

38. Boulangé CL, Neves AL, Chilloux J, Nicholson JK, Dumas M-E. Impact of the gut microbiota on inflammation, obesity, and metabolic disease. *Genome medicine*. 2016;8:1-12.
39. Moen B, Berget I, Rud I, Hole AS, Kjos NP, Sahlstrøm S. Extrusion of barley and oat influence the fecal microbiota and SCFA profile of growing pigs. *Food & function*. 2016;7(2):1024-32.
40. Lopez-Moreno J, Garcia-Carpintero S, Jimenez-Lucena R, Haro C, Rangel-Zuniga OA, Blanco-Rojo R, et al. Effect of dietary lipids on endotoxemia influences postprandial inflammatory response. *Journal of agricultural and food chemistry*. 2017;65(35):7756-63.
41. Do MH, Lee E, Oh M-J, Kim Y, Park H-Y. High-glucose or-fructose diet cause changes of the gut microbiota and metabolic disorders in mice without body weight change. *Nutrients*. 2018;10(6):761.
42. Nettleton JE, Reimer RA, Shearer J. Reshaping the gut microbiota: Impact of low calorie sweeteners and the link to insulin resistance? *Physiology & behavior*. 2016;164:488-93.
43. Poulsen MW, Hedegaard RV, Andersen JM, de Courten B, Bügel S, Nielsen J, et al. Advanced glycation endproducts in food and their effects on health. *Food and Chemical Toxicology*. 2013;60:10-37.
44. Huang M, Jiao J, Wang J, Chen X, Zhang Y. Associations of hemoglobin biomarker levels of acrylamide and all-cause and cardiovascular disease mortality among US adults: National Health and Nutrition Examination Survey 2003–2006. *Environmental pollution*. 2018;238:852-8.
45. Steele EM, Buckley JP, Monteiro CA. Ultra-processed food consumption and exposure to acrylamide in a nationally representative sample of the US population aged 6 years and older. *Preventive medicine*. 2023;174:107598.
46. DeJarnett N, Conklin DJ, Riggs DW, Myers JA, O'Toole TE, Hamzeh I, et al. Acrolein exposure is associated with increased cardiovascular disease risk. *Journal of the American Heart Association*. 2014;3(4):e000934.
47. Zinöcker MK, Lindseth IA. The Western diet–microbiome-host interaction and its role in metabolic disease. *Nutrients*. 2018;10(3):365.
48. Fiolet T, Srour B, Sellem L, Kesse-Guyot E, Allès B, Méjean C, et al. Consumption of ultra-processed foods and cancer risk: results from NutriNet-Santé prospective cohort. *Bmj*. 2018;360:k322.
49. Mendonça RD, Pimenta AM, Gea A, de la Fuente-Arrillaga C, Martinez-Gonzalez MA, Lopes AC, et al. Ultraprocessed food consumption and risk of overweight and obesity:

International Journal of Basic and Clinical Studies, Bakkal LZ et al., 2024; 13(2): 1-17, 13201.

- the University of Navarra Follow-Up (SUN) cohort study. *Am J Clin Nutr.* 2016;104(5):1433-40.
50. Matta M, Huybrechts I, Biessy C, Casagrande C, Yammine S, Fournier A, et al. Dietary intake of trans fatty acids and breast cancer risk in 9 European countries. *BMC Medicine.* 2021;19(1):81.
 51. Yammine S, Huybrechts I, Biessy C, Dossus L, Aglago EK, Naudin S, et al. Dietary and Circulating Fatty Acids and Ovarian Cancer Risk in the European Prospective Investigation into Cancer and Nutrition. *Cancer Epidemiol Biomarkers Prev.* 2020;29(9):1739-49.
 52. Buckley JP, Kim H, Wong E, Rebholz CM. Ultra-processed food consumption and exposure to phthalates and bisphenols in the US National Health and Nutrition Examination Survey, 2013-2014. *Environ Int.* 2019;131:105057.
 53. Seachrist DD, Bonk KW, Ho SM, Prins GS, Soto AM, Keri RA. A review of the carcinogenic potential of bisphenol A. *Reprod Toxicol.* 2016;59:167-82.
 54. Riboli E, Beland FA, Lachenmeier DW, Marques MM, Phillips DH, Schernhammer E, et al. Carcinogenicity of aspartame, methyleugenol, and isoeugenol. *Lancet Oncol.* 2023;24(8):848-50.
 55. Debras C, Chazelas E, Srour B, Druet-Pecollo N, Esseddik Y, Szabo de Edelenyi F, et al. Artificial sweeteners and cancer risk: Results from the NutriNet-Santé population-based cohort study. *PLoS Med.* 2022;19(3):e1003950.
 56. Seitz HK, Stickel F. Molecular mechanisms of alcohol-mediated carcinogenesis. *Nat Rev Cancer.* 2007;7(8):599-612.
 57. Steck SE, Murphy EA. Dietary patterns and cancer risk. *Nat Rev Cancer.* 2020;20(2):125-38.
 58. Narula N, Wong ECL, Dehghan M, Mente A, Rangarajan S, Lanus F, et al. Association of ultra-processed food intake with risk of inflammatory bowel disease: prospective cohort study. *Bmj.* 2021;374:n1554.
 59. Monteleone I, Marafini I, Dinallo V, Di Fusco D, Troncone E, Zorzi F, et al. Sodium chloride-enriched Diet Enhanced Inflammatory Cytokine Production and Exacerbated Experimental Colitis in Mice. *J Crohns Colitis.* 2017;11(2):237-45.
 60. Schnabel L, Buscail C, Sabate JM, Bouchoucha M, Kesse-Guyot E, Allès B, et al. Association Between Ultra-Processed Food Consumption and Functional Gastrointestinal Disorders: Results From the French NutriNet-Santé Cohort. *Am J Gastroenterol.* 2018;113(8):1217-28.