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*Review*

# A Review of the Relationship between Gut Microbiome and Obesity

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**Abstract:** Obesity is a rapidly growing problem of public health on a worldwide scale, responsible for more than 60% of deaths associated with high body mass index. Recent studies underpinned the augmenting importance of the gut microbiota in obesity. Gut microbiota alterations affect the energy balance of the host organism; namely, as a factor affecting energy production from the diet and as a factor affecting host genes regulating energy expenditure and storage. Gut microbiota composition is characterised by constant variability, and is affected by several dietary factors, suggesting the probability that manipulation of the gut microbiota may promote leaning or prevent obesity. Our narrative review summarizes the results of recent years that stress the effect of gut microbiota in the development of obesity. It investigates the factors (diet, dietary components, lifestyle, and environment) that might affect the gut microbiota composition. Possible strategies for the prevention and/or treatment of obesity include restoring or modifying the composition of the microbiota by consuming prebiotics and probiotics, fermented foods, fruits, vegetables, and avoiding foods of animal origin high in saturated fat and sugar.

**Keywords:** gut microbiome; obesity; weight loss



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## 1. Introduction

Research on the microbiome developed rapidly over the past decades, creating a high-interest scientific and public area. As early as the mid-1880s, a report on microorganisms was published by the Austrian pediatrician Theodor Escherich, associated with the isolation of *Escherichia coli*. Several microorganisms were isolated from the human body in the following years, including *Veillonella parvula* in 1898 and the isolation of *Bifidobacteria* in 1900. Throughout the 20th century, isolation of microorganisms continued to take place from the nasal mucosa, oral cavities, skin, gastrointestinal tract, and urogenital tract, characterised as part of the human microbiota. In the 21st century, the field of human microbiome and microbiome research has become a frontier scientific field [1]. In the 1990s, polymerase chain reaction (PCR) and electrophoresis methods, among others, provided the potential for new findings, and until the early 2000s, this field of research was revolutionized by the introduction of next-generation sequencing [2]. The term "microbiome" itself was first used by Lederberg and McCray in 2001 [1]. The gut microbiota represents the largest part

of the human microbiome, with alternative terms for it including gut microbiome and gut flora, although the latter is now an obsolete term [1].

Microbiome is the ecological community of microorganisms living in the human gut that evolved over thousands of years with the host body, forming complex and mutually beneficial relationships [3]. The number of microorganisms living in the gastrointestinal tract is close to $10^{13}$, consisting predominantly of anaerobic bacteria and containing ≈500–1000 species (spp.), with a total genome estimated to have 100 times more genes than the human genome [4,5]. Current studies of the gut microbiota focus mainly on bacteria. Other symbiotic microorganisms (e.g., virus, fungi, etc.) are basically ignored in gut microbiota analyses [2].

Gut microbiota plays an important role in the physiology of the human body including the fermentation of water-soluble fibres to produce short-chain fatty acids and energy not available to the host and the synthesis of vitamins (e.g., vitamin $B_2$, folic acid, vitamin K, biotin). In addition, it metabolizes xenobiotics, preventing the colonization of pathogens, protecting the integrity of the intestinal epithelium, and promoting the development of a mature immune system [6,7]. It also plays a key role in the regulation of intestinal transit, thereby influencing the amount of nutrients and energy absorbed from food [8]. When the composition of the gut microbiota is altered by a number of factors, the homeostasis of human health can be disturbed, resulting in the development of metabolic diseases (obesity, diabetes, non-alcoholic fatty liver disease (NAFLD), cardiovascular diseases, etc.) [9]. These and other functions shed light on the crucial role of the microbiome in weight gain and metabolism, discussed in more detail in this review [4,5].

## 2. The Relationship between Gut Microbiota and Obesity

Obesity is still a rapidly growing public health issue worldwide, responsible for more than sixty percent of deaths associated with high body mass index (BMI) [10]. If the increasing trend continues, it is estimated that by 2025, the prevalence of obesity will rise to 18% in men and over 21% in women worldwide [11]. Obesity is considered a complex disease where we must take several factors in account, mainly due to genetic, behavioural, socioeconomic, and environmental risk factors, but the role of gut microbiota in obesity is one of the most promising discoveries of the last decade [2].

The first assumption of a connection between obesity and the gut microbiota was established after studies in germ-free mice. A subgroup of germ-free mice was reared in a sterile environment, in comparison to mice reared in a normal environment. The body fat percentage of mice raised in a conventional environment was 40% higher and the fat percentage around the reproductive organs 47% higher than of the germ-free mice, despite consuming lower amount of food compared to their germ-free counterparts. Transplantation of the gut microbiota from regular mice into the germ-free mice resulted in a sixty percent raise in body fat within fourteen days without increasing their food intake significant changes in energy expenditure. The finding suggests that gut microbiota influences the phenotypic characteristics of the host associated with obesity. The transplanted microbiota simultaneously increased the availability of energy from dietary plant polysaccharides, but also modified genes carbohydrate response element binding protein (ChREBP) and sterol response element binding protein 1 (SREBP-1) in the host that affect energy storage in adipocytes [12].

Obesity may alter the gut microbiota structurally and functionally [5], and gut microbiota can also modulate nutritional status [13–15]. The abundant and diverse quantity of certain bacteria may facilitate energy storage and metabolic pathways leading to obesity [4,5]. This indicates that altercating the gut microbiota by dietary or other means may provide beneficial effects by restoring functional integrity of the gut and reversing the dysbiosis that characterizes obesity [5,16]. Animal studies show favorable results in obese models based on changes in physical and biochemical parameters, metabolic and inflammatory markers (e.g., increased IL-10 secretion, increased AMPK, reduction of acetyl-CoA carboxylase, fatty acid synthase), and gut microbiota diversity, whereas results in

humans are limited and controversial [6,7]. The microbiota can influence both aspects of the energy balance of the host organism; namely, as a factor affecting energy harvest from the diet and as a factor influencing host genes affecting the deposition of energy (e.g., fasting-induced adipocyte factor), regulating energy expenditure and storage. Gut microbiota composition is characterised by constant variability, and it can be influenced by several dietary components, such as probiotics, including fermented foods, or prebiotics, such as inulin, other oligosaccharides, lactulose, and resistant starch, suggesting the possibility that manipulation of the gut microbiota may promote weight loss or prevent obesity in humans [17].

## 3. Relationships between Dietary Patterns, Gut Microbiota Composition, and Obesity in Certain Populations

Long-term follow-up of a given type of diet leads to different microbiome communities in different ethnic groups/populations, and in some cases, this may be associated with obesity.

In the hunter–gatherer Hadza tribe of Tanzania, the prevalence of obesity is very low, explained by the researchers in terms of their microbiome diversity and diet. During the African rainy season, they maintain a predominantly plant-based diet dominated by roots, baobab, and wild honey, consuming meat very rarely [18]. On the other hand, the Inuit of the Canadian Arctic have had a traditional diet for thousands of years, low in carbohydrates and rich in animal fats and proteins [19,20]. These characteristics are similar to Western-type diets, suggesting that the Inuit microbiome is close to the microbiome of southern Canadians and other Western populations, reflected in their nutritional status, with 52.4% of men and 58% of women being overweight or obese [19].

The typical dietary patterns, gut microbiota diversity, and prevalence of obesity of different populations are summarized in Table 1.

**Table 1.** Obesity prevalence and microbiome diversity characteristics in specific population group ↑: increased; ↓: decreased.

| Population | Dietary Pattern | Microbiome Diversity | Obesity Prevalence | Reference |
|---|---|---|---|---|
| Hadza tribe | Predominantly plant-based diet | ↑*Prevotella*<br>↑*Bacteroidetes*<br>↑*Treponema* | <5% | [18] |
| Inuit | High in animal fat and protein, low in dietary fibre | ↓*Prevotella*<br>↓*Akkermansia muciniphila* | 20.6% | [19,20] |
| Western population<br>US<br>Netherlands<br>Italy<br>Spain | Western diet (high in fat, sugar, sodium, animal protein, processed food; low in fruits, vegetables, whole grains, and dietary fibre) | ↑*Bacteroides*<br>↓*Prevotella* | 38.2% (US)<br>12.8% (Netherlands)<br>9.8% (Italy)<br>16.7% (Spain) | [21,22] |
| Non-western populations<br>parts of central and northern India<br>Peru<br>Madagascar | Agricultural diets, predominantly containing plant-based components with the presence of animal-based components | ↑*Prevotella*<br>↓*Bacteroides* | 5% (India)<br>26.3% (Peru)<br>4% (Madagascar) | [22–24] |

## 4. The Role of Certain Bacterial Phylum and Species

In the context of energy balance, the diversity and microbial stability are important factors for gut health, the changes in which lead to dysbiosis [5,16,25]. Dysbiosis has been associated with three different phenomena that can occur together: (1) loss of beneficial microbiota, (2) overgrowth of potentially harmful bacteria, and (3) a decrease in overall microbial diversity [26]. Diseases that were found to have possible connection to microbial alterations involve autoimmune and allergic diseases, inflammatory bowel diseases, obesity,

and central nervous system diseases [26,27]. About 90% of the bacterial species within the microbiome community belong to the *Firmicutes* (i.e., *Bacillus* spp.) and *Bacteroidetes* (*Bacteroides* spp.) phyla [7,27] with other important phyla including *Actinobacteria* (Bifidobacterium spp.), *Proteobacteria* (*Escherichia, Helicobacter*), and *Verrucomicrobia* (*Akkermansia* spp.) [5,7]. Nevertheless, a wide range of individual species could be found, resulting in an increased amount of individual variability.

The *Firmicutes/Bacteroidetes* ratio has often been considered as a possible predictor of obesity risk [28]. In a mouse model, the gut microbiota of obese subjects was found to have higher *Firmicutes* and lower *Bacteroidetes* ratios compared to lean subjects, but after 1 year of dietary therapy, a reversed profile was found [4,5]. A metagenomic study comparing the gut microbiome of obese and lean twins found lower bacterial diversity and *Bacteroidetes* ratios, but higher *Actinobacteria* ratios in obese individuals compared to lean individuals, but no significant difference in *Firmicutes* ratios [29]. However, further studies and meta-analyses have not found a certain relationship between *Firmicutes* and *Bacteroidetes* ratios and obesity [2], suggesting a more complex role for the gut microbiome in the regulation of obesity than a simple imbalance of these phylum.

A 6 week randomised controlled clinical trial investigated the difference in body weight change in healthy people based on the abundance of *Prevotella* in participants who consumed an ad libitum diet containing whole grain or refined wheat. They found that *Prevotella* abundances were inversely correlated with body weight change. Subjects with high *Prevotella* abundance spontaneously lost more body weight on a diet containing whole grain wheat than on a diet containing refined wheat, whereas the weight of subjects with low *Prevotella* abundance remained stable. The authors suggest *Prevotella* as a potential biomarker in the management of obesity [30].

Probiotics regulate the gut microecosystem, host energy metabolism, and reduce low grade inflammation and oxidative stress, and may, therefore, influence the prevention and management of obesity by regulating the gut microbiota [31,32].

The composition of gut microbiota also varies depending on the severity of obesity. With obesity, the genera Bacteroidales, such as a *Lactobacillus spp*., *Bifidobacterium spp*., *Bacteroides* spp., and *Enterococcus* spp., as well as *Firmicutes* and *Bacteroidetes* and *Enterobacteriaceae* species increased, while the proportion of Clostridia, including *Clostridium leptum* and *Enterobacter* spp. decreased [33,34]. Particularly, a significant decrease in the composition of bacterial genus *Akkermansia*, *Faecalibacterium*, *Oscillibacter* and *Alistipes* has been shown in obese people compared to normal weight people [35,36]. Higher levels of *Lactobacillus reuteri* and lower levels of *Methanobrevibacter smithii* are associated with obesity leading to significant weight gain, while *Bifidobacterium animalis* and *Methanobrevibacter smithii* and other *Lactobacillus species* are found in higher abundance in normal weight individuals [37]. Several studies confirm that *Akkermansia muciniphila* abundance is negatively correlated with being overweight, obesity, metabolic syndrome, and untreated type 2 diabetes in mice [38,39]. In animal models, a study showed that *Christensenella minuta* inhibited weight gain and altered the gut microbiome pattern of the recipient mice. The exact mechanism of action of the bacteria in human models is not yet clear, but it has the potential to be effective in reducing body weight including via the production of SCFA (acetic acid, butyric acid) and via the strong inhibition of de novo lipogenesis in the regulation of hepatic lipid metabolism [40,41].

Dietary interventions with probiotics, prebiotics, or synbiotics may be effective in reversing the disturbances observed in the gut microbiota during obesity or unbalanced diets, as they may be able to reduce and maintain body weight [42,43]. In a randomised controlled clinical trial, a symbiotic was administered to individuals participating in a weight loss program. The probiotics used were *Lactobacillus acidophilus*, *Bifidobacterium lactis*, *Bifidobacterium longum,* and *Bifidobacterium bifidum* and the prebiotic component was a mixture of galactooligosaccharides. No significant differences in body weight and body composition were found between the placebo and the synbiotic groups during the 3 month intervention. However, synbiotic supplementation increased the abundance of *Bifidobac-*

*terium* and *Lactobacillus*, which have been associated with positive health effects [43,44]. In addition, supplementation with probiotics may be associated with an increase in appetite, and it should be considered ineffective without adequate diet, and can only be used as a supplement [45]. There is some evidence that probiotics can regulate not only the balance of the gut microbiota but also hormones related to appetite. However, a systematic review has found that probiotics have minimal influence on hormone levels playing a role in appetite regulation (e.g., leptin, fasting insulin, resistin) in overweight/obese individuals [46].

## 5. Effect of Diet or Dietary Components on the Gut Microbiota

As a substrate for microbial metabolism, diet plays a significant role in widening the individual microbiome, modulated positively or negatively by different diets and dietary components [2]. Western diets (low in fibre, vegetables, fruits; high in saturated fat, sugar and animal protein) have consequences beyond metabolic aspects (hyperinsulinemia, insulin resistance, dyslipidemia, overstimulation of sympathetic nervous system and renin–angiotensin system, oxidative stress), in addition to dysbiosis, intestinal barrier dysfunction, increased intestinal permeability, and leakage of toxic bacterial metabolites into the blood circulation, may contribute significantly to the development of low-grade systemic inflammation [34,47]. However, these dietary patterns—high fat, carbohydrate and animal protein, low fibre intake—induce changes in the gut microbiota in different ways.

The effects of certain diets or dietary components on the gut microbiota and host are shown in Table 2.

**Table 2.** Effect of diet and dietary components on the gut microbiome and host (↑: increased; ↓: decreased).

| Diet or Dietary Pattern | Impact on Microbiome | Impact on Host | Reference |
|---|---|---|---|
| Vegan/vegetarian diet | ↑*Prevotella*<br>↑*Roseburia*<br>↑*Ruminococcus*<br>↑*Bifidobacterium*<br>↓*E. coli*<br>↓*Firmicutes*<br>↑*E. rectale*<br>↑*F. prausnitzii*<br>↑*Anaerostipes*<br>↑*Streptococcus*<br>↑*Odoribacter*<br>↑*Clostridium sensu stricto* | ↓Visceral fat<br>↓Body mass<br>↓Inflammation<br>Promote gut barrier integrity via anti-tumorigenesis | [48–52] |
| Vegan diet with low fat | ↑*Bacteroidetes*<br>↑*C.clostridioforme*<br>↑*Faecalibacterium prausnitzii*<br>↓*Firmicutes* | ↓Body mass<br>↓Body fat<br>↓Visceral fat<br>↑Insulin sensitivity | [53] |
| Dietary fibre | ↑*Prevotella*<br>↑*Lactobacillus*<br>↑*Ruminococcus bromii*<br>↓*Firmicutes* | ↑SCFA synthesis<br>↓Body mass | [49] |
| Inulin | ↑*Actinobacteria*<br>↓*Clostridia*<br>↓*B. obeum*<br>↓*B. luti*<br>↓*B. faecis*<br>↓*R. faecis*<br>↓*Oscillibacter*<br>↑*Bifidobacterium*<br>↑*Catenibacterium*<br>↓*Desulfovibrio*<br>↓*Roseburia* | ↑Insulin sensitivity<br>↓Body weight<br>↓BMI<br>↓Fat mass<br>↓Visceral fat | [54,55] |

**Table 2.** *Cont.*

| Diet or Dietary Pattern | Impact on Microbiome | Impact on Host | Reference |
|---|---|---|---|
| Mixed fibre (mixture of soluble and insoluble fiber with a greater proportion of insoluble) | ↑*Barnesiellaceae*<br>↑*Lachnospira*<br>↓*Actinomycetaceae*<br>↓*Enterobacteriaceae* | ↑Acetate production<br>↓Isovalerate production<br>Moderate effect on microbiota composition | [56,57] |
| Resistant starch | ↓*Firmicutes*<br>↑*Bacteroidetes* | ↓Abdominal fat | [58] |
| Polyphenols | ↑*Lactobacillus*<br>↑*Bifidobacterium*<br>↑*Akkermansia muciniphila*<br>↓*Clostridium* | Increase or maintenance of body mass<br>↓Inflammation | [48,59,60] |
| Western diet | ↑*E. coli*<br>↑*Firmicutes*<br>↑*Alistipes*<br>↑*Bilophila*<br>↑*Bacteroides*<br>↓*Roseburia*<br>↓*Eubacterium rectale*<br>↓*Ruminococcus bromii* | ↑Dysbiosis<br>↑Inflammation<br>↑Obesity<br>↑Inflammatory bowel disease | [42,49,51] |
| High saturated fat | ↑*Proteobacteria*<br>↑*Firmicutes*<br>↓*Bacteroidetes*<br>↓*Akkermansia muciniphilia*<br>↑*Anaerotruncus genus*<br>↑*Eisenbergiella*<br>↑*Lachnospiraceae*<br>↑*Campylobacter*<br>↑*Flavonifractor*<br>↑*Erysipelatoclostridium* | Correlations with obesity<br>Weight gain<br>↓Gut microbiome diversity | [6,49,61,62] |
| High protein | ↑*Bacteroides*<br>↑*Faecalibacterium*<br>↑*Sutterella*<br>↑*Clostridium*<br>↑*Eisenbergiella*<br>↓*Bifidobacterium*<br>↓*Roseburia* | ↓SCFA synthesis<br>↑Formation of nitrogen compounds | [49,63–65] |
| High sugar | ↑*Acinetobacter*<br>↑*Blautia*<br>↑*Dorea*<br>↑*Lactococcus*<br>↑*Escherichia coli*<br>↑*Proteobacteria*<br>↓*Bacteroidetes* | Bacterial overgrowth associated with obesity<br>↑Production of endogenous ethanol<br>↑The risk of non-alcoholic fatty liver disease<br>↑Pro-inflammatory properties promoting metabolic endotoxemia and low-grade inflammation | [66–68] |
| Fermented foods | ↑*All gut diversity* | ↓Inflammation<br>Body mass maintenance | [69,70] |
| *Fasting* | ↑*Akkermansia muciniphilia*<br>↑*Spirochaetes*<br>↑*Roseburia* | ↓Body fat<br>↑SCFA production<br>↓Levels of LPS | [38,71,72] |

## 6. Impact of Lifestyle and Environmental Factors on the Gut Microbiome

Besides diet, several lifestyle and environmental factors play a role in the development and subsequent influence on the normal gut microbiota, and can affect our body weight (Table 3).

**Table 3.** Effect of certain lifestyle and environmental factors on gut microbiota ↑: increased; ↓: decreased.

| Lifestyle and Environment Factors | Model | Impact on Microbiome | Impact on Host | Reference |
|---|---|---|---|---|
| Birth by caesarean section | 6–12 month old infants | ↑*Staphylococcus*<br>↓*Bacteroidetes* | ↑Risk of obesity | [73,74] |
| Maternal smoking | 3 month old infants | ↑*Firmicutes* | ↑Risk of obesity between 0–3 years | [75] |
| Antibiotics consumption | Healthy children | ↓*Bifidobacterium*<br>↓*Akkermansia muciniphilia* | ↑Risk of obesity | [76] |
| Stress | Norwegian soldiers | ↑*Firmicutes*<br>↓*Bacteroidetes* | Increase in intestinal permeability under stress | [77] |
| Physical activity | Subjects with prediabetes and type 2 diabetes | ↓*Firmucites*<br>↑*Bacteroidetes*<br>↑Clostridium genus | ↓Endotoxemia<br>↑Insulin sensitivity | [78] |
| Alcohol | Alcohol dependent patients with high or low intestinal permeability | ↓*Ruminococcus*<br>↓*Faecalibacterium*<br>↓*Subdoligranulum*<br>↓*Oscillibacter*<br>↓*Anaerofilum* | ↓In the overall bacterial load lead to dysbiosis | [79] |

A high carbohydrate and fat diet leads to dysbiosis, decreasing the expression of angiopoietin-like protein 4 (Angptl4), the protein that regulates lipid metabolism, [12], resulting in an increase in lipoprotein lipase (LPL) activity, causing elevated uptake of fatty acids, increased fat storage, and fat accumulation in peripheral tissues [80]. This may be one of the mechanisms of gut-bacteria-induced obesity.

High-fat diets reduce the population of *Bifidobacterium* spp., *Lactobacillus* spp., and *Prevotella* spp., and play a role in the overactivation of the endocannabinoid system [6,61]. These changes can adversely alter the gut microbial composition, leading to increased gut permeability, thus, allowing translocation [6,61]. However, changes in the gut microbiota also depend on the type of fatty acids ingested. Omega-3 intake is directly related to the growth of *Lactobacillus*, whereas monounsaturated fatty acids (MUFA) and omega-6 polyunsaturated fatty acids (PUFA) are inversely related to the growth of Bifidobacterium [47]. Furthermore, high-fat diets increase the overgrowth of Gram-negative pathogens, promoting the diffusion of bacterial fragments such as lipopolysaccharides (LPS) across the intestinal barrier. The LPS endotoxin can activate the nuclear factor kappa B (NF-κB) pathway in the bloodstream. LPS can activate the NF-κB pathway in the blood, and it functions as a ligand for Toll-like receptors with a proinflammatory cytokine CD14 (cluster of differentiation 14), causing an increased intestinal permeability, thereby facilitating the weight gain process. LPS translocation caused by a high-fat diet may be associated with low-grade chronic inflammation induced by obesity [81].

In high-protein diets, *Bacteroides* and *Propionibacterium* species convert dietary proteins into amino acids and their derivatives (ammonia, amines, phenols, and sulphides) [63]. Gut health may be compromised by increasing the protein content of the diet, but recent data are unclear about a probable link with obesity.

A total of 40 overweight or obese individuals were randomized to high protein and calorie-restricted diets for 8 weeks. The dietary intervention changed the microbial composition and diversity, increased the relative abundance of *Akkermansia* spp. and *Bifidobacterium* spp., and decreased the enrichment of *Prevotella*-9 [82], which increases in obesity [83].

According to epidemiological data, a high intake of dietary fibre is beneficial for maintaining a normal body weight. Prebiotics are non-digestible oligosaccharides that can

stimulate the growth of selective and beneficial intestinal bacteria, especially *Lactobacilli* and *Bifidobacteria* [84]. From indigestible fibers, some bacteria species can produce metabolites and short-chain fatty acids (SCFA), including acetate, propionate, and butyrate, during fermentation, playing a metabolic role in the regulation of energy expenditure and may influence the pathogenesis of obesity [85]. High fibre intake is associated with an increase in the gut microbiome of *Prevotella*, *Lactobacillus,* and *Ruminococcus bromii* species, among others, and a decrease in *Firmicutes* strain members, and these characteristics are associated with lower body weight [49]. However, the correlation between obesity and short-chain fatty acids is not yet fully clarified. SCFAs are considered to contribute about 200 kcal/day to the human energy balance. Short-chain fatty acids are released into the bloodstream and then bind to G-protein-coupled receptors, participating in cellular signaling pathways including lipid, glucose, and cholesterol metabolism [85]. In high-carbohydrate diets and obesity, the binding of SCFAs as signal transduction molecules to G-protein-coupled receptors may be impaired, leading to increased intestinal energy storage and hepatic lipogenesis. The acetate produced functions as a precursor for acetyl-CoA and fatty acids for de novo lipogenesis in the liver, thus, the overproduction of acetate may contribute to obesity [86]. Not all short-chain fatty acids have the same metabolic effects, as propionate is gluconeogenic in the liver, whereas butyrate and the previously mentioned acetate are lipogenic, but results from studies in humans are controversial [85]. Riva et al. reported that obese children had more SCFA in their stools than non-obese children, and this was positively correlated with a higher BMI Z score, and a higher proportion of *Firmicutes* and lower proportion of *Bacteroidetes* in the gut [87].

The prebiotic found in nature is inulin, its dietary sources include asparagus, Jerusalem artichokes, artichokes, onions, garlic, bananas, oats, and soya. However, these dietary sources are not considered to be biologically valuable, as a daily intake of 4–8 g of fructooligosaccharide would significantly increase the *Bifidobacteria* [32,88]. In overweight young children, after 16 weeks of supplementation with oligofructose-enriched inulin, body weight decreased by 3.1% and body fat by 2.4%, compared to children taking a placebo [89,90]. The prebiotic selectively altered the gut microbiota by causing a significant increase in *Bifidobacterium spp*. and a decrease in *Bacteroides vulgatus* [90]. Kaczmarek et. al. carried out a study based on broccoli consumption to investigate the effect of fibre on the gut microbiota. The study suggests that consuming broccoli decreases the relative abundance of *Firmicutes* by 9%, while increasing the abundance of *Bacteroidetes* by 10%, and increased the relative abundance of *Bacteroides* by 8% compared to the control group [91].

In a randomised controlled trial, overweight or obese subjects were divided into three groups, with one group consuming wholegrain cereals, a second group consuming fruit and vegetables, and a control group consuming a diet of refined cereals for 6 weeks. Significant reductions in LPS were found in the group consuming whole grains and the group consuming fruits/vegetables. Fruit and vegetable consumption significantly reduced interleukin-6 (IL-6), whereas the whole grain diet significantly reduced tumor necrosis factor alpha (TNF-α) levels [92,93]. There is also a potential benefit to consuming probiotics in the form of fermented foods such as fermented vegetables, tempeh, miso, pickles, sauerkraut, kimchi, kombucha, and other beverages such as apple cider vinegar and fermented dairy products. These foods may be effective in maintaining body weight, balancing intestinal permeability and barrier functions, and controlling dysbiosis [94]. In a randomised clinical trial of obese Korean women, consumption of fermented kimchi for 8 weeks increased the relative abundance of *Bacteroides* and *Prevotella,* and caused a non-significant reduction in body weight, waist circumference, and body fat percentage. Bacteroides show a negative correlation with obesity, and *Prevotella* is the dominant genus in the microbiota of individuals who follow a low-fat, high-fibre diet [95].

Another clinical study proved the beneficial effects of kimchi on the gut microbiota; kimchi interventions resulted in higher abundance of SCFA-producing genera such as *Phascolarctobacterium, Faecalibacterium,* and *Roseburia* [96].

During a 4 week weight-loss intervention, obese participants consumed 30 g of fermented cheese per day. The natural probiotic intake increased the abundance of *Lactobacillales*, *Streptococcaceae*, *Lactococcus,* and *Streptococcus*, as well as SCFA-producing *Phascolarctobacterium* and *Butyricimonas* [97].

Interestingly, the excessive use of food additives such as emulsifiers may be connected to the obesity crisis. These substances can alter the gut microbiome and cause dysbiosis, and these changes contribute to many undesirable conditions such as obesity, inflammation, and metabolic syndrome inflammatory bowel diseases [98–100].

Animal studies show an association between prenatal and perinatal antibiotic use and an increased risk of childhood obesity [101]. Mice treated with low-dose penicillin at birth had a greater increase in body weight at weaning compared to control mice. Following 4 weeks of antibiotic administration, adult mice showed increased body weight and fat mass from 20 weeks of age. According to the authors, this was not a consequence of prolonged dysbiosis, as the microbiota recovered 4 weeks after treatment was stopped, but they believe that a long-term effect of a temporary disruption of the gut microbiota may be responsible. Other studies report that antibiotic use can increase the risk of obesity in healthy children associated with a decrease in *Bifidobacterium*, *Akkermansia muciniphilia*, while abnormal obesity has been reported in patients with Q-fever endocarditis with a decrease in *Bacteroidetes* and *Lactobacillus* and an increase in *Firmicutes* [76,102].

Physical activity has an impact on the gastrointestinal system, as it can reduce the transit time of faeces, increase the number of beneficial microbial species, and enrich its diversity [103]. Both moderate intensity and intense physical activity can reduce endotoxemia and improve insulin sensitivity and *Firmicutes/Bacteroidetes* ratio [78]. Moreover, athletes tend to have more *Akkermansia muciniphilia,* associated with a lower BMI, compared to non-athletes [104].

For many years, the infant's gut was considered sterile and was thought to be colonized after birth by the maternal microbiota, diet, and environment. Recent research suggests that microbial colonization of the infant starts before birth because the womb is not sterile [105]. Several researchers question the evidence for the "intrauterine colonisation hypothesis" due to the controversial results. However, this area of research is currently under debate [106]. Earlier findings suggest that microbial exposure can start during pregnancy, and colonization with microbes from the maternal microbiota and the environment begins immediately after birth [107]. The mode of delivery influences differences in the composition of the gut microbiome of infants, which persist for at least 6 months after birth [108]. There is a link between caesarean delivery and childhood obesity, suspected to affect later body weight [74,109–112]. Birth by caesarean section, especially if the mother was overweight or obese, increases the risk of overweight or obesity in the first 3 years of life [74,112]. The main difference is that vaginally born infants typically have higher concentrations of *Bacteroides*, *Bifidobacteria,* and *Lactobacillus* in the first days of life and greater microbial variability in the following weeks. The microbiome of infants born by caesarean section, similar to the maternal skin and the hospital environment, is mainly composed of *Staphylococcus, Streptococcus,* and *Clostridium* [113]. A cohort study monitoring the body mass of 943 infants born vaginally and 362 by caesarean section found that the mean BMI of infants born by caesarean section was significantly higher than that of infants born vaginally six months after birth. However, no significant differences were found in the BMI of the children at either 2 or 5 years of age, thus, it is suggested that the method of birth has no long-term effect on the children's BMI [114]. Infant feeding is also found to be a significant factor in the risk of obesity, as breastfeeding is a protective factor against childhood obesity, increasing intestinal *Bifidobacteriaceae, Veillonellaceae* species, and diversity in 12 month old infants [115].

In addition to these factors, alcohol leads to a drastic reduction in several beneficial species (*Akkermansia muciniphilia, Faecalibacterium prausnitzii, Lactobacillus*), and, therefore, has the potential to contribute to microbiome imbalances and dysbiosis. It also contributes to intestinal hyperpermeability, leading to inflammation through the influx of LPS [116].

Obesity is multifactorial, influenced by several factors. Figure 1 summarizes the influence of both dietary and environmental factors.

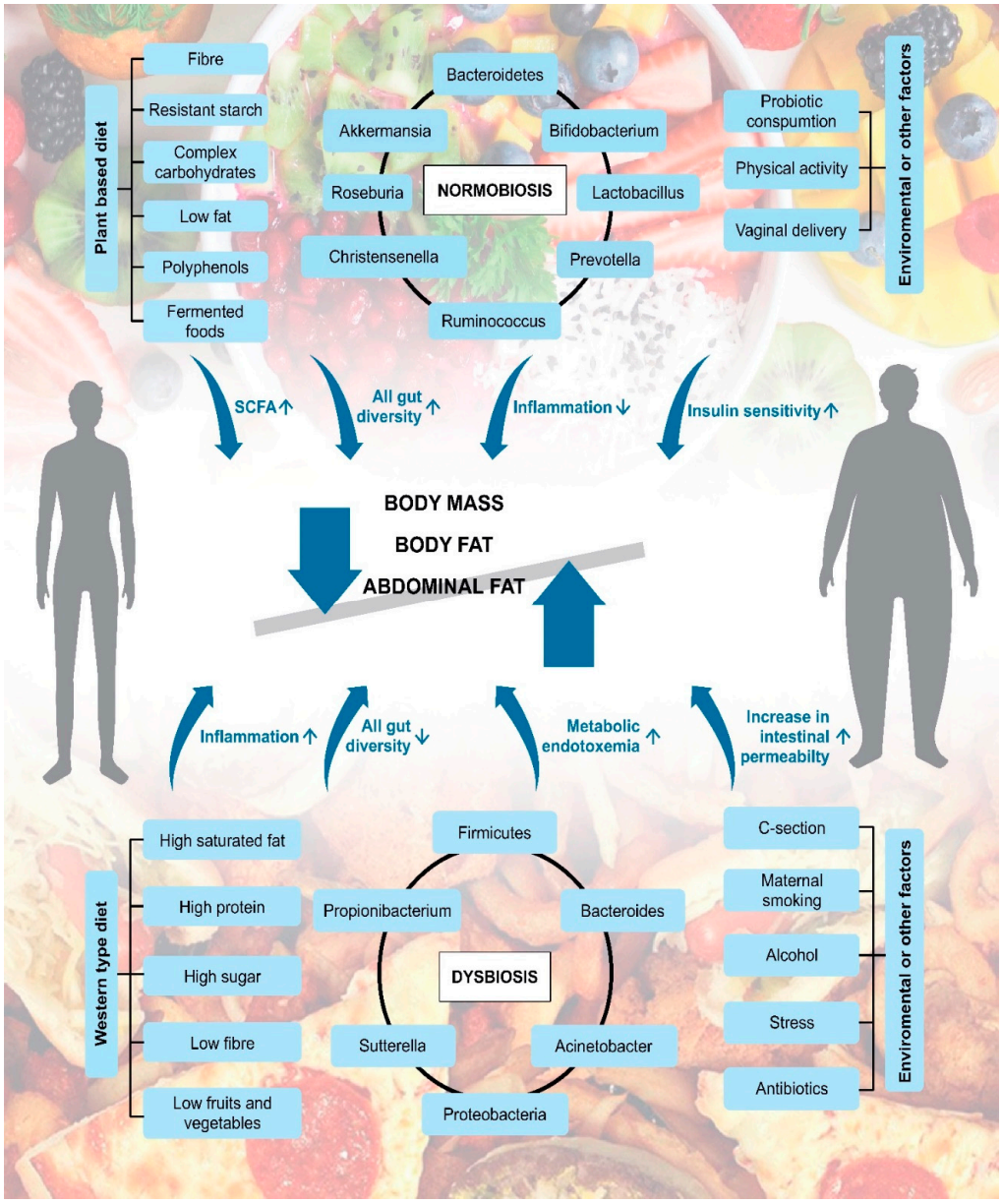


**Figure 1.** Dietary and environmental factors influencing the growth of some bacteria responsible for normobiosis or dysbiosis, causing an increase or decrease in body weight through various mechanisms.

## 7. Conclusions

Current evidence suggests that changes in the gut microbiota composition may contribute to the pathogenesis of obesity. The results of studies confirm that altering the composition of the gut microbiota may be an additional effective way to achieve stable weight loss. Possible strategies for the prevention and/or treatment of obesity include restoring or modifying the composition of the microbiota by consuming probiotics and prebiotics, fermented foods, fruits, vegetables, and avoiding foods of animal origin high in saturated fat and sugar. Further studies are needed to better understand the mechanisms of the observed association between the gut microbiota and obesity, the role of the gut microbiota, and to determine whether manipulation of the gut microbiota through diet,

with or without increased intake of pre/probiotics, may offer potential therapeutic options for obesity prevention.

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