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HOW THE MICROBIOME RESHAPES OBESITY RESEARCH: FROM ALTERED GUT MICROBIAL COMPOSITION TO IMPORTANT CO-FACTOR IN WEIGHT LOSS STRATEGIES

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Abstract – ***Introduction:*** Obesity has become one of the most common chronic conditions, causing a large number of comorbidities. During the last decades, a growing number of studies have associated obesity with altered microbiome composition. Moreover, numerous studies reported the effects of diet- and surgery-induced weight loss on the microbiome. This narrative review aims to give an overview of studies published between 2021 and early 2022 about the microbiome in obesity.
Material and Methods: A literature search using the search term 'Obesity AND (Microbiota OR Microbiome)' was conducted in Medline. Only research studies in humans published between March 2021 and March 2022 were eligible for inclusion.
Results: Out of 1877 studies, 69 discussed the microbiome composition in obesity or reported how weight loss by a diet or bariatric surgery influenced the microbiome. In general, obesity is associated with the upregulation of the Firmicutes phylum compared to the Bacteroidetes phylum. However, the microbiome is also modified due to changes at all levels of the microbiome. No studies were able to unravel a causal link between certain microbial patterns and the development of obesity. The intestinal microbiome in obesity was affected by genetic, environmental, and phenotypic factors. Similarly, weight loss was also associated with extensive modifications of the gut microbiome. More changes in the microbiome were seen after bariatric surgery compared to diet-induced weight loss.
Conclusions: Although a large number of studies have demonstrated that obesity and weight loss modify the intestinal microbiome, it is unclear how these changes occur. Future studies should focus on the mechanisms by which the microbiome interacts with the metabolism in obesity.

Keywords: Obesity, Microbiome, Bariatric surgery.

Abbreviations: F/B ratio: Firmicutes/Bacteroidetes ratio; NS: Not Significant; N/A: Not Available; RYGB: Roux-en-Y Gastric Bypass; SG: Sleeve Gastrectomy; BPD: Biliopancreatic Diversion.

INTRODUCTION

During the last decades, obesity has become one of the most frequently encountered chronic conditions in the Western World. Recent numbers of the World Health Organization

indicate that the worldwide prevalence of obesity has tripled since 1975 with over 650 million being obese in 2016[1]. Meanwhile, global obesity rates rose tenfold in children and adolescents[2]. The strong association of obesity with multiple acute and chronic medical comorbidities, such as cardiovascular disease, type 2 diabetes, sleep apnea, and cancer has led to a strongly increased scientific interest in the prevention, pathophysiology, and treatment of obesity.

One of these promising and blooming topics in the field of obesity research is the involvement of microbiota in the pathology and management of obesity. This recently increased interest in the function of the microbiome in health and disease has led to a massive surge in the number of papers published. According to Medline, only 105 papers reported on the role of the microbiome in obesity in 2011. Ten years later, the yearly number of publications on this subject has risen to 1600 publications. These studies cover a wide range of topics and discuss subjects such as the role of microbiota in the development, pathophysiology, and treatment of obesity. Meanwhile, other studies investigate how microbiota and the microbiome affect the progression of obesity into a life-threatening metabolic syndrome characterized by complications, such as diabetes and cardiovascular disease. Due to the strong growth in the number of publications, that cover a wide range of topics within the domain of microbiome research, staying up to date has become a real challenge. For this reason, this narrative review aims to provide an overview of the literature published during the last year on the microbiome composition in obesity and how microbiota diversity changes during conventional and surgery-induced weight loss.

MATERIALS AND METHODS

A literature review was performed in Medline using the search term 'Obesity AND (Microbiota OR Microbiome)'. Only studies published between March 2021 and March 2022 were included. Papers not in English were also excluded. Subsequently, all studies were screened on their topic and methodology. During this selection process, only studies covering the microbiome composition or discussing the effects of diets and bariatric surgery on the microbiome were selected for inclusion. Reviews, experimental studies in animal models, or manuscripts discussing the microbiome in unrelated medical conditions were excluded.

RESULTS

Between January 2000 and March 2022, a total of 7566 publications about obesity and microbiota were indexed. Out of these, 1877 unique studies (25.0%) were published between March 2021 and March 2022, and thus, eligible for inclusion. A large bulk of these studies were reviews or editorials (n=689), which were excluded. Furthermore, the topic shifted during the last two decades. While initially studies mostly investigated the differences between lean and obese subjects in terms of microbiome composition, current research is more focused on determining how the microbiome affects weight loss, determines outcomes of other diseases in obese patients, or describes how lifestyle, diet or probiotics modulate the microbiome in obese patients (Figure 1). Eventually, the full-text version of only 69 articles was reviewed for this review. A selection of these studies contained information that fully fitted within the scope of this review.

DISCUSSION

The Microbiome in Obese Subjects

During the last decade, a large number of studies[3-9] have been focusing on the composition of the gut microbiome in obese subjects and how it differs from lean subjects. Several studies[3-9] described significant differences in microbiome composition between obese and lean subjects (Table I). In short, a significantly increased presence of taxa belonging to the

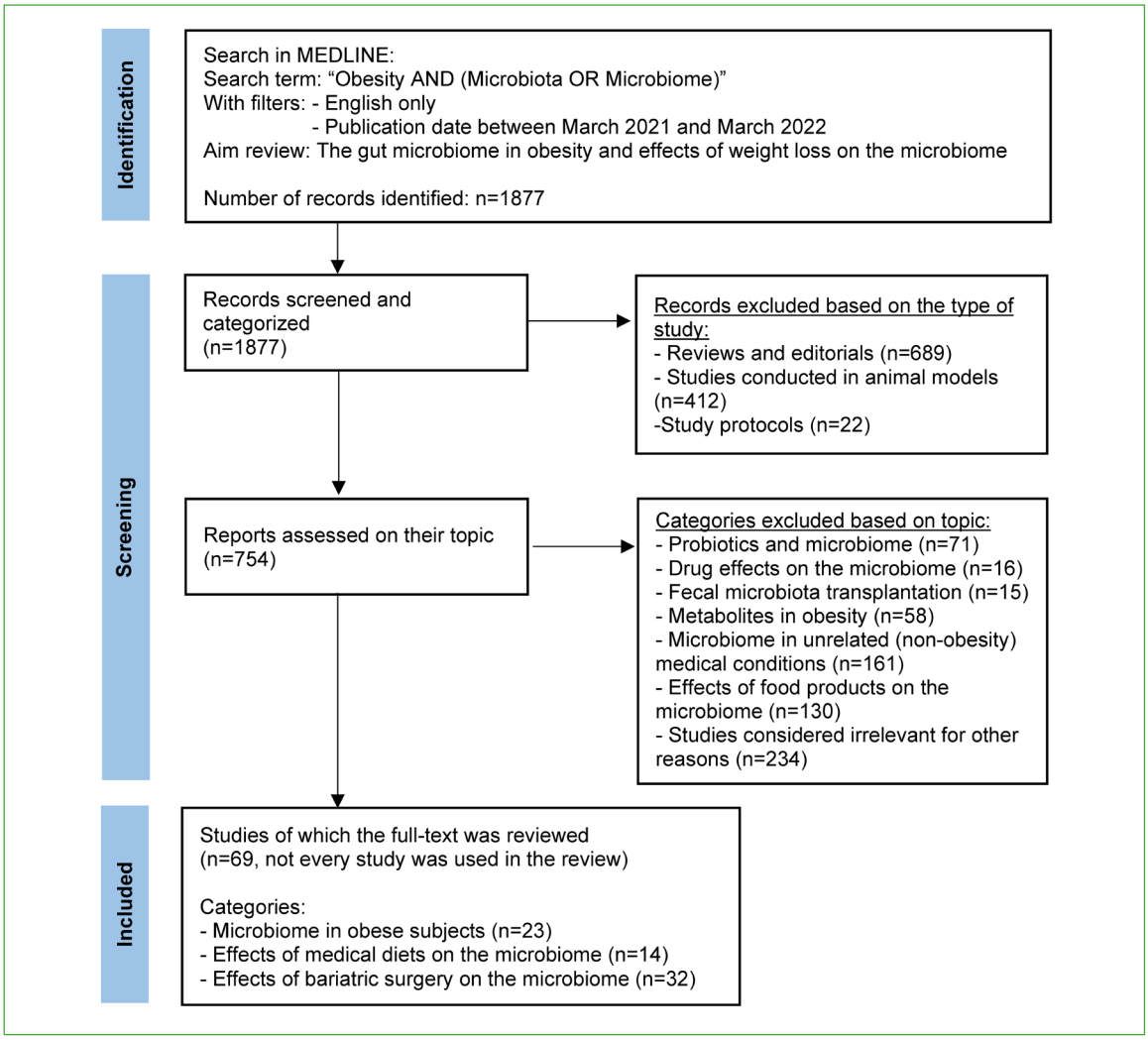

Figure 1. Screening and selection flow chart. Overview of the screening and selection process. The literature search in Medline with the search term "Obesity AND (Microbiota OR Microbiome)" was conducted on March 29, 2022 selecting studies published from March 2021 until March 2022. Only studies describing the microbiome in obese subjects or reporting on the effects of conventional medical diets or bariatric surgery on the microbiome were selected for this review. Not every study assessed in the final step was included in the review because some lacked necessary information.

Firmicutes phylum (*Lachnospiraceae, Gemellaceae, Paenibacillaceae, Streptococcaceae, Thermicanaceae, Gemella, Mitsuokella, Streptococcus, Acidaminococcus spp., Eubacterium spp., Ruminococcus spp., Megamonas spp., Streptococcus, Thermicanus, Megasphaera spp. and Veillonella spp.*) is seen in people with obesity[5,7]. Meanwhile, a significant reduction in taxa of the Bacteroidetes phylum (*Flavobacteriaceae, Porphyromonadaceae, Sphingobacteriaceae, Flavobacterium, Rikenella spp., Pedobacter spp., Parabacteroides spp., Bacteroides spp.*) and Proteobacteria phylum (*Candidatus Blochmannia rufpes*) was observed[5,7,10]. These changes are typically illustrated by the Firmicutes-Bacteroidetes ratio. Other studies[11-13] confirmed this composition but also showed that alterations in gut microbiota in obese subjects depend on phenotypical, ethnical and geographical properties as well.

Additionally, recent literature[14-16] has investigated the role of the gut virome in the development of obesity. In their study, Yang et al[14] demonstrated differences in the fecal viral distribution between obese and lean subjects (e.g., Geobacillus phage). In contrast, no such difference was seen in another study[15] in a pediatric population. Finally, seropositivity for certain members of the Herpesviridae family, most dominantly herpes simplex virus 1, was also reported to be higher in obese subjects16. Similarly, it is unknown by which mechanisms the virome would affect obesity.

TABLE 1. ALTERED MICROBIOME COMPOSITION IN OBESITY AT THE PHYLUM AND GENUS LEVEL.

Author, year	Age group	F/B ratio	Phylum level		Genus level	
			Increased in obesity	Decreased in obesity	Increased in obesity	Decreased in obesity
Atzeni et al[3], 2021	Adult	NS			None	None
Chen et al[4], 2022	Pediatric	N/A			*Sutterella* (p=0.020)	*Oscillospira* (p=0.001)
Companys et al[5], 2021	Adult	Increased	Actinobacteria (p<0.001), Firmicutes (p=0.056), Euryarchaeota (p<0.001)	Tenericutes (p<0.001), Lentisphaerae (p=0.013), Bacteroidetes (p=0.021)	No Differences	No Differences
Duan et al[6], 2021	Adult	Decreased	Bacteroidetes (p<0.001), Fusobacteria (p=0.028)	Firmicutes (p<0.001), Actinobacteria (p=0.018)	*Prevotella* (p=0.004), *Megamonas* (p=0.004), *Blautia* (p=0.022), *Fusobacterium* (p=0.031)	Alistipes (p<0.001), *Faecalibacterium* (p< 0.001), *Oscillibacter* (p<0.001), *Lachnospiracea* (p<0.001), *Clostridium* (p<0.001), *Barnesiella* (p<0.001), *Gemmiger* (p = 0.002), *Parabacteroides* (p=0.023), *Coprococcus* (p=0.032), *Ruminococcus* (p=0.040), Bifidobacterium (p=0.043)
Palmas et al[7], 2021	Adult	Increased	Firmicutes (Sig)	Bacteroidetes (Sig), Proteobacteria (Sig)	*Acidaminococcus* (Sig), *Eubacterium* (Sig), *Gemella* (Sig), *Ruminococcus* (Sig), *Megamonas* (Sig), *Mitsuokella* (Sig), *Streptococcus* (Sig), *Thermicanus* (Sig), *Veillonella* (Sig), *Megasphaera* (Sig), *Desulfovibrio* (Sig), *Enterobacter* (Sig), *Escherichia* (Sig), *Klebsiella* (Sig), *Serratia* (Sig)	*Bacteroides* (Sig), *Flavobacterium* (Sig), *Rikenella* (Sig), *Pedobacter* (Sig), *Sphingobacterium* (Sig), *Parabacteroides* (Sig), *Oscillospira* (Sig), *Candidatus Blochmannia* (Sig), *Sutterella* (Sig)
Qin et al[8], 2021	Adult	NS	No differences	No differences		
Stefura et a[l9], 2021	Adult	N/A			*Ruminococcus* (Sig)	*Bacteroides* (Sig), *Odoribacter* (Sig), *Blautia* (Sig), *Parabacteroides* (Sig)

Role of Microbiota in the Development of Obesity

Although to date some scholars[17] have described an association of altered microbiota composition with obesity, the causality between these changes and the development of obesity is often unclear. In fact, the development of obesity seems to be a multifactorial process, depending on genetics, environmental factors, dietary factors and lifestyle[18,19]. Moreover, obesity is not just something that develops from one day to another, it requires time to develop. For this reason, causality studies often fail because they are unable to adjust for the large number of confounding factors. One study[10] in 2021 analyzed gut microbiota of 1126 twin pairs of the TwinsUK study. While adjusting for numerous covariates, including age, gender and genetic data, the study discovered a significant positive association between the *Lachnospiraceae* family and the truncal fat mass[10]. In contrast, the abundance of the *Bifidobacterium* genus and presence of *Faecalibacterium prausnitzii* were negatively associated with obesity[10]. While these observations are in line with previous results in observational studies[20], a clear mechanistic explanation for the association remains to be established. Furthermore, although correcting for covariates, the mean age of the participants was 59 years indicating a lot of room for interference from lifestyle and environmental factors.

Effect of Weight Loss on the Gut Microbiome

With worldwide obesity rates on the rise, obesity nowadays is considered a global pandemic. Correspondingly, weight loss has become one of the most studied topics in current medical research. Numerous weight-loss strategies have been developed. Although conventional weight loss by diet and lifestyle changes is still the most practiced method to lose weight, the number of surgical interventions for obesity, grouped under the term bariatric surgery or metabolic surgery, have strongly increased during the last decades. Together with the uprise in microbiome research, studies investigating the interaction between conventional or surgery-induced weight loss and microbiota are published on a daily base. In the following two sections of this review, we summarize some of the key findings published during the last year and discuss how such findings could influence daily clinical practice.

The Microbiome During Conventional Weight Loss

To date, a large number of studies[17] have investigated how weight loss through certain diets and lifestyle modifications affect the microbiome. Between 2021 and 2022 numerous new studies have emerged, confirming earlier studies or bringing new ideas to the microbiome table. One of the first remarkable observations is that, in general, the diversity of the microbiome is only altered to a limited extent. This is shown by the fact that most studies that investigated the effects of diet-induced weight loss observed no differences with 16SrRNA gene sequencing on the alpha and beta diversity. It is not clear why in some other studies[21-26], overall diversity was nevertheless significantly modified (Table II). One reason could be that overall microbial diversity is a poor marker in showing the effects of an intervention. This was seen in the study of Alili et al[27] where stratification of subjects in a pre-intervention low and high diversity group, did result in a significant alpha and beta diversity within these groups. Similarly, seemingly unaffected overall diversities proved to be significant but only in a subpopulation (e.g., men, children)[21,22]. Additionally, in some studies[21,23,24] the alpha diversity was significantly altered as demonstrated by the Shannon index and indicating a modulated within-sample diversity, yet the beta between-sample diversity was unaffected and vice versa. Another reason could be the influence of external factors beyond the diet itself.

Specific changes in the microbiome at the phylum and genus level are displayed in Table II. Few studies[21,22,25,26,28] did focus on finding how diet influenced the microbiome at the phylum level. Those who did, observed an altered presence of different microbial phyla. However, no clear pattern was present at the phylum level. Bacteroidetes and Firmicutes numbers were frequently affected by a diet, yet while in the studies of Cho[21] and Cuevas-Sierra et al[22] the amount of Firmicutes increased and the number of Bacteroidetes decreased, the opposite was seen by

TABLE 2. WEIGHT LOSS-INDUCED INTESTINAL MICROBIOMAL COMPOSITION CHANGES AT THE PHYLUM AND GENUS LEVEL.

Author, year	Diet length	Sample size	Microbial diversity		Phylum level		Genus level	
			Alpha	Beta	Increased by diet	Decreased by diet	Increased by diet	Decreased by diet
Alili et al[27], 2021	3 m	163	NS†	NS†			*Bacteroides 1* (Sig)	*Bacteroides 2* (Sig)
Benitez-Paez et al[46], 2021	12 w	80	NS	NS†				
Biemann et al[29], 2021	6 m	33	NS	NS				
Cho[21], 2021	57 d	17	$p<0.05$	NS	Firmicutes ($p=0.009$)	Bacteroidetes ($p=0.014$)	NS	*Bacteroides* ($p<0>05$)
Cuevas-Sierra et al[22], 2021	4 m	179	$p=0.02$†	$p=0.01$†	Firmicutes (NS, trend)	Bacteroidetes (NS, trend)	*Peptococcus* ($p=0.04$)	*Acidaminococcus* ($p=0.02$)
Diener et al[28], 2021	6-12 m	105	N/A	N/A	Bacteroidetes ($p=0.002$), Verrucomicrobia (<0.01)	Actinobacteria ($p<0.001$)		
Dong et al[23], 2021	16 w	80	NS	$p=0.001$			*Coprococcus* ($p<0.05$), *Collinsella* ($p<0.05$)	*Enterococcus* ($p<0.05$), *Klebsiella* ($p<0.05$)
Gutiérrez-Repiso et al[24], 2021	6 m	39	$p=0.016$	NS			*Parabacteroides* ($p<0.05$), *Alistipes* ($p<0.05$)	*Lactobacillus* ($p<0.05$)

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TABLE 2 *(CONTINUED)*. WEIGHT LOSS-INDUCED INTESTINAL MICROBIOMAL COMPOSITION CHANGES AT THE PHYLUM AND GENUS LEVEL.

Author, year	Diet length	Sample size	Microbial diversity		Phylum level		Genus level	
			Alpha	Beta	Increased by diet	Decreased by diet	Increased by diet	Decreased by diet
Nogacka et al[47], 2021	6-8 m	18	NS	N/A			*Clostridium sensu stricto 1* ($p<0.01$)	*Parabacteroides*, ($p<0.05$) *Bacteroides* ($p<0.01$)
Stanislawski et al[25], 2021	3 m	55	$p<0.001$	$p<0.001$	Bacteroidetes (Sig)	Firmicutes (Sig)	*Lachnoclostridium*, ($p=0.02$) *Ruminococcus* ($p=0.04$), *Phascolarctobacterium* ($p=0.04$), *Bacteroides* ($p<0.1$) *Alistipes* ($p<0.1$) Parabacteroides ($p<0.1$)	Coprococcus 3 ($p=0.02$), *Subdoligranulum* ($p<0.1$), Collinsella ($p<0.1$)
Yu et al[26], 2022	20-231 d	65	$p=0.031$	$p=0.001$	Bacteroidetes (Sig)	Firmicutes (Sig), Proteobacteria (Sig)	Parabacteroides ($p<0.05$), Bacteroides ($p<0.05$)	*Ruminococcus 2* ($p<0.05$), Lachnoclostridium ($p<0.05$), Parasutterella ($p<0.05$), *Escherichia-Shigella* ($p<0.05$), *Klebsiella* ($p<0.05$)
Yuan et al[48], 2021	12 w	15	NS	NS	NS	NS	*Ruminococcus* ($p<0.05$), *Holemania* ($p<0.05$)	*Eubacterium* ($p<0.05$), *Pseudomonas* ($p<0.05$), *Blautia* ($p<0.05$)

m, months; w, weeks; d, days; NS, not significant; N/A, not available; Sig, indicated as significant difference but no p-values available. Changes in alpha and beta diversity are indicated by their corresponding p-value. †Alpha and/or beta diversity was significant after stratification into certain subgroups but not overall significant.

Yu et al[25], Stanislawski et al[26] and Diener et al[28] (Table II). These differences also translated to the genus and species level with the presence of genera *Bacteroides*, *Alistipes* and *Parabacteroides* most often being altered by a diet. Other studies described alterations in the microbiome composition at different levels. Biemann et al[29] noticed significantly increased levels of the *Desulfovibrionaceae*, *Syntrophomonadaceae,* and *Thermotogaceae* families, while members of the *Leptospiraceae* family significantly decreased. Similarly, diet-induced changes in the *Clostridiaceae* and *Lachnospiraceae* families have been reported[24,25]. All these changes on the phylum, family and genus level were caused by increased diversity at the species level.

Although studies[21-29] seem to indicate that the microbiome is indeed highly affected during dietary attempts to lose weight, it is currently unclear whether the changed microbial composition is just a by-product of the diet change or whether altered microbiota play a leading role in achieving weight loss. Therefore, some scholars[30] are now focusing on determining which modifications in the microbiome increase the probability of having a successful weight loss. Other studies[25,31,32] are looking into methods to assess whether the pre-diet microbiome composition can predict the amount of weight loss that is to be expected with a certain diet or behavioral intervention. Although current research is still in an early stage and requires expansion to large cohorts, the ability to predict how successful one can be with a certain diet could have a significant clinical impact. It could potentially assist clinicians in choosing the most suitable diet for the right patient, thus increasing the success rates of conventional dietary measures.

Bariatric Surgery and the Microbiome

Although dietary measures can lead to significant weight loss, the amount of weight loss is usually limited to around <10% of the body weight. This was observed in the studies above, which described diet-induced weight loss; many of the participants reached less than 5% of weight loss or dropped out of the program. Bariatric or metabolic surgery has nowadays become one of the most successful methods of losing a significant portion of body weight. Such surgical procedures are based on creating an anatomical way of food restriction or intestinal malabsorption.

Throughout the years several surgical techniques have been developed. Currently, the gastric bypass procedure and sleeve gastrectomy are being used the most often. During a gastric bypass procedure, the stomach is surgically reduced in size, and the small intestine is rerouted by performing a Roux-en-Y reconstruction. In short, the reduced stomach, called the gastric pouch, is connected to an alimentary limb of around 100-150 cm. This alimentary limb is connected with the gastric remnant and biliary system by a biliopancreatic limb, thus forming a common limb. The result is a reduced stomach size limiting the food intake and lowering the food absorption.

The sleeve gastrectomy procedure converts the stomach into a tube-shaped structure by surgically removing around 80% of the stomach and thus restricting the amount of food a patient is able to consume. The rest of the intestinal tract remains unaffected following a sleeve gastrectomy.

During the last year, several studies[33-42] have been focusing on investigating changes in the microbiome following bariatric surgery (Table III). These studies[33-42] demonstrated highly altered fecal microbiome compositions after bariatric surgery and this on the phylum, family, genus and species level. These changes were usually already present within the first 6 months after bariatric surgery. Although some conflicting results were seen between studies, increased presence of the phyla Proteobacteria, Fusobacteria, and Verrucomicrobia were repeatedly observed. Two phyla typically altered in obesity, Firmicutes and Bacteroidetes, were decreased in three out of four and two out of four studies respectively (Table III). It is uncertain what caused these differences. On the family level, increased levels of *Enterobacteriaceae* and *Sinobacteriaceae* were detected, while the presence of *Clostridiaceae* and *Lachnospiraceae* decreased[38]. The majority of changes in the microbiome diversity can currently not be pathophysiologically explained. Moreover, it is currently unclear how bariatric procedures differ in terms of their effect on the microbiome. Unfortunately, many of the included studies failed to report differences in alpha and beta diversity.

TABLE 3. EFFECTS OF BARIATRIC SURGERY ON THE INTESTINAL MICROBIOMAL COMPOSITION.

Author, year	Follow-up	Sample size	Procedure	%BMI change	Microbial diversity		Phylum level		Genus level	
					Alpha	Beta	Increased by diet	Decreased by diet	Increased by diet	Decreased by diet
Ben Izhak et al[33], 2021	1.5 y	66	SG, RYGB, omega loop	-35.8%	N/A	N/A	Proteobacteria (Sig), Fusobacteria (Sig)	Firmicutes (Sig)		
Fouladi et al[34],	6 m	61	RYGB	N/A	NS	N/A			*Veillonella* (Sig), *Streptococcus* (Sig) *Gemella* (Sig), *Fusobacterium* (Sig), *Escherichia/* Shigella (Sig)	*Akkermansia*, (Sig), *Rothia* (Sig), *Actinomyces* (Sig), *Atopobium* (Sig), *Granulicatella* (Sig), *Blautia* (Sig)
Fukuda et al[35], 2022	12 m	10	SG	-24.1%	p=0.017	NS	Bacteroidetes (p=0.037), Fusobacteria (p=0.017)	NS		
Han et al[36], 2022	6 m	52	RYGB, SG	-20.0%	NS	p=0.001	Fusobacteria (Sig), Proteobacteria (Sig), Verrucomicrobia (Sig)	NS	*Streptococcus* (Sig), *Oscillospira* (Sig), *Akkermansia* (Sig)	*Bifidobacterium* (Sig), *Turicibacter* (Sig), *Prevotella* (Sig)
Hong et al[37], 2021	4 m	16	SG	-19.4%	N/A	N/A			*Clostridium* (Sig), *Streptococcus* (Sig)	NS

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TABLE 3 *(CONTINUED)*. EFFECTS OF BARIATRIC SURGERY ON THE INTESTINAL MICROBIOMAL COMPOSITION.

Author, year	Follow-up	Sample size	Procedure	%BMI change	Microbial diversity		Phylum level		Genus level	
					Alpha	Beta	Increased by diet	Decreased by diet	Increased by diet	Decreased by diet
Juárez-Fernández et al[38], 2021	4 y	9	SG, BPD, RYGB	-31.6 %	NS	N/A	Proteobacteria (p<0.05), Lentisphaerae (p<0.05)	Firmicutes (p<0.05)	*Butyricimonas* (p<0.05), *Parabacteroides* (p<0.05), *Slackia* (p<0.05)	*Acinetobacter* (p<0.05), *Coprococcus* (p<0.05), *Lachnospira* (p<0.05), *Lactococcus* (p<0.05), *Megamonas* (p<0.05), *Oribacterium* (p<0.05), *Phascolarctobacterium* (p<0.05)
Karami et al[39], 2021	6 m	30	SG, RYGB	-25.1 %	N/A	N/A	NS	Bacteroidetes (p<0.05)[†]		
Kural et al[40], 2022	N/A	27	SG	N/A	N/A	N/A	*Firmicutes* (p<0.001), *Verrucomicrobia* (p<0.001), *Lentisphaerae* (p<0.05)	Bacteroidetes (p<0.05)	*Akkermansia* (Sig), *Alistipes* (Sig), *Streptococcus* (Sig), *Ruminococcus* (Sig), *Parabacteroides* (Sig), *Bacteroides* (Sig)	
Lau et al[41], 2021	12 m	10	RYGB	-26.8 %	NS	p=0.004			*Klebsiella* (Sig), *Enterobacter* (Sig)	Ruminococcus (Sig), Faecalibacterium (Sig)
Tabasi et al[42], 2021	12 m	126	SG	-31.7 %	N/A	N/A	Bacteroidetes (p<0.0001)	*Firmicutes* (p<0.0001), *Actinobacteria* (p=0.0012)	*Bifidobacterium* (p<0.0001), *Roseburia* (p<0.0001)	Prevotella (p=0.0081)

m, months; w, weeks; d, days; y, years; SG, sleeve gastrectomy; RYGB, Roux-en-Y Gastric Bypass; BPD, Biliopancreatic Diversion; NS, not significant; N/A, not available; Sig, indicated as significant difference but no p-values available. Changes in alpha and beta diversity are indicated by their corresponding p-value. [†]Only Significant after RYGB. Only significantly changed phyla and genera are displayed.

One randomized controlled trial consisting of 20 patients compared the effects of a RYGB against those of a conventional medical diet on the gut microbiome[41]. Following a RYGB, significantly higher genus richness was reported compared to the diet group. This was in line with studies published earlier[43]. The changes in the microbiome were strongly associated with anthropometric, metabolic and inflammatory improvements, indicating that not only the altered anatomy after a RYGB, but also the extensive metabolic effects of bariatric surgery have an impact on the gut microbiome[41].

Finally, since the anatomy of the stomach is highly altered in bariatric surgery, Gutiérrez-Repiso et al[44] focused on the effects of a sleeve gastrectomy on gut microbiota. Although this study determined the microbial composition before surgery and linked them with the use of proton-pump inhibitors and the presence of *Helicobacter pylori*, they did not report how the gastric microbiota changed after one year. This study, however, observed reduced weight loss in patients with preoperative *H. pylori* colonization, confirming an observation reported earlier in bariatric surgery patients and suggesting the involvement of microbiota at different levels of the gastrointestinal tract[45-48].

CONCLUSIONS

The intestinal microbiome is a complex, environment-dependent, and dynamic community of microorganisms, comprising trillions of bacteria, fungi, archaea, phages, and viruses. Since the discovery and widespread availability of sampling techniques, many scholars[17] have demonstrated altered microbiome composition in obesity. Similarly, medical diets and bariatric surgery also seem to highly influence the microbiome.

Currently, most microbiome research projects in obese subjects are descriptive. As a result, increased or decreased microbiota numbers in obese subjects cannot be fully explained, nor are the mechanisms for altered microbiome composition after weight loss fully understood. As a result, in 2022 the intestinal microbiome still remains a yet to be opened black box in which environmental, genetic, dietary, anatomical, behavioral, and microbial factors are most likely working hand in hand to cause obesity and likewise assist in achieving weight loss. With more knowledge about the microbiome in obesity, causal mechanisms that link microbiota with body weight are likely to be unraveled in the near future.

Conflict of Interest

None of the authors have a conflict of interest.

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