REVIEW

The Gut Potential: exploring the modulatory effects of exercise and diet on the structure of the gut microbiota

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ABSTRACT

Microbiomes can shape the health status of an individual as certain microbiome profiles are associated with positive or negative health attributes. Promotion of a proper diet has been always essential in achieving good health and well-being. Consumption of certain foods has been known to directly affect the composition of the gut microbiome. A healthy diet promotes beneficial microorganisms that also foster host health. However, another factor that contributes to overall health and well-being is exercise and physical activity. Exercise and physical activity are associated with good health and wellness outcomes. Recent studies have also shown that exercise affects the gut microbiome composition but the contribution of how exercise shapes the gut microbiota is still limited. Dietary recommendations are generally recommended in conjunction with exercise for individuals with lifestyle-related disease. While both diet and exercise work using different pathways to induce health changes, they may also help identify certain microorganisms that may advance host health. In this narrative review, we described the effects of exercise and dietary interventions in modulating the gut microbiota. We found that exercise interventions promote beneficial microorganisms, while dietary interventions promote microorganisms that would likely adapt in a certain dietary composition. The results prompt the identification of a healthy gut microbiome profile as a recommendation for further research endeavors. Moreover, we discussed the potential benefits of exercise and diet as interventions to promote community health and well-being, especially in the Philippines.

INTRODUCTION

The definition of a healthy gut microbiota (GM) differs per individual, and each person has a unique gut microbiome profile

KEYWORDS

gut microbiota, diet, exercise, physical activity, exercise science

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(Rinninella et al. 2019). Albeit unique for each individual, there is still a baseline information about the abundant taxa in human GM. Based on the numerous data on the human microbiome, the dominant phyla in GM are Firmicutes, Bacteroidetes, Proteobacteria, Verrucomicrobia, and Actinobacteria (Magne et al. 2020; Reiss et al. 2016). Interestingly, shifts in the GM structure can be attributed to a number of external factors, such as diet (Ghosh et al. 2020; Kisuse et al. 2018; De Filippis et al. 2016), antibiotics (Elvers et al. 2020; Zimmermann and Curtis 2019), age (Xu et al. 2019), and physical activities (Ortiz-Alvarez et al. 2020; Codella et al. 2018). Changes in the GM may potentially affect the health status of an individual; therefore, the influence of the external factors should be studied and understood.

Several studies have already highlighted the importance of diet and nutrition in maintaining a healthy GM or disrupting the GM structure. Recently, there is a growing interest in the effect of exercise on GM. Several studies have explored the gut-muscle axis, which provides a framework on the bi-directional channel of exercise and GM, and its application to disease and immune function (Przewłócka et al. 2020; Ticinesi et al. 2019). Exercise has also been implicated in neural function establishing the role of exercise within the gut-brain axis (Shin et al. 2019).

This review focuses on diet and exercise as modulators of the GM (Fig. 1A). Furthermore, we attempt to categorize changes in GM composition in terms of dietary patterns and exercise types. The studies included for review were articles published from January 2011 to June 2021. In the evaluation of these modulations in GM, we aim to integrate the results from diet and exercise studies to generate information for future interventions in the Philippines.

DIET AND THE GUT MICROBIOTA

Several studies have established that nutrition and diet play a huge role in shaping the GM structure of humans. In return, the diet-GM dynamics influences specific metabolic functions and human health (Sonnenburg and Bäckhed 2016). Modifications in the GM at family and species level, especially in the core bacterial taxa, are observed during major compositional changes in the dietary patterns over a long period of time (Leeming et al. 2019; Oriach et al. 2016). In contrast, short-term dietary interventions alter some microbial taxa but not the core bacterial taxa (Leeming et al. 2019). These observations show the complex relationship between diet and the GM. Dynamics within each phylum are unique depending on the health, nutrition, and metabolic status of humans. In this section, we discuss the effects of different dietary patterns on the structure of GM (Table 1).

Western Dietary Pattern

Although there are several kinds of nutrition and dietary patterns, two of the most commonly studied diets are the Western diet (WD) and the Mediterranean Diet (MD). The typical WD is rich in animal protein and fats, with high dietary intake of saturated fats and refined carbohydrates and low intake of fiber (García-Montero et al. 2021; Shankar et al. 2017). This dietary pattern is associated with several metabolic complications, such as obesity and diabetes (García-Montero et al. 2021). Nowadays, the dietary patterns of several countries are becoming westernized because of globalization, leading to changes in the GM structure. In general, the WD increases the Firmicutes/Bacteroidetes (F/B) ratio in the gut in animal studies (Clarke et al. 2012). This trend was observed in children from the urban city of Ormoc in Leyte, Philippines (Nakayama et al. 2017). Compared with the children from rural Baybay city who maintained their traditional dietary habits, children from Ormoc consumed westernized diets that led to a decrease in abundance of *Prevotella*, a genus belonging to phylum Bacteroidetes. Intake of sugar-sweetened beverages was found to be positively associated with F/B ratio and negatively associated with butyrate producer *Lachnobacterium* (Ramne et al. 2020). Interestingly, Kisuse et al. (2018) observed a lower F/B ratio in children from urban Bangkok who consume high-fat diet (HFD) and WD. The difference in the observed F/B ratio in WD in human studies highlights that studies on GM structure should explore taxonomic units up to genera or species level, especially that these taxa have different functions in the gut.

In Asian studies, the urban and rural population can also be classified into *Bacteroides*-type and *Prevotella*-type, respectively (Kisuse et al. 2018). The *Bacteroides* and *Prevotella* enterotypes are also observed in African Americans and native Americans, respectively (Ou et al. 2013). The Bacteroides enterotype is found to be associated with high animal protein intake, possibly because of their ability to utilize proteins for growth (Senghor et al. 2018; Shankar et al. 2017). Moreover, *Bacteroides* are also known to produce short fatty chain acids (SCFAs), which may help in alleviating gut inflammation (Macfarlane and Macfarlane 2011). The abundance of *Bacteroides* during consumption of WD suggests that diet may also enrich microorganisms that would aid in digestion. Moreover, at genus level, the population accustomed to WD had increased *Clostridia, Akkermansia, and Bilophila* (Kisuse et al. 2018; Nakayama et al. 2017; Ou et al. 2013; Shankar et al. 2017). Mucin-degrading *Akkermansia* is known to be correlated with leanness and to have anti-inflammatory properties (Zhou et al. 2020). However, the increase in *Akkermansia* suggests host- and diet-driven adaptation in the GM (Shankar et al. 2017). This adaptation may serve as protection to the gut barrier and lessen the chances of inflammation during WD consumption.

Mediterranean Diet: The Ideal Diet

Contrary to WD, the typical MD is the standard of a healthy diet, with increased consumption of vegetables, legumes, fruits, and low consumption of meat, dairy products, and unsaturated fats (Ghosh et al. 2020). Adherence to MD is also associated with weight loss and enrichment of microorganisms associated with weight loss (McLeod et al. 2020). This dietary pattern is often associated with increased GM diversity and improved gut barrier function (García-Montero et al. 2021; McLeod et al. 2020). Moreover, a decrease in F/B ratio is associated with adherence to MD (García-Montero et al. 2021; Pisanu et al. 2020). Enrichment of butyrate-producing taxa *Faecalibacterium praunitzii, Roseburia*, and *Eubacterium* was observed in MD adherence of different healthy individuals with or without metabolic diseases or risk factors (Ghosh et al. 2020; Haro et al. 2017; Meslier et al. 2020). Butyrate is essential in maintaining gut integrity and preventing gut inflammation (Bailey and Holscher 2018). Probiotic microorganisms such as *Bifidobacterium* and *Lactobacillus* are also enriched in MD (Haro et al. 2017; Jain et al. 2018). Plant-based diets such as MD may act as substrates for *Bifidobacterium* and *Lactobacillus* fermentation, subsequently producing short-chain fatty acids (García-Montero et al. 2021). The enrichment of beneficial microorganisms during MD adherence supports the idea of MD as a standard to healthy nutrition.

Vegetarian and Vegan Diets

Although the MD involves high consumption of vegetables, adherence to MD entails consuming meat or fish. People adhering to vegetarian and vegan diets do not consume any kind of meat, so we expect differences in their GM structure when compared with people on WD and/or MD. Interestingly, microbial richness increased in strict vegetarians (Losasso et al. 2018). Moreover, the *Prevotella*/*Bacteroides* (P/B) ratio increased

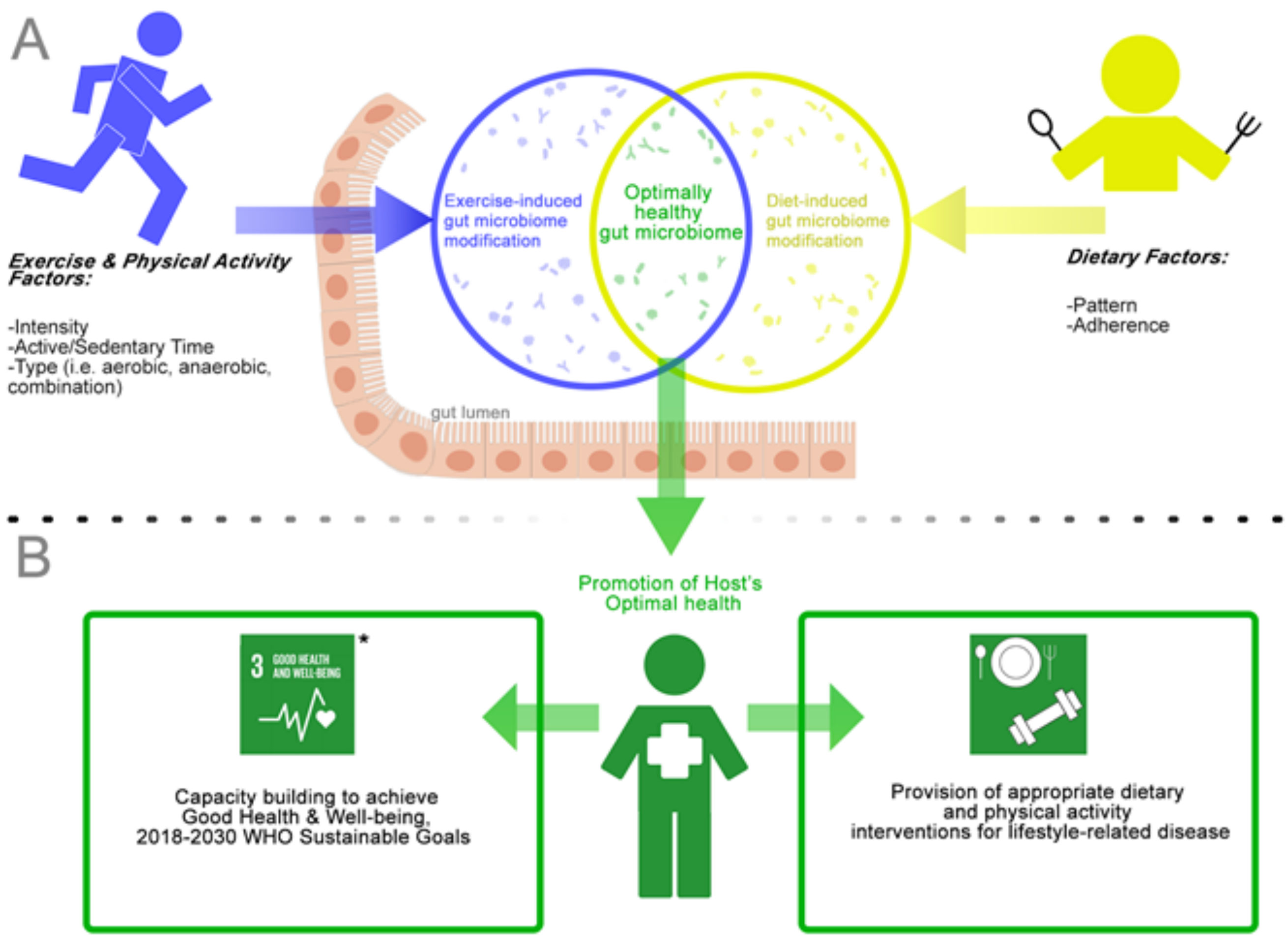

Figure 1: Conceptual framework on the interaction of exercise and diet on the gut microbiome and implications on host health. (A) Microbiota changes independently brought about by either exercise or diet may give rise to a shared microbiome structure associated with optimal health. (B) Identification of an optimal microbiome structure leads to sustainable goal development for the community. [*lifted from World Health Organization (2018)]

in some studies (De Filippis et al. 2016; Matijašić et al. 2014). A high P/B ratio was previously found to be a potential biomarker to weight loss (Hjorth et al. 2018). Similar to MD, the increase in *Prevotella* may be attributed to its ability to break down polysaccharides (Precup and Vodnar 2019). Interestingly, several studies have observed an increase in *Faecalibacterium prausnitzii* in vegetarians, similar with MD-adherent individuals (Matijasic et al. 2014; Kabeerdoss et al. 2012). The similarities in the abundant taxa in vegetarian diet and MD suggest similar health benefits for the two diet interventions.

Between vegetarian and vegan diets, the difference is that vegan diet does not include from dairy products (Wong et al. 2018). Interestingly, Reiss et al. (2016) found a decrease in abundance of lactic acid bacteria in vegans. Fecal bile acids were also lowered in vegan diet from a previous study (van Faassen et al. 1987). Because there is low to no consumption of dairy products, the substrates that allow for lactobacilli growth are lost (Reiss et al. 2016).

The Neurotherapeutic Ketogenic Diet

The ketogenic diet (KD) constitutes a low carbohydrate, adequate protein, high fat diet that enhances ketone production (Ang et al. 2020). KD is originally used as treatment for epileptic patients, but recent studies have shown its promising therapeutic effects on certain neurodegenerative diseases, metabolic diseases, and obesity (Paoli et al. 2019). However, as of writing, there is a limited knowledge on the effect of KD on the GM. Microbial diversity in the GM of obese participants increased after KD intervention (Gutiérrez-Repiso et al. 2019; Heinsen et al. 2016). Moreover, the effect of KD in the GM structure of obese and overweight individuals is different from HFD (Ang et al. 2020). The F/B ratio increases during HFD, whereas it decreases during KD. This trend in KD may be affected by the ketogenic bodies produced by the body during KD. *Oscillospira* and butyrate-producer *Butyricimonas* were increased after KD (Gutiérrez-Repiso et al. 2019). In KD, a decrease in *Bifidobacterium* significantly alters the intestinal pro-inflammatory Th17 levels (Ang et al. 2020). These results suggest that KD may be a potential dietary intervention to restore gut homeostasis and improve inflammation during obesity and metabolic syndrome.

Moreover, Xie et al. (2017) found that the GM structure of epileptic infants differed from that of healthy infants. KD decreased the abundance of Proteobacteria, especially the opportunistic pathogen *Cronobacter*, and increased the abundance of *Bacteroides* (Xie et al. 2017). Similarly, *Bacteroides* was enriched after KD treatment in epileptic children (Zhang et al. 2018). However, fiber-consuming bifidobacteria and butyrate-producing *Eubacterium rectale* were decreased following KD in children with severe epilepsy (Lindefeldt et al. 2019). *Bifidobacterium* was also observed to be decreased in KD (Ang et al. 2020). The decrease in abundance of some health-promoting bacteria may be attributed to the nature of KD wherein there is restriction of glucose metabolism pathways due to the low carbohydrate composition of the diet (Lindefeldt et al. 2019). In particular, *Bifidobacterium*

Table 1: Effects of dietary patterns and fermented foods in the structure of human gut microbiota.

Dietary Factors	Study Design	Participants	Structure of the Gut Microbiota	Reference
Dietary Pattern				
Westernized diet	Observational	Participants form the Malmö Offspring Study	↑ Firmicutes/Bacteroidetes ratio ↑ *Dialister, Lactobacillus, Eubacterium* ↓ *Lachnobacterium*	Ramne et al. 2020
	Observational	Healthy Chinese in Singapore, aged 22-35	↑ *Bifidobacterium, Blautia* ↓ *Prevotella*	Jain et al. 2018
	Observational	Children from urban Bangkok	↑ *Bacteroidales, Selenomonadales* ↓ Firmicutes/Bacteroidetes ratio ↓ Clostridia ↓ microbial diversity	Kisuse et al. 2018
	Observational	Healthy preadolescent and adolescent males from Dayton, Ohio	↑ *Bacteroides, Clostridia, Verrucomicrobia, Bilophila, Akkermansia* ↑ starch-degrading bacteria	Shankar et al. 2017
	Observational	Children aged 7-9 from urban Ormoc city	↑ Firmicutes/Bacteroidetes ratio, *Bacteroides* ↓ *Prevotella*	Nakayama et al. 2017
	Observational	Healthy volunteers aged 50-65	↑ *Bacteroides* ↑ Actinobacteria, Synergistes	Ou et al. 2013
Mediterranean diet	Experimental	Non-frail or pre-fail elderly individuals across five European countries	↑ *Prevotella, Faecalibacterium prausnitzii*, *Roseburia, Eubacterium* ↓ *Ruminococus torques, Clostridium ramosum, Veillonella dispar* ↓ microbial diversity	Ghosh et al. 2020
	Experimental	Healthy overweight and obese subjects	↑ *Faecalibacterium prausnitzii, Roseburia, Lachnospiraceae* ↓ *Ruminococcus gnavus, Streptococcus thermophilus*	Meslier et al. 2020
	Experimental	Overweight and Obese subjects	↑ Bacteroidetes, Proteobacteria ↑ *Prevotella* ↓ Firmicutes	Pisanu et al. 2020

	Experimental	Healthy, lean volunteers	↑ *Bifidobacterium, Lactobacillus* ↑ *Desulfovibrio, Oscillospira*	Garcia-Mantrana et al. 2018
	Experimental	Metabolic syndrome patients	↑ *Bacteroides, Eubacterium, Lactobacillus* ↓ *Parabacteroides distasonis, Faecalibacterium prausnitzii*	Haro et al. 2018
	Observational	Healthy Indian adults in Singapore, aged 22-35	↑ *Prevotella, Bifidobacterium, Megasphaera, Catenibacterium, Lactobacillus*	Jain et al. 2018
Vegan/Vegetarian diet	Observational	Strictly vegans, vegetarians	↑ Bacteroidetes ↑ Ruminococcaceae (vegans) ↑ microbial richness (vegetarians)	Losasso et al. 2018
	Observational	Healthy volunteers	↑ Firmicutes, Bacteroidetes ↑ *Prevotella/Bacteroides* ratio	De Filippis et al. 2016
	Observational	Vegetarians aged 40-61 years	↑ *Prevotella copri, Clostridium nexile, Eubacterium eligens, Klebsiella pneumoniae* ↓ potential pathogens compared with non-vegetarians	Reungsomwong et al. 2016
	Observational	Healthy, vegan individuals	↑Verrucomicrobia, Archaea ↓ lactic acid bacteria	Schwiertz et al. 2016
	Observational	Healthy vegan and vegetarian individuals aged 1.5-67	↑ *Bacteroides/Prevotella* ratio ↑ *B. thetaiotaomicron, Clostridium clostridioforme, Faecalibacterium prausnitzii* ↓*Clostridium* cluster XIVa	Matijasic et al. 2014
	Observational	Vegetarian and non-vegetarian young women aged 18-27	↑ *Faecalibacterium prausnitzii* ↓ *Clostridium* cluster XIVa bacteria compared with omnivore group	Kabeerdoss et al. 2012

	Observational	Strictly vegans or vegetarians who attended a congress in Dresden, Germany	↓ *Bacteroides, Bifidobacterium, Escherichia coli* ↓ Enterobacteriaceae	Zimmer et al. 2012
Ketogenic diet (very low carbohydrate ketogenic diet, high-fat)	Experimental	Overweight or class I obese nondiabetic adult men	↑ *Fusobacteria, Escherichia* ↓ *Bifidobacterium,* Actinobacteria	Ang et al. 2020
	Experimental	Participants aged 18-65 years, with body mass index > 30 kg/m^2	↑ microbial diversity ↑ Ruminococcaceae, Mogibacteriaceae ↑ *Oscillospira, Butyricimonas* ↓ Proteobacteria, Enterobacteriaceae, Sinobacteraceae ↓ *Serratia, Erwinia, Citrobacter*	Gutiérrez-Repiso et al. 2019
	Experimental	Children with refractory epilepsy	↑ Bacteroidetes ↓ Firmicutes ↓ microbial diversity	Zhang et al. 2018
	Experimental	Pediatric patients with refractory epilepsy	↑*Bacteroides*, *Prevotella* ↓*Cronobacter, Erysipelatoclostridium, Alistepes, Enterococcus*	Xie et al. 2017
	Experimental	Obese human subjects	↑ microbial diversity	Heinsen et al. 2016
Fermented Foods and Probiotics				
Cha-Koji (fermented green tea leaves)	Experimental	Healthy adults	↑*Clostridium* subcluster XIVa ↓ acetate and propionate	Yamamoto et al. 2018
Kefir	Experimental	Patients with metabolic syndrome	↑ Actinobacteria	Bellikci-Koyu et al. 2019
Kimchi	Experimental	Korean males and females (ages 20-30)	↑ lactic acid bacteria (*Leuconostoc mesenteroides*) ↓ Gammaproteobacteria	Kim et al. 2016
	Experimental	Obese Korean women (ages 30-60)	↑ Proteobacteria, Actinobacteria, *Bacteroides, Prevotella* ↓ Firmicutes/Bacteroidetes ratio, *Blautia*	Han et al. 2015

Fermented milk	Experimental	Healthy volunteers	↑ Firmicutes, Actinobacteria ↑ microbial diversity ↓ Proteobacteria	Lisko et al. 2017
	Experimental	Healthy adults	↑ Bacteroidetes, Bacteroidaceae, Prevotelaceae	Unno et al. 2015
	Experimental	Women with IBS with predominant constipation	↑ butyrate-producing taxa ↓ *Bilophila wadsworthia*	Veiga et al. 2014
Fermented papaya	Experimental	Tube-fed patients with neurological dysfunctions	↓ *Clostridium scindens, Eggerthella lenta*	Fujita et al. 2017

utilizes a wide range of carbohydrates, and in turn produces SCFAs (Pokusaeva et al. 2011). Further studies are needed to understand the shift in levels of health-promoting bacteria and provide an intervention to compensate for the loss of these "good" bacteria, especially now that there is a growing interest in KD as a weight loss strategy. Synbiotic intervention during or after KD may promote SCFA-producing bacteria (Gutiérrez-Repiso et al. 2019), and this highlights the potential of pre- and probiotics as dietary interventions.

Fermented Foods and Probiotics

Fermented foods are foods inoculated with microorganisms and undergo a controlled process that regulates microbial growth (Marco et al. 2017). Because of the production of fermentation end-products, fermented foods have enhanced nutritional and functional properties. The presence of probiotics can also classify fermented foods as functional foods, which are ordinary foods added with components to confer a specific health benefit other than their own nutritional value (Linares et al. 2017). A review paper by Stiemsma et al. (2020) summarized the potential of fermented foods as dietary interventions to prevent gut dysbiosis in humans. Several fermented milk products increased the abundance of butyrate-producing bacteria (Unno et al. 2015; Veiga et al. 2014). Meanwhile, fermented yogurts decreased F/B ratio and enriched abundance of probiotic strains in the gut (Lisko et al. 2017; Unno et al. 2015).

Most Asian fermented foods can be potential sources of probiotics, especially lactic acid bacteria (Swain et al. 2014). Intervention studies showed the potential of Asian fermented food against metabolic and immune-mediated diseases (Stiemsma et al. 2020). Although current results are promising, studies on the effects of fermented foods on the structure of GM are still limited. Some recent studies suggested the potential effects of Asian fermented foods on gut microbiota composition, but further investigation is needed. For example, consumption of Cha-Koji, which is a product comprising green tea leaves fermented with *Aspergillus luchuensis*, increased the relative abundance of *Clostridium* subcluster XIVa and decreased the overall acetate and propionate levels (Yamamoto et al. 2018). *Clostridium* subcluster XVIa is found to be related to butyrate production (Yamamoto et al. 2018). Kefir, a fermented milk, was found to increase the abundance of *Lactobacillus, Bifidobacterium,* and Actinobacteria in patients with metabolic syndrome, albeit not significantly different from control group (Bellikci-Koyu et al. 2019). Meanwhile, papaya fermented with *Enterococcus faecalis* and *A. oryzae* reduced the abundance of Firmicutes, especially *Clostridium scindens* and *Eggerthella lenta,* in tube-fed patients with neurological dysfunctions (Fujita et al. 2017). *Clostridium scindens* is associated with toxic secondary bile acids (Ridlon et al. 2013), while *Eggerthella lenta* causes bacteremia (Ugarte-Torres et al. 2018). These results suggest the health-promoting properties of fermented foods and the potential use of fermented foods as adjunct therapy. Interestingly, the probiotic *Lactobacillus kefiri* isolated from kefir was previously found to modulate the GM (Toscano et al. 2017), which suggests that kefir as a food may potentially change the structure of the GM. Consumption of fermented kimchi, a traditional side dish in Korea, decreased the F/B ratio in the gut of obese Korean women (Han et al. 2015). Moreover, the relative abundance of *Bacteroides* and *Prevotella* increased, while *Blautia*, which is recognized as butyrate-producing species, decreased. This may indicate that consumption of fermented kimchi did not restore the population of *Blautia,* which may have been affected by the status of the participants. Decreased abundance of *Blautia* is commonly associated in diabetes, obesity, and other diseases (Liu et al. 2020). Although fresh kimchi may also exert the same changes in the GM structure, fermented kimchi was found to be more associated with functional metabolic gene expression (Han et al. 2015). Lactic acid bacteria were also increased following kimchi intervention (Kim et al. 2016). These studies highlight the important role of lactic acid fermentation in traditional fermented foods and emphasize the potential of fermented foods as interventions that may modulate the GM into a healthier profile.

EXERCISE AND PHYSICAL ACTIVITY

Aerobic Exercise and Endurance Training

The studies included in this review mostly employed endurance-related criteria either through an intervention or a factor of interest such as in individual profiles in cross-sectional designs. Endurance exercises are characterized by activities where there are repeated or continuous muscular isotonic contractions (Morici et al. 2016) relying on aerobic metabolism for energy production in which improvements are assessed in terms of change in maximal oxygen consumption (VO_2 max) (Patel et al. 2017). In this section, we highlighted the relative changes of abundant phyla in the human GM following endurance exercise.

Durk et al. (2019) has identified a positive association between F/B ratio and VO_2 max, which explained 22% of compositional variance among healthy young adults under free-living conditions. This trend among healthy participants is quite similar with the athletic population. A case study which focused on an ultra-endurance athlete was by Grosicki et al. (2019) wherein there was an observed higher abundance in F/B ratio at post-race, which may be attributed to a 69% decrease in Bacteroidetes. Similarly, marathon runners and cross-country skiers had a higher F/B ratio than healthy controls (Kulecka et al 2020). This may imply that aerobic exercise engagement in athletic and healthy population may have comparable outcomes on GM.

On the contrary, insulin resistant middle-aged participants had a decline in F/B ratio that was due to an increase in Bacteroidetes in all groups despite having a significant improvement in peak oxygen uptake only for the sprint interval but not moderate intensity continuous training group (Motiani et al. 2020). Other studies on adults with diabetes indicated that F/B ratio is inversely associated with plasma glucose levels regardless of BMI (Larsen et al. 2010). However, there is a need to point out that despite a decrease in F/B ratio in Motiani et al. (2020), change in plasma glucose was not significant after the endurance exercise intervention. This may imply that the decline in F/B ratio may be linked closely to participant profile (e.g. insulin resistance, plasma glucose) in the context of exercise. Having said that, F/B ratio has not been consistently associated to diabetes (Gurung et al. 2020). This means that the effects of endurance exercise on F/B ratio needs further examination especially for populations with certain health conditions.

In the context of age, GM may have certain differences across age groups (de la Cuesta-Zuluaga et al. 2019). Participant age groups in the mentioned studies involved young adults (Durk et al. 2019) and middle-aged adults (Grosicki et al 2019; Motiani et al 2020). This suggests that endurance exercise may influence F/B ratio regardless of age. Furthermore, disease states may affect the influence of endurance exercise to F/B ratio as opposed to healthy states. Factors such as physical activity, diet, and pharmacological treatment, which contributes to contradicting results when comparing certain participant profiles (Magne et al. 2020). Reasoning from these evidence, endurance-exercise-induced changes in F/B ratio may be influenced by participant profile. Specifically, comparative research that involves an aggregate of endurance athletes, healthy individuals, and subjects with certain disease, may be warranted to create a robust pool of knowledge on endurance exercise, GM and health outcomes.

Butyrate-producing bacteria have been shown to shift in abundance under aerobic exercise conditions. *Roseburia* is more abundant in individuals who have higher peak oxygen uptake (Estaki et al. 2016), participate in ultra-endurance activities (Keohani et al. 2019), and supervised aerobic exercise (Allen et al. 2018). Similarly, Lachnospiraceae is also increased in endurance training (Allen et al 2018), and is associated with oxygen uptake (Estaki et al 2016). *Lachnospira* had a greater relative abundance among female endurance athletes (Morishima et al 2020). A prominent butyrate-producing microorganism which has been mentioned in several articles in this review is *Faecalibacterium*. Elite endurance level athletes have increased *Faecalibacterium* (Morishima et al. 2020; O'Donovan et al. 2020). *Faecalibacterium prausnitzii* abundance is enhanced by moderate intensity continuous training (Motiani et al. 2020). *Faecalibacterium* spp. increased at post-intervention but were reduced after a 6-week washout period (Allen et al. 2018). In relevance to this specific study, a temporal aspect in exercise-induced effect on GM may be explored. Based on the available evidence, the moderate-to-vigorous endurance exercise may potentially promote the abundance in *Faecalibacterium*. Other butyrate-producing microorganisms that had a higher abundance associated with endurance-related factors include *Clostridium bolteae, Anaerostipes hadrus* (O'Donovan et al. 2020), *Dorea* (Munukka et al. 2018; Keohane et al. 2019), and Erysipelotrichaceae (Estaki et al. 2016). On the contrary, *Clostridium* cluster XIVa was decreased in participants who were encouraged walk briskly at least at ≥3 METS (Metabolic Equivalent of Task) (Morita et al. 2019), which is the lower limit value for moderate intensity (Mendes et al. 2018). The contrasting result in this specific study compared to previously mentioned articles may provide further insights on the minimum intensity level by which butyrate-producing taxa may be modulated by endurance exercise. Butyrate-producing bacteria cross-feed metabolites, such as lactate from other bacteria (Cook et al. 2016), which may have implications in terms of aerobic exercise dynamics on the gut microbiome. In terms of exercise, lactate is formed from contracting muscles (Adeva-Andany et al. 2014). Although the link between microorganisms and exercise-induced lactate lacks sufficient evidence, Scheiman et al (2019) demonstrated in mice that systemic lactate may be able to cross through the gut epithelium.

Lactate-utilizing *Veillonella* was found to have an increased relative abundance among endurance athletes (Scheiman et al. 2019; Grosicki et al. 2019) and in non-athletes who underwent endurance training (Motiani et al. 2020). This may additionally support the need to focus on the role of endurance exercise in lactate-utilizing bacteria which also includes butyrate-producers. Furthermore, the current evidence presents that there may be distinct interspecies interactions that occur during aerobic exercise that need to be explored.

Meanwhile, *Subdoligranulum* abundance are inconsistent in elite level endurance activities (Keohane et al. 2019; Grosicki et al. 2019). Despite the conflicting results and lack of direct cause for such phenomenon, it is worth considering that *Subdoligranulum* is positively associated with high density lipoprotein levels and negatively associated with body fat, insulin resistance, and systemic inflammatory markers such as IL-6 (Van Hul et al. 2020).

These results further strengthen the existence of a modulatory pathway of endurance exercise to certain bacteria from the order Clostridiales, namely the certain taxa under Lachnospiraceae and Ruminococcaceae. Endurance exercise engagement and cessation also play a role in the GM profile. Furthermore, the modulation of these microorganisms through exercise implies a cascading effect towards host health through currently unidentified exercise-microbiota-host mechanisms which are recommended to be studied in future research endeavors.

Blautia abundance was highly variable in reviewed articles. Changes due to vigorous exercise such as improved aerobic capacity and its adjunct metabolic benefits (e.g. improved insulin sensitivity) was associated with decreased abundance in *Blautia* among insulin-resistant participants (Motiani et al. 2020) and overweight participants (Rettedal et al. 2020). In contrast, cross-country endurance athletes had an increased abundance in *Blautia* following a graded maximal volitional running session (Tabone et al. 2021). Given the distinct conditions in both participant and intervention characteristics, it is difficult to provide a definitive insight. In the context of diabetes, a decline in *Blautia* is regarded as a possible driver genus in the shift from healthy to a diabetic state (Diener et al. 2021). However, a restored *Blautia* abundance among participants with diabetes may be attributed to anti-diabetic drugs (Gaike et al. 2020; Tong et al. 2018). This means that there may be other mechanisms that need to be considered in the interpretation of exercise-induced effects on GM. A critical aspect from this inconsistency is that exercise may have a distinct

Table 2: Effects of exercise and physical activity in the structure of the human gut microbiota.

Cohort	Study Design	Physical Activity	Gut Microbiome Structure	Reference
Adults with lifestyle-related disease				
Chinese males who have prediabetic condition	Experimental	Combined High-Intensity Aerobic and Resistance Training	Improved insulin resistance ↑Lachnospiraceae ↑ *Akkermansia mucinphila* (compared to exercise non-responders) ↓ *Akkermansia mucinphila* (when compared to post-intervention results within groups) ↓ *Streptococcus mitis, Alistipes putredinis, Alistipes shahii, Bacteroides xylanisolvens* ↓*Prevotella copri* replication rate ↑*Bacteroides* growth rate No improvements in insulin resistance ↑*Alistipes shahii* ↓*Ruminococcus gnavus*	Liu, et al. 2020
Sedentary participants with Prediabetes, Diabetes, and Control	Experimental	Group 1: Sprint Interval Training Group 2: Moderate-intensity Continuous Training (60% VO_2 peak)	Both Groups ↓Firmicutes/Bacteroidetes ratio ↓*Blautia, Clostridium* ↑Bacteroidetes Group 1 ↑*Lachnospira, Akkermansia* Group 2 ↑*Veillonella, Faecalibacterium prausnitzi*	Motiani et al. 2020
Elderly patients with Type 2 Diabetes	Experimental	6-month endurance, resistance, and flexibility training	↓*Candida albicans* ↓Mycetes	Pasini et al. 2019
Geriatric				
Elderly and Adults	Experimental	Exercise Intervention (Frequency-based)	Frequent Exercise ↑Turicibacteraceae ↓Pseudomondaceae. Odoribacteraceae, Barnesiellaneae, Oxalobacteraceae	Zhu, Jiang, & Du, 2020
Japanese Elderly Males	Experimental	5-week progressive aerobic exercise (60-75% VO_2 peak)	↓*Clostridium difficile*	Taniguchi et al. 2018
Japanese Elderly Females	Experimental	Group 1: 12-week trunk muscle strength program Group 2: 12-week 60-min brisk walk at ≥3 METS	Group 1 ↑*Clostridium* cluster IX Group 2 ↑*Bacteroides* ↓*Clostridium* subcluster XIVa	Morita et al. 2019
Community Dwelling Elderly and Active Senior Orienteers	Observational		Physically Active Seniors ↑*Faecalibacterium prausnitzi*	Fart et al. 2020
Older Community Dwelling Men	Observational		Higher Step counts ↑*Cetobacterium*, *Faecalibacterium*, *Prevotella*, *Clostridium*, Peptococcaceae, Paraprevotellaceae, Lachnospiraceae ↓*Coprobacillus*, *Adlercreutzia*, Erysipelotrichaceae, *Alistipes*, *Clostridia*	Langsetmo et al. 2019

			SHA-98, *Anaerotruncus*, *Eggerthella*, *Megasphaera*	
Athletes and Recreational Athletes				
Elderly Athletes	Observational		Elderly Athletes ↑*Bacteroides, Prevotella* ↓*Bacteroides/Prevotella* Ratio Elderly Controls ↑ *Bacteroides/Prevotella* Ratio	Soltys et al. 2021
Polish Endurance Athletes	Observational		Endurance athletes (Marathon Runners & Cross-Country Skiers) ↑Firmicutes/Bacteroidetes Ratio Sedentary ↓Firmicutes/Bacteroidetes Ratio Both ↑*Prevotella* ↓*Bacteroides*	Kulecka et al. 2020
Cyclists	Observational		Exercise Volume per week (+) *Prevotella*	Petersen et al. 2017
4 Male athletes	Observational	4998.55 km transatlantic rowing race in 33.92 days	During the race period ↑*Dorea longicatena*, *Roseburia hominis*, unclassified genus *Subdoligranulum* ↓*Bacteroides finegoldii*	Keohane, et al. 2019
An elite male ultramarathon runner	Observational	163km mountain footrace (uphill and downhill)	Post-race (2 hours) ↑Proteobacteria ↑*Haemophilus, Veillonella, Streptococcus* ↓Bacteroidetes ↓*Alloprevotella*, *Subdolingranulum* ↑ Firmicutes-Bacteroidetes Ratio	Grosicki, Durk. & Bagley, 2019
36 Elite Irish athletes from 16 sports	Observational		40-70% VO_2 max (n=3) *Streptococcus suis*, *Clostridium bolteae*, *Anaerostipes hadrus* >70% VO_2 max, >50% maximal voluntary contraction *Bacteroides caccae*	O'Donovan et al. 2020
Female Endurance Runners, Healthy Control	Observational		Endurance Runners ↑Deferribacteres ↑*Acinetobacter*, *Faecalibacterium*, *Haemophilus*, *Lachnospira*, *Mucispirillum*, Paraprevoteillaceae, *Prevotella*, *Rothia*, unclassified *p_OD1* Control ↑*Actinomyces*	Morishima et al. 2020
Professional Wushu routine athletes	Observational		Longer Training years and Higher Training Volume ↑Porphyromonadaceae, *Parabecteroides*, *Phascolarctobacterium*, *Bilophila*, *Oscillobacter* Lower Training years and Lower Training Volume ↑*Megasphaera*, Veillonellaceae	Liang et al. 2019
Male elite professional rugby players and healthy controls	Observational		Athletes ↓Bacteriodetes Athletes (vs high BMI control) ↑Akkermansiaceae, *Akkermansia*	Clarke et al. 2014

			Athletes (vs low BMI control) ↓Lactobacillaceae, *Bacteroides*, *Lactobacillus* High BMI (vs low BMI) ↑*Pseudobutyrvibrio*, *Dorea* ↓*Akkermansia*	
Endurance athletes	Experimental	Treadmill Run until volitional exhaustion	↑*Romboutsia* genus, Ruminococcocaceae UCG-005, *E. coli* TOP498, *Blautia* genus ↓*Ruminiclostridium* 9, *Clostridium phoceensis*	Tabone et al. 2021
Amateur Runners	Experimental	Half Marathon	Pre-marathon ↑*Bacteroides coprophilus* Post-marathon ↑*Pseudobutyrivibrio*, *Coprococcus_2*, *Collinsella*, *Mitsuokella*, Coriobacteriaceae	Zhao, et al. 2018
Endurance Athletes	Observational		Post-marathon ↑*Veillonella*	Scheiman et al. 2019
Athletes (non-sport-specific)	Observational		Adult Athlete ↑ Ruminococcaceae*, Ruminococcus* Youth Athlete ↑ *Bacteroides,* Ruminococcaceae Youth Non-athlete (+) *Prevotella*	Han et al. 2020
Sedentary, Overweight, or Obese				
Sedentary (BMI = 20 -45kg/m^2)	Experimental	24-week concurrent progressive exercise (no control)	↑Bifidobacteriaceae, Bifidobacterium ↑Oscillospira, Anaerostipes ↓Prevotella, Oribacterium ↑Stool butyrate	Erlandson et al. 2021
Sedentary and Active Premenopausal Women	Observational		Sedentary ↑Odoribacteraceae, Barnesiellaceae Active ↑*Faecalibacterium prausnitzi*, *Roseburia hominis, Akkermansia mtucinphila* Correlation with Time per Sedentary factors (+) Desulfovibrionaceae with maximum sedentary time (+) *Paraprevotella* with average sedentary time Correlation with Body Fat (+) Barnesiellaceae Correlation with appendicular muscle mass index (+) *Coprococcus*	Bressa et al. 2017
Sedentary Females (BMI >27.5 kg/m^2)	Experimental	6-week Low to Moderate Intensity Cycling	Post-Exercise ↑*Verrucomicrobia*, *Dorea*, *Anaerofilum*, *Akkermansia* ↓unidentified *Porphyromonadaceae*, *Odoribacter*, unidentified *Desulfovibrionaceae*, unidentified *Enterobacteriaceae*, *Streptococcus*, Proteobacteria	Munukka, et al. 2018

Overweight Females (BMI: 25-32 kg/m^2)	Experimental	10-week progressive endurance exercise training (55-65% HRR to 70-75%)	Exercise Group ↑*Lactobacillus*, *Bifidobacterium*	Mahdieh et al. 2021
Obese Children (trained vs control) and Healthy controls (7-12 years old)	Experimental	12-week combined strength and endurance exercise	Obese and exercise ↓ Proteobacteria, *Clostridium*, *Alkaliphilus*, Gammaproteobacteria ↑*Lachnospira*, *Veillonella*, *Roseburia*, *Blautia*, *Dialister*	Quiroga et al. 2020
Free-living individuals (18-40 years old)	Observational		Sedentary ↑ *Bacteroides*, *Parabacteroides* Active ↑*Coprococcus*, *Blautia*, *Eubacterium*	Castellanos et al. 2020
Sedentary Males and Females (Lean vs Obese)	Experimental	6-week, 3x/week endurance-based exercise at 60-75% HR reserve	Post-training (irrespective of BMI) ↑Butyrate producers: *Clostridiales* spp, *Lachnospira* spp, *Roseburia* spp, *Lachnospiraceae* unclass, *Faecalibacerium* spp) Post-washout (irrespective of BMI) ↓Butyrate producers	Allen et al. 2018
Healthy Adults				
18 to 33 year-old Females	Experimental	Study 1: Aerobic exercise at 60-90% HR$_{max}$ (Study 1) Study 2: Resistance Training at 70-85% 1-RM (Study 2)	Study 1 High Respiratory Exchange Ratio (Post) ↑*Prevotella, Romboutsia, Dialister* Low Respiratory Exchange Ratio (Post) ↑*Bacteriodes, Bacteriodes B, Parabacteriodes* Study 2 High 3RM Squat Change ↑Firmicutes, *Ruminococcus*, unidentified Lachnospiraceae, *Turicibacter*, *Clostridium* Low 3RM Squat Change ↑*Siccibacter, Bacteroides, Bacteroides B* ↑*Alistipes, Oscillibacter*	Bycura, et al. 2021
Males and Females, 25.7±2.2 years old	Observational		VO_2 max (+) Firmicutes/Bacteroidetes Ratio	Durk et al. 2019
Adults (18-35 years old)	Observational		Cardiorespiratory fitness (+) *Coprococcus* (+) *Roseburia* (+) *Adlercreutzia* (+) unknown *Clostridiales* (+) Lachnospiraceae (+) Erysipelotrichaceae	Estaki et al. 2016
Slovenian Healthy Cohort	Observational		More Frequent Physical Activity ↑Fungal Diversity ↓*Saccharomyces cerevisiae*	Mahnic & Rupnik 2018

↑ = increase, ↓ = decrease, (+) = positively correlated

mechanism by which it affects GM as compared to other interventions (e.g. diet, drugs). Subsequently, similar health outcomes may still be achieved despite the differences among health interventions. Moreover, these divergent results may imply that exercise-induced modulation of certain taxa may depend on the participant profile, and exercise intensity. These recommendations open several research opportunities especially in establishing the unique mechanisms underlying the role of exercise on GM and health outcomes.

Clostridium difficile (Taniguchi et al. 2018) and *Streptococcus* (Munukka et al. 2018) were decreased following an endurance exercise program among non-athletes. Meanwhile, *Streptococcus* was higher among three athletes who engaged in moderately dynamic sports (O'Donovan et al. 2020), and an ultra-endurance athlete post-race (Grosicki et al. 2019). Based on the limited results presented, it appears that a reduction in opportunistic bacteria may be modulated by engaging in endurance exercise. *Streptococcus* in the athlete GM may shift to a higher abundance based on the evidence presented but its concomitant factors, which may include exercise intensity, need to be further elucidated.

Bacteroides were increased after moderate-to-vigorous aerobic program among young adults (Bycura et al. 2021) and brisk walking program of at least light-to-moderate intensity among the elderly (Morita et al 2019). Likewise, elderly athletes who have been engaging in a structured lifelong endurance exercise training had an increased Bacteroides profile (Soltys et al 2021). *Bacteroides caccae* (O'Donovan et al. 2020), *Bacteroides finegoldii* (Keohani et al. 2019) and *Bacteroides coprophilus* (Zhao et al. 2018) were identified species among athletes engaging in aerobic-dominant sports. Among the three species, *Bacteroides finegoldii* was decreased throughout an ultra-endurance rowing competition in four male athletes (Keohani et al. 2019). The role of *Bacteroides* spp. (i.e. commensal, beneficial, pathogenic) on host health varies depending on specific environmental conditions (Zafar & Saier 2021). While the role of *Bacteroides* may be elusive in terms of overall health, it seems like endurance-related activities and characteristics may enhance the abundance of *Bacteroides* in general. For this reason, aerobic exercise- and profile-associated changes on *Bacteroides* should be examined at species level. Furthermore, there is a need for future studies on endurance activity intensity since this may facilitate or hinder setting a conducive environment for certain *Bacteroides* species.

Abundance of *Prevotella* is high among endurance athletes (Morishima et al. 2020; Kulecka et al 2020; Soltys et al. 2021) and among University students who had a high respiratory exchange ratio after an 8-week cardiorespiratory training program (Bycura et al 2021). Additionally, *Prevotella* was positively associated with exercise volume per week among cyclists (Petersen et al. 2017). Meanwhile, *Bacteroides/Prevotella* ratio is lower among elderly athletes compared to controls (Soltys et al. 2021). *Prevotella* is generally known to be a commensal bacterium but may be involved only in certain inflammatory mechanisms (Precup & Vodnar 2019; Larsen 2017). This suggests that endurance exercise may facilitate health-promoting functions of *Prevotella*.

Mucin-degrading bacteria, *Akkermansia muciniphila*, is increased in elite athletes (Clarke et al. 2014), and participants with prediabetes (Liu et al. 2020). *Akkermansia* was also increased in overweight sedentary women after a 6-week endurance intervention (Munnuka et al. 2018). Another mucin-degrading bacterium, *Mucispirullum* had a higher abundance among endurance runners compared to healthy volunteers (Morishima et al. 2020). The studies presented appear to have similar increased trends with endurance exercise. To further support this insight, Lopetuso et al. (2020) found a significant relationship between the decline in *Akkermansia muciniphila* and dysbiosis in disease states. Combining this information to the evidence from the reviewed articles, health benefits from endurance exercise may be related or augmented by *Akkermansia* supporting the feasibility of potential exercise-initiated GM modulatory mechanism for future studies.

Studies on aerobic exercise and Actinobacteria are limited. Current evidence points to certain taxa, namely Coriobacteraceae (Zhao et al. 2018), *Bifidobacterium* (Mahdieh et al. 2021), and *Rothia* (Morishimia et al. 2021) having increased abundance with endurance activities. Zhao et al. (2018) also determined Coriobacteraceae may be a potential biomarker for exercise-induced health benefits. Relevant studies suggest that Coriobacteraceae (Kim et al. 2020) and *Bifidobacterium* (O'Callaghan et al. 2016) are linked to positive health outcomes. Thus, modulatory effects of aerobic exercise on certain taxa under Actinobacteria may be worth considering for future research.

Proteobacteria is a biomarker for dysbiosis and certain disease states (Shin et al 2015). Immensely demanding exercise, especially at very high intensity or very long durations, may induce intestinal injury, permeability, and endotoxemia (Costa et al 2017). Evidence from these studies, in conjunction with the rise in Proteobacteria following extreme physical exertion in Grosicki et al (2019), and Tabone et al (2021) may implicate a potential connection between exercise-related dysbiosis marked by an increase in Proteobacteria. This is because extreme levels of physical exertion may induce systemic and gut-specific inflammatory response after intense endurance activity (Smith et al. 2020). Additionally, there was a decrease in Desulfovibrionaceae and an unidentified Enterobacteriaceae but increased *Akkermansia* following exercise bordering moderate-to-vigorous intensity (Munnuka et al. 2018). This further suggests that GM changes influenced by endurance exercise intensity may have specific optimal ranges for certain commensal and opportunistic microbiota.

Anaerobic Exercise and Resistance Training

There is a very limited number of studies which examine the effect of sole strength or resistance training on the gut microbiome composition. Muscular strength is measured in terms of repetition maximum (RM), that is the maximum weight an individual can carry given a certain number of repetitions. Activities that require a high level of voluntary contraction dominantly utilize ATP through anaerobic pathways include weightlifting, gymnastics, and throwing events (Mitchell et al. 2005). Other examples include sprints, high-intensity interval training, and powerlifting (Patel et al. 2017).

Some taxa under Clostridiales were increased after an improved 3 RM squat (Bycura et al. 2021), after performing a trunk muscle strength program (Morita et al. 2019), and after sprint interval training (Motiani et al. 2020). *Ruminoccous*, Lachnospiraceae, *Clostridum*, (Bycura et al. 2021), and *Lachnospira* (Motiani et al. 2020) were among the identified bacteria to have been modulated by anaerobic and resistance training which were also identified in the discussion on aerobic training. Sprint interval training consisting of 30-second maximal bouts had an increase in *Akkermansia* (Motiani et al. 2020). This also implies that *Akkermansia* responds to relevant mechanisms resulting from either aerobic or anaerobic exercise. While anaerobic exercise has physiologically different adaptations compared to endurance exercise, anaerobic exercise may still exert beneficial effects related to cardiovascular fitness (Patel et al. 2017). This suggests there are certain taxa that may be modulated by exercise regardless of the dominant energy pathway for specific activities.

This section shows that with the current evidence, there is yet a need to investigate athletes participating in highly anaerobic sports (e.g. weightlifting, powerlifting, gymnastics, throwing events) to provide further insights such as the role of anaerobic-dominant activities on GM.

Concurrent Strength and Endurance Training

Clostridiales (e.g. *Lachnospira*, *Clostridium*, *Alkaliphilus*, *Roseburia*, *Blautia*) and Veillonellaceae (e.g. *Veillonella, Dialister*) increased in obese children after a combined endurance and strength program (Quiroga et al. 2020). Butryate-producing bacteria, *Bifidobacterium*, and stool butyrate were increased in older adults post-intervention (Erlandson et al 2021). As mentioned in the earlier section, aerobic training increases *Bifidobacterium* and butyrate-producing bacteria as well. In relevant studies, these microorganisms may have cross-feeding interactions related to butyrate production in the context of diet (De Vuyst and Leroy 2011) but have yet to be explored in the context of exercise. Meanwhile, possible opportunistic microorganisms such as Gammaproteobacteria (Quiroga et al. 2020), and pathogenic fungi *Candida albicans* (class Saccharomycetes) were reduced after exercise training (Pasini et al. 2019). The collective evidence coincides with findings from the aerobic exercise discussion, that is, the promotion of butyrate-producing taxa and the reduction in opportunistic bacteria. This is perhaps due to the influence of aerobic components in this combined training modality. Furthermore, concurrent training intensity may still exert a significant influence on GM. This is demonstrated in Liu et al. (2020) wherein a combined resistance training program was aimed to be at 80-95% heart rate maximum suggesting a moderate to almost maximal exercise effort. Liu et al. (2020) found a significant increase in *Streptococcus mitis*, an opportunistic bacterium associated with the onset of diabetes (Vatanen et al. 2018), and a reduction in health-promoting bacteria (e.g. *Akkermansia muciniphila*) among responders (i.e. improved insulin resistance) compared to non-responder group (Liu et al. 2020). While aerobic and anaerobic training induce varied physiological responses and adaptations (Jabbour et al. 2015), it seems that the training programs in the reviewed studies lean towards aerobic-exercise-related adaptations. This further strengthens the need to investigate anaerobic training effects on GM composition in addition to the combined effect with aerobic training.

Physical Activity and Sedentary Time

Physical activity time and sedentary time are two independent activity factors that affect individual health outcomes. Physical activity frequency is associated with a lowered risk for developing cardiovascular disease and diabetes (de Souto Baretto et al. 2017). Several studies focused on participant activity time and sedentary behavior and how these factors translate to GM profile. Physically active individuals had a higher abundance of taxa under Clostridiales, such as *Faecalibacterium* (Fart el al. 2020; Bressa et al. 2017; Langsetmo et al. 2019), Lachnospiraceae (Bressa et al. 2017; Langsetmo et al. 2019), Ruminococcus (Langsetmo et al. 2019), and *Blautia* (Castellanos et al. 2020). On the other hand, *Clostridia* SHA-98 and *Anaerotruncu*s were lower in abundance among active participants compared to participants with lower levels of physical activity (Langsetmo et al. 2019). Integrating the results provided, butyrate-producing taxa under Clostridiales may generally have positive associations with habitual physical activity.

Megasphaera was lower in participants with a higher step count (Langsetmo et al. 2019) and higher among Wushu athletes with lower training volume per week (Liang et al. 2019). Despite having varied participant profiles, these results may warrant further studies on the possible inverse association between physical activity level and *Megasphaera*.

Odoribacteraceae and Barnesiellaceae were increased in sedentary time among women (Bressa et al. 2017) but were reduced in elderly adults who frequently exercised (Zhu et al 2020). Corroborating to these results, metabolically unhealthy overweight/obese participants have a lower abundance in Odoribacteraceae compared to metabolically healthy overight/obese participants (Kim et al. 2020). In addition, Odoribacteraceae is also correlated with body fat percentage (Bressa et al. 2017). The result indicates that physical activity or reduction in sedentary time may modulate the abundance of Odoribacteraceae possibly through modifications in lipid-related profiles.

Parabacteroides were observed in athletes who had a greater number of training years and hours of training per week (Liang et al. 2019). Meanwhile, *Parabacteroides* and *Bacteroides* are predominant among sedentary individuals (Castellanos et al. 2020).

Participants who are more frequently active have a lowered prevalence of *Saccharomyces cerevisiae* (Mahnic and Rupnik 2018). This result including the previously mentioned effect of concurrent training on *Candida albicans* elicits the need to establish potential exercise-related modifications in the gut fungal microbiome. In fact, 4.2% of interindividual differences in the gut fungal microbiome was associated with physical activity levels (Mahnic and Rupnik 2018), positing the importance in exploring this area. Furthermore, these pathogenic fungi seem to have a similar trend with pathogenic bacteria as discussed in previous sections suggesting the role of exercise in reducing risks for disease brought about by opportunistic microorganisms.
More active individuals had a higher abundance in *Akkermansia muciniphila* compared to sedentary participants (Bressa et al. 2017). While there is a limited number of research done on strictly focusing on active or sedentary time and *Akkermansia*, the evidence that have been presented including from other sections strongly suggest that exercise closely modulates *Akkermansia*.

To summarize, most exercise and physical activity studies in this review have aerobic- or endurance-related factors (Table 2). There is a gap in identifying GM composition or modulation in highly anaerobic types of training such as power lifting or weight training. Further studies that involve highly anaerobic types of training implicates concurrent resistance and aerobic training effects on the GM. The result of the review also supports the notion of physical activity time and sedentary time as independent factors that are associated with certain health outcomes. This is observed in the GM modifications wherein identified taxa were also associated with certain health outcomes. This means that interventions such as physical activity promotion that aims to increase physical activity time and reduce sedentary time may have effects on the GM and promote host health. Extreme levels of exercise activity may induce specific gut composition changes which are different from lower intensities. Inclusion of exercise-related parameters such as frequency, intensity, type of exercise, and physiological measures are recommended in future studies to help identify potential mechanisms on how the changes in GM composition may have occurred.

IDENTIFICATION OF KNOWLEDGE GAPS AND FUTURE DIRECTIONS IN THE PHILIPPINE SETTING

Several studies have shown the combined influence of diet and exercise in the GM in rodents and mice (McNamara et al. 2021; Batacan et al. 2017). Moreover, a review by Hughes and Holscher (2021) highlighted the effect of combined diet and exercise in the GM of athletes. However, these studies may not be sufficient to characterize the combined influence of diet and exercise to identify a healthy GM. Therefore, this review analyzed the GM profile with respect to particular modulatory effects of diet and exercise.

Notable findings on GM modulation through diet and exercise are observed in the studies reviewed (Table 3). Several gut

Table 3: Summary of Key Findings

	DIET	EXERCISE
F/B Ratio	Increased in western diet Decreased in ketogenic diet	Requires further research
Butyrate-producing Bacteria	Increased in Mediterranean, vegan, and vegetarian diets, and diet with fermented food Decreased in ketogenic diet	Increased in aerobic exercise, and frequent physical activity
Bacteroides	Increased in western diet	Requires further research
Prevotella	Increased in vegan and vegetarian diets	Increased in aerobic and concurrent exercise
Probiotic	Increased in Mediterranean diet and diet with fermented food Decreased in ketogenic diet	Requires further research
Pathogenic	Increased in ketogenic diet	Increased with sedentary time Decreased in aerobic and concurrent exercise
Lactate-utilizing Bacteria	Increased in diet with fermented food	Increased in aerobic exercise
Mucin-degrading Bacteria	Increased in western diet	Increased in aerobic exercise, anaerobic exercise, concurrent exercise, and frequent physical activity

microbes that have health-promoting properties, such as *Prevotella* and *Faecalibacterium*, are generally abundant in individuals who engage in a healthy diet or endurance activities. Meanwhile, other species of health importance, including *Akkermansia* and *Bacteroides*, are increased during gut dysbiosis brought about by certain diets, indicating possible adaptations in the gut community to protect the gut barrier and lessen inflammation. Aerobic exercise activities and profiles correspond to notable GM modulation which involve butyrate-producing microorganisms, Clostridiales, *Faecalibactereium*, Ruminococcaceae, and *Bacteroides.* Meanwhile, *Akkermansia* generally increases in both aerobic and anaerobic physical activities. *Prevotella* appears to be connected to endurance athlete profiles. Relevant markers of health and disease, such as changes in F/B ratio, P/B ratio, and pathogenic microorganisms, which are observed in both diet and exercise interventions, can be further utilized in examining the interplay between diet and exercise that may influence GM and health since the current body of knowledge regarding this is lacking or inconsistent.

Furthermore, physical activity levels and sedentary behavior may also have an influence in the GM profile. However, valid measures on levels of physical activity and sedentary behavior such as questionnaires and accelerometer are warranted to clearly define participant profile, which can affect the identification of associated GM profile for specific subject composition. How diet may affect the GM profile and how it may serve as an intervention in these situations should be elucidated.

Although this review has shown that exercise and diet have beneficial effects in the GM, there is a lack of research within the Philippine setting. This gap necessitates generation of exercise and GM studies since the Philippine population have distinct factors such as lifestyle, culture, and geographic factors compared to other populations which may affect the modulatory effects of exercise and diet on GM. In the Philippines, insufficient physical activity is highly prevalent among children (93.4%) (Guthold et al. 2020), and among Filipino adults (42.5%) (Food and Nutrition Research Institute 2015). This follows that Filipino GM profiles may have distinct characteristics. Furthermore, exercise may both address the inactivity levels and potential detrimental GM characteristics among Filipinos.

On the other hand, the typical Filipino diet has a limited diversity, given that white rice, pork, and breads contribute to the daily intake of nutrients (Angeles-Agdeppa et al. 2019a). Moreover, nutrient inadequacy and sub-optimal energy and macro- and micronutrient intake were observed in Filipino working adults and school children (Angeles-Agdeppa and Custodio et al. 2020; Angeles-Agdeppa et al. 2019b). Therefore, dietary interventions that would promote nutrient intake and foods with health benefits should be explored. Functional foods may be developed to address the nutritional inadequacy observed in the Filipino diet. The Philippines has a number of fermented food products of their own importance (Elegado et al. 2016). Local production and consumption of traditional fermented foods are becoming relevant, especially that lactic acid bacteria strains have been isolated and characterized (Banaay et al. 2013). These fermented food products may be developed as dietary interventions and further utilized as functional foods to alleviate the present problem of nutritional intake, ensure healthy lives, and promote well-being for all Filipinos.

The previous sections addressing the effect of diet and exercise on the structure of GM emphasize the need for similar research in the Philippines. Moreover, the effects of the Filipino diet and exercise on the GM structure will provide points for comparison among other diets presented in this review and utilize the data for health interventions for Filipinos. As of writing, only two studies have characterized the GM of Filipino children based on their diet (Golloso-Gubat et al. 2020; Nakayama et al. 2017) while there are no studies available on exercise and GM in the Philippine context. Further studies should be conducted to explore the GM in other age groups, as well as how physical activity affects the GM structure of Filipinos. In turn, a combined approach involving functional and healthy foods and exercise will provide stronger support in achieving not only good health and well-being goals but also other sustainable development goals in the country (Fig. 1B).

CONCLUSION

There is an evident gap on identifying exact physiological mechanisms in GM modulation by exercise and diet. However, there were several prominent taxa present in both healthy diet and exercise studies which can potentially characterize a profile for a healthy gut microbiome. Indeed, healthy diet and exercise have been empirically proven to shape a healthy gut microbiome by generally promoting beneficial microbiota and reducing pathogenic taxa.

Exercise and diet play a huge role in modulating the structure of the human gut microbiota. The interplay among diet, exercise, and GM may also be explored to improve the health status of humans. By adapting the theoretical and practical approaches presented in this review, an aggregate of exercise and diet intervention utilizing local resources will be a promising program for Filipinos to achieve a community of good health and well-being.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

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