Effects of Dietary Interventions on Gut Microbiome in Overweight or Obese Adults: A Systematic Review of Randomized Controlled Trials

Tri Ayu Setiyaning Tiyas¹,², Mochammad Sulchan¹, Endang Sri Lestari³, Etika Ratna Noer¹, Adriyan Pramono¹*

ABSTRACT

Background: It has been shown that gut microbiota dysbiosis may induce intestinal permeability, and systemic inflammation, leading to metabolic dysregulation. Furthermore, it has been implicated in the etiology of obesity. Dietary intake is known to affect the gut microbiota. These RCTs suggested that different dietary interventions may exhibit different effects on the composition of gut microbiota in overweight or obese individuals.

Objectives: This systematic review aimed to determine the effect of dietary intervention on the gut microbiota profiles in overweight or obese adults. The primary outcome of this systematic review is alpha-beta diversity and its changes at the species level.

Materials and Methods: This systematic review followed the PRISMA guidelines and was registered in the PROSPERO database with registration number CRD42022298891. A systematic search was conducted through the databases PubMed, MEDLINE, CINAHL, and Scopus literature using the terms: “gut microbiota”, “microbiome”, “overweight”, “obesity”, “insulin sensitivity”, “insulin resistance”, “blood glucose”, “randomized controlled trial”. After screening abstracts and full texts, 18 articles were extracted by two authors.

Results: Among the 18 RCT studies, dietary intervention gave an impact on gut microbiota alpha diversity changes in four studies. However, 7 studies showed no significant changes or differences compared to the placebo group. Beta diversity analysis was reported in 7 among 11 studies that performed alpha diversity analysis. Significant changes were found in food nutrients group (fiber supplementation) studies conducted over 8-12 weeks period. Seven more studies did not report any analysis of variance in either alpha or beta diversity. Changes in the composition of gut microbiota could be observed in dietary pattern interventions and resulting in improved metabolic status, except in the fried meat group diet. Interventions with food groups, food nutrients, and probiotics did not change the composition of gut microbiota.

Conclusion: The effects of dietary interventions on alpha-beta diversity are inconsistent, but rather showed more consistent effects on the changes in microbiota composition, especially in dietary pattern interventions.

Keywords: dietary interventions; gut microbiota; obesity; insulin resistance; randomized controlled trial

BACKGROUND

The prevalence of obesity worldwide has sharply increased according to the World Health Organization in 2016¹, indicating that 39% of adult population are overweight and more than 13% of them are obese¹. Obesity is characterized by increase in body-fat mass² and low-grade inflammation³ which may determine chronic diseases such as type 2 diabetes mellitus, stroke, coronary heart disease, several types of cancer, and recently, increasing in mortality caused by COVID-19 infection⁴⁵.

Obesity is caused by a long-term energy surplus, can be influenced by genetic, neurobiology, and environmental factors⁶⁷. Recently, the gut microbiota has been implicated in the etiology of

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obesity. The gut microbiota contains genes that encode thousands of microbial enzymes and metabolites that interact with human as the host to play a role in the immune system and metabolic regulation. Furthermore, the gut microbiota has been shown to regulate glucose homeostasis and lipid metabolism. In addition to that, the gut microbiota metabolites such as short-chain fatty acid are also known to regulate satiety by stimulating the production of hormone peptide YY (PYY) and glucagon-like peptide-1 (GLP-1) via the gut-brain axis.

Dietary intake is known to affect the gut microbiota. Cumulative evidence has shown that western diet rich in saturated fat and low in fibre decreases the composition of gut microbiota towards dysbiosis. It has been shown that gut microbiota dysbiosis may induce intestinal permeability, fat colonization, and systemic inflammation, leading to metabolic dysregulation. An intervention study with 40% of the total energy consisted of high-fat diet (HFD) showed changes in the composition of gut microbiota in which associated with an increase in Alistipes, a decrease in Faecalibacterium and concentration of short-chain fatty acids (SCFA), as well as an increase in arachidonic acid, lipopolysaccharide biosynthesis and inflammatory cytokines (CRP).

On the other hand, the dietary pattern of Mediterranean diet, which is rich in vegetables, fruit, nuts, whole grains, fish, and olive oil, showed a decrease in the phylum Firmicutes and was followed by the level of Ruminococcus gnavus species which has potential for pro-inflammatory conditions. Supported by an acute intervention study of the Mediterranean diet for four days, it showed changes in the abundance of fibre-fermenting bacteria, such as Lachnospiraceae and Butyrivibrio, which increased significantly and decreased after being given a high-fat diet. Another study of probiotic strain A. muciniphila supplementation was able to increase insulin sensitivity index by 30% compared to placebo. Moreover, an intervention using inulin and resistant starch within 24 hours showed an increasing trend of SCFA production.

These randomized controlled trials (RCT) suggested that different dietary interventions may exhibit differences effect in the composition of gut microbiota in overweight or obese individuals. Therefore, we conducted this systematic review to determine the effect of dietary intervention on the gut microbiota profiles in overweight or obese adults. The primary outcome of this systematic review is alpha-beta diversity and its changes at species level.

MATERIALS AND METHODS

This systematic review was carried out by published protocols and refers to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guideline 2020. This systematic review protocol has been registered in the Prospective Register of Systematic Reviews, PROSPERO (reg.no. CRD42022998891).

Data Source and Collection

A comprehensive literature search was conducted through PubMed, MEDLINE (Medical Literature Analysis and Retrieval System Online), CINAHL (Cumulative Index to Nursing and Allied Health Literature), and Scopus. The main keywords used were as follows: gut microbiota, microbiome, overweight, obesity, insulin sensitivity, insulin resistance, blood glucose, randomized controlled trial. These keywords were combined with Boolean operators (e.g. OR, AND, NOT), and all fields or MeSH (Medical Subject Heading) terms.

The interest of primary outcome was the change in gut microbiota profile seen from alpha diversity, beta diversity, and richness or abundance on specific species levels. The association of specific species with fasting insulin and fasting glucose could also be reported as a secondary outcome.

Study Selection

Eligibility criteria included studies that met the PICOS (Patients/participants, Intervention, Comparison/control group, Outcome, and Study design) in which the study population consisted of 1) individuals with overweight and/or obesity (with or without insulin resistance, metabolic syndrome; 2) adults only (more than 18 years old); 3) the minimum duration of the intervention is 1 month (4 weeks); 4) diet intervention is performed daily; 5) the reported outcome is gut microbiota profile included alpha-diversity, beta diversity and richness/abundance of species level, fasting insulin, fasting glucose; and 6) the experiment is in RCT. Exclusion criteria were consisted of individual with type 1 diabetes, type 2 diabetes, gestational diabetes, NASH, NAFLD, infectious diseases (e.g. HIV, TB, COVID-19), cancer disease, gastrointestinal disease, end-stage renal disease, neurological disease, and studies performed in adolescents or children.
During the collection process, duplicate studies were manually identified and removed. The articles were then analyzed using two-steps procedure. Initially, the retrieved titles and abstracts were independently analyzed by two authors. Next, the full text of all included articles were subjected to other analysis, then the eligible articles based on the inclusion and exclusion criteria were identified. Disagreements were resolved by consensus-based discussion or by another author’s opinion.

**Data Extraction and Quality Assessment**

Two authors (TAST and AP) independently extracted data from each study using an extract table template (Ms. Excel). Data extracted included: first author, year of publication, study design, place of study, participants’ characteristics (n, age, BMI), dietary intervention (whole diet or specific diet), duration of interventions, and outcome measures (change of alpha -beta diversity is derived from any tools such as Shannon or Simpsons Index, Chao-1, UniFrac distance, specific species level of richness or abundance, and associated of specific species with fasting insulin and fasting glucose). Each RCT was assessed for its quality using the National Heart, Lung, and Blood Institute (NHLBI) tool for intervention studies. Four of these items represented fatal flaws if answered “No/Not reported/ Can't determine”: (i) randomization (#1), (ii) dropout rate <20% (#7), (iii) valid/reliable outcome measure (#11), (iv) intent-to-treat analysis (#14). Study quality was determined based on the number of fatal flaws: good quality (0 fatal flaws), fair quality (1 fatal flaws), or poor quality (≥ 2 fatal flaws).

**Data Synthesis**

The findings from the included studies would be presented as a narrative synthesis and illustrated in a table, including the following information; authors, year, subject characteristics, type of intervention, duration, primary outcome, and secondary outcome. Subgroups analysis would be conducted for different types of dietary interventions and based on durations.

**RESULTS**

**Study Selection**

The literature search identified 130 studies that have been reported in PubMed (63); Medline (10); CINAHL (19); Scopus (38), and after excluding the duplicates and non-eligible titles and abstracts, 29 original articles were included. The identification and study selection detail are presented in the PRISMA flow chart (Figure 1).

![Flowchart Diagram for Study Selection of Systematic Review (based on PRISMA Guideline)](image)
After a review of the full text some studies were excluded: 2 non-RCT studies, 6 ineligible studies according to the inclusion criteria, 1 study without fecal microbiota analysis, 1 study with less than 4 weeks duration, and 1 study without comparison to the control or placebo group. Finally, 18 studies were selected for review.

**Study Characteristics**

Characteristics of these studies are shown in Table 1. In relation to this review, study design, study location, participants, sample size, age, body composition (e.g., body mass index/BMI), health status, dietary intervention, and duration were also included. In total, 18 RCTs were selected, with publication year between 2013-2021. There were 9 studies enrolled healthy overweight or obese participants, meanwhile the remaining studies were conducted on overweight or obese individual with insulin resistance, metabolic syndrome. Among the 18 RCT studies, 1 was single-blinded, 11 were double-blinded, 3 were open-labelled, and 3 had no report on the study design.

Any dietary interventions in the studies were classified into many sub-categories such as dietary patterns (e.g., Mediterranean diet, high fat diet, vegan diet, multifunctional diet), food groups (e.g., kimchi, the red wine polyphenol, pea fiber, and whole grain), food nutrients (inulin, arabinoxylan oligosaccharides, genistein supplementation) and probiotic supplementation which was compared to the control or placebo group. The duration the intervention vary from a minimum of 4 weeks to 1 year.

**Dietary Interventions and Gut Microbiota Diversity (α and -diversity)**

Table 2 shows an alpha-beta diversity analysis. Alpha diversity was only measured in 11 out of 18 reviewed studies. The measurement of alpha diversity used the Shannon index, Simpson index, and Chao1. Dietary intervention gave impact in in gut microbiota diversity changes in four studies. However, 7 studies showed no significant changes or differences compared to the control/placebo group. Dietary intervention with a period of more than four weeks showed changes in alpha diversity, both enrichment and decreased diversity. One of them, Vitale et al., 8 weeks intervention of Mediterranean diet showed a significant increase in gut microbiota diversity compared to the Western diet. Similar intervention in obese adults with metabolic syndrome within one year of period by Muralidharan et al. showed no change in alpha diversity compared to baseline.

Beta diversity analysis reported in 7 among 11 studies which performed alpha diversity analysis. Significant changes were found in food nutrients group (fiber supplementation) studies conducted over 8-12 weeks period. Seven more studies did not report any analysis of variance in either alpha or beta diversity.

Changes in the diversity of the gut microbiota were not only from food intake and food composition, but also from dietary patterns and the environment (such as lighting settings) affecting circadian rhythms which influence the composition of microbiota. It is interesting to consider it during the intervention which was not found in this review.

**Dietary Interventions, Bacterial Taxa, and Metabolic Marker Changes**

The abundance of bacterial taxa is reported in this study review; 15 studies were analyzed up to species level and 3 studies were analyzed up to genus levels. Details of the results are reported in Figure 2.
Dietary Pattern Interventions

Mediterranean Diet

There were 3 clinical trials that used Mediterranean diet for the intervention. The main characteristics of this diet is high in fiber, indicated by consumption patterns rich in fruits, vegetables, whole grain foods, and low in saturated fat (e.g. olive oil). A study by Muralidharan et al. reported that subjects with metabolic syndrome experienced a decrease in body weight and an increase in the ration of Bacteroidetes/Firmicutes after one year of intervention with the combination of Mediterranean diets, calorie restriction, and physical activity, compared to the control group\(^{28}\). This study is in line with the study by Remely et al. revealing that there was an increase in the abundance of Bacteroidetes after a weight loss in obese individuals \(^{45}\). In taxa composition, there were differences in abundance between the two intervention and control groups. Reduction was observed in the genus of Firmicutes, *Butyrivibrio*, *Eubacterium hallii*, and *Ruminiclostridium 5*, meanwhile in the intervention group, the genus of Coprobacter was seen increased, as well as the species of *Ruminococcaceae NK4A214* and *Lachnospiraceae NK4A136* from the family of Lachnospiraceae \(^{28}\).

In other intervention studies using Mediterranean diet, Tagliamonte et al. and Vitale et al. found that the healthy-obese group under treatment for eight weeks showed consistent results in the increasing amount of *Akermansia muciniphila* \(^{26,37}\), which are markers for healthy gut bacteria from the phylum of Verrucomicrobia \(^{46}\).

Three interventions with Mediterranean diets demonstrated favorable metabolic changes to lower glucose and insulin levels \(^{26,28,37}\). There was also an increase in postprandial plasma butyric acid after intervention \(^{37}\), considering that butyric acid provides health benefits in several studies \(^{47}\). On the other side, a study by Muralidharan et al. did not report SCFA metabolome analysis. It only included an analysis on related producer bacteria (*Lachnospira* and *Lachnospiraceae NK4A136*) which number was increased in both intervention and control groups \(^{28}\).

Multifunctional Diet (MFD)

Marungruang et al. mentioned that a multifunctional dietary intervention (MFD) diet enriched with natural antioxidant food and omega-3 supplementation also showed a significant increase in the ratio of Prevotella/Bacteroides, including the species of *Prevotella copri*. Metabolic improvement which marked by lowered diastolic blood pressure, total cholesterol, LDL-cholesterol, and triglycerides. Following those improvements, weight loss was observed after eight weeks compared to the baseline. However, there was no statistical report of tax abundance correlated between them \(^{23}\).

Vegan Diet

In study by Kahleova et al., the intervention group was given low-fat-vegan diet and vitamin B12 supplementation. Participants were requested to consistently eat a diet rich in vegetables, grains, legumes, and fruit, while avoiding animal products and added oils. The results showed a non-significant increase in the abundance of Bacteroidetes. However, reduction in body weight and improved insulin sensitivity were observed, although it had negative correlation with *Bacteroidetes fragilis* species. SCFA-producing bacteria, the species *Faecalibacterium praunzii* (butyrate producer) showed increasing in abundance in the low-fat vegan diet group. Although there was a decrease in *Bacteroidetes fragilis* in both intervention groups, but in the vegan diet group was slightly higher compared to the control group \(^{35}\).

Low Fiber Diet / High Fat Diet

A study by Gao Jian et al., using fried meat as the diet \(^{40}\), showed contradictory results to those in Mediterranean diet. This finding strengthened the evidence of gut microbiota changes following the high fiber diet especially in individuals consuming Mediterranean diet \(^{26,28,37}\). An increase in the abundance of *Dialister* and *Veillonella* from the Firmicutes group occurred in the fried meat group. Deep-frying was used as cooking method to fry the meat during 4 weeks and resulted in a drop of SCFA producing bacteria (*Lachnospiraceae* and *Flavonifractor*). This proved that the result of fried meat intervention was identical to the high-fat diet, in which a significant decrease of butyric acid, valeric acid, and an increase in lipopolysaccharide were observed. Insulin levels was also amplified by an increase in muscle insulin resistance index (MIRI) and several inflammatory cytokines.TNF-α, IL-10, and IL-1β \(^{40}\).

Fava et al. reported that total bacteria was decreased after subjects were given high-fat diet. Interestingly, reduction in fat intake accompanied by increasing in carbohydrate intake (thigh carbohydrate

Food Groups

Whole Grain vs Refined Grain

Roager et al. investigated two dietary intervention studies, in which each duration was 8 weeks. The subjects were given either whole-grain diet or refined-grain diet. A total of 60 adults at risk of developing metabolic syndrome participated in these randomized controlled cross-over design studies. It was found that the whole-grain dietary intervention did not significantly impact the changes of bacterial species composition and diversity in the gut microbiota (even after FDR correction for multiple tests was performed). However, among several species, *Faecalibacterium prausnitzii* and *Prevotella copri* responded with an increase in abundance after being given whole-grain diet, while decreased immediately after consumption of refined-grain diet. Decreasing in body weight, fat-free mass, and inflammatory biomarkers (IL-6) after adjusting for weight loss was observed.32

Kimchi

Kimchi is a traditional food from South Korean. It is a fermented food with main ingredients are Chinese cabbage, garlic, red pepper, green onion, and ginger. Han et al. compared the difference of giving fresh kimchi vs fermented kimchi to overweight/obese individuals during 8 weeks. The result showed that the group receiving fermented kimchi had greater proportion of bacterial strains than those receiving fresh kimchi. Some changes observed towards the ratio of bacteria after fermented kimchi administration were as follow: 1) the number of Firmicutes and Bacteroidetes were dropped; 2) *Bacteroides* and *Prevotella* were escalated; and 3) *Blautia* was decreased. On the other side, in the group consuming fresh kimchi, there was a slight reduction in fasting glucose and insulin levels in comparison to the baseline. This result was not found in the group consuming fermented kimchi.33

Red wine

A cross-over RCT study with red wine polyphenol supplementation in individuals with metabolic syndrome by Moreno et al. reported that there was an increase in *Bifidobacterium bifidum* species after 30 days of red wine supplementation. At baseline, microbiota analysis showed low abundance of several species such as *Bifidobacterium*, *Eggerthella lenta*, *Prevotella*, *Blautia coccosides–Eubacterium rectale group*, *Lactobacillus*, *Faecalibacterium prausnitzii* and *Roseburia*. A consistent increase in *Faecalibacterium prausnitzii* from the phylum Firmicutes in both intervention and control groups, although there was no significant difference between the two groups. This might happen because red wine polyphenols have prebiotic capacity that presents positive effect towards fasting blood glucose levels, LPS concentrations, and CRP levels in Mets individuals.36

Food nutrients

Fiber

The composition, diversity, and abundance of gut microbiota are largely influenced by fiber consumption. Fiber provides a number of metabolic substrates that are used for fermentation reactions carried out by the gut microbiota.48. In this review, there are three studies with fiber supplementation that consistently show increasing in the Firmicutes phylum. 24,30,38

An intervention study by Chambers et al. that supplemented the subjects with 20 g/day of inulin-propionate ester (IPE), resulted in a rise of Firmicutes phylum, with species bacteria from *B. obenum*, *E. ruminantium*, meanwhile in the inulin group the subject experienced an increase in *B. obenum*, *B. luti*, *B. faecis*, *R. faecis*, *Oscillibacter spp*. Similarly, supplementation of IPE or inulin only significantly improved insulin sensitivity (HOMA index, Matsuda index) when compared to cellulose administration.38

A crossover-RCT study about supplementation of arabinoxylan (AXOS) and PUFA on central obese individuals with metabolic syndrome by Kjolbaek at al., resulted in a drop of Bacteroidetes phylum abundance and a rise in the abundance of Actinobacteria and Bifidobacteria phylum. It also showed an abundance increasing of butyrate-producing species from Firmicutes phylum and Clostridiales order such as *Eubacterium rectale*, *Faecalibacterium prausnitzii*, *Blautia wexlerae*, *Dorea longicatena*, *Eubacterium hallii*, *Blautia luti*, *Ruminococcus obeum*, *Fusobacterium saccharivorans*. Unfortunately, there was no washout period between supplementation of AXOS and PUFA. On the other hand, both AXOS and PUFA...
supplementation did not result in the changes of metabolic parameters.\textsuperscript{24} Meanwhile, there was no change observed in the composition of gut microbiota after PUFA supplementation.

Supplementation of 15 g/d yellow pea fiber for 12 weeks in a study conducted by Lambert et al. showed a non-significant increase in total bacteria. However, there was a trend of increasing gut microbiota abundance, which was followed by an increase in the abundance of \textit{Clostridium leptum}, \textit{Clostridium cluster I}, and \textit{Roseburia spp} when compared to the placebo group. This supplementation has a slightly significant metabolic effect to improve body fat profile and glucose tolerance\textsuperscript{30}.

**Genistein**

Genistein is an isoflavone compound found in foods, especially soybeans. Genistein is able to modulate the composition of the gut microbiota and reduce metabolic endotoxemia (LPS) and is able to increase insulin sensitivity as indicated by the HOMA index or Matsuda index. A study by Guevara et al. showed a decrease in the Firmicutes/Bacteroidetes ratio, an increase in the Verrucomicrobia phylum, and abundance increasing \textit{A. muciniphila}, \textit{Ruminococcus bromii}, and \textit{B. uniformis} after 50 mg/day of genistein supplementation for 2 months in comparison to the placebo group\textsuperscript{39}.

**Probiotic Supplementation**

There are 4 studies of probiotic supplementation in this review; all of them reported changes in the composition of gut microbiota and metabolic markers after supplementation\textsuperscript{25,27,29,34} although there was no change in total composition of bacteria\textsuperscript{27}. The metabolic markers observed were reduced insulin levels\textsuperscript{25}, fasting blood glucose\textsuperscript{29}, improved insulin sensitivity\textsuperscript{34}, and improvement of cell-mediated incretin function occurred in \textit{L.reuteri} probiotic supplementation.

A study by Teronio et al. using Lactobacillus spp supplementation with dosage of 9log10 cfu/capsule and omega-3 in individuals with metabolic syndrome resulted in increasing of \textit{Verrucomicrobia} phylum with specific genus is Akkermansia. Significant differences in changes of the metabolic markers between both groups (prebiotic and omega-3) were also observed. A trend of reduced insulin levels, inflammatory cytokines (IL-6), and soluble vascular cell adhesion molecule 1 (sVCAM) which were closely associated with cardiovascular disease risk was also seen\textsuperscript{25}.

Similar results in a study by Depomnier et al. showed an inclined number of \textit{A. muciniphila} after administration of living \textit{A. muciniphila} or pasteurized \textit{A. muciniphila}\textsuperscript{34}. Pasteurized \textit{A. muciniphila} markedly and significantly improved insulin sensitivity index by about 30% as compared to the placebo group.

A double blind RCT probiotic supplementation by Rajkumar et al. (group 1: placebo, group 2: VSL3, group 3 = omega 3, group 4 =VSL3 and omega 3 capsules) showed a significant increase in total bacteria aerobes, \textit{Lactobacillus}, \textit{Bifidobacteria} and \textit{Streptococcus} in groups 2 and 4. Interestingly, the total bacteria Bacteroides, Cloforms, and \textit{Escherichia coli} was changed in group 4. It was only group 3 that showed no changes\textsuperscript{29}.

**Quality of Included Studies**

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Table 3. Quality Assessment of Studies

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e-ISSN : 2338-3119, p-ISSN: 1858-4942
**Table 3: Methodological quality scores of included studies.**

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<td>Poor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitale et al. 2020</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>NR</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Good</td>
<td></td>
</tr>
<tr>
<td>Gao Jian et al. 2021</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Good</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muralidharan et al. 2021</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
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<td>N</td>
<td>Poor</td>
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<tr>
<td>Tagliamonte et al. 2021</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Fair</td>
<td></td>
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</tr>
</tbody>
</table>

Of the 18 included studies in this review (Table 3), the methodological qualities of three studies were stated to be good, ten were classified as fair, and five were placed as poor. Related the prominent flaws, four studies did not use randomized controlled design; two studies presented dropout rates above 20%, and eight studies did not perform intention to treat analysis.

**DISCUSSION**

In general, it is difficult to draw conclusions about the effect of dietary intervention in this regard. Metabolic health status, type of dietary intervention, duration of intervention, study design, and sample size may lead to different outcomes among studies. Although there are differences in study results, most of the studies showed association between taxa-specific changes after dietary intervention was given and the metabolic health parameters such as glucose metabolism, fat, insulin sensitivity, inflammation, and some SCFA metabolites due to changes in tax composition.

Dietary intervention is an important external factor because it influenced the composition and abundance of the gut microbiota. The nutrients contained in the foods are used for survival of the microbes in the digestive tract. Beneficial bacteria is associated with high-fiber intake in either dietary pattern intervention (Mediterranean diet, MFD diet, vegan diet), food groups (kimchi), or food nutrients (insulin, axos supplementation). Similar effects were confirmed by the systematic review by Wagenaar et al.

There is an increase in the genus of Lachnospiraceae NK4A136 from the family of Lachnospiraceae, species of Faecalibacterium prausnitzii, Eubacterium rectale, Eubacterium hallii, and Roseburia spp. Several types of these bacteria are believed to be part of the butyrate-producing taxa. A rising number of Akkermansia muciniphila also occurred after the administration of Mediterranean diet and fiber supplementation (AXOS). Akkermansia muciniphila has an important role to maintain intestinal barrier function as a feature of healthy gut profile. The number of Prevotella copri was inclined after being given whole-grain diet but immediately dropped when the diet was replaced with refined-grains.

High-fat and low-fiber consumption pattern such as in typical Western diet can reduce total bacteria, as well as the abundance of the Lachnospiraceae and Flavonifractor families (SCFA-producing bacteria), meanwhile the amount of pathogenic bacteria which is closely related to obesity was increased. In another study conducted by Mocanu et al., low-fiber diet did not change the composition and diversity of bacteria, but on the other side, changes after fecal microbial transplantation (FMT) was found.

High-fiber intake in a whole-diet intervention showed improvements in metabolic parameters such as improved insulin sensitivity, diastolic blood pressure, total cholesterol, LDL and triglycerides, an inflammatory cytokine (IL-6), reduced glucose levels, and an increase in postprandial butyric acid after Mediterranean diet intervention.

Some supplements such as IPE and inulin improved insulin sensitivity compared to cellulose administration. On the other hand, AXOS supplementation did not show significant changes in blood pressure, glucose metabolism, and lipids. Similarly, fiber supplementation from yellow pea resulted in a slight improvement on body fat and glucose tolerance.

Phytochemicals (polyphenols) are able to provide two effects on the gut microbiota: 1) inhibiting the growth of certain taxa, and 2) increasing the growth of bacteria because they can be metabolized into substrates for the host. Regarding these properties, red wine-polyphenols administration can increase the abundance of Faecalibacterium prausnitzii and affect the metabolic health by decreasing fasting blood glucose levels, LPS concentrations and CRP levels. Another type of phytochemicals is genistein, which in some studies were shown a rising number of Akkermansia muciniphila after genistein supplementation and significantly improved the insulin sensitivity by 30% compared to the control group.

Faecalibacterium prausnitzii is butyrate-producing microbiota that consistently presents in high-fiber intake (Mediterranean, Vegan, and AXOS) and in red wine-polyphenol interventions. Dietary fibre is a carbohydrate polymer that cannot be metabolised by amylase and cannot be absorbed in small intestine.

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Dietary fibre can only be processed by certain species of gut microbiota through an anaerobic fermentation process, with the main product being SCFA (butyrate, propionate, acetate)\(^{48}\). Short-chain fatty acid is a metabolite products that play a role in energy regulation processes, immune system, and cell proliferation\(^{58}\). Butyrate is present in a greater proportion in the intestinal lumen\(^{58}\).

Gram-positive butyrate-producing bacteria plays important role in gut health, by carrying out the fermentation process in the colon. The process takes place by obtaining ATP through substrate-level phosphorylation during the breakdown of oxidative-substrate\(^{48}\). Then, combination of two molecules of acetyl-CoA to form acetoacetyl-CoA, accompanied by a gradual reduction to butyryl-CoA for the next step in the formation of butyrate\(^{51}\). Intestinal mucosa requires butyrate as its main energy and plays a role in the regulation of gene expression, inflammation, differentiation, and apoptosis in host cells. Butyrate is able to reduce the negative effects of lipopolysaccharides and simultaneously increase the regulation of intestinal barrier function by stimulating the production of mucin, as well as activation of G-protein receptors (GPR41 and GPR43) in the large intestine, stimulation of the production of hormone peptide YY (PYY) and glucagon-like peptide-1 (GLP-1) which affects glucose homeostasis\(^{11}\).

High-fat and low-fibre diets cause gut bacteria to use mucin glycans for self-metabolism by inducing the expression of enzyme genes that result in decreased the mucin\(^{57}\), leading to a risk of leaky gut barrier which is characterised by increased permeation of luminal contents into the mucosa and submucosa layer around immune cells. This condition has potential to cause translocation of lipopolysaccharide compounds (LPS) into the blood circulation\(^{59}\) which leads to metabolic dysregulation\(^{16}\).

In the fried-meat intervention group, a drop in butyric and valeric acid, a rise in lipopolysaccharide and insulin levels were occurred due to amplification by an increase in muscle insulin resistance index (MIRI) and several inflammatory cytokines (TNF-α, IL-10, and IL-1β)\(^{60}\). In addition, the study reported by Fava et al in the high showed a significant increase in fecal butyrate and propionate. In this perspective, the increase in fecal SCFA in obese individuals is interesting to understand in regard to the intestinal absorption function and/or activity modulation of the composition of gut microbiota present\(^{44}\). Moreover, it is probably the choice of plasma SCFA measurement as in the study of Vitale et al can be considered to assess the exact amount of SCFA levels\(^{37}\).

Probiotic supplementation also provides significant changes in the composition and abundance of gut microbiota, excluding symbiotic supplementation\(^{60}\) and only omega-3 supplementation without any combination with probiotics\(^{39}\). An increase in Akkermansia muciniphila appeared after supplementation with the probiotic Lactobacillus, in the form of living or pasteurized A. Muciniphila\(^{86,52}\). Reduced insulin levels\(^{25}\) and fasting blood glucose\(^{29}\), improvement in insulin sensitivity\(^{34}\) and cell-mediated incretin function occurred with probiotic supplementation of L. reuteri\(^{27}\).

The plausible mechanism that might explain the improvement in metabolic health is the ability of probiotics to repair the intestinal epithelial barrier and reduce intestinal permeability due to previous dietary consumption patterns, leading to inflammation suppression and translocation of endotoxins into the blood vessels\(^{61,62}\). Positive correlation in regards to improved insulin sensitivity was reported in relation to bacterial species of A. Muciniphila\(^{34}\), Bacteroides fragilis\(^{35}\), Bacteroides stercoris, Bacteroides caccae, Phascolarctobacterium faecum\(^{54}\), Intestimonas butyriciproducens, Desulfovibrio piger, Coprobacter fastidiosus\(^{25}\), one OTU (unpublished species name) classified as Prevotella genus\(^{44}\), and also Lactobacillus reuteri\(^{37}\). Meanwhile, negative correlation was found in the types of bacteria Dialister succinifilus, Turibacter sanguinis, Alloprevotella\(^{34}\). In addition, Faecalibacterium prausnitzii\(^{28}\), Eubacterium eligens\(^{37}\) has negative correlation with blood glucose levels.

Akkermansia muciniphila is one of species that appears consistently for a minimum of eight weeks duration\(^{25,26,37,39}\) (more details in Table 3). Nine dietary intervention studies were administered to healthy overweight/obese individuals. Seven studies (78%) demonstrated significant improvements in metabolic health, occurring at a minimum duration of four weeks of intervention\(^{23,26,30,35,37,38,40}\). Two studies in the obese group with insulin resistance showed improvement in metabolic status beginning at week 6\(^{25,29}\). One study in pre-diabetic individuals did not report any change in metabolic markers\(^{63}\).

Inconsistent changes were also still visible at long duration of 10-12 weeks\(^{24,25,34,36,54}\), but starting at 28 weeks up to one year of the duration, it showed significant change results\(^{28,33}\). These results possibly indicated that individuals with metabolic syndrome require a long-term diet to achieve significant change. Several other studies suggest the possibility that there is no significant effect of diet on gut microbiota and metabolic health, depending on interpersonal variability in enterotype composition, even if the individuals have been subjected to appropriate extreme diets\(^{64}\). Therefore, further mechanisms need to be investigated.
In this review, differences in the diversity and composition of gut microbiota taxa may be influenced by factors such as metabolic health status, duration of intervention and types in the dietary intervention itself. In general, a high-fibre diet and dietary interventions rich in polyphenols (there is prebiotic capacity) have a positive effect on the diversity and composition of beneficial microbes that are beneficial in improving metabolic function. It could be partly associated with increased levels of SCFA through the process of bacterial fermentation. Furthermore, the effectiveness of probiotic administration depends on the specific strain used on the initial composition of the individual gut microbiota. Finally, the limited included studies in this review might also be a major limitation of this systematic review; thus, further investigation in a large well-controlled study is needed to confirm these findings.

CONCLUSIONS

In conclusion, the effects of dietary interventions on alpha-beta diversity are inconsistent but showed more consistent effects on microbiota composition changes. Meanwhile, interventions with food groups, food nutrients, and probiotic did not change gut microbiota composition. Changes in gut microbiota composition could be observed after modifying the diets, resulting in improved metabolic status. However, this does not include the group receiving dietary interventions with fried meat. Future studies on the effects of cooking methods on the gut microbiota and metabolic health status are interesting to investigate further.
## Table 1. Characteristic of Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Design</th>
<th>Location</th>
<th>N (subject)</th>
<th>n, GM was analyzed</th>
<th>age (years)</th>
<th>BMI (kg/m²)</th>
<th>Health Status</th>
<th>Intervention</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fava et al. 2013</td>
<td>SB-RCT</td>
<td>UK</td>
<td>130</td>
<td>88 (HS group = 11,</td>
<td>54±9.5</td>
<td>28.8±4.9</td>
<td>obese with metabolic</td>
<td>Following a high saturated fat diet (HS) - high glycemic index (GI) diet (total fat 38%E fat, SFA 18%E, MUFA 12%E, PUFA 6%E, CHO 45%E, GI 64%), after which participants were randomly assigned to one of four experimental diets (HM/HGI: total fat 38%E, SFA 10%E, MUFA 20%E, PUFA 6%E, CHO 45%E, GI 64%; HM/LGI: total fat 38%E, SFA 10%E, MUFA 20%E, PUFA 6%E, CHO 45%E, GI 53%; HC/HGI: total fat 38%E, SFA 10%E, MUFA 20%E, PUFA 6%E, CHO 45%E, GI 53%; HC/LGI: total fat 28%E, SFA 10%E, MUFA 11%E, PUFA 6%E, CHO 55%E, GI 51%)</td>
<td>28 weeks (4 weeks run out HS diet, 24 weeks one of four diet intervention HM/HGI; HM/LGI; HC/HGI; HC/LGI)</td>
</tr>
<tr>
<td>Marungruang et al. 2017</td>
<td>RCT</td>
<td>Sweden</td>
<td>52</td>
<td>(multifunctional diet = 25, control diet = 27)</td>
<td>50-73</td>
<td>25-33</td>
<td>obese</td>
<td>MFD group were given foods rich in natural antioxidants, omega-3 fatty acids, high (prebiotic) fiber, low glycemic, blood cholesterol-normalizing ingredients. MFD provided 2 g stanol/d for women and 2.7 g/d for males. Total dietary fiber content was 62 g/day vs control. Both diets were designed in agreement with the Nordic Nutrition Recommendations and supplied 2500–2600 Kcal/day for men and 2000–2100 Kcal/day for women, combining foods from plant and animal origins.</td>
<td>8 weeks</td>
</tr>
<tr>
<td>Author</td>
<td>Design</td>
<td>Location</td>
<td>N (subject)</td>
<td>n, GM was analyzed</td>
<td>age (years)</td>
<td>BMI (kg/m²)</td>
<td>Health Status</td>
<td>Intervention</td>
<td>Duration</td>
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<tr>
<td>Kahleova et al. 2020</td>
<td>open label-RCT</td>
<td>Columbia</td>
<td>168 (vegan group = 65; control group = 84)</td>
<td>115 (vegan group = 65; control group = 50)</td>
<td>&gt;18</td>
<td>28-40</td>
<td>healthy overweight adult</td>
<td>low fat vegan diet vs control. Vitamin B12 was supplemented for vegan group (500µg/day)</td>
<td>16 weeks</td>
</tr>
<tr>
<td>Vitale et al. 2020</td>
<td>DB-RCT Parallel Group</td>
<td>Italy</td>
<td>Mediterranean diet = 16; Control Diet (western diet) = 13</td>
<td>Mediterranean diet = 16; Control Diet (western diet) = 13</td>
<td>41.6 ± 12.3</td>
<td>Mediterranean diet = 28.9±2.3; Control Diet = 29.3±3.5</td>
<td>The control diet was instructed to keep their habitual diet unvaried during the intervention and did not consume extra virgin olive oil Mediterranean Diet was designed to have fruit and vegetable 500gr/day, nuts 30gr/day, refined cereal products replaced with wholegrain products 200gr/day, meat and derived meat products, fish 300gr/day, legumes 200gr/day, extra virgin olive oil</td>
<td>8 weeks</td>
<td></td>
</tr>
<tr>
<td>Gao Jian et al. 2021</td>
<td>DB-RCT</td>
<td>China</td>
<td>117 (control group = 58; fried meat group = 59)</td>
<td>117 (control group = 58; fried meat group = 59)</td>
<td>21.73; fried meat group = 21.13</td>
<td>26.39; fried meat group = 26.06</td>
<td>Fried meat was provided four times per week in the experimental the group with cooking methods, which was frying at 150 C for &lt;3 min; and boiling, steaming, or dressing with sauce at 100 C in the control group.</td>
<td>4 weeks</td>
<td></td>
</tr>
<tr>
<td>Author</td>
<td>Design</td>
<td>Location</td>
<td>N (subject)</td>
<td>n, GM was analyzed</td>
<td>age (years)</td>
<td>BMI (kg/m²)</td>
<td>Health Status</td>
<td>Intervention</td>
<td>Duration</td>
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<tr>
<td>Muralidharan et al. 2021</td>
<td>DB-RCT</td>
<td>Spain</td>
<td>400 (intervention group = 200; control group = 200)</td>
<td>262 (intervention group = 183; control group = 179)</td>
<td>intervention group = 64.3 ± 5.1; control group = 65.1 ± 4.9</td>
<td>ow/ob with metabolic syndrome</td>
<td>intervention group = individualized behavioral support, restricted caloric Mediterranean Diet, and physical activity promotion; control group = information on maintaining ad libitum unrestricted caloric Mediterranean Diet with no advice on weight loss strategies</td>
<td>1 year</td>
<td></td>
</tr>
<tr>
<td>Tagliamonte et al. 2021</td>
<td>DB-RCT</td>
<td>Italy</td>
<td>82 (Mediteranean Diet = 43, Control Diet =39)</td>
<td>82 (Mediteranean Diet = 43, Control Diet =39)</td>
<td>Mediterranean Diet = 31.1±0.5 ; Control Diet = 31.2±2.0)</td>
<td>ow/obese group 1 = Isocaloric Tailored Mediterranean Diet; group 2 = control</td>
<td>8 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Han et al. 2015</td>
<td>RCT</td>
<td>Korea</td>
<td>fresh kimchi group = 12; fermented kimchi group = 11</td>
<td>fresh kimchi group = 10; fermented kimchi group = 10</td>
<td>30 - 60</td>
<td>fresh kimchi group = 28 ± 2.31; fermented kimchi group = 27.8 ± 2.20</td>
<td>ow/obese consuming 180 g of fresh or fermented kimchi per day (60 g/pkg × 3 meals)</td>
<td>8 weeks</td>
<td></td>
</tr>
</tbody>
</table>

**Food groups**

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<table>
<thead>
<tr>
<th>Author</th>
<th>Design</th>
<th>Location</th>
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<th>BMI (kg/m²)</th>
<th>Health Status</th>
<th>Intervention</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moreno et al.</td>
<td>RCT-cross</td>
<td>Spain</td>
<td>MetS group 10, control group = 10</td>
<td>MetS group = 10, control group = 10</td>
<td>48±2</td>
<td>MetS vs control group: 35.2±4.21 vs 27.5±2.10</td>
<td>Metabolic syndrome</td>
<td>Divided into three periods; the first period was the washout period (participants did not consume any red wine), the second period was drunk only red wine (272 ml/d), the third period was drunk de-alcoholized red wine (272 ml/d)</td>
<td>10 weeks (two weeks/15 days of washout period, followed by two intervention periods of 30 days each)</td>
</tr>
<tr>
<td>Lambert et al.</td>
<td>DB-RCT cross</td>
<td>Canada</td>
<td>pea fiber group = 29; placebo group = 22</td>
<td>pea fiber group = 22, placebo group = 22</td>
<td>44±15</td>
<td>33.4±1.3 (PG); 32.8±1.3 (Pea fiber group)</td>
<td>Obesity</td>
<td>The pea fiber group received 15 g/d pea fiber supplementation with the dose was increased incrementally during the first 3 weeks of the study (week 1 ¼ 5 g/d; week 2 ¼ 10 g/d; week 3 ¼ 15 g/d. Pea fiber is packaged in wafers containing 5 g/serving of yellow pea fiber vs placebo group received an isocaloric dose of control wafers with no pea fiber</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Roager et al.</td>
<td>DB-RCT cross</td>
<td>Denmark</td>
<td>60 (men = 18; women = 32)</td>
<td>20-65</td>
<td>25-35</td>
<td>ow/ob at risk of developing metabolic syndrome</td>
<td>group 1 = whole-grain ≥ 75 gr/day; group 2 = &lt; 10 gr/day of refined grain</td>
<td>8 weeks for each group, with washout period 6 weeks</td>
<td></td>
</tr>
<tr>
<td>Author</td>
<td>Design</td>
<td>Location</td>
<td>N (subject)</td>
<td>n, GM was analyzed</td>
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<td>Duration</td>
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<tr>
<td>Chambers et al. 2019</td>
<td>DB-RCT-cross over</td>
<td>UK</td>
<td>14</td>
<td>12</td>
<td>12</td>
<td>18-65</td>
<td>29.8±0.9</td>
<td>ow/obese</td>
<td>42 days each in random order. The washout period for the next intervention was carried out for 28 days</td>
</tr>
<tr>
<td>Kjolbaek et al. 2019</td>
<td>Opened label RCT-cross over</td>
<td>Denmark</td>
<td>30</td>
<td>27</td>
<td>27</td>
<td>18 - 60</td>
<td>25-40</td>
<td>central obese and one criterion of metabolic syndrome</td>
<td>12 weeks (two diet periods of 4 weeks each separated by a 4-week washout period)</td>
</tr>
<tr>
<td>Guevara et al. 2020</td>
<td>DB-RCT</td>
<td>Mexico</td>
<td>45 (PG = 23; GTG = 22)</td>
<td>45 (PG = 23; GTG = 22)</td>
<td>20-60</td>
<td>PG = 34.5 ± 0.98; GTG = 34.6 ± 0.86</td>
<td>obese with insulin resistance</td>
<td>The subjects were randomly selected to form part of the placebo group (PG) or the genistein-treated group (GTG) with genistein capsules (50mg/day)</td>
<td>8 weeks</td>
</tr>
</tbody>
</table>

Food nutrients

20 g/day of inulin , 20 g/day inulin-propionate ester / IPE (14.6 g/day of inulin and 5.4 g/day of esterified propionate vs 20 g/day of cellulose (placebo - negative control)

Probiotic

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<table>
<thead>
<tr>
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<th>n, GM was analyzed</th>
<th>age (years)</th>
<th>BMI (kg/m²)</th>
<th>Health Status</th>
<th>Intervention</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rajkumar et al.</td>
<td>DB-RCT</td>
<td>India</td>
<td>placebo (n = 15), VSL#3 probiotic capsules (n = 15), omega-3 fatty acid capsules (n = 15), omega-3 capsule + VSL#3 probiotic capsule (n = 15)</td>
<td>placebo (n = 15), VSL#3 probiotic capsules (n = 15), omega-3 fatty acid capsules (n = 15), or omega-3 capsule + VSL#3 probiotic capsule (n = 15)</td>
<td>40-60</td>
<td>± 28.79 (range 27-30)</td>
<td>obese, dyslipidemia and insulin resistance</td>
<td>Group 1 = nothing; group 2 = 1 capsule probiotic of VSL#3 everyday; group 3 = 1 capsule of omega 3 everyday; group 4 = 1 capsule of omega 3 and VSL#3 probiotic everyday</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Simon et al.</td>
<td>DB-RCT</td>
<td>Jerman</td>
<td>21</td>
<td>21 (men = 10, women = 11)</td>
<td>lean group = 49 ± 7; obese group = 51 ± 7</td>
<td>392</td>
<td>obese</td>
<td>placebo group = receive Nutraceutix capsule placebo; intervention group = Nutraceutix capsule contain 10^10 cells of L. reuteri</td>
<td>8 weeks</td>
</tr>
<tr>
<td>Depomnier et al.</td>
<td>DB-RCT</td>
<td>Belgium</td>
<td>40</td>
<td>32 (n placebo = 11; n pasteurized = 12; n alive = 9)</td>
<td>placebo = 37.63±5.82; pasteurized = 39.81±4.77; alive = 36.82±3.68</td>
<td>32</td>
<td>18-70</td>
<td>ow/obese with insulin resistance and metabolic syndrome</td>
<td>Alive A. muciniphila (live 10^10 bacteria per day); pasteurized A. muciniphila (pasteurized 10^10 bacteria per day); Placebo</td>
</tr>
<tr>
<td>Teronio et al.</td>
<td>DB-RCT</td>
<td>Spanyol</td>
<td>53 (group 1 = 28, group 2 = 25)</td>
<td>53 (group 1 = 28, group 2 = 25)</td>
<td>&gt; 30</td>
<td>obese with metabolic syndrome</td>
<td>placebo group = maltodextrin; intervention group = probiotic Lactobacillus spp 9 log10 cfu/capsule, 1 capsule/day, with wash out periode (6 weeks)</td>
<td>12 weeks</td>
<td></td>
</tr>
</tbody>
</table>
**Table 2. Primary Outcome for Gut Microbiome Following Dietary Interventions (Alpha-Beta Diversity)**

<table>
<thead>
<tr>
<th>Author</th>
<th>Health Status</th>
<th>Dietary pattern</th>
<th>Food Groups</th>
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Ow/ob: overweight/obese, Mets: metabolic syndrome, IR: insulin resistance
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