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Efficacy of Probiotic Supplementation for Weight Loss in Overweight and Obese Adults

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Abstract

The purpose of this literature review is to assess current studies investigating the efficacy of using probiotic supplementation to promote weight loss in the overweight and obese adult populations. Three databases were used including PubMed, ClinicalKey, and Embase with a time frame of 15 years. A total of 17 studies met the research criteria and were therefore reviewed. Body weight loss and decrease in BMI were used as measurements of efficacy. Studies used were peer reviewed, randomized-control trials, double-blind, and placebo-controlled. Current research shows insufficient evidence to support the use of a specific genus and/or species of probiotic to promote weight loss in the overweight and obese adult populations. *L. gasseri, L. acidophilus*, *L. curvatus* in combination with *L. plantarum*, and several genus combinations have studies supporting their use for weight loss. Additionally, studies evaluating *L. amylovorus* and *L. rhamnosus* showed significant weight loss with supplementation; however, their results were gender specific. Significant decrease in BMI was exhibited in groups supplemented with *L. amylovorus, L. gasseri, L. plantarum, L. curvatus* with *plantarum*, and several genus combinations when compared to placebo groups. Several studies found that benefits ceased after the probiotic supplementation was discontinued, suggesting that ongoing supplementation may be required. Finally, the side effects associated with probiotic supplementation were minimal, regardless of the strain, gender, or duration. This may suggest that potential benefits could outweigh risks.

Keywords*: probiotics, probiotic supplement, probiotic therapeutic use, probiotic agent, weight loss, body weight loss, body mass index, obesity, Lactobacillus*

Introduction

With the prevalence of obesity continually on the rise and estimated to affect over 50% of adults in the United States by the year 2030, causative factors and potential treatments have become an area of increasing interest to researchers and health care providers. While genetics, caloric intake, and caloric expenditure are known to play a role in the development and treatment of obesity, there has been a growing curiosity regarding the effects of gastrointestinal (GI) microbiome on weight change. There have been over 1000 bacterial species identified as having the ability to inhabit the human GI tract, and it is estimated that at least 160 species colonize the gut of each individual at any given time (Grahmn, Mullen & Whelan, 2015). Erraticism of gut microbiome has been related to socioeconomic status, age, and diet, among other demographic variables (Ding & Schloss, 2014). The potential functions of GI bacteria include fermentation, catabolism of toxins, synthesis of micronutrients, complex sugar digestion, and alteration in metabolism. It is suspected that the location of the bacterial strain within the gut may actually alter its role. There are limited human studies at this time comparing the microbiome composition at different regions of the intestinal tract, making it difficult to assess or compare the changeability of the bacterial role based on location (Devaraji, Hemarajata & Versalovic, 2014). Understanding the intricate relationship between the human microbiome and its impact on pathology and metabolism is vital in order to assess the efficacy of utilizing probiotics to alter weight in obese and overweight populations. Though the outcomes of GI microbiome manipulation are still relatively new to research, there is theory that probiotic supplementation, leading to altered GI microbiome, may be beneficial for therapeutic use to promote weight loss and other favorable anthropometric changes. The purpose of this literature review is to investigate current studies exploring the efficacy of using probiotic supplementation to promote weight loss and improvement in body mass index (BMI) in the overweight and obese adult population.

Statement of the Problem

According to the Centers for Disease Control and Prevention (2020), those with obesity are at increased risk for numerous co-morbidities, including hypertension (HTN), hyperlipidemia (HLD), type two diabetes (NIDDM), coronary heart disease (CHD), osteoarthritis (OA), and many others. While organizations continue to work toward the development of tools and potential intervention options for the treatment of obesity, the percentage of adult Americans with obesity continues to rise (CDC, 2021). Although we know lifestyle plays a crucial role in weight management, a study completed by Foster-Schubert et al. in 2012 concluded that lifestyle modification alone resulted in weight loss of only about 5-10% of baseline weight and was often inadequate to achieve and maintain a normal weight. When considering these findings, it is evident that health care providers are in need of additional treatment options to offer to this population. Although alternatives such gastric bypass and weight loss medications are currently available, it is important for providers to be aware of complementary or supplementary interventions that may improve the success rates for patients seeking weight loss.

Research Questions

In overweight and obese adults, does probiotic supplementation promote greater weight loss when compared to weight changes with no probiotic supplementation? Furthermore, do the benefits of using probiotic supplementation for weight loss outweigh the risks?

Methods

A literature review was conducted using the following databases: PubMed, ClinicalKey, and Embase. Keywords and mesh terms were used to delineate a set of literature discussing use of probiotic supplements for weight loss and then specifically for the overweight and/or obese populations. A BMI of 25 or greater, as established by the CDC (2021), was used to define the overweight and obese population. The search revealed 87 results. Only 6 of the studies met final criteria, and for this reason, the time frame was expanded from literature published within the last five years to literature published over the past 15 years. Studies which focused on the use of probiotic supplementation in the animal, pediatric, or neonatal populations were excluded. Additionally, studies which discussed only the effect of probiotic supplementation on bariatric surgery or chronic disease outcomes were excluded. A total of 17 studies met criteria and were therefore reviewed. Body weight loss and decrease in BMI were used as measurements of efficacy.

Keywords: probiotics, probiotic supplement, probiotic therapeutic use, probiotic agent, weight loss, body weight loss, body mass index, obesity, *Lactobacillus*

Review of Literature

A review of literature revealed several studies investigating the efficacy of probiotic supplementation for weight loss in overweight and obese populations. Since research on this topic is early in its development, no guidelines have been established regarding strain of probiotic, dosage, or length of use. Variable probiotic strains were used throughout the studies, and thus, conclusions regarding efficacy were strain specific. *Lactobacillus gasseri, Lactobacillus acidophilus*, combination of *Lactobacillus curvatus* and *plantarum*, and several combination strain probiotics had studies supporting their use for weight loss. Additionally, studies evaluating *Lactobacillus amylovorus* and *Lactobacillus rhamnosus* showed significant weight loss with supplementation; however, their results were gender specific. Significant decrease in BMI was shown in groups supplemented with *L. amylovorus, L. gasseri, L.*

plantarum, L. curvatus with *plantarum,* and several combination strains when compared to placebo groups. Several studies found that benefits ceased after the probiotic supplementation was discontinued, suggesting that ongoing supplementation may be required for results. Finally, the side effects associated with probiotic supplementation were minimal, regardless of the strain, gender, or duration. This may suggest that potential benefits could outweigh risks.

Lactobacillus Supplementation for Weight Loss

Lactobacillus is one of the most studied and well understood strains of human gut bacteria. It has gained notable attention due to its suggested capability to provide multiple health benefits including cancer prevention and improved immunity.

Chan, Jones, Jones, Omar, and Prakash (2012) conducted a study assessing the efficacy of supplemental *Lactobacillus fermentum* (LF) and *Lactobacillus amylovorus* (LA) based on their proposed ability to lower serum lipids and ultimately alter body adipose tissue. Partakers in the study included 28 overweight and obese (BMI between 25-32 kg/m^2) adults (males = 10, females = 18) ages 18-60 years. It included three separate phases (43 days in length each) with a six-week washout period between each phase. Subjects were randomly assigned to one of three groups for each phase: control yogurt, yogurt containing 1.39 x 10^9 cfu of live LA bacteria, or yogurt containing 1.08 x 10^9 cfu of live LF bacteria. Throughout the three phases, each participant received one phase using each supplemental form. Anthropometric measurements, including weight and body composition, were measured at the beginning and end of each phase. Additionally, fecal specimens were collected in order to assess the fecal microbial composition and compliance to supplementation. Results of the study indicated no significant difference in weight change for any groups at endpoint when compared to baseline. Additionally, there were no statically significant differences in weight change between the endpoints of the groups. Levels of *Lactobacillu*s in fecal samples did significantly increase in the LF and LA groups compared to control group (p = 0.008), which validated compliance to supplementation and alteration of gut microbiome. Ultimately, Chan et al. concluded that probiotic supplementation with LF or LA under controlled-diet conditions does not result in increased weight loss. This finding supports the rationale that weight loss is associated with mechanisms independent of probiotic supplementation with LF or LA. Strengths of this study include a controlled diet and individualized calculation of caloric needs for participants. This allowed for improved isolation of the probiotic supplement assessment. Additionally, providing each individual with all three supplement types, separated by washout periods, allowed for decreased likelihood of genetic or lifestyle differences between participants to alter results of the trial. One major limitation of this study was small sample size and no differentiation of gender outcomes. In addition, physical activity was not monitored or documented throughout the study which may have significantly impacted results due to the ability of exercise to change energy expenditure (Chan et al., 2012).

In another study, Chung et al. (2016) postulated that *Lactobacillus acidophilus* JBD301 supplementation would result in significant weight loss in the obese adult population. This hypothesis was based on the theory that the mechanism of *L. acidophilus* JBD301 is similar to the weight loss medication orlistat. Orlistat works through inhibition of dietary fat digestion into free fatty acids. In order to test their hypothesis, Chung et al. recruited a total of 37 adults between ages 25 and 65 years with a BMI between 25 and 35 kg/m^2. The participants were split into two groups, either receiving a placebo capsule containing vegetable cream (n = 19) or an experimental capsule containing 1×10^{10} cfu *L. acidophilus* JBD301 (n = 18). Ingestion of supplemental *L. acidophilus* JBD301 for a duration of 12 weeks resulted in a significant decrease in body weight (p = 0.026) as well as BMI (p = 0.036) when compared to the control group.

Chung et al. concluded that, like the weight loss medication orlistat, *L. acidophilus* may be effective at decreasing the absorption of free fatty acids which could indicate effectiveness for the promotion of weight loss. Due to the limited negative side effects associated with *L. acidophilus* supplementation, these findings could indicate a safer alternative to orlistat for the treatment of obesity. Strengths of this study include using a double-blind, randomized, placebo-controlled outline. Additionally, while phase one was not discussed in detail in this review, having two phases involving both animal and human subjects was beneficial in that the animal study provided insight to expectations of the human study. Limitations include a small sample size, short study duration, failure to consider the role of participant's sex and age in results, and no assessment of diet and physical activity compliance. Also, there was no comparison regarding effect on the overweight versus obese population. Compliance to the supplement was also not assessed which may have significantly impacted outcomes (Chung et al., 2016).

Another study, completed by Jung et al. in 2013, assessed the effect of supplemental *Lactobacillus gasseri* BNR17 on obesity and diabetes. A total of 57 volunteers with a BMI of 23 kg/m^2 or greater, fasting blood sugar of 100 mg/dL or greater, and age 19 to 60 years were enrolled in the study. Participants were randomly assigned either placebo capsules (n = 29: 9 males and 20 females) or BNR17 probiotic capsules containing 10^{10} cfu of *L. gasseri* (n = 28: 13 males and 15 females). Each participant took two capsules before breakfast, lunch, and supper (total of 6 capsules per day) for 12 weeks. Weight, body fat, biochemical parameters, vital signs, and computed tomography were obtained at weeks zero, four, eight, and twelve. There was no increase in weight loss in the BNR17 group when compared to the control group upon completion of 12 weeks of supplementation ($p = 0.09$). Outcomes on diabetes control will not be discussed for the purpose of this review. While results did not support utilizing this specific probiotic strain at this dosage for the promotion of weight loss in the studied population, there were no significant side effects reported. Therefore, it was suggested there may still be a use for supplemental *L. gasseri* BNR17 at different dosages in the treatment of obesity, pending results of additional studies. Strengths of this study include single center, placebo controlled, randomized, and double-blind conditions. The exclusion of participants with potential metabolism alterations as a result of disease, medication, or previous probiotic supplementation allowed for better assessment of *L. gasseri* supplementation alone. Additionally, obtaining measurements at intervals throughout the study provided important information regarding the length of supplementation required in order to see effects. A major limitation of the study was including participants with a BMI of 23 to 24.9, as the CDC defines overweight and obesity as a BMI of 25 or greater. This may be misleading, as the target population and the studied population were not defined by the same parameters. Another limitation is a short duration of the supplementation period as well as lack of monitoring standardizing diet and exercise throughout the study. The study also failed to compare the results of men versus women or other demographics that may have provided insight to benefits in specific populations. This is likely due to the small sample size (Jung et al., 2013).

An additional study completed by Jung et al. in 2015 assessed the efficacy of *Lactobacillus curvatus* and *Lactobacillus plantarum* supplementation for weight loss and reduction in body fat in the overweight and obese adult population. Obese or overweight subjects (BMI >25 kg/m^2) from Seoul, Korea were recruited for the study. It was required they be between ages 20 and 65 years. The participants were divided into a placebo group (n=60) and a probiotic group (n=60). The intervention group consumed two grams of powder containing the *Lactobacillus* strains, while the placebo group received two gm of powder without added probiotic. Body weight, height, BMI, waist circumference, abdominal fat, and body composition were measured and recorded at baseline and again after 12 weeks using standardized measurement tools. Additionally, blood was collected, and serum profiles were documented. A total of 14 participants from the placebo group and 11 participants from the probiotic group dropped out of the study and were not included in results; however, adverse reactions were not reported as a reason for dropping out of the study. Individuals who received supplemental *L. curvatus* and *L. plantarum* experienced significant reduction in body weight ($p = 0.001$) and BMI ($p = 0.001$) after 12 weeks of supplementation when compared to the control group. While the mechanisms of *L. curvatus* and *L. plantarum* have not been fully established, the findings of Jung et al. suggest reduction of body weight and body fat could be achieved through 12 weeks of supplementation with these probiotic strains. One strength of this study was utilizing a dietitian to provide diet education to participants in order to improve compliance to diet maintenance recommendations. Additionally, assessing intake records to compare macronutrient profiles allowed for more accurate comparison of the groups. While this study was double-blind, placebo-controlled, and randomized, it had several limitations. The only geographical region involved in the study was Seoul, Korea; therefore, it may not accurately represent a diverse population. A baseline diet within a Korean household may provide a significantly different microbial environment for the probiotics being supplemented to flourish versus a baseline diet found in other cultures. In addition, diet and physical activity were reported through participant recall which is subject to error. There was no follow up on participation weight maintenance or continued weight loss after the 12-week study was completed. Due to the chronicity of obesity, long term follow-up would be beneficial in supporting the findings and applicability of this study (Jung et al., 2015).

In 2010, Kadooka et al. completed a double-blind, randomized, placebo-controlled intervention study to assess the effect of fermented milk (FM) containing *Lactobacillus gasseri* LG2055 on anthropometric measurements in overweight and obese adults. Based on the results of the 2010 study, Kadooka et al. (2013) completed a follow-up control trial to further investigate the use of *L. gasseri* FM supplementation using different dosages.

Kadooka et al. (2010) studied a total of 87 participants (men = 59, women = 28), ages 33 to 63 years. It was required that subjects had a BMI of 24.2 to 30.7 kg/m^2 as well as visceral fat of the abdomen measuring 81.2 to 178.5 cm^2. During a four-week lead-in period, blind matching of participants in age, weight, and BMI occurred. They were then randomly assigned to either the active probiotic supplement group (200 g/day FM with added LG2055) (n = 43; male: 29, female: 14) or the control group (200 g/day FM without added LG2055) (n = 44; male: 30, female: 14) for 12 weeks. Anthropometric measurements were obtained at weeks zero, four, eight, and upon completion of the trial. Results of the study showed significant decrease in body weight ($p < 0.001$) and BMI ($p<0.01$) in the probiotic supplemented group compared to the control group at week 12. The intervention group had significant decreases in weight and BMI at weeks eight ($p<0.01$) and 12 ($p<0.01$) when compared to baseline measurements but not at week four. In contrast, the control group did not see significant changes in any anthropometrics throughout the duration of the study. No significant differences in energy intake or number of steps per day between the groups were noted. There were no negative side effects reported from the probiotic supplementation throughout the study (Kadooka et al., 2010).

The study completed by Kadooka et al. (2013) assigned 210 healthy Japanese adults (men = 105, women = 105) into one of three groups depending on their baseline characteristics. It was required that the subjects have a visceral fat area of at least 80 cm^2 and be over age 18 years. One intervention group received FM containing 10^7 cfu/g of LG2055, another intervention group received 10^6 cfu/g LG2055, and the control group received 0 cfu/g LG2055. All groups were supplemented with 200 g/day of FM for a total of 12 weeks. Anthropometrics including abdominal visceral fat, BMI, waist and hip circumference, and body fat mass were measured at weeks zero, four, eight, upon trial completion, and four weeks following completion of the study. Results indicated significant decreases in BMI ($p<0.01$) for both the LG2055 10^6 and LG2055 10^7 groups from week zero to week 12. The difference in BMI ($p<0.05$) for both probiotic-supplemented groups was smaller at the four-week follow-up than week 12 but still statistically significant from baseline. Differences in diet and physical activity between the groups were not statistically significant. There were no significant changes in the control group from baseline throughout the study. There were no adverse effects reported (Kadooka et al., 2013).

The findings of both studies were suggestive of beneficial effects of LG2005 supplementation at dosages ranging from 10^6 to 10^8 cfu/g on decreasing body weight and BMI. Changes in other anthropometric measurements will not be discussed for the focus of this review. Based on the results found by Kadooka et al. (2013) at four weeks following the trial, the beneficial effects may be short term and/or require ongoing supplementation. The mechanism responsible for the results of these studies are still unknown. It is suspected that decreased lipid absorption may be partially responsible for the trial outcomes. In addition, alterations in systemic inflammation may have contributed. The results of the studies may prove beneficial when considering long term treatment of overweight and obesity. Both studies appropriately organized double-blind, randomized, placebo-controlled intervention studies. Kadooka et al. (2013) utilized a larger sample size and also evaluated an equal number of males and females. The four-week follow-up completed by Kadooka et al. (2013) also provided strong insight to the potential longevity of the supplementation benefits. In both studies, standardized measurements were used to assess weight change, BMI, and other anthropometrics which allowed for consistency in comparisons. In contrast, several limitations were recognized. Significantly more men than women were included in the study completed by Kadooka et al. (2010), and while they appear to have been evenly distributed between control and intervention groups, the gender difference may not accurately represent women as well as men. Kadooka et al. (2013) studied equal numbers of males and females but failed to differentiate results based on gender. Due to the limited geographical region in one study and failure to recognize geographical origin in the other, it is difficult to assess how well the results represent a diverse population with variable baseline diets. Finally, FM was used as a control which, by some standards, could be considered a probiotic itself. Therefore, one could argue that the studies are comparing dosages of natural probiotic versus dosages of added probiotic rather than probiotic versus no probiotic supplementation (Kadooka et al., 2010; Kadooka et al., 2013).

A study completed by Nakamura et al. (2016) evaluated the efficacy and safety of fragmented *Lactobacillus amylovorus* CP1563 on weight and body fat in Class I obese participants. A total of 197 partakers, made up of healthy adult men and women, completed the study. They were required to have a BMI of 25 to 30 kg/m^2. Participants were given either a placebo beverage or beverage containing CP1563 and instructed to consume one bottle of the supplement daily for 12 weeks. Body weight and BMI were recorded every four weeks throughout the trial and four weeks after the trial was completed. Results indicated no significant differences in age, gender, demographics, anthropometrics or clinical characteristics between the test groups ($p<0.05$). Men who received the CP1563 supplement showed significantly more weight loss upon completion of the study than those in the placebo group ($p=0.035$). There was a reduction in weight for women, but it was not statistically significant. There was a significant decrease in BMI between the probiotic group and the placebo group for both gender subgroups ($p<0.001$). Four subjects from the placebo group and two subjects from the intervention group reported transient diarrhea as a side effect. Constipation was reported by two subjects from the placebo and one from the probiotic group. Nakamura et al. concluded that beverages containing fragmented CP1563 may be beneficial in promoting weight loss in Class I obese men only. However, the intervention group did have significant improvement in BMI for both genders with Class I obesity. While constipation and diarrhea were reported by a small number of participants, there were actually fewer complaints of these side effects in the intervention group than the control group. This could suggest that the benefits of supplementation may outweigh the risks. One strength of this study is a larger sample size than other *Lactobacillus* supplementation trials. Also, having participants report subjective side effects of the supplement provides strong information regarding the likelihood of long-term compliance, as side effects are often a cause of discontinuation. Limitations include only incorporating those classified as obesity Class I in the study. This limits the application of the findings. There is also lack of information regarding macronutrient and micronutrient makeup of the individualized diets. Because subjects were documenting their own lifestyle habits, misreporting may have occurred (Nakamura et al., 2016).

In 2014, Sanchez et al. completed a 24-week study investigating *Lactobacillus rhamnosus* (LPR) supplementation impact on weight loss and weight maintenance for obese men and women. Further analysis was completed by Sanchez et al. (2017) in a follow-up study investigating the effects of LPR supplementation on eating behaviors and mood in obese individuals enrolled in a weight-loss program in the Quebec, Canada region. The studies hypothesized that participants receiving probiotic supplementation with LPR would have improved eating behaviors and subsequent weight loss. Methods used in the studies were essentially the same. Participants included in the Sanchez et al. (2014) study were 45 obese men and 60 obese women, between ages 18 to 55 years, with a BMI 29 to 41 kg/m^2. A total of 48 men and 77 women with the same BMI and age parameters were included in the Sanchez et al. (2017) study. Both trials involved two phases consisting of a weight loss period and a weight maintenance period. Phase one for both studies involved 12 weeks of attempted weight loss through a supervised dietary reduction of 500 kcal/day. Following phase one, phase two involved 12 weeks of weight maintenance with a supervised but unrestricted, personalized diet. In both studies, participants either received one capsule of LPR or one capsule of placebo once in the morning 30 minutes prior to breakfast and again in the evening 30 minutes prior to dinner throughout the entire 24-week study. The LPR capsules in both studies provided approximately 1.62 10^8 cfu LPR, totaling 3.24 10^8 cfu/day. In both studies, body weight was recorded at baseline and every two weeks throughout phase one. Weight was also recorded every four weeks throughout phase two using a digital scale. The results of the Sanchez et al. (2017) study showed no statistical difference in weight loss between the intervention and control groups for men. The women receiving LPR supplementation experienced statistically significant weight loss compared to the control group at the end of the trial, with at least 77% of the weight loss made up of body fat (Sanchez et al., 2017). Results reported by Sanchez et al. (2014) showed no significant difference in weight change during either phase between the control and intervention groups overall. However, when sex was considered as a subgroup, women who received the LPR supplement had significantly greater losses in weight ($p = 0.02$) and body fat mass ($p = 0.01$) than the control group. There was no significant difference seen in men (Sanchez et al., 2014). Both studies found that women did experience increased weight loss when receiving supplemental LPR when compared to the placebo group, but there were no statistically significant differences in men. Furthermore, neither study reported negative side effects of LPR supplementation in male or female groups, suggesting the benefits of probiotic supplementation with LPR may outweigh the risks. One major strength of both studies was the implementation of a two-week participant washout period prior to beginning phase one in order to eliminate probiotic-containing items from the diet. This ultimately decreased the risk skewed results from intake of natural probiotics in baseline diets. Additionally, both studies provided results for male and female subgroups which allowed for more thorough assessment of the results and how they may be applied. The standardization and close monitoring of diet and physical activity was another strength of these studies. Since obesity is a chronic condition, the length of the studies may have been too short to obtain true insight to the ability of participants to maintain the weight loss over an extended period of time. Additionally, the participants were all from the Quebec, Canada region which may have limited the diversity of the population studied (Sanchez et al., 2014; Sanchez et al., 2017).

Sharafedtinov et al. completed a pilot study in 2013 to evaluate if a diet supplemented with cheese containing *Lactobacillus plantarum* TENSIA would reduce weight and other symptoms of metabolic syndrome in Russian adults with obesity. The various proposed functional properties of *L. plantarum* such as “antioxidative effects, cholesterol-lowering effects, and antimicrobial activity against pathogens” were reasons for selecting the strain. A total of 40 subjects participated in the three-week study. Selected participants were required to be between ages 30 to 69 years with diagnosed metabolic syndrome and without chronic diseases requiring intervention. The 40 subjects were divided into two groups: 15 consumed 50 gm of control cheese without added probiotic (males = 4, females = 11), and 25 consumed 50 gm of cheese with added *L. plantarum* providing 1.5 x 10^{11} cfu/g (males = 9, females = 16). It was noted that the microbial content of the cheeses used in the control and the probiotic cheese did not differ. The subjects in both groups were placed on a 1500 kcal, hypocaloric diet. Fecal counts of *Lactobacilli* were evaluated to assess compliance. Results showed a significant decrease in BMI ($p = 0.031$) in the group supplemented with probiotic cheese when compared to the control group. Weight loss experienced by the probiotic group was greater than the control group but was not statistically significant ($p = 0.083$). Other anthropometric measures showed no statistically significant differences between the groups. There were no adverse effects, aside from temporary constipation, reported by the participants in either group. In summary, Sharafedtinov et al. found that daily supplementation with *L. plantarum* cheese, in addition to a calorie-restricted diet, may result in greater reduction in BMI when compared to diet-restriction alone. Sharafedtinov et al. suspected longer supplement duration may be needed to see additional benefits for weight loss based on the lack of change in fecal levels of *L. plantarum*. Although additional research regarding this topic was suggested, authors revealed promising potential in utilizing *L. plantarum* TENSIA supplementation in conjunction to a calorically restricted diet to decrease BMI and ultimately lower risk for metabolic syndrome in overweight and obese individuals. Strengths of this study include controlled caloric, macronutrient, and micronutrient intake. The study was performed under randomized, double-blind, placebo-controlled, and parallel conditions. Due to the small sample size of the pilot study, the data may not accurately represent a larger population. For this reason, it would be beneficial to conduct a larger follow-up study to include a more populous and diverse group of individuals. One major limitation to this study is utilizing cheese as a delivery method for the probiotic under investigation. Authors did not disclose the type of cheese used which could dramatically impact results. While the cheeses provided to the control and the study groups were microbially the same, the underlying prebiotic or probiotic activity of the cheese may have inhibited or amplified the activity of the *L. plantarum.* Implementing a 1500 kcal/day restriction may have provided a larger restriction in calories compared to basal energy needs for some participants than others which may have also impacted results. In addition, physical activity of the participants at baseline and throughout the study was not regulated or recorded. Due to the impact of physical activity on weight and BMI changes, variable levels of physical activity between subjects and groups may have altered results and therefore conclusions of the study. Finally, differences in outcomes for men versus women were not provided (Sharafedtinov et al., 2013).

Akkermansia Supplementation for Weight Loss

While *Lactobacillus* is the most widely recognized gut bacteria, studies have also investigated the relationship of *Akkermansia muciniphila* and the prevalence of obesity in humans. Depommier et al. conducted a study in 2019 which explored the use of supplemental *A. muciniphila* and outcomes on weight, safety, and other metabolic parameters that will not be covered in detail in this literature review. The study involved 32 overweight or obese adult volunteers. Participants were required to be ages 18 to 70 years and have a BMI of >25 kg/m^2. They additionally required a diagnosis of metabolic syndrome according to the NCEP ATP III definition. All participants were located in Brussels, Belgium. Partakers were assigned to one of three groups: placebo (n = 11), 10^{10} cfu of *A. muciniphila* in live form (n = 12), or *A. muciniphila* in pasteurized form (n = 9). They were instructed to take the supplement on an empty stomach every morning for eight weeks. Baseline and end measurements were obtained for anthropometrics, blood specimens, and stool samples. Results showed a mild decrease in body weight in the intervention groups compared to the control group (p = 0.091), but this was not considered statistically significant. There was no significant change in BMI. Depommier et al. concluded that supplementation with *A. muciniphila* did not result in significant reduction in weight or other anthropometric measurements. No significant side effects of supplementation were reported, and therefore, the study still concluded that the benefits of administering *A. muciniphila* may outweigh the risks pending the findings of future studies. Strengths of this study include implementation of a randomized, double-blind, placebo-controlled pilot study. Additionally, Depommier et al. monitored side effects of the supplement which can provide important insight to the risks versus benefits of utilizing the intervention. Additionally, completing the trial using both pasteurized and live *A. muciniphila* provides important awareness of the variability within even one strain of probiotic that must be considered. This was the only study reviewed that indicated if the bacteria were live or pasteurized. Limitations of the study include monitoring compliance to diet and physical activity through patient-reported survey, as this is subject to misreporting. The sample size used for the study was small and failed to incorporate a large geographical area. Finally, outcomes for males and females were not differentiated (Depommier et al., 2019).

Bifidobacterium Supplementation for Weight Loss

Studies have suggested there is a correlation between low levels of GI *Bifidobacterium breve* and obesity in humans. Moreover, there has been evidence suggesting anti-obesity effects of *B. breve* on obese mice. Based on these findings, Minami et al. (2015) conducted a study investigating the effectiveness of supplemental *B. breve* B-3 on improving body composition and blood parameters in obese adults. A total of 44 adults, aged 40 to 69 years, with a BMI of 24 to 30 kg/m^2 were enrolled in the trial. They were then randomly assigned either three capsules daily containing 5 x 10^{10} cfu of B-3 (n = 19: male = 6 and female = 13) or three capsules daily of placebo (n = 25: male = 11 and female = 14) for a total of 12 weeks. Blood samples and anthropometric measurements were taken using standardized devices and recorded at weeks zero, four, eight, and 12. At weeks four and 12, body weight was significant lower in the probiotic group when compared to baseline weight (p=<0.05 at both weeks four and twelve); however, it was not significantly different from the placebo group. BMI and other anthropometric measurements were not statistically different between the placebo and intervention groups. There were no significant adverse effects reported throughout the study. In conclusion, the study found that 12 weeks of *B. breve* B-3 supplementation did not significantly improve weight loss or other anthropometric measurements when compared to the placebo group. Strengths of this study include the implementation of a run-in period. This allowed for a strong understanding of each participant's baseline habits in order to compare and monitor any changes made throughout the study that may have impacted results. Incremental measurements throughout the study allowed for better determination of when effects of the supplement may begin to take place. One major limitation was failing to exclude patients taking metabolism-altering medications. This may have significantly impacted results. The study did not divide males and females into subgroups for assessment which may have provided insightful data for application within a specific gender. Finally, the study incorporated participants with a BMI of 24 to 24.9, which is not considered overweight or obese according to the guidelines established by the CDC. Ultimately, this would alter the target audience (Minami et al., 2015).

Multiple Genus Supplementation for Weight Loss

After reviewing studies which utilized only a single bacterial genus, it is important to address studies which incorporated multiple genus into the supplements provided to participants.

Chang et al. conducted a study in 2011 investigating the efficacy of supplemental yogurt enriched with *Streptococcus thermophilus*, *Lactobacillus acidophilus*, and *Bifidobacterium infantis* on different components of metabolic syndrome including body weight and BMI. The study was completed over a course of eight weeks and included a total of 101 participants (males = 31 and females = 70). Individuals were required to be ages 20 to 65 years and have a BMI between 18 and 30 kg/m^2. Subjects consumed either functional (probiotic) yogurt NY-YP901 (n = 53: 16 men and 37 women) or placebo yogurt (n = 48: 15 men and 33 women) twice daily. BMI and body weight were measured prior to and following supplementation. Results showed that participants who consumed probiotic yogurt lost significantly more weight (p=0.006) than those who received the placebo supplement. Additionally, there was a significant decrease in BMI (p=0.006) and low-density lipoprotein (p=0.044). There were no other significant differences seen between groups. Based on their results, Chang et al. concluded that eight weeks of supplementation with yogurt enriched with *S. thermophilus, L. acidophilus*, and *B. infantis* may be beneficial in promoting weight loss and decreased BMI in the overweight and obese populations. Strengths of the Chang et al. study include the use of a randomized, double-blind, placebo-controlled, and parallel parameters. Additionally, the researchers closely monitored compliance to supplement consumption, diet, physical activity, and other lifestyle habits that could have impacted results. By requiring participants to avoid intake of FM or other sources of probiotics, the risk for altered results through consumption of uncontrolled probiotic strains via the diet was minimized. This study had several limitations. In addition to participants considered overweight or obese, the study included those with a BMI of 18 to 24.9 kg/m^2 which is considered normal body weight according to the CDC. More women than men were studied which may have impacted results. It was noted that participants were to continue with their routine smoking and alcohol habits, but smokers and those who consumed alcohol were not put into subgroups and therefore were compared to those who did not use tobacco or alcohol. Furthermore, the study used three different genus and species of bacteria, therefore, posing the question if one single bacteria strain was responsible for the results or if it is required to have all three in order to produce benefits. Finally, using yogurt as a carrier for supplementation may have provided skewed results due to potential prebiotic, symbiotic, or probiotic activity naturally provided by the yogurt (Chang et al., 2011).

Another multi-genus study was completed by Gomes et al. in 2017. The study evaluated the effect of *Lactobacillus* and *Bifidobacterium* supplementation on weight change, body composition, inflammation, and antioxidant profiles in obese women only. Overweight and obese women aged 20 to 59 years with a BMI of 24.9 to 40 were recruited through advertisement flyers. A mix containing 2×10^{10} cfu/day (*L. acidophilus*, *L. casei, L, lactis, B. bifidum*, and *B. lactis*) was provided to the intervention group (n = 21), and a placebo mix was provided to the control group (n = 22) for a total of eight weeks. Follow-up visits were completed for anthropometric measurement and diet recall collection, and subjects that were lost to follow-up were excluded from results. The study showed no significant difference in weight loss between the groups (p = 0.33); however, there were no adverse events reported in either group. In conclusion, the findings of this study may be beneficial to consider when evaluating the benefits of utilizing a probiotic mix of *L. acidophilus*, *L. casei*, *L. lactis*, *B. bifidum*, and *B. lactis* for overweight and obese women. Strengths of this study include the application of double-blind, two-arm, parallel-group, and randomization. The results were likely made more accurate by excluding participants who were following restricted or previously probiotic-supplemented diets. While participants were instructed to maintain baseline diet and physical activity, and regular recalls were collected, there was no formal comparison of diet composition between groups. The contribution of total caloric intake from carbohydrates, fats, proteins, and micronutrients may have significantly varied between the groups and therefore altered the validity of the results. Furthermore, variability in baseline intake between the groups may have yielded results not truly accurate of the probiotic supplementation alone. The small sample size made up of only females would make it difficult to apply the findings to the male gender. In addition, the study only spanned for a total of eight weeks which may not be an accurate timeline when considering the need for ongoing treatment of a chronic condition (Gomes et al., 2017).

An additional multi-genus study, completed by Michael et al. in 2020, tested the theory that daily supplementation with Lab4P consortium, made up of *L. acidophilus, B. bifidum, B. animalis, L. lactis and L. plantarum,* for six months would provide beneficial effects on body weight and overall well-being of healthy, overweight or obese adults. Adults aged 30 to 65 years with a waist circumference >89 cm (women) or >100 cm (men), BMI 25 to 34.9 kg/m^2, and no statin use within the last 3 months were recruited for participation. Eligible participants were randomly assigned one capsule of either Lab4P or microcrystalline placebo daily for six months. Body weight, quality of life, and other measurements were obtained at baseline, three months, and six months. Results showed a significant difference in weight loss between the groups upon completion of the trial at six months. The group receiving Lab4P experienced a 1.5% weight reduction ($p < 0.0001$) with no significant changes noted in the placebo group. Additionally, the probiotic supplementation group had significant reduction in BMI ($p < 0.0001$), while the placebo group had no significant changes. It was noted that minimal changes were observed after three months of supplementation, suggesting that long term (greater than six months) of supplementation may be needed in order to be effective. Weight loss from baseline in the overweight population (BMI <30) supplemented with Lab4 was greater than those considered obese (BMI >30). Weight loss in women receiving the probiotic supplement was 1.6%, while men receiving the probiotic supplement had weight loss of 1.4%. It was also noted that participants over age 50 who received probiotic supplementation experienced the greatest amount of weight loss (-1.72 kg). There were no significant changes in weight for placebo male, female, BMI, or age subgroups. The study mentions a large population size as a strength but fails to provide the actual number of participants. The measurements taken at three- and six-month intervals provide beneficial information regarding the duration of supplementation required to promote significant change within this population. Limitations of this study include failing to obtain baseline dietary and exercise patterns. Alterations in dietary or exercise patterns throughout the study have the potential to significantly alert results. Additionally, the study reported that 15.9% of the participants in the placebo group and 12.7% of participants in the supplement group received antibiotic therapy at some point throughout the study, and therefore, this may have altered results due to the effect of antibiotics on intestinal microbiota (Michael et al., 2020).

Finally, two studies completed by Zarrati et al. (2014) and Zarrati et al. (2013) investigated “whether probiotics have synergistic effects with weight-loss diets” and “effects of probiotic yogurt on fat distribution and gene expression of proinflammatory factors in peripheral blood mononuclear cells in overweight and obese people with or without weight-loss diet”. Subjects within both studies were randomly divided into three groups using a computer-generated, blocked, randomized list accounting for sex and BMI. The groups received either probiotic yogurt without a low-calorie diet (PWLCD) (n = 25), probiotic yogurt with a low-calorie diet (PLCD) (n = 25), or regular yogurt with a low-calorie diet (RLCD) (n = 25) for a total of eight weeks in both studies. The strains of probiotic incorporated into the yogurt contained *L. acidophilus* La5, *Bifidobacterium* BB12, and *L. casei* DN002 which provided a total of 10^8 cfu/gm. Participant data was the same for both studies: 75 healthy, overweight or obese adults (men = 24 and women = 51) with a BMI between 25 and 35 kg/m^2. Anthropometric data and blood samples were collected and analyzed. Due to becoming pregnant during the trial, two subjects were excluded from results. There were statistically significant changes in BMI between the PLCD and PWLCD ($p < 0.001$) as well as the RLCD and the PWLCD ($p < 0.001$) groups. Likewise, both groups that followed a low-calorie diet (LCD) had significant weight changes from week zero to week eight ($p < 0.001$). There were no statistically significant differences in anthropometric measurements between the PLCD and the RLCD groups. The studies concluded that supplementation with probiotic yogurt containing *L. acidophilus* LA5, *L. casei* DN001, and *B. lactis* Bb12 may promote weight loss and decrease gene expression of proinflammatory factors in the overweight and obese adult population. Furthermore, following a calorie-restricted diet may promote weight loss. While associations have been made, there is still limited understanding regarding the mechanism in which energy restriction and weight loss may result in improved inflammatory conditions. Due to the many adverse effects associate with chronic inflammation, supplementation with probiotics may be beneficial in the overweight and obese population. Strengths of the studies include randomization and double-blind format. Computer software was used to blindly distribute the participants evenly based on sex and BMI which allows for more accurate comparison between groups (Zarrati et al., 2014). It would have been beneficial to also consider age when dividing the groups, as this can have a significant impact on baseline metabolism and inflammation. While they were divided evenly, the studies had significantly more women than men and did not report them separately as subgroups. There may be significant fluctuations in weight and inflammatory changes when comparing sexes. Another limitation of the study was the small sample size and short duration. While the sample size in these studies is larger than many published articles investigating the benefits of probiotic supplementation, it is still limited and may not accurately represent all ethnicities. Although the study mentioned that most participants followed an Iranian diet, typically consisting of rice, herbs, cheeses, and bread, they did not differentiate macronutrient or micronutrient breakdowns. The geographic location of participants was also not discussed which may alter results and therefore conclusions (Zarrati et al., 2014) (Zarrati et al., 2013).

Discussion

In overweight and obese adults, does probiotic supplementation promote greater weight loss when compared to weight changes with no probiotic supplementation?

While there is still limited research investigating the efficacy of specific strains of probiotic for weight loss and/or improved BMI, it is important to evaluate the effectiveness of each individually in order to assess our current understanding of their applicability to clinical practice.

There were no studies that evaluated *L. fermentum* as a sole supplemental strain. The study by Chan et al. (2012) concluded that probiotic supplementation with both *L. fermentum* and *L. amylovorus,* under controlled-diet conditions, does not result in increased weight loss in the overweight and obese adult population. The study did not look at dosage or gender outcomes, so the overall conclusions are difficult to apply to a specific population that would be seen in a clinic setting. Ultimately, there is insufficient evidence at this time to support utilizing supplemental *L. fermentum* for weight loss in the overweight and obese populations.

While the Chan et al. (2012) study, which provided both *L. fermentum* and *L. amylovorus*, did not prove to be efficacious in promoting weight loss, the study completed by

Nakamura et al. (2016) concluded that beverages containing fragmented *L. amylovorus* CP1563 may be beneficial in promoting weight loss in men with Class I obesity. It also showed significant improvement in BMI for both genders. Additional studies with larger participant groups should be completed in order to provide recommendations regarding the utilization of *L. amylovorus* as a lone probiotic supplement for weight loss or improved BMI.

The analysis completed by Chung et al. (2016) concluded that *L. acidophilus* may be effective at promoting weight loss. There were no recommendations provided regarding gender-specific usage or dosage required to yield results. Follow-up studies investigating specific dosage and effect on sex, age, and obesity class subgroups would be beneficial in developing guidelines for application of these findings.

L. gasseri was investigated by three studies. Jung et al. (2013) did not support utilizing supplemental *L. gasseri* BNR17 for the promotion of weight loss in individuals with a BMI of 23 or greater. The authors clearly indicated the need for additional studies in order solidify the findings of this study, as the sample size used was quite small. The studies completed by Kadooka et al. (2013) and Kadooka et al. (2010) were suggestive of short-term beneficial effects of FM containing LG2005 supplementation at dosages ranging from 10^6 to 10^8 cfu/g on decreasing body weight and BMI. The studies provided insight regarding the longevity of effects following supplementation with these specific probiotic strains at these dosages. Due to the contradictory findings of the two Kadooka et al. studies and the Jung et al. study, additional trials with a larger number of participants, similar dosages, and similar controls would be required in order to formulate recommendations regarding the use of *L. gasseri* supplementation for weight loss.

There were no studies available at this time which used supplemental *L. curvatus* alone. However, Jung et al. (2015) concluded that reduction of body weight and body fat could be achieved through 12 weeks of supplementation with *L. curvatus* in combination with *L. plantarum* in the overweight and obese adult population of Seoul, Korea. Due to the population used in this study, it may be difficult to apply the findings to a generalized population that would be seen in a primary care setting the United States based on differences in diet as explained earlier in this literature review.

When providing supplemental *L. plantarum* alone, Sharafedtinov et al. (2013) found that a calorie-restricted diet in conjunction with *L. plantarum* cheese may result in greater reduction in BMI when compared to diet-restriction alone. Sharafedtinov et al. suspected longer supplement duration may be needed to see additional benefits for weight loss. The authors did acknowledge the need for additional research using a larger sample size in order to provide clinical application recommendations for *L. plantarum* supplementation. With only one study and a limited number of participants, there is insufficient evidence at this time to firmly recommend *L. plantarum* supplementation to the overweight and obese adult populations in order to promote weight loss.

The studies completed by Sanchez et al. (2014) and Sanchez et al. (2017) found that women experienced increased weight loss when receiving supplemental *L. rhamnosus*; however, there were no significant changes noted in men. Ultimately, the sample sizes of both studies were fairly small, and more women than men were included in the studies which may have attributed to the findings. For these reasons, it would be beneficial to complete follow-up studies with a larger number of partakers, ideally with equal numbers of males and females, before recommending the use of *L. rhamnosus* in clinical practice.

Only one study has been completed to investigate the use of the *Akkermansia* genus for weight loss in the overweight and obese adult population. Depommier et al. (2019) found no significant change in weight or BMI when participants were supplemented with live or pasteurized *A. muciniphila*. These findings suggest a lack of evidence to support the use of *A. muciniphila* to promote weight loss. The study was small, only involving 32 participants. Larger studies would be warranted in order to obtain a better understanding of the efficacy of supplemental *A. muciniphila* for weight loss.

Similarly, only one study has been completed to assess the use of the *Bifidobacterium* genus alone for weight loss. The study completed by Minami et al. in 2015 concluded that 12 weeks of *B. breve* supplementation did not significantly improve weight loss or other anthropometric measurements for adults with a BMI 24 or greater. Only 44 participants were included in the study; therefore, larger studies would be warranted in order to obtain a better understanding of the efficacy of supplemental *B. breve* for weight loss.

A total of four studies were completed assessing the effectiveness of supplementation with multiple genus. Chang et al. (2011) concluded that eight weeks of supplementation with yogurt enriched with *S. thermophilus, L. acidophilus*, and *B. infantis* may be beneficial in promoting weight loss and decreased BMI in the adult population with a BMI of 18 kg/m^2 or greater. Gomes et al. (2017) concluded that there is limited benefit in providing *L. acidophilus*, *L. casei*, *L. lactis*, *B. bifidum*, and *B. lactis* supplementation for overweight and obese women. The trial completed by Michael et al. in 2020 showed a significant weight and BMI reduction upon receiving supplemental *L. acidophilus, L. lactis, L. plantarum, B. bifidum, and B. animalis*. Finally, the studies completed by Zarrati et al. (2014) and Zarrati et al. (2013) concluded that supplementation with probiotic yogurt containing *L. acidophilus* LA5, *L. casei* DN001, and *B.*

lactis Bb12 may promote weight loss and decrease gene expression of proinflammatory factors in the overweight and obese adult population. It is difficult to draw conclusions from the findings of the studies, as each investigated a different combination of genus and species. Ultimately, there would need to be significantly more research done in order to provide recommendations regarding the use of multiple genus supplementation to promote weight loss in the clinical setting.

Do the benefits of using probiotic supplementation for weight loss outweigh the risks?

Sharafedtinov et al. (2013) reported temporary constipation with supplementation of cheese containing *L. plantarum*. While constipation and diarrhea were reported by a small number of participants, Nakamura et al. (2016) concluded there were actually fewer complaints of these side effects in the group supplemented with *L. amylovorus* than the control group. There were no negative side effects noted in any of the other studies that were reviewed. Ultimately, the risks associated with probiotic supplementation appear to be minimal based on the findings of the studies. It must be noted that the studies were not completed on participants with immunosuppression, infection, or other factors that may place an individual at increased risk for complications or negative side effects.

Applicability to Clinical Practice

With overweight and obesity affecting a significant percentage of the adult population in the United States, it is undoubtedly a disease that primary care providers will encounter and be required to manage within their clinical practice. Not only are overweight and obese individuals at increased risk for other comorbidities, but the disease may also impact overall quality of life. While aspects such as genetics, caloric intake, and caloric expenditure are known to play a role in the development and treatment of obesity, it is important to understand where current literature stands regarding the efficacy of alternative treatment options. Upon analysis of the research presented in this literature review, medical providers will be able to inform overweight and obese patients on the efficacy of using probiotic supplementation as an alternative or supplementary treatment option. Additionally, providers will be able to educate interested participants on the risks versus benefits of utilizing probiotics to promote weight loss. While this topic is still new to research and requires further investigation, this literature review provides insight to what we currently know about the utilization of different probiotic genus and strains to promote weight loss in overweight and obese individuals.

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