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PROBIOTICS FOR IRRITABLE BOWEL SYNDROME : A SYSTEMATIC REVIEW

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Abstract

It has been demonstrated that dysbiosis, also known as imbalances or aberrations of microbiota, plays a significant role in FGIDs and allergens, including infection and antibiotic-associated diarrhea, food allergy, atopic eczema, inflammatory bowel syndrome, and irritable bowel syndrome. It has been demonstrated via research that the mechanisms of action of probiotics in irritable bowel syndrome are diverse, heterogeneous, and strain specific. For the purpose of understanding irritable bowel syndrome (IBS), the mechanism of action of probiotics has to be translated into a language that is more comprehensible from a clinical and a practical standpoint. The competitive exclusion mechanism of pathogens by luminal pH, competition for nutritional sources, and production of bacteriocins, SCFAs, and biosurfactants are all involved in the modulation of the gut microbiota. These factors all work together to prevent the proliferation of pathogens and inhibit their adhesion to the gut epithelia. Because the use of synbiotics as an alternative treatment for IBS is still in its infancy, and because the outcomes of synbiotic administration may be dependent on the probiotic component of the synbiotic, greater emphasis should be placed on determining patients' probiotic responses before beginning treatment with synbiotics.

Keyword: *Bacteria; Irritable Bowel Syndrome; Probiotics; Synbiotic*

INTRODUCTION

Irritable bowel syndrome, often known as irritable bowel syndrome (IBS), is a type of functional gastrointestinal disorder (FGID) that does not have one specific cause.[1] Epidemiologic and demographic studies that investigated IBS suggest that the disease has a variable worldwide prevalence that averages around 11% of the population. Furthermore, these studies suggest that 55.0% (95% CI, 46.2–69.4%) of IBS patients are women, and that the average age of IBS patients is 40 (95% CI, 31.2–50.0) years old.[2] IBS causes persistent stomach discomfort and irregular gastrointestinal habits including constipation, diarrhea, or alternating constipation and diarrhea, which may or may not cause abdominal bloating.[3]

In addition, recent research has demonstrated that IBS affects the gut–brain axis, which links mental health symptoms such as depression and anxiety to the disease, thereby complicating its diagnosis and treatment.[3–6] Moreover, brain structural alterations were associated with subgroups of IBS patients, suggesting the involvement of specific microbes and their predicted metabolites in this condition.[7] IBS causes GI motility disorders, bile acid malabsorption, gut microbiota, and enteric nervous system abnormalities. Some studies also linked IBS to persistent intestinal mucosa micro-inflammation that alters GI function.[8]

The complex character of IBS presents a challenge when it comes to developing an effective therapy for the condition as a whole. Both the absence of an effective therapy for IBS and the wide variety of therapies that have been tried are significant indications that the biology of the condition is not yet completely understood.[9,10] New therapies, including prebiotics, probiotics, synbiotics, and fecal microbiota transfer (FMT), are being used to try to change the gut microbiota of people with irritable bowel syndrome (IBS) such that it has a more favorable composition.[3–6]

This article aims to look at research studies related to ussage probiotics for irritable bowel syndrome (IBS).

METHODS

Protocol

The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines were followed to make sure that the way this investigation was done was in line with what those standards said to do.

Criteria for Eligibility

This literature review seeks to investigate ussage probiotics for irritable bowel syndrome (IBS) by evaluating or analyzing prior studies on the issue. This is a significant problem raised by the present investigation. Researchers participate in studies that satisfy the following requirements: 1) To be accepted for publication, publications must be published in English and focus on effectiveness of probiotics for irritable bowel syndrome (IBS). 2) This assessment included articles published after 2013 but prior to the period covered by this systematic review. Examples include editorials, submissions without a DOI, already published review articles, and entries that are substantially similar to those previously published in a journal.

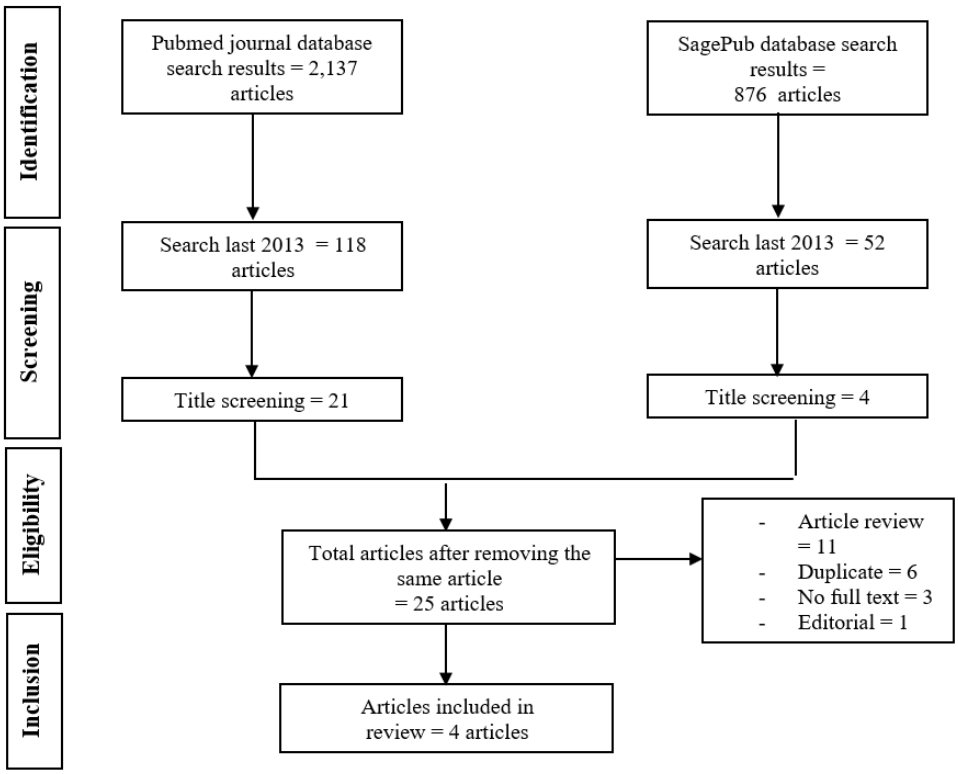

Figure 1. Article search flowchart

Search Strategy

The search for studies to be included in the systematic review was carried out from February, 4th 2023 using the PubMed and SagePub databases by inputting the words: "*probiotic*" and "*irritable bowel syndrome*". Where *("probiotic s"[All Fields] OR "probiotical"[All Fields] OR "probiotics"[MeSH Terms] OR "probiotics"[All Fields] OR "probiotic"[All Fields]) AND ("irritable bowel syndrome"[MeSH Terms] OR ("irritable"[All Fields] AND "bowel"[All Fields] AND "syndrome"[All Fields]) OR "irritable bowel syndrome"[All Fields])* is used as search keywords.

Data retrieval

After reading the titles and abstracts of past research, the author changed the inclusion criteria. The revised criteria are detailed in this study's supplementary materials. This revealed the breadth and numerous dimensions of the problem that need additional examination. The author reached this result after reviewing several studies using a similar format. Systematic reviews only considered studies that met all inclusion criteria. This restricted the search to relevant material. Our personnel rejected research ideas that didn't meet our requirements. This ensured a comprehensive inquiry. This investigation revealed crucial research information, including names, authors, publication dates, locations, study activities, and parameters. Available product categories are listed below. Practice can teach these talents. The source of this information may determine its presentation.

Quality Assessment and Data Synthesis

Before deciding which papers to look into further, each author first carried out their own individual analysis of a separate piece of study that was described in the titles and abstracts of the publications. After that, we will read the totality of the publications that meet the inclusion criteria and are therefore suitable for inclusion in the systematic review.

Then, depending on our results, we will decide which papers should be included in the review. The pieces of writing that are going to be looked at have been chosen on the basis of these criteria. in order to make the process of picking articles for the evaluation as straightforward as possible. Which previous studies have been carried out, and what are the characteristics of those studies that make them suitable for inclusion in the review?

RESULT

When compared with a sham diet, a low FODMAP diet caused significant changes in the abundance of major *saccharolytic* genera. These changes included a higher abundance of *Bacteroides* (LFD 34.1% [15.7%] vs. sham 23.3% [15.2%], q = 0.01) and a lower abundance of *Bifidobacterium* (0.9% [1.0%] vs 2.1%, [2.5%] q = 0.029). Supplementation with probiotics resulted to greater levels of *Lactobacillus* (probiotic 0.08% [0.1%] vs. placebo 0.03% [0.2%], q = 0.001; placebo 0.03% [0.2%]), and Streptococcus abundance (2.0% [2.2%] vs. 0.6% [1.2%], q = 0.001).[11]

The effect that the low-FODMAP diet had on *Bifidobacterium* was reduced as a result of the probiotic therapy. Even though dietary changes can affect the microbiota in the gut, a straightforward bivariate correlation analysis may only provide a limited understanding of the complex interactions that dietary changes have with the different types of gut bacteria in irritable bowel syndrome (IBS). Irritable bowel syndrome (IBS) patients have access to dietary interventions that have the potential to modify their microbiota.[11]

Other study showed at week 6, 14 of 22 patients in the BL group had reduction in depression scores of 2 points or more on the Hospital Anxiety and Depression scale, vs 7 of 22 patients in the placebo group (P = .04). BL had no significant effect on anxiety or IBS symptoms. The groups had similar fecal microbiota profiles, serum markers of inflammation, and levels of neurotrophins and neurotransmitters, but the BL group had reduced urine levels of methylamines and aromatic amino acids metabolites. At week 10, depression scores were reduced in patients given BL vs placebo.[12]

Xu, et al (2021)[13] showed IBS-symptom severity score ($P < 0.01$), serum levels of IL-6 ($P < 0.01$) and TNF-α ($P < 0.001$) were significantly lower in the probiotic group than the control group at day 28. The probiotic adjunctive treatment resulted in significant decreases in some bacterial genera that worsen IBS, such as *Bacteroides* ($P < 0.01$), *Escherichia* ($P < 0.05$), and *Citrobacter* ($P < 0.05$), significant decreases were also observed in some beneficial genera in the control group, including *Bifidobacterium* ($P < 0.05$), *Eubacterium* ($P < 0.05$), *Dorea* ($P < 0.01$), and *Butyricicoccus* ($P < 0.05$).

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Period	Species	Result
Staudacher, 2021[11]	United Kingdom (UK)	Randomized controlled trial	95 individuals with IBS participating	No data	Bifidobacterium abundance, Lactobacillus, Streptococcus abundance	Low FODMAP diet resulted to alterations in the abundance of key saccharolytic taxa compared to sham diet, including increased Bacteroides (LFD 34.1% (15.7%) vs. sham 23.3% (15.2%), q = 0.01) and decreased Bifidobacterium (0.9% (1.0%) versus 2.1%, (2.5%), q = 0.029). Probiotic treatment increased Lactobacillus (0.08% (0.1%) vs. 0.03% (0.2%), p 0.001) and Streptococcus abundance (2.0 (2.2%) vs. 0.6% (1.2%), p = 0.001). The probiotic therapy mitigated Bifidobacterium's response to the low FODMAP diet. Microbiota at baseline failed to predict clinical response to either intervention.
Pinto-Sanchez, 2017[12]	Canada	Randomized, double-blind, placebo-controlled study	44 adults with IBS and diarrhea or a mixed-stool pattern	March 2011 to May 2014	Bifidobacterium longum	At week 6, 14 of 22 patients in the BL group had reduction in depression scores of 2 points or more on the Hospital Anxiety and Depression scale, vs 7 of 22 patients in the placebo group (P = .04). BL had no significant effect on anxiety or IBS symptoms. Patients in the BL group had a mean increase in quality of life score compared with the placebo group. The fMRI analysis showed that BL reduced responses to negative emotional stimuli in multiple brain areas, including amygdala and fronto-limbic regions, compared with placebo. The groups had similar fecal microbiota profiles, serum markers of inflammation, and levels of neurotrophins and neurotransmitters, but the BL group had reduced urine levels of methylamines and aromatic amino acids metabolites. At week 10, depression scores were reduced in patients given BL vs placebo.
Xu, 2021[13]	China	Randomized controlled trial	Forty-five patients with IBS	No data	Bifidobacterium, Eubacterium, Dorea, Butyricicoccus, Bacteroides, Escherichia, and Citrobacter	At day 28, the probiotic group had a lower IBS-symptom severity score, serum IL-6, and TNF-α than the control group. In the control group, Bifidobacterium, Eubacterium, Dorea, and Butyricicoccus decreased significantly, as did Bacteroides, Escherichia, and Citrobacter. Some observed metrics correlated with compositional changes in the fecal microbiota, suggesting that gut microbiota modification may benefit IBS clinically. Enterotype study showed that feces microbiota makeup can affect clinical outcomes.
Oh, 2019[14]	Vietnam	Randomized, Double-Blind, Placebo-Controlled Trial	Fifty Vietnamese patients with unconstipated IBS	No data	Lactobacillus species, L. paracasei, L. salivarius, and L. plantarum	During the 4-week trial, patients documented their SGA weekly and were rated with the VAS. Responders had 2 or more SGA points or a 30% VAS score drop. Overall responders were patients who reacted weekly for more than 2 of the 4 weeks. Group demographics were similar. Probiotics significantly improved overall IBS symptoms by SGA score (80.8%) compared to placebo (45.8%) (p = 0.009). Probiotics also had higher VAS score responder rates (69.2%, 41.7%, p = 0.048). Neither group had adverse events during the research.
Ankersen, 2021[15]	Denmark	Randomized, Double-Crossover Clinical Trial	34 IBS patients without comorbidities and 6 healthy controls	August 23, 2018, to October 18, 2019	Streptococcus thermophilus, Bifidobacteria longum	Taken from participating subjects, 180 fecal samples were analyzed for their microbiota composition. Out of 21 IBS patients, 12 (57%) responded to the LFD and 8 (38%) completed the reintroduction of FODMAPs. Out of 21 patients, 13 (62%) responded to their first treatment of VSL#3 and 7 (33%) responded to multiple VSL#3 treatments. A median of 3 (IQR 2.25-3.75) probiotic treatments were needed for sustained symptom control. LFD responders were reintroduced to a median of 14.50 (IQR 7.25-21.75) high-FODMAP items. No significant difference in the median reduction of IBS-SSS for LFD versus probiotic responders was observed, where for LFD it was -126.50 (IQR -196.75 to -76.75) and for VSL#3 it was -130.00 (IQR -211.00 to -70.50; P>0.99).
Lewis, 2020[16]	Canada	Randomized, Placebo-Controlled Study	251 adults with either constipation (IBS-C), diarrhea (IBS-D), or mixed-pattern (IBS-M)	No data	Lactobacillus paracasei HA-196 (L. paracasei); Bifidobacterium longum	Both L. paracasei and B. longum supplementation increased emotional well-being and social functioning relative to baseline (all p <0.05).
Skrzydło-Radomańska, 2021[17]	Poland	Randomized, Placebo-Controlled Study	51 patients	November 2019 and May 2020	Mixture of Lactobacillus, Bifidobacterium, and Streptococcus thermophilus strains	The probiotic in comparison with placebo significantly improved the IBS symptom severity (the change of total IBS-SSS score from baseline −165.8 ± 78.9 in the probiotic group and −105.6 ± 60.2 in the placebo group, p = 0.005) and in the specific scores related to the severity of pain (p = 0.015) and the quality of life (p = 0.016) after eight weeks of intervention. The probiotic group indicated an improvement in symptoms with the use of the IBS-GIS compared with the placebo group after four (p = 0.04) and eight weeks (p = 0.003).

Furthermore, significant correlations were found between some monitored parameters and compositional changes in the fecal microbiota, suggesting that the clinical improvement of IBS was likely associated with gut microbiota modulation. The enterotype analysis revealed that the initial fecal microbiota composition could influence clinical outcomes.[13] Oh, et al (2019)[14] showed that patients with SGA score of 2 points or more or a decrease of more than 30% in VAS score were considered responders. Patients who responded weekly for more than 2 of the 4 weeks were considered overall responders. There was no significant difference in demographic characteristics between the groups. Overall responder rates of improvement of global IBS symptoms assessed by SGA score were significantly higher in the probiotics group (80.8%)

than in the placebo group (45.8%) (p = 0.009). The overall responder rates assessed by VAS score were also higher in the probiotics group (69.2%, 41.7%, p = 0.048). There were no adverse events in either group during the study period.
Ankersen, et al (2021)[15] conducted a study with 180 fecal samples were analyzed for their microbiota composition. Out of 21 IBS patients, 12 (57%) responded to the LFD and 8 (38%) completed the reintroduction of FODMAPs. Out of 21 patients, 13 (62%) responded to their first treatment of VSL#3 and 7 (33%) responded to multiple VSL#3 treatments. A median of 3 (IQR 2.25-3.75) probiotic treatments were needed for sustained symptom control. LFD responders were reintroduced to a median of 14.50 (IQR 7.25-21.75) high-FODMAP items. No significant difference in the median reduction of IBS-SSS for LFD versus probiotic responders was observed, where for LFD it was -126.50 (IQR -196.75 to -76.75) and for VSL#3 it was -130.00 (IQR -211.00 to -70.50; P>.99). Study in Canada by Lewis, et al (2020) showed that supplementation with either L. paracasei or B. longum increased quality of life in terms of emotional well-being and social functioning when compared to the baseline (all p-values <0.05). In conclusion, L. paracasei and B. longum may lessen the intensity of gastrointestinal (GI) symptoms and enhance the psychological well-being of those who have specific subtypes of IBS.[16]

Study in Poland showed the probiotic in comparison with placebo significantly improved the IBS symptom severity (the change of total IBS-SSS score from baseline –165.8 ± 78.9 in the probiotic group and –105.6 ± 60.2 in the placebo group, p = 0.005) and in the specific scores related to the severity of pain (p = 0.015) and the quality of life (p = 0.016) after eight weeks of intervention. The probiotic group indicated an improvement in symptoms with the use of the IBS-GIS compared with the placebo group after four (p = 0.04) and eight weeks (p = 0.003). The occurrence of adverse events did not differ between study groups. In conclusion, the multi-strain probiotic intervention resulted in a significant improvement in IBS symptoms evaluated with the use of both IBS-SSS and IBS-GIS scales.[17]

DISCUSSION

Irritable bowel syndrome (IBS) is a chronic and recurrent functional gastrointestinal illness that affects between 9 and 23 percent of the global population. Patients with IBS are frequently referred to gastroenterology, have a variety of diagnostic procedures, take several medications, miss work, and have a low quality of life. The pathogenesis of irritable bowel syndrome is not well known and appears to be complex. Numerous pathogenetic variables, in varying combinations, and not necessarily all present in every patient, can play a significant impact. Irritable bowel syndrome is characterized by stomach discomfort or pain that is relieved by defecation and a change in stool consistency.[10,18]

.Numerous variables, including emotional stress and diet, might increase the symptoms.[18] To present, little is known about the genesis of irritable bowel syndrome; however, the intestinal microbiota is receiving increasing attention as a role in the disease's development. For this reason, several studies have been undertaken on medicines that alter the microbiota, including probiotics, prebiotics, and synbiotics. Numerous studies have demonstrated the effectiveness of prebiotics and synbiotics. To date, probiotics have been the subject of the majority of research. The purpose of this review was to examine the efficacy of probiotics, prebiotics, and synbiotics in treating irritable bowel syndrome.[19]

Dysbiosis, also known as imbalances or aberrations of microbiota, has been shown to play an important role in FGIDs and allergies such as infectious and antibiotic-associated diarrhea, food allergy, atopic eczema, inflammatory bowel syndrome, and IBS.[20] As a result, the influence and importance of the gut microbiota in the health of the host became increasingly clear. The processes of probiotics that are involved in the modification of gut microbiota rely on the capacity of probiotic strains or combinations of probiotic strains to block, displace, or interfere with the process of adhesion of pathogenic strains. This ability may be seen in probiotic strains.[21]

Previous research has demonstrated that several probiotic strains each have their own unique effects on the reduction of clinical symptoms associated with IBS. For instance, *L. acidophilus* DDS-1 and *B. lactis* UABla12 have the potential to lessen the intensity of stomach discomfort in addition to other symptoms associated with IBS.[22] *Lactobacillus acidophilus* CL1285, *L. casei* LBC80R, and *L. rhamnosus* CLR2 could improve the quality-of-life and IBS symptoms, but *B. longum* NCC3001 showed only weak clinical efect to improve depression in patients with IBS.[23,24]

The severity of IBS was assessed with the overall IBSQoL, IBS-SSS, and fve serum factors (IL-6, IL-8, TNF-α, d-lactate, and LPS). At day 28, both the control and probiotic groups demonstrated an increase in the IBS-QoL score and a decrease in the IBS-SSS; however, the IBS-SSS declined significantly more in the probiotic group, indicating that the adjunctive treatment enhanced the clinical efficacy of managing IBS compared to the routine regimen alone. Serum pro-inflammatory cytokines, such as IL-6, IL-8, and TNF-, are believed to have a role in the development of IBS.[6]

Kefir, yogurt, and several other fermented foods are well-known sources of probiotics. All of them include various bacteria with the potential to improve gut health. *Streptococcus thermophilus, Lactobacillus strains, Lactobacillus delbrueckii subsp. bulgaricus*, and *Bifidobacterium strains* are the most prevalent organisms in these sources. These have been shown to improve gut health, as well as anti-inflammatory and immunological responses in general, according to studies. Other than the usual *Lactobacillus* and *Bifidobacterium species*, some commonly used microorganisms in probiotic preparations include the *Enterococcus* and *Streptococcus species*. Different formulations of probiotic products are available, ranging from *Bacillus* species to yeasts (*Saccharomyces cerevisiae* and *S. boulardii*) and even *Aspergillus oryzae*, which is a

filamentous fungus, all of which can be made available in the form of capsules, powders, pastes, tablets, or sprays depending on the feasibility.[25]

Bifdobacterium is an essential genus in a healthy human digestive system. Members of this genus perform crucial functions in degrading complex carbohydrates and stimulating the maturation of the host's immune system. It has been found that the bifdobacterial population in the gut microbiota of IBS patients decreased significantly. Although the probiotic adjunctive treatment did not increase the proportion of Bifdobacterium, less Bifdobacterium was detected in the control group on day 7, indicating that the routine drug treatment had an adverse effect on the gut microbiota, at least in the early phase of treatment, which was mitigated by the probiotic adjunctive treatment.[13,26]

The mechanisms of action of probiotics in irritable bowel syndrome have been studied, and it was shown that they are varied, heterogeneous, and strain specific. Understanding the mechanism of action of probiotics in IBS has to be translated into a language that is more functionally and clinically meaningful. Therefore, the modulation of the gut microbiota involves the competitive exclusion mechanism of pathogens by luminal pH, competition for nutritional sources, and production of bacteriocins, SCFAs, and biosurfactants, all of which prevent the proliferation of pathogens and inhibit their adhesion to the gut epithelia.[3,6]

In addition, one of the mechanisms by which probiotics improve the barrier function and the exclusion of pathogens is the promotion of mucus secretion. Mucus secretion is a gel layer that offers protection to epithelium from harmful bacteria or antigens by acting as a lubricant improving the gut motility and binding the carbohydrates to the epithelial cell's surface. Other probiotic mechanisms within the gut barrier function involve the improvement of the integrity of the tight junctions between intestinal epithelial cells and the production of antimicrobial peptides by epithelial cells (cationic peptides).[27,28]

These peptides prevent the reach of pathogens to the epithelium and exhibit antimicrobial activity. Other probiotic mechanisms within the gut barrier function involve the improvement of the integrity of the tight junctions between intestinal epithelial cells. In terms of the control of the immune system, probiotics function in the differentiation of T-regulatory cells as well as the elevation of anti-inflammatory cytokines and growth factors. Additionally, probiotics strengthen the immunity of the gut by promoting the synthesis of secretory IgA. At the level of the gut–brain axis, probiotics assist the regulation of endocrine and neurologic activities for the purpose of enhancing communication between the gut and the brain.[27,28]

There is an increasing body of evidence that reveals the modulatory interaction of probiotics and prebiotics with the human intestinal microbiota and its alteration towards a healthier composition for the host. This interaction is revealed by the fact that there is a rising body of evidence that reveals this interaction. Even though technical advancements have been made in the field of "omics," their mechanisms of action are not yet fully understood, and the scientific community is still debating whether or not they are beneficial in alleviating the symptoms of IBS.[27,29]

CONCLUSION

Given the infancy of the use of synbiotics in the field of alternative IBS therapy, as well as the potential dependency of synbiotic administration outcomes on their probiotic component, greater emphasis should be placed on establishing patients' probiotic response beforehand.

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