Probiotic Therapy for Irritable Bowel Syndrome

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By

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Abstract

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It is estimated that 20% of Americans suffer from Irritable Bowel Syndrome (IBS) which is a functional gastrointestinal disorder characterized by abdominal pain, constipation and diarrhea (National Digestive Diseases Information Clearinghouse, 2011). Many IBS sufferers have attempted to manage their symptoms through probiotic therapy, which is the ingestion of microorganisms, similar to those normally present in the gastrointestinal tract, to achieve health benefits (American Gastroenterological Association, 2011). The information about probiotics for IBS was confusing and conflicting.

This paper examined the evidence for the relationship between IBS symptoms and gastrointestinal microorganisms, the species of bacteria that are identified as probiotics, and the efficacy of utilizing probiotic therapy to manage IBS symptoms. It addressed the following question; “Does the current research provide evidence for the efficacy of probiotic therapy for the treatment of IBS symptoms?” A variety of internet sources and 20 research articles were examined and a summary of the research suggested (a) there is likely a relationship between gastrointestinal microorganisms and IBS symptoms; (b) the term “probiotics” encompasses a variety of species of bacteria; (c) although a variety of bacteria species have been studied, there is not yet conclusive evidence about the most effective species to treat IBS symptoms; (d) the genera Bifidobacterium and Lactobacillus have been the most studied and produced the most favorable data; and (e) few adverse effects are reported in the literature. Further research is necessary to establish guidelines for the use of probiotics to manage IBS symptoms.

Key Words: probiotics, Irritable Bowel Syndrome, digestive health, gastrointestinal symptoms, constipation, diarrhea, abdominal pain, microorganisms
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**Problem Statement**

Gastrointestinal symptoms are one of the most common reasons that people seek medical care and utilize prescription and over-the-counter medications. Often the etiology of these symptoms is an infection, inflammatory disease, or malignancy; however, approximately 41% of the time, the work-up does not reveal a cause for the symptoms. These individuals are diagnosed with a functional gastrointestinal disorder; such as dyspepsia, Irritable Bowel Syndrome, incontinence, gastrointestinal reflux disease, or chronic constipation (International Foundation for Functional Gastrointestinal Disorders, 2012). There is symptom overlap between many of the disorders, but the most common of these conditions is Irritable Bowel Syndrome (IBS). It includes a variety of symptoms such as cramping, abdominal pain, bloating, constipation, gas and diarrhea, and affects approximately one in five Americans (National Digestive Diseases Information Clearinghouse, 2011).

According to Rome III diagnostic criterion (2012), Irritable Bowel Syndrome is defined as recurrent abdominal pain or discomfort, at least 25% of the time, that is associated with two or more of the following, (a) improvement with defecation, (b) onset associated with a change in frequency of stool, and (c) onset associated with a change in form (appearance) of stool. Symptom onset must be six months prior to diagnosis; however, the aforementioned criteria must only be met for three months prior to diagnosis. There must be no evidence of inflammatory, anatomic, metabolic, or neoplastic process to explain the symptoms. The Rome Foundation encourages that a pain/discomfort frequency of at least 2 days/week be utilized as inclusion criteria for conducting pathophysiology research and clinical trials of IBS (Rome Foundation, 2012).

Many IBS sufferers experience a lack of symptom relief from conventional treatments. These include lifestyle interventions such as avoiding foods that triggers symptoms (especially caffeine and alcohol), regular exercise, stress reduction, ingestion of at least 30 grams of fiber per day, and drinking at least eight glasses of water per day. Conventional pharmacologic strategies include

- management of pain and cramping with anti-cholinergics or anti-spasmodics;
• management of constipation with osmotic or stimulant laxatives, polyethylene glycol, or lubiprosotone;
• management of diarrhea with anti-diarrheals or bile acid binding agents;
• management of stress with antidepressants and antianxiety agents;
• modulation of neurotransmitters, especially serotonin, with antidepressants.

Research has suggested that people with IDS have reduced serotonin receptor activity causing abnormal levels of serotonin in the GI tract. This results in problems with bowel motility and visceral hypersensitivity (National Digestive Diseases Information Clearinghouse, 2012). The conventional medications for IBS are often ineffective or produce undesirable side effects such as anti-cholinergic effects or dependence. Many IBS sufferers attempt alternative treatment strategies, such as over-the-counter probiotics, which are live microorganisms that are ingested for a health benefit (National Center for Complementary and Alternative Medicine, 2011).

These microorganisms are similar to the microbiota already present in the human gastrointestinal tract. A preliminary understanding of the microbial make-up of the human gut has been accomplished through: (a) quantitative real-time polymerase chain reaction (qPCR), a laboratory technique used to amplify and quantify a targeted DNA or RNA molecule in order to identify the microorganisms, and (b) the human intestinal tract chip (HITChip) which is a probe that identifies gut microbiota by their 16S rRNA subunit gene sequence. It is believed that there are thousands of species of microbiota in the human gut, but the common core is composed of the phylum; Actinobacteria, Bacteroidetes and Firmicutes, especially the Clostridium Cluster XIVa (Rajilic-Stojanovic et al, 2009). It is hypothesized that certain phylogenotypes may be associated with IBS symptoms. Table 1: Microbiota with Possible Association with IBS Symptoms contains a list of the microbiota discussed within this paper.

The mechanism of action of probiotics is believed to be based on their ability to modify the microbiota of the gut, thus decreasing the symptoms experienced by the IBS sufferer. The most common probiotics utilized for IBS symptoms are from the genera, *Lactobacillus* and *Bifidobacterium*; however,
phylogenotypes from other genera are utilized as well. Table 2: Probiotics for IBS Symptoms contains a list of the different species examined in the paper.

There is a recent surge of interest in the use of probiotics for treatment of IBS symptoms. However, information about the efficacy of treating IBS symptoms with probiotics may be unavailable, inconsistent, or confusing for the general public. Nurse practitioners must be prepared to provide information about probiotics to their patients. The question that faces nurse practitioners is, “Does the current research provide evidence for the efficacy of probiotic therapy for the treatment of IBS symptoms?” The purposes of this paper are to explore the evidence for (a) the relationship between gastrointestinal microorganisms and IBS symptoms, and (b) the efficacy of treating IBS symptoms with probiotics.

**Literature Search Strategies**

General information about IBS and probiotics was gathered and synthesized from a variety of internet sources, and a narrowed search about the efficacy of probiotic therapy for IBS was conducted through EBSCOhost: Advanced Search Engine Pubmed Database. Information was obtained from the American Gastroenterological Association, National Center for Complementary and Alternative Medicine, Rome Foundation, International Foundation for Functional Gastrointestinal Disorders, National Digestive Diseases Clearinghouse, and Current Nursing. The taxonomic classifications of the microbiota discussed herein were obtained from Pathosystems Resource Integration Center and the Genome Institute at Washington University.

The following Pubmed search terms were used: “digestive health,” “gastrointestinal symptoms,” “Irritable Bowel Syndrome,” “constipation,” “diarrhea,” and “abdominal pain” were each paired with “probiotics.” The search was further limited to the parameter “research and review articles.” Each article was selected for inclusion because it met the following criterion; (a) it was a research article or meta-analyses; (b) it examined IBS or gastrointestinal symptoms that are characteristic of IBS and not explained by inflammatory disease, infection, or malignancy; and (c) it examined microorganisms that are either actively or passively present in the human gastrointestinal tract. Nineteen articles were chosen for
Theoretical Framework

The theoretical framework for this paper is based on the nursing theory, Self-Care Model, by Dorothea Orem. The model defines self-care as those activities performed independently by the individual to promote personal health and wellness (Current Nursing, 2012). The utilization of complementary and alternative methods of treatment for IBS, such as probiotics, is an example of independent self-care. People are using available resources for health promotion, when conventional medical interventions have failed. Orem defined the role of the nurse practitioner as supportive and educative (Current Nursing, 2012). Because people have demonstrated an interest in providing self-care for IBS symptoms through the use of probiotics, it is the role of the nurse practitioner to educate people regarding the efficacy of utilizing probiotic therapy to manage IBS symptoms, and to support people in their decision-making process (Current Nursing, 2012).

Literature Review

The Relationship Between Microorganisms and IBS Symptoms

Jalanka-Tuovinen et al. (2011) performed a longitudinal study of 9 healthy subjects by regularly assessing their intestinal microorganisms through qPCR and HITChip. The results demonstrated that a healthy individual’s quantity and quality of gut microbiota tended to remain constant over time (high overall temporal stability; r=0.96, ±0.02), and most of the species of microbiota were present in all subjects, but in variable proportions between subjects. There was a correlation between a variety of microbiota and common intestinal symptoms, abdominal pain and bloating (p<0.05). There was an inverse correlation between Bifidobacteria and abdominal pains (r=−0.45,±0.03). The strengths of this study included its examination of healthy individuals in order to provide a baseline or control group for
future study of gastrointestinal disease. Its limitations included a small sample and employment of one of the authors by a commercial food production company.

Kerckhoffs et al. (2009) completed a fluorescence in situ hybridization (FISH) analysis of fecal samples for total microbiota and a qPCR analysis fecal and duodenal brush samples for bifidobacteria in 41 persons with IBS and 26 healthy participants. They discovered a 2-fold lower level of bifidobacteria in the fecal samples of persons with IBS. Specifically, Bifidobacterium catenulatum was significantly lower in duodenal and fecal samples in IBS participants when compared to healthy people (p<0.001). The strengths of this study included the examination of both fecal and duodenal flora, and the limitations included the lack of a matched sample of IBS and healthy participants by age.

Ponnusamy, Choi, Kim, Lee, and Lee (2011) performed a fecal analysis of 11 participants with IBS and 8 without IBS using 16S rRNA-specific denaturing gradient gel electrophoresis and qPCR analysis. The results of this study demonstrated that IBS subjects had a significantly higher diversity of total bacteria (p = 0.004), but not a higher total quantity. The variations in microbiota were associated with alterations in protein and carbohydrate metabolism in the gut. The strengths of this study included the examination of a variety of metabolites to measure bacterial presence and activity, and the limitations included its small sample and its single effort at obtaining data.

Malinen et al. (2010) examined the fecal samples of 44 persons who had IBS to identify correlations between quantity of various organisms and IBS symptoms. The investigators collected fecal samples and performed PCR assays of the phylotypes that have been demonstrated to have possible association with IBS symptoms by previous studies, and analyzed symptom scores with the Inflammatory Bowel Disease (IBD) questionnaire (modified to suit IBS patients). The phylotypes included species from Bifidobacterium catenulatum, Bifidobacterium spp., Clostridium cocoides/Eubacterium rectale-group, Clostridium cocleatum, Collinsella aerofaciens, Corpoccus eutactus, Desulfovibrio desulfuricans, Eubacterial 16S, Lactobacillus spp., Ruminococcus torques, Streptococcus bovis, and Veillonella spp. The results suggested that increased Ruminococcus torques and decreased Clostridium cocleatum, Collinsella aerofaciens, and Corpoccus eutactus were associated with increased symptoms scores. The
strengths of the study included the consideration of a variety of strains of organisms and the limitations included the use of an IBD questionnaire with unknown reliability and validity in a sample of persons with IBS.

Lyra et al (2009) analyzed eight diarrhea prominent (IBS-D), eight constipation prominent (IBS-C), four mixed symptom (IBS-M) and fifteen control participants (N= 35) using qPCR at three time intervals (0, 3 and 6 months). The qPCR analyzed phylotypes with possible association with IBS symptoms; *Bacterioides intestinalis*, *Bifidobacterium catenulatum*, *Butyrivibrio crosstus*, *Clostridium cocleatum*, *Clostridium thermosuccinogenes*, *Collinsella aerofaciens*, *Corpobacillus catenaformis*, *Coprococcus eutactus*, *Ruminococcus bromii*, *Ruminococcus torques*, *Slackia faecicanis*, and *Spiropasma chinense*. The following bacterial phylotypes were present in significantly different quantities in the four groups; *Clostridium cocleatum*, *Clostridium thermosuccinogenes*, *Corpobacillus catenaformis*, *Ruminococcus bromii*-like, and *Ruminococcus torques*, which suggested that different bacteria phylotypes may be responsible for different symptoms. The strengths of this study included replication of a previously conducted study and its most serious limitation was the small sample size.

Although a majority of the core microbiota of the human gastrointestinal tract have been identified, new species are continuing to be discovered. Evidence suggested that the variety, stability and quantity of certain phylotypes present in IBS sufferers may be different than those in healthy individuals. In addition, that certain species may be associated with specific gastrointestinal symptoms.

**The Efficacy of Treating IBS Symptoms with Probiotics**

There are many studies about the use of probiotics to modify the naturally occurring microbiota of the gastrointestinal tract and/or alleviate IBS symptoms; however, most of the studies utilize different species of bacteria either alone or in combination. There is little information to support the researchers' rationale for selecting one species over another. See Table 2: *Probiotics for IBS Symptoms* for a complete list of the probiotics discussed within the paper.

Lyra et al. (2010) used qPCR to examine the fecal microbiota of 42 IBS sufferers at 0, 3 and 6 months after supplementation with the following probiotic formula, which has shown association with
reduced IBS symptoms in previous studies; *Lactobacillus rhamnosus* GH, *Lactobacillus rhamnosus Le705*, *Propionibacterium freudenreichii* (ssp Shermanii JS) and *Bifidobacterium breve Bb99*. The qPCR examined phylotypes with possible association with IBS symptoms; *Bacteroides intestinalis*, *Clostridium cocleatum*, *Clostridium thermosuccinogenes*, *Collinsella aerofaciens*, *Coprococcus eutactus*, and *Ruminococcus torques*. The intervention group possessed decreased levels of *Ruminococcus torques* and increased levels of *Clostridium thermosuccinogenes*. These findings demonstrated alterations in microbiota that were associated with decreased IBS symptoms in previous studies. The strengths of this study included placebo-controlled double-blinded design and utilization of previously studied probiotic formula and bacterial targets. The study was limited by a small sample size.

Barrett, Canale, Gearry, Irving, and Gibson (2008) performed a study to determine if the consumption of Yakult (*Lactobacillus casei* shirota) altered the fermentation patterns in the small bowel. The 18 participants were people with IBS who demonstrated Early Rise in Breath Hydrogen After Lactulose (ERBHAL) at study onset, which is presumed to be associated with small intestinal bacterial overgrowth (SIBO). The intervention consisted of 65 ml of Yakult daily for 6 weeks followed by a retest of ERBHAL and symptom assessment by a visual analogue scale. The results demonstrated that 64% of participants experienced loss of ERBHAL (no hydrogen production in response to lactulose), and loss of ERBHAL was associated with reduced IBS symptoms. Therefore, fermentation patterns were found to be altered in a manner that was consistent with small bacterial intestinal overgrowth (SIBO) reduction. A strength of this study was the appropriate use of an uncontrolled, proof-of-concept, pilot study research design. The findings may have been biased since funding support was provided by Yakult Ltd.

McFarland and Dublin (2008) performed a meta-analysis of the effectiveness of probiotics in reducing the symptoms of IBS that included 20 randomized controlled trials, a total of 23 products and 1404 participants. The analysis suggested that probiotic use was associated with improvement in global IBS symptoms and decreased abdominal pain; however, too few studies on other IBS symptoms or specific probiotic strains limited the amount of information available on these topics. The strengths of the
study included limiting its resource pool to randomized, controlled, blinded trials, and its weaknesses included the methodological diversity of contributing studies.

Hoveyda et al. (2009) completed a systematic review and meta-analysis to evaluate the efficacy of probiotics for relieving IBS symptoms that included 14 randomized placebo controlled trials and (11 of which were included McFarland and Dublin (2008)) and 11 strains of probiotics. The analysis suggested that probiotics produced improvement in IBS symptoms and that further studies were indicated to identify the specific organisms and optimal dose of probiotics as well as which subgroups would most likely benefit. The strengths of the study included its limitation to randomized placebo controlled trials. Its weaknesses included the wide variation amongst contributing studies in regards to the length of treatment (4-26 weeks), dose, organisms, and strengths of probiotics used.

Yu-jing, Shu-je, Ying-cong, Jian-min, and Bin (2006) found that the symptoms of IBS gradually improved and then remained stable for two weeks, without any reported side effects, with the use of 1260 mgs of Bifidobacterium, Lactobacillus and Enterococcus three times per day for four weeks. Seventy-four patients completed the study and the information was obtained through utilization of IBS scales (which considered pain time, pain frequency, stool character, stool urgency, passage of mucous frequency, and abdominal distention). In addition, fecal analysis of 20 patient’s samples revealed the following results Lactobacillus (increased), Bifidobacterium (increased), Bacteroides (decreased), Clostridium (decreased), Enterococci (decreased), and Enterobacteriaceae (no change) before and after treatment. The strengths of the study included its consideration of the possibility of side effects or adverse reactions from probiotics, and the limitations of the study included is failure to identify the species of bacteria used in the probiotic, the open label nature of the trial, the lack of a control group, and the examination of only 20 of the 74 participants’ fecal samples.

Hong et al. (2009) demonstrated that Bifidobacterium bifidum BGNA, Bifidobacterium lactis AD011, Lactobacillus acidophilus AD031, and Lactobacillus casei IBS041 were safe and effective in decreasing IBS symptoms, especially in people with normal or loose stools. The study involved 70 patients who had IBS, 34 received placebo and 36 received 20 billion lyophilized bacteria twice daily for
8 weeks. The primary outcomes were abdominal pain, flatulence, and defecation discomfort as measured by the sum of visual analogue symptom scores. The secondary outcomes of quality of life and bowel habits including defecations frequency and stool form were measured using a daily bowel diary and a questionnaire at baseline, 4 and 8 weeks. After completion of the 8 week course of treatment, significant reductions in abdominal pain were identified; The baseline pain symptom score was 50.3, and it reduced to 18.4 in the treatment group and 32.6 in the placebo group (p=0.045). In addition, no significant adverse effects were reported. The strengths of the study included its double-blind randomized placebo controlled format, data collection by single trained interviewer, and its inclusion of participants who met Rome III criteria. A limitation was the use of single-item visual analogue scales to measure the outcome variables.

Martens, Enck, and Zieseniss (2010) found that 203 children, 4-18 years of age, with IBS who were treated with a probiotic containing *Escherichia coli* type bacteria at a dose of 1.5-4.5x10⁷ CFU (Symbioflor 2) for 43 days, reported a significant improvement in abdominal pain, stool frequency, bloating, mucus and blood in stool, the need for straining at stools, and urge to defecate. No adverse effects were reported. The strengths of this study included its large sample size, its inclusion solely of children who meet Rome III criteria, and its examination of an understudied population. The limitations included its observational format, lack of a control group, variable treatment dosage, variable duration of therapy, variable assessment intervals, and lack of adoption of a standard for subjective global assessment.

A variety of probiotic bacterial species and combinations of species have produced alterations in the quantity, diversity and stability of gastrointestinal microbiota. These alterations have demonstrated association with decreased IBS symptoms. The bacteria that have demonstrated initial benefit are predominantly from the genera *Bifidobacterium* and *Lactobacillus*, and a few from *Escherichia, Pediococcus, Propionibacterium*, and *Streptococcus*.

The following articles addressed probiotic use in the gastrointestinal symptoms of constipation, flatulence and abdominal pain. Although the participants of these studies did not have a diagnosis of IBS,
their symptoms had similar characteristics to IBS symptoms because they were functional gastrointestinal symptoms with an etiology that was not based on infection, inflammatory disease, or malignancy. The information from these studies provided evidence about the efficacy of probiotic treatment in specific gastrointestinal symptoms that are common to IBS, which aided in the understanding of therapy with specific strains of probiotics for specific IBS symptoms.

Kalman et al. (2009) determined that Digestive Advantage Gas Defense Formula (*Bacillus coagulans*, also known as *Lactobacillus sporogenes*) improved quality of life and reduced gastrointestinal symptoms in adults with post prandial intestinal gas-related symptoms and no GI diagnosis. The researchers randomly assigned 30 people to the treatment group and 31 to control, and gathered information about abdominal pain, abdominal distention, bloating, and flatus by administering the Gastrointestinal Symptom Rating Scale (GSRS) and the Severity of Dyspepsia Assessment (SODA) at 0, 2, and 4 weeks. The strengths of the trial included that it was a randomized double blind placebo controlled dual site trial and the limitation was the potential for bias since the authors received funding for this study from Ganeden Biotech.

An et al. (2010) established that lactic acid bacteria (LAB), specifically *Lactobacillus acidophilus*, *Pediococcus pentosaceus*, and *Bifidobacterium longum*, when used as a supplement to the standard treatment plan for nursing home residents with chronic constipation, increased frequency of defecation, and the amount and state of stool. The administration of LAB (3.0 X 10^{11} CFU/g) twice a day for two weeks resulted in a significant increase in fecal LAB levels (p<0.05) and a significant decrease in tryptophanase and urease (p<0.05) which are harmful enzyme activities of intestinal microflora. The strengths of the study included the measurement of multiple defecation habits as well as multiple elements of microbial activity. The weaknesses included its small sample size of only 19 participants and reliance on a self-report questionnaire to measure defecation habits.

Yang et al. (2008) found that a probiotic intervention had beneficial effects on stool frequency, defecation condition, and stool consistency in constipated adult women. The researchers randomly assigned 135 women to receive either fermented milk with *Bifidobacterium lactis* DN-17301 (1.25 X 10^{10}
and Streptococcus thermophilus and Lactobacillus bulgaricus (1.2 X 10^9 cfu) or acidified milk (control) for two weeks. Data was recorded at 0, 1 and 2 weeks. The strengths of this study included its large sample size and the identification of three specific species and doses of the probiotic. A weakness was the authors’ failure to report the source of data, e.g., stool frequency, stool consistency, and food intake.

Bekkali, Bongers, Van den Berg, Liem, and Benninga (2007) demonstrated that the probiotic mixture containing Bifidobacteria bifidum, Bifidobacteria infantis, Bifidobacteria longum, Lactobacilli casei, Lactobacilli plantarum, and Lactobacilli rhamnosus (Ecologic Relief®) had positive effects on childhood constipation as evidenced by increased number of bowel movements, decreased number of “hard” stools, decreased episodes of fecal incontinence, decreased abdominal pain, and no reported side effects. The study enrolled 20 children aged 4-16 who underwent treatment for four weeks. The strengths of the study included its consideration of multiple primary and secondary outcomes and limitations included its nature as a pilot study.

Tabbers, de Milliano, Roseboom, and Benninga (2011) found that bifidobacterium breve was effective in decreasing childhood constipation as evidenced by increased stool frequency, improved stool consistency, decreased fecal incontinence, and decreased abdominal pain. Twenty children, 3-16 years of age, consumed 10^8 x 10^{10} CFU of Yakult (bifidobacterium breve) once daily for four weeks. Symptoms were recorded in a daily bowel diary from seven days before onset of treatment through the commencement of therapy. No adverse effects were reported. The strengths of the study included its utilization of a standardized diary and the Bristol stool scale and limitations included the use of a non-randomized, non-controlled small pilot study design.

Chmielewska and Szajewska (2010) performed a meta-analysis of the literature to evaluate the efficacy and safety of probiotic therapy to treat constipation. The analysis suggested that Bifidobacterium lactis DN-173010, Lactobacillus casei Shirota, and Escherichia coli Nissle 1917 improved defecation frequency and stool consistency in adults. In children, Lactobacillus casei rhamnosus Lcr35 showed beneficial effects, but Lactobacillus rhamnosus GG did not. The strengths of the study were the analysis
of randomized controlled trials only and its inclusion of both adults and children. It’s most serious limitation was a small sample of five studies.

It has been presumed that probiotics required refrigeration in order to maintain the beneficial properties of the live bacteria, which placed a major limitation on their practicality. Rerksuppaphol and Rerksuppaphol (2010) found that Infioran (Lactobacillus acidophilus and Bifidobacterium bifidum) reduced the duration of acute diarrhea in children, and that efficacy was not affected by storage temperature. The researchers randomly assigned 23 children to receive probiotics that were stored in a refrigerator at 4°C, 22 to receive probiotics that were stored at room temperature at 28-32°C for one month prior to administration, and 22 to receive a placebo (N=67). A major limitation of this article was that it addressed acute diarrhea (greater than 72 hours), rather than IBS. However, the bacterial strains utilized were also commonly studied for the treatment of IBS. Therefore, a strength of this study was that the information it provided about the comparative effects of treatment with probiotics at alternative storage temperatures may have implications for other types of probiotic therapy, such as for IBS symptoms.

Discussion

Significance to Nursing Practice

The current research identified that IBS affects up to 20% of the worldwide population and has a negative impact on quality of life (Kerckhoffs et al. 2009; Malinen et al. 2010). The cause of this disorder is not well understood, but the research suggested that there may be a correlation between IBS symptoms and gastrointestinal microorganisms. IBS symptoms appeared be related to two factors (a) the diversity and instability of bacterial phylotypes (Ponnusamy et al. 2011), and (b) the quantity of a variety of bacterial species from specific genera. For example,

- decreased levels of Bifidobacteria spp were associated with increased IBS symptoms (Kerckhoffs et al., 2009; Jalanka-Tuovinene et al., 2011);
- increased levels of Ruminococcus torque were associated with increased levels of IBS symptoms (Lyra et al., 2009; Malinen et al., 2010);
other genus of bacteria that may have implications for IBS symptoms include Bacteroides spp., Clostridium spp., Coprococcus spp., Collinsella spp., Escherichia spp., of Lactobacilli spp, Streptococcus spp., and Veillonella spp. (Jalanka-Tuovinene et al., 2011; Kerckhoffs et al., 2009; Lyra et al., 2009; Lyra et al., 2010; Ponsumay et al., 2011); and

preliminary evidence suggested that certain bacterial phylotypes may be associated with specific gastrointestinal symptoms or IBS-subtypes (Lyra et al., 2009).

The lack of successful treatment of IBS with traditional interventions has led to the exploration of alternative methods such as probiotic therapy. Supplementation with probiotic formulas have demonstrated alterations in the gastrointestinal microbiota; (a) improved stability of gut microbiota, and (b) shifts from predominantly IBS-associated bacterial phylootypes to predominantly non-IBS associated (healthy) phylootypes (Lyra et al., 2010). Supplementation with probiotic formulas have also demonstrated symptom improvement as measured by pre and post treatment scores for a variety of IBS related symptoms. At least 18 bacterial phylootypes have shown initial success in treatment. The effective phylootypes are predominantly from the genera Bifidobacterium and Lactobaccillus, and a few from Escherichia, Pediococcus, Propionibacterium, and Streptococcus. Research suggested that probiotics containing multiple species may be more beneficial than probiotics containing a single species. Two meta-analyses of the research stated that overall evidence supported the use of probiotic therapy for IBS, but more research is necessary (McFarland et al. 2008; Hoveyda et al. 2009).

The evidence from multiple studies presented in this paper was not definitive; however, a review of the literature demonstrated that the preliminary data was consistent among studies. Therefore, nurse practitioners can inform patients that

- there is likely a relationship between gastrointestinal microorganisms and IBS symptoms;
- the term “probiotics” encompasses a variety of species of bacteria;
- although a variety of species have been studied, there is not yet conclusive evidence about the most effective species to treat IBS symptoms;
the genera *Bifidobacterium* and *Lactobacillus* have been the most studied and produced the most favorable data; and

- few adverse effects were reported in the literature.

There was no evidence to suggest that the use of probiotics should be discouraged while additional research is conducted. Because a variety of specific phylotypes from the genera *Bifidobacterium* and *Lactobacillus* demonstrated beneficial outcomes for a variety of symptoms, nurse practitioners can advise their patients to select a probiotic that contains a variety of species from these two genera. IBS sufferers may begin to see results after one week, but should continue supplementation for at least a month to determine efficacy. Because the benefit of probiotics appeared to be associated with improving the stability of the gut microbiota, probiotic supplementation will likely require continued treatment in order for benefits to be retained. There are no studies at this time to identify the cost/benefit ratio; therefore, this is a factor that the IBS sufferer must decide for themselves.

According to Dorothea Orem’s Self-Care Model, it is the role of the nurse practitioner to educate and support people in their personal promotion of health and wellness (Current Nursing, 2012). The current utilization of probiotics by IBS sufferers suggests that people are inclined to utilize this treatment option in their personal promotion of health and wellness. Therefore, it is the role of the nurse practitioner to educate and support people as they make decisions about this treatment option. Nurse practitioners can utilize the information presented in this paper to facilitate discussion.

**Recommendations for Future Research**

Major design strengths of the extant research included the (a) availability of multiple meta-analysis and synthesis publications; (b) availability of primarily randomized, controlled, double blinded trials; (c) utilization of many different methods to collect symptom reports; and (d) quantitative analysis of microorganisms. Major design weaknesses of current research included (a) an over reliance on self-report assessment, (b) the use of questionnaires with unknown reliability and validity for the sample of interest, (c) the lack of matching by age between experimental and control groups, (d) the relatively short length of many of the clinical trials, (e) the lack of studies that compared different microorganisms, and
(f) possible conflict of interest when the research on commercial products was funded by the manufacturer (An et al., 2010; Barrett et al., 2008; Bekkali et al., 2007; Chmielewska et al., 2010; Hong et al., 2009; Hoveya et al., 2009; Jalanka-Tuovinene et al., 2011; Kalman et al., 2009; Kerckhoffs et al., 2009; Lyra et al., 2009, Lyra et al., 2010; Malinen et al., 2010; Martens et al., 2010 McFarland et al., 2008; Ponnusamy et al., 2011; Rerksuppahol et al., 2010; Tabbers et al., 2011; Yang et al., 2008; Yu-jing et al., 2006).

Future research is needed to continue to identify the core microbiota of healthy individuals and to identify common variations of phylotypes associated with IBS symptoms. Once this knowledge is obtained, it will guide the choices for research on probiotic interventions. Although there are many studies about probiotics, there are too few studies about each individual species to produce conclusive data. More studies are necessary to understand the effects of specific species when used alone and in combination with other species.

Additional areas of study include the relationship between individual microorganisms in the gut and specific IBS symptoms, and the relationship between quantities of microorganisms in the gut and severity of IBS symptoms. In addition, further research should be conducted to determine the most effective doses for different populations, treatment schedule (daily, BID, TID, association with meals, etc.), duration of use, potential adverse effects, populations that need to avoid probiotic supplementation, and storage requirements. This research would help to establish treatment guidelines for probiotics.
Table 1

*Microbiota with Possible Association with IBS Symptoms*

<table>
<thead>
<tr>
<th>Genus</th>
<th>Phylum (Class)</th>
<th>Presence in IBS sufferers</th>
<th>Studies Included</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaerostipes spp</td>
<td>new eubacterium-like isolate</td>
<td>Insufficient data, unlikely a significant contributor</td>
<td>Jalanka-Tuovinene et al. (2011)</td>
</tr>
<tr>
<td>Bacteroides spp</td>
<td>Bacteroidetes</td>
<td>*Imbalance (Inconsistent data as to increased or decreased)</td>
<td>Jalanka-Tuovinene et al. (2011), Kerckhoffs et al. (2009), Ponnsumay et al. (2011), Lyra et al. (2009), Lyra et al. (2010)</td>
</tr>
<tr>
<td>Bifidobacteria spp</td>
<td>Actinobacteria</td>
<td>Decreased</td>
<td>Jalanka-Tuovinene et al. (2011), Kerckhoffs et al. (2009), Ponnsumay et al. (2011), Malinen et al. (2010), Lyra et al. (2009)</td>
</tr>
<tr>
<td>Bryantella spp</td>
<td>Firmicutes, Clostridia</td>
<td>Insufficient Data, unlikely a significant contributor</td>
<td>Jalanka-Tuovinene et al. (2011)</td>
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<td>Butyrivibrio spp</td>
<td>Firmicutes, Clostridia</td>
<td>*Imbalance (Insufficient data as to increased or decreased)</td>
<td>Jalanka-Tuovinene et al. (2011), Lyra et al. (2009)</td>
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<td>Clostridium spp</td>
<td>Firmicutes, Clostridia</td>
<td>*Imbalance (insufficient data as to increased or decreased)</td>
<td>Jalanka-Tuovinene et al. (2011), Kerckhoffs et al. (2009), Ponnsumay et al. (2011), Malinen et al. (2010), Lyra et al. (2009), Lyra et al. (2010)</td>
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<tr>
<td>Coprobacillus spp</td>
<td>New Eubacterium-like isolate</td>
<td>*Imbalance (Insufficient data as to increased or decreased)</td>
<td>Lyra et al. (2009)</td>
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<tr>
<td>Coprococcus spp</td>
<td>Firmicutes, Clostridia</td>
<td>*Imbalance (inconsistent data as to increased or decreased)</td>
<td>Jalanka-Tuovinene et al. (2011), Malinen et al. (2010), Lyra et al. (2009), Lyra et al. (2010)</td>
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<tr>
<td>Collinsella spp</td>
<td>Actinobacteria</td>
<td>*Imbalance (inconsistent data as to increased or decreased)</td>
<td>Malinen et al. (2010), Lyra et al. (2009), Lyra et al. (2010)</td>
</tr>
<tr>
<td>Dorea spp</td>
<td>Firmicutes, Clostridia</td>
<td>*Imbalance (inconsistent data as to increased or decreased)</td>
<td>Jalanka-Tuovinene et al. (2011)</td>
</tr>
<tr>
<td>Desulfovibrio spp</td>
<td>Proteobacteria</td>
<td>*Imbalance (inconsistent data as to increased or decreased)</td>
<td>Malinen et al. (2010)</td>
</tr>
<tr>
<td>Escherichia spp</td>
<td>Proteobacteria</td>
<td>*Imbalance</td>
<td>Barret et al. (2008)</td>
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</tbody>
</table>

Studies Included:
- Jalanka-Tuovinene et al. (2011)
- Kerckhoffs et al. (2009)
- Ponnsumay et al. (2011)
- Lyra et al. (2009)
- Lyra et al. (2010)
- Malinen et al. (2010)
- Lyra et al. (2009)
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<tr>
<th></th>
<th>Kingdom</th>
<th>Phylum</th>
<th>Class</th>
<th>Order</th>
<th>Imbalance</th>
<th>Reference(s)</th>
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<tr>
<td><em>Eubacterium spp</em></td>
<td>Firmicutes</td>
<td>Clostridia</td>
<td></td>
<td></td>
<td>Imbalance</td>
<td>Jalanka-Tuovinene et al. (2011), Malinen et al. (2010)</td>
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<td><em>Faecalibacterium spp</em></td>
<td>Firmicutes</td>
<td>Clostridia</td>
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<td>Jalanka-Tuovinene et al. (2011), Kerckhoffs et al. (2009)</td>
</tr>
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<td><em>Lactobacillus spp</em></td>
<td>Firmicutes</td>
<td>Bacilli</td>
<td></td>
<td></td>
<td>Decreased</td>
<td>Kerckhoffs et al. (2009), Ponnsunlay et al. (2011), Malinen et al. (2010)</td>
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<td><em>Lachnobacillus spp</em></td>
<td>(Associated with Clostridium Cluster XIVa)</td>
<td>Firmicutes</td>
<td>Clostridia</td>
<td></td>
<td></td>
<td>Jalanka-Tuovinene et al. (2011)</td>
</tr>
<tr>
<td><em>Oscillospira</em></td>
<td>Firmicutes</td>
<td>Clostridia</td>
<td></td>
<td></td>
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<td>Jalanka-Tuovinene et al. (2011)</td>
</tr>
<tr>
<td><em>Peptococcus</em></td>
<td>Firmicutes</td>
<td>Clostridia</td>
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<td></td>
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<td>Jalanka-Tuovinene et al. (2011)</td>
</tr>
<tr>
<td><em>Ruminococcus spp</em></td>
<td>Firmicutes</td>
<td>Clostridia</td>
<td></td>
<td></td>
<td>Increased</td>
<td>Jalanka-Tuovinene et al. (2011), Ponnsunlay et al. (2011), Malinen et al. (2010), Lyra et al. (2009), Lyra et al. (2010)</td>
</tr>
<tr>
<td><em>Slackia spp</em></td>
<td>Actinobacteria</td>
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<td>Imbalance</td>
<td>Lyra et al. (2009)</td>
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<tr>
<td><em>Spiroplasma spp</em></td>
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<td>Clostridia</td>
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<td></td>
<td>Imbalance</td>
<td>Lyra et al. (2009)</td>
</tr>
<tr>
<td><em>Sporobacter</em></td>
<td>Firmicutes</td>
<td>Clostridia</td>
<td></td>
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<td></td>
<td>Jalanka-Tuovinene et al. (2011)</td>
</tr>
<tr>
<td><em>Streptococcus spp</em></td>
<td>Firmicutes</td>
<td>Coccus</td>
<td></td>
<td></td>
<td>Imbalance</td>
<td>Jalanka-Tuovinene et al. (2011), Malinen et al. (2010)</td>
</tr>
<tr>
<td><em>Tannerella spp</em></td>
<td>Bacteroidetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Jalanka-Tuovinene et al. (2011)</td>
</tr>
</tbody>
</table>
**Veillonella spp**

| Firmicutes, Negativicutes | Imbalance (Insufficient data as to increased or decreased) | Jalanka-Tuovinene et al. (2011), Malinen et al. (2010) |

*Imbalance: Most studies suggested a variation from levels associated with non-IBS sufferers; some suggested an increased level, some suggested a decreased level, and some suggested fluctuation over time.*

### Table 2

**Probiotics for IBS Symptoms**

<table>
<thead>
<tr>
<th>Probiotic: Genus, Species (Phylum, Class)</th>
<th>Major Findings</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bifidobacterium animalis</strong> (Actinobacteria, Actinobacteria)</td>
<td>1) Improved symptom scores in constipation predominant IBS (in combination with <em>Streptococcus thermophilus</em> and <em>Lactobacillus bulgaricus</em>)</td>
<td>1) Hoveyda et al. (2009)</td>
</tr>
<tr>
<td><strong>Bifidobacteria bifidum</strong> (Actinobacteria, Actinobacteria)</td>
<td>1) Improved symptom scores in IBS (in combination with <em>Bifidobacterium lactis</em>, <em>Lactobacillus acidophilus</em>, <em>Lactobacillus casei</em>) 2) Effectiveness for treating acute diarrhea maintained at ambient temperature (with <em>Lactobacillus acidophilus</em>) 3) Improved defecation scores for childhood constipation (part of <em>Ecologic®Relief</em> product)*</td>
<td>1) Hong et al. (2009), 2) Rerksuppaphol &amp; Rerksuppaphol (2010), 3) Bekkali et al. (2007)</td>
</tr>
<tr>
<td><strong>Bifidobacteria breve</strong> (Actinobacteria, Actinobacteria)</td>
<td>1) Caused changes in gut microbiota; decreased <em>Ruminococcus torques</em>, increased <em>Clostridium</em> (in combination with <em>Lactobacillus rhamnosus</em>, <em>Propionibacterium freudenreichii</em>) 2-3) Improved symptom score in IBS (in same combination as described above) and Improved symptom score in IBS (in combination with <em>Lactobacillus plantarum</em>, <em>Lactobacillus acidophilus</em>) 3) Decreased abdominal pain in IBS (in combination with <em>Lactobacillus plantarum</em>, <em>Lactobacillus acidophilus</em>) 4) Increased stool frequency in childhood constipation</td>
<td>1) Lyra et al. (2010), 2) McFarland and Dublin (2008); 3) Hoveyda et al. (2009); Same study as discussed in McFarland and Dublin (2008) and study not already discussed, 4) Tabbers et al. (2011)</td>
</tr>
<tr>
<td><strong>Bifidobacteria infantis</strong> (Actinobacteria, Actinobacteria)</td>
<td>1-2) Improved symptom score in IBS 3) Improved defecation scores for childhood constipation (part of <em>Ecologic®Relief</em> product)*</td>
<td>1) McFarland and Dublin (2008) 2) Hoveyda et al. (2009); Same study as discussed in McFarland and Dublin (2008), 3) Bekkali et al. (2007)</td>
</tr>
<tr>
<td><strong>Bifidobacteria lactis</strong></td>
<td>1) Improved symptom score (in combination with <em>Lactobacillus casei</em>, <em>Lactobacillus</em></td>
<td>1) McFarland and Dublin (2008), 2) Hong et al. (2009),</td>
</tr>
<tr>
<td><strong>Probiotic</strong></td>
<td><strong>Improvements</strong></td>
<td><strong>References</strong></td>
</tr>
<tr>
<td>-------------</td>
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<td>---------------</td>
</tr>
<tr>
<td><strong>Actinobacteria, Actinobacteria</strong></td>
<td><em>acidophilus</em> 2) Improved symptom scores in IBS (in combination with <em>Bifidobacterium bifidum, Lactobacillus acidophilus, Lactobacillus casei</em>) 3) Improved defecation in constipated women (in combination with <em>Streptococcus thermophilus, and Lactobacillus bulgaricus</em>) 4) Improved defecation habits in constipated adults</td>
<td>3) Yang et al. (2008), 4) Chmielewska &amp; Szajewska (2010)</td>
</tr>
<tr>
<td><strong>Bifidobacteria longum</strong> (Actinobacteria, Actinobacteria)</td>
<td>1) No improvement 2) Improved defecation scores in nursing home residents (in combination with <em>Lactobacillus acidophilus, Pediococcus pentosaceus</em>) 3) Improved defecation scores for childhood constipation (part of Ecologic®Relief product)*</td>
<td>1) McFarland and Dublin (2008), 2) An et al. (2010), 3) Bekkali et al. (2007)</td>
</tr>
<tr>
<td><strong>Lactobacillus acidophilus</strong> (Firmicutes, Bacilli)</td>
<td>1) Improvement in symptoms of IBS 2) Improvement in symptoms IBS (in combination with <em>Lactobacillus plantarum, Bifidobacterium breve.</em>) 3) Improved symptom scores in IBS (in combination with <em>Bifidobacterium bifidum, Bifidobacterium lactis, Lactobacillus casei</em>) 4) Effectiveness for treating acute diarrhea maintained at ambient temperature (with <em>Bifidobacterium bifidum</em>) 5) Improved defecation scores in nursing home residents (in combination with <em>Pediococcus pentosaceus and Bifidobacterium longum</em>)</td>
<td>1) McFarland and Dublin (2008) x2, 2) Hoveyda et al. (2009), 3) Hong et al. (2009), 4) Rerksuppaphol &amp; Rerksuppaphol (2010), 5) An et al. (2010)</td>
</tr>
<tr>
<td><strong>Lactobacillus bulgaricus</strong> (Firmicutes, Bacilli)</td>
<td>1) Improved symptom scores in constipation predominant IBS (in combination with <em>Streptococcus thermophilus and bifidobacterium animals</em>) 2) Improved defecation in constipated women (in combination with <em>Streptococcus thermophilus, and Bifidobacteria lactis</em>)</td>
<td>1) Hoveyda et al. (2009), 2) Yang et al. (2008)</td>
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<tr>
<td><strong>Lactobacillus casei</strong> (Firmicutes, Bacilli)</td>
<td>1) Alters fermentation patterns in the small bowel and reduced symptom in IBS 2) No significant improvement 3) Improved symptom scores in IBS (in combination with <em>Bifidobacterium bifidum, Bifidobacterium lactis, Lactobacillus acidophilus</em>) 4) Improved defecation scores for childhood constipation (part of Ecologic®Relief product)*</td>
<td>1) Barret et al. (2008), 2) McFarland and Dublin (2008), 3) Hong et al. (2009), 4) Bekkali et al. (2007), 5) Chmielewska &amp; Szajewska (2010) x2</td>
</tr>
</tbody>
</table>
| Lactobacillus plantarum (Firmicutes, Bacilli) | 1) Improved symptoms in IBS  
2) Improvement in symptom score in IBS (in combination with Bifidobacterium breve, Lactobacillus acidophilus)  
3) Improved defecation scores for childhood constipation (part of Ecologic®Relief product)* | 1) McFarland and Dublin (2008)  
2) Hoveyda et al. (2009); Same study as discussed in McFarland and Dublin (2008) and study not already discussed  
3) Bekkali et al. (2007) |
| Lactobacillus reuteri (Firmicutes, Bacilli) | 1-2) Data not significant | 1) McFarland and Dublin (2008),  
2) Hoveyda et al. (2009); Same study as discussed in McFarland and Dublin (2008) |
| Lactobacillus rhamnosus (Firmicutes, Bacilli) | 1) Caused changes in gut microbiota; decreased Ruminococcus torques, increased Clostridium (in combination with, Propionibacterium freudenreichii, Bifidobacterium breve)  
2-3) Improved symptom score in IBS (in same combination as described above)  
4) Improved defecation scores for childhood constipation (part of Ecologic®Relief product)*  
5) No improvement in defecation habits with constipated kids when used alone | 1) Lyra et al. (2010),  
2) McFarland and Dublin (2008)  
3) Hoveyda et al. (2009); Same study as discussed in McFarland and Dublin (2008)  
4) Bekkali et al. (2007),  
5) Chmielewska & Szajewska (2010) |
| Lactobacillus salivarius (Firmicutes, Bacilli) | 1-2) Data not significant | 1) McFarland and Dublin (2008),  
2) Hoveyda et al. (2009); Same study as discussed in McFarland and Dublin (2008) |
| Lactobacillus sporogenes (a.k.a. Bacillus coagulans) (Firmicutes, Bacilli) | 1) Reduced GI symptoms in adults with post prandial gas symptoms | 1) Kalman et al. (2009) |
| Pediococcus pentosaceus (Firmicutes, Bacilli) | 1) Improved defecation scores in nursing home residents (in combination with Lactobacillus acidophilus and Bifidobacterium longum) | 1) An et al. (2010) |
| Propionibacterium freudenreichii (ssp shermani JS) (Actinobacteria, Actinobacteridae) | 1) Caused changes in gut microbiota; decreased Ruminococcus torques, increased Clostridium (in combination with Lactobacillus rhamnosus, Bifidobacterium breve)  
2-3) Improved symptom score in IBS (in same combination as described above) | 1) Lyra et al. (2010),  
2) McFarland and Dublin (2008)  
3) Hoveyda et al. (2009); Same study as discussed in McFarland and Dublin (2008) |
| Streptococcus thermophilus (Firmicutes, Coccus) | 1) Improved symptom scores in constipation predominant IBS (in combination with Bifidobacteria animalis and Lactobacillus bulgaricus)  
2) Improved defecation in constipated women (in combination with Bifidobacteria lactis and Lactobacillus bulgaricus) | 1) Hoveyda et al. (2009),  
2) Yang et al. (2008) |
| **Streptococcus faecium (a.k.a Enterococcus faecium)** (Firmicutes, Coccus) | 1-2) Improvement of IBS symptoms based on physician assessment and improvement in symptom score (in combination with *Escherichia coli*) | 1) McFarland and Dublin (2008) 2) Hoveyda et al. (2009); Same study as discussed in McFarland and Dublin (2008) |

*Ecologic®Relief: Bifidobacterium bifidum, Bifidobacterium infantis, Bifidobacterium longum, Lactobacillus casei, Lactobacillus plantarum, Lactobacillus rhamnosus*
RUNNING HEAD: PROBIOTIC THERAPY, IRRITABLE BOWEL

References


