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Probiotics – a blessing for some, a burden for others. The positive and negative effects of their use among different groups of patients – journal review

Abstract

Introduction. The increasing interest in the use of bacterial cultures and complex microbial products in medical treatment has become more and more noticeable. Each year, a growing number of such products are introduced to the pharmaceutical market. With the development of methods for isolating and culturing specific bacterial strains, numerous concepts have emerged on the potential benefits of supplementation. We agree that probiotic supplementation yields scientifically proven positive effects in certain medical conditions. However, our attention is drawn to the tendency to expand the use of probiotics to vulnerable populations. This raises important questions concerning the safety, efficacy, and potential risks associated with probiotic use among the most sensitive patient groups. In our work, we focused on reviewing the current scientific literature , and we would like to propose several insights into safe probiotic administration among different groups of patients.

Materials and methods. We reviewed the literature from early 2000 to 2025 for articles on the probiotics in different groups of patients. The review of the available literature was conducted by searching official databases such as PubMed and Google Scholar using the following keywords: probiotics, prebiotics, antibiotics, microflora, sepsis, acute diarrhea, preterm infants, SIBO, IBS, acute pancreatitis etc.. We also queried references cited from original research, meta-analyses, and reviews in both Polish and English language, published in scientific journals and articles.

Results. Probiotics demonstrate therapeutic benefits in preventing antibiotic-associated diarrhea and reducing necrotizing enterocolitis in preterm infants. They may also support treatment of ulcerative colitis, pouchitis, travelers' diarrhea and acute childhood diarrhea, as well as possibly prevent atopic dermatitis when taken maternally. However, the evidence remains inconclusive for several other conditions, including IBS and Crohn's disease. Probiotic use remains not recommended in immunocompromised states, such as ICU settings, due to the risk of sepsis. Safety concerns include antibiotic resistance and microbiota disruption, which requires thorough data from high-quality clinical trials, including strain-specific assessments. Finally, the available data suggests that synbiotics may offer enhanced benefits, while postbiotics are emerging as safer alternatives.

Conclusions. The available data and existing studies do not provide sufficient grounds to unequivocally support the use of probiotics and related products in clinical treatment. There is a lack of robust evidence based on well-designed clinical trials. Current recommendations regarding the use of probiotics for the management of travelers' diarrhea and antibiotic-associated diarrhea remain in place, as do contraindications for their use in individuals with sepsis or compromised immune function. However, for other medical conditions, stronger evidence and formal guidelines from scientific societies are still awaited.

Keywords: Probiotics, Prebiotics, Sepsis, Antibiotics, Microflora, Acute Diarrhea, Preterm Infants, SIBO, IBS, Acute Pancreatitis.

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INTRODUCTION

In XVII century, Robert Hooke and Antoni Van Leeuwenhoek discovered tiny life forms using simple prototypes of microscope [1]. Those first mentions led to extensive reasearch that created the foundation of nowadays microbiology which made and makes possible studies of human microbiota today [2].

Human body is considered as one of the most complex bio structure on whole planet, containing about 30 trillion of cells. However, the part of the success and sometimes of failure has to be given to microorganisms living inside and on us. The concept of microbiota comprises all living organisms residing in specific anatomical sites on human tissues or in fluids form microbiome. These organisms include not only bacteria, fungi, archaea and protists but nowadays extends to viruses, phages and what's more - mobile genetic elements [3,4].

Advanced technology along with latest research prove that previously bacteria free sites now can be considered as microbiome such as respiratory system [5] or urinary bladder [6].

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The scope of this research is focused generally on the gut microbiome, given the fact that probiotics are generally taken orally, however the market offers products for skin care like creamsor gels with addition of probiotics [7].

The gastrointestinal tract consists of oral cavity, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon and rectum which can be simplified to oral cavity, stomach, small and large intestine. Every above-mentioned parthas physiologically different pH levels, includes different enzymes thus creating various condition for different species of present bacteria.

The oral cavity with pH levels balancing between 6.6-7.1 [8]. According to Lea Sedghi et all, the oral microbiome consists of over 700 identified bacterial species. The most common ones in adults were family Streptococcus (S.oralis, S. Mitis, and S.peroris) lesscommon but still frequently found were family of Pasturellaceae, Lactobacillales, Gemella, Veillonella, Prevotella, Fusobacterium, Actinomyces, Corynebacterium, Capnocytophaga and Neisseria.

The authors point out the differences in newborn's microbiome and child's microbiome which changes since early days. Starting from Streptococcus, Fusobacterium and Staphylococcus species [9]. Interestingly, maternal smoking was correlated to higher levels of C.conisus and F. nucleatum in infant microbiome [9,10].

The stomach keeps high pH levels usually,however that differs with age stages. Infants tend to keep pH > 4, elderly pH > 6.6 both groups prone to enteric infections [11-13]. Adults generally have pH close to 1.5 depending of health condition, diet etc. It is worth noting that the 2015 study, authors discussed interesting research findings that human gastric pH levels are evolutionary closer to that of carrion feeders than to that of carnivores and omnivores [11]. The harsh environment enables to kill

most of incoming microorganism via food. However not all of them see it as hostile as it seems. Notorious Helicobacter pylori, known to be the strongest risk factor for gastric ulcers and gastric cancer is the main possible inhabitant. We know it now thanks to discovery by Nobel prize winner Dr. Barry J. Marshall who purposefully infected himself with H.Pylori live culture [14].

Helicobacter secretes urease and by inducing inflammation cause destruction of acid secreting glands, increasing the local gastric pH levels, in which conditions no other microorganism is able to compete. However, when the pH goes above 2-4 it is possible to colonise gastric mucosa by commensal bacteria.

In 2006 biopsy samples were studied with PCR technique. Bik et al. Found 128 bacterial phylotypes in gastric mucosa of 23 patients, where most phyla were characterised by Proteobacteria, Firmicutes, Bacteroidetes, Actinobacteria, and Fusobacteria.

Bik et al. found that the result of few H.Pylori negative patients obtained via conventional methods actually positive in PCR. Stewart et all. discussed it as the possibility of underestimation of infected patients examined via conventional tests [15,16].

Moving further to the small intestine (duodenum, jejunum and ileum) with much higher pH levels from 5 up to 9 where are usually found phylum Bacteroidetes, Clostridiales and Enterobacteriacae. The biomass levels are higher than in the stomach but lower compared to the oral cavity and large intestine. This is due to the rapid lumenal flow, the antibacterial activity of bile salts and the production of antimicrobial compounds such as defensins etc. Jens Walter and Ruth Ley described IgA immunoglobulin as one of the factors of keeping bacterial numbers in check. Although authors stated that the mechanism requires further research, they believe that it has possibility to shape the diversity of gut microbiota [17].

Lastly, large intestine comprised of cecum, colon and rectum. It is the best habitat for large quantities of bacteria due to the low concentration of antibactericial bile salts, much slower peristalsis and higher pH estimated from 5 to 7. Firmicutes, Facteroidetes Actinobacteria, Proteobacteria and Fusobacteria phylas can be found there [17].

All microorganisms, just like humans, have their preferences regarding the environment in which they thrive best. By examining different sections of the digestive system, it is easy to observe that various bio-physical and chemical factors influence the presence of different species as well as the estimated amounts of the microbiota.

These factors include pH levels, temperature, osmolarity, pressure, oxygen concentration, the presence of enzymes and immune proteins, as well as nutrients. As an example, in the intestines, peristalsis makes it difficult for microorganisms to attach to the surface. External influences such as diet, lifestyle (especially with high levels of stress), geographical location, seasons and, of course, medications taken also affect the microbiome [3].

Most of the factors mentioned above are difficult to change, and even if possible, such changes often come with serious implications. For this reason, it is easiest for us to influence diet, lifestyle, and, of course, medications, which have indirect effects – such as proton pump inhibitors that lower the pH of gastric juice – or direct effects, like antibiotics since 1928 when the discovery of penicillin by Alexander Fleming laid the foundation for the wide range of antibiotics available worldwide today. These drugs, which have saved humanity from bacterial diseases, not only eliminate pathogenic bacteria but also eradicate native microbiota.

Nowadays, we not only have bacterial killers available but methods to deliver pure, selected strains of bacteria and fungi in the form of probiotics, nutrients that promote colony growth known as prebiotics, or a combination of both called synbiotics.

How do probiotics affect microflora?

The human microbiota is a vast community of living organisms existing in symbiosis within the body. Maintaining this state is a multifaceted mechanism largely based on a properly functioning intestinal barrier and relatively stable environmental conditions. Any change in this state will lead to dysbiosis.

The contemporary use of probiotics for control and prevention is a direct intervention in the processes occurring within the microbial community.

In general, the concept of probiotic action refers to the directinfluence on the microbiota by promoting the growth or displacement of existing colonies, activating and enhancing the immune system, or affecting enterocytes.

Colin Hill et al. categorised the mechanisms of probiotic action based on their frequency of occurrence as follows:

Widely observed and common mechanisms include competition against existing colonies, supporting depleted colonies by providing fresh colonisers, promoting enterocytes, and synthesising acids and short-chain fatty acids. Direct antagonism at the species level is also frequently observed, including the production of additional chemical compounds such as vitamins, enzymes, or metabolites from bile salt breakdown. Much less frequently, strain-specific effects on the neurological, immunological and hormonal systems have been observed [18].

Additionally, the authors, citing studies available at that time, mention Akkermansia muciniphila, Faecalibacterium prausnitzii, Roseburia spp., and Eubacterium hallii as bacterial strains producing butyrate with evidence of anti-inflammatory, immune-boosting, and intestinal barrier-enhancing effects. All of these possess potential as noteworthy therapeutic tools, although further research and safety maintenance are required.

The study published in 2023 describes how probiotic bacteria exert their beneficial effects on the host immune system through multiple, complex mechanisms based on key probiotic genera, focusing on Lactobacillus, Lacticaseibacillus, Limocaseibacillus, Bifidobacterium, Escherichia coli, Bacteroidales, and Streptococcus. The significant immunomodulatory capability of probiotics is facilitated by their direct interactions with immune cells (such as lymphocytes, monocytes, macrophages, and dendritic cells) and intestinal epithelial cells. Probiotics effectively bolster intestinal immune function by stimulating B cells to produce IgA antibodies. Oral probiotic strains, containing *Lactobacillus casei*, *acidophilus*, *rhamnosus*, *delbrueckii*, has been shown to increase the number of IgA-producing cells in the gut in a dose-dependent manner. This occurs as probiotics trigger the clonal expansion of B cells, leading to IgA release, notably without affecting the count of CD4+ T cells. Furthermore, specific probiotic bacteria like *Lactobacillus casei* CRL 431 and *Lactobacillus helveticus* R389 have been observed to increase intestinal IgA-producing cell numbers by prompting the release of IL-6 through a TLR2-dependent mechanism. This suggests that certain lactobacilli encourage B cell proliferation via IL-6 production to enhance IgA secretion [19].

In 2020, Fang Yang et al. Summaries that Probiotics help regulate the functions of the intestinal epithelium by supporting the integrity of the epithelial barrier, encouraging cell survival, boosting the production of antibacterial agents and protective proteins, strengthening beneficial immune responses, and reducing the production of proinflammatory cytokines. Many of these effects are achieved through the modulation of specific intracellular signaling pathways in intestinal epithelial cells, such as mitogen-activated protein kinases (MAPK) and nuclear factor kappa B (NF-κB) [20].

Probiotics, prebiotics, synbiotics and postbiotics – overview

Nowadays there is a growing trend to consume concentrated nutrients in the form of supplements. We may ask ourselves whether this is influenced by marketing itself or is it a defense mechanism of societies increasingly affected by civilization diseases?

There are many preparations available on the pharmaceutical market with alleged positive effects on intestinal microflora. The most common are the aforementioned dietary supplements, which are available in pharmacies. Individual preparations are registered as OTC drugs. Unfortunately, they are attributed with many more properties than have actually been confirmed. Under normal conditions, the bacterial flora is in a state of equilibrium, but certain factors, such as antibiotic therapy, stress, poor diet or disease, can disrupt this state.

Among the available preparations we distinguish:

- prebiotics,
- probiotics,
- synbiotics,
- postbiotics.

Each of these has its own specific definitions, which we would like to briefly outline.

1. **Prebiotics:** according to the International Scientific Association for Probiotics and Prebiotics (ISAPP), prebiotic is "a substrate that is selectively utilised by host microorganisms for health benefits." The definition has been updated to include both carbohydrate-based products, such as oligosaccharides and dietary fiber, as well as other compounds (e.g., phenols, CLA-Conjugated Linoleic Acid and PUFA-Polyunsaturated Fatty Acids, including omega-3 and omega-6) that have been demonstrated beneficial effects on the target host. The best known and most widely used prebiotics are fructooligosaccharides: inulin and oligofructose. They can be found in some plant-based foods, including chicory, artichokes, asparagus and garlic. Dietary fiber is a mixture of carbohydrate polymers that are not digested by human enzymes in the small intestine. These compounds have the ability to ferment and subsequently release short-chain fatty acids, which have a beneficial effect on the growth of microorganisms, including Bifidobacterium and Lactobacillus [21].
2. **Probiotics** are "live microorganisms that, when administered in adequate amounts, provide health benefits to the host." Probiotic bacteria increase the good microflora by creating a favorable intestinal environment. In addition, in the event of an imbalance of the intestinal microflora, they reduce the number of pathogenic bacteria, thereby restoring eubiosis [22]. The condition for creating a product containing a particular microorganism is the fulfillment of a number of important criteria. This applies to both dietary supplements and probiotic-enriched foods.
   - human origin from the gastrointestinal tract of a healthy donor
   - its beneficial effects must be scientifically documented
   - accurate determination of the type, species and strain of bacteria
   - ability to colonise the intestines and resistance to gastric juices and bile
   - confirmed safety of use (safe coexistence with natural bacterial flora)
   - information on proper storage of the product
   - minimum concentration in the product (minimum 106 colony forming units, or CFU)

   The best studied and popularly used probiotic strains are:
   - Lactic acid bacteria: Lactobacillus rhamnosus, Lactobacillus helveticus, Lactobacillus casei, Lactobacillus lactis oraz Lactobacillus acidophilus
   - Yeasts: Saccharomyces bouldardii
   - Bifidobacteria: Bifidobacterium breve, Bifidobacterium animalis, Bifidobacterium bifidum
   - Streptococcus thermophilus
3. **Synbiotics:** they are preparations consisting of probiotics, which are live microorganisms, and prebiotics, substances that are a nutrient for them. This combination implies the use of synergistic action, which can bring more health benefits than with a single product. The prebiotic and a probiotic must separately meet minimum criteria and interact safely together to form a synbiotic. Examples of synbiotics are formulations containing strains of Lactobacillus and Bifidobacterium in combination with fructooligosaccharides (FOS) or inulin [23].

4. **Postbiotics:** they are also known as metabiotics or parabiotics and are preparations containing inactive microorganisms or their components that provide health benefits. They must contain a sufficient amount of inactivated cells or their components, with or without metabolites. They have an indirect effect on the health of the host. Products of the microbiome released by living bacteria include metabolites, proteins and vitamins, among others. The advantage of postbiotics over probiotics is their greater stability. They are inactive, so they do not react with substances in their environment. They feature a simple chemical structure making them easier to produce, dose, store and transport [24].

Examples of postbiotics:
- nucleotides,
- peptides e.g. bacteriocins,
- short-chain fatty acids (SCFAs) e.g. butyric acid,
- lipopolysaccharides (LPS) and exopolysaccharides (EPS),
- enzymes,
- vitamins.

Indications for probiotics:

The pharmaceutical market offers probiotics in various forms, from oral capsules to face creams. Probiotic manufacturers attribute many properties to them. Unfortunately, few of them have been scientifically confirmed. Their marketing and the popularity are disproportionately positive compared to what the research says.

However, there are specific indications where there is reliable evidence that probiotics work.

- **Antibiotic therapy:**

It is well known that the use of probiotics during antibiotic therapy can reduce the risk of diarrhea associated with the therapy. They are widely used by primary care physicians and by specialists. To date, very little clinical data has been generated on this topic despite many animal studies. We believe that the results of several meta-analyses are noteworthy because they indicate a beneficial effect of probiotics in preventing this diarrhea. As an example, in 2002, Cremonini et al. analysed seven randomised controlled trials involving 881 participants. Two strains of bacteria, Lactobacillus spp. and Saccharomyces boulardii, were included in this study. It is worth noting that only pediatric patients participated in the study, so the conclusions drawn should not be extended to adult patients. The subjects also came from different geographic areas and socioeconomic backgrounds, with developing countries making up the bulk of the population. The drawn conclusion was that probiotics are beneficial in treating diarrhea associated with antibiotic therapy. Despite this, it should be remembered that not all probiotics work in the same way or have a comparable end result. Therefore, no firm conclusions should be drawn [25].

Another important study was a meta-analysis conducted by McFarland in 2006, which included 25 randomised trials involving 2,810 people. It showed a significant reduction in the number of diarrhea cases after the use of probiotics. In addition, the analysis also focused on another important disease that is a serious complication of antibiotic therapy in hospitals, Clostridium difficile infection. The conclusions were that three types of probiotics (Saccharomyces boulardii, Lactobacillus rhamnosus GG and probiotic mixtures) significantly reduced the development of antibiotic-associated diarrhea, and six randomised controlled trials showed that only S. boulardii, used together with oral metronidazole and/or vancomycin, significantly reduced the risk of C. difficile infection [26].

- **Travelers' diarrhea:**

Affects about 60% of travelers, it is one of the most common diseases accompanying tourists on vacation. The etiology of 50-80% is bacterial, while the remaining cases of diarrhea are caused by viruses and protozoa. The most commonly reported pathogens are Escherichia coli, Campylobacter jejuni, Salmonella species and Shigella species [27]. Therefore, antibiotics are recommended for the treatment of traveler's diarrhea. The pathological mechanism associated with this disease entity is associated with an imbalance of the intestinal flora. This has led many researchers to conclude that taking probiotics may have a positive effect in preventing traveler's diarrhea. However, clinical studies have shown inconclusive results in the use of probiotics to treat traveler's diarrhea. The well-known meta-analysis conducted by McFarland in 2007 found that probiotics significantly reduce the risk of traveler's diarrhea. The analysis included 12 studies that confirmed a reduced relative risk of diarrhea in people taking probiotics while traveling [28]. In contrast, a recent meta-analysis published in 2018 showed statistically significant efficacy in TD prevention. The study authors showed that probiotics are a valuable adjunct to rehydration therapy in the treatment of acute infectious diarrhea. It is noteworthy that the meta-analysis did not address which probiotic strains or probiotic combinations are most effective for TD prevention, and it is this information that clinicians and travelers care most about [29].

- **Acute diarrhea in children:**

Rotavirus is the most common virus associated with acute diarrhea in children aged 1 month to 3 years. So far conducted studies have shown the effectiveness of probiotics together with adequate hydration in treating acute diarrhea. It has been claimed that taking probiotics can shorten the duration of diarrhea from 0.7 to 1 day. In 2024, Minaz et al. wrote a review article covering 98 studies involving a total of 17,236 participants. The studies were divided into categories. The WHO definition of diarrhea and that defined by the author were put under the microscope. They also investigated the effectiveness of probiotics among children with chronic diarrhea. It was proven that probiotics reduced the duration of diarrhea by 95 hours in this group of patients [30]. Unfortunately, the conclusions that have been made are very uncertain. The high level of heterogeneity i.e. the use of different probiotic strains, different doses and treatment durations reduced the certainty of the evidence.

- **Atopic dermatitis:**

This is a chronic, recurrent, inflammatory dermatosis most commonly diagnosed in infants and young children. Research findings suggest that certain probiotic strains may be helpful in treating this condition, but data on the type of strains with the greatest efficacy are currentlynot available . The exact mechanism of action of probiotics in the treatment of atopic dermatitis is not fully understood. It is likely that the mechanism involves immunomodulatory effects [31]. According to one study, Lactobacillus rhamnosus GG was administered to women in the last weeks of pregnancy and during breastfeeding. This was compared to a group of women taking a placebo. The study included women with a strong family history of AD. The study found that infants of mothers who received LGG had a significantly lower risk of atopic dermatitis during the

first 2 years of life [32]. Additionally, many of the papers we analysed focused on comparing probiotics with prebiotics in single therapy or in combination. In summary, the most commonly studied probiotics were Lactobacilli and Bifidobacteria strains. The SCORAD index was used to measure treatment efficacy. However, the conclusions are inconclusive, as in many studies the authors suggest that the disease tends to improve over time in certain groups of patients [33].

- **Necrotising enterocolitis (NEC):**

Probiotics appear to be revolutionary in the prevention of necrotising enterocolitis (NEC) in premature infants, reducing its risk and overall mortality. They promote the maturation of the gastrointestinal tract of premature infants. Ultimately stimulating intestinal maturity, probiotics help premature infants better tolerate nutrition. In 2025, a systematic analysis of 51 randomised controlled trials examined the effect of probiotics on NEC in preterm infants. According to the most recent sources, the most recommended probiotic strains were a combination of Bifidobacterium, Lactobacillus and Enterococcus. This mixture has been shown to be most effective in reducing mortality and the incidence of NEC (Bell II or higher) in premature infants. In addition, Lactobacillus alone has the best results in reducing hospitalisation and time to full enteral feeding in preterm infants [34]. This is due to the fact that it induces adhesive secretion and inhibits cell apoptosis.

It is worth adding that, in addition to the inclusion of probiotics, early enteral feeding should be promoted and unnecessary monitoring of gastric contents should be minimised. In 2011, a double-blind, randomised, controlled clinical trial was conducted involving 231 preterm infants with very low birth weight (750 to 1499 g). The study group of infants received human milk with probiotic supplementation (B. breve and L. casei), while thethe control group received human milk containing no probiotics. The results of the conducted study were promising. Oral supplementation with B. breve and L. casei reduced the incidence of NEC (Bell stage ≥2). The improvement in intestinal motility was manifested by a reduction in the time to achieve full enteral feeding [35]. Given that the effect of probiotics is closely related to a specific strain, the question still remains whether there are probiotic strains particularly effective in preventing necrotising enterocolitis (NEC) in preterm infants.

In many disease entities, there is no official statement concerning the use of probiotics. There is insufficient evidence supported by clinical trials to influence treatment guidelines. Many clinicians today question whether there is a noticeable benefit or harm to a patient undergoing oral probiotic supplementation. Such disease include:

- **Neonatal sepsis:**

There is insufficient evidence to suggest that probiotics increase or decrease the risk of sepsis in preterm infants. One clinical study showed that prophylactic supplementation with probiotics, specifically a mixture consisting of 4 strains: L. acidophilus LA-5, L. plantarum, B. lactis BB-12 and S. boulardii, reduced the incidence of VAP in patients, a pneumonia caused by prolonged mechanical ventilation [36]. Sepsis is a common problem in premature infants connected to invasive life-saving devices. We need to consider that in addition to the existing benefits of probiotic supplementation in reducing the risk of NEC and death in very low birth weight infants, we need to keep in mind the risk of invasive infection due to live bacteria in probiotics. Based on reports to date, this risk is very rare, but still exists.

In the face of such reports, we cannot pass by indifferently, because the life of the child may depend on this decision. Therefore, it is very important to use only probiotics of the highest production quality, with the best proven effectiveness in scientific studies, for premature babies. These preparations are administered to premature infants under close supervision in the conditions of neonatal units.

- **Irritable bowel syndrome (IBS):**

A review from 2023 and Meta-analysis of 82 trials with data from over 10,000 patients resulted in no clear conclusion about recommendations of use. The study authors specify need for further, better planned clinical randomized trials to give data sufficient for confident treatment with probiotics. However, support for some strains, specific species and combination of probiotics is reported, the data indicates that certainty in the evidence to the GRADE criteria is low or very low [37].

Another review from 2024 found that prebiotics especially inulin and GOS (galacto-oligosaccharides) may be helpful. In the authors' view, probiotics appears to improve symptoms and synbiotics were found helpful. All of them seems to be promising help in treatment but there is still not enough evidence, data and clinical trials to determine their importance [38].

- **Inflammatory bowel diseases (IBD):**

Ulcerative collitis (UC) and Crohn disease (CD) have been the aim of studies for asignificant amount of time . Sameeha rau et al. reviewed RCTs of prebiotics in UC. The evidence suggests that while certain prebiotics like FOS 1-kestose and higher-dose OF-IN (oligofructose-enriched inulin) show specific therapeutic benefits, results are inconsistent across compounds and study designs. Dose-response relationships appear to be critical, particularly for OF-IN's anti-inflammatory effects. Larger trials with standardised outcome measures are required to clarify clinical utility, particularly given the heterogeneity in control groups and endpoints across existing studies.

According to Crohn's disease, two RCTs found that prebiotics like oligofructose-enriched inulin (OF-IN) at 15–20 g/day did not induce clinical remission. No trials have assessed prebiotics for preventing relapse. The OF-IN may cause bloating and flatulence, but other prebiotics show no increased adverse effects. Overall, the evidence is very limited and of low quality, so prebiotic supplementation is not currently recommended. As a plant-based diets rich in soluble fiber may help to reduce symptoms and inflammation, but caution is needed in patients with ileal strictures to avoid fiber-related complications. Fruits and vegetables remain key components of anti-inflammatory diets beneficial for IBD.

Probiotics have shown effectiveness in inducing clinical remission and improving symptoms in ulcerative colitis, particularly multi-strain formulations like VSL#3®, while single-strain probiotics are generally ineffective. Evidence for maintaining remission or preventing relapse in UC is limited. In the case of pouchitis, probiotics may help prevent recurrence, with VSL#3® conditionally recommended by the American Gastroenterological Association (AGA), though data for primary prevention and treatment are low quality. Concerning Crohn's disease, current evidence is sparse and does not support probiotic use for inducing or maintaining remission. Overall, probiotics appear to be safe but should be used with consideration of the limited and variable evidence across different IBD conditions.

The study authors reviewed synbiotic use in a 4-week RCT with 94 participants. Only the synbiotic group (psyllium plus *Bifidobacterium longum*) showed improvements in CRP levels

and quality of life, while psyllium or probiotics alone did not show such effects. This suggests that synbiotics may offer greater benefits than prebiotics or probiotics alone [38].

Estevinho et al. conducted a meta-analysis of 67 eligible studies (22 systematic reviews and 45 RCTs) from 2,613 results, finding that probiotics significantly increased clinical remission in ulcerative colitis (UC) but not in Crohn's disease (CD). Subgroup analysis showed that combining 5-ASA with probiotics further improved remission in mild-to-moderate UC. Probiotics greatly reduced recurrence in relapsing pouchitis and tended to decrease clinical recurrence in inactive UC, with no protective effect in CD. Additionally multi-strain probiotics achieved better results for remission and recurrence prevention in UC compared to single strain probiotics. No improvement in endoscopic outcomes was observed, and adverse events were similar to controls. The overall evidence certainty was low due to study limitations and heterogeneity.

Probiotics appear to be promising adjunct therapies for IBD, particularly effective in UC and pouchitis, especially with multi-strain formulations in combination with 5-ASA, while showing a favorable safety profile. They are generally ineffective for CD, including after ileocecal resection. The difference in efficacy likely reflects variations in disease location, immune response, and microbiota interactions between UC and CD. Despite encouraging findings, evidence quality remains moderate to low, highlighting the need for further research to optimise probiotic strains, dosages, treatment durations, and patient selection, with future potential in genetically enhanced bacteria for the CD treatment [39].

Contraindications to probiotics:

A lot of attention has been devoted to convince readers that probiotics can have positive effects on the human body, especially on the intestinal microflora. As we already know, there are certain clinical conditions they there are used for. Therefore, it is appropriate to discuss the topic of cases and diseases in which the use of probiotic preparations is not advisable, and may even be harmful to health.

Probiotic supplementation is contraindicated in the following situations:

- **Sepsis and decreased immunity:**

According to the latest definition, it is a life-threatening reaction of the body to an infection, resulting in significant failure of at least one organ. The infection is usually caused by bacteremia, or the presence of bacteria in the blood. One risk factors for sepsis appears to be an impaired gut microbiome. At this point, there are no guidelines for the use of probiotics in patients with organ failure, immune deficiency or intestinal barrier dysfunction [40]. A link between abnormal development of the gut microbiome and the onset of sepsis has been found in newborns [41]. In his meta-analysis, Rao compared the risk of late onset sepsis in early-term infants who received probiotics with those who did not receive this supplementation. The study included two groups of low-birth-weight premature infants: those fed exclusively with human milk and those receiving formula. According to the study results, preterm infants fed exclusive human milk and supplementing with probiotics had a lower risk of LOS [42]. In this case, the use of probiotics is justified, but requires strict control of the strains administered. The management of adult patients, who are hospitalised for a long time, e.g. in an intensive care unit, immunocompromised patients, and patients having a central line insertion is quite different. Probiotic supplementation among these groups of patients is not recommended.

Over the years, an increase in the risk of probiotic strains penetrating from the intestinal epithelium into the portal circulation has been observed in these patients. This phenomenon is referred to as probiotic translocation.

In this scenario, the "good" probiotic bacteria, which were supposed to help rebuild the bacterial flora, become a serious threat in immunocompromised patients, causing a systemic infection of the body. A review paper by Kullar et al. found that strains of Lactobacilli caused bacteremia and sepsis in immunocompromised patients or those hospitalised for severe illness. Patients exposed to antibiotic therapy were characterised by a disrupted intestinal barrier, resulting in probiotic strains entering the bloodstream from the gut. In addition, it was noted that hospitalised patients, who were not taking probiotics were also at risk of bacteremia. In the cases described, it was hypothesised that patients with intravenous catheters who were not taking probiotics orally may have been infected by both the airborne and contact routes by medical personnel. This is explained by the fact that the probiotic used was taken by patients in powder form, which could have easily spread and contaminate central line catheters [43]. In 2011, there was a case report of a 24-year-old patient who developed sepsis as a result of preoperative administration of probiotics after aortic valve replacement. The woman had previously been suspected of having infective endocarditis. She received empirical antibiotic therapy along with probiotics for 6 weeks. Blood analyses showed that the causative agent of the sepsis was a probiotic strain: Lactobacillus rhamnosus. It was the same strain that she received along with the antibiotic. Unfortunately, most infections in humans result from mucosal transmission. In this case, the heart failure patient may have had a weakened intestinal barrier associated with ischemia. The immune system acting properly in a situation of bacterial movement from the intestinal lumen into the blood kills bacteria in the mesenteric lymph nodes. In the case described here, it has been shown that probiotic supplementation in immunocompromised or organ failure patients can carry dangerous consequences [40].

- **Acute pancreatitis:**

Currently, probiotic preparations are not recommended for use in patients with acute pancreatitis. In the characteristics of probiotic products registered asmedicines , it is stated that precautions should be taken in the use in this group of patients.

The mortality rate associated with this disease ranges from 2% to 10%, while it rises to as high as 14-25% in patients with the more severe form, which affects 10-20% of patients [44]. The meta-analysis conducted by Hou and colleagues suggested that the use of probiotics could reduce the length of hospital stay (MD ¼ 6.01,95% CI ¼ 8.95-3.07), shorten the length of ICU stay (RR ¼ 2.31,95% CI ¼ 4.61-0.01) and lower the overall infection rate (RR ¼ 0.57, 95% CI ¼ 0.38-0.87) in both the study and control groups. However, there were no statistically significant differences between the study groups in reducing patient mortality, the rate of pancreatic complication rates, the need for surgery, as well as drainage rates and systemic complications [45]. This year's comprehensive review paper by Celestino Nist and colleagues examined the role of gut microbiota and probiotics in acute pancreatitis and found that microbiota-targeted therapy, including probiotics, can help to reduce the inflammation associated with AP. However, they stressed that the effectiveness of its action varies depending

on the strain and severity of the patient's clinical condition [46]. Two years ago, the University of Bangkok studied the effect of probiotics on pancreatic inflammation and intestinal integrity in mice with acute pancreatitis. Male mice were divided into 4 groups: a control group receiving intraperitoneal saline injections, a study group with AP receiving injections with L-arginine only, and 2 groups of mice with AP plus probiotics, which received L-arginine plus 1 strain of the probiotic L. plantarum B7 or a probiotic mixture of L. rhamnosus L34 and L. paracasei B13. After induction, these mice were sacrificed 72 hours later. Subsequently, tissue sections of the pancreas and intestine were taken for histological examination and blood for amylase analysis. The results showed that the levels of pancreatic amylase and pancreatic myeloperoxidase were higher in the AP group than in the control group, and the lowest in the probiotic supplemented groups. Histopathology analysis showed increased inflammation, swelling and necrosis in the AP, which improved after administration of the probiotic mixture. In conclusion, probiotic supplementation, especially with a mixed strain, alleviated L-arginine-induced acute pancreatitis by reducing inflammation and improving the intestinal barrier [47].

In contrast to these promising new studies, it was the work from 2008 that shaped the guidelines for the use of probiotics in AP. The results of the PROPATRIA (Probiotics in Pancreatitis) study, conducted by Besselinket al. , showed no beneficial effect of probiotic prophylaxis on the incidence of infectious complications. In addition, mortality in the probiotic group was about twice as high as in the placebo group. This study showed that probiotics should not be routinely used in acute pancreatitis [48].

- **Immunosuppression:**

This group includes patients taking immunosuppressive drugs, after transplants, during radio- or chemotherapy, with impaired immune systems, prematurely born children, patients with AIDS, lymphoma or undergoing long-term corticosteroid therapy. In these cases, the risk may outweigh the benefits of probiotic supplementation. Special caution should be taken when introducing probiotics so as not to risk a general inflammatory reaction. On the contrary, it is worth mentioning that in recent years, several studies have been conducted, which focused on the effect of probiotics on increasing the number of CD4+ cells in patients infected with HIV. According to Mortezazadeh et al. daily administration of probiotics in appropriate doses may lead to a temporary increase in the number of CD4+ cells. Through their action, bacteria promote the healing process of the intestinal epithelium. Then, by changing the intestinal flora, they reduce the risk of virus transmission. This results in less frequent hospitalization due to co-infections [49].

- **SIBO:**

There is no clear position regarding the effectiveness of probiotics in eliminating SIBO symptoms. The results of studies are varied, and many of them are based on small groups of patients and different endpoints. Probiotics in SIBO are primarily intended to modulate the composition of the intestinal microbiota and protect the intestines from colonisation with pathogens. Therefore, attempts have been made to supplement SIBO therapy with probiotic strains with proven clinical effects. The effects of probiotic therapy are strongly dependent on the specific strain of bacteria. Thus, not all probiotics work equally, so the choice of strain should be always individually consulted with a doctor. The meta-analysis from 2017 showed that the use of probiotics reduces the amount of hydrogen produced in a breath test (OR = 1.61; 95% CI: 1.19-2.17) [50]. Other studies indicate that probiotics may improve the effectiveness of antibiotics, e.g. rifaximin administered with Lactobacillus casei, compared to antibiotics alone [51]. However, the study form 2018 noted an exacerbation of symptoms such as bloating, abdominal pain, lactic acidosis, and "brain fog" in SIBO patients taking probiotics. These symptoms resolved after discontinuing the probiotics [52].

In summary, the current state of knowledge indicates the need for further research to better understand the effect of probiotics on the course and symptoms of SIBO.

Side effects of probiotic supplementation:

Like any substance with a therapeutic effect, probiotics can cause side effects. The most common of them include: bloating, excessive gas, abdominal pain. In very rare cases, hypersensitivity reactions have been reported, manifesting as a rash or diarrhea. It should be emphasised that side effects of using probiotics occur sporadically. To avoid side effects, attention should be paid to the way probiotics are stored. These preparations contain heat-sensitive live bacterial cells, which should be kept in a dry, dark place at a constant temperature. However, if side effects occur, the use of the product should be discontinued and it should be consulted with a doctor. Pregnant or breastfeeding women should also obtain the consent of their doctor to supplement probiotics.

Safety concerns:

The gut microbiota significantly influences drug metabolism, impacting both efficacy and toxicity through various microbial enzymatic processes such as azoreduction, decarboxylation, sulfation, and β-glucuronidase activity. Probiotics can modify these microbial functions, potentially altering drug metabolism and safety. Current evidence is preliminary, and more research is needed to confirm how probiotic enzymes affect drug function in vivo and to develop strategies to manage potential probiotic–drug interactions.

Microbiome profiling holds promise for tailoring probiotic therapy and predicting individual responses but is not yet a standard requirement for probiotic safety assessments. A major safety concern remains the potential for probiotics to transfer antibiotic resistance (AR) genes, especially those linked to mobile genetic elements or clinically important antibiotics. This necessitates rigorous phenotypic and genotypic screening and thorough risk analysis to minimise AR gene dissemination.

Long-term colonisation by probiotics derived from common commensal microbes is generally considered safe at low levels, but increased exposure from persistent colonisation may pose risks, such as displacing beneficial native microbes, disrupting the microbiota structure and function, or causing invasive infections if the gut barrier is compromised, as observed in rare cases that include Lactobacillus bacteremia in ICU patients. Conversely, sustained colonisation could offer efficient, lasting health benefits by filling vacant ecological niches and providing essential metabolic functions, such as metabolising human milk oligosaccharides or delivering enzymes to treat metabolic disorders like phenylketonuria. Given these potential benefits and risks, the development of long-term colonising probiotics should becarefully approached, with a clear therapeuticpurpose, thorough risk-benefit assessment, and dedicated research to establish relevant safety data, exposure tests, and biomarkers to ensure their safe use. Long-term safety concerns remain difficult to address due to limited data. Regulatory approaches for probiotics should align with those

for other bioproducts . Research is needed to identify high-risk groups which require closer long-term follow-up [53].

In the review published in 2024, researchers used the United States Preventive Services Task Force (USPSTF) standards to evaluate idea of broad, safe prevention use of probiotics in healthy humans. The USPSTF sets a very high standard for recommending preventive interventions in healthy individuals, and while probiotics are generally safe and may be considered for specific uses, such as preventing antibiotic-associated diarrhea, recurrent urinary tract infections, or frequent respiratory infections, current evidence is insufficient to support broad preventive recommendations [54].

SUMMARY

Probiotics offer therapeutic benefits in several clinical contexts, but their effects on microbiota composition, antibiotic resistance, and drug metabolism require careful evaluation. Continued research and the development of improved screening methodologies are essential to ensure their safe and effective use, particularly in support of personalised treatment approaches and to minimise potential risks. Among the strongest indications for probiotic use is the prevention of antibiotic-associated diarrhea, where strains such as Lactobacillus rhamnosus GG and Saccharomyces boulardii have shown consistent efficacy. In preterm infants, probiotics significantly reduce both the incidence and mortality associated with necrotising enterocolitis (NEC). For conditions such as ulcerative colitis (UC) and pouchitis, some multi-strain formulations, such as VSL#3®, have been effective as adjunct therapies.

There is also some evidence supporting probiotic use in the treatment of travelers' diarrhea and acute childhood diarrhea, though results vary depending on the specific strains and dosages used. Additionally, maternal probiotic supplementation may help to prevent atopic dermatitis in infants. The mechanism of function of probiotics can enhance the intestinal barrier, stimulate immune responses (such as IgA production), produce beneficial metabolites like short-chain fatty acids (SCFAs), and compete with pathogenic microorganisms. Synbiotics, which combine probiotics with prebiotics, may offer greater benefits than either component alone, while postbiotics,non-active microbial products,present a safer and more stable alternative.

However, evidence remains unclear or inconclusive for several conditions, including irritable bowel syndrome (IBS), Crohn's disease, small intestinal bacterial overgrowth (SIBO), neonatal sepsis, and general immune modulation. Moreover, the preventive use of probiotics in healthy individuals is not currently recommended by high-standard bodies such as the UnitedState Preventive Services Task Force (USPSTF), due to insufficient supporting evidence. The use of probiotics also carries contraindications, particularly in individuals with sepsis, immunocompromisedpatients , or acute pancreatitis, who are at a heightened risk of probiotic-induced bacteremia or systemic infection. This risk is especially concerning for patients in intensive care units, those with compromised gut barriers, or individuals with catheters.

Safety concerns include the potential for horizontal transfer of antibiotic resistance genes and the possibility of long-term disruption of the gut microbiota. Consequently, strain-specific safety assessments are critical. In conclusion, while probiotics show clear benefits in specific, well-studied clinical conditions, their routine or preventive use,especially among healthy or vulnerable populations,should be approached with caution. The review underscores the urgent need for better-designed, large-scale clinical trials and rigorous strain-specific research to optimise probiotic use.

Disclosure:

Author's contribution:

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REFERENCES

1. Gest H. The discovery of microorganisms by Robert Hooke and Antoni Van Leeuwenhoek, fellows of the Royal Society. Notes Rec R Soc Lond. 2004;58(2):187-201. doi:10.1098/RSNR.2004.0055
2. Milestones in Human Microbiota Research. Accessed June 18, 2025. https://www.nature.com/immersive/d42859-019-00041-z/index.html
3. Aggarwal N, Kitano S, Puah GRY, Kittelmann S, Hwang IY, Chang MW. Microbiome and Human Health: Current Understanding, Engineering, and Enabling Technologies. Chem Rev. 2022;123(1):31. doi:10.1021/ACS.CHEMREV.2C00431
4. Berg G, Rybakova D, Fischer D, et al. Microbiome definition re-visited: old concepts and new challenges. Microbiome. 2020;8(1):103. doi:10.1186/S40168-020-00875-0
5. Beck JM, Young VB, Huffnagle GB. The Microbiome of the Lung. Transl Res. 2012;160(4):258. doi:10.1016/J.TRSL.2012.02.005
6. Zasloff M. Antimicrobial peptides, innate immunity, and the normally sterile urinary tract. J Am Soc Nephrol. 2007;18(11):2810-2816. doi:10.1681/ASN.2007050611
7. Gao T, Wang X, Li Y, Ren F. The Role of Probiotics in Skin Health and Related Gut–Skin Axis: A Review. Nutrients. 2023;15(14):3123. doi:10.3390/NU15143123
8. Matzeu G, Naveh GRS, Agarwal S, et al. Functionalized Mouth- Conformable Interfaces for pH Evaluation of the Oral Cavity. Advanced Science. 2021;8(12):2003416. doi:10.1002/ADVS.202003416
9. Sedghi L, DiMassa V, Harrington A, Lynch S V., Kapila YL. The oral microbiome: Role of key organisms and complex networks in oral health and disease. Periodontol 2000. 2021;87(1):107. doi:10.1111/PRD.12393

10. Mason MR, Chambers S, Dabdoub SM, Thikkurissy S, Kumar PS. Characterizing oral microbial communities across dentition states and colonization niches. Microbiome. 2018;6(1):67. doi:10.1186/S40168-018-0443-2
11. Beasley DE, Koltz AM, Lambert JE, Fierer N, Dunn RR. The Evolution of Stomach Acidity and Its Relevance to the Human Microbiome. PLoS One. 2015;10(7):e0134116. doi:10.1371/JOURNAL.PONE.0134116
12. Carrion V, Egan EA. Prevention of neonatal necrotizing enterocolitis. J Pediatr Gastroenterol Nutr. 1990;11(3):317-323. doi:10.1097/00005176-199010000-00006
13. Husebye E, Skar V, Høverstad T, Melby K. Fasting hypochlorhydria with gram positive gastric flora is highly prevalent in healthy old people. Gut. 1992;33(10):1331-1337. doi:10.1136/GUT.33.10.1331
14. Marshall BJ. Barry J. Marshall - Nobel Lecture. Published online 2005.
15. Stewart OA, Wu F, Chen Y. The role of gastric microbiota in gastric cancer. Gut Microbes. 2020;11(5):1220. doi:10.1080/19490976.2020.1762520
16. Bik EM, Eckburg PB, Gill SR, et al. Molecular analysis of the bacterial microbiota in the human stomach. Proc Natl Acad Sci U S A. 2006;103(3):732. doi:10.1073/PNAS.0506655103
17. Walter J, Ley R. The human gut microbiome: ecology and recent evolutionary changes. Annu Rev Microbiol. 2011;65:411-429. doi:10.1146/ANNUREV-MICRO-090110-102830
18. Hill C, Guarner F, Reid G, et al. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nature Reviews Gastroenterology & Hepatology 2014 11:8. 2014;11(8):506-514. doi:10.1038/nrgastro.2014.66
19. Mazziotta C, Tognon M, Martini F, Torreggiani E, Rotondo JC. Probiotics Mechanism of Action on Immune Cells and Beneficial Effects on Human Health. Cells. 2023;12(1). doi:10.3390/CELLS12010184
20. Yan F, Polk DB. Probiotics and Probiotic-Derived Functional Factors—Mechanistic Insights Into Applications for Intestinal Homeostasis. Front Immunol. 2020;11:1428. doi:10.3389/FIMMU.2020.01428
21. Luzzi A, Briata IM, Di Napoli I, et al. Prebiotics, probiotics, synbiotics and postbiotics to adolescents in metabolic syndrome. Clinical Nutrition. 2024;43(6):1433-1446. doi:10.1016/J.CLNU.2024.04.032
22. Salminen S, Collado MC, Endo A, et al. The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. Nat Rev Gastroenterol Hepatol. 2021;18(9):649. doi:10.1038/S41575-021-00440-6
23. Swanson KS, Gibson GR, Hutkins R, et al. The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of synbiotics. Nat Rev Gastroenterol Hepatol. 2020;17(11):687. doi:10.1038/S41575-020-0344-2
24. Vinderola G, Sanders ME, Salminen S. The Concept of Postbiotics. Foods. 2022;11(8):1077. doi:10.3390/FOODS11081077
25. Cremonini F, Di Caro S, Nista EC, et al. Meta-analysis: the effect of probiotic administration on antibiotic-associated diarrhoea. Aliment Pharmacol Ther. 2002;16(8):1461-1467. doi:10.1046/J.1365-2036.2002.01318.X
26. McFarland L V. Meta-analysis of probiotics for the prevention of antibiotic associated diarrhea and the treatment of Clostridium difficile disease. Am J Gastroenterol. 2006;101(4):812-822. doi:10.1111/J.1572-0241.2006.00465.X
27. Fan H, Gao L, Yin Z, Ye S, Zhao H, Peng Q. Probiotics and rifaximin for the prevention of travelers' diarrhea: A systematic review and network meta-analysis. Medicine. 2022;101(40):E30921. doi:10.1097/MD.0000000000030921
28. McFarland L V. Meta-analysis of probiotics for the prevention of traveler's diarrhea. Travel Med Infect Dis. 2007;5(2):97-105. doi:10.1016/J.TMAID.2005.10.003
29. Bae JM. Prophylactic efficacy of probiotics on travelers' diarrhea: an adaptive meta-analysis of randomized controlled trials. Epidemiol Health. 2018;40(40):e2018043. doi:10.4178/EPIH.E2018043
30. Minaz A, Alam R, Jiwani U, et al. Efficacy of probiotics for treatment of acute or persistent diarrhoea in children from birth till 10 years: Systematic review and meta-analysis. J Glob Health. 2024;14:04236. doi:10.7189/JOGH.14.04236
31. Islam SU. Clinical Uses of Probiotics. Medicine. 2016;95(5):e2658. doi:10.1097/MD.0000000000002658
32. Rautava S, Kalliomäki M, Isolauri E. Probiotics during pregnancy and breast-feeding might confer immunomodulatory protection against atopic disease in the infant. Journal of Allergy and Clinical Immunology. 2002;109(1):119-121. doi:10.1067/mai.2002.120273
33. Fanfaret IS, Boda D, Ion LM, et al. Probiotics and prebiotics in atopic dermatitis: Pros and cons (Review). Exp Ther Med. 2021;22(6):1376. doi:10.3892/ETM.2021.10811
34. Dai Y, Yu Q, Zhang F, et al. Effect of probiotics on necrotizing enterocolitis in preterm infants: a network meta-analysis of randomized controlled trials. BMC Pediatr. 2025;25(1). doi:10.1186/S12887-025-05469-Z
35. Braga TD, Da Silva GAP, De Lira PIC, De Carvalho Lima M. Efficacy of Bifidobacterium breve and Lactobacillus casei oral supplementation on necrotizing enterocolitis in very-low-birth-weight preterm infants: a double-blind, randomized, controlled trial. Am J Clin Nutr. 2011;93(1):81-86. doi:10.3945/AJCN.2010.29799
36. Tsilika M, Thoma G, Aidoni Z, et al. A four-probiotic preparation for ventilator-associated pneumonia in multi-trauma patients: results of a randomized clinical trial. Int J Antimicrob Agents. 2022;59(1). doi:10.1016/J.IJANTIMICAG.2021.106471
37. Goodoory VC, Khasawneh M, Black CJ, Quigley EMM, Moayyedi P, Ford AC. Efficacy of Probiotics in Irritable Bowel Syndrome: Systematic Review and Meta-analysis. Gastroenterology. 2023;165(5):1206-1218. doi:10.1053/J.GASTRO.2023.07.018
38. Rau S, Gregg A, Yaceczko S, Limketkai B. Prebiotics and Probiotics for Gastrointestinal Disorders. Nutrients. 2024;16(6). doi:10.3390/NU16060778
39. Estevinho MM, Yuan Y, Rodríguez-Lago I, et al. Efficacy and safety of probiotics in IBD: An overview of systematic reviews and updated meta-analysis of randomized controlled trials. United European Gastroenterol J. 2024;12(7):960. doi:10.1002/UEG2.12636
40. Kochan P, Chmielarczyk A, Szymaniak L, et al. Lactobacillus rhamnosus administration causes sepsis in a cardiosurgical patient--is the time right to revise probiotic safety guidelines? Clin Microbiol Infect. 2011;17(10):1589-1592. doi:10.1111/J.1469-0691.2011.03614.X
41. Adelman MW, Woodworth MH, Langelier C, et al. The gut microbiome's role in the development, maintenance, and outcomes of sepsis. Crit Care. 2020;24(1):278. doi:10.1186/S13054-020-02989-1
42. Rao SC, Athalye-Jape GK, Deshpande GC, Simmer KN, Patole SK. Probiotic Supplementation and Late-Onset Sepsis in Preterm Infants: A Meta-analysis. Pediatrics. 2016;137(3). doi:10.1542/PEDS.2015-3684
43. Kullar R, Goldstein EJC, Johnson S, McFarland L V. Lactobacillus Bacteremia and Probiotics: A Review. Microorganisms. 2023;11(4):896. doi:10.3390/MICROORGANISMS11040896
44. DąbrowskaA,SłotwińskiR,KędzioraS.Probiotics–panaceaorplacebo?Gastroenterology Review/Przegląd Gastroenterologiczny. 2010;5(6):321-328. doi:10.5114/PG.2010.18475
45. Hou X, Yang J, Zhao Z, Liu L. A meta-analysis of the effects of probiotics on acute pancreatitis. Asian J Surg. 2023;46(9):3885-3889. doi:10.1016/J.ASJSUR.2023.03.153
46. Nista EC, Parello S, Brigida M, et al. Exploring the Role of Gut Microbiota and Probiotics in Acute Pancreatitis: A Comprehensive Review. Int J Mol Sci. 2025;26(7). doi:10.3390/IJMS26073433
47. Werawatganon D, Vivatvakin S, Somanawat K, et al. Effects of probiotics on pancreatic inflammation and intestinal integrity in mice with acute pancreatitis. BMC Complement Med Ther. 2023;23(1). doi:10.1186/S12906-023-03998-7
48. Besselink MG, van Santvoort HC, Buskens E, et al. Probiotic prophylaxis in predicted severe acute pancreatitis: a randomised, double-blind, placebo-controlled trial. Lancet. 2008;371(9613):651-659. doi:10.1016/S0140-6736(08)60207-X
49. Mortezazadeh M, Kalantari S, Abolghasemi N, et al. The effect of oral probiotics on CD4 count in patients with HIV infection undergoing treatment with ART who have had an immunological failure. Immun Inflamm Dis. 2023;11(6). doi:10.1002/IID3.913
50. Zhong C, Qu C, Wang B, Liang S, Zeng B. Probiotics for Preventing and Treating Small Intestinal Bacterial Overgrowth: A Meta-Analysis and Systematic Review of Current Evidence. J Clin Gastroenterol. 2017;51(4):300-311. doi:10.1097/MCG.0000000000000814
51. Rosania R, Giorgio F, Principi M, et al. Effect of probiotic or prebiotic supplementation on antibiotic therapy in the small intestinal bacterial overgrowth: a comparative evaluation. Curr Clin Pharmacol. 2013;8(2):169-172. doi:10.2174/15748847113089990048
52. Rao SSC, Rehman A, Yu S, De Andino NM. Brain fogginess, gas and bloating: a link between SIBO, probiotics and metabolic acidosis. Clin Transl Gastroenterol. 2018;9(6). doi:10.1038/S41424-018-0030-7
53. Merenstein D, Pot B, Leyer G, et al. Emerging issues in probiotic safety: 2023 perspectives. Gut Microbes. 2023;15(1):2185034. doi:10.1080/19490976.2023.2185034
54. Merenstein DJ, Tancredi DJ, Karl JP, et al. Is There Evidence to Support Probiotic Use for Healthy People? Advances in Nutrition. 2024;15(8):100265. doi:10.1016/J.ADVNUT.2024.100265

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