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Review

Probiotics in Gastrointestinal Health: Current Status and Future Applications

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Abstract

Probiotics are defined as live microorganisms that confer health benefits to the host when administered in adequate amounts and have gained increasing attention for their role in gastrointestinal health. The gut microbiota plays a critical role in pathogen resistance, maintenance of intestinal epithelial integrity, metabolism of dietary and pharmaceutical compounds, regulation of immune responses, and modulation of the gut-brain axis. Disruption of this microbial balance, termed dysbiosis, has been implicated in the pathogenesis of various gastrointestinal health disorders. Probiotics exert strain-specific effects through multiple mechanisms, including competition with pathogens for nutrients and adhesion sites, production of antimicrobial substances, enhancement of gut barrier function via stimulation of mucus secretion and tight junction proteins, and modulation of innate and adaptive immune responses. Clinical evidence suggests potential therapeutic and preventive roles for selected probiotic strains in several gastrointestinal conditions; however, findings remain heterogeneous. In irritable bowel syndrome, strains such as *Bifidobacterium infantis* and *Lactobacillus plantarum* 299v have demonstrated modest improvements in abdominal pain, bloating, and global symptoms, though results are inconsistent across studies. In inflammatory bowel disease, certain *Bifidobacterium*-containing formulations show benefit in ulcerative colitis, while evidence for Crohn's disease remains limited. Meta-analyses indicate that probiotics can reduce the incidence of antibiotic-associated diarrhoea and *Clostridioides difficile* infection, with efficacy varying by strain and formulation. Probiotics may also support *Helicobacter pylori* eradication and reduce treatment-related adverse effects. In neonates, specific multi-strain products have been associated with reduced necrotizing enterocolitis. Overall, probiotic benefits are strain-dependent, product-specific, and generally modest. Further well-designed, strain-level clinical trials are required to establish standardized dosing, long-term safety, and definitive clinical utility.

Keywords

Probiotics, Gut microbiota, Dysbiosis, Irritable bowel syndrome, Inflammatory bowel disease, Antibiotic-associated diarrhoea, *Clostridioides difficile* infection, *Helicobacter pylori*, Necrotizing enterocolitis, Gastrointestinal health

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1. Introduction

The word "probiotic" was first used in 1965 by Lilly and Stillwell to describe substances made by one organism that help another one grow. Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer specific health benefits by modulating the host's microbial ecology, particularly within the gastrointestinal tract. These include well-characterized yeasts such as *Saccharomyces boulardii* (*S. boulardii*) and bacterial genera such as *Lactobacillus* and *Bifidobacterium*, whose effects are strain-dependent and linked to targeted physiological or immunomodulatory mechanisms. According to World Health Organization (WHO), and Food and Agriculture Organization, probiotics are "live microorganisms which when administered in adequate amounts confer a health benefit on the host" [1]. Recent global guidance has expanded the definition to include engineered live biotherapeutic strains used for targeted gastrointestinal modulation [2].

The human gastrointestinal tract harbours a diverse and complex community of microorganisms collectively referred to as the gut microbiota, which plays a critical role in maintaining physiological homeostasis and influencing health and disease state. Many factors affect these gut microbes, especially early influences, which can significantly impact them, particularly during early life. One of the biggest factors is diet**,** which continues to shape the gut bacteria as we grow. These bacteria help keep the immune system strong**,** control how the body uses energy**,** and fight off harmful germs**.** However, disruption of the normal microbial equilibrium–referred to as dysbiosis–has been associated with a wide range of pathological conditions and infectious diseases. Recent large-scale multi-omic analyses have confirmed that diet-microbiota-immune system interactions are central determinants of gastrointestinal health, with integrative profiling approaches uncovering functional links between dietary intake, microbial community structure, metabolite production, and host immune responses [3].

The human gastrointestinal tract represents one of the largest interfaces (250-400 m^2) between the host, environmental factors and antigens in the human body. In an average lifetime, tonnes of food pass through the human gastrointestinal tract, along with an abundance of microorganisms from the environment, which impose a huge threat on gut integrity [4].

The collection of bacteria, archaea and eukarya colonising the gastrointestinal tract is termed the 'gut microbiota' and has co-evolved with the host over thousands of years to form an intricate and mutually beneficial relationship [5,6]. Advances in next-generation sequencing, metagenomics, meta-transcriptomics, and other multi-omics approaches have greatly expanded our ability to characterize these communiti-es and understand their functional roles. A 2025 bioinformatics update demonstrated that integrating metagenomics with metabolomics improves the prediction of probiotic response [7].

Recent bioinformatics advances show that integrating metagenomic and metabolomic data enhances the prediction of host functional responses to microbiome perturbations and therapeutic interventions, laying a foundation for future models that may predict probiotic responsiveness. Aya et al. demonstrated this in energy metabolism, and Chen et al. applied it to disease-associated microbiome profiling [7].

The number of microorganisms inhabiting the gastrointestinal tract has been estimated to exceed 10^{14}, which encompasses 10 times more bacterial cells than the number of human cells and over 100 times the amount of genomic content (microbiome) as the human genome [8]. However, more recent analyses estimate the ratio of microbial to human cells to be closer to 1:1**,** indicating that earlier figures may have been overstated while still underscoring the substantial genomic and metabolic capacity of the gut microbiome.

The gut microbiota contributes to host health through multiple physiological functions, including maintenance of epithelial integrity, modulation of energy harvest, protection against pathogenic microorganisms, and regulation of mucosal and systemic immunity. While these activities are generally beneficial, alterations in microbial composition–referred to as dysbiosis–may also give rise to detrimental interactions, such as impaired barrier function, aberrant immune activation, or enhanced colonization by opportunistic pathogens. With the advent of increasingly sophisticated tools to profile and characterize complex microbial ecosystems, the involvement of the microbiota in a wide spectrum of intestinal and extra-intestinal disorders has become progressively evident.

Therapeutic interventions such as antibiotics, immunosuppressive agents, and radiation therapy can disrupt the composition and functional stability of the gut microbiota. Consequently, the administration of specific probiotic strains has been explored as a strategy to support microbial restoration and reduce the risk of treatment-associated complications. Because of this, adding probiotics might help bring back balance and prevent sickness. A prebiotic is a type of food ingredient that feeds the beneficial gut microbiota, especially in the colon, and helps them grow, which is good for your health.

Probiotics have demonstrated potential clinical benefit in specific conditions such as acute infectious diarrhoea (particularly rotavirus-associated cases) and pouchitis, although evidence remains variable and strain-dependent. In general, probiotics are safe and easy to take, though they can sometimes cause bloating or gas. However, the benefits of one type of probiotic may not be the same as another. More research is still needed to see how well probiotics work for other issues, like antibiotic-related diarrhoea**,** infections like *Clostridium Difficile*, traveller's diarrhoea**,** irritable bowel syndrome (IBS), and diseases like ulcerative colitis and Crohn's disease.

Proposed mechanisms of probiotic action include strain-specific modulation of luminal pH, competitive interactions that may limit the expansion of pathogenic microorganisms, and regulation of host immune responses; however, these effects vary among strains and do not necessarily require–or result in–stable colonization of the gut. It is unclear exactly how many probiotics are needed to be effective, but they typically need to contain billions of bacteria for the best chance of colonising the gut. Probiotics should be used carefully in critically ill patients, those with weakened immune systems, or people with certain medical devices, as they can rarely cause infections. It is important to take probiotics at least two hours after antibiotics.

Probiotics can help with many conditions, including infant diarrhoea, intestinal infections, antibiotic-related diarrhoea, and inflammatory bowel disease. *Lactobacillus rhamnosus* (*L. rhamnosus*) strain GG, for example, is beneficial for gut immunity, as it helps the body produce more protective immune cells and enhances the immune response in the intestines.

Because probiotics consist of live microorganisms, their use carries a small but clinically relevant risk of adverse events, including bacteremia, sepsis, or fungemia–particularly in immunocompromised individuals, critically ill patients, or those with indwelling medical devices. The potential risk of infection should be balanced with the benefits they offer in preventing or treating diseases. More well-designed studies are needed to fully understand the health benefits of probiotics. Selecting an appropriate probiotic requires consideration of strain specificity, clinically supported dosing, and documented therapeutic effects; however, this process is complicated by the lack of standardization, variable potency, and inconsistent quality control across many commercially available products.

2. Mechanism of Action of Probiotics

(1) Certain probiotic strains may contribute to competitive exclusion by occupying ecological niches and utilizing available nutrients within the gut, thereby limiting the expansion of pathogenic microorganisms; however, this effect is not universal across all strains.

(2) Some probiotic strains produce antimicrobial metabolites–such as organic acids, hydrogen peroxide, or bacteriocins–that can inhibit the growth of pathogenic microorganisms, although these effects are highly strain-specific.

(3) Specific probiotic strains can synthesize antimicrobial metabolites, including organic acids, hydrogen peroxide, and bacteriocins, which inhibit the proliferation of pathogenic microorganisms; however, these biochemical activities are strain-dependent and not uniformly exhibited across all probiotics.

(4) Probiotics protect the gut lining by making more mucus and strengthening the gut wall, stopping harmful germs from entering the blood.

(5) Certain probiotic strains can modulate host immunity through mechanisms such as promoting dendritic cell maturation, influencing Toll-like receptor signaling pathways, and altering macrophage activity, although these immunological effects are highly strain-dependent.

(6) Certain probiotic strains can modulate immune function by influencing cytokine profiles–such as enhancing IL-10 production–or by promoting regulatory T-cell (Treg) induction, thereby contributing to the regulation of both innate and adaptive immune responses; however, these immunomodulatory effects are not shared by all strains.

3. Evidence-Based Applications in gastrointestinal Disorders

3.1 Irritable Bowel Syndrome

Irritable bowel syndrome is a gastrointestinal disorder characterized by altered bowel habits in association with abdominal discomfort or pain in the absence of detectable structural and biochemical abnormalities [9]. According to the Rome IV diagnostic criteria, symptoms must occur at least one day per week over the past three months and be related to defecation or changes in stool frequency or form. IBS is further classified into subtypes based on predominant stool pattern: IBS with constipation (IBS-C), IBS with diarrhoea (IBS-D), mixed IBS (IBS-M), and unclassified IBS (IBS-U).

According to published guidelines, the main treatment options for abdominal pain include anti-spasmodics or anti-depressants at low dose, while anti-diarrheal or laxative drugs are given to improve transit disturbance [10]. Despite the availability of multiple therapeutic modalities, achieving adequate symptom control–particularly for abdominal pain–in patients with IBS remains challenging, with many individuals demonstrating only partial or inconsistent treatment responses. This is likely because IBS isn't caused by just one thing; many different factors can be at play, such as: Multiple pathophysiological mechanisms have been proposed to contribute to IBS, although the strength of evidence supporting each varies. These include alterations in gastrointestinal motility, heightened visceral hypersensitivity, and dysregulation of the brain-gut axis signaling. Additional hypotheses involve diet-related triggers and food intolerances, increased intestinal permeability, and post-infectious or post-inflammatory changes that may precipitate symptom onset in a subset of patients.

Recently, scientists have highlighted dysbiosis, when IBS symptoms start. Because of this, there is a good reason to talk about using probiotics as a treatment. When you take enough of them, they can offer health benefits. In fact, new research is showing that some specific probiotic strains can indeed help improve IBS symptoms. A meta-analysis on the efficacy of *Bifidobacterium infantis* (*B. infantis*) 35624 in patients with IBS was conducted in 2017 [11].

The meta-analysis by Yuan et al. evaluated five randomized controlled trials assessing *B. infantis* 35624, either as a single strain or within composite probiotic formulations, for the management of IBS. However, the overall evidence base was limited by small sample sizes and substantial methodological heterogeneity.

Trials differed in probiotic composition, dosage, treatment duration, symptom assessment scales, and diagnostic criteria, complicating direct comparison and reducing the reliability of pooled estimates. Notably, only composite probiotic formulations demonstrated modest improvements in abdominal pain and bloating, whereas the efficacy of the single-strain *B. infantis* 35624 remained unconfirmed. Additional limitations included potential publication bias, short follow-up periods, and inconsistent reporting of adverse events. Collectively, these issues highlight the need for larger, well-powered, and methodologically harmonized clinical trials to determine the true therapeutic value, strain specificity, and safety profile of *B. infantis* 35624 in IBS. The standardized mean difference method was used to combine data since scales to measure the efficacy of probiotics were different among studies

On analysis, it was found that, when *B. infantis* was used alone, it did not clearly help with belly pain, bloating, or bowel habits in people with IBS. When *B. infantis* was part of a probiotic, patients had less belly pain and less bloating. The improvement was great and reliable based on the numbers. Even after adding one more study (making it six total) to check for bloating, the bloating still showed clear improvement. It seems that probiotic mixes that contain *B. infantis* might be an option for IBS patients. These mixes could significantly help reduce IBS symptoms like pain and bloating, and they do not seem to cause serious side effects. However, the study could not confirm that *B. infantis* by itself is effective for IBS. As evidence are limited, more large-scale, well-designed studies are needed to prove if *B. infantis* alone really helps.

A clinical trial was done in 2012 to assess the symptomatic efficacy of *Lactobacillus plantarum* 299v (DSM 9843) for the relief of abdominal symptoms in a large subset of IBS patients [12]. In this double blind, placebo-controlled, parallel-designed study, subjects were randomized to receive either one capsule of *Lactobacillus plantarum* 299v (DSM 9843) or a placebo for 4 weeks. Frequency and intensity of abdominal pain, bloating and feeling of incomplete rectal emptying were assessed weekly on a visual analogue scale, while stool frequency was calculated. However, the trial had several important limitations, including its short duration**,** reliance on subjective self-reported symptom scores, and enrolment of a single patient population, which may limit the generalizability and long-term interpretability of its findings. This study included 214 patients with IBS. After just 4 weeks, those who took a specific probiotic called *Lactobacillus plantarum* 299v (also known as DSM 9843) experienced noticeable improvements compared to those who took a placebo: Abdominal pain: They had less severe pain and fewer days with pain. Bloating: They also had similar improvements in bloating.

In fact, at the end of the 4 weeks, a large majority (78.1%) of patients taking the probiotic rated its effect on their symptoms as "excellent" or "good," while only a very small number (8.1%) of those taking the placebo felt the same way. This difference was very significant. However, this outcome reflects a subjective patient-reported satisfaction measure, which, while valuable for understanding perceived benefit, does not necessarily equate to objective clinical improvement and should be interpreted alongside more rigorous symptom and physiological endpoints. This study suggests that taking *Lactobacillus plantarum* 299v (DSM 9843) for 4 weeks is an effective way to relieve common IBS symptoms, especially abdominal pain, and bloating.

3.2 Inflammatory Bowel Disease

Crohn’s disease and ulcerative colitis are chronic inflammatory disorders of the gastrointestinal tract that arise from a complex interplay of immune dysregulation, genetic susceptibility, and environmental factors. Alterations in the gut microbiome are strongly associated with these conditions and are thought to contribute to disease initiation and progression, although they represent only one component of a multifactorial pathogenic process. The gut microbiome partly determines the pathogenesis of both diseases. This research was performed according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [13]. The final analysis included 33 studies from 14 countries, encompassing 2,713 adult participants, to evaluate the effects of probiotics compared with placebo or no treatment in inflammatory bowel diseases. However, interpretation of the findings is limited by substantial heterogeneity across studies, including variation in probiotic strains and combinations, differences in dosing regimens and treatment durations, and inconsistent outcome measures, all of which reduce the comparability and strength of the overall conclusions.

3.2.1 Crohn's Disease

Out of eleven studies on Crohn’s disease, only four reported significant improvements in remission outcomes. However, these findings should be interpreted with caution, as the results were influenced by substantial heterogeneity in probiotic strains, definitions of remission, and overall study design. Although some of the positive studies involved interventions

lasting three to six months, the current evidence does not support a clear duration-response relationship, and the benefits remain inconsistent across trials.

3.2.2 Ulcerative Colitis

In contrast, evidence for ulcerative colitis is comparatively more favourable. In 21 out of 25 studies, probiotics demonstrated some benefit in achieving or maintaining remission, though the magnitude of effect varied notably by formulation. Certain multispecies products–such as high-potency combinations like VSL#3–tended to show stronger and more consistent outcomes than single-strain preparations. While Bifidobacterium species have been beneficial in some trials, other strains and multispecies formulations have also contributed to these effects, underscoring the strain-specific nature of probiotic efficacy. Overall, the evidence supporting probiotic use in ulcerative colitis is moderate, not definitive, and effectiveness depends heavily on the specific product used. For Crohn's disease, findings remain inconsistent, with many studies showing minimal or no benefit, and current clinical guidelines do not recommend routine probiotic use for its management.

3.3 Antibiotic-associated Diarrhoea and *Clostridium Difficile*

Clostridioides difficile is a bacterium that affects the gastrointestinal tract and is a major–but not the sole–cause of antibiotic-associated diarrhoea (AAD). *Clostridium difficile* is a Gram-positive, spore, and toxin-forming bacterium that can affect the gastrointestinal tract [14]. Antibiotics lead to the loss of gut microbial communities that normally prevent colonization, creating conditions that allow the *Clostridioides difficile* bacterium to germinate and proliferate–particularly in the colon–where it produces its major toxins, TcdA and TcdB. The risk is especially elevated with certain antibiotic classes, including clindamycin, cephalosporins, and fluoroquinolones, and is most pronounced in defined high-risk groups such as older adults, hospitalized patients, and those with immunosuppression or recent broad-spectrum antibiotic use. Table 1 shows the various studies that involve a review of antibiotic-associated diarrhoea and *Clostridium Difficile.*

Table 1. Analysis of various studies that involve a review of antibiotic-associated diarrhoea and *Clostridium Difficile.*

Study Design	Population	Key Findings	Ref.
Systematic review (31 RCTs)	8,672 adults & children receiving antibiotics	Probiotics significantly reduced CDAD; evidence graded as moderate certainty.	[15]
Systematic review & meta-analysis (26 RCTs)	7,957 antibiotic-treated patients	Probiotics lowered CDAD risk by 60.5%; the greatest benefit was in hospitalized patients.	[16]
Systematic review & meta-analysis (16 RCTs)	Adult inpatients (mean age 33-79.9 yrs)	Reduced AAD risk (RR 0.61; 95% CI 0.47-0.79) and CDI (RR 0.37; 95% CI 0.23-0.61).	[17]
Narrative review	Not reported	Probiotics provide a modest reduction in CDI risk among high-risk antibiotic users.	[18]
Systematic review with meta-regression (19 RCTs)	14,933 patients	Probiotics reduced CDI incidence; strongest effect in high-risk groups.	[19]
Randomized controlled trial	32 ICU patients	Enteral probiotic drinks were safe and may prevent AAD/CDI.	[20]
Meta-analysis (25 RCTs)	4,476 pediatric & adult patients	Certain probiotic strains are effective for primary CDI prevention; only two strains are effective for secondary prevention.	[21]
Large randomized controlled trial	2,981 inpatients ≥65 years	No benefit of a multistrain probiotic for the prevention of AAD or CDI.	[22]
Meta-analysis & review	Adults with spinal cord injury	Probiotics suppressed pathogenic bacteria through bacteriocin production.	[23]
Review	Not reported	*S. boulardii* reduces pathogen adhesion and modulates inflammatory pathways.	[24]
Experimental preclinical study	Animal and *in vitro* models	*Lactobacillus acidophilus* inhibited *Clostridium Difficile*, downregulated virulence genes, and prevented disease in murine models.	[25]
Review (Non-probiotic: FMT)	Not reported	Faecal microbiota transplantation (FMT) prevents CDI recurrence via bile acid modulation.	[26]
Review (non-probiotic: microbial metabolites)	Not reported	Butyrate reduces intestinal inflammation and enhances immune homeostasis.	[27]

Notes: "Not reported" indicates review studies that did not specify sample size or demographic details. Preclinical studies include *in vitro* and animal experiments. Non-probiotic interventions (FMT, microbial metabolites) are included for mechanistic comparison only. RCTs, randomized controlled trials; CDAD, *Clostridium difficile*-associated diarrhoea; AAD, antibiotic-associated diarrhoea; CDD, *Clostridium Difficile* diarrhoea. CDI, *Clostridium difficile* infection. CD, *Clostridium difficile*.

3.4 *Helicobacter Pylori* Infection

Helicobacter pylori (*H. pylori*) is a type of bacteria that is a main cause of several serious stomach problems, including Peptic ulcers, Gastric adenocarcinoma, a rare type of lymphoma (MALT lymphoma) that affects the stomach and it is also classified as a WHO Group 1 carcinogen. *H. pylori* can establish chronic gastric infection through several well-characterised mechanisms. It produces urease, which breaks down urea into ammonia and carbon dioxide, creating a locally alkaline environment that protects the organism from stomach acid. Its helical shape and flagellar motility enable it to penetrate the gastric mucus layer and reach the epithelium, where the pH is more favourable. Additionally, *H. pylori* employ multiple immune-evasion strategies–including altering surface antigens, modulating host immune signaling, and interfering with antigen presentation–which allow it to persist for years within the host. The triple therapy for *H. pylori* treatment involves taking two antibiotics and a proton pump inhibitor for 7 to 14 days. However, this treatment is failing more often. The main reason for this is that the bacteria are becoming resistant to the commonly used antibiotics, making them harder to kill. Table 2 demonstrates the potential influence of probiotics as adjuncts to standard therapy on *H. pylori* eradication rate and also the pediatric trial undertaken for *H. pylori* eradication.

Table 2. Analysis of several studies that examined the potential influence of probiotics as adjuncts to standard therapy on *H. pylori* eradication rate.

Regimen (Duration)	Probiotic (Strain / Dose / Duration)	Sample Size	Eradication Rate (Control → Probiotic)	Adverse Effects	Ref.
Adult Clinical Trial					
PPI + AC (14 days)	*S. boulardii* CNCM I-745 (14 days)	124 adults	~71% → ~84%	Significant reduction (mainly diarrhoea)	[28]
PPI + CT (7 days)	*S. boulardii* CNCM I-745 (14 days)	43 adults	No major change	Reduced gastrointestinal side effects	[29]
PPI + AC (14 days)	*S. boulardii* (14 days)	389 adults	Not reported	Lower incidence of side effects	[30]
PPI + AC (10 days)	*S. boulardii* (28 days)	90 adults	Improvement vs control	Fewer gastrointestinal events	[31]
PPI + AC (14 days)	*S. boulardii* (14 days)	160 adults	Slight improvement	Reduced side effects	[32]
PPI + AC (7 days)	*S. boulardii* (28 days)	661 adults	Small improvement	Reduced diarrhoea/nausea	[33]
PPI + AC (7 days)	*L. acidophilus* (7 days)	120 adults	~70% → ~87%	Not reported	[34]
PPI + CT (7 days)	*L. rhamnosus* GG (14 days)	60 adults	No major improvement	Symptom reduction	[35]
PPI + AC (7 days)	*L. rhamnosus* GG (14 days)	83 adults	Minimal or no change	Fewer side effects	[36]
PPI + CT (7 days)	*L. rhamnosus* GG (14 days)	85 adults	Modest improvement	Better tolerability	[37]
PPI + AL (14 days)	*L. reuteri* DSM 17938 (14 days)	90 adults	No improvement	Symptom relief	[38]
PPI + ACT (10 days)	*L. reuteri* DSM 17938 (20 days)	42 adults	Minimal difference	Fewer gastrointestinal symptoms	[39]
PPI + AC (14 days)	*L. reuteri* DSM 17938 (28 days)	70 adults	No major difference	Reduced side effects	[40]
PPI + AC (7 days)	*B. animalis* + *L. casei* (35 days)	160 adults	Slight improvement	Lower gastrointestinal complication rate	[41]
PPI + AC (7 days)	*B. animalis* + *L. casei* (90 days)	65 adults	No meaningful difference	Not reported	[42]
PPI + AC (7 days)	*L. gasseri* OLL2716 (28 days)	229 adults	~75-85%	Fewer treatment-related symptoms	[43]
PPI + AC (7 days)	*B. clausii* (14 days)	120 adults	Minor change	Significant reduction in diarrhoea	[44]
Paediatric Clinical Trials					
PPI + AC (7 days)	*L. casei* DN-114001 (14 days)	86 children	~57% → ~85%	Significant reduction in side effects	[45]
PPI-based therapy	*L. reuteri* (multiple strains) (60 days)	100 children	Not significantly changed	Reduced abdominal	[46]

Note: Statistically significant ($P < 0.05$). -, Data are not available; PPI, Proton pump inhibitor; UBT, Urea breath test; Hist., Histology; RUT, Rapid urease test; A, Amoxicillin; C, Clarithromycin; T, Tinidazole; L, Levofloxacin.

Key findings: (1) Eradication success. Most probiotics do *not* significantly increase *H. pylori* eradication rates. A few specific strains showed modest improvements: *S. boulardii* CNCM I-745, *L. acidophilus*, *L. gasseri* OLL2716, *L. casei* DN-114001 (in children). (2) Consistent benefit across studies. The strongest and most reproducible effect is→

Probiotics reduce antibiotic-related side effects (especially diarrhoea, nausea, bloating). (3) Heterogeneity. Wide variation in strains, doses, durations, regimens, and patient types. Some early tables in literature contain inconsistent or misreported eradication rates, which were corrected/standardized here. (4) Adults vs paediatric outcomes. Paediatric efficacy appears slightly stronger for eradication improvement. In adults, probiotics mainly improve tolerability, not eradication.

Conclusion of this study- Having *H. pylori* bacteria in your stomach for a long time can lead to significant clinical concern like ulcers, a type of stomach cancer, and a specific kind of lymphoma. Because of these risks, getting rid of *H. pylori* is a main goal for people who have symptoms.

However, the triple therapy, which is a combination of a proton pump inhibitor and two antibiotics, often does not work as well as it used to. The success rates are often low, ranging from about 60% to 80%.

There are two main reasons for this: (1) Antibiotic resistance. The *H. pylori* bacteria have become resistant to the antibiotics used, meaning the medicines cannot kill them effectively anymore. (2) Difficulty sticking to treatment. Many people struggle to complete the full course of antibiotics, mainly because of unpleasant stomach side effects like nausea, diarrhoea, or stomach pain.

Because of these challenges, probiotics are now being suggested as a helpful addition to the standard treatment. The idea is that adding probiotics could improve the chances of getting rid of *H. pylori* and reduce those side effects, making it easier for patients to complete their treatment.

3.5 Necrotizing Enterocolitis in Neonates

Necrotizing enterocolitis (NEC) is a devastating and destructive syndrome of intestinal necrosis primarily affecting the immature intestine of newborns–particularly preterm and low birth weight infants [47].

Diagnosing NEC right now is difficult because there is no one clear test. Instead, clinicians rely on a combination of clinical and radiologic findings in preterm infants, including:
Feeding intolerance or sudden difficulty tolerating enteral feeds, Abdominal distentions, Hematochezia (bloodstools)**,** Systemic signs of infection or sepsis, such as abnormalities in heart rate, respiratory rate, temperature regulation, and blood pressure, Radiologic markers; most notably pneumatosis intestinalis**,** with possible portal venous gas or pneumoperitoneum in advanced cases. These features are typically evaluated within the framework of Bell's staging classification, which helps determine disease severity and guide clinical management.

How probiotics may help prevent NEC: Preclinical studies in cell culture and animal models indicate that specific probiotic strains may modulate inflammatory pathways and enhance barrier function in the immature intestine. While these findings provide mechanistic insight into how probiotics could potentially reduce the risk of NEC, results from animal models do not directly predict clinical efficacy in human neonates.

Here are some of the ways probiotics can act in the gut: (1) They may modulate key molecular pathways–such as suppressing TLR4 signaling**,** downregulating NF-κB activation, and reducing pro-inflammatory mediators like IL-6–thereby supporting intestinal epithelial health. (2) They may indirectly enhance short-chain fatty acid production–such as acetate and propionate–by supporting beneficial microbial communities, which in turn help maintain epithelial integrity and inhibit pathogen overgrowth; however, most probiotic strains evaluated in NEC do not produce butyrate themselves. (3) Enhance intestinal barrier function by promoting tight-junction integrity and reducing epithelial permeability. (4) Inhibit pathogenic colonization through competitive exclusion and modulation of the local microbial ecosystem. (5) Regulate mucosal immune responses by promoting balanced cytokine signaling and limiting excessive inflammatory activation.

4. Limitations and Challenges

4.1 Strain Specificity and Variation in Efficacy

A major challenge in probiotic research is that strain-level differences–including variations in genome content, metabolic capacity, and surface proteins–can lead to markedly different biological effects even within the same species. For example, while *L. rhamnosus* GG is well studied and shows benefit in reducing AAD, other *L. rhamnosus* strains may exhibit different or more limited efficacy, depending on their adhesion properties, immune-modulatory profiles, and metabolite production. Similar distinctions are seen in other species, such as *Bifidobacterium longum* versus *B. longum* subsp. *infantis*, or among strains within *Lactobacillus plantarum*, each displaying unique functional attributes. These strain-specific characteristics influence not only therapeutic potential but also safety profiles**,** including risks of bacteremia or translocation in vulnerable neonatal or immunocompromised populations.

4.2 Survival Through the Gastrointestinal Tract

For many live probiotic formulations, achieving their intended effects–such as modulating immune responses, influencing microbial ecology, or enhancing barrier function–requires surviving gastric acidity and exposure to bile

salts and digestive enzymes to reach the lower gastrointestinal tract in sufficient numbers. However, survival rates vary widely across commercial products, and many preparations deliver suboptimal levels of viable organisms by the time they reach their target site.

At the same time, it is important to note that survival is not universally required: emerging categories such as postbiotics (non-viable microbial metabolites) and paraprobiotics (inactivated microbial cells or components) can exert beneficial effects without the need for colonization or viability.

Advances in delivery systems–including microencapsulation, enteric-coated capsules, lipid-based carriers, and polymeric protective matrices–have improved viability during transit, but the effectiveness of these technologies remains highly product-specific.

4.3 Regulatory and Labeling Issues

Regulation of probiotics varies substantially across regions. In many countries, most probiotic products are classified as dietary supplements rather than therapeutic agents**,** which subjects them to less rigorous requirements for demonstrating safety, efficacy, and quality. For example, in the United States, probiotics sold as dietary supplements fall under the FDA's DSHEA framework, which does not require pre-market clinical evidence. In the European Union, probiotics intended for therapeutic use must meet the stricter standards applied to medicinal products, whereas food or supplement formulations are regulated under food-safety laws and cannot make medical claims without robust evidence. In parts of Asia, such as Japan and South Korea, certain probiotics may be approved as Foods for Specified Health Uses or similar health-claim categories, which involve regulatory pathways distinct from both supplements and pharmaceuticals. These differences highlight the need to distinguish clearly between probiotics marketed as general wellness supplements and those evaluated as therapeutic biological products.

4.4 Lack of Standardization in Probiotic Trials

Another significant limitation is the extensive heterogeneity across clinical trials evaluating probiotics. Studies offer differences in Strain and strain-combination selection**,** each with distinct mechanistic properties. Dosage and viable cell count (CFU) administered. Duration of treatment and timing relative to disease activity. Study populations**,** including age, baseline microbiota composition, comorbidities, and disease severity. Outcome measures**,** which vary widely–from symptom scores and quality-of-life indices to biochemical markers, stool microbiome profiles, and endoscopic or histologic endpoints–making cross-study comparisons difficult and limiting the ability to draw firm, generalizable conclusions. This lack of standardization makes it difficult to compare results or draw meaningful conclusions across studies. Furthermore, many trials are underpowered, poorly controlled, or industry-funded, raising concerns about bias and reproducibility.

Although probiotics are being explored for diverse health applications, their clinical utility remains limited by several substantial challenges. Strain-specific variability, uncertain survival and activity within the gastrointestinal environment, inconsistent regulatory oversight, inaccurate or misleading product labeling, and highly heterogeneous clinical trial methodologies all contribute to the lack of clear, reliable evidence. Moving forward, meaningful progress will require comprehensive strain-level genomic characterization**,** standardized methods for verifying viability and functional activity, and harmonized clinical trial frameworks with uniform endpoints and rigorous controls. Strengthened regulatory pathways and improved product quality assurance will also be essential for critically evaluating–and more accurately defining–the true therapeutic potential of probiotic interventions.

5. Future Applications and Innovations

5.1 Genetically Engineered Probiotics

Microbiome research–the study of the diverse microbial communities inhabiting the human body–has substantially advanced our understanding of host physiology and disease. By revealing how microbial metabolites, immune interactions, and ecological imbalances contribute to various health conditions, this field has opened new avenues for therapeutic development, including probiotics, postbiotics, and microbiome-targeted interventions.

The effectiveness of probiotics can vary considerably across individuals and disease states due to differences in dietary patterns, host genotype, baseline microbiome composition, medication exposures**,** and underlying immune status. These sources of interindividual variability make it difficult to identify universally effective strains for targeted therapeutic use.

Similarly, current probiotics might not survive the harsh conditions of the gastrointestinal tract, limiting their effectiveness [48]. This limitation is less relevant for engineered strains with enhanced stress tolerance and for postbiotics, which do not require microbial viability to exert their effects.

Advancing beyond the limitations of conventional probiotics will require the development of Next-Generation Probiotics microbial candidates with well-defined mechanisms and disease-specific functions. Prominent examples under investigation include Akkermansia muciniphila, associated with improved metabolic and barrier function, and Faecalibacterium prausnitzii, known for its anti-inflammatory activity and butyrate production. These Next generation

probiotics aim to provide targeted therapeutic effects, interact more precisely with an individual's existing gut microbiota, and exhibit enhanced biological resilience–such as tolerance to bile salts, resistance to oxidative stress, and improved mucosal adhesion–to ensure functional activity within the gastrointestinal tract.

Scientists are also looking at ways to improve probiotics by: Genetically engineering microbial strains: This entails intentionally modifying naturally occurring microorganisms to enhance specific, well-characterised functional properties–such as metabolite production or immune modulation–while incorporating safeguards to minimise risks related to horizontal gene transfer, unintended ecological effects, and biocontainment.

Applying synthetic biology approaches: This involves constructing new biological systems or redesigning existing microbial chassis to perform defined therapeutic functions. Engineered strains must meet emerging regulatory standards for live biotherapeutic products, including stringent assessments of genomic stability, environmental safety, and controlled biological activity.

Synthetic biology enables the design of microbial cells with defined therapeutic functions, allowing engineered strains to target and operate within specific anatomical sites that are often inaccessible to conventional pharmacological agents. In addition, there are fewer side effects because smaller amounts of therapeutic molecules are delivered through engineered microbes in situ, which show similar efficacy as orally administered doses [49].

5.2 Synthetic Biology to Deliver Therapeutic Molecules

In the traditional delivery methods, the therapeutic molecules are easily degraded in the host system, such as the acidic stomach [50]. In addition, engineered microbes do not go through the endocytosis process due to the oral tolerance in the gut, which is an immune repression against the antigens administered orally [51]. These concepts, however, are based largely on preclinical models, and their stability, safety, and efficacy in humans remain to be fully validated.

Importantly, many of these engineered strains function as therapeutic chassis–microbial platforms that are genetically modified to synthesise and deliver specific bioactive molecules while minimizing host immune activation. Strains such as *Bacteroides thetaiotaomicron* and *Lactococcus lactis*, which are naturally associated with the human gut, are being explored because their commensal origin reduces the likelihood of eliciting strong immune responses and allows them to exploit mechanisms such as oral tolerance. This makes them promising candidates for oral delivery of therapeutic payloads, though their clinical translation is still under investigation.

Some examples are: Keratinocyte growth factor-2 is a human epithelial growth factor with therapeutic potential in inflammatory bowel diseases, but its rapid degradation *in vivo* limits clinical usefulness. To address this, researchers have engineered *Bacteroides fragilis* as a therapeutic chassis capable of producing and delivering Keratinocyte growth factor-2 directly within the gut. In this system, the modified bacterium is designed to synthesize Keratinocyte growth factor-2 in response to xylan, a dietary fiber, and to secrete it using a native *B. fragilis* secretion signal. While this strategy enables spatially targeted delivery of Keratinocyte growth factor-2, it also introduces important considerations–namely, the diet-dependent activation of the inducible promoter and the potential variability in gene expression based on fiber intake, as well as broader concerns surrounding the stability, reliability, and safety of inducible expression systems in complex and fluctuating gut environments.

When xylan was orally administered in DSS-induced mice models, improvements in colitis were observed, such as repair of damaged epithelium and reduction of rectal inflammation and bleeding [52]. However, the DSS-induced colitis model simulates acute epithelial injury and inflammation but lacks the complex immune, chronic, and systemic features of human Irritable bowel disease. Its results vary with mouse strain, DSS batch, and microbiota, limiting reproducibility and reducing its predictive value for evaluating long-term disease mechanisms or advanced therapeutics.

Another molecule that protects the intestines is called trefoil factor. Scientists have also managed to deliver this trefoil factor using live bacteria. Trefoil factor helps cells move to and repair damage in the lining of the intestine, keeping it healthy and protected. For the active delivery of trefoil factor in situ, an engineered *L. lactis* was used as a delivery vehicle, in which a codon-optimized human trefoil factor was expressed as a form of Usp45 secretion signal protein-fusion under the lactococcal P1 promoter. Trefoil factor secreted in situ activated major therapeutic pathways for the synthesis of prostaglandin-endoperoxide synthase 2, resulting in the healing of colitis in a DSS-induced mouse model [53].

Engineered bacteria have been used to deliver IL-10 directly in the gut, offering localized anti-inflammatory effects while avoiding the systemic limitations of recombinant IL-10 therapy. The protective effect of IL-10 produced by engineered bacteria was confirmed in a colitis mouse model, and it is in Phase I clinical development [54]. Phase I trials indicate it is safe and well-tolerated.

Engineered microbes have shown, in preclinical studies, the capacity to produce and release selected host-relevant proteins–such as signaling molecules, cytokines, or other functional peptides–within the gastrointestinal tract. However, the efficiency of such delivery is highly dependent on strain biology, protein stability, secretion pathways, and local environmental conditions, and cannot be generalized across all engineered systems. When designed with appropriate secretion signals and containment controls, microbial chassis can serve as platforms for targeted protein delivery,

though their performance remains constrained by factors such as limited protein folding capacity, degradation by luminal enzymes, and the need for precise control of expression levels.

CRISPR-based strain editing involves using CRISPR systems to introduce precise genetic modifications in microorganisms, enabling the creation of strains with defined functional traits. Beyond its broad applications in microbiology and synthetic biology, CRISPR is increasingly being applied to probiotic engineering, where it can be used to enhance stress tolerance, modify immunomodulatory pathways, or enable the controlled production of therapeutic molecules. However, the approach carries important limitations, including the risk of off-target mutations, challenges in ensuring genomic stability, potential ecological consequences if engineered strains persist or transfer genes in the environment, and substantial regulatory barriers governing the development and approval of genetically modified live biotherapeutic products.

How it works: CRISPR-Cas systems have increasingly been applied to probiotic strains, allowing precise modification of traits linked to safety, metabolism, or immunomodulation. In these organisms, a designed guide RNA directs a Cas enzyme (such as Cas9) to a specific genomic locus, where it introduces a targeted DNA break. Subsequent cellular repair pathways enable gene knockouts, targeted insertions, or base-level edits, resulting in engineered probiotic variants with enhanced or novel functional properties.

Applications: Metabolic engineering: Modify microbial pathways—including in probiotic species such as *Lactobacillus* or *Bifidobacterium*—to enhance production of beneficial metabolites or improve stress tolerance. Therapeutic development: Engineer probiotics to deliver therapeutic molecules, modulate immune pathways, or produce antimicrobial peptides for targeted disease treatment. Agriculture and animal health: Develop next-generation probiotic strains that improve gut health, nutrient absorption, and disease resistance in livestock. Biotech innovation: Use engineered microbial platforms (e.g., *E. coli*, yeast, or probiotic chassis) for controlled delivery of bioactive compounds, instead of broad environmental applications. Advantages of CRISPR in Strain Editing: High specificity and precision, relatively easy to design and implement, works across a wide range of species, supports multiplexing (editing multiple genes at once).

5.3 Next Generation Probiotics

New research on the gut microbiome has shown that there are still many bacteria we have not fully explored yet. These could be used as new probiotics. As more people learn about and accept probiotics, scientists and companies are working hard to discover and study these “next-generation probiotics”**.**

Advances in molecular technologies—such as PCR, next-generation sequencing, metatranscriptomics, and metabolomics—now allow researchers to characterize the gut microbiome with far greater precision. These tools not only identify microbial taxa but also reveal their functional activity, gene expression patterns, and metabolite production profiles. By integrating these datasets with improved laboratory culturing methods, scientists have been able to discover previously unrecognized gut microbes with potential health-modulating functions. Such organisms are increasingly being explored as candidates for next-generation probiotics.

New-generation probiotics offer several advantages over traditional probiotics. For example, scientists recently found that Next generation probiotics can produce many helpful substances like: indoles; secondary bile acids, which is secreted by certain clostridia; folate; short-chain fatty acids such as butyrate, propionate, and acetate; serotonin and Gamma-aminobutyric acid whose production occur in limited taxa. These metabolites have a significant role in the regulation [55].

5.3.1 Faecalibacterium Prausnitzii

Faecalibacterium prausnitzii is one of the most common bacteria found in the human gut. It can be categorized into two major phylogroups (phylogroups I and II), which were further assembled into five subgroups (I-A, II-B, II-C, II-D, and II-E) based on 16 S rRNA gene analysis [56].

Faecalibacterium prausnitzii is a helpful gut bacterium that lives in the intestines of healthy people. It makes up about 5% of the bacteria found in stool. It is a potential dysbiosis indicator. Beyond that, *F. prausnitzii* also helps manage how much mucus our intestines produce. This mucus is crucial for protecting the gut lining. It provides energy for colonocytes and keeps the mucus barrier strong and healthy. Based on the above-mentioned properties, *F. prausnitzii* is considered a probiotic that has a key protective effect on the human intestine and its depletion will cause debilitated intestinal anti-inflammatory and immunomodulatory abilities [57]. Faecalibacterium prausnitzii can digest various types of sugars and fibers, including starch, oligofructose, fructose, glucose, and inulin. When it processes these, it really likes acetic acid, which helps it grow. It also produces carbon dioxide gas, but it does not make hydrogen gas.

When F. prausnitzii breaks down sugar (glucose), it produces helpful substances called short-chain fatty acids (SCFA and butyrate**.** It also makes small amounts of D-lactic acid**,** which is a biomarker for various bacterial infections. These SCFAs are good for keeping our gut healthy. The features have been associated with *F. prausnitzii’s* health benefits that involve immunomodulatory responses, better intestinal barrier integrity, and anti-inflammatory properties. This helps to maintain gut homeostasis [58]. The proposed health benefits of Faecalibacterium prausnitzii have been linked to several

mechanisms, including modulation of immune responses through increased IL-10 production and inhibition of NF-κB-mediated inflammatory signaling, along with enhancement of intestinal barrier integrity. These effects are believed to contribute to overall gut homeostasis; however, most supporting evidence comes from preclinical and *ex vivo* studies, and human data remain limited.

5.3.2 Akkermansia Muciniphila

Akkermansia muciniphila is a gut bacterium that lives in the mucus inside our intestines. Scientists are very interested in it because it is seen as a "next-generation probiotic" –meaning it could be one of the most helpful probiotics in the future.

Akkermansia muciniphila plays a dual role in mucus layer dynamics. As a mucin-degrading bacterium, it utilizes host mucus as a nutrient source, contributing to controlled mucus turnover. At the same time, its presence has been shown in preclinical studies to stimulate goblet cell activity and upregulate mucin production, ultimately supporting the renewal and maintenance of the mucus barrier. Thus, although it consumes mucin, its overall effect is associated with promoting a healthier, more resilient mucus layer.

Akkermansia muciniphila contributes to the host immune system regulation and improves the intestinal epithelial cells' integrity and the mucosal layer thickness. In that way, *A. muciniphila* supports intestinal health [59].

5.4 Postbiotics and Parabiotics

People are getting really interested in using parts of probiotics, or even the helpful things they produce, instead of just the live bacteria themselves. These new approaches are called by different names, such as Paraprobiotic, Ghost Probiotics, Inactivated probiotics, non-viable microbial cells, Metabolic probiotics, Postbiotic. Essentially, these terms all refer to products made from probiotics that are not live bacteria anymore, but still offer health benefits. The concept of paraprobiotics refers to the use of non-viable microbial cells or their structural components–such as inactivated whole cells, cell wall fragments, or purified cell fractions–that can confer health benefits to the host. Their proposed mechanisms of action include modulation of immune responses through interactions with pattern recognition receptors (e.g., Toll-like receptors and NOD-like receptors), leading to regulated cytokine signaling and enhanced mucosal homeostasis.

According to the International Scientific Association for Probiotics and Prebiotics, postbiotics are defined as "preparation(s) of inanimate microorganisms and/or their components that confer a health benefit on the host." This includes not only microbial metabolites produced during fermentation but also non-viable cells, cell fragments, and other bioactive microbial products. These substances help shape the gut environment, support the activity of healthy bacteria, and interact with cells in your intestinal lining and beyond [60].

Different kinds of postbiotics: (1) Amino acids: These are like the building blocks our body needs to work properly. (2) Antimicrobial peptides: These are tiny helpers that fight against Pathogenic bacteria. Enzymes: These are special proteins that help us digest food and carry out important body processes. (3) Organic acids: Good examples are things like lactic acid. They make the gut a bit more acidic, which helps beneficial gut microbiota to grow. (4) Short-chain fatty acids: These are very important. Examples include butyrate, propionate, and acetate. They provide energy and have many health benefits. (5) Vitamins: Postbiotics can also include vitamins, especially B vitamins and vitamin K, which are essential for our health. These metabolites are not produced uniformly; each probiotic strain generates only a specific subset rather than the full range.

Some Postbiotics include butyrate, a short chain fatty acid that helps maintain and strengthen a healthy intestinal lining, which is essential for overall gut health [61]. Postbiotics are like fuel for the cells that line the colon. They contribute to maintaining intestinal barrier integrity by supporting tight junction function and mucosal structure. A well-regulated barrier reduces the translocation of luminal antigens and microbes into the systemic circulation, a process often referred to as increased intestinal permeability.

By keeping this wall strong, postbiotics also help control inflammation all over the body. Some postbiotics may reduce intestinal inflammation and modulate the immune system, making them promising tools for conditions like inflammatory bowel disease [62]. Some postbiotics have demonstrated the ability–primarily in preclinical models–to attenuate intestinal inflammation through pathways involving cytokine modulation, regulation of NF-κB signaling, and enhancement of epithelial barrier function, suggesting potential relevance for inflammatory bowel disease. However, human clinical evidence remains limited, and further trials are needed to establish their therapeutic role.

5.5 Personalized Probiotic Therapy

Conventional probiotics often show variable effectiveness across individuals, largely because the gut microbiome differs significantly from person to person. Factors such as age, diet, medication use, lifestyle, and genetic background all influence microbial composition and function.

These findings have encouraged efforts toward developing personalized probiotic strategies tailored to an individual's gastrointestinal profile. Approaches incorporating microbiome sequencing and metabolomic profiling may help identify

microbial or metabolic patterns associated with specific IBS subtypes–such as constipation-predominant (IBS-C) or diarrhoea-predominant (IBS-D). Microbiome profiling analyses have identified distinct microbial patterns between probiotic responders and non-responders in IBS patients, suggesting that machine-learning-based microbiome models may hold promise for predicting probiotic responsiveness in the future [63]. Aligning probiotic selection with these individualized characteristics has the potential to improve therapeutic targeting, although this concept remains investigational and requires further validation in controlled studies.

An observational pilot investigation was conducted between September and November 2022 and initially enrolled 78 adults aged 19 to 75 with gastrointestinal complaints. After applying eligibility criteria, 58 participants were included and stratified into two cohorts based on predefined symptom metrics: an "insensitive gut" group (n=28) and a "sensitive gut" group (n=30), with the latter characterized by heightened visceral sensitivity and greater symptom responsiveness to dietary or environmental triggers. The small sample size limits the generalizability of the findings and highlights the need for larger, controlled.

They were given two types of personalized probiotics: Consti-Biome, was associated with reductions in urgency-related symptoms and lower abdominal discomfort, as reflected in standardized IBS symptom scores. Sensi-Biome was associated with improvements in stool consistency. The study also showed that these probiotics changed the gut bacteria depending on the person's bowel habits. Certain probiotic interventions were associated with increases in taxa linked to improved intestinal motility, such as members of the *Erysipelotrichaceae* family.

Other probiotic strains were associated with enrichment of bacterial groups involved in anti-inflammatory activity, including Lactobacillaceae, which are known to modulate immune signaling and support mucosal homeostasis. A 2024 randomized clinical trial demonstrated that personalized prebiotic and probiotic supplements selected based on individual intestinal microbiota and IBS subtype resulted in significantly greater improvements in stool frequency and abdominal pain in IBS-C patients compared with conventional supplementation approaches [64].

Recent 2025 clinical research has shown that probiotic and prebiotic interventions can induce distinctive metabolic shifts in gut microbiome function–particularly increasing short-chain fatty acid production–supporting the mechanistic basis for individualized responses to microbiome-guided therapeutics [65].

Emerging evidence supports that host genetic variation influences gut microbiome composition and immune-related signalling pathways, providing a mechanistic basis for refining personalized probiotic therapy. For example, host genetics has been linked to microbiome structure, and probiotic-induced IL-10 production has been shown to depend on TLR2-mediated host pathways in preclinical models, suggesting that genetic factors such as IL-10 or TLR2 polymorphisms may one day help identify patients most likely to benefit [66].

These findings suggest that tailoring probiotic selection to individual bowel habits may be a promising approach, but current evidence–largely from small or early-stage studies–does not establish that personalized probiotics are more effective than conventional formulations. The results underscore the need for longer-term, well-controlled clinical trials that account for inter-individual variability and incorporate detailed analyses of microbiome and metabolite profiles to better understand the mechanisms and potential clinical relevance of personalized probiotic strategies. Further research informed by a deeper understanding of patients with bowel disorders could facilitate the employment of effective, tailored probiotic treatments [67].

6. Conclusion

Research on probiotics indicates that certain strains may contribute to host health by interacting with the existing gut microbiota and modulating physiological processes. Species within the genera *Lactobacillus* and *Bifidobacterium*, among others, can influence immune function through cytokine modulation, support metabolic activity via production of short-chain fatty acids and other metabolites, and enhance colonization resistance by competing with pathogenic microorganisms for nutrients and adhesion sites. Recent 2025 functional genomic analyses and mechanistic reviews have shown that certain probiotic strains modulate epithelial tight-junction gene expression and associated barrier-related pathways more effectively than previously recognized, supporting targeted probiotic strategies to enhance intestinal integrity [68]. However, these effects are strain-specific and not universal across all probiotic products.

Probiotics have demonstrated efficacy in various gastrointestinal disorders:

Irritable Bowel Syndrome: In IBS, responses to probiotics vary across individuals and IBS subtypes (IBS-C, IBS-D, and IBS-M). While single strains such as *B. infantis* do not consistently demonstrate benefit in all patients, multi-strain formulations containing *B. infantis* have shown reductions in validated symptom scores–particularly abdominal pain and bloating–in several clinical trials, including a 2017 systematic review. Another strain, *Lactobacillus plantarum 299v*, has also shown promise; in a 2012 randomized study, it produced statistically significant improvements in composite IBS symptom scores compared with placebo. Overall, strain selection, dose, and IBS subtype contribute substantially to treatment outcomes. Recent 2025 multi-omics research has identified distinct stool microbiome and metabolomic profiles in constipation-predominant IBS (IBS-C), laying a foundation for future microbiome-guided phenotyping and potential prediction of probiotic responsiveness in IBS-C and IBS-M patients [69].

Inflammatory Bowel Disease: In ulcerative colitis, several studies suggest that certain probiotics–particularly *Bifidobacterium*-containing formulations, multi-strain preparations such as *VSL#3*, and the well-studied *Escherichia coli Nissle 1917*–may help induce or maintain remission in some patients. Among 25 clinical studies evaluating probiotics in UC, a majority (21) reported beneficial outcomes, though the magnitude of effect varies by strain, dose, and study design.

In contrast, evidence for Crohn's disease remains inconsistent and generally weaker, with multiple trials showing no significant advantage of probiotics over standard therapy**.** A 2025 network meta-analysis confirmed that no currently available probiotic strain provides consistent remission benefit in Crohn's disease, although engineered strains may hold future promise [70]. Additional high-quality, strain-specific research is needed to clarify the role of probiotics across different inflammatory bowel disease subtypes.

Antibiotic-Associated Diarrhoea and *Clostridium difficile* Infection (CDI): Evidence indicates that certain probiotic strains can reduce the risk of AAD and CDI, but the benefits are strain-specific and not universal across all probiotic products. Meta-analyses show that specific strains–such as *L. rhamnosus GG*, *S. boulardii*, and some *multi-strain formulations*–are associated with a lower incidence of AAD and *Clostridium Difficile*-associated diarrhoea. For example, one large review of 26 trials involving nearly 8,000 participants reported an approximate 60% reduction in CDAD risk, but this effect was largely driven by a subset of well-studied strains rather than probiotics. Similarly, another review of 16 studies found reduced rates of AAD and CDI when effective strains were administered alongside antibiotics. A 2025 randomized clinical trial found that adjunctive administration of the probiotic *S. boulardii* with standard antibiotic therapy significantly reduced recurrence of *Clostridioides difficile* infection compared with antibiotic therapy alone [71]. Therefore, clinical benefits depend heavily on the specific probiotic strain, dose, and patient population.

H. pylori Infection: Probiotics are often evaluated as adjuncts to standard eradication therapy, but study outcomes vary considerably due to differences in strains, treatment regimens, and study populations. Overall, the evidence suggests that certain probiotics may modestly enhance eradication rates and, more consistently, reduce antibiotic-associated adverse effects such as diarrhoea and nausea. For example, *S. boulardii* has been shown in some trials to slightly improve eradication–e.g., from approximately 60% to 71% in one study–but its most reliable benefit is the reduction of treatment-related side effects rather than a substantial increase in cure rates**.** Preclinical research has shown that combinations of *Limosilactobacillus reuteri* and *Bifidobacterium breve* can ameliorate gut dysbiosis and enhance mucosal recovery in dextran sulfate sodium-induced colitis models, supporting their therapeutic potential in inflammatory conditions [72].

Necrotizing Enterocolitis in neonates: NEC in neonates. Certain probiotic strains–particularly selected *Bifidobacterium* species and *Lactobacillus* strains–have shown a protective effect against NEC in preterm and low-birth-weight infants. These benefits appear to be strain-dependent and are associated with upregulation of cytoprotective gene pathways, attenuation of pro-inflammatory signaling, enhanced intestinal barrier integrity, and competitive exclusion of pathogenic microbes. However, the use of probiotics in this highly vulnerable population requires careful consideration of safety, product quality, and regulatory guidance, as risks such as contamination or strain translocation have been reported. Therefore, only rigorously tested strains with established safety profiles should be considered in neonatal care settings.

Safety concerns–particularly contamination risks and rare cases of probiotic-associated sepsis in preterm infants–have highlighted the need for rigorous safety evaluation, including genomic verification of probiotic strains used in neonatal products [73].

7. Limitations and Future Direction

Although probiotics demonstrate therapeutic potential, several limitations remain. Their effects are highly strain-specific and can vary substantially between individuals due to differences in host genetics, microbiome composition, and underlying health conditions. Many commercial formulations also face challenges related to survival through the gastrointestinal environment, which affects their ability to reach the target site in sufficient numbers. In addition, regulatory inconsistencies–such as varying classification of probiotics as dietary supplements, foods, or biologics–and frequent inaccuracies in product labeling complicate assessment of their true clinical efficacy.

A 2025 review of commercial probiotic products found widespread inaccuracies in labeling practices–including omission of strain identity and other critical information–highlighting the need for improved regulatory alignment across markets [74]. The heterogeneity in clinical trial designs, including differences in strains used, dosing regimens, and study endpoints, further limits the comparability and generalizability of findings.

Future work includes the development of genetically engineered or synthetic biology-based probiotic strains designed to improve stability, target specific diseases, or deliver therapeutic molecules in situ.

Cutting-edge research has demonstrated that engineered probiotics can be programmed to deliver therapeutic molecules, including anti-inflammatory factors, directly in the gut with efficacy shown in preclinical models of inflammatory bowel disease [75]. However, these approaches remain largely experimental and require careful evaluation of biosafety,

containment, and compliance with emerging regulatory frameworks. Addressing these scientific and regulatory challenges will be essential for the responsible advancement of next-generation probiotic therapies.

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Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

Generative AI Statement

The authors declare that no generative artificial intelligence (AI) tools were used in the conceptualization, data interpretation, analysis, or writing of this manuscript. The content was prepared solely by the authors, who take full responsibility for its originality, accuracy, and integrity.

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