

The ISAPP quick guide to probiotics for health professionals: History, efficacy, and safety

A resource prepared by the International Scientific Association for Probiotics and Prebiotics

1. What are probiotics?

The term “probiotic” comes from Latin “pro” and the Greek “bios”, together meaning “for life.” Probiotics are [defined as](#) “live microorganisms that, when administered in adequate amounts, confer a health benefit on the host”. The definition was proposed by a panel of experts convened by the International Scientific Association for Probiotics and Prebiotics (ISAPP). It was a grammatical correction of the definition put forward in 2001 by an Expert Consultation of international scientists, chaired by Prof. Gregor Reid and convened by the Food and Agriculture Organization of the United Nations (FAO) of the World Health Organizations (WHO). In 2002, an FAO/WHO Working Group issued [Guidelines for the Evaluation of Probiotics in Food](#).

Probiotics encompass different modes of administration (oral, intravaginal, topical), various regulatory categories (foods, dietary supplements, infant formula, drugs and medical devices), target different hosts (humans, animals, and fish) and multiple mechanisms of action (see below for more details). Probiotics are commonly delivered in foods, such as yogurt, or as nutritional supplements. Probiotic drugs, also known as live biotherapeutic agents, are also available in some geographical regions. Probiotics are also used to maintain animal health (companion and livestock) and can be included in animal supplements, pet foods, and animal feed. Different regulations regarding safety standards, permissible claims and manufacturing requirements are applicable to each product category and to each geographical region.

Most commercial probiotics are specific microbial strains from the genera *Bifidobacterium*, *Lactobacillus*, and *Saccharomyces*, and less commonly from *Bacillus*, *Propionibacterium*, *Enterococcus*, *Pediococcus*, *Streptococcus*, and *Escherichia*. Note that in 2020, an international team of scientists reorganized the genus *Lactobacillus*, which now comprises 25 genera (see [here](#) and [here](#) for related infographics). There is active research on identifying novel candidate probiotics isolated from different body sites of healthy human subjects.

See [here](#) for infographics on probiotics (in multiple different languages) and [here](#) for short educational videos on probiotics.

2. History of probiotics

From ancient times, people have taken advantage of live microbes naturally present on raw foods to make fermented foods. These fermented foods were a source of live dietary microbes in their diets and were often believed to provide therapeutic benefits. See [here](#) for a useful review on fermented foods. However, the live microbial components of these foods were not known at the time. One of the founders of modern microbiology, Louis Pasteur discovered the microbial basis for food fermentations. This early research was followed by other discoveries, including the isolation of bacteria that are now used as probiotics. For example, in 1890, *Lactobacillus acidophilus* was [first discovered](#) by the Australian physician Ernst Moro; this was followed by the discovery of *Bifidobacterium* in 1899 by Henry Tissier (pediatrician, Pasteur Institute, France). Tissier found that bifidobacteria were dominant in the gut microbiota of breastfed babies and he observed clinical benefits from treating infant diarrhea with the same bacteria.

Probiotics were first conceptualized over a century ago by the Russian scientist and Nobel Prize winner, [Elie Metchnikoff](#) of the [Pasteur Institute](#) in Paris. Metchnikoff was the first to introduce the idea that consuming live microbes may be beneficial to health. He suggested that it is possible to replace harmful microbes in the gut microbiota with beneficial ones. In 1907, while working in Bulgaria, Metchnikoff was intrigued by the observation that certain Bulgarians lived longer, healthier lives than others. Metchnikoff proposed that putrefactive (proteolytic)

microbes producing toxic substances in the colon contribute to aging. For example, bacteria such as clostridia (part of the normal gut microbiota), can produce toxic substances including phenols, indols, amines and ammonia from protein digestion. Metchnikoff suggested that these compounds were responsible for what he called "intestinal autointoxication," leading to the physical changes associated with aging. He also suggested that the [fermented milk](#) (yogurt) consumed by these villagers, which contained live *Lactobacillus bulgaricus*, countered this autointoxication. This yogurt bacillus was discovered two years earlier in 1905 by [Stemen Grigorov](#). In honor of the country where it was discovered, this species was named *Lactobacillus bulgaricus*, currently named [Lactobacillus delbrueckii subsp. bulgaricus](#). Based on these observations, Metchnikoff proposed that consumption of fermented milk could "seed" the human intestine with healthful bacteria, which would suppress the growth of proteolytic bacteria. Metchnikoff himself consumed sour milk containing the "Bulgarian Bacillus" and believed his health benefited. Friends in Paris soon followed his example, and physicians began prescribing the sour-milk diet for their patients.

A decade later, during an outbreak of shigellosis in 1917, the German professor Alfred Nissle (University Freiburg, Germany) isolated a strain of *Escherichia coli* from the feces of a soldier unaffected by the disease. This strain, named [E. coli Nissle 1917](#), was later used to help prevent acute gastrointestinal salmonellosis and shigellosis.

In 1920, the American scientists Leo Rettger and Harry Cheplin (Yale University, USA) reported that Metchnikoff's "Bulgarian Bacillus" could not live in the human intestine. Although it is not necessary for probiotics to colonize the intestine, their ability to remain alive during transit was considered important for them to mediate health benefits. This led them to conduct animal and human experiments on *Lactobacillus acidophilus*, which was isolated from human feces. Professor Rettger further explored *L. acidophilus* and reasoned that bacteria originating from the gut were more likely to be beneficial to gut health.

In 1930, the Japanese microbiologist [Minoru Shirota](#) subsequently isolated what is now known as *Lactocaseibacillus paracasei* subsp. *paracasei* strain *Shirota*. These efforts led to the first commercially marketed fermented dairy drink. It was marketed as Yakult starting in 1935 and continues to be manufactured and sold worldwide today.

The word probiotic was first used by the German bacteriologist [Werner Kollath](#) (University of Breslau, Germany) in 1953 to describe various organic and inorganic supplements that were believed to have the ability to restore the health of malnourished patients. In 1954, the German researcher Ferdinand Vergin proposed the term *probiotika* to describe “active substances that are essential for healthy development of life.” The American scientist Daniel Lily and Rosalie Stillwell (St. John’s University, New York, USA) published an article in Science in 1962 wherein they expanded the definition of probiotics to include “the anaerobic bacteria that are able to produce lactic acid and stimulate the growth of other organisms.” Robert Parker in 1974 proposed that the term probiotic include not only microbes but also other substances that contributed to intestinal microbial balance. Our current usage of the term probiotic was first proposed by Professor Roy Fuller (Reading, UK) who removed “other substances” from the definition and defined probiotics as “live microbial feed supplements which beneficially affect the host animal by improving its intestinal microbial balance.” Professor Fuller's definition emphasized the requirement of viability for probiotics and introduced the aspect of a beneficial effect on the host. The current definition, “live microorganisms that, when administered in adequate amounts, confer a health benefit on the host”, retains the essence of Fuller’s definition, but does not restrict the mechanism driving health benefits.

3. Beneficial effects of probiotics

Decades of research have explored the role of probiotics in supporting health, managing symptoms, and prevention of various diseases. Numerous clinical trials have evaluated the safety and efficacy of different probiotics for several conditions including: **prevention of antibiotic-associated diarrhea, management of some mild to moderate digestive symptoms associated with irritable bowel syndrome or functional bowel conditions, reducing symptoms associated with lactose maldigestion, reducing colic symptoms and eczema in infants, treating infectious diarrhea, and decreasing common infections of the respiratory tract, gut, or vaginal tract.** Recommendations based on these clinical trials should emphasize use of the specific strain or strain combinations tested, as well as the dose tested. Since probiotics [differ at the](#)

[strain level](#), results from one probiotic cannot be extrapolated to all probiotic products available on the market.

Reviews have been published that summarize available information on health benefits of probiotics for human use (see [here](#), [here](#), and for some GI indications, [here](#)). Much evidence for probiotics has been generated in patient populations, with less information available documenting a value of probiotics for healthy people. Although documenting improved health in a population that is already healthy is difficult, evidence suggests that certain probiotics can **reduce the incidence and duration of common respiratory tract infections (i.e., the common cold), decrease antibiotic usage, improve blood lipid profiles in hypercholesterolemic adults, help manage occasional digestive symptoms, help manage common oral cavity symptoms and may even help with some psychological symptoms such as stress, depression and anxiety.**

As for any therapeutic intervention, null studies, which fail to demonstrate a benefit for probiotics, have been published. For example, two well-conducted studies investigating the effect of two different probiotic preparations on acute pediatric gastroenteritis failed to find the tested probiotics to be beneficial (see [here](#) and [here](#)). Although studies to date have led to [recommendations](#) for certain probiotics to reduce the duration of acute pediatric diarrhea, these new studies suggest that the tested probiotics (*L. rhamnosus* GG or a combination product containing *L. rhamnosus* R0011 and *L. helveticus* R0052) might not be effective in the setting of North American emergency departments when administered to children who have been experiencing symptoms for several days (studies [here](#) and [here](#)). Such null studies are important to help zero in on which strains and doses work for which indications. For a given product on the market, benefits may occur in other populations or for different conditions. A careful examination of the literature is important because one probiotic does not work for all indications or sub-populations.

Translating the research findings into product recommendations can be challenging, because product names often do not appear in published studies. These two guides (for [USA](#) and [Canada](#)) are evidence-based, consumer-friendly lists of some probiotics products backed by clinical evidence.

3.1. Gut health

- *Antibiotic-associated diarrhea (AAD) and Clostridioides (formerly Clostridium) difficile infections*

Although essential for treating bacterial infections, antibiotics may also disturb the beneficial bacterial community in our gastrointestinal tract. This microbial perturbation may play a role in a common side effect of antibiotic treatment, known as antibiotic-associated diarrhea (AAD).

Further, disruption of the gut microbiota risks onset of secondary infections caused by opportunistic pathogens such as *Clostridioides (Clostridium) difficile*, which is of particular concern in hospitalized older adults.

[Clinical trials](#) have been conducted with different probiotic preparations and suggest a beneficial effect of certain probiotics in reducing the incidence of *Clostridioides difficile*-associated diarrhea and AAD (see [here](#) for recommendations by the American Gastroenterological Association). Among the various probiotics evaluated, evidence suggests that *Lactocaseibacillus rhamnosus* GG, *Saccharomyces cerevisiae* var *bouardii* Lyo, and a combination product containing *Lactobacillus acidophilus* CL1285, *Lactocaseibacillus casei* LBC80R, and *Lactocaseibacillus rhamnosus* CLR2 are able to reduce the risk of AAD (see [here](#), [here](#), and [here](#)). Note that probiotics have not been shown to treat *C. difficile*-associated diarrhea.

A few studies also investigate the effectiveness of probiotics as an adjunct to antibiotic therapy to improve *Helicobacter pylori* eradication rates and to manage side effects of the antibiotics. A [meta-analysis](#) including a broad range of probiotics, did not demonstrate improved eradication of *H. pylori* infection. A [2019 meta-analysis](#) concluded that probiotic therapy improved both *H. pylori* eradication rates and side effects from antibiotic therapy in children, and a [2015 meta-analysis](#) noted the effectiveness of probiotics to reduce side effects of *H. pylori* antibiotic treatment in adults. Finally, a [2020 meta-analysis](#) based on 40 clinical studies concluded that probiotics supplementation improved *H. pylori* eradication rates and individual gastrointestinal symptoms, with longer probiotic treatment providing better positive effect.

- *Inflammatory bowel disease (IBD)*

Probiotic interventions have been studied for their ability to extend remission of the inflammatory bowel diseases (IBD), Crohn's disease (CD) and ulcerative colitis (UC). In general, probiotics are [ineffective in Crohn's disease](#). However, probiotic use in conjunction with standard medications has been effective in extending remission of ulcerative colitis. A [meta-analysis](#) indicated that probiotic treatment was useful for relieving the disease activity, increasing the remission induction rate, and preventing the relapse of disease in UC patients as effectively as the administration of mesalazine (used to treat and prevent flare-ups of acute UC). A [meta-analysis and systemic review](#) concluded that probiotics show a significant efficacy for remission rates in UC patients. According to this [meta-analysis](#), probiotics have been shown to induce remission rate of UC during the active phase, significantly more effectively than the control group, but did not have an obvious therapeutic advantage in maintaining CD and UC remission.

A live formulation of eight different lyophilized strains from the species *Bifidobacterium breve* DSM24732, *Bifidobacterium longum* DSM24736, *Bifidobacterium infantis* DSM24737, *Lactobacillus acidophilus* DSM24735, *Lactiplantibacillus plantarum* DSM24730, *Lactocaseibacillus paracasei* DSM24733, *Lactobacillus bulgaricus* DSM24734, and *Streptococcus thermophilus* DSM24731 has shown effectiveness in small clinical trials (see [here](#) and a summary [here](#)). Of note, the tested preparation has been now accepted in some UK hospitals and prescribed by some gastroenterologists in addition to standard ulcerative colitis treatment.

- *Irritable bowel syndrome (IBS)*

Certain probiotics have been shown to relieve the symptoms of IBS and improve the quality of life of IBS patients. A [guideline and meta-analysis](#) involving children and adults with IBS found that probiotics significantly improved IBS symptoms, bloating, and flatulence, but the quality of evidence was low and a recommendation regarding probiotic species and strains could not be made. Another [meta-analysis](#) focusing on adults with IBS found that probiotics significantly improved overall symptom response and quality of life compared to placebo, but did not have an effect on individual IBS symptoms. A [systematic review and meta-analysis](#) of children and adolescents with IBS found that probiotics increased the likelihood of treatment success compared to placebo and decreased abdominal pain intensity. Probiotics are a promising option

to mitigate some symptoms of IBS; however, the overall quality and quantity of evidence is low. Therefore, studies are still needed to clarify which probiotic species, specific strains, and dose of probiotics are most effective for patients with IBS.

- *Infant colic*

Infant colic is a common condition, currently without effective medical treatment options. In recent clinical trials, *Lactobacillus reuteri* DSM 17938 was shown to safely relieve symptoms of infant colic in breast fed infants, as demonstrated in an [individual patient data meta-analysis](#) (see the meta-analysis [here](#)).

- *Necrotizing enterocolitis*

Necrotizing enterocolitis (NEC) is a neonatal disease with a 30% mortality rate and risks life-long morbidity in survivors. The cause of the disease is not yet clear, but intestinal microbiota differs between NEC patients and healthy infants. Prophylactic probiotic use can reduce the incidence of NEC [[number needed to treat](#) (NNT)=25], overall death (NNT=34), and neonatal sepsis (NNT=34) in preterm newborns and can reduce NEC stage ≥ 2 in very low birth weight infants (NNT=33) (see [here](#) and [here](#)). One [Cochrane systematic review](#) and meta-analysis on [all probiotic preparations](#) showed that probiotics reduced these risks by more than 50% compared to controls. However, not all probiotic preparations studied for NEC are effective, as *Bifidobacterium breve* BBG-001 did not improve the incidence of, or mortality from, NEC. Additional research is needed to determine optimal probiotic formulations and dosing, as suggested by a [meta-analysis](#), which looked at efficacy of specific probiotic preparations and concluded that sufficient evidence exists for 3 of 25 probiotic formulations to reduce mortality from NEC, whereas 7 of 25 strains reduced incidence of NEC. The American Gastroenterological Association [recommends the use of specific probiotic strain combinations](#) for NEC prevention in preterm, low-birth-weight infants. A neonatologist provided perspective in how to select strains to prevent NEC [here](#).

3.2. Urogenital health

- *Bacterial vaginosis (BV)*

[Lactobacilli](#) are the dominant bacteria species in the vaginal niche, with *L. crispatus*, *L. gasseri*, *L. jensenii* and *L. iners* being the most commonly isolated species. A microbiota deficient in lactobacilli, accompanied by the overgrowth of anaerobic bacteria, is [associated with the development of bacterial vaginosis](#) (BV). BV is sometimes asymptomatic, but if symptomatic it is characterized by fishy odor, increased vaginal pH and vaginal discharge. Since lactobacilli are typically the dominant bacterial species in a healthy vaginal ecosystem, clinical trials have been performed to establish the role of exogenously applied probiotic strains to restore the commensal vaginal microbiota following BV. Several clinical studies (described in this [systematic review](#)) showed that use of a single probiotic strain or mixture of multiple probiotic strains administered orally or intravaginally successfully treated BV. However, available studies are heterogeneous with regard to probiotic interventions (selected strains, dosing, and administration), duration of treatment, and the goals of treatment. Therefore, more properly powered, well-controlled and less heterogeneous studies would facilitate knowledge about probiotic use for this condition. [Other evidence](#) demonstrates that probiotics combined with antimicrobial therapy with probiotics led to improved cure of BV and restoration of the indigenous lactobacilli.

- *Vulvovaginal candidiasis*

Probiotics have been used for the treatment of vulvovaginal candidiasis (VVC), estimated to be the second most common form of vaginal infection after BV. A [Cochrane analysis](#) determined that probiotics used as adjuvant therapy to conventional antifungal therapy improve the rate of short-term (within five to 10 days) clinical cure, short-term mycological cure (no abnormal laboratory results) and relapse of VVC at one month. However, probiotics alone were not able to influence the rate of long-term (within one to three months) clinical cure and long-term mycological cure. While [further research](#) is needed to determine the exact role of probiotics for the treatment of VVC, studies suggest they may function by penetrating *Candida* biofilms and altering the yeast's susceptibility to anti-fungal agents (see [here](#) and [here](#)).

3.3. Skin health

- *Eczema*

Atopic dermatitis (eczema) is an inflammatory skin condition often associated with asthma and allergic rhinitis. Based on two meta-analysis and systemic reviews (see [here](#) and [here](#)), probiotics have been shown to reduce the risk of developing eczema in infants when consumed by women in the last trimester of the pregnancy, when used by breastfeeding mother and when given to infants. Based on these promising and positive results, the World Allergy Organization (WAO) recommended (1) using probiotics in pregnant women at high risk for having an allergic child; (2) using probiotics in women who breastfeed infants at high risk of developing allergy; and (3) using [probiotics in infants at high risk of developing allergy](#). However, it remains unclear which probiotic strains should be used. More studies need to be conducted because existing data, although promising and positive, constitute a low evidence level due to a high risk of bias and inconsistency. Nevertheless, the limited data were sufficiently convincing for a recommendation to be made by WAO.

3.4. Upper respiratory tract infections

Probiotics [have been shown](#) to reduce incidence of upper respiratory tract infections (URTIs) and reduce the duration of illness in healthy children and adults. A [Cochrane Review](#) reported that probiotics were better than placebo in reducing the number of participants experiencing episodes of acute URTI and the duration of an episode of acute URTI. This has the potential for large [savings](#) for national healthcare budgets. Probiotics also slightly reduce antibiotic use and cold-related school absence (as shown [here](#) and [here](#)).

4. Safety of probiotics

Safety of commercial probiotic products entails several aspects:

- Inherent safety of probiotic strain
- Safety of product as manufactured
- Safety of probiotic product for the intended use
- Limitations of regulatory oversight

Inherent safety of probiotic strain

Historically probiotics were associated with the consumption of foods such as yogurt. Today, probiotic bacteria are provided to the final consumer as foods, dietary or nutritional supplements, dried products, infant formula, drinks, foods for special dietary uses, medical foods, and even devices. Different safety considerations and consequently, regulations, exist for these different uses. In many regions of the world, probiotic products are often marketed as dietary or nutritional supplements, which have less stringent manufacturing and regulatory requirements than drugs. The European Union provides a list of microbes deemed safe for use in foods, such as bacteria, yeasts, filamentous fungi and viruses; this list is known as the [“Qualified Presumption of Safety”](#) (QPS) list. Before using strains of species on the QPS list in food, strains must be assessed for antibiotic resistance phenotypes that are atypical for the species, as this could indicate the presence of transferrable antibiotic resistance genes. In addition to phenotypic testing, it is also advisable that a well-annotated sequence of the bacterial genome is obtained for probiotic strains, which can be searched for such genes. If the strain is free of antibiotic resistance phenotypes and genotypes of concern, the strain does not require specific safety testing for use in foods. Most of the bacterial species used as probiotics have QPS status.

In the United States, safety for use in foods typically entails obtaining “generally recognized as safe” (GRAS) status for use in foods or, if the probiotic was not marketed in the United States prior to October 15, 1994, undergoing the new dietary ingredient process for use in a dietary supplement. No premarket approval of safety is required for probiotics used in foods or supplements; it is the manufacturer’s responsibility to meet safety requirements.

Safety of product as manufactured

Product safety can be impacted by poor product quality; an intrinsically safe probiotic strain can be rendered dangerous if contaminated with potentially dangerous microbes or other contaminants. A [contaminated probiotic product](#) was linked with the death of a premature

infant from mucormycosis, although conceivably this product could have met the common standard for mold in such products (>1000 yeast and mold/gram). As with any consumer product, probiotic products must be manufactured using good manufacturing practices consistent with the product's regulatory category. Suitable standards for product purity, identity and potency must be met, and ideally these are communicated to the end-user of the product through transparent label declarations. A [paper](#) discussed the need for improved transparency on product labels, and the role that third-party verification can play to achieve this end.

A [more stringent approach](#) to assuring quality in probiotic products would go far to assuring end-users about probiotic product quality. Problems exist with regard to strains being misidentified and misclassified, products being contaminated, and products not providing the labeled number of CFUs through the end of shelf life. Third party verification using [validated methodology of identity, purity and potency is needed](#).

Safety of probiotic product for the intended use

One challenge in the probiotic field is that often products are marketed as dietary supplements, but have evidence for clinical uses. Probiotics may be used in a variety of clinical settings, sometimes in high-risk patients, even though they are not approved as drugs. Although probiotics have been shown to be safe for many uses, their safety must be considered carefully for some uses. People with immunodeficiency, short bowel syndrome, and premature infants may be at higher risk for adverse events. Use of *Lactocaseibacillus rhamnosus* GG in critically ill children led to [bacteremia](#). This serves as a caution, even though [no clinical outcomes were reported](#). In some cases, adverse events after consumption of probiotics have been reported, but they are rare and limited to people with underlying disease.

Even among vulnerable populations, such as preterm infants and patients with HIV (see [here](#) and [here](#)), [those with cancer](#), and other immunocompromised conditions, strains of lactobacilli, *Bifidobacterium* and *Saccharomyces* have been used safely. However, manufacturers should meet specific quality needs for the target population and make testing results available for review before recommending probiotic products to at-risk individuals.

Other considerations needed for safety assessments include route of administration, dose and final product formulation. Deviations in any of these parameters from those used in safety evaluations trigger a re-evaluation of safety.

In summary, many probiotic species have a history of safe use and many clinical trials of strains of these species show a low risk for adverse events. However, the safety of probiotics comprising newly identified species [remains to be established](#).

Limitations of regulatory oversight

For certain categories of products, no premarket approval of safety is required. This is the case in the United States for dietary supplements, where it is up to manufacturer to assure safety. [Some have criticized](#) this lack of regulatory oversight and cited common violations by manufacturers when FDA inspections are conducted. Although the lack of compliance of probiotic manufacturers with FDA regulations is not known, submitting to and passing third party audits would likely alleviate such concerns.

5. Mode of action

Understanding the exact mechanisms by which probiotics exert their beneficial effects is important for several reasons. It can provide a rationale for logical selection of probiotic strains, increasing the likelihood of selecting the best strain(s) for a specific condition(s). It has the potential to enable researchers to do a better job of predicting responders and non-responders among subjects in clinical trials to probiotic interventions. Knowing mechanisms provides targets for improving probiotic functionality, through strain improvement efforts or optimizing manufacturing conditions. Sophisticated quality control could be achieved by enabling measurement of a mechanism rather than only live cell count. Overall, the credibility of the field would be enhanced. But this research is complicated, in part because it is likely that probiotics, being live cells, express numerous mechanisms simultaneously. An observed clinical effect may be the sum result of these multiple functions.

Well-documented and well-studied [probiotic effector molecules](#) in lactobacilli and *Bifidobacterium* strains include cell wall-associated structures such as specific pili, S-layer proteins, exopolysaccharides. For example, the unique spaCBA pili present on the surface of *Lactocaseibacillus rhamnosus* GG [has been shown](#) to [competitively exclude](#) various pathogenic bacteria. Further, the pili play a role in immunomodulation of macrophages and dendritic cells, and promote the probiotic's ability to be [retained](#) in the intestine. Some widely produced tryptophan-related and histamine-related metabolites, such as those that induce regulatory T-cells in *Limosilactobacillus reuteri* strains, have been mechanistically linked to promoting probiotics benefits. Other probiotic-produced substances such as GABA, CpG-rich DNA, CpG-rich DNA [has been shown](#) to inhibit allergy-specific IgE in mice and bacteriocins produced by *Ligilactobacillus salivarius* UCC118 reduce *Listeria monocytogenes* [infection](#) in mice. Specific molecules, such as pili, mucus-binding proteins, exopolysaccharides, glycoproteins, lectins, have been shown to play a crucial role in the host-microbe and bacteria-bacteria interaction of lactobacilli and *Bifidobacterium* strains, promoting adhesion to host epithelial cells or inhibiting bacterial and viral pathogens.

Various [attributes that convey beneficial effects](#) by probiotic strains include ability to replicate in the host and persist for a suitable time to impart effects, production of antimicrobial substances and those that interfere with pathogen adherence and virulence, the ability to modulate host immunity, and improve epithelial barrier function.

Typically, probiotics do not take up residence in the gut after they are consumed. Many studies show that within a week or two of stopping probiotics, they are no longer isolated from a subject's feces, although some studies have shown persistence of some administered probiotics (see [here](#) and [here](#)). But failure to colonize long-term does not render a probiotic unbeneficial. As they traverse through your alimentary canal, they can interact with your immune system and with the microbes residing in different parts of your body. The important point is that health benefits are established; colonization is not required.

Although probiotics are viewed as important modulators of gut microbiota, available studies suggest that probiotics likely do not elicit big changes to the fecal microbiota of healthy adults. But research on this topic is limited to fecal samples, which do not reveal possible impacts

upstream from the distal colon, and would not detect small, but potentially significant, changes in gut microbial composition. Future studies may identify ways that probiotics might impact metabolic functions of the microbiota or directly interact with pathogens. Further, during passage through our gut, probiotics and the substances they produce can interact with immune cells, gut epithelial cells, gut microbes and dietary components. These interactions may lead to observed health benefits. Likewise, probiotic strains do not colonize the vagina or oral cavity, but during their presence they can relay benefits to the host.

Molecular mechanisms of action employed by probiotics might be strain-specific, or they might be [shared](#) among most members of a larger taxonomic group, providing in-common benefits. Understanding probiotic modes of action and how they provide health benefits is an important area for future research.

6. Acknowledgements

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