

There's a widespread belief that probiotic supplementation can replenish the good bacteria lost during antibiotic treatment. What is the evidence for this belief, and is it beneficial for probiotics to be taken alongside antibiotics?

How do antibiotics impact the gut microbiome?

Antibiotics are important for the treatment of many bacterial infections, but their use can have unintended consequences, including disruption of the commensal gut microbiota. The degree of disruption varies between different antibiotic types, but in general, they can reduce microbial diversity, deplete specific groups of microorganisms and enhance others, promote antibiotic-resistant pathogens, and alter functionality of the microbiome. The impact of antibiotics also depends on the method and duration of administration, and other characteristics of the host.¹

What are the potential consequences of antibiotic-related microbiome disruption?

Microbiome disruption is believed to contribute to a number of side effects of antibiotics. Antibiotic-associated diarrhea affects about 17% of patients on antibiotics, and while typically self-limiting, it can be unpleasant and reduce patient compliance with antibiotics. The more severe *Clostridioides difficile*-associated diarrhea is also associated with antibiotic use. It occurs in around 4% of patients on antibiotics, and if left untreated can lead to serious outcomes. Antibiotics also increase the risk for other gastrointestinal infections, likely due to compromised colonization resistance and resulting pathogen expansion.¹ Both oral and intravenous antibiotics can cause antibiotic-associated diarrhea.

What are probiotics?

Probiotics are defined as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host".² Probiotics are typically delivered in nutritional supplements or foods, such

as yogurt. However, not all products with live microbes contain validated probiotics - for a microbe to be classified as a probiotic it must be proven in intervention studies to have a health benefit. Some of the most common commercial probiotics include specific strains within the genera of *Bifidobacterium*, *Lactobacillus*, *Lactocaseibacillus*, *Lactiplantibacillus*, *Limosilactobacillus*, *Saccharomyces*, and *Bacillus*. Decades of research have explored the role of probiotics in supporting health, managing symptoms, and prevention of various diseases. Probiotics should be chosen based on the specific strains, combinations, and doses tested in clinical trials, as results cannot be generalized to all probiotic products.³ To learn more about probiotics, visit <https://isappscience.org/infographics>.



Are there benefits of probiotics when taken alongside antibiotics?

There are several reasons clinicians may consider the recommendation of a probiotic alongside an antibiotic. Specific probiotics have been shown to mitigate some of the clinical harms associated with antibiotic use, such as antibiotic-associated diarrhea and *Clostridioides difficile*-associated diarrhea. While their primary documented benefit is preventing diarrhea, probiotics may help mitigate other side effects such as bloating and cramping. Probiotics may also increase the efficacy of antibiotic treatment for certain conditions. See Table 1.

Table 1. Evidence and clinical guidelines on the use of probiotics alongside antibiotic therapy.

Indication	Effects	Clinical society guidelines	Strain and dosage resources
Prevention of antibiotic-associated diarrhea (AAD)	Coadministration of selected probiotics can help reduce the incidence of AAD in adults ⁵ and both the incidence and duration in children. ^{6,7,8}	<u>Adults and children:</u> - WGO (lists probiotics with at least one well-designed clinical trial) ⁸ <u>Children:</u> - ESPGHAN (strong recommendation, moderate certainty evidence) ⁶	Resources for specific strain and dosage recommendations can be found within these clinical guidelines: <u>WGO</u> ⁸ Access online at: https://www.worldgastroenterology.org/guidelines/probiotics-and-prebiotics/probiotics-and-prebiotics-english
Prevention of <i>Clostridioides difficile</i> -associated diarrhea (CDAD)	Research suggests a beneficial effect of certain probiotics in reducing the incidence of <i>Clostridioides difficile</i> -associated diarrhea (CDAD). ^{8,9} Probiotic use is more effective in situations where there is a high baseline risk of CDAD (>5%). ¹⁰	<u>Adults:</u> - AGA (conditional recommendations, low quality evidence) ⁹ - ACG (negative recommendation) ¹¹ <u>Adults and children:</u> - WGO (lists probiotics with at least one well-designed clinical trial) ⁸ <u>Children:</u> - ESPGHAN (conditional recommendation, low quality evidence) ¹²	<u>ESPGHAN (AAD 2023)</u> ⁶ Access online at: https://onlinelibrary.wiley.com/doi/pdf/10.1097/MPG.00000000000003633 <u>ESPGHAN (CDAD 2016)</u> ¹² Access online at: https://onlinelibrary.wiley.com/doi/full/10.1097/MPG.0000000000001081 <u>AGA</u> ⁹ Access online at: https://www.gastrojournal.org/article/S0016-5085(20)34729-6/fulltext
Augment efficacy of antibiotic therapy for <i>Helicobacter</i> eradication	Probiotic supplementation used in conjunction with standard antibiotic therapy may provide a modest increase in eradication rates and treatment compliance. ⁸ Use of probiotics for more than 10 days was most effective. ¹³	- Maastricht VI/Florence consensus report (weak recommendation, moderate quality evidence) ¹⁴ - WGO (lists probiotics with at least one well-designed clinical trial) ⁸	Resources for specific strain and dosage recommendations can be found within these clinical guidelines: <u>WGO</u> ⁸ https://www.worldgastroenterology.org/guidelines/probiotics-and-prebiotics/probiotics-and-prebiotics-english
Augment efficacy of antibiotic therapy for bacterial vaginosis	Specific probiotics may improve the therapeutic effectiveness of antibiotic treatments for bacterial vaginosis. Start probiotic before or as soon as possible after starting antibiotic and continue at least 1 week after antibiotics have ceased. ¹⁵	None known.	A review of evidence based on AAFP SORT Grade A/Level 1 evidence contains strain and dose recommendations. ¹⁵ Access online at: https://www.mdedge.com/familymedicine/article/220474/preventive-care/probiotics-tx-resource-primary-care

WGO – World Gastroenterology Organisation, ESPGHAN – European Society for Paediatric Gastroenterology Hepatology and Nutrition, AGA – American Gastroenterological Association. ACG – American College of Gastroenterology, AAFP – American Academy of Family Physicians

What is the impact of probiotics on antibiotic-induced microbiome disruption?

While many studies have documented the clinical benefits of probiotic administration with antibiotics, far fewer have investigated the effect on the microbiota. When taken together, studies comparing probiotic-treated groups to control groups show no overall impact of probiotics on antibiotic-induced changes in microbiota diversity⁴ and some limited shifts in microbiome composition or function between groups. While some studies have interpreted these changes as protective, classifying differences in microbiota recovery as ‘beneficial’ or ‘harmful’ may be oversimplifying a complex situation. The field lacks both a clear definition of a healthy microbiota composition and an understanding of how it adapts to change. Further, available evidence does not fully address the influence of significant interindividual microbiome variation or provide long-term follow-up for post-treatment outcomes.¹

It is also important to note that while probiotics are often thought to ‘replace’ the missing beneficial bacteria, the species enriched within the microbiome by probiotic treatment are generally not the same as the administered probiotic species. Any probiotic-mediated impact on the microbiome is likely due to interactions of the administered probiotic with the microbiota and/or the host, rather than direct colonisation by the probiotic.

Based on available studies, it is not possible to conclude that probiotics are able to restore an antibiotic-disrupted microbiome to a pre-antibiotic exposure state. The mechanisms through which probiotics achieve the documented clinical benefits when administered with antibiotics remain unclear. Clinicians are advised to focus on clinical outcome data when considering probiotics for their patients on antibiotics.

Are there any contraindications for use of probiotics?

Probiotics have a long history of safe use and adverse events are rare. Using well-studied strains permitted by local regulatory authorities and delivered within products made by trusted manufacturers is recommended. As probiotics are live microorganisms, the rare possibility exists for invasive infections. Although clinical trials exist in a

number of the following populations showing low to no serious side effects, caution is still warranted in the immunocompromised, severely ill, premature infants and those with indwelling intravenous catheters.¹⁶

Should probiotics be recommended to everyone taking antibiotics?

Many clinicians commonly recommend probiotics to be taken with an antibiotic. Conditional recommendations issued by some clinical societies suggest an informed discussion between clinicians and patients about the relevant benefits and risks of probiotic use. Factors which may be taken into consideration in each case include the class of antibiotic, duration of treatment, cost of probiotics, age, comorbidities, hospitalisation status, and background risk or previous episodes of antibiotic or *Clostridioides* associated diarrhea.⁶



Which probiotic and dose should be used?

Many probiotic benefits are species- and strain-specific, meaning not all probiotic products will provide the same clinical benefits. Recommendations should be based on clinically tested doses of specific strains shown to provide the desired benefits in the relevant population. A higher dose is not necessarily more beneficial. Clinical societies have provided specific recommendations per indication and population - see Table 1 for resources to identify effective strains and dosages.

How long should probiotics be taken? Should they be continued after antibiotics?

Studies demonstrating efficacy of probiotics have typically commenced dosing as soon as is practical, either before or within 1-2 days after antibiotic initiation.¹⁷ While protocols vary among studies, continuing probiotics for 7–14 days post-antibiotics is a commonly tested dosing strategy.

Does probiotic dosing need to be spaced apart from antibiotics?

There are no studies that compare different dosing regimens, so optimal approaches are unknown. Most bacterial probiotics are sensitive to a range of

antibiotics; therefore, to reduce the possibility of inactivating the probiotic, a 2-hour gap between the antibiotic and probiotic may be prudent, provided this does not reduce compliance. Yeast probiotics, such as *Saccharomyces* spp, are unaffected by antibiotics.

Do probiotics impact the efficacy of antibiotics?

Some patients have questioned whether probiotics might negatively affect the efficacy of antibiotics. There is no evidence for this concern. Antibiotics encounter a large number of resident microbes within the gastrointestinal tract and still remain effective.

References

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