World Gastroenterology Organisation Global Guidelines

Probiotics and prebiotics

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WGO Review Team

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Table 8 Evidence-based *adult* indications for probiotics, prebiotics, and synbiotics in gastroenterology. * Oxford Centre for Evidence-Based Medicine levels of evidence (see Table **7**)

ADULT Disorder, action	Probiotic strain, prebiotic, synbiotic	Recommended dose	Evidence level*	Refs.	Comments
Diarrhea					
Treatment of acute diarrhea in adults	*Lactobacillus paracasei* B 21060 or *L. rhamnosus* GG	10^9 CFU, twice daily	3	[8]	–
	Saccharomyces boulardii CNCM I-745, strain of *S. cerevisiae*	$5x10^9$ CFU/capsule or 250 mg twice daily	2	[9,10]	–
Antibiotic-associated diarrhea	Yogurt with *Lactobacillus casei* DN114, *L. bulgaricus,* and *Streptococcus thermophilus*	≥ 10^{10} CFU daily	1	[11]	Prevention of AAD in various clinical settings (in-patients and outpatients)
	Lactobacillus acidophilus CL1285 and *L. casei* (Bio-K+ CL1285)	≥ 10^{10} CFU daily	1	[11]	
	Lactobacillus rhamnosus GG	10^{10} CFU/capsule twice daily	1	[11]	
	Saccharomyces boulardii CNCM I-745	$5x10^9$ CFU/capsule or 250 mg twice daily	1	[11,12]	
	Lactobacillus reuteri DSM 17938	1×10^8 CFU twice daily	3	[13]	Prevention of AAD in hospitalized patients
	Lactobacillus acidophilus NCFM, *L. paracasei* Lpc-37, *Bifidobacterium lactis* Bi-07, *B. lactis* Bl-04	1.70^{10} CFU	2	[14]	
	Bifidobacterium bifidum W23, *B. lactis* W18, *B. longum* W51, *Enterococcus faecium* W54, *Lactobacillus acidophilus* W37 and W55, *L. paracasei* W72, *L. plantarum* W62, *L. rhamnosus* W71, and *L. salivarius* W24	10^9 CFU/g (5 g twice daily)	2	[15]	–
Prevention of *Clostridium difficile*–associated diarrhea (or prevention of recurrence)	*Lactobacillus acidophilus* CL1285 and *L. casei* LBC80R	5×10^{10} CFU daily and $4–10 \times 10^{10}$ CFU daily	2	[16]	–
	Yogurt with *Lactobacillus casei* DN114 and *L. bulgaricus* and *Streptococcus thermophilus*	$10^7–10^8$ CFU twice daily	2	[17]	–

ADULT Disorder, action	Probiotic strain, prebiotic, synbiotic	Recommended dose	Evidence level*	Refs.	Comments
	Saccharomyces boulardii CNCM I-745	$5x10^9$ CFU/capsule or 250 mg twice daily	3	[17]	–
	Lactobacillus rhamnosus HN001 + *L. acidophilus* NCFM	10^9 CFU once daily	3	[18]	Reduced fecal counts of *Clostridium difficile* in healthy elderly patients without diarrhea
	Lactobacillus acidophilus + *Bifidobacterium bifidum* (Cultech strains)	2×10^{10} CFU, once daily	3	[19]	–
	Oligofructose	4 g, three times daily	3	[20]	–
***Helicobacter pylori* (HP)**					
Coadjuvant therapy for HP eradication	*Lactobacillus rhamnosus* GG	6×10^9 twice daily	2	[7]	Reduction in therapy-related side effects in first line therapy
	Bifidobacterium animalis subsp. *lactis* (DSM15954), *Lactobacillus rhamnosus* GG	10^8–10^{10} living bacteria twice daily	2	[21]	Reduction in therapy-related side effects
	Lactobacillus reuteri DSM 17938	1×10^8, CFU three times daily	2	[22]	Reduction in therapy-related side effects in levofloxacin second-line therapy
	Mixture of *Lactobacillus acidophilus* and *L. bulgaricus* and *Bifidobacterium bifidum* and *Streptococcus thermophilus* and galacto-oligosaccharides	$5 \times 10^8 + 1 \times 10^9$, live cells twice daily	2	[23]	Improves treatment compliance in sequential therapy
	Lactobacillus acidophilus, Streptococcus faecalis, Bacillus subtilis	5×10^6, 2.5×10^6, 5×10^3	3	[24]	Improves eradication rates in first-line therapy
	Saccharomyces boulardii CNCM I-745	$5x10^9$ CFU/capsule or 250 mg twice daily	1	[7]	Reduction in therapy-related side effects
	Kefir	250 mL twice daily	3	[25]	

ADULT Disorder, action	Probiotic strain, prebiotic, synbiotic	Recommended dose	Evidence level*	Refs.	Comments
	Bacillus clausii (Enterogermina strains)	2×10^9 spores, three times daily	2	[26]	
	Lactobacillus reuteri DSM 17938 and *L. reuteri* ATCC 6475,	1×10^8 CFU of each strain, twice daily	2	[27,28]	–
Liver disease					
Hepatic encephalopathy	Nonabsorbable disaccharides (lactulose)	45–90 g/daily	1	[29]	–
	Mixture containing strains of *Lactobacillus plantarum, Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus delbrueckii subsp. bulgaricus, Bifidobacterium infantis, Bifidobacterium longum, Bifidobacterium breve* and *Streptococcus salivarius subsp. thermophilius*.	1×10^8 CFU three times daily	2	[30]	Primary prophylaxis of HE
	Mixture containing strains of *Lactobacillus plantarum, Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus delbrueckii subsp. bulgaricus, Bifidobacterium infantis, Bifidobacterium longum, Bifidobacterium breve* and *Streptococcus salivarius subsp. thermophilius*.	1×10^8 CFU three times daily	2	[31,32]	Secondary prophylaxis of HE
	Yogurt with *Streptococcus thermophilus, Lactobacillus bulgaricus, L. acidophilus,* bifidobacteria, and *L. casei*	12 ounces daily	2	[33]	Improvement in minimal hepatic encephalopathy
NAFLD	Yogurt (with *Lactobacillus bulgaricus* and *Streptococcus thermophilus*) enriched with *L. acidophilus* La5 and *Bifidobacterium lactis* Bb12	300 g daily	3	[34]	Improvement in aminotransferases
	Mixture of *Lactobacillus casei, L. rhamnosus, Streptococcus thermophilus, Bifidobacterium breve, L. acidophilus, B. longum,* and *L. bulgaricus* + fructo-oligosaccharides	At least 10^7 CFU twice daily	3	[35,36]	Improvement in aminotransferases, along with improve HOMA-IR and transient elastography

ADULT Disorder, action	Probiotic strain, prebiotic, synbiotic	Recommended dose	Evidence level*	Refs.	Comments
NASH	*Lactobacillus bulgaricus* and *Streptococcus thermophilus*	A tablet with 500 million, once daily	3	[37]	Improvement in aminotransferases
	Bifidobacterium longum W11 + FOS	5,000 million live bacteria once daily	2	[38]	Improvement in aminotransferases and NASH histological activity score
IBS					
	Bifidobacterium bifidum MIMBb75	1×10^9 CFU once daily	3	[39]	Improvement in global IBS symptoms and QOL
	Lactobacillus plantarum 299v (DSM 9843)	10 billion CFU once daily	2	[40,41]	Improvement in severity of abdominal pain
	Escherichia coli DSM17252	10^7 CFU three times daily	2	[41]	–
	Lactobacillus rhamnosus NCIMB 30174, *L. plantarum* NCIMB 30173, *L. acidophilus* NCIMB 30175, and *Enterococcus faecium* NCIMB 30176.	10 billion bacteria	2	[42]	Improvement in IBS score, mainly in pain and bowel habit score
	Bacillus coagulans and fructo-oligosaccharides	15×10^7, three times daily	2	[43]	Decrease pain, improve constipation
	Lactobacillus animalis subsp. *lactis* BB-12®, *L. acidophilus* LA-5®, *L. delbrueckii* subsp. *bulgaricus* LBY-27, *Streptococcus thermophilus* STY-31	4 billion CFU, twice daily	3	[44]	Improvement in abdominal pain and bloating
	Saccharomyces boulardii CNCM I-745	$5x10^9$ CFU/capsule or 250 mg twice daily	2	[45]	Improvement in IBS QOL score
	Bifidobacterium infantis 35624	10^8 CFU, once daily	2	[46,47]	Improvement in subjects global assessment of IBS symptoms
	Bifidobacterium animalis DN-173 010 in fermented milk (with *Streptococcus thermophilus* and *Lactobacillus bulgaricus*)	10^{10} CFU, twice daily	2	[48,49]	Improvement in HRQOL in constipation-predominant IBS

ADULT Disorder, action	Probiotic strain, prebiotic, synbiotic	Recommended dose	Evidence level*	Refs.	Comments
	Lactobacillus acidophilus SDC 2012, 2013	10^{10} CFU, once daily	3	[41,50]	–
	Lactobacillus rhamnosus GG, *L. rhamnosus* LC705, *Propionibacterium freudenreichii* subsp. *shermanii* JS DSM 7067, *Bifidobacterium animalis* subsp. *lactis* Bb12 DSM 15954	10^{10} CFU, once daily	2	[41,51]	–
	Short-chain fructo-oligosaccharides	5 g/daily	3	[52]	–
	Galacto-oligosaccharides	3.5 g/daily	2	[53]	–
	Bacillus coagulans GBI-30, 6086	2×10^9 CFU, once daily	3	[54]	–
	Pediococcus acidilactici CECT 7483, *Lactobacillus plantarum* CECT 7484, *L. plantarum* CECT 7485	$3–6 \times 10^9$ CFUs/capsule, once daily	3	[55]	–
Functional constipation					
	Bifidobacterium bifidum (KCTC 12199BP), *B. lactis* (KCTC 11904BP), *B. longum* (KCTC 12200BP), *Lactobacillus acidophilus* (KCTC 11906BP), *L. rhamnosus* (KCTC 12202BP), and *Streptococcus thermophilus* (KCTC 11870BP)	2.5×10^8 viable cells once daily	3	[56]	Improvement in elderly, in nursing-home population
	Lactobacillus reuteri DSM 17938	1×10^8, CFU twice daily	3	[57]	Improvement in bowel movement frequency per week
	Lactulose	20–40 g/d	2	[58]	–
	Oligofructose	20 g/d	3	[59]	–
	Fructo-oligosaccharide (FOS) and *Lactobacillus paracasei* (Lpc-37), *L. rhamnosus* (HN001), *L. acidophilus* (NCFM) and *Bifidobacterium lactis* (HN019)	6 g (FOS) + 10^8–10^9 CFU once daily	3	[60]	–
Uncomplicated symptomatic diverticular disease					
	Lactobacillus casei subsp. DG	24 billion viable lyophilized bacteria daily	2	[61]	Improvement in symptoms in uncomplicated diverticular disease

ADULT Disorder, action	Probiotic strain, prebiotic, synbiotic	Recommended dose	Evidence level*	Refs.	Comments
	Lactobacillus paracasei B21060	5×10^9 CFU daily	3	[62]	Improvement in symptoms in uncomplicated diverticular disease
Postoperative sepsis in elective gastrointestinal surgery patients					
	Lactobacillus acidophilus, L. plantarum, and *Bifidobacterium longum* 88	2.6×10^{14} CFU daily	1	[63]	–
Small-bowel injury from NSAIDs					
	Lactobacillus casei strain Shirota	45×10^8 to 63×10^9 CFU, once daily	3	[64]	Decreased the incidence and severity of low-dose aspirin-associated small-bowel injury
IBD—pouchitis					
Treatment of active pouchitis	Mixture containing strains of *Lactobacillus plantarum, Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus delbrueckii subsp. bulgaricus, Bifidobacterium infantis, Bifidobacterium longum, Bifidobacterium breve* and *Streptococcus salivarius subsp. thermophilius*.	900 billion bacteria daily	2	[65]	–
Maintenance of clinical remission	Mixture containing strains of *Lactobacillus plantarum, Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus delbrueckii subsp. bulgaricus, Bifidobacterium infantis, Bifidobacterium longum, Bifidobacterium breve* and *Streptococcus salivarius subsp. thermophilius*.	1800 billion bacteria daily	1	[66]	–
IBD—ulcerative colitis					

ADULT Disorder, action	Probiotic strain, prebiotic, synbiotic	Recommended dose	Evidence level*	Refs.	Comments
Inducing remission	Mixture containing strains of *Lactobacillus plantarum, Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus delbrueckii subsp. bulgaricus, Bifidobacterium infantis, Bifidobacterium longum, Bifidobacterium breve* and *Streptococcus salivarius subsp. thermophilius*.	1800 billion bacteria twice daily	3	[67]	–
Maintenance of clinical remission	*Escherichia coli* Nissle 1917	5×10^{10} viable bacteria twice daily	2	[68,69]	–
Lactose maldigestion—reducing associated symptoms					
	Yogurt with live cultures of *Lactobacillus delbrueckii* subsp. *bulgaricus* and *Streptococcus thermophilus*	At least 10^8 CFU of each strain per gram of product	1	[70]	–
Healthy population—reducing incidence of hard or lumpy stools					
	Lactobacillus casei strain Shirota	6.5×10^9 in fermented milk, once daily	3	[71]	–

AAD, antibiotic-associated diarrhea; CFU, colony-forming unit(s); HE, hepatic encephalopathy; HRQOL, Health-Related Quality of Life (score); IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; NSAID, nonsteroidal anti-inflammatory drug; QOL, quality of life.

Table 9 Evidence-based *pediatric* indications for probiotics, prebiotics, and synbiotics in gastroenterology. * Oxford Centre for Evidence-Based Medicine levels of evidence (see Table **7**)

PEDIATRIC **Disorder, action**	**Probiotic strain, prebiotic, synbiotic**	**Recommended dose**	**Evidence level***	**Refs.**	**Comments**
Treatment of acute gastroenteritis	LGG	≥ 10^{10} CFU/day (typically 5–7 days)	1	[72,73]	ESPGHAN/ESPID recommendations 2014; ESPGHAN Working Group on Probiotics. Meta-analysis of RCTs
	Saccharomyces boulardii CNCM I-745	250–750 mg/day (typically 5–7 days)	1	[72,74]	
	Lactobacillus reuteri DSM 17938	10^8 to 4 × 10^8 CFU (typically 5–7 days)	2	[72,73,75,76]	
	Escherichia coli Nissle 1917		3	[72]	ESPGHAN/ESPID: insufficient evidence to make a recommendation (methodological issues)
	Lactobacillus acidophilus	10 × 10^9 CFU	3	[72,77]	ESPGHAN/ESPID: Insufficient evidence to make a recommendation (no strain specification)
	Lactobacillus acidophilus and *Bifidobacterium bifidum*	3 × 10^9 CFU, for 5 days	3	[72,78]	
	Lactobacillus acidophilus and *Bifidobacterium infantis*	3 × 10^9 CFU of each organism for 4 days	3	[72,79]	
	Lactobacillus acidophilus rhamnosus 573L/1, 573L/2, 573L/3	1.2 × 10^{10} CFU twice daily, for 5 days)—effect only in RV diarrhea	2	[72,80]	ESPGHAN/ESPID: Insufficient evidence to make a recommendation (only one RCT available)
	Lactobacillus helveticus R0052 and *L. rhamnosus* R0011		2	[72,81]	
	Lactobacillus delbrueckii var. *bulgaricus, L. acidophilus, Streptococcus thermophilus, Bifidobacterium bifidum* (strains LMG-P17550, LMG-P 17549, LMG-P 17503, and LMG-P 17500)	10^9 CFU, 10^9 CFU, 10^9 CFU, and 5 × 10^8 CFU	2	[72,82]	

PEDIATRIC Disorder, action	Probiotic strain, prebiotic, synbiotic	Recommended dose	Evidence level*	Refs.	Comments
	Bacillus mesentericus and *Clostridium butyricum* and *Enterococcus faecalis*	1.1 × 10^7 CFU) & *Clostridium butyricum* (2.0 × 10^7 CFU) and *Enterococcus faecalis* (3.17 × 10^8 CFU)	3	[72,83]	ESPGHAN/ESPID: Insufficient evidence to make a recommendation (only one RCT available and no strain identification))
	Mixture containing strains of *Lactobacillus plantarum, Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus delbrueckii subsp. bulgaricus, Bifidobacterium infantis, Bifidobacterium longum, Bifidobacterium breve* and *Streptococcus salivarius subsp. thermophilius*.		3	[72,84]	
	Lactobacillus acidophilus & *L. rhamnosus* & *Bifidobacterium longum* & *Saccharomyces boulardii* CNCM I-745		3	[72,85]	
Prevention of antibiotic-associated diarrhea	LGG	1–2 × 10^{10} CFU	1	[86,87]	ESPGHAN Working Group on Probiotics
	Saccharomyces boulardii	250–500 mg	1	[12]	
Prevention of nosocomial diarrhea	LGG	10^{10}–10^{11} CFU, twice daily	1	[12]	Meta-analysis of RCT
	Bifidobacterium bifidum and *Streptococcus thermophilus*		2	[88]	–
Infections in children attending day-care centers	LGG		1	[89–91]	Prevention of AAD in hospitalized patients
	Lactobacillus reuteri DSM 17938	1 × 10^8 CFU/day for 3 months	2	[92,93]	

PEDIATRIC Disorder, action	Probiotic strain, prebiotic, synbiotic	Recommended dose	Evidence level*	Refs.	Comments
	Lactobacillus casei DN-114 001 in fermented milk	10^{10} CFU, once daily	2	[94–96]	–
	Lactobacillus casei Shirota in fermented milk	10^{10} CFU, once daily	2	[97]	–
Eczema (prevention)	(Probiotics) There is no clear indication yet regarding which probiotic(s) to use.			[98,99]	WAO suggests the use of probiotics in high-risk populations to reduce the risk of eczema
Necrotizing enterocolitis (prevention)	(Probiotics) No clear indications from scientific societies regarding which probiotic strain(s) should be recommended. The following strains are found NOT to be effective: *Saccharomyces boulardii* CNCM I-745, *Bifidobacterium breve* BBG-001, Bb12			[100,101]	Reduced risk of NEC and mortality in infants with birth weight < 1500 g
	Lactobacillus reuteri DSM 17938		2	[102]	–
H. pylori infection	*Saccharomyces boulardii* CNCM I-745	500 mg (in two doses, for 2–4 weeks)	2	[103]	Reduced risk of side effects and increased eradication rate
	Lactobacillus casei DN-114 001 in fermented milk	10^{10} CFU daily, for 14 days	2	[104]	–
Infantile colic—management	*Lactobacillus reuteri* DSM 17938	10^{8} CFU, once daily, for 21 days	1	[105–110]	Reduced crying time (documented mainly in breastfed infants). Meta-analysis of RCTs
Infantile colic—prevention	*Lactobacillus reuteri* DSM 17938	10^{8} CFU, once daily, up to 3 months of age	1	[111]	–
	LGG	10^{10}–10^{11} CFU, twice daily	1	[112]	Meta-analysis of RCTs

PEDIATRIC Disorder, action	Probiotic strain, prebiotic, synbiotic	Recommended dose	Evidence level*	Refs.	Comments
Abdominal pain–related functional gastrointestinal disorders	Mixture containing strains of *Lactobacillus plantarum, Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus delbrueckii subsp. bulgaricus, Bifidobacterium infantis, Bifidobacterium longum, Bifidobacterium breve* and *Streptococcus salivarius subsp. thermophilius*.	1 sachet (once per day for children 4–11 years of age; twice per day for those 12–18 years old)	3	[113]	–
	Lactobacillus reuteri DSM 17938	10^8 CFU/d for 4 weeks	1	[114,115]	–
Induction of remission in ulcerative colitis	*Escherichia coli* Nissle 1917		2	[116,117]	ESPGHAN/ECCO: Limited evidence suggests that probiotics added to standard therapy may provide modest benefit
	Mixture containing strains of *Lactobacillus plantarum, Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus delbrueckii subsp. bulgaricus, Bifidobacterium infantis, Bifidobacterium longum, Bifidobacterium breve* and *Streptococcus salivarius subsp. thermophilius*.	4 to 9 × 10^{11} CFU, twice daily	2	[118,119]	–

AAD, antibiotic-associated diarrhea; CFU, colony-forming unit(s) ECCO, European Crohn's and Colitis Organization; ESPGHAN, European Society for Paediatric Gastroenterology, Hepatology, and Nutrition; ESPID, European Society for Paediatric Infectious Diseases; LGG, *Lactobacillus rhamnosus* GG ; NEC, necrotizing enterocolitis; RCT, randomized controlled trial.

5 References

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