Modulare il microbiota:
dalle evidenze scientifiche alle applicazioni terapeutiche in gastroenterologia

Massimo Bellini

U.O. Gastroenterologia

Dip.Ricerca Traslazionale in Medicina e Chirurgia

Azienda Ospedaliero Universitaria Pisana

Batteri, Virus, Archea, Funghi Lieviti, Protozoi, Elminti …

Microbiota: l'insieme dei microrganismi che convivono con un organismo senza danneggiarlo, in condizione di normale funzionamento del suo sistema immunitario.

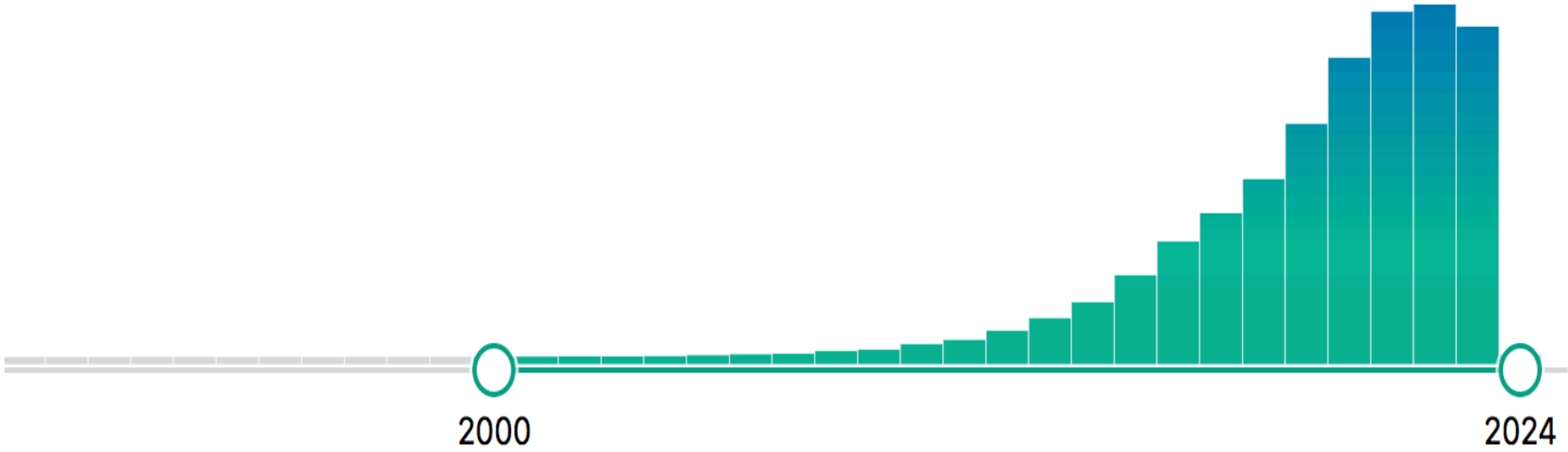
10^{14} Cellule batteriche **10^{13} Cellule umane**

Microbioma: patrimonio genetico dei microrganismi presenti (150 volte > genoma umano)

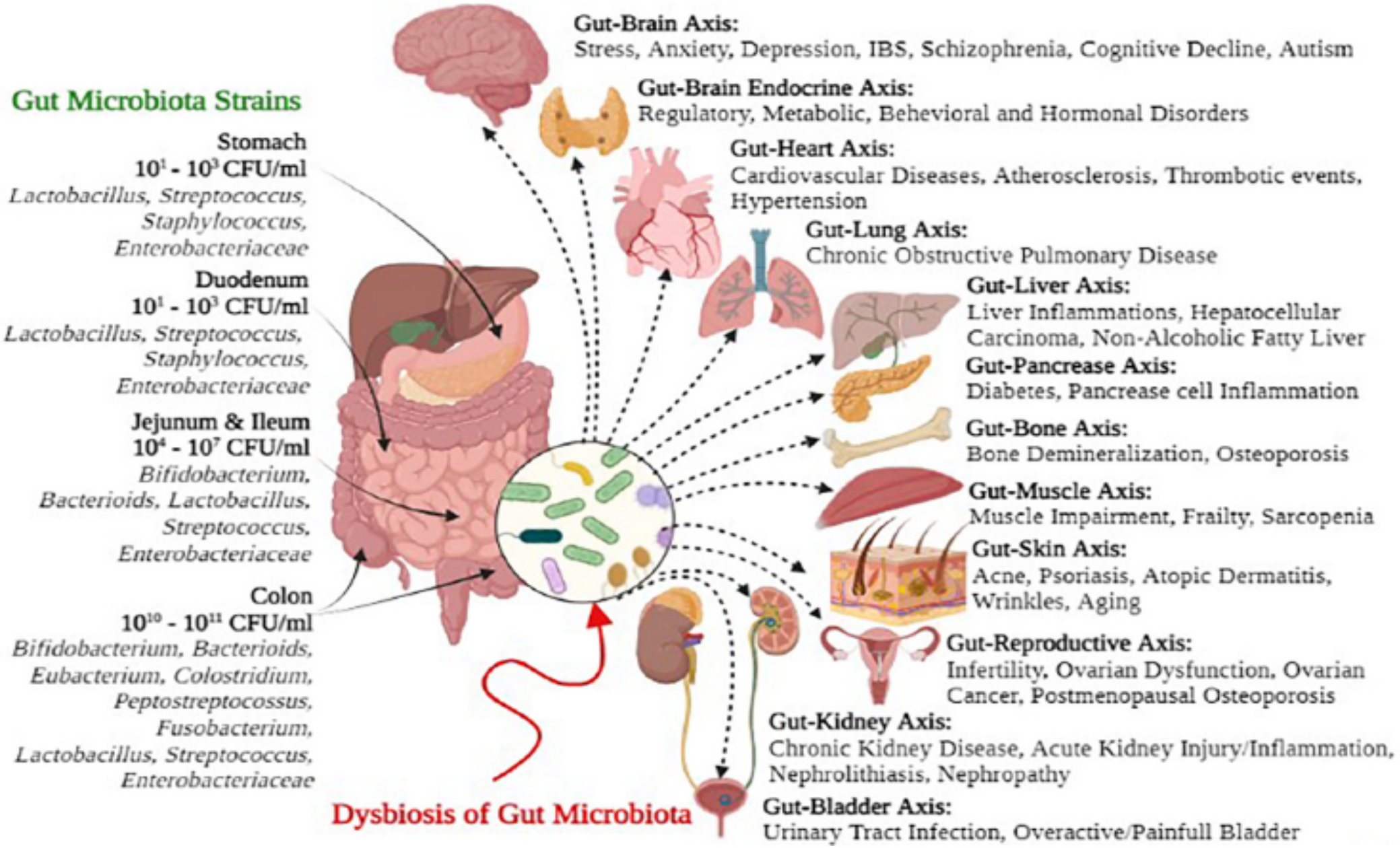
73572 results: GUT MICROBIOTA

PubMed

26 Novembre2023



Human gut microbiota and disease



Microbiota plays a significant role in maintaining normal gut physiology and health.

(Afzaal M, et al. Front Microbiol. 2022)

The gut microbiota has a lot of significant functions in human body:

-protection from **pathogens** (colonizing mucosal surfaces and creation of antimicrobial substances)

-enhancing the **immune system (**increasing macrophages activity)

-playing a vital role in **digestion and metabolism**

-modifying **insulin** resistance and affecting its secretion

-involved in the synthesis and metabolism of **bile acids** and **cholesterol**

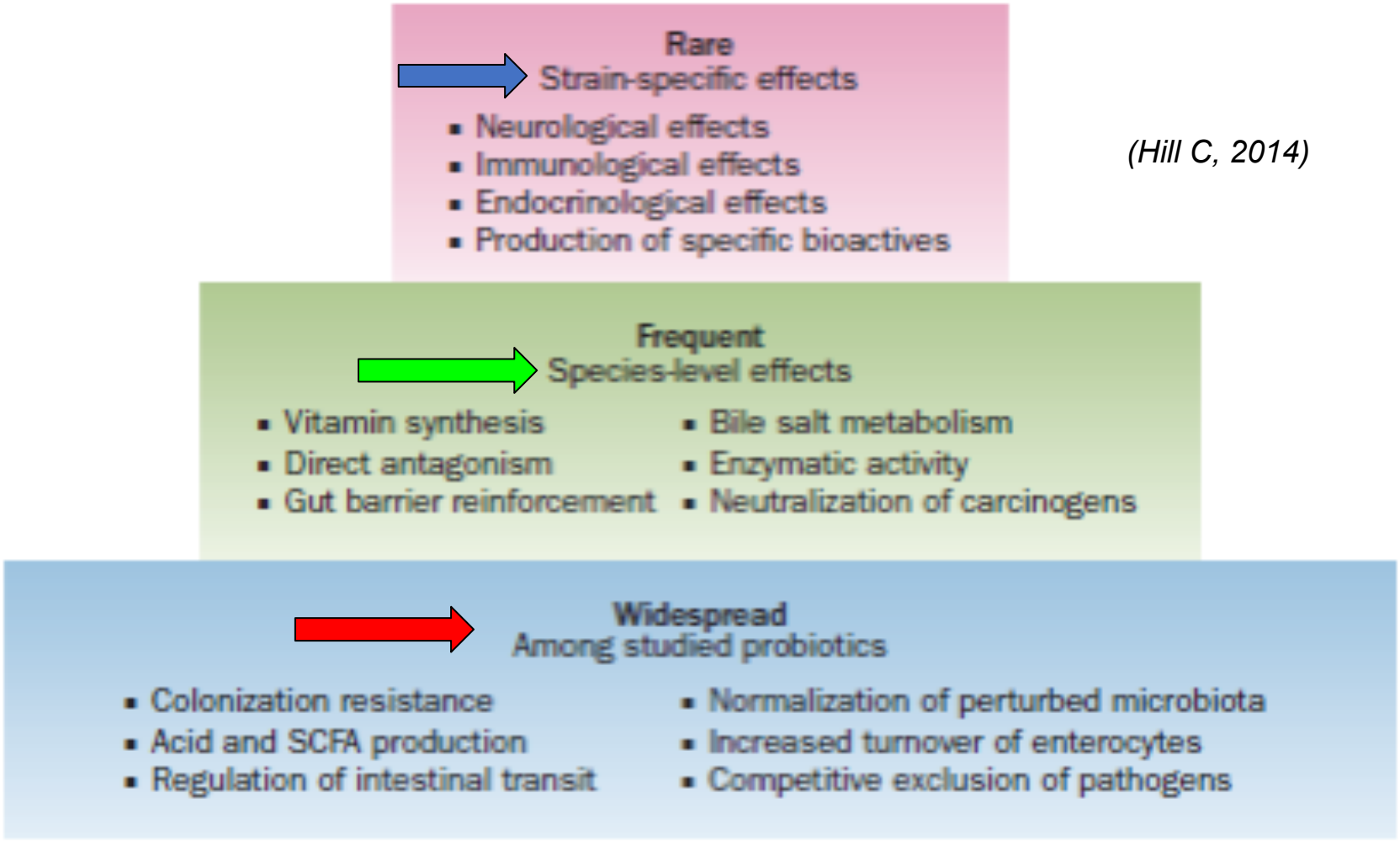
-**vitamin** synthesis (biotin, thiamine, cobalamin, riboflavin, nicotine and pantothenic acids, vitamin B and K)

-controlling epithelial cell **proliferation and differentiation**

-influencing **brain–gut communication** (neutrotrasmitters synthesis, e.g. GABA >psychobiotics)

(LeBlanc, 2013)
(Mills, 2019)
(Rothschild, 2018)
(Wiley, 2017)
(Kelly, 2015),
(Zheng, 2019),
(van Leeuwenhoek, 2020)

Possible distribution of mechanisms



(Hill C, 2014)

"No individual strain would be expected to have all the effects".

"Every strain is different and probably elicits a different outcome in the host".

Microbioma; grande diversità tra gli individui

Esseri umani:
-**uguali** al 99% in termini di genoma
-**differenti** sino all' 80-90% in termini di genoma del microbiota

The gut microbiota evolves with the human evolution. It is also in constant and dynamic interaction with the host gastrointestinal microenvironment.

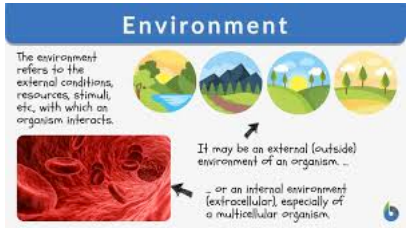
"Exploiting the variation contained within the microbiome will be much more fruitful in PERSONALIZED MEDICINE than the use of an individual patient's genetic data that targets the relatively constant host genome"

Microbioma è l'unica porzione modulabile del nostro patrimonio genetico e conferisce adattabilità alle perturbazioni e ai cambiamenti

Delivery

Breast Feeding

Aging (intestinal permeability)

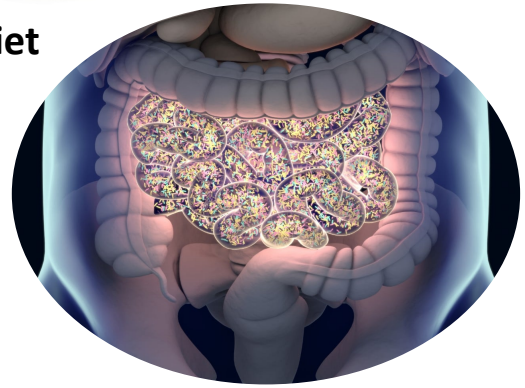


Pollution, Stress, Trauma

Diet

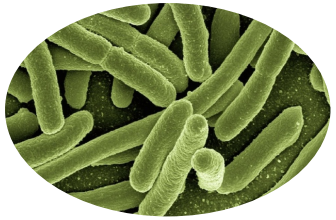
FMT

Prebiotics



Drugs

Lifestyle



Probiotics

Exercise and associated dietary extremes impact on gut microbial diversity

Siobhan F Clarke,[1,2,3] Eileen F Murphy,[2,4] Orla O'Sullivan,[1] Alice J Lucey,[5]

REVIEW Open Access

International Society of Sports Nutrition Position Stand: Probiotics

Jäger[1*], Alex E Mohr[2], Katie C Carpenter[3], Chad M Kerksick[4], Martin Purpura[1], Adel Moussa[5]

- La composizione del microbiota riflette il livello di attività fisica dell'ospite
- Il Microbiota di un atleta è differente rispetto a quello di un sedentario (Akkermansia muciniphila)
- Esercizio e aumentato introito proteico incrementano la diversità e la abbondanza delle specie batteriche

Interaction between drugs and the gut microbiome

Rinse K Weersma [1], Alexandra Zhernakova,[2] Jingyuan Fu[2,3]

Gut 2020;**0**:1–10. doi:10.1136/gutjnl-2019-320204

Table 1 Effect of common drugs on the microbiome in population studies

Name (analogue UK)	NL% n=1124	UK% n=2737	Effect on alpha div	Effect on beta-div/prop. of core genera	Decreased taxa	Increased taxa
ACE inhibitors	3.91	11.7			s_Dorea_longicatena (1)	g_Rothia (1); g_Blautia (1)
Alpha blockers	0.89	2.73				f_Lactobacillaceae (1); g_Lactobacillus (1); f_Veillonellaceae (1); g_Dialister (1)
Angiotensin-II-receptor antagonists (Sartan)	2.94	6.84		Yes (2)		
Antibiotics (previous month antibiotics)	1.16	6.45	0.45*	Yes (1, 2, 3, 4)	f_Bifidobacteriaceae (1); g_Bifidobacterium (1); s_Bifidobacterium_longum (1); s_Bifidobacterium_adolescentis (1); f_Prevotellaceae (3); f_Peptococcaceae (3); f_Odoribacteraceae (3); f_Clostridiaceae (3); f_Alcaligenaceae (3); f_Anaeroplasmataceae (3); g_unclassified_Lachnospiraceae (4)	f_Enterococcaceae (3); g_Bacteroides (4); g_Oscillibacter (4); g_unclassified_Ruminococcaceae (4)
Antihistamines (H1 inhibitor)	6.14	4.93		Yes (4)	f_Dehalobacteriaceae (3); f_Christensenellaceae (3)	s_Clostridium_bolteae (1)
Beta blockers	5.43	7.42		Yes (1 to 2)	0	f_Streptococcaceae (1); g_Streptococcus (1); s_Streptococcus_mutans (1); g_Rothia (1)
Calcium	1.25	15.7		Yes (1,2)		f_Gemellaceae (3)
Laxatives	1.87	3.19		Yes (1, 2, 4)	g_Collinsella (1); s_Collinsella_aerofaciens (1); f_Lachnospiraceae (1); s_Ruminococcus_obeum (1); g_Coprococcus (1); s_Coprococcus_catus (1); s_Coprococcus_comes (1); g_Dorea (1); g_Faecalibacterium (4)	s_Bifidobacterium_pseudocatenulatum (1); g_Bacteroides (1); s_Bacteroides_stercoris (1); s_Bacteroidales_bacterium_ph8 (1); f_Enterobacteriaceae (1); g_Escherichia (1); g_unclassified_Rhodospirillaceae (4); g_Bacteroides (4); g_Oscillibacter (4); g_Barnesiella (4)
Metformin	1.33	2.9	0.9*	Yes (1, 2, 3)	s_Bacteroides_dorei (1); g_Coprococcus (1); s_Coprococcus_comes (1); g_Dorea (1); s_Dorea_longicatena (1); f_Clostridiaceae (3); f_Ruminococcaceae (3); f_Barnesiellaceae (3); f_Christensenellaceae (3)	f_Streptococcaceae (1); g_Streptococcus (1); f_Enterobacteriaceae (1,3); g_Escherichia (1); s_Escherichia_coli (1)
Opiates (opioid)	1.16	8.58		Yes (3)	f_Dehalobacteriaceae (3);	f_Streptococcaceae (3); f_Micrococcaceae (3); f_Lactobacillaceae (3); f_Eubacteriaceae (3)
Oral contraceptives	10.1	2.61		Yes (2 to 4)		g_Rothia (1)
Paracetamol	0.98	10.6	0.6*	Yes (3)	f_Lachnospiraceae (1); g_Dorea (1); f_Christensenellaceae (3); f_Dehalobacteriaceae (3); f_Oxalobacteraceae (3)	s_Bifidobacterium_dentium (1); s_Streptococcus_salivarius (1); f_Streptococcaceae (3); f_Peptostreptococcaceae (3); f_Eubacteriaceae (3); f_Micrococcaceae (3);
Platelet aggregation inhibitors (aspirin)	2.85	7.83		Yes (1 to 2)	f_Bifidobacteriaceae (1); g_Bifidobacterium (1); s_Bifidobacterium_adolescentis (1)	g_Rothia (1); s_Bifidobacterium_dentium (1); s_Bacteroides_ovatus (1); f_Streptococcaceae (1); g_Streptococcus (1); s_Streptococcus_mutans (1); s_Streptococcus_parasanguinis (1); s_Streptococcus_sanguinis (1); s_Clostridium_bolteae (1); g_Blautia (1); s_Lachnospiraceae_bacterium_3_1_57FAA_CT1 (1); s_Lachnospiraceae_bacterium_7_1_58FAA (1); f_Eubacteriaceae (3)

Continued

Table 1 Continued

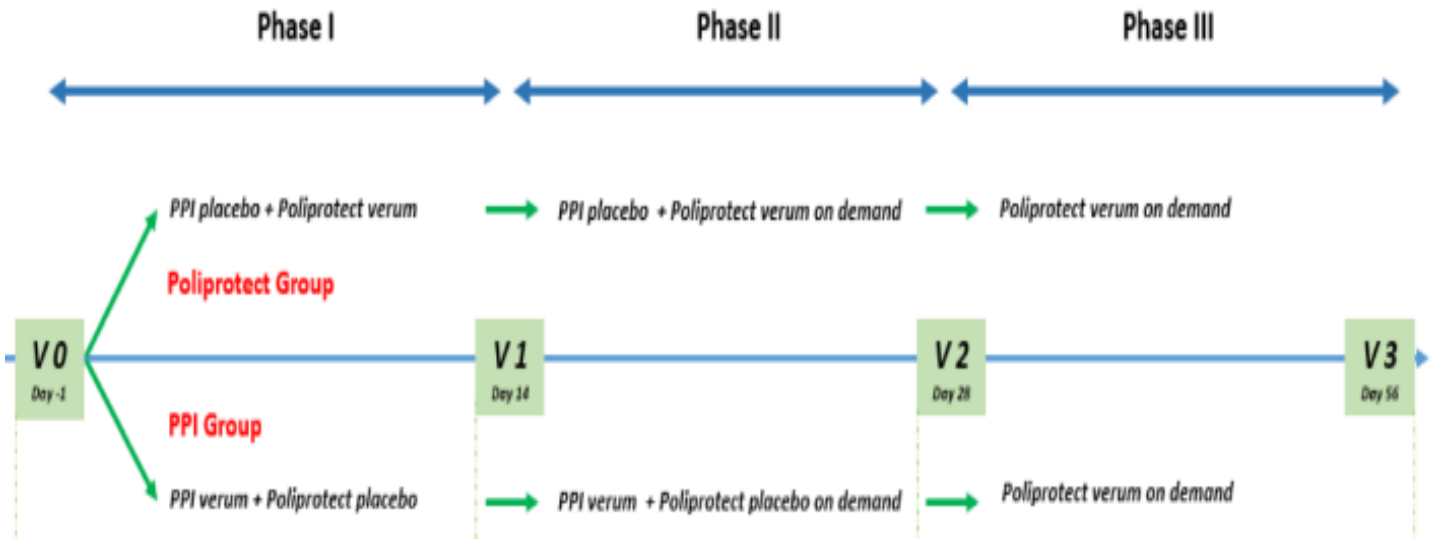
Name (analogue UK)	NL% n=1124	UK% n=2737	Effect on alpha div	Effect on beta-div/prop. of core genera	Decreased taxa	Increased taxa
Proton pump inhibitors	8.27	18.7	8.7*	Yes (1, 2, 3, 4)	s_Eubacterium_hallii (1); s_Eubacterium_ventriosum (1); s_Coprococcus_catus (1); g_Dorea (1); s_Dorea_longicatena (1); f_Ruminococcaceae (1, 3); f_Alcaligenaceae (3); f_Peptococcaceae (3); f_Dehalobacteriaceae (3); f_Coriobacteriaceae (3)	f_Actinomycetaceae (1, 3); g_Actinomyces (1); s_Bifidobacterium_dentium (1); f_Lactobacillaceae (1, 3); g_Lactobacillus (1); f_Streptococcaceae (1, 3); g_Streptococcus (1); s_Streptococcus_anginosus (1); s_Streptococcus_mutans (1); s_Streptococcus_parasanguinis (1); s_Streptococcus_sanguinis (1); s_Streptococcus_salivarius (1); s_Clostridium_bolteae (1); g_Erysipelotrichaceae_noname (1); g_Veillonella (1); s_Veillonella_parvula (1); s_Veillonella_unclassified (1); f_Pasteurellaceae (1, 3); g_Haemophilus (1); s_Haemophilus_parainfluenzae (1); f_Micrococcaceae (3); f_Gemellaceae (3); f_Enterococcaceae (3); f_Fusobacteriaceae (3); f_Enterobacteriaceae (3)
SSRI antidepressants	2.49	6.55		Yes (1, 2, 3)	f_Turicibacteraceae (3); f_Clostridiaceae (3); f_Bifidobacteriaceae (3); f_Peptostreptococcaceae (3); f_.Paraprevotellaceae (3); f_Coriobacteriaceae (3)	
Statins	4.89	25.7		Yes (1, 2, 3)	s_Methanobrevibacter_unclassified (1); g_Coprococcus (1); s_Coprococcus_comes (1); g_Dorea (1); s_Dorea_longicatena (1); f_Peptostreptococcaceae (1); g_Peptostreptococcaceae_noname (1); s_Peptostreptococcaceae_noname_unclassified (1); s_Faecalibacterium_prausnitzi (1)	g_Rothia (1); f_Streptococcaceae (1); g_Streptococcus (1); s_Clostridium_bolteae (1); g_Blautia (1); s_Lachnospiraceae_bacterium_2_1_58FAA (1); s_Lachnospiraceae_bacterium_3_1_57FAA_CT1 (1); s_Coprobacillus_unclassified (1)
Tricyclic antidepressants	0.89	3.77		Yes (1 to 2)	f_Bifidobacteriaceae (1); g_Bifidobacterium (1); f_Streptococcaceae (3); f_Enterobacteriaceae (3); f_Lactobacillaceae (3)	
Vitamin D (cholecalciferol)	1.25	16.5		Yes (1 to 2)		s_Streptococcus_salivarius (1)

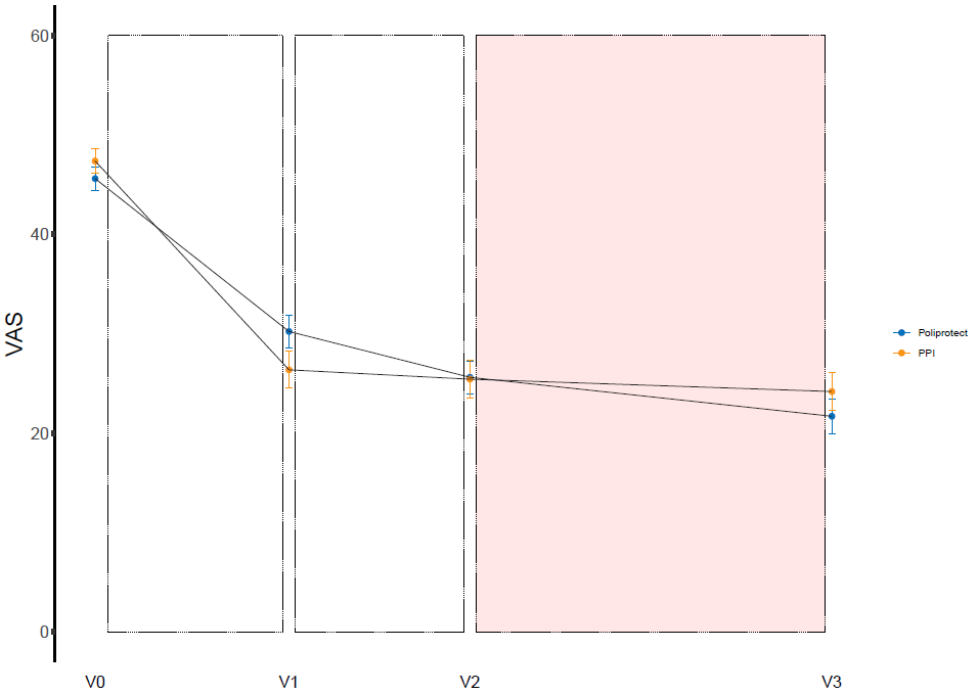
Data extracted from four population studies in three populations: Dutch: (1) Vich Vila *et al*, Nat Communications, 2019,[19] and (2) Zhernakova *et al*, Science, 2016;[16] UK: (3) Jackson *et al*, Nat. Communications, 2018[18] and Belgium: (4) Falony *et al*, Science, 2016.[15] The table includes drugs used by >2.5% of population in either a Dutch (1) or UK (3) study that showed association to the gut microbiome diversity, composition or taxa. As both Dutch studies (1 and 2) have largely overlapping samples, we only present the taxonomic association results from Vich Vila, which were generated using the more recent MetaPhlAn pipeline and included association on all taxonomic levels.
Name (analog UK): Name of the drug in the Dutch study (1). In brackets, the name of the drug in UK study (3) if another group name is used.
%NL and %UK: Proportion of drug users in the corresponding populations.
Effect on alpha div: Evidence that the drug has an effect on alpha diversity of gut microbiome, * decrease.
Effect on beta-div/prop. of core genera: Evidence that the drug has an effect on beta-diversity or the proportion of core genera (proportion of core genera is only addressed in study 4).
Decreased taxa: Bacterial taxa negatively associated with drug use.
Increased taxa: Bacterial taxa positively associated with drug use.
SSRI, selective serotonin reuptake inhibitor.

- **<u>Frazione polisaccaridica</u> aderente all'epitelio da *Aloe vera*, *Malva sylvestris* e *Althaea officinalis***
  per rafforzare la barriera epiteliale

- **Componenti <u>antiacidi dai minerali naturali</u> limestone e nahcolite incorporati nella frazione polisaccaridica**
  per tamponare l'acido sull'epitelio al quale aderisce

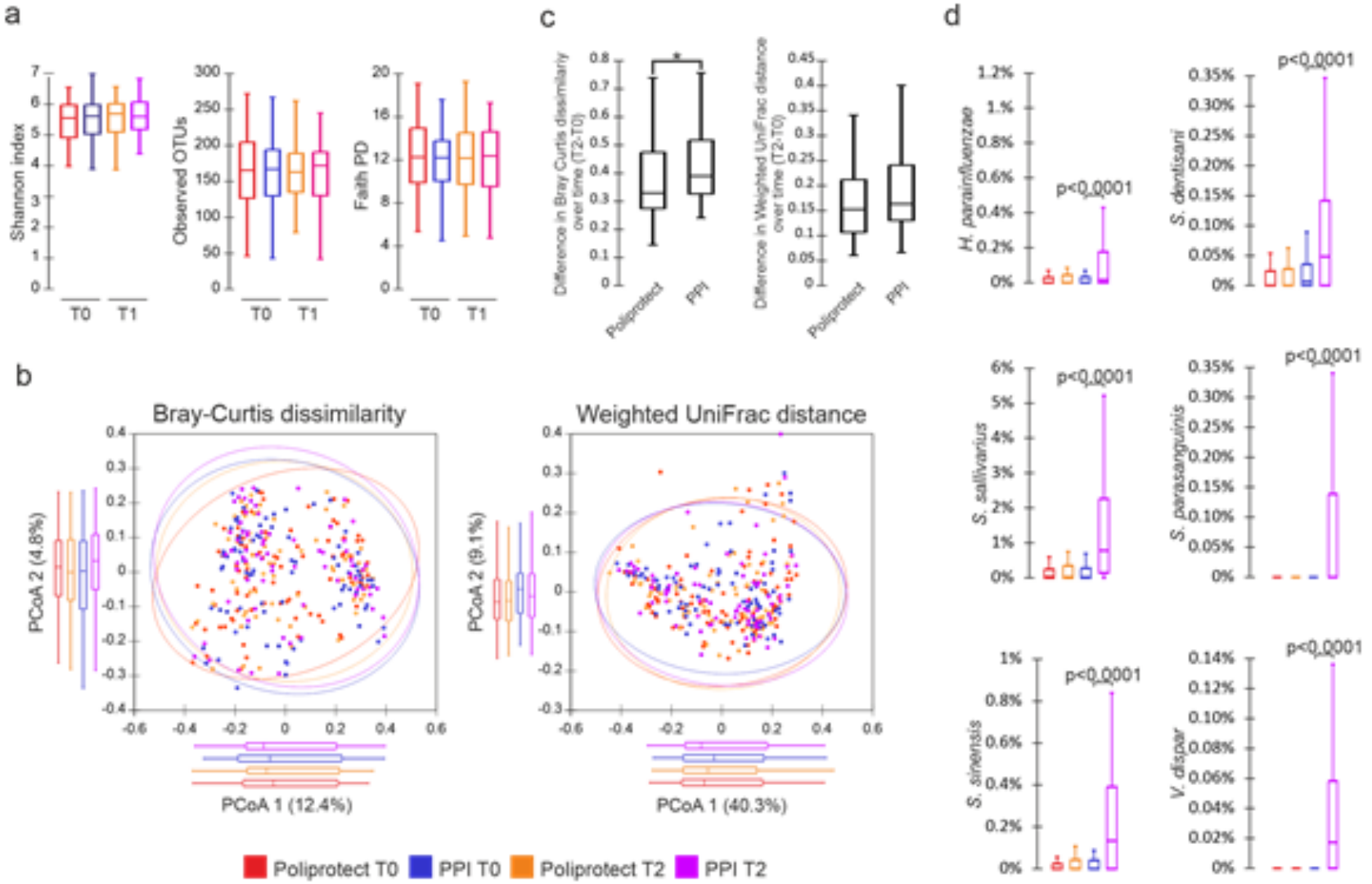
275 pts GERD e/o EPS





Symptom score mean absolute values

Poliprotect, unlike PPI, does not produce a breakdown of the gastric acid antimicrobial barrier.



Corazziari ES, et al. Poliprotect vs Omeprazole in the Relief of Heartburn, Epigastric Pain, and Burning in Patients Without Erosive Esophagitis and Gastroduodenal Lesions: A Randomized, Controlled Trial *Am J Gastroenterol*. 2023 Sep 11. doi: 10.14309/ajg.0000000000002360.

Table 1 Studies conducted to verify the effect of bowel preparation on the microbiota composition

Bachmann R, 2017)

	Year	n	Type	Sample type	Design of the study	Results
Mai *et al.*[45]	2006	5	–	L	Comparing intraluminal microbiota precolonoscopy, shortly after colonoscopy and 6–8 weeks after colonoscopy using PCR-DGGE.	MBP has a significant effect on the luminal gut bacteria, with NO clear trends detected in precolonoscopy and postcolonoscopy samples.
Bucher *et al*[46]	2006	50	PEG	M	Prospective randomised study of 50 patients who did or did not receive MBP before left-sided colorectal surgery for benign or malign disease with the purpose to determine whether MBP is associated with histological alterations in the colon. All patients received intravenous antibiotics prophylaxis.	The most striking alterations associated with MBP were the loss of superficial mucus and epithelial cells. In addition, inflammatory changes, that is, lymphocytes and polymorphonuclear cell infiltration were more prevalent after MBP.
Harrel *et al*[47]	2011	12	PEG	M	Mucosa-associated microbiota analysis via biopsies carried out during sigmoidoscopy. The subjects were split into three groups to compare the impact of MBP or liquid diet for 24 hours with no preparation.	Changes in the microbiota composition after MBP and no changes in both control groups were observed. Reduction in overall mucus-associated microbiota diversity after MBP. Changes in the microbiota composition at the genus level but not at phylum level were found.
O'Brien *et al*[48]	2013	15+5	PEG	L	Analysis of microbiota in stool samples collected 1 month and 1 week before and 1 week, 1 month and 3 months after by PCR-DGGE and HTS.	Short-term non-specific changes in the microbiota with no lasting effect on the composition of the intestinal microbiota.
Jalanka *et al*[49]	2015	23	PEG	L	Randomised study analysing the microbiota in two groups that consumed a bowel preparation treatment (Moviprep) either in two separate doses of 1 L or as a single 2 L dose.	Immediately after the lavage the amount and composition of the microbiota altered drastically. Restoration of the bacteria levels and community composition within 14 days. Consumption of the purgative in a single dose had a more severe effect on the microbiota composition than that of a double dose and notably increased the levels of *Proteobacteria*, *Fusobacteria* and bacteria related to *Dorea formicigenerans*.
Drago *et al.*[50]	2016	10	PEG	L	Study of the microbiota composition immediately after MBP and 1 month thereafter.	MBP has a long-lasting effect on the gut microbiota composition and homeostasis, with a particular decrease in *Lactobacillaceae*, a population of protective bacteria.
Shobar *et al*[51]	2016	18	½ PEG ½ NaCl	L+M	The effect of bowel preparation on the mucosa-associated and luminal colonic microbiota in healthy subjects and IBD patients by harvesting the sampling during an unprepped sigmoidoscopy and 1 week later during a prepped colonoscopy using HTS. No probiotics or antibiotics within the past 3 months before the study.	MBP massively affected the composition and diversity of the faecal and luminal microbiota in the short term. Luminal samples were similar to mucosal samples immediately post MBP. Both the luminal and mucosal compartments of the gut microbiota are affected.

DGGE, denaturing gradient gel electrophoresis; HTS, high-throughput sequencing; M, mucus-associated bacteria; L, luminal content bacteria; MBP, mechanical bowel preparation; Type, type of bowel preparation: polyethylene glycol solutions (PEG) or saline solutions (NaCl).

Preparations for colonoscopy

-remove intestinal mucus and flush-out luminal bacteria > altering microbiota balance.
-alter quality and production of the protective mucus layer
-convey oxygen into the lumen, thus negatively affecting anaerobes populations (Proteobacteria);
-increase in pH;
-accelerate intestinal transit time, possibly reducing availability of nutrients (e.g. fibres) for bacterial metabolism

(Drago L, 2019)

A drastic change in the ratio of Gram-positive to Gram-negative species. Similar changes were observed when studying the microbiota in diarrhoea diseases.

(Bachmann R, 2017)

Conflicting results (no unique pattern of microbial modification, duration of the effects, restitutio ad integrum, etc.) are probably due to the small number of subjects, the inclusion of healthy and diseased subjects, the lack of a non-procedure control group, and a lack of analytical depth in these studies. Different ways of sample collection

Antibiotics

Different classes > very different effects on the gut microbiota

Beta-lactamics, fluoro-quinolones, glycylcyclines, lincosamide, nitroimidazole, and various combinations of antibiotics > alteration of the gut microbiota composition with a **reduction of autochthonous taxa** and an increase of **potentially pathogenic bacteria**, such as Enterobacteriaceae.

In contrast, Bifidobacteria, Faecalibacterium prausnitzii and Lactobacilli, seem to be reduced after antibiotic treatment.

(Ponziani FR, 2016)

Table 1. Impact of different antimicrobial classes on gut microflora and immunity; adapted from references [13, 37, 48]

	Changes in microbial composition			Emergence of drug-resistant bacteria		Effects on gut immunity
	Gram-positive	entero-bacteria	anaerobes	Gram-positive	entero-bacteria	
Ceftriaxone	↑	↓↓	–	–/↑	↑	sIgA ↓
Amoxicillin ± BLI	↑	↑	–	–	–	APC ↓ AMP ↓
Ciprofloxacin	–	↓↓	–	–	↑	AMP ↓
Clindamycin	↑	↑	↓↓	↑	↑	?
Metronidazole	–	–	–	–	–	AMP ↑
Metronidazole + clarithromycin	↓	↑	↓	↑	↑	AMP ↓* IIC ↓
Vancomycin	↓/↑	–	↓	↑	↑	AMP ↓* ILF ↓

↓: Reduction; ↓↓: strong reduction; ↑: increase; ↑↑: strong increase; –: not relevantly altered; ↓/↑: discrepant reports; ?: not reported; *: in combination with other antimicrobial substances.

APC = Antigen presenting capacity; AMP = antimicrobial peptides (e.g. LL-37, REG3-γ); BLI = beta-lactamase inhibitor; sIgA = secretory immunglobulin A; IIC = intestinal innate immune cells; ILF = intestinal lymphoid follicles.

(Lange K, 2016)

Rifaximin

Non-aminoglycoside, semisynthetic, non-systemic antibiotic derived from rifamycin SV. Originally licensed in Italy as polymorphic form α in 1985.

(Tursi A, 2018)

Rifaximin inhibits bacterial protein synthesis by binding to the β-subunit of bacterial DNA-dependent RNA polymerase.
Strong activity (bactericidal and bacteriostatic) against Gram-positive and Gram-negative bacteria, both aerobic and anaerobic

Intrinsic **anti-inflammatory activity (**down-regulates the release of pro-inflammatory cytokines and TNF production). It reduces gut inflammation modulating the activity of the inflammasome NLRP3 (nucleotide-binding oligomerization domain leucine rich repeat and pyrin domain containing protein 3).

Rifaximin can modulate **the bacterial adhesion** to the intestinal mucosa reestablishing an effective **epithelial mucosal barrier** and, consequently, the **intestinal permeability**

(Ponziani FR, 2016)

Rifaximin reduces the total load of the gut microbiota

Eubiotic effects: Rifaximin promotes the growth of beneficial bacteria, such as Bifidobacteria and Lactobacilli

Table 1 Studies investigating the effects of rifaximin on gut microbiota composition

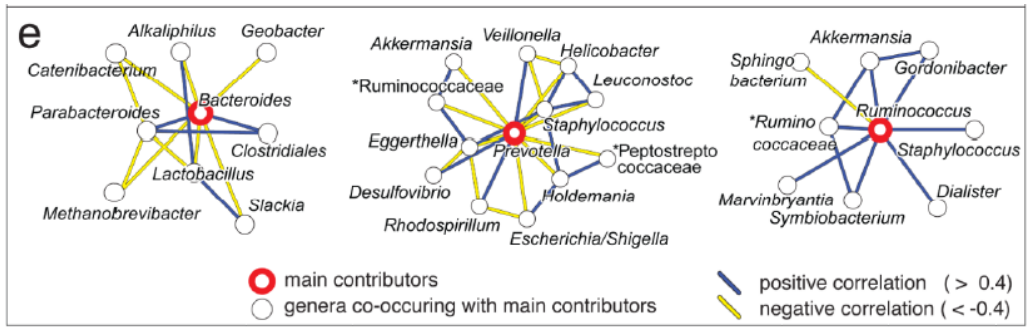
Ref.	Patients/model	Technique	Rifaximin dose	Changes in gut microbiota after rifaximin
Brigidi *et al*[77], 2002	12 pts UC	Standard bacteriological procedures	1800 mg/d, 3 cycles of 10 d followed by 25 d of wash-out	*Enterococci*: < *Coliform*: = *Bifidobacteria*: > *Lactobacilli*: < *Clostridium perfrigens*: > than < *Bacteroides*: unpredictable variations *Candida*: = Overall composition: not explored
Maccaferri *et al*[78], 2010	4 pts colonic active CD	Continuous culture colonic model system, FISH, quantitative PCR, PCR-denaturing gradient gel electrophoresis	1800 mg/d	Bifidobacterium: > Atopobium: > *Faecalibacterium prausnitzii*: > Overall composition: =
Bajaj *et al*[76], 2013	20 pts HE	454 pyrosequencing	1100 mg/d	Overall composition: =
Xu *et al*[79], 2014	Rat model of visceral hyperalgesia	Quantitative PCR, 454 pyrosequencing	150 mg/kg, twice daily	Overall composition: = *Lactobacillus*: > Clostridiaceae, Erysipelotrichaceae, and Peptostreptococcaceae: < Overall composition: 84% reduction in bacterial load
Soldi *et al*[80], 2015	15 pts non-C IBS	Real-time PCR, Illumina pyrosequencing	1650 mg/d for 14 d	Faecalibacterium prausnitzii: > Clostridiaceae, Streptococcaceae: < Bacteroidaceae, Prevotellaceae: > Overall composition: =
Ponziani *et al*[81], 2016	20 pts CD, UC, non-C IBS, DD, HE	454 pyrosequencing	1200 mg/d for 14 d	*Lactobacillus*: > *Roseburia, Haemophilus, Veillonella* and *Streptococcus*: < Overall composition: =

Pts: Patients; UC: Ulcerative colitis; CD: Crohn's disease; FISH: Fluorescence in situ hybridization; PCR: Polymerase chain reaction; HE: Cirrhosis with hepatic encephalopathy; non-C IBS: Irritable bowel syndrome without constipation; DD: Diverticular disease.

(Ponziani FR, 2016)

(Arumugam M, Nature 2011)

Diet and Enterotypes



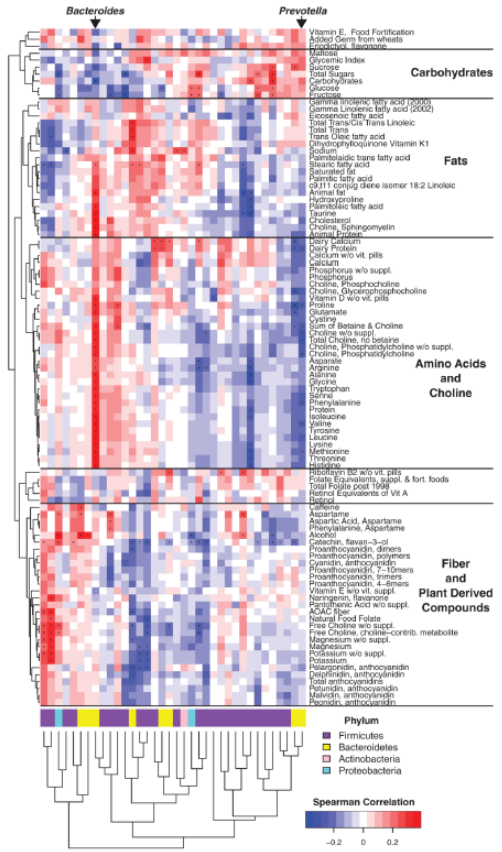
Bacteroides enterotype: associated with animal protein, a variety of aminoacids, and saturated fats > meat consumption (Western diet) characterized this enterotype.

Prevotella enterotype: associated with carbohydrates and simple sugars > diet more typical of agrarian societies

Vegetarian diets: dominance of Firmicutes and Bacteroidetes

Diet rich in **protein and fats:** abundance of bile-tolerant species (Bacteroides, Bilophila and Alistipes) and a suppression of Firmicutes

(David, 2014)
(Forouhi, 2018)



Wu GD, et al. Science. 2011

Early in **infancy,** the gut microbiota is enriched in genes involved in the digestion of oligosaccharides (breast milk); later (introduction of solid foods) it is enriched in genes associated with the metabolism of polysaccharides and vitamins

(Backhed et al. 2015).

The method of feed affects microbial composition in infant microbiota.

Breast-fed infants: overgrowth of Actinobacteria and an inhibition of Firmicutes and Proteobacteria. Breast milk includes oligosaccharides that can be metabolized effectively by these bacterial species, resulting in an increase in SCFAs > increased expression of IgG.

(Thompson, 2015)

Formulafed infants: increasing of Clostiridia, Streptococci, Bacteroides and Enterobacteria

(Azad, 2013) (Lee, 2015)

The halophilic archae such as Halorubrum koreense, Halorubrum alimentarium, Halorubrum saccharovorum, and Halococcus morrhuae were isolated from Korean, not IBS, subjects. It could be due to Koreans'high-salt food intake.

(Nam, 2008)

(Bibbò S, 2016)

High-fiber diet vs High-fat diet

Table I. Effect of carbohydrates on gut microbiota composition.

Resistant starch 2	↑ Ruminococcus spp, Eubacterium rectale, Bifidobacterium adolescentis
Resistant starch 3	↑ Eubacterium rectale, Roseburia spp, Ruminococcus bromii
Resistant starch 4	↑ Parabacteroides diastasonis
	↓ Eubacterium rectale, Ruminococcus bromii
High soluble fiber diet	↑ Bacteroides spp., C. leptum group, and E. rectale
Complex carbohydrates	↑ Bifidobacteria spp, Prevotella spp
Low fiber diet	↓ Roseburia spp, Eubacterium rectale

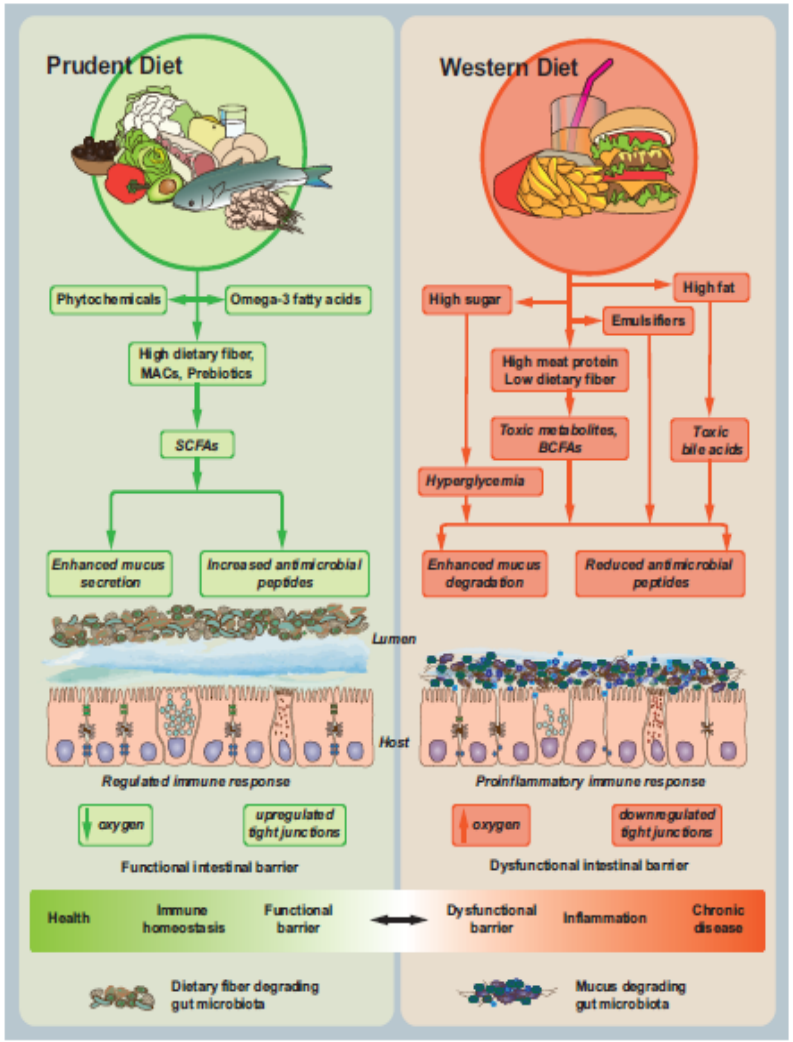
Table II. Effect of oligosaccharides on gut microbiota composition.

Fructo-oligosaccharides	↑ Bifidobacterium spp, Lactobacillus spp
Inulin	↑ Bifidobacterium spp, Lactobacillus spp
Fructans	↓ Bacteroides spp, Clostridium spp
Galacto-oligosaccharides	↑ Bifidobacterium spp, F. prausnitzii
Arabinoxylan-oligosaccharides	↑ Bifidobacterium spp

Table III. Effect of high-fat diet on gut microbiota composition.

Safflower oil (ω-6 PUFA)	↑ Firmicutes, Actinobacteria, Proteabacteria
	↓ Bacteroides
PUFA	↓ Lactobacillus spp
ω -6 PUFA	↓ Bifidobacteria spp
↓PUFA	↑ L. casei Shirota
MUFA	↓ Bifidobacteria spp
High-fat diet	↑ delta-proteabacteria spp, Bilophila wadsworthia
	↓ Roseburia spp

RS 1 plant cell wall polymers (grains, seeds, legumes)
RS 2 granular structure (raw potatoes, green bananas)
RS3 retro-gradation resulting from heating and cooling (cooked potatoes and rice)
RS4 chemical cross-linking



(Makki K, 2018)

Prebiotics

- **Oligosaccharide** (XOS, GOS, lactulose, inulin, FOS, TGOS)
- **Polysaccharides** (Algae polysaccharides)
- **Polyphenols isolated from fruits** (black raspberries and blueberries)*
- **Polypeptide polymers** (Poly-gamma-glutamate)

Prebiotics can help to:

- correct dysbiosis by promoting positive alterations in the microbial flora, for instance **enhancing the proliferation of gut bacteria including *Bifidobacterium*** ***(Paineau, 2008; Silk, 2009).***
- regulate immunity
- improve intestinal barrier function
- increase mineral absorption
- lower blood lipid levels
- …….. ***(Chong PP, 2019)***

*inhibit the growth of pathogenic bacteria

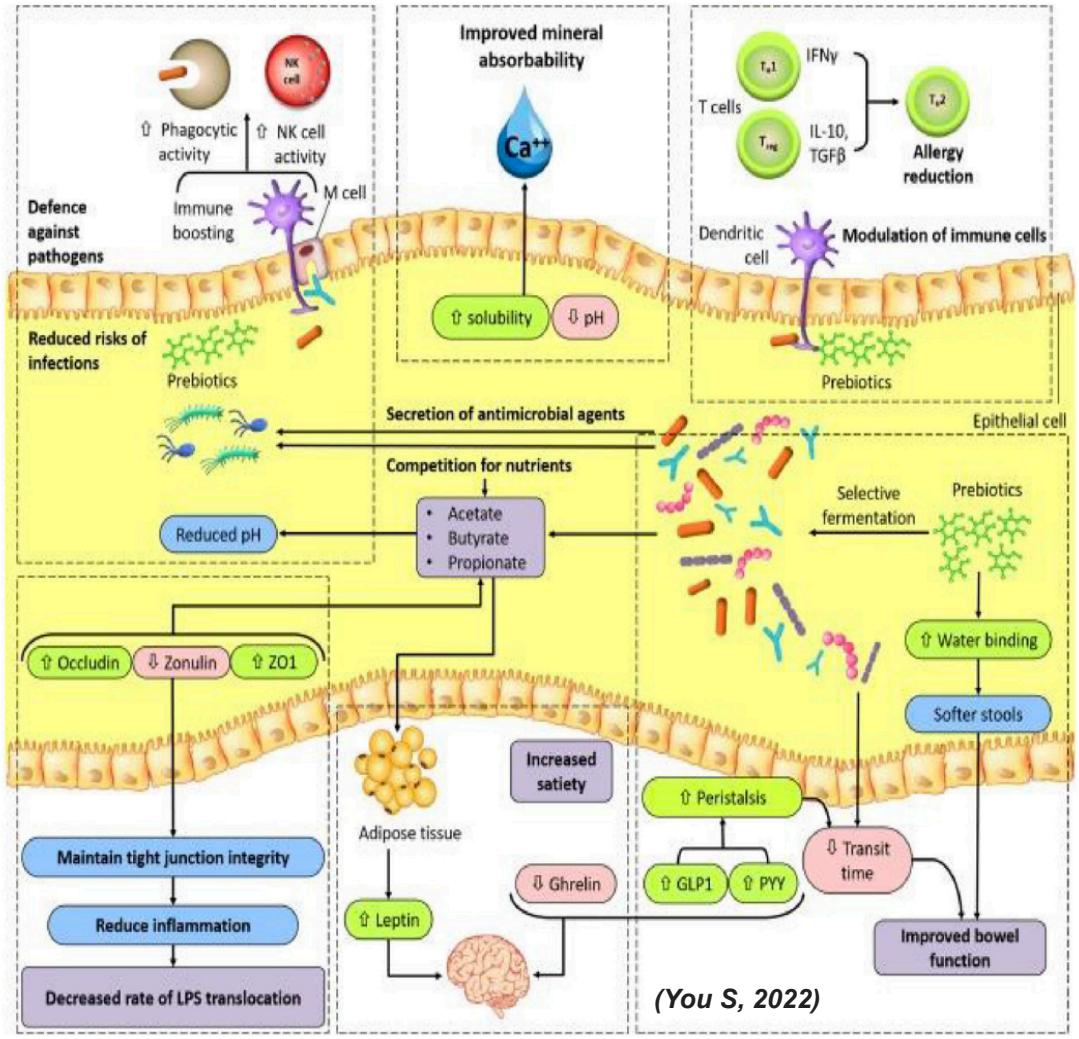
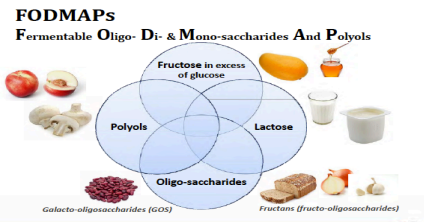


FIGURE 2
A model for possible mechanisms of prebiotic benefits to human health (66). GLP1, glucagon like peptide1; M cell, microfold cell; NK, natural killer; PYY, peptide YY; TGFβ, transforming growth factor-β; TH1, TH2, type 1 T helper, type 2 T helper; Treg, regulatory T; ZO1, zonula occludens 1.

Table 2. Randomized controlled trials investigating the effect of low FODMAP diet on gut microbiota and microbiota metabolites.

Authors, Years	Study Design and Duration	Diagnostic Criteria and Materials	Gut Microbiota		Microbiota Metabolites	
			Microbial Analysis	Findings	Methods	Findings
Halmos EP et al., 2015 [44]	RCT, crossover (single blind), 3 weeks	Rome III IBS and healthy controls. LFD vs. ordinary diet. IBS $n = 27$, Healthy controls $n = 6$	qPCR	Lower absolute abundance of Bifidobacteria, *F. prausnitzii*, Clostridium Cluster IV and lower relative abundance *Akkermansia muciniphila* in LFD than ordinary diet. Lower total bacteria in LFD at baseline. Greater diversity Clostridium Cluster XIV in LFD than ordinary diet at baseline	Gas liquid chromatography	No difference in total or individual stool SCFAs in LFD compared to ordinary diet, baseline.
McIntosh K, et al., 2017 [53]	RCT (single blind), 3 weeks	Rome III IBS. LFD $n = 19$, HFD $n = 18$	16S rRNA sequencing (Illumina)	Higher richness of Actinobacteria, Firmicutes, Clostridiales in LFD than HFD. No difference in α- or β-diversity after LFD vs. baseline. Higher richness in LFD than HFD. Higher abundance of Clostridiales family XIII *Incertae sedis* spp. and *Porphyromonas* spp. in LFD than baseline. Lower abundance of Propionibacteriaceae, Bifidobacteria in LFD than baseline.	Mass spectroscopy	Urinary metabolomic profile at baseline in LFD vs. HFD showed no difference but separated after intervention. Three metabolites (histamine, p-hydroxybenzoic acid and azelaic acid) discriminated groups. Correlations between metabolite concentrations and abundance of various taxa.
Staudacher HM et al., 2012 [54]	RCT (unblind), 4 weeks	Rome III IBS. LFD $n = 19$, Habitual diet $n = 22$	Fluorescence in situ hybridization	Lower abundance of Bifidobacteria in LFD than habitual diet. No difference in total abundance of other groups (*F. prausnitzii*)	Gas liquid chromatography	No difference in total or individual stool SCFAs in LFD compared to habitual diet
Staudacher HM et al., 2017 [52]	RCT (single blind), 4 weeks	Rome III IBS. LFD $n = 51$, Sham $n = 53$	qPCR	Lower abundance of Bifidobacteria in LFD compared to sham	Gas liquid chromatography	Lower stool acetate concentration in LFD compared to control

IBS: irritable bowel syndrome; RCT, randomized controlled trial; LFD, low FODMAP diet; HFD, high FODMAP diet; SCFA, short chain fatty acid; qPCR, quantitative polymerase chain reaction. All differences reported are significant ($p < 0.05$).



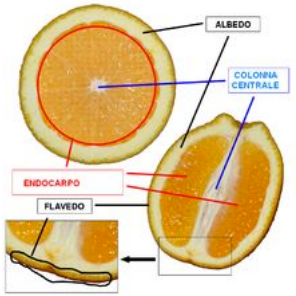


TABLE 1 Different kinds of emerging prebiotics.

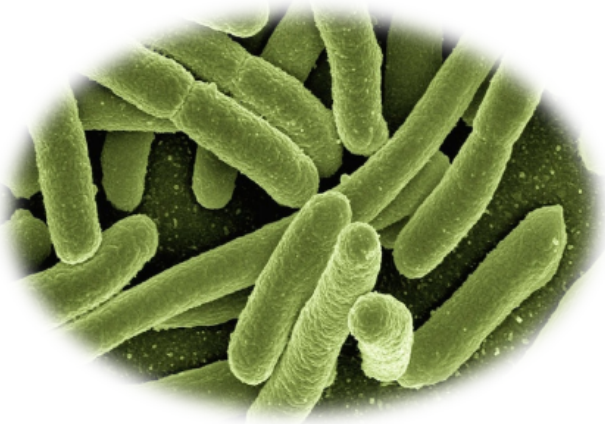
Prebiotic	Component	Source	Function	References
Polyphenol	Blueberry polyphenol extract	Blueberry	Reduce weight and normalize lipid metabolism	(22)
	Wine grape seed flour	Grape seed	Intestinal permeability is enhanced, and adipocyte gene expression is altered to inhibit high-fat-induced obesity and inflammation.	(56)
	Orange albedo	Orange	Stimulates the growth, reproduction, and metabolism of *Lactobacillus acidophilus* and *Lactobacillus animalis*	(57)
	Catechin and punicalagin	Fermented pomegranate juice	Increases antioxidant capacity and improves survival of lactic acid bacteria	(58)
Polypeptide polymers	Poly-gamma-glutamate (PGA)	Bacillus fermentation	Increases abundance of *Lactobacillus* and reduces abundance of *Clostridium*, helping to regulate the intestinal microbiota.	(59)
Polysaccharides	Algae polysaccharides	Algae	Improves the activity of some beneficial flora and stimulates the production of functional metabolites in the intestinal microbiota.	(60)
	Lotus seed resistant starch (LRS3-20%)	Lotus seed	Shows high probiotic activity against *Bifidobacterium* and *Lactobacillus acidophilus*.	(61)
	Longan pulp polysaccharides	Logan	Promotes the growth of *Lactobacillus plantarum*, *Lactobacillus bulgaricus* and *Lactobacillus fermentum*	(62)

(You S, 2022)

Probiotics

«Living microorganisms (bacteria and yeast), which are friendly to the gut and confer health benefits to the host when given in adequate amounts»

- ***Bifidobacterium* ++** *(B. infantis*, *B. lactis*, *B. bifdum*, *B. Animalis)*
- ***Lactobacillus* +** (*L. plantarium*, *L. rhamnosus*, *L. casei*, *L. reuteri*)
- ***Escherichia*** (*E. coli Nissle 1917*)
- ***Saccharomyces*** (*S. cerevisiae*, *S. boulardi*)
- Indications: IBS, IBD, gastroenteritis, diarrhoea…
- Single strain / Multi-strain ?
- Symbiotics?
- Dosage and treatment duration
- Effects (short termed)



(Herndon CC, Kaohsiung J Med Sci. 2020)

Efficacy, Safety, and Concerns on Microbiota Modulation, Antibiotics, Probiotics, and Fecal Microbial Transplant for Inflammatory Bowel Disease and Other Gastrointestinal Conditions: Results from an International Survey

Tommaso Lorenzo Parigi [1,2], Sophie Vieujean [3], Kristine Paridaens [4], Kira Dalgaard [5], Laurent Peyrin-Biroulet [6,7,8,9,10,11] and Silvio Danese [1,2,*]

Microorganisms 2023, *11*, 2806.

Microbiota modulation remains a relatively underutilized clinical practice, with limited adoption in healthcare settings…while there is consensus on the relevance of the gut microbiota in IBD and other GI disease pathogenesis

European guidelines on microscopic colitis: United European Gastroenterology and European Microscopic Colitis Group statements and recommendations 2020

Is there a role for probiotics in MC?
We recommend against use of probiotics for treatment of MC. LE: low; GR: strong against; agreement: 100%, strong consensus

Italian guidelines for the management of irritable bowel syndrome 2022

Should probiotics be used to treat global IBS symptoms?	We recommend for the use of probiotics, as a group, for improving overall symptoms or abdominal pain	Yes	Low	Conditional

European society of neurogastroenterology and motility guidelines on functional constipation in adults 2019

Insufficient evidence to recommend FMT for routine treatment of functional constipation
- Level of evidence: Low
- Recommendation: Weak
- Level of agreement: 100%

Limited evidence for a positive effect of probiotics on acceleration of intestinal transit time and improvements in stool frequency
- Level of evidence: Low
- Recommendation: Weak
- Level of agreement: 100%

Functional bowel disorders with diarrhoea: Clinical guidelines of the United European Gastroenterology and European Society for Neurogastroenterology and Motility

UEG/ESNM recommends FOR the use of probiotics that may improve overall symptoms and diarrhoea in some patients with IBS-D, but there is no evidence for FDr.	Yes	Low	Conditional

British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults

…probiotic therapy may have modest benefits in UC, but should not be routinely used. No evidence of any benefit for these treatments in Crohn's disease

Efficacy of Probiotics in Irritable Bowel Syndrome: Systematic Review and Meta-analysis

Gastroenterology 2023;165:1206–1218

Vivek C. Goodoory,[1,2,*] Mais Khasawneh,[1,2,*] Christopher J. Black,[1,2] Eamonn M. M. Quigley,[3] Paul Moayyedi,[4] and Alexander C. Ford[1,2]

82 trials; >10000 pts.

Efficacy of Probiotics Persistence of **Global Symptoms** in IBS

BENEFIT

Moderate certainty for Escherichia strains,

Low certainty for Lactobacillus strains and Lactobacillus plantarum 299V,

Very low certainty for combination probiotics and Bacillus strains.

Paucity of trials of probiotics in IBS-C, meaning their use in this subtype is less evidence-based

	Number of trials	Number of patients	RR of persistence of global symptoms (95% CI)	*P* value for the difference	I^2 (*P* value for χ^2)
All combination probiotics	32	3369	0.78 (0.71–0.87)	<.001	71% (<.001)
VSL#3	4	155	0.78 (0.53–1.16)	.23	47% (.13)
Lactobacillus paracasei ssp paracasei F19, Lactobacillus acidophilus La5, and *Bifidobacterium lactis Bb12*	3	269	0.92 (0.76–1.11)	.38	14% (.31)
Enterococcus faecalis DSM16440 and *Escherichia coli DSM17252*	2	686	0.71 (0.33–1.51)	.37	97% (<.001)
LacClean Gold S	2	130	0.59 (0.37–0.93)	.02	0% (.56)
Duolac 7s	2	76	0.62 (0.43–0.89)	.009	0% (.62)
All *Lactobacillus* strains	16	1498	0.84 (0.72–0.98)	.03	69% (<.001)
Lactobacillus plantarum 299V	5	453	0.73 (0.59–0.92)	.007	59% (.04)
All *Bifidobacterium* strains	5	1161	0.82 (0.67–1.02)	.07	74% (.004)
Bifidobacterium bifidum MIMBb75	2	565	0.69 (0.46–1.04)	.07	83% (.01)
All *Bacillus* strains	3	216	0.44 (0.34–0.57)	<.001	0% (.48)
All *Saccharomyces* strains	2	469	0.94 (0.80–1.11)	.49	0% (.86)
All *Escherichia* strains	2	418	0.86 (0.79–0.93)	<.001	0% (.78)
All *Blautia* strains	1	366	0.93 (0.84–1.03)	.15	N/A
All *Clostridium* strains	1	200	0.80 (0.64–0.99)	.04	N/A
All *Streptococcus* strains	1	54	0.72 (0.53–0.99)	.04	N/A
Patients with IBS-D					
All combination probiotics	13	1272	0.78 (0.67–0.92)	.002	69% (<.001)
VSL#3	2	49	0.42 (0.04–4.85)	.49	82% (.02)
Duolac 7s	2	76	0.62 (0.43–0.89)	.009	0% (.62)
All *Lactobacillus* strains	4	157	0.57 (0.36–0.89)	.01	27% (.25)
All *Saccharomyces* strains	2	169	0.99 (0.76–1.28)	.92	0% (.81)
All *Clostridium* strains	1	200	0.80 (0.64–0.99)	.04	N/A
All *Blautia* strains	1	202	0.94 (0.82–1.08)	.36	N/A
All *Escherichia* strains	1	54	1.00 (0.57–1.74)	1.00	N/A
All *Bifidobacterium* strains	1	44	0.64 (0.36–1.16)	.14	N/A
All *Bacillus* strains	1	40	0.57 (0.31–1.05)	.07	N/A
Patients with IBS-C					
All combination probiotics	4	295	1.01 (0.89–1.14)	.87	8% (.35)
All *Saccharomyces* strains	1	180	0.82 (0.62–1.08)	.16	N/A
All *Blautia* strains	1	164	0.92 (0.78–1.07)	.26	N/A
All *Escherichia* strains	1	35	0.84 (0.41–1.73)	.64	N/A

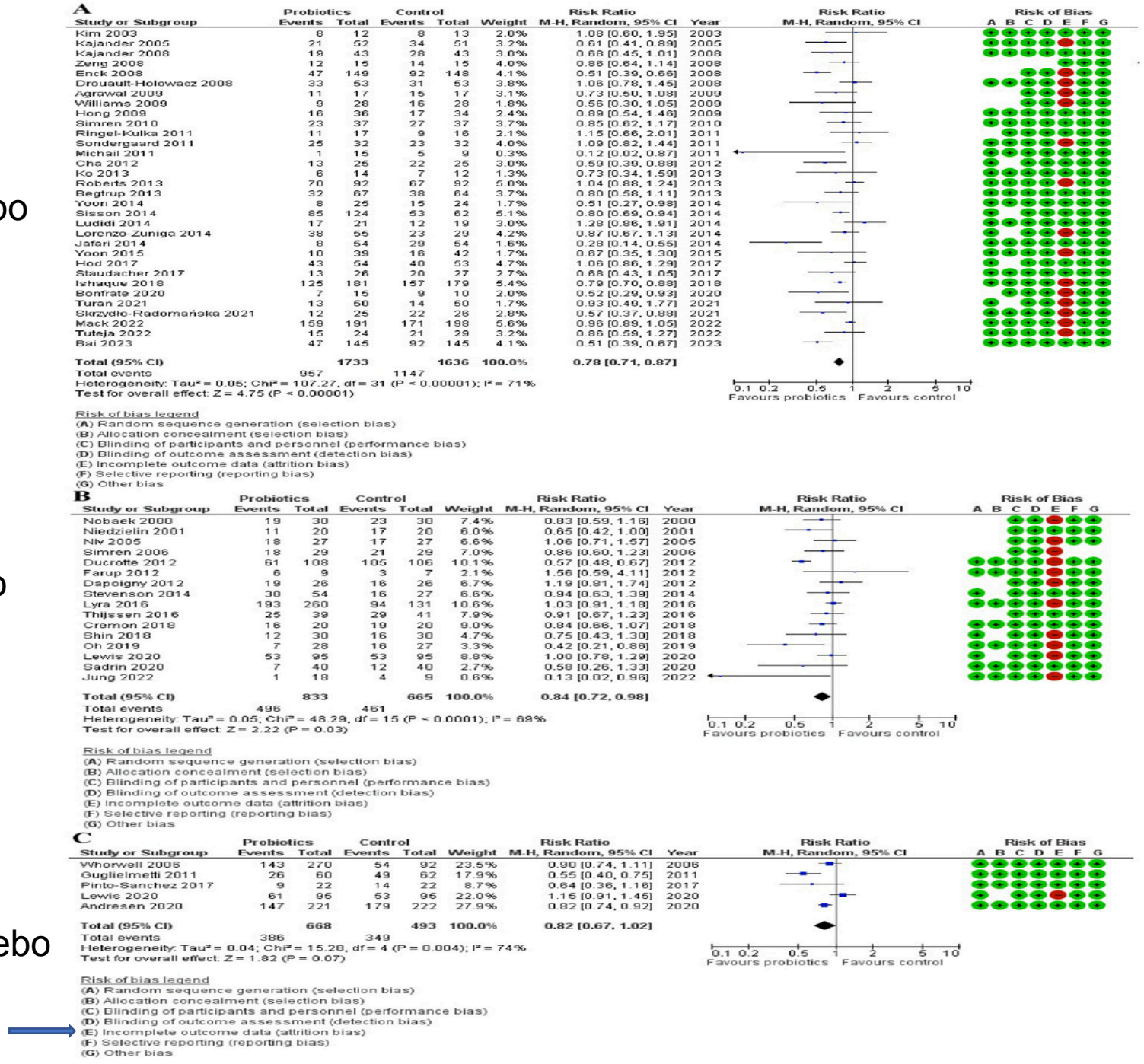
CI, confidence interval; IBS, irritable bowel syndrome; IBS-C, IBS with constipation; IBS-D, IBS with diarrhea; N/A, not applicable; RR, relative risk.

Persistence of Global IBS Symptoms

Combination Probiotics vs. placebo

Lactobacillus strains vs. placebo

Bifidobacterium strains vs. placebo



Efficacy of Probiotics in Irritable Bowel Syndrome: Systematic Review and Meta-analysis

Gastroenterology 2023;165:1206–1218

Vivek C. Goodoory,[1,2,*] **Mais Khasawneh**,[1,2,*] Christopher J. Black,[1,2] Eamonn M. M. Quigley,[3] Paul Moayyedi,[4] and Alexander C. Ford[1,2]

Efficacy of Probiotics in Persistence of **Abdominal Pain** in IBS

<u>BENEFIT</u>

Low certainty for Saccharomyces cerevisiae I-3856 and Bifidobacterium strains,

Very low certainty for combination probiotics, Lactobacillus, Saccharomyces, and Bacillus strains.

	Number of trials	Number of patients	RR of persistence of abdominal pain (95% CI)	*P* value for the difference	I^2 (*P* value for χ^2)
All combination probiotics	32	3469	0.72 (0.64–0.82)	<.001	72% (<.001)
VSL#3	4	144	0.87 (0.64–1.18)	.36	19% (.29)
Lactobacillus paracasei ssp paracasei F19, Lactobacillus acidophilus La5, and Bifidobacterium lactis Bb12	3	269	0.97 (0.83–1.14)	.74	0% (.91)
Enterococcus faecalis DSM16440 and *Escherichia coli DSM17252*	2	686	0.67 (0.37–1.22)	.19	92% (<.001)
Bifidobacterium animalis DN173 010, Streptococcus thermophilus, and *Lactobacillus bulgaricus*	2	308	0.89 (0.70–1.12)	.32	33% (.22)
LacClean Gold S	2	130	0.76 (0.52–1.10)	.14	0% (.72)
Duolac 7s	2	76	0.55 (0.18–1.65)	.28	73% (.05)
All *Lactobacillus* strains	11	1183	0.59 (0.45–0.76)	<.001	73% (<.001)
Lactobacillus plantarum 299V	3	220	0.45 (0.15–1.35)	.16	78% (.010)
All *Saccharomyces* strains	9	1744	0.75 (0.57–0.99)	.04	89% (<.001)
Saccharomyces cerevisiae I-3856	5	1482	0.64 (0.45–0.90)	.01	93% (<.001)
Saccharomyces boulardii	3	232	1.21 (0.87–1.67)	.26	44% (.17)
All *Bifidobacterium* strains	3	389	0.78 (0.64–0.95)	.02	37% (.20)
All *Bacillus* strains	3	212	0.33 (0.23–0.47)	<.001	10% (.33)
All *Blautia* strains	1	366	0.92 (0.79–1.06)	.25	N/A
All *Escherichia* strains	1	298	0.87 (0.79–0.95)	.002	N/A
All *Clostridium* strains	1	200	0.93 (0.76–1.14)	.49	N/A

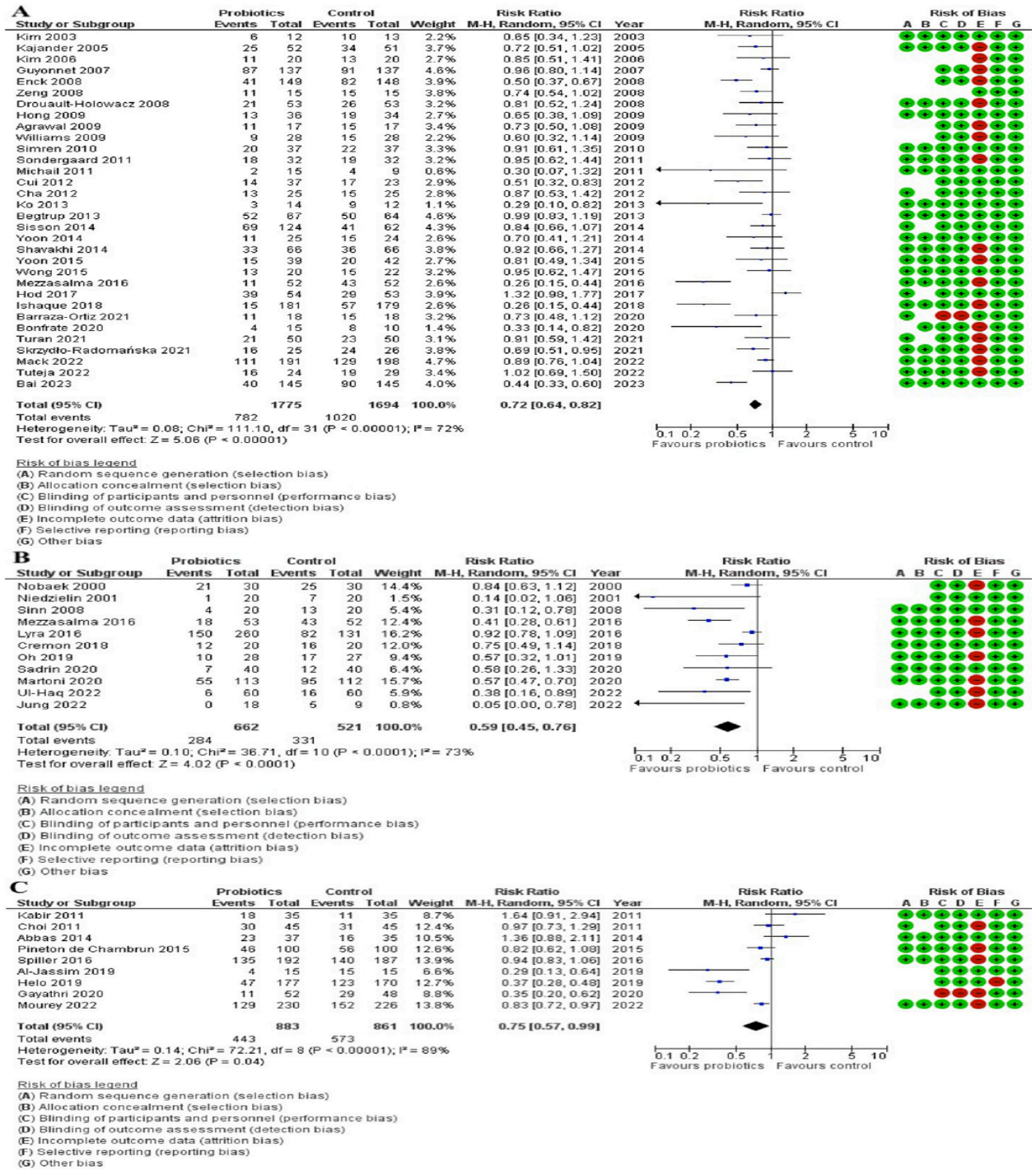
CI, confidence interval; N/A, not applicable; RR, relative risk.

Abdominal pain in IBS

Combination Probiotics vs. placebo

Lactobacillus strains vs. placebo

Saccharomyces strains vs. placebo



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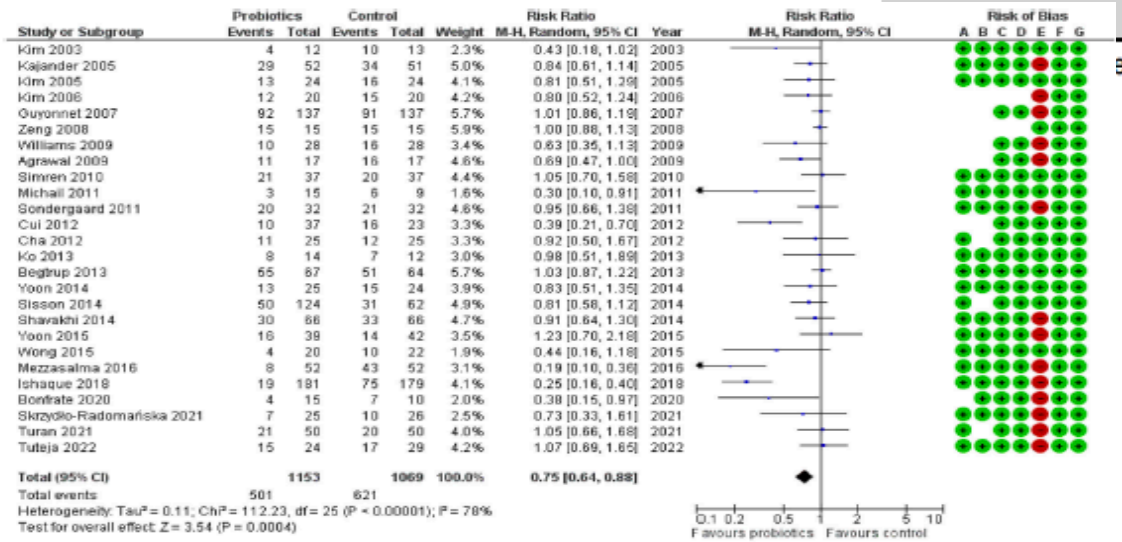
Efficacy of Probiotics Persistence of **Abdominal Bloating or Distension** in IBS

	Number of trials	Number of patients	RR of persistence of abdominal bloating or distension (95% CI)	*P* value for the difference	I^2 (*P* value for χ^2)
I combination probiotics	26	2222	0.75 (0.64–0.88)	<.001	78% (<.001)
VSL#3	5	192	0.65 (0.42–1.02)	.06	52% (.08)
Lactobacillus paracasei ssp paracasei F19, Lactobacillus acidophilus La5, and *Bifidobacterium lactis Bb12*	3	269	1.02 (0.89–1.18)	.78	0% (.92)
Bifidobacterium animalis DN173 010, Streptococcus thermophilus, and *Lactobacillus bulgaricus*	2	308	0.86 (0.60–1.26)	.45	71% (.06)
LacClean Gold S	2	130	0.98 (0.67–1.45)	.94	8% (.30)
Duolac 7s	2	76	0.94 (0.61–1.47)	.80	0% (.88)
All *Lactobacillus* strains	5	723	0.67 (0.43–1.04)	.07	88% (<.001)
All *Saccharomyces* strains	5	641	0.87 (0.64–1.17)	.34	60% (.04)
Saccharomyces boulardii	3	232	0.97 (0.77–1.23)	.80	0% (.79)
All *Bacillus* strains	3	212	0.41 (0.31–0.56)	<.001	0% (.83)
All *Clostridium* strains	1	200	0.97 (0.81–1.16)	.75	N/A
All *Bifidobacterium* strains	1	122	0.66 (0.49–0.88)	.005	N/A

erval; N/A,

Combination Probiotics vs. placebo



LIMITATIONS

Few trials were low risk of bias and there was heterogeneity between studies and evidence of publication bias.

Some combinations of probiotics or strains may be beneficial in IBS, but certainty in the evidence (GRADE) is low or very low

United European Gastroenterology Journal
0(0) 1–10

DOI: 10.1177/2050640617736478
journals.sagepub.com/home/ueg
SAGE

Effect of *Lactobacillus paracasei* CNCM I-1572 on symptoms, gut microbiota, short chain fatty acids, and immune activation in patients with irritable bowel syndrome: A pilot randomized clinical trial

Cesare Cremon[1], Simone Guglielmetti[2], Giorgio Gargari[2], Valentina Taverniti[2], Anna Maria Castellazzi[3], Chiara Valsecchi[3], Carlotta Tagliacarne[3], Walter Fiore[4], Massimo Bellini[5], Lorenzo Bertani[5], Dario Gambaccini[5], Michele Cicala[6], Bastianello Germanà[7], Maurizio Vecchi[8], Isabella Pagano[1], Maria Raffaella Barbaro[1], Lara Bellacosa[1], Vincenzo Stanghellini[1] and Giovanni Barbara[1]

Lactobacillus paracasei CNCM I-1572 induces a significant reduction in genus Ruminococcus, a significant increase in the fecal short chain fatty acids acetate and butyrate, and a significant reduction in the proinflammatory cytokine interleukin-15 in patients with IBS.

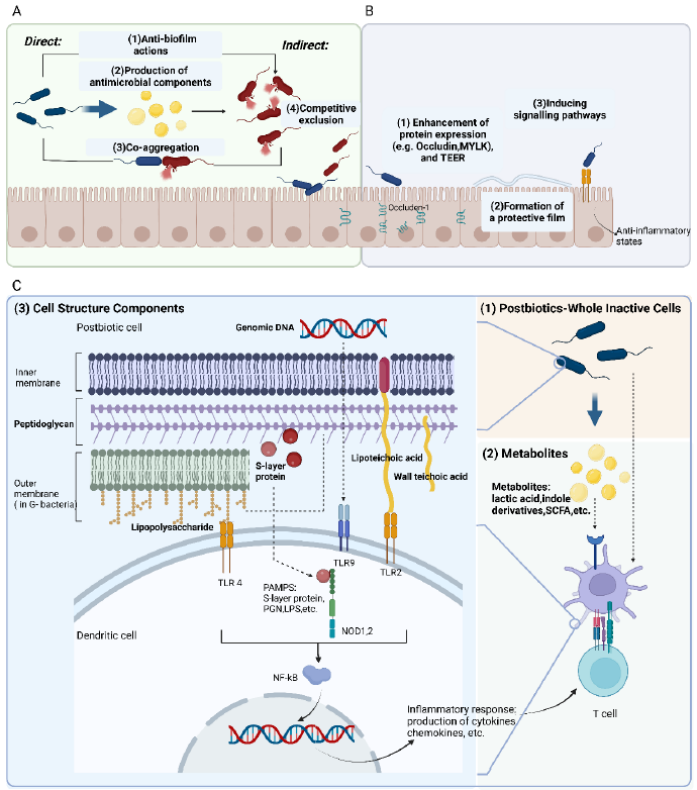
Live bacteria are not required for achieving beneficial effects when utilizing probiotics in treating symptoms of gut disorders (Postbiotics are the non-living components of the microbiome)

«..of further interest is determining if there are functional metabolic changes (measured in the metabolome) associated with microbiome perturbations, beyond simply measuring composition»

(Powles ST, 2022)

Postbiotics

Preparation of inanimate microorganisms and/or their components that confers a health benefit on the host



(Ma L, et al. Nutrients 2023)

PROTECTIVE MODULATION AGAINST PATHOGENS

- **Anti-microbial actions:**

Lactobacillus and *Bifidobacterium* → bacteriocins against the invasion of enteroinvasive *E. coli*; exopolysaccharides (EPS) *Bifidobacterium bifidum* → lactobacilli and other anaerobic bacteria grew more readily and enterobacteria, enterococci, or *Bacteroides fragilis* are inhibited.

- **Anti-biofilm actions:**

teichoic acid (Lactobacillus strains) → inhibits biofilm formation of pathogens (e.g. *Streptococcus mutans*, *Staphylococcus aureus* and *Enterococcus faecalis)*

FORTIFY THE EPITHELIAL BARRIER

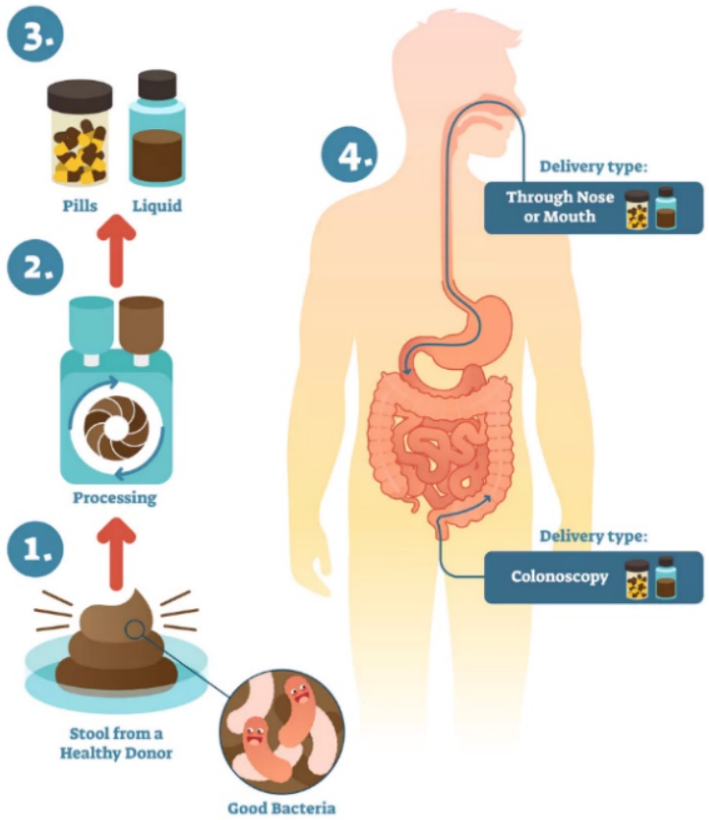
MODULATION OF IMMUNE RESPONSES.

Table 1 Examples of gut microbiota-derived metabolites and their beneficial effects on human health

Metabolite	Pathway	Microbial agent	Health benefits
Butyrate	Carbohydrate metabolism	*Clostridia*	Increased intestinal barrier function (Kelly et al. 2015a, b)
		Faecalibacterium prausnitzii	Modulate intestinal macrophage function (Chang et al. 2014)
		Coprococcus catus	Suppression of colonic inflammation (Simeoli et al. 2017)
		Anaerostipes hadrus	Improvements in insulin sensitivity (Khan and Jena 2016)
Propionate	Carbohydrate metabolism	*Blautia obeum*	Suppression of colonic inflammation (Tong et al. 2016)
		Coprococcus catus	Decreased innate immune responses to microbial stimulation (Ciarlo et al. 2016)
		Roseburia inulinivorans	Protection from allergic airway inflammation (Trompette et al. 2014)
		Prevotella copri	Improvements in insulin sensitivity and weight control in obese mice (den Besten et al. 2015)
Indole	Tryptophan metabolism	*Lactobacillus* spp.	Maintenance of host–microbe homeostasis at mucosal surfaces via IL-22 (Zelante et al. 2013)
		Bifidobacterium longum	Increased barrier function (Bansal et al. 2010)
		Bacteroides fragilis	Modulation of host metabolism (Chimerel et al. 2014)
Indole-3-aldehyde	Tryptophan metabolism	*Lactobacillus* spp.	Maintenance of mucosal homeostasis and intestinal barrier function via increased IL-22 production (Zelante et al. 2013)
			Protection against intestinal inflammation in mouse models of colitis (Lamas et al. 2016)
Indole-3-propionate	Tryptophan metabolism	*Clostridium sporogenes*	Maintenance of intestinal barrier function and mucosal homeostasis (Venkatesh et al. 2014)
			Increased production of antioxidant and neuroprotectant products (Hwang et al. 2009)
10-hydroxy-cis-12-octadecoate	linoleic acid derivative) (lipid metabolism	*Lactobacillus* spp.	Maintenance of intestinal barrier function (Miyamoto et al. 2015)
			Decreased inflammation (Kaikiri et al. 2017)
			Increased intestinal IgA production (Kaikiri et al. 2017)

(van Leeuwenhoek A, 2020)

Fecal Microbiota Transplantation (FMT)



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Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Guidelines

European Society of Clinical Microbiology and Infectious Diseases: 2021 update on the treatment guidance document for *Clostridioides difficile* infection in adults

Contents lists available at ScienceDirect

The Lancet Regional Health - Europe

journal homepage: www.elsevier.com/lanepe

Research paper

The use of Faecal Microbiota Transplantation (FMT) in Europe: A Europe-wide survey

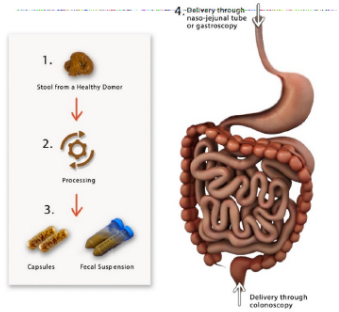
Indication	n*	%
Routine clinical indications. (n = 30 centres)		
Clostridioides difficile infection (CDI):		
Recurrent CDI	30	100%
Antibiotic refractory CDI	27	90%
Critical CDI	14	47%
Experimental (outside trials) indications. (n = 30 centres)		
Ulcerative colitis	4	13%
Multidrug resistant organisms carriage	3	10%
Graft versus host disease	2	7%
Irritable bowel syndrome	1	3%
Pouchitis	1	3%
Antibiotic-associated diarrhoea, not CDI.	1	3%
Investigational (within trials) indications. (n = 24 centres)		
Ulcerative colitis	11	46%
Irritable bowel syndrome	7	30%
Multidrug resistant organisms carriage	5	21%
Recurrent CDI	3	13%
Index CDI	3	13%
Refractory CDI	2	8%
Crohn's disease	2	8%
Pouchitis	2	8%
Graft versus host disease	2	8%
Obesity	2	8%
Spondyloarthropathy	2	8%
Liver cirrhosis, hepatic encephalopathy	2	8%
Critical CDI	1	4%
Antibiotic-associated diarrhoea, not CDI	1	4%
Parkinson's disease	1	4%
Chemotherapy-related diarrhoea	1	4%
Non-alcoholic fatty liver disease (NAFLD)	1	4%
Chronic fatigue syndrome	1	4%
Microscopic colitis	1	4%

FMT: Evidenza per indicazione al FMT nel 2023

	Metanalyses	RCTs	Open label trials	Case series/reports	Efficacy data
C. difficile infection	+++	+++	++++	++++	Outstanding
Ulcerative colitis	+	+	++	+++	Promising
Hepatic encefalopathy		+		+	Quite promising
Metabolic syndrome		+		+	Quite promising
Crohn's disease			+	+	Poor
IBS		+	+	+	Poor
Multi-resistant infections			+	+	Poor
Autism			+	+	Poor
GVHD				+	Poor

(gc R. Vassallo)

Recruitment and Screening of the donors: physical and laboratory investigations by blood and stool analysis and culture to rule out organic disorders, infectious agents and contagious diseases, most importantly, HIV, viral hepatitis, syphilis, malaria, tuberculosis and trypanosomiasis.
It is advisable that the donors have not recently used antibiotics, travelled to tropical areas, had high-risk sexual behavior or had a bout of gastroenteritis or diarrhea within 4 weeks of donation



(Mazzawi T, 2022)

It remains to be investigated whether **single or mixed donors** is the preferred choice and at which time intervals should FMT be performed.

Fresh/frozen **fecal material** might be superior to frozen **oral capsules** in improving IBS global symptoms and having lasting alteration of gut microbiota

The beneficial effect of FMT on IBS symptoms tends to **fade over time**

Risk of transferring microbial pathogens, or undesired disease phenotypes, such as obesity, diabetes, chronic and cardiovascular diseases as well as metabolic syndromes.

Lowering the risk: defined preparations of fecal microbiota with their constituent therapeutic factors may be a suitable alternation. In addition, mixtures of defined species or strains, or cocktails of microbiota-derived molecules targeting specific microbial species or pathways that are enriched in the disease state, in an effort to treat or prevent various common di

FMT is a promising treatment for many diseases but still, there remains a lot that is unknown and missing knowledge gaps that has prevented this therapeutic modality from obtaining FDA approval for treatments beyond CDI

The exact might be because o profiles, involvement of new species of gut microbiota found in healthy donor feces, and the presentation of peptides from the donor that modify host immune responses

(Gianotti & Moss, 2017)

FMT increased the total fecal **SCFAs levels**, namely butyric acid *(van Leeuwenhoek A, 2020)*

FVT (Fecal Viroma Transplantation)

Importance of phages in **eliminating the gastroenteritis-associated pathogenic bacteria**, and in modulating the beneficial bacteria by **adding new functions** such as metabolites biosynthesis (SCFA, H_2S) in the management of metabolic and neurological disorders

Potential applications of bacteriophages include **designing phage to "correct" microbiota dysbiosis,** creating phage therapies to **target certain bacterial species** that causes a gut disease, and developing compounds that block phage induction to **inhibit the growth of certain bacteria**

A programmed phage λ can be used to repress E. coli genes in the mammalian gut.
Oral delivery using an aqueous-based encapsulation formulation.

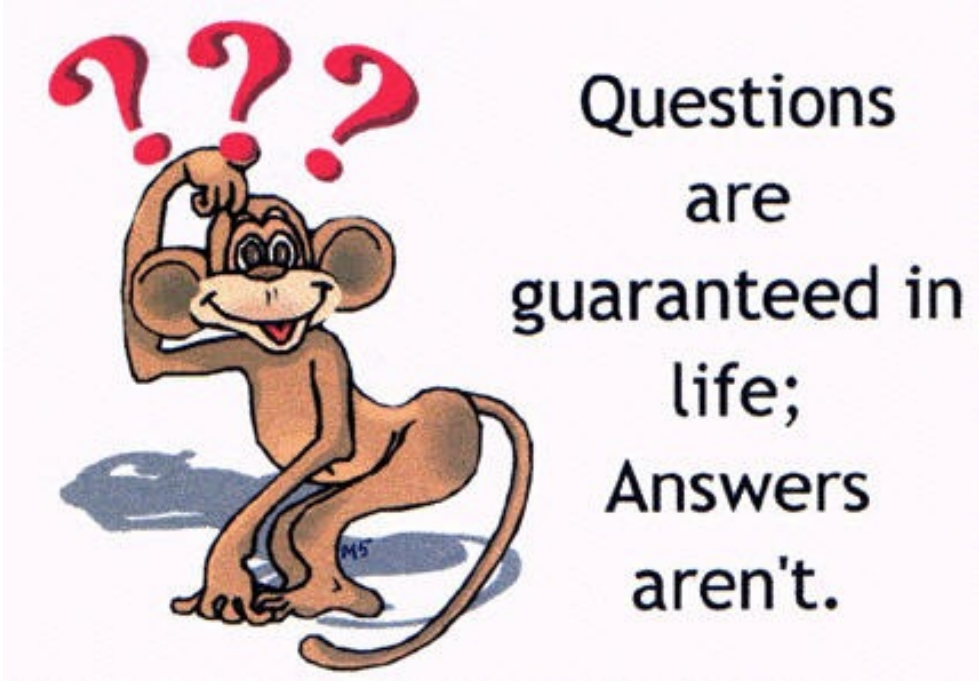
(Hsu BB, 2020)

The prophage-encoded virulence factors remain a **safety issue**, which limits the use of phages in medicine

(Rasmussen TT, 2020)

Essential data for the approval of phages as antibacterial drugs still needed and studies to address these points are necessary

Thank you for your attention!



La spinta migliore, viene da te

Most studies: massive **impact on the bacterial load** and **alfa diversity** of the gut microbiota composition in the samples taken after MBP

No unique general pattern of microbial modification has emerged;
Duration of the effect: most studies report a short effect on microbial composition, up to 2 weeks; in some cases up to 4 weeks after colonoscopy.
Almost restitutio ad integrum of the microbiota occurs a few weeks after MBP in healthy patients
Overall, studies suggest that microbiota variations seem more sustained in patients suffering from diseases per se associated to intestinal dysbiosis, such IBS or IBD.

(Drago L, 2019)

These **conflicting results** are probably due to the small number of subjects, the inclusion of healthy and diseased subjects, the lack of a non-procedure control group, and a lack of analytical depth in these studies. Different ways of sample collection