Webinar ‘building blocks’

Available ingredients for magistral preparations

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1. Intro: recently added building blocks
2. Interactive choice of BBs to discuss
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1. Intro: recently added building blocks

Limosilactobacillus fermentum ME-3

- Isolated from healthy child in Estonia in 1995[1].
- Extensively studied for its antioxidative function. It has complete glutathione system[1-3]. Clinically it is shown to have:
  - Systemically increased antioxidative potential[3-6] (fig)
- In addition, there is evidence for:
  - Anti-inflammatory effects[7,8]
  - Improve gut barrier function[8]
  - Metabolic dysfunction[7,9]
  - Pathogen inhibition, including Salmonella (e.g.[10]) and H. pylori (e.g.[11])
- Typical use: oxidative stress

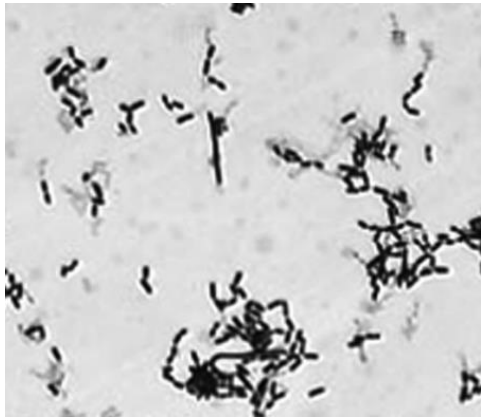

Table 1. The glutathione status and redox ratios of the skin and blood.

Skin						
	GSSG (μg/g skin)		GSH (μg/g skin)		GSSG/GSH	
	Before	After	Before	After	Before	After
ME-3 (n=10)	31±8	13±2	184.8±26.1	149.2±58.4	0.18±0.04	0.13±0.03*
		P=0.001				P=0.05
Control (n=6)	38±11	29±8	124±94	166±44	0.16±0.03	0.16±0.03
Blood						
	GSSG (μM/L)		GSH (μM/L)		GSSG/GSH	
	Before	After	Before	After	Before	After
ME-3	38±5	38±8	1075±73	1313±81*	0.032±0.003	0.025±0.006
				P=0.001		P<0.05
Control	40±12	35±11	1105.0±59.3	1153±89	0.036±0.010	0.030±0.007

**P<0.05 as compared to control group*

1. Kullisaar, T. et al.International Journal of Food Microbiology.72,.215–224.(2002)
2. Mikelsaar, M. et al.Microbial Ecology in Health and Disease.21,.1–27.(2009)
3. Kullisaar, T. et al.Appl Biochem Microbiol.46,.481–486.(2010)
4. Songisepp, E. et al.Nutr J.4,.22.(2005)
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7. Kullisaar, T. et al.Nutr J.15,.93.(2016)
8. De Gregorio, A. et al.IJMS.24,.6225.(2023)
9. Kullisaar, T.Endocrinol Diabetes Metab J.3,.(2019)
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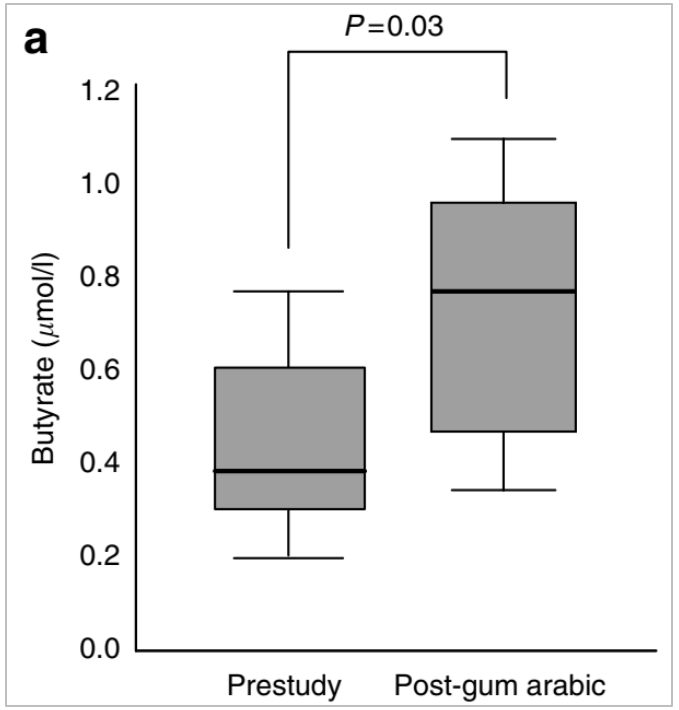
Acacia Senegal fiber

- This fiber is derived from the gum of acacia Senegal trees.
- This fiber is extremely well-studied, hundreds of clinical studies have been conducted since 1980's.
- Although often studied in daily doses of 25g, there is also evidence for effects at daily doses of ~5g.
- Known for butyrate production stimulation[6,7] (fig)



1. Bongartz, U. et al.FNS.13,.424–438.(2022)
2. Babiker, R. et al.FFHD.7,.222.(2017)
3. JanssenDuijghuijsen, L. et al.Eur J Nutr.(2024)
4. Mohamed Widatalla, A. et al.73–76.(2013)
5. Jarrar, A. H. et al.Nutrients.13,.194.(2021)
6. Alarifi, S. et al.Int J Food Sci Nutr.69,.696–704.(2018)
7. Elamin, S. et al.International Journal of Nephrology.2017,.1–6.(2017)
8. Kamal, E. et al.International Journal of Rheumatology.2018,.1–6.(2018)
9. Ali, N. E. et al.International Journal of Nephrology.2020,.1–7.(2020)

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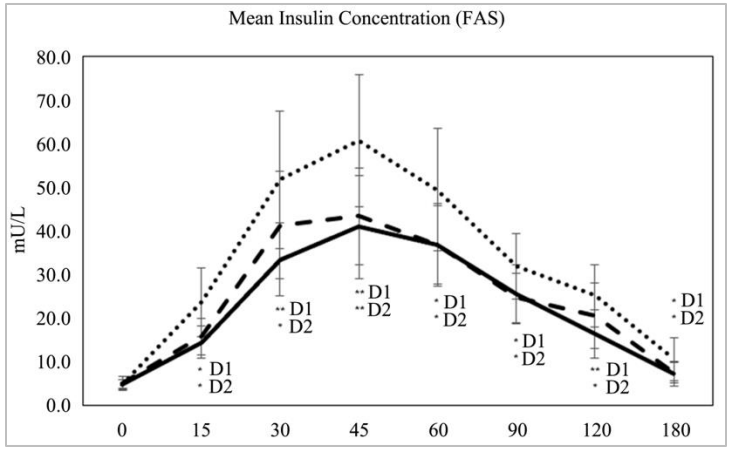
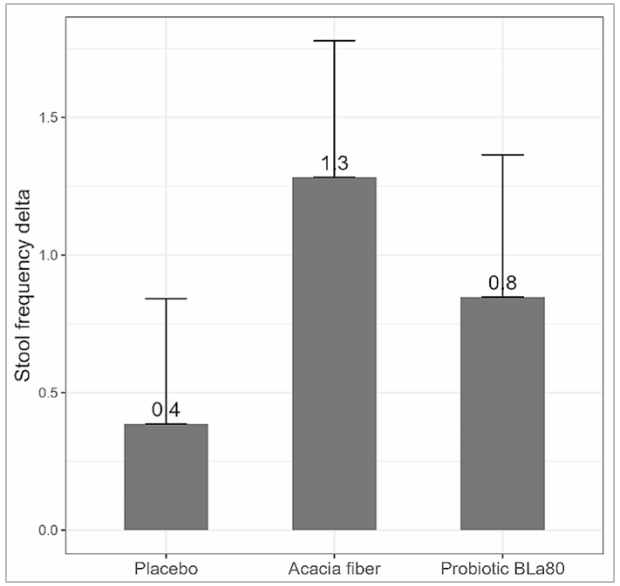
Acacia Senegal fiber



- Important therapeutic uses:
  - Insulin resistance (several studies, e.g.[1,2], fig)
  - Constipation (e.g.[3,4]. fig)
- Other evidence-based uses:
  - Bloating[5]
  - Inflammation (e.g.[7,8])
  - Oxidative stress (e.g.[9])
- Typical use: Metabolic dysfunction, low butyrate



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4. Mohamed Widatalla, A. et al.73–76.(2013)
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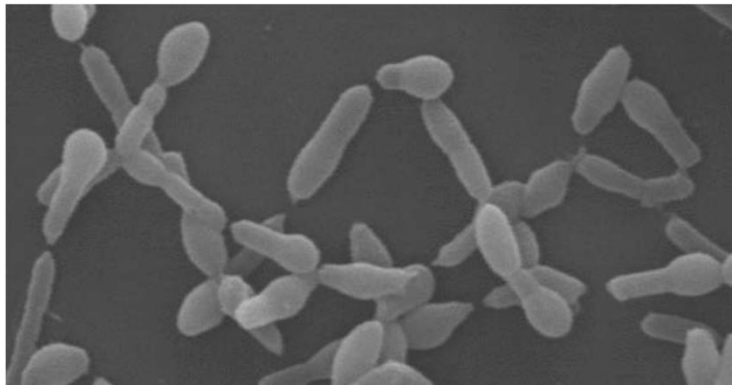
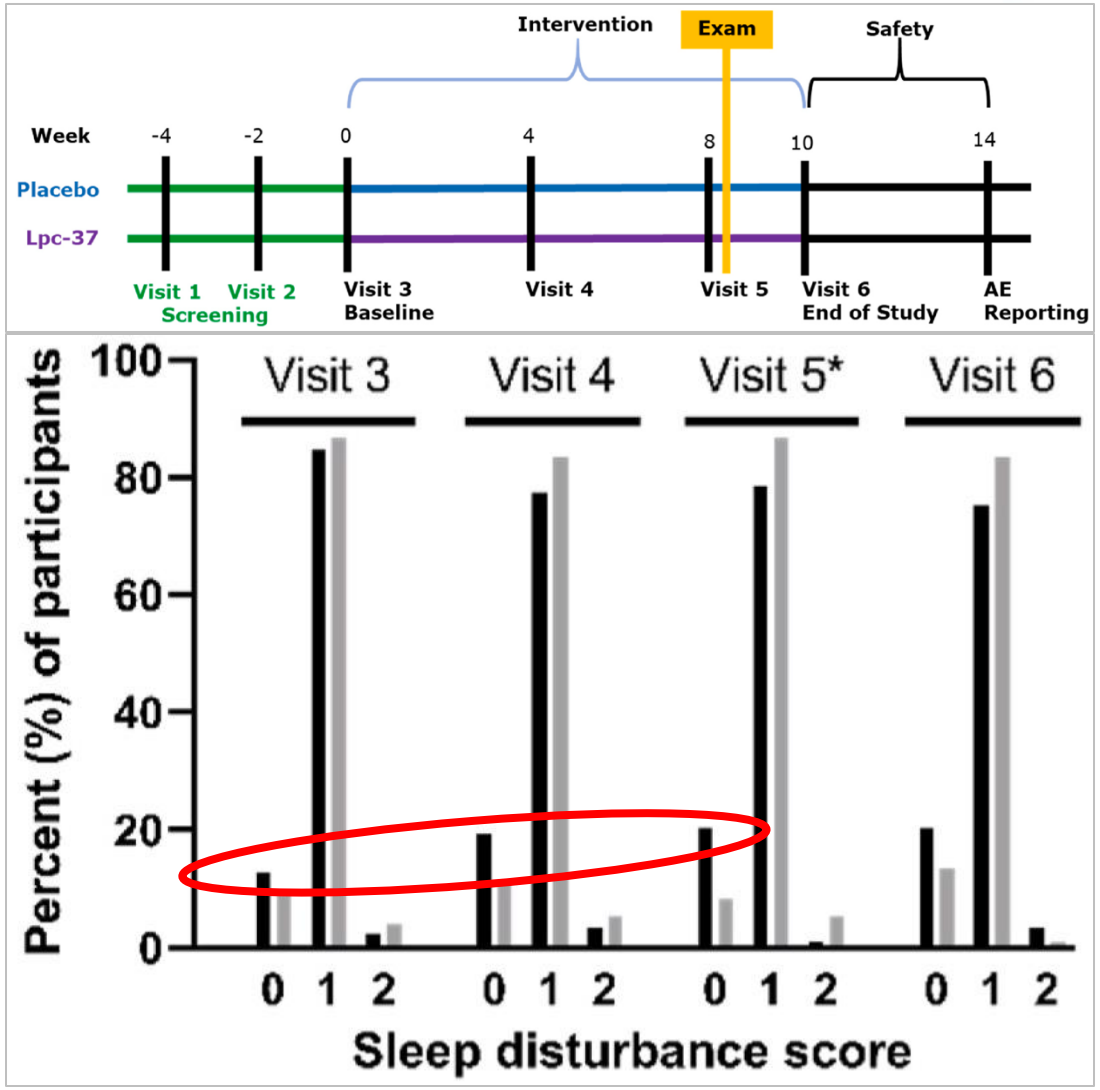
9. Ali, N. E. et al.International Journal of Nephrology.2020,.1–7.(2020)

Lacticaseibacillus paracasei Lpc-37

- Isolated from a dairy source.
- Has been studied in many trials alone or as part of mixture
- One very interesting indication is improving sleep quality (sleep disturbance, fig)[3,4]





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2. Ouwehand, A. C. et al.Vaccine.32,.458–463.(2014)
3. Mäkelä, S. M. et al.Brain, Behavior, & Immunity - Health.32,.100673.(2023)
4. Patterson, E. et al.Neurobiol Stress.13,.100277.(2020)
5. Li, L. et al.Front. Microbiol.14,.1202858.(2023)
6. Waitzberg, D. L. et al.Clinical Nutrition.32,.27–33.(2013)
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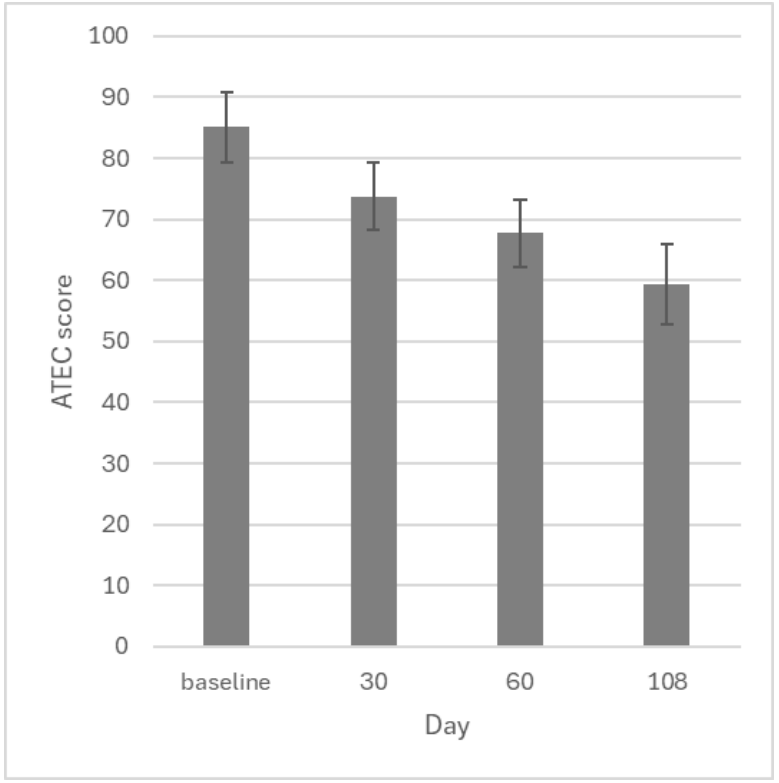
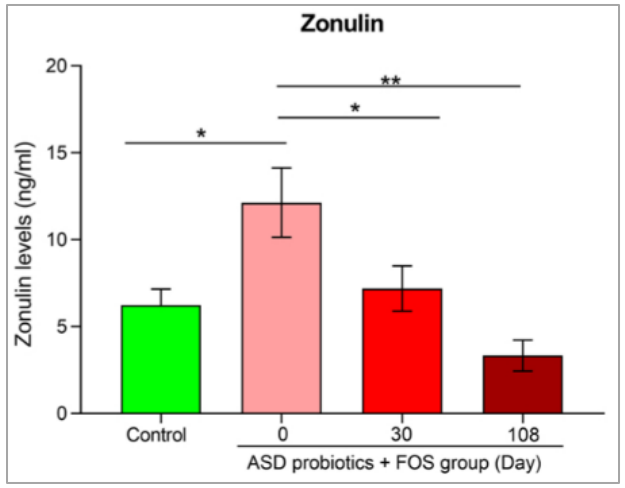
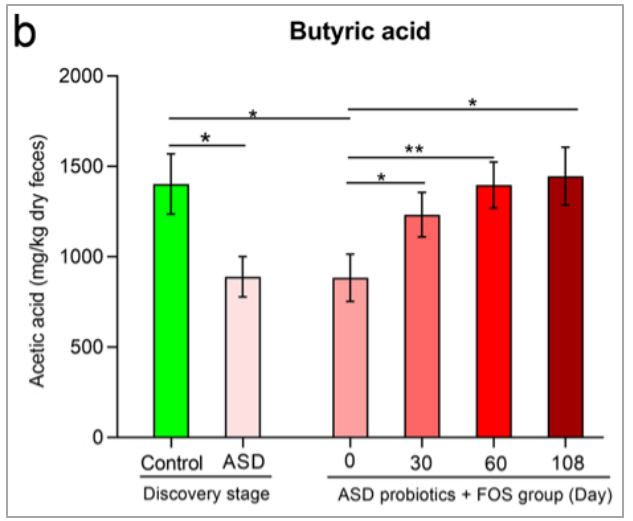
Lacticaseibacillus paracasei Lpc-37

- Another exciting study, though small and with a mixture, is autism (fig)[8]
- In addition, there is evidence for:
  - Prevention of diarrhea and fever[1]
  - AAD and *C. difficile* infection e.g.[2]
  - Stress[3,4]
  - Hay fever[5]
  - Constipation e.g.[6]
  - Mucositis[7]
- Typical use: sleep quality under stress combined with GI complaints







1. Hemalatha, R. et al.European Journal of Nutrition & Food Safety.4,.325–341.(2014)
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4. Patterson, E. et al.Neurobiol Stress.13,.100277.(2020)
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6. Waitzberg, D. L. et al.Clinical Nutrition.32,.27–33.(2013)
7. Santana, S. I. et al J Clin Periodontol.49,.828–839.(2022)
8. Wang, Y. et al.Pharmacological Research.157,.104784.(2020)

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Our own strain: *Escherichia coli* MC231

- Selected from a large set of potential strains
- Why this strain?
  - Bacterial species *E. coli* plays an important beneficial role in the microbiome
  - Genetically almost identical to extensively studied *E. coli* Nissle 1917
  - Safe! *E. coli* Nissle 1917 has a very long history of use.

4.3.2 Mapping Statistics with Reference Genome

The mapping rates of samples reflect the similarity between each sample and the reference genome. The depth and coverage are indicators of the evenness and homology with the reference genome.

Table 4.5 Statistics of mapping rate, depth and coverage

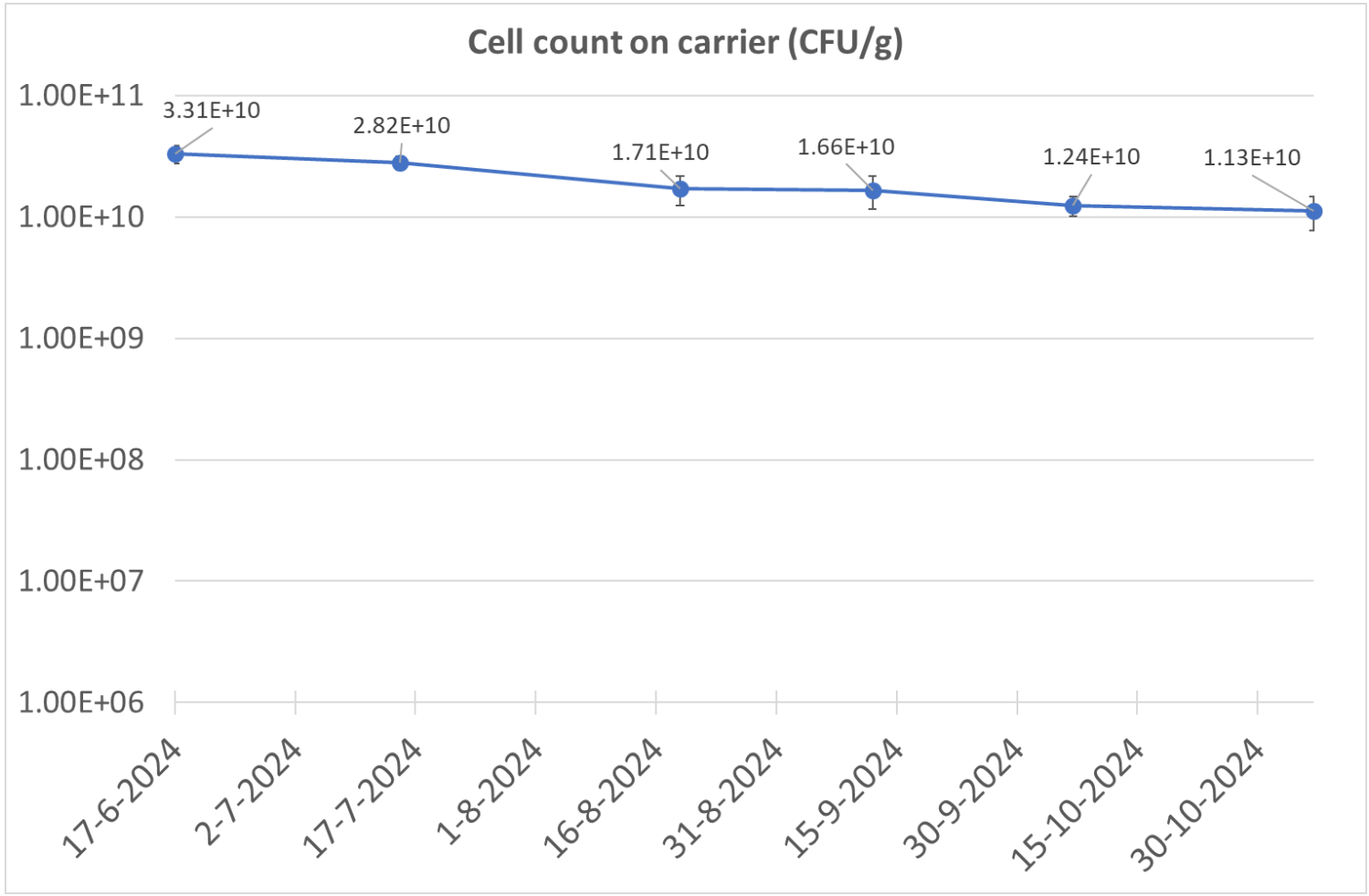
Sample	Mapped reads	Total reads	Mapping rate (%)	Average depth(X)	Coverage at least 1X (%)	Coverage at least 4X (%)
MC231_02	9,119,407	9,130,850	99.87	201.96	100.00	100.00

4.3.3 Mapping Summary

For the current 5,064,093 bp reference genome, the mapping rate of this sample is 99.87%. Refer to the reference genome (without Ns),the average depth is 201.96X, and more than 1X coverage reaches 100.00%. This result is in the qualified normal range and may serve in the subsequent variation detection and related analyses.

Development of *E. coli* MC231

Stability



What can this strain be effective for?
→ Ulcerative colitis

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Maintaining remission of ulcerative colitis with the probiotic Escherichia coli Nissle 1917 is as effective as with standard mesalazine

W Kruis, P Frič, J Pokrotnieks, M Lukáš, B Fixa, M Kaščák, M A Kamm, J Weismueller, C M Stolte, C Wolff, J Schulze

Gut 2004;53:1617–1623. doi: 10.1136/

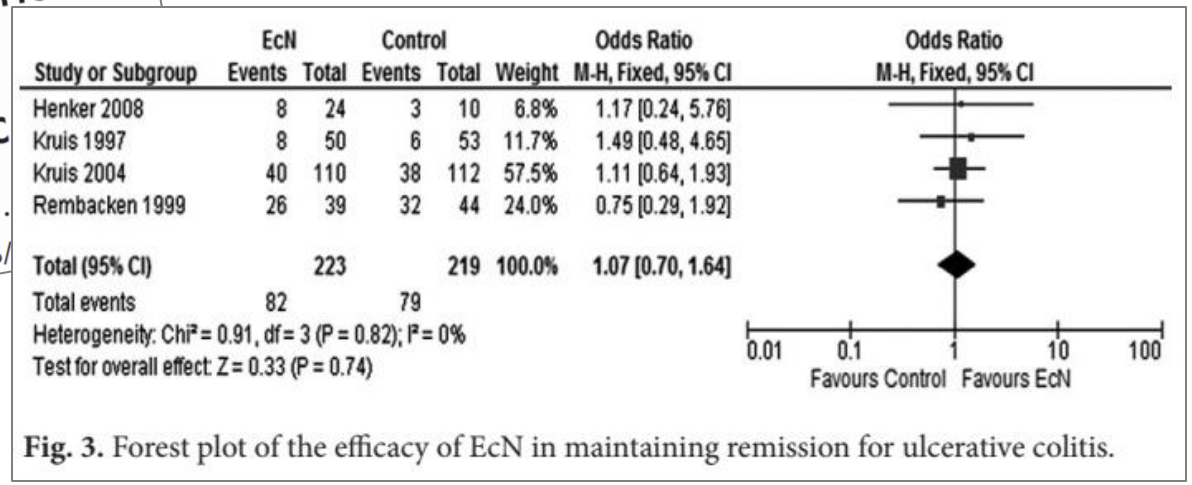


Fig. 3. Forest plot of the efficacy of EcN in maintaining remission for ulcerative colitis.

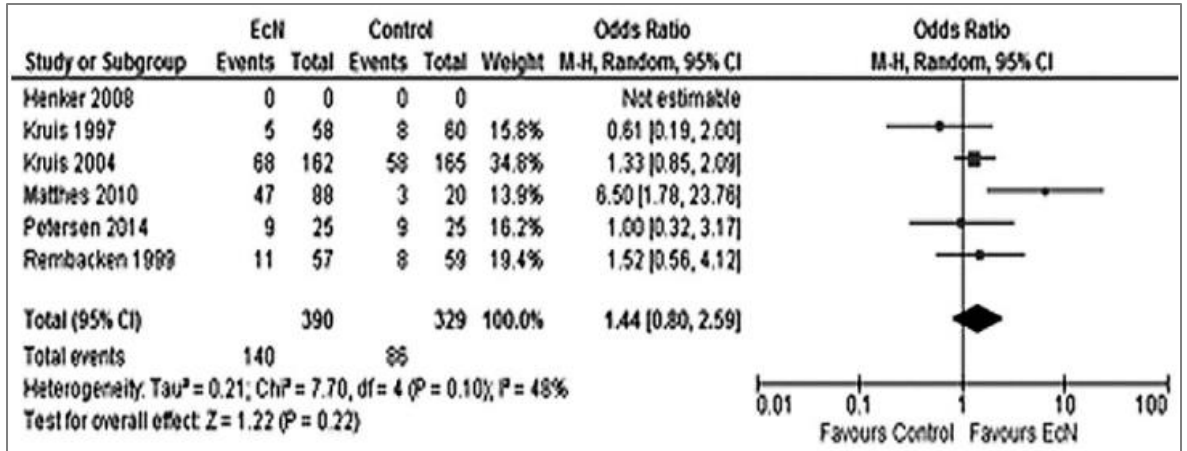
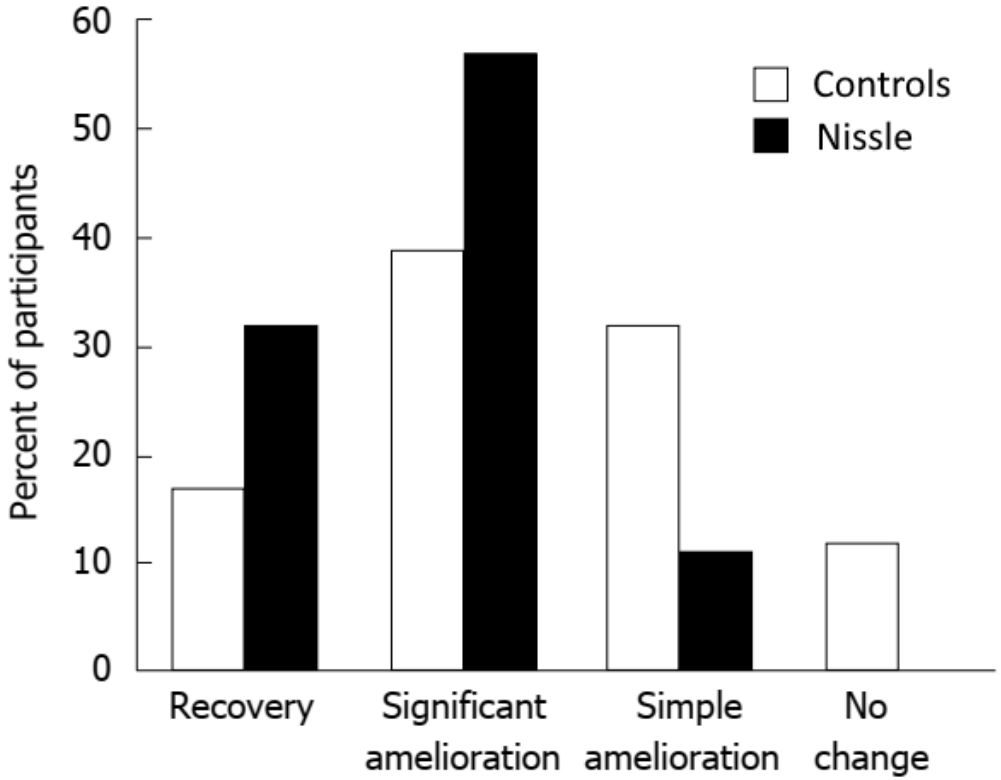


Fig. 4. Forest plot of the side effects observed in EcN treatment.

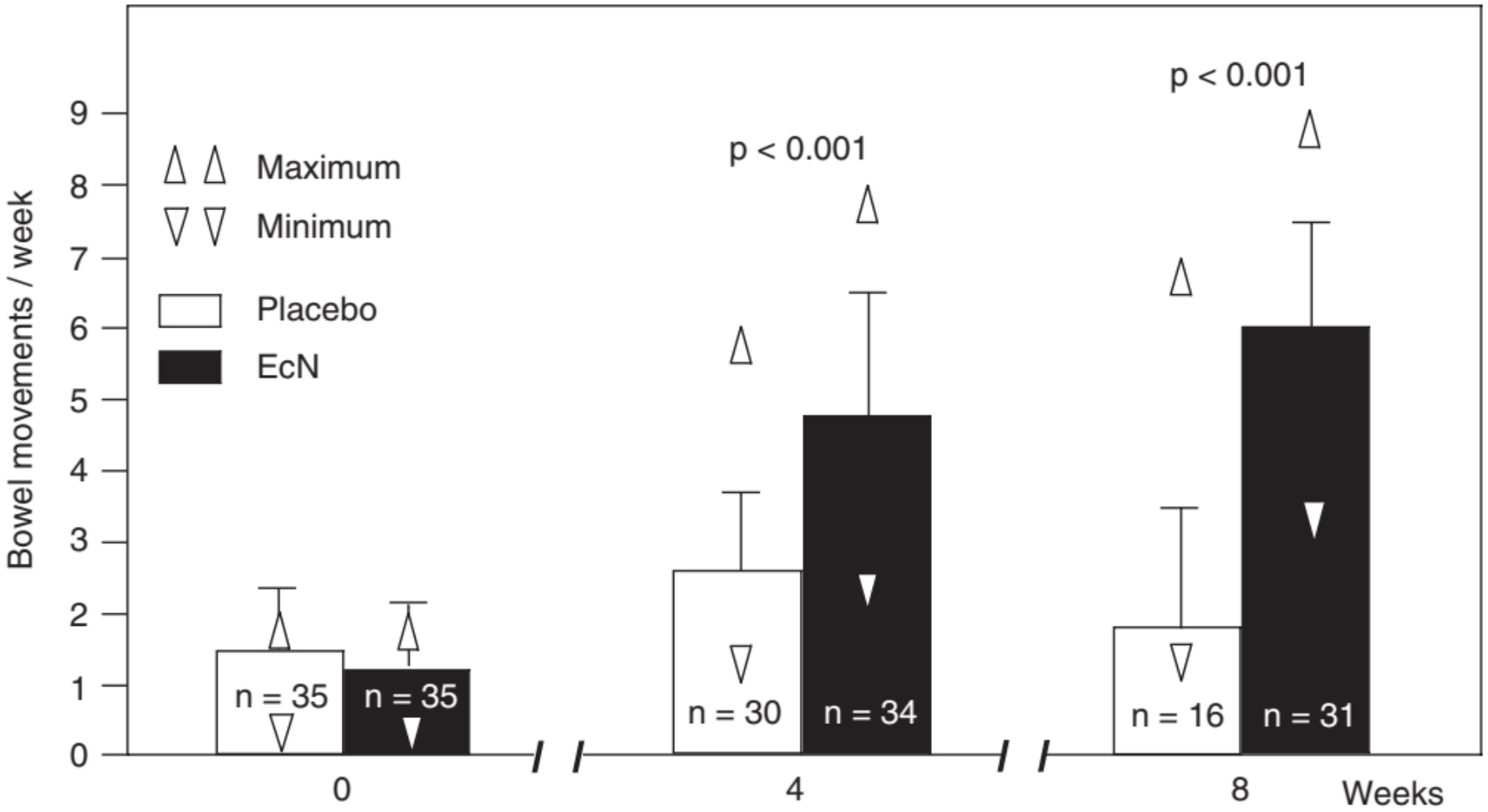
1. Losurdo, G. et al.Journal of Gastrointestinal and Liver Diseases.24,.499–505.(2015)

What can this strain be effective for?
→ Dermatosis with pimples (acne, rosacea, seborrheic dermatitis)



1. Manzhalii, E. et al.World J Gastroenterol.22,.5415–5421.(2016)

What can this strain be effective for?
→ Constipation



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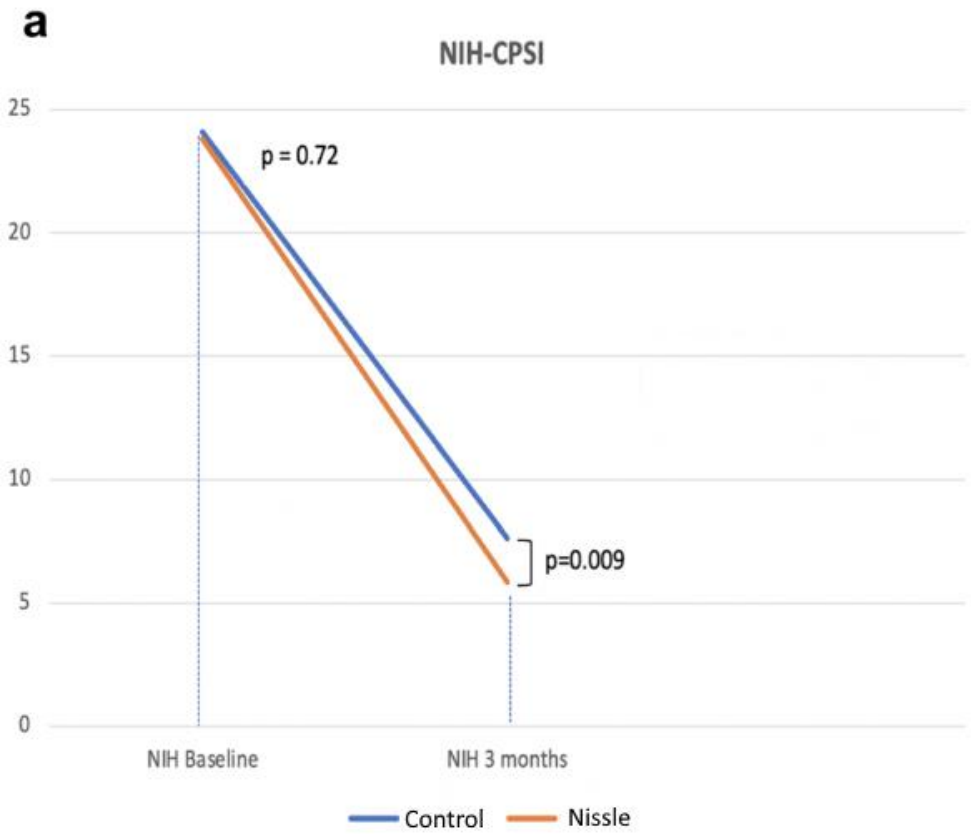
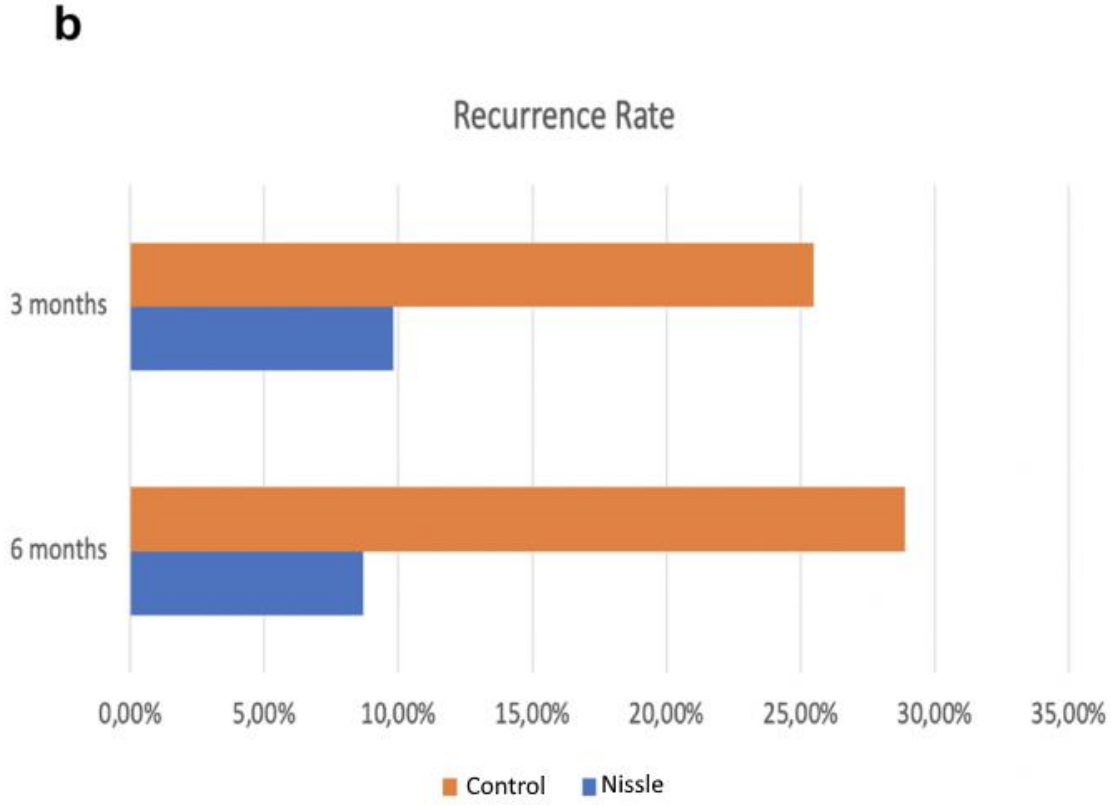
What can this strain be effective for?
→ Chronic bacterial prostatitis





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2. Interactive part:
What do you  want to know about the building blocks?

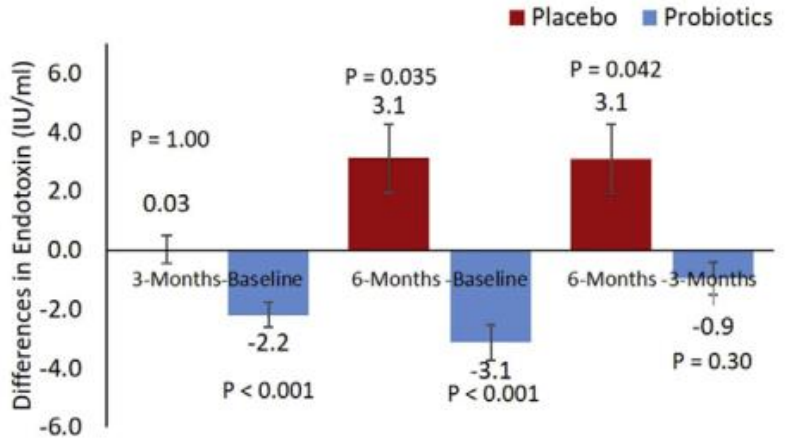
Building block overview

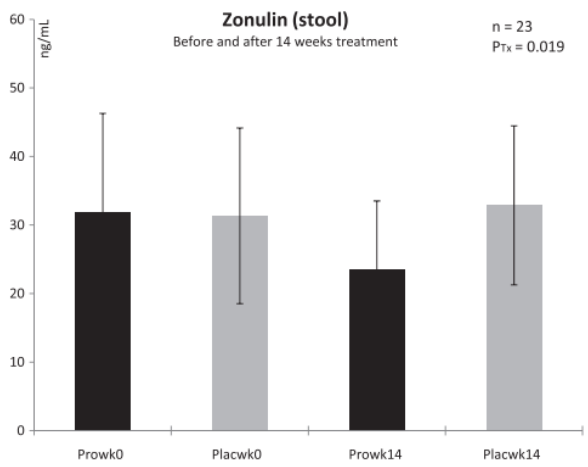
2020	1	Barrier
	2	Bifido booster
	3	DJ repair
	4	IL-10 Immune balancer
	5	TH1/TH2 Immune balancer
	6	Pathogene reduction
	7	Yeast reduction
	8	Vitamin K2 booster
	9	Butyraat generator
	10	Microbiotia booster – fiber complex
	11	*S. Boulardii*
	12	*L. acidophilus* LA02
	13	*L. rhamnosus* GG
2021	14	*Bacillus clausii* UBBC-07
	15	*Bacillus coagulans* Unique IS-2
	16	*E. faecium* Rosell-26 + *B.* Rosell-179
	17	2'-Fucosyllactose
	18	*L. plantarum* P8

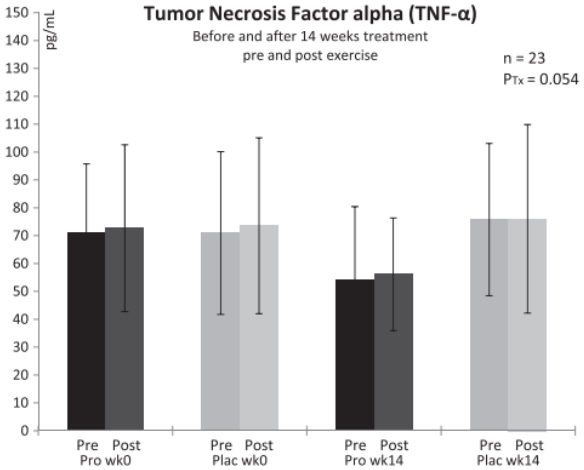
2022	19	PHGG
	20	*L. sakei* probio65
	21	*Anaerobutyricum soehngenii*
	22	Gut enricher
	23	*L. Plantarum* DR7
2023	24	*L. rhamnosus* SP1
	25	*Akkermansia*
	26	*Bifidobacterium lactis* HN019
	27	Vaginal suppositories
2024	28	*Limosilactobacillus fermentum* ME-3
	29	Acacia fiber
2025	30	*Lacticaseibacillus paracasei* Lpc-37
	31	*Eschericia coli* MC231

Barrier

- This BB contains four strains:
  - *Bifidobacterium bifidum* W23
  - *Lactobacillus acidophilus* W37
  - *Bifidobacterium lactis* W51
  - *Lactobacillus brevis* W78
- It is developed to improve gut barrier integrity, for which there is both in vitro and in vivo evidence (fig)[1-4].
- Other evidence for therapeutic uses, often linked to barrier integrity, include:
  - Anti-inflammatory effects[4,5]
  - Type 2 diabetes[2,3]
  - Sad mood/depression[6,7]
  - Respiratory tract infections[8]
- Typical use: one of these disorders with leaky gut







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4. Lamprecht, M. et al. J Int Soc Sports Nutr 9, 45 (2012)
5. Niers, L. E. M. et al. Clin. Exp. Allergy 35, 1481–1489 (2005)
6. Chahwan, B. et al. Journal of Affective Disorders 253, 317–326 (2019)
7. Papalini, S. et al. Neurobiology of Stress 10, 100141 (2019)
8. Strasser, B. et al. Nutrients 8, (2016)

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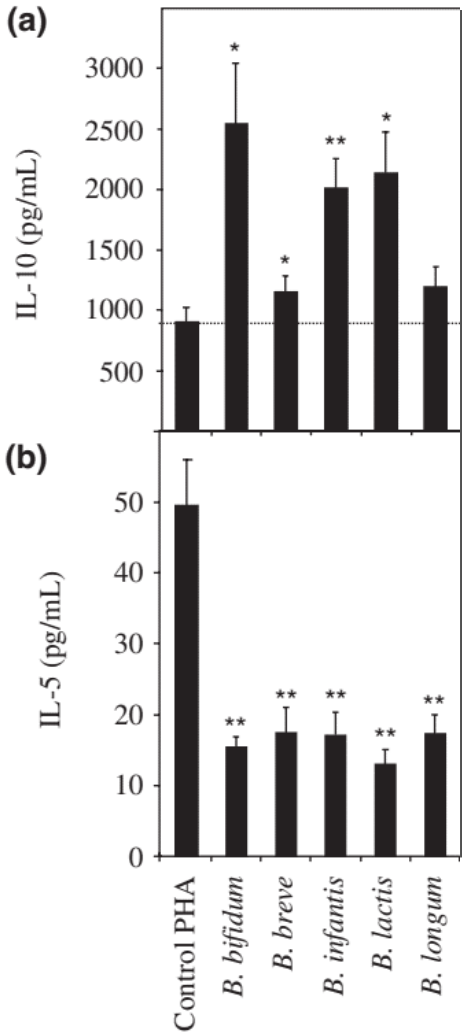
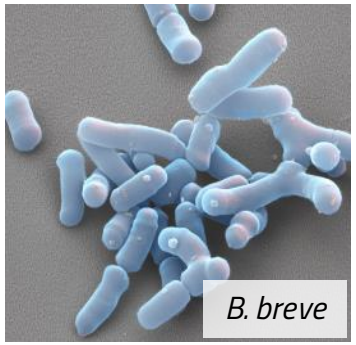
Bifido booster

- This BB contains six bacterial species of the genus Bifidobacterium:
  - *Bifidobacterium bifidum* W23
  - *Bifidobacterium breve* W25
  - *Bifidobacterium bifidum* W28
  - *Bifidobacterium lactis* W51
  - *Bifidobacterium lactis* W52
  - *Bifidobacterium longum* W108
- Bifido's are known for their immune-modulating properties.
- There is in vitro evidence for:
  - Anti-inflammatory effects (fig)[1,2]
  - Th2 to Th1 skewing[1,3]
  - Pathogen inhibition[4]
- Clinical evidence for an effect on constipation (fig)[5,6]
- Typical use: low abundance of bifido's with inflammation





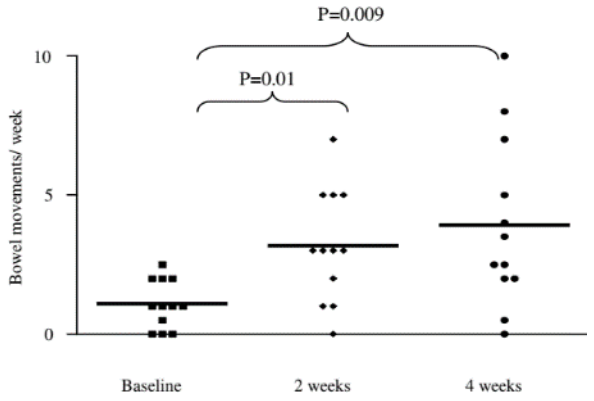


Figure 2
Bowel movements (BMs) per week in children presenting with <3 BMs/week.

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4. Campana, R. et al. Gut Pathog 9, (2017)
5. Bekkali, N.-L.-H. et al. Nutr J 6, 17 (2007)
6. de Milliano, I. et al. Nutr J 11, 80 (2012)

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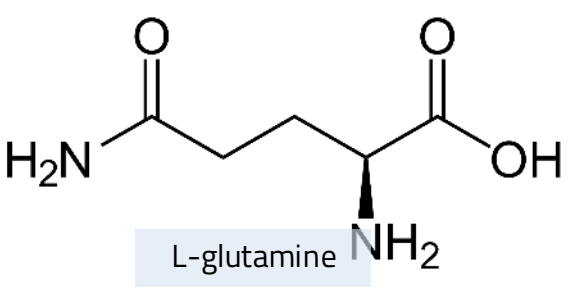
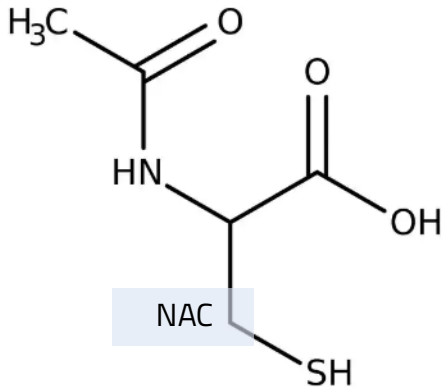
DJ repair

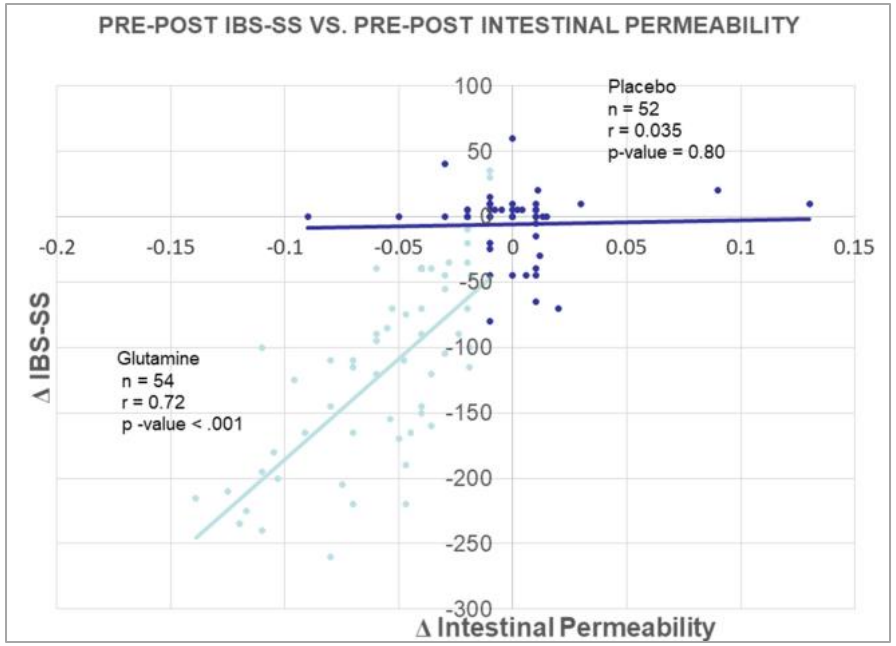
- This BB consists of L-glutamine (90%), N-acetyl-cysteine (9.9%), and zinc (0.1%).
- This mixture is designed to aid the intestinal barrier function. Evidence shows that:
  - L-glutamine[1,2] and zinc[3,4] improve barrier function (fig).
  - NAC decreases oxidative stress[5,6]
- Other evidence-based therapeutic uses include:
  - IBS[2]
  - Side effects of radio or chemotherapy[7,8]
  - Improve fatigue[9]
- Typical use: one of these disorders with leaky gut



L-glutamine



NAC



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4. Wessells, K. R. et al. J Pediatr Gastroenterol Nutr 57, 348–355 (2013)
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6. Shahbazian, H. et al. Saudi Journal of Kidney Diseases and Transplantation 27, 88 (2016)
7. Li, Y. et al. Tumori Journal 92, 396–401 (2006)
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9. Maes, M. et al. Neuro Endocrinol. Lett. 29, 902–910 (2008)

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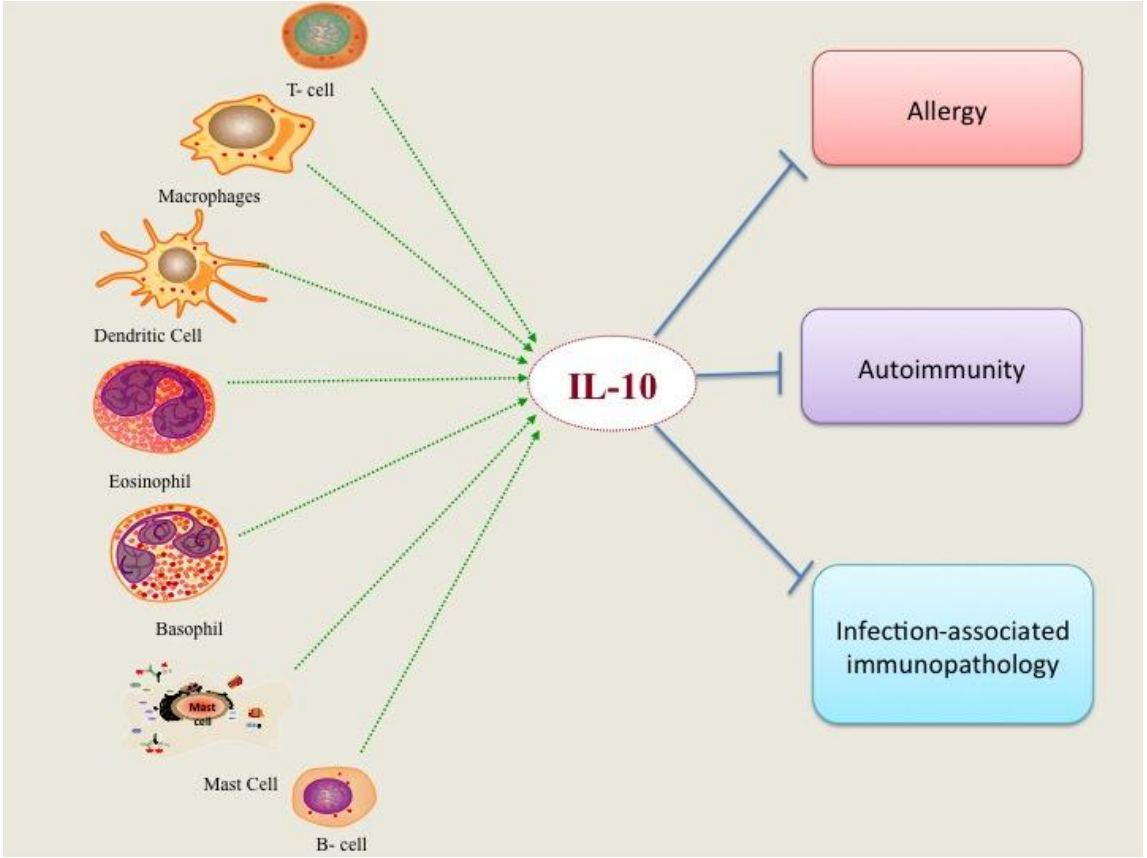
IL-10 immune balancer

- This BB contains four strains from three genera:
  - Bifidobacterium bifidum W28
  - Bifidobacterium animalis subsp lactis W53
  - Enterococcus faecium W54
  - Lactobacillus acidophilus W55
- This BB is designed for an anti-inflammatory via, among other things, the induction of IL-10[1,2].
- IL-10 is a key regulatory cytokine that prevents damage from prolonged inflammation[3,4].
- Some strains stimulate FOXP3 release[5], which is indicative of the activation of regulatory T cells (Treg) that play an important role in inhibiting autoimmune diseases and allergic reactions.
- Typical use: patients with allergic or auto-immune diseases



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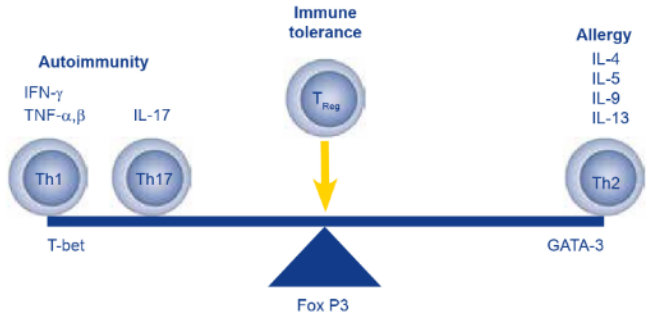
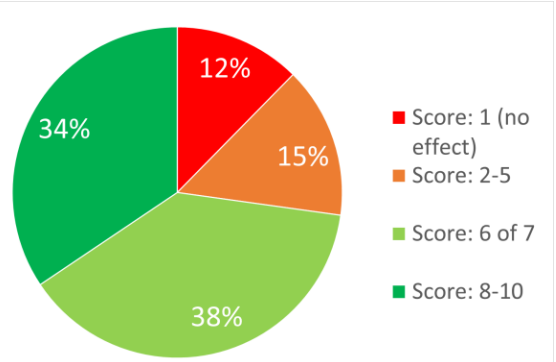
Th1/Th2 immune balancer

Microbiome Center

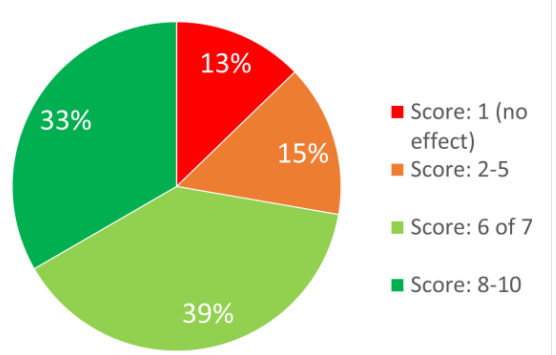
Data till December 2023

- This BB contains four strains from three genera:
  - *Bifidobacterium lactis* W28
  - *Bifidobacterium animalis subsp lactis* W53
  - *Lactobacillus casei* W56
  - *Lactococcus lactis* W58
- It is designed to skew the Th1/Th2 balance towards Th1. This balance, which is also affected by Treg expression, is crucial in allergic diseases[1].
- The strains are selected for dampening Th2, stimulating Th1 and Treg[2-4].
- Other evidence for therapeutic uses:
  - Pathogen inhibition[5]
  - Anti-inflammatory effect[2-4]
  - Type 2 diabetes[6,7]
  - Sad mood/depression[8,9]
- Data analysis: indeed favorable effect in allergies (fig)
- Typical use: patients with allergies

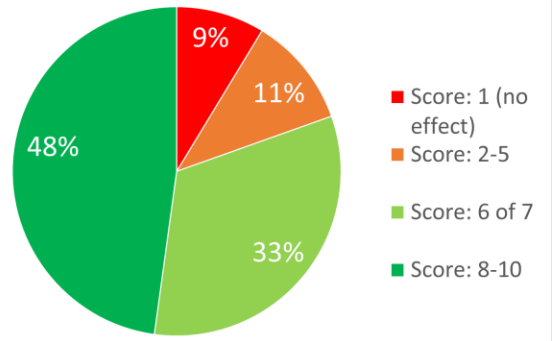




All patients (n=1195)



All patients with allergy (n=321)



Patients with allergy using Th1/Th2 immune balancer (n=46)

1. Akdis, C. A. et al. (European Academy of Allergy and Clinical Immunology, 2014)
2. Niers, L. E. M. et al. Clin. Exp. Allergy 35, 1481–1489 (2005)
3. Kepert, I. et al. Journal of Allergy and Clinical Immunology 139, 1525–1535 (2017)
4. Niers, L. E. M. et al. Clin Exp Immunol 149, 344–352 (2007)
5. Campana, R. et al. Gut Pathog 9, (2017)
6. Sabico, S. et al. Clinical Nutrition (2018)
7. Szulińska, M. et al. Nutrients 10, 773 (2018)
8. Chahwan, B. et al. Journal of Affective Disorders 253, 317–326 (2019)
9. Papalini, S. et al. Neurobiology of Stress 10, 100141 (2019)

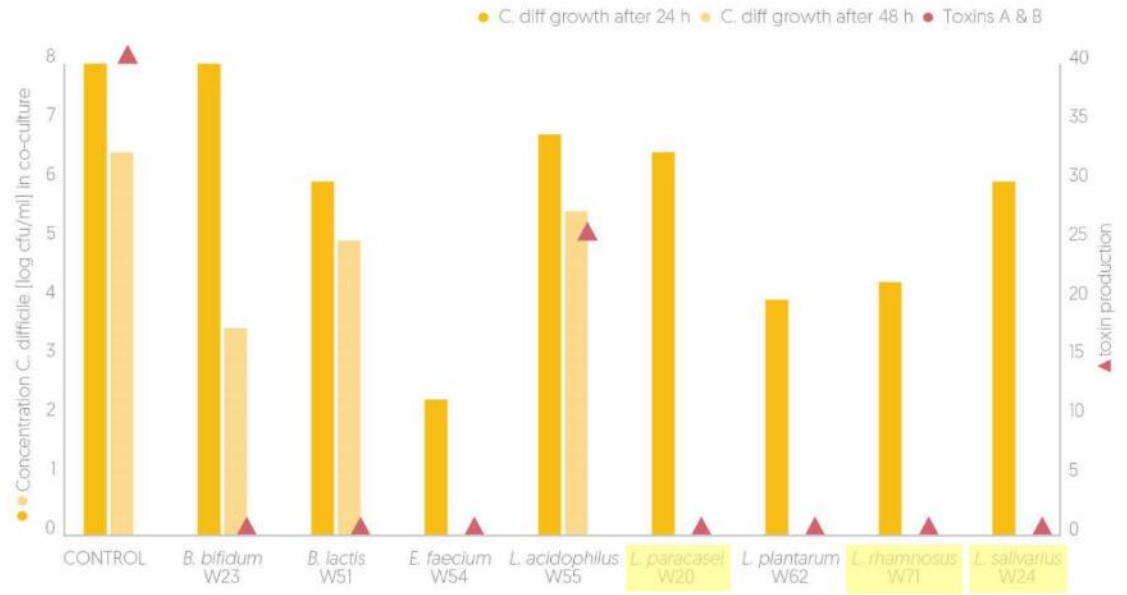
Return to overview

Pathogen reduction

- This BB consist of:
  - *Lactobacillus paracasei* W20
  - *Lactobacillus plantarum* W21
  - *Lactobacillus salivarius* W24
  - *Lactobacillus rhamnosus* W71
- These strains were selected for their strong pathogen inhibiting effects.
- For these strains in vitro evidence shows strong inhibition of *Clostridium difficile*, pathogenic *Enterococcus faecalis*, pathogenic *Escherichia coli*, *Salmonella enteritidis*, and *Listeria monocytogenes* (fig)[1,2]
- Typical use: patients with overgrowth of pathogenic bacteria

Table 2 Antimicrobial activity of the cell-free supernatants (CFCSs) produced by the different LAB strains toward human intestinal pathogens strains performed by agar well diffusion method

CFCSs	Inhibition zone (mm ± sd)				
	S. enteritidis ATCC 13076	*L. monocytogenes* ATCC 7644	*E. coli* O157: H7 ATCC 35150	*C. sakazakii* ATCC 29544	*C. jejuni* ATCC 33291
B. bifidum W23	–	10.1 ± 0.25	11.0 ± 0.35	12.1 ± 0.25	12.1 ± 0.32
L. salivarius W24	10.1 ± 0.32	–	–	10.2 ± 0.11	10.1 ± 0.28
L. acidophilus W37	–	11.1 ± 0.12	–	–	12.1 ± 0.36
L. casei W56	–	11.1 ± 0.51	–	10.2 ± 0.21	17.1 ± 0.21
L. lactis W58	11.0 ± 0.15	11.0 ± 0.27	12.0 ± 0.28	11.1 ± 0.15	10.5 ± 0.51
L. plantarum W21	10.1 ± 0.31	14.1 ± 0.34	10.0 ± 0.20	10.1 ± 0.28	13.5 ± 0.52
L. rhamnosus W71	10.1 ± 0.24	12.1 ± 0.31	11.0 ± 0.15	10.2 ± 0.25	17.2 ± 0.21
Positive control	16.3 ± 0.53 (Gen)	19.3 ± 0.63 (W)	15.6 ± 0.64 (Gen)	16.3 ± 0.52 (Strep)	32 ± 0.51 (Gen)

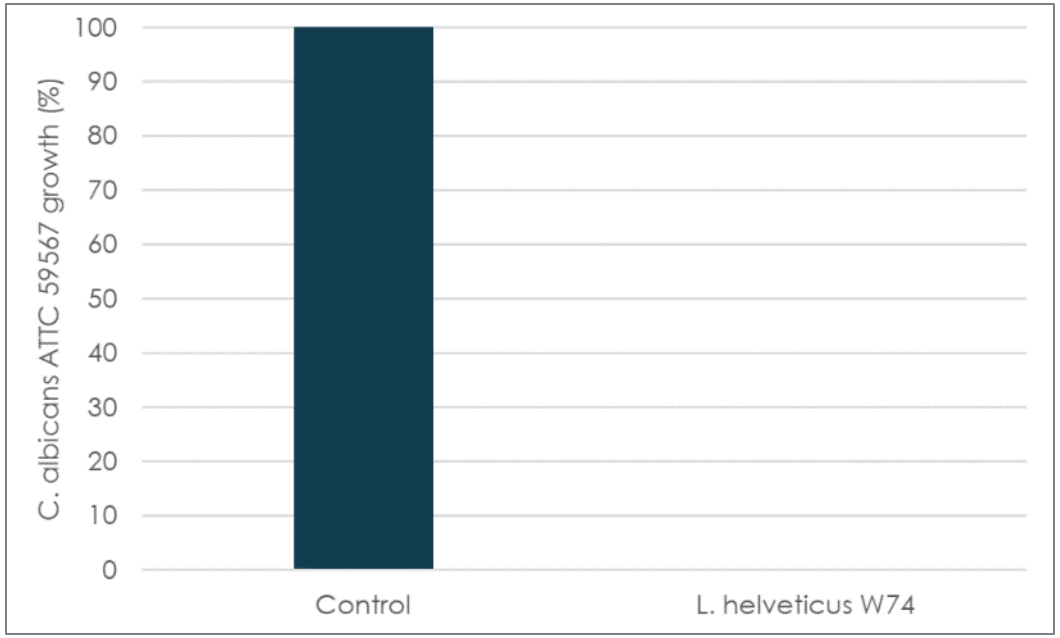


1. Campana, R. et al. Gut Pathog 9, (2017)
2. Proprietary data

Return to overview

Yeast reduction

- This BB consists of:
  - *Lactobacillus plantarum* W21
  - *Lactobacillus acidophilus* W22
  - *Lactobacillus salivarius* W57
  - *Lactobacillus helveticus* W7
- The strains are selected for their ability to inhibit pathogenic yeasts such as *Candida albicans* ATCC 14053, *Candida albicans* ATCC 59567 and *Candida glabrata* ATCC 90030 (fig)[1].
- In addition, there is some evidence for:
  - Pathogen inhibition[1,2]
  - Th1/Th2 balancing[3]
- Typical use: patients with overgrowth of candida



1. Proprietary data
2. Campana, R. et al. Gut Pathog 9, (2017)
3. Kepert, I. et al. Journal of Allergy and Clinical Immunology 139, 1525–1535 (2017)

Return to overview

Vitamin K2 booster

- This BB consists of:
  - *Lactobacillus brevis* W78
  - *Bacillus coagulans* W183
  - *Propionibacterium freudenreichii* W200
  - *Bacillus subtilis* W201
- These strains are selected for their capacity to produce vitamin K2 in various subtypes (fig)[1].
- Vitamin K2 produced by bacteria in the gut can be absorbed and contributes to vitamin K2 use by other commensals[2,3].
- Evidence for therapeutic uses of vitamin K2:
  - Osteoporosis (meta-analysis of RCTs, fig)[4]
  - Arterial stiffness[5]
  - Glycemic control / T2DM[6-8]
  - Depression[9]
- Typical use: patients with osteoporosis or atrial stiffness combined with metabolic dysfunction

	MK4	MK5	MK6	MK7	MK8	MK9	MK9-4H	MK10
B.subtilis W201		0,1	0,4	105,9	1,9	0,2		
P. freudenreichii W200		0,2		0,02	0,3	20,1	1040	
B. coagulans W64		0,1	0,1	23,7	1,3	0,1		0,1
L. brevis W63				0,01	0,004	0,007		

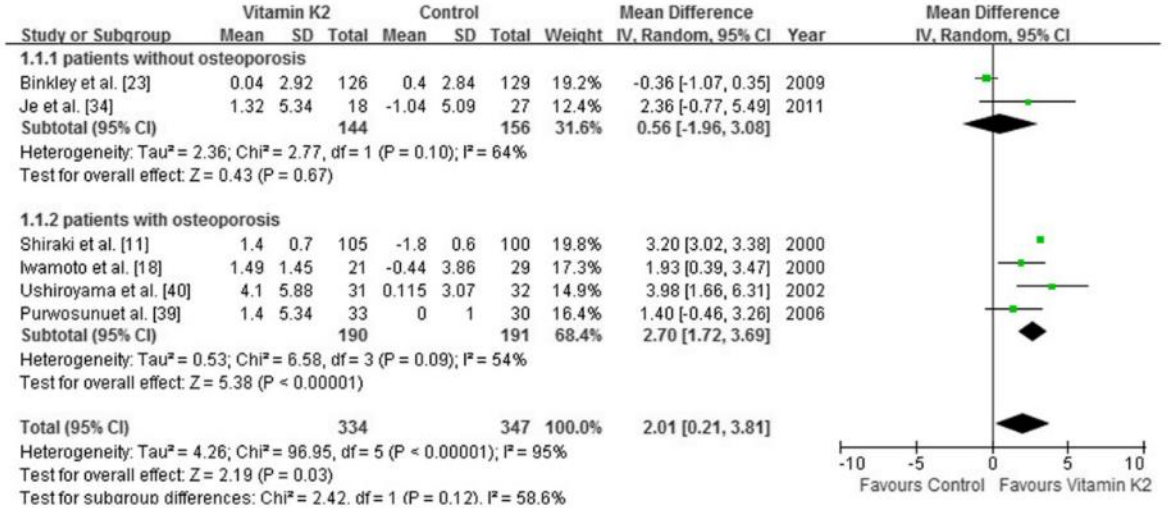


Fig. 2 Forest plot of the medium-term follow-up of vertebral BMD changes, showing a significant improvement of vertebral BMD in osteoporosis subgroup analysis and overall effect for vitamin K2 over control group

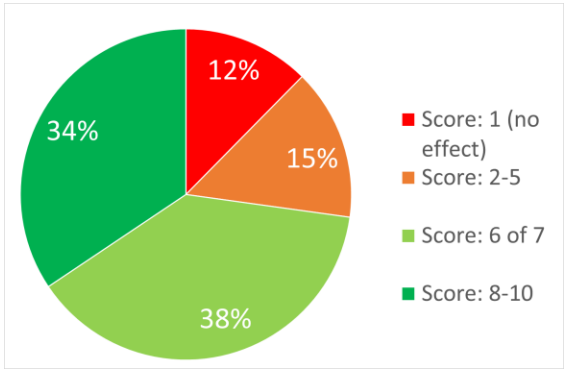
1. Proprietary data
2. Walther, B. et al. Adv Nutr 4, 463–473 (2013)
3. Halder, M. et al. Int J Mol Sci 20, (2019)
4. Huang, Z.-B. et al. Osteoporos Int 26, 1175–1186 (2015)
5. Knapen, M. H. J. et al. Thrombosis and Haemostasis 113, 1135–1144 (2015)
6. Rahimi Sakak, F. et al. European Journal of Nutrition (2020)
7. Karamzad, N. et al. Diabetes Metab Syndr Obes 13, 2239–2249 (2020)
8. Aguayo-Ruiz, J. I. et al. Diabetology & Metabolic Syndrome 12, (2020)
9. Tarkesh, F. et al. BMC Womens Health 22, 315 (2022)

Return to overview

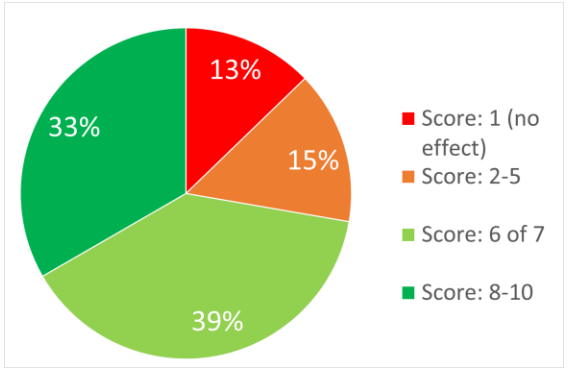
Interventions - Butyrate generator

- This building block contain three strains:
  - *Bacillus mesentericus*
  - *Enterococcus faecalis*
  - *Clostridium butyricum*
- On the Japanese market as medicine since 1963
- Strains act symbiotically, yielding *in situ* butyrate production of *C. butyricum*
- Butyrate has strong anti-inflammatory properties[1-3]
  - Exemplified by effect of this building block on ulcerative colitis[4-6]
- For this building block there is also evidence for:
  - Anti-inflammatory effects[4,7,8]
  - Infectious diarrhea[7,8]
- Data analysis: favorable effect in patients with allergy.
- Typical use: inflammation with low butyrate-producing capacity.

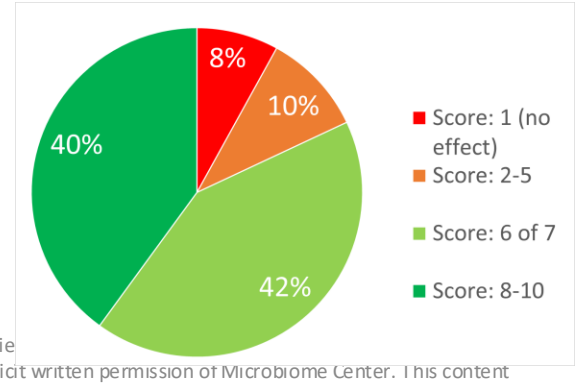
Data till December 2023



All patients (n=1195)



All patients with allergy (n=321)



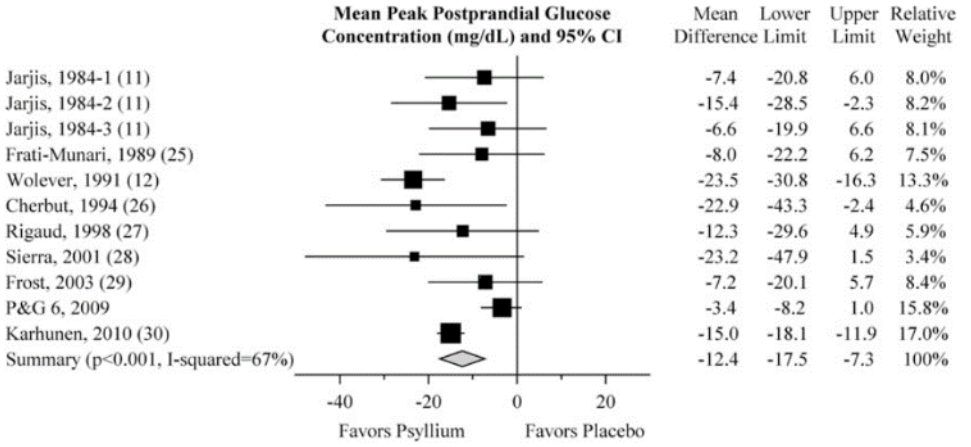
Patients with allergy using butyrate generator (n=100)

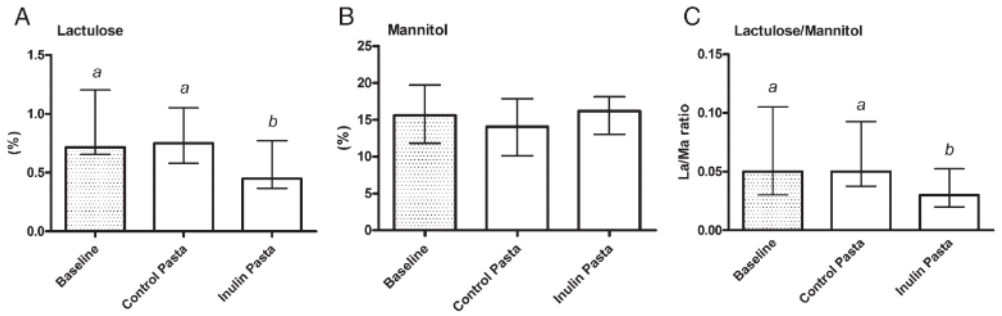
1. Brahe, L. K. et al. Obesity Reviews 14, 950–959 (2013)
2. Chang, P. V. et al. PNAS 111, 2247–2252 (2014)
3. Stoeva, M. K. et al. Gut Microbes 13, 1907272 (2021)
4. Yoshimatsu, Y. et al. World J Gastroenterol 21, 5985–5994 (2015)
5. Tsuda, Y. et al. Scand. J. Gastroenterol. 42, 1306–1311 (2007)
6. Lee, J. et al. Gastroenterology Research and Practice 2022, 1–5 (2022)
7. Chen, C.-C. et al. Pediatr. Infect. Dis. J. 29, 135–138 (2010)
8. Huang, Y.-F. et al. J. Clin. Gastroenterol. 48, 37–42 (2014)
9. Aisu, N. et al. Experimental and Therapeutic Medicine 10, 966–972 (2015)

Return to overview

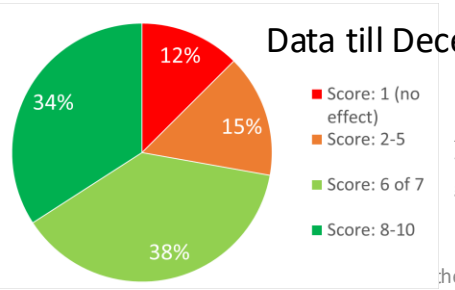
Microbiotia booster – fiber complex

- This BB contains five different fibers:
  - Psyllium fibers
  - acacia fibers
  - inulin fibers
  - pea fibers
  - konjac fibers (glucomannan)
- Not studied in this combination, but at individual level.
- There is evidence for effects in:
  - Diabetes type 2 (meta-analyses, fig)[1-3]
  - Intestinal permeability (fig)[4,5]*
  - Constipation[6,7]
- *Often with higher daily doses, but data analysis shows positive results on intestinal permeability (fig).
- Typical use: patients with intestinal permeability and T2DM or constipation, without severe food intolerances

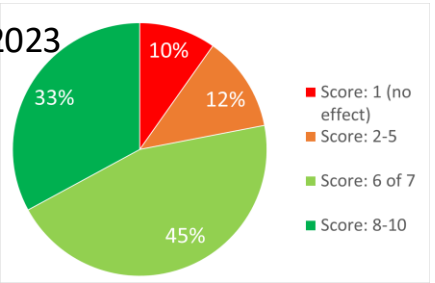




Data till December 2023



All patients with leaky gut (n=665)



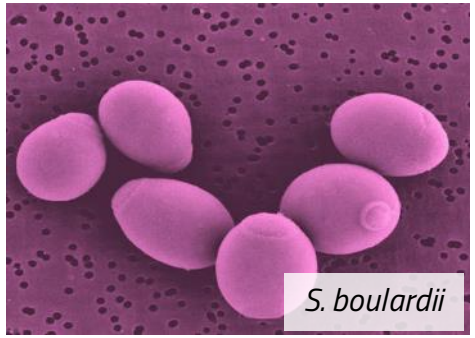
Patients with leaky gut using fiber complex (n=82)

1. Gibb, R. D. et al. The American Journal of Clinical Nutrition 102, 1604–1614 (2015)
2. Liu, F. et al. European Journal of Clinical Nutrition 71, 9–20 (2017)
3. Sood, N. et al. The American Journal of Clinical Nutrition 88, 1167–1175 (2008)
4. Russo, F. et al. Nutrition Research 32, 940–946 (2012)
5. Christodoulides, S. et al. Alimentary Pharmacology & Therapeutics 44, 103–116 (2016)
6. Gabrielli, F. et al. Minerva Chir 71, 98–105 (2016)
7. Collado Yurrita, L. et al. Nutr Hosp 30, 244–252 (2014)

Return to overview

S. Boulardii

- *Saccharomyces cerevisiae var boulardii* CNCM-I-1079 is a yeast.
  - Much bigger than most bacteria.
- Isolated in 1923 by Henri Boulard from skin of tropical fruits in Southeast Asia, after he observed that people who ate these did not get diarrhea from cholera[1,2].
- Extensively studied, >120 clinical trials. Most studied for several types of diarrhea (meta-analyses):
  - Antibiotics-associated diarrhea[3,4]
  - Travelers' diarrhea[5]
  - Infectious diarrhea[6]
- Other evidence-based therapeutic uses:
  - Helicobacter pylori erradication (fig)[7]
  - Parasitic infections (fig)[8-10]
  - Anit-inflammatory effects[11]
  - SIBO[12]
  - Etc.
- Typical use: diarrhea, parasites, or SIBO



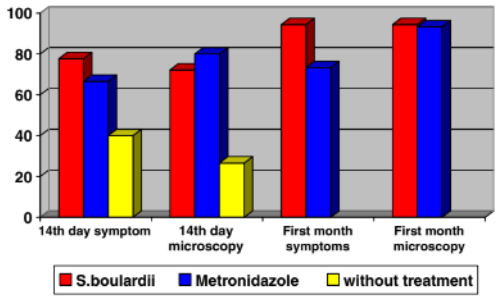


Fig. 1 Cure rate for clinical findings and parasitological examinations between study groups on the 14th day and first month

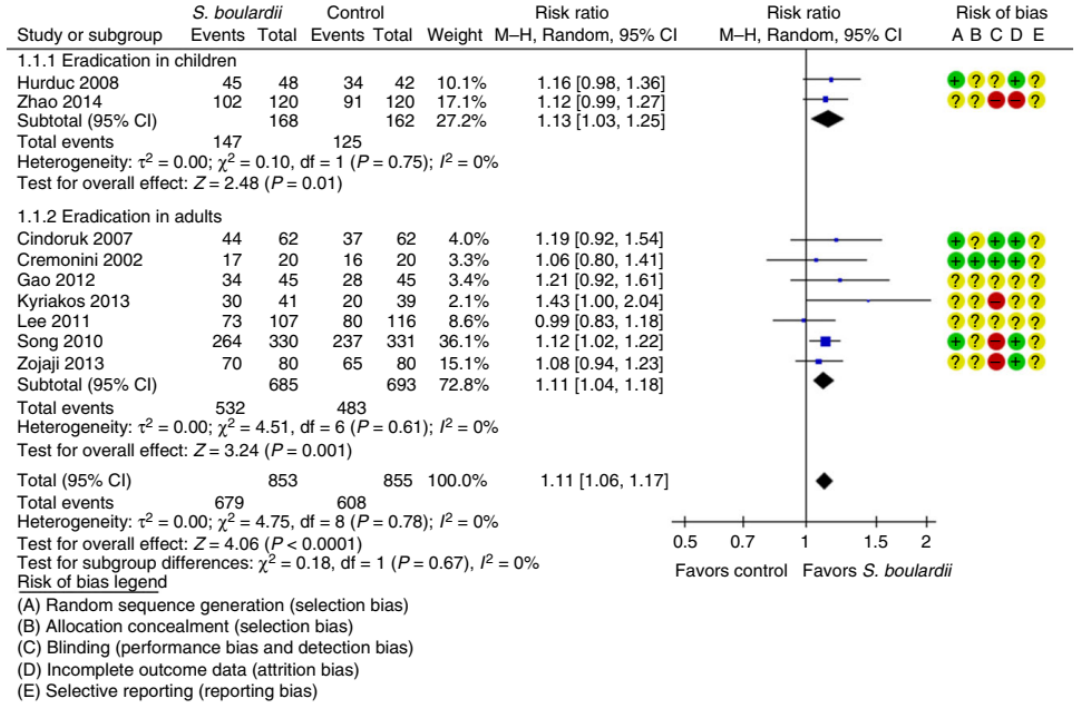


Figure 1 | Primary outcome: Effect of *Saccharomyces boulardii* (SB) on *Helicobacter pylori* eradication rates.

1. Czerucka, D. et al. World J Gastroenterol 25, 2188–2203 (2019)
2. McFarland, L. V. World J Gastroenterol 16, 2202–2222 (2010)
3. Szajewska, H. et al. Aliment Pharmacol Ther 42, 793–801 (2015)
4. Blaabjerg, S. et al. Antibiotics 6, 21 (2017)
5. McFarland, L. V. Travel Med Infect Dis 5, 97–105 (2007)
6. Feizizadeh, S. et al. PEDIATRICS 134, e176–e191 (2014)
7. Szajewska, H. et al. Alimentary Pharmacology & Therapeutics 41, 1237–1245 (2015)
8. Dinleyici, E. C. et al. Am. J. Trop. Med. Hyg. 80, 953–955 (2009)
9. Dinleyici, E. C. et al. Parasitol. Res. 108, 541–545 (2011)
10. Besirbellioglu, B. A. et al. Scandinavian Journal of Infectious Diseases 38, 479–481 (2006)
11. Abbas, Z. et al. European Journal of Gastroenterology & Hepatology 1 (2014)
12. García-Collinot, G. et al. Dig Dis Sci 65, 1134–1143 (2020)

Return to overview

L. acidophilus LA02

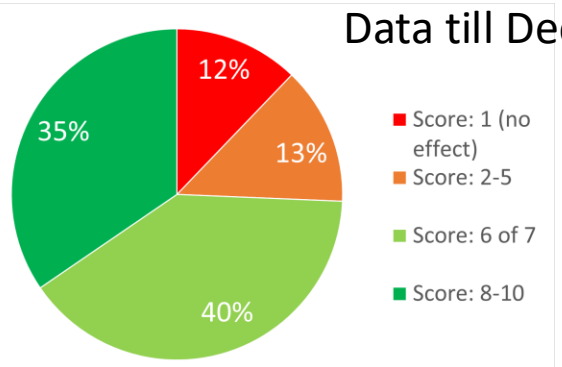
- The *Lactobacillus acidophilus* La02 is selected for its oxalate metabolizing capacity[1].
  - Oxalate metabolization may lower the risk of kidney stones.
- Other evidence-based therapeutic uses:
  - Inhibiting pathogens[2]
  - Inhibiting candida[5]
  - Improving intestinal barrier[2]
  - IBS[3]
  - Vaginosis (vaginal application)[4,5]
- Data analysis: promising in inflammation (fig)
- Typical uses: low oxalate-metabolizing capacity, candida, IBS

Time	Sample	*C. albicans* ATCC 10231	*Candida parapsilosis* ATCC 22019	*Candida krusei* ATCC 6258	*C. albicans* ATCC 90028	*Candida glabrata* ATCC 2001
(A) Fresh broth cultures						
Time 0 (inoculum)	Yeast alone	2450	3100	1870	1300	1000
24 h	Yeast alone	3,860,000	600,000	660,000	4800,000	12,000,000
	Yeast + LA02	260,000	260,000	280,000	470,000	2,280,000
48 h	Yeast alone	4,500,000	3,500,000	2,700,000	8,800,000	34,000,000
	Yeast + LA02	61,000	120,000	1500	59,000	1,170,000

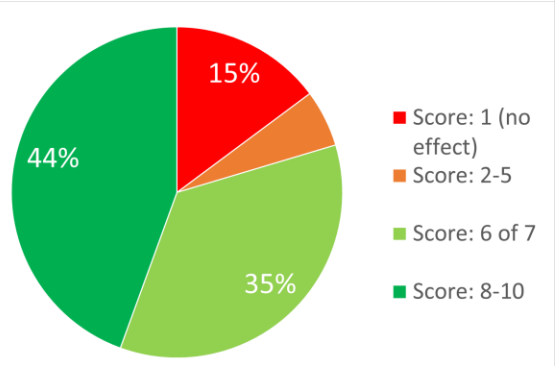
TABLE 1. Clinical Outcome (Efficacy Analysis) of Study Population

Time	n/N (%) Cure	Recurrence
Prophylactic phase		
I phase—10 d	58/57 (98.3)	58/1 (1.7)
II phase—10 wk	57/49 (86.0)	57/8 (14.0)
Observation phase (mo)		
1	49/45 (91.8)	49/4 (8.2)
3	45/43 (95.6)	45/2 (4.4)
7	43/42 (97.7)	43/1 (2.3)
Cumulative rate	58/42 (72.4)	58/16 (27.6)

Data till December 2023



All patients with inflammation (n=304):



Patients with inflammation using La02 (n=54)

1. Mogna, L. et al. Journal of Clinical Gastroenterology 48, S91–S95 (2014)
2. Magistrelli, L. et al. Front. Immunol. 10, (2019)
3. Saggioro, A. Journal of Clinical Gastroenterology 38, S104–S106 (2004)
4. Murina, F. et al. Journal of Clinical Gastroenterology 48, S102–S105 (2014)
5. Vicariotto, F. et al. Journal of Clinical Gastroenterology 46, S73–S80 (2012)

Return to overview

L. acidophilus LA02

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  - Oxalate metabolization may lower the risk of kidney stones.
- Other evidence-based therapeutic uses:
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  - Inhibiting candida[5]
  - Improving intestinal barrier[2]
  - IBS[3]
  - Vaginosis (vaginal application)[4,5]
- Data analysis: promising in inflammation (fig)
- Typical uses: low oxalate-metabolizing capacity, candida, IBS

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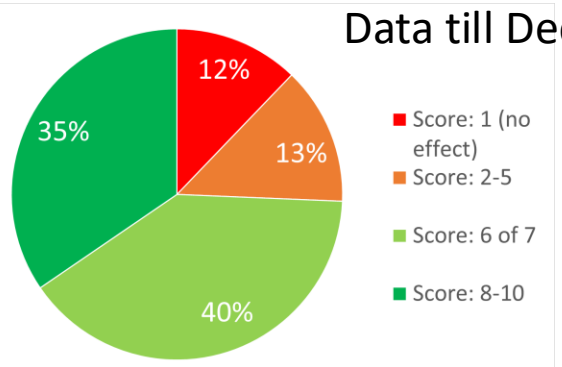
Data till December 2023



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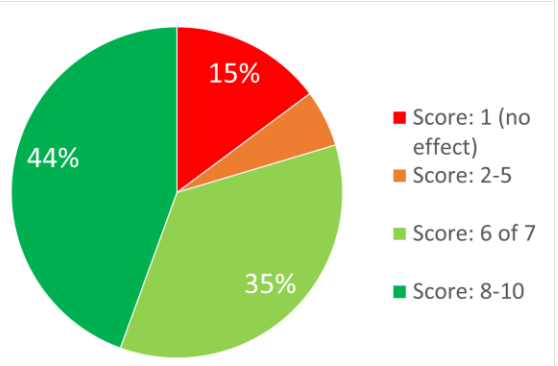


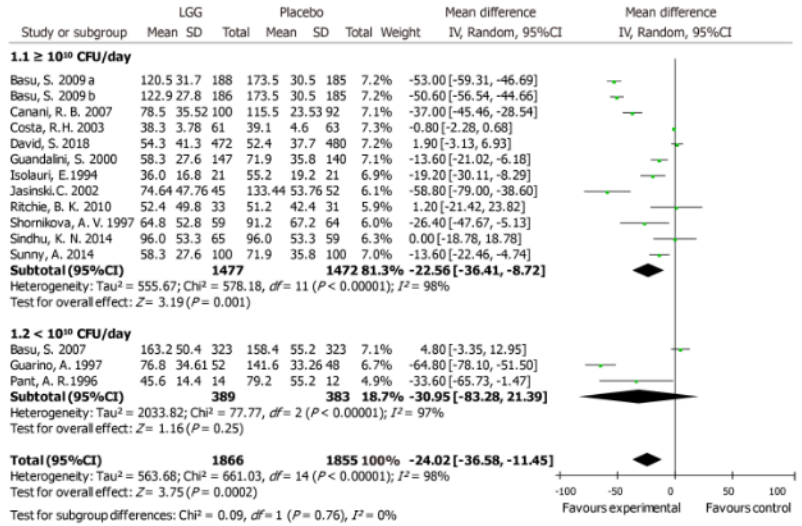
Patients with inflammation using La02 (n=54)

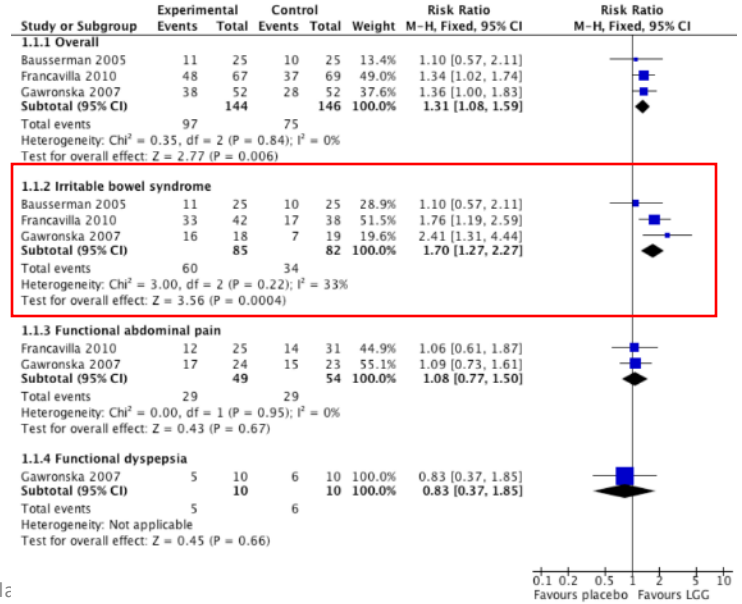
1. Mogna, L. et al. Journal of Clinical Gastroenterology 48, S91–S95 (2014)
2. Magistrelli, L. et al. Front. Immunol. 10, (2019)
3. Saggioro, A. Journal of Clinical Gastroenterology 38, S104–S106 (2004)
4. Murina, F. et al. Journal of Clinical Gastroenterology 48, S102–S105 (2014)
5. Vicariotto, F. et al. Journal of Clinical Gastroenterology 46, S73–S80 (2012)

Return to overview

L. rhamnosus GG

- *Lacticaseibacillus rhamnosus* GG is world's most studied probiotic strain (>1650 articles in Pubmed (Feb '24)).
- It is the go-to strain for researchers who want to study a probiotic, often without a rationale selection.
  - Not effective in all studied indications
- Indications with meta-analyses of RCTs:
  - Acute diarrhea (fig)[1,2]
  - Antibiotics-associated diarrhea[3,4]
  - IBS (fig)[5,6]
- Other evidence-based indications:
  - Liver steatohepatitis[7]
  - Respiratory tract infections[8]
  - Candida infection[9,10]
  - Intestinal permeability[11]
  - Etc.
- Typical uses: diarrhea, IBS, candida overgrowth





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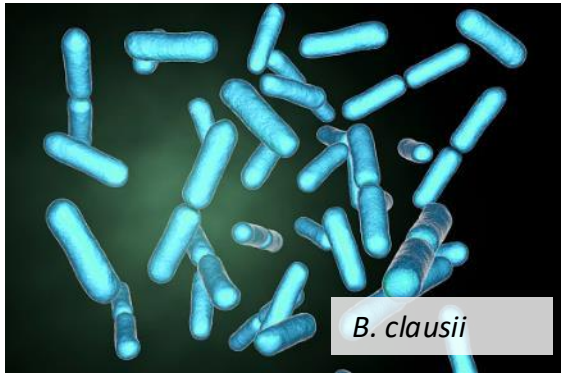
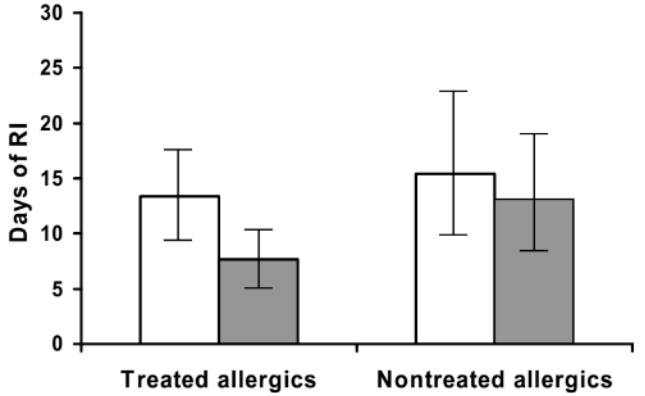
Return to overview

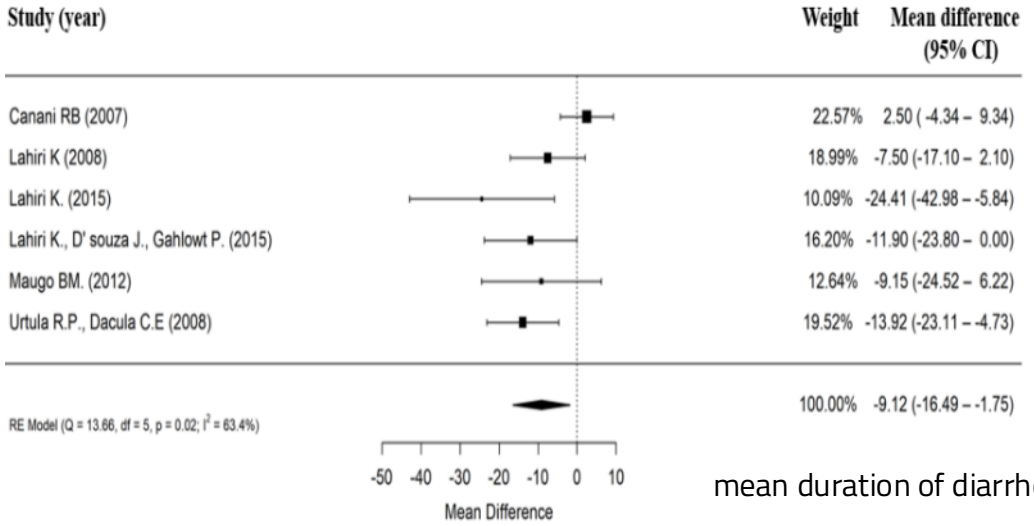
Bacillus clausii UBBC-07

- *Bacillus clausii* UBBC-07 is a spore-forming strain, making it extremely stable.
- It is genetically closely related to the metagenome of a set of *B. clausii* strains that have been studied extensively[1].
- The evidence-based therapeutic uses consist of:
  - Acute diarrhea[2-4] (fig)
  - Antibiotics-associated diarrhea[5,6]
  - SIBO[7,8]
  - Respiratory tract infections (fig)[9]
  - Gingivitis (as mouth wash)[10]
  - Pathogen inhibition[11,12]
  - Ulcerative colitis[13]
  - Mucositis[14]
  - Etc.
- Typical uses: SIBO with pathogens, diarrhea





Duration of resp.tract inf.



mean duration of diarrhea

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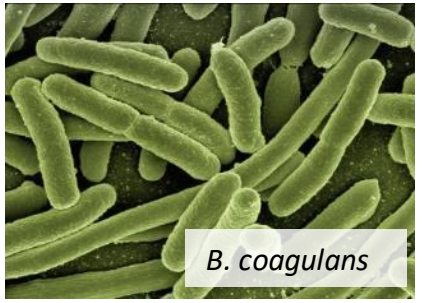
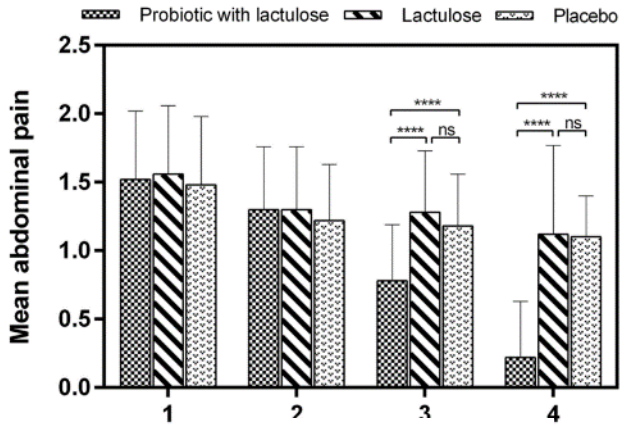
Return to overview

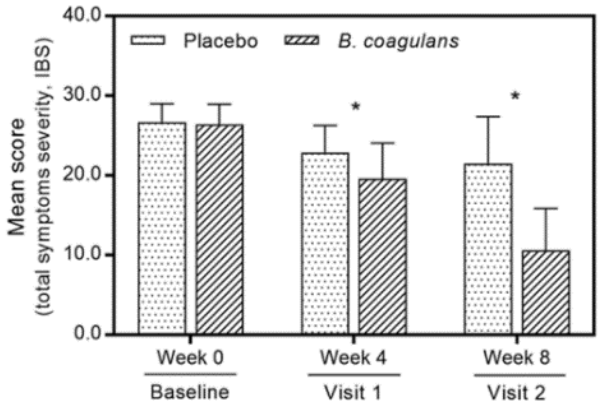
Bacillus coagulans Unique IS-2

- *Bacillus coagulans* Unique IS-2 is a spore-forming strain, making it extremely stable.
- Bacillus species are often called 'soil-based' probiotics, but this strain is isolated from a human stool sample[1].
- The evidence-based therapeutic uses consist of:
  - Constipation (fig)[2,3,9]
  - IBS (fig)[4-6]
  - SIBO[7]
  - Liver cirhosis[8]
  - Vaginosis (oral use)[9]
  - Ulcerative colitis[10]
- Typical uses: constipation, SIBO/IBS

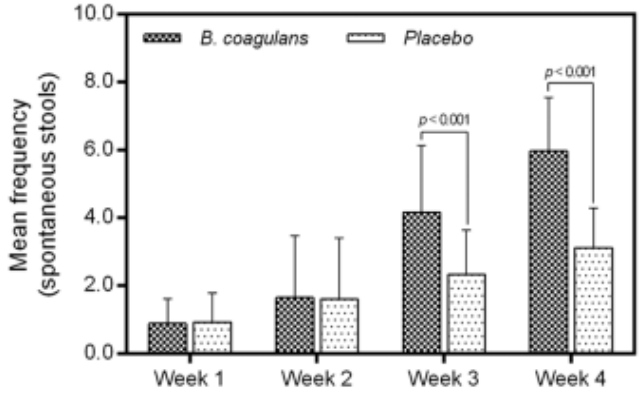




Constipation



IBS



Constipation

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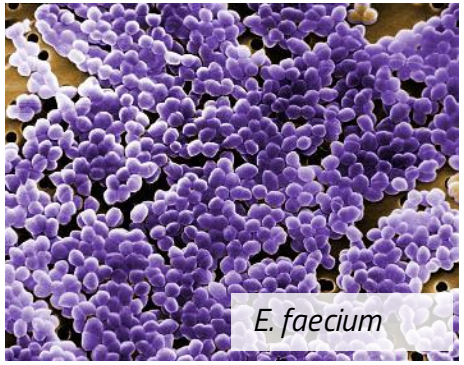
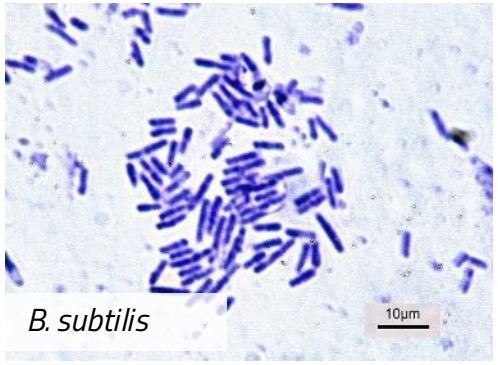
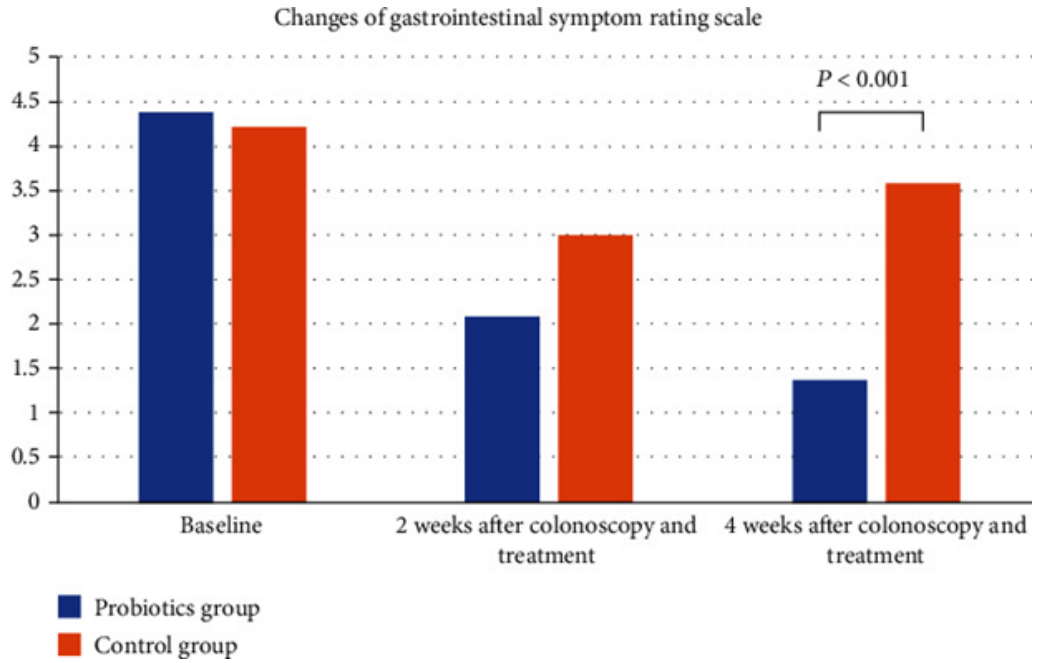
Return to overview

E. faecium + B. subtilis

- This ingredient is a combination of two strains: *Enterococcus faecium* Rosell-26 + *Bacillus subtilis* Rosell-179
- On the market as a drug in Asia.
- This drug has been studied extensively, primarily for ulcerative colitis, as shown in a meta-analysis of >50 RCTs[1].
- There is also scientific evidence for:
  - Anti-inflammatory effects[1,2]
  - IBS and abdominal pain[3,4]
  - Respiratory tract infections[5]
  - SIBO (fig)[6,7]
  - Etc.
- Typical use: inflammation (or UC) or SIBO







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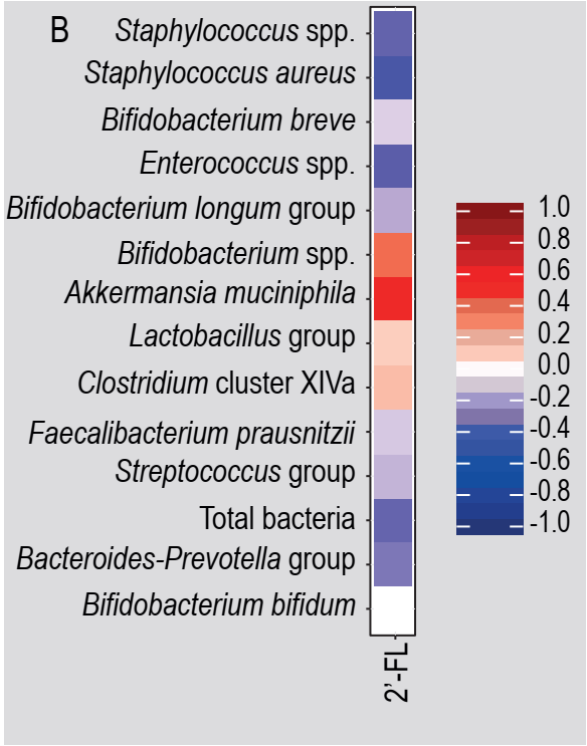
2’fucosyllactose

- This building block consists of the most abundant Human Milk Oligosaccharide (HMO) in breast milk: 2’fucosyllactose (2’FL).
- Typical daily dose: 5g/d
  (N.B.: most food supplements use 0.25g/d)
- 2’FL contributes to the development of the microbiome (prebiotic, anti-pathogenic), tuning of the immune system, and gut-brain axis[1].
- Therapeutic effects include:
  - Anti-inflammatory effects[2,3]
  - Stimulate *Akkermansia* and *A. soehngenii*[4,5]
  - Inhibit pathogens[6,7]
  - Management of allergies (fig)[8,9].
- Typical use: low Akkermansia, allergies



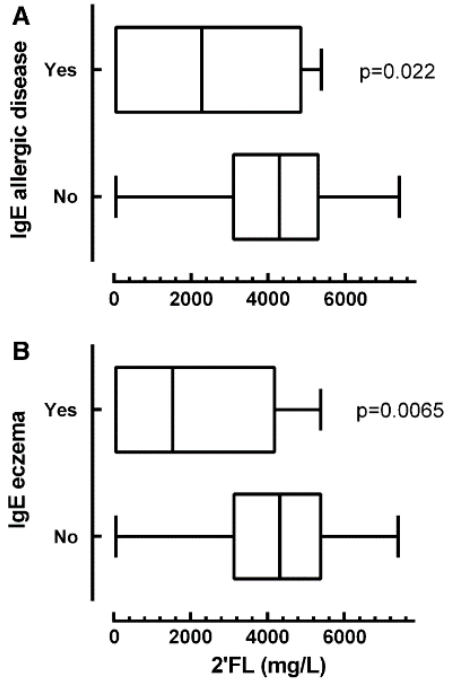


Fig. 2 Breast milk consumed by C-section-born infants who did not show IgE-associated allergic disease and IgE-associated eczema contained higher levels of 2′-fucosyllactose a proxy for FUT2-dependent oligosaccharides. 2′-Fucosyllactose (2′FL) levels in early breast milk (2.6 ± 1.1 days *postpartum*) that was consumed by C-section-born infants who showed IgE-associated allergic disease (**a**) or IgE-associated eczema (**b**) at 2 years or not. Box and whisker plots are shown with median and minimal and maximal values. Two-tailed *p* values from unpaired *t* test are indicated

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Return to overview

L. plantarum P-8

- The *Lactiplantibacillus plantarum* P-8 is isolated from a traditional fermented dairy product from Mongolia.
- A well-designed RCT shows an effect on **depression, stress and anxiety**[2], which is expected to be caused by changes in microbial production of neuro-active substances such as GABA[3].
- In addition, there is evidence for:
  - IBS[4]
  - Anti-inflammatory effect[4,2]
  - Increasing sIgA excretion[5]
  - Reduction of bile acids[5]
- Typical use: depression/anxiety, IBS

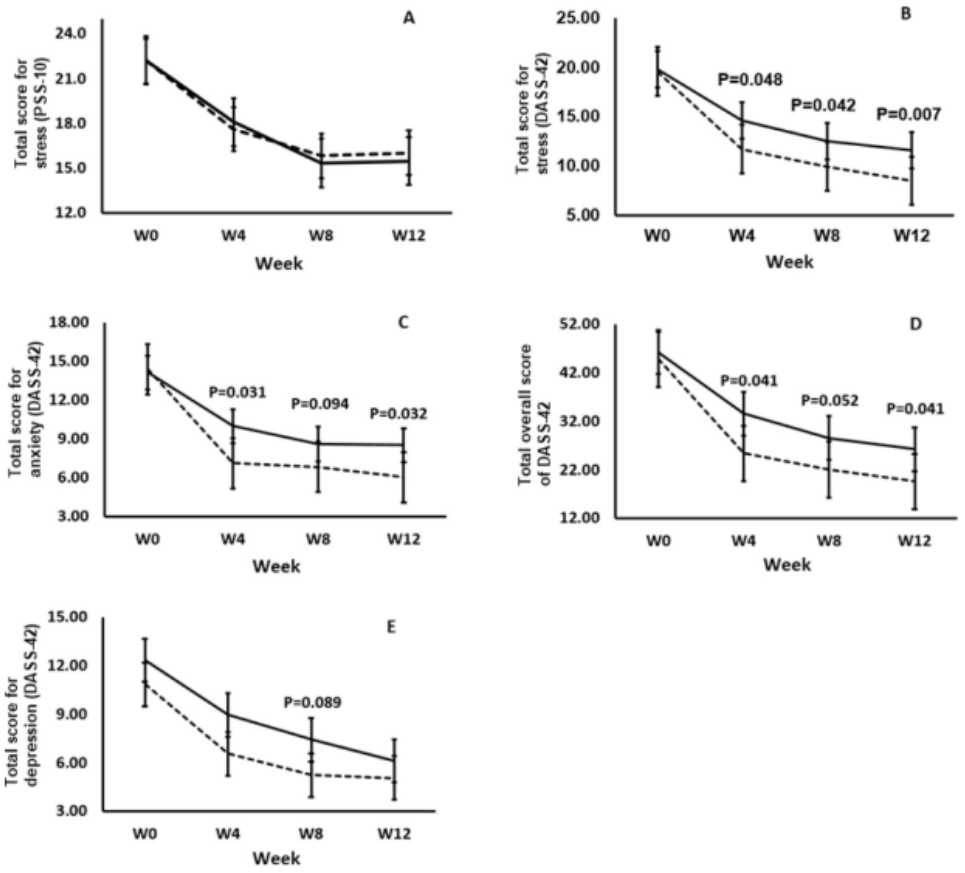

Fig. 2. Effects of a 12-week administration of probiotic *L. plantarum* P8, P8 (---) or placebo (—) on the total scores of (A) stress based on the PSS-10 questionnaire (W: $P < 0.001$, T: $P = 0.788$, TxW: $P = 0.820$), (B) stress (W: $P < 0.001$, T: $P = 0.030$, TxW: $P = 0.293$), (C) anxiety (W: $P < 0.001$, T: $P = 0.077$, TxW: $P = 0.170$), (D) total scores (W: $P < 0.001$, T: $P = 0.054$, TxW: $P = 0.427$), and (E) depression (W: $P < 0.001$, T: $P = 0.163$, TxW: $P = 0.787$) based on the DASS-42 questionnaire. P-values indicated difference between treatment groups at individual time points. Results are expressed as mean; error bars (SEM); n = 103. Repeated measures ANOVA provided statistical significance on W: effect of weeks; T: effect of treatment groups P8 and placebo; TxW: interaction between weeks and treatment.

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Return to overview

PHGG

- This fiber is derived from the guar bean (*Cyamopsis tetragonoloba*) and partially hydrolyzed enzymatically to make it less viscous[1].
- This fiber is extremely well-studied, hundreds of clinical studies have been conducted since 1970's.
- Contrary to most other fibers, PHGG has found to be efficacious at daily doses of ~5g.
- Important therapeutic uses:
  - Insulin resistance (dozens of studies, e.g., fig[2,3])
  - IBS, abdominal pain, bloating[1,4,5]
  - Constipation[6,7]
  - Diarrhea[8,9]
  - Depression and anxiety[1]
  - SIBO[10]
- Typical use: IBS and symptoms, SIBO, diabetes

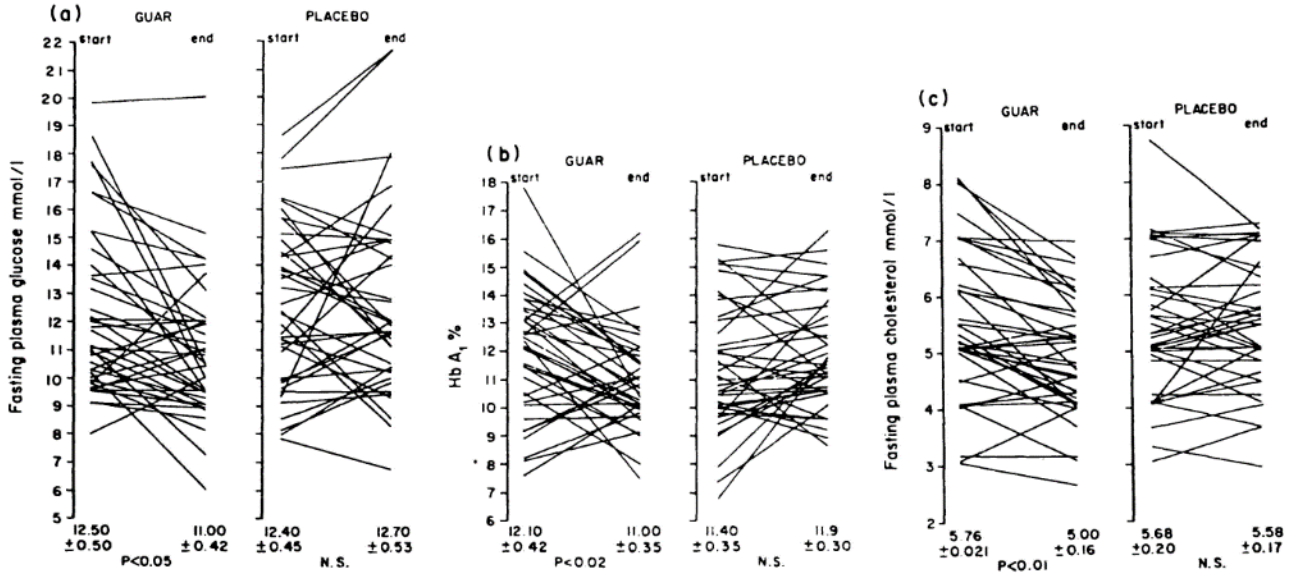

FIGURE 1. Individual changes in fasting plasma glucose (a), glycosylated hemoglobin (b), and cholesterol (c) in all 39 patients.

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Return to overview

L. sakei probio65

- *L. sakei* probio65 is isolated from kimchi
- Mostly studied for its effect on atopic dermatitis (fig)
  - Two RCTs[1,2]
  - Several animal studies
- In addition, in vitro and preclinical studies show:
  - Anti-inflammatory effects[3,4]
  - Pathogen inhibition[5]
  - Increasing insulin sensitivity[6,7]
- Typical use: allergies (dermatitis)

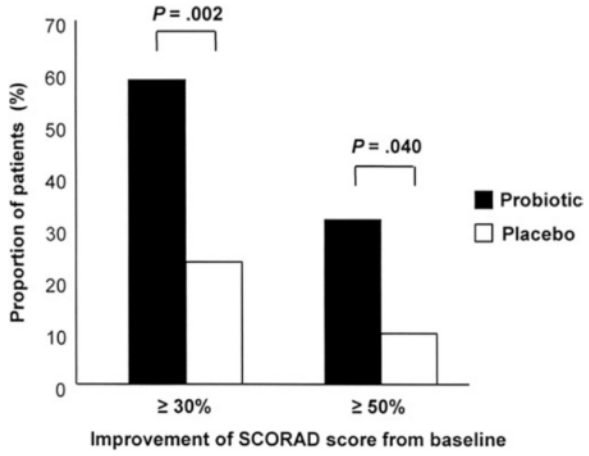

Figure 2. Patients achieving at least 30% and 50% improvement in SCORing of Atopic Dermatitis (SCORAD) scores at the study end point.

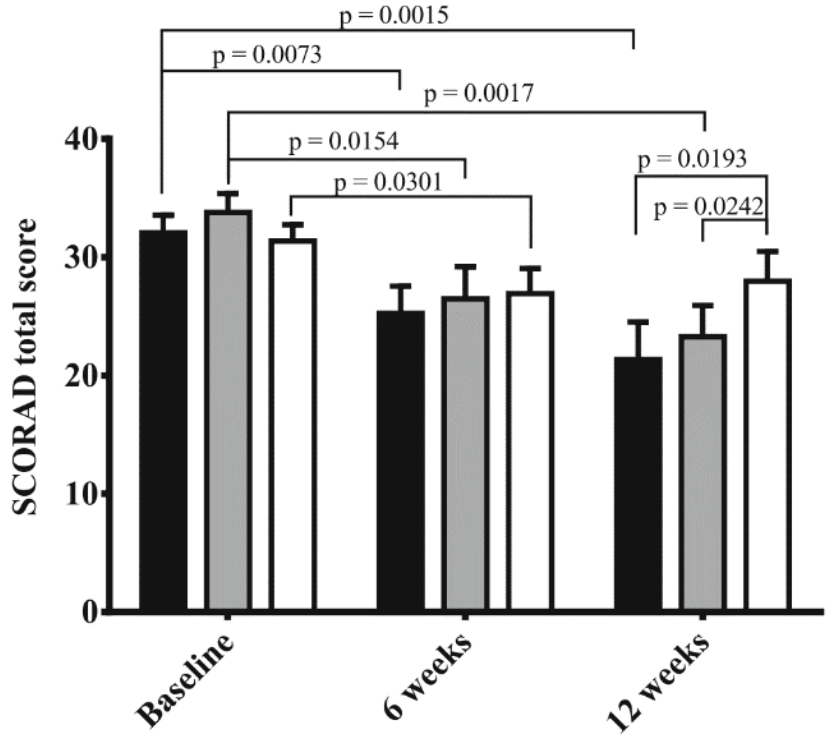

Fig. 2 Assessment of SCORAD total score. Results are expressed as mean; error bars (SEM). Statistical analysis was performed using paired t-tests when comparing within same group while Wilcoxon rank sum test was used when comparing between groups. I. Live cell (bar in black): freeze-dried *Lactobacillus sakei* proBio65 (1×10^{10} cells/day; $n = 16$). II. Dead cell (bar in gray): freeze-dried dead *Lactobacillus sakei* proBio65 (1×10^{10} cells/day; $n = 22$). III. Placebo (bar in white): microcrystalline cellulose only ($n = 20$). Statistical analysis was performed using paired *t* tests

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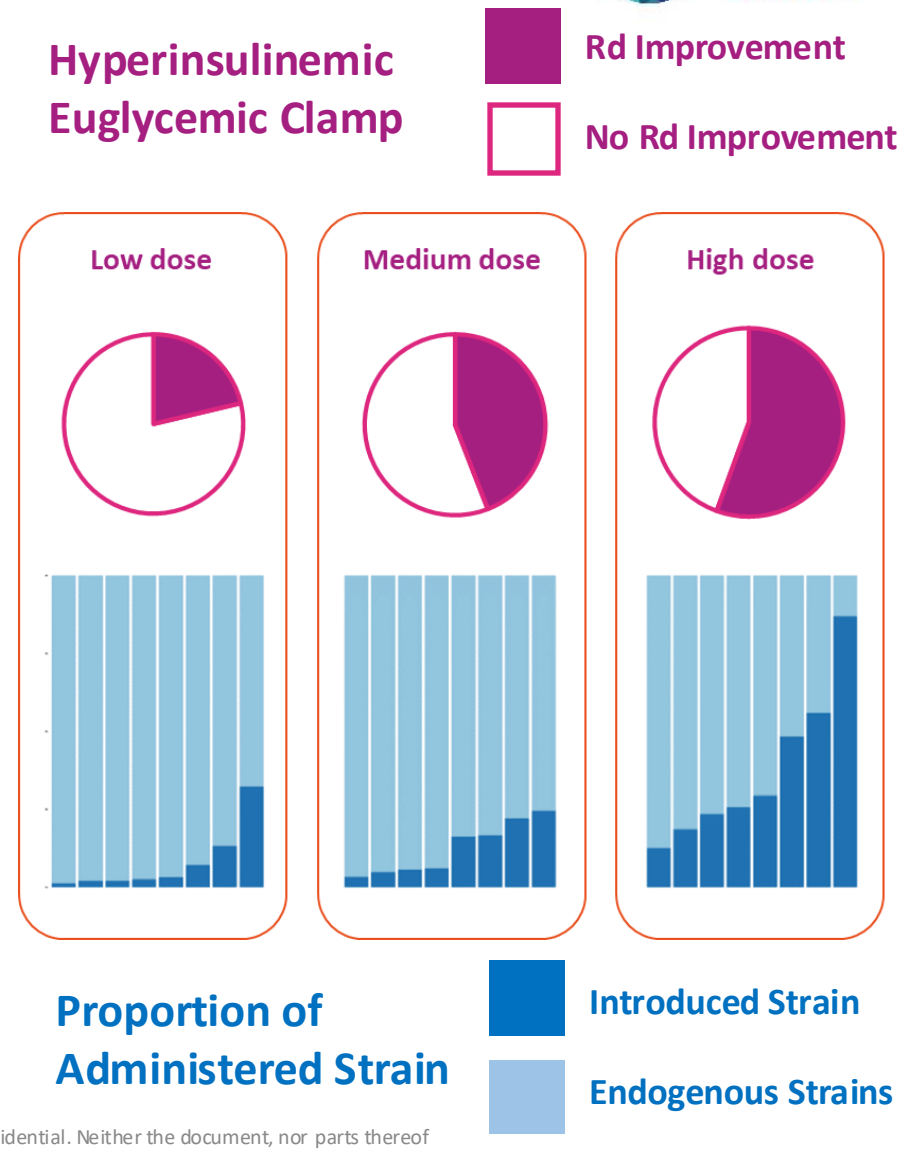
Return to overview

Anaerobutyricum soehngenii

- *A. soehngenii* is isolated from stool of an 11-month-old healthy infant[1].
- In fact, *A. soehngenii* (*E. hallii*) is one of the earliest butyrate-producing colonizers, already found at in healthy infants 2 weeks of age[2].
- It has the capacity to also produce butyrate from lactate in a low pH environment such as the proximal small intestine[3].
  - Other butyrate producers (e.g. *F. prausnitzii* or *Ruseburia* spp.) cannot utilize lactate.
  - *A. soehngenii* can thrive in the small intestines as well.
- This specific strain has been shown:
  - To be safe at even a high dose[5].
  - To stimulate GLP-1 production and lower **insulin resistance**[4,5].
- Butyrate has anti-inflammatory effects and often lowered in IBD:
  - *A. soehngenii* abundance is found to be lowered in IBD[6].
  - Conversely, high relative abundance of *A. soehngenii* is best predictor of success of fecal transplantation in ulcerative colitis[7].



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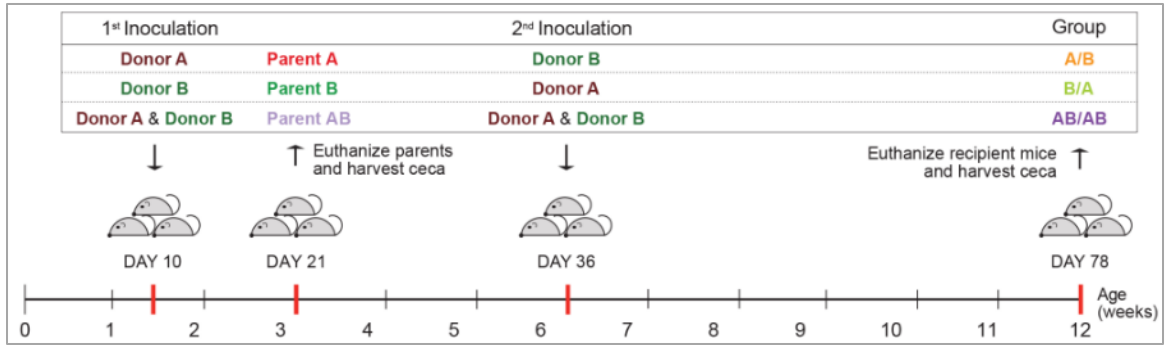
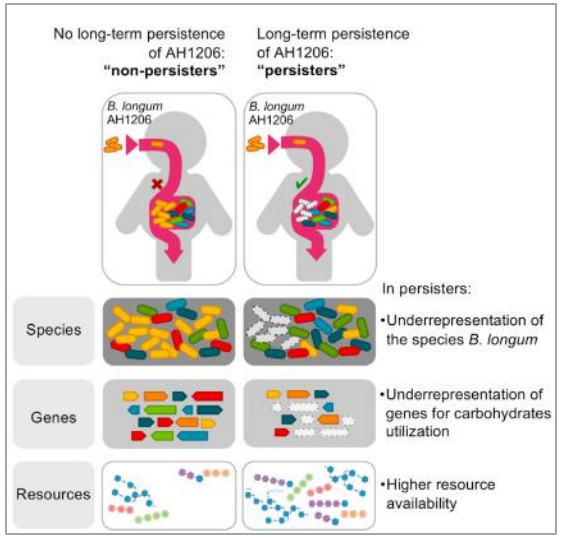
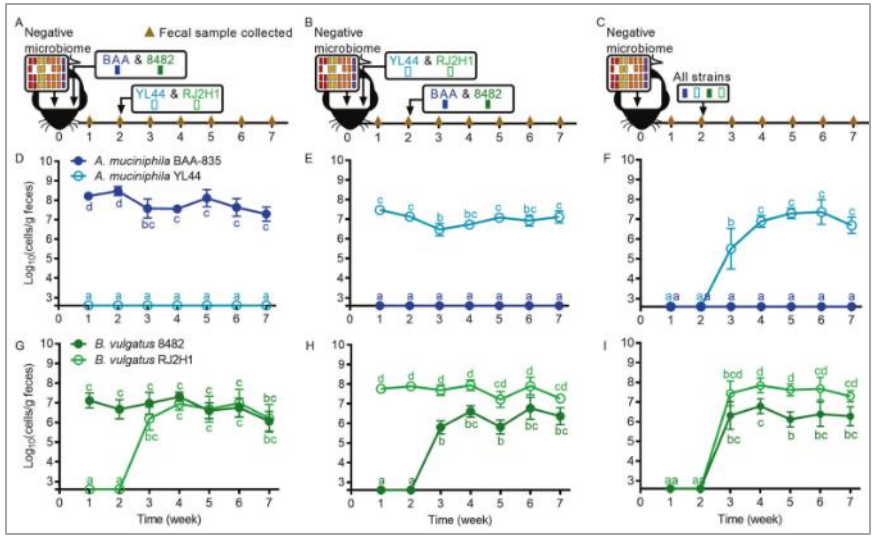
Gut enricher

- Recent insights have shown that ecological principles define the microbiome (fig):
  - Order of colonization[1]
  - Open niches allow colonization[2,3]
  - Strains adapt to host/niche[4]
- Host actively selects/supports bacteria:
  - Bacterial entero-mammary transfer[5-7]
  - Prevents commensals from starvation, curates composition of microbiome[8]
- Low microbiome diversity and richness is associated with many diseases[9,10].
- This BB consists of all currently available strains (~40 strains) at low dose (~10^6 cfu/g).
- This BB supports selection of strains by individual ecology and host factors in patients with low diversity (≤4).
- Typical use: low diversity







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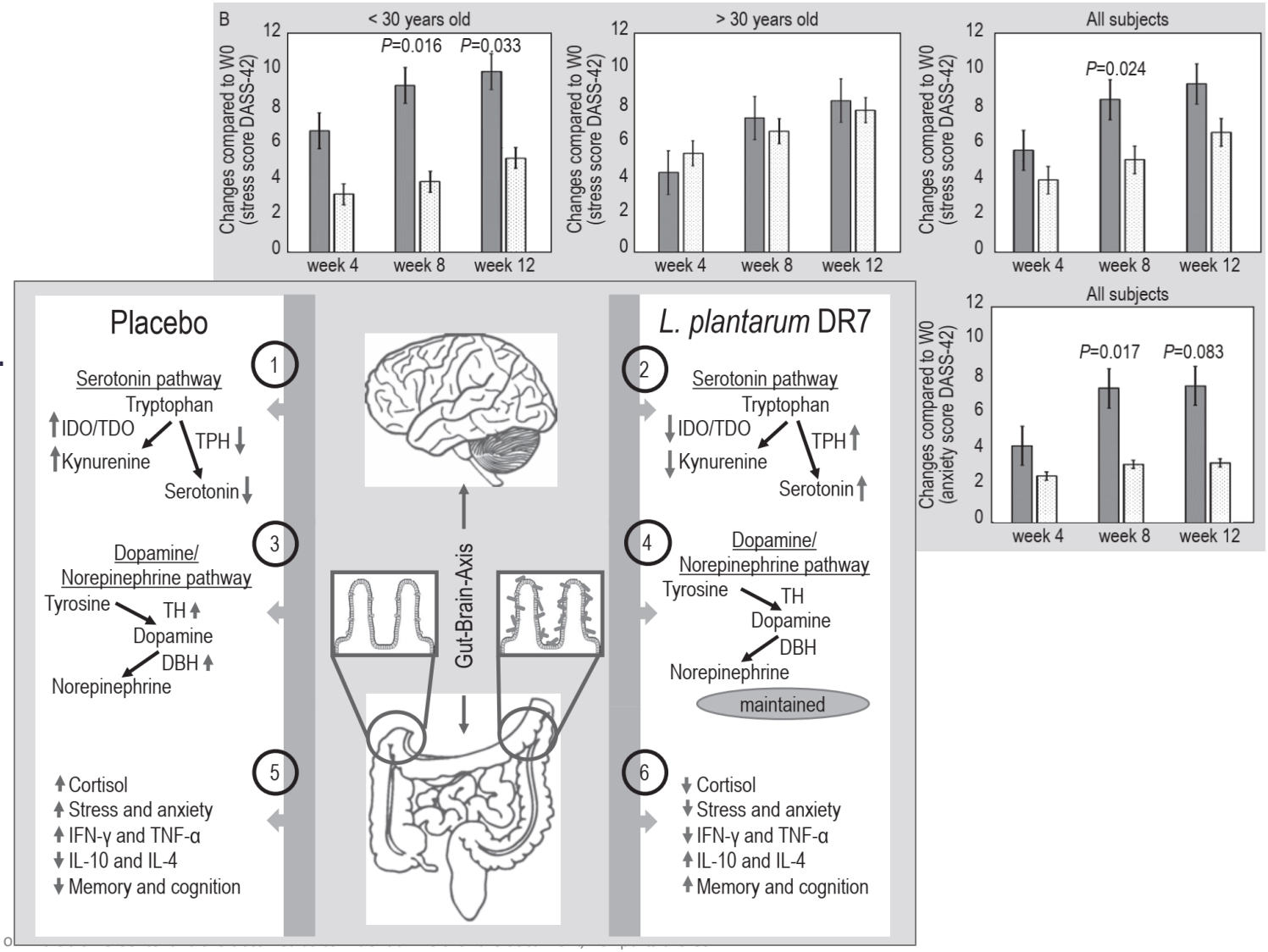
Return to overview

L. plantarum DR7

- The *Lactiplantibacillus plantarum* DR7 is isolated from cow's milk from Penang, Malaysia.
- A well-designed RCT shows an effect on **stress and anxiety**[2], which is expected to be caused by changes in the tryptophan and tyrosine pathways and inflammatory activity[2].
- In addition, there is evidence for:
  - Respiratory tract infection[3,4]
  - Anti-inflammatory effect[2,3]
  - Increasing AMPK activty[1,6,7]
    → Improved insulin signaling
- Typical use: stress/anxiety, airway infections



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Lacticaseibacillus rhamnosus SP1

- The *Lacticaseibacillus rhamnosus* SP1 is a human isolate.
- A small but well-designed RCT shows an effect on **acne**[1]; insulin sensitivity is expected to a mechanism of action.
- In addition, there is evidence for:
  - Denture stomatitis[2]
  - Inhibition of Candida[2]
  - Prevention of caries[3,4] (fig, lower beta-defensi probably due to healthier oral microbiome)
  - Degrading immunogenic gluten peptides[5]
- Typical use: acne, caries, gluten sensitivity

Table 2. Dental Caries in the Intervention Group (n = 123) and Control Group (n = 82) at Baseline and at the End of the Study.

	Probiotic Group	Control Group	Odds Ratio
Nursery schools, n	8	8	
Participants, n	123	82	
ICDAS 2–6 >0, baseline, %	39.3	42.3	0.94 (0.62–1.44)
ICDAS 2–6 >0, 12 mo, %	54.4	65.8	0.76 (0.51–1.14)
ΔICDAS 2–6 >0, 12 mo – baseline, %	16.2	20.8	0.76 (0.38–1.51)
ICDAS 5–6 >0, baseline, %	23.3	22.5	1.17 (0.68–2.01)
ICDAS 5–6 >0, 12 mo, %	33.3	45.1	0.71 (0.43–1.15)
ΔICDAS 5–6 >0, 12 mo – baseline, %	9.7	24.3	**0.35 (0.16–0.79)**[a]

Table 2. Change from baseline to 12 weeks in the investigator's global improvement rating of adult acne in the two study groups (data are given as counts and percentages).

Rating	Probiotic group (n=10)	Placebo group (n=10)
Worsened	0 (0%)	0 (0%)
Unchanged	2 (20%)	9 (90%)
Improved	6 (60%)	1 (10%)
Markedly improved	2 (20%)	0 (0%)
Resolved	0 (0%)	0 (0%)

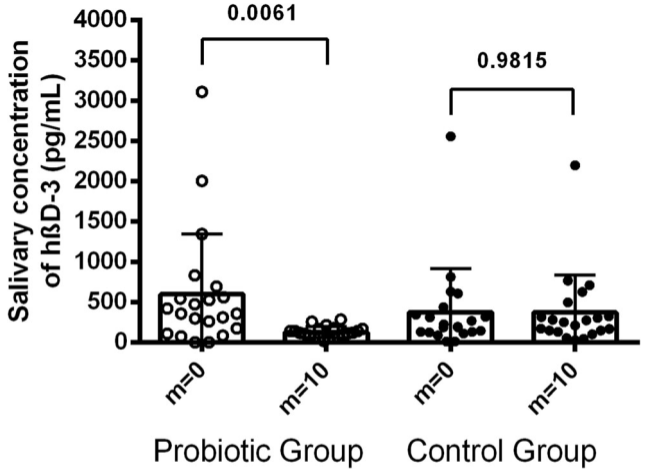


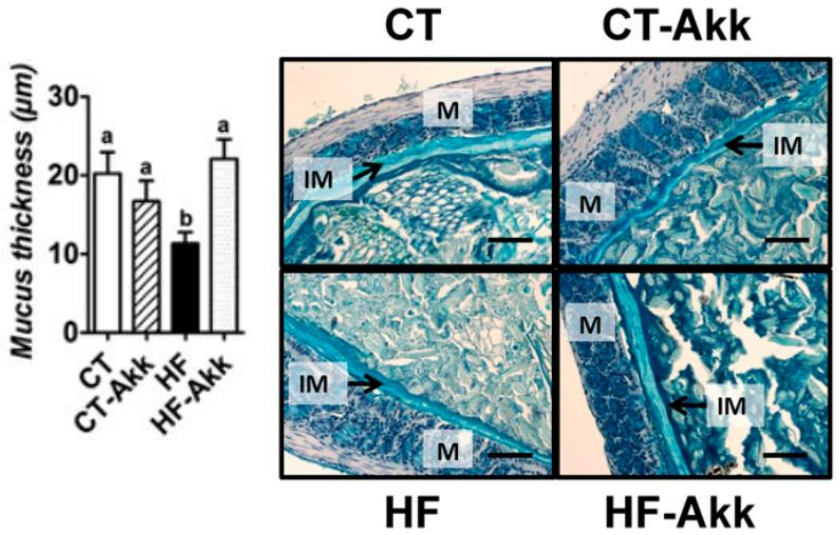
Fig. 2 Salivary concentration of hβD-3, expressed as pg/mL, of the groups at baseline (m = 0) and the end of the intervention (m = 10). The probiotic group showed a significant decrease in salivary concentration of hβD-3 (p = 0.0061) and a decrease in variability once the probiotic was consumed. No changes were observed in the control group

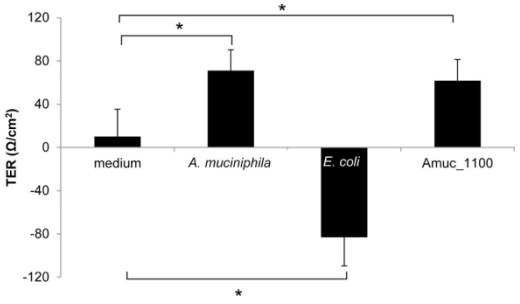
1. Fabbrocini, G. et al. Beneficial Microbes 7, 625–630 (2016)
2. Lee, X. et al. Australian Dental Journal 64, 229–236 (2019)
3. Rodríguez, G. et al. J Dent Res 95, 402–407 (2016)
4. Sandoval, F. et al. Clin Oral Invest (2021)
5. Francavilla, R. et al. Appl Environ Microbiol 83, e00376-17 (2017)

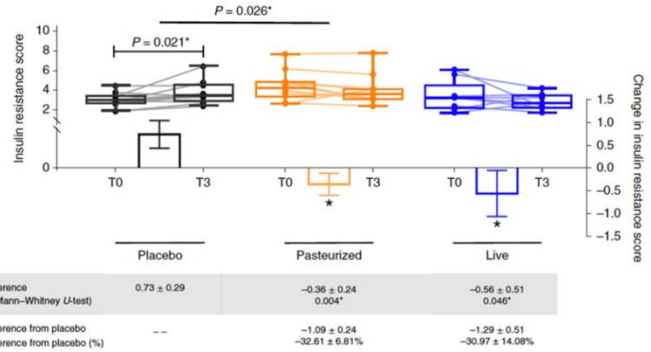
Return to overview

Pasteurized *Akkermansia muciniphila*

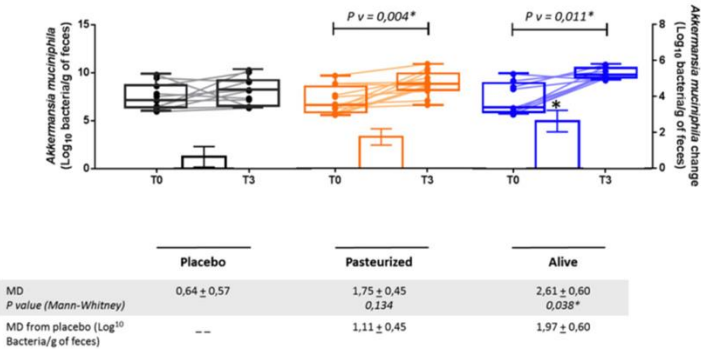
- First isolated in 2004 from the stool of a healthy Dutch Caucasian female[1]. Highly abundant: relative abundance of approx. 3%[2].
- Lives in mucus layer. Restores mucus layer thickness[3] (fig).
- Mediated via TLR-2 through Amuc_1100 pili[4] (fig). Survives pasteurization.
- Improves insulin resistance (fig), can yield weight loss, and increases Akkermansia abundance (fig)[5].
- In addition, there is observational evidence for:
  - Ulcerative colitis[6]
  - Atopic dermatitis/allergies[7]
  - Anti-inflammatory effects[5,6]
  - Improved barrier function and mucus layer thickness[5,6,8]
- Typical use: leaky gut/low mucus, metabolic dysfunction







	Placebo	Pasteurized	Live
Mean difference *P* value (Mann–Whitney *U*-test)	0.73 ± 0.29	−0.36 ± 0.24 0.004*	−0.56 ± 0.51 0.046*
Mean difference from placebo Mean difference from placebo (%)	--	−1.09 ± 0.24 −32.61 ± 6.81%	−1.29 ± 0.51 −30.97 ± 14.08%



	Placebo	Pasteurized	Alive
MD *P value (Mann-Whitney)*	0,64 ± 0,57	1,75 ± 0,45 *0,134*	2,61 ± 0,60 *0,038**
MD from placebo (Log10 Bacteria/g of feces)	--	1,11 ± 0,45	1,97 ± 0,60

1. Derrien, M. *et al. Int J Syst Evol Microbiol* 54, 1469–1476 (2004)
2. de Vos, W. M. Microbiology 163, 646–648 (2017)
3. Everard, A. et al. Proceedings of the National Academy of Sciences 110, 9066–9071 (2013)
4. Ottman, N. et al. PLOS ONE 12, e0173004 (2017)
5. Depommier, C. et al. Nat Med 25, 1096–1103 (2019)
6. Bian, X. et al. Front Microbiol 10, 2259 (2019)
7. Lee, Y. et al. Sci Rep 12, 7324 (2022)
8. Everard, A. et al. Proceedings of the National Academy of Sciences 110, 9066–9071 (2013)

Return to overview

Bifidobacterium animalis subsp. lactis HN019

- Isolated from yogurt in the late 1990s[1].
- Extensively studied, for example:
  - Periodontitis (fig)[2-4]
  - Cellular immunity (fig)[5]
  - Respiratory tract infections (fig)[6-8]
- In addition, there is evidence for:
  - Constipation, flatulence, abdominal pain[(e.g. 9)]
  - Depression and anxiety[10]
  - Pathogen inhibition
  - Anti-inflammatory effects
- Typical use: periodontitis, airway infections

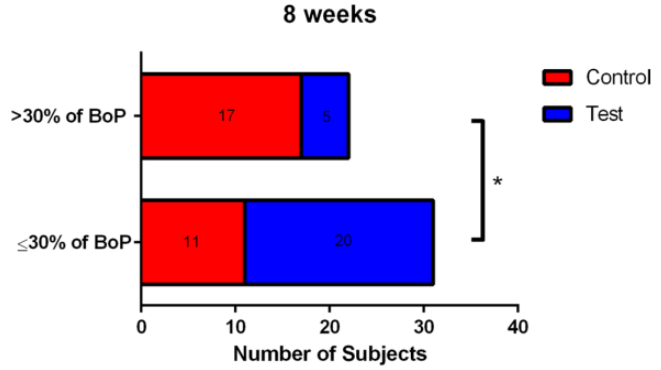


Fig. 3 Frequency of patients of the test and control groups presenting > 30% bleeding sites (generalized gingivitis) and ≤ 30% bleeding sites (without generalized gingivitis) at 8 weeks. *Significant difference between groups (chi-square test, $p = 0.0027$)

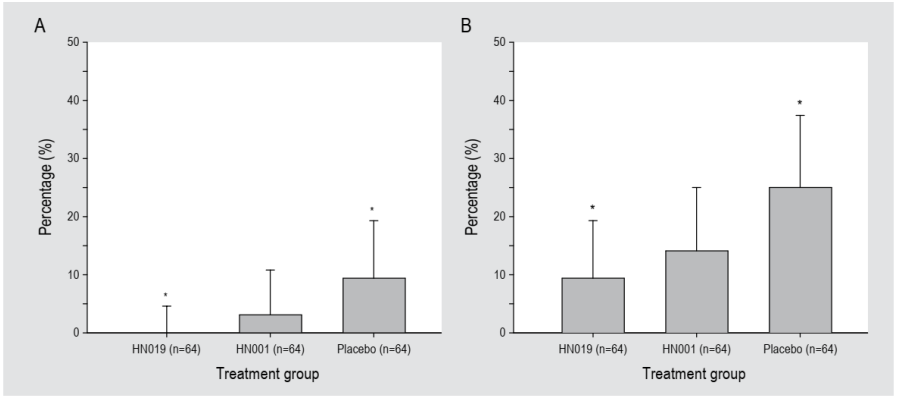


Figure 2. Incidence of (A) confirmed and (B) parentally reported (i.e. confirmed and unconfirmed) upper respiratory tract infections

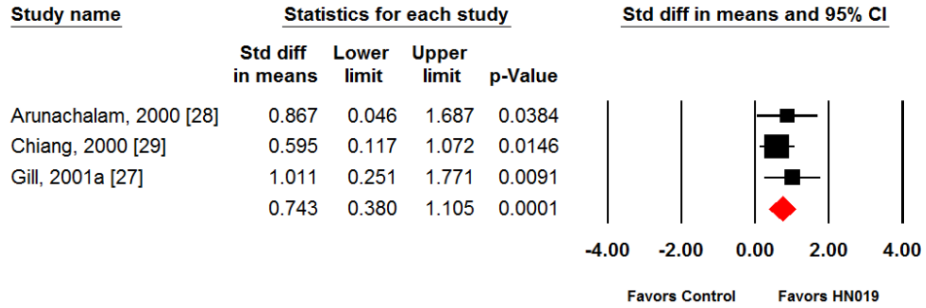


Figure 2. Forest plot of polymorphonuclear phagocytic capacity with consumption of *B. lactis* HN019 vs. control. Random effects meta-analysis using the standardized mean difference (SMD) statistic.

1. Prasad, J. et al. International Dairy Journal 8, 993–1002 (1998)
2. Invernici, M. M. et al. J Clin Periodontol 45, 1198–1210 (2018)
3. Invernici, M. M. et al. PLoS One 15, e0238425 (2020)
4. de Almeida Silva Levi, Y. L. et al. Clin Oral Investig 27, 387–398 (2023)
5. Miller, L. E. et al. Nutrients 9, 191 (2017)
6. Sazawal, S. et al. in (2004)
7. Sazawal, S. et al. PLoS One 5, e12164 (2010)
8. Dekker, J. et al. Benef Microbes 13, 341–353 (2022)
9. Waller, P. A. et al. Scand J Gastroenterol 46, 1057–1064 (2011)
10. Huang, L. et al. Front Psychiatry 13, 990465 (2022)

Return to overview

Vaginal suppositories

- Fixed composition vaginal suppositories:
  - Contains three active strains:
    - *Lactobacillus crispatus* SP28 (2.5x10^9 cfu/pc)
    - *Lactobacillus crispatus* LCR01 (2.5x10^9 cfu/pc)
    - *Lactobacillus acidophilus* La02 (2.5x10^9 cfu/pc)
  - Matrix from cacao butter with coconut butter.
- *L. crispatus* is consistently associated with good vaginal health[1], and e.g. with lower risk of preterm birth[2].
- RCTs with different L. crispatus strain show decreased risks of: recurring vaginosis[3] and recurring urinary tract infections[4].
- Two open label studies with vaginal product containing *L. acidophilus* La02 showing effect on vulvovaginal candidiasis[2,3].
- Typical use: UTI, vulvovaginal candidiasis, fertility

TABLE 3. Overview of Data and Statistical Analysis

Parameters	Time 0	Time 28	p (T28 vs. T0)	Time 56	p (T56 vs. T0)	p (T56 vs. T28)
Total women with infection	30	4	< 0.001	7	< 0.001	—
Total women without infection	0	26	—	23	—	—
Percentage of healing	—	86.67%	—	76.67%	—	—
Total women with recurrences	—	0	—	3	—	0.083
Percentage of recurrences	—	—	—	11.54%	—	—

Bacterial Vaginosis Recurrence Status in the Intention-to-Treat Population.

Variable	Lactin-V (N = 152)	Placebo (N = 76)	Risk Ratio (95% CI)*	P Value
	no. (%)			
Status of recurrence by wk 12				
Recurrence†	46 (30)	34 (45)	0.66 (0.44–0.87)	0.01
No recurrence	87 (57)	30 (39)		
Unknown	19 (12)	12 (16)		
Status of recurrence by wk 24				
Recurrence	59 (39)	41 (54)	0.73 (0.54–0.92)	
No recurrence	63 (41)	21 (28)		
Unknown	30 (20)	14 (18)		

Table 2. Urinary Tract Infection Rates by Intervention and *Lactobacillus crispatus* Colonization Pattern

Intervention	No. (%) of participants developing recurrent UTI	Relative risk (95% CI)
Lactin-V (*n* = 48)	7 (15)	.5 (.2–1.2)
Placebo (*n* = 48)	13 (27)	…
Intervention, *L. crispatus* colonization pattern		
Lactin-V, high level (*n* = 41)	2 (5)	.07 (.02–.3)
Lactin-V, low level (*n* = 7)	5 (71)	…
Placebo, high level (*n* = 32)	9 (28)	1.1 (.4–3.1)
Placebo, low level (*n* = 16)	4 (25)	…

1. Chee, W. J. Y. et al. Microb Cell Fact 19, 203 (2020)
2. Fettweis, J. M. et al. Nat Med 25, 1012–1021 (2019)
3. Cohen, C. R. et al. N Engl J Med 382, 1906–1915 (2020)
4. Stapleton, A. E. et al. Clinical Infectious Diseases 52, 1212–1217 (2011)
5. Vicariotto, F. et al. Journal of Clinical Gastroenterology 46, S73–S80 (2012)
6. Murina, F. et al. Journal of Clinical Gastroenterology 48, S102–S105 (2014)

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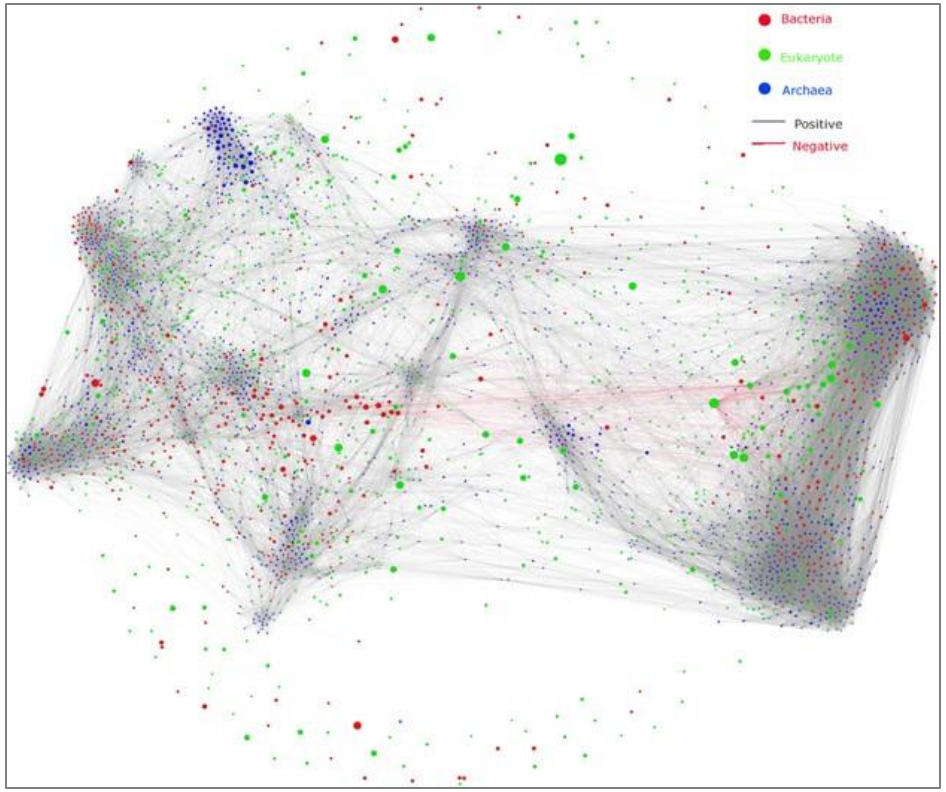
3. Outlook: expected additions

3. Outlook for future



Microbiome Center is expanding

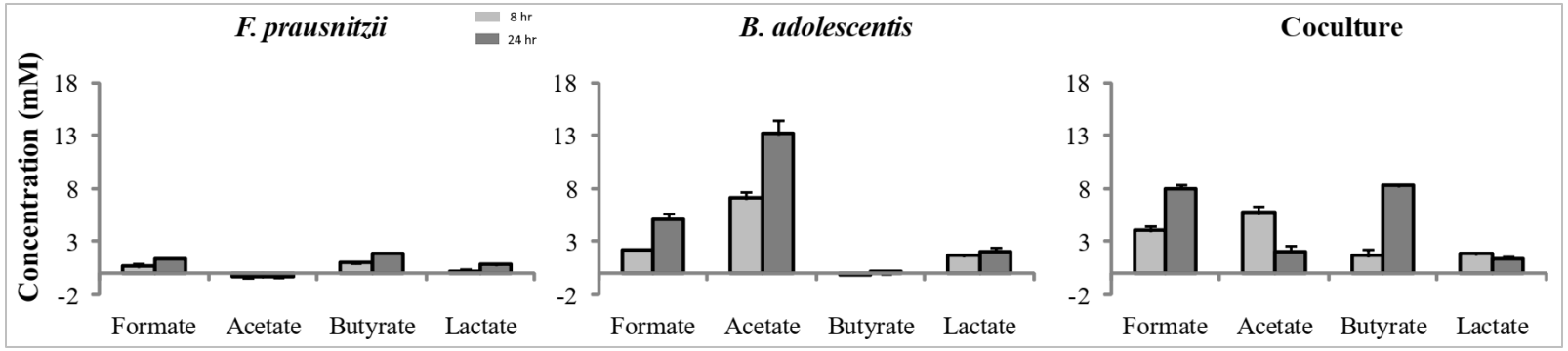
Cumulative numbers	2019	2020	2021	2022	2023	2024	June 2025
Patients	670	1,500	2,800	5,000	8,000	13,000	16,500
Doctors	113	133	222	359	482	729	873

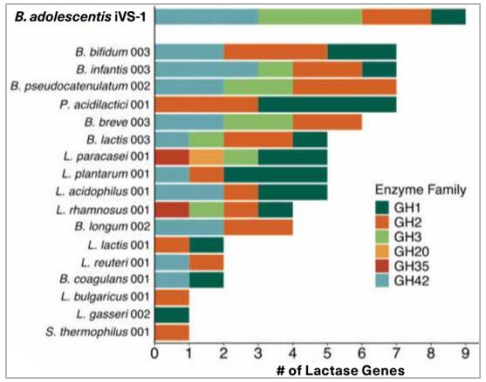
We now have made the platform available in:

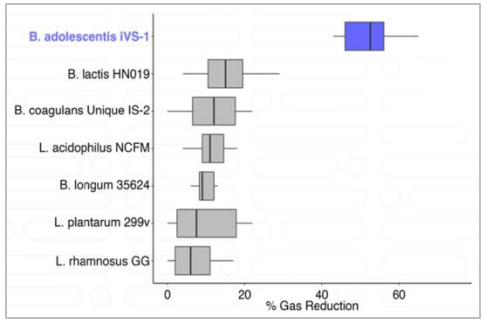
- The Netherlands
- Germany
- Switzerland
- Austria
- United Kingdom
- Belgium
- Italy
- Slovakia
- Poland
- …

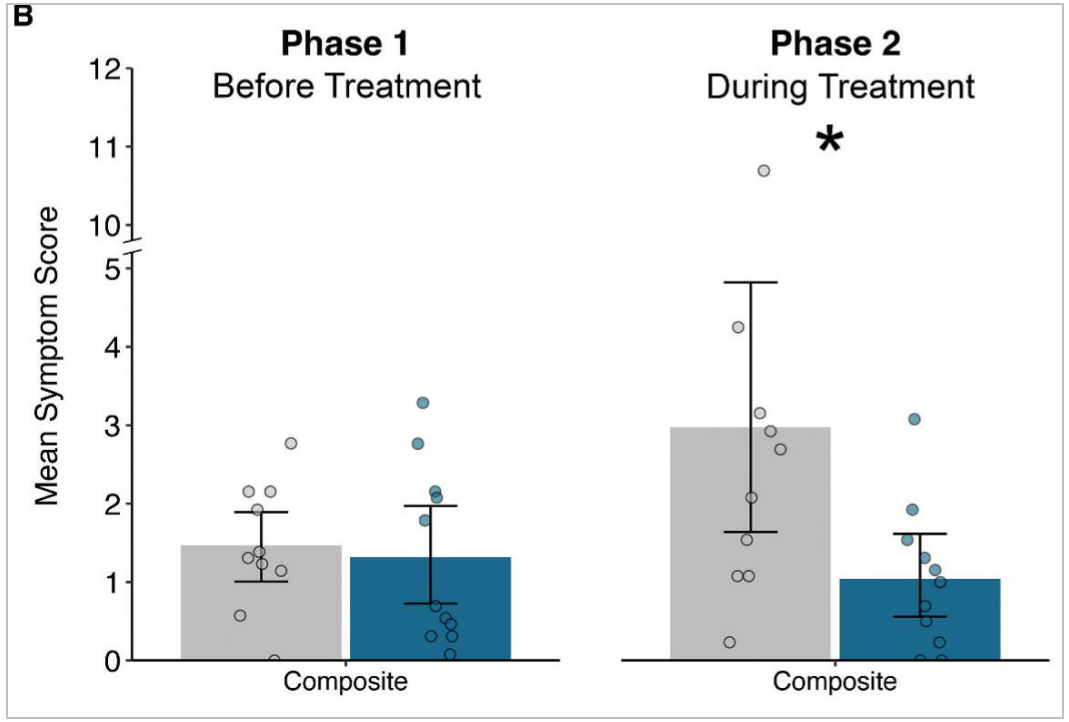
Bifidobacterium adolescentis SH001

- *Bifidobacterium adolescentis* SH001 is identical to strain iVS-1. Isolated from healthy human consuming high level of GOS[1].
- Interesting because:
  - *B. adolescentis* is known cross-feeder for F. prausnitzii (most abundant butyrate producer in our gut) e.g.[1] (fig)
  - Highest amount of lactase enzymes (fig) and reduces gas production the most
- There is evidence for:
  - Reduction of lactose intolerance symptoms (fig)[2]
  - Reduction of bloating, flatulence, abdominal pain[2]
  - Improve gut barrier3
- Typical use: GI diseases and symptoms, immune related problems









1. Rios-Covian, D. et al.FEMS Microbiology Letters.362,.fnv176.(2015)
2. Ramakrishnan, M. et al.Gut Microbes Reports.2,.2508199.(2025)
3. Krumbeck, J. A. et al.Microbiome.6,.121.(2018)

Other BBs that we expect to add soon

- Synbio (L. rhamnosus IMC501 + L. paracasei IMC502)
  - Evidence for: **bloating**, **constipation**, **fatigue**, **etc**.

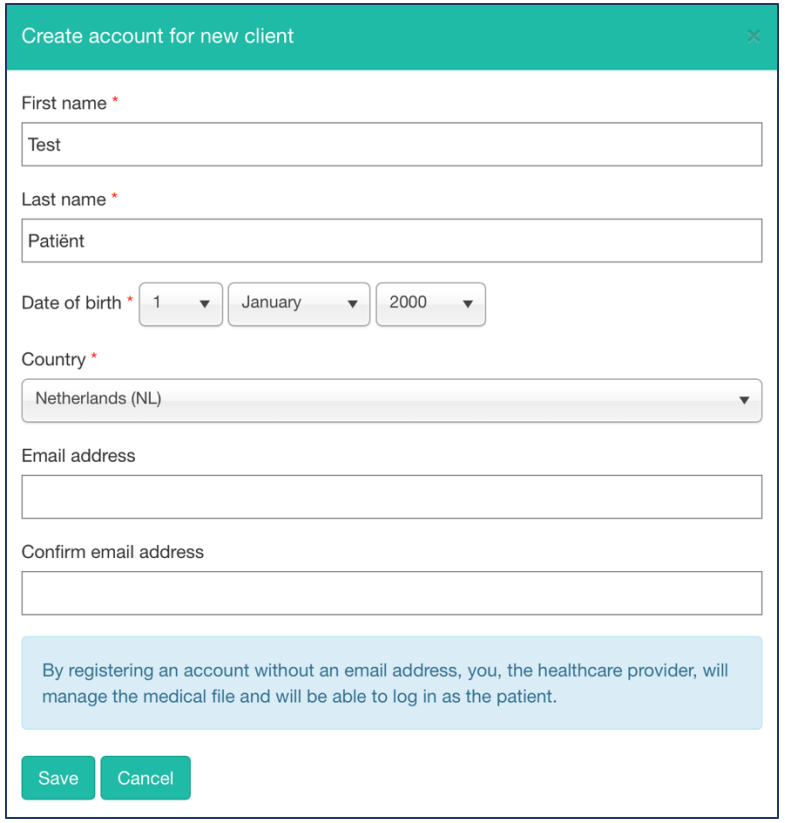
- *Bifidobacterium longum* ES1
  - Evidence for: **IBS**, **abdominal pain**, **anxiety**, **headache**, **gluten sensitivity/celiac disease, etc**

- *Christensenella minuta* M03
  - Evidence for: **weight management among others**

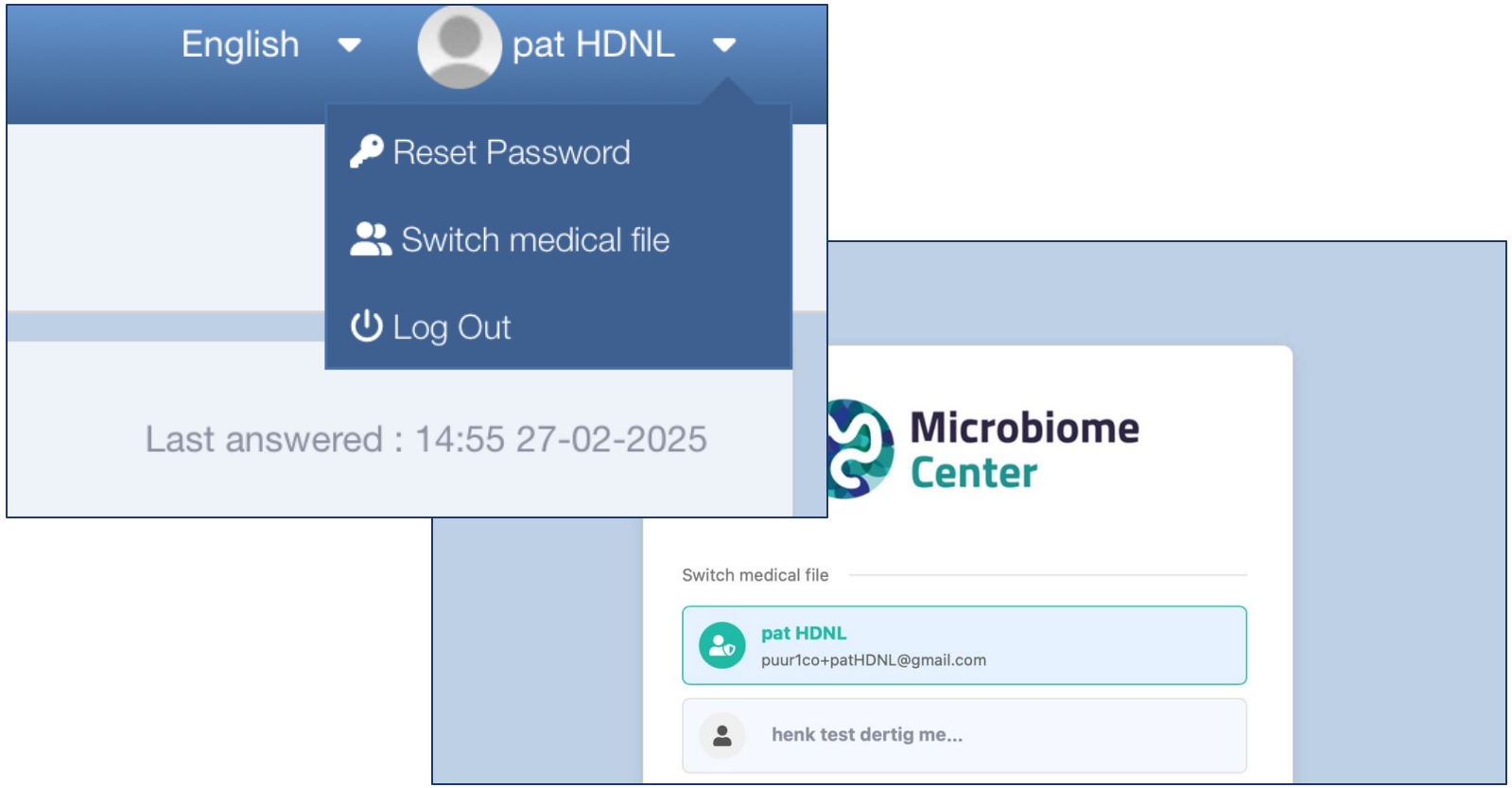
1. BLA

Support patients without email (5y child or 85y grandma)

Add a medical file to an existing account

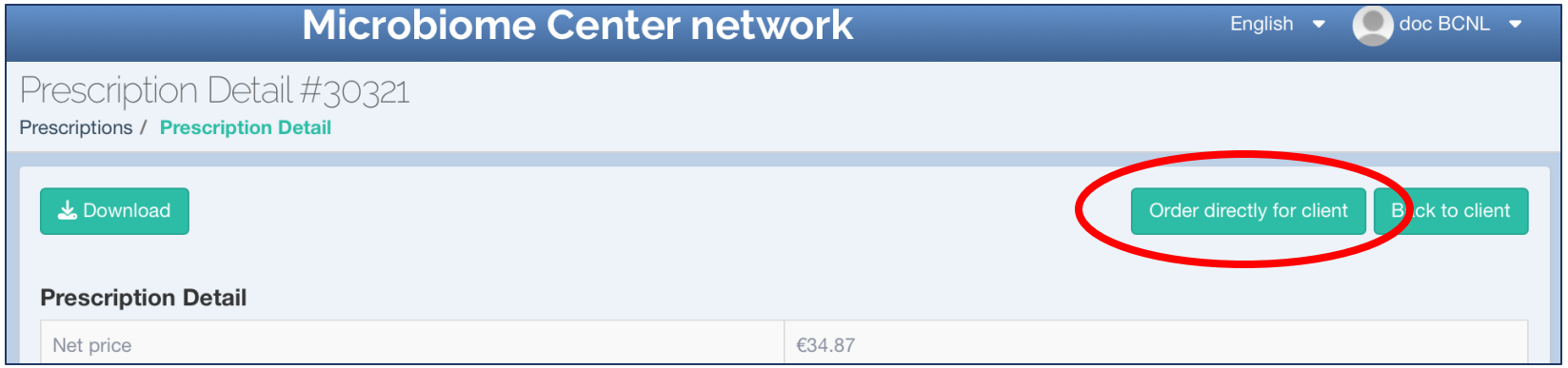


Then simply switch between medical files



Generate invoice for manual payment by patient

1.



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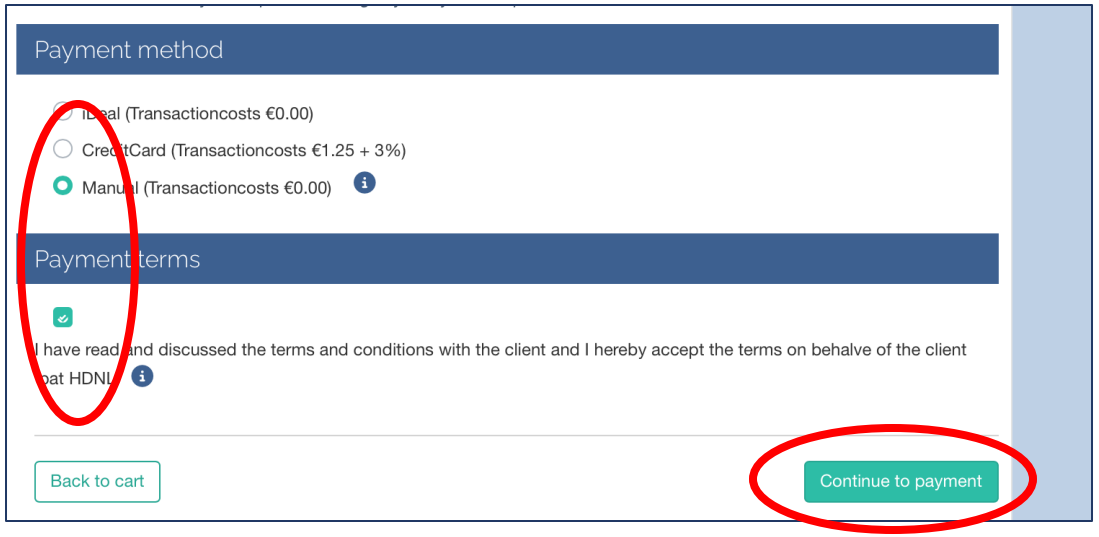

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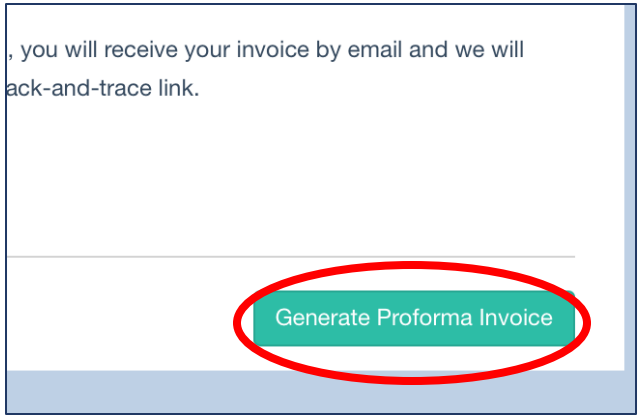
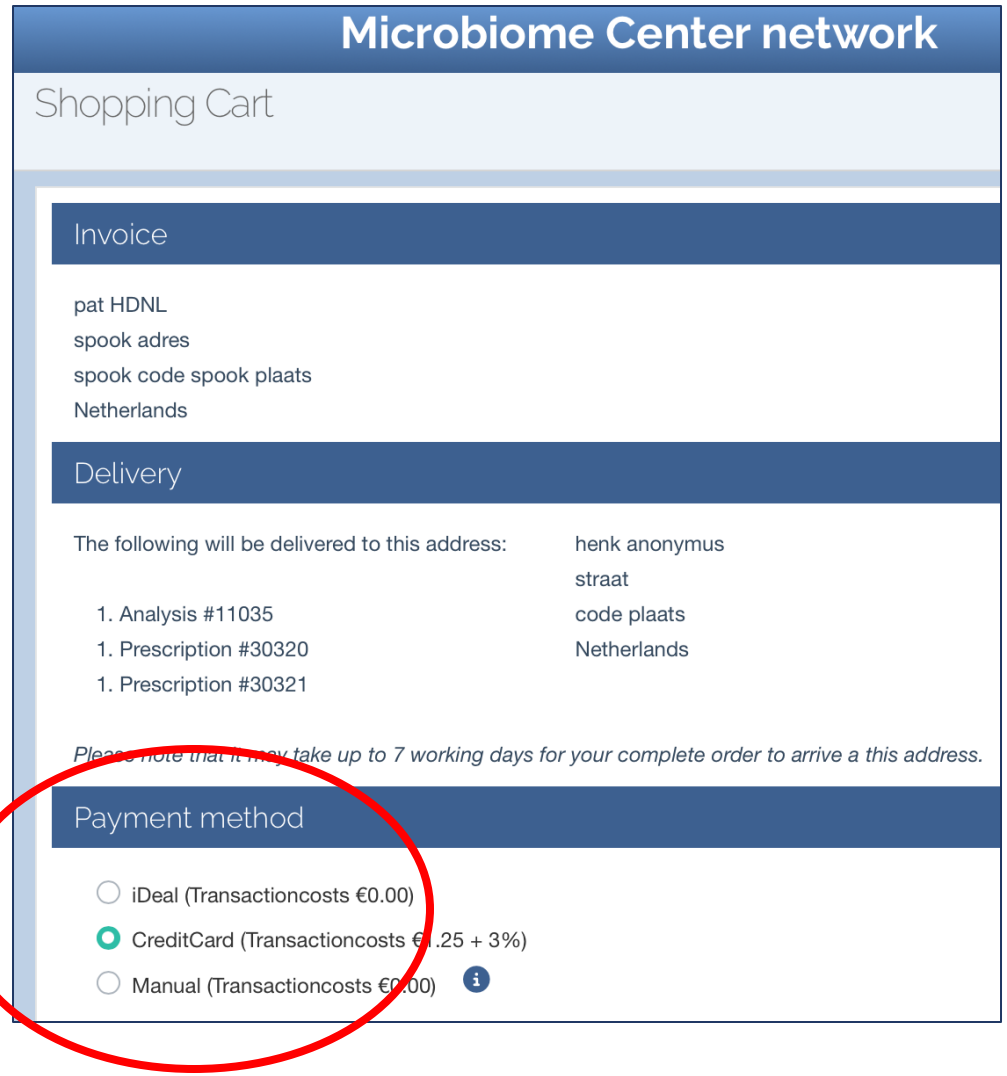


Payment by worldwide accepted creditcards



Calender

Starters, intervision, Arbeitskreis

- 8th of July, Arbeitskreis 1. (DE)
- 10th of July Starter session (NL)

- 9th of September Starter session (NL)
- 11th of September, Arbeitskreis 1. (DE)
- 15th of September, Discussing case reports (NL)
- 23rd of September, Arbeitskreis 2. (DE)

Thematic webinars

- 3rd of July Building blocks (EN)
- 9th of July Building blocks (DE)

- 16th of September Implement microbiome treatment in your praxis part 1. (DE)
- 18th of September Implement microbiome treatment in your praxis part 1. (NL)
- 30th of September Implement microbiome treatment in your praxis part 2. (DE)
- 2nd of October Implement microbiome treatment in your praxis part 2. (NL)

Thank you for your attention!