

Clinical Studies on Alleviating the Symptoms of Irritable Bowel Syndrome

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**Kajsa Kajander
Research Scientist**

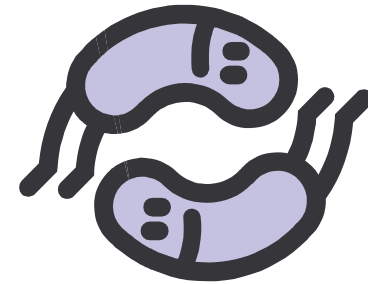
Institute of Biomedicine, Pharmacology, University of Helsinki,
Finland
Valio Ltd, Research Centre, Helsinki, Finland

IBS: the most common diagnosis in gastroenterology

- Symptoms: abdominal pain, distension, flatulence, constipation, diarrhoea
- Unknown etiology
 - Imbalanced microbiota, visceral hypersensitivity, inflammation, gastroenteritis, brain-gut axis, motility
- Reduces quality of life
- A major economic burden to society
- Current treatments ineffective
 - Some probiotics have shown promising effects



Is IBS an imbalanced microbiota...?



- Studies on microbiota in IBS by culturing
 - Coliforms, bifidobacteria and lactobacilli ↓ (Balsari et al. 1982)
 - Anaerobes ↓ (Madden et al. 2001)
 - Bifidobacteria ↓, *Enterobacteriaceae* ↑ (Si et al. 2004)
 - Coliforms ↑, aerobe/anaerobe ratio ↑ (Mättö et al. 2005)
- Changes in metabolic activity
 - Changes in short chain fatty acids (Treem et al. 1996)
 - Increased hydrogen (King et al. 1998)
 - Abnormal lactulose breath test (Pimentel et al. 2000)

Molecular biology reveals instability in microbiota

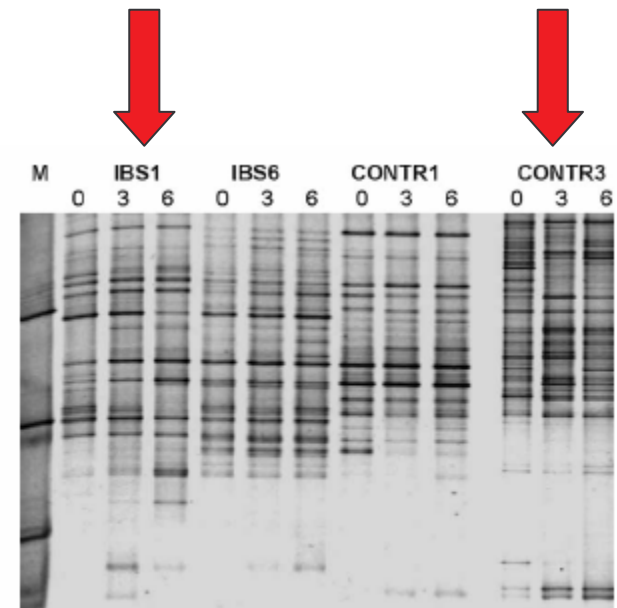
- 27 IBS patients (Rome II criteria)
- 22 age- and gender-matched healthy controls
- Fecal samples at 0, 3 and 6 months

Real-Time PCR

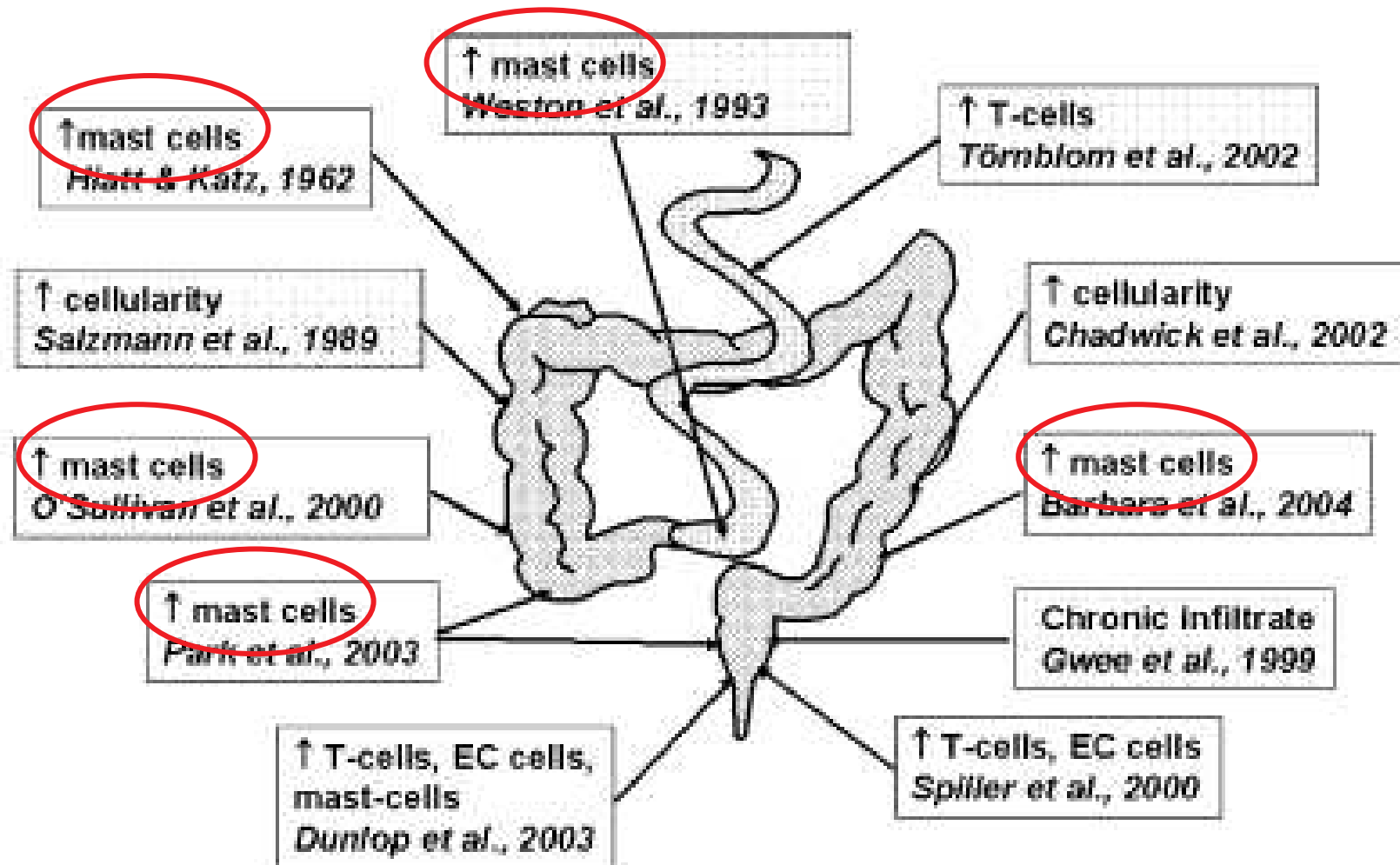
- *Lactobacillus* ↓ in D-IBS
- *Veillonella* ↑ in C-IBS

PCR-DGGE

- Instability in microbiota



Is IBS a low-grade inflammation?

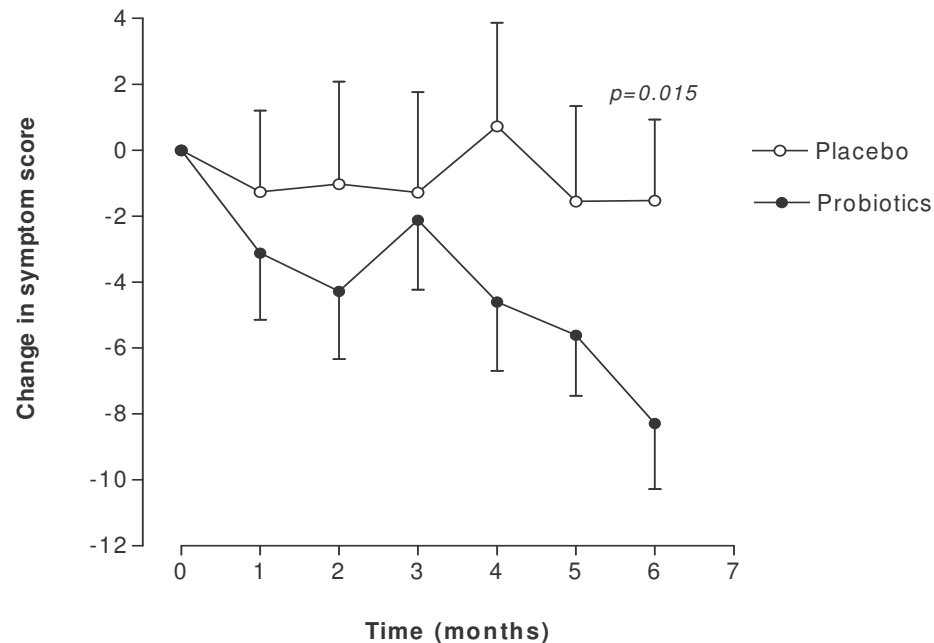




Study I: Material & Methods

- 103 IBS adult patients (Rome II criteria: 68%)
- Double-blind, placebo-controlled, parallel groups
- 6 months
- 1 probiotic capsule or placebo capsule daily
 - LGG, *L. rhamnosus* Lc705, *P. freudenreichii* JS and *B. breve* Bb99
- Regular symptom diary
 - Abdominal pain, distension, flatulence, rumbling
 - Bowel habits
- A subsample (n=55) gave faecal samples at 0, 3 and 6 months

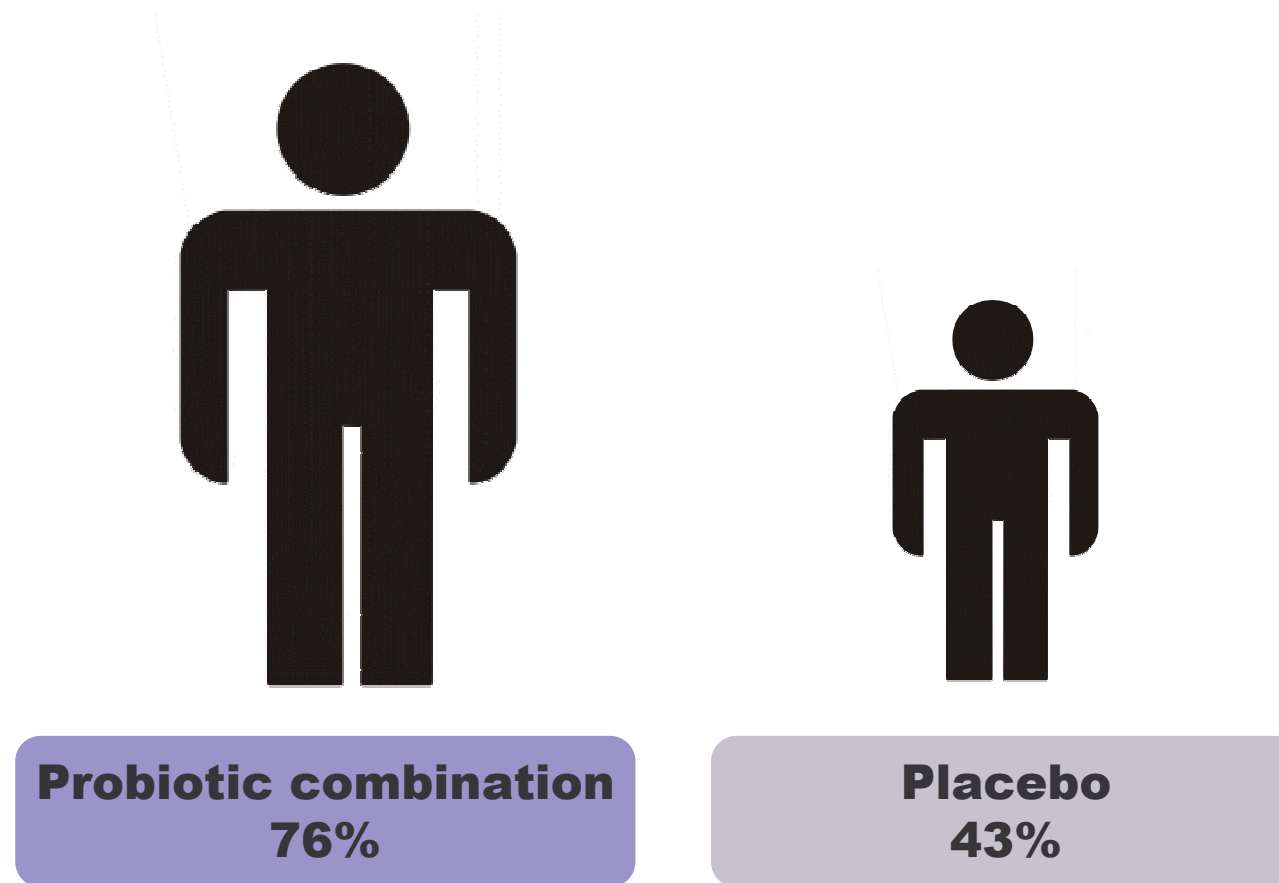
The probiotic supplementation alleviates IBS symptoms



- The IBS symptom score (=abdominal pain + distension + flatulence + rumbling) during the 6-month intervention

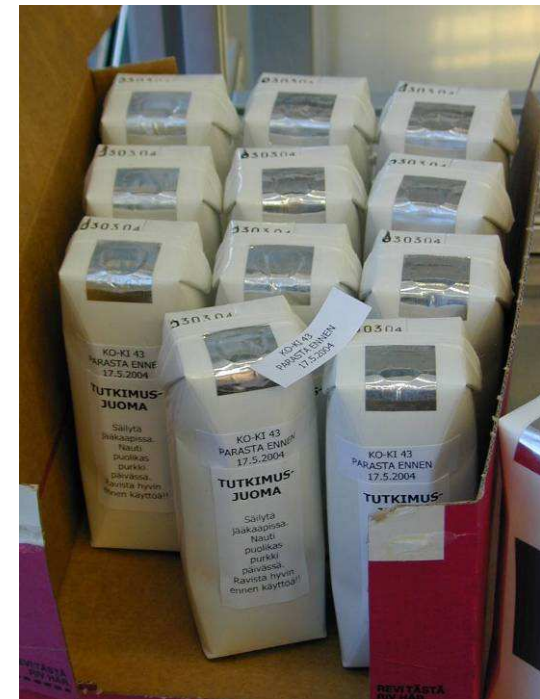
- $p=0.015$ at 6 months; $n=81$

The probiotic relieves symptoms in 3/4



Study II: Material & Methods

- 86 adult IBS patients (Rome II criteria)
- Double-blind, placebo-controlled, parallel groups
- 5 months
- Daily either probiotic milk-based drink or placebo drink or placebo drink
 - LGG, *L. rhamnosus* Lc705, *P. freudenreichii* ssp. *shermanii* JS, Bb-12
- Regular symptom diary and health-related quality of life (HRQoL) questionnaire
- Faecal and blood samples

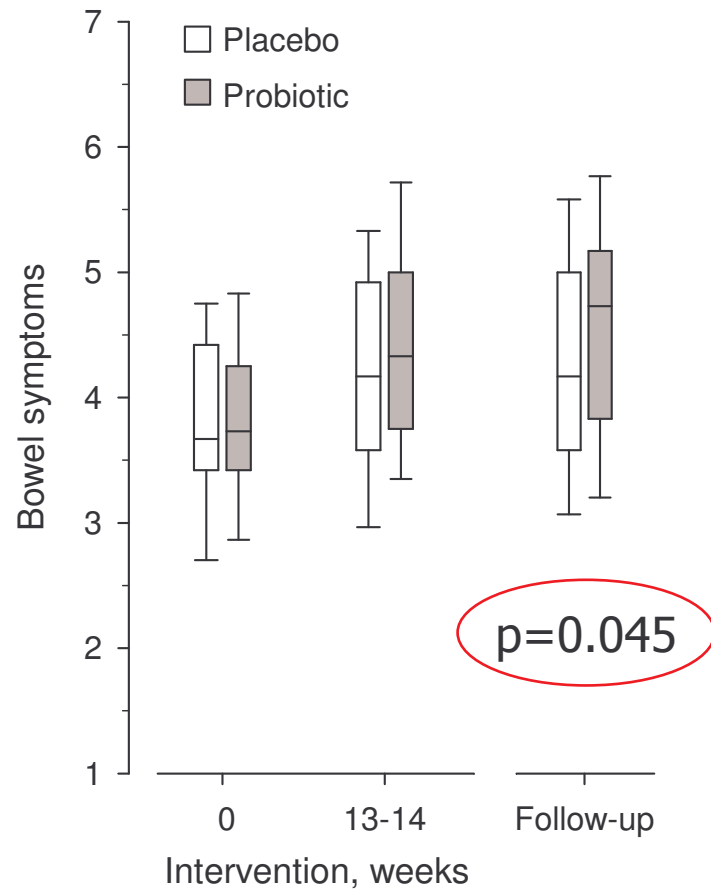


The probiotic alleviates especially bloating and pain

	Baseline		Change to end of trial		P-value [†]
	Placebo Mean (SD)	Probiotic Mean (SD)	Placebo Mean (95% CI)	Probiotic Mean (95% CI)	
Total sympt.	33 (16)	38 (21)	-3 (-8 to 1)	-14 (-19 to -9)	0.0083
Abd. pain	6 (4)	8 (6)	0 (-2 to 2)	-3 (-5 to -2)	0.052
Bloating	10 (7)	11 (7)	-1 (-3 to 1)	-4 (-6 to -2)	0.023
Flatulence	12 (6)	12 (6)	-2 (-4 to -0)	-4 (-6 to -2)	0.11
Rumbling	5 (5)	6 (6)	-1 (-2 to 0)	-3 (-4 to -1)	0.086

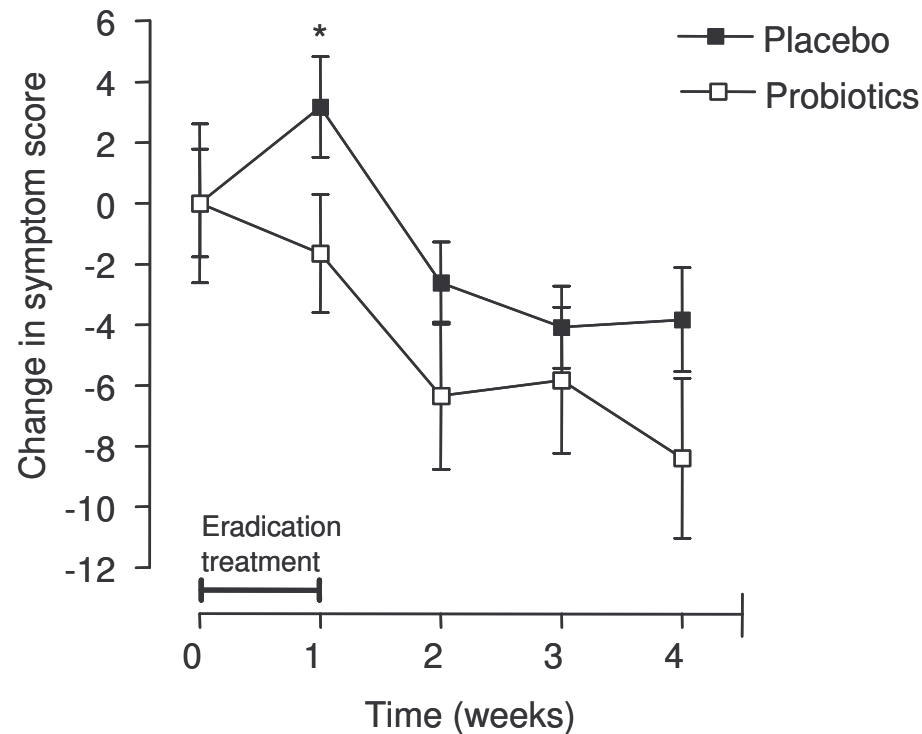
† Analysis of covariance, baseline as covariate

Health-related QoL is improved



- HRQL: four domains
- Difference between groups
 - Bowel symptoms (p=0.045)
 - Fatigue (p=0.087)
 - Activity limitations (p=0.81)
 - Emotional function (p=0.72)

H. Pylori treatment associated symptoms

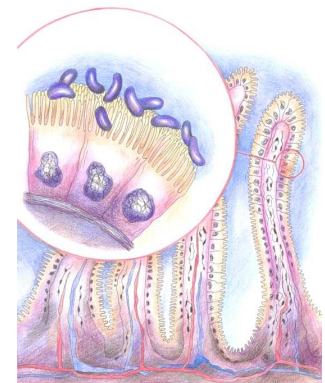


- n=47
- Eradication rate in probiotics vs. placebo 91.3% vs. 79.2% (ns.)

Putative mechanisms behind probiotic action in IBS

Probiotics can...

- Balance the microbiota (SCFA, enzymes, gases)
- Normalise intestinal permeability
- Activate immunomodulation
 - The probiotic combination has been shown to modulate immunity differently vs. LGG alone (Pohjavuori et al. 2004; Viljanen et al. 2005)
- Normalise dysmotility and relax the GI tract (Massi et al. 2004; Verdu et al. 2004 and 2006)
 - *L. paracasei*, bifidobacteria
- Induce μ -opioid and cannabinoid receptors (Rousseaux et al. 2006)
 - *L. acidophilus*



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