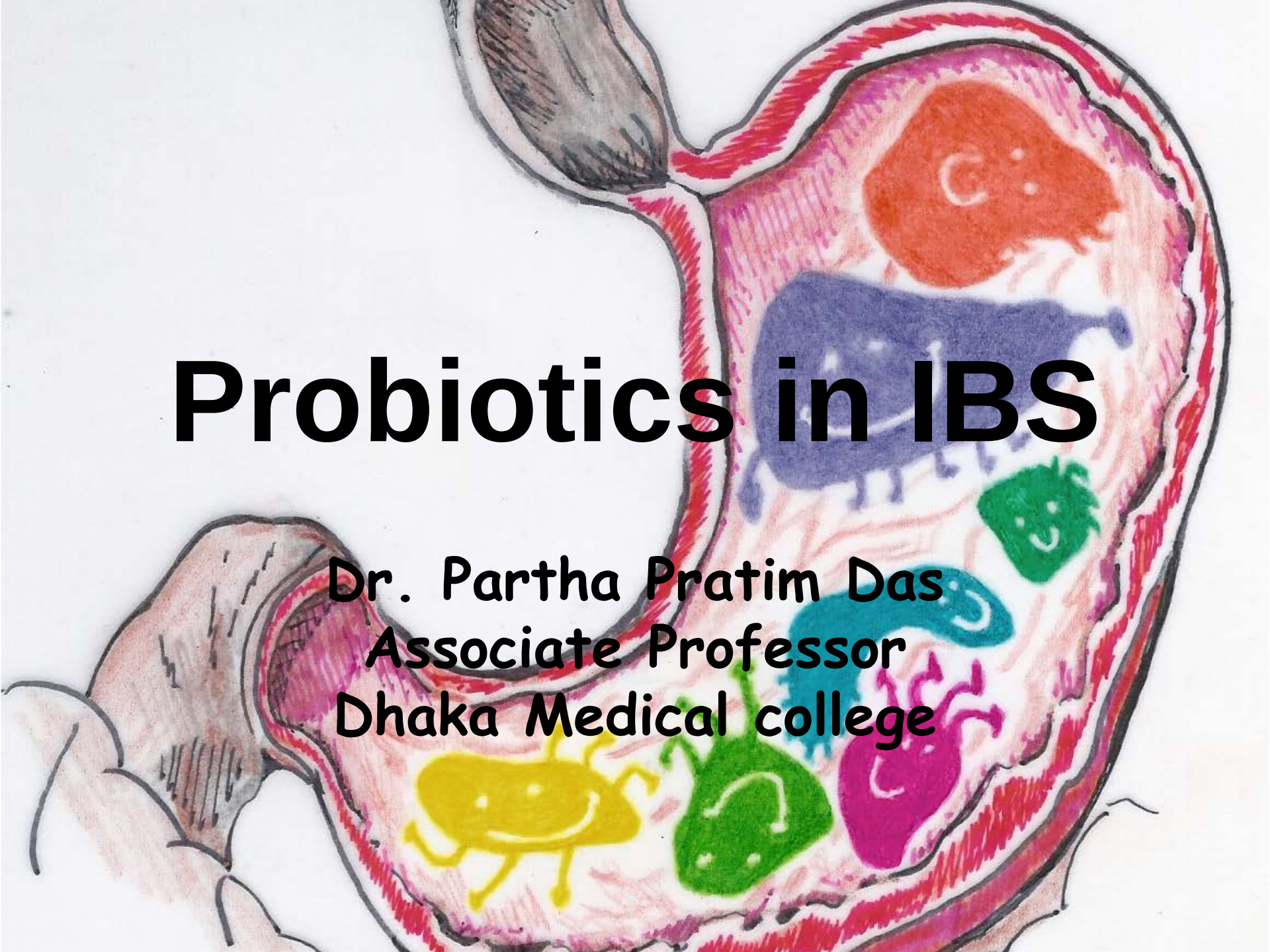


Probiotics in IBS

Dr. Partha Pratim Das
Associate Professor
Dhaka Medical college


BURP!
What are probiotics

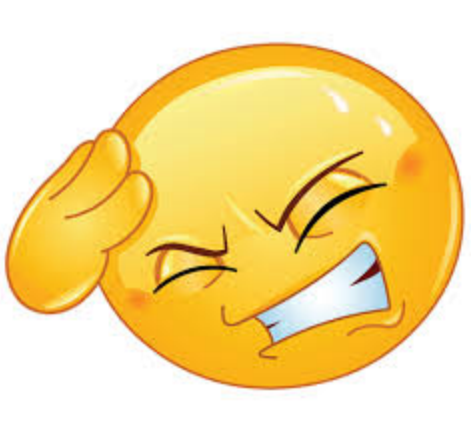
Definitions

- Probiotics: Live microorganisms that confer a health benefit on the host when administered in adequate amounts. (WHO, 2002)

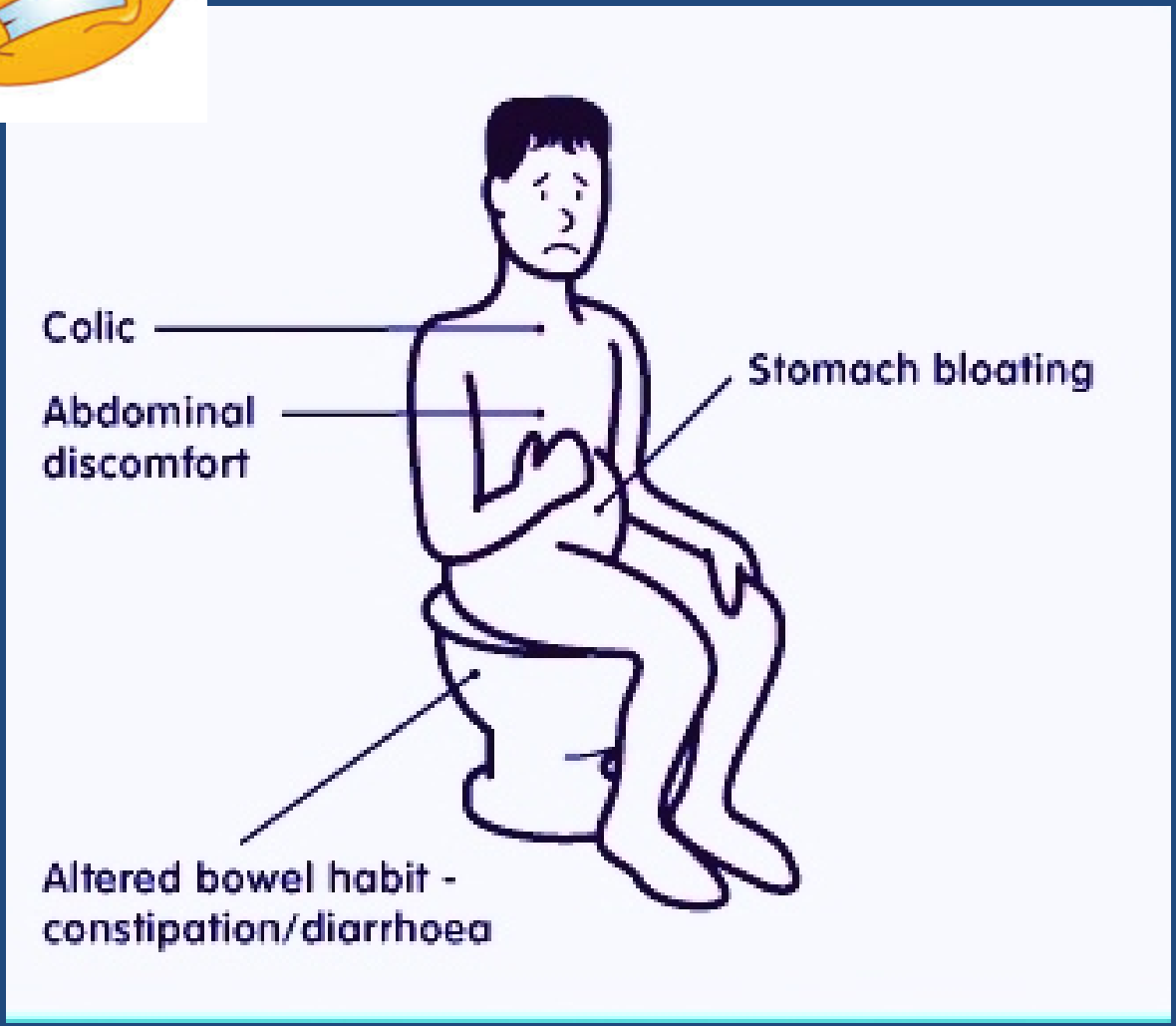
The minimum criteria that have to be met for probiotic products

Probiotic must be:

- Specified by genus and strain.
- Alive.
- Delivered in adequate dose through the end of shelf-life (with minimal variability from one batch to another).
- Shown to be efficacious in controlled human studies.
- Non-toxic



What is IBS


Colic
Abdominal discomfort
Stomach bloating
Altered bowel habit - constipation/diarrhoea

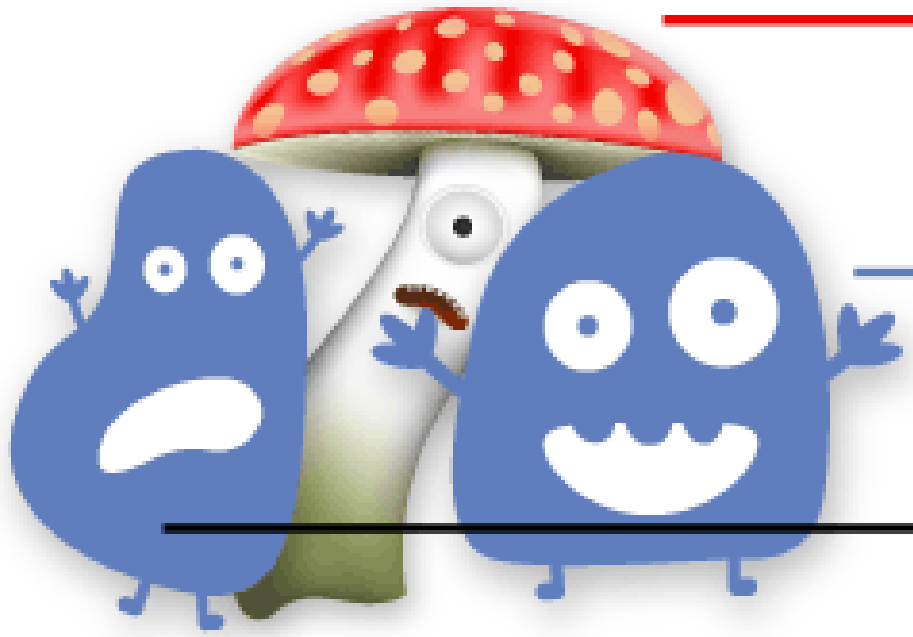
Rome III diagnostic criteria for Irritable bowel Syndrome

Recurrent abdominal pain or discomfort (an uncomfortable sensation not described as pain) at least 3 days per month in the past 3 months, associated with two or more of the following:

- Improvement with defecation.
- Onset associated with a change in frequency of stool.
- Onset associated with a change in form (appearance) of stool.

The criteria must be fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.

Which microorganisms are probiotics



Good Fungi

Good Bacteria

Both Probiotics!

Microorganisms	Genus	Species
Bacteria	*Lactobacillus*	*L.acidophilus, L.brevis, L.reuteri, L.casei, L.rhamnosum, L.bulgaricus, L.cellobiosus, L.delbrueckii, L. fermentum.*
	Bifidobacterium	*B.thermophilus, B.infantis, B .longum, B.bifidum, B.animalis.*
	Streptococcus	*S.lactis, S.thermophilus, S.cremonis, S.alivarius.*
	Bacillus	*B.Coagulans* ***B. Clausii***
	Pediococcus	*P.acidilactici*
	Leuconostoc	*L.mesenteroides*
	Enterobacter	*E.faecium, E.faecalis.*
Fungi	*Aspergillus*	*A.niger, A.oryzae.*
Yeast	*Saccharomyces*	*S.boulardii, S.cerevisiae, S.carlsbergensis.*

PROBIOTICS IN IBS
Mechanisms of action

- Change gut bacterial composition
- Potentially return abnormal gut flora to normal
- Competitive interactions with pathogens
- Produce chemical products, that are toxic to pathogenic bacteria or viruses.
- Reinforce the mucosal barrier
- Inhibit the movement of bacteria across the gut wall
- Produce neurotransmitters that influence the motility and sensation of the gut
- Produce cytokines, neuroactive peptides, fatty acids, gas and other substances.

Ref: J Gastroenterol. 2014; 146 (6)

Justification—research and proof

- Lots of clinical studies have been done on efficacy and safety of probiotics
- The most common claims are those that relate probiotics to the normal structure and functioning of the human body, known as “structure–function claims.” Often considered “soft” claims.

Summary of Studies on the Compositional Changes of Gut Microbiota in Patients With IBS

Study	Method of confirmation	No. of patients (Diagnostic criteria)	Results
Si et al[47]	Culture	25 (Rome II)	Decreased amounts of *Bifidobacteria* species. Increased amount of *Enterobacteriaceae* species in IBS patients.
Tana et al[45]	Culture	26 (Rome II)	Increased *Lactobacillus* in IBS patients.
Mättö et al[48]	Culture/ DGGE	26 (Rome II)	Increased number of aerobes in IBS patients. Temporal instability in IBS patients revealed by DGGE.
Malinen et al[52]	qPCR	27 (Rome II)	Decreased amounts of *Lactobacillus* in IBS-D patients. Increased amounts of *Veillonella* in IBS-C patients.
Tana et al[45]	qPCR	26 (Rome II)	Increased *Veillonella* in IBS patients.
Malinen et al[49]	qPCR	44 (Rome I)	*R. torques*-like phylotype was associated with severity with bowel symptoms. *C. cocleatum* 88%, *C. aerofaciens*-like and *C. eutactus* 97% phylotypes were significantly reduced among IBS patients with *R. torques* 94% detected.
Noor et al[53]	qPCR -DGGE	11 (Rome II)	Biodiversity of bacterial species were significantly lower in UC and IBS patients than healthy controls. In UC and IBD patients, loss of *Bacteriodes* species. was observed.
Swidsinski et al[51]	FISH	20 (Unidentified)	*E. rectale-C. coccoides* accounted for > 40% of the biofilm in IBS patients.
Kassinen et al[5]	Nucleic acid fractionation / sequencing	24 (Rome II)	Significant differences in the levels of *Coprococcus*, *Collinsella* and *Coprobacillus* species between IBS patients and healthy controls.

IBS, irritable bowel syndrome; DGGE, denaturing gradient gel electrophoresis; PCR, polymerase chain reaction; IBS-D, diarrhea-predominant IBS; IBS-C, constipation-predominant IBS; *R. torques*, *Ruminococcus torques*; *C. cocleatum*, *Clostridium cocleatum*; *C. aerofaciens*, *Collinsella aerofaciens*; *C. eutactus*, *Coprococcus eutactus*; UC, ulcerative colitis; IBD, inflammatory bowel disease; *E. rectale*, *Eubacterium rectale*; *C. coccoides*, *Clostridium coccoides*.

Ref:Lee BJ, Bak YT. J Neurogastroenterol Motil. 2011; 17(3): 252-66.

EMB-Randomized Controlled Trials of Probiotics in Patients With IBS

Probiotics significant reduction in symptom

- Abdominal pain/discomfort
- bloating/distention and flatulence
- bowel movement difficulty/ diarrhea/ constipation

Summary of Randomized Controlled Trials of Probiotics in Patients With Irritable Bowel Syndrome

Study	Probiotics		Dosage (CFU/mL)	No. of patients (Diagnostic criteria)	Duration (wk)	Results
	Single					
Sinn et al[108]	*Lactobacillus* species	*L. acidophilus* SDC 2012, 2013	2×10^9	40 (Rome III)	4	Significant reduction in abdominal pain and discomfort ($P = 0.011$)
Sen et al[102]		*L. plantarum* 299V	5×10^7	12 (Rome II)	4	Failed to improve IBS symptoms and to alter colonic fermentation
Niedzielin et al[101]			5×10^7	40 (not characterized)	4	IBS symptom improvement (pain, constipation, diarrhea and flatulence): 95% vs 15% ($P < 0.001$)
Nobaek et al[65]			5×10^7	60 (Rome II)	4	Significant improvement in flatulence over placebo: 44% vs 18% ($P < 0.05$)
Bausserman et al[100]		*L. rhamnosus* GG	1×10^{10}	50 (children) (Rome II)	6	Not superior to placebo in relieving abdominal pain
Gawronska et al[109]			3×10^9	37 (children) (Rome II)	4	Treatment success (resolution of pain and relaxed face): 33% vs 5.1% ($P = 0.04$); reduced frequency of pain ($P = 0.02$)

O'Mahony et al[74]		*L. salivarius* UCC 4331	1×10^{10}	67 (Rome II)	8	No significant improvement in composite and individual score (abdominal pain/discomfort, bloating/distention and bowel movement difficulty) over placebo
Niv et al[99]		*L. reuteri* ATCC 55730	1×10^{8}	54 (Rome II)	6 months	No significant improvement of IBS symptoms over placebo
O'Mahony et al[74]	*Bifidobacteria* species	*B. infantis* 356724	1×10^{10}	67 (Rome II)	8	Significant improvement in composite and individual scores (abdominal pain/discomfort, bloating/distention and bowel movement difficulty) over placebo ($P < 0.05$)
Whorwell et al[95]			1×10^{8}	362 (women) (Rome II)	4	Improvement in global symptom assessment exceed placebo by more than 20% ($P < 0.01$)
Guyonnet et al[96]		*B. animalis* DN 173010[a]	1.2×10^{10}	274 (Rome II, IBS-C)	6	Although health-related quality of life and digestive symptom was improved over baseline, there was no significant difference comparing to placebo.
Enck et al[97]	*Escherichia* species	*E. coli* DSM 17252	Symbioflor 2[b]	298 (criteria of 1 care physicians)	8	Improvement of global symptom score and abdominal pain score comparing to placebo: 18.4% vs 4.7%, 18.9% vs 6.67% ($P < 0.001$)

Study	Probiotics	Dosage (CFU/mL)	No. of patients (Diagnostic criteria)	Duration (wk)	Results
Kajander et al[104]	*L. rhamnosus* GG, *L. rhamnosus* LC705, *B. breve* Bb99 and *P. freudenreichii* spp. *shermanii* JS	8-9 × 10^9	86 (Rome II)	20	Significant reduction in IBS symptoms (pain, distension, flatulence and rumbling) ($P = 0.008$)
Kajander et al[103]		8-9 × 10^9	103 (Rome I or II)	26	Significant reduction in total symptom score (abdominal pain, distension, flatulence and borborygmi) ($P < 0.015$)
Williams et al[110]	*L. acidophilus* (NCIMB 30157 and NCIMB 30156), *B. lactis* (NCIMB 30172) and *B. bifidum* (NCIMB 30153)	2.5 × 10^{10}	52 (Rome II)	8	Significant reduction in symptom severity score and number of days with pain and improvement of satisfaction of bowel habit, quality of life over placebo ($P < 0.05$)
Tsuchiya et al[111]	*L. helviticus*, *L. acidophilus*, *Bifidobacterium*	10 mL t.i.d.[c]	68 (Rome II)	12	Symptom improvement of IBS: 80% vs 10% ($P < 0.01$)
Drouault-Holowacz et al[112]	*B. longum* LA 101 (29%), *L. acidophilus* LA 102 (29%), *L. lactis* LA 103 (29%) and *S. thermophilus* LA 104 (13%)	1 × 10^9	100 (Rome II)	4	No significant improvement of IBS symptom over placebo
Hong et al[107]	*B. bifidum* BGN4, *B. lactis* AD011, *L. acidophilus* AD031 and *L. casei* IBS041	2 × 10^9	70 (Rome III)	8	Significant reduction in pain over placebo ($P = 0.045$)

Ref:Lee BJ, Bak YT. J Neurogastroenterol Motil. 2011; 17(3): 252-66.

The safety of probiotics

There are 3 theoretical concerns regarding the safety of probiotics:

- (1) the occurrence of disease, such as bacteremia or endocarditis;
- (2) toxic or metabolic effects on the gastrointestinal tract; and
- (3) the transfer of antibiotic resistance in the gastrointestinal flora.

- Most studies found probiotics are safe.
- However, there has also been a case of L.acidophilus bacteremia in a patient who had HIV infection and Hodgkin disease and a case of Lactobacillus infection after a bone marrow transplant.

Ref: 1. Ledoux D, Labombardi VJ, Karter D . Lactobacillus acidophilus bacteraemia after use of a probiotic in a patient with AIDS and Hodgkin's disease. Int J STD AIDS 2006;17:280-2.

2. Kalima P, Masterton RG, Roddie PH, Thomas AE . Lactobacillus rhamnosus infection in a child following bone marrow transplant. J Infect 1996;32:165-7.

SUMMARY

- The gut contains numerous bacteria.
- Disruption of gut micro-organism may cause symptoms of IBS.
- probiotics help to keep a healthy micro-organisms environment in the body.
- However, beneficial health claims and safety of probiotics are not yet supported by strong clinical trials.