

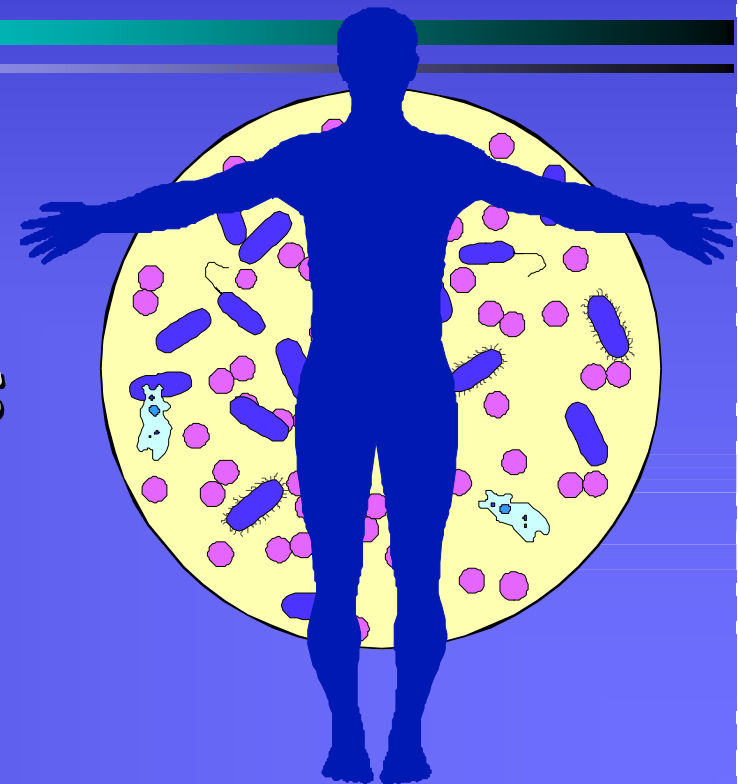


Dairy probiotics and gut health

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Health claims for probiotics



- *'Help maintain the balance of the gut flora'*
- *'Help the body's natural defences'*
- *'Maintain a healthy digestive system'*

Health claims for probiotics



Natasha's Probiotic Face Cream

'Beneficial Bacteria Promotes a Youthful Glow'

'Enriched with DNA fragments of beneficial bacterial cells, which speed up the skin's natural renewal process'

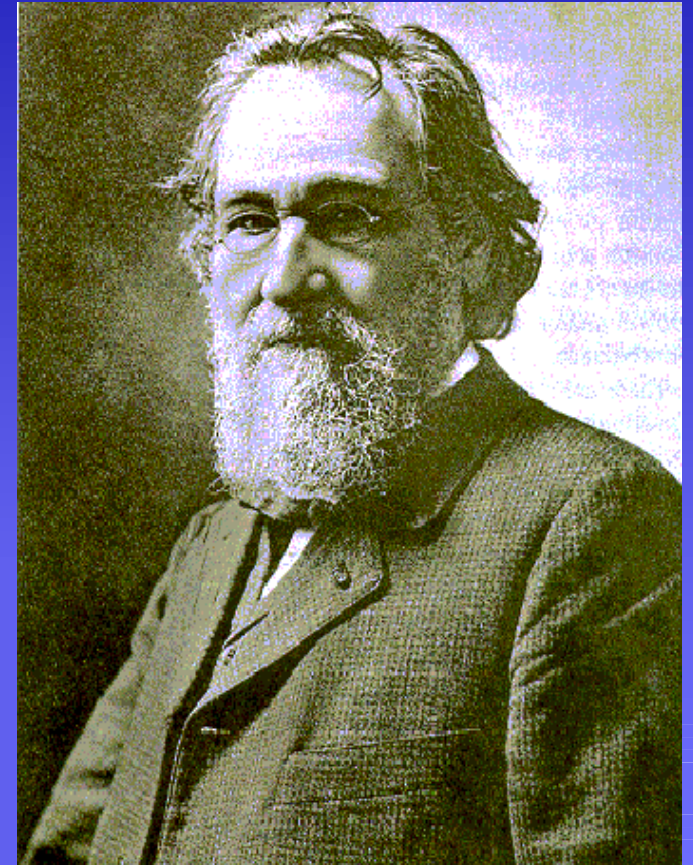
Why are LAB considered beneficial?

Elie Metchnikoff

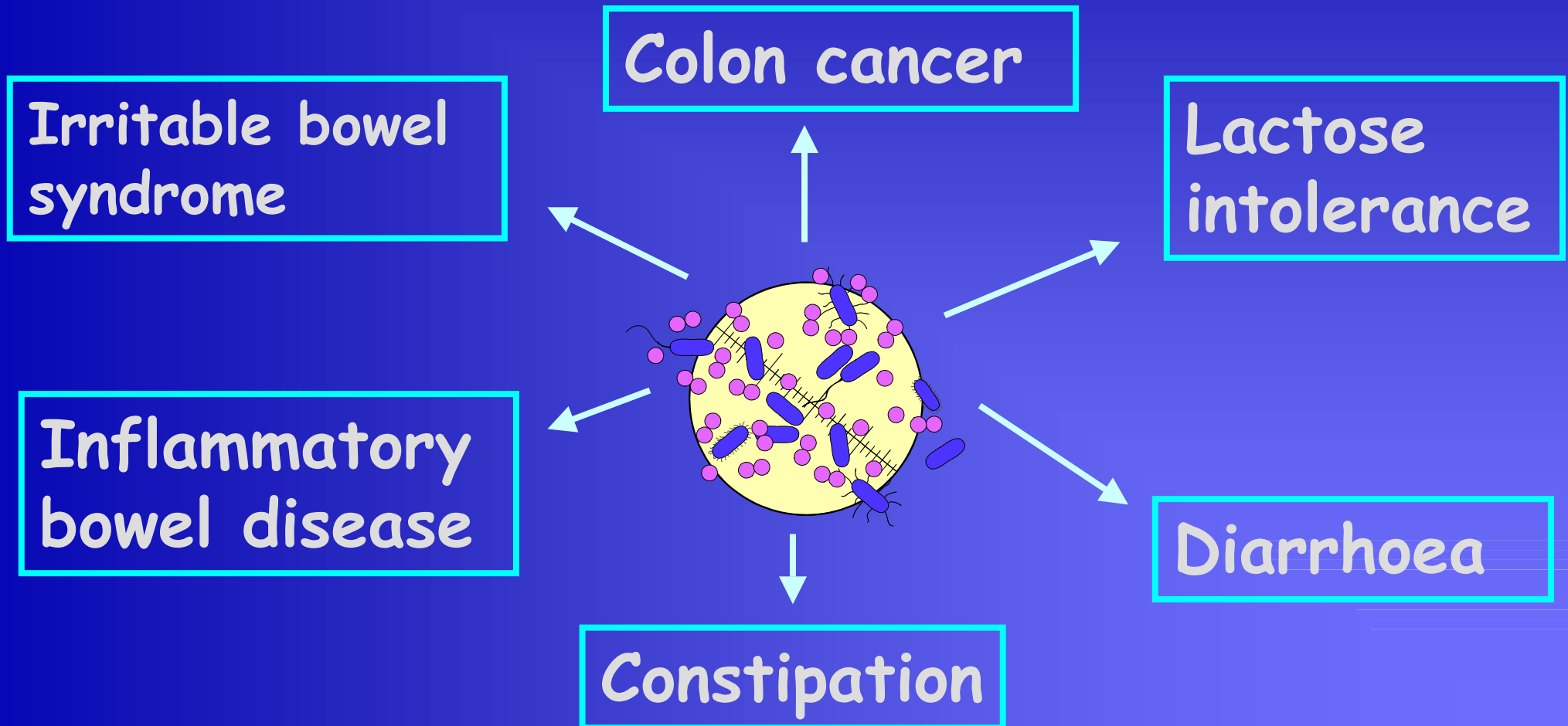
born May 15, 1845, in Kharkov, Ukraine

1907 proposed ingested lactobacilli could displace toxin producing 'putrefactive' bacteria from the gut, thus prolonging life.

- Claimed Bulgarian peasants consumed fermented milks and lived >100y



Postulated health benefits of probiotics in the gut



Lactose Intolerance



Probiotics and lactose intolerance

- Lactose intolerance is due to lactose maldigestion -lactase deficiency.
- About 15% of lactose maldigesters are intolerant
- Undigested, the milk sugar lingers in the colon and ferments, creating intestinal distress - abdominal pain, bloating and diarrhoea

Probiotics and lactose intolerance

- Lactose from yoghurt is digested better than lactose from milk (fermented milk drunk in countries where lactase deficiency is common)

Probiotics and lactose intolerance How many bacteria? Are live bacteria necessary?

- Probiotics possess lactase activity and degrade lactose in small intestine - Pasteurization reduces digestibility of yoghurt lactose -therefore **LIVE** bacteria are important.
- For optimum effect, yoghurts containing **10^8 bacteria/ml** (100 million) are needed

Yoghurt	Breath H2	Intestinal complaints
10^8 bacteria/ml	+/-	+
10^6 bacteria/ml	++	++
10^5 bacteria/ml	++	++
Heat treated	++	++
Milk	++++	+++

Pelletier et al EJCN 55, 509 2001

Probiotics and diarrhoea

- Acute gastro-enteritis diarrhoea in children
- Antibiotic associated diarrhoea
- Travellers diarrhoea

Probiotics and infant diarrhoea

Acute gastro-enteritis diarrhoea in children

- Usually due to **Rotavirus**
- Trials show *reduction in duration* of diarrhoea in infants given specific probiotics → **Therapeutic**
- Trials indicate lower *incidence* of diarrhoea with specific probiotics → **Preventive**
- Mechanism unknown but may be via immune stimulation

Acute gastro-enteritis diarrhoea in children

<i>Disease</i>	<i>Probiotic</i>	<i>Effect</i>	<i>Ref</i>
<u>Therapy</u>			
Rotavirus diarrhoea	L GG	Duration ↓	Isolauri 1991 Kaila 1992 Majamaa, 1995
Acute severe diarrhoea	L GG	No effect	Salazar-Lindo 2004
<u>Prevention</u>			
Acute diarrhoea	<i>B. bifidum+</i> <i>S. thermophilus</i>	Incidence ↓ Rotavirus ↓	Saavedra 1994
	L casei DN11400	Incidence ↓ Duration no effect	Pedone 1999
	BB12; L reuteri	Incidence/duration ↓	Weizman 2005
	<i>B breve</i> <i>S therm</i>	Incidence/duration no effect; severity ↓	Thibault 2004

Acute gastro-enteritis diarrhoea in children -therapy

Acute rotavirus diarrhoea (Isolauri et al, Pediatrics 88, 90, 1991)

- Placebo controlled, randomized study
- Duration of diarrhoea shortened by Lactobacillus GG 5d → 3d
- LGG enhanced Ig secreting cell nos.
- IgA specific Ab-secreting cell response to rotavirus in 90% of LGG vs 46% placebo

Infant diarrhoea - Prevention

Group	Incidence	Rotavirus +ve
1. Yoghurt	22.0%	2.20%
2. L casei	15.9%*	0.29%

Children (6-24 m; n=928,) given supplements of yoghurt or Actimel for 3 m. (* P=0.029)

No effect on duration

Pedone et al, Int J Clin Prac 54 568 (2000).

Infant diarrhoea - Prevention

Parameter	Control	<i>BB-12</i>	<i>L reuteri</i>
n	60	73	68
Episodes	0.31	0.13**	0.02**
Duration d	0.59	0.37**	0.15**
Fever d	0.41	0.27**	0.11**
Ab prescrip	0.19	0.21	0.06**

RDBPCT Children (4-10 m;) given Formula milk \pm probiotics ($10^7/g$) for 12 weeks

Weizman et al, *Pediatrics* 2005;115;5-9

Antibiotic-associated diarrhoea

- Patients treated with broad-spectrum antibiotics usually have diarrhoea, sometimes due to *Clostridium difficile*
- 8 clinical trials show reduction in diarrhoea when specific probiotics consumed

Pediatric AAD- Meta analysis (Cochrane)

9/10 studies sig reduction in incidence

(RR 0.49 CI 0.32-0.74) (Johnston Cochrane Syst Rev 2007)

Probiotics and diarrhoea

➤ Travellers diarrhoea

➤ Can be due to a wide range of bacteria and viruses

➤ No consistent evidence for protective effect of probiotics

Constipation and transit time

- 10 studies on constipation, usually in elderly subjects, with yoghurt, yoghurt enriched with probiotics or probiotic tablets
 - 5 studies showed some benefits for constipation
- 4 studies on transit time
 - 3 studies showed improvement
- Probiotic-enriched yoghurts appeared more effective

Inflammatory bowel disease

Crohn's disease and ulcerative colitis/pouchitis are chronic, painful diseases

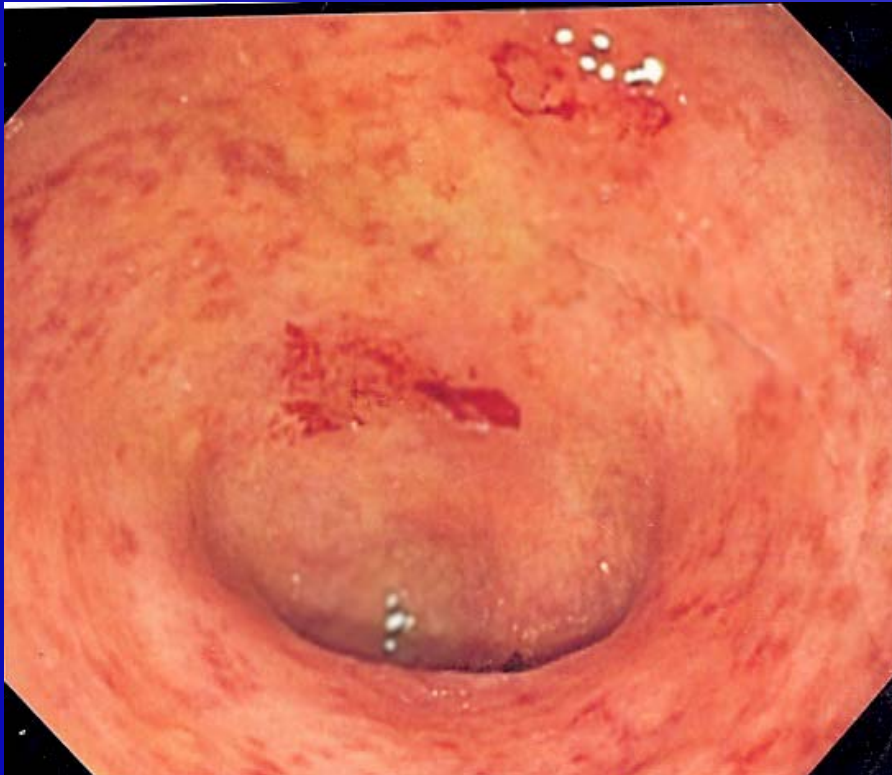
Crohns - No effect of probiotics (8 small studies: Rolfe et al Cochrane Database Syst Rev Oct 2006)

Pouchitis patients given a mixture of probiotics (4 lactobacilli, 3 bifido, 1 strep - VSL#3)

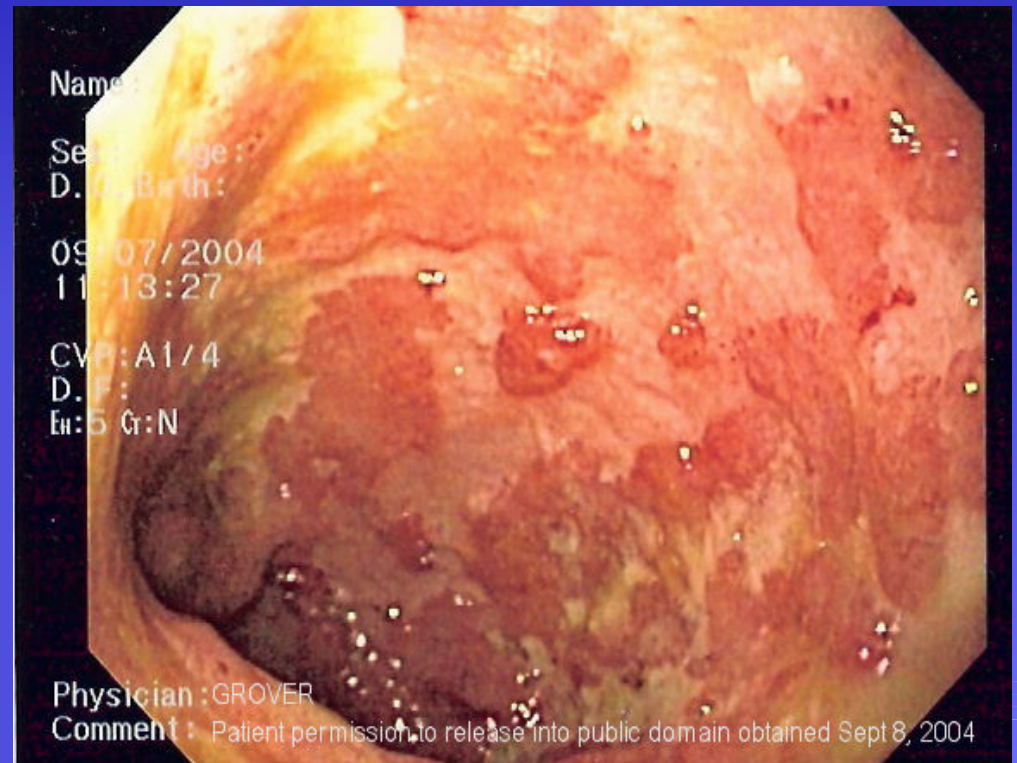
- **20/20** patients on placebo relapsed in 8 months
- **3/20** patients given probiotics relapsed in 8 months (Gionchetti et al 1998, 2000,)
- VSL also prevented dev of pouchitis after surgery
- LGG - no effect

Inflammatory bowel disease

Ulcerative colitis



UC Sigmoid colon



UC left colon

Probiotics and ulcerative colitis

Induction of remission 4/4 studies +ve

2 x fermented milks, 1 VSL#3, 1 E coli Nissle

Maintenance of remission 2/4 studies +ve

+ve E coli Nissle, VSL #3

-ve LGG, L. salivarius/B. infantis

(NB not all RPCT, VSL#3 open label/no placebo)

IBD & probiotics - mechanisms

- Modulation of cytokines
 - \uparrow IL10, TGF- β ; \downarrow TNF α , interferon- γ
- Improved barrier function
- Inhibition of pathogenic bacteria

Irritable Bowel Syndrome (IBS)

- Common GI disorder
- Affects 15 - 20 % of adults in Western world at some point in their lives
- Accounts for 10% of GP visits
- Symptoms vary (abdominal pain, distension, flatulence, diarrhoea, constipation)
- No underlying pathology
- Evidence for association with low grade inflammation in colon & immune activation?
- Abnormal microflora/colonic fermentation?

Probiotics in the Treatment of IBS

13 Studies of probiotics vs IBS, most RDPCT,
N= 12 - 360; dose variable

2- 6weeks.

Beneficial

Lb plantarum (2)

B infantis (2)

VSL#3 (2),

LGG/L rham/B breve/P freundenreichii

Lb acidophilus

No effect

Lb GG (2),

Lb plantarum

Lb salivarius,

Lb reuteri

8/13 studies showed some improvement in some symptoms,
usually not all, often only one symptom changed

Protective effects of probiotics and prebiotics towards cancer

- Prevention of DNA damage *in vitro/in vivo*
- Suppression of pre-neoplastic changes in the colon
- Suppression of tumours in animals
- Evidence for protective effects in humans



Human Intervention Study

Subjects:

Patients with high risk of CRC (polypectomized) n=40

Patients with history of CRC (Dukes B) n=40

Treatments: parallel design, 12 wk intervention

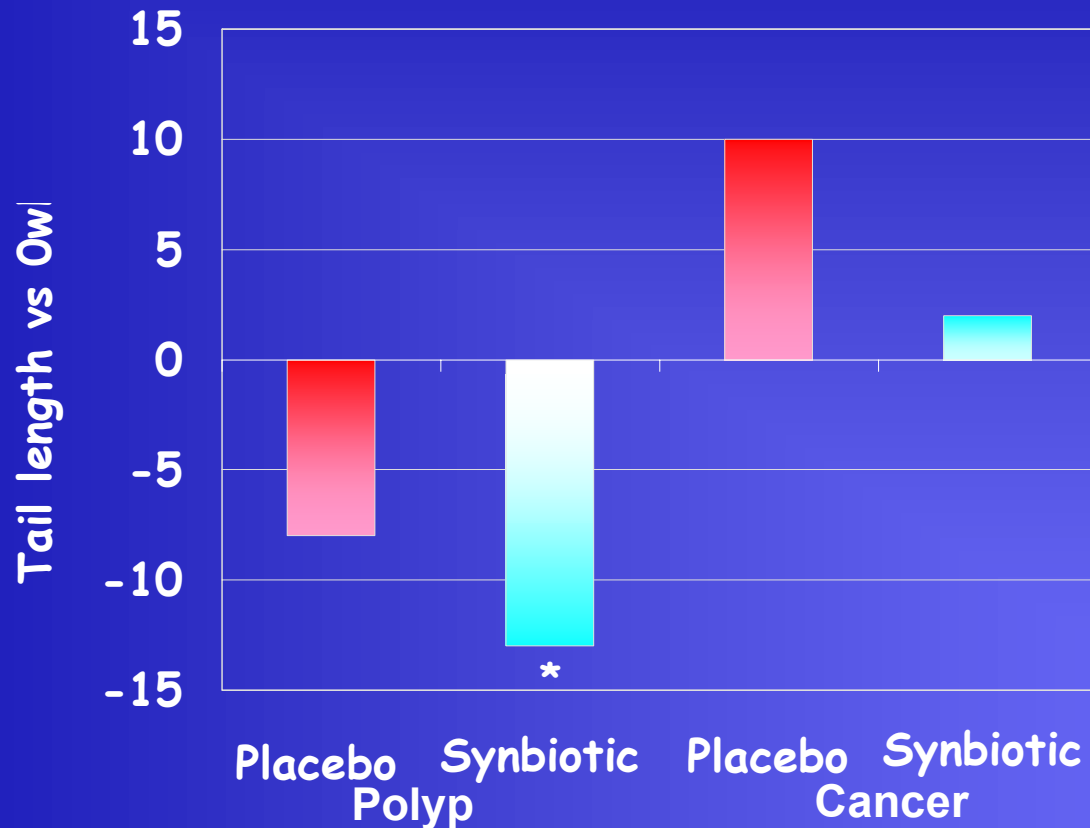
1. Placebo

2. Probiotics LGG, BB12 plus Prebiotic (Synergy 1)

Samples:

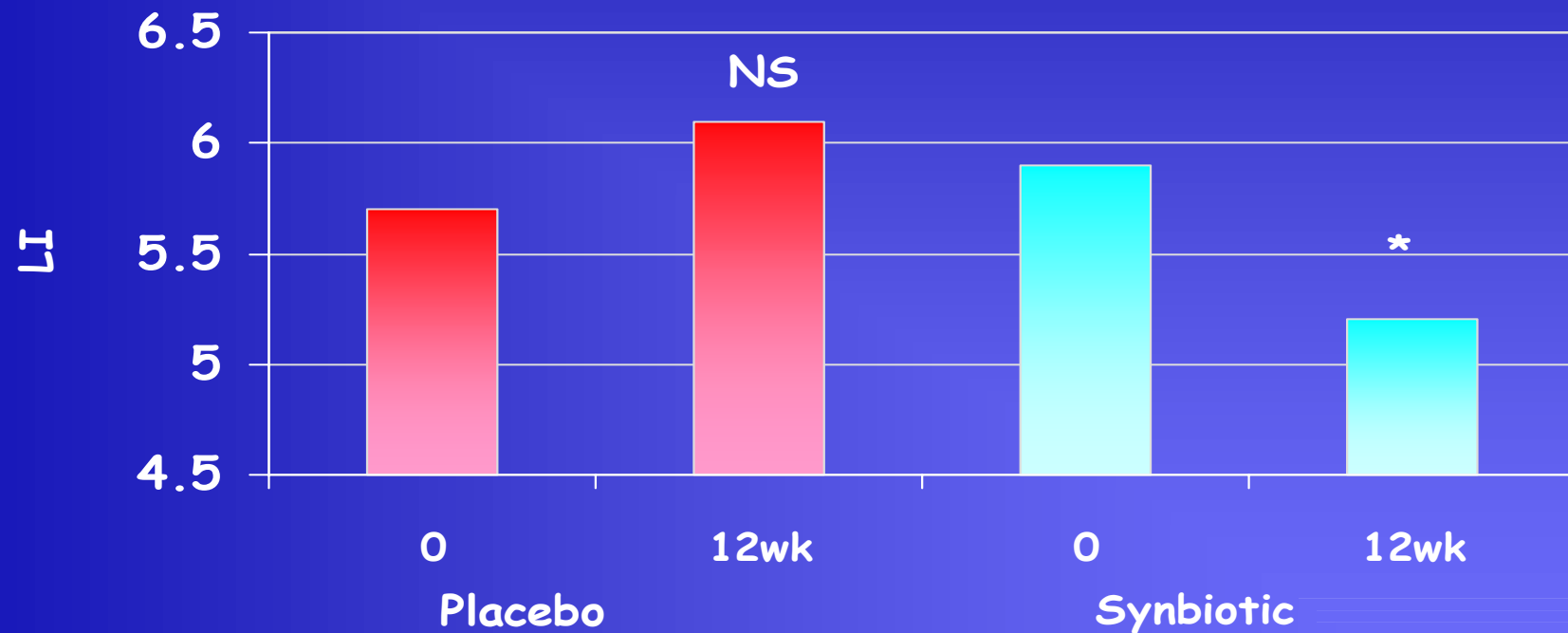
Rectal tissue samples and stool samples assessed for indicators of cancer risk

Synbiotics and DNA damage in biopsies



Effect of synbiotic consumption on DNA damage (Comet assay) in rectal biopsies in polyp patients n=14, 15 Rafter et al AJCN 85:488-96

Synbiotics and cell proliferation



Effect of synbiotic consumption on cell proliferation rectal biopsies in polyp patients n=14, 15

Randomized Trial of *Lactobacillus casei* Administration for Prevention of Colorectal Tumors

Subjects: 40 - 65 years old patients
with resected multiple colorectal tumor
(Adenoma and/or Carcinoma)

Lactobacillus casei powder 1.5×10^9 - 2.1×10^{10} viable cells/g

End point: Presence or absence of new colorectal
adenoma (after 2 years ~67% of control
subjects developed a new adenoma)

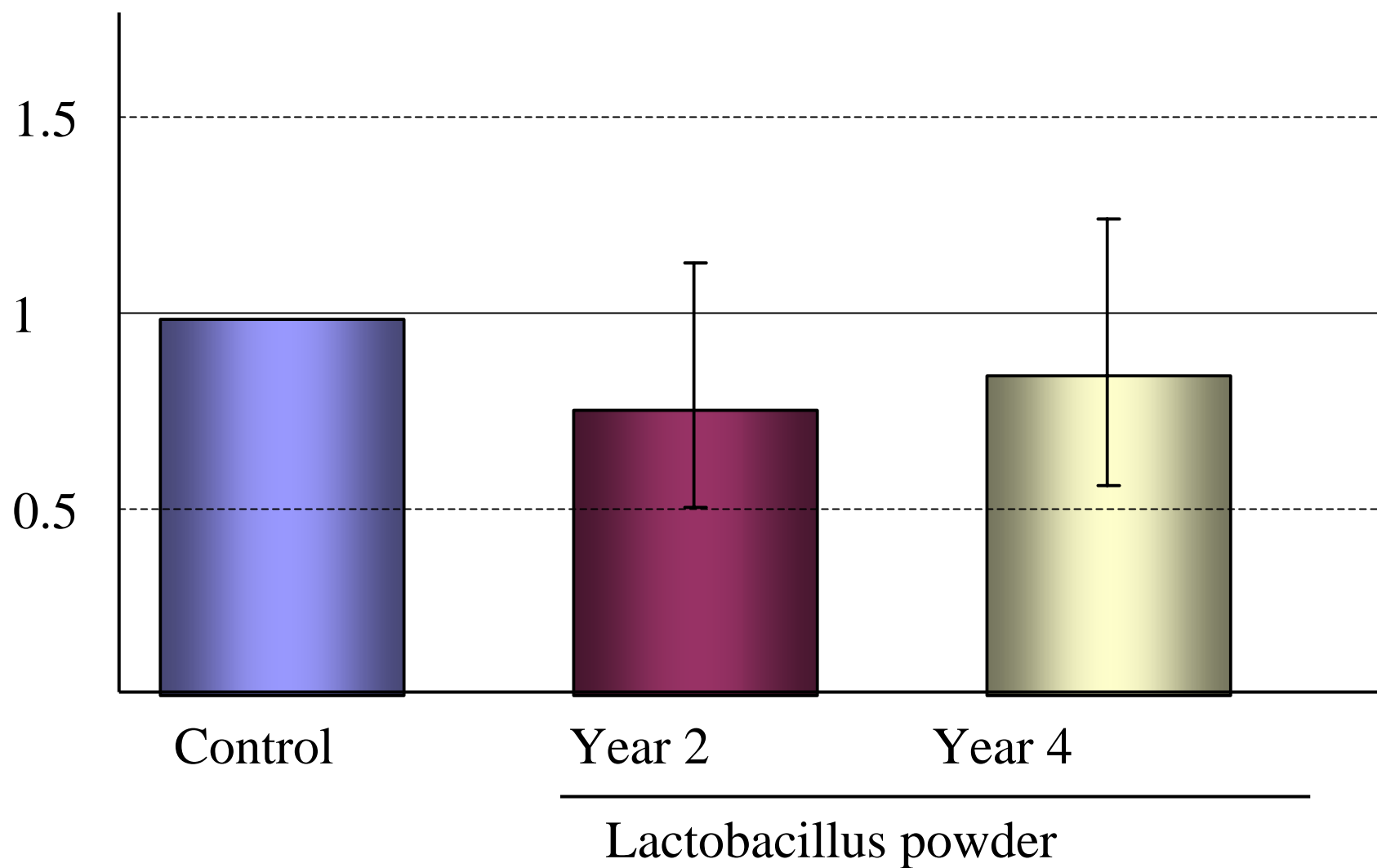


Ishikawa H. et al.. Int. J. Cancer, 116: 762-767, 2005

Lactobacillus casei adenoma recurrence

Relative Risk

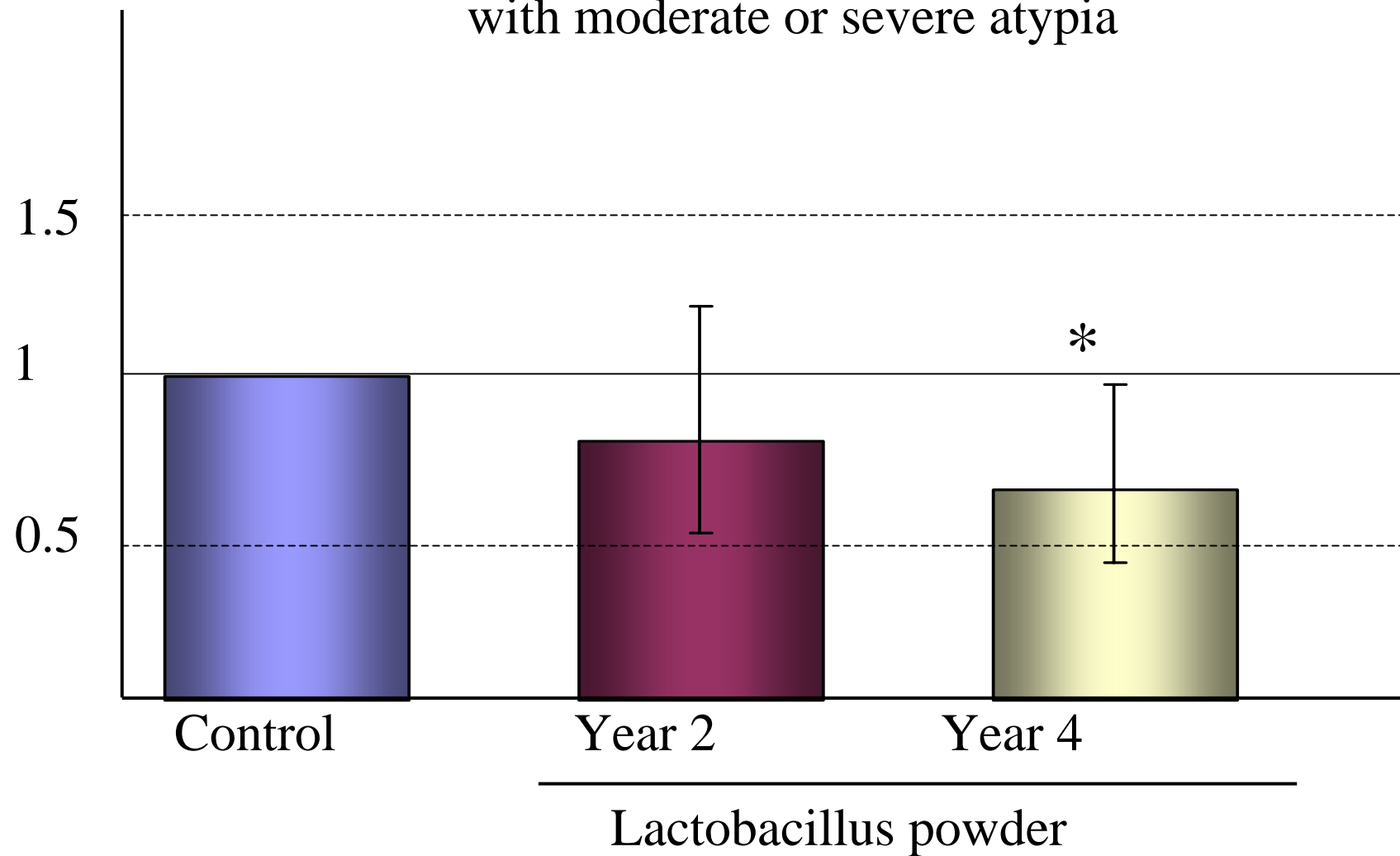
Presence of tumor



Lactobacillus casei - adenoma recurrence

Relative Risk

Presence of adenoma
with moderate or severe atypia



Postulated health benefits of probiotics in the gut - *conclusions*

Lactose intolerance	***
Diarrhoea	***
Constipation	**
IBD	*
IBS	*
Colon cancer	*