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First you add knowledge...

Pro- (and pre) biotics in relation to allergy and obesity

Arthur Ouwehand

Health & Nutrition

Human intestinal microbiota

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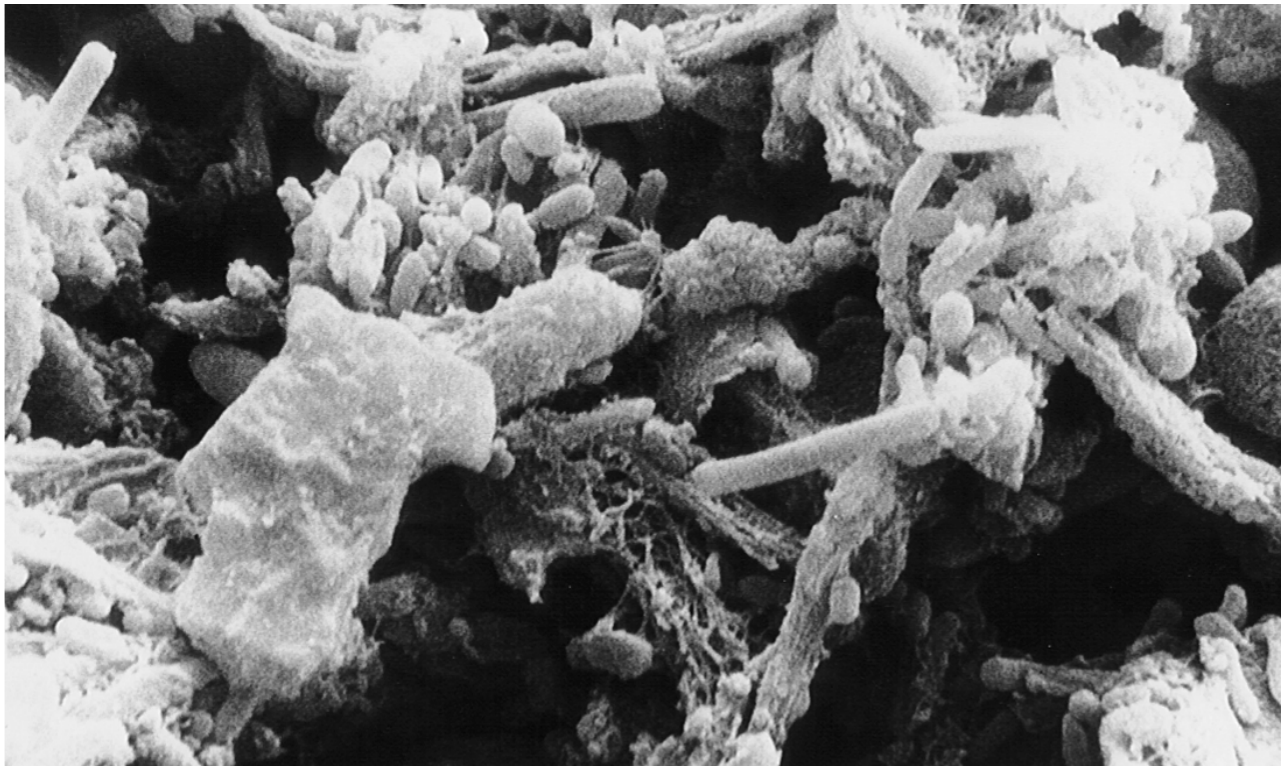
- ☺ Colon contains approx. 1-1½ kg bacteria
- ☺ Estimated over 1000 different bacterial species in the intestine
- ☺ Bacteria outnumber human cells in the body by 10:1
- ☺ Many have no known function,
  some are potentially detrimental others are beneficial



How to influence the (intestinal) microbiota

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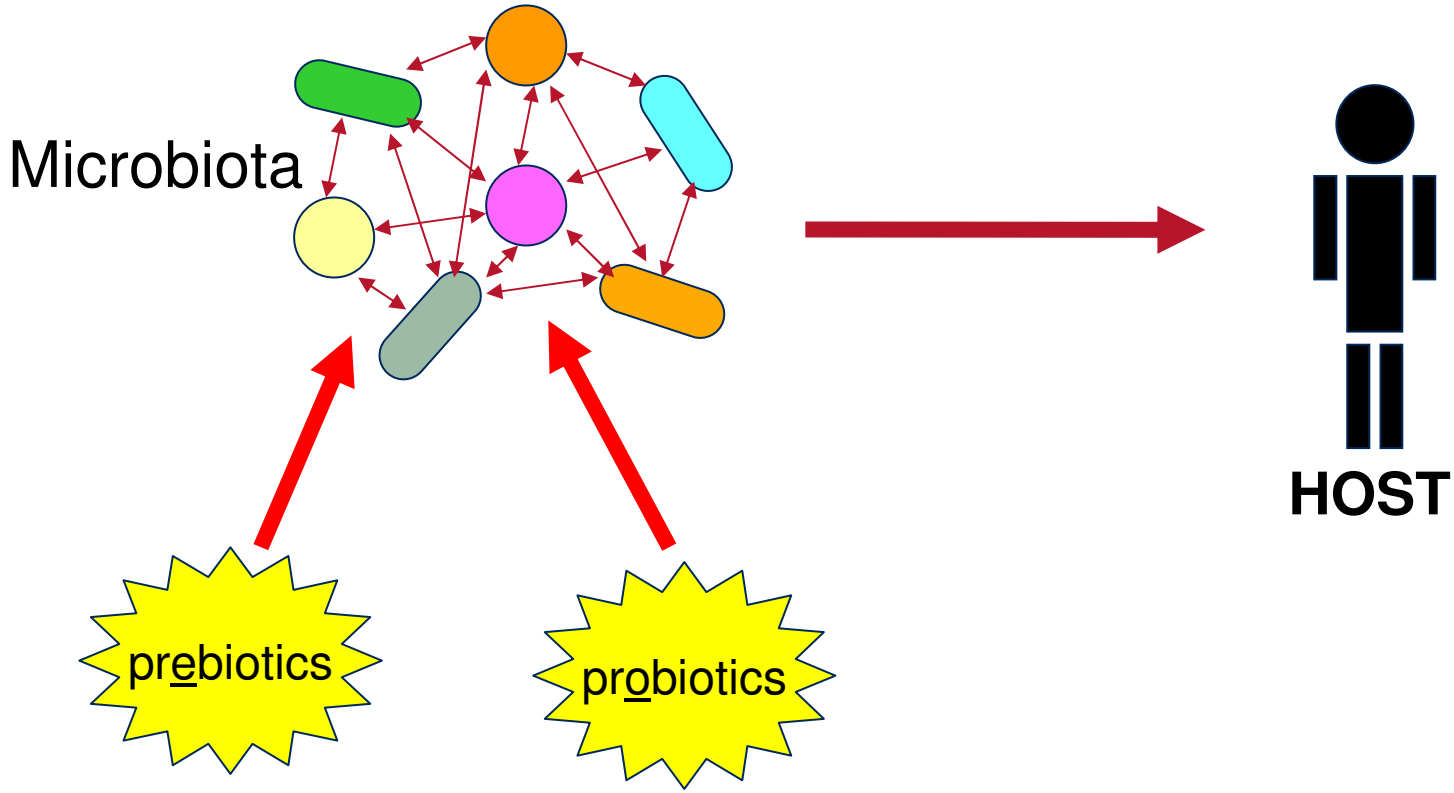

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Weight management

Differences in microbiota composition in lean and genetically obese mice

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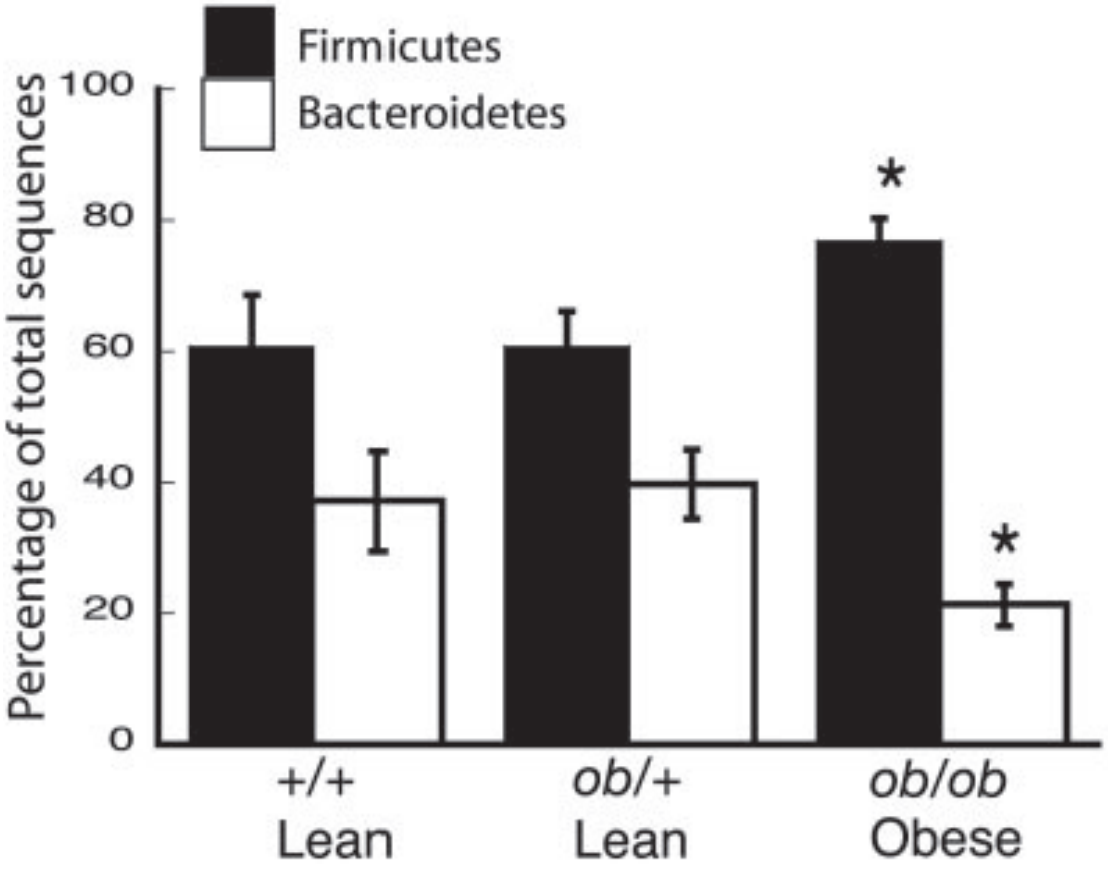

Phyla	Representative genera
Bacteria	
Firmicutes	*Ruminococcus*
	Clostridium
	Peptostreptococcus
	Lactobacillus
	Enterococcus
Bacteroidetes	*Bacteroides*
Proteobacteria	*Desulfovibrio*
	Escherichia
	Helicobacter
Verrucomicrobia[b]	
Actinobacteria	*Bifidobacterium*
Cyanobacteria[b]	
Synergistes[b]	
Archaea	
Euryarchaeota	*Methanobrevibacter*

Ley et al 2006

Production of VFA, Residual energy in faeces
A more energy efficient microbiota

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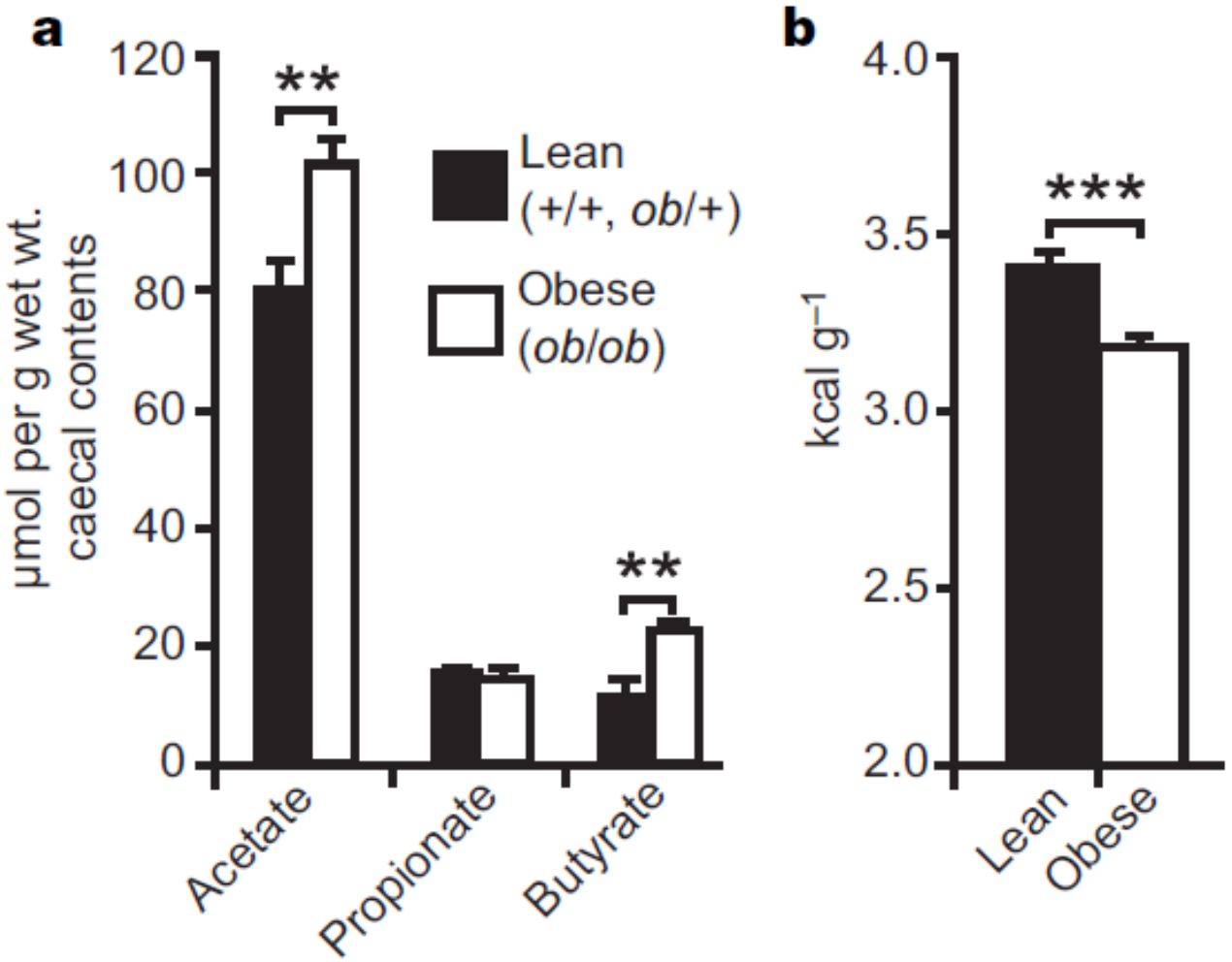

Turnbough et al 2006

Change in microbiota in response to dieting

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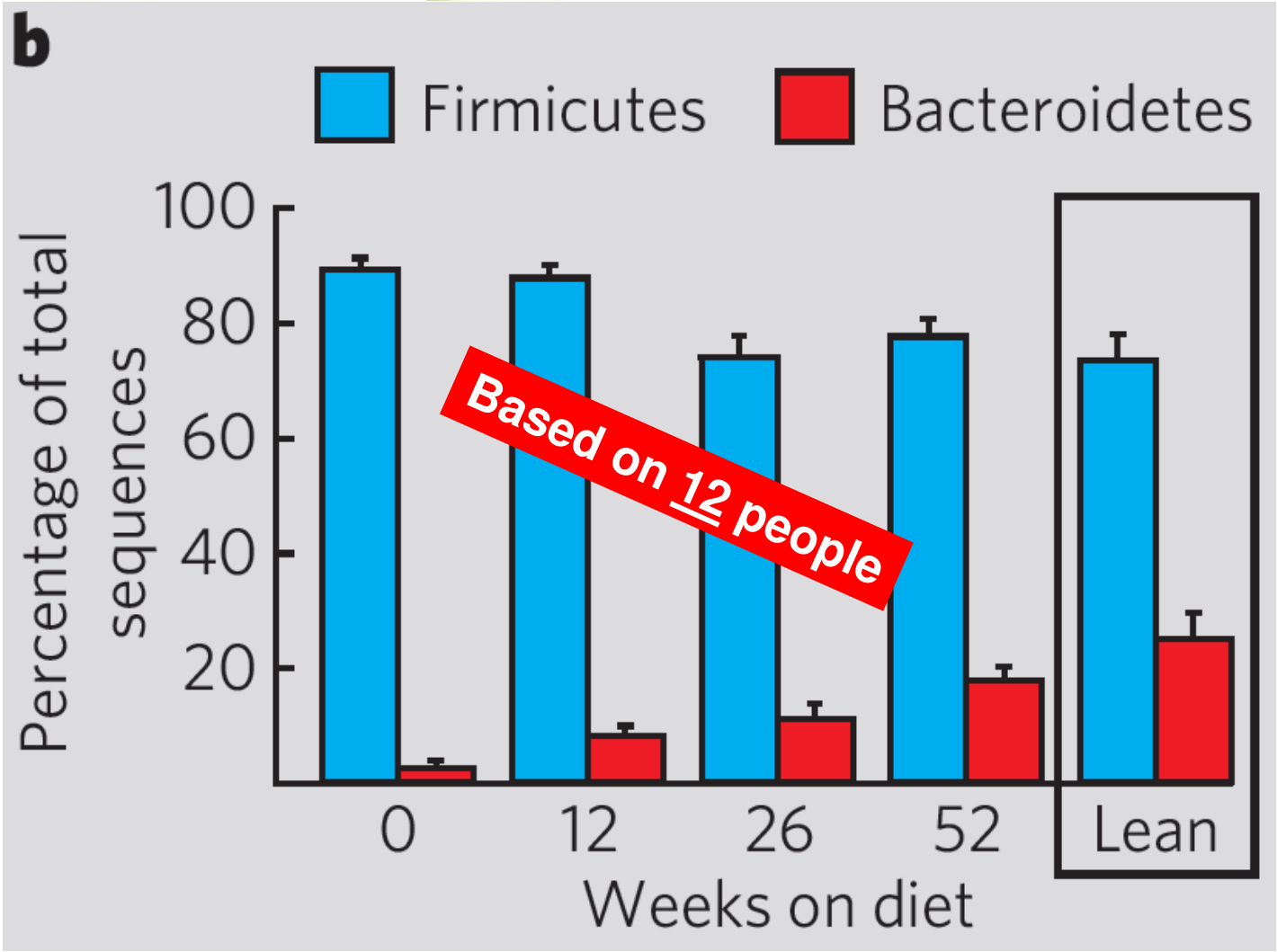

Ley et al 2006

Mechanism remains to be explained!

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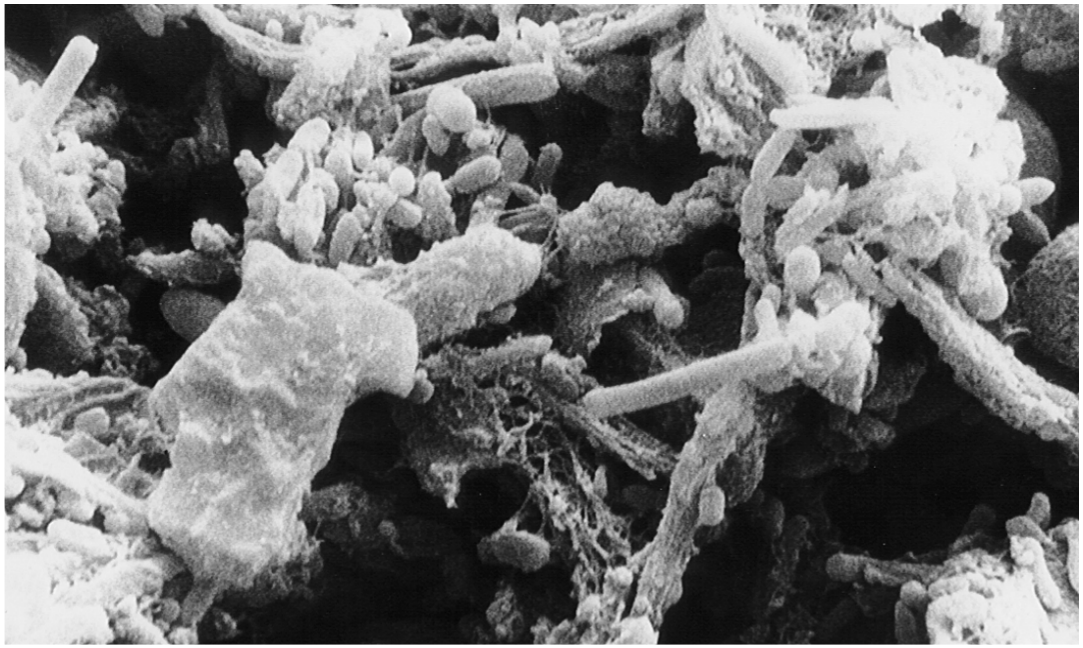
- Fermicutes — Lean<Obese
- Bacteroidetes — Lean>Obese
- Energy harvesting — Lean<Obese (more efficient)
- Dieting (energy restriction)

Obese microbiota → Lean microbiota

Efficient microbiota → less efficient microbiota



Microbiota of children whom are lean or obese in later life

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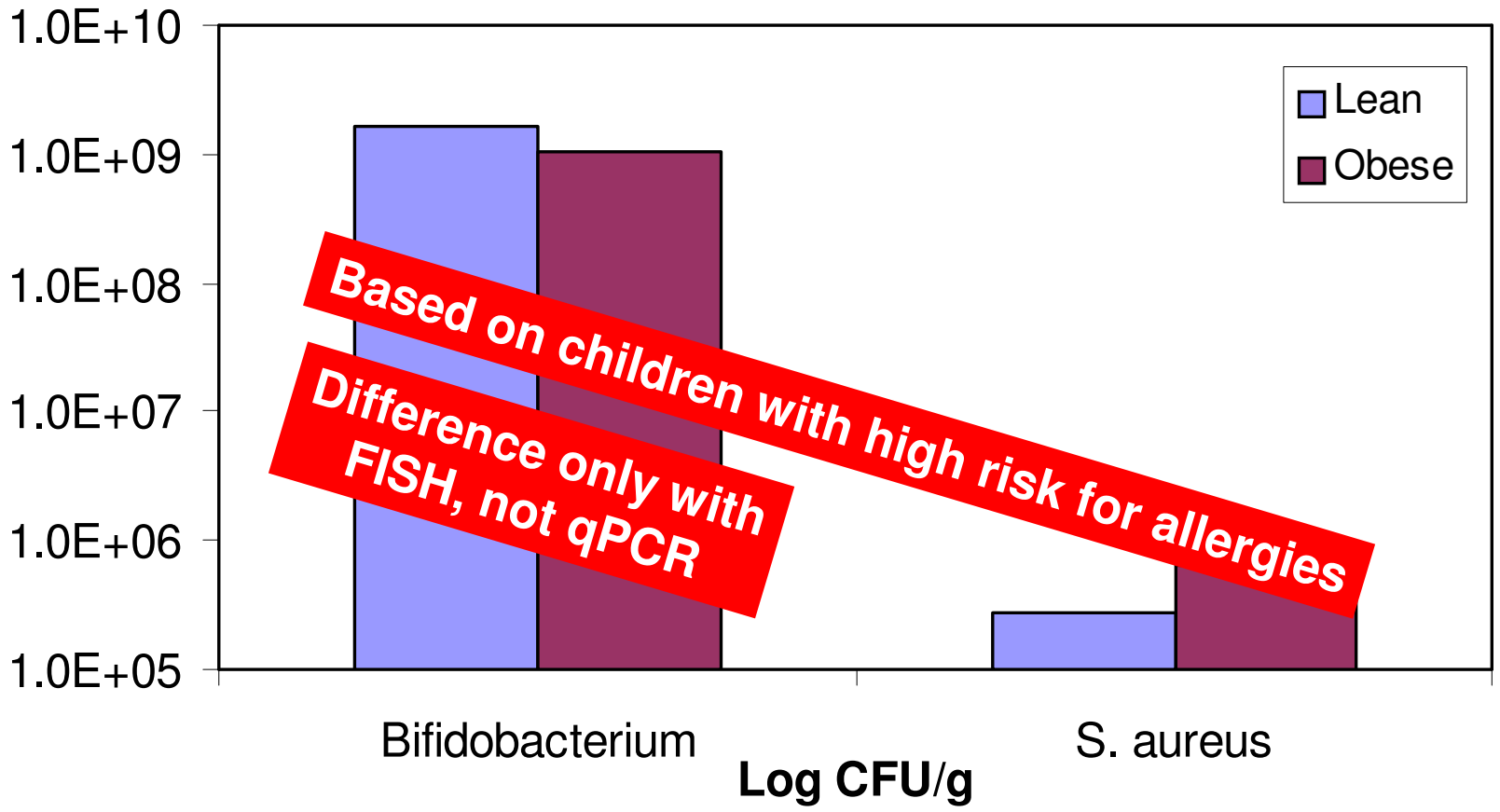

Kalliomäki et al. 2005

Helicobacter pylori and obesity

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Age (years)	Obese subjects (fraction Hp positive)	Control subjects (fraction Hp positive)
10-19	4/22	63/154
20-29	71/193	77/111
30-39	56/118	89/140
>40	50/81	201/278
All	181/414	410/683

H. pylori colonisation is also associated with reduced risk for allergy

Wu et al. 2005

Weight management;
Potential targets for probiotics

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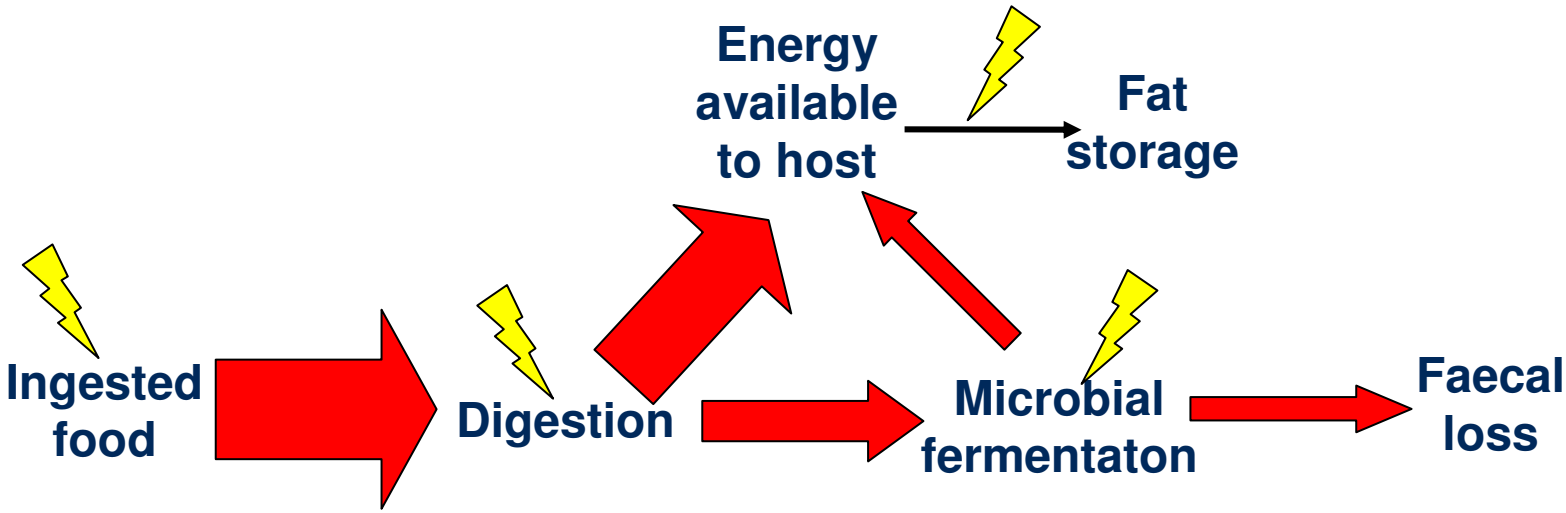

Korczyńska et al. 2008

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THE PROBIOTIC SOLUTION

Dr. Mark A. Brudnak

In this treatment strategy, the goal is to use a very high dose of probiotics in order to prevent the food from being digested by the body and turned into fat. Put differently, the food that would ordinarily be absorbed will be consumed by the probiotics. So, you can have your cake and the probiotics will eat it, too! One particularly interesting

More 'mouths' to feed, more energy available

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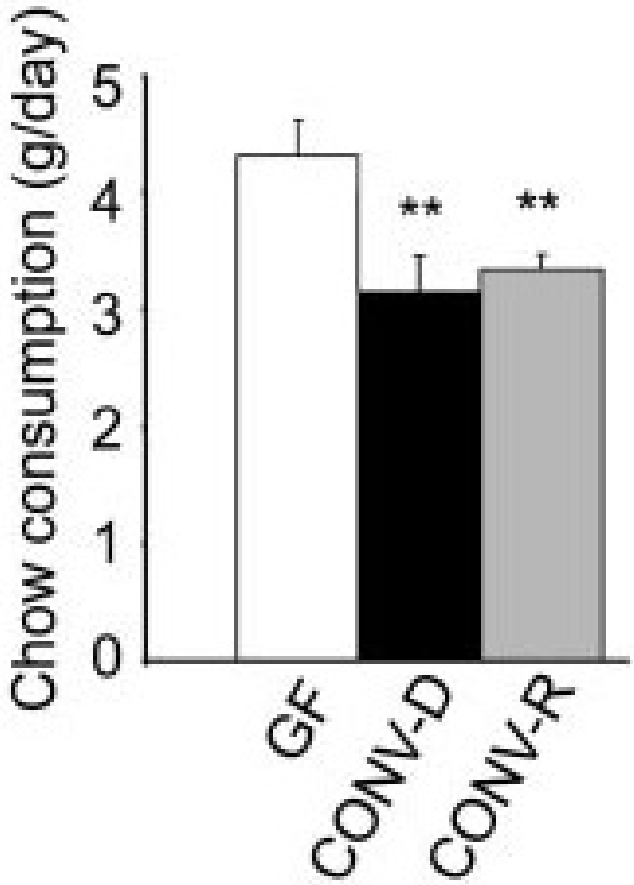

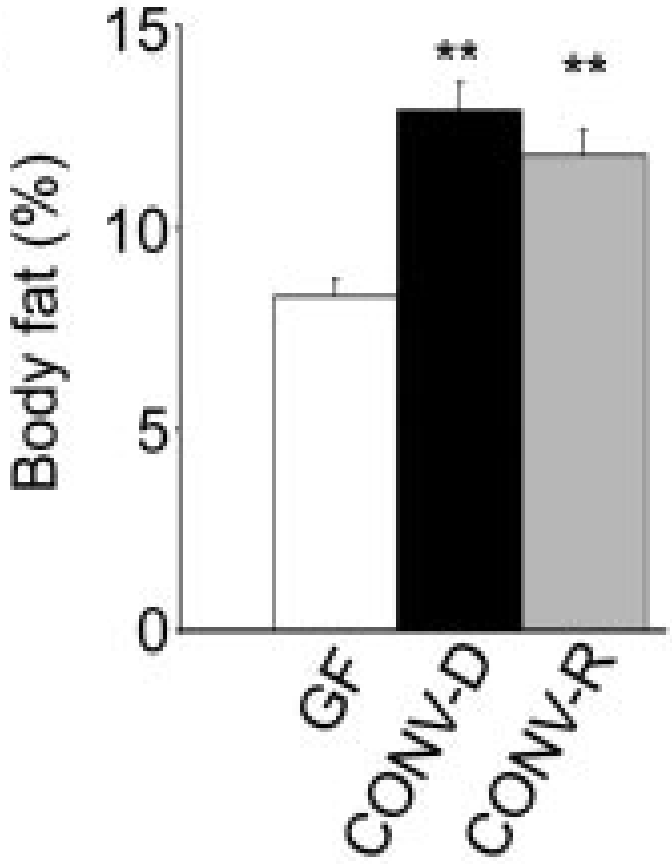

Bäckhed et al 2004

Yogurt and satiety

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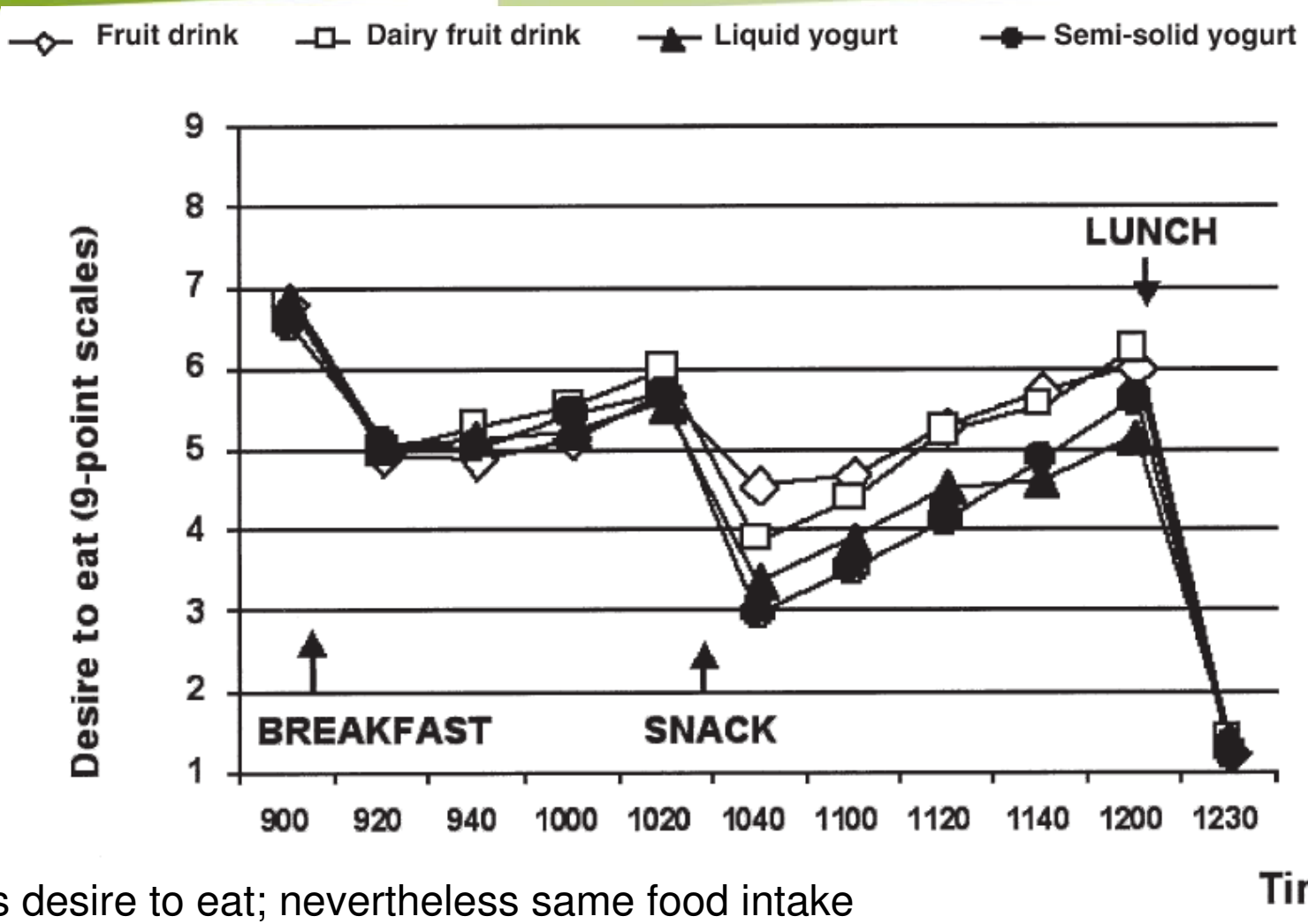

Less desire to eat; nevertheless same food intake
Would they have eaten their lunch later?

Tsuchiya et al. 2006

Change microbiota composition
Influence energy harvesting

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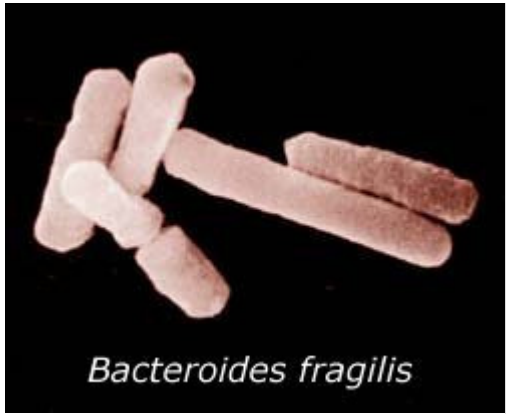
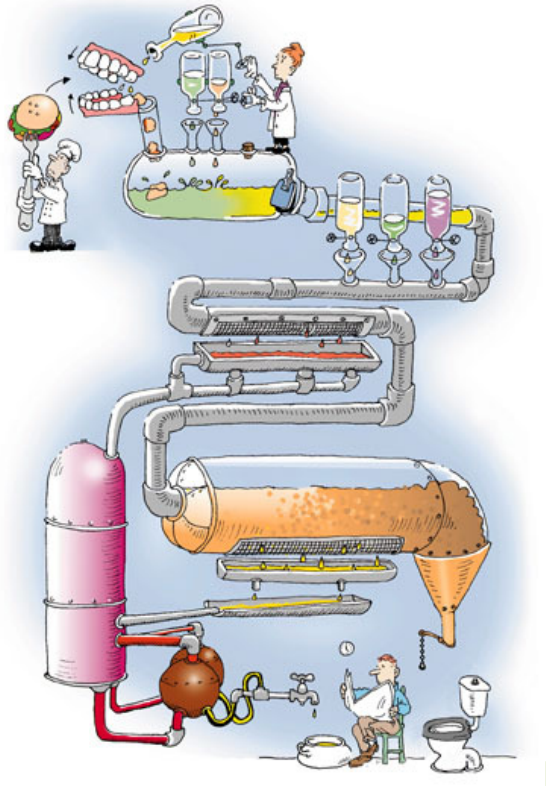


- Increase Bacteroidetes
  - *Bacteroides* probiotics?
    - Novel food

- Interfere with digestion
  - Reduce effectiveness of digestion
  - Reduce absorption of digesta
    - Risk for deficiencies



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Allergic disease

Intestinal microbiota and allergic disease

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	Prevalence (%)									
	1 week		1 mo		3 mo		6 mo		12 mo	
Microorganisms	Healthy	Allergic	Healthy	Allergic	Healthy	Allergic	Healthy	Allergic	Healthy	Allergic
S aureus	62	56	65	56	50¶	50	23*¶	61*	27	39
Enterococci	96*	67*	96†	72†	96	89	96	100	96	89
Lactobacilli	8*‖	39*	46‖	56	34	56	38	39	38	44
Bifidobacteria	50†	17†	69	39	62‡	28‡	42	28	69§	22§
Bacteroides	46	61	62	72	65	83	81	94	96	89
Clostridia	27	50	27	28	46	28	65	50	54	67

↘↙Colonisation level

Björkstén et al. 2001

Bifidobacteria and allergic disease

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	Percentage of isolates (frequency of isolation)		
Bifidobacterium species	Allergic	Healthy	*P* value*: healthy vs allergic
B adolescentis	50 (6/7)	0 (0/6)	.005
B bifidum	2 (1/7)	58 (5/6)	.029
B breve	15 (1/7)	27 (2/6)	>.05
B infantis	21 (4/7)	15 (1/6)	>.05
B longum	12 (1/7)	0 (0/6)	>.05

Ouwehand et al. 2001

Bifidobacteria and allergic disease (2)

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Child	Allergic								Nonallergic							
Species	*B. adolescentis*	*B. catenulatum/ pseudocatenulatum*	*B. longum*	*B. bifidum*	*B. breve*	*B. angulatum*	*B. dentium*	Total	*B. adolescentis*	*B. catenulatum/ pseudocatenulatum*	*B. longum*	*B. bifidum*	*B. breve*	*B. angulatum*	*B. dentium*	Total
1	•		•	•						•	•					
2	•					•				•	•					
3	••									•	•					
4	•	•	•						•	•	•			•		
5			••							••	••			•	•	
6			••						•		•			•		
7	•	•	•	••						••	••					
8			•							•	••					
9	•	•							•		•					
10	•					•				••	•	•				
11			•							•	•					
12			•••								••					
13	••	•	••								•					
14	••		•••							••	•		•	•		
15	•		•							•••	••		•			
16	•		•							•••	•		•	•		
17	••	•	••		•					••	••		•	•		
18	•		•		•				•	•	••			•		
19			•								••		•	•		
20	•		•			•			•	••	••			•		
Sum of positive subjects/total clones	14†/18*	5/5	16/24	2/3	2/2	3/3	0/0	**20/55**	5/5	14‡/23#	20/29	1/1	5/5	9/9	1/1	**20/73**

Stsepetova et al. 2007

Serum status of Russian and Finnish Karelian children; correlation to atopy

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	OR	95% CI	Change in OR, %
No antibodies in the model			
(only country)	1.78	1.34–2.35	100
Stepwise addition of seropositivities			
H. pylori	1.53	1.07–2.21	–32
A. actinomycetemcomitans	1.47	1.01–2.13	–40
T. gondii	1.41	0.97–2.05	–47
HSV	1.40	0.96–2.06	–49
C. pneumoniae	1.37	0.92–2.02	–53
P. gingivalis	1.39	0.93–2.07	–50
HAV	1.43	0.87–2.37	–44

von Hertzen et al. 2006

Nasal microbiota and allergic disease

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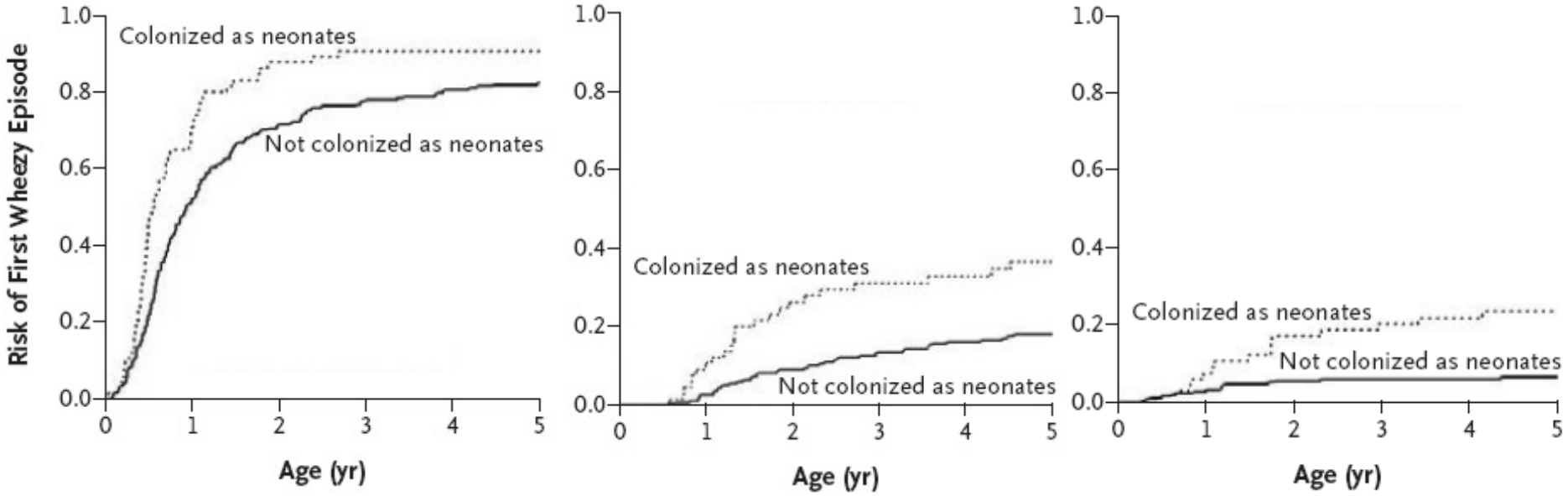
Colonisation with:

Streptococcus pneumoniae ***Moraxella catarrhalis*** ***Haemophilus influenzae***



Bisgaard et al. 2007

Lactobacillus GG or *B. lactis* Bb-12 in the treatment of atopic eczema

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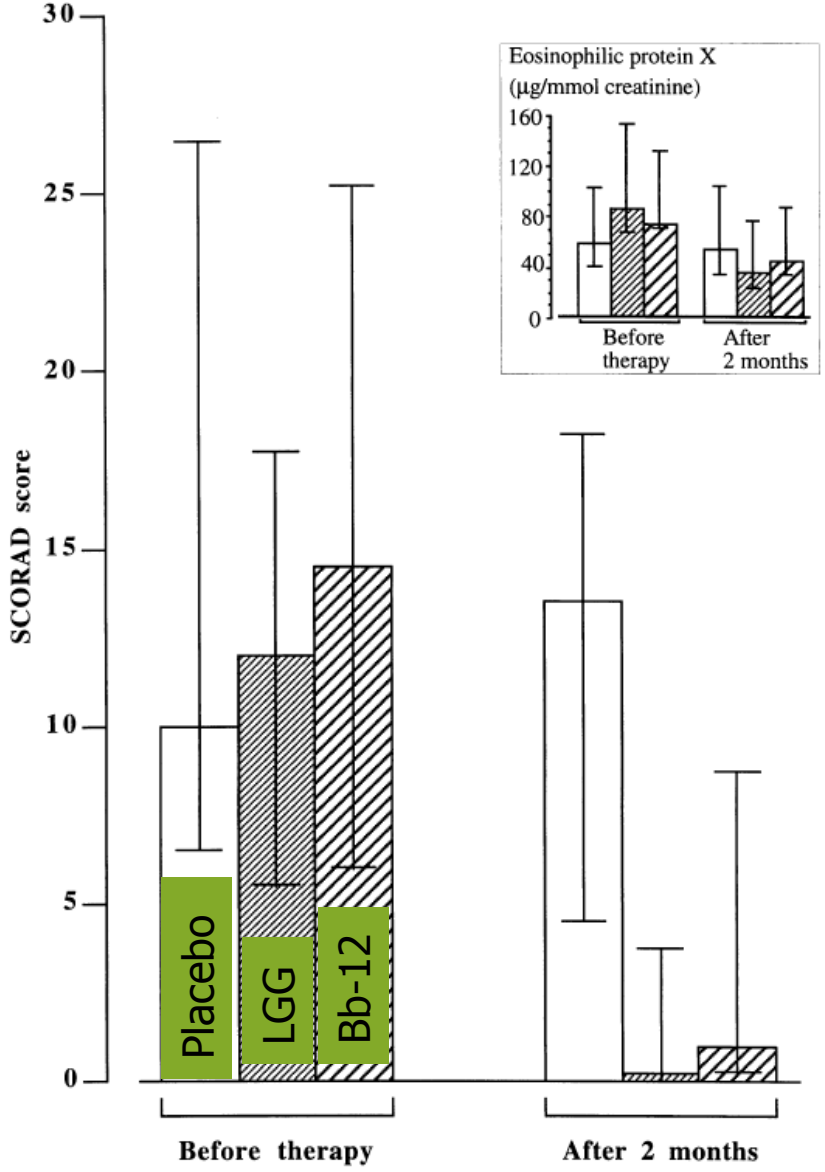

Isolauri et al. 2000

Lactobacillus GG or *L. rhamnosis* in the treatment of atopic eczema

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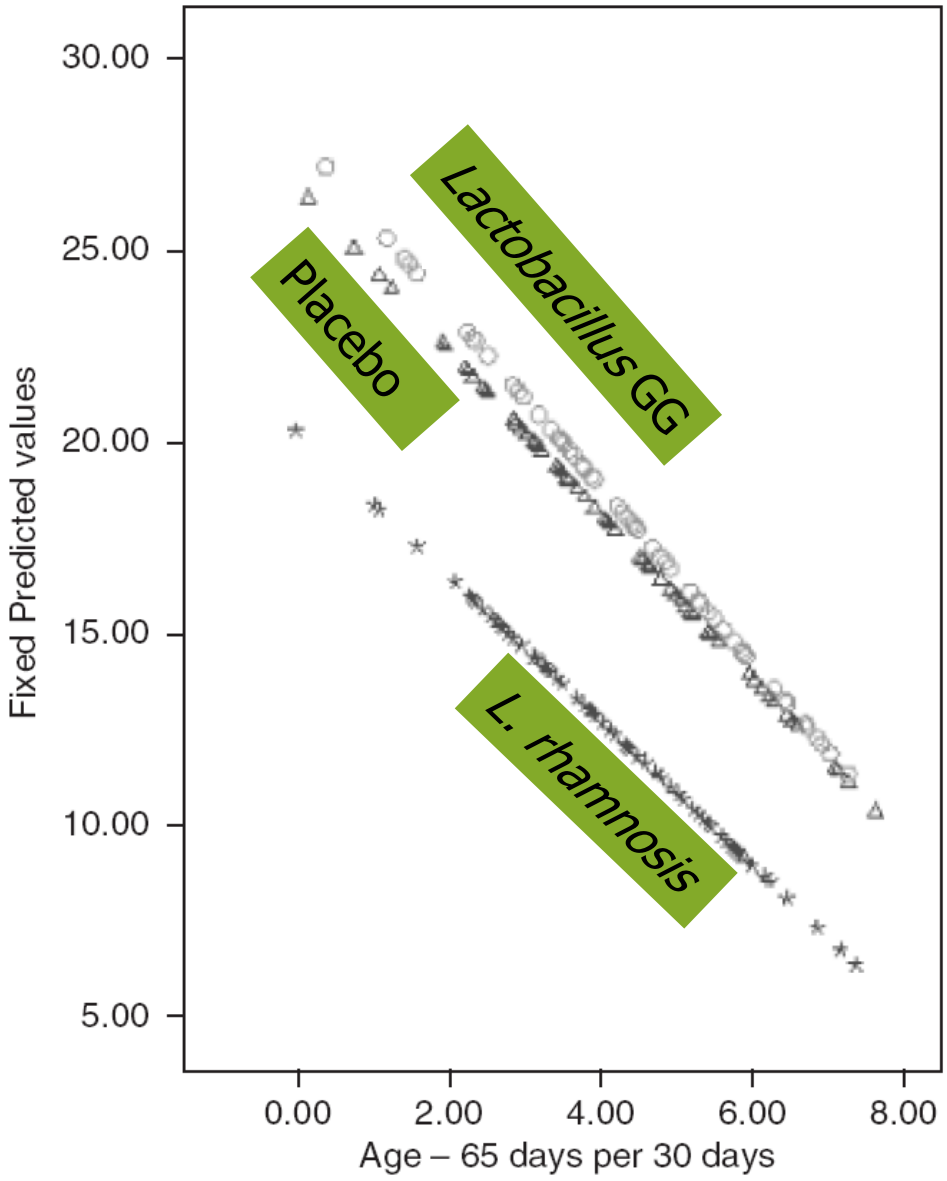

Brouwer et al. 2006

Lactobacillus GG in the treatment of atopic eczema

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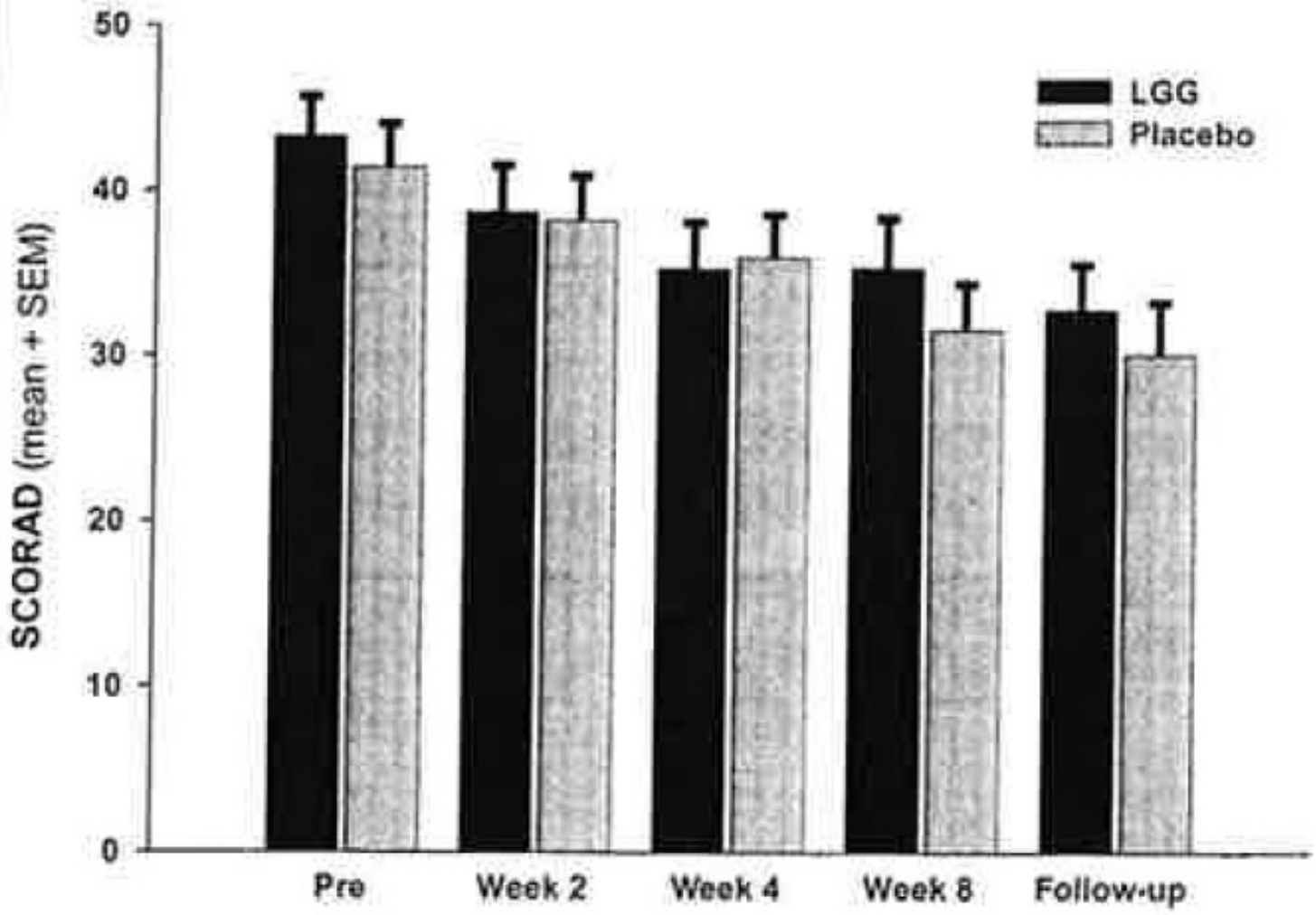

Fölster-Holst et al. 2006

Probiotics in treatment of atopic eczema

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	Strain	Dose	'Diet'	Antihistamins etc.	Age (mo.)	Out come
Isolauri et al. 2000	*B. lactis* Bb-12 or *L. rhamnosus* GG	3-8x10^{10} CFU	No prior formula	?	4.6	+
Brouwer et al 2006	*L. rhamnosis* or *L. rhamnosus* GG	3x10^{8} CFU/g formula	Cows milk allergy	+	3.8	-
Fölster-Holst et al. 2006	*L. rhamnosus* GG	10^{10}CFU	?	+	19	-

Lactobacillus GG to reduce risk for atopic eczema

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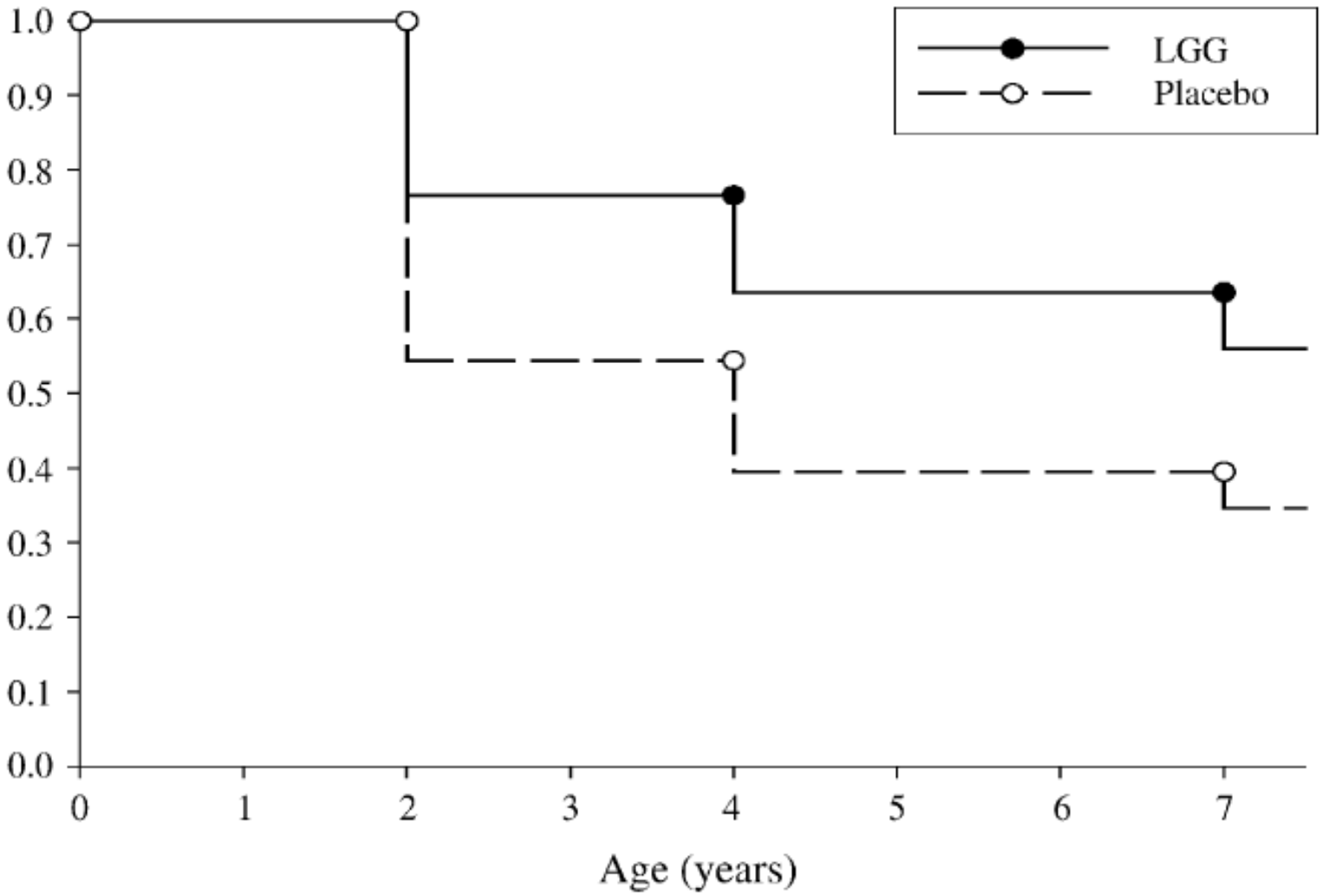

Kalliomäki et al. 2007

Lactobacillus GG et al. + GOS to reduce risk for atopic eczema

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	Probiotic		Placebo		Unadjusted		Adjusted*	
	n	%	n	%	OR (95% CI)	*P* value†	OR (95% CI)	*P* value†
Primary outcome								
Allergic disease‡	145/461	31.5	163/464	35.1	0.85 (0.64-1.12)	.236	0.82 (0.61-1.08)	.159
IgE-associated allergic disease§	64/456	14.0	87/463	18.8	0.71 (0.50-1.00)	.052	0.65 (0.45-0.94)	**.022**
Secondary outcome								
Eczema	120/461	26.0	150/464	32.3	0.74 (0.55-0.98)	**.035**	0.69 (0.52-0.93)	**.015**
Atopic eczema‖	57/459	12.4	82/463	17.7	0.66 (0.46-0.95)	**.025**	0.61 (0.42-0.90)	**.012**
Sensitization¶	127/454	28.0	144/462	31.2	0.86 (0.65-1.14)	.289	0.82 (0.61-1.10)	.184

Kukkonen et al. 2007

L. reuteri 55730 to reduce risk for atopic eczema

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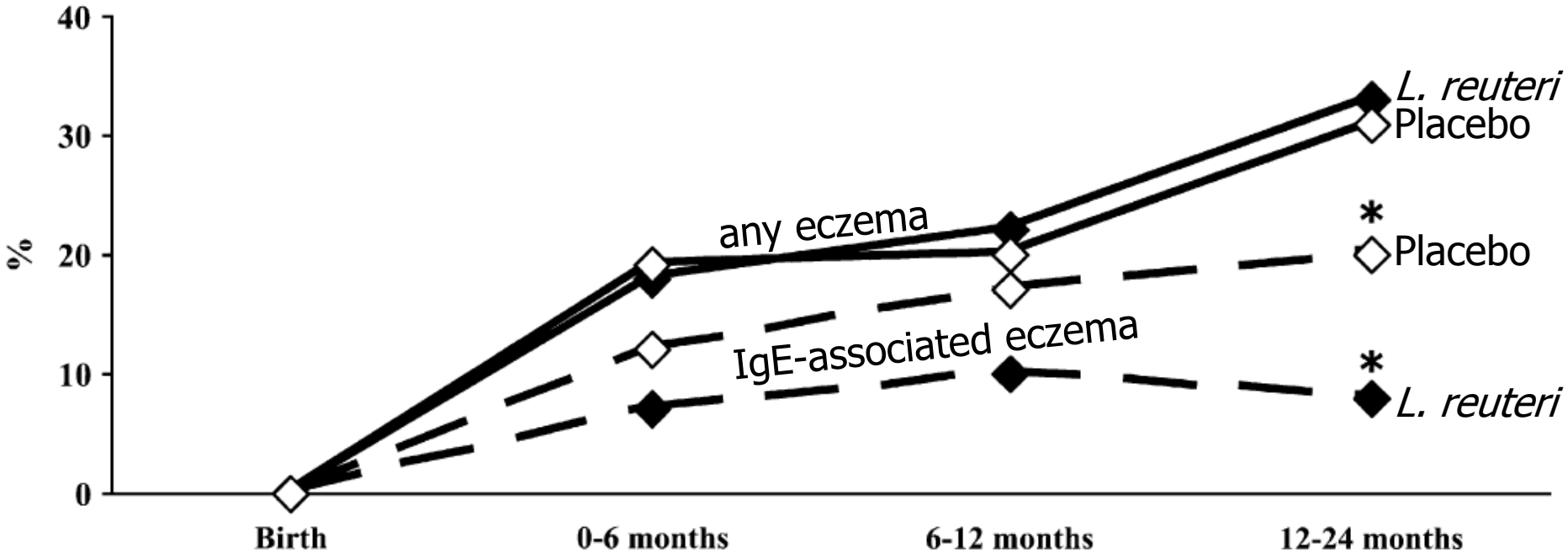

Abrahamsson et al. 2007

L. acidophilus LAFTI-L10 to reduce risk for atopic eczema

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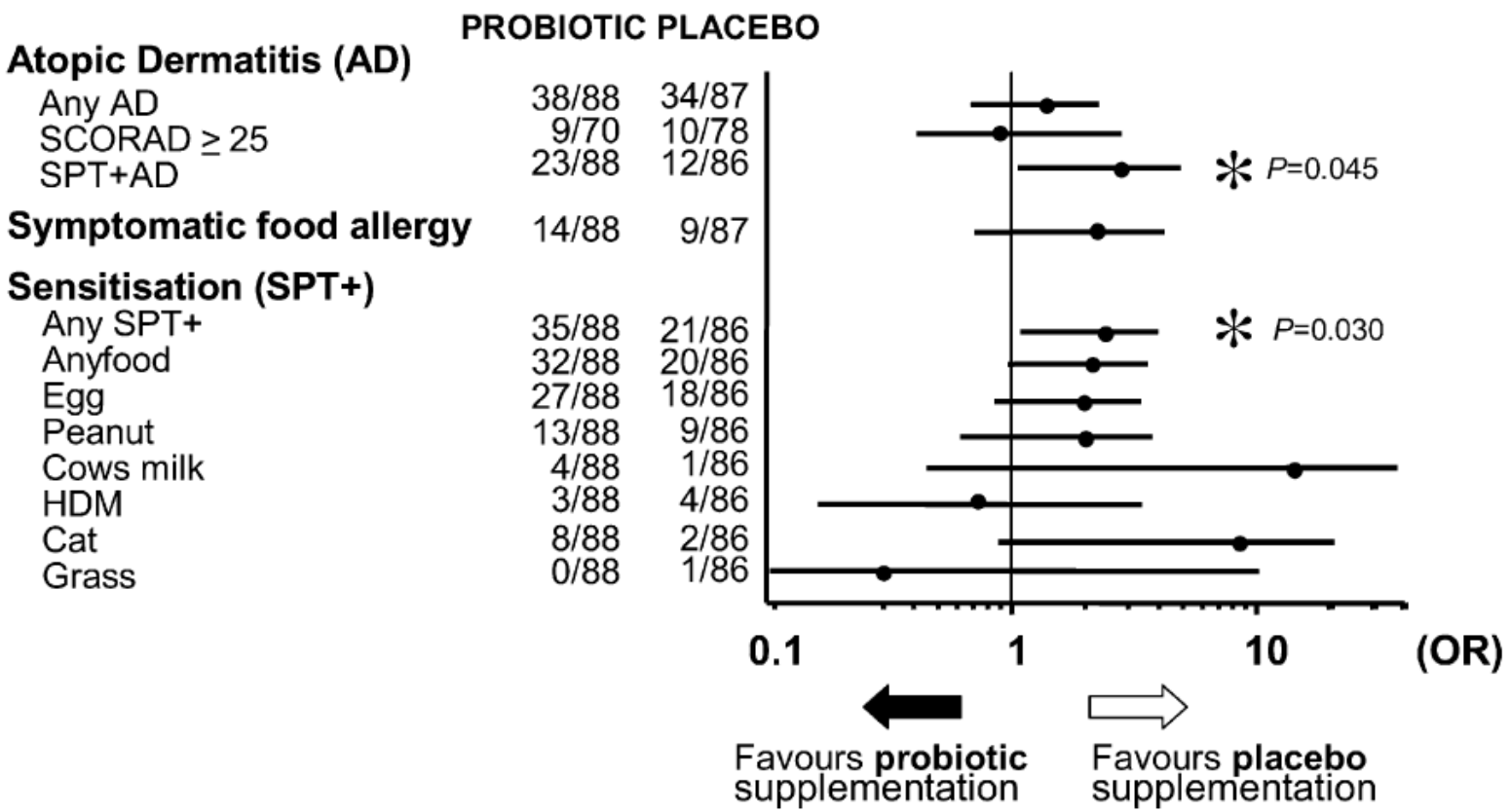
Risk (odds ratio, 95%CI) of early allergic outcomes in children on probiotics relative to the placebo group



Taylor et al. 2007

L. rhamnosus HN001 and *B. lactis* HN019 to reduce risk for atopic eczema

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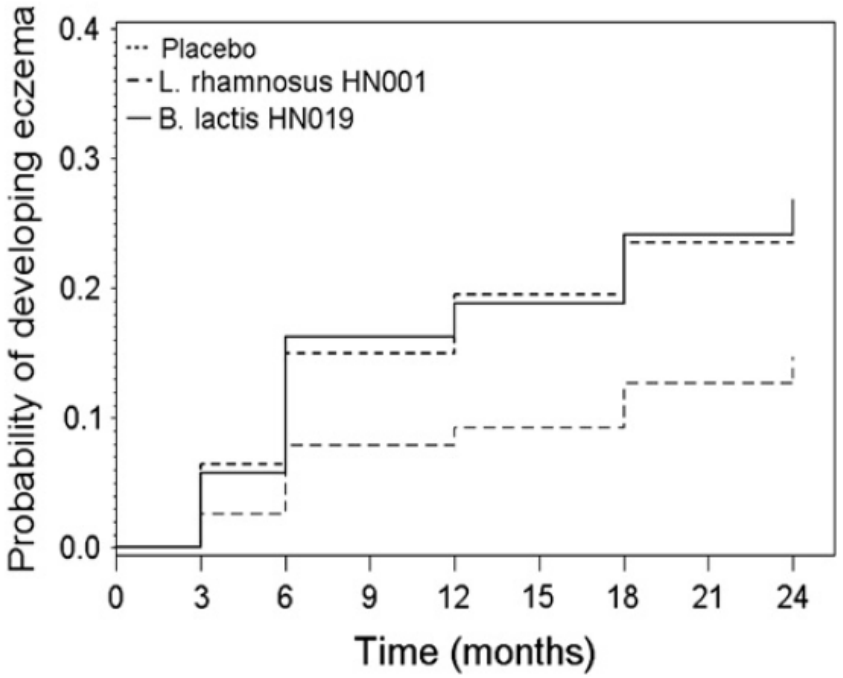
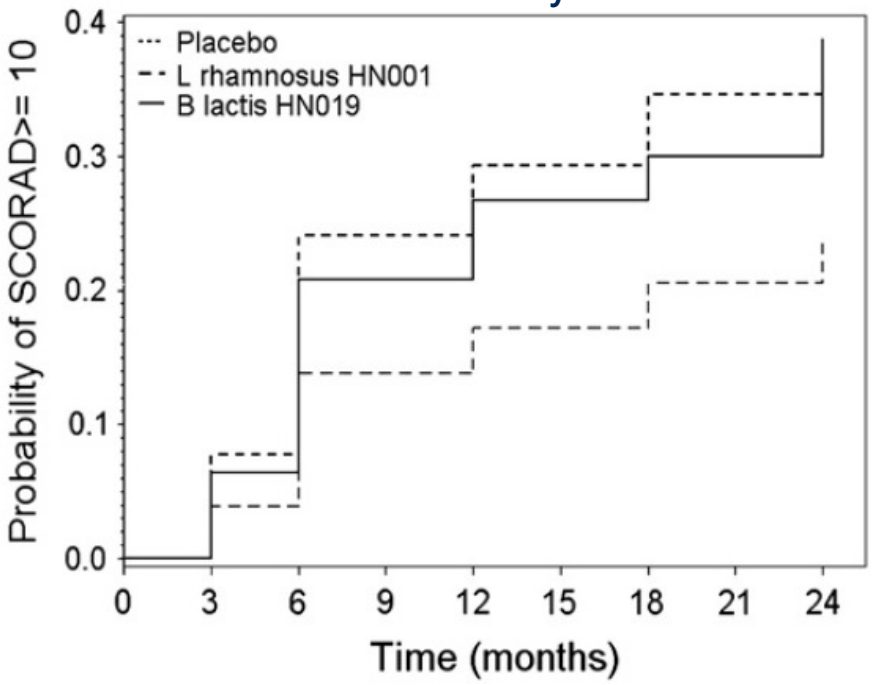
incidence



severity



Wickens et al. 2008

Probiotics to reduce risk for atopic eczema

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	Strain	Dose (CFU)	Age at start	Duration	'Out come'
Kalliomäki et al. 2001	*L. rhamnosus* GG	$1x10^{10}$	-28 days	6 months	+ (wheezing)
Kopp et al. 2008	*L. rhamnosus* GG	$6x10^{9}$	-28 days	6 months	wheezing
Kukkonen et al. 2007	L. rhamnosus GG+ Lc705+B. breve Bb99 +P. freudenreichii JS	$1.2x10^{10}$	-14/28 days	6 months	+
Abrahamsson et al. 2007	*L. reuteri* ATCC 55730	$1x10^{8}$	-28 days	12 months	'+'
Taylor et al. 2007	*L. acidophilus* LAFTI L10	$3x10^{9}$	0-2 days	6 months	AD
Wickens et al. 2008	*L. rhamnosus* HN001	$6x10^{9}$	-28/35 days	24 months	+
	B. lactis HN019	$9x10^{9}$	-28/35 days	24 months	0

Microbial Ecology in Health and Disease. 2008; 20: 171–176

informa
healthcare

Should long-term prophylactic use of probiotics for infants and young children give cause for concern?[1]

SIAMAK P. YAZDANKHAH[1], JUDITH A. NARVHUS[2], MERETE EGGESBØ[3], TORE MIDTVEDT[4], JØRGEN LASSEN[5] & RAGNHILD HALVORSEN[6]

Some studies even indicate that early inclusion of LGG into the diet may provoke allergic sensitization. Long-term effects on immune function in general, or on the gut in particular, when LGG is consumed on a daily basis are not known and warrant caution.

Prebiotics (GOS+FOS) to reduce risk for atopic eczema

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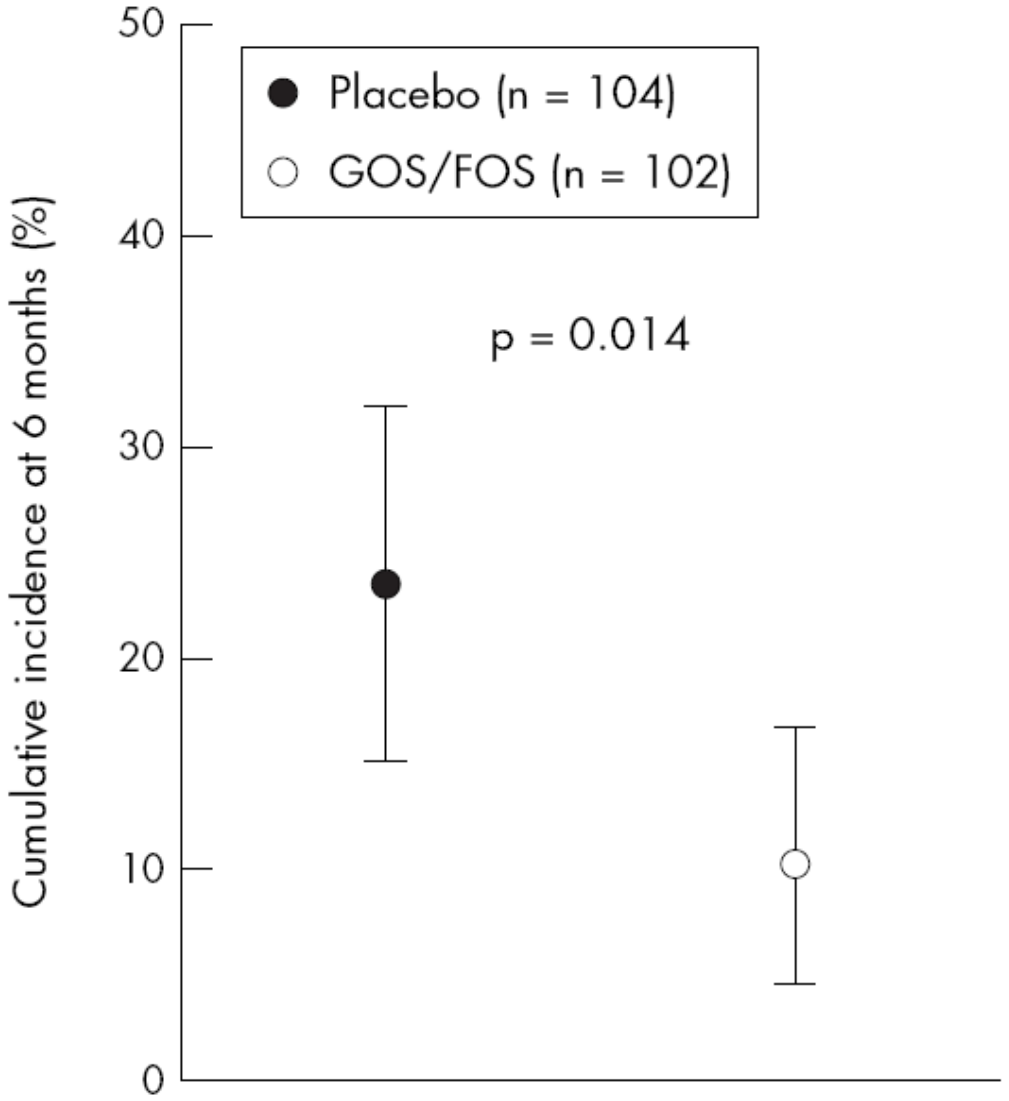

Moro et al. 2006

Conclusions

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Weight management

- Current data on the relation between microbiota and weight management is based on:
  - Animal studies (with genetically obese animals)
  - Small human populations
  - Particular sub-populations
- Will probiotics work? If they work, they propably have a limited influence

Allergy

- Current information suggests a causal relation between microbiota composition and allergy
- Probiotics do not seem to treat atopic dermatitis (pollen allergy?)
- Selelcted probiotic strains may contribute to primary prevention of atopic dermatitis (increased risk for wheezing?)