Learn more about probiotics and prebiotics

Yvan.vandenplas@uzbrussel.be

Universitair Ziekenhuis Brussel

KidZ Health Castle

VUB

- Introduction
- Are all prebiotics the same?
- Are all probiotics the same?
- Conclusion

It’s all about micro-organisms

History: eastern world

Should we standardize
the 1,700-year-old fecal microbiota transplantation?

Zhang F. Am J Gastroenterol. 2012;107:1755

4th century: Ge Hong:
human fecal suspension by mouth for food poisoning/severe diarrhea

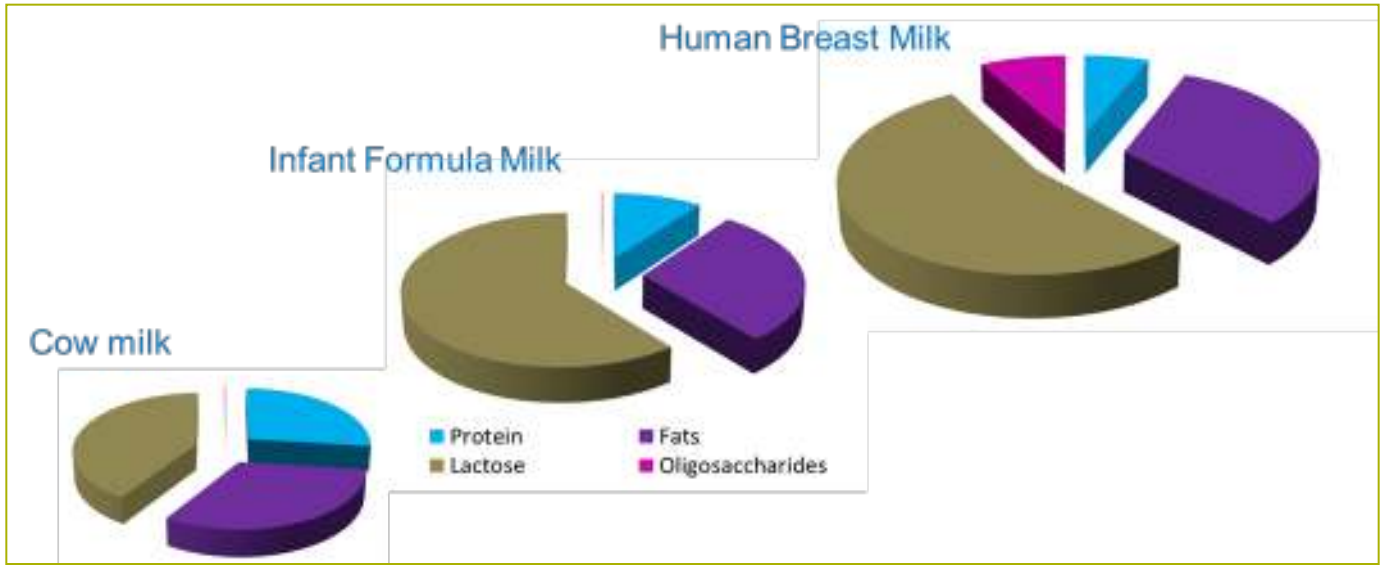
16th century: yellow soup
Fermented fecal solution; fresh fecal suspension; dry feces; infant feces
for severe diarrhea, constipation, and other abdominal disease

History: western world

- ✓ Bedoins: camel faeces to human with dysentery
- ✓ Veterinary medicine: faeces from healthy to sick horse
  Italian Fabricus Aquapendente (17th century)

Composition of human milk

Lactose	53-61 g/l
Fat	30-50 g/l
Oligosaccharides (HMOs)	**10-12 g/l**
Proteins	8-10 g/l



Anal Biochem 1994; 223:218-226

Prebiotic oligosaccharides in human milk

Prebiotic: a substrate that is selectively utilized by host microorganisms conferring a health benefit.

Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP)
consensus statement on the definition and scope of prebiotics. Gibson GR. Nat Rev Gastroenterol Hepatol. 2017;14:491-502

- Unique for human milk
- Partially digested,
  act as prebiotic stimulating bifidogenic microbiome
- > 200 different
- Changing composition between mothers,
  during lactation, during breastfeeding
- Some resemble epithelial pathogen receptors

Human milk: a source of more life than we imagine.

Jeurink PV. Benef Microbes 2013;4:17-30.

The presence of bacteria in human milk has been acknowledged since the seventies.

During the last decades, the use of more sophisticated culture-dependent and -independent techniques, and the steady development of the -omic approaches are opening up the new concept of the 'milk microbiome', a complex ecosystem with a greater diversity than previously anticipated.

Complete genome sequence of Streptococcus salivarius PS4, a strain isolated from **human milk**.
Martin V, J Bacteriol. 2012;194:4466-7

Characterization of Lactobacillus salivarius CECT 5713, a strain isolated from **human milk**: from genotype to phenotype.
Langa S, Appl Microbiol Biotechnol. 2012 Jun;94(5):1279-87

Assessment of the bacterial diversity of **breast milk** of healthy women by quantitative real-time PCR.
Collado MC, Lett Appl Microbiol. 2009;48:523-8.

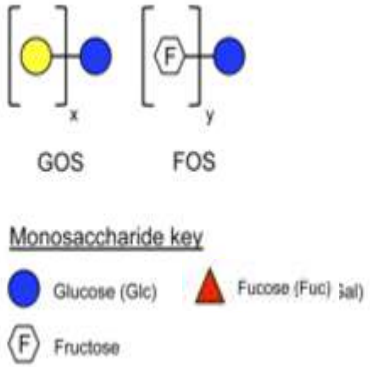
- *Introduction*
- Are all prebiotics the same?
- Are all probiotics the same?
- Conclusion

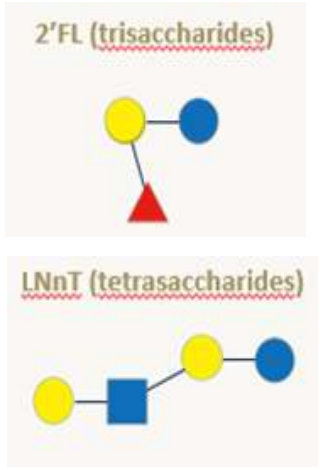
Structural differences between HMOs and non-human oligosaccharides

GOS, FOS and other non-human oligosaccharides are structurally very different from HMOs[1]

GOS are built mainly from galactose with a glucose and a galactose ending, while FOS predominantly contain fructose with a glucose and a fructose ending[2]

GOS and FOS contain fructose, but HMOs do not[1]





Fucose and sialic acid are present only in HMOs[1]

The effects of HMOs are highly structure specific. It is unlikely that GOS, FOS or other non-human oligosaccharides can mimic HMO benefits[1]

FOS, Fructo-oligosaccharides; GOS,Galacto-oligosaccharides.

Sela DA. Trends Microbiol. 2010;18(7):298-307.; Bode L. Advances in Nutrition. 2012 May 1;3(3):383S-91S

Impact of non-human oligosaccharides on Enterobacteriaceae Growth- In Vitro

None of the selected Enterobacteriaceae strains grew on the HMOs 2´FL, 6´SL or LNnT.

Several Enterobacteriacea including obligate pathogenic strains grew well on FOS & GOS

GOS/FOS promote the growth of pathogenic bacterial strains, but HMOs do not[1]

	Glucose	FOS	GOS-V	GOS-P	HMO-2'FL	HMO LNnt	HMO 6'FL
EC13047	✓	✗	✓	✓	✗	✗	✗
CM51329	✓	✗	✓	✓	✗	✗	✗
CF8090	✓	✗	✓	✗	✗	✗	✗
CSBAA894	✓	✗	✓	✓	✗	✗	✗
CS29544	✓	✗	✓	✓	✗	✗	✗
KO13182	✓	✓	✓	✓	✗	✗	✗
KP13883	✓	✓	✓	✓	✗	✗	✗
SD13313	✓	✗	✓	✗	✗	✗	✗
EC29425	✓	✗	✓	✗	✗	✗	✗
EC1000	✓	✗	✓	✗	✗	✗	✗
EC11775	✓	✗	✓	✓	✗	✗	✗

EC1000: Escherichia coli EC1000, CF8090: Citrobacter f reundii, CSBAA894 and CS29544: Cronobacter sakazakii, CM51329: Cronobacter muytjensii, EC13047: Enterobacter cloacae subsp., EC11775: Escherichia coli O1:K1:H7, EC29425: Escherichia coli K12, KP13883: Klebsiella pneumoniae subsp., KO13182: Klebsiella oxytoca, SD13313: Shigella dysenteriae FOS: fructooligosacharides, GOS-V: galactooligosaccharides-vivinal; GOS-P: galactooligosaccharides-purimune, 2'FL: 2′-fucosyllactose, 6'SL: 6′-sialyllactose, LNnt: lacto-N-neotetraose

Effect of non-human oligosaccharides on immune defence

HMOs offer various immuno-protective benefits that are not shown by GOS/FOS[1,2]

GOS/FOS[1,2]

- Do not strengthen gut barrier function
- Do not block pathogen binding
  by acting as decoy receptors

The immune benefits of HMOs are structure specific, which non-human oligosaccharides such as GOS and FOS fail to offer[1,2]

FOS, Fructo-oligosaccharides; GOS,Galacto-oligosaccharides.

Bode L. Adv Nutr. 2012;3(3):383S-391S.
Smilowitz J. Annu Rev Nutr. 2014;34(1):143-69

- *Introduction*
- *Are all prebiotics the same?*
- Are all probiotics the same?
- Conclusion

Not all microorganisms are probiotics

- ***Natural strains for fermentation***
  - fermented milk products : yogurt, kefir, buttermilk, lassi
  - ceviche, sauerkraut, kimchi

- ***Commercialised fermented milk/food (supplement)***
  - ~ natural "strain" but industrial preparation
  - milk as vehicle

- ***Commercialised fermented food supplements***
  - ~ natural strain but industrial preparation
  - in "health care shops", etc.
  - capsule as vehicle ("medication-like")

- ***Drugs***

Not all microorganisms are probiotics

Fermented milk — yoghurt, kefir and buttermilk (are this postbiotics??)

viable bacteria — Bifidobacterium bifidum
Lactobacillus acidophilus, L. bulgaricus,
Streptococcus lactis, S. cremoris
Roffe C. J Infect 1996;32:1-10

need for cold storage / limited shelf life

difficult for patients to consume sufficient large quantities (litres ...)

poor resistance of most yoghurt bacteria to bile and acid

vehicle : survival L. acid. gastric acid in milk > yoghurt > buttermilk

IV antibiotics : inactivation microorganism via hepatoenteric cycle

Alm L. Am J Clin Nutr 1980;33:2543.

Marteau P. Microbiology Reviews 1993;12:207-220

Does eating yoghurt prevent antibiotic-associated diarrhea? A placebo-controlled randomised controlled trial in general practice.

Conway S. Br J Gen Pract. 2007;57:953-9.

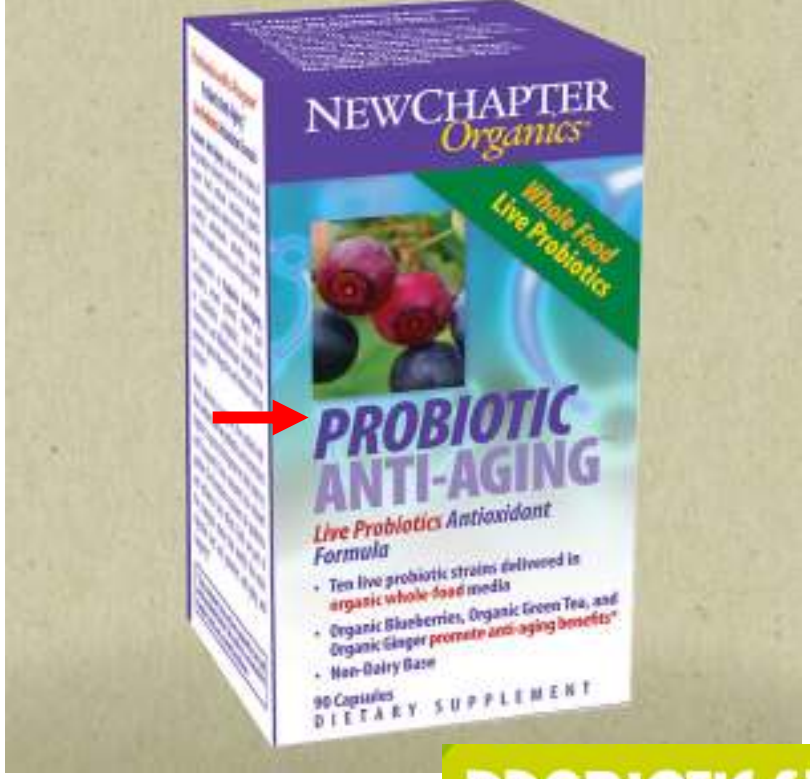
This study was a three-arm (bio yoghurt, commercial yoghurt, no yoghurt) randomised controlled trial with double blinding between the two yoghurt arms.

Patients > 1 year requiring 1-week course of antibiotics (n: 369)
consumption of 150 ml of live strawberry-flavoured yoghurt for 12 days,
starting on the first day of taking the antibiotic
Diarrhea = ≥ 3 or more loose stools / day over at least 2 consecutive days'
within 12 days of starting the antibiotics.

	n	
no-yoghurt group	120	17 (14%, 95% CI = 9.0 to 21.5)
commercial yoghurt	118	13 (11%, 95% CI = 6.6 to 17.9)
bio-yoghurt	131	9 (7%; 95% CI = 3.7 to 12.5) (P = 0.17)

Failure to demonstrate that yoghurt has any effect on AAD

Should the better tolerance of yoghurt compared to milk
by a lactose-intolerant individual be considered as
a health benefit of the fermentation process (lactobacilli..)
or a health benefit of the reduced lactose?


NEWCHAPTER
Organics
Whole Food
Live Probiotics
PROBIOTIC
ANTI-AGING
Live Probiotics Antioxidant
Formula
• Ten live probiotic strains delivered in organic whole-food media
• Organic Blueberries, Organic Green Tea, and Organic Ginger promote anti-aging benefits*
• Non-Dairy Base
90 Capsules
DIETARY SUPPLEMENT


PROBIOTIC SPRAY
Crèche Guard
Probiotic Oral Spray has been specifically formulated to improve your child's immune system by balancing the intestinal microflora.


NATREN®
JOURDAN'S
CRÈME APRÈS RASSAGE
PROBIOTIC AFTER SHAVE

PIP Allergy Free.

PIP = Probiotics in Progress.

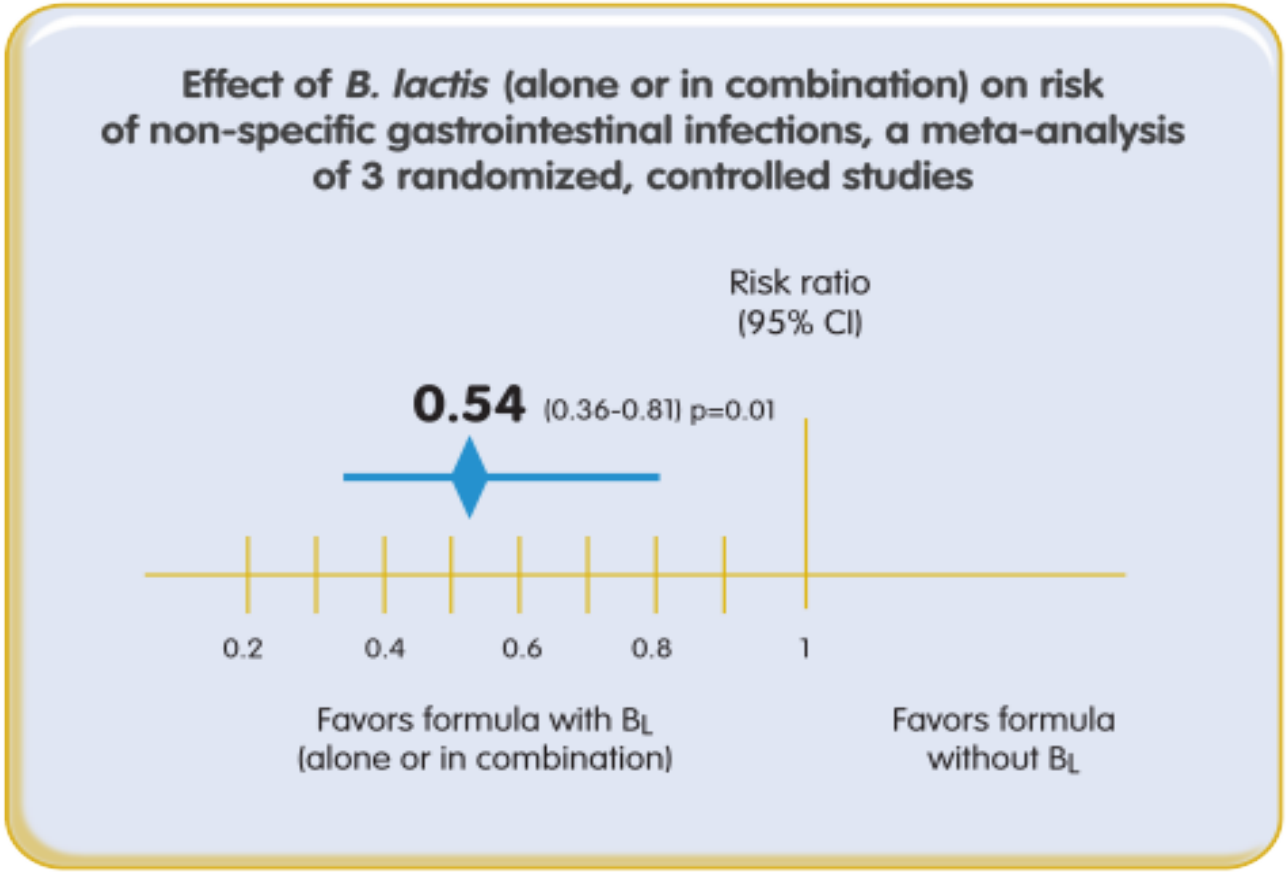
How does PIP Allergy Free work?

PIP Allergy Free contains bacteria, who, when in contact with air and a warm and humid environment (your bed), leave their “cocon” looking for food.

Probiotics in food…

Probiotics as food supplement…

Supplementation of infant formula with probiotics and/or prebiotics:
a systematic review and comment by the ESPGHAN committee on nutrition.
Braegger C; ESPGHAN Committee on Nutrition. JPGN 2011;52:238-50



B. lactis (B_L): 46% reduced risk of diarrhea

Probiotics for the Management of Infantile Colic.

Szajewska H, J Pediatr Gastroenterol Nutr. 2016 Jul;63 Suppl 1:S22-4

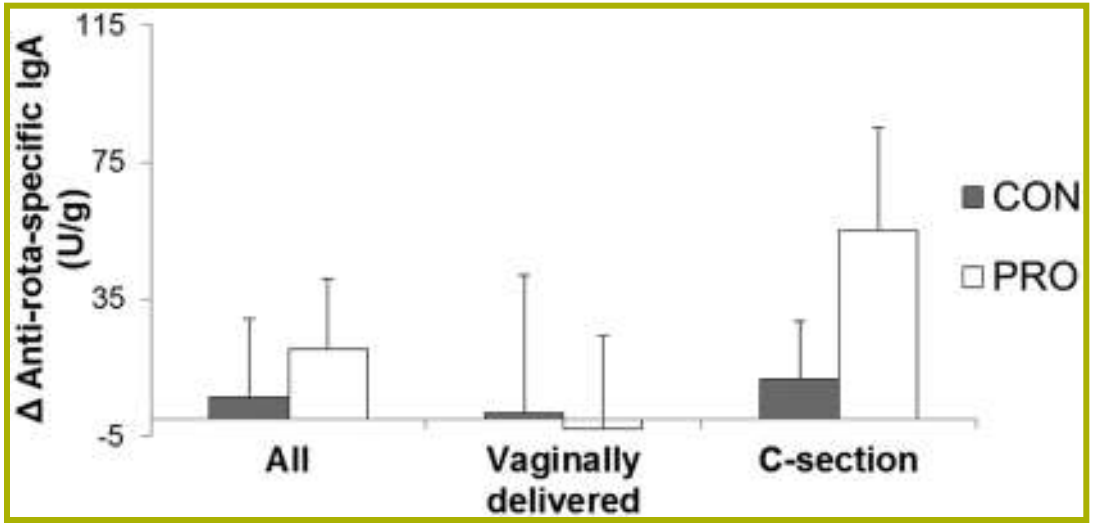
Reference	Study design	Population	Intervention	Comparison	Primary outcome (main findings)	
TREATMENT						
Savino et al., 2010 (13)	RCT, DB	N = 50, exclusively BF	*L reuteri* DSM 17938	Placebo	Responders were significantly higher in the *L reuteri* group versus placebo group.	+
Szajewska et al., 2013 (12)	RCT, DB	N = 80, exclusively or predominantly (>50%) BF	*L reuteri* DSM 17938	Placebo	Treatment success was significantly higher in the probiotic group compared with the placebo group.	+
Sung et al., 2014 (16)	RCT, DB	N = 167, BF or FF	*L reuteri* DSM 17938	Placebo	The probiotic group cried or fussed 49 min more than the placebo group.	-
Chau et al., 2015 (14)	RCT, DB	N = 52, BF	*L reuteri* DSM 17938	Placebo	The total average crying and fussing times (minutes) for the duration of treatment were significantly shorter in the probiotic group.	+
Mi GL et al., 2015 (15)	RCT, SB	N = 42, exclusively or predominantly (>50%) BF	*L reuteri* DSM 17938	Placebo	Treatment success was significantly higher in the probiotic group compared with the placebo group.	+
Pärtty et al., 2015 (20)	RCT, DB	N = 30, BF & FF	*Lactobacillus rhamnosus* GG	Placebo	No effect of probiotic on the daily crying time at the end of the intervention in the probiotic group.	=
Kianifar et al., 2014 (21)	RCT, DB	N = 50, BF	*Synbiotic**	Placebo	The treatment success was significantly higher in the synbiotic group.	+
PREVENTION						
Indiro et al., 2014 (19)	RCT, DB	N = 589, BF & FF	*L reuteri* DSM 17938	Placebo	At 3 mo of age, a significant reduction in the duration of crying time in the probiotic group compared with the placebo group.	+

BB = breastfed infants; DB = double blind; FF = formula-fed infants; RCT = randomized controlled trial.

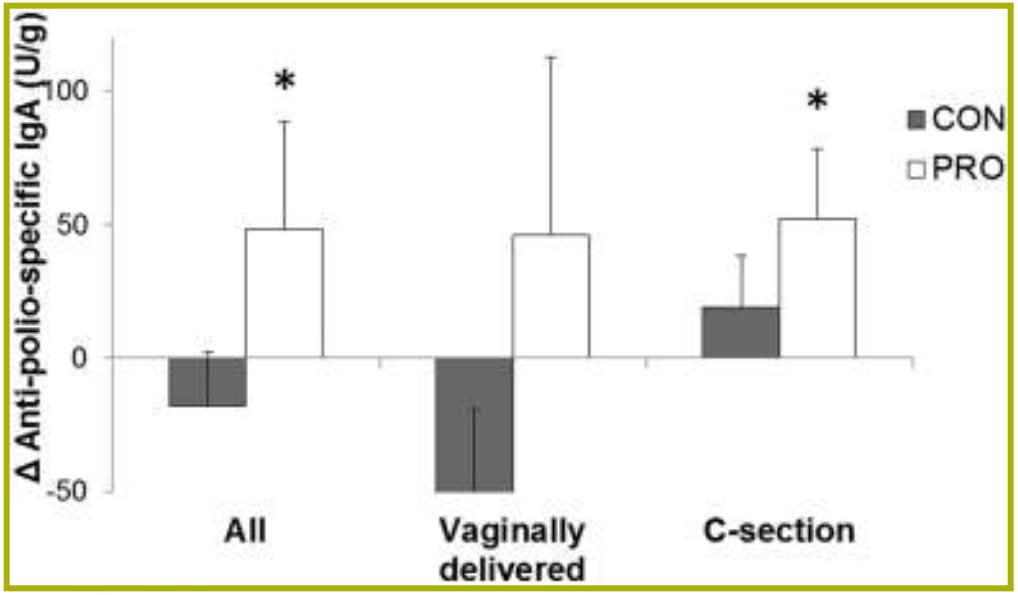
* *L casei*, *L rhamnosus*, *Str thermophilus*, *Bifidobacterium breve*, *L acidophilus*, *B infantis*, *L bulgaricus*, and fructooligosaccharides.

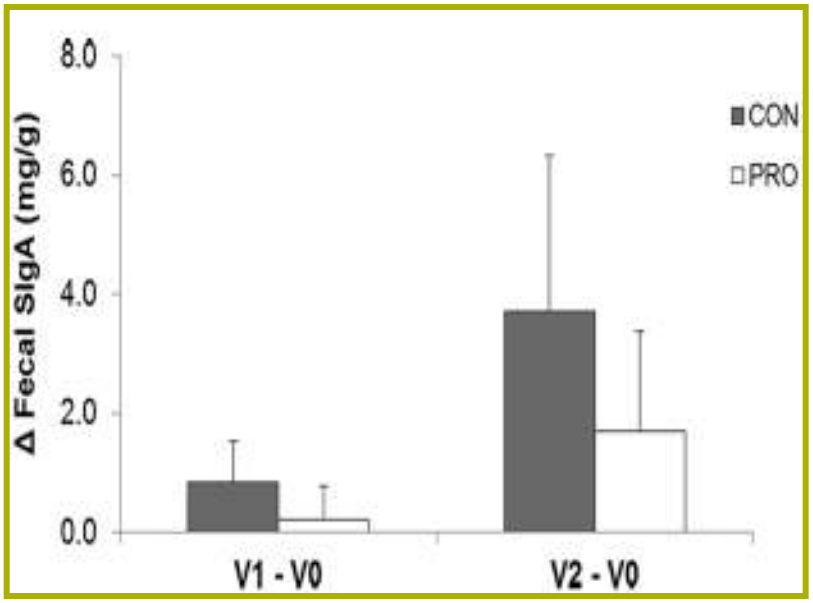
Bifidobacterium lactis Bb12 enhances intestinal antibody response in formula-fed infants: a RDBC trial.

Holscher HD. JPEN J Parenter Enteral Nutr. 2012;36(1 Suppl):106S-17S



↑ sIgA
↑anti-Rota IgA
↑ anti-polio IgA





Universitair Ziekenhuis Brussel

VUB

Evidence demonstrated

What is evidence?

Necrotizing enterocolitis

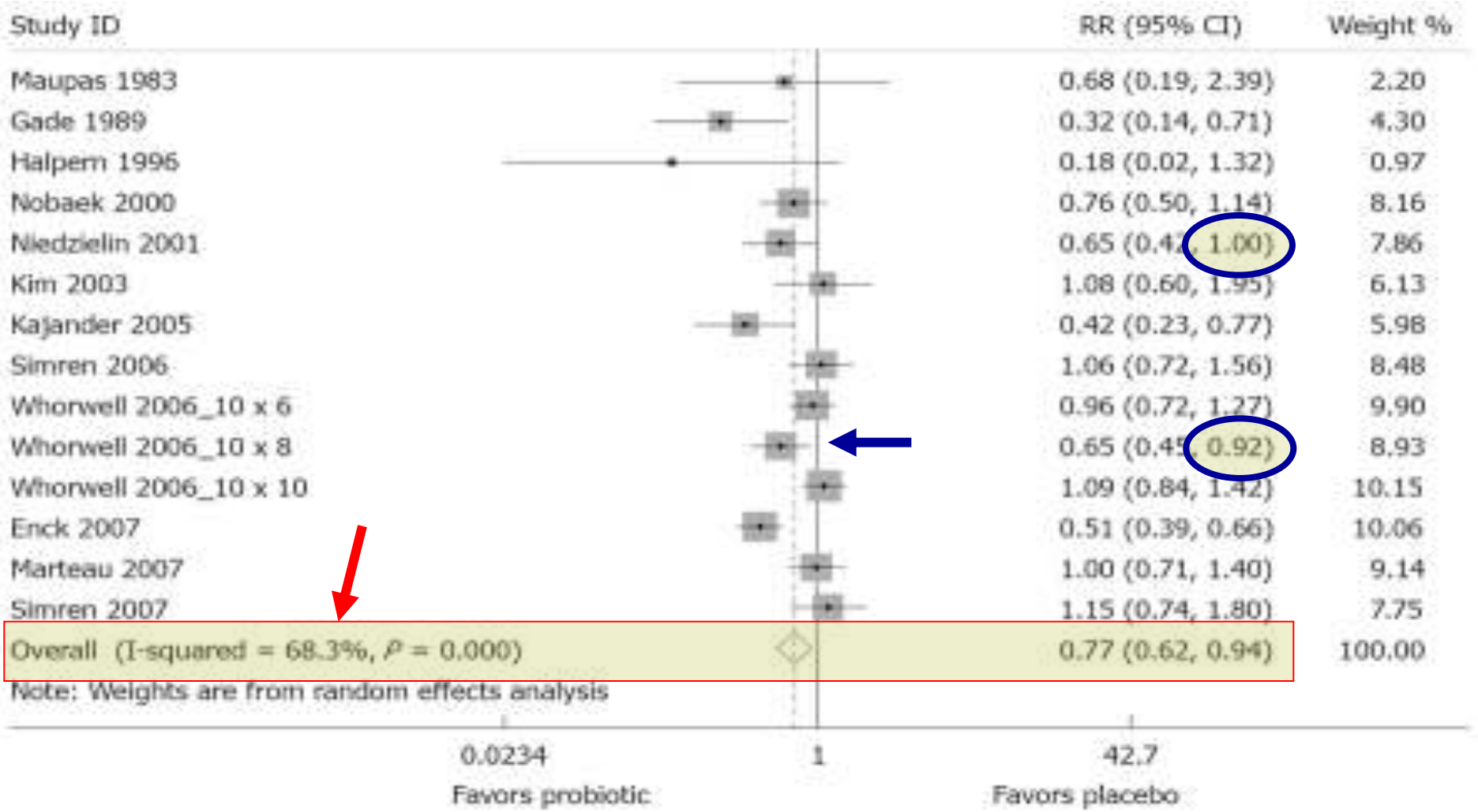
ESPGHAN 2009	AAP 2010	ASPEN 2012
No	**No**	**No**
Efficacy and safety should be established for each product. **Further studies are needed.**	There is some evidence that probiotics prevent NEC in VLBW infants (birth weight between 1000 and 1500 g), but **more studies are needed.**	There are insufficient data to recommend the use of probiotics in infants at risk for NEC. **Further research needed.**
JPGN 2009;49:1-9.	Pediatrics 2010;126:1217-31.	JPEN 2012;36:506-23.

Number needed to treat

Intervention	NNT
Statins for myocardial infarction for one year	100-427
Aspirin for cardiovascular protection	40
Probiotics for the prevention of NEC	33

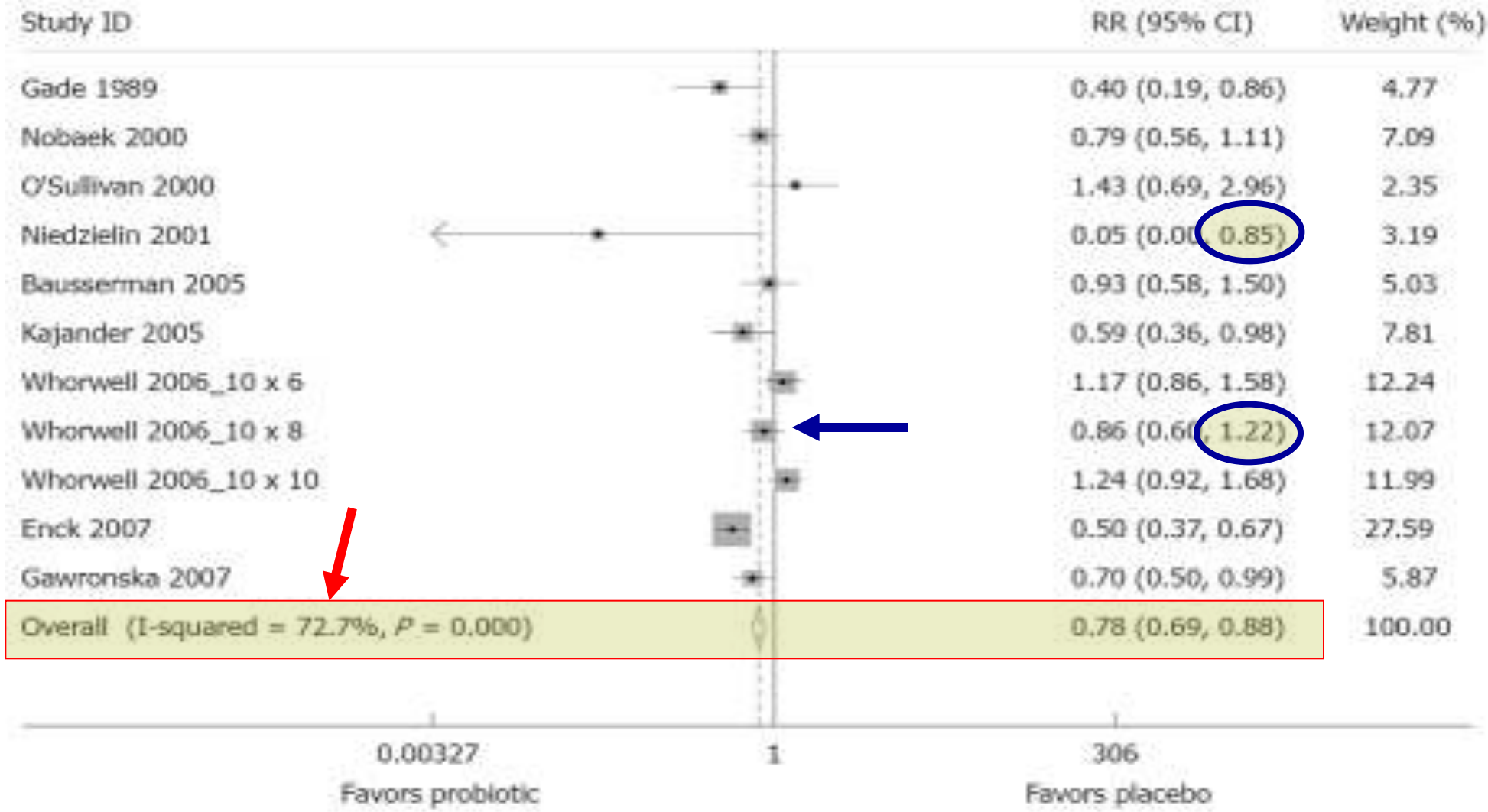
Meta-analysis of probiotics for the treatment of irritable bowel syndrome.

McFarland LV. World J Gastroenterol. 2008;14:2650-61



Efficacy of probiotics in irritable bowel syndrome: a meta-analysis of randomized, controlled trials.

Nikfar S. Dis Colon Rectum. 2008;51:1775-80



Evidence depends on

Registration as medication:

differs from country to country

RCT: Study design, primary outcome

Meta-analysis:

selection of trials

primary outcome

Commercial probiotic products: A call for improved quality control.
A Position Paper by the ESPGHAN Working Group for Probiotics and Prebiotics.

Kolaček S, Hojsak I, Canani RB, Guarino A, Indrio F, Orel R, Pot B, Shamir R, Szajewska H, Vandenplas Y, van Goudoever J, Weizman Z; ESPGHAN Working Group for Probiotics and Prebiotics.
J Pediatr Gastroenterol Nutr. 2017

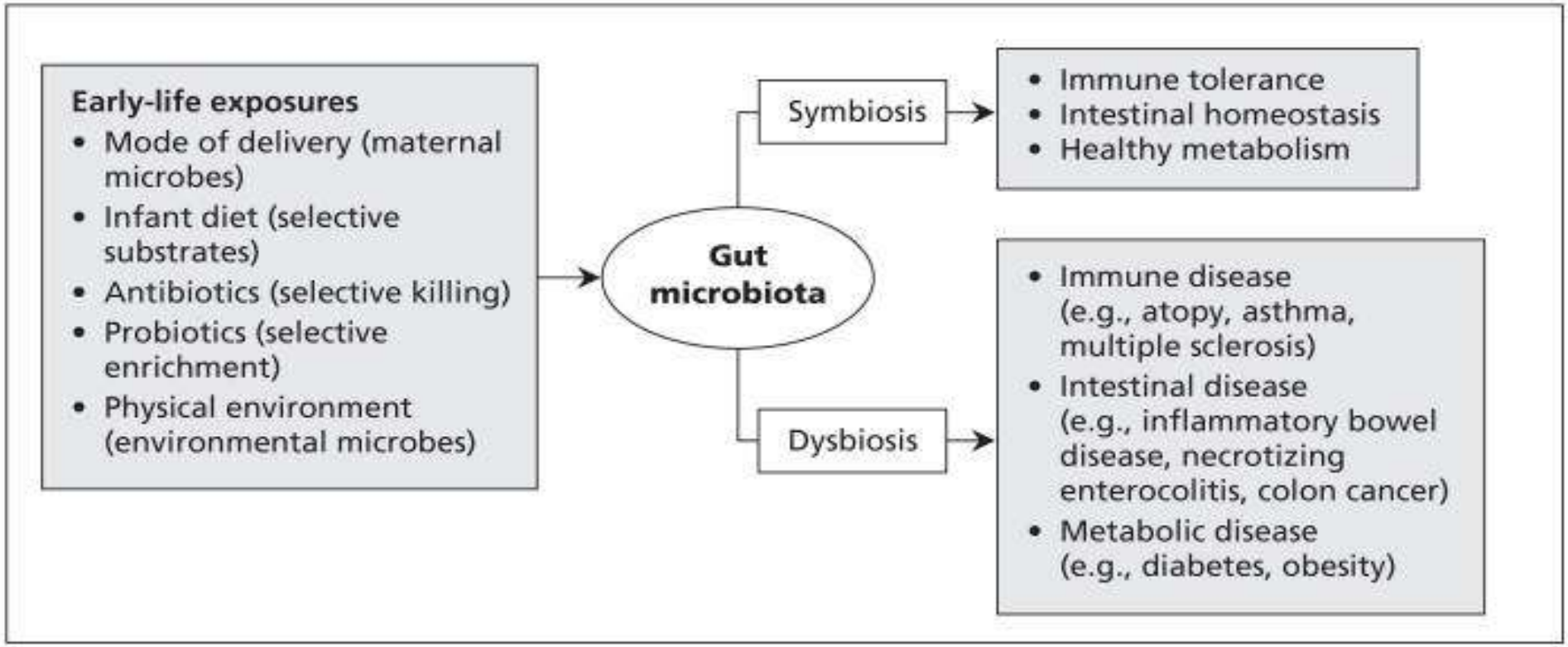
Based on the results obtained,
we strongly suggest a more stringent quality control process.

This process should ensure that the probiotic content as mentioned on the label meets the actual content throughout the shelf life of the product, while no contamination is present.

- *Introduction*
- *Are all prebiotics the same?*
- *Are all probiotics the same?*
- Conclusion

Gut microbiota of healthy Canadian infants: profiles by mode of delivery and infant diet at 4 months.

Azad MB CMAJ. 2013;185:385-941



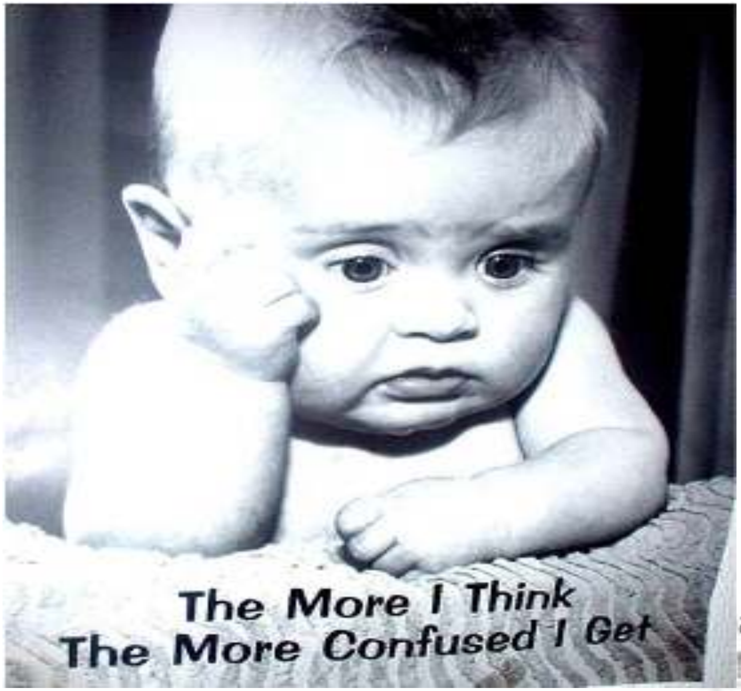
If Sporebiotic

Postbiotic

Prebiotic

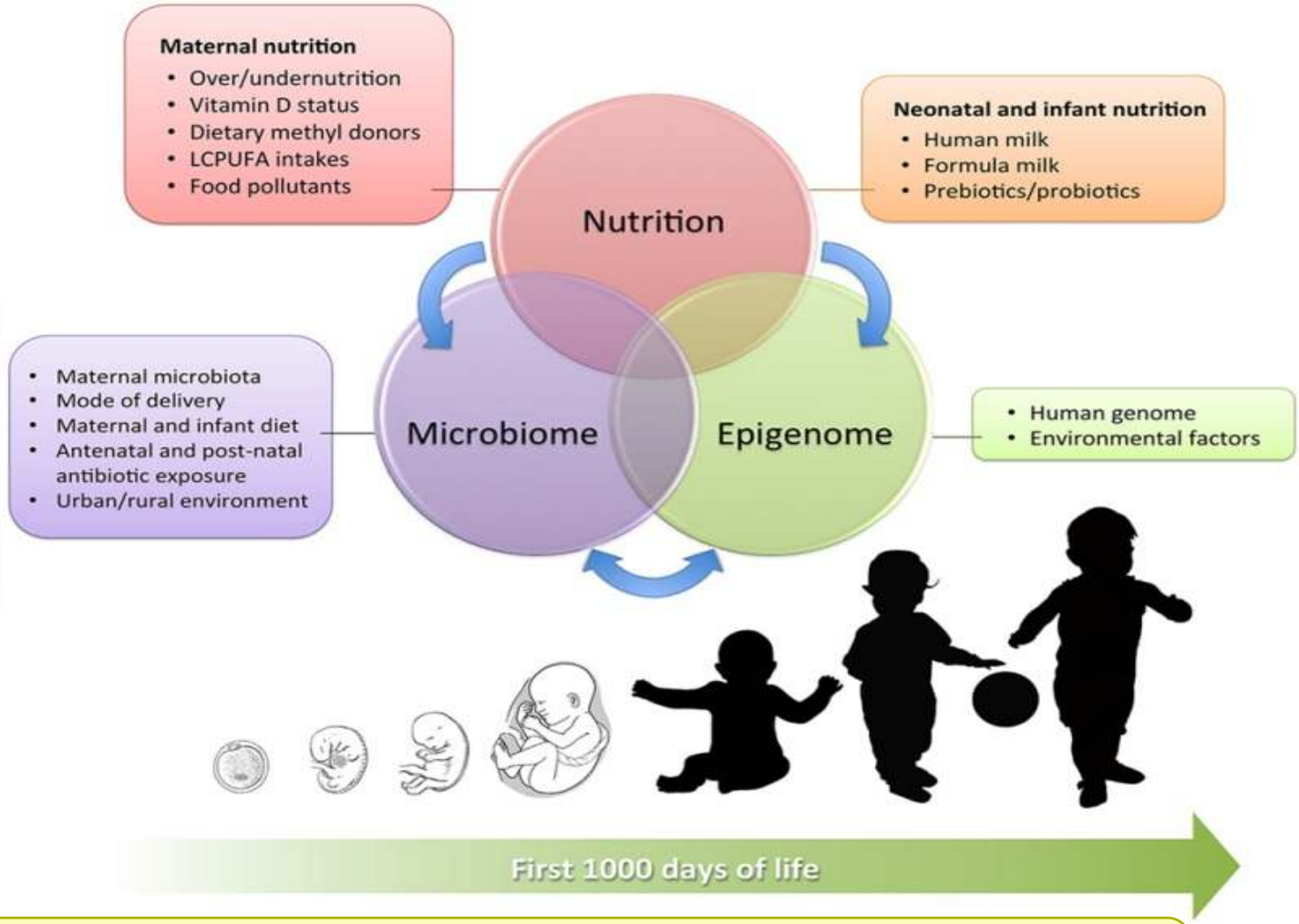
can be used, why not

Probiotic


The More I Think
The More Confused I Get


danke
謝謝
ngiyabonga
teşekkür ederim
thank you
gracias
dank je
dziękuję
obrigado
sukriya
kop khun krap
go raibh maith agat
mochchakkeram
arigatō
dakujem
grazie
merci
мерси
감사합니다
terima kasih
tapadh leat
ありがとう

The First Semester of Life is Crucial



The first months of life of the infant are crucial for the development of the gastrointestinal microbiome

Probiotic

- Regulatory status of probiotic differs in different parts of the world (often no regulation)
- Every probiotic is a live microbial culture,
  but not every live microbial culture is a probiotic

- Probiotics (lactic acid bacteria, gram pos bacteria, yeast,…)
  - ✓ Strain level identification
  - ✓ Survive in the GI tract
  - ✓ Acid resistance; bile tolerance
  - ✓ Evidence of health promoting properties

Prebiotic
Probiotic

Postbiotic

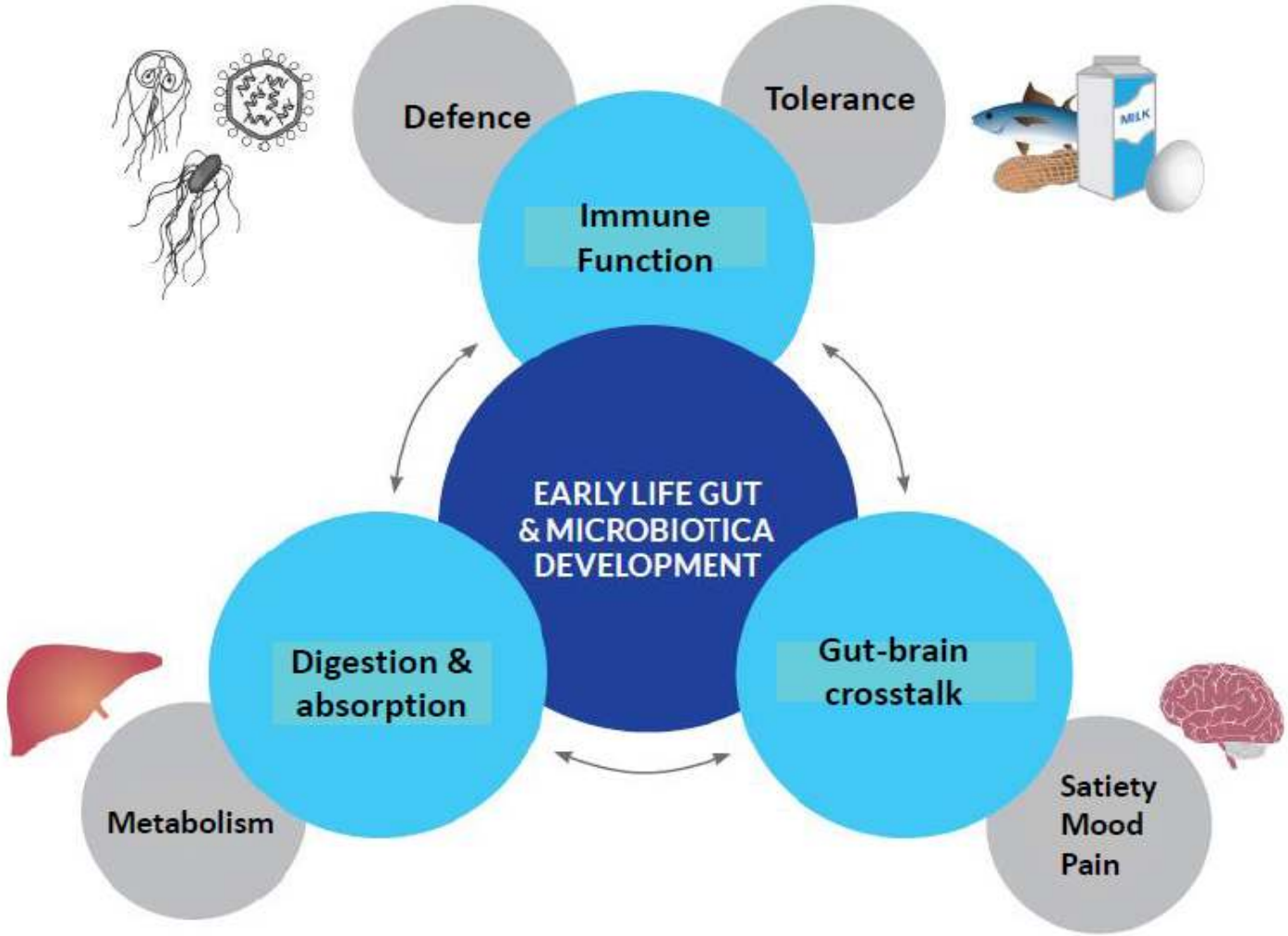
dead bacteria (eg. heat killed…) + metabolites

infant formula
commercialized food supplements (capsules)

both have clinical trials showing health benefit

formula: prevention colic
food supplement: duration acute GE

Vital role of gastrointestinal (GI) tract & gut microbiota



(Vandenplas Y et al. Gut health in early life: implications and management of gastrointestinal disorders. Wiley 2015)

Functions of gut microbiota: beyond gut health

Functions	Mechanisms/effects
Protective functions against pathogenic bacteria	• Pathogen displacement • Nutrient competition • Production of antimicrobial factors • Activation of local immune response • Contribution to the intestinal barrier function
Immune development	• IgA production • Control of local and general inflammation • Tightenning of juntions • Induction of tolerance to foods
Digestive and metabolic functions	• Vitamin production • Fermentation of non-digestible carbohydrates • Dietary carcinogens metabolism
Neuronal development	• Modulation brain gut axis during neuronal development • Motor control and anxiety behavious

Buccigrossi et al. Curr Opin Gastroenterol 2013;29:31-8.

Claims should be on products, not strains

Consider

production process

Shelff life

Contains « good » microorganisms

products with bacteria that should be somehow beneficial

no clinical proof

fermented food, sprays, ….

dietary and non-diatary microorganisms

« Probiotic »: if registered as medication ?

« dietary probiotic » food supplement

(no matter formulation: infant formula, yoghurt, …)

products with 2 RCTs

from different centers showing benefit

with similar design

« claim » only for primary outcome of trial

Strain specificity !

We are all created different

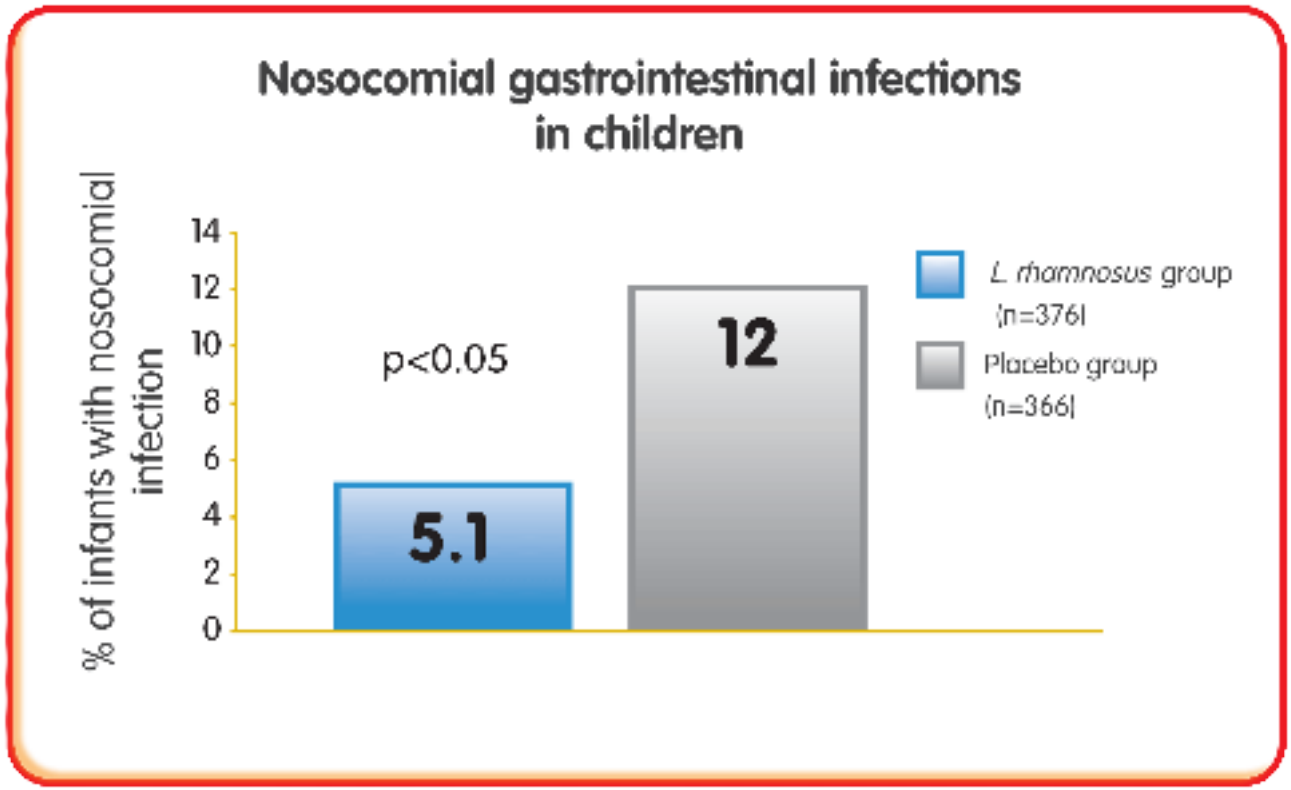
Improved 1,3-Propanediol synthesis from glycerol by the robust Lactobacillus reuteri strain DSM 20016.
Ricci MA. J Microbiol Biotechnol. 2015 Jan 15.

Lactobacillus reuteri I5007 modulates tight junction protein expression in IPEC-J2 cells with LPS stimulation and in newborn piglets under normal conditions.
Yang F. BMC Microbiol. 2015 Dec;15(1):372.

Changes in bile acids, FGF-19 and sterol absorption in response to bile salt hydrolase active L. reuteri NCIMB 30242.
Martoni CJ. Gut Microbes. 2015 Jan 2;6(1):57-65.

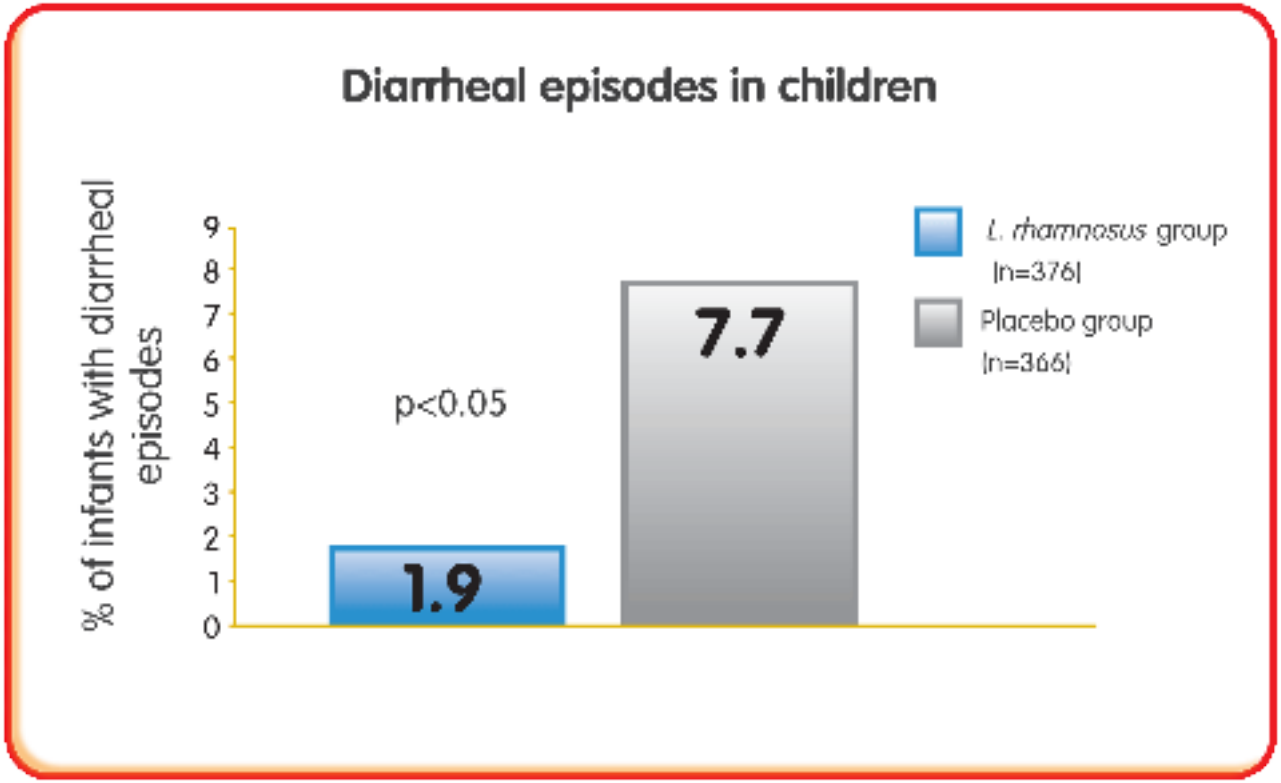
Lactob GG in the prevention of nosocomial GI and resp tract infections.

Hojsak I. Pediatrics. 2010;125:e1171-7



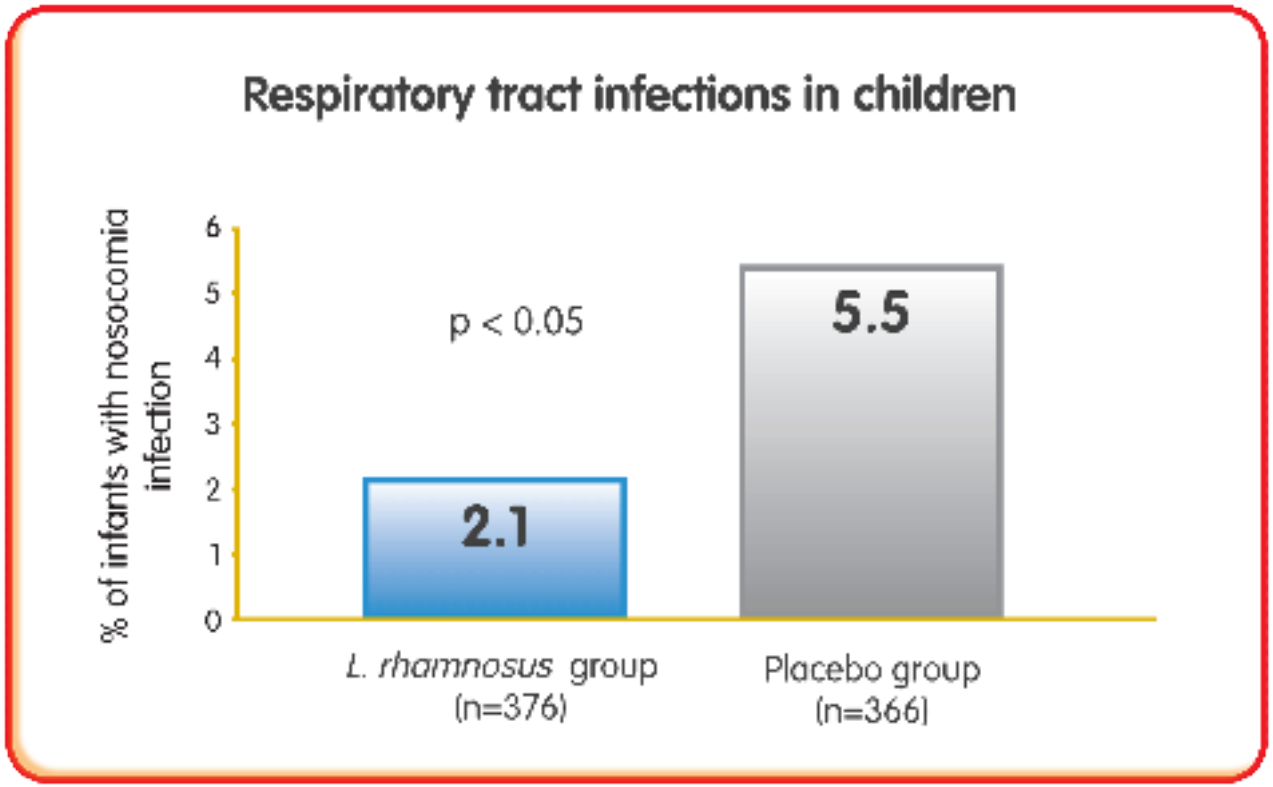
L. rhamnosus: reduced risk of nosocomial GI

Lactob GG in the prevention of nosocomial GI and resp tract infections.
Hojsak I. Pediatrics. 2010;125:e1171-7



L. rhamnosus: reduced risk of diarrheal episodes

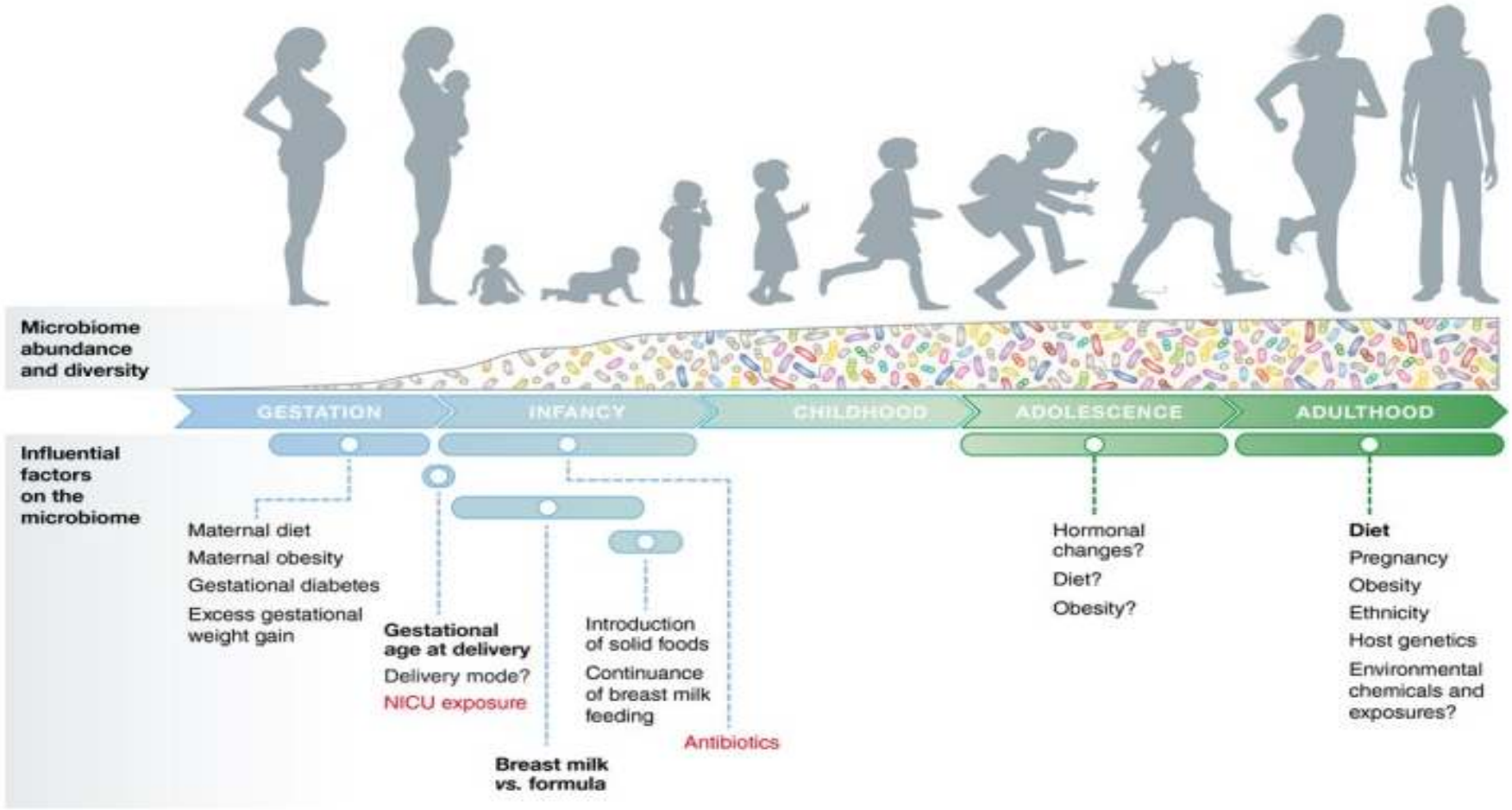
Lactob GG in the prevention of nosocomial GI and resp tract infections.
Hojsak I. Pediatrics. 2010;125:e1171-7



L rhamnosus: reduced risk of respiratory tract infections

- Micro-organisms: “good” and “bad” (pathogens)

- Every probiotic is a “good” micro-organism but not every “good” micro-organism is a probiotic



Universitair Ziekenhuis Brussel

Kidz Health Castle

VUB

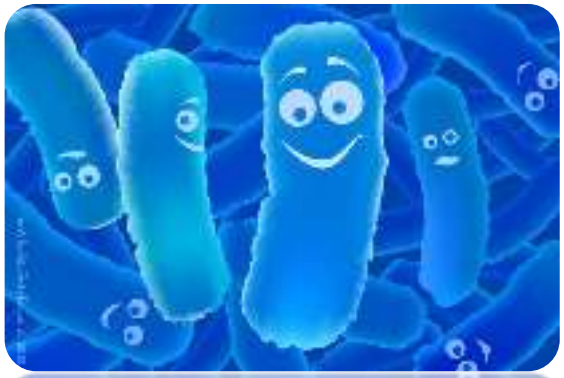
Should every living microorganism be considered as - Pathogen ?
- Probiotic

Lactobacillus reuteri DSM 17938

- ✓ **Management of infantile colic**
  Szajewska H, J Pediatr Gastroenterol Nutr. 2016 Jul;63 Suppl 1:S22-4

- ✓ **Superior compared to other treatment in infantile colic management**
  Gutiérrez-Castrellón P. Medicine (Baltimore). 2017 ;96(51):e9375.

- ✓ **Shortens acute infectious diarrhea**
  Dinleyici EC, J Pediatr (Rio J). 2015; 91(4): 392 – 396



Bifidobacterium lactis

- ✓ **Reduces risk of diarrhea**
  Braegger C; ESPGHAN Committee on Nutrition. JPGN 2011;52:238-50
- ✓ **Enhances antibody sIgA**
  Mohan R· Pediatr Res. 2008;64:418-22
- ✓ **Increase vaccination response**
  Holscher HD. JPEN J Parenter Enteral Nutr. 2012;36(1 Suppl):106S-17S
- ✓ **Reduces incidence NEC in very low birth weight infants**
  Bin-Nun. J Pediatr. 2005;147:192-6.

Lactobacillus rhamnosus GG

Reduces respiratory tract infections
Hojsak I, Pediatrics. 2010;125:e1171-7

Reduces gastrointestinal tract infections
Hojsak I, Pediatrics. 2010;125:e1171-7

Reduces risk of atopic eczema
Kukkonen K, J Allergy Clin Immunol, 2007 Jan;119(1):192-8

Products that claim to effective in AAD need to be resistant to ABs...

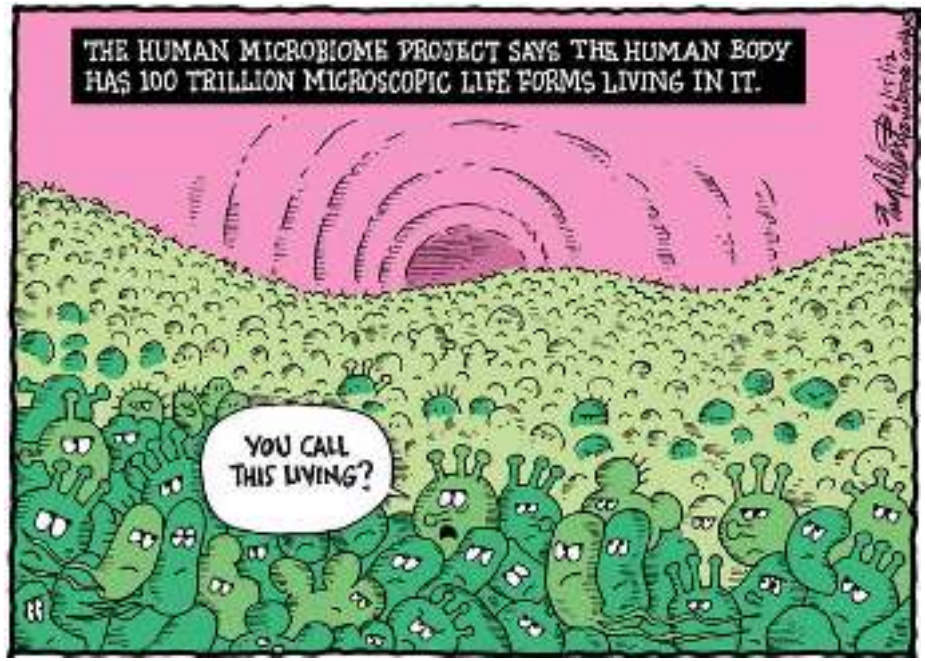
Product “X” (on Belgian market)

	resistant up to
Amoxicilline + clavulanate	200 mg/ml
Cefalosporin I, II, III	500 mg/ml
Tetracyclin	100 mg/ml
Macrolide	200 mg/ml
Penicilline	200 mg/ml
Metronidazole	32 µg/ml
Clindamycin	32 µg/ml
Chloramphenicol	200 mg/ml
Rifampycin	200 mg/ml
Ceftametazon	32 µg/ml
Gentamycin	200 mg/ml
Vacomycin	500 µg/ml

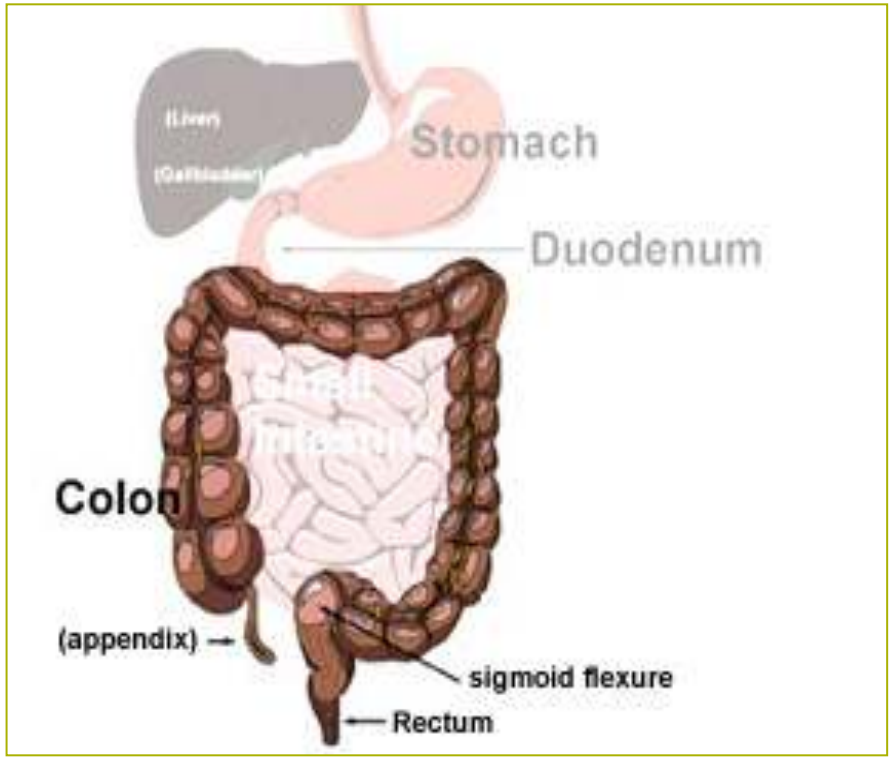
The microbiome

The ecological community of commensal, synbiotic and pathogenic microorganisms that literally share our body space = **Eubiosis**

This term was originally coined by **Joshua Lederberg**, who argued the importance of microorganisms inhabiting the human body in health and disease.



Intestinal Microbiota



- **sterile at birth ???**
- complex ecosystem
- > 1000 species
- 10^{14} bacteria
- 10^{6} bacteria/cm² GI tract
- **> 1 – 1.5 kg**
- **10-100 X > than human cells**
- highest concentration in the colon
- transient and resident flora

Zoetendal EG. A microbial world within us. *Mol Microbiol. 006;59:1639-50*

The Gut: a complex organ

60 -70% of immune cells

100 million neurons

Surface ~**300m²**

100 trillion bacteria
" Gut Microbiota"

Expert Consensus

The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics.
Gibson GR· Nat Rev Gastroenterol Hepatol. 2017;14:491-502

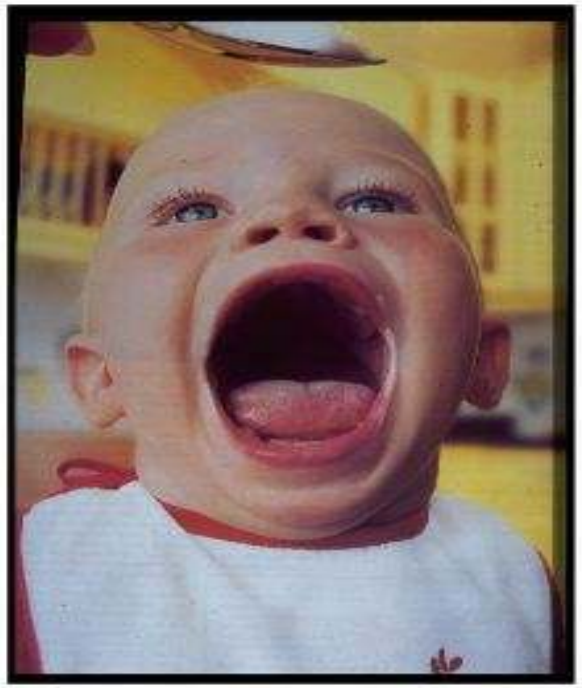
Probiotic

living microorganisms when ingested in sufficient large amount have a health promoting effect on the host present in breast milk

Not all probiotics are the same

Each strain / each product needs clinical proof of efficacy

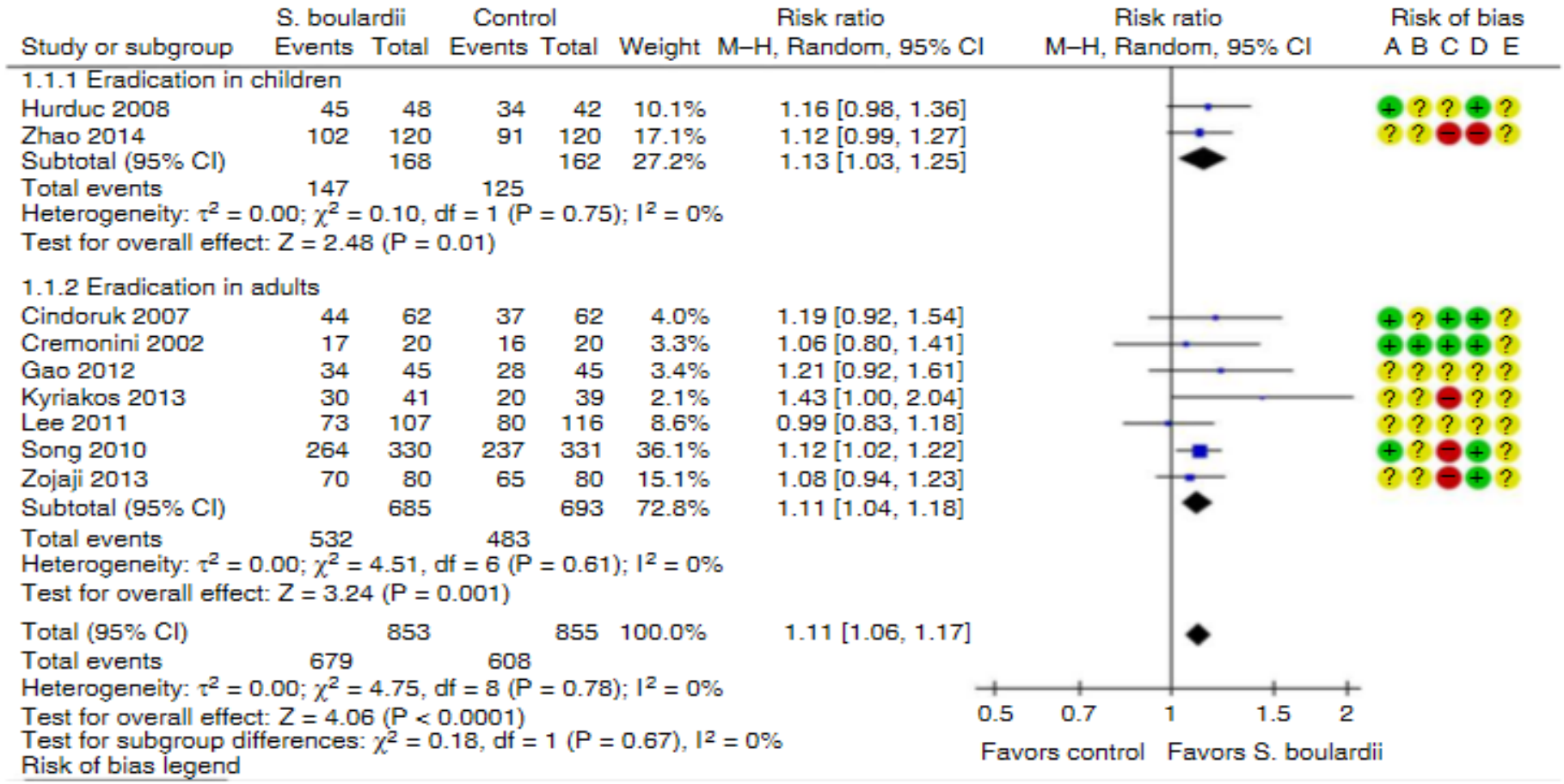
PROBIOTIC MATTERS,



THANK YOU!

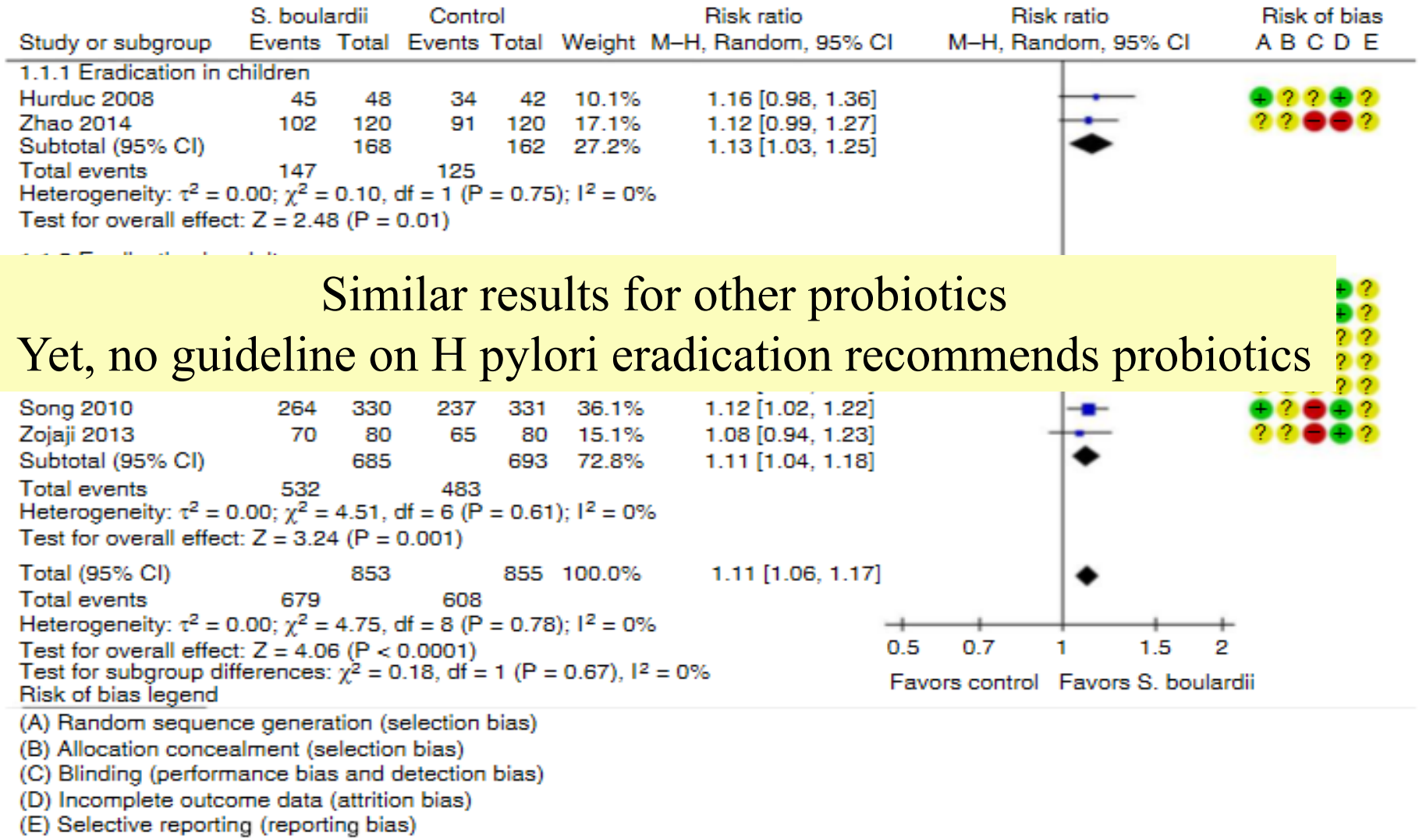
Systematic review with meta-analysis: S boulardii supplementation and eradication of Helicobacter pylori infection.

Szajewska H. Aliment Pharmacol Ther. 2015;41:1237-45.



Systematic review with meta-analysis: S boulardii supplementation and eradication of Helicobacter pylori infection.

Szajewska H. Aliment Pharmacol Ther. 2015;41:1237-45.



Similar results for other probiotics

Yet, no guideline on H pylori eradication recommends probiotics

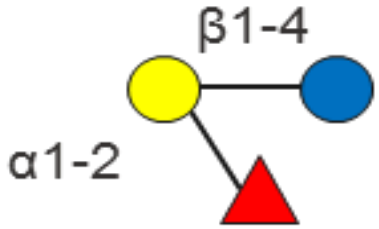
Commonly Used Probiotics

Lactobacillus	Bifidobacteria	Yeast
L. reuteri	*B. lactis (B. infantis)*	*S. boulardii*
L. rhamnosus	*B. breve*	
L. plantarum	*B. longum*	
L. casei		

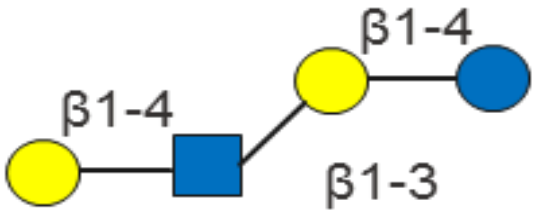
Fermentation process was intended for conservation of food

Is healthy eating a health benefit?

Human milk oligosaccharides



2'fucosyl-lactose (2'FL)



Lacto-N-neotetraose (LNnT)

Glucose Galactose Fucose N-acetylglucosamine

It’s all about micro-organisms

What happens early in life?

2nd choice infant feeding

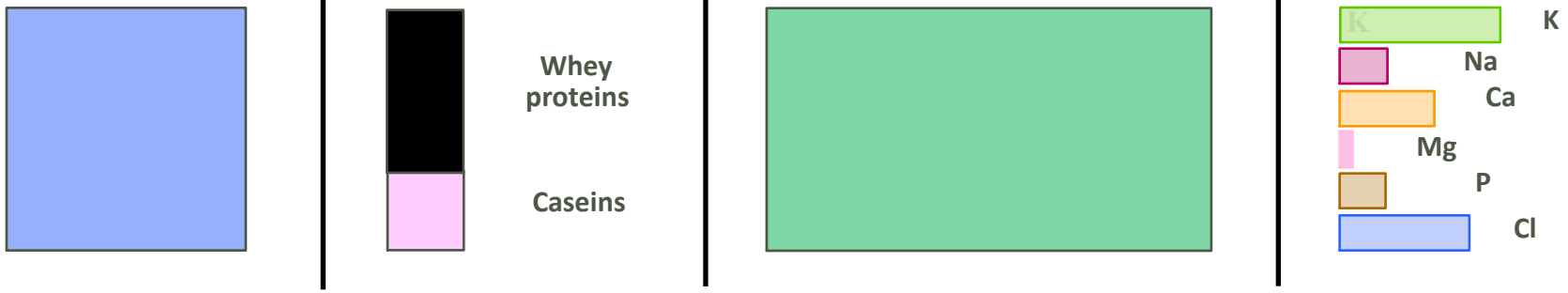
Infant formula: Cow milk based

- Many cows
- Cows provide large amounts of milk
- Not because cow's milk resembles mother's milk

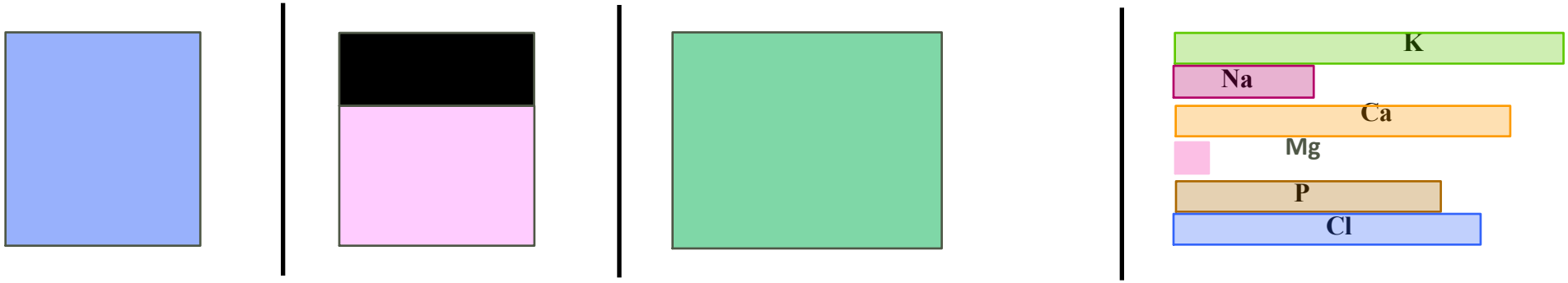
The challenge: breast milk and cow milk differ

Lipids | Proteins | Carbohydrates | Minerals

Breast milk



Cow milk



Introduction to HMOs

Human Breast Milk

- Most suitable nutrition for infants
- Has a unique composition
- Offers health benefits to infants

1900

Breastfed infants have a survival advantage

Difference in stool bacterial composition of breastfed and formula-fed infants discovered

Mothers milk discovered to have an unidentified carbohydrate fraction

1930

Bifidogenic factor in human milk consists of oligosaccharides

1954

Discovery and characterization of the most abundant oligosaccharides in human milk

Non-human Oligosaccharides

Some infant formulae are currently supplemented with non-human oligosaccharides[1]

Galacto-oligosaccharides (GOS)	• Enzymatically synthesised from galactose[1]
Fructo-oligosaccharides (FOS)	• Commonly extracted as inulin from chicory/other plant sources[1]
Pectin-derived acidic oligosaccharides (pAOS)	• Extracted from citrus fruit or cellulose[2]

GOS & FOS are prebiotic oligosaccharides, promoting the growth of beneficial gut microbiota[3-5]

Sela DA. Trends Microbiol. 2010;18(7):298-307; Bernard H. J Infect Dis. 2014;211(1):156-65; Kunz C. Adv Nutr. 2012;3(3):430S-9S.; Gibson G. Nutr Res Rev. 2004;17(02):259.; Roberfroid M. Br J Nutr. 2010;104(S2):S1-S63.

The Specific GOS/FOS Prebiotic Mixture:

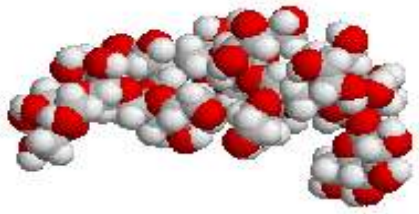
Mimicking Size, Linkage, partly Building Blocks and Prebiotic function of HMOS

90 % scGOS: **low molecular weight (short chain)**
Galacto-OligoSaccharides
(enzymatic from lactose)

$$[Gal(\beta 1\text{-}]_{1\text{-}4}\ 3/4/6)Gal(\beta 1\text{-}4)Glc$$

Lactose

10% IcFOS: **high molecular weight (long chain)**
Fructo-OligoSaccharides
(fraction from chicory)



$$[Frc(\beta 2\text{-}]_{n\geq 8}\ 1)Frc(\beta 2\text{-}1)Glc$$

Sucrose

- Today, 2-FL and LNnT are added to infant formula

- Are it HMOs ? = NO

- industrially made.
- produced by fermentation of lactose.
- but….The molecular structure is IDENTICAL
- to the 2'FL present in mother's milk

➢ "synthetized HMO" is added to infant formula

Not all prebiotics are the same

Mis-use of wording “HMO” ?

A randomized clinical trial measuring the influence of kefir on AAD: The measuring the influence of Kefir (MILK) Study.

Merenstein DJ. Arch Pediatr Adolesc Med 2009;163:750-4

Primary care patients in the Washington, DC, metropolitan area.
125 children (1 - 5 years) Kefir / heat-killed placebo

No difference in rates of diarrhea per group

18% in the active group

21.9% in the placebo group

(relative risk, 0.82; 95% confidence interval, 0.54-1.43)

No differences in any secondary outcomes