The role of nutrition in optimum gastrointestinal health

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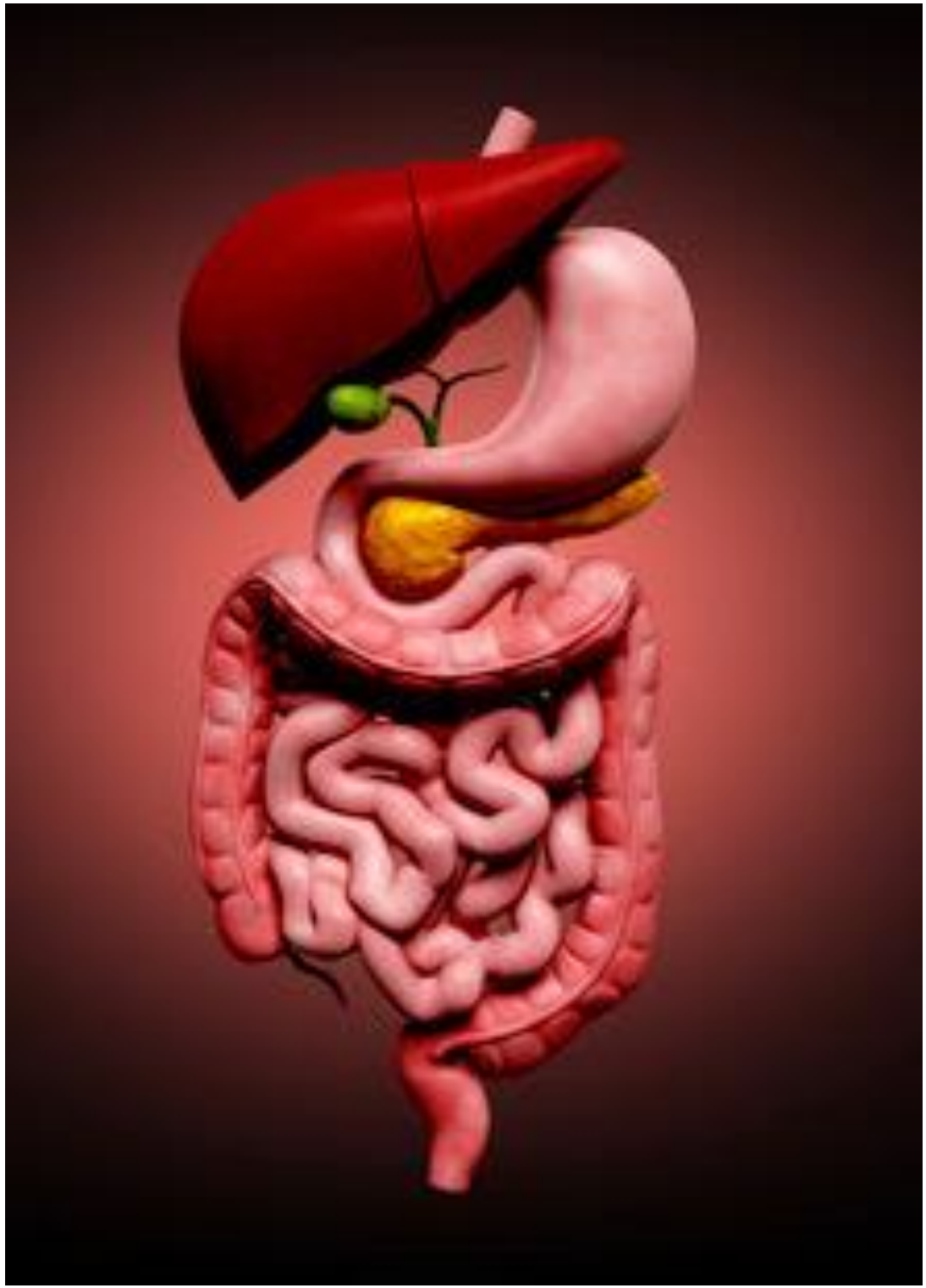
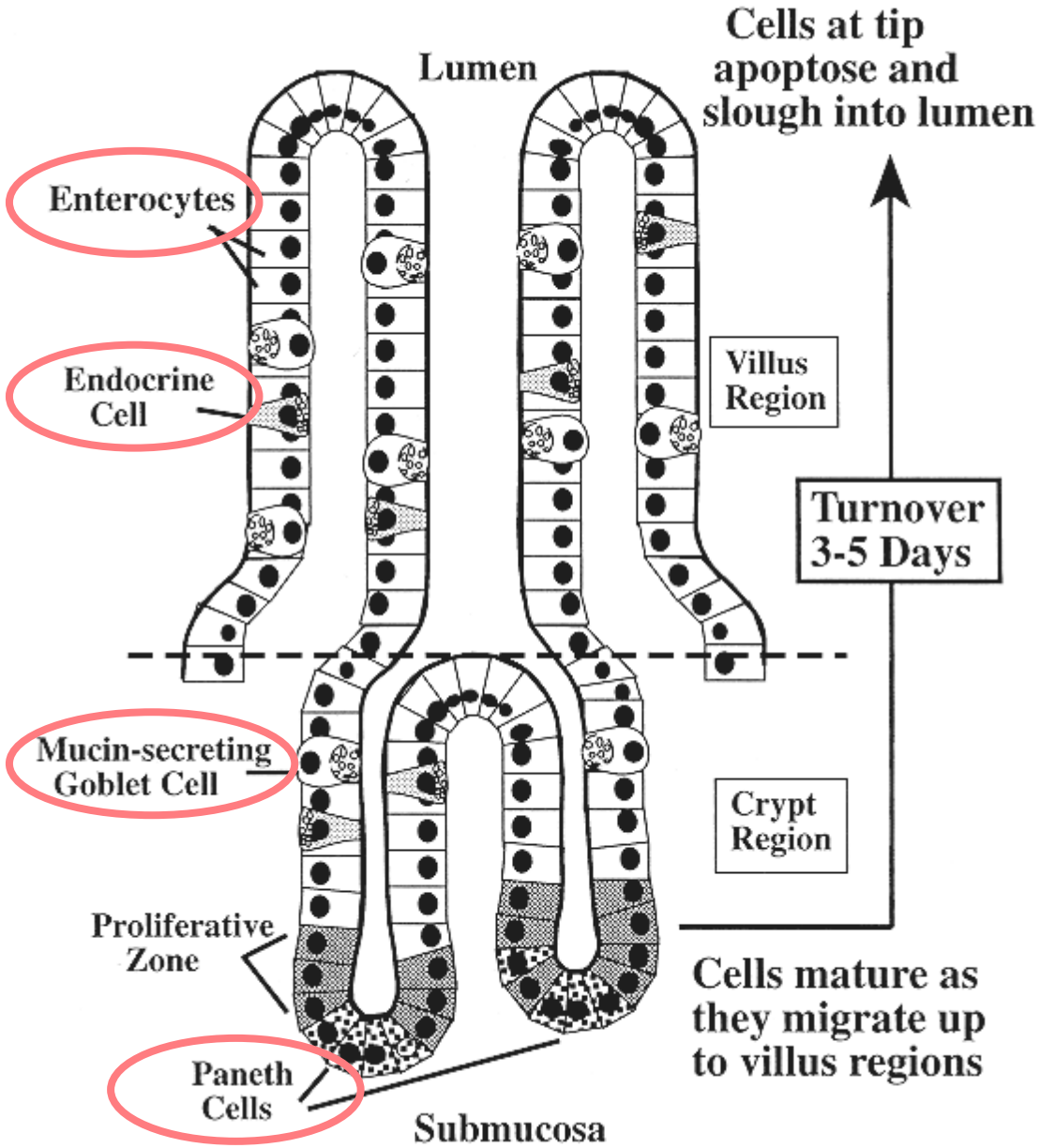
Outline

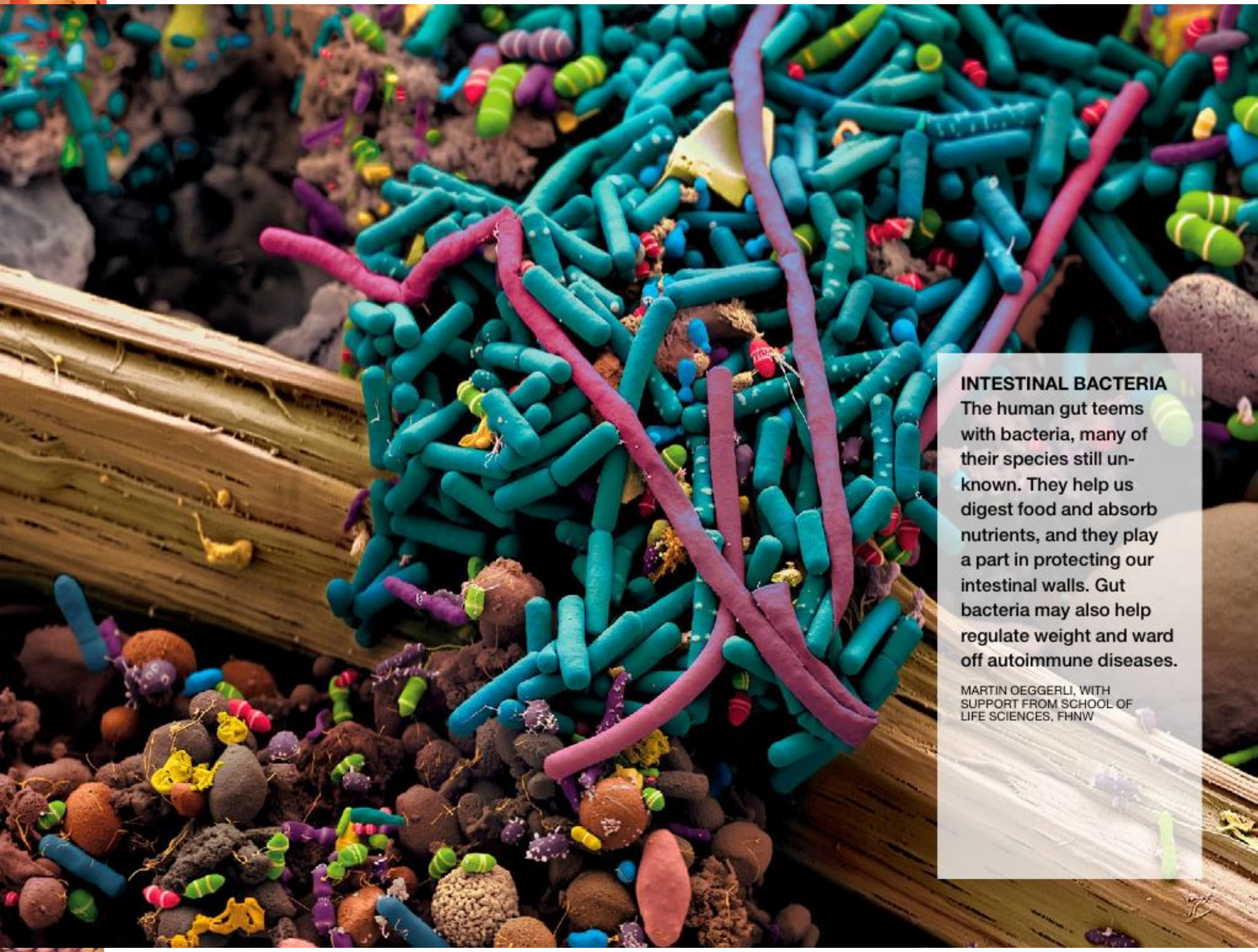
1. Development of the human gastrointestinal tract
2. Optimal nutrition provided by human milk
3. Definition of pre- and probiotics
4. Impact of pre- and probiotics on intestinal health



Specialized structure facilitates function

Multiple epithelial cell types

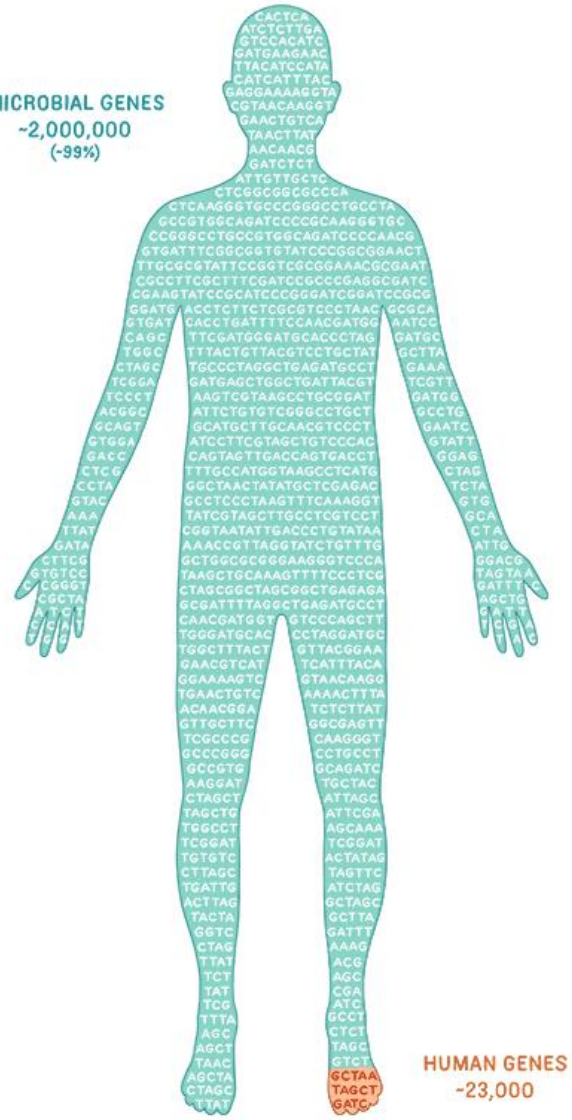




INTESTINAL BACTERIA
The human gut teems with bacteria, many of their species still unknown. They help us digest food and absorb nutrients, and they play a part in protecting our intestinal walls. Gut bacteria may also help regulate weight and ward off autoimmune diseases.

MARTIN OEGGERLI, WITH SUPPORT FROM SCHOOL OF LIFE SCIENCES, FHNW

Who are we?



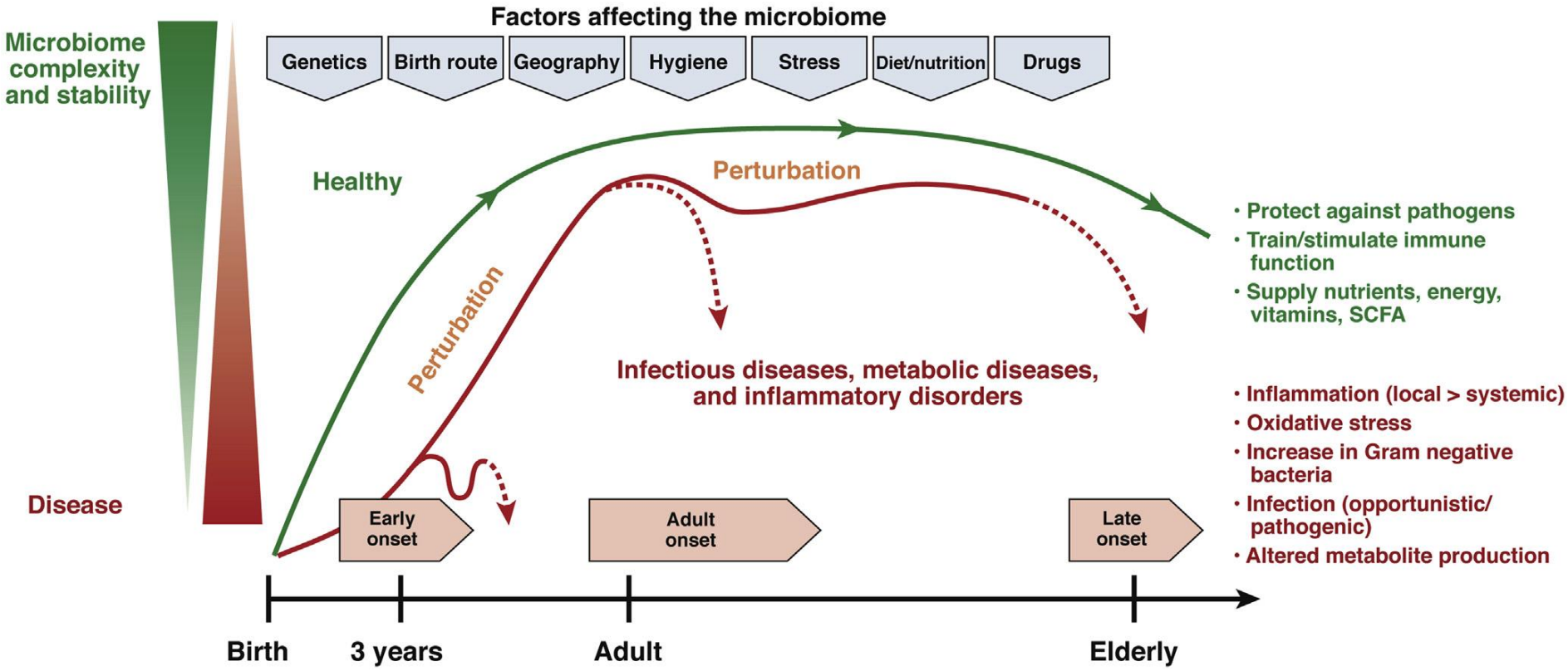
American Museum of Natural History, 2016

Functions of the Intestinal Microbiota

Functions	Mechanisms/Effects
Digestive and metabolic functions	• Vitamin production • Fermentation of nondigestible CHO → SCFA • Dietary carcinogens metabolism
Neuronal development	• Modulation of brain gut axis during neuronal development • Motor control and anxiety behavior
Protective functions against pathogenic bacteria	• Pathogen displacement • Nutrient competition • Production of antimicrobial factors • Activation of local immune response • Contribute to the intestinal barrier function
Immune development	• IgA production • Control of local and general inflammation • Tightening of junctions • Induction of tolerance to foods

Buccigrossi et al., Curr Opin Gastroenterol 2013, 29:31–38.

Factors affecting stability and complexity of gut microbiome in health and disease



Kostic et al., Gastroenterology 2014;146:1489-1499.

Microbiota: breast vs bottle?

- Breast-fed infants
  - stable developing microbiota
  - dominated by bifidobacteria (‘bifidofactor’)
  - decreased pathogens

- Formula-fed infants
  - Less stable microbiota
  - assoc with higher incidence of pathogenic infections, pneumonia, diarrhea, and allergy

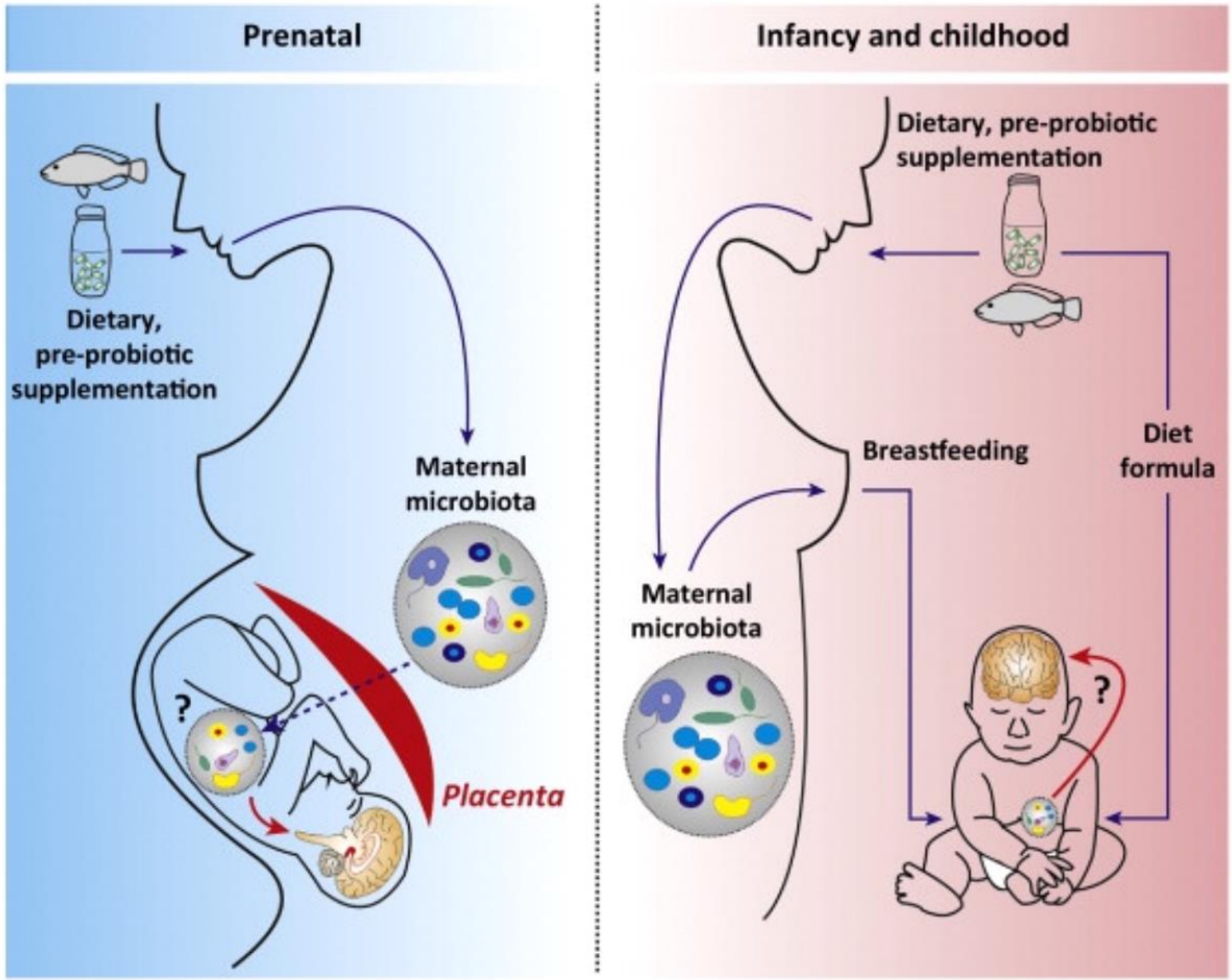
Harmsen et al., JPGN 2000:30;61-67

Dysbiosis with childhood diseases

Disease	Microbiota composition changes
Celiac Disease	Lack of bacteria of the phylum Bacteroidetes along with an abundance of Firmicutes
IBD	↓ concs of Faecalibacterium prausnitzii and Bifidobacteria ↑ levels of Escherichia coli Reduced diversity of gut microbiota
IBS	Significantly ↑ % of the class Gammaproteobacteria Presence of unusual Ruminococcus-like microbes
NEC	Predominance of Gammaproteobacteria ↓ diversity of gut microbiota
Obesity	↑ Firmicutes at expenses of the Bacteroidetes group
CF	↓ counts of lactic acid bacteria, clostridia, Bifidobacterium spp., Veillonella spp., and Bacteroides-Prevotella spp.
Allergy	↓ counts of Lactobacilli, Bifidobacteria, and Bacteroides ↑ counts of Clostridium difficile ↓ diversity of gut microbiota

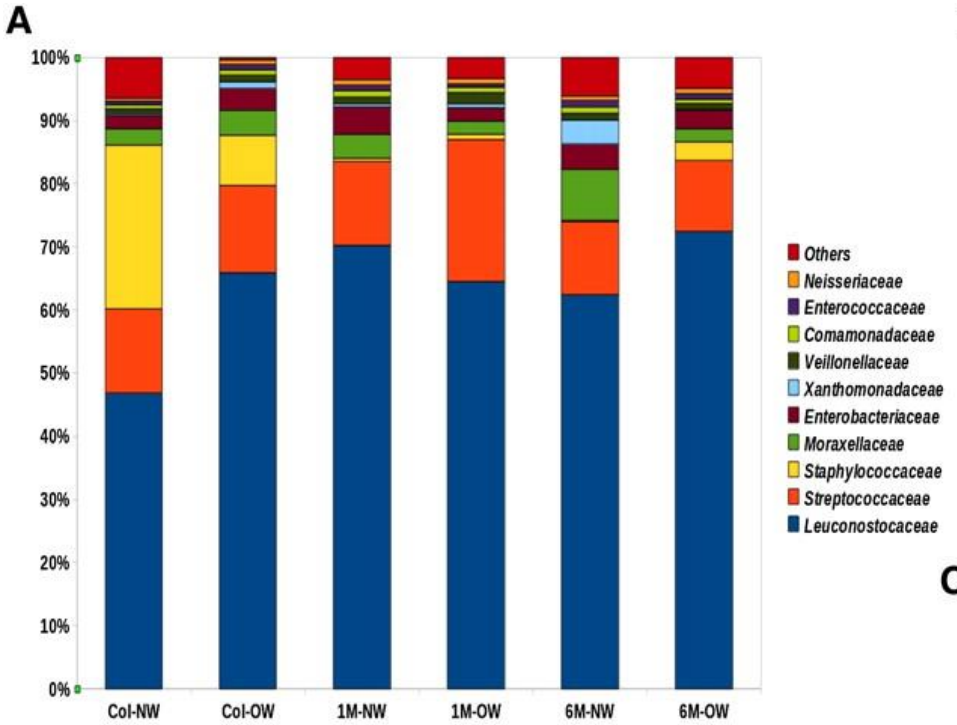
Buccigrossi et al., Curr Opin Gastroenterol 2013;29:31–38.

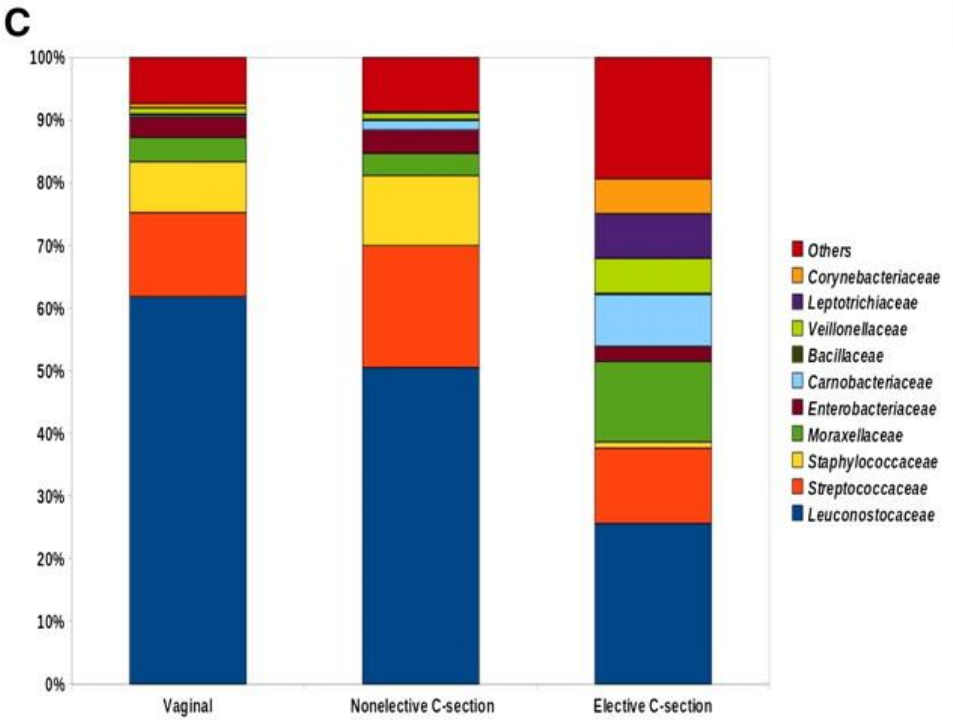
Microbe contact begins *in utero*



Borre et al., Trends Mol Med 2014;20:509-518.

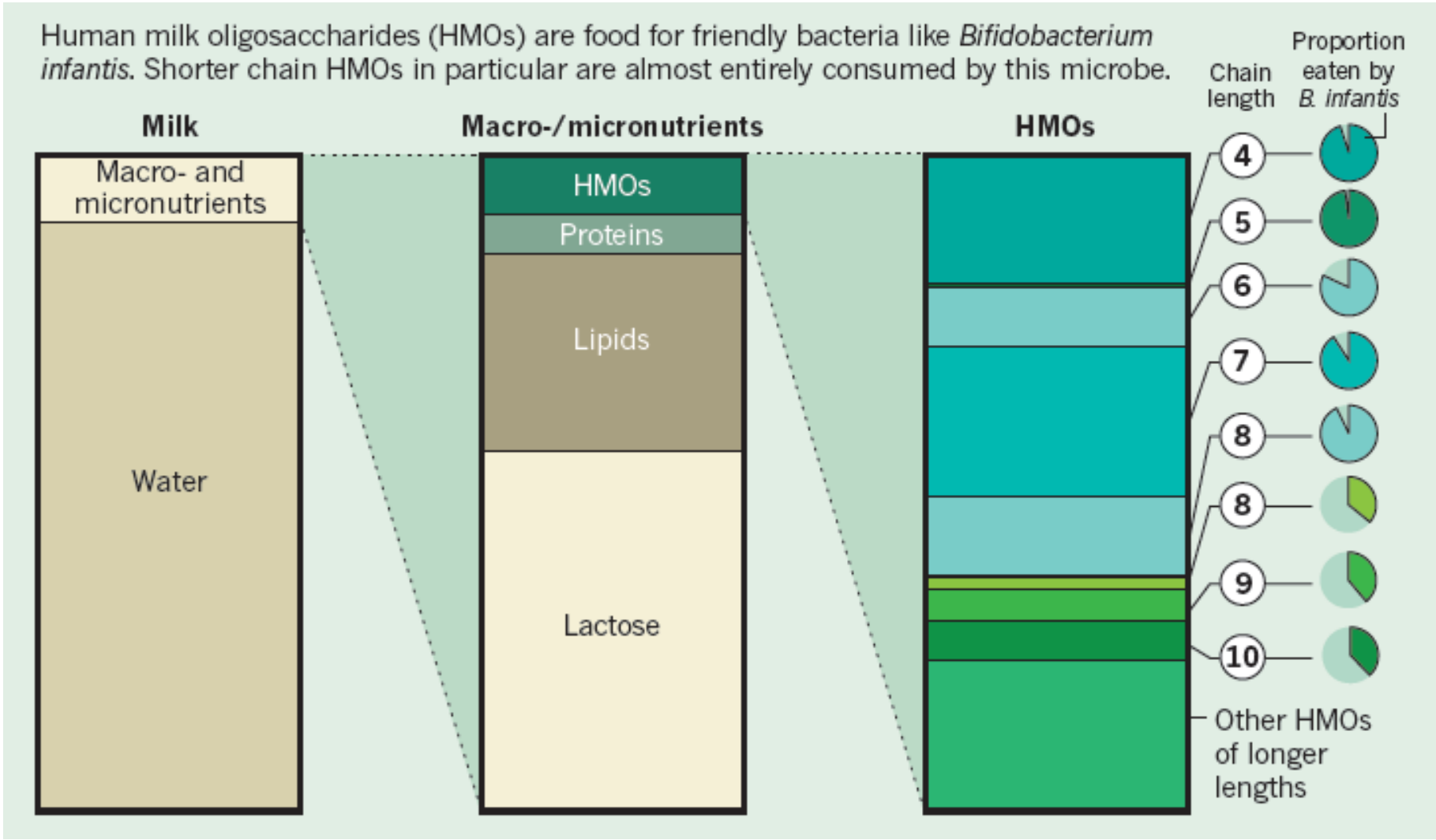
Human milk microbiome varies with stage of lactation, obesity and route of delivery





Cabrera-Rubio R et al. Am J Clin Nutr 2012;96:544-551.

Human milk = the ultimate **SYNbiotic**!



Petherick Nature 2010;65:S5-S7

Can nutritional formulas be modified

- using a **SYNbiotic** approach -

to alter the intestinal microbiota and

improve clinical outcomes in children?

What is a PRObiotic?

- Oral probiotics are *living* microorganisms that upon ingestion in specific numbers, exert health benefits beyond those of inherent basic nutrition
- Probiotics are sometimes also referred to as “good bacteria”.

Strong evidence supporting PRObiotic use

Clinical Condition	Organism
Diarrhea	
Infectious adult – treatment	Saccharomyces boulardii, LGG
Infectious childhood – treatment	LGG, Lactobacillus reuteri
Prevention of antibiotic-associated diarrhea	S. boulardii, LGG, L. casei, . Bulgaricus, S. thermophilus
Inflammatory Bowel Disease	
Pouchitis - Preventing and maintaining remission	VSL#3
Immune response	LGG, L. acidophilus, L. plantarum, B. lactis, L. johnsonii, VSL#3
Atopic eczema associated with cow's milk allergy	
Treatment	LGG, B. lactis
Prevention	LGG, B. lactis

Recommendation for Use of PRObiotics in Diarrhea in Children

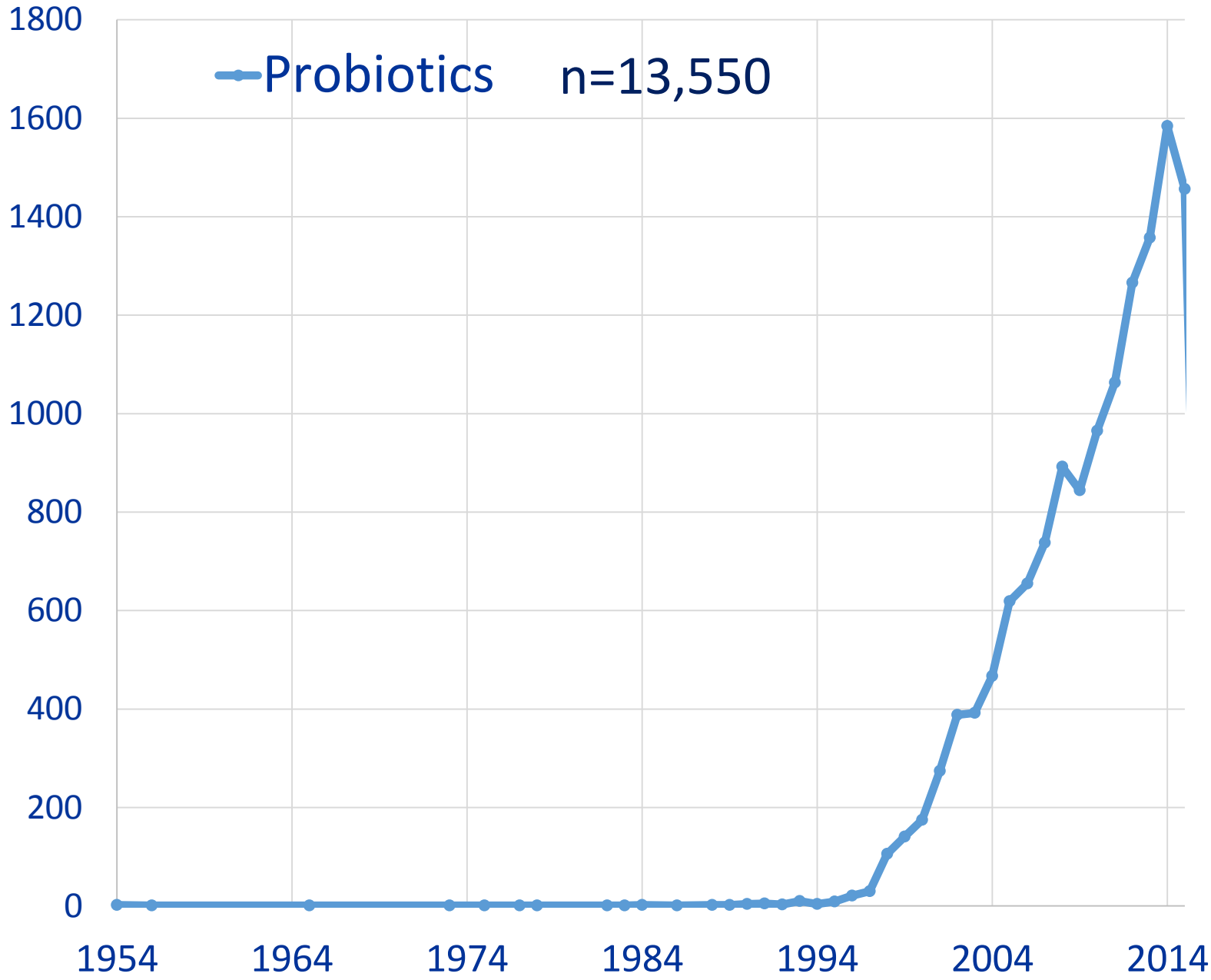
Condition	Sample Size	Probiotics Studied	Efficacy
Prevention of day-care diarrhea	1700	B. lactis/S.thermophilus LGG	+
Prevention of nosocomial diarrhea	356	LGG B. lactis/S.thermophilus	+/-
Antibiotic-associated diarrhea	2000	LGG Saccharomyces boulardii	+++
Infectious diarrhea	3000	LGG Saccharomyces boulardii L. acidophilus LB	+++
Persistent diarrhea	235	LGG	++

Guandalini S. J Clin Gastro 2008;42(S2):S53-S57.

Moderate Evidence Supporting PRObiotic Use

Clinical Condition	Organism
Diarrhea	
Prevention of infection	Saccharomyces boulardii, LGG
Treatment of recurrent C. difficile-associated diarrhea	S. boulardii, LGG
Prevention of recurrent C. difficile-associated diarrhea	S. boulardii, LGG
Necrotizing Enterocolitis	B. infantis, S. thermophilus, B. bifidus
Irritable Bowel Syndrome	B. infantis

PubMed Citations by Year



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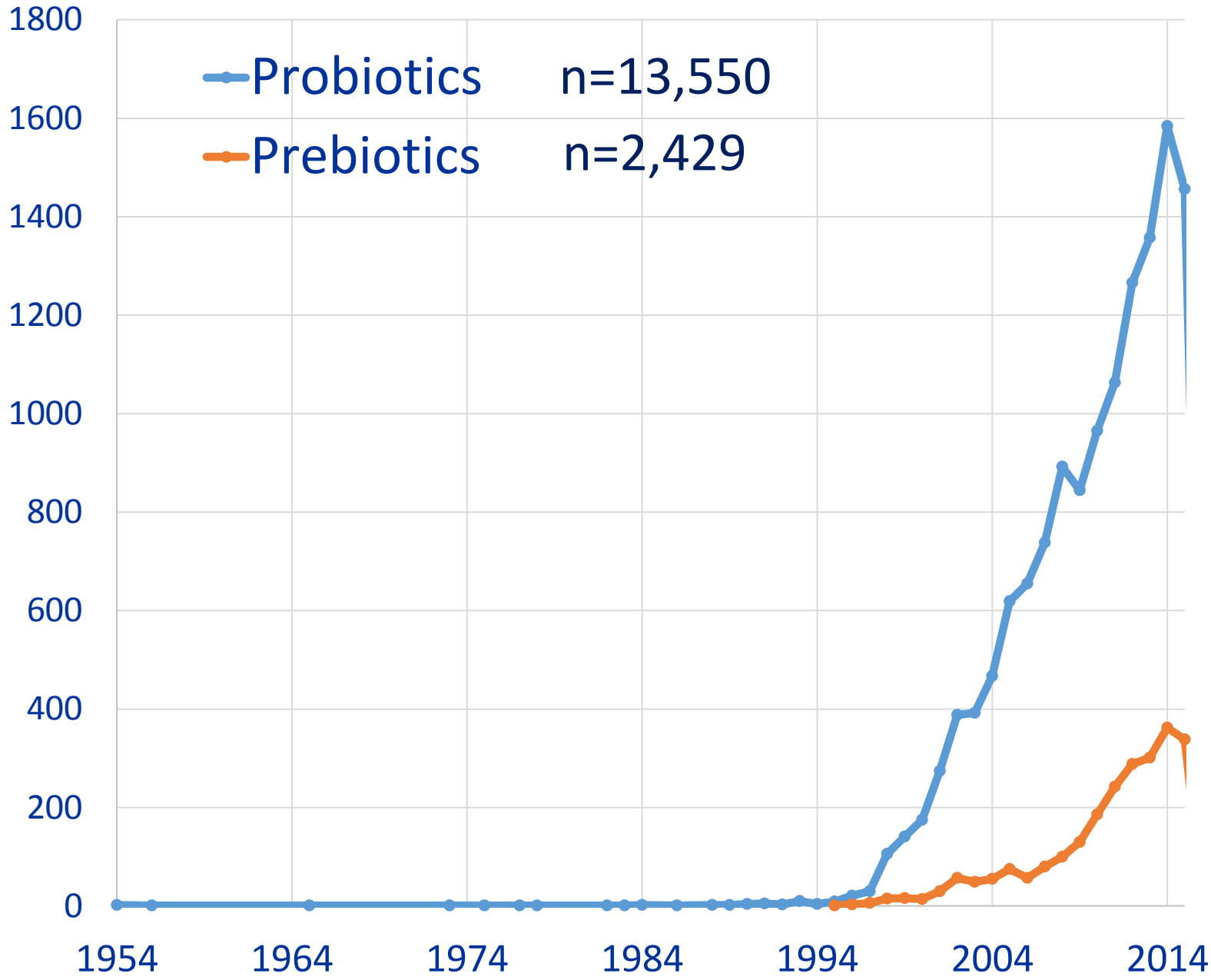


What is a PREbiotic?

- A prebiotic is a non-digestible *food* ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one of a limited number of bacteria in the colon, and thus improves host health.

  (Gibson and Roberfroid,1995; Gibson et al., 2004)

- Many prebiotics are classified as a functional *fiber*

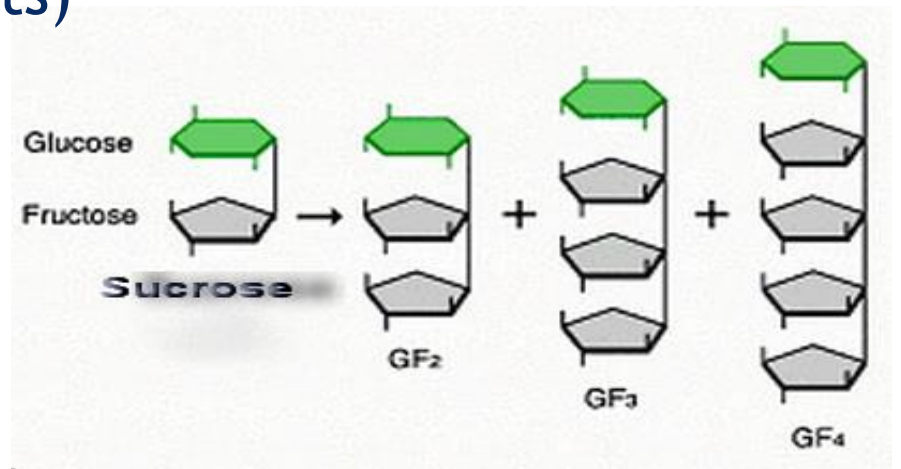





Different types of prebiotics

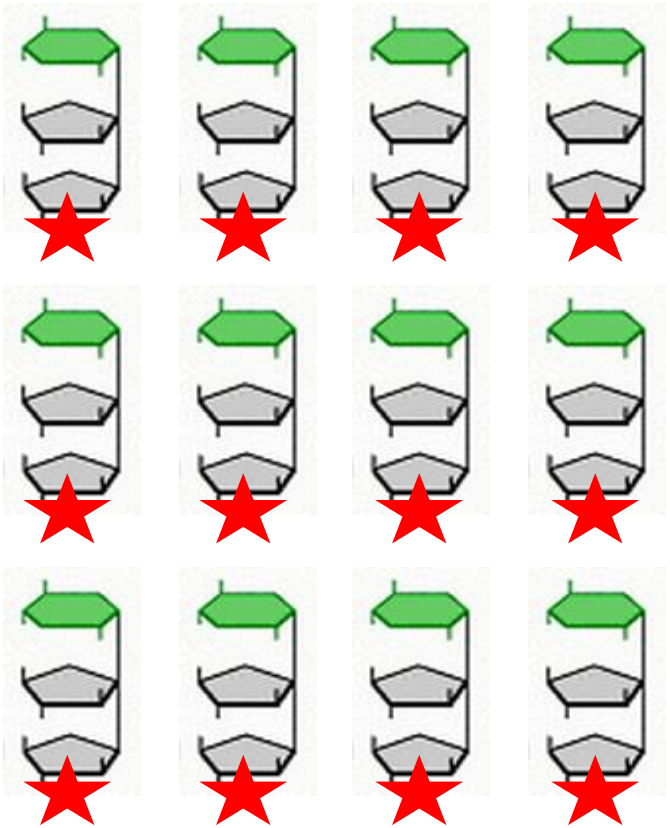
- GOS-type: Galacto-oligosaccharides
  - Derived from lactose
  - Present in human milk (traces)

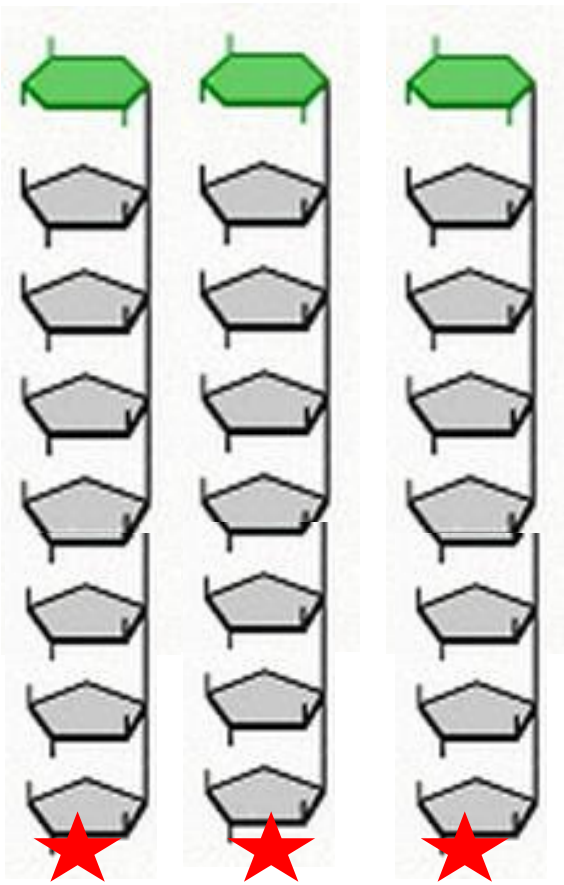
- FOS-type: Fructo-oligosaccharides
  - Derived from plants (e.g. chicory, artichoke, banana)
  - Also referred to as ‘inulin-type’
  - Polymers of different lengths of fructose units
    - **scFOS** (2-5 units)
    - **Oligofructose** (≤10 units)
    - **Inulin** (>10 units)



Prebiotic structure impacts functional characteristics

- Particles present in equal dose varies based on MW of product
- Rate of fermentation impacted by microbes access to each particle





Compared to probiotics…

…prebiotics are

~100 yr younger

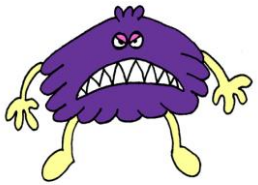
5.6X ↓ studied

less exciting?

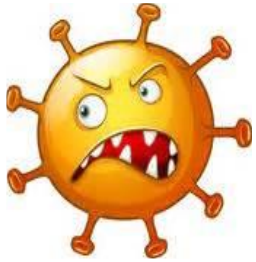
Top Reasons Why Prebiotics Should Not Be Overlooked

Evoke similar benefit as probiotic interventions.

Provide necessary substrate for microbiota.

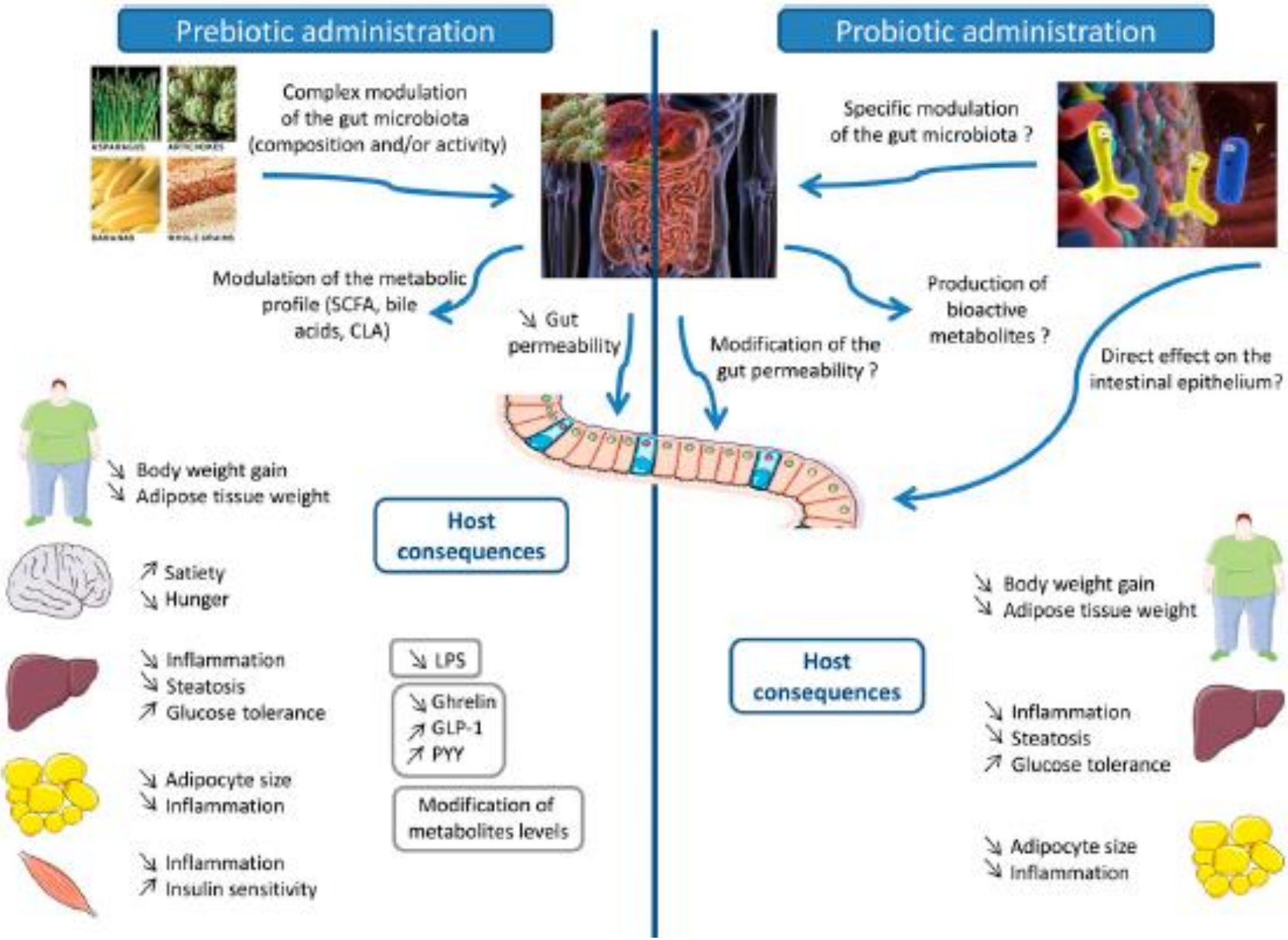


Lasting impact on microbiota and clinical outcomes.



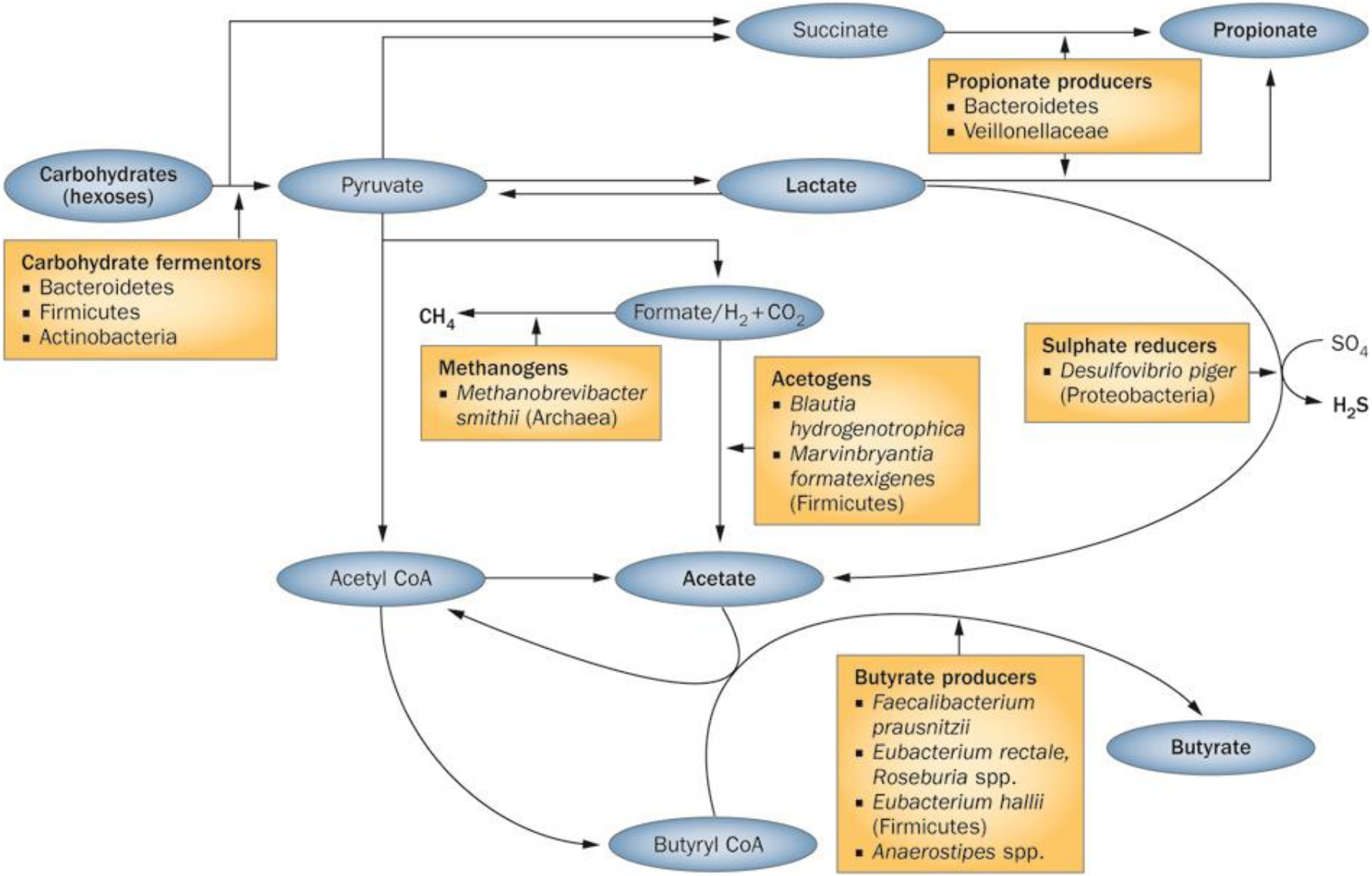
Safe, food-based strategy associated with wealth of data

Prebiotics evoke many similar physiological responses as probiotics.



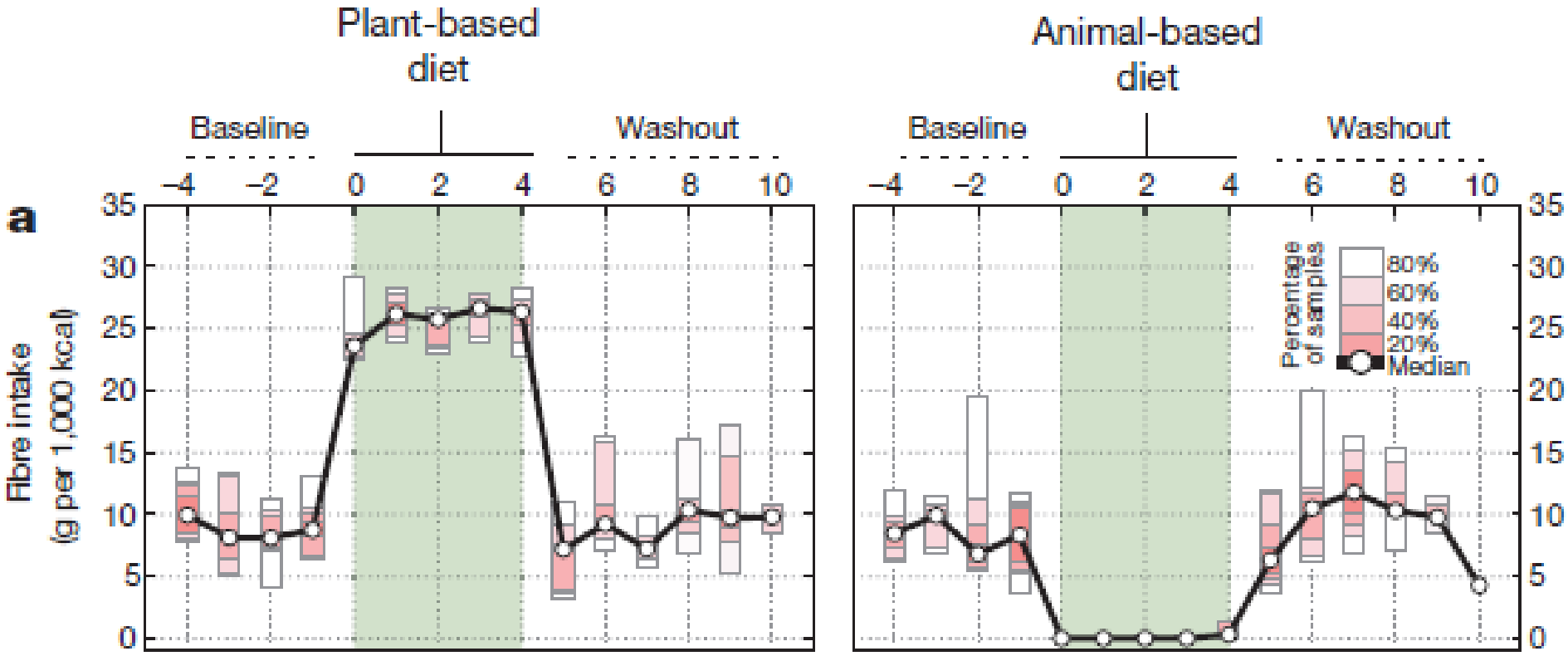
Druart et al., Adv Nutr 2014; 5: 624S–633S.

Prebiotics provide necessary substrate to sustain the microbiota.



Flint et al. Nat Rev Gastroenterol Hepatol, 2012; 9,577-589.

Short-term diet alters the intestinal microbiota

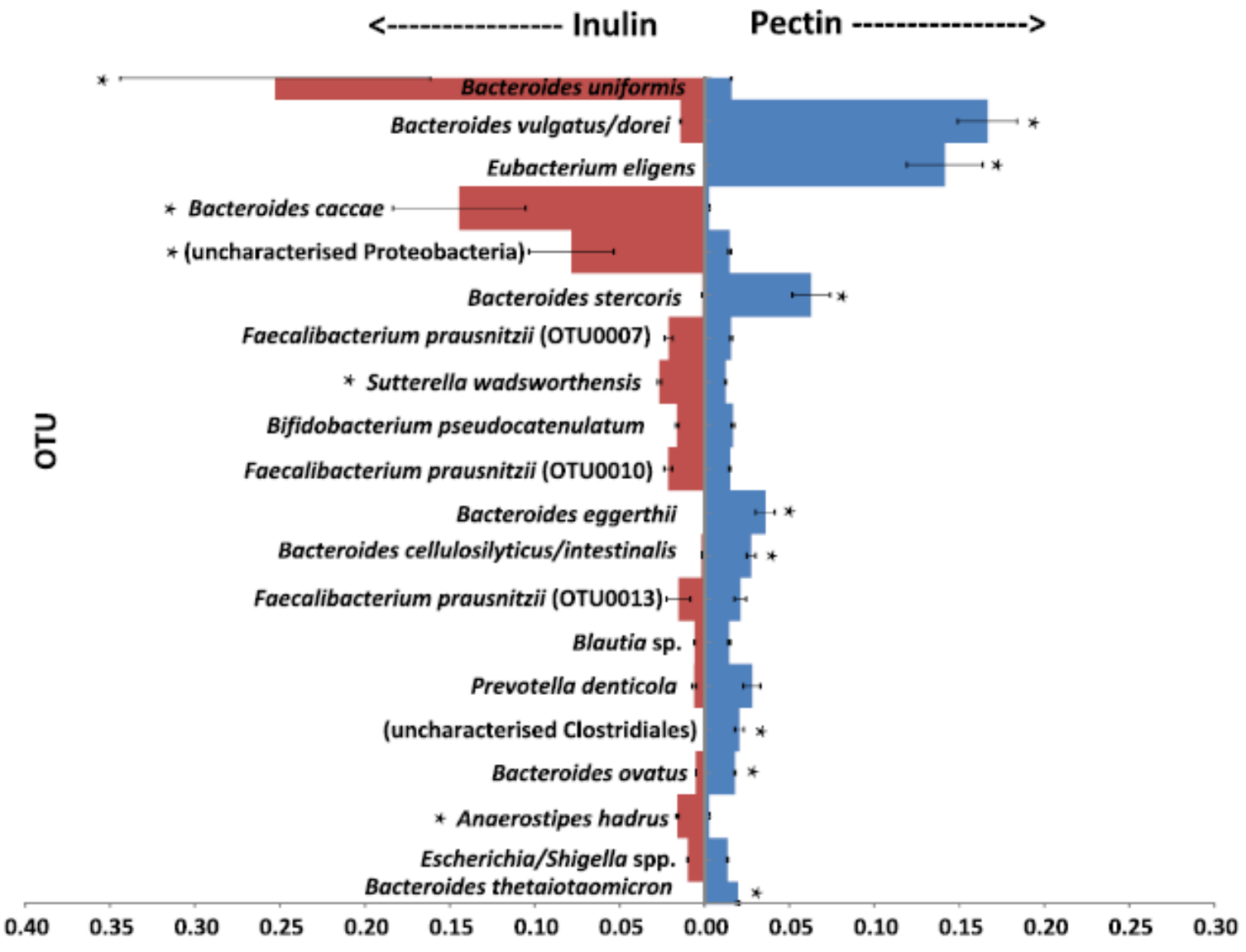


Animal-based diet:

- ↑ bile-tolerant microorganisms
- ↓ Firmicutes that metabolize dietary plant polysaccharides
- link between dietary fat, bile acids growth of microorganisms capable of triggering IBD

David et al., Nature 2014;505:559.

Prebiotics alter the microbial community, not just isolated species.

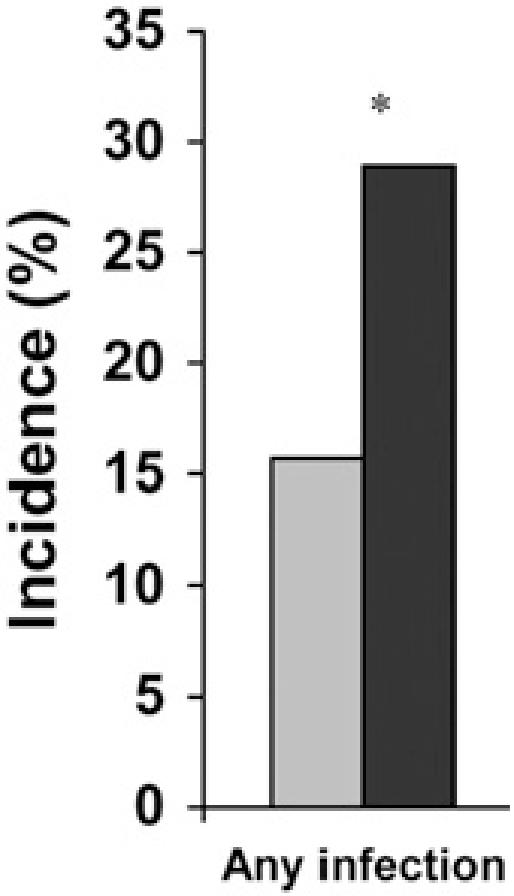


Chung et al. BMC Biology 2016;14:3

Infants consuming formula with prebiotic have microbiota more similar to that of breast fed infants.

Oozeer R. Am J Clin Nutr 2013;98(suppl):561S–71S.

Prebiotic formula reduces cumulative incidence of infections during first 6 months of life



scGOS/lcFOS ■ Placebo

*p<0.05
**p<0.01

Arslanoglu et al., J. Nutr. 2007;137:2420–2424.

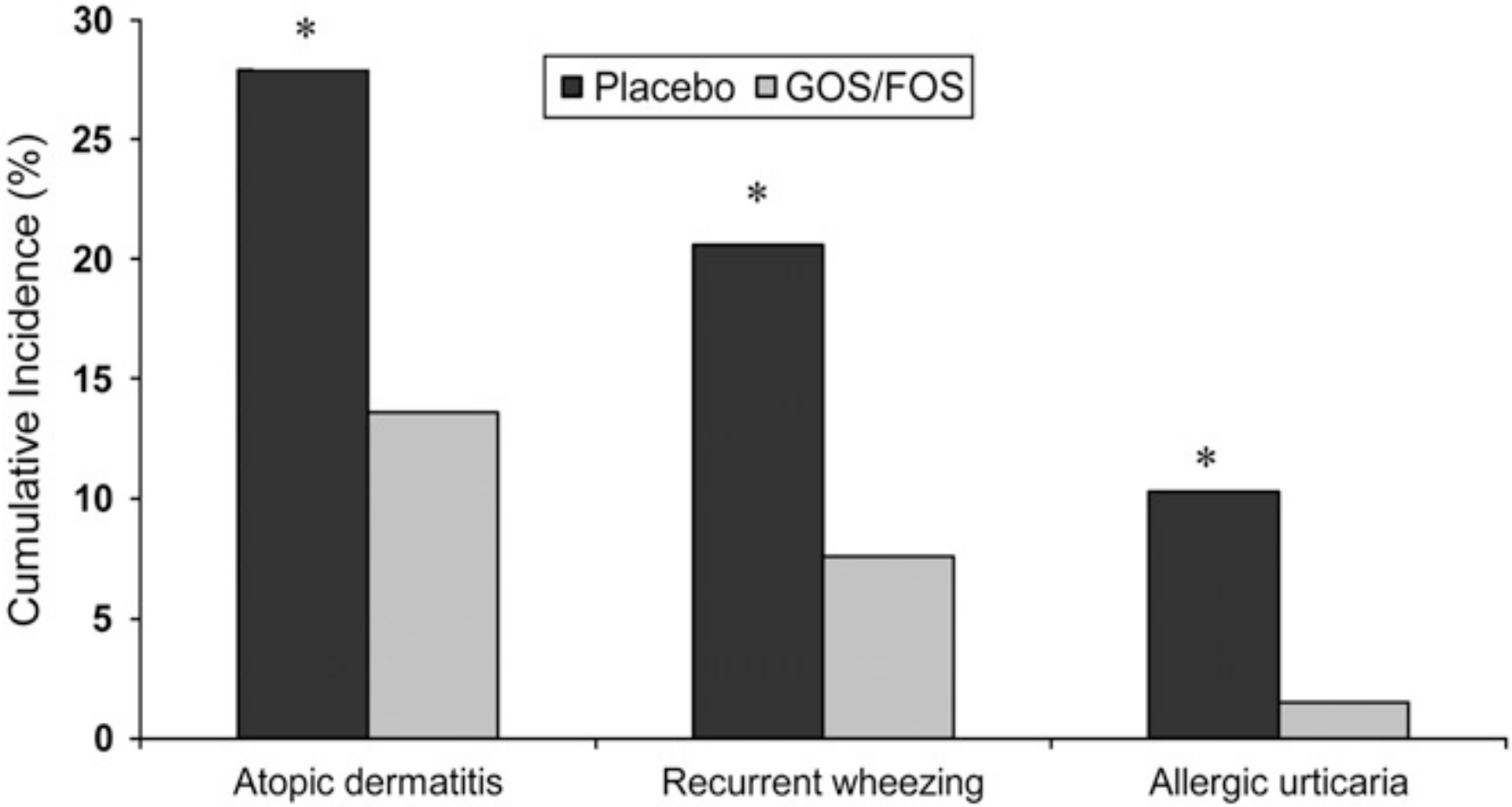
Prebiotic formula reduces episodes of infections and fever during first 2 years of life.

	Placebo	scGOS/lcFOS
	episode/infant	
n	68	66
Physician-diagnosed infections		
Overall (any kind of infection)**	5.9 ± 4.1	4.1 ± 3.1
URTI†	3.2 ± 2.2	2.1 ± 1.8
Lower respiratory tract infections	1.3 ± 0.8	0.9 ± 1.1
Otitis media	0.7 ± 1.2	0.5 ± 1.0
Gastrointestinal infections	0.6 ± 0.9	0.4 ± 0.7
Urinary tract infections	0.1 ± 0.5	0.0 ± 0.0
Infections requiring antibiotic prescriptions*	2.7 ± 2.4	1.8 ± 2.3
Fever episodes recorded by parents‡	3.9 ± 2.5	2.2 ± 1.9

[1] Values are means + SD. *Different from placebo, $P < 0.05$, **$P = 0.01$, †$P < 0.01$, ‡$P < 0.0001$.

Arslanoglu et al., J. Nutr. 2008;138:1091–1095.

Prebiotic formula reduces incidence of allergic manifestations during first 2 years of life



Arslanoglu et al., J. Nutr. 2008;138:1091–1095.


Prebiotics
produce
lasting impact
on microbiota
and clinical
outcomes.

World Allergy Organization-McMaster University Guidelines for Allergic Disease Prevention (GLAD-P): PREbiotics

Objective. The World Allergy Organization (WAO) convened a guideline panel to develop evidence-based recommendations about the use of prebiotics in the prevention of allergy.

Methods. Used Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to develop recommendations (evidence up to July 2015).

Recommendation. Based on GRADE evidence to decision frameworks, the **WAO guideline panel suggests using prebiotic supplementation in not-exclusively breastfed infants.**

Cuello-Garcia et al., World Allergy Organization Journal (2016) 9:1-10

World Allergy Organization-McMaster University Guidelines for Allergic Disease Prevention: **PRObiotics**

Recommendations. Currently available evidence does not indicate that probiotic supplementation reduces the risk of developing allergy in children. However, considering all critical outcomes in this context, the WAO guideline panel determined that there is a likely net benefit from using probiotics resulting primarily from prevention of eczema.

The WAO guideline panel suggests:

a) using probiotics in pregnant women at high risk for having an allergic child;

b) using probiotics in women who breastfeed infants at high risk of developing allergy; and

c) using probiotics in infants at high risk of developing allergy.

All recommendations are conditional and supported by very low quality evidence.

Conclusion

Country	Recommendation	Source of recommendation
France	25–30 g*	Agence Française de Sécurité Sanitaire des Aliments, 2001
Germany	30 g*	German Nutrition Society, 2000
Netherlands	30–40 g: 3.4 g/MJ*	Health Council of The Netherlands, 2006
Nordic countries	25–35 g*	Nordic Nutrition Recommendations, 2004
UK	18 g **	Department of Health, 1991
USA	38 g, men 19–50 years 31 g, men 50+ years 25 g, women 19–50 years 21 g, women 50+ years***	Institute of Medicine, 2002

Recommended dietary fiber intake

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