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BIODIVERSITÉ ET LE MICROBIOME HUMAIN

Caroline Roduit, Children‘s Hospital Zürich, Allergy Research Group and CK-CARE

Bern, 15 Januar 2016

The incidence of allergic, autoimmune and inflammatory diseases

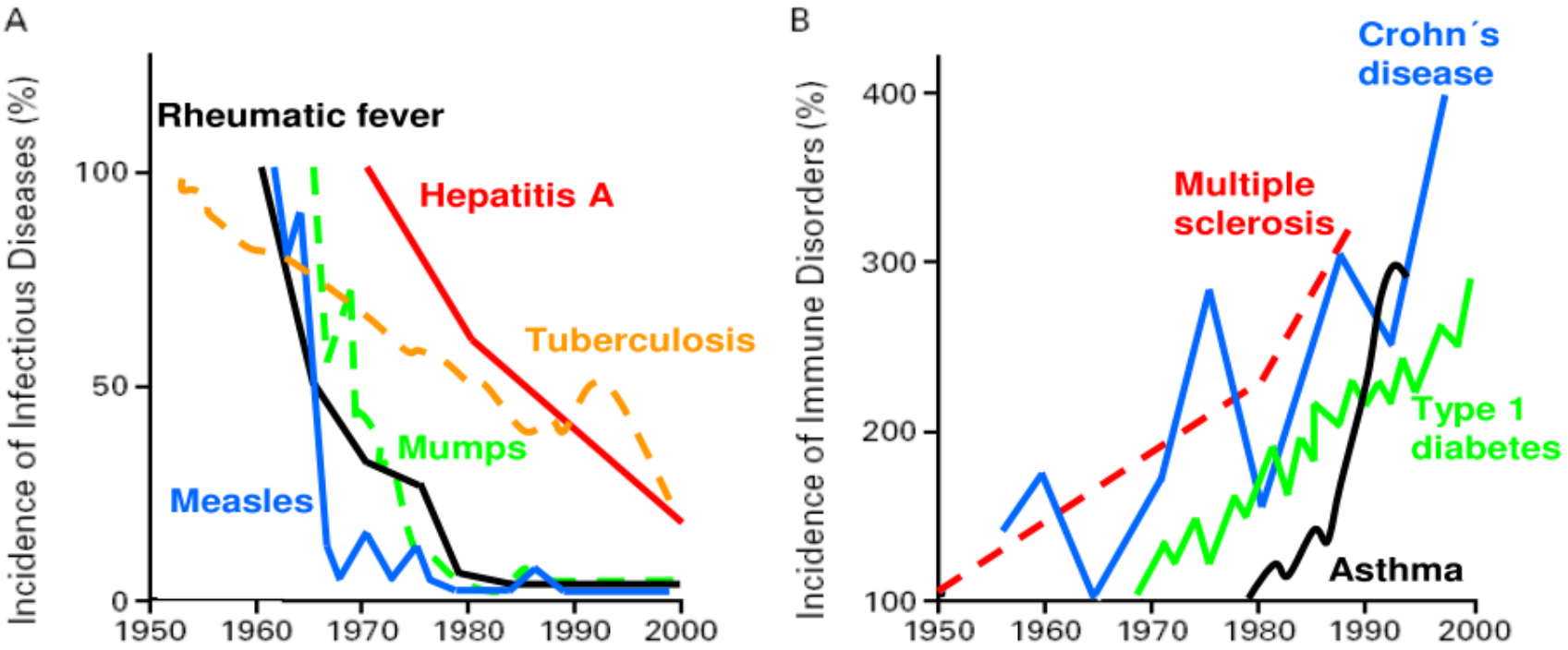
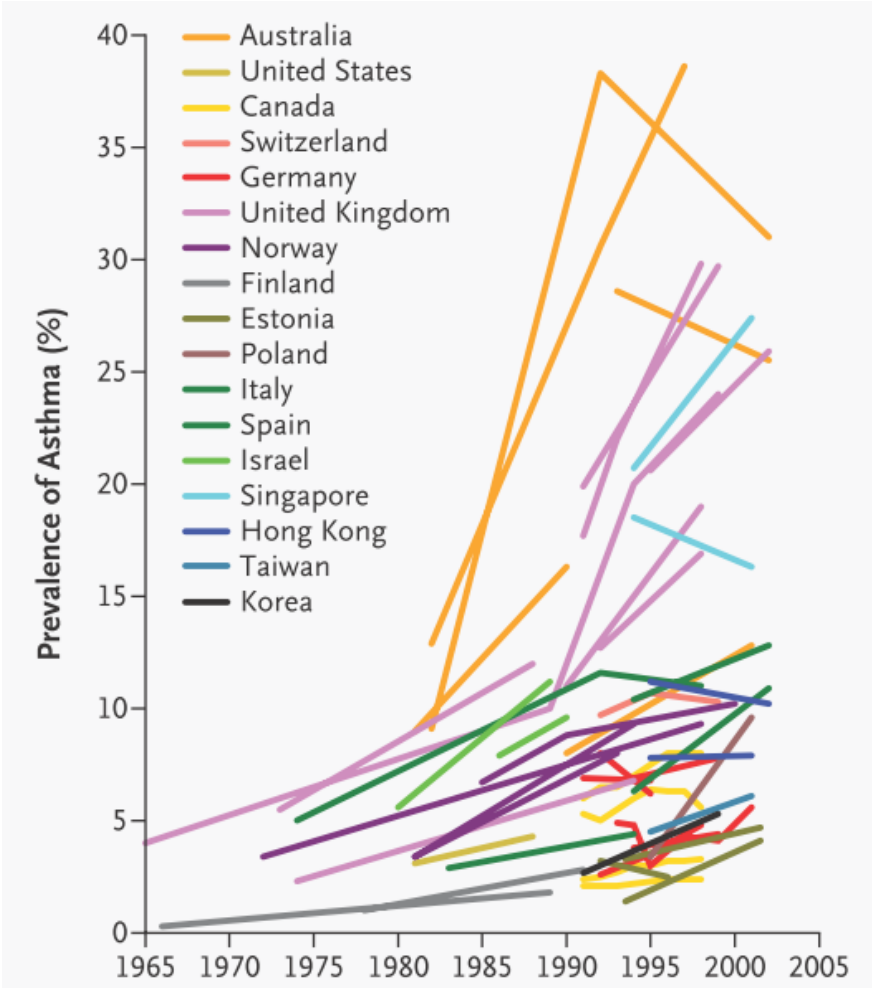


Figure 1. Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1950 to 2000.

J.F. Bach, NEJM 2002

The incidence of asthma in childhood



Eder, Ege, von Mutius, NEJM 2006

The hygiene hypothesis

Hay fever, hygiene, and household size

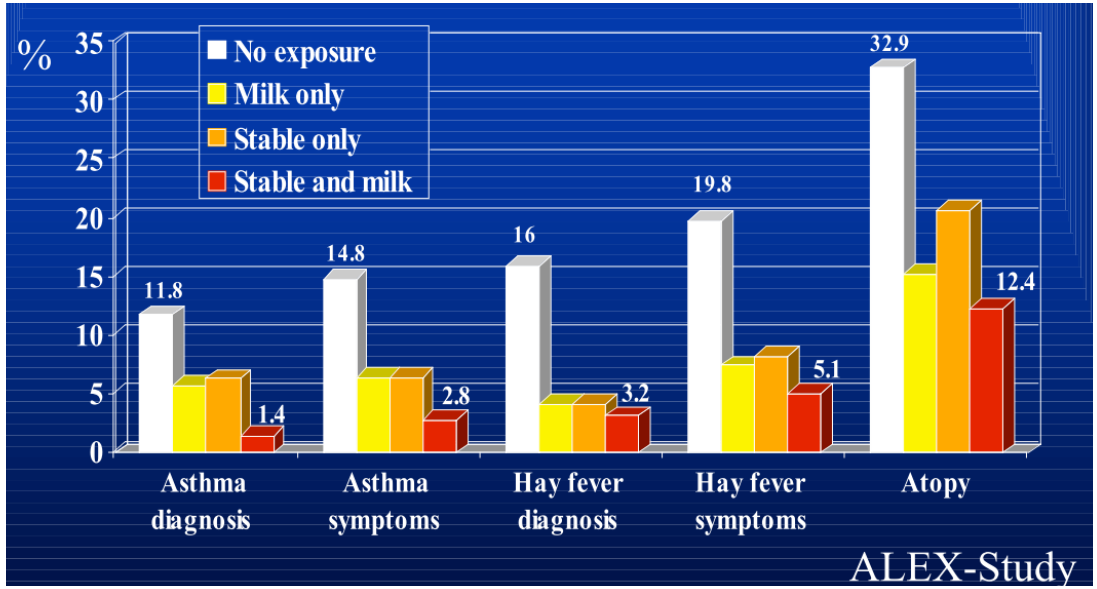
David P Strachan

- Less hay fever and atopic dermatitis among children with siblings, large families, having most likely more infections by contact as single children.

- Evidences from various studies suggested that “the hygiene hypothesis” plays a large role in the allergy epidemic.

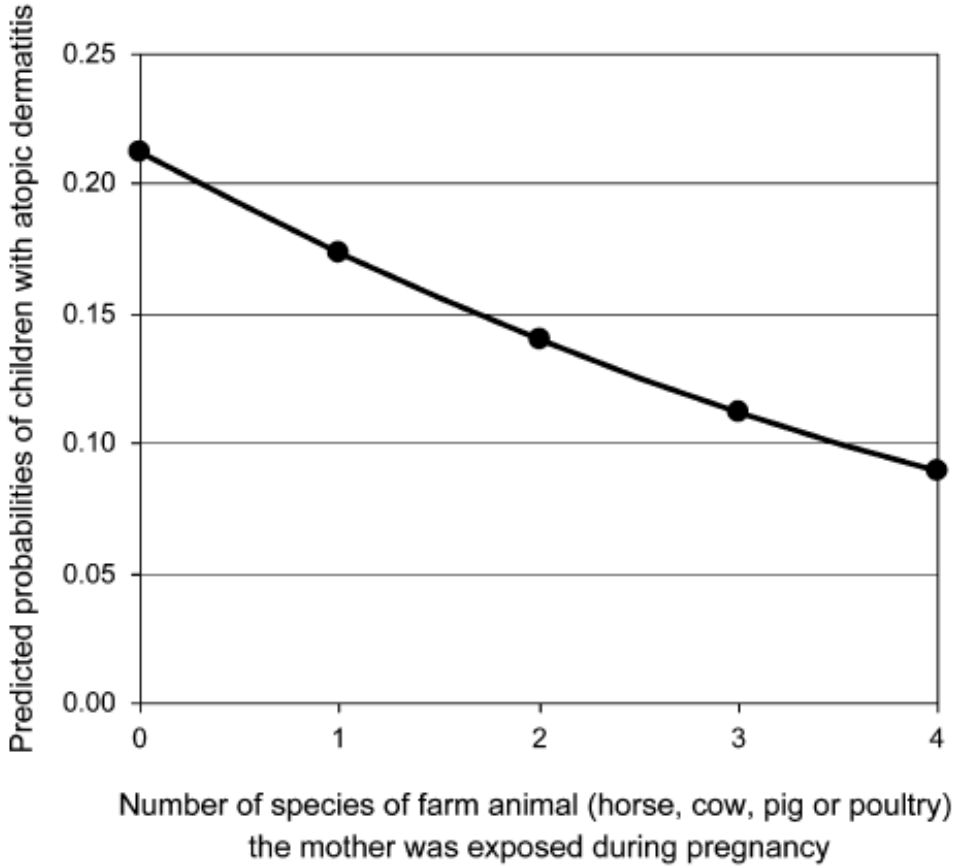
Strachan D. Br. Med J. 1989

Farm environment protects against allergies



Riedler et al. Lancet 2001

Prenatal exposure to an increasing number of farm animal species protects against atopic dermatitis



Roduit et al. JACI 2011

Exposure to a large diversity of microbes reduces the risk of asthma

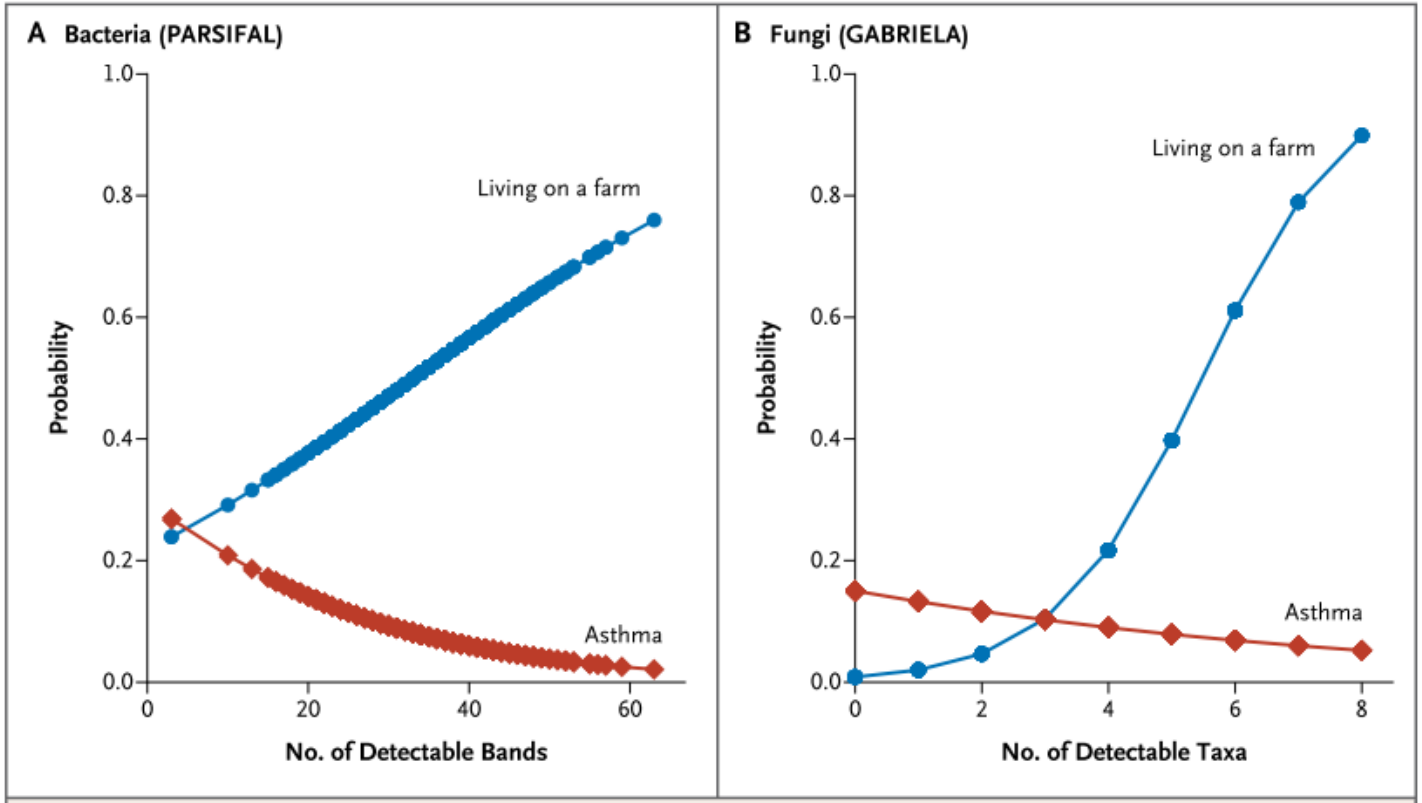
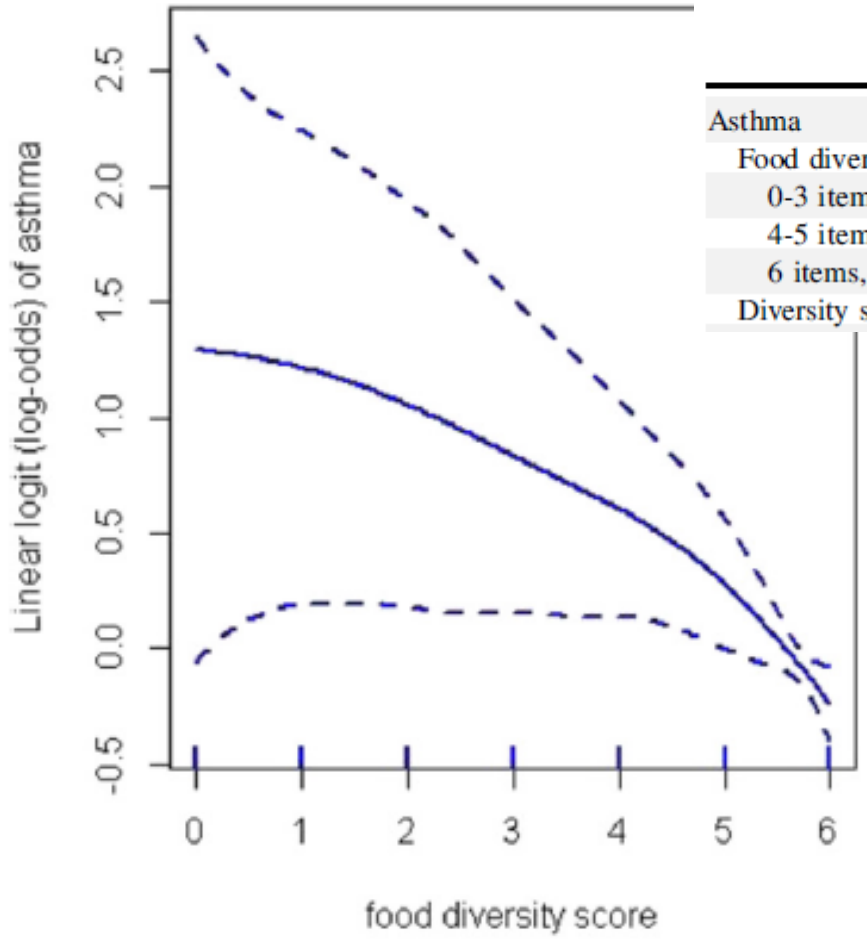


Figure 3. Relationship between Microbial Exposure and the Probability of Asthma.

In both the PARSIFAL study and GABRIELA, the range of microbial exposure was inversely associated with the probability of asthma.

Ege et al. NEJM 2011

Early postnatal environment: increased diversity of food introduced in the 1st year protects against asthma



	Model 1		
	No.	OR	95% CI
Asthma			
Food diversity score within 1st year			
0-3 items	7/37	**3.58**	**1.47-8.75**
4-5 items	33/263	**2.20**	**1.33-3.64**
6 items, reference	34/556	1	
Diversity score, continuous	74/856	**0.73**	**0.61-0.87**

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**Diversity score with major food items: vegetables or fruits, any cereals, meat, bread, cake and yogurt*

Roduit et al. JACI 2014

Lifestyle changes in westernised countries:
Reduction of consumption of fiber in industrialized countries compared to developing countries

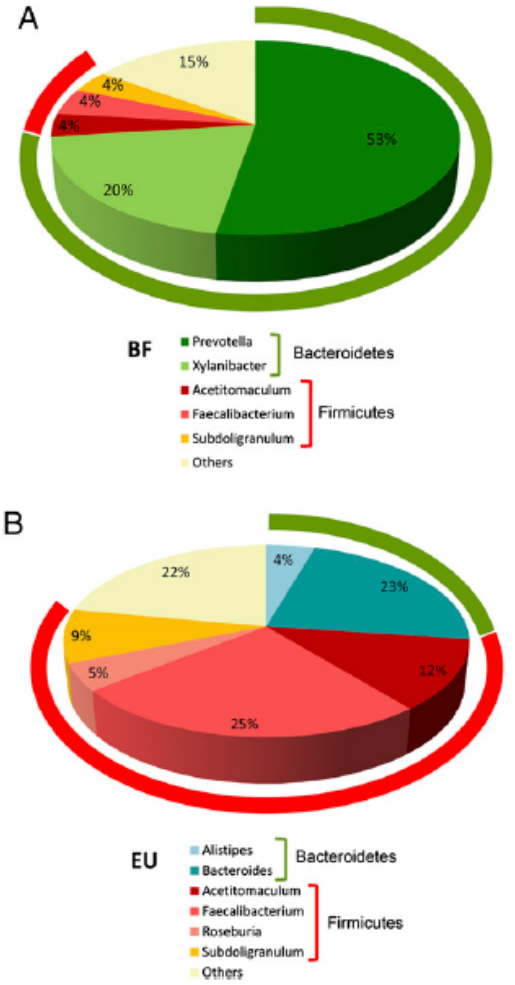
- In **industrialized countries**:
average consumption of fibers: **20-25 g per day**

- While in **developing countries**:
100 g per day, (great consumption of vegetal products)

Impact of diet on gut microbiota

- Comparison of the fecal microbiota of European children (EU) and that of children from a rural African village of Burkina Faso (BF), where the diet is high in fiber content.

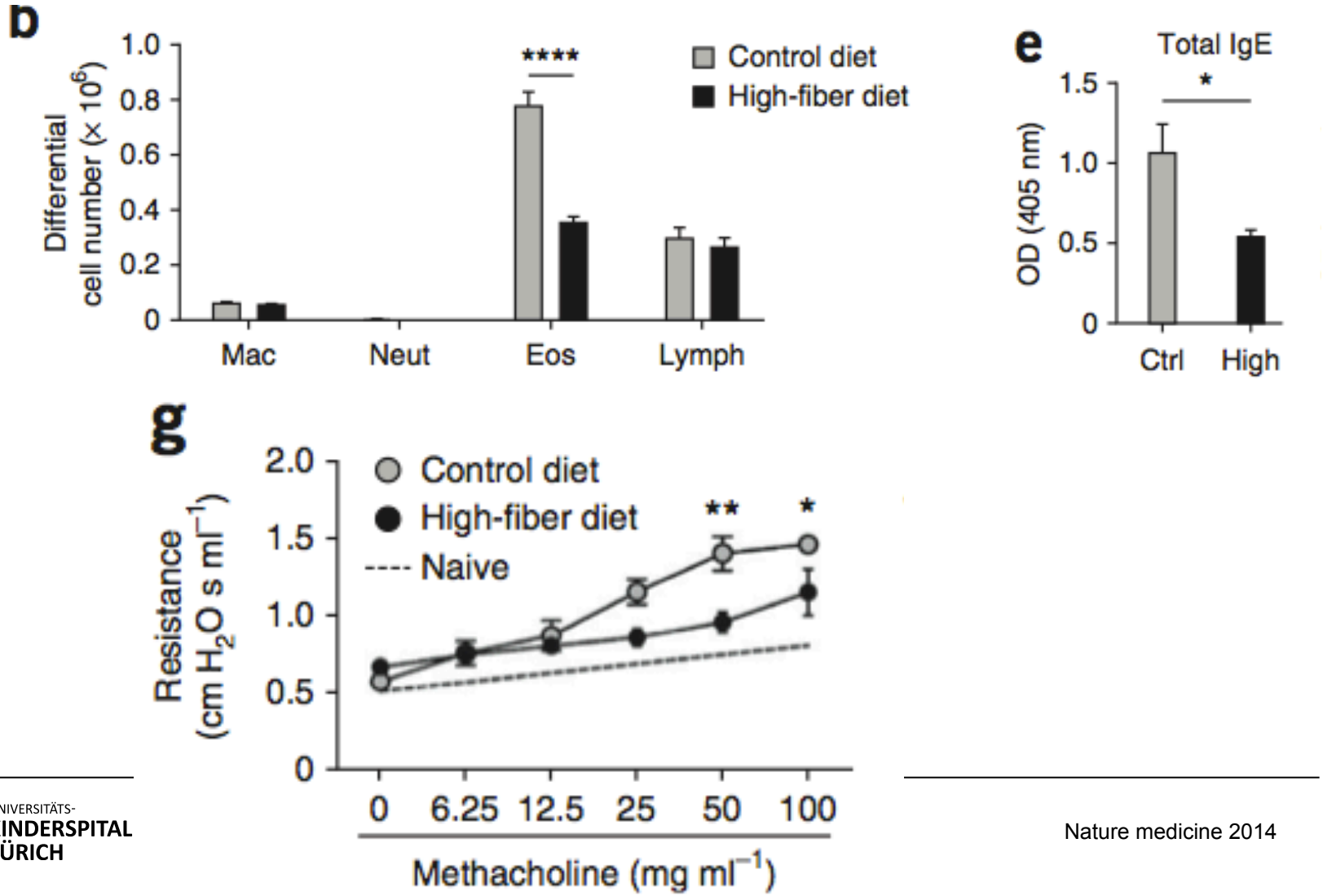
- Among children from Africa: a lower prevalence of allergic diseases was observed compared with the prevalence seen in children from western Europe



De Filippo C, et al. Proc Natl Acad Sci U S A 2010

Gut microbiota metabolism of dietary fiber influences allergic airway disease and hematopoiesis

Aurélien Trompette[1], Eva S Gollwitzer[1], Koshika Yadava[1], Anke K Sichelstiel[1], Norbert Sprenger[2], Catherine Ngom-Bru[2], Carine Blanchard[2], Tobias Junt[3], Laurent P Nicod[1], Nicola L Harris[4] & Benjamin J Marsland[1]



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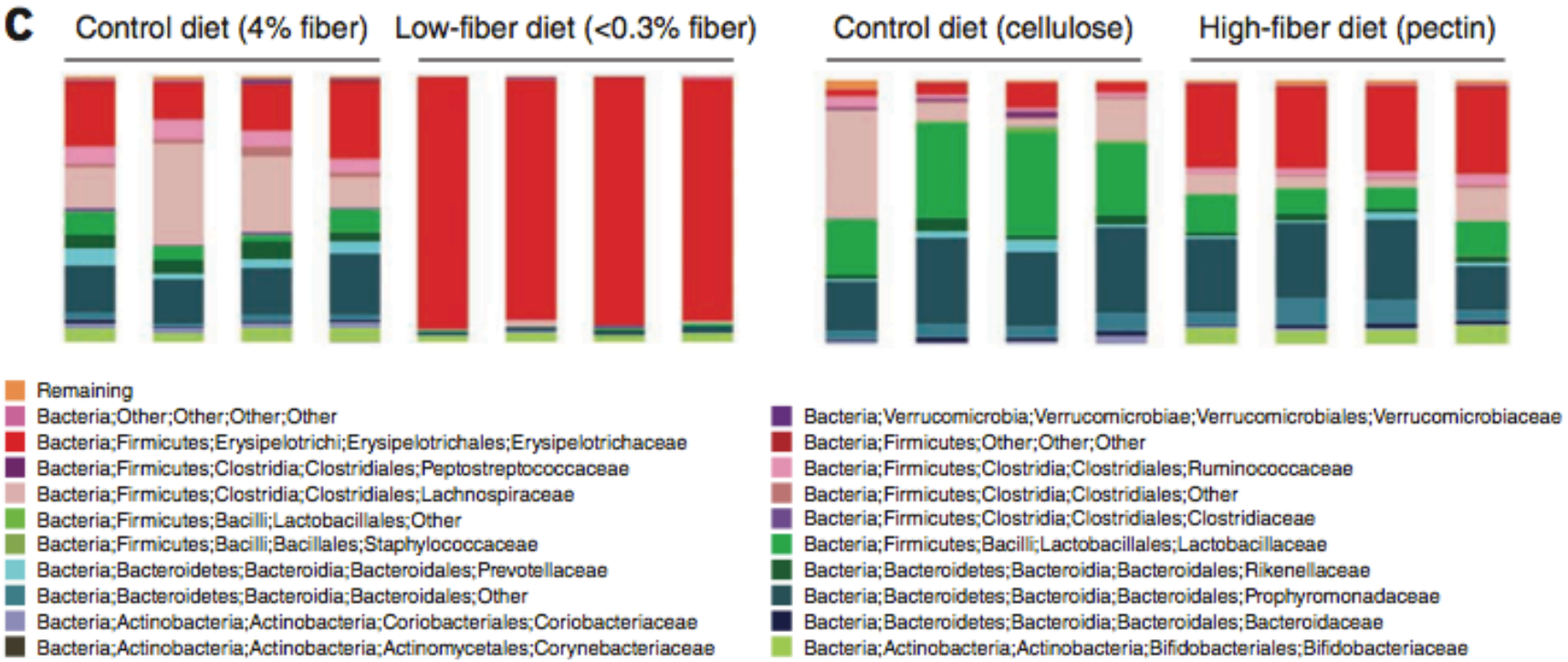


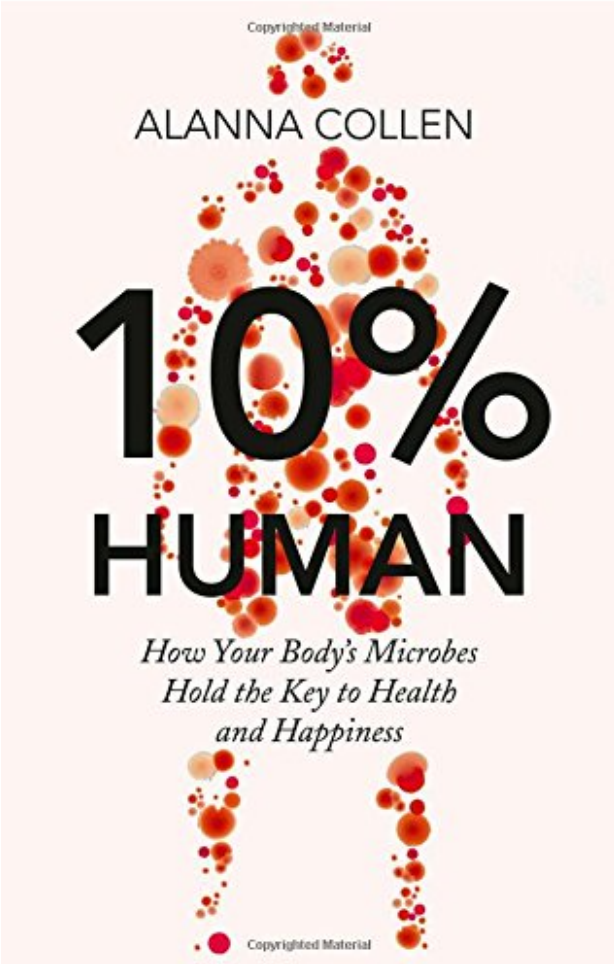
Human microbiome

Cells:
- 10% human
- 90% microbes

-> **Microbiota** = micro-organism within a given niche

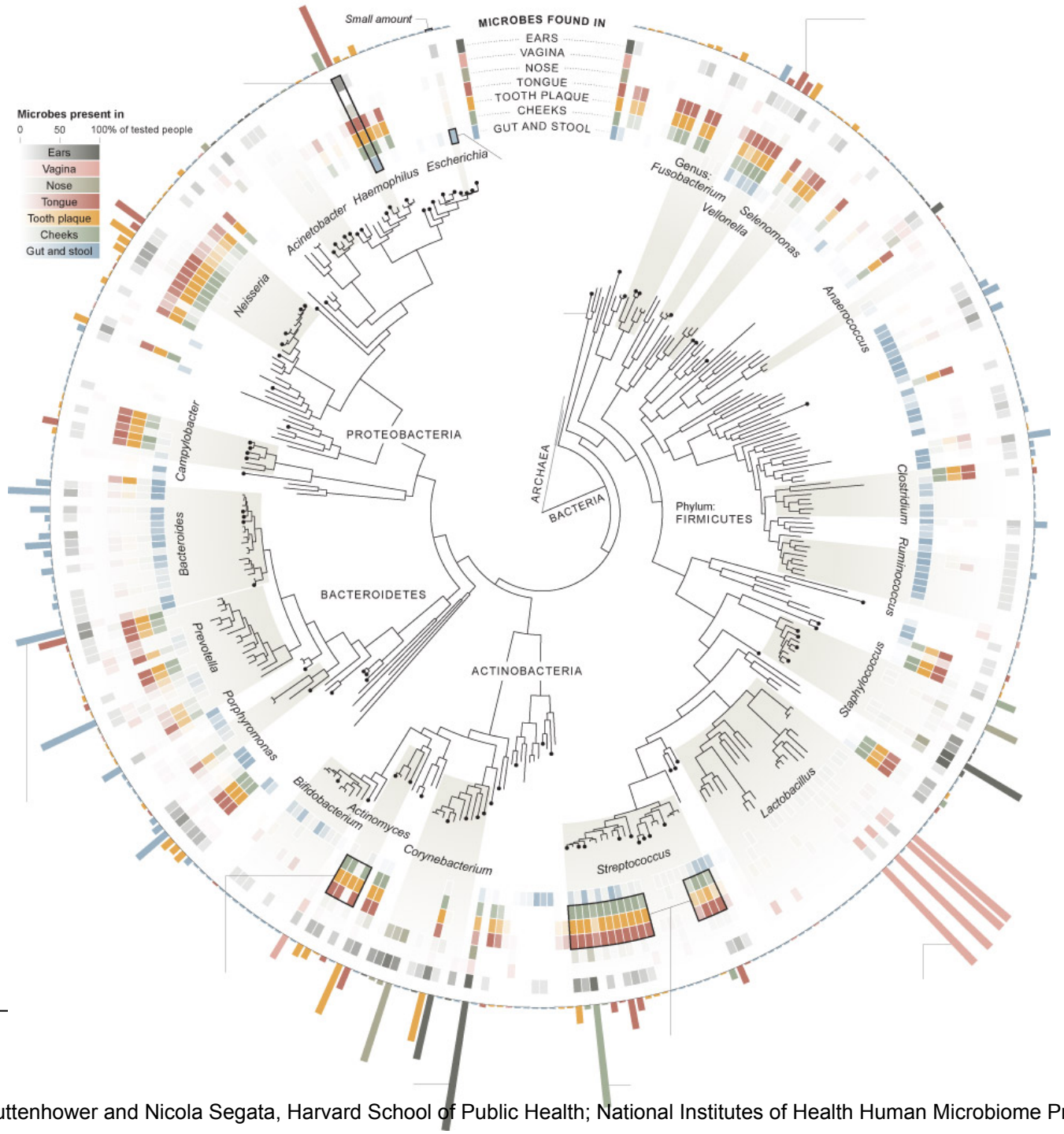
Genes:
- 1% human
- 99% microbes

-> **Microbiome** = all the genetic material of micro-organisms within a given niche



- Ley R., et al. Ecological and evolutionary forces shaping microbial diversity in the human intestine. Cell 2006
- Qin J., et al. A human gut microbial gene catalogue established by metagenomic sequencing. Nature 2010

Human microbiome



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Curtis Huttenhower and Nicola Segata, Harvard School of Public Health; National Institutes of Health Human Microbiome Project

Are we born with bacteria?

Review
Microbial Programming of Health and Disease Starts during Fetal Life

Petya T. Koleva*[1], Ji-Sun Kim[2], James A. Scott[2], and Anita L. Kozyrskyj[1,3]

The pioneer microbiota of the neonatal gut are essential for gut maturation, and metabolic and immunologic programming. Recent research has shown that early bacterial colonization may impact the occurrence of disease later in life (microbial programming). Despite early conflicting evidence, it has long been considered that the womb is a sterile environment and human microbial colonization begins at birth. In the last few years, several findings have reiterated the presence of microbes in infant first stool (meconium) and pointed to the existence of in utero microbial colonization of the infant gut. The dominant bacterial taxa detected in meconium specimens belong to the *Enterobacteriaceae* family (*Escherichia* genus) and lactic acid bacteria (notably members of the genera *Leuconostoc*, *Enterococcus*, and *Lactococcus*). Maternal atopy promotes dominance of *Enterobacteriaceae* in newborn meconium, which in turn may lead to respiratory problems in the infant. This microbial interaction with the host immune system may in fact, originate during fetal life. Our review evaluates the evidence for an intrauterine origin of meconium microbiota, their composition and influences, and potential clinical implications on infant health.

Birth Defects Research (Part C) 105:265–277, 2015.

Key words: meconium; microbiota; fetal programming; infancy; childhood diseases

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ming; infancy; childhood

Gut microbiota alterations are associated with diseases:

- Crohn's disease	Diversity decrease – reduced *F. prausnitzii*
- Ulcerative colitis	Diversity decrease – reduced *A. muciniphila*
- Irritable bowel syndrome	Increased *Dorea* and *Ruminococcus*
- *Clostridium difficile* infection	Strong diversity decrease
- Obesity	Specific bacterial ratios (*Bacteroidetes/Firmicutes*)
- Colorectal cancer	Variation in *Bacteriodes* spp
- Celiac disease	Altered composition
- Allergy, asthma	Altered diversity
- Diabetes	
- Mental health disorders	
- Alzheimer	

➡ **Low diversity of the microbiome appears to be less healthy**

doi: 10.1111/cea.12253

Clinical & Experimental Allergy, **44**, 842–850

ORIGINAL ARTICLE Clinical Mechanisms in Allergic Disease

Low gut microbiota diversity in early infancy precedes asthma at school age

T. R. Abrahamsson[1], H. E. Jakobsson[2], A. F. Andersson[3], B. Björkstén[4,5], L. Engstrand[2,3] and M. C. Jenmalm[1,6]

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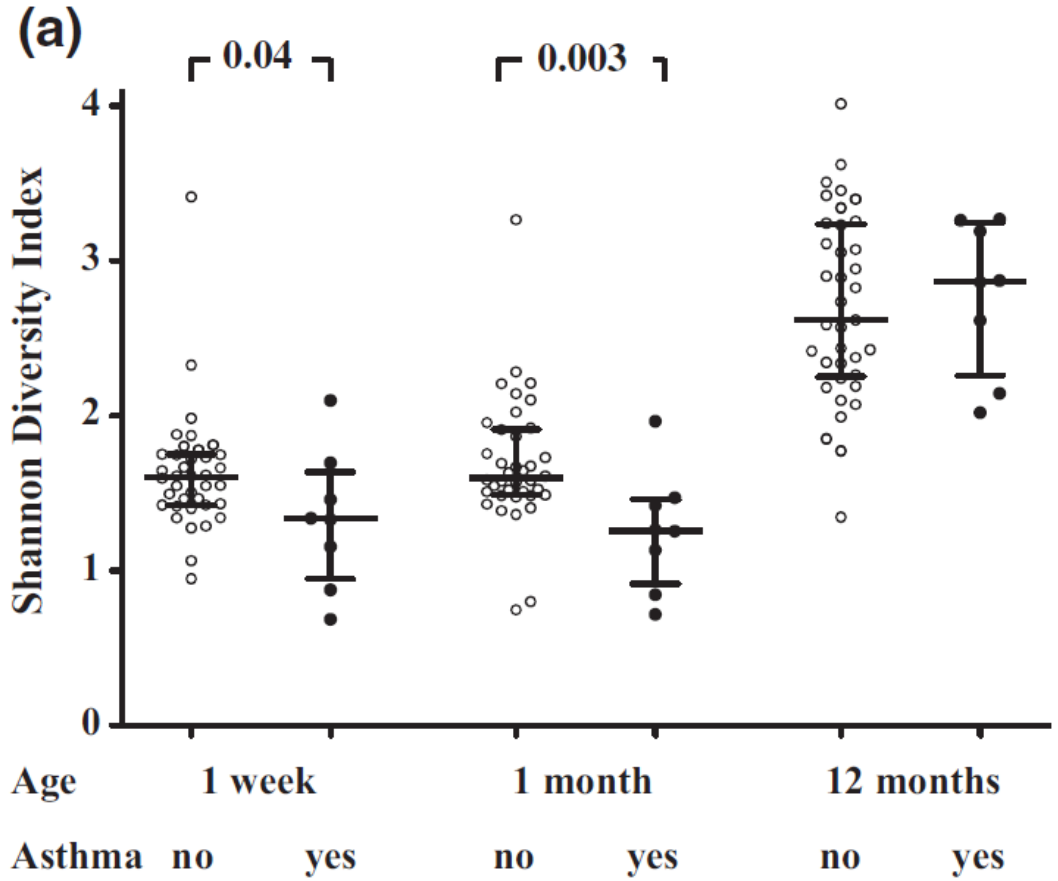
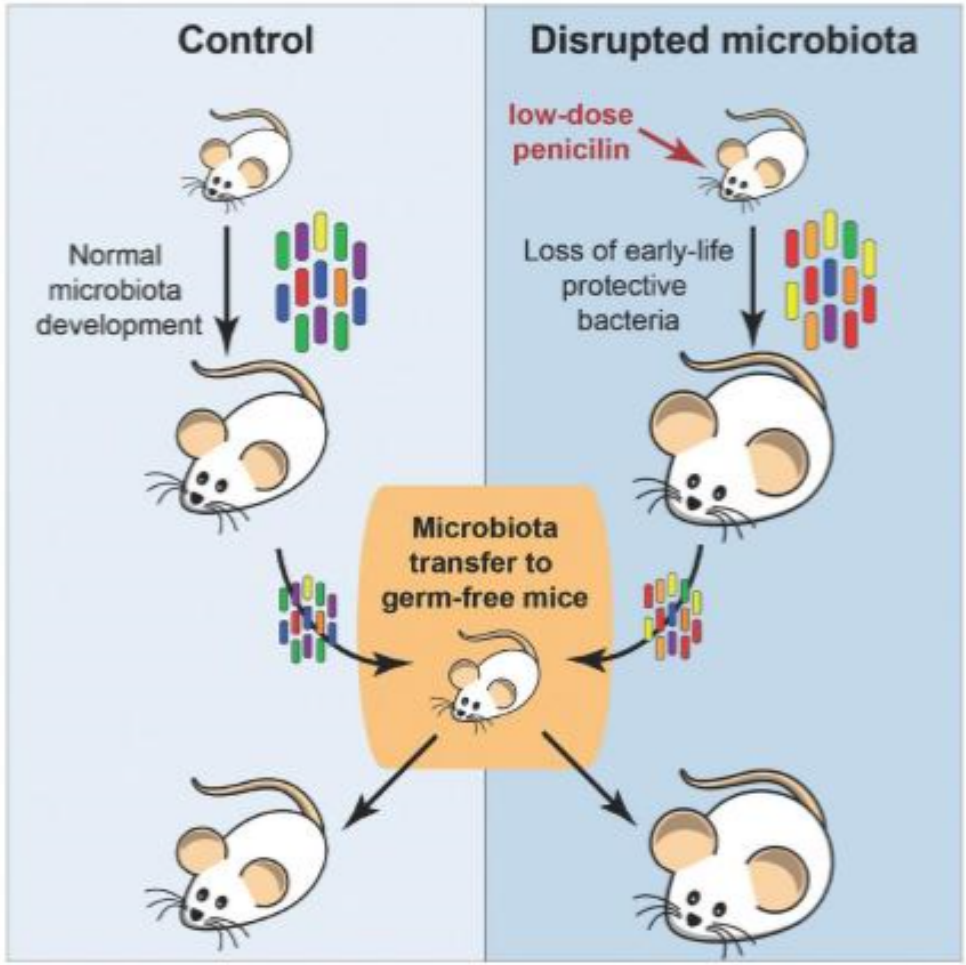


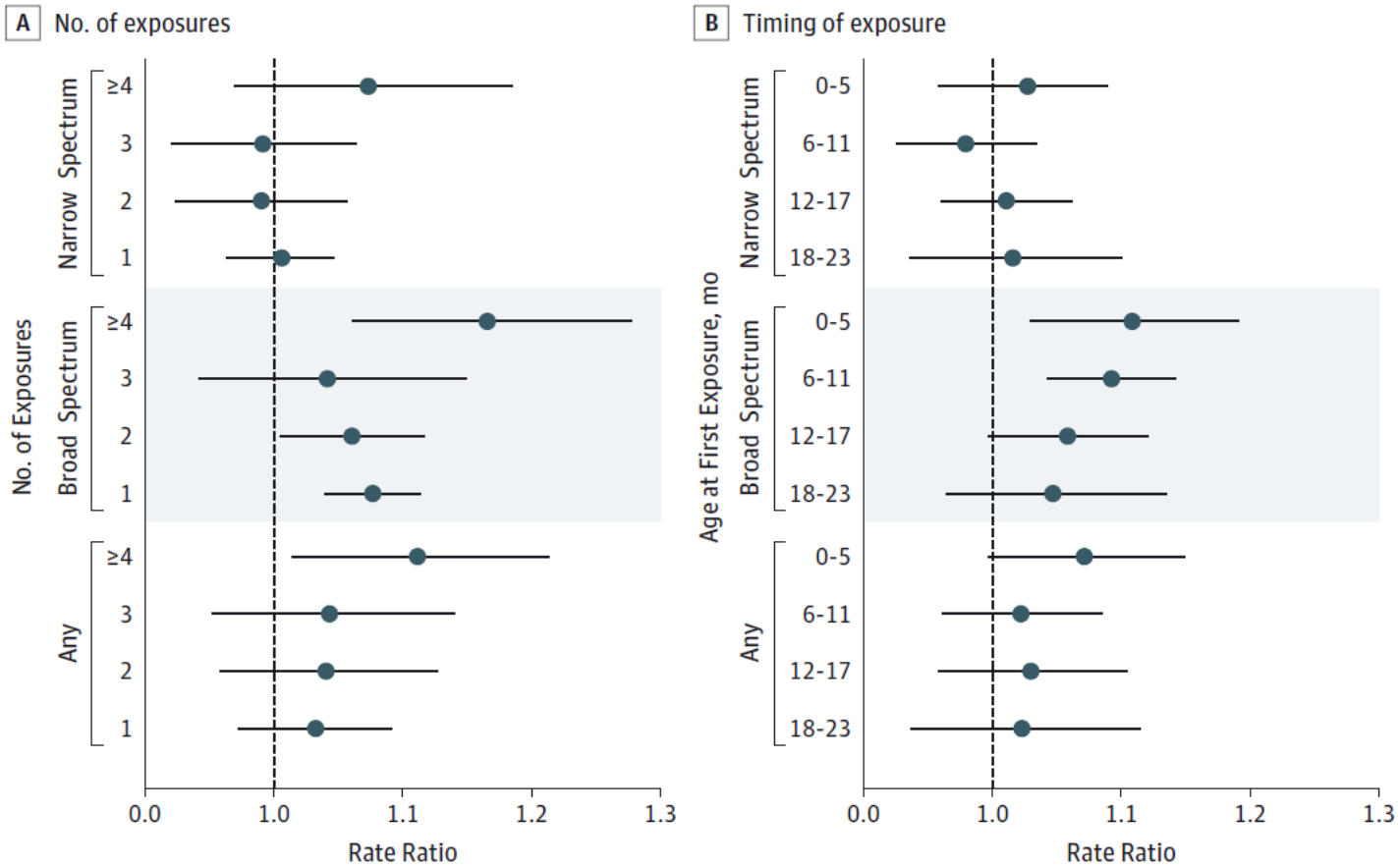
Gut microbiota and obesity



Transferring the gut microbes of mice treated with low dose of penicillin from early life into germ-free mice results in weight gain in the recipient mice

Ellekilde M. et al. Transfer of gut microbiota from lean and obese mice to antibiotic-treated mice. Scientific Reports 2014

Antibiotic exposure during the first 24 months promotes obesity later in life



Bailey LC. et al. Association of antibiotics in infancy with early childhood obesity. JAMA Pediatr. 2014

frontiers in NEUROLOGY

OPINION ARTICLE
published: 04 April 2014
doi: 10.3389/fneur.2014.00043

The gastrointestinal tract microbiome and potential link to Alzheimer's disease

James M. Hill[1,2,3], *Surjyadipta Bhattacharjee*[1], *Aileen I. Pogue*[4] and *Walter J. Lukiw*[1,3,4,5]*

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[3] Department of Ophthalmology, Louisiana State University Health Sciences Center, New Orleans, LA, USA
[4] Alchem Biotek, Toronto, ON, Canada
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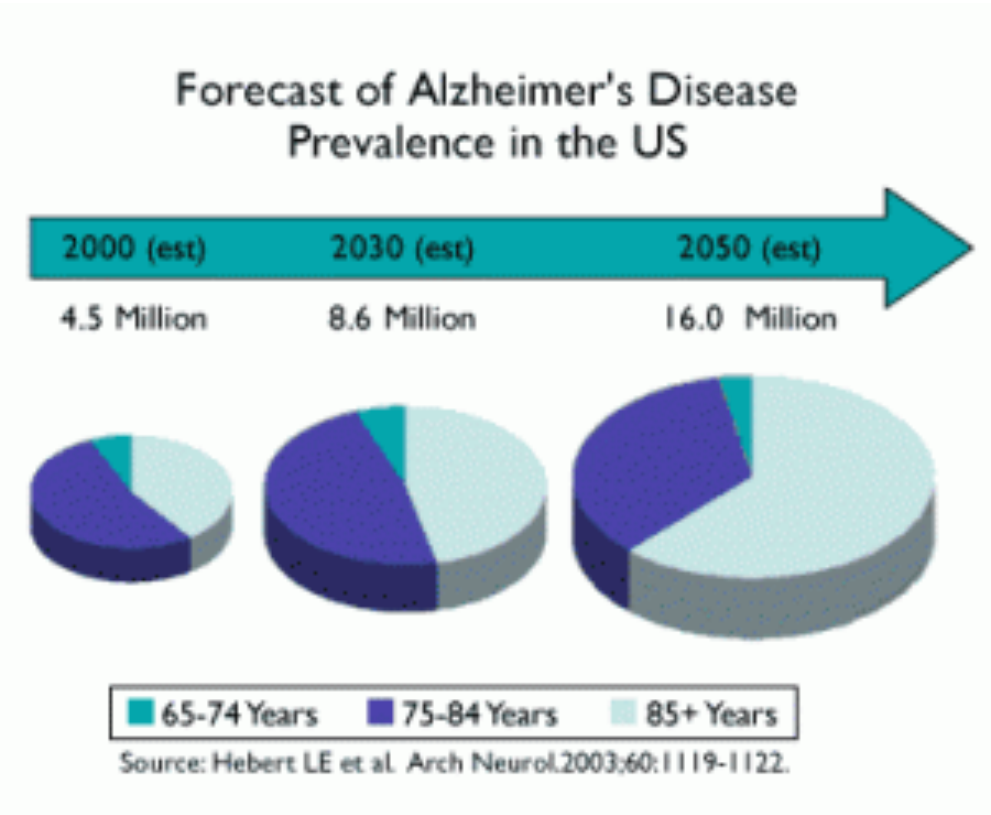
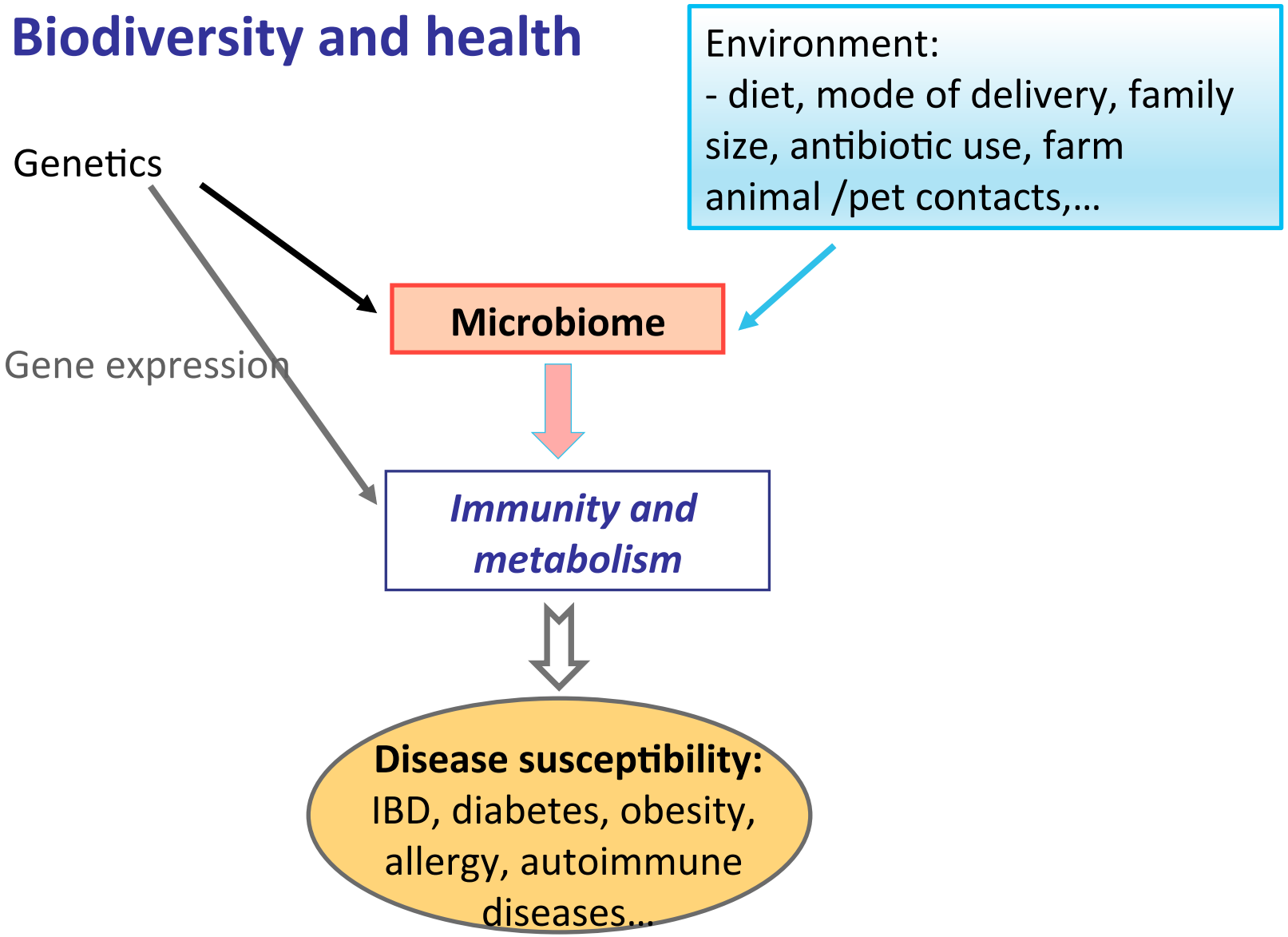
Keywords: Alzheimer's disease, microbiome, genetic complexity, evoluti



Biodiversity and health



The biodiversity hypothesis

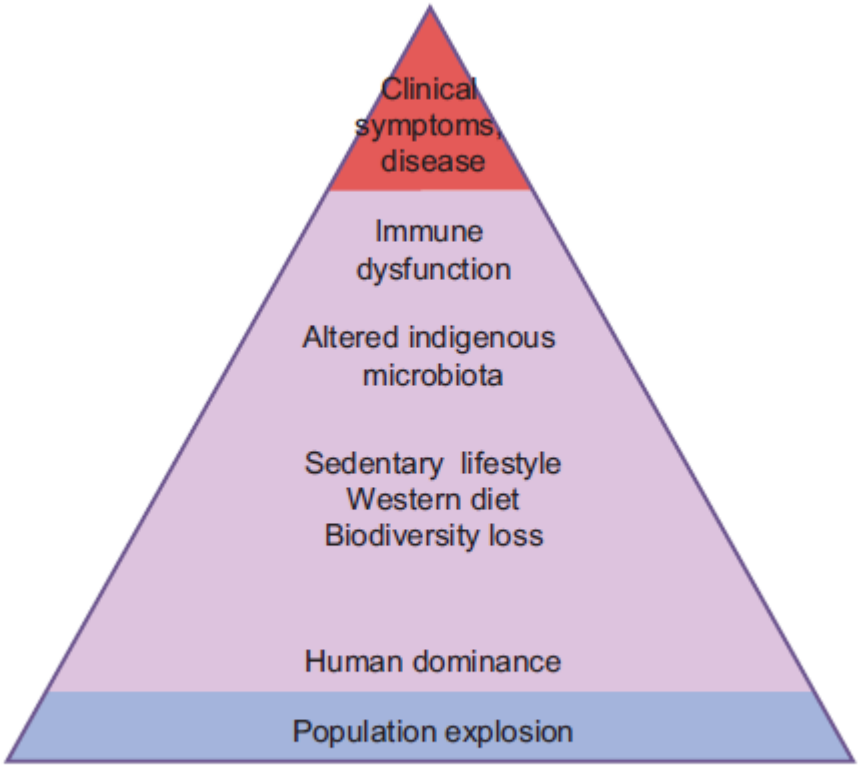


Figure 1. Biodiversity loss, together with sedentary lifestyle and unhealthy diet, may lead to immune dysregulation, poor tolerance, and ultimately to clinical disease. Modified from (116).

Von Hertzen L., et al. Annals of Medicine 2015

Haahtela *et al. World Allergy Organization Journal* 2013, **6**:3
http://www.waojournal.org/content/6/1/3

WAO journal
WORLD ALLERGY ORGANIZATION

POSITION ARTICLE AND GUIDELINES **Open Access**

The biodiversity hypothesis and allergic disease: world allergy organization position statement

Tari Haahtela[1*], Stephen Holgate[2], Ruby Pawankar[3], Cezmi A Akdis[4], Suwat Benjaponpitak[5], Luis Caraballo[6], Jeffrey Demain[7], Jay Portnoy[8], Leena von Hertzen[1], and WAO Special Committee on Climate Change and Biodiversity

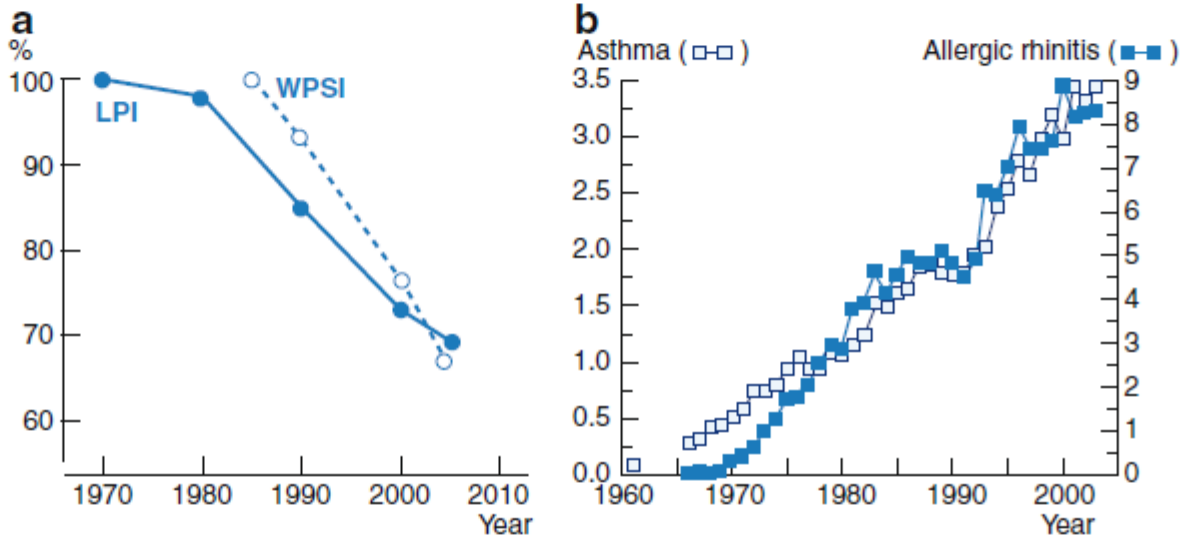
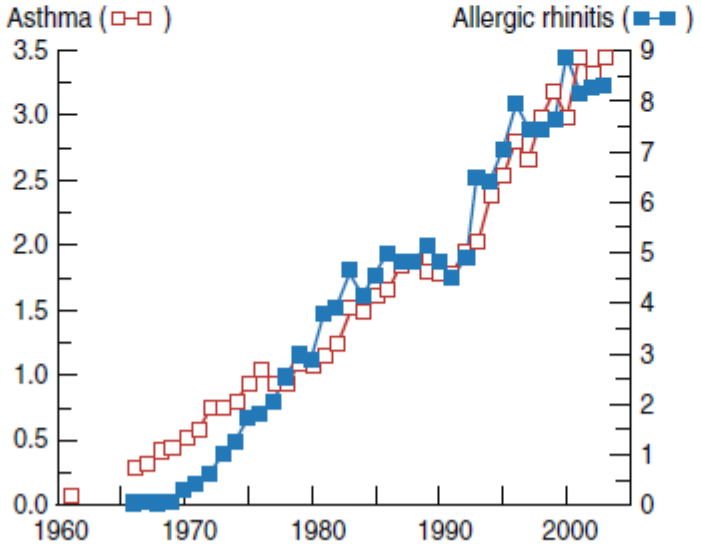
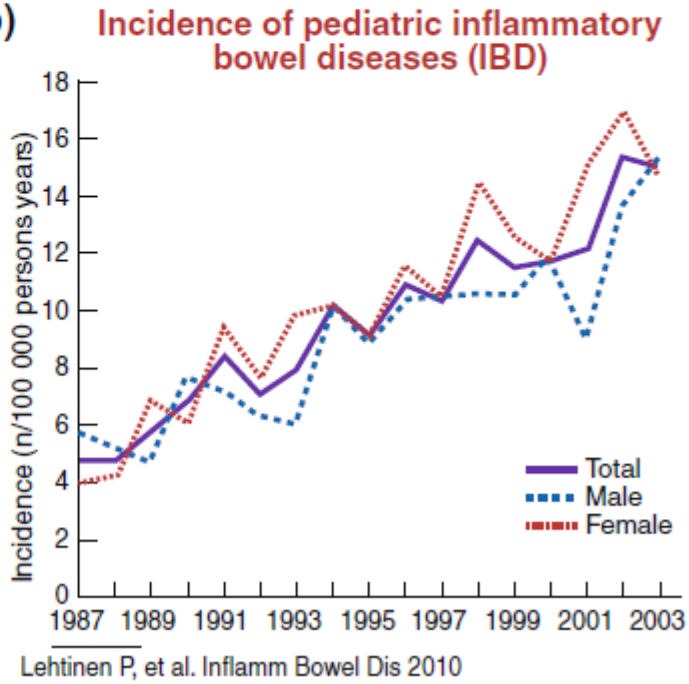


Figure 1 Two global megatrends in biodiversity and public health. (**a**) Declining biodiversity (percentage change) since 1970 as measured by two indices. WPSI=Waterbird Population Status Index; LPI=Living Planet Index [14]. (**b**) Increasing trends in the prevalence of inflammatory civilization diseases, asthma and allergic rhinitis among military conscripts in 1966-2003 [165] as an example (modified from ref. [14]).

a)

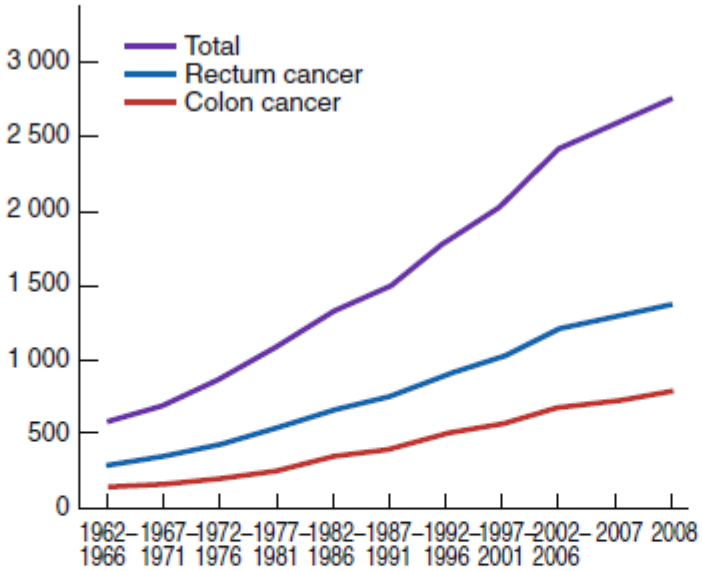


b)



Lehtinen P, et al. Inflamm Bowel Dis 2010

c)



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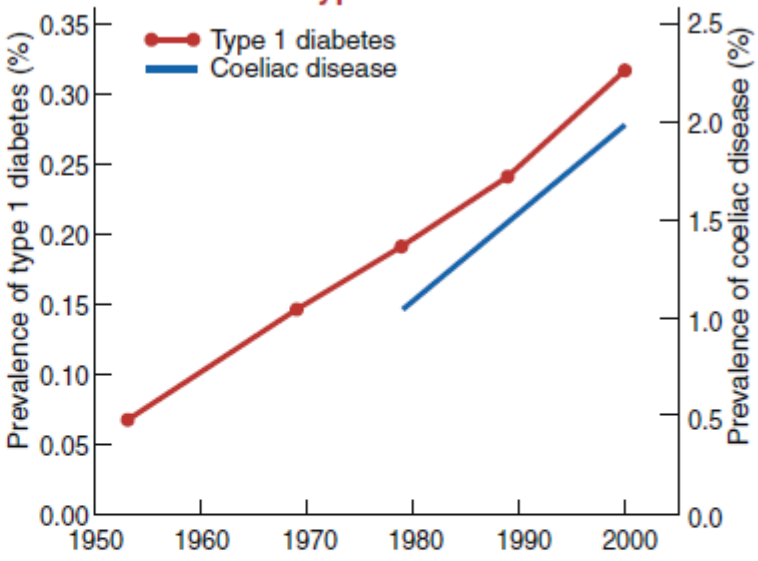

Lohi S, et al. Aliment Pharmacol Ther 2007

Everything that we eat, drink, touch, and breathe is reflected in our microbiota

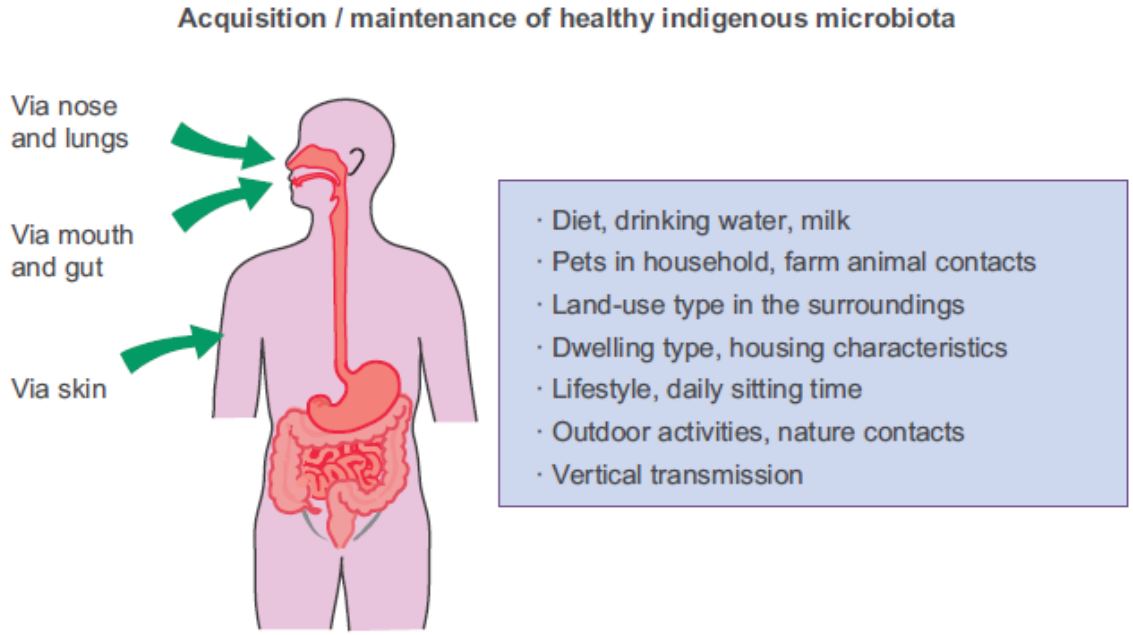

Figure 2. 'We are what we host, and we host what we eat, touch, and breathe'. Outdoor activities in biodiverse environments together with unprocessed food can provide us with microbial exposures necessary for the development and maintenance of healthy balanced microbiota and immunoregulatory circuits.

Von Hertzen L., et al. Annals of Medicine 2015

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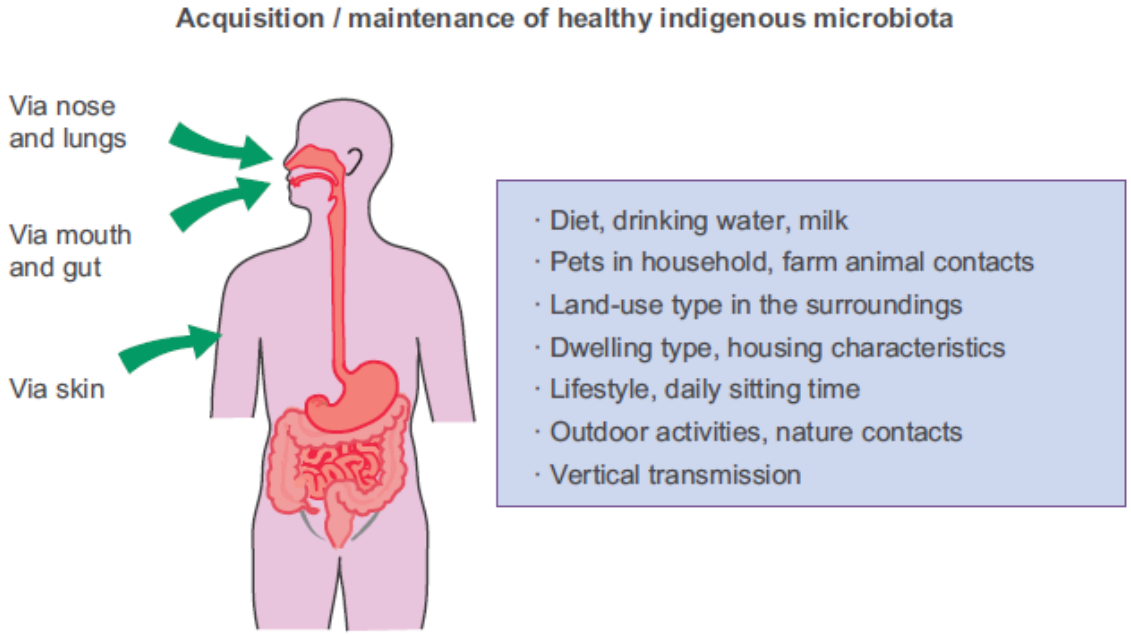

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