

Eric Claassen, Lisette de Jong en Heidi Klijsen

Eric Claassen, Immunoloog
Professor Athena Institute VU Amsterdam

Herewith declared conflict of interest as a non-exclusive and independent expert advisor to numerous industrial, NGO, private and public academic institutions and (EU) consortia (over 160 clients).

prof.eric.claassen@gmail.com



MY SLIDES ARE AVAILABLE THROUGH TODAY'S ORGANISERS

RESEARCH ARTICLE

How ownership rights over microorganisms affect infectious disease control and innovation: A root-cause analysis of barriers to data sharing as experienced by key stakeholders

Carolina dos S. Ribeiro¹*, Martine Y. van Roode², George B. Haringhuizen¹, Marion P. Koopmans², Eric Claassen³, Linda H. M. van de Burgwal^{3,4}



SCIENCE sciencemag.org

26 OCTOBER 2018 • VOL 362 ISSUE 6413 405

POLICY FORUM

GLOBAL HEALTH

Threats to timely sharing of pathogen sequence data

The Nagoya Protocol may impose costs and delays

RESEARCH COOPERATION: COVID-19

BLOCKCHAIN
OUTBREAK

Blockchain-facilitated sharing to enhance outbreak R&D

Technology may help overcome nontechnological barriers

van der Waal, M. B., Ribeiro, C. D. S., Ma, M., Haringhuizen, G. B., Claassen, E., & van de Burgwal, L. H. (2020). Science, 368(6492), 719-721.

VU



VRIJE
UNIVERSITEIT
AMSTERDAM

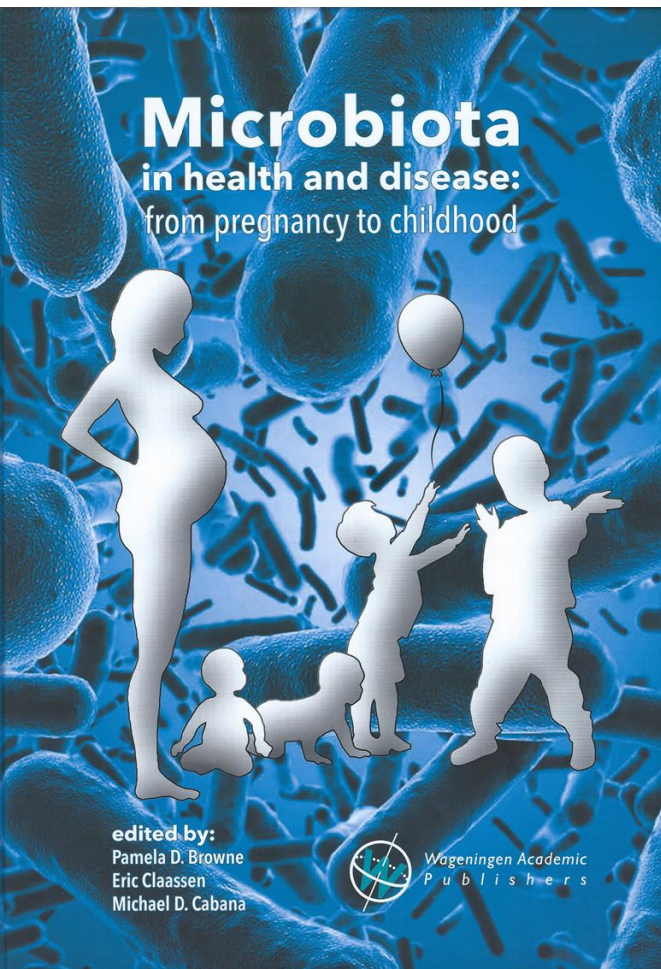
Faculteit der
Aard- en Levens-
wetenschappen



**My day job is
starting
companies for
infectious
disease
diagnostics and
vaccines in a
One Health
setting mainly
for zoonoses
(animal to man)**

Ik werk sinds 1980 aan de immunologie van slijmvliezen van de darm en sinds 1987 aan melkzuur bacterieen

Gerritse, Posno, Schellekens, Boersma & Claassen E. (1990) Oral administration of TNP-lactobacillus conjugates in mice: a model for evaluation of mucosal and systemic immune responses and memory formation elicited by transformed Lactobacilli. *Res. Microbiology*, 141, 955-962.



Eric Claassen, Lisette de Jong en Heidi Klijsen



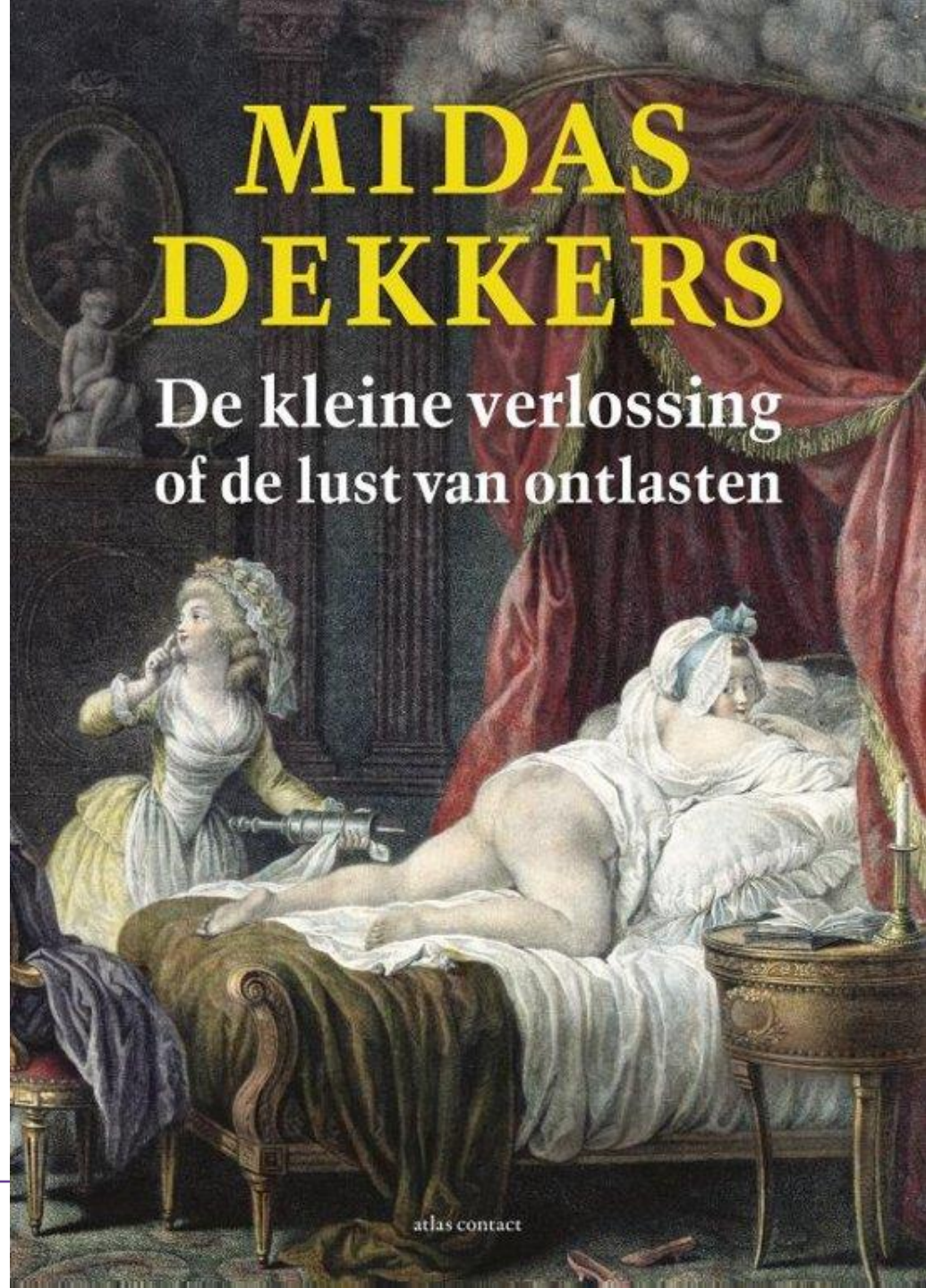
KOMRIJ'S
Kaka
fonie

*Encyclopedie
van de Stront*



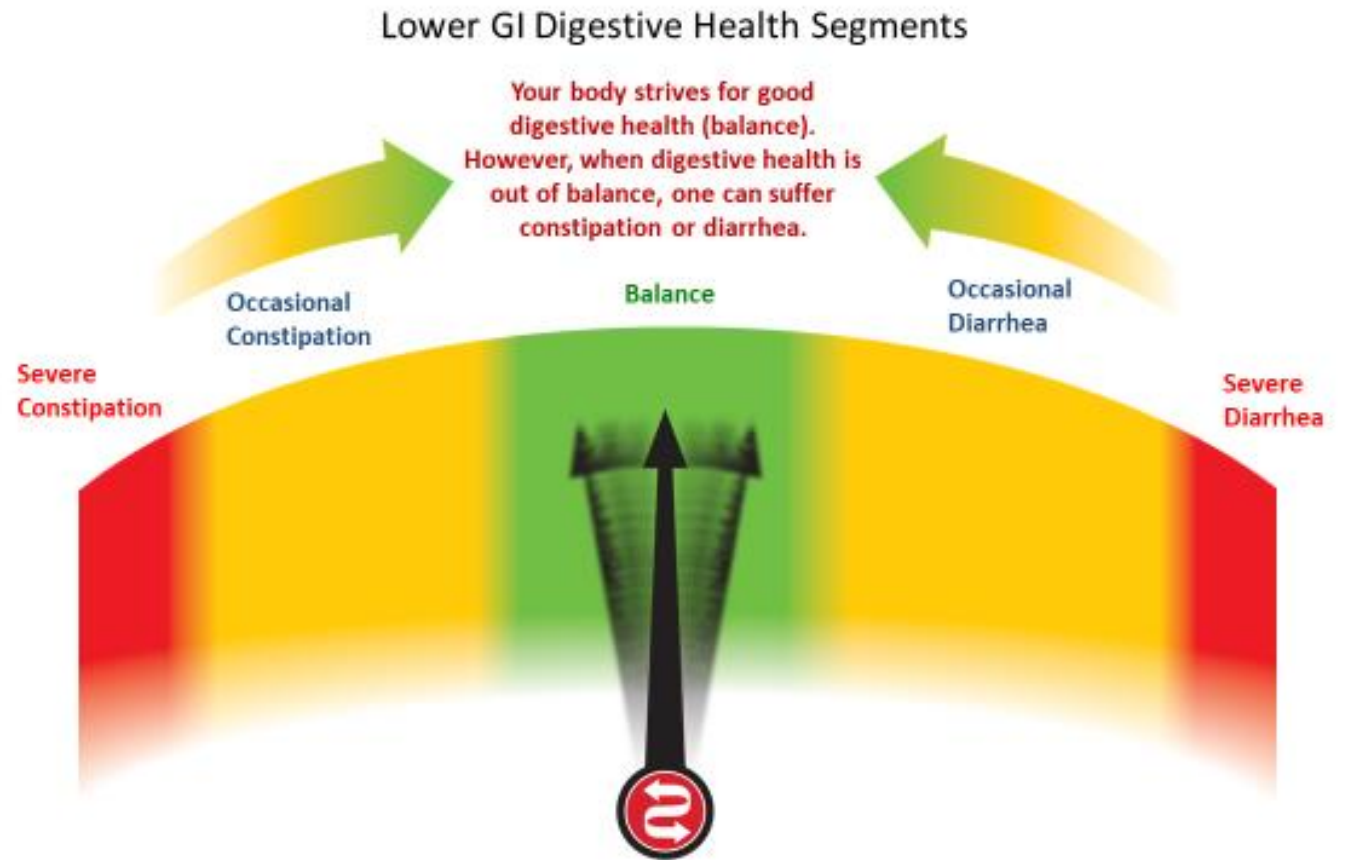
MIDAS
DEKKERS

De kleine verlossing
of de lust van ontlasten

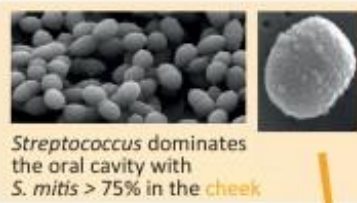


Bristol Stool Chart

Type 1		Losse harde keutels, zoals noten (moeilijk uit te scheiden)
Type 2		Als een worst, maar klonterig
Type 3		Als een worst, maar met barstjes aan de buitenkant
Type 4		Als een worst of slang, glad en zacht
Type 5		Zachte keutels met duidelijke randen (makkelijk uit te scheiden)
Type 6		Zachte stukjes met gehavende randen, een papperige uitscheiding
Type 7		Waterig, geen vaste stukjes. Helemaal vloeibaar



A map of diversity in the human microbiome



Streptococcus dominates the oral cavity with *S. mitis* > 75% in the cheek



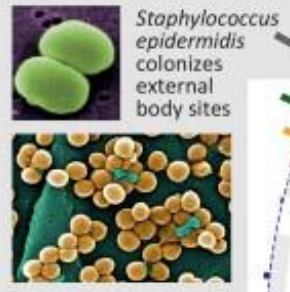
Propionibacterium acnes lives on the skin and nose of most people



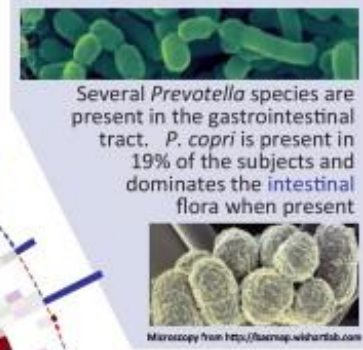
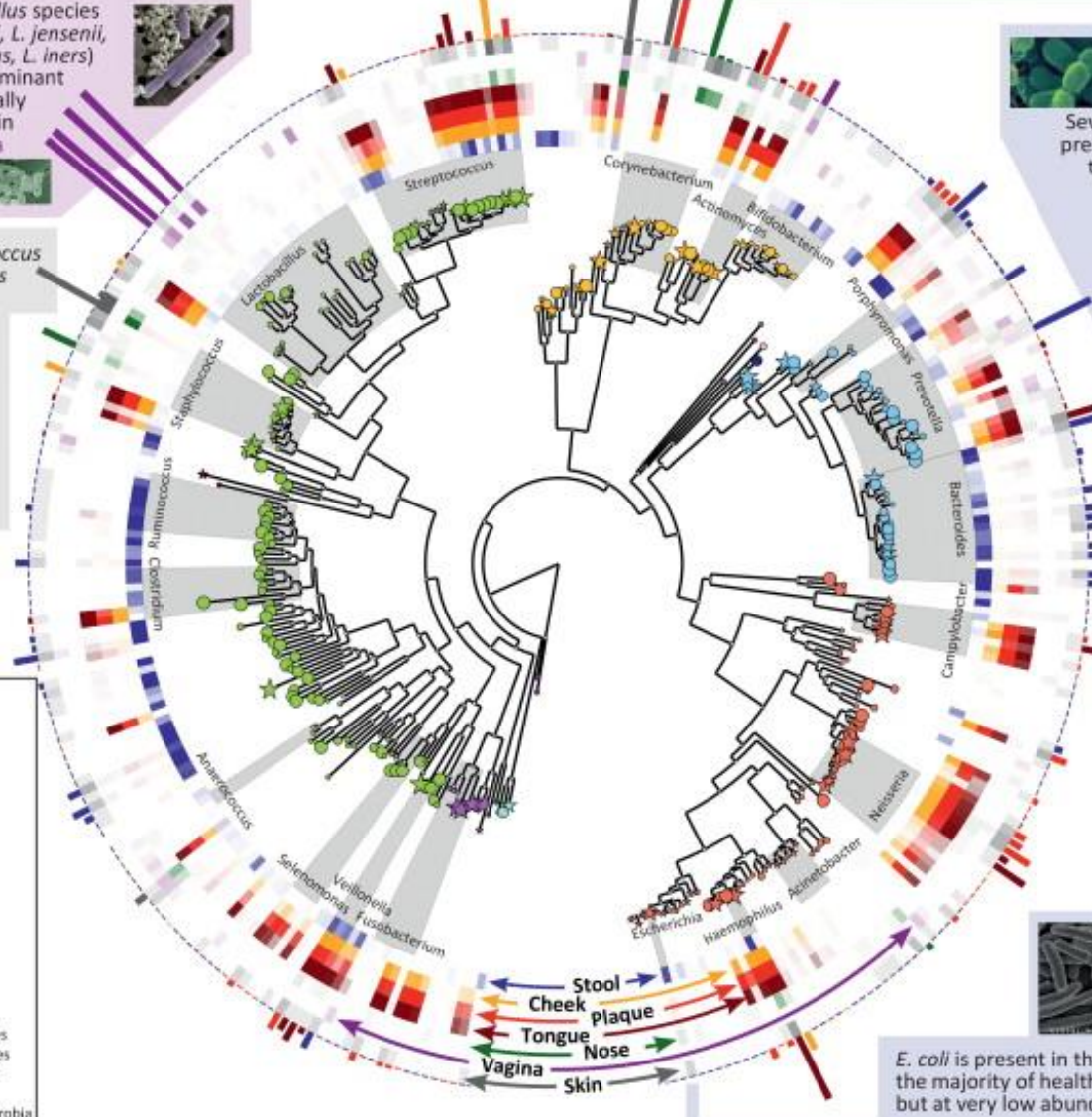
Many *Corynebacterium* species characterize different body sites:
C. matruchoti the plaque
C. accolens the nose
C. croppenstedtii the skin



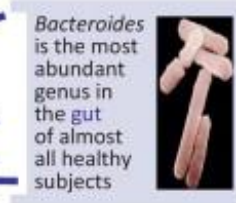
Lactobacillus species (*L. gasseri*, *L. jensenii*, *L. crispatus*, *L. iners*) are predominant but mutually exclusive in the vagina



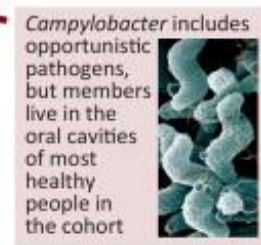
Staphylococcus epidermidis colonizes external body sites



Several *Prevotella* species are present in the gastrointestinal tract. *P. copri* is present in 19% of the subjects and dominates the intestinal flora when present



Bacteroides is the most abundant genus in the gut of almost all healthy subjects



Campylobacter includes opportunistic pathogens, but members live in the oral cavities of most healthy people in the cohort



E. coli is present in the gut of the majority of healthy subjects but at very low abundance

Key:

- Commensal microbes
- ☆ Potential pathogens

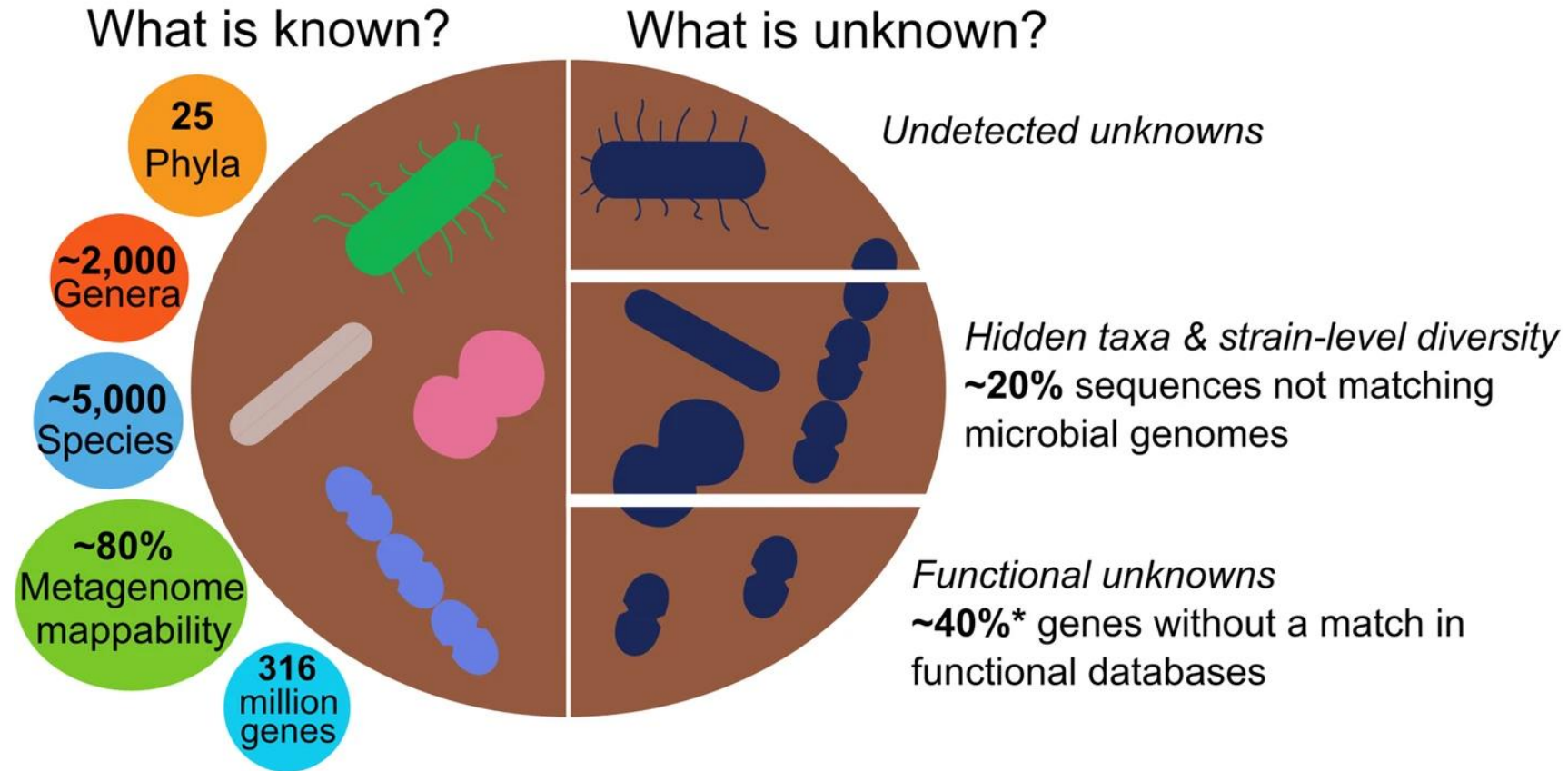
The four most abundant phyla

- Actinobacteria
- Bacteroidetes
- Firmicutes
- Proteobacteria

Low abundance phyla

- Chloroflexi
- Cyanobacteria
- Euryarchaeota
- Fusobacteria
- Lentisphaerae
- Spirochaetes
- Synergistetes
- Tenericutes
- Thermi
- Verrucomicrobia

The human microbiome



The New York Times

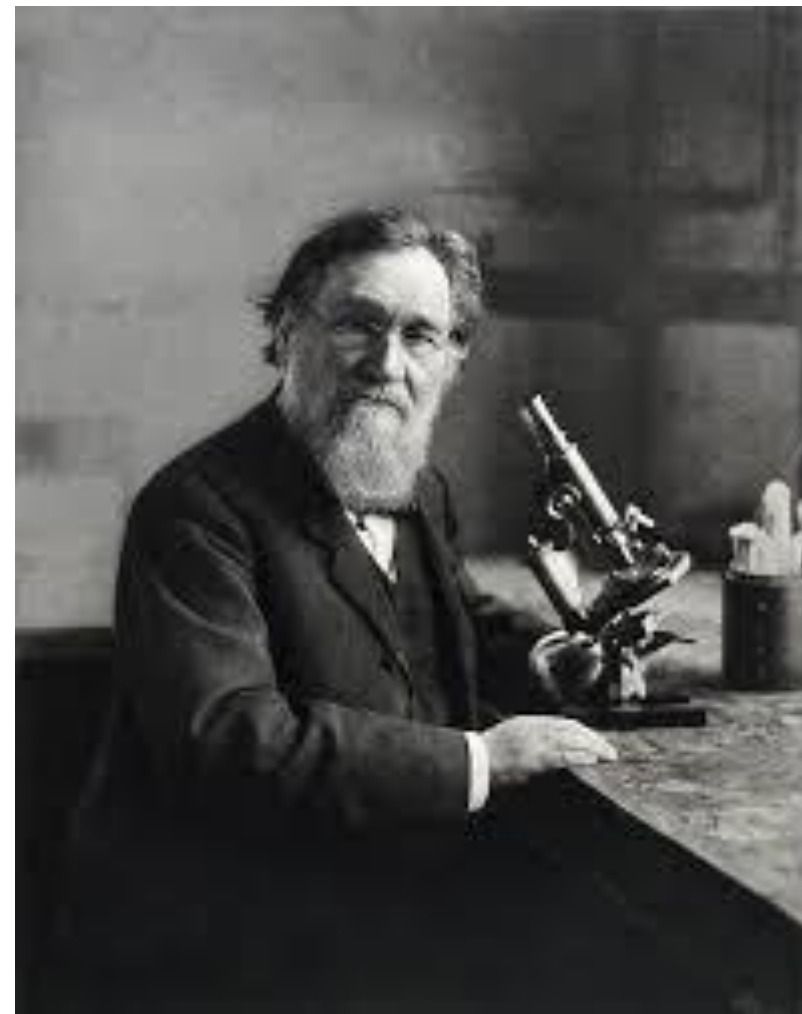
Published: January 21, 1912

Copyright © The New York Times

METCHNIKOFF CONFIRMED IN HIS THEORY OF LONG LIFE



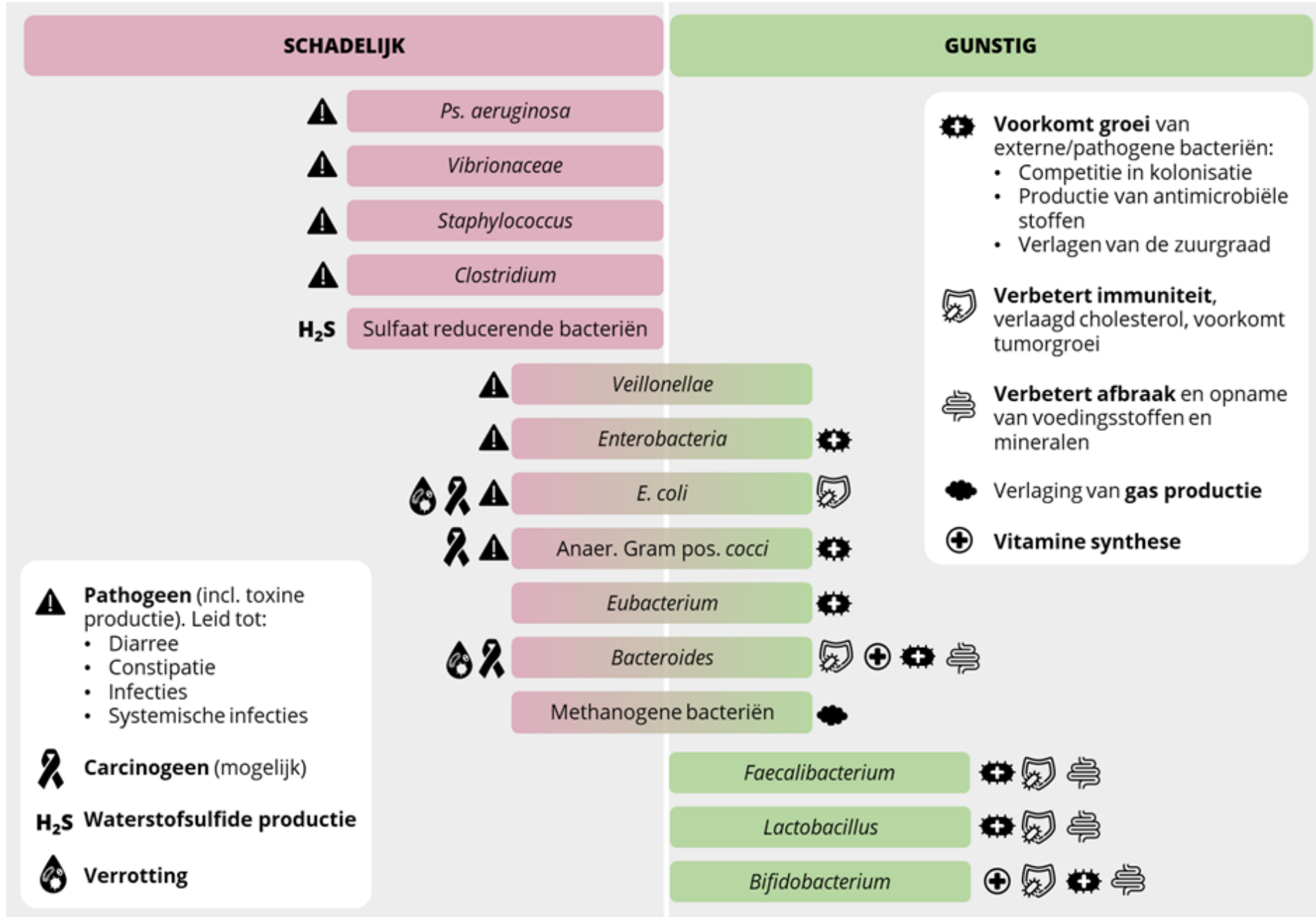
De putrefactie van de dikke darm

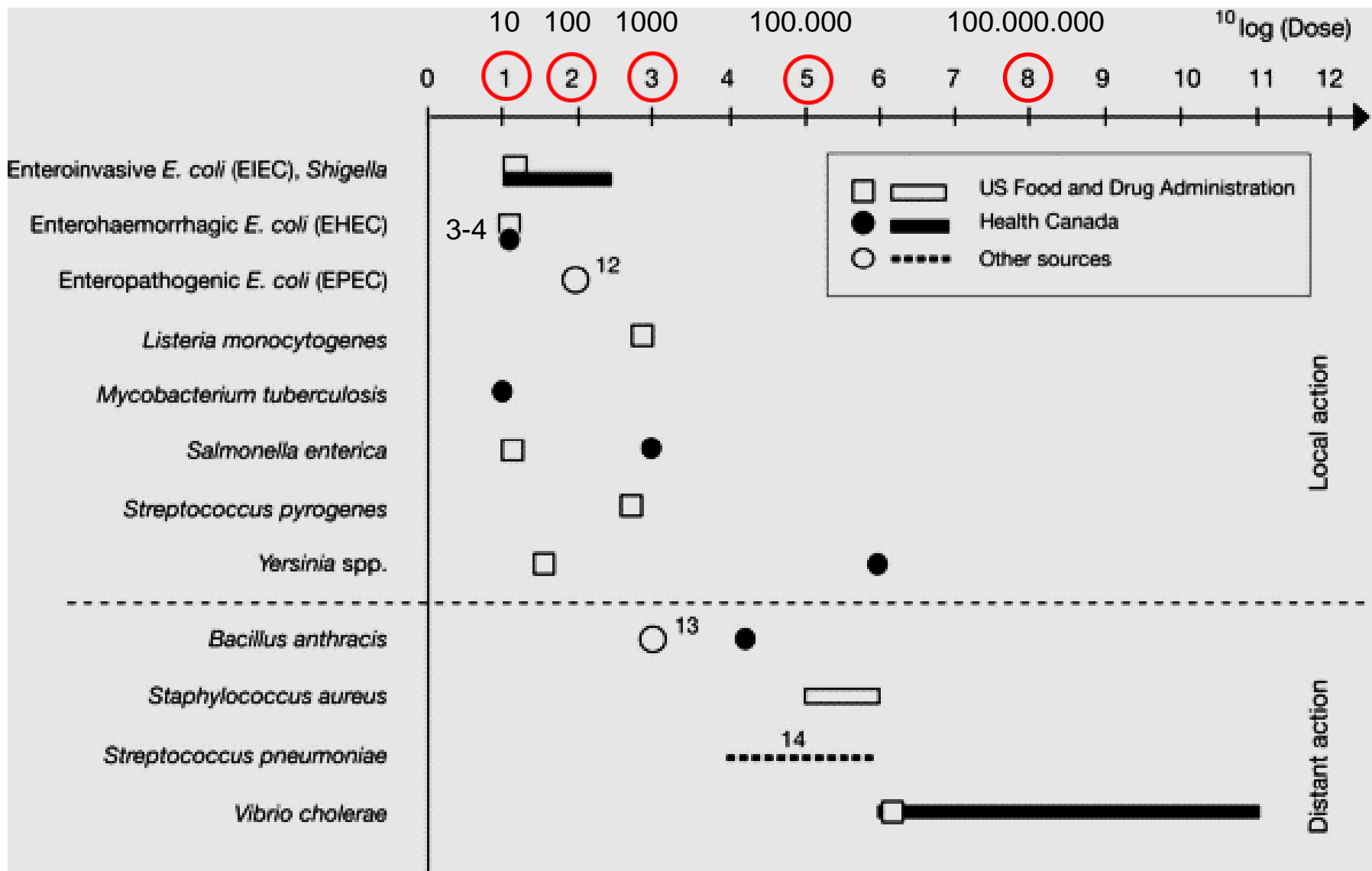


Het humane microbioom heeft 1-10 maal zoveel bacteriën als lichaamscellen!



- Er leven ongeveer 10^{14} (honderd-duizend-miljard!) micro-organismen in de mens
- Dat is 1-1½ kilogram per gezonde volwassene
- 100x meer bacteriële genen in vergelijking met humaan genoom





- 1 Prewearing
- 2 Weaning
- 3 Weaned-3 years old
- 4 4–9 years old
- 10 10–19 years old
- 20 20–29 years old
- 30 30–39 years old
- 40 40–49 years old
- 50 50–59 years old
- 60 60–69 years old
- 70 70–79 years old
- 80 80–89 years old
- 90 90–99 years old
- 100 Over 100 years old

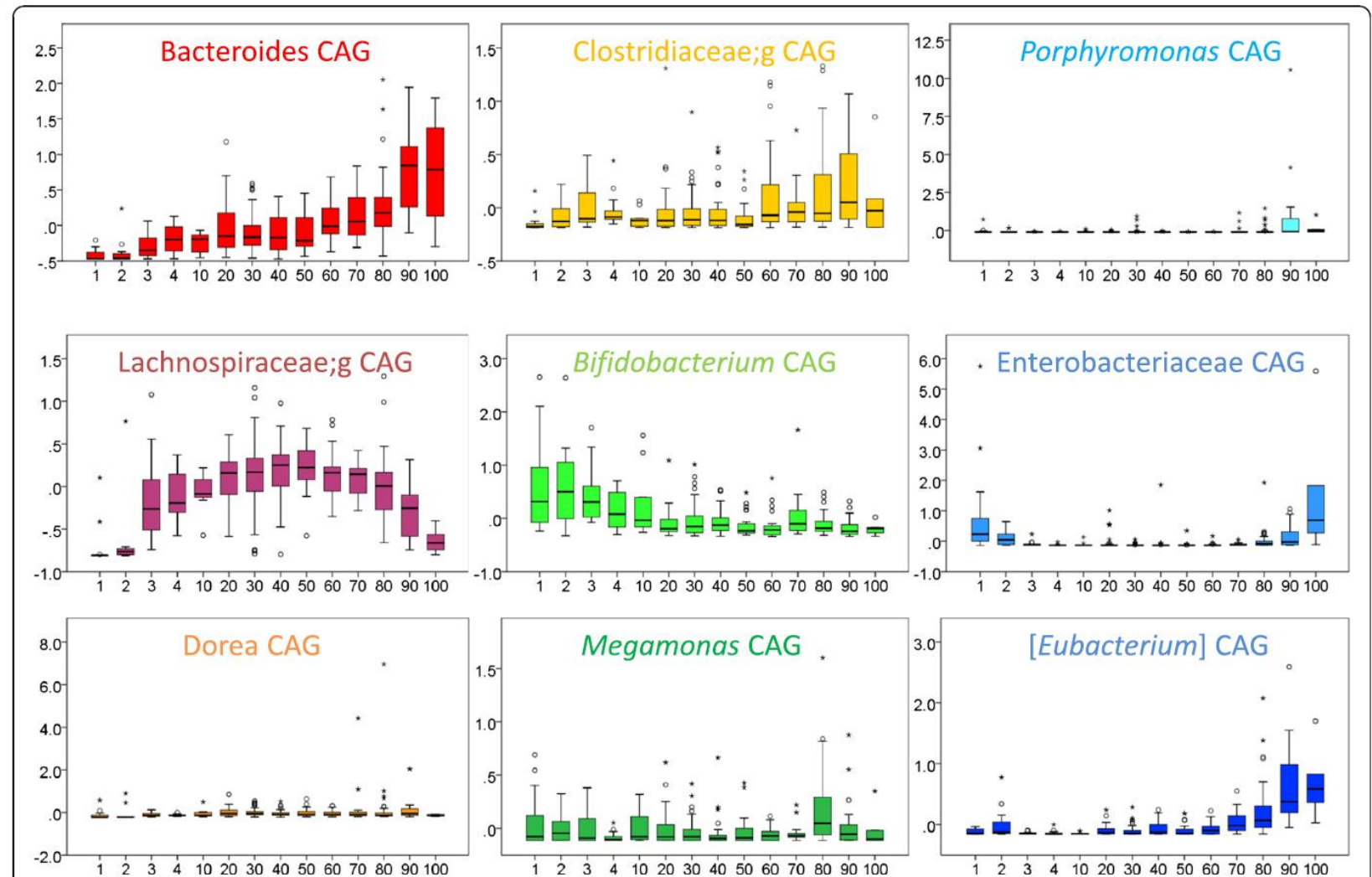
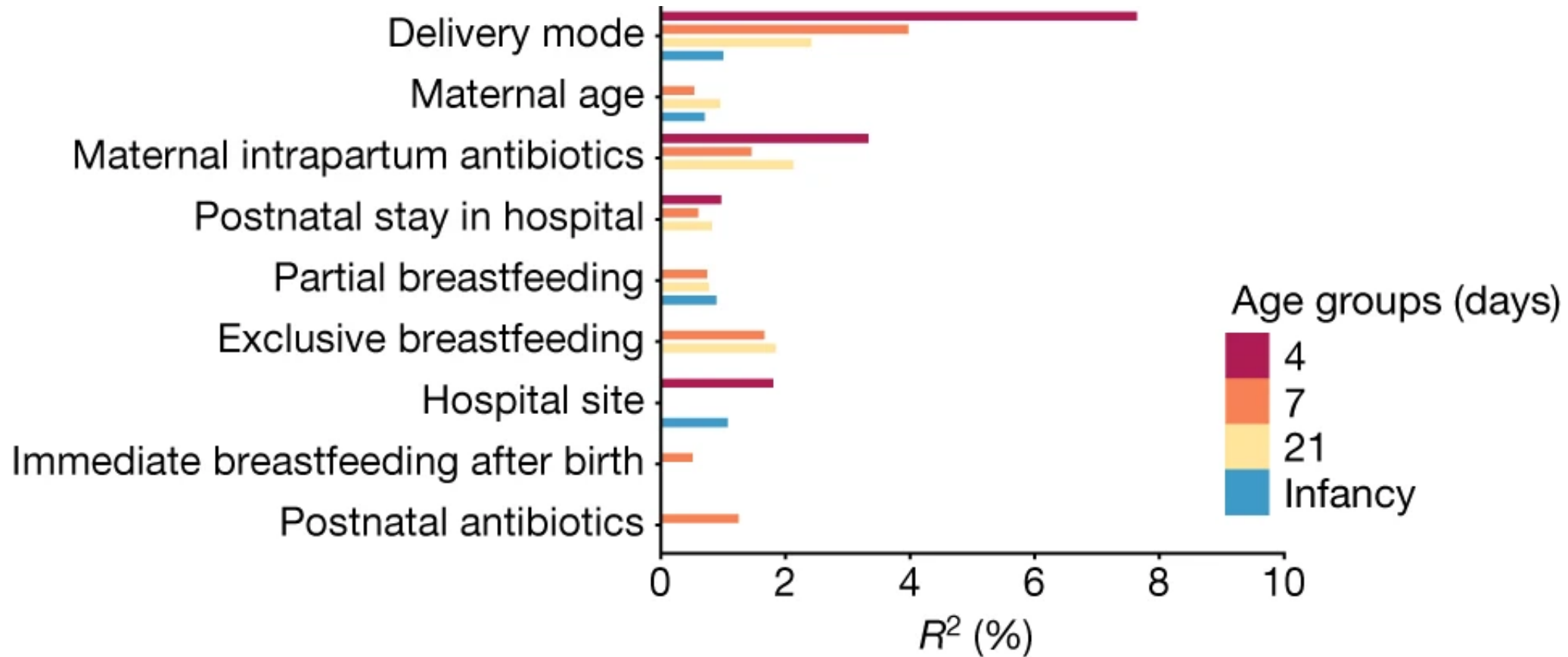


Fig. 3 Transition type of each co-abundance group (CAG) from infant to centenarian. Each number indicates a group as shown in Table 1. Box-plots show the interquartile range (IQR) of the sum of z-scores converted from the relative abundance of genera belonging to the same CAG. Open circles and asterisks indicate outliers from 1.5- to 3.0-fold IQR and over 3.0-fold IQR, respectively

When children are born, they emerge from the relatively sterile environment of the uterus into a world teeming with bacteria . . .

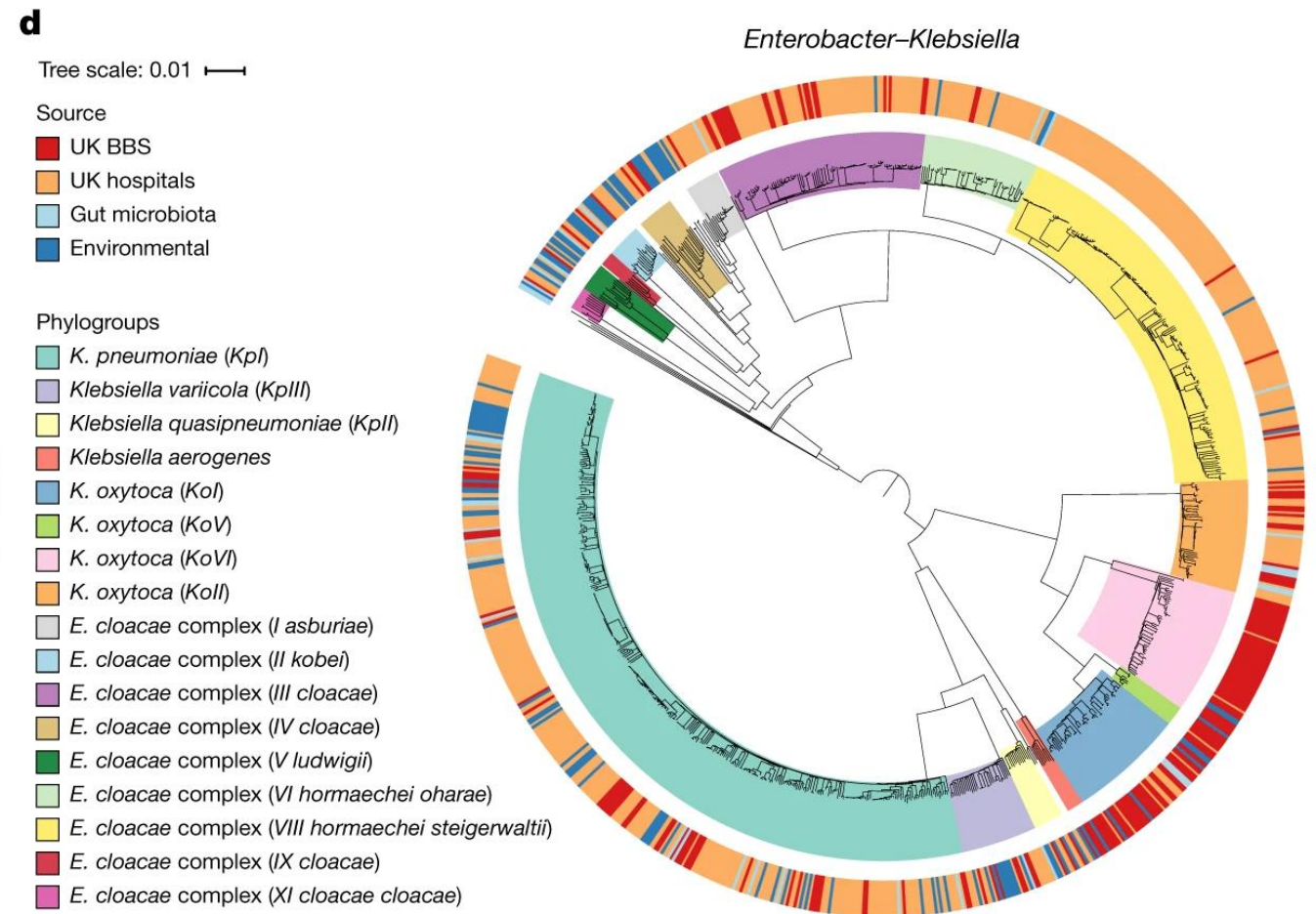
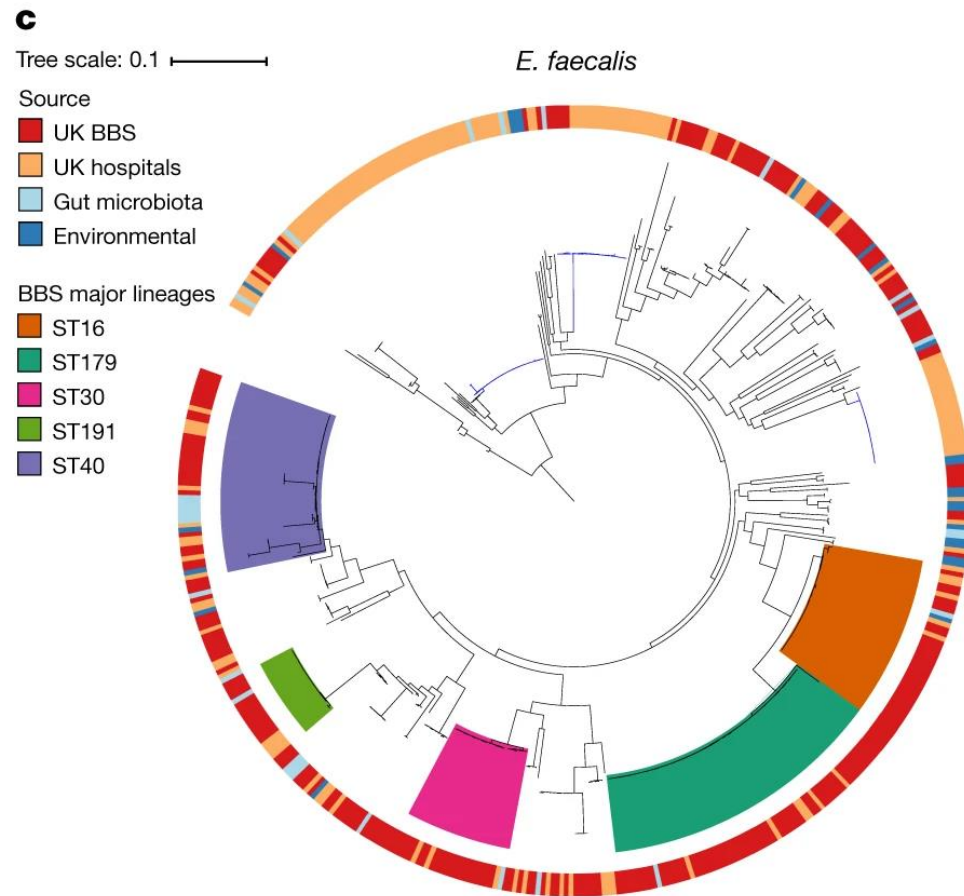


KEIZERSNEDE GEEFT MICROBIOTA ACHTERSTAND



Stunted microbiota and opportunistic pathogen colonization in caesarean-section birth

Yan Shao, Samuel C. Forster, Evdokia Tsaliki, Kevin Vervier, Angela Strang, Nandi Simpson, Nitin Kumar, Mark D. Stares, Alison Rodger, Peter Brocklehurst, Nigel Field & Trevor D. Lawley **Nature (2019)**



Stunted microbiota and opportunistic pathogen colonization in caesarean-section birth

Yan Shao, Samuel C. Forster, Evdokia Tsaliki, Kevin Vervier, Angela Strang, Nandi Simpson, Nitin Kumar, Mark D. Stares, Alison Rodger, Peter Brocklehurst, Nigel Field & Trevor D. Lawley **Nature (2019)**



Mouth
 $10^5 - 10^7$
polymorph germs

stomach
 $10^2 - 10^3$
Streptococcus

duodenum
 $< 10^{4-5}$
Streptococcus

jejunum
 $10^5 - 10^6$
Streptococcus

ileum
 $10^3 - 10^7$
Streptococcus
Bacteroides

colon
 $10^9 - 10^{11}$
Bacteroides
Clostridium
Streptococcus
Bifidobacteria
Enterobacteria



Darmvlokken (*villi*) geven oppervlakte vergroting



- De totale oppervlakte van de 'uitgespreide darm' komt daarmee op meer dan 300 vierkante meter
- Dat is een tennisveld

A microscopic cross-section of a plant stem, likely a dicot, showing various tissues. The outermost layer is the epidermis, followed by the cortex. The vascular bundles are arranged in a ring, each containing primary xylem, a vascular cambium, and primary phloem. The central pith is visible. The image is stained, with different tissues showing varying colors. Overlaid on the image is red text.

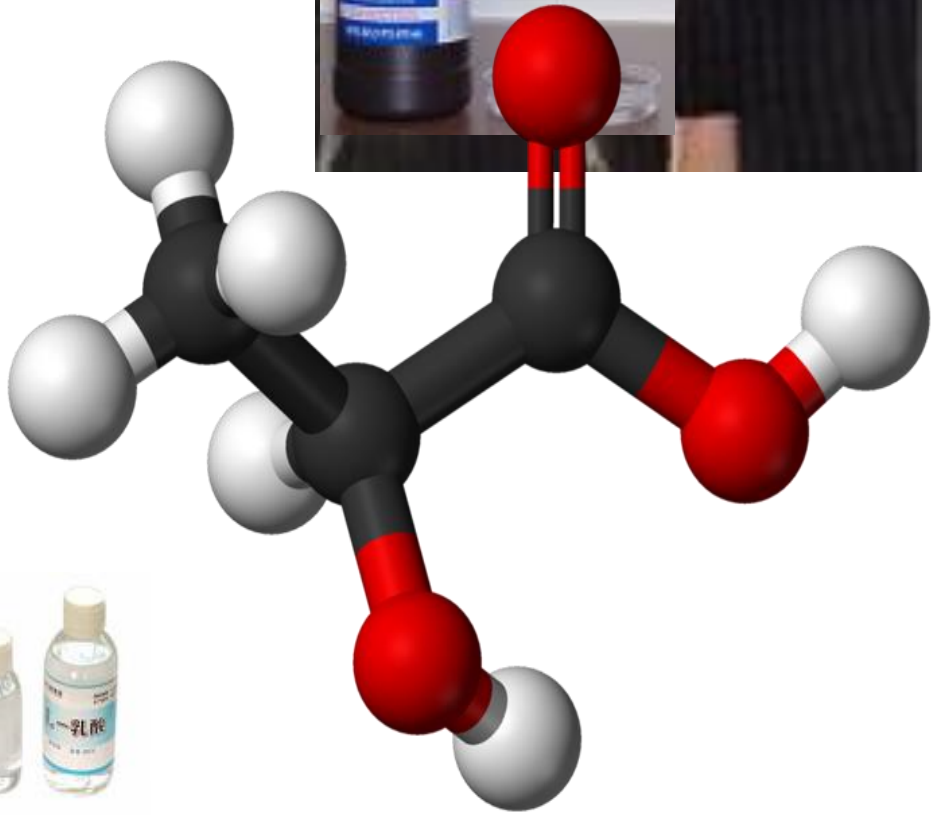
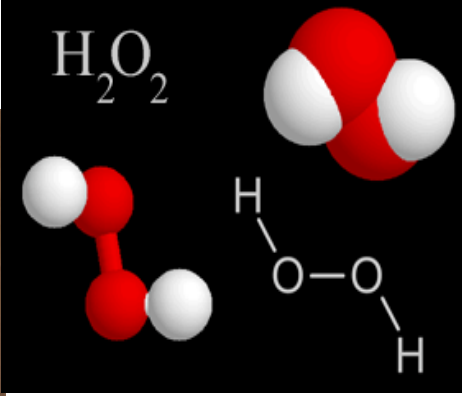
Hier zit uw
BROODJE met uw
levende bacteriële
gasten!!





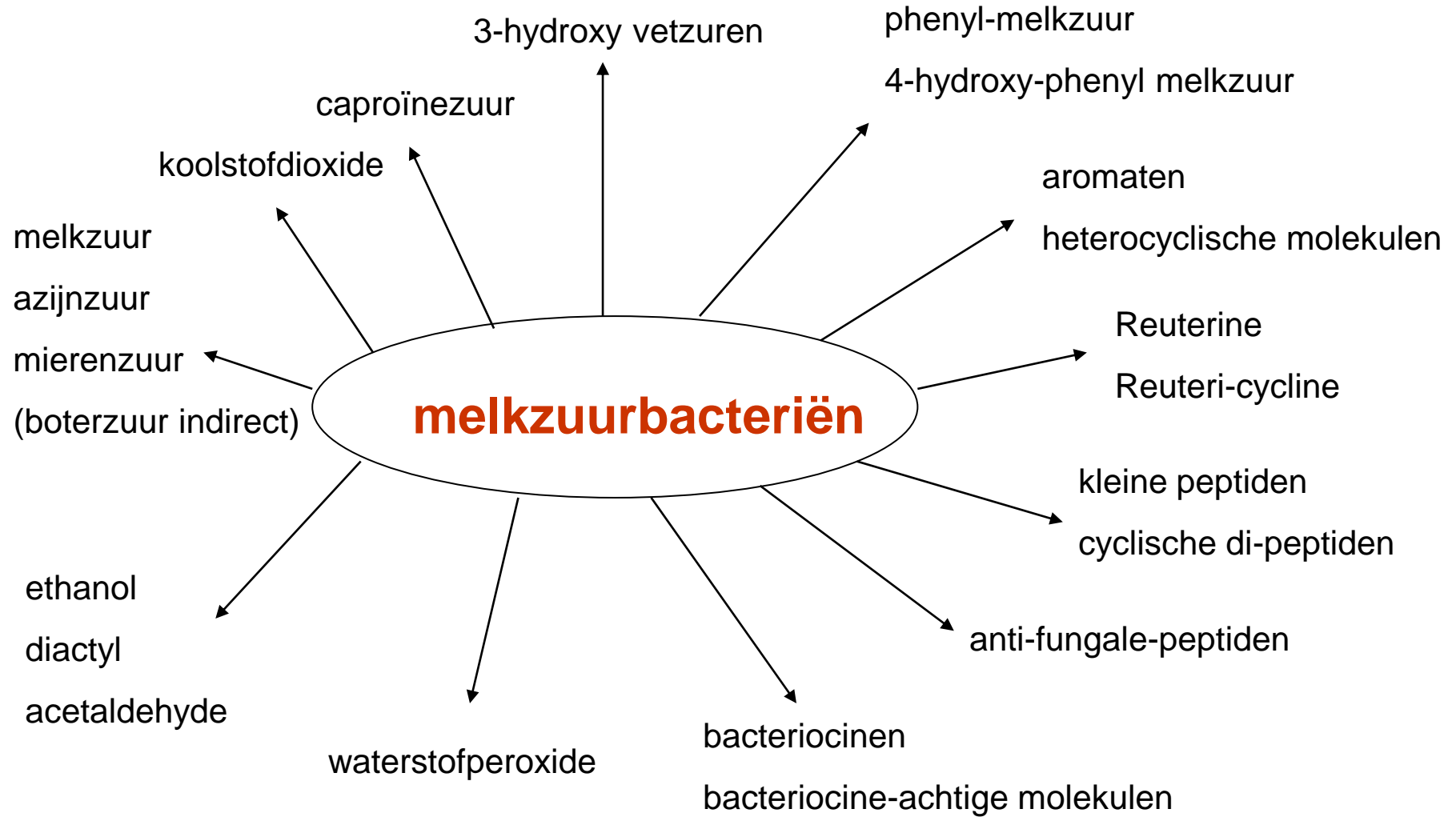
Bacterieen moeten aanhechten aan darm eptiheel om te koloniseren: competitie





suikerkatabolieten

vet- en aminozuurmetabolieten

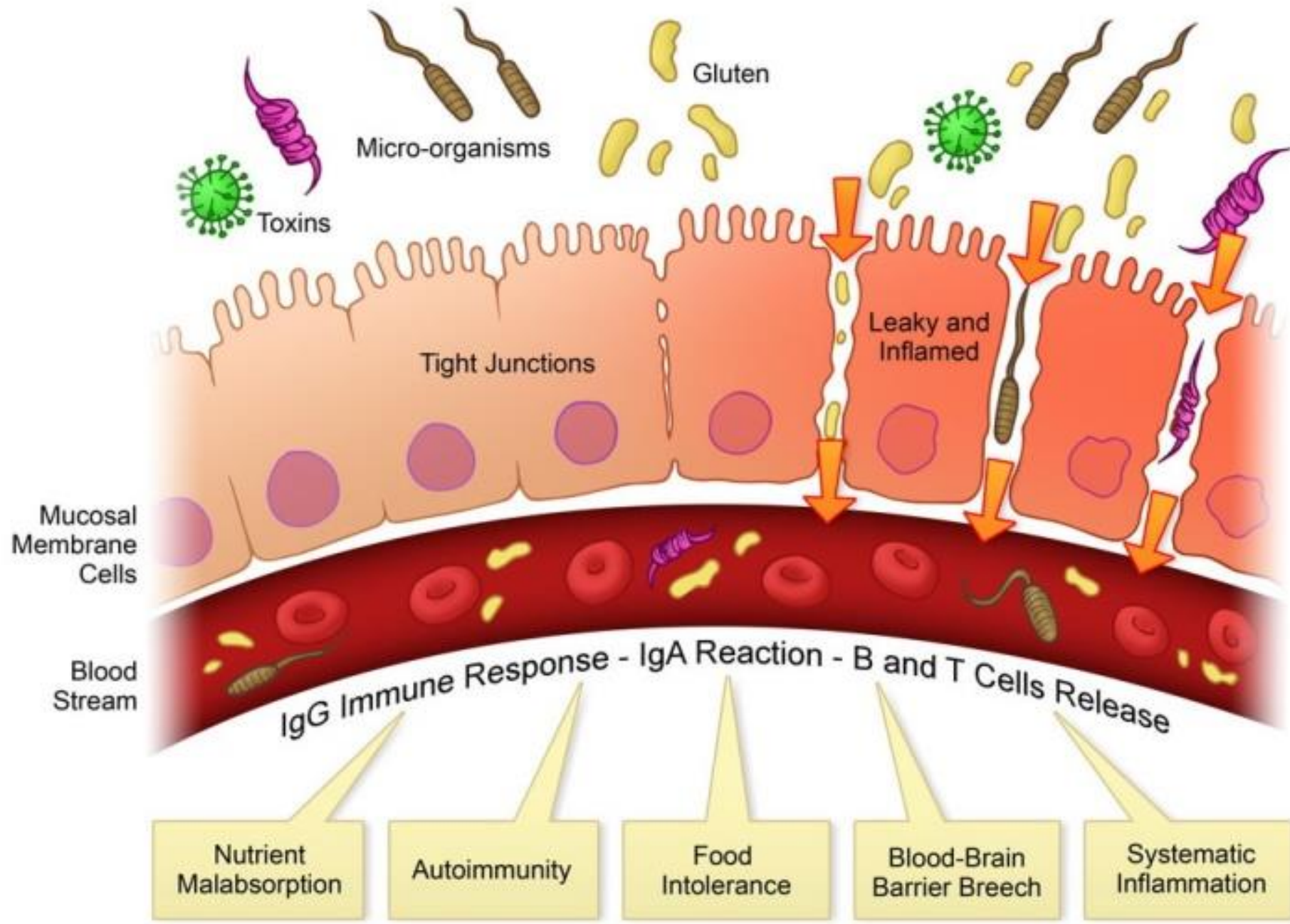


zuurstofkatabolieten

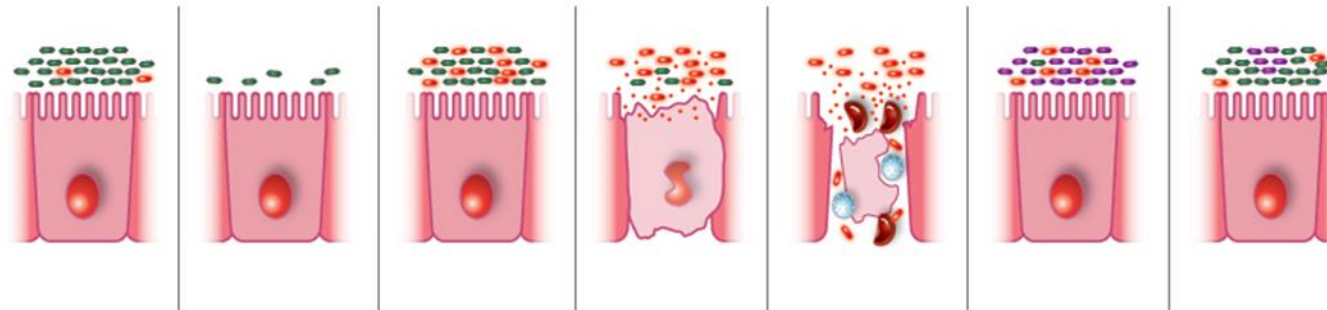
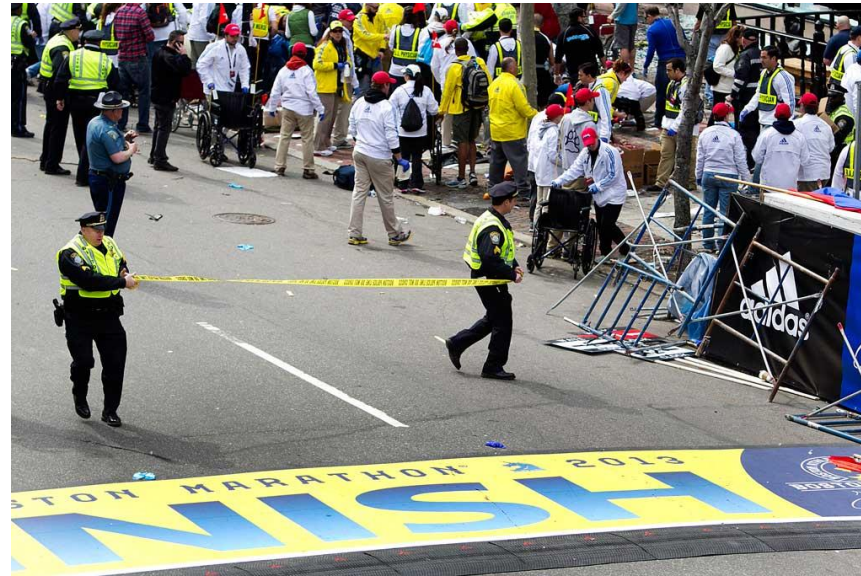
eiwitachtige stoffen

Darmwand en gezond epitheel is een barriere



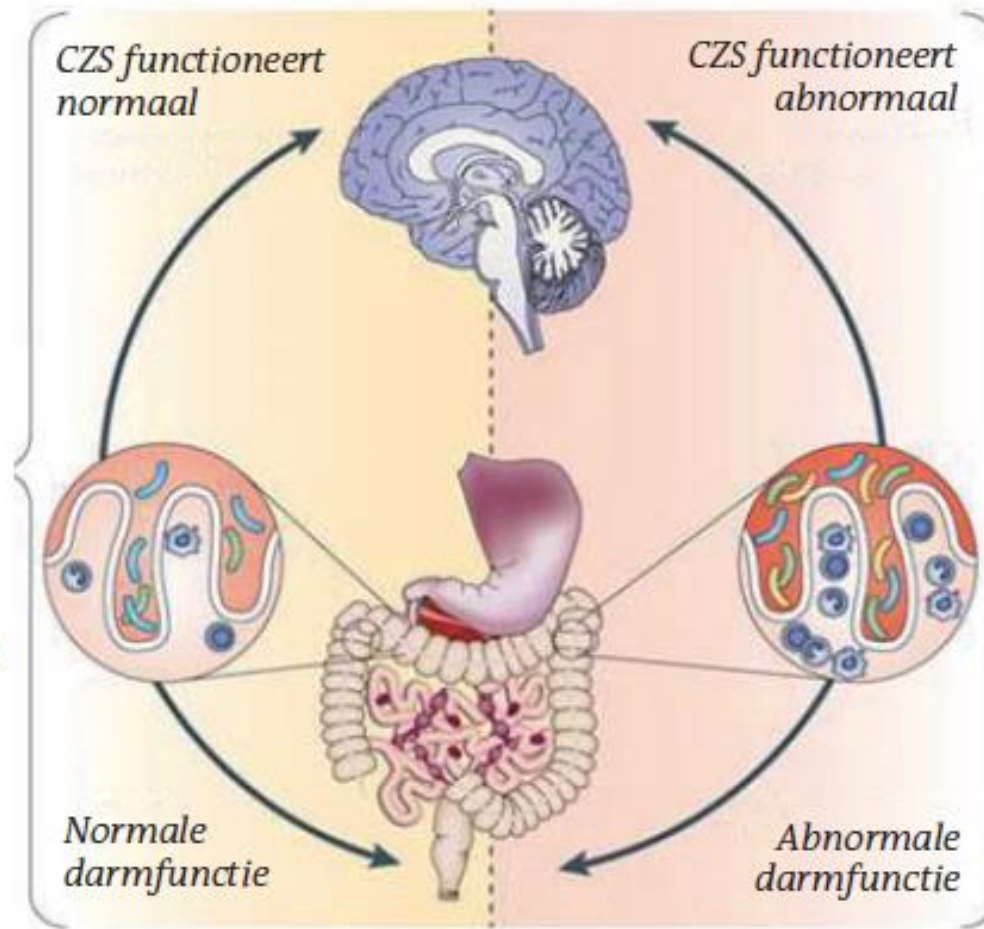


Afbraak van de barriere functie -> opportunisten & ontsteking



Gezonde situatie

- * Normaal gedrag, cognitie emotie en nociceptie (pijnzin)
- * Gezonde waarden van ontstekingscellen en/of mediators
- * Normale darmmicrobiota



Stress/ziekte

- * Veranderingen in gedrag, cognitie, emotie en nociceptie
- * Veranderde waarden van ontstekingscellen en/of mediators
- * Intestinale dysbiose

Triggers die lekkende darm kunnen veroorzaken:

proteïnen uit dieet

weinig maagzuur & enzymen

antibiotica

infecties

afwijkend bloedsuiker

antistoffen

zwangerschap

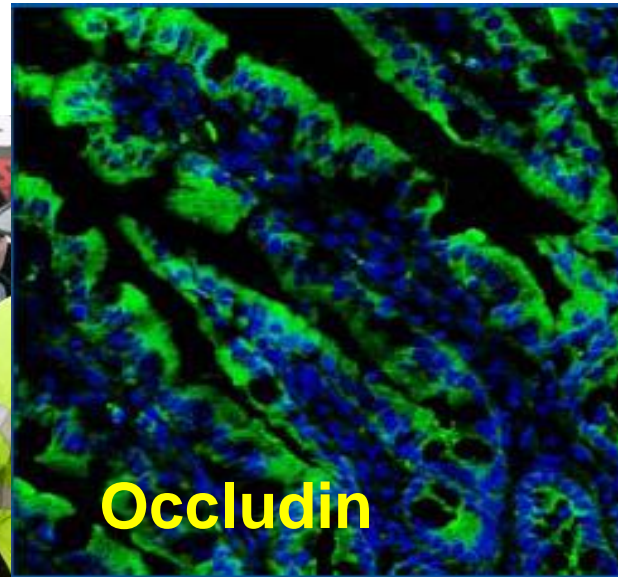
stress

menopauze

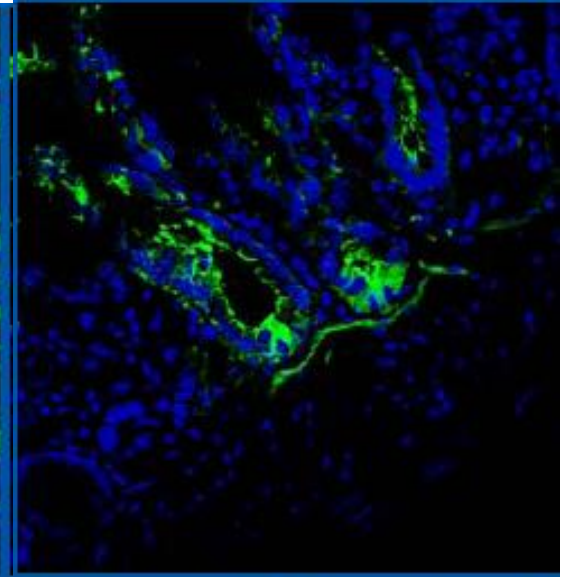
toxische stoffen

voedselallergieën & -intoleranties

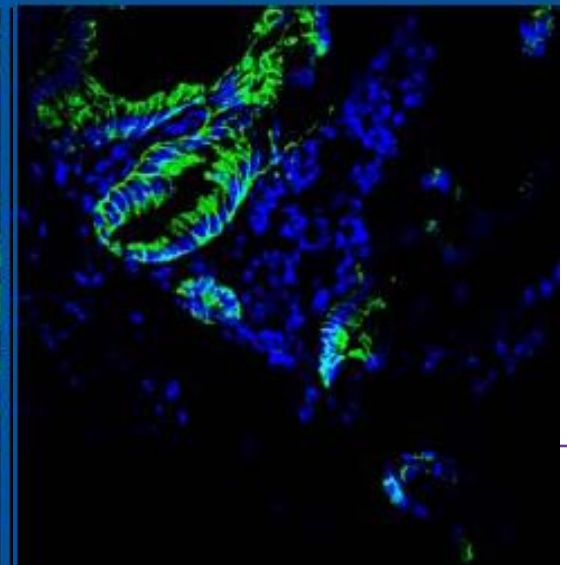
Lactobacilli versterken tight junctions



Occludin

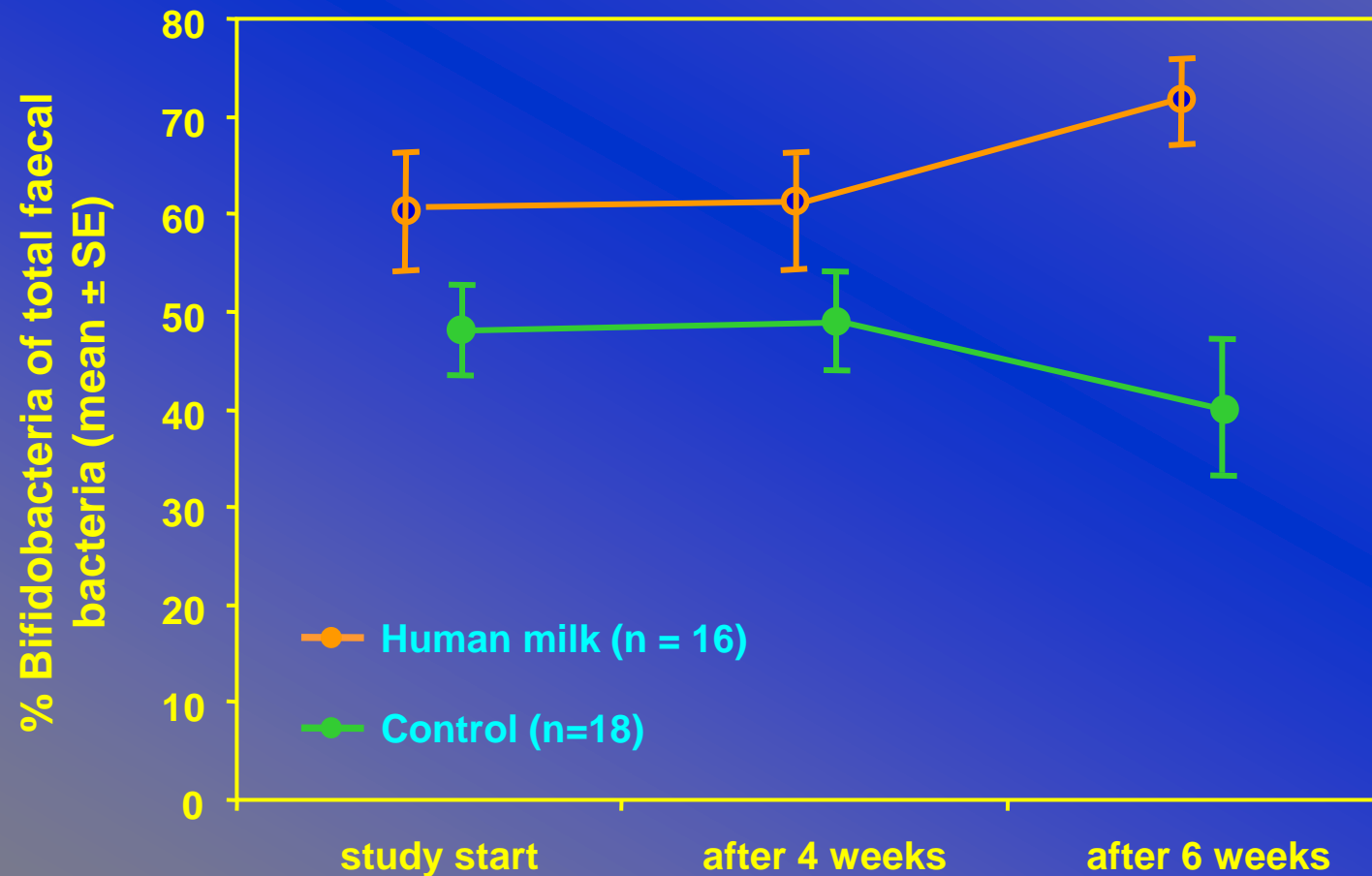


Claudin 1



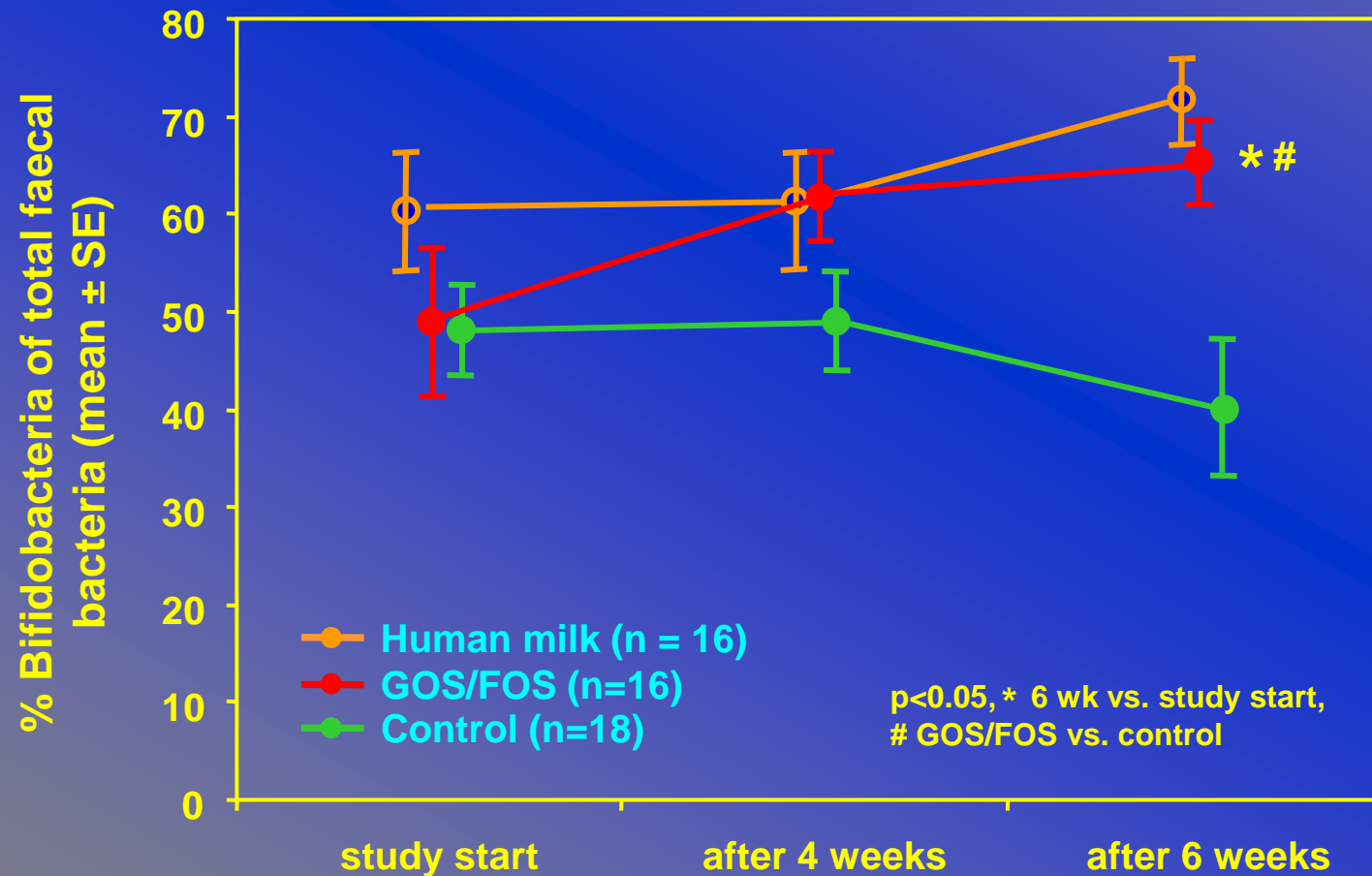
Clinical Studies: Effects of the Prebiotic GOS/FOS Mixture in Infants 4-12 Weeks

- Bifidogenicity -



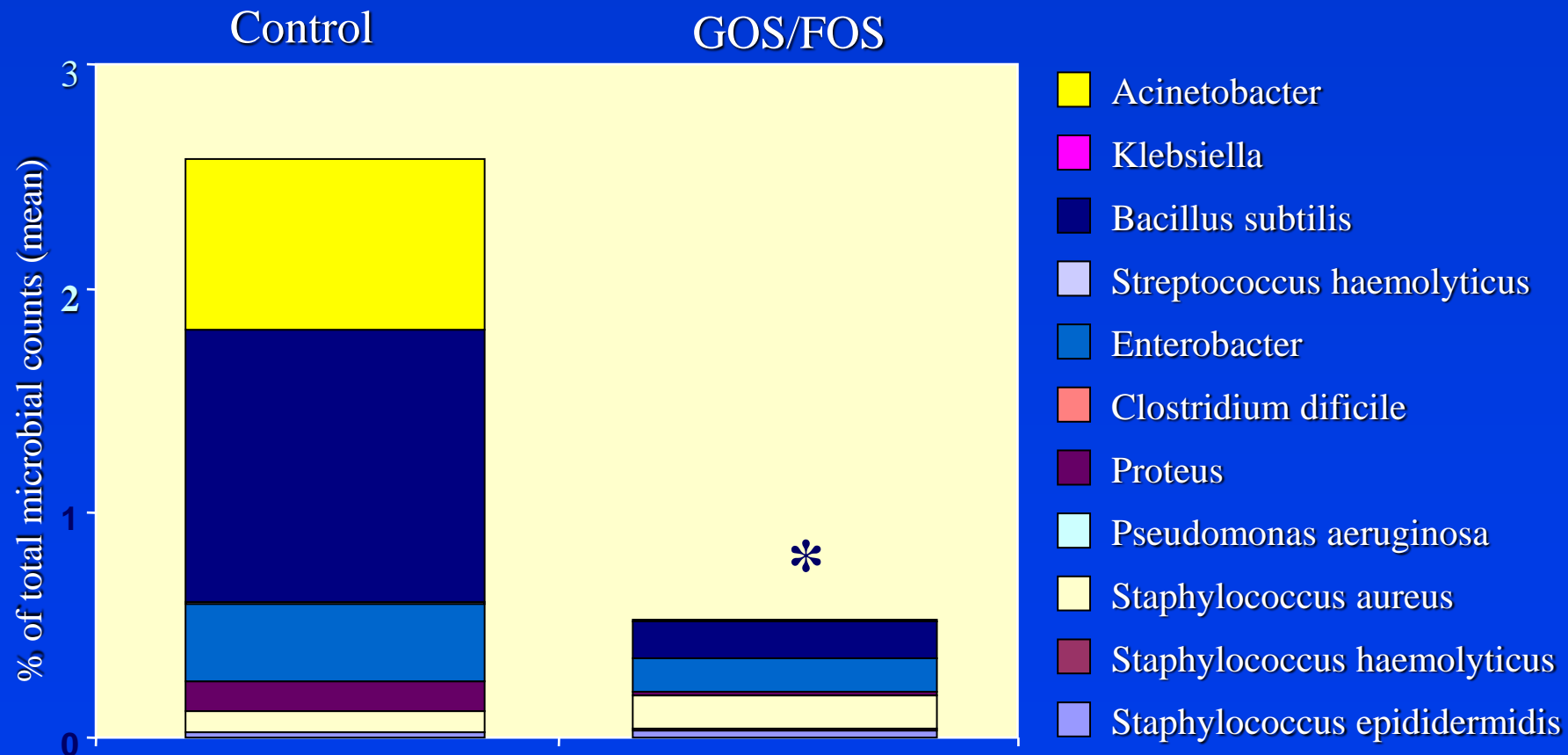
Clinical Studies: Effects of the Prebiotic GOS/FOS Mixture in Infants 4-12 Weeks

- Bifidogenicity -



Reduction of pathogens in the gut after GOS&FOS

Difference group
Mann-Whitney U-test:
Sum of all pathogens:
* p=0.01 vs. Control



% w/w (vers)

Witlof / Cichorei	15-20
Knoflook	9 - 16
Schorseneer	4 - 10
Prei	3 - 10
Ui	2 - 6
Artisjok	2 - 6
Asperge	2 - 3
Tarwemeel	1 - 4
Borstvoeding Mens	0.5 - 1.5
Haver	0.5 - 1.5
Banaan	0.3 - 0.7
Zoogdier melk	0.01 - 0.1



CONTORNI (GUARNICIÓN)

Cicoria (Achicoria)

€ 5,00

Spinaci (Espinacas)

€ 5,00

Grigliati Misti (Mixtos Vegetales a la Parrilla)

€ 6,00

Puntarelle (di stagione) (Puntarelle en salsa de anchoas)

Puntarelle is soort roodlof

Asparagi (espárragos)

€ 7,00

Carciofi alla Romana (di stagione) (alcachofas cocidas alla romana) (en estación)

€ 4,00

Patate fritte (Frances Fritas)

€ 4,00

Patate Saltate (Patatas Salteadas)

€ 4,00

Lenticchie (Lentejas)

€ 4,00

Fagioli (Frijoles)

€ 4,00



From Holland witlof
designed © by slappo

Probiotische en prebiotische voedingsmiddelen



Probiotisch

- Sommige soorten gatenkaas, waaronder Emmentaler en Maasdammer
- Yoghurt met levende melkzuurbacteriën
- Gefermenteerde zuivel
- Kimchi en augurken
- Tempeh
- Miso & natto
- Kefir
- Echt zuurdesembrood
- Zuurkool en olijven
- Gefermenteerde salsa
- Wijn met levende micro-organismen
- Bier met nagisting
- Gefermenteerde cacao (dat zit in doorsnee chocola)
- Kombucha



Prebiotisch

- Cichorei en witlof
- Knoflook
- Prei en schorseneer
- Ui, asperge en artisjok
- Tarwe
- Aardappel en mais
- Zoete aardappel
- Boerenkool, broccoli, spruitjes, paksoi en andere groenten die tot de familie van 'kruisbloemige planten' horen
- Avocado
- Kombucha (thee)
- Bosbes, thee en koffie
- Hennep & chiazaadjes
- Walnoten
- Quinoa
- Paardenbloem en moerbeibes
- Bonen
- Fruit

probiotisch	10 log CFU/gr-ml		referentie
NB gefermenteerd en niet gepasteuriseerd	9-12	dagelijkse dosis bij dieet rijk aan gefermenteerde voeding	15
belangrijke actieve ingrediënt(en)			
sommige kazen	3-9	<i>Propionibacterium freudenreichii</i> (Emmentaler)	16
'levende' yoghurt	1-10	<i>Lactobacillus</i> , <i>Bifidobacterium</i> , <i>Lactococcus</i> , <i>Streptococcus</i> (alle spp.)	17
gefermenteerde zuivel	4-9	<i>Lactobacillus</i> , <i>Bifidobacterium</i> , <i>Lactococcus</i> , <i>Streptococcus</i> (alle spp.)	18
kimchi, augurken en dergelijke	6-10	<i>Lactobacillus plantarum</i> , <i>Leuconostoc sp</i>	19
tempeh	3-9	<i>Rhizopus spp</i> , <i>Fusarium spp.</i> (plus gisten en melkzuurbacteriën)	20
miso en natto	2-7	<i>Penicillium spp.</i> en <i>Aspergillus spp.</i>	21
kefir (incl. kefiran)	6-9	melkzuur- en azijnzuurbacteriën en gisten op een polysaccharide matrix	22
echt zuurdesembrood	6-8	<i>Lactobacillus casei</i> , <i>Bifidobacterium pseudocatelunatum</i>	18
zuurkool en olijven	4-8	<i>Lactobacillus spp</i> , <i>Leuconostoc spp.</i>	23
salami en ham	2-11	<i>Lactobacillus plantarum spp.</i>	24
gefermenteerde salsa	5-7	<i>Lactobacillus fermentum</i>	25
'levende' wijn	2-5	<i>Saccharomyces cerevisiae</i> (en soms ook melkzuurbacteriën)	26
'levend' bier	2-5	melkzuurbacteriën (bijv. Lambiek en Geuze)	27
gefermenteerde cacao	3-8	<i>Saccharomyces boulardii</i> ; <i>Lactobacillus fermentum</i> , <i>L. plantarum</i>	28
kombucha	6-7	<i>Pichia</i> ; <i>Bretanomyces</i> ; <i>Zygosaccharomyces</i> , <i>Komagataeibacter</i> , <i>Gluconobacter</i>	29
prebiotisch			
		vorming microbloom (bij kinderen) met oplosbare vezels	30
cichorei en witlof	0.15-0.2 g/g	MAC (microbiotatoegankelijke koolhydraten, bijv. GOS en FOS)	31, 32
knoflook	0.09-0.16 g/g	MAC (microbiotatoegankelijke koolhydraten, bijv. GOS en FOS)	31
prei en schorseneer	0.04-0.1 g/g	MAC (microbiotatoegankelijke koolhydraten, bijv. GOS en FOS)	31
ui, asperge en artisjok	0.02-0.06 g/g	MAC (microbiotatoegankelijke koolhydraten, bijv. GOS en FOS)	31
tarwe	0.01-0.04 g/g	MAC (microbiotatoegankelijke koolhydraten, bijv. GOS en FOS)	31
aardappel en mais	n.a.		33
zoete aardappel		anthocyanines en fenolzuren resulteren in korteketenvezuren	34
boerenkool en kruisvormigen		glucosinolaat geeft isothiocyanaat (rauw beter i.v.m. myrosinase)	35
avocado		oplosbare vezels	36
kombucha (thee)		glucuronzuur, azijnzuur, polyfenolen, fenolen, B-complex vitamines en foliumzuur	37
bosbes, thee en Koffie		polyfenolen	38
hennep en chiazaadjes		antioxidanten en flavonoiden,	39
walnoten		antioxidanten en bevordering boterzuurproductie door het microbloom	40
quinoa		antioxidanten en verlaging van de pH door productie korteketenvezuur	41
paardenbloem en moerbeibes		microbloom versnelt ethanolafbraak en glucosemetabolisme	42
bonen		antioxidanten	43
fruit		oplosbare vezels, pectine en resistent zetmeel	44

Tabel 1. Voedingsproducten die een positieve werking kunnen hebben op het microbloom.

Probiotische en prebiotische voedingsmiddelen



Probiotisch

- Sommige soorten gatenkaas, waaronder Emmentaler en Maasdammer
- Yoghurt met levende melkzuurbacteriën
- Gefermenteerde zuivel
- Kimchi en augurken
- Tempeh
- Miso & natto
- Kefir
- Echt zuurdesembrood
- Zuurkool en olijven
- Gefermenteerde salsa
- Wijn met levende micro-organismen
- Bier met nagisting
- Gefermenteerde cacao (dat zit in doorsnee chocola)
- Kombucha



Een carrièreswitch op je zestigste. Op je zeventigste met een snowboard de berg af. En als tachtigplusser op safari naar Afrika. Wie gezond oud wordt, kan zijn bucketlist blijven vullen. Tot in de eeuwigheid leven is te hoog gegrepen, maar volgens recent onderzoek moeten we in de toekomst de 115 kunnen aantikken. Dat klinkt veelbelovend, alleen zijn de extra jaren die we erbij krijgen vaak niet onze beste. Broze botten, diabetes, een hartziekte of een haperend geheugen: allemaal kwalen die niet echt handig zijn op skivakantie of safari. Het kan anders, daar zijn de auteurs van *Gezond naar 115* van overtuigd. In dit boek gaan ze op zoek naar het geheim van een gelukkig, lang en gezond leven. Ze bestuderen wetenschappelijk onderzoek en bezoeken experts en ervaringsdeskundigen uit de hele wereld. Gezond naar 115? Je kunt in ieder geval een serieuze poging wagen. Lang actief blijven dus, want die geraniums wachten wel. Eet regelmatig witlof, en altijd groene groente bij je biefstukje. Houd je darmen in tiptop conditie voor een gezonde bovenkamer. En ga schapen hoeden.



Heidi Klüjzen (1970) is journaliste, gespecialiseerd in gezondheid, personal finance en recht. Ze is eindredacteur van de *Consumantengids* en schrijft en schreef voor onder meer *Elsevier*, *NRC*, *Zin* en de *Gezondgids*.

Ir. Lisette de Jong (1973) is voedingskundige en wetenschapsjournalist. Ze schrijft over gezond leven, duurzame technologie en andere zaken die de wereld mooier maken. Lisette is coauteur van *Ons mooie voedselboek*.

Prof. dr. Eric Claassen (1957) is immunoloog, ondernemer en hoogleraar ondernemerschap aan de VU in Amsterdam. Hij werkt al meer dan dertig jaar aan innovatie in voeding en darmgezondheid.

www.uitgeverijprometheus.nl



Claassen, De Jong en Klüjzen **GEZOND NAAR HONDERDVIJFTIEN**

Eric Claassen, Lisette de Jong en Heidi Klüjzen



probiotisch	10 log CFU/gr-ml		referentie
NB gefermenteerd en niet gepasteuriseerd	9-12	dagelijkse dosis bij dieet rijk aan gefermenteerde voeding	15
		belangrijke actieve ingrediënt(en)	
sommige kazen	3-9	<i>Propionibacterium freudenreichii</i> (Emmentaler)	16
'levende' yoghurt	1-10	<i>Lactobacillus</i> , <i>Bifidobacterium</i> , <i>Lactococcus</i> , <i>Streptococcus</i> (alle spp.)	17
gefermenteerde zuivel	4-9	<i>Lactobacillus</i> , <i>Bifidobacterium</i> , <i>Lactococcus</i> , <i>Streptococcus</i> (alle spp.)	18
			19
			20
			21
			22
			18
			23
			24
			25
			26
			27
			28
			acter 29
			30
			31, 32
			31
			31
			31
			31
			33
			34
			35
			36
			37
			38
			39
			40
			41
			42
paardenvoer en moerbes		microbiom versniet ethanolafbraak en glucosemetabolisme	42
bonen		antioxidanten	43
fruit		oplosbare vezels, pectine en resistent zetmeel	44

Tabel 1. Voedingsproducten die een positieve werking kunnen hebben op het microbiom.

- Bonen
- Fruit

Disturbance microbiota (=dysbiosis)



Directly linked to gut dysbiosis

- Inflammatory Bowel Disease (IBD)
- Irritable Bowel Syndrome (IBS)
- Diarrhea
- Antibiotic associated diarrhea
- Travelers diarrhea
- Infantile diarrhea (Rotavirus)
- Caused by food pathogens
- Constipation
- Helicobacter pylori infections



Indirectly linked to gut dysbiosis

- Allergies
- Cancer
- Cardiovascular disease
- Urinary tract infections
- Bacterial vaginosis
- Upper respiratory tract infections

Downloaded from gut.bmj.com on August 22, 2013 - Published by group.bmj.com

Recent advances in clinical practice



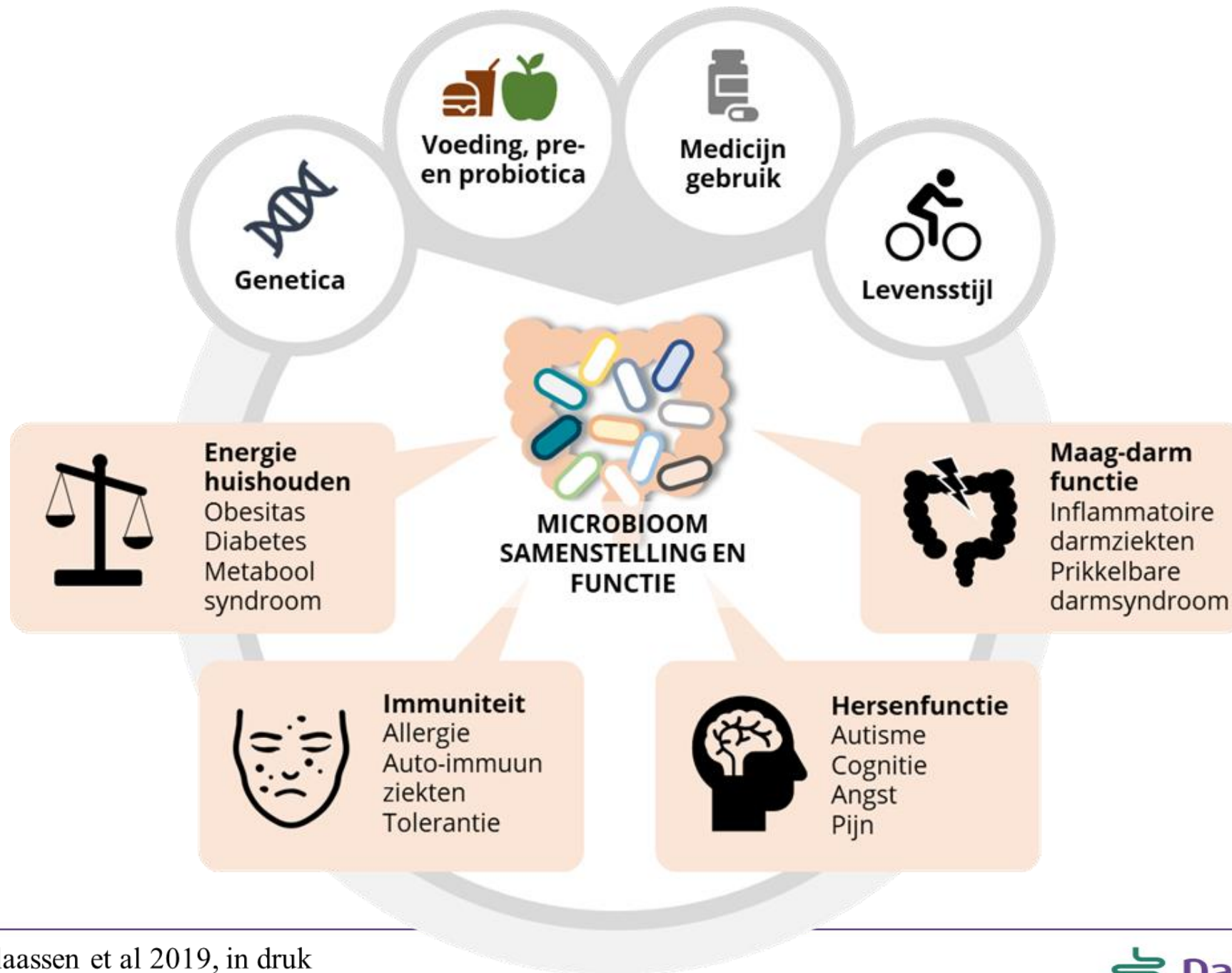
OPEN ACCESS



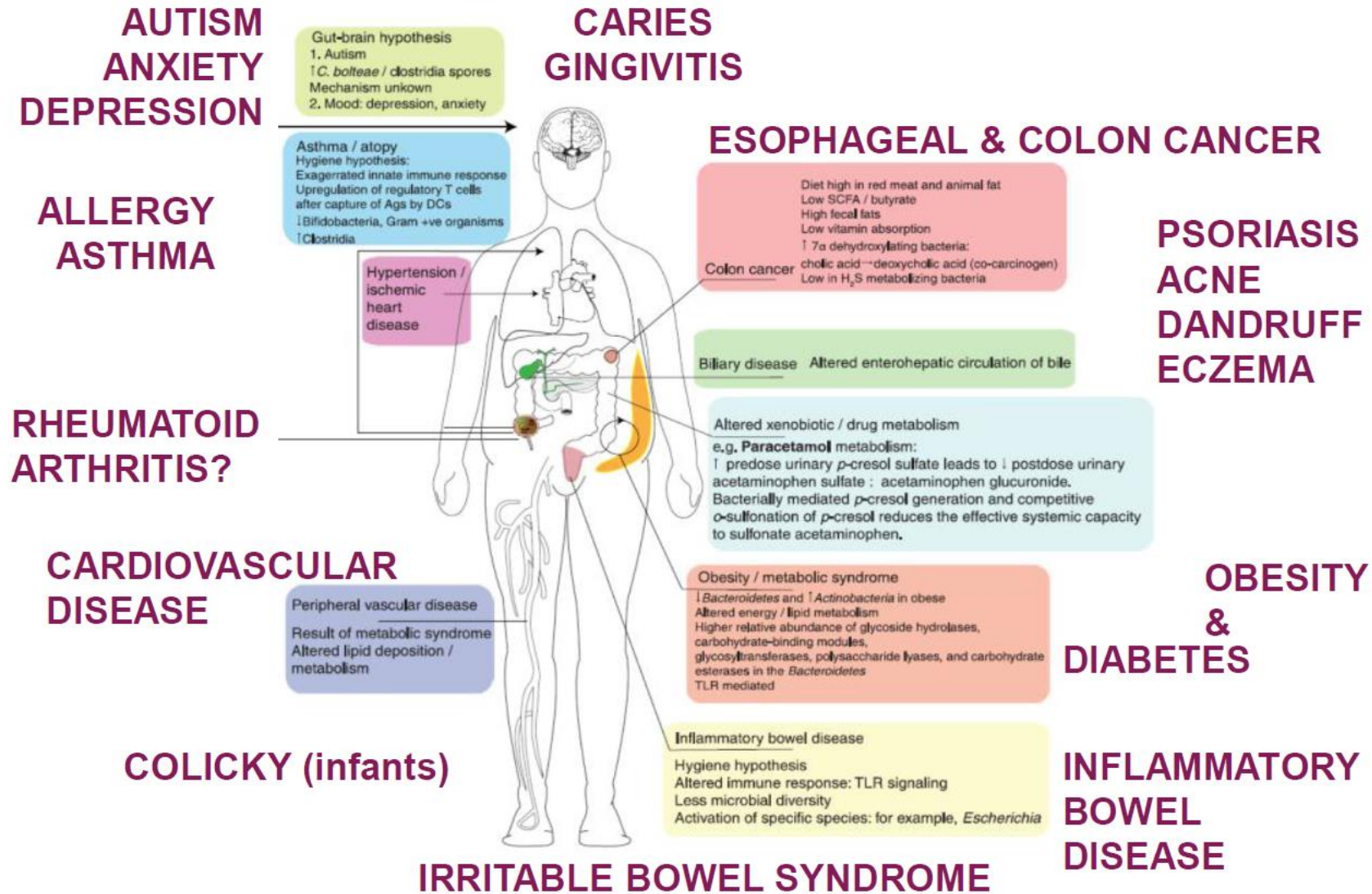
Editor's choice
Scan to access more
free content

An update on the use and investigation of probiotics in health and disease

Mary Ellen Sanders,¹ Francisco Guarner,² Richard Guerrant,³ Peter R Holt,⁴ Eamonn MM Quigley,^{5,6} R Balfour Sartor,⁷ Philip M Sherman,⁸ Emeran A Mayer³



The human microbiota In health and disease



ORIGINAL ARTICLE

Duodenal Infusion of Donor Feces for Recurrent *Clostridium difficile*

Els van Nood, M.D., Anne Vrieze, M.D., Max Nieuwdorp, M.D., Ph.D.,
Susana Fuentes, Ph.D., Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D.,
Caroline E. Visser, M.D., Ph.D., Ed J. Kuijper, M.D., Ph.D.,
Joep F.W.M. Bartelsman, M.D., Jan G.P. Tijssen, Ph.D.,
Peter Speelman, M.D., Ph.D., Marcel G.W. Dijkgraaf, Ph.D.,
and Josbert J. Keller, M.D., Ph.D.

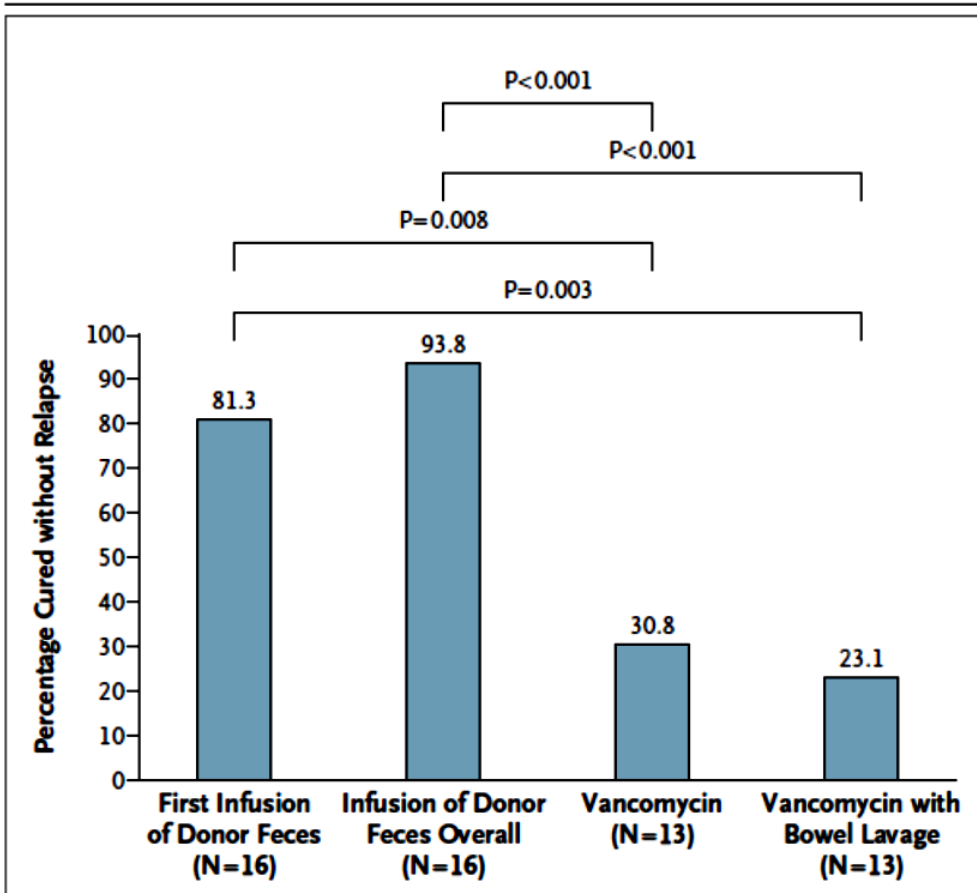


Figure 2. Rates of Cure without Relapse for Recurrent *Clostridium difficile* Infection.

Shown are the proportions of patients who were cured by the infusion of donor feces (first infusion and overall results), by standard vancomycin therapy, and by standard vancomycin therapy plus bowel lavage.

Table 2. Adverse Events in 16 Patients in the Infusion Group.*

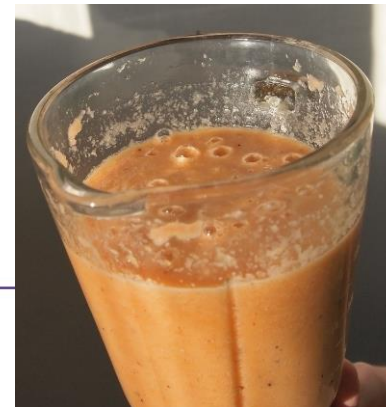
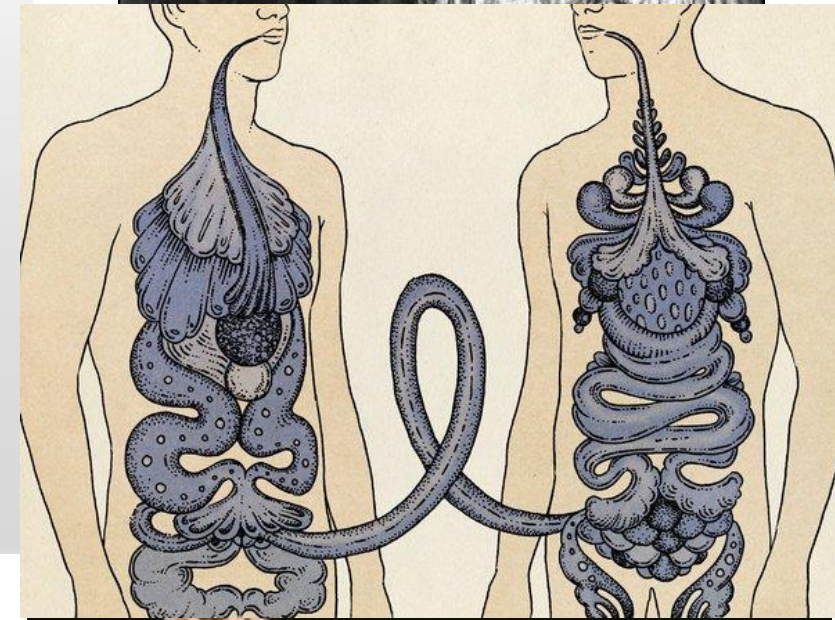
Adverse Event	On Day of Infusion of Donor Feces	During Follow-up
	no. of events	
Belching	3	0
Nausea	1	0
Vomiting	0	0
Abdominal cramps	5	0
Diarrhea	15	0
Constipation	0	3
Abdominal pain	2 (associated with cramping)	0
Infection	0	2†
Hospital admission	NA	1‡
Death	0	0
Other adverse event	1§	1‡

* Adverse events that were reported on the day of donor-feces infusion and those that were reported during follow-up are listed separately. NA denotes not applicable.

† During follow-up, one patient with recurrent urinary tract infections had a urinary tract infection for which antibiotics were prescribed. Another patient had fever during hemodialysis for which antibiotics were prescribed; cultures remained negative.

History

- First documented in 4th Century China as “Yellow Soup”
- In some countries, maternal feces is inserted into the newborn's mouth to “jumpstart” the colon
- June 17th, 2013: FDA approved the procedure for recurrent C. diff.
- 0 documented serious side effects
- 92% - 95% success rate



SCIENTIFIC REPORTS



OPEN **The mechanistic link between health and gut microbiota diversity**

Olaf F. A. Larsen  & Eric Claassen

Although numerous reports link a decreased diversity of the gut microbiota to a declined health status, to date no mechanistic motivation for this exists. Here, we show a theory on small networks that higher diversity within such a network increases resilience to perturbations, systems and redundancy. Our results quantitatively support earlier findings that higher gut microbiota richness with respect to these parameters. Our simulation shows that higher diversity leads to higher resilience within small microbiological ecosystems. This notion should provide an ingredient when developing strategies for microbiota management.

Received: 25 September 2017


Accepted: 12 January 2018

Published online: 01 February 2018

SCIENTIFIC REPORTS



OPEN **Towards a rational design of faecal transplant analogues**

Olaf F. A. Larsen ¹, Anton H. J. Koning², Peter J. van der Spek² & Eric Claassen¹

Faecal transplants (microbiota transfer) have shown to be promising therapies having a wide range of therapeutic applications. However, current safety considerations hamper further valorisation. As such, well designed faecal transplant analogues provide an interesting alternative to minimize possible safety aspects. However, to date little knowledge on how to rationally design such analogues exists. Here, we show by applying first order basic graph theory that such analogues dedicated to restoring a specific physiological functionality (a microbial guild) should consist of 5–6 species to maximize stability, efficiency, and minimize safety issues and production costs.

Received: 10 October 2018

Accepted: 21 March 2019

Published online: 03 April 2019

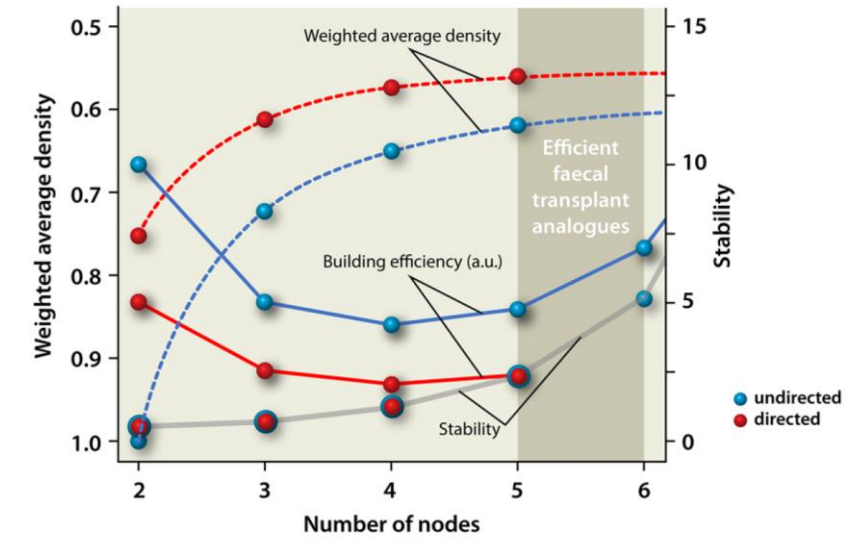
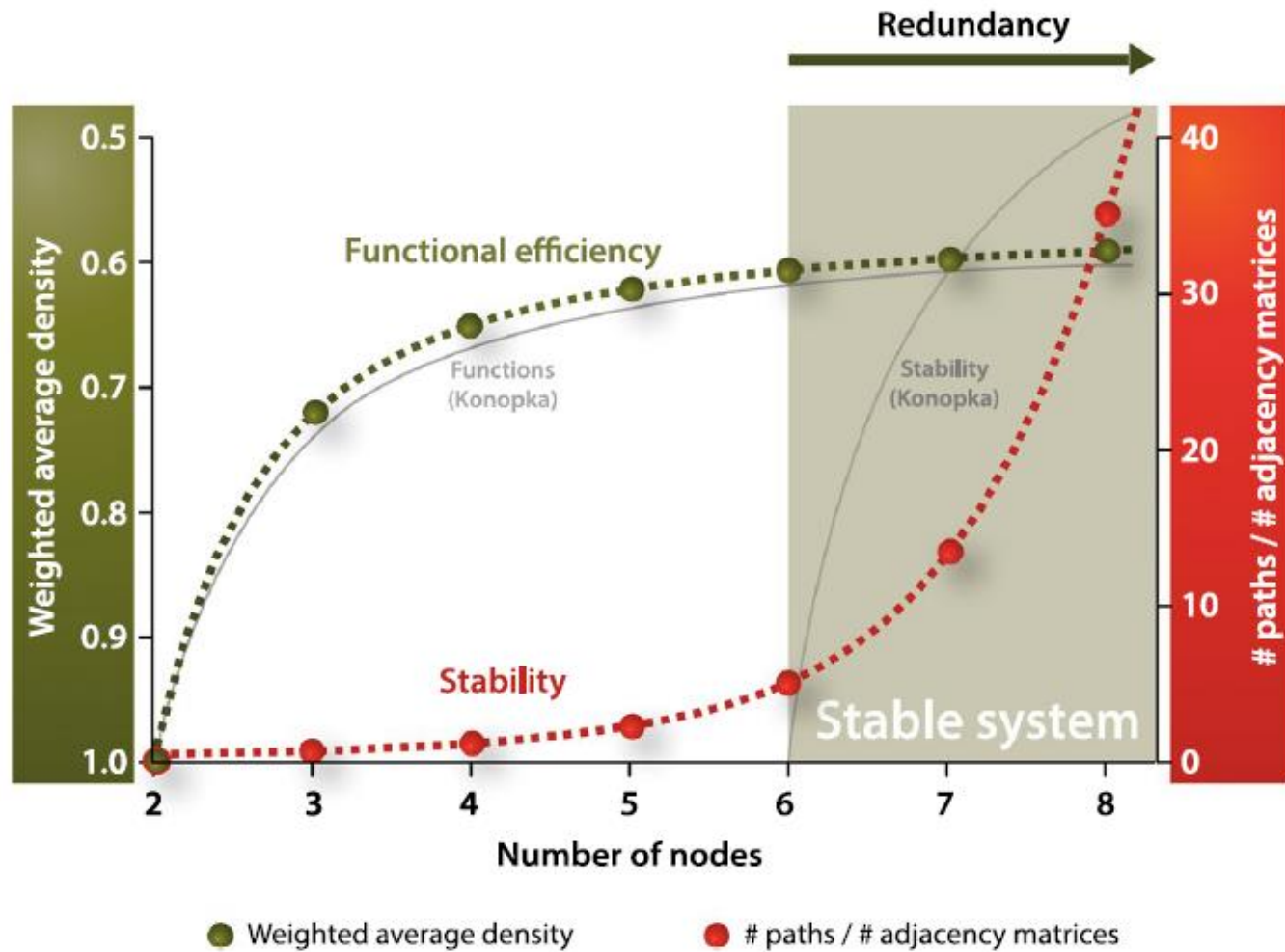
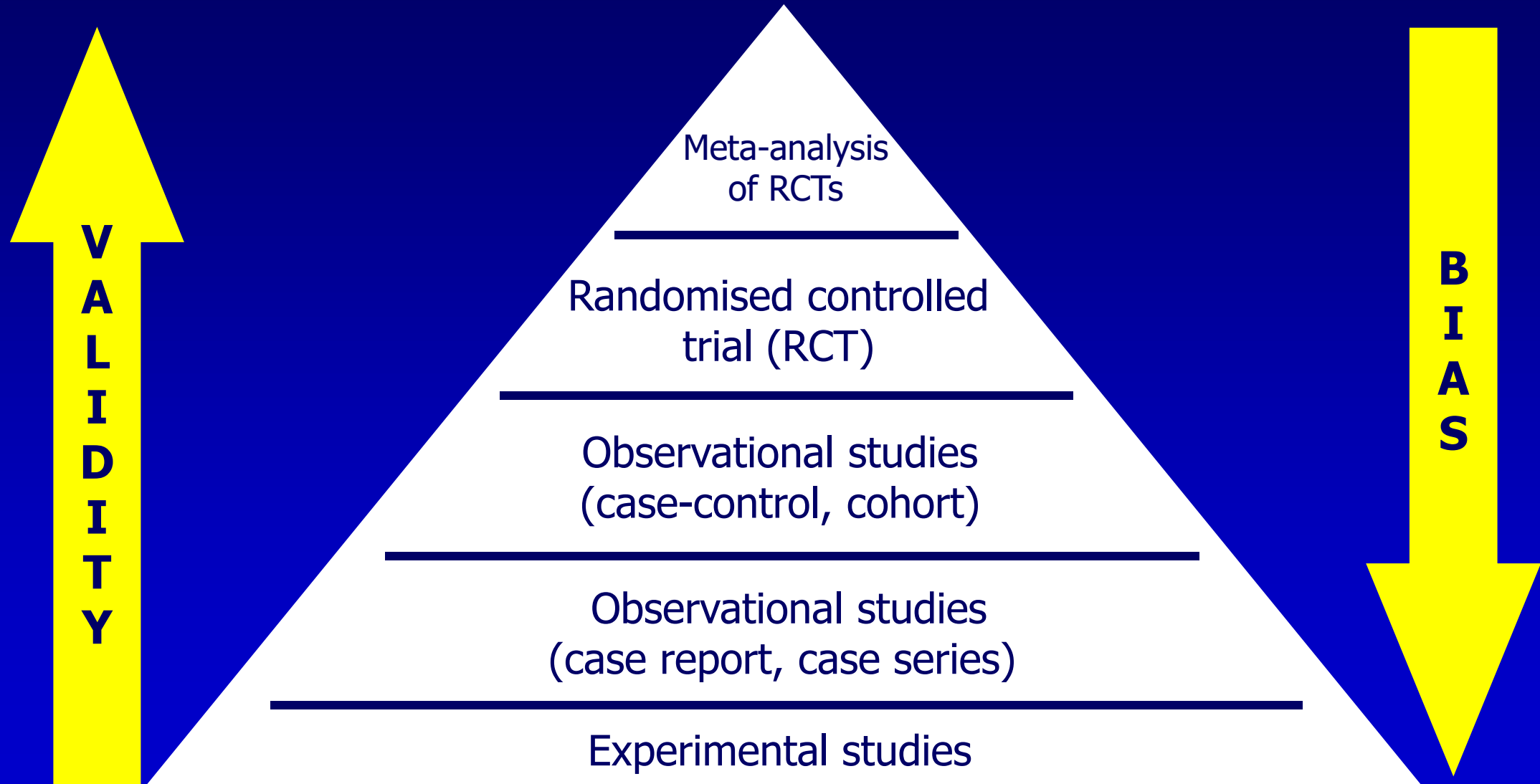


Figure 4. Graphical summary of our findings (adapted from Konopka¹⁴). Green: weighted average density reflecting functional efficiency. Red: number of paths divided by the number of adjacency matrices, reflecting stability. Grey: trends as proposed earlier by Konopka¹⁴.

Hierarchy of evidence

For questions about the effectiveness of an intervention



The forest plot

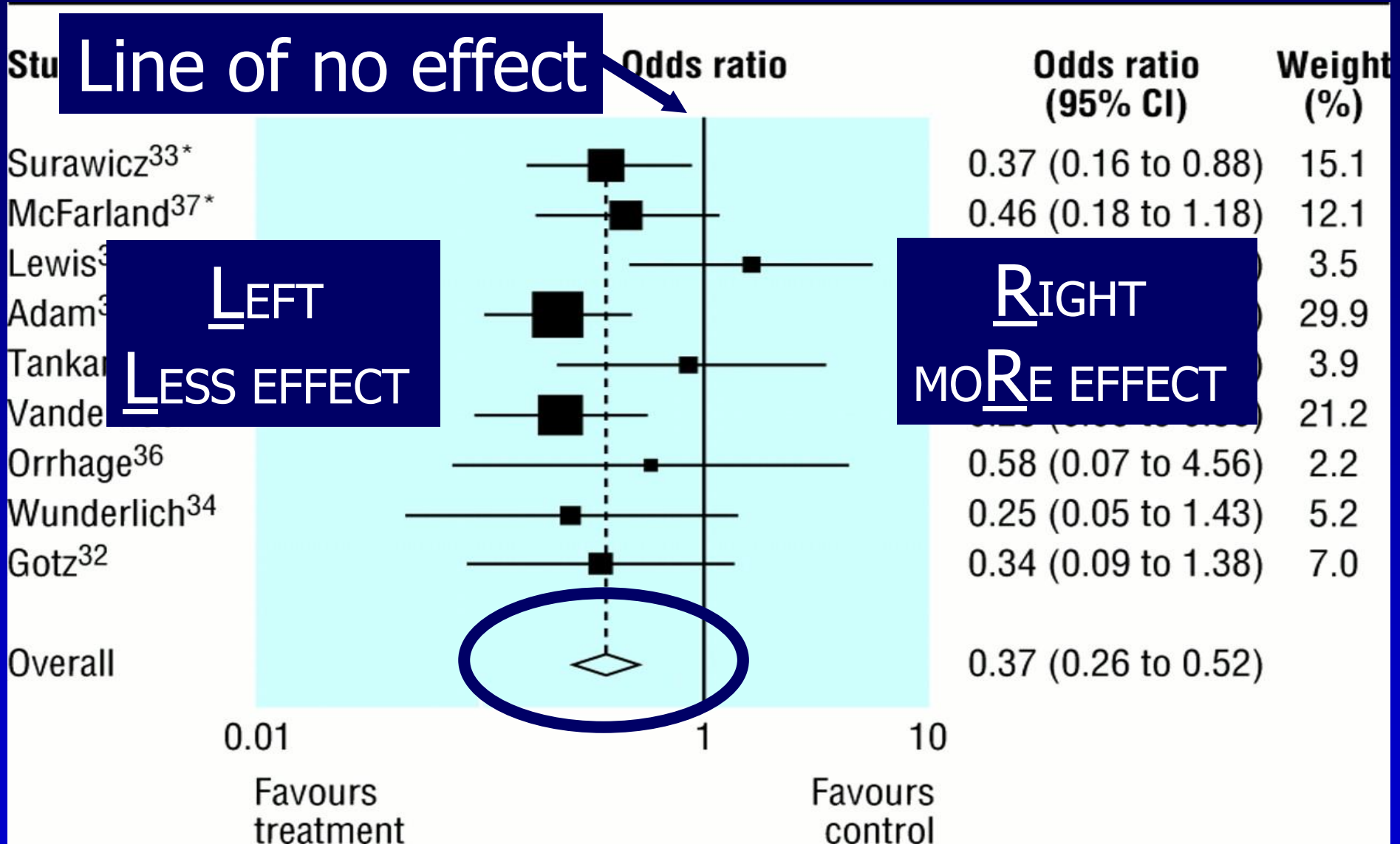
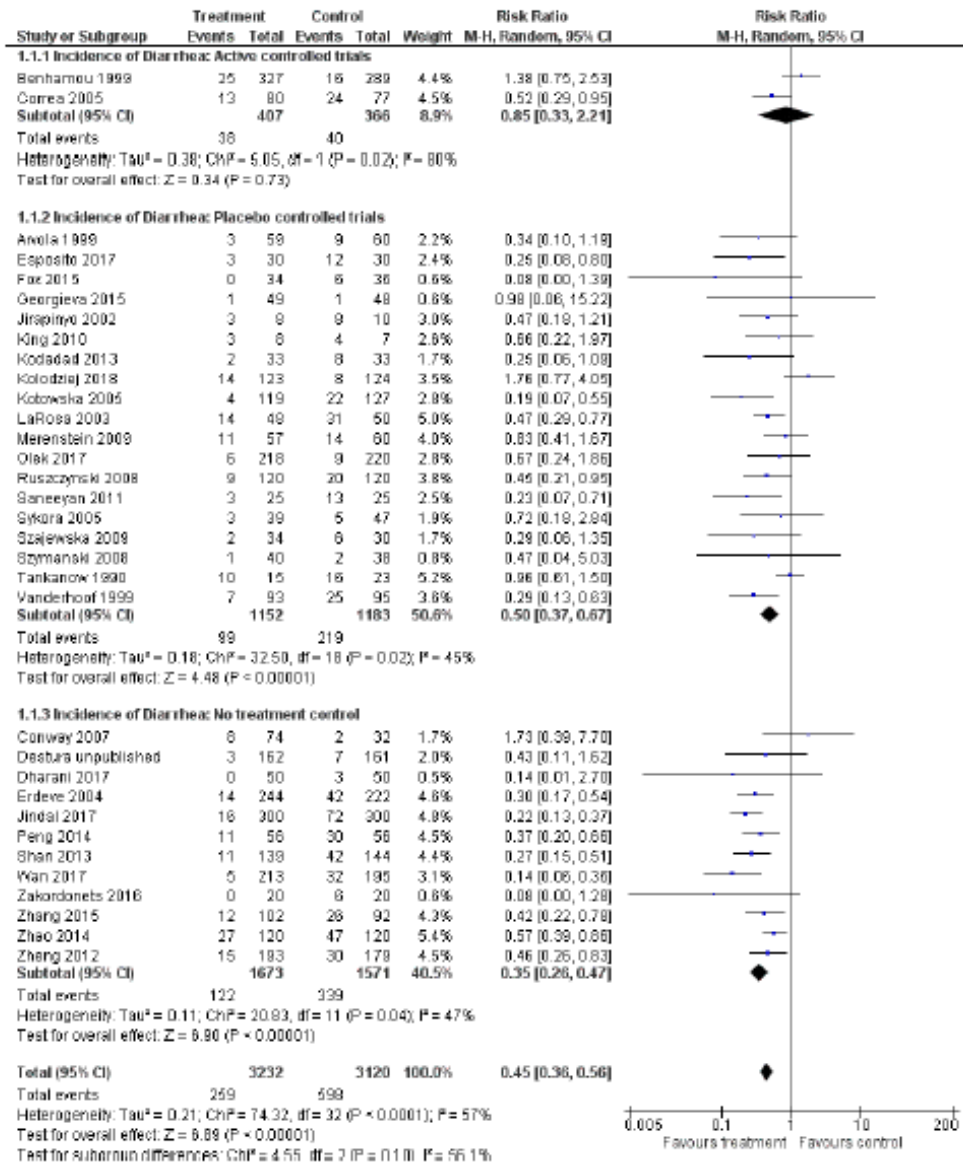
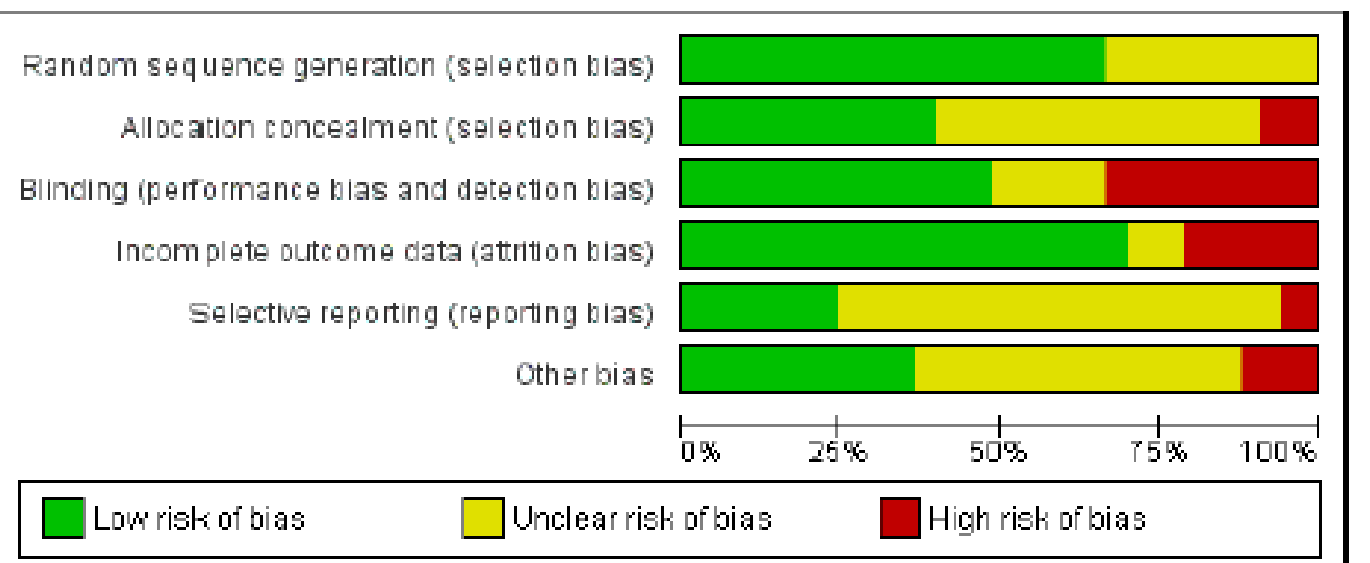


Figure 6. Forest plot of comparison: 1 Probiotics versus control, outcome: 1.1 Incidence of diarrhea Complete case.



Guo Q, Goldenberg JZ, Humphrey C, El Dib R, Johnston BC. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. Cochrane Database of Systematic Reviews **2019**, Issue 4. Art. No.: CD004827. DOI: 10.1002/14651858.CD004827.pub5.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



The overall evidence suggests a **moderate protective effect of probiotics** for preventing AAD (NNTB 9, 95% CI 7 to 13). Using five criteria to evaluate the credibility of the subgroup analysis on probiotic dose, the results indicate the subgroup effect based on high dose probiotics (**≥ 5 billion CFUs per day**) was credible. Based on high-dose probiotics, the NNTB to prevent one case of diarrhea is **6** (95% CI 5 to 9). The overall certainty of the evidence for the primary endpoint, incidence of AAD, based on high dose probiotics was moderate due to the minor issues with risk of bias and inconsistency related to a diversity of probiotic agents used. Evidence also suggests that probiotics may moderately reduce the duration of diarrhea, **a reduction by almost one day**. The benefit of high dose probiotics (e.g. *Lactobacillus rhamnosus* or *Saccharomyces boulardii*) needs to be confirmed by a large well-designed multi-centered randomized trial. It is premature to draw firm conclusions about the efficacy and safety of 'other' probiotic agents as an adjunct to antibiotics in children. Adverse event rates were low and no serious adverse events were attributable to probiotics.

Examples Atopic / Constitutional Eczema



Epidemiologic Associations between Antibiotic Use and Allergies; 14 STUDIES AND OVER 90 THOUSANDS PERSONS

Year	Design ^a	Subjects		
		Number	Residence	Description
1998	Retro (PB-BC)	1934	UK	General
1999	Retro (PB)	5067+	Germany	General
1999	Retro (CSS)	456	New Zealand	Anthroposophic (RS) ⁱ
2000	Retro (PB)	742 ----- 438	Belgium	General
2001	Pro (PB-BC)	939	Germany	General (38% atopy risk factors)
2001	Retro (PB)	2512	Germany	General
2002	Pro (FH)	498	US	FH of atopy
2002	Pro (PB-BC)	29,238	UK	General
2003	Retro (C-C)	7098-7098	UK	hayfever-control
2004	Pro (PB)	4408	US	General
2004	Retro (CSS)	1584 ----- 2539	New Zealand	"childhood infections" ----- "general population"
2004	Retro (PB)	746	UK	General
2005	Retro (PB)	26,400	Korea	General
2005	Pro (PB-BC)	448	US	General

Epidemiologic Associations between Fecal Microbiota Composition and Allergies

Subjects			Allergies		Experiments		Microflora Associations with Allergic Disease ^f	
Number ^b	Residence	Age	Disease ^c	Diagnosis ^d	Sample	Assay ^e	Negative ^g	Positive ^h
27-35	Estonia + Sweden	2 yr	AD (FA)	clinical and SPT	feces	microbiol	Lactobacilli, Bifidobacteria, CONS, Anaerobes, Bacteroides	Aerobes, Coliforms, <i>S. aureus</i> , Bacteroides
25-47	Sweden	12 mo	AD, asthma, FA	clinical and SPT	feces	molecular	propionic, butyric, i-butyric, i-valeric, and valeric FA	i-caproic FA ⁱ
44 (18)	Estonia + Sweden	0-2 yr	AD (FA)	clinical and/or SPT	feces	microbiol	Enterococci, Bifidobacteria, <i>Bacteroides</i>	<i>S. aureus</i> , Lactobacilli, Clostridia
4-6	NR	2-7 mo	AD and FA	clinical	feces	microbiol	<i>Bifidobacterium bifidum</i>	<i>Bifidobacterium adolescentis</i>
76 (22)	Finland	0-12 mo	atopy (+/- AD/FA)	SPT (clinical)	feces	microbiol, molecular, genetic	Similarity (%) of bacterial FA profile	Clostridia
27-10	Finland	0-14 mo	AD (FA)	clinical and SPT	feces	microbiol, genetic	Gram-positive species within aerobes, <i>S. viridans</i> , Clostridia ⁱ	Lactobacilli/enterococci ⁱ
7-6	NR	2-7 mo	AD	clinical and SPT	feces	microbiol	<i>Bifidobacterium bifidum</i>	<i>Bifidobacterium adolescentis</i>
10-10	UK	12 mo	atopic wheeze	clinical and SPT	blood	molecular		<i>C. difficile</i> -specific IgG
30-68	Japan	< 20 yr	AD	clinical	feces	microbiol	<i>Bifidobacterium</i>	<i>Staphylococcus</i>
33-33 (8-8) ^k	UK	3-5 yr	atopic wheeze (AD) ^k	clinical and SPT	feces	genetic	(Bifidobacteria) ^k	
19-19	Estonia	5 yr	AD, asthma, allergic rhinitis	clinical and SPT and/or IgE	feces	microbiol	Bifidobacteria	Clostridia
21-28	Singapore	~3 yr	AD	clinical	feces	microbiol, genetic	<i>Bifidobacterium</i> spp., <i>Clostridium</i> spp.	Lactic acid bacteria, enterococci

Identification and antibiotic resistance of isolates from probiotic products

T. Temmerman, Ghent, Belgium

55 European probiotic products

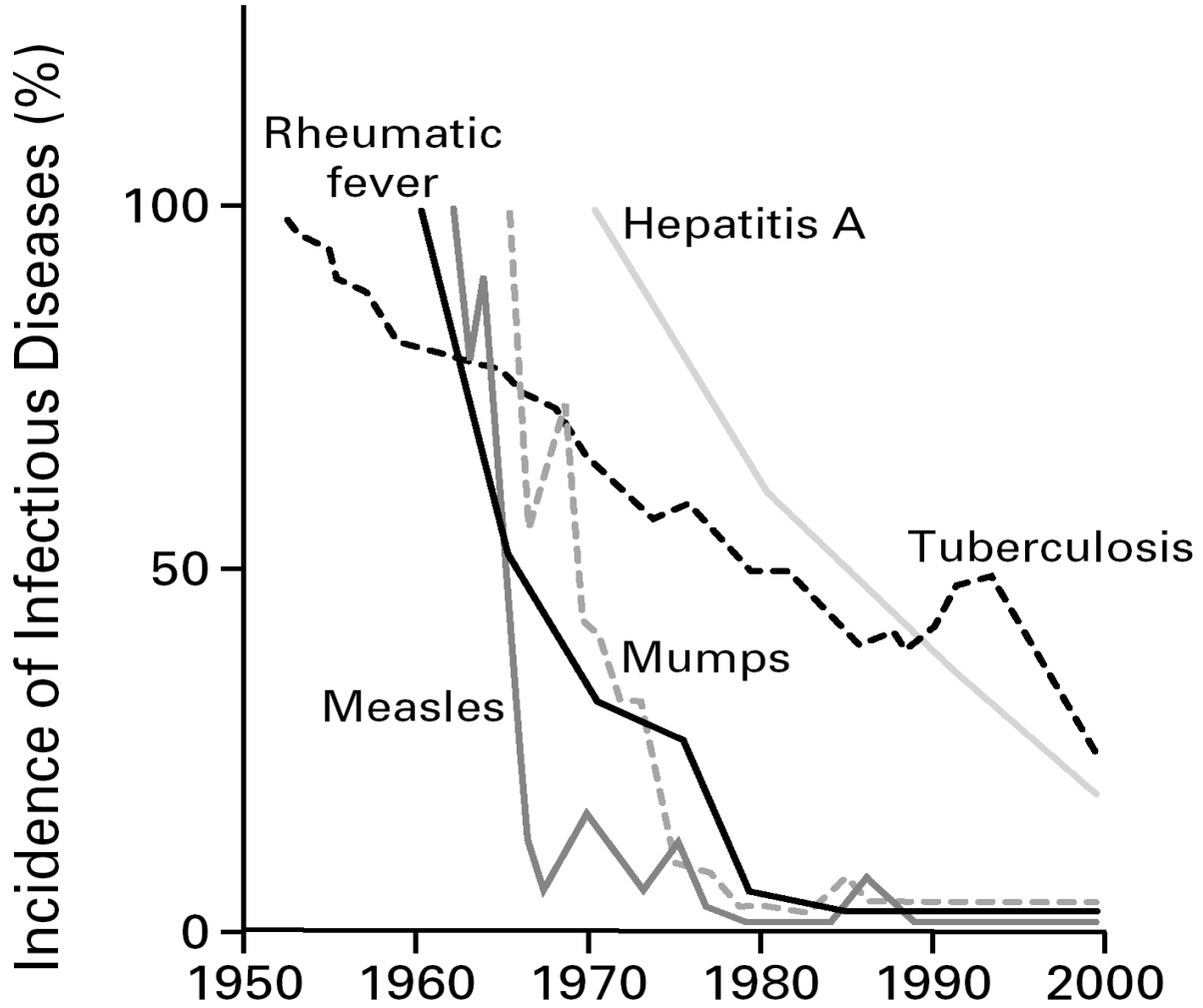
25 dairy products

20 dried food supplements

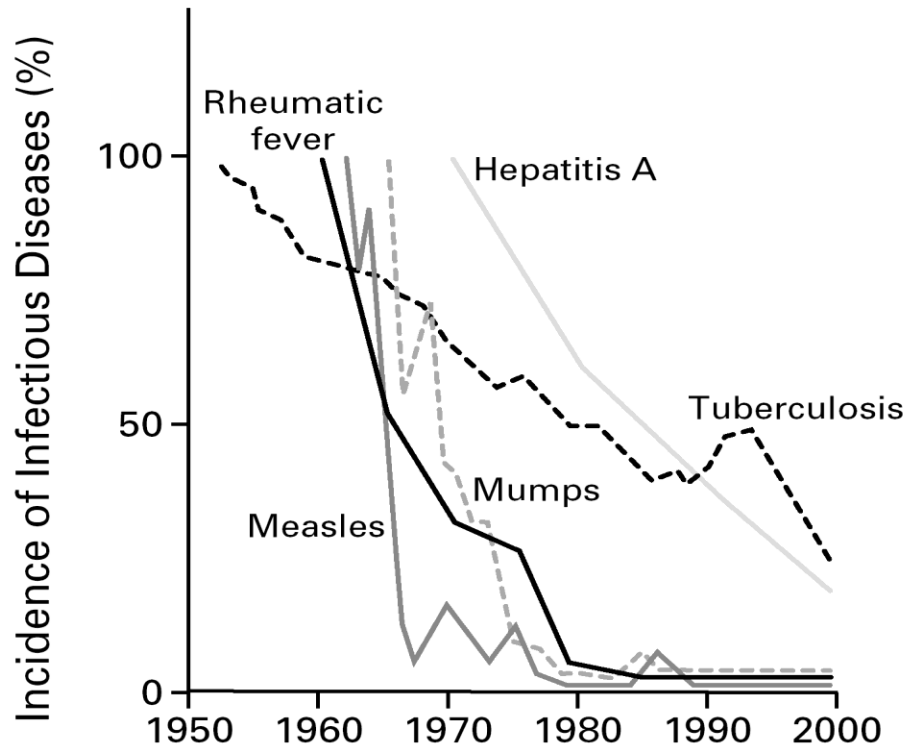
Antibiotic resistance

antibiotic	% resistance
Kanamycin	79 %
Vancomycin	65 %
Tetracycline	26 %
Pencillin G	23 %
Erythromycin	16 %
Chloramphenicol	11 %

A



A



B

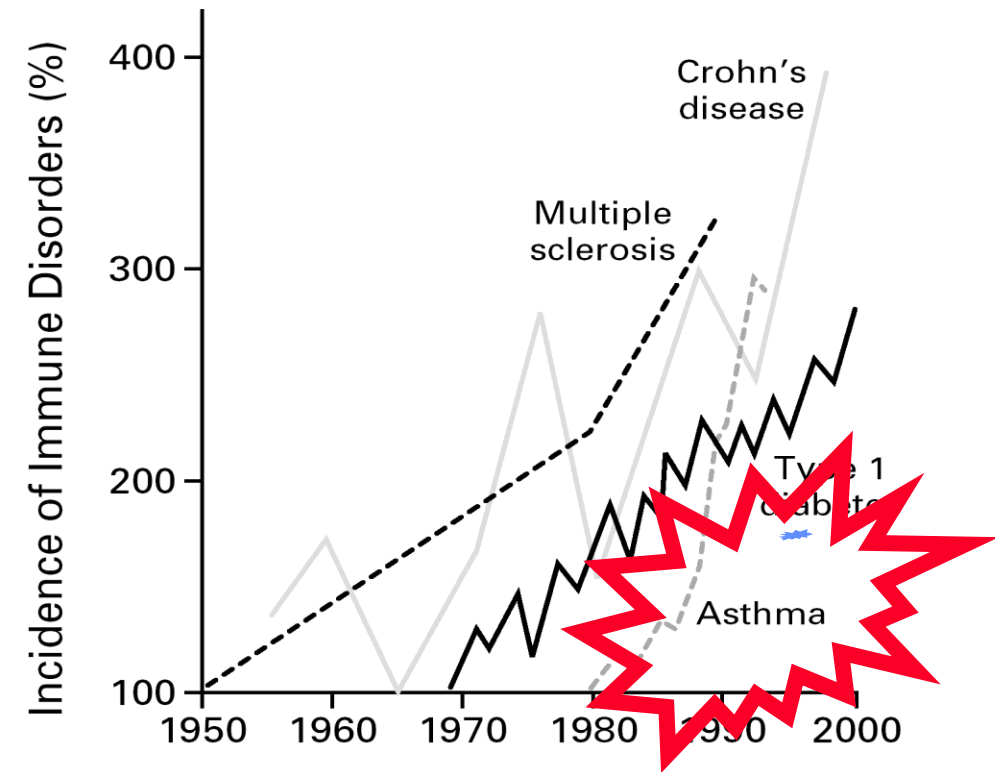


Figure 1. Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1950 to 2000.

In Panel A, data concerning infectious diseases are derived from reports of the Centers for Disease Control and Prevention, except for the data on hepatitis A, which are derived from Joussemet et al.¹² In Panel B, data on immune disorders are derived from Swarbrick et al.,¹⁰ Dubois et al.,¹³ Tuomilehto et al.,¹⁴ and Pugliatti et al.¹⁵

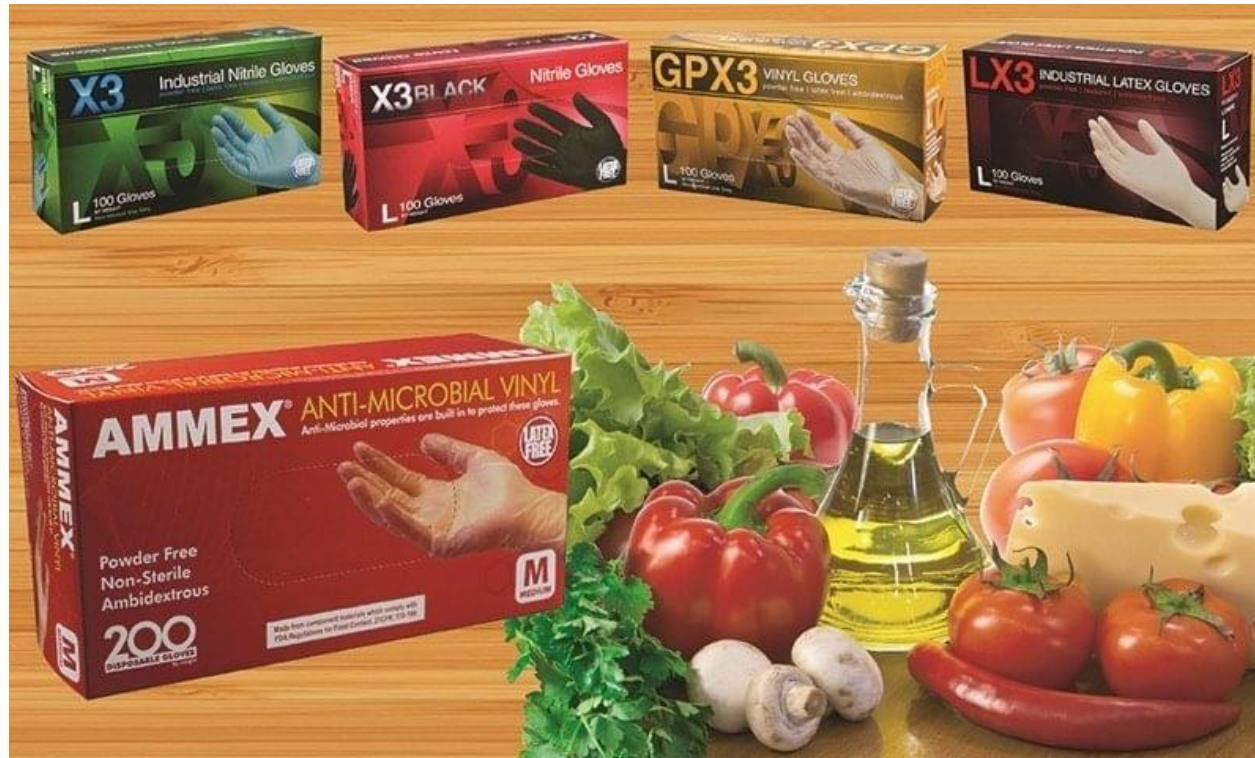
Examples Atopic / Constitutional Eczema



Hygiene hypothesis: relevant microbial exposures?

- **Childhood infections (Hep A?): NO**
- **Domestic hygiene (bathing, soaps, detergents, antibacterial kitchen cutting boards etc.): NO**
- **“Old Friends” (helminths, mites, saprophytic mycobacteria, lactobacilli): YES?**

With increased food safety our food has also become more and more sterile



Every advantage has its disadvantage.

— Johan Cruijff —

Breast is Best

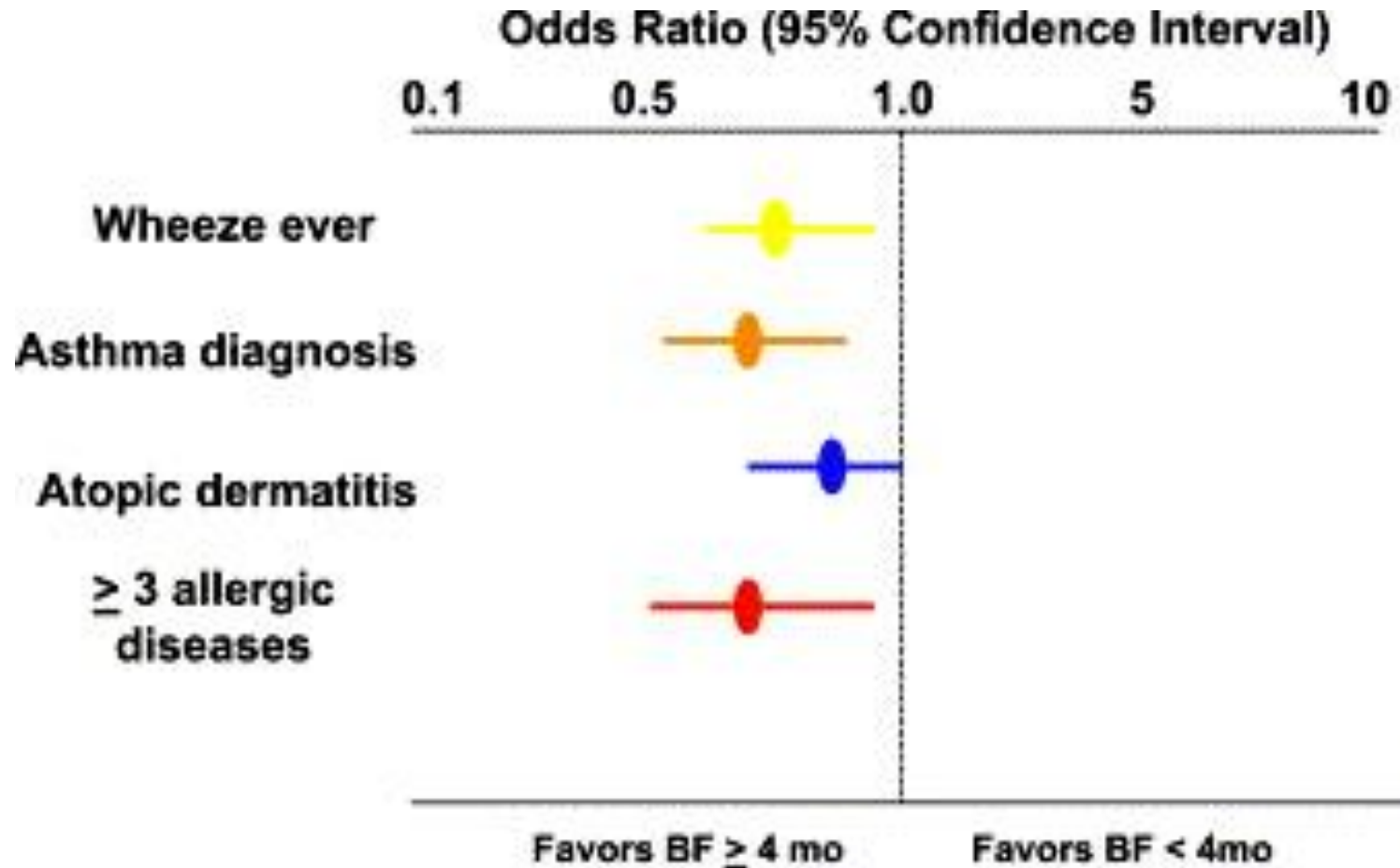


Breastfeeding - my best role ever.

Xenia Warrior Princess



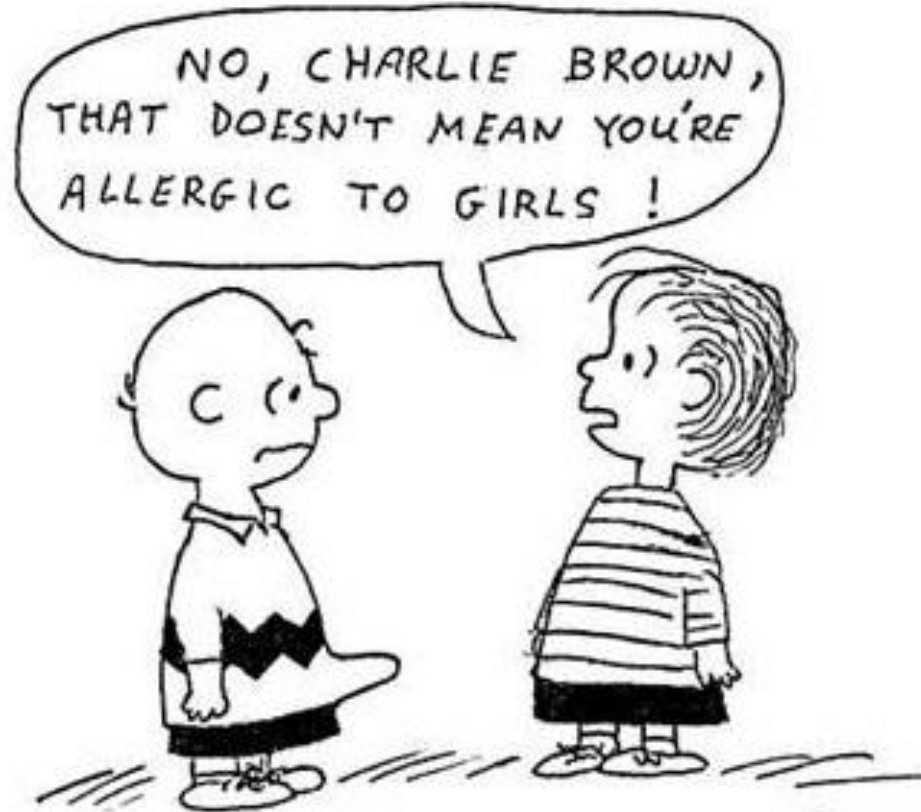
Breastfeeding reduces chance on allergy





Allergisch meisje of?

Allergisch voor meisjes?



**Rautava S. J. Allergy Clin Immunol 2002: 109 pp 119-121
& reviews by E. Isolauri**



Now in its 15th year the probiotic use by pregnant mothers + breastfeeding study still shows a 45% reduction in children's clinical manifestations of IgE+ve allergy over placebo

Breastfeeding remains key!!!!!!

MOTHERISK ROUNDS

Probiotic Safety in Pregnancy: A Systematic Review and Meta-analysis of Randomized Controlled Trials of *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces spp.*

Jean-Jacques Dugoua, HBSc, ND,^{1,2} Marcio Machado, PhD,³ Xu Zhu, MSc,¹ Xin Chen, HBSc,¹ Gideon Koren, MD, FABMT, FRCPC,^{1,2,4} Thomas R. Einarson, PhD^{1,2,4}

¹Graduate Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto ON

²Motherisk Program, Hospital for Sick Children, Toronto ON

³Toronto Health Economics and Technology Assessment Collaborative (THETA), University of Toronto, Toronto ON

⁴Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto ON

The Africa Paradox and the hygiene hypothesis



Skin prick tested children

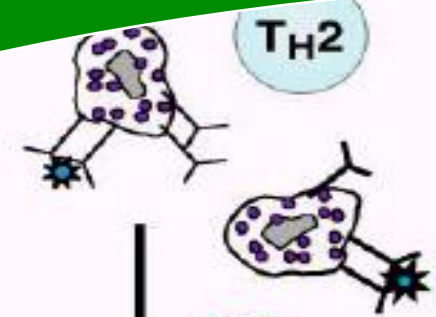


High exposure to pathogens:
strong stimulation of
TH2 responses.

Vaccines, antibiotics, and antiparasitics: little TH2 stimulation

Low exposure to pathogens: weak regulatory network

High exposure to pathogens: strong regulatory network



Allergic responses:
Asthma,
Rhinoconjunctivitis

Seropositive for allergens: but little allergic disease



'Old friends trigger regulation through innate dendritic cell receptors'

Mechanisms of Disease: the hygiene hypothesis revisited

Francisco Guarner*, Raphaëlle Bourdet-Sicard, Per Brandtzaeg, Harsharnjit S Gill, Peter McGuirk, Willem van Eden, James Versalovic, Joel V Weinstock and Graham AW Rook

NATURE CLINICAL PRACTICE GASTROENTEROLOGY & HEPATOLOGY

MAY 2006 VOL 3 NO 5

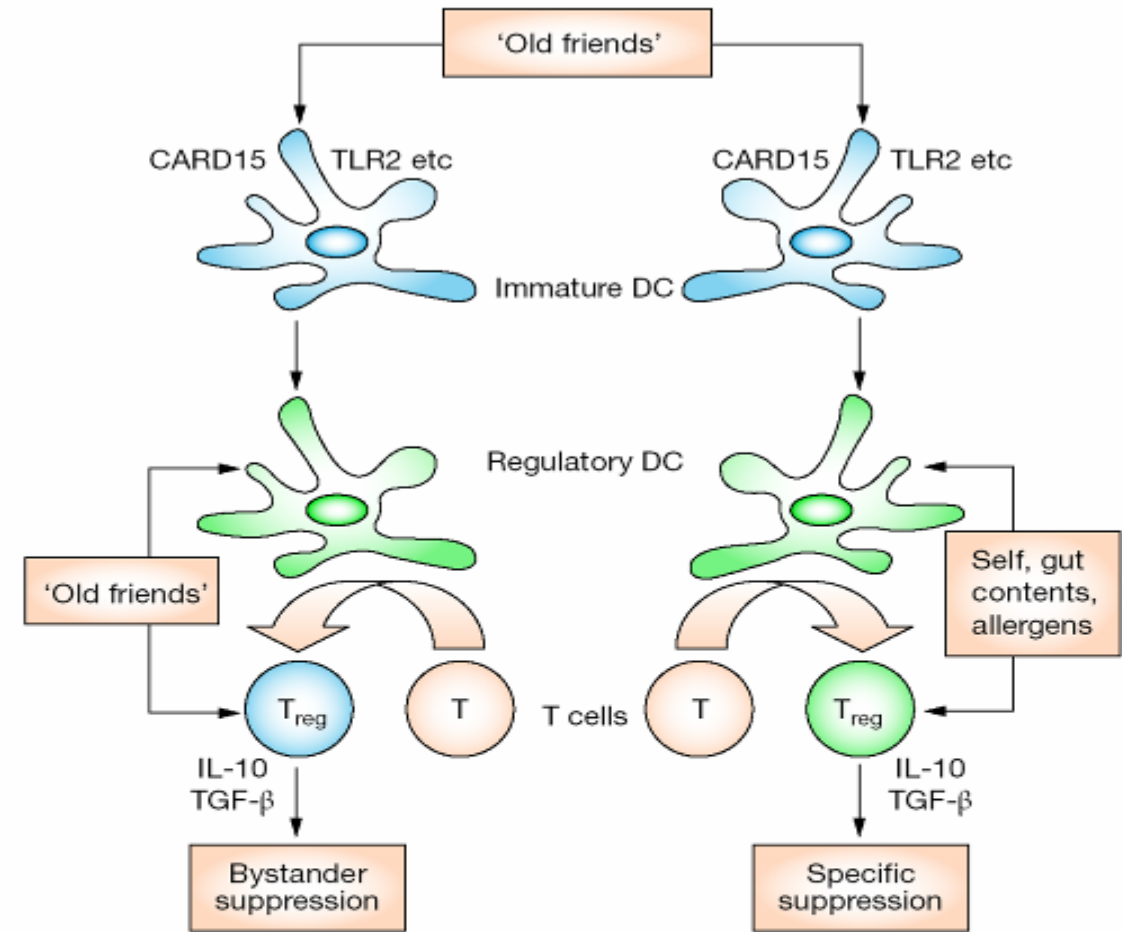


Figure 3 The 'old friends' hypothesis. Organisms recognized as harmless by the innate immune system (through pattern-recognition receptors, such as CARD15 and Toll-like receptor 2) cause dendritic cells to mature into regulatory dendritic cells that drive regulatory-T-cell polarization. Some of these cells will recognize the 'old friends' themselves, and so provide a continuous background bystander regulation. Regulatory dendritic cells, however, might also process and present epitopes from self, allergens and gut content (antigens, bacterial DNA motifs, microbial heat-shock proteins) and so drive specific immunoregulation. DC, dendritic cells; IL, interleukin; TGF- β , transforming growth factor- β ; TLR2, Toll-like receptor 2; T_{reg}, regulatory T cell.

Scout senses
no danger
(sees “old
friends”): info to
officer “steady
state of
tolerance”
“Hold your fire”



Allergy: Scout
senses danger &
no old friends:
info to officer and
command to fire



The possible link between de-worming and the emergence of immunological disease

JOEL V. WEINSTOCK, ROBERT W. SUMMERS, DAVID E. ELLIOTT, KHURRAM QADIR, JOSEPH F. URBAN, JR, and ROBIN THOMPSON

IOWA CITY, IOWA, and BELTSVILLE, MARYLAND

A major objective of our laboratory is the study of the various complex host immunological responses to helminths. Helminths are a group of worm-like organisms, some of which live in the intestinal lumen or host tissue. Helminths include

experimental data from both human and animal research now provide substantial support for this hypothesis.

Exposure to helminths in early life may have a protective effect on the immune system. Weinstock: "We're opening up the possibility of whole new classes of drugs."



Man and his worm. Joel Weinstock holds a dose of eggs from *Trichuris suis* (inset), which he is using to treat inflammatory bowel disease.

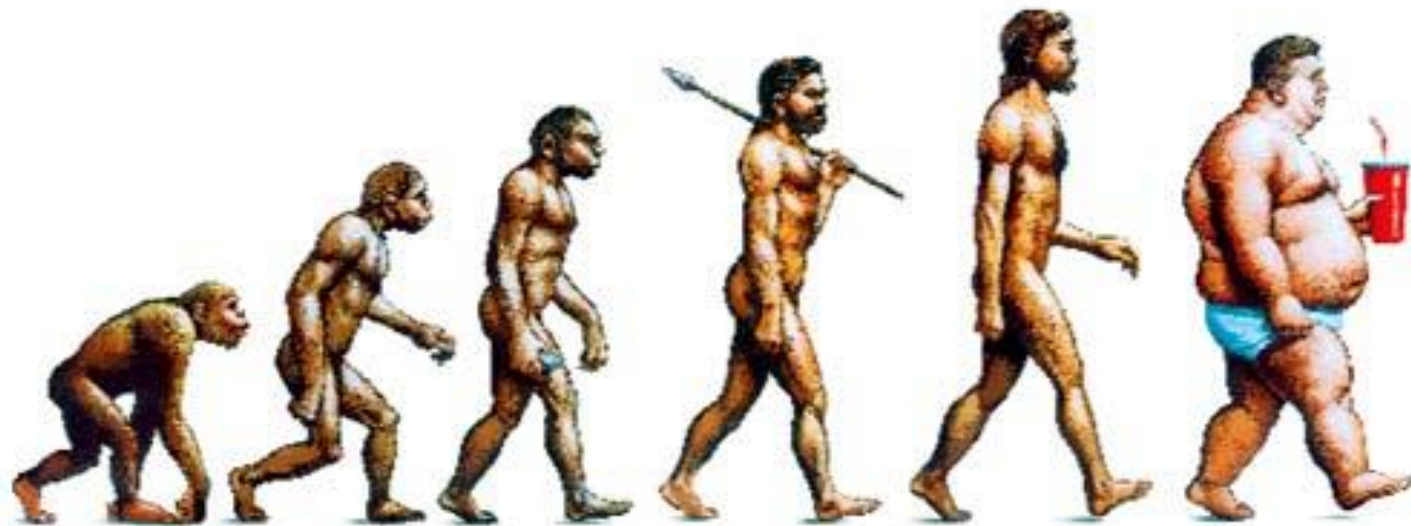
children in
with the
haematob
lergic to h
for asthma
free of we
concentrat
uct of reg
higher in i

HYGIËNE

Vroeger: minder
hygiëne en
minder allergie

Beetje vies is gezond





The development of probiotic treatment in obesity: a review

M.C. Mekkes^{1*}, T.C. Weenen^{2,3*}, R.J. Brummer⁴ and E. Claassen^{1,3}

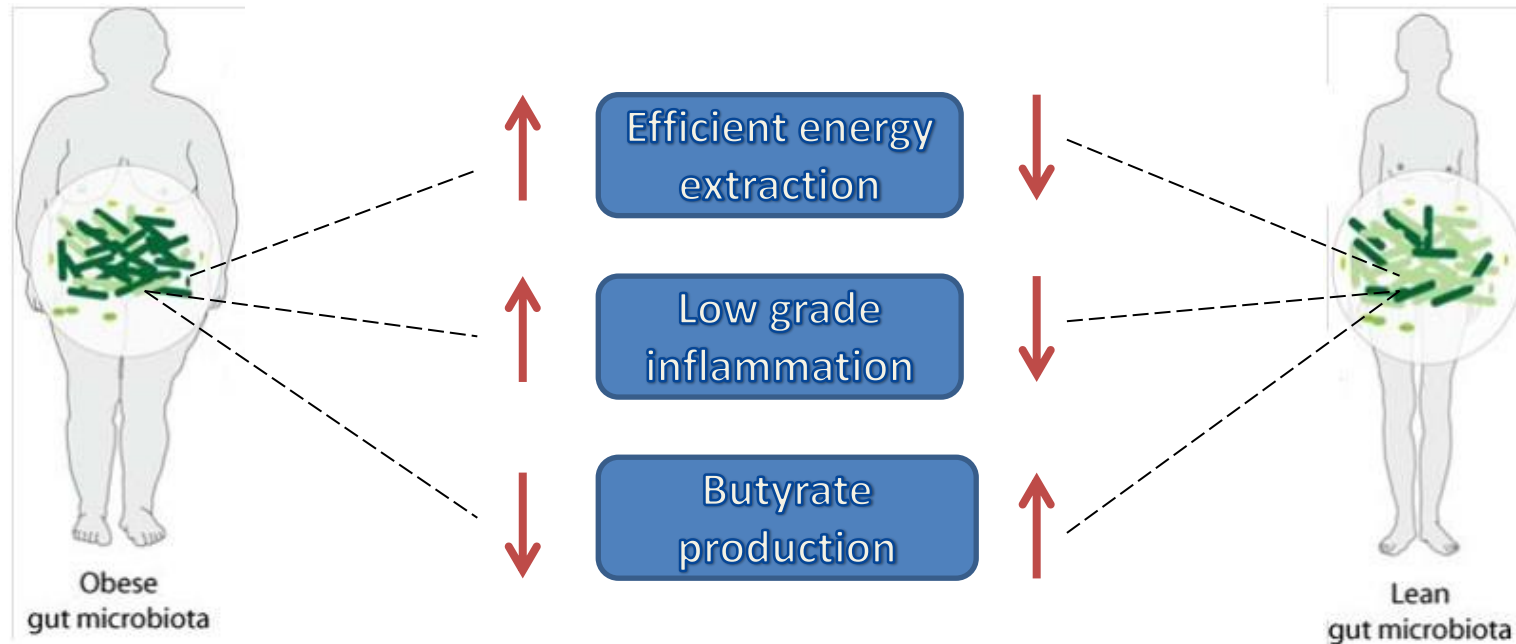
¹VU University Amsterdam, Athena Institute, De Boelelaan 1085, 1081 HV Amsterdam, the Netherlands; ²Erasmus School of Economics Rotterdam, Burgemeester Oudlaan 50, 3062 PA Rotterdam, the Netherlands; ³Erasmus Medical Center Rotterdam, Dr. Molewaterplein 50, 1315 GE Rotterdam, the Netherlands; ⁴School of Health and Medical Sciences, Örebro University, 701 82 Örebro, Sweden; marcel.mekkes@gmail.com; *Co-first author

Received: 18 December 2012 / Accepted: 3 March 2013

© 2013 Wageningen Academic Publishers

REVIEW ARTICLE

The influence on metabolism

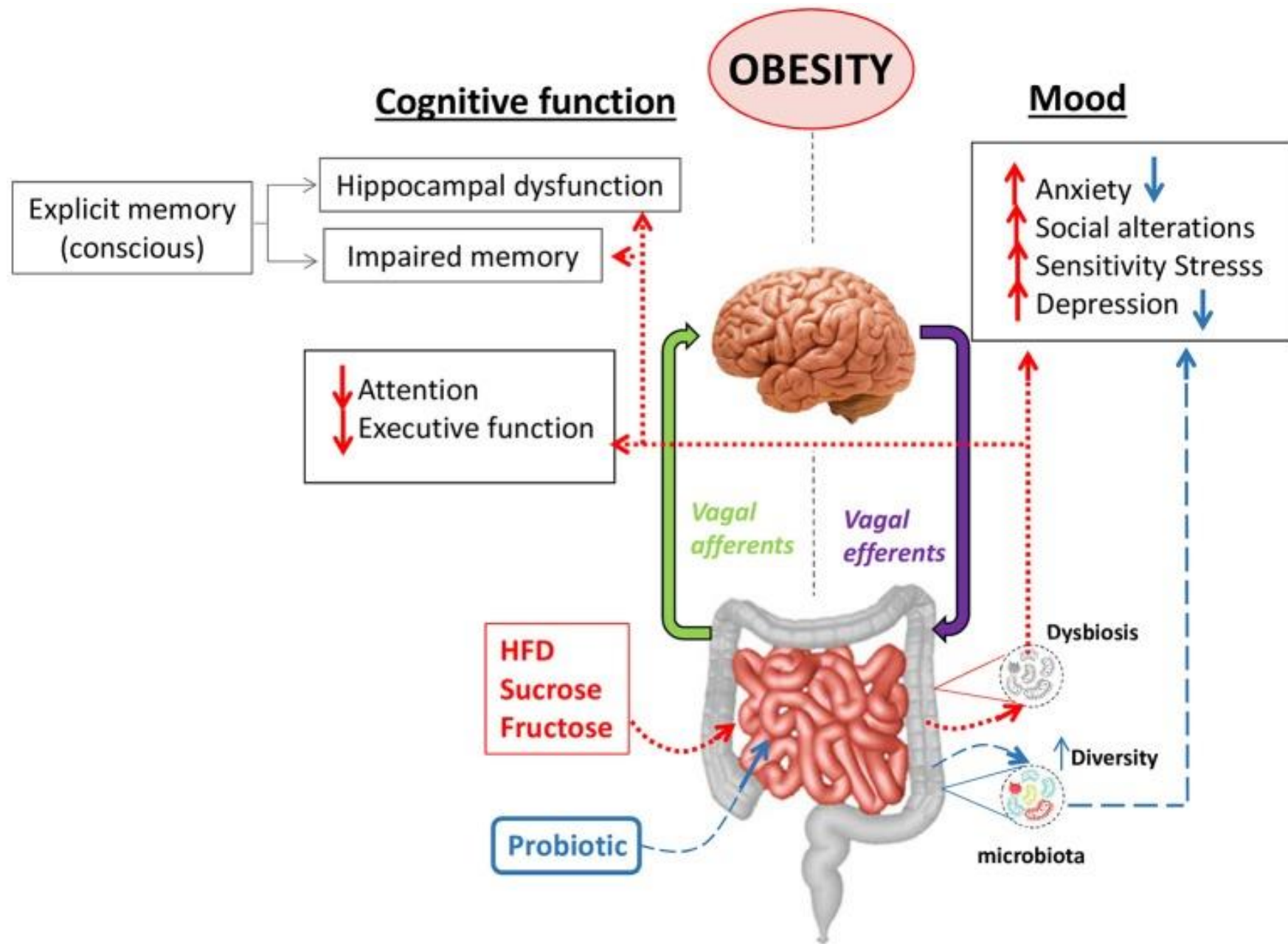


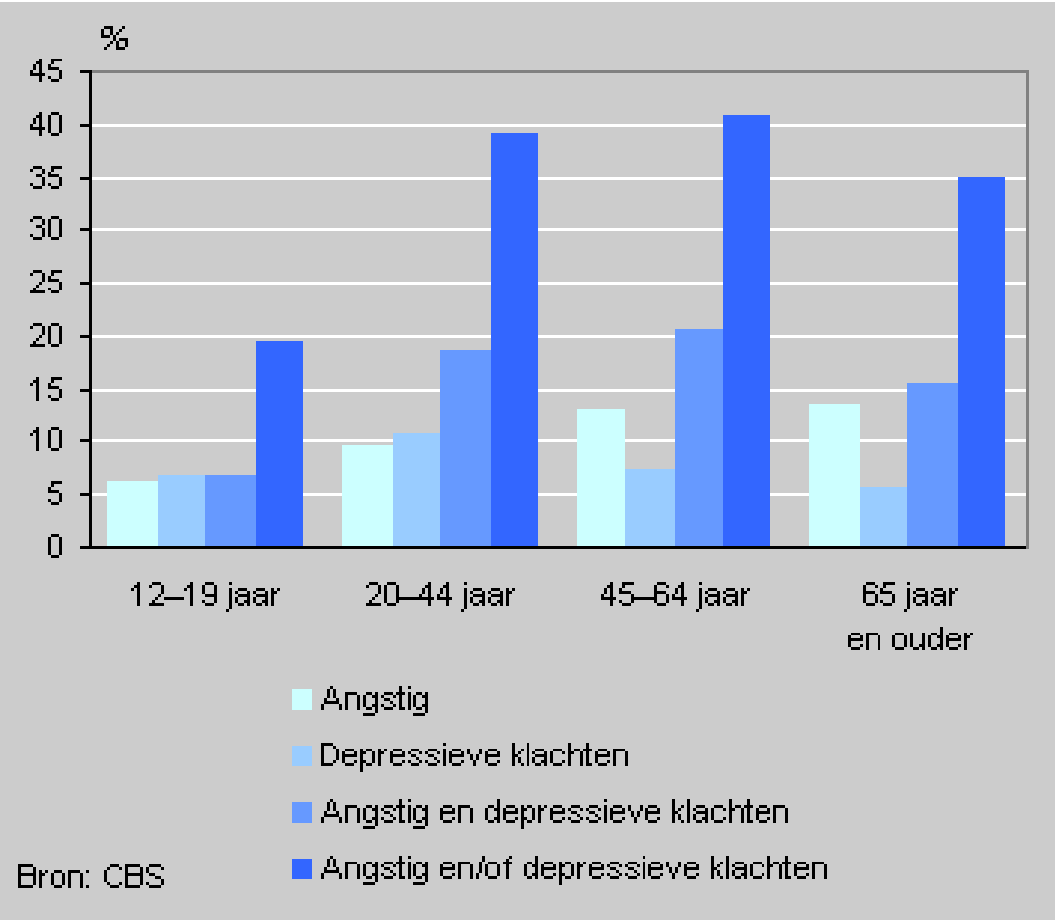
- This explains the differences in metabolic mechanisms
- These insights are a base to understand the Mechanism Of Action (MOA) of future probiotic treatment
- Probiotic microorganism might manipulate these mechanisms
 - Reducing effect on weight and weight gain

eat until **80%** full. はら
はち
ぶ



HARA HACHI BU





Darmmicrobiota bepalen gedrag: *Angst zit in je darm en niet in je brein!*

GASTROENTEROLOGY 2010;139:2102-2112

Chronic Gastrointestinal Inflammation Induces Anxiety-Like Behavior and Alters Central Nervous System Biochemistry in Mice

PREMYSL BERCIK,* ELENA F. VERDU,* JANE A. FOSTER,^{±,5} JOSEPH MACRI,[¶] MURRAY POTTER,[¶] XIAXING HUANG,* PAUL MALINOWSKI,[¶] WENDY JACKSON,* PATRICIA BLENNERHASSETT,* KAREN A. NEUFELD,^{±,5} JUN LU,* WALIUL I. KHAN,^{*,¶} IRENE CORTHESEY-THEULAZ,[#] CHRISTINE CHERBUT,^{**} GABRIELA E. BERGONZELLI,[#] and STEPHEN M. COLLINS*

GASTROENTEROLOGY 2011;141:599-609

Cell 155, 1451-1463, December 19, 2013

The Intestinal Microbiota Affect Central Levels of Brain-Derived Neurotrophic Factor and Behavior in Mice

PREMYSL BERCIK,* EMMANUEL DENOUE,* JOSH COLLINS,* WENDY JACKSON,* JUN LU,* JENNIFER JURY,* YIKANG DENG,* PATRICIA BLENNERHASSETT,* JOSEPH MACRI,[‡] KATHY D. McCoy,* ELENA F. VERDU,* and STEPHEN M. COLLINS*

Microbiota Modulate Behavioral and Physiological Abnormalities Associated with Neurodevelopmental Disorders

Elaine Y. Hsiao,^{1,2,*} Sara W. McBride,¹ Sophia Hsien,¹ Gil Sharon,¹ Embriette R. Hyde,³ Tyler McCue,³ Julian A. Codelli,² Janet Chow,¹ Sarah E. Reisman,² Joseph F. Petrosino,³ Paul H. Patterson,^{1,4,*} and Sarkis K. Mazmanian^{1,4,*}

Cell 155:1451-1463; 2013



Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

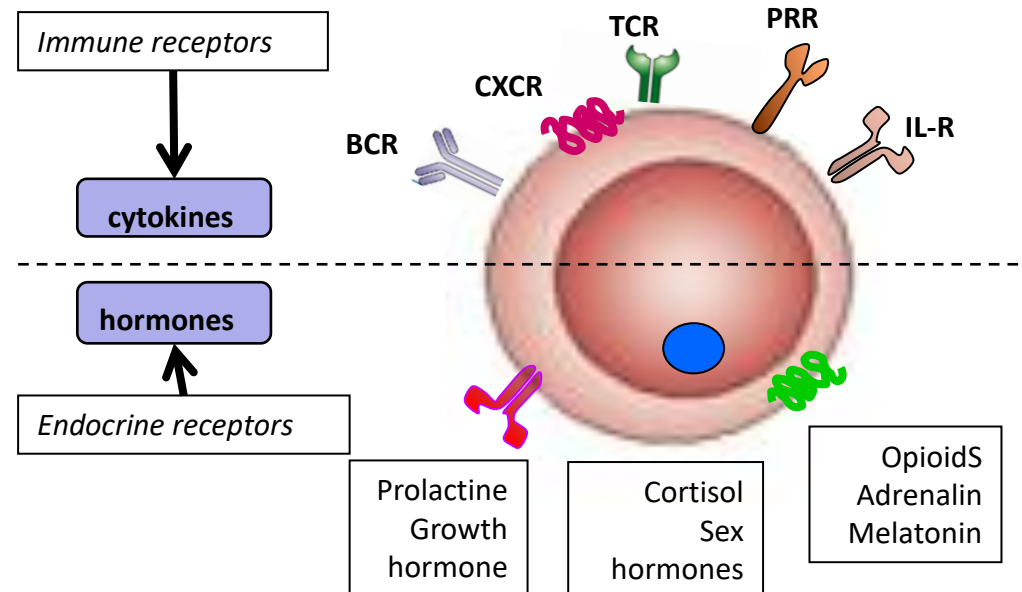


A randomized controlled trial to test the effect of multispecies probiotics on cognitive reactivity to sad mood ☆



Laura Steenbergen^{a,b,*}, Roberta Sellaro^{a,b}, Saskia van Hemert^c, Jos A. Bosch^d, Lorenza S. Colzato^{a,b}

Gezonde studenten: probiotica gedurende weken
→ minder gevoelig voor negatieve gedachten typisch voor depressie
→ ondersteunende/preventieve therapie bij PDS?




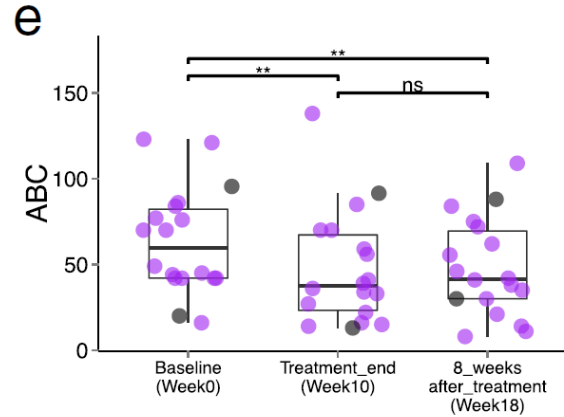
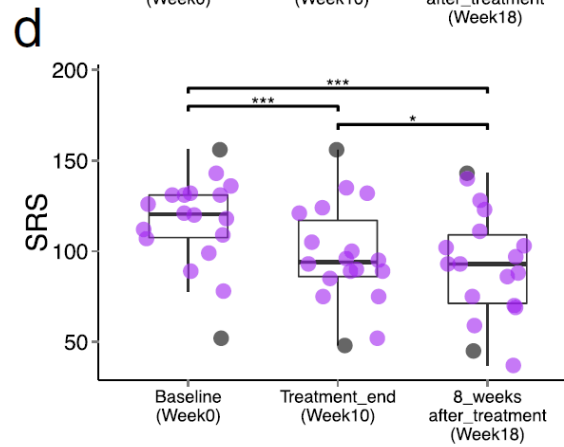
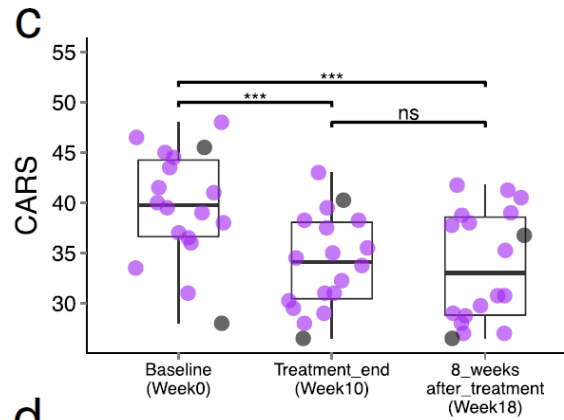
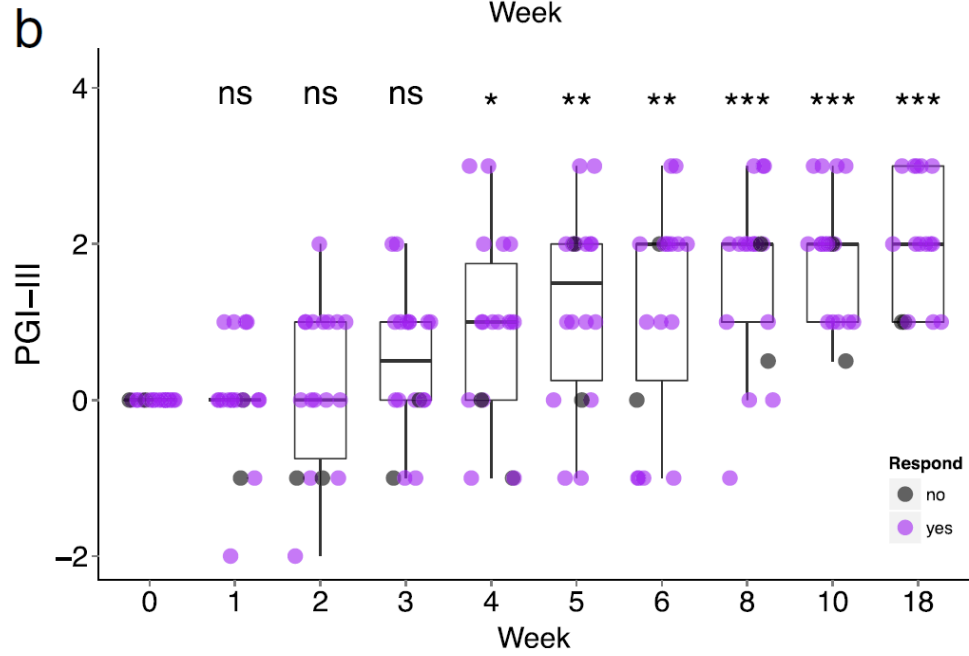
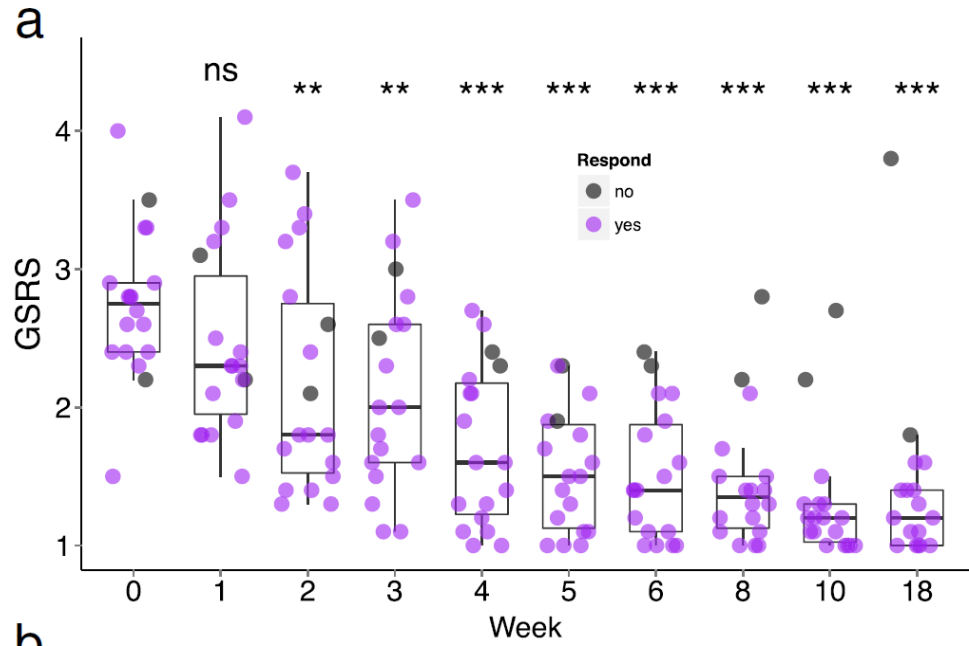
RESEARCH

Open Access



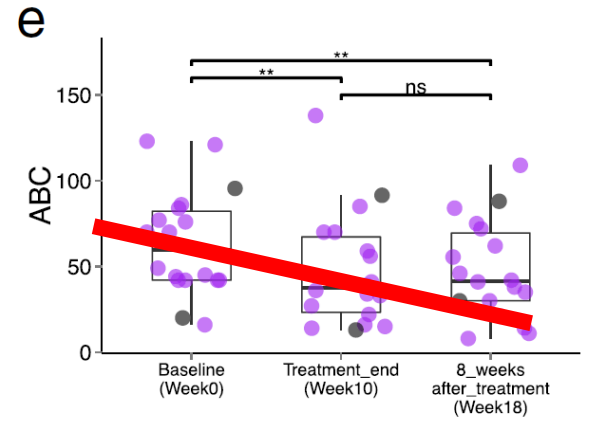
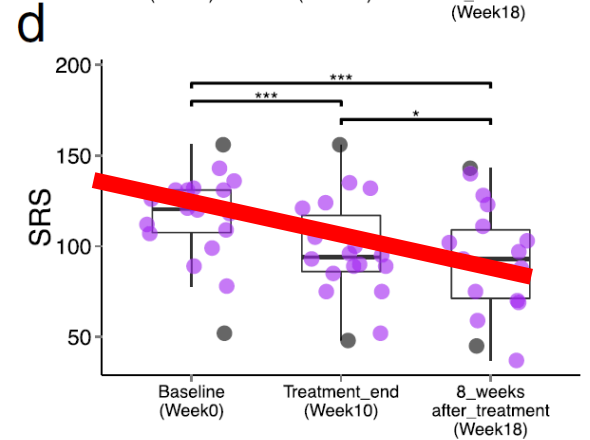
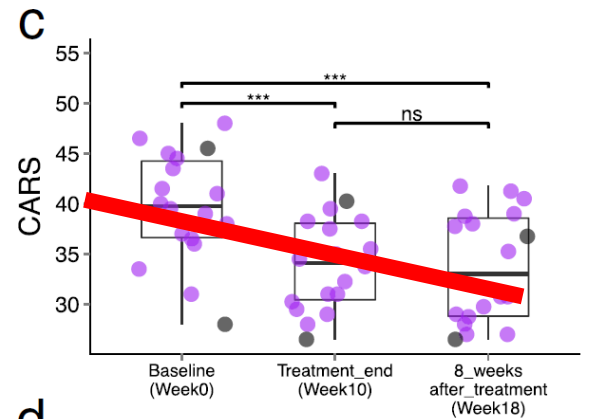
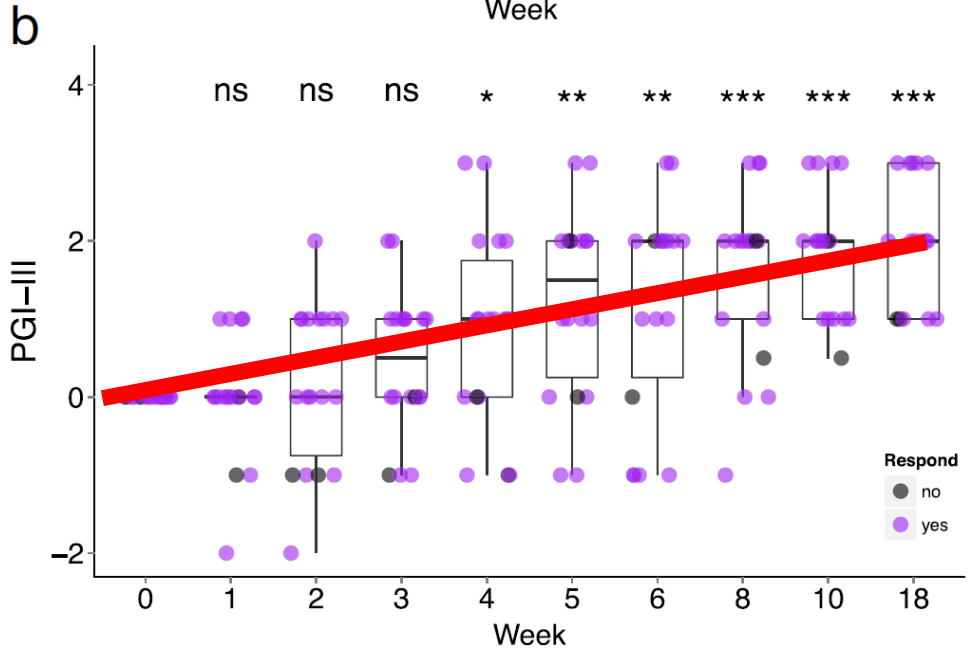
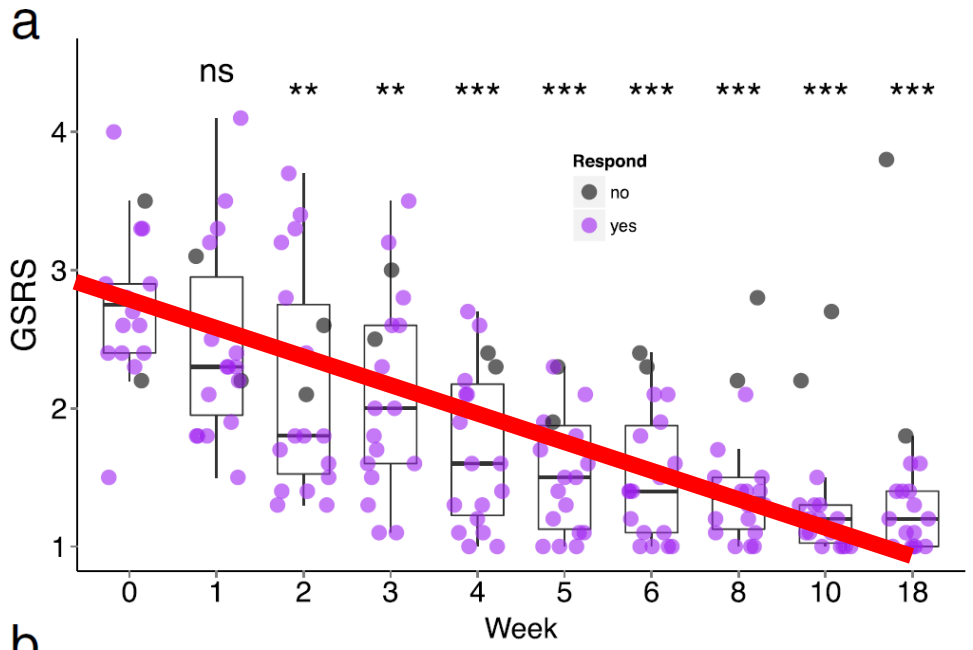
Microbiota Transfer Therapy alters gut ecosystem and improves gastrointestinal and autism symptoms: an open-label study

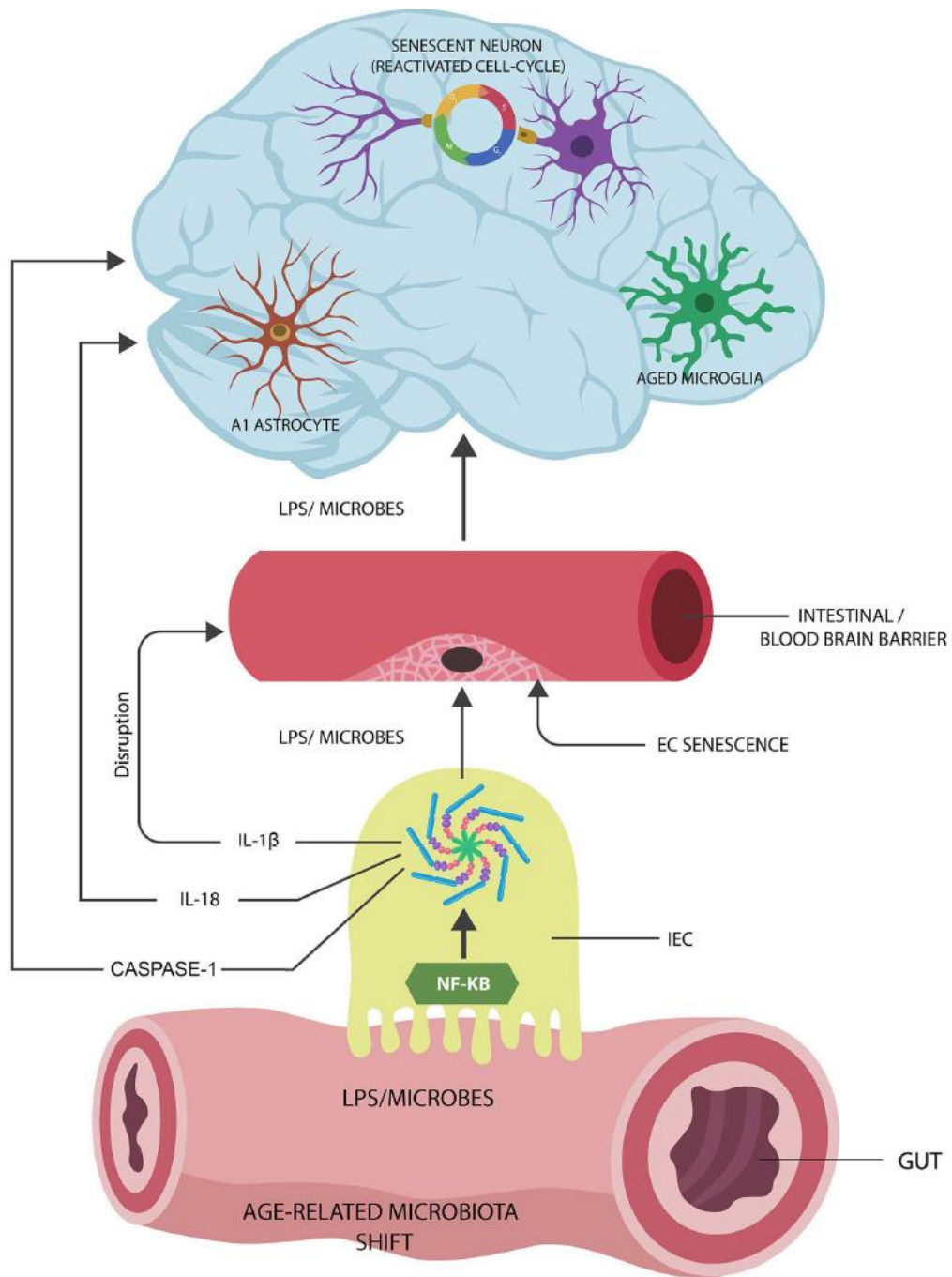
Dae-Wook Kang^{1†}, James B. Adams^{2†}, Ann C. Gregory^{3,15†}, Thomas Borody⁴, Lauren Chittick^{5,15}, Alessio Fasano⁶, Alexander Khoruts^{7,8,9}, Elizabeth Geis², Juan Maldonado¹, Sharon McDonough-Means¹⁰, Elena L. Pollard², Simon Roux^{5,15}, Michael J. Sadowsky^{8,11}, Karen Schwarzberg Lipson¹², Matthew B. Sullivan^{3,5,15,16*}, J. Gregory Caporaso^{12,13*} and Rosa Krajmalnik-Brown^{1,14*} 



- a) Gastrointestinal symptom rating scale
- b) Parent global impressions-III
- c) Childhood autism rating scale
- d) Social responsiveness scale
- e) Aberrant behavior checklist

- a) Gastrointestinal symptom rating scale
- b) Parent global impressions-III
- c) Childhood autism rating scale
- d) Social responsiveness scale
- e) Aberrant behavior checklist





The Post-amyloid Era in Alzheimer's Disease: Trust Your Gut Feeling

Carolina Osorio¹, Tulasi Kanukuntla², Eddie Diaz², Nyla Jafri², Michael Cummings² and Adonis Sfera^{2*}

History of Health Claims

- **Persian version of the Old Testament (Genesis 18:8) states “ Abraham owed his longevity to the consumption of sour milk.”**
- **In 76 BC the Roman historian Plinius recommended the administration of fermented milk products for treating gastroenteritis .**

The history of probiotics: the untold story.

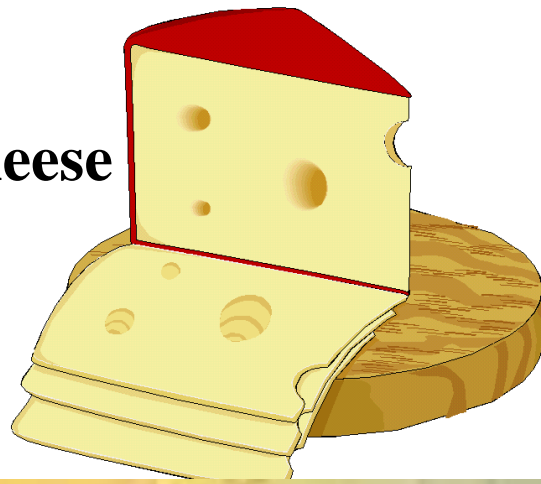
Ozen M, Dinleyici EC

Probiotic, a word derived from Latin, means 'for life'. A long time before the awareness of probiotic microorganisms, fermented products, such as beer, bread, wine, kefir, kumis and cheese had been very frequently used for nutritional and **therapeutic** purposes.

Yoghurt is most likely resulted from a fermentation process within the animal skin bags used for transportation of water and milk in regions with low humidity and high temperatures (Middle Asia and Middle East).

The history of probiotics goes parallel with the evolution of human race and, thanks to the sophisticated techniques at the moment, can be traced back to the ancient times, nearly **10,000 years ago**.

Cheese



Yogurt



**MILK KEFIR BENEFITS
A PROBIOTIC POWERHOUSE**



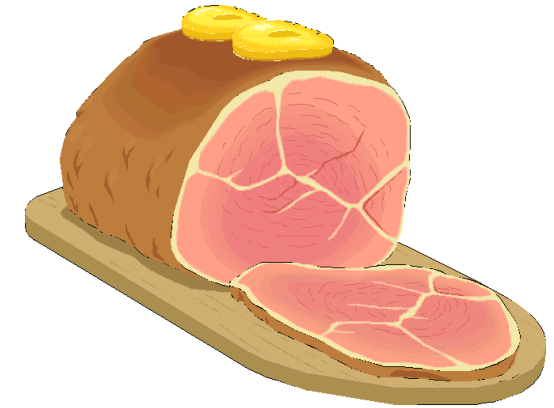
Beer



Sauerkraut

**Sourdough
bread**

Salami and pickles



cured ham

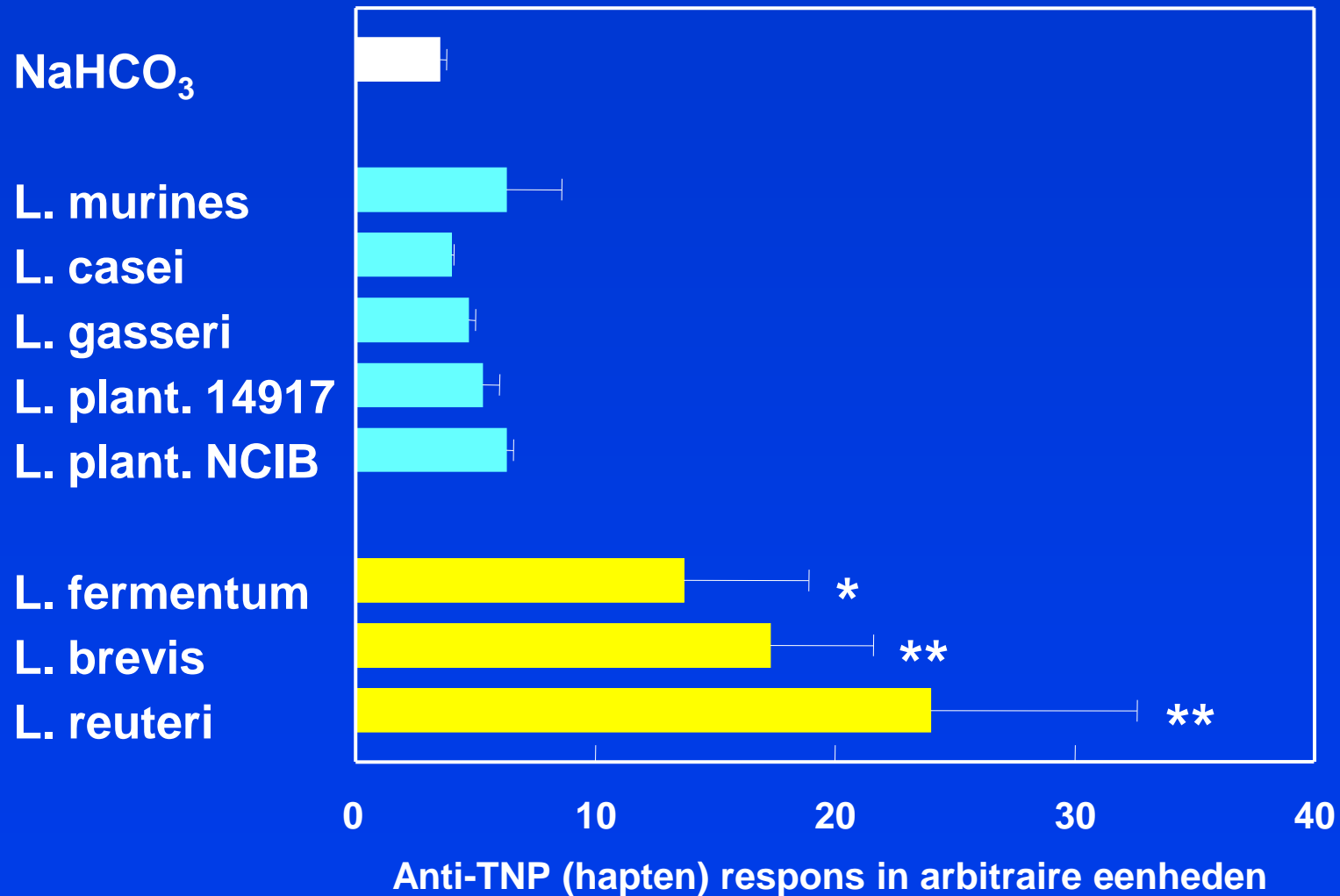
Vinegar



ADJUVANT

- From Latin “adjuvare” meaning to support or to help.
- In the immunesystem this help is non-specific, so “general help” a sort of “code red” alarm

Strain dependent intrinsic adjuvanticity





1935

concept of probiotic in medicine

“biotherapy”





DEALING WITH THE REMAINING CONTROVERSIES OF PROBIOTIC SAFETY

M. van den Nieuwboer and E. Claassen. Beneficial Microbes

PROBIOTICS REDUCE COMPLICATIONS

REDUCED COMPLICATIONS - Probiotic intake is associated with a reduction in symptoms and AEs compared to the placebo. Examples are:

- ✓ In the prevention of *Clostridium difficile* associated diarrhoea, probiotics reduce the risk of **AEs by 17%**
- ✓ Probiotic intake for preventing necrotizing enterocolitis is associated with fewer infections and gastrointestinal symptoms and **50% reduced mortality rate**
- ✓ **Lower rates of respiratory and gastrointestinal infections** in healthy infants as a result of probiotic intake
- ✓ **Reduced incidence of catheter related bloodstream infections** in mechanically ventilated individuals
- ✓ **Lower incidence of complications** after surgery with probiotic intake.

Due to **heterogeneity and publication bias**, the evidence for this reduction in adverse events is low. In order to make these general conclusions, additional data is required.

- It is difficult for an investigator to discriminate whether an AE is a result of the patient condition or from the investigated product.
- Effects of probiotics can be widespread, exerting a subtle positive influence extending far beyond the gut
- Experienced AEs in placebo and probiotic groups are often a result of the health condition of the individual



Health Maintenance of Athletes with Probiotics

Marta Oliveira

School of Sport, Exercise & Health Sciences
Loughborough University, UK

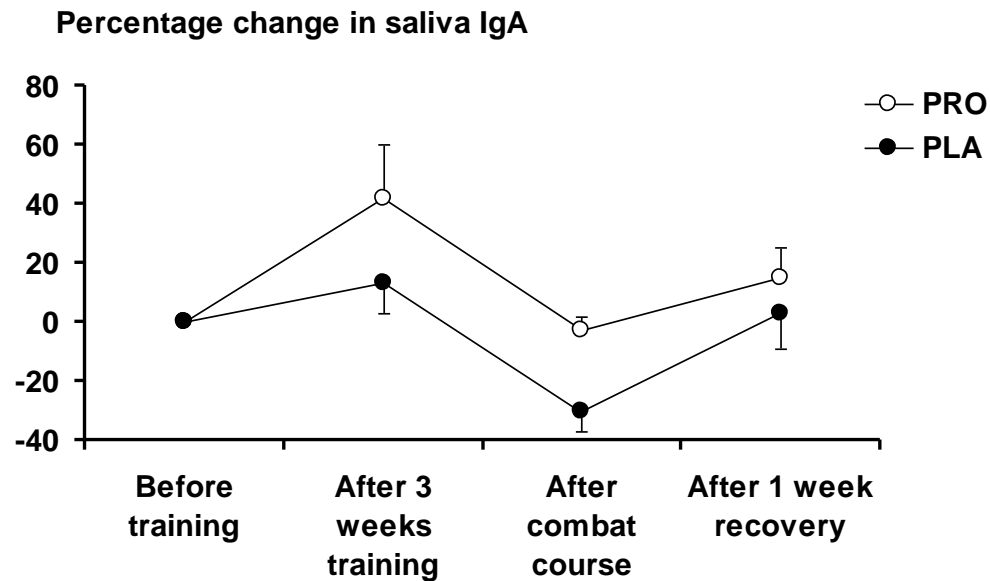


The Official
Preparation
Camp
Headquarters
for Team GB



EFFECT OF A PROBIOTIC ON RESPIRATORY INFECTIONS AND SALIVA IGA DURING INTENSE MILITARY TRAINING

- 47 army cadets
- Daily 100 ml *L. casei* DN-114 001 probiotic drink or placebo for 3 weeks training, followed by a 5-day combat course
- No difference in incidence of respiratory illness
- Significant saliva IgA decrease only in placebo group



Research

Open Access

Increasing work-place healthiness with the probiotic *Lactobacillus reuteri*: A randomised, double-blind placebo-controlled study

Py Tubelius¹, Vlaicu Stan¹ and Anders Zachrisson^{*2}

- ‘Healthy’ Shift-workers Probiotics and resistance to infections
 - Gastro-intestinal and respiratory

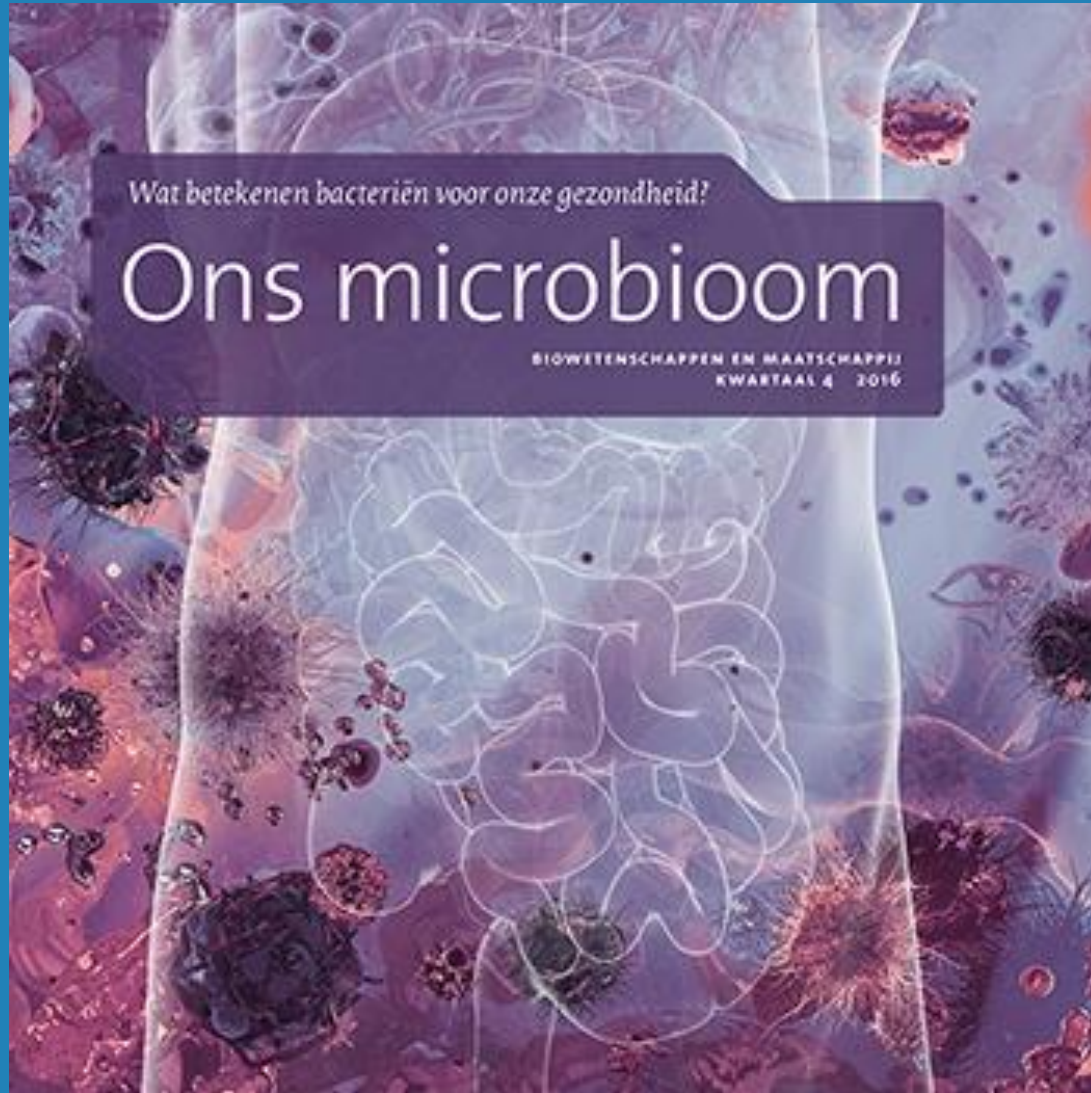
Voedingsadvies

- Groente en fruit zijn de basis van dagelijkse voeding
- Verwen je darm eet witlof, asperge, artisjok, ui, knoflook, prei
- Eet gefermenteerde producten
- Eet elke dag een handje ongezouten noten
- Eet ten minste 2x per week vette vis
- Eet matig vlees (gevogelte is beter dan rood) en altijd met groene groente
- Let op en beperk je suiker inname waar je maar kunt
- Drink water/koffie/thee in plaats van fris- of fruitdrank
- Wees zuinig met zetmeel (brood, pasta, rijst, aardappelen)
- Gebruik liever altijd volkoren graanproducten (met mate)
- Gebruik volvette melkproducten, vooral yoghurt, kwark en kaas
- Vermijd industrieel geproduceerde voedingsmiddelen
- Gebruik olijfolie als dressing en om te braden

Disclaimer for use and copyright



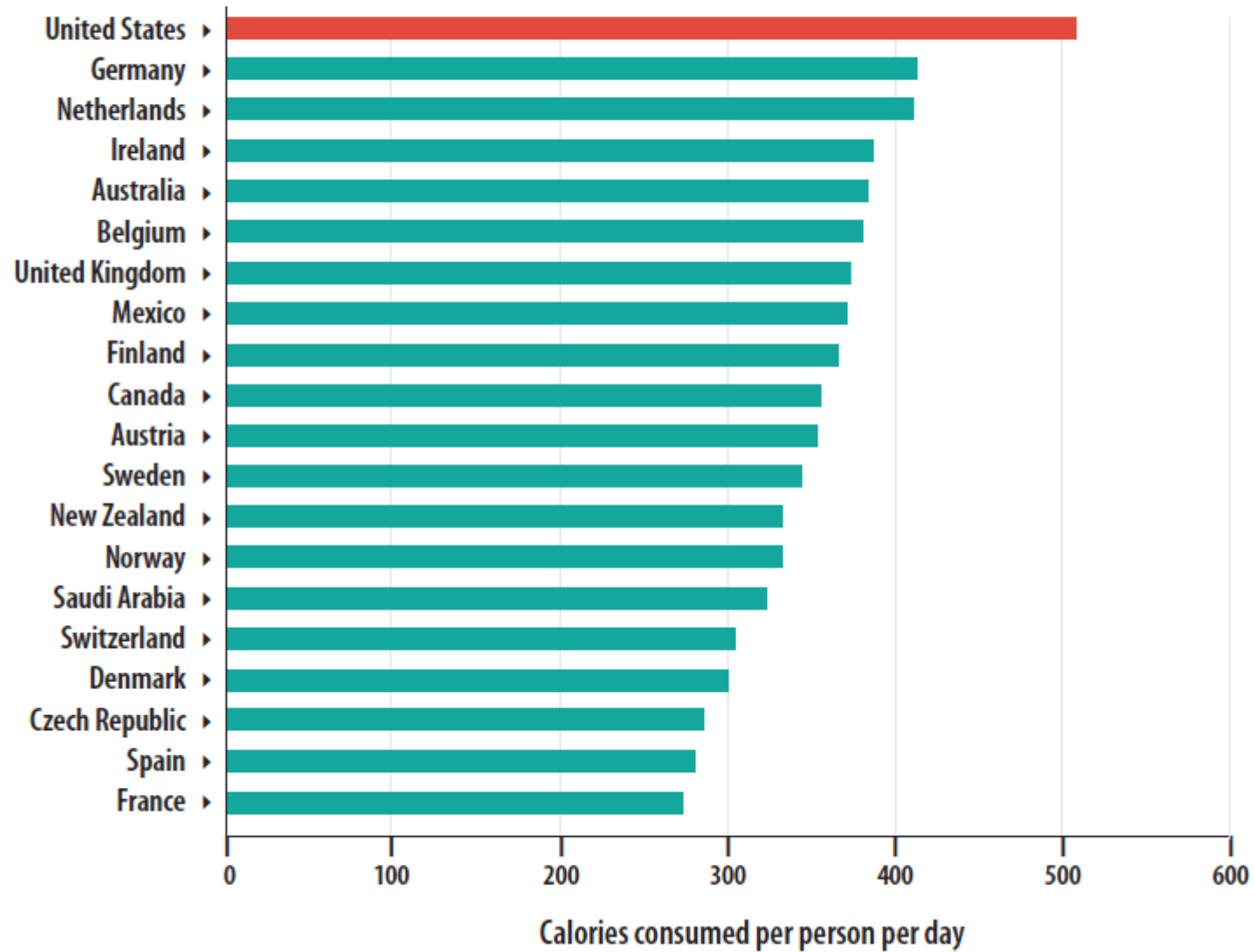
- **THIS SERIES OF SLIDES IS FOR PERSONAL USE ONLY. ANY OTHER APPLICATION MIGHT INFRINGE ON COPYRIGHTS or other rights of third parties (other than myself). DO NOT COPY UNLESS PERMITTED.**
- **Prof.eric.claassen@gmail.com**
- **tel: +31 6 20443098**



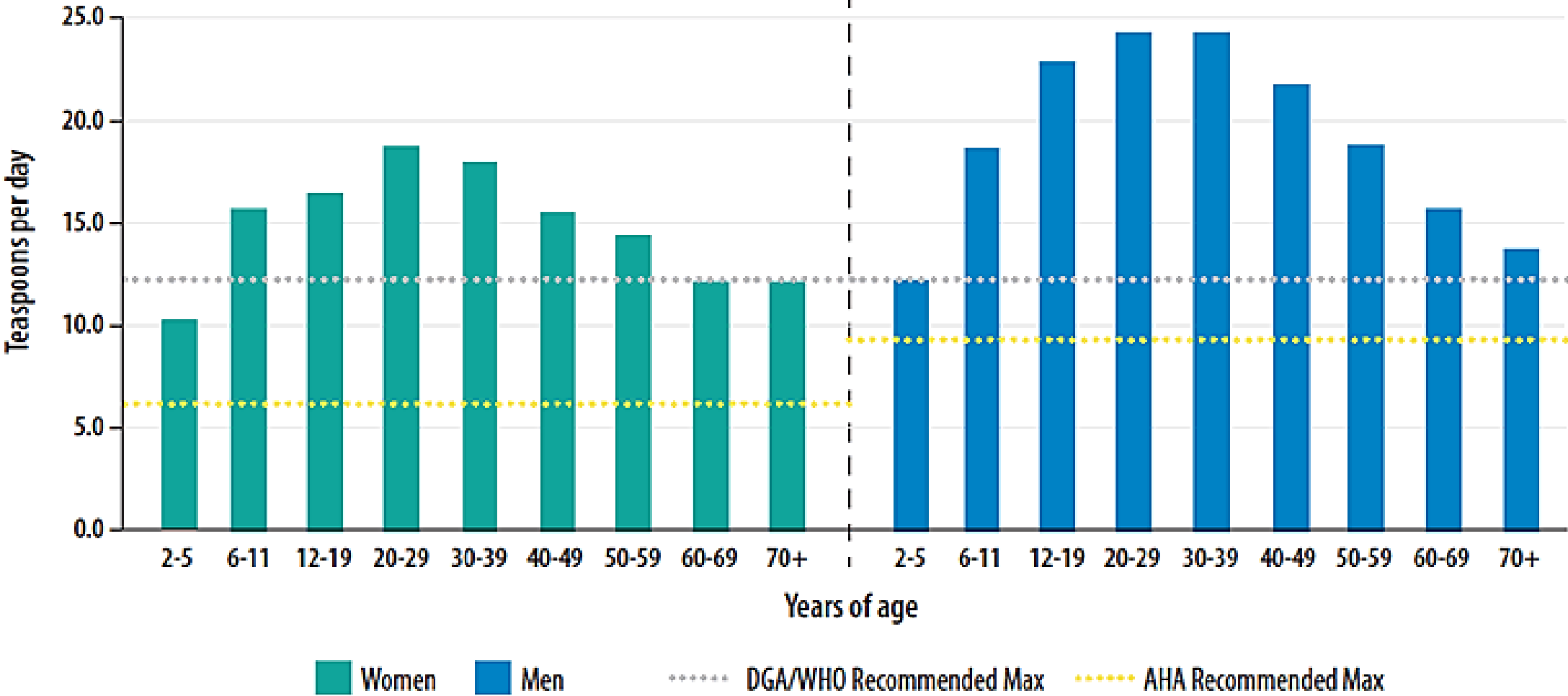
bio WETENSCHAP+
MAATSCHAPPIJ

<http://www.biomaatschappij.nl/product/ons-microbioom/>

Global consumption of caloric sweeteners,* calories/person/day



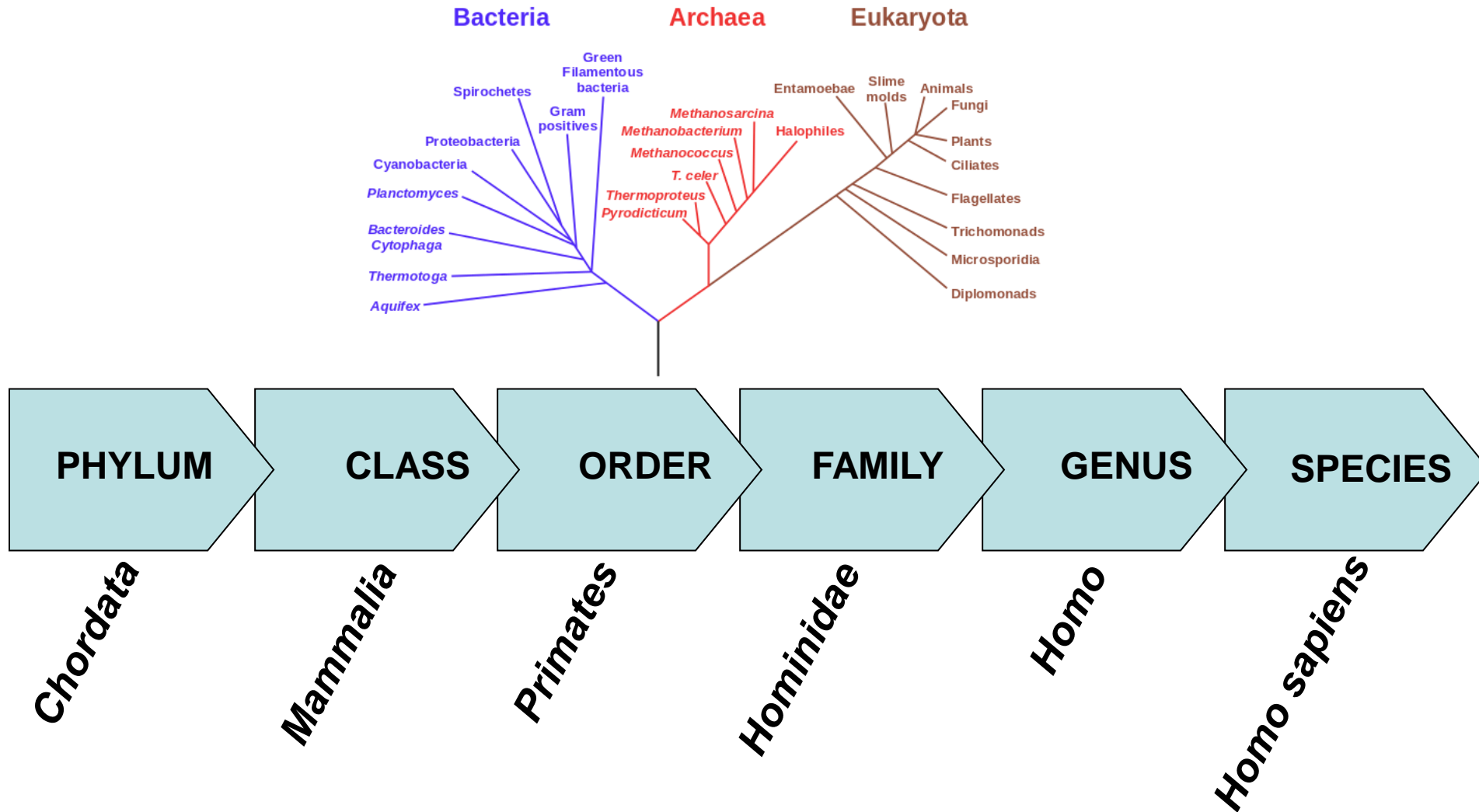
Average daily added sugar intake by age-sex group, compared to the 2015 Dietary Guidelines for Americans (DGA), World Health Organization (WHO), and American Heart Association (AHA) recommendations





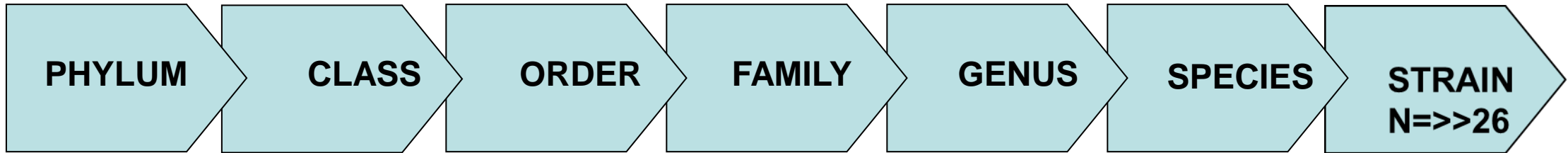
Phylogeny; 'a reminder....'

Human phylogeny & namegiving



Phylogeny; 'a reminder....'

Automobile phylogeny & namegiving 😊



Wheeled motor vehicles

Person transporting cars

Four-wheeled-cars

Volkswagen

Golf

Golf GTI

Golf GTI 1980

1980

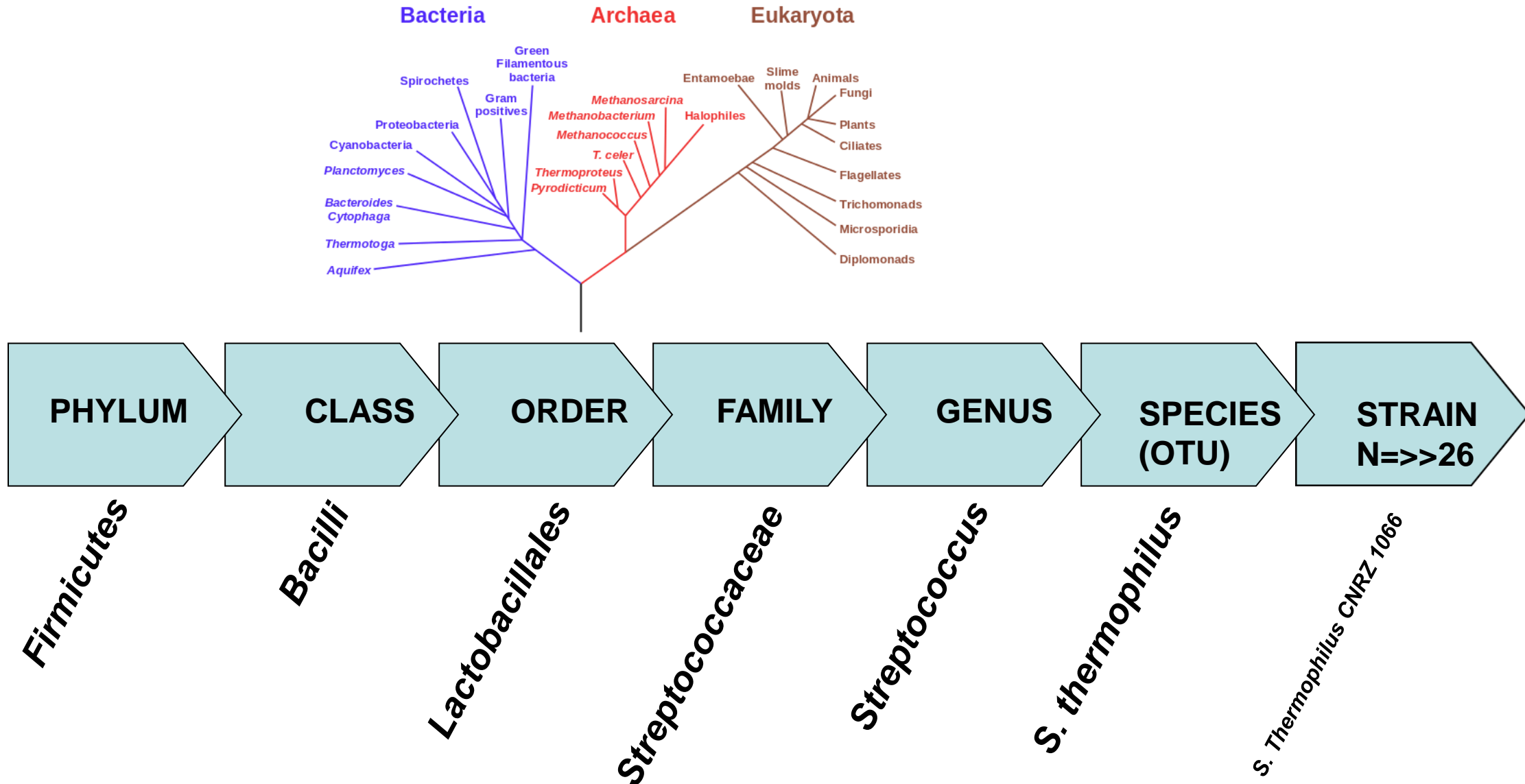


2018



Bacterial phylogeny; 'a reminder....'

The yoghurt workhorse *S. thermophilus*





NEW STUDY PROVES MELATONIN EFFECTIVE SLEEP AID FOR CHILDREN WITH AUTISM



www.AutismParentingMagazine.com

Common Mediators of Placebo Effects

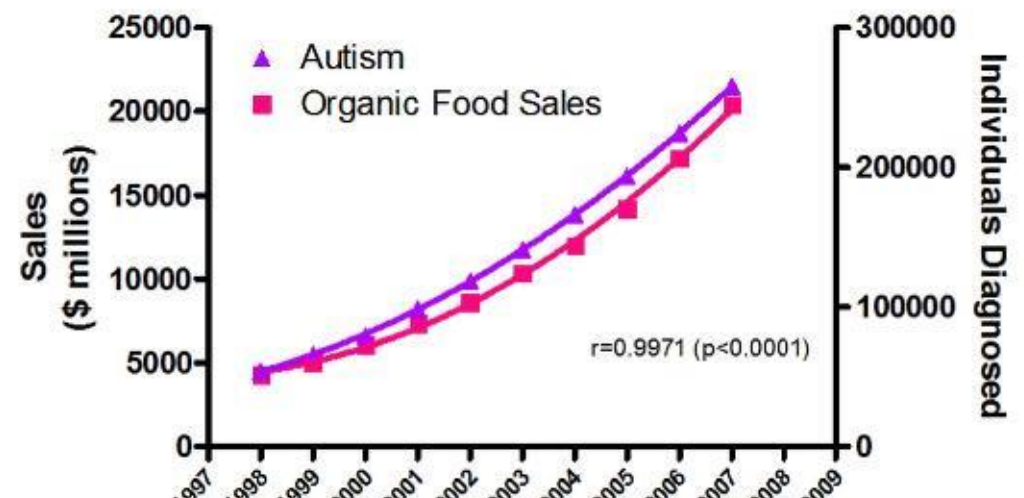
1. Expectancy: strengthened by verbal suggestions, desire for relief, reward, increased self-efficacy, anxiety reduction, and positive transference.
2. Conditioning.
3. Meaning effects.
4. Therapeutic relationship: includes practitioner qualities, attitudes, styles of communication, treatment setting, patient's experience of the relationship, and personality factors.

AUTISM MAY BENEFIT FROM OXYTOCIN TREATMENT

- Overall, there is partial scientifically validated evidence supporting the effectiveness of pharmacotherapy as a treatment for autism.
 - Medication - Placebo studies
 - Flawed Methodologies
 - Core deficits versus associated behavioral symptoms?
 - Very few studies comparing pharmacotherapy and applied behavior analysis



The real cause of increasing autism prevalence?



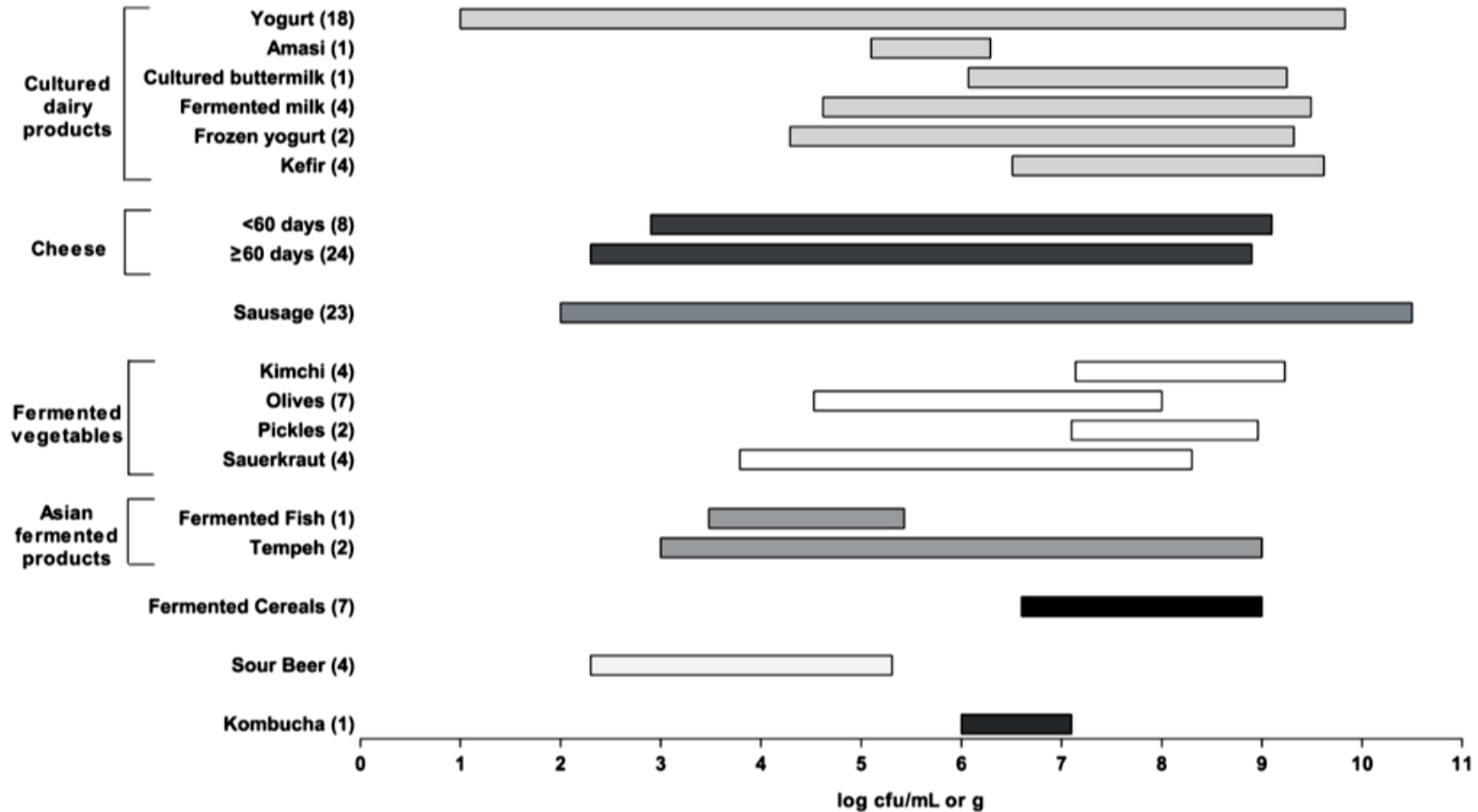


FIGURE 1 | Summary of lactic acid bacteria (LAB) counts in all fermented foods as reported in **Tables 1–8**. The bar plots represents a range (minimum to maximum) of counts found across the studies surveyed. The number of studies used here for each fermented food is shown in brackets. Products were excluded if they had no viable counts or when LAB counts were not reported. For yogurt, initial counts were used for products that had counts for more than one timepoint. For cheese, the products were divided by aging time (60 days) and were excluded if aging time was not reported.

Fermented Foods as a Dietary Source of Live Organisms

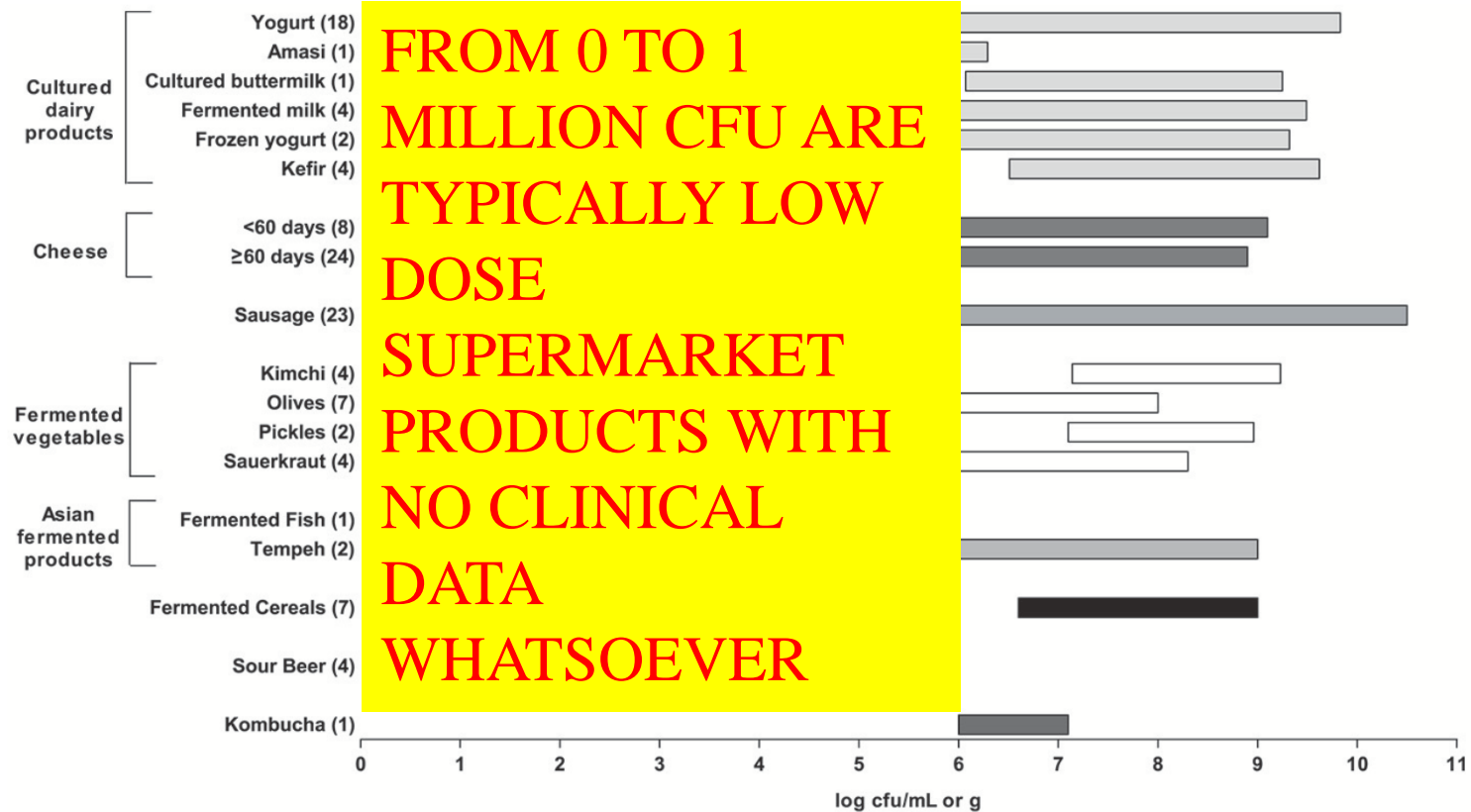


FIGURE 1 | Summary of lactic acid bacteria (LAB) counts in all fermented foods as reported in **Tables 1–8**. The bar plots represents a range (minimum to maximum) of counts found across the studies surveyed. The number of studies used here for each fermented food is shown in brackets. Products were excluded if they had no viable counts or when LAB counts were not reported. For yogurt, initial counts were used for products that had counts for more than one timepoint. For cheese, the products were divided by aging time (60 days) and were excluded if aging time was not reported.

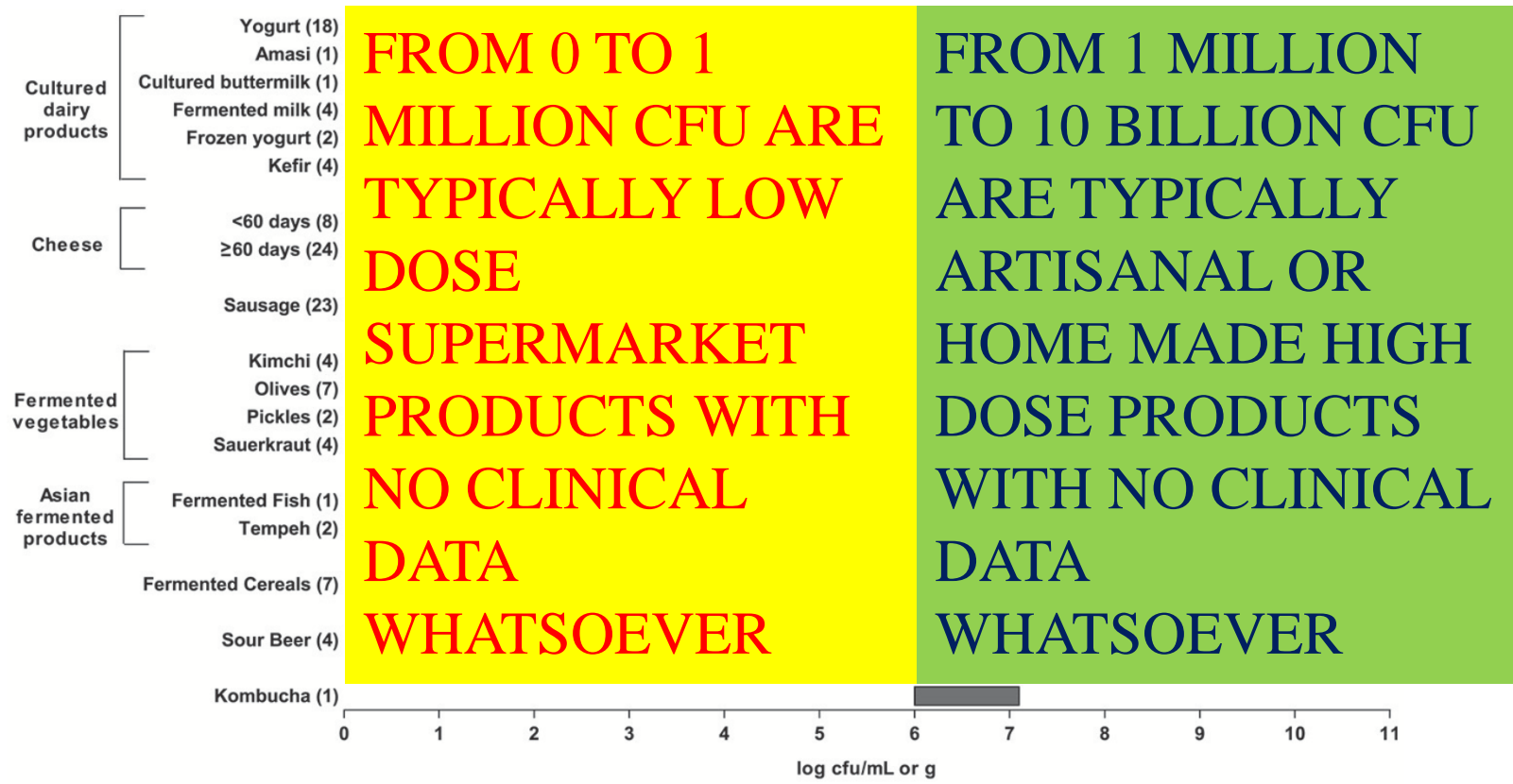


FIGURE 1 | Summary of lactic acid bacteria (LAB) counts in all fermented foods as reported in **Tables 1–8**. The bar plots represents a range (minimum to maximum) of counts found across the studies surveyed. The number of studies used here for each fermented food is shown in brackets. Products were excluded if they had no viable counts or when LAB counts were not reported. For yogurt, initial counts were used for products that had counts for more than one timepoint. For cheese, the products were divided by aging time (60 days) and were excluded if aging time was not reported.

NOTABLE EXCEPTIONS HIGH DOSE CLINICALLY TESTED SUPERMARKET PRODUCTS

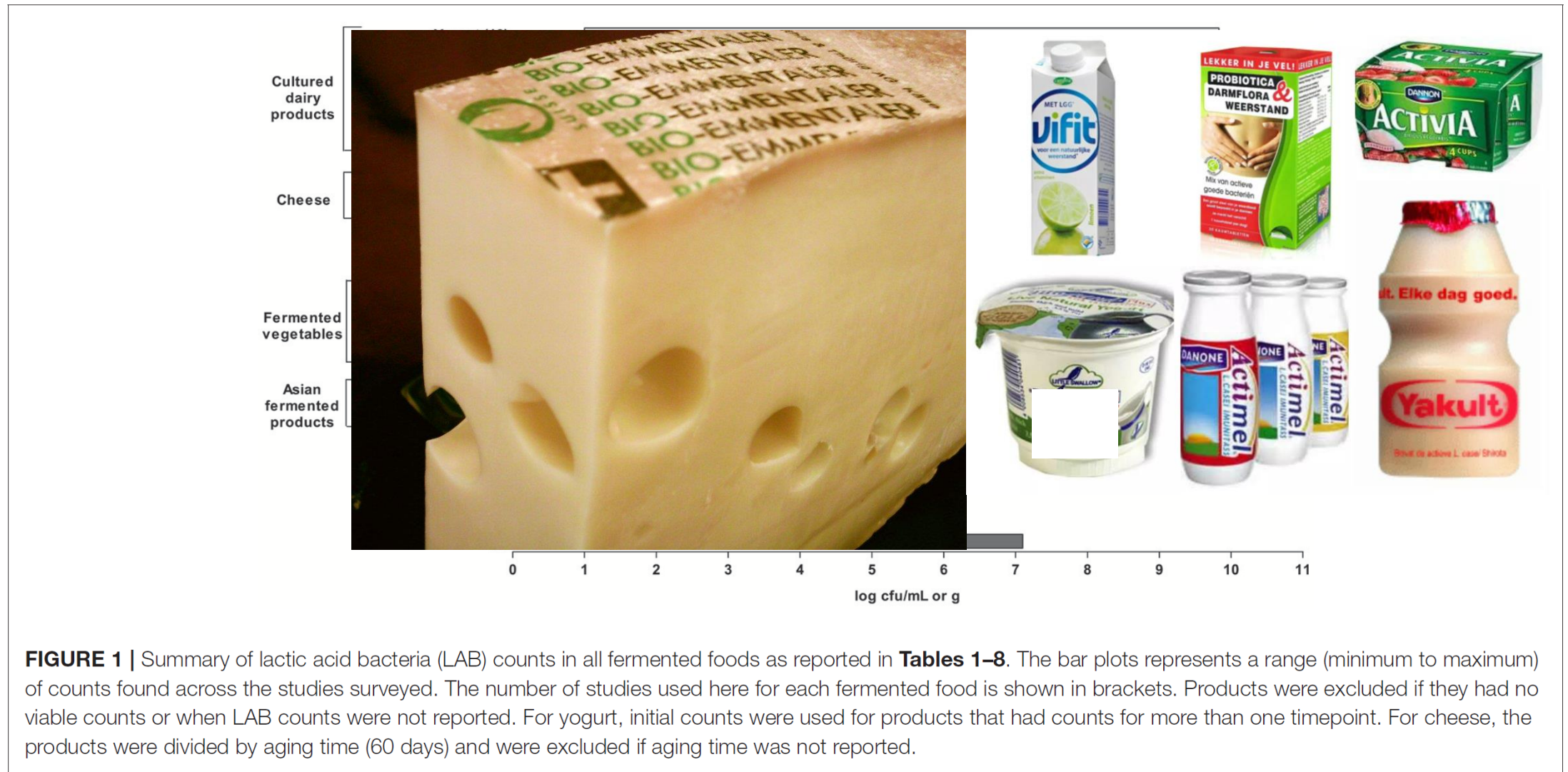


FIGURE 1 | Summary of lactic acid bacteria (LAB) counts in all fermented foods as reported in **Tables 1–8**. The bar plots represents a range (minimum to maximum) of counts found across the studies surveyed. The number of studies used here for each fermented food is shown in brackets. Products were excluded if they had no viable counts or when LAB counts were not reported. For yogurt, initial counts were used for products that had counts for more than one timepoint. For cheese, the products were divided by aging time (60 days) and were excluded if aging time was not reported.

Fermented Foods as a Dietary Source of Live Organisms