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 instutions and (EU) consortia (over 160 clients).

prof.eric.claassen@gmail.com

MY SLIDES ARE AVAILABLE THROUGH TODAYS ORGANISERS

PLOS ONE

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. Ribeiro[1☯]*, Martine Y. van Roode[2☯], George B. Haringhuizen[1], Marion P. Koopmans[2], Eric Claassen[3], 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

BLOCKC
OUTBRE

RESEARCH COOPERATION: COVID-19

Blockchain-facilitated sharing to enhance outbreak R&D

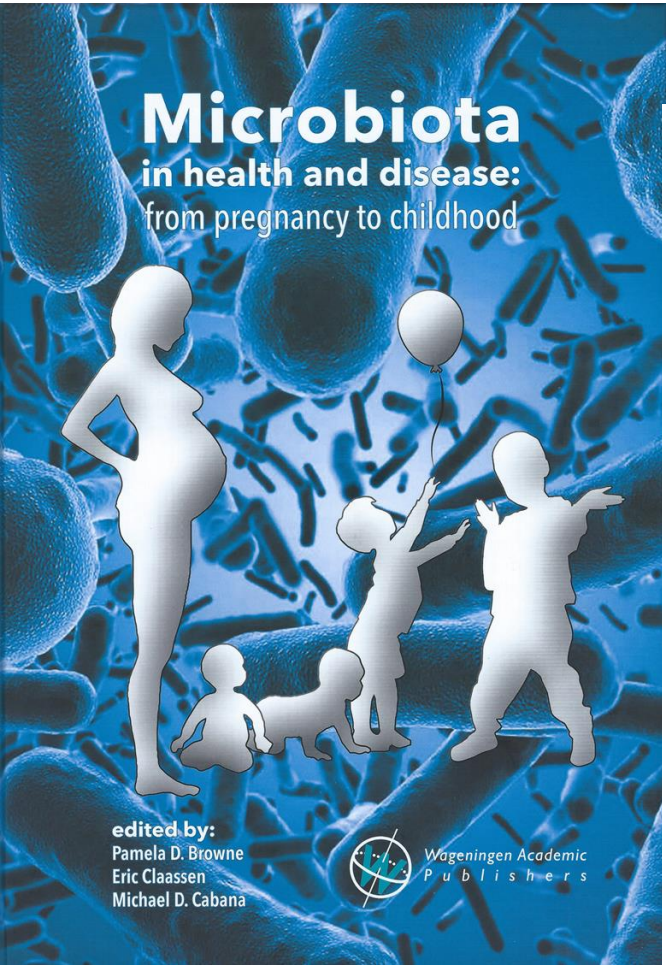
Technology may help overcome nontechnological barriers

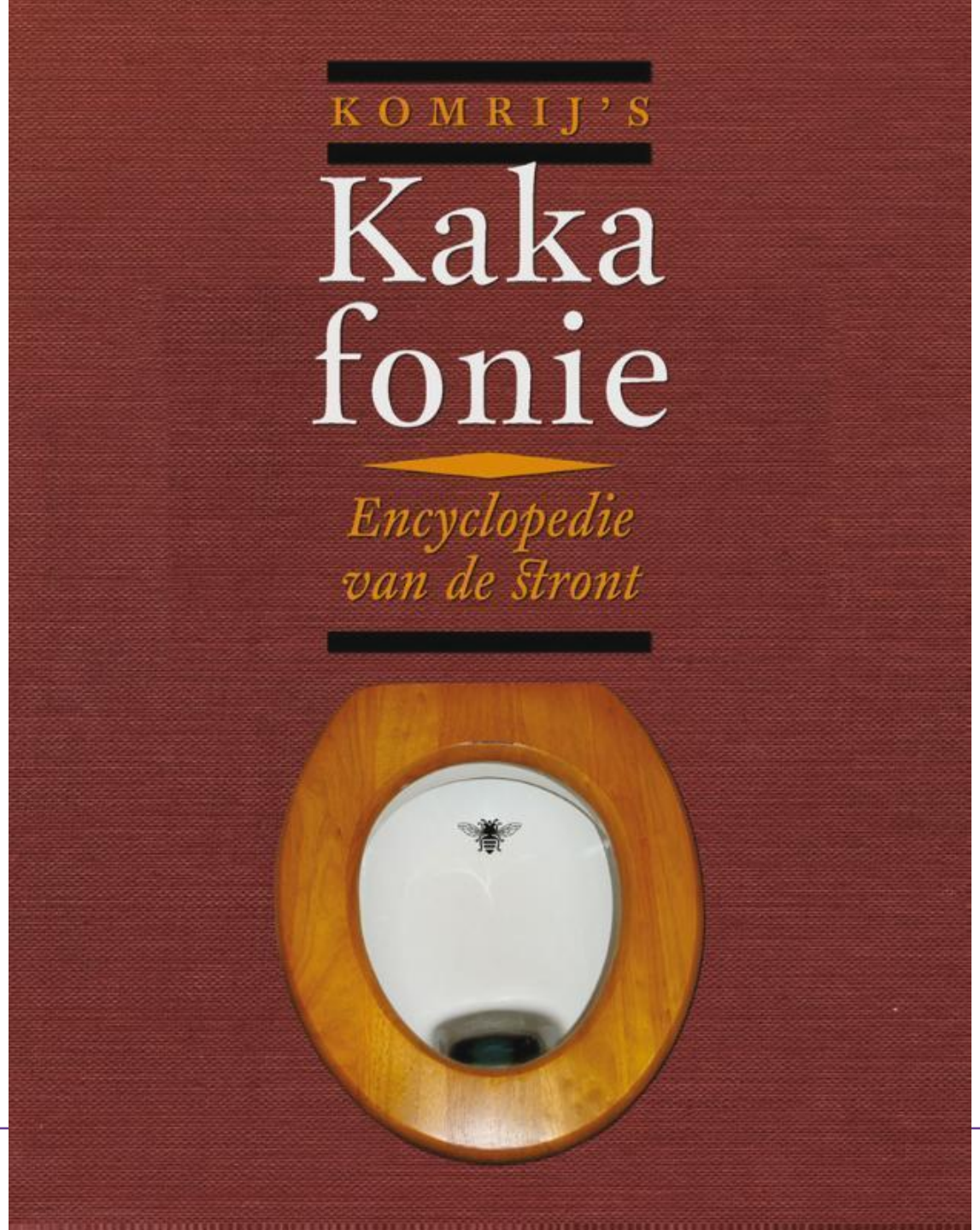
van der Waal, M. B., Ribeiro, C. D. S., Ma, M., Haringhuizen, G. B., Claassen, E., & van de Burgwal, L. H. (2020). Science, 368(6492), 719-721.

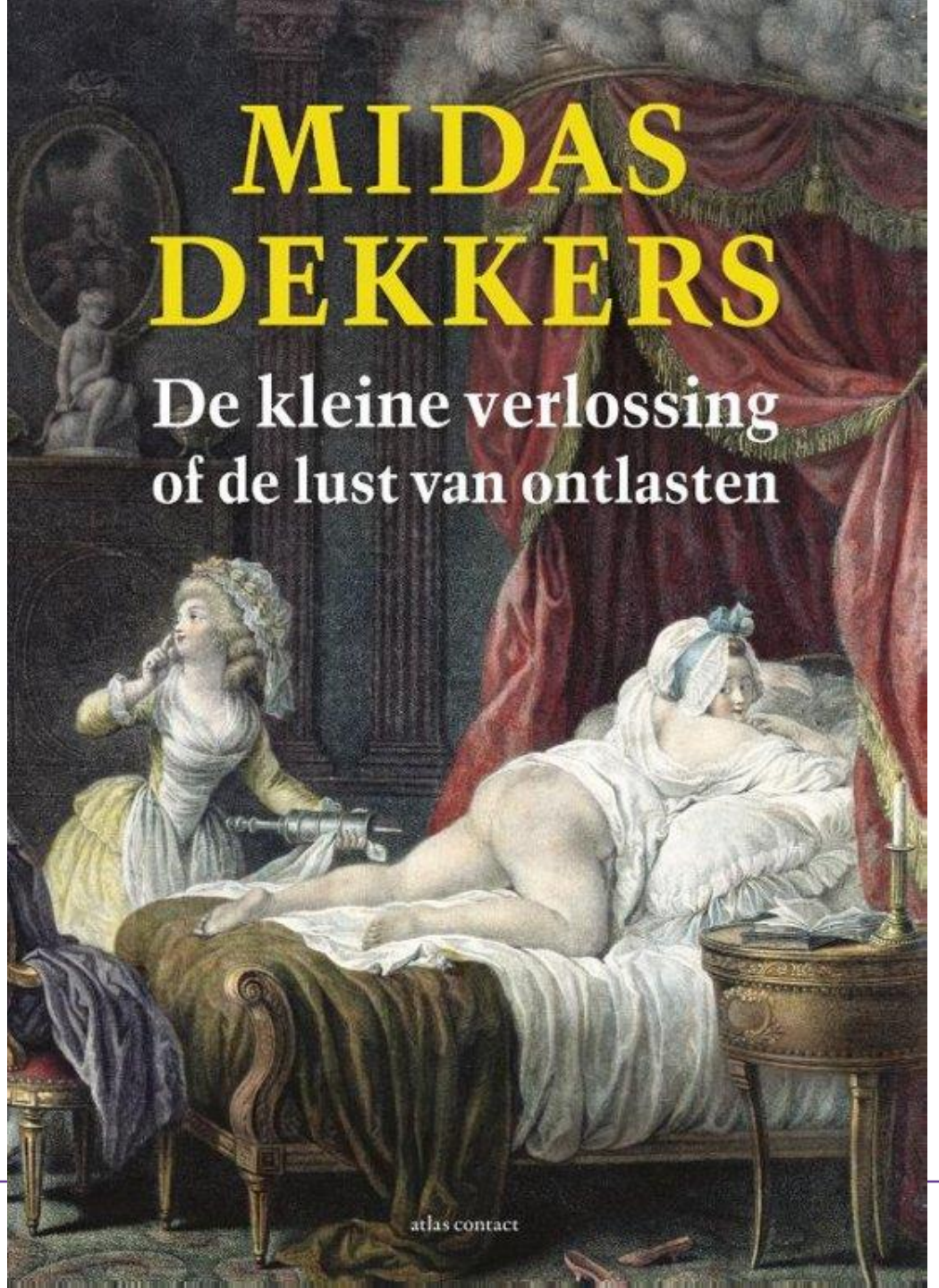
My day job is starting companies for infectious disease diagnostics and vaccines in a One Health setting mainly for zoonoses (animal to man)

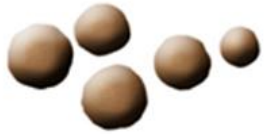
Ik werk sinds 1980 aan de immunologie van slijmvliezen van de darm
en sinds 1987 aan melkzuur bacterieen

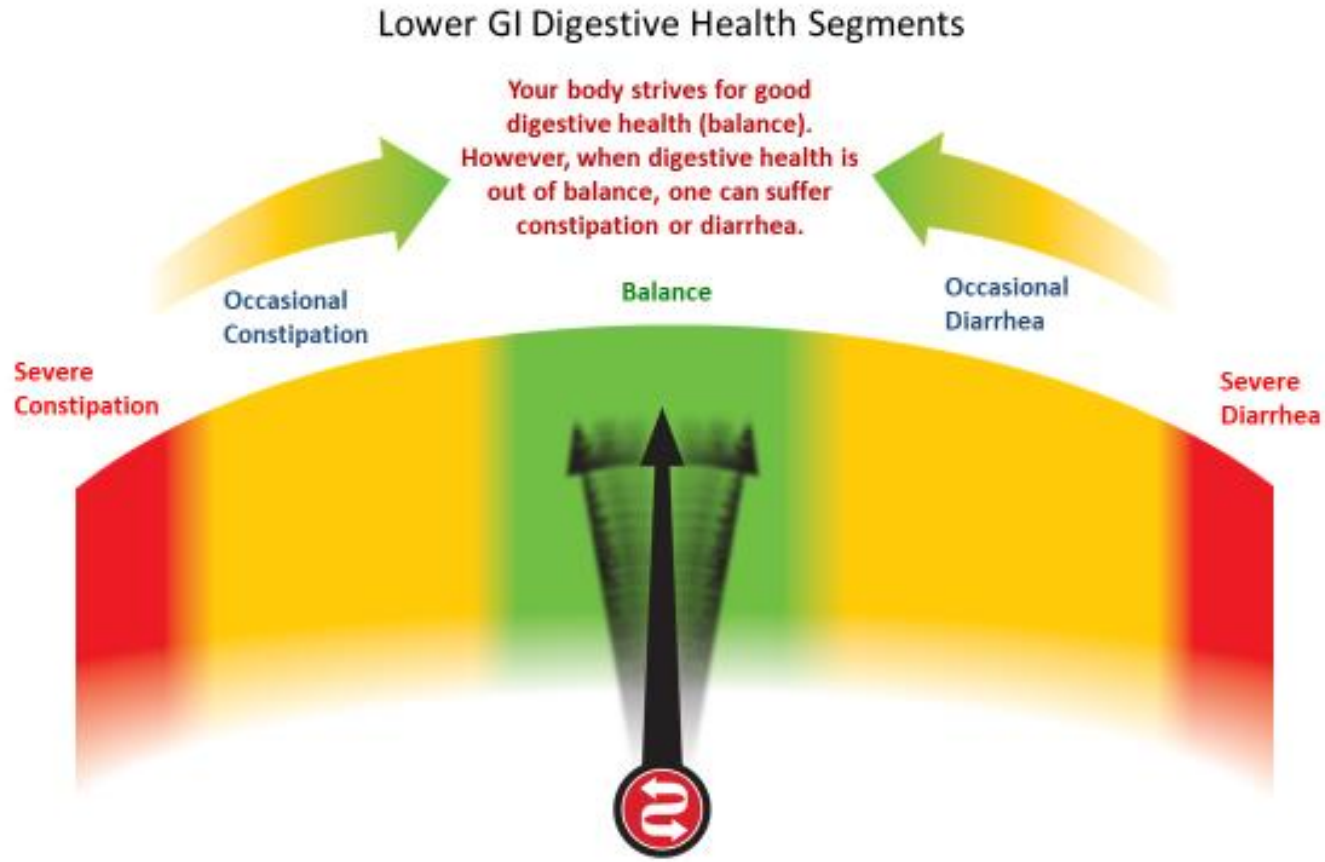
Gerritse, Posno, Schellekens, Boersma & Claassen E. (1990) Oral administration of TNP-lactobacillus conjugates in mice: a model for evaluation of mucosal and systemic immune responses and memory formation elicited by transformed Lactobacilli. Res. Microbiology, 141, 955-962.




KOMRIJ'S
Kaka
fonie
Encyclopedie
van de Stront


MIDAS
DEKKERS
De kleine verlossing
of de lust van ontlasten
atlas contact

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. Entirely liquid



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

Microscopy from http://basemap.wikhantlab.com

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

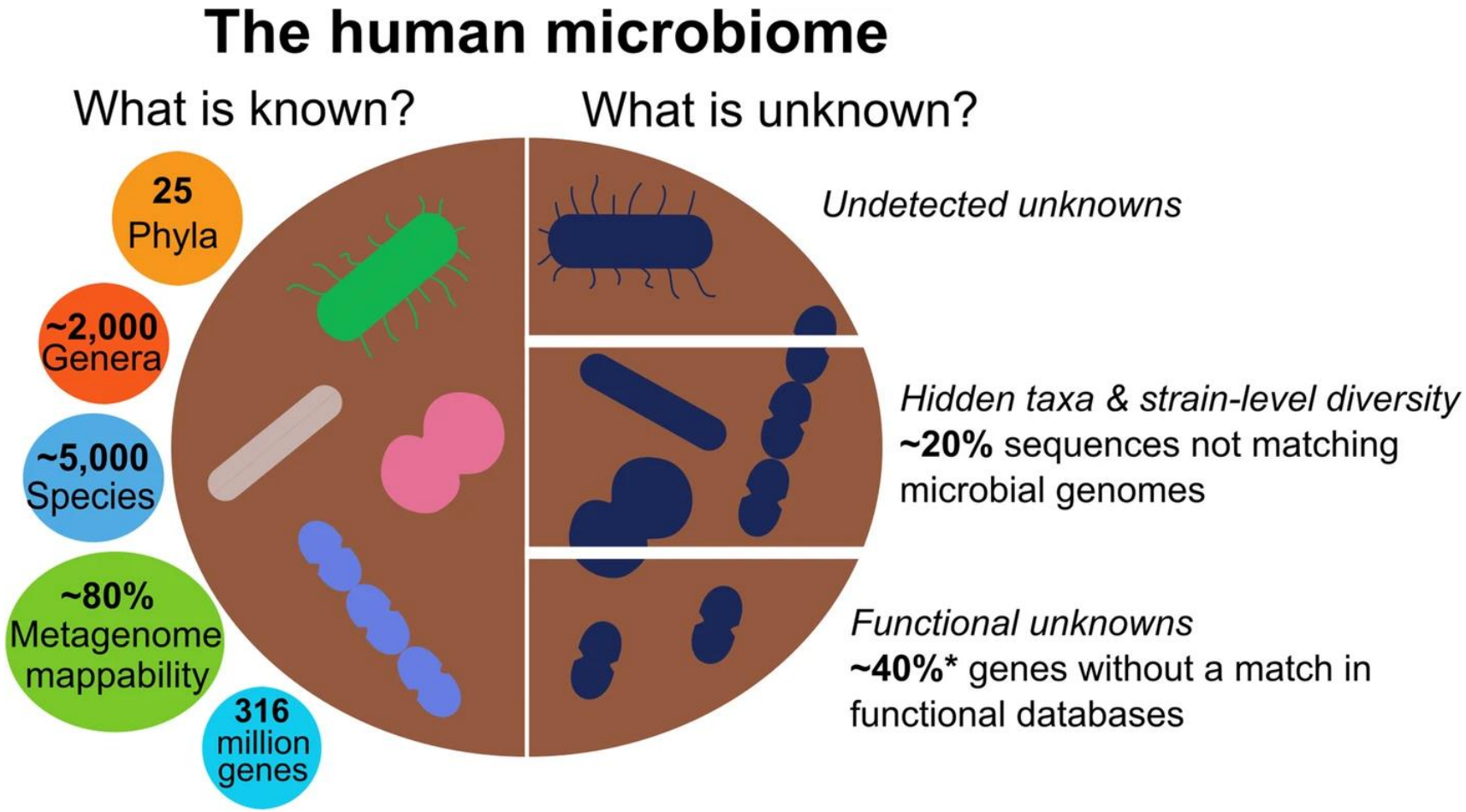
The four most abundant phyla

- Actinobacteria
- Bacteroidetes
- Firmicutes
- Proteobacteria

Low abundance phyla

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

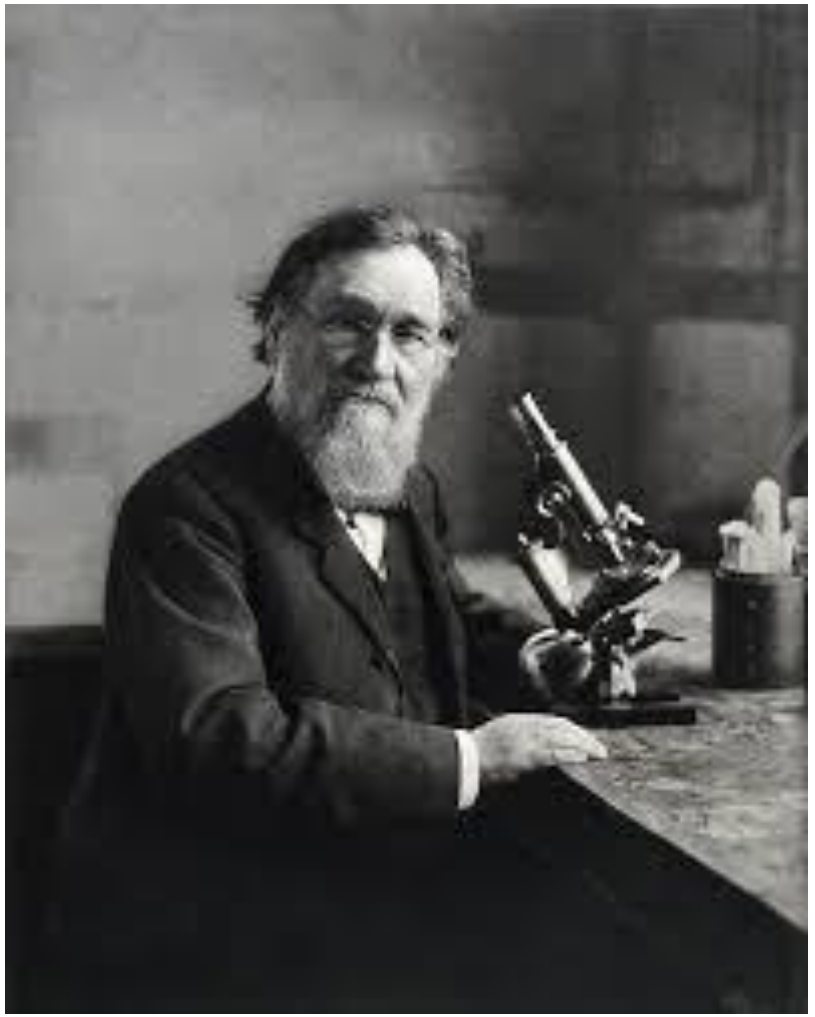
TRENDS in Genetics



Andrew Maltez Thomas & Nicola Segata BMC Biology 17: 48 (2019)

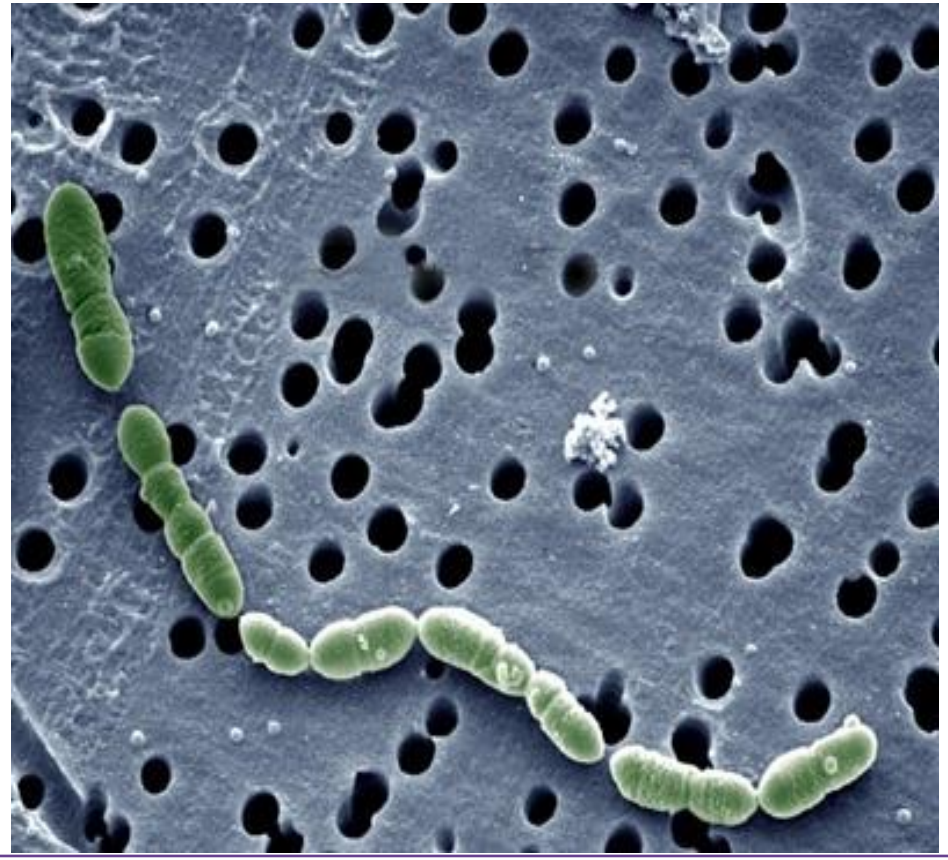
The New York Times
Published: January 21, 1912

METCHNIKOFF CONFIRMED IN HIS THEORY OF LONG LIFE

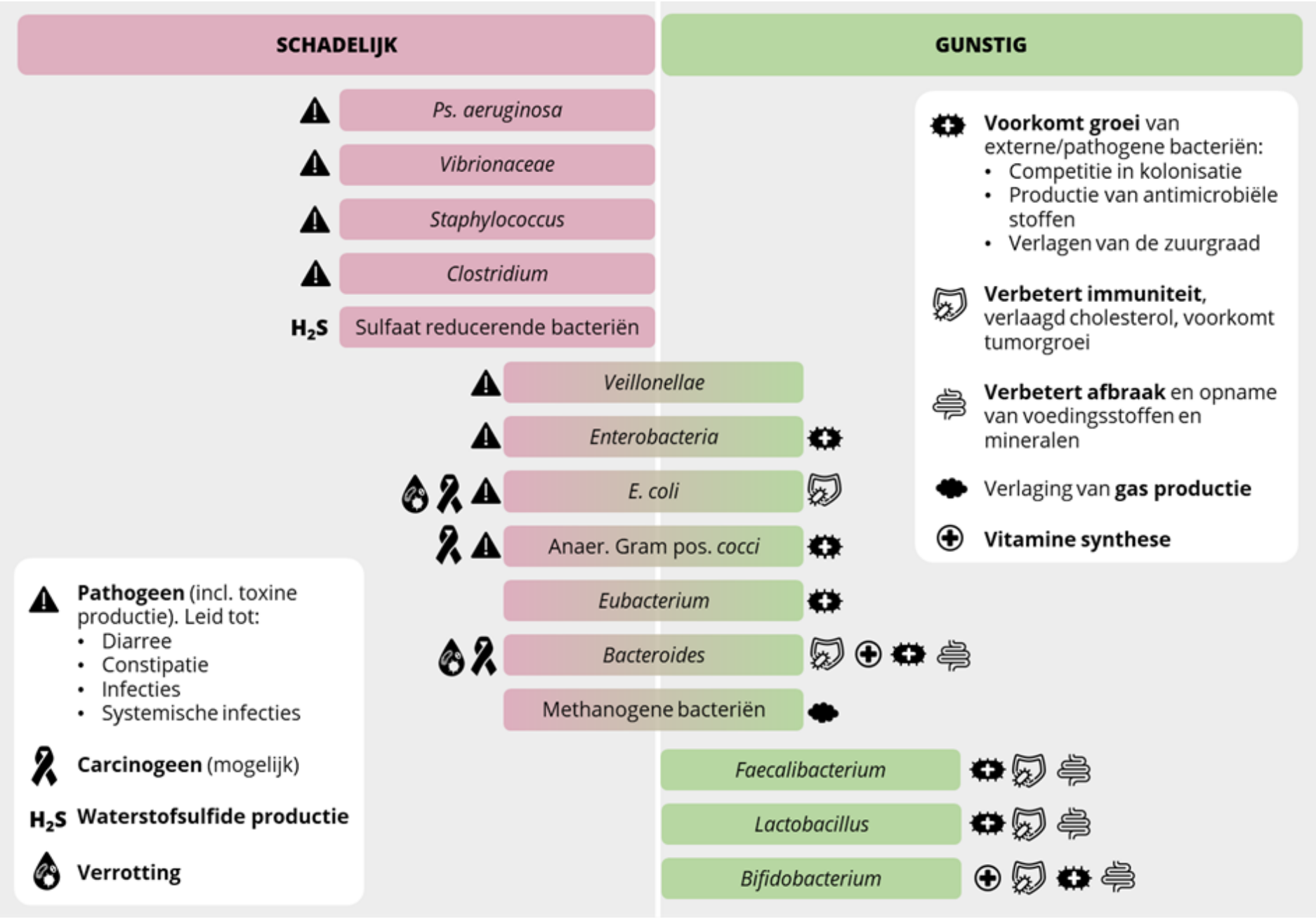


De putrefactie van de dikke darm

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



Nieuwboer, Claassen et al 2019, in druk

1	Preweaning
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

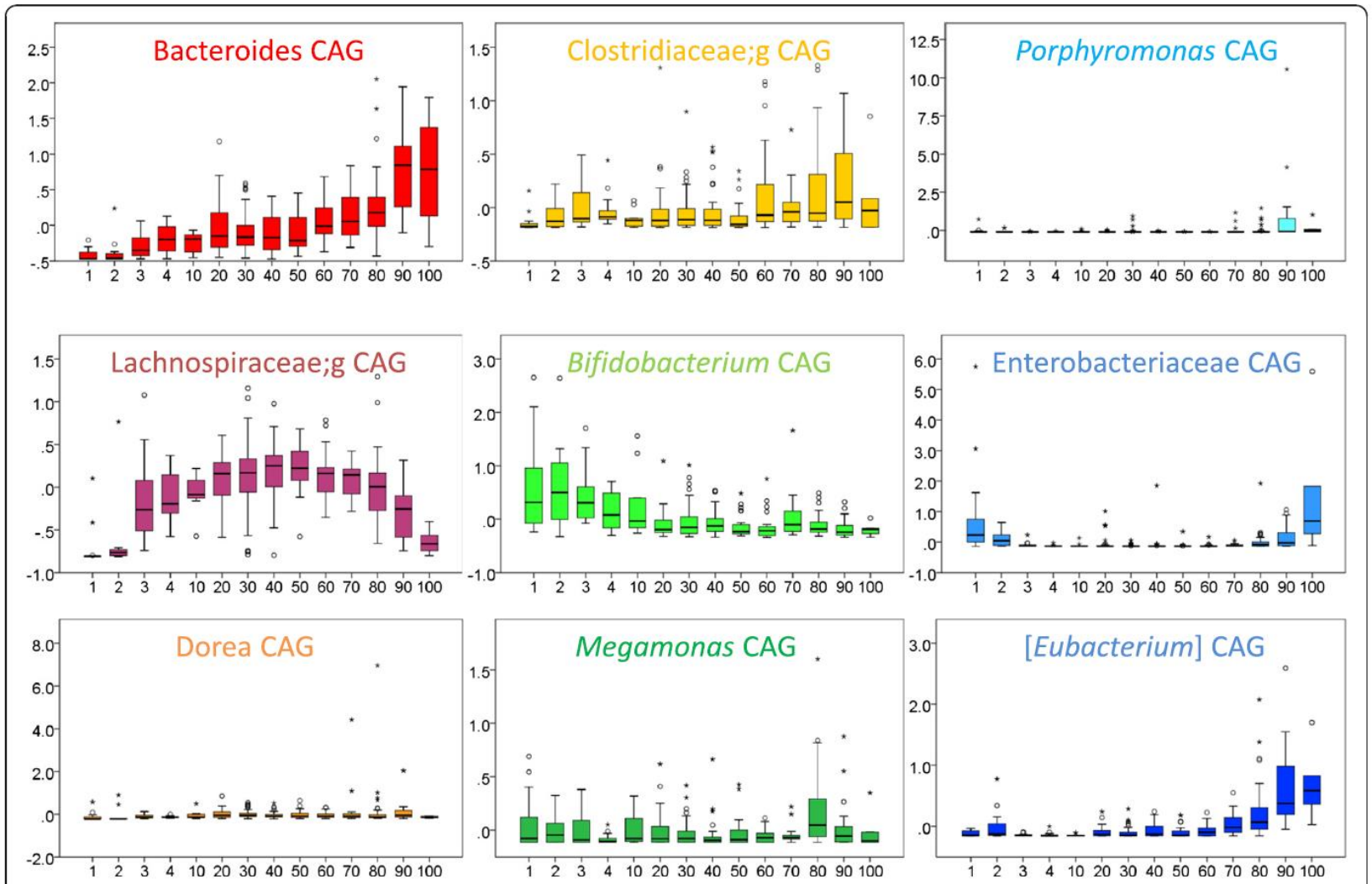
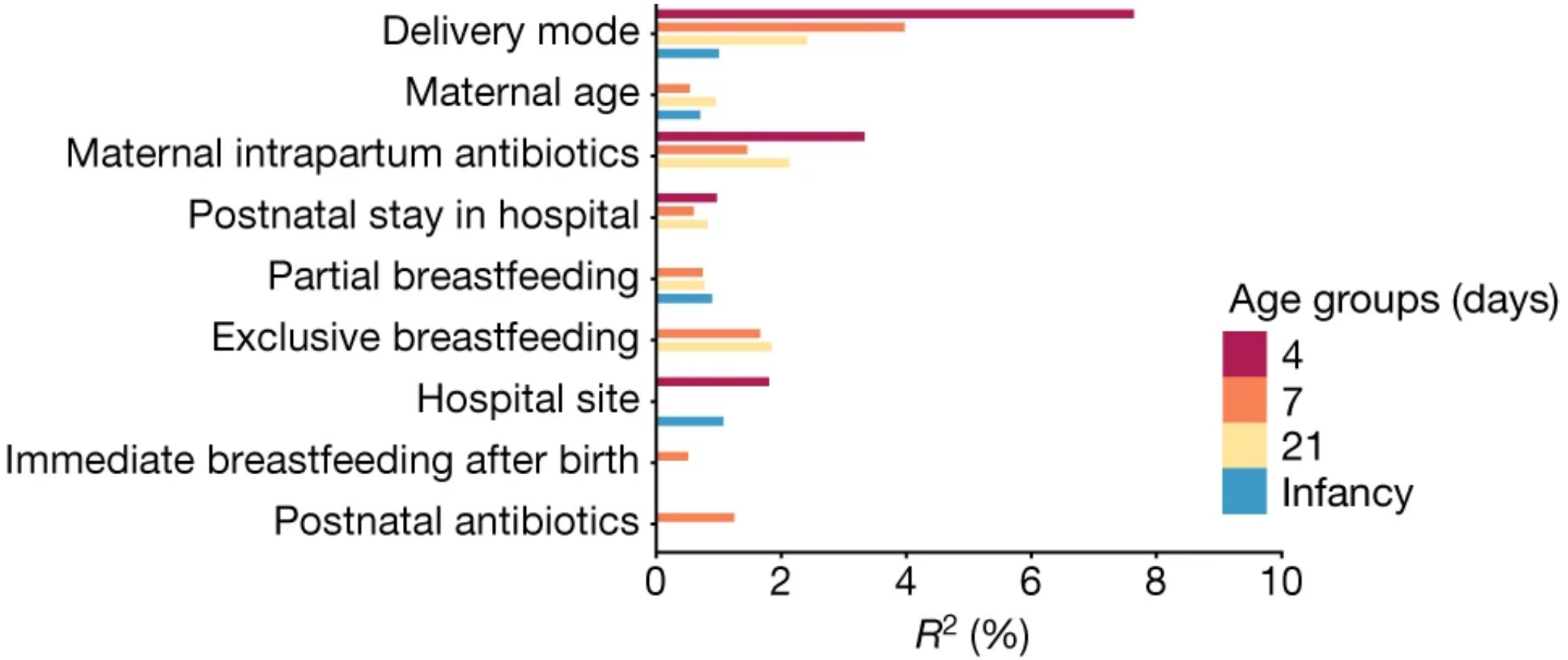


Fig. 3 Transition type of each co-abundance group (CAG) from infant to centenarian. Each number indicates a group as shown in Table 1. Box-plots show the interquartile range (IQR) of the sum of z-scores converted from the relative abundance of genera belonging to the same CAG. Open circles and asterisks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

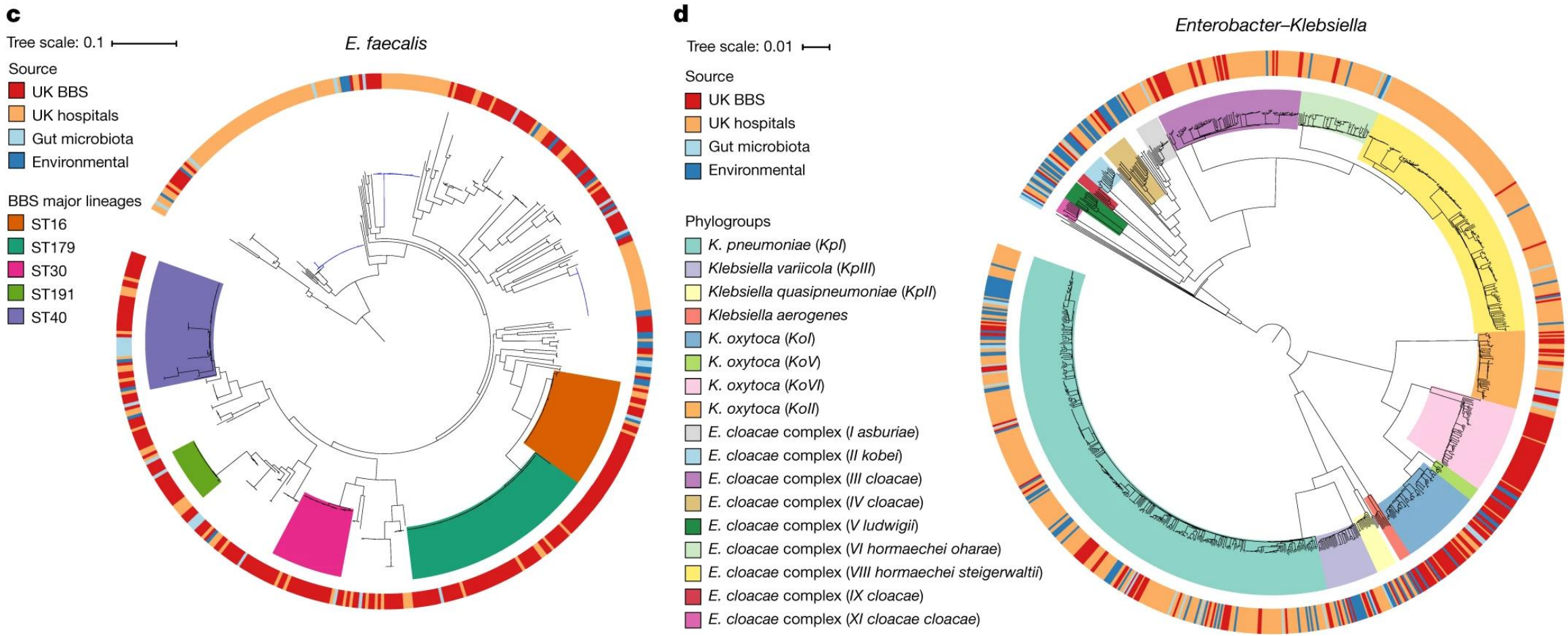
When children are born, they emerge from the relatively sterile environment of the uterus into a world teeming with bacteria . . .

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)**



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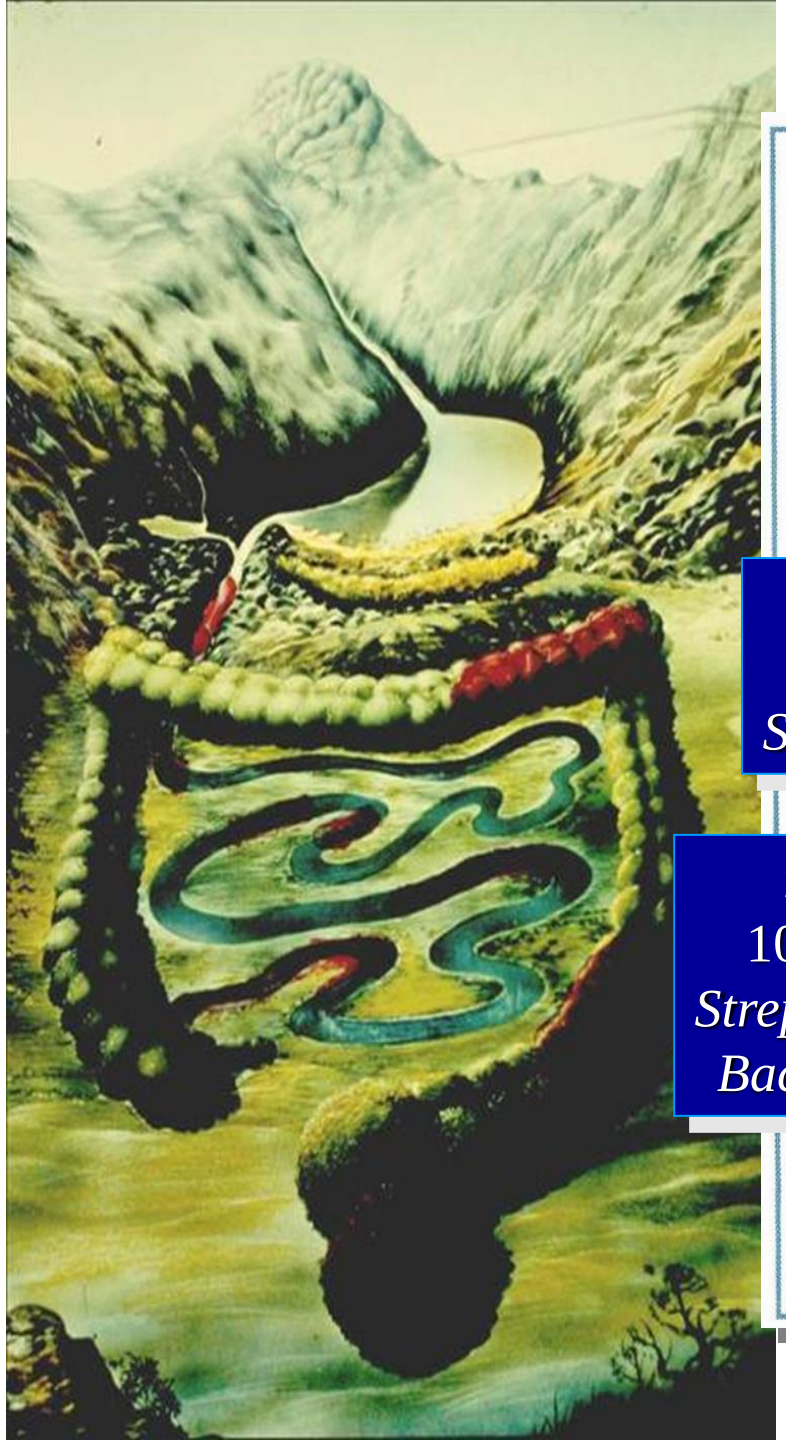


Mouth
10^5 – 10^7
polymorph germs

stomach
10^2 – 10^3
Streptococcus

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

jenunum
10^5 – 10^6
Streptococcus

ileum
10^3 – 10^7
Streptococcus
Bacteroides

colon
10^9 – 10^{11}
Bacteroides
Clostridum
Streptococcus
Bifidobacteria
Enterobacteria

Darmvlokken (*villi*) geven oppervlakte vergroting

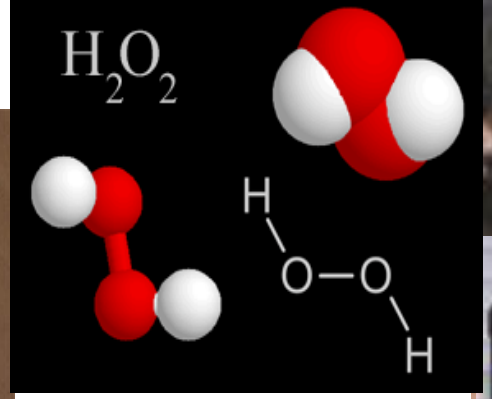
- De totale oppervlakte van de ‘uitgespreide darm’ komt daarmee op meer dan 300 vierkante meter

- Dat is een tennisveld

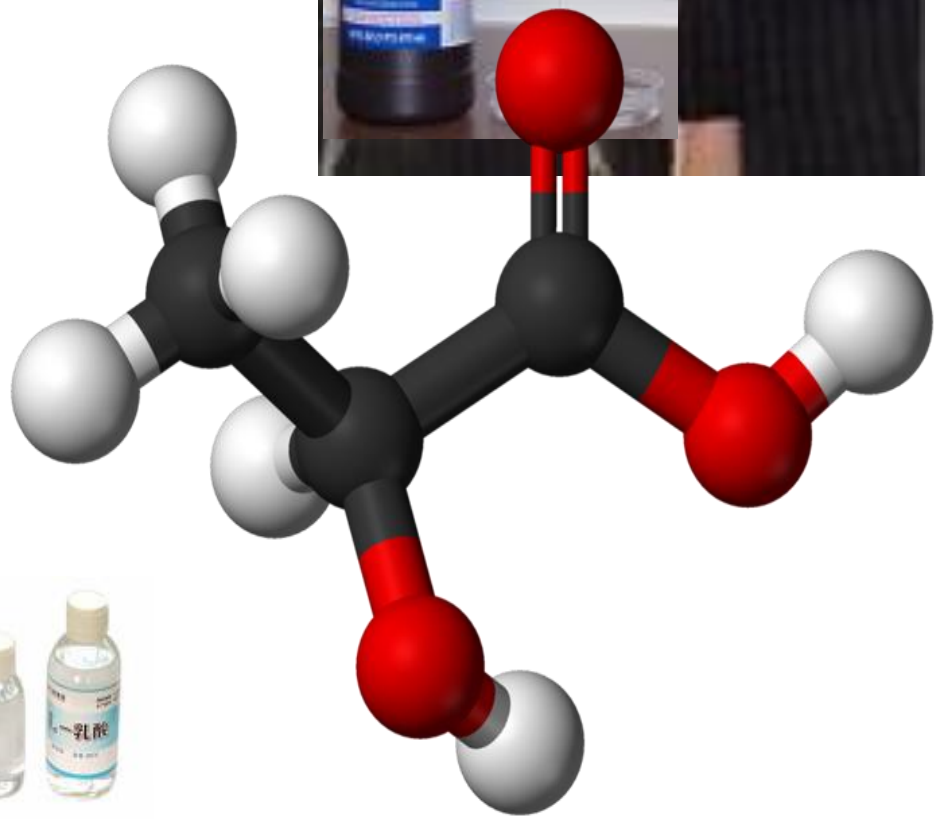

Hier zit uw
BROODJE met uw
levende bacteriële
gasten!!

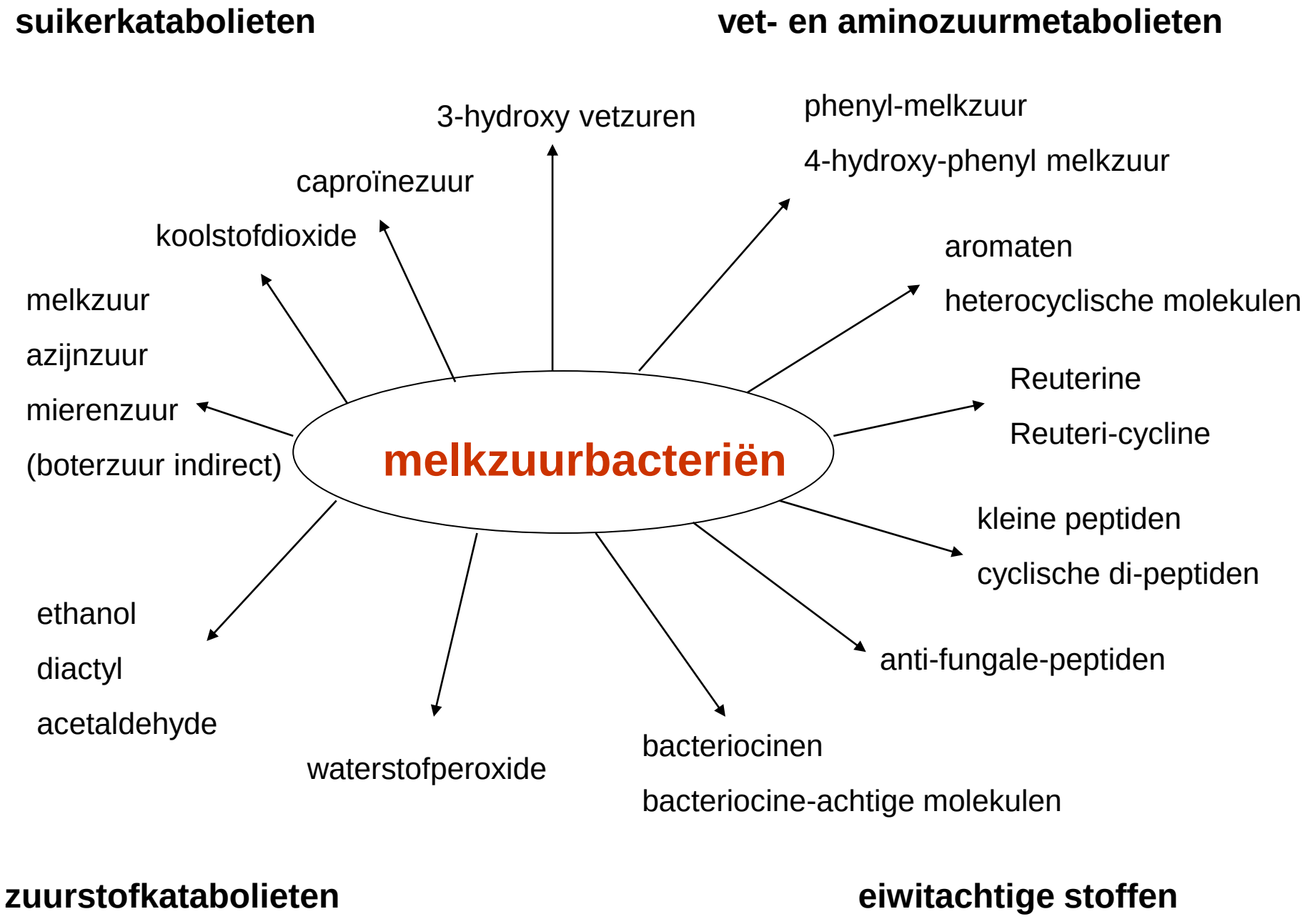

パパパーク!
6.15
オープンキャンパス

Bacterieen moeten aanhechten aan darm eptiheel om te koloniseren: competitie

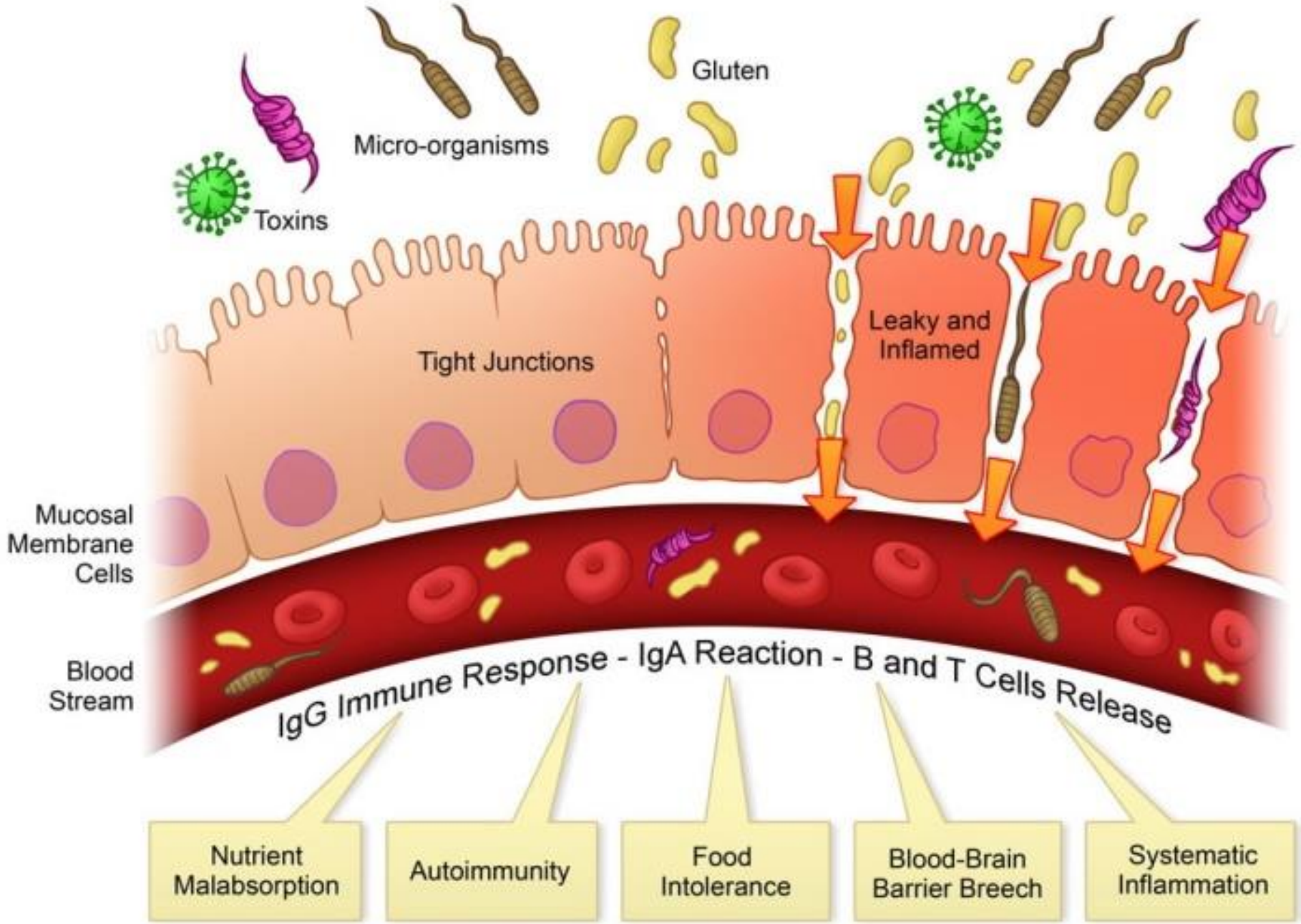

H_2O_2
H
O—O
H


BLONDIE
Hydrogen Peroxide

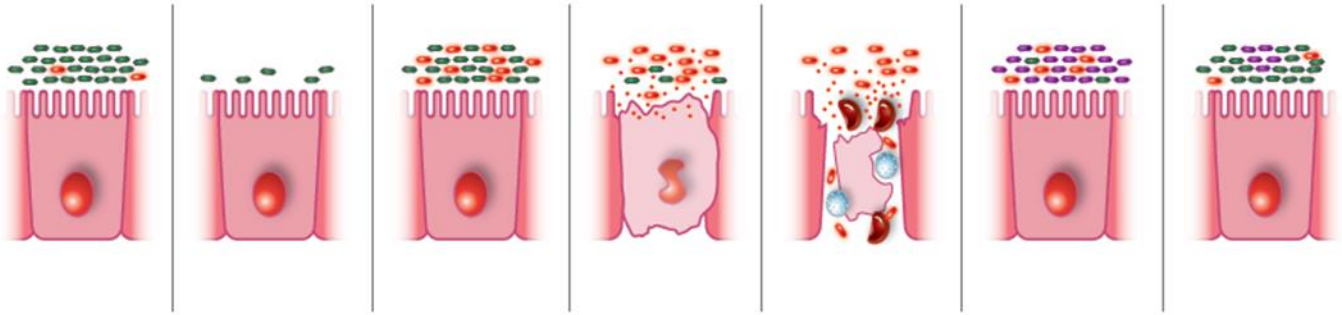



suikerkatabolieten
vet- en aminozuurmetabolieten
3-hydroxy vetzuren
caproïnezuur
koolstofdioxide
melkzuur
azijnzuur
mierenzuur
(boterzuur indirect)
phenyl-melkzuur
4-hydroxy-phenyl melkzuur
aromaten
heterocyclische molekulen
Reuterine
Reuteri-cycline
kleine peptiden
cyclische di-peptiden
anti-fungale-peptiden
melkzuurbacteriën
ethanol
diactyl
acetaldehyde
waterstofperoxide
bacteriocinen
bacteriocine-achtige molekulen
zuurstofkatabolieten
eiwitachtige stoffen

Darmwand en gezond epitheel is een barriere

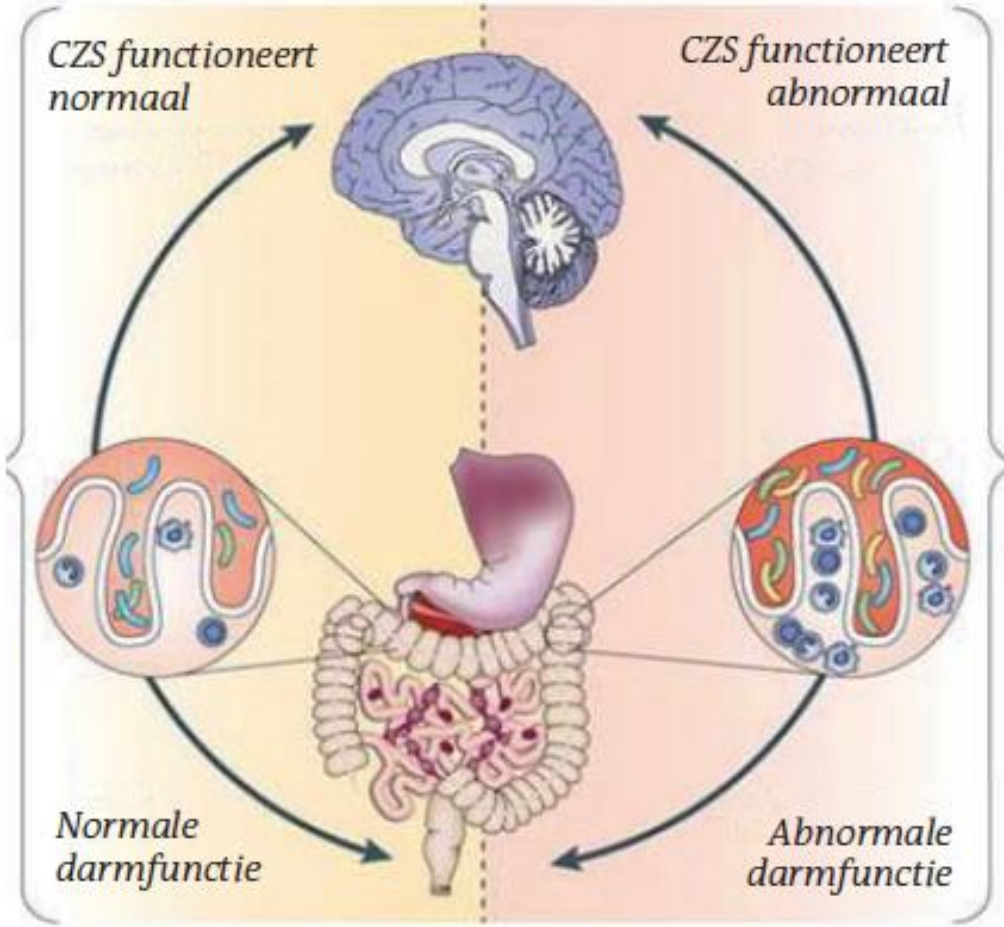

Gluten
Micro-organisms
Toxins
Tight Junctions
Leaky and Inflamed
Mucosal Membrane Cells
Blood Stream
IgG Immune Response - IgA Reaction - B and T Cells Release
Nutrient Malabsorption
Autoimmunity
Food Intolerance
Blood-Brain Barrier Breech
Systematic Inflammation

Afbraak van de barriere functie -> opportunisten & ontsteking



Gezonde situatie

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



Stress/ziekte

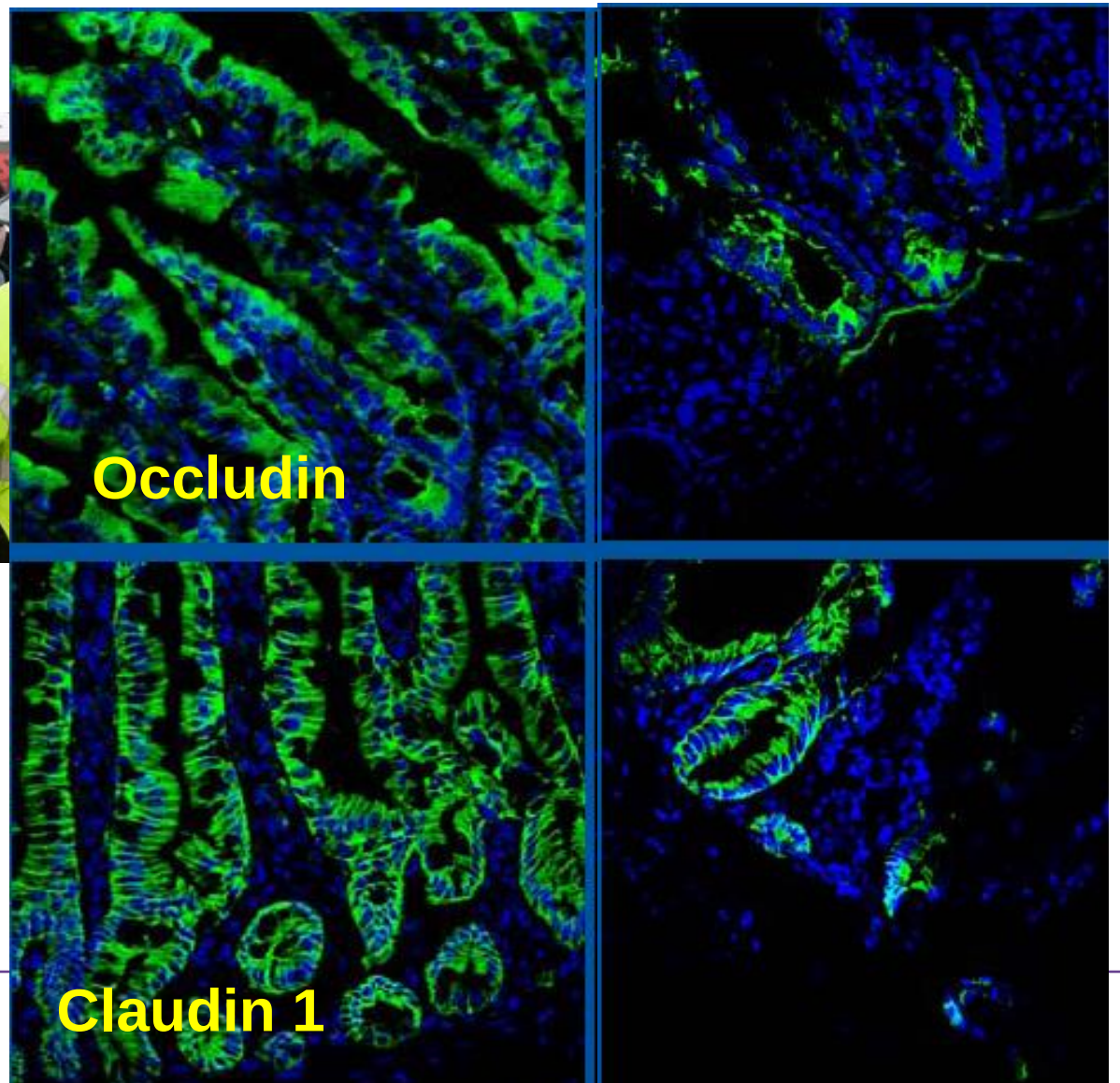
* Veranderingen in gedrag, cognitie, emotie en nociceptie
* Veranderde waarden van ontstekingscellen en/of mediatoren
* Intestinale dysbiose

Triggers die lekkende darm kunnen veroorzaken:

proteïnen uit dieet | weinig maagzuur & enzymen | antibiotica | infecties | afwijkend bloedsuiker

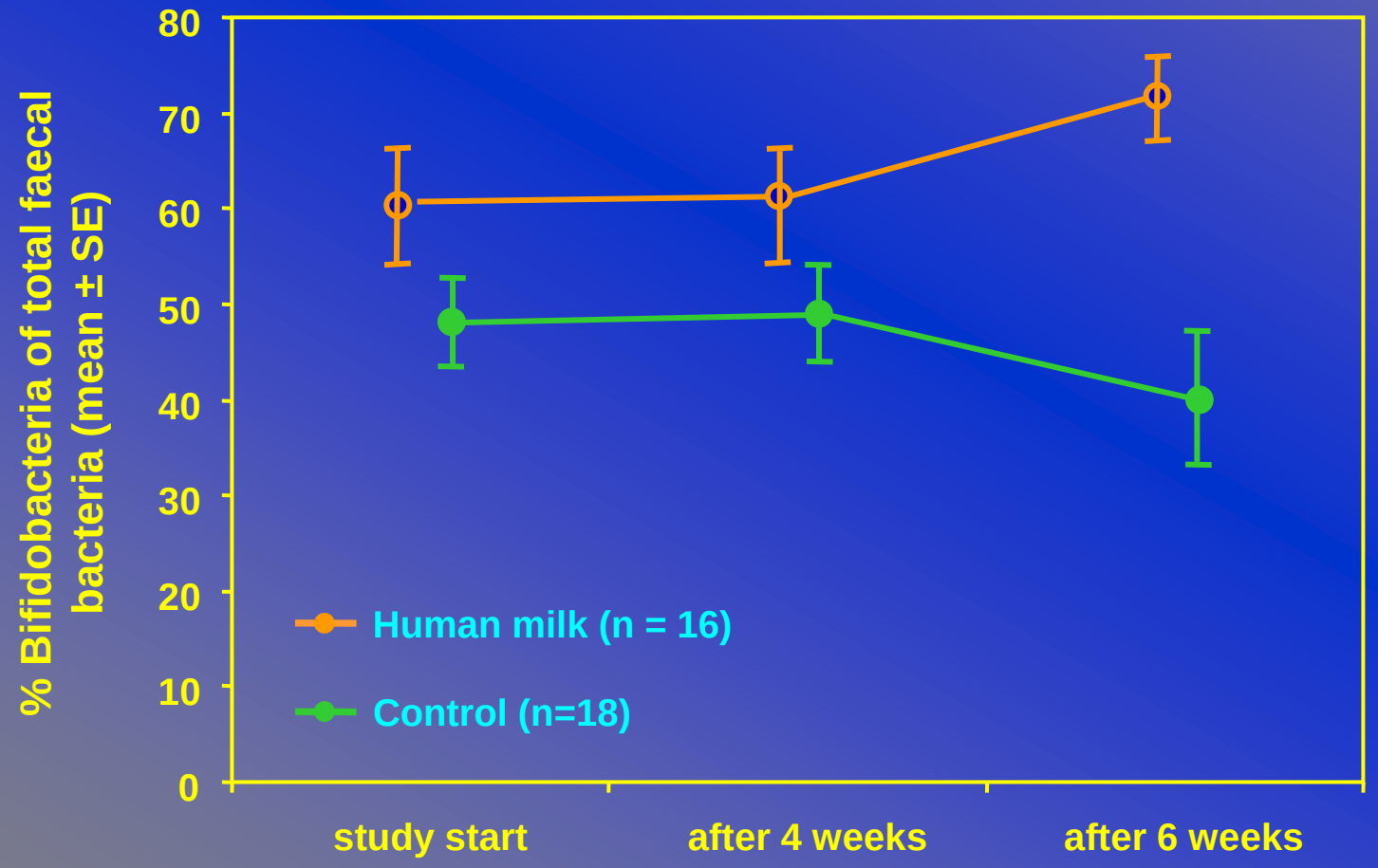
antistoffen | zwangerschap | stress | menopauze | toxische stoffen | voedselallergieën & –intoleranties

Lactobacilli versterken tight junctions



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

- Bifidogenicity -



Knol et al., 2002

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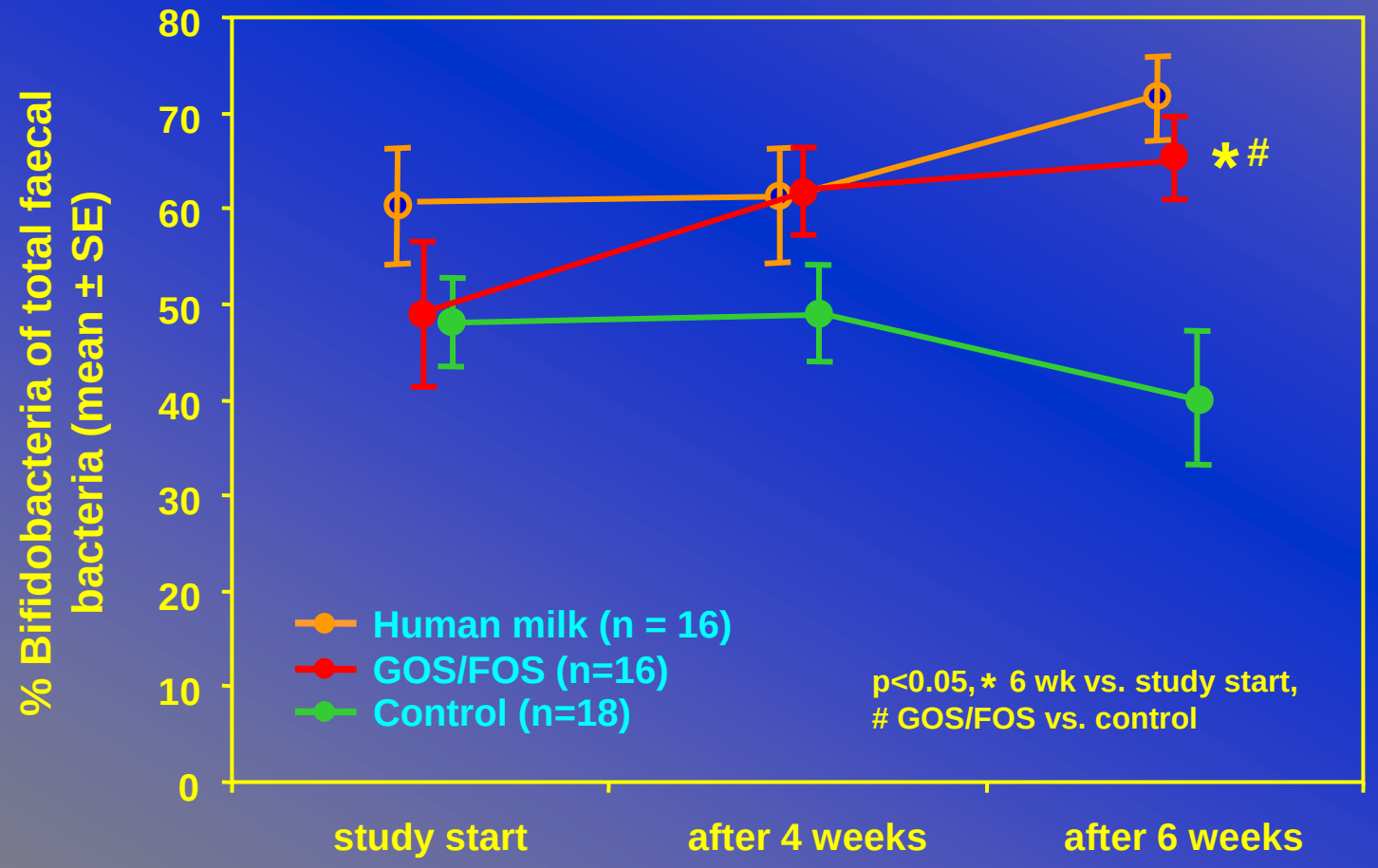
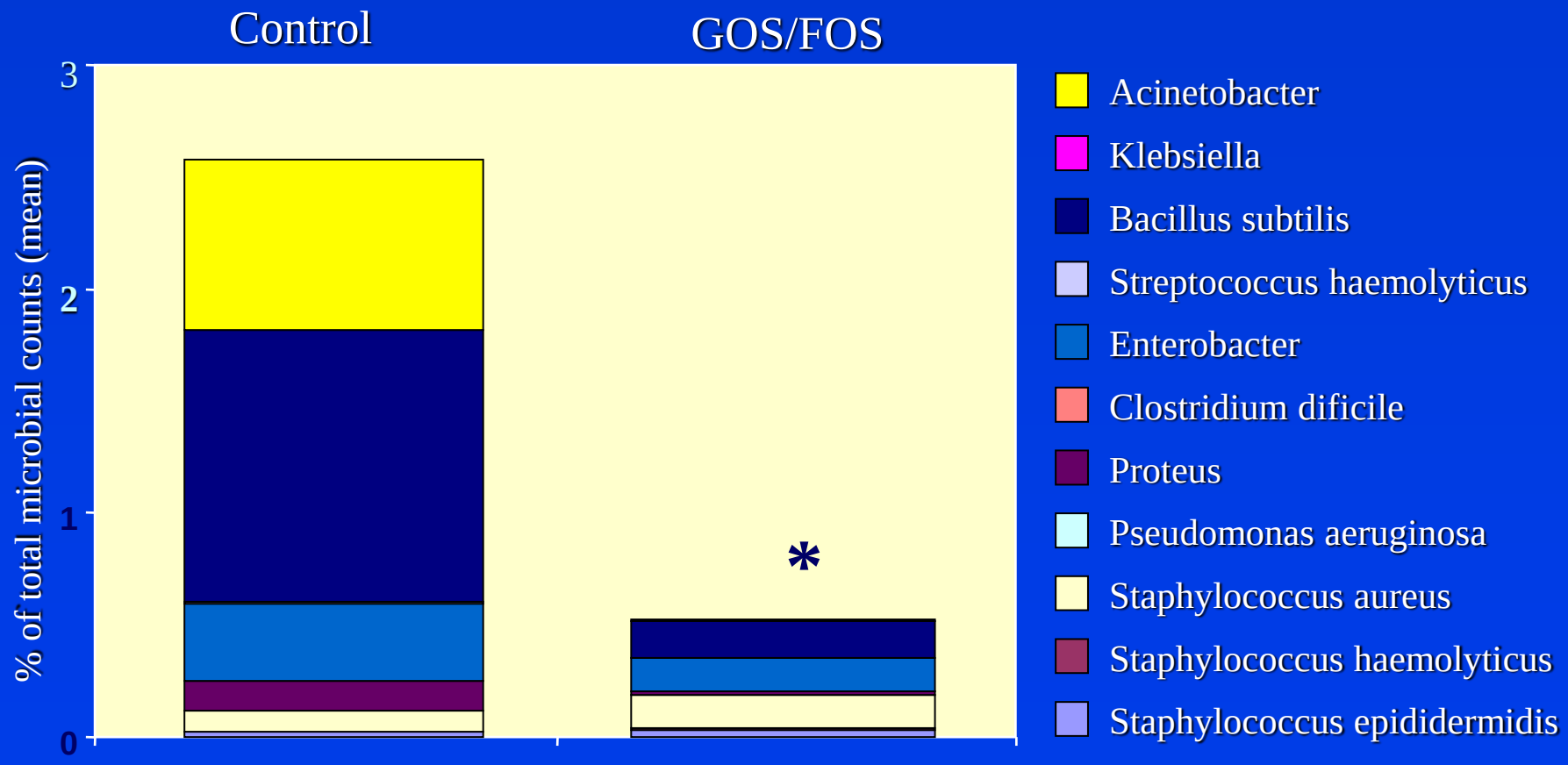


Knol et al., 2002

Reduction of pathogens in the gut after GOS&FOS

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

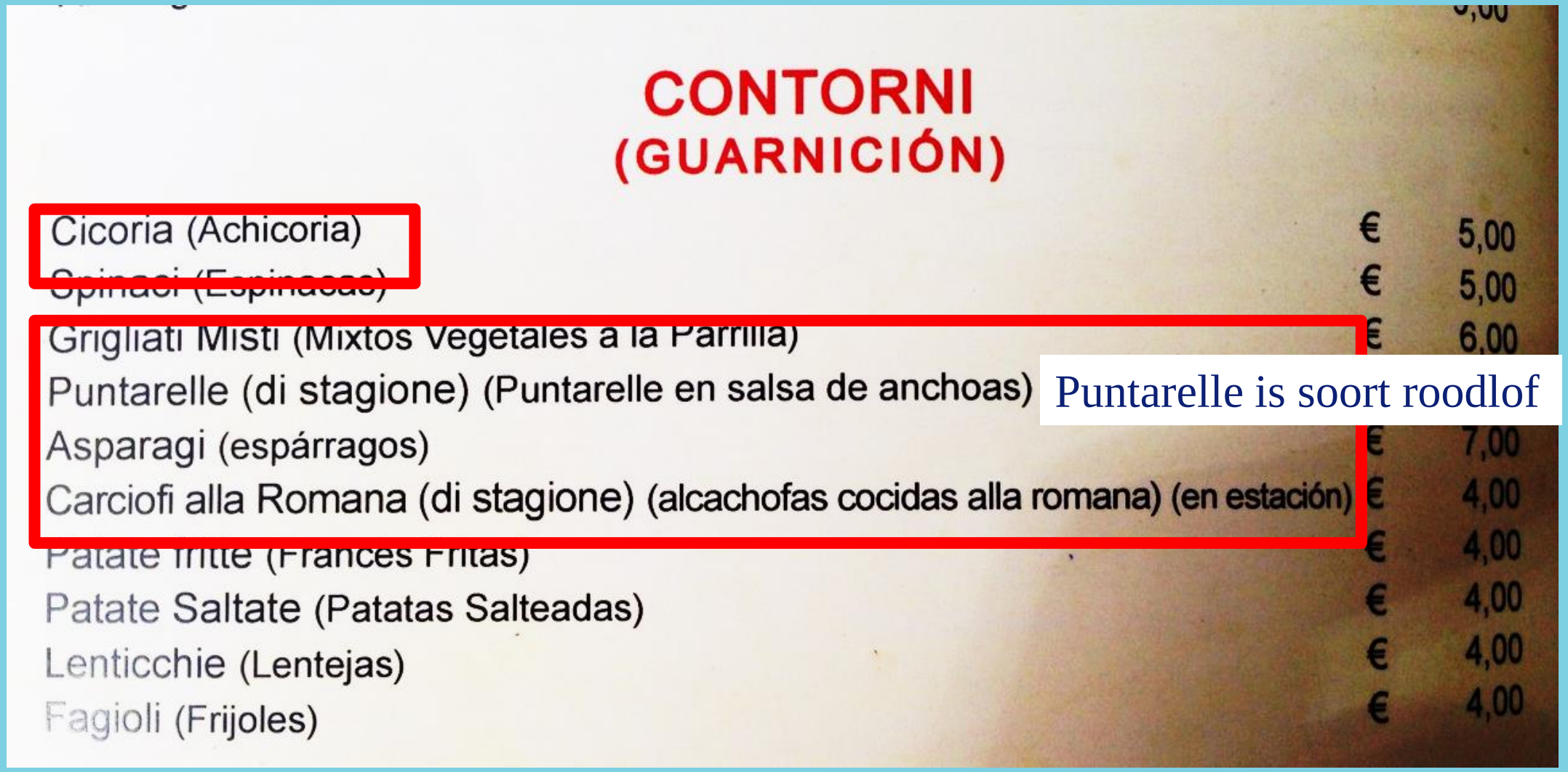


Boehm et al., JPGN, 2003

Slide from Yvan van den Plas

Citation: Claassen E (2014) Cost-benefit relation of diet and probiotics in iatrogenic bowel irregularity (IBI). Front. Pharmacol. 5:14. doi: 10.3389/fphar.2014.00014

	% 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



Puntarelle is soort roodlof

From Holland witlof
designed © by slappo

Probiotische en prebiotische voedingsmiddelen

Probiotisch

- Sommige soorten gatenkaas, waaronder Emmenthaler 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 ingredient(en)	
sommige kazen	3-9	*Propionibacterium freudenreichii* (Emmentaler)	16
'levende' yoghurt	1-10	*Lactobacillus, Bifidobacterium, Lactocccus, Streptococcus* (alle spp.)	17
gefermenteerde zuivel	4-9	*Lactobacillus, Bifidobacterium, Lactocccus, Streptococcus* (alle spp.)	18
kimchi, augurken en dergelijke	6-10	*Lactobacillus plantarum, Leuconostoc sp*	19
tempeh	3-9	*Rhizopus spp, Fusarium spp.* (plus gisten en melkzuurbacteriën)	20
miso en natto	2-7	*Penicillium spp.* en *Aspergillus spp.*	21
kefir (incl. kefiran)	6-9	melkzuur- en azijnzuurbacteriën en gisten op een polysacharide matrix	22
echt zuurdesembrood	6-8	*Lactobacilus casei, Bifidobacterium pseudocatelunatum*	18
zuurkool en olijven	4-8	*Lactobacillus spp, Leuconostoc spp.*	23
salami en ham	2-11	Lactobacillus plantarum spp.	24
gefermenteerde salsa	5-7	Lactobacillus fermentum	25
'levende' wijn	2-5	*Saccharomyces cerevisiae* (en soms ook melkzuurbacteriën)	26
'levend' bier	2-5	melkzuurbacteriën (bijv. Lambiek en Geuze)	27
gefermenteerde cacao	3-8	*Saccharomyces boulardii; Lactobacillus fermentum, L. plantarum*	28
kombucha	6-7	*Pichia; Bretanomyces; Zygosaccharomyces, Komagataeibacter, Gluconobacter*	29
prebiotisch			
		vorming microbioom (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 korteketenvetzuren	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 chiazaden		antioxidanten en flavonoïden,	39
walnoten		antioxidanten en bevordering boterzuurproductie door het microbioom	40
quinoa		antioxidanten en verlaging van de pH door productie korteketenvetzuur	41
paardenbloem en moerbeibes		microbioom 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 microbioom.

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			37
			38
			39
			40
			41
paardenbloem en moerbeibes		microbioom verstiet 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 microbioom.

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 Klijsen (1970) is journalist, gespecialiseerd in gezondheid, *personal finance* en recht. Ze is eindredacteur van de *Consumentengids* 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 Klijsen

GEZOND NAAR HONDERDVIJFTIEN

Eric Claassen, Lisette de Jong en Heidi Klijsen

Disturbance microbiota (=dysbiosis)

World Health Organization

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

Food and Agriculture Organization of the United Nations

Indirectly linked to gut dysbiosis

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

Recent advances in clinical practice

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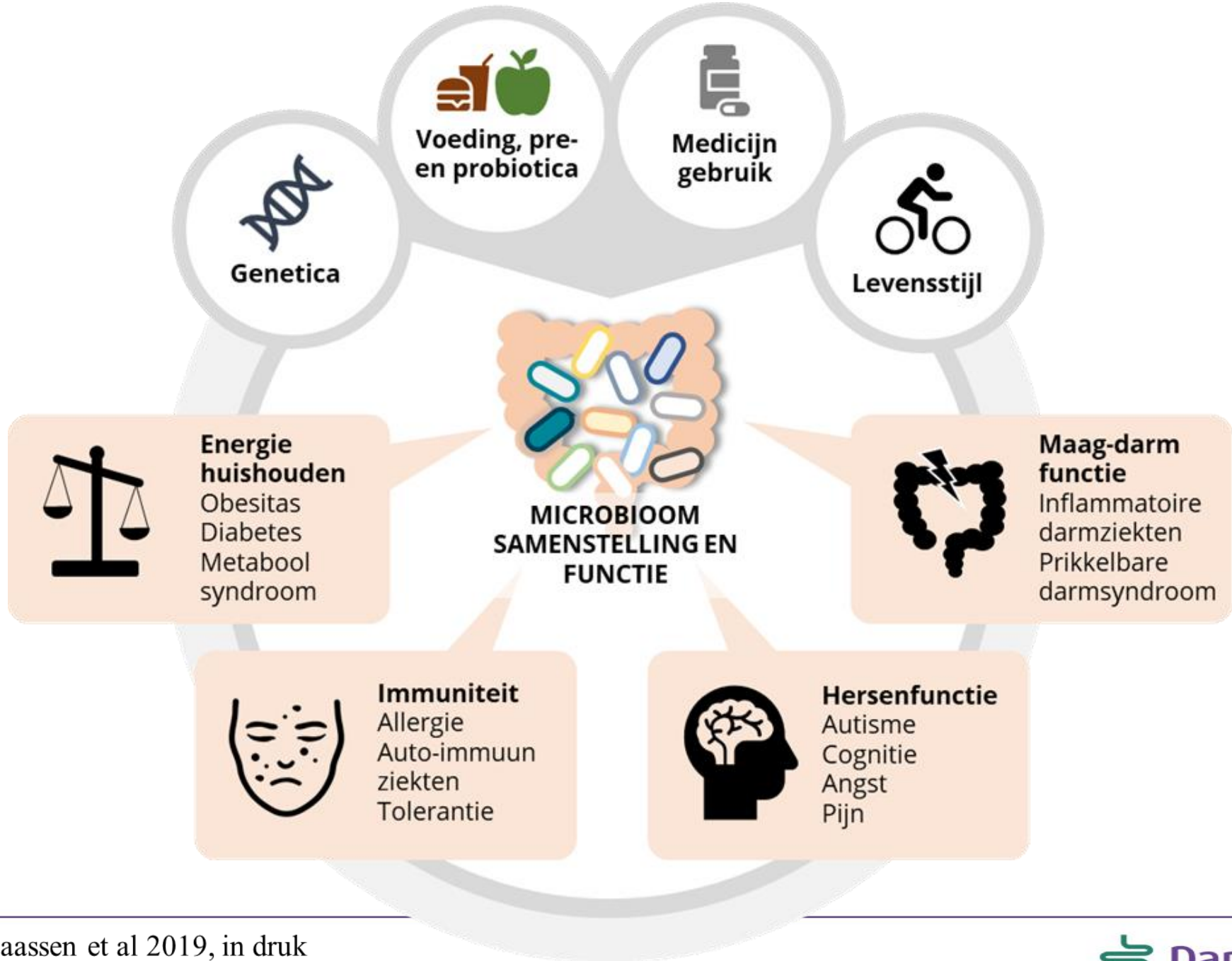
An update on the use and investigation of probiotics in health and disease

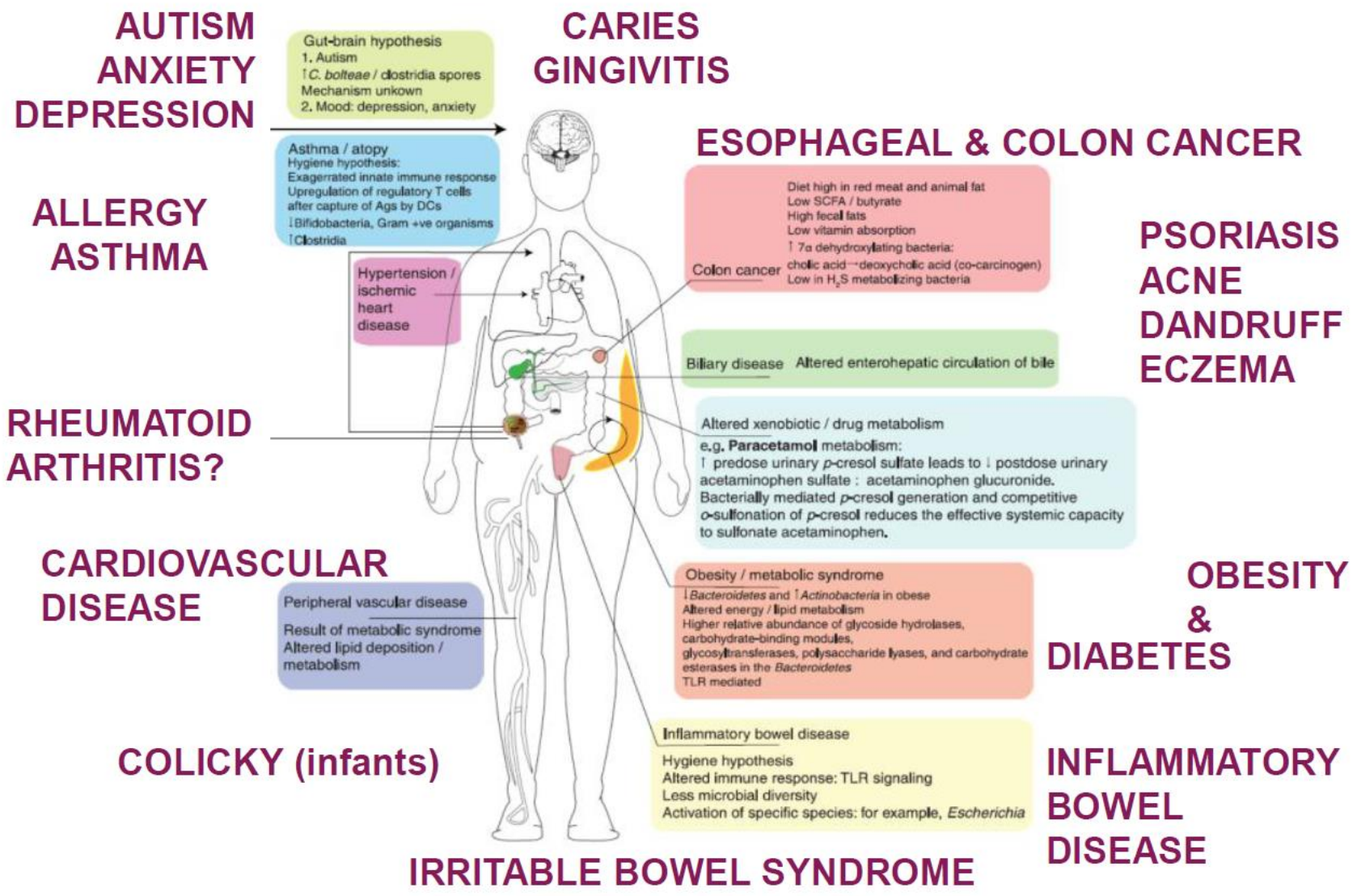
Mary Ellen Sanders,[1] Francisco Guarner,[2] Richard Guerrant,[3] Peter R Holt,[4] Eamonn MM Quigley,[5,6] R Balfour Sartor,[7] Philip M Sherman,[8] Emeran A Mayer[9]



Nieuwboer, Claassen et al 2019, in druk

STICHTING Darmgezondheid

The human microbiota
In health and disease



Poll 1 Wat zijn de functies van de microbiota?

- Competitie om aanhechtingsplaatsen
- Alert houden immuunsysteem
- Productie korte-keten-vetzuren
- Alle bovenstaande zijn juist

The NEW ENGLAND JOURNAL of MEDICINE

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.

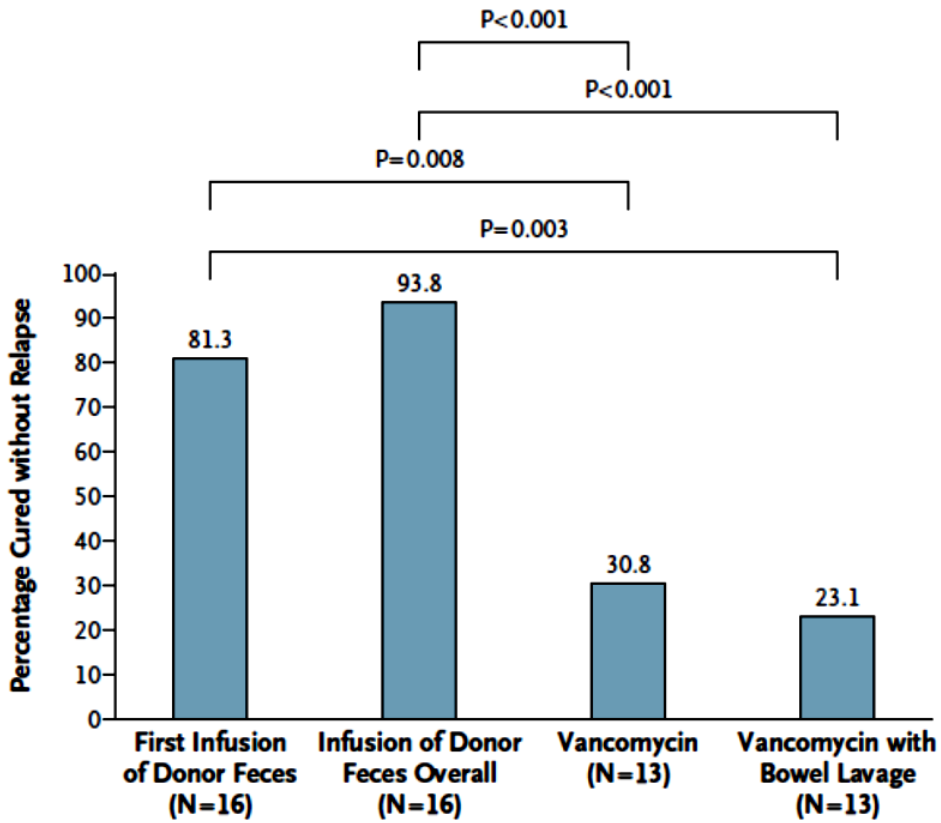


Figure 2. Rates of Cure without Relapse for Recurrent *Clostridium difficile* Infection.

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.*

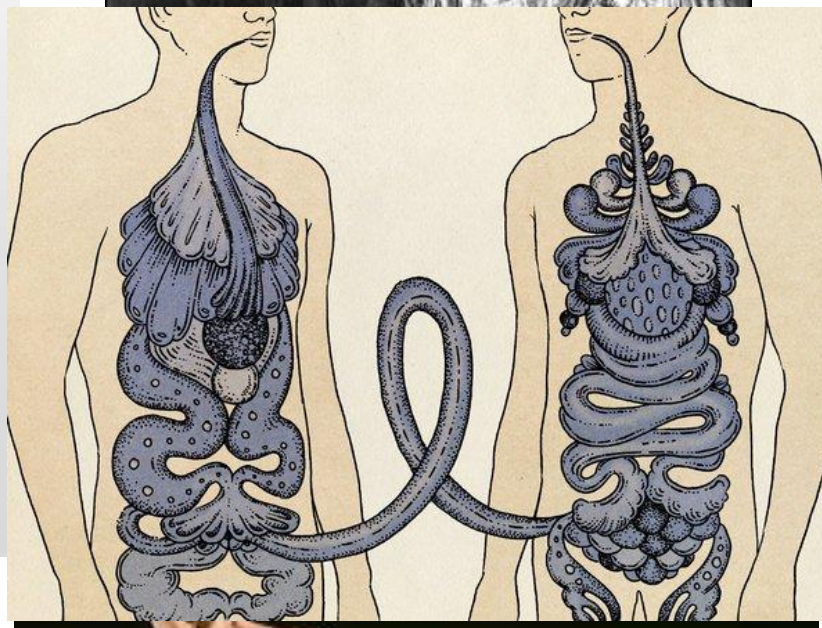
Adverse Event	On Day of Infusion of Donor Feces	During Follow-up
	no. of events	
Belching	3	0
Nausea	1	0
Vomiting	0	0
Abdominal cramps	5	0
Diarrhea	15	0
Constipation	0	3
Abdominal pain	2 (associated with cramping)	0
Infection	0	2†
Hospital admission	NA	1‡
Death	0	0
Other adverse event	1§	1‡

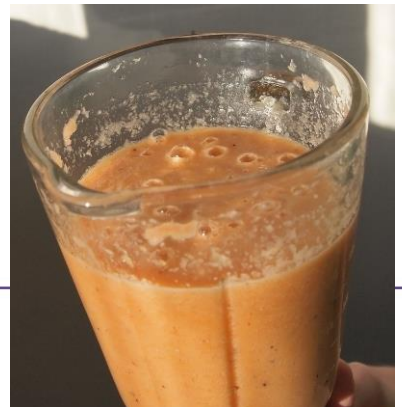
* Adverse events that were reported on the day of donor-feces infusion and those that were reported during follow-up are listed separately. NA denotes not applicable.

† 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





Fecal transplantation NOT SAFE but “Poopular”

SCIENTIFIC REPORTS

OPEN

The mechanistic link between health and gut microbiota diversity

Olaf F. A. Larsen & Eric Claassen

Received: 25 September 2017
Accepted: 12 January 2018
Published online: 01 February 2018

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 by applying first principles basic graph theory on small networks that higher diversity within such a netw systems and redundancy. Our results quantitatively support earl gut microbiota richness with respect to these parameters. Our si diversity leads to higher resilience within small microbiological e microbiota. This notion should provide an ingredient when devel within the domain of microbiota management.

www.nature.com/scientificreports

SCIENTIFIC REPORTS

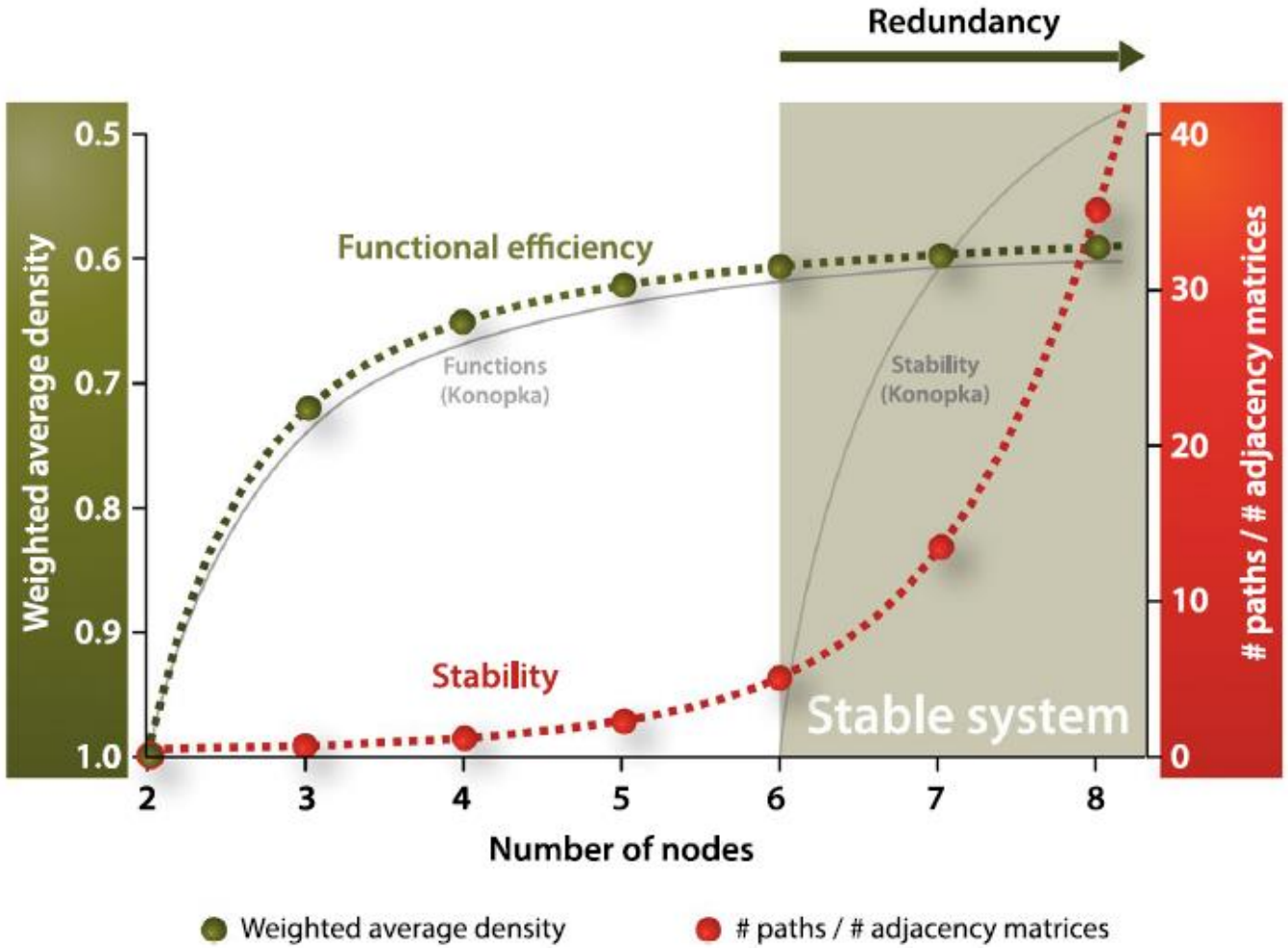
OPEN

Towards a rational design of faecal transplant analogues

Olaf F. A. Larsen[1], Anton H. J. Koning[2], Peter J. van der Spek[2] & Eric Claassen[1]

Received: 10 October 2018
Accepted: 21 March 2019
Published online: 03 April 2019

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.



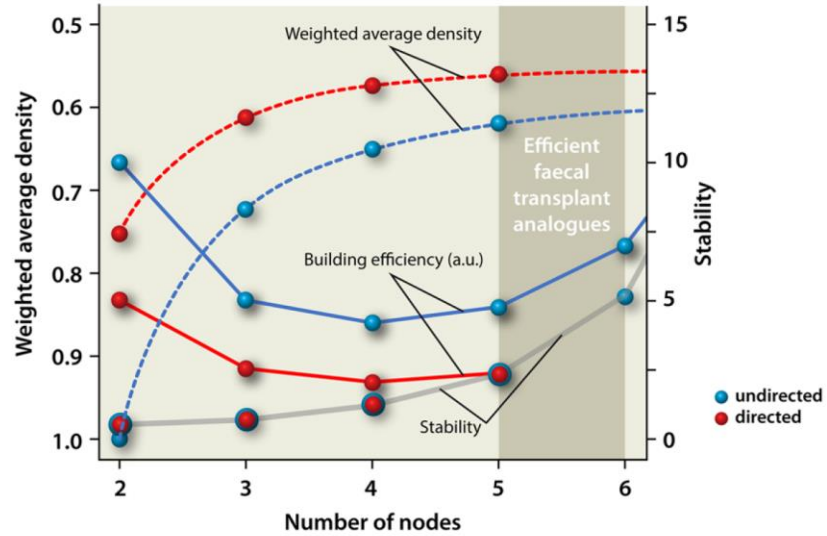
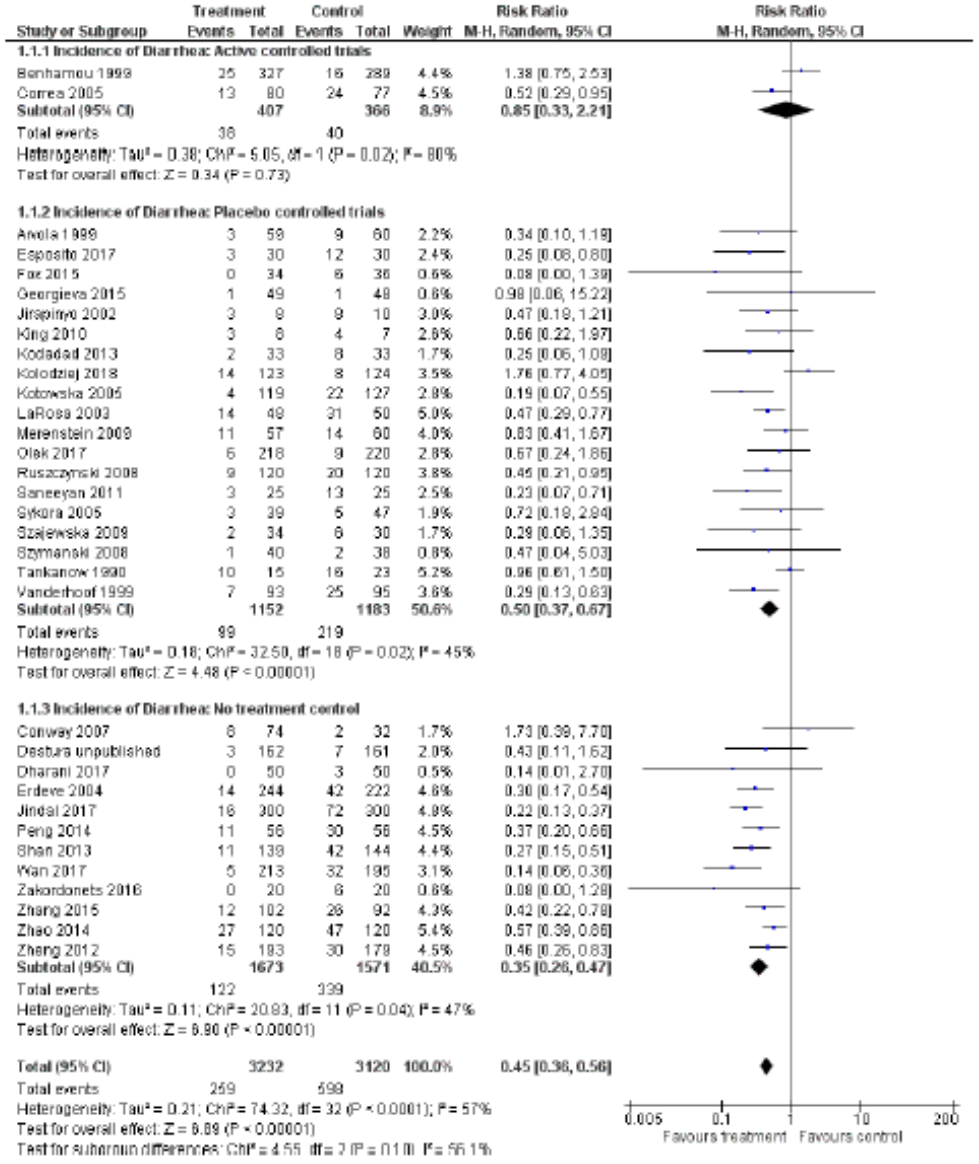


Figure 4. Graphical summary of our findings (adapted from Konopka[14]). Green: weighted average density reflecting functional efficiency. Red: number of paths divided by the number of adjacency matrices, reflecting stability. Grey: trends as proposed earlier by Konopka[14].

Poll 2 Je hebt meer bacteriën in je maag-darmkanaal dan cellen in je lichaam

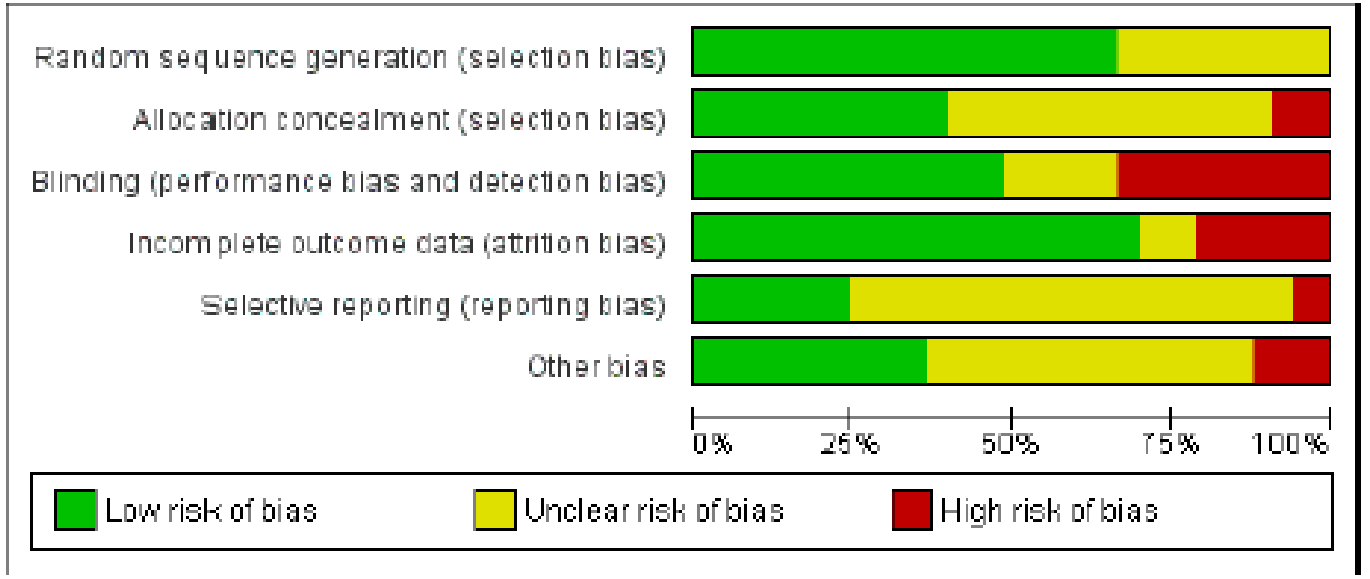
- Juist
- Onjuist
- Weet niet

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.

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**

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

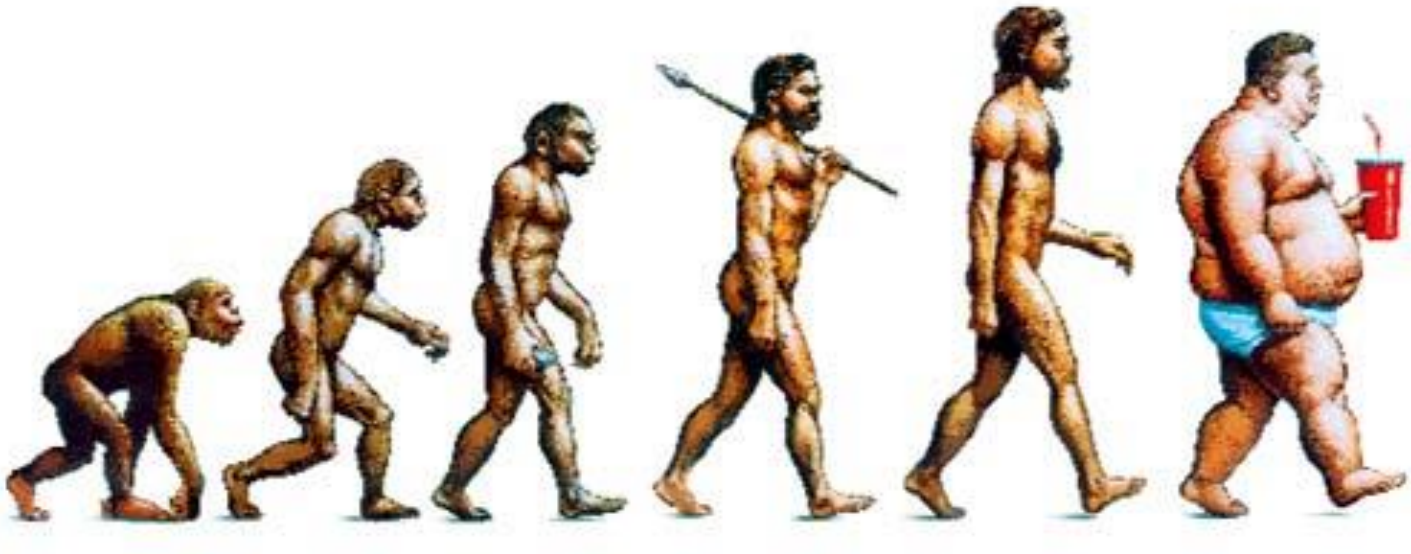
Subjects			Allergies		Experiments		Microflora Associations with Allergic Disease[a]	
Number[b]	Residence	Age	Disease[c]	Diagnosis[d]	Sample	Assay[e]	Negative[g]	Positive[h]
27-35	Estonia + Sweden	2 yr	AD (FA)	clinical and SPT	feces	microbiol	Lactobacilli, Bifidobacteria, CONS, Anaerobes, Bacteroides	Aerobes, Coliforms, *S. aureus*, 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, *Bacteroides*	*S. aureus*, Lactobacilli, Clostridia
4-6	NR	2-7 mo	AD and FA	clinical	feces	microbiol	*Bifidobacterium bifidum*	*Bifidobacterium adolescentis*
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, *S. viridans*, Clostridia[j]	Lactobacilli/enterococci[j]
7-6	NR	2-7 mo	AD	clinical and SPT	feces	microbiol	*Bifidobacterium bifidum*	*Bifidobacterium adolescentis*
10-10	UK	12 mo	atopic wheeze	clinical and SPT	blood	molecular		*C. difficile*-specific IgG
30-68	Japan	< 20 yr	AD	clinical	feces	microbiol	*Bifidobacterium*	*Staphylococcus*
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	*Bifidobacterium* spp., *Clostridium* 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

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




♂
30 tot 40 jaar
11%
40 tot 50 jaar
23%
50 tot 60 jaar
32%
60 tot 70 jaar
40%
♀
30 tot 40 jaar
28%
40 tot 50 jaar
33%
50 tot 60 jaar
44%
60 tot 70 jaar
58%

Beneficial Microbes, March 2014; 5(1): 19-28

Wageningen Academic Publishers

The development of probiotic treatment in obesity: a review

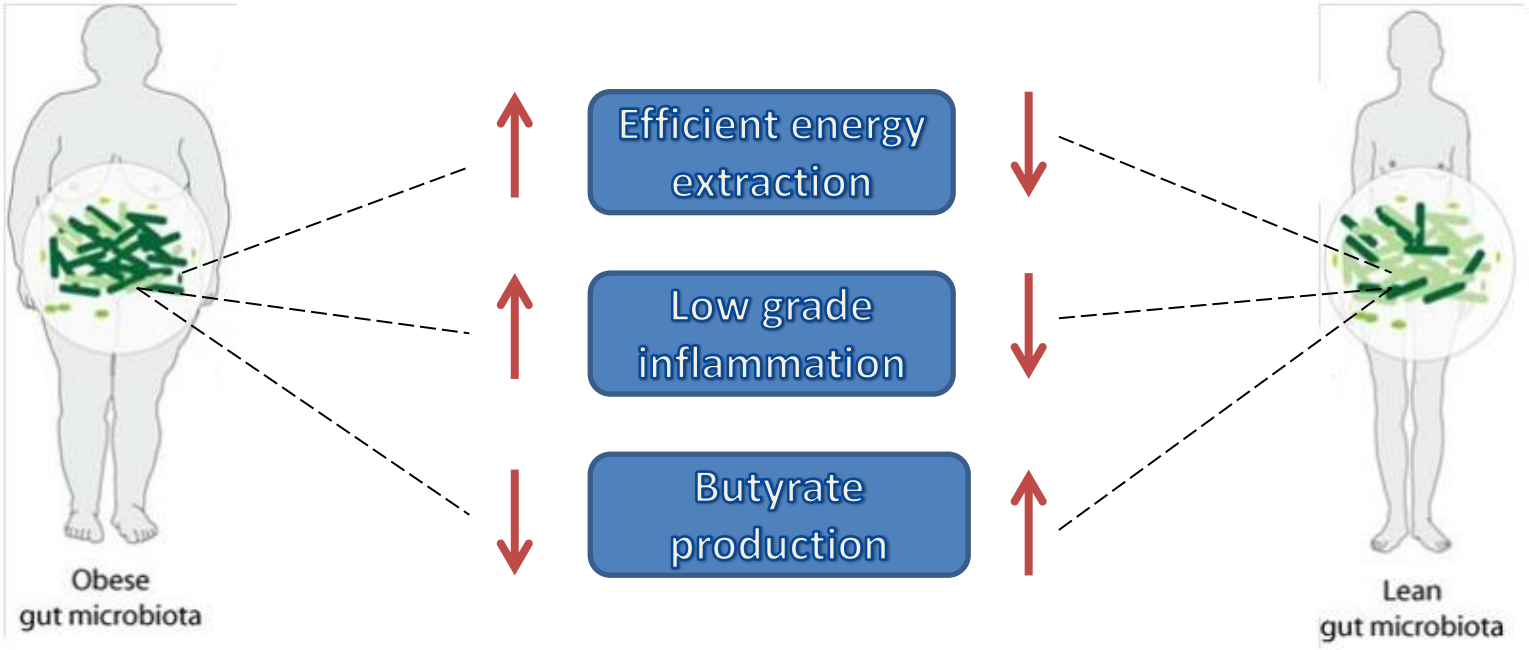
M.C. Mekkes[1*], T.C. Weenen[2,3*], R.J. Brummer[4] and E. Claassen[1,3]

*[1]VU University Amsterdam, Athena Institute, De Boelelaan 1085, 1081 HV Amsterdam, the Netherlands; [2]Erasmus School of Economics Rotterdam, Burgemeester Oudlaan 50, 3062 PA Rotterdam, the Netherlands; [3]Erasmus Medical Center Rotterdam, Dr. Molewaterplein 50, 1315 GE Rotterdam, the Netherlands; [4]School 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

REVIEW ARTICLE

The influence on metabolism

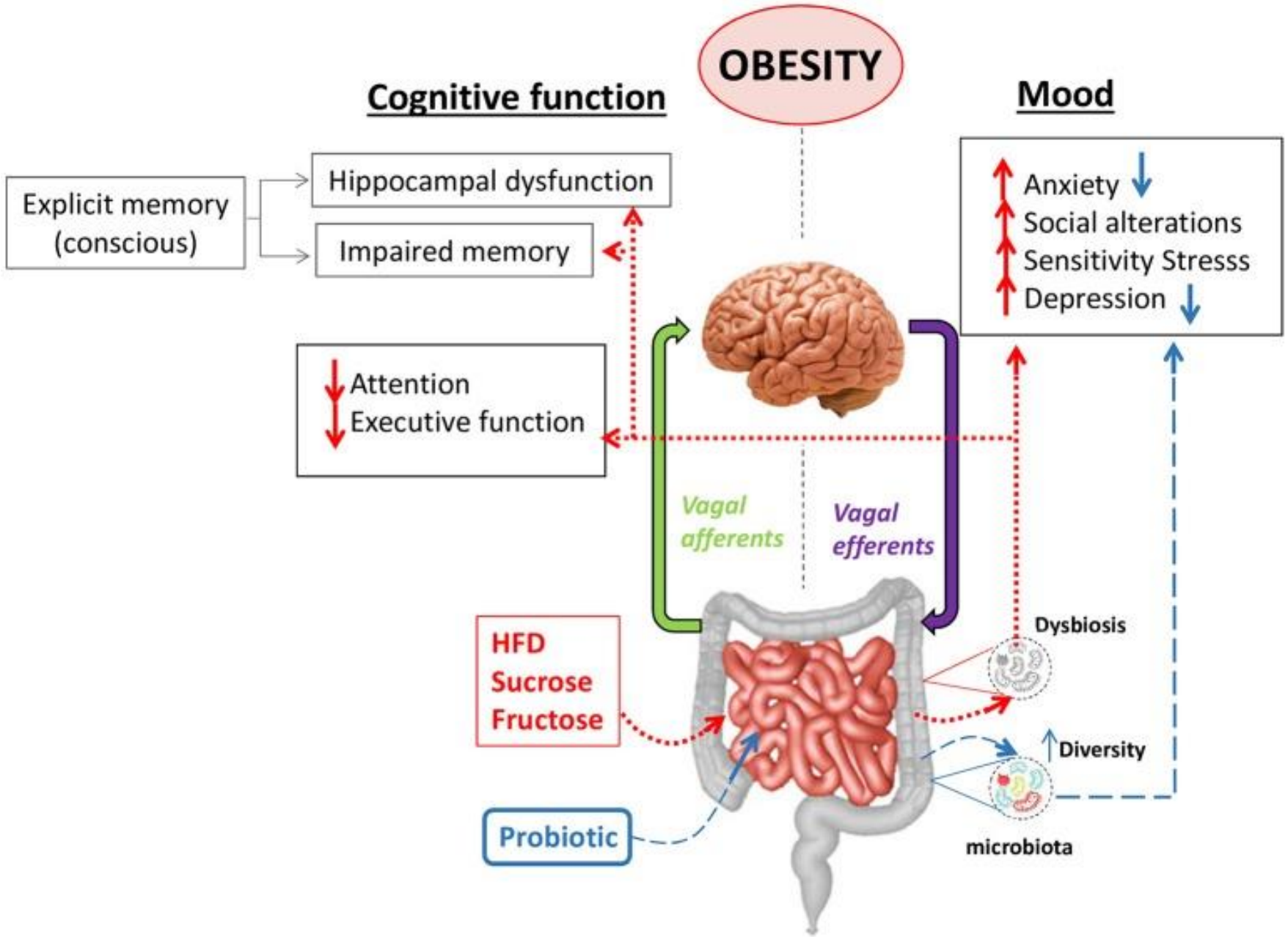


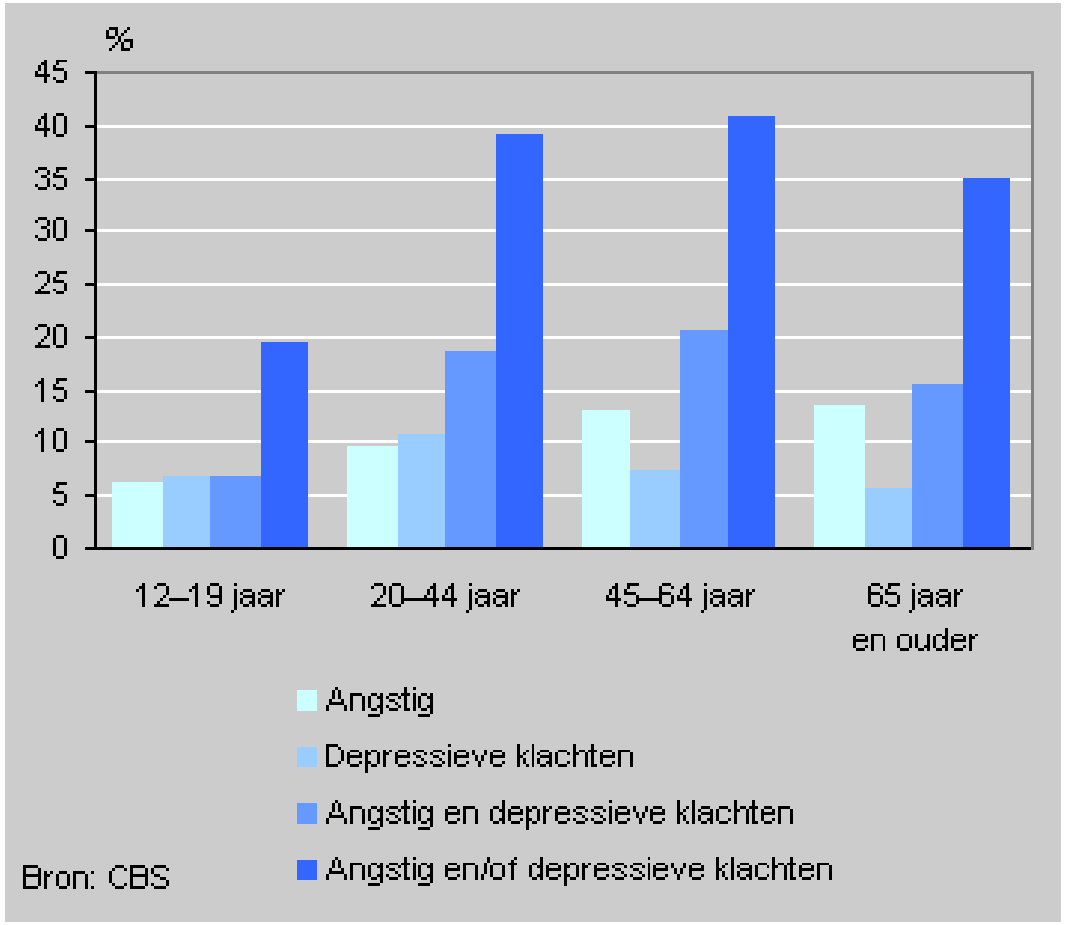
- This explains the differences in metabolic mechanisms
- These insights are a base to understand the Mechanism Of Action (MOA) of future probiotic treatment
- Probiotic microorganism might manipulate these mechanisms
  - Reducing effect on weight and weight gain

HARA HACHI BU

Poll 3 Het is zinvol om met probiotica te beginnen tijdens de antibioticumkuur

- juist
- onjuist
- Weet niet


OBESITY
Cognitive function
Mood
Explicit memory (conscious)
Hippocampal dysfunction
Impaired memory
Attention
Executive function
Anxiety
Social alterations
Sensitivity Stresss
Depression
Vagal afferents
Vagal efferents
HFD
Sucrose
Fructose
Probiotic
Dysbiosis
Diversity
microbiota


%
45
40
35
30
25
20
15
10
5
0
12–19 jaar
20–44 jaar
45–64 jaar
65 jaar en ouder
Angstig
Depressieve klachten
Angstig en depressieve klachten
Angstig en/of depressieve klachten
Bron: CBS

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,‡,§ JOSEPH MACRI,¶ MURRAY POTTER,‖ XIAXING HUANG,* PAUL MALINOWSKI,¶ WENDY JACKSON,* PATRICIA BLENNERHASSETT,* KAREN A. NEUFELD,‡,§ JUN LU,* WALIUL I. KHAN,*,‖ IRENE CORTHESY–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 Neurotropic Factor and Behavior in Mice

PREMYSL BERCIK,* EMMANUEL DENOU,* 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

Brain, Behavior, and Immunity 48 (2015) 258–264

Contents lists available at ScienceDirect

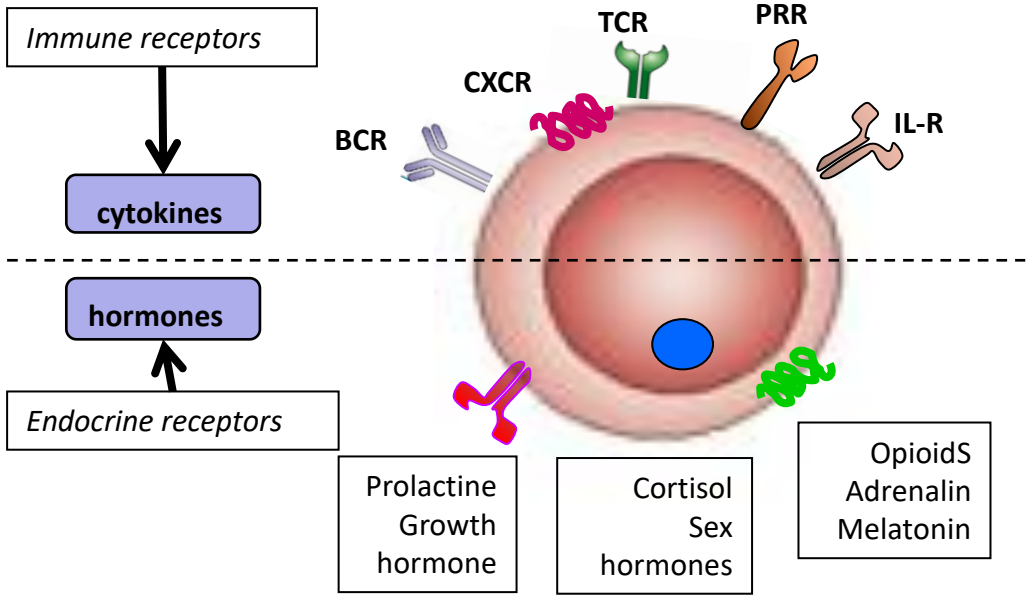
Brain, Behavior, and Immunity

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?



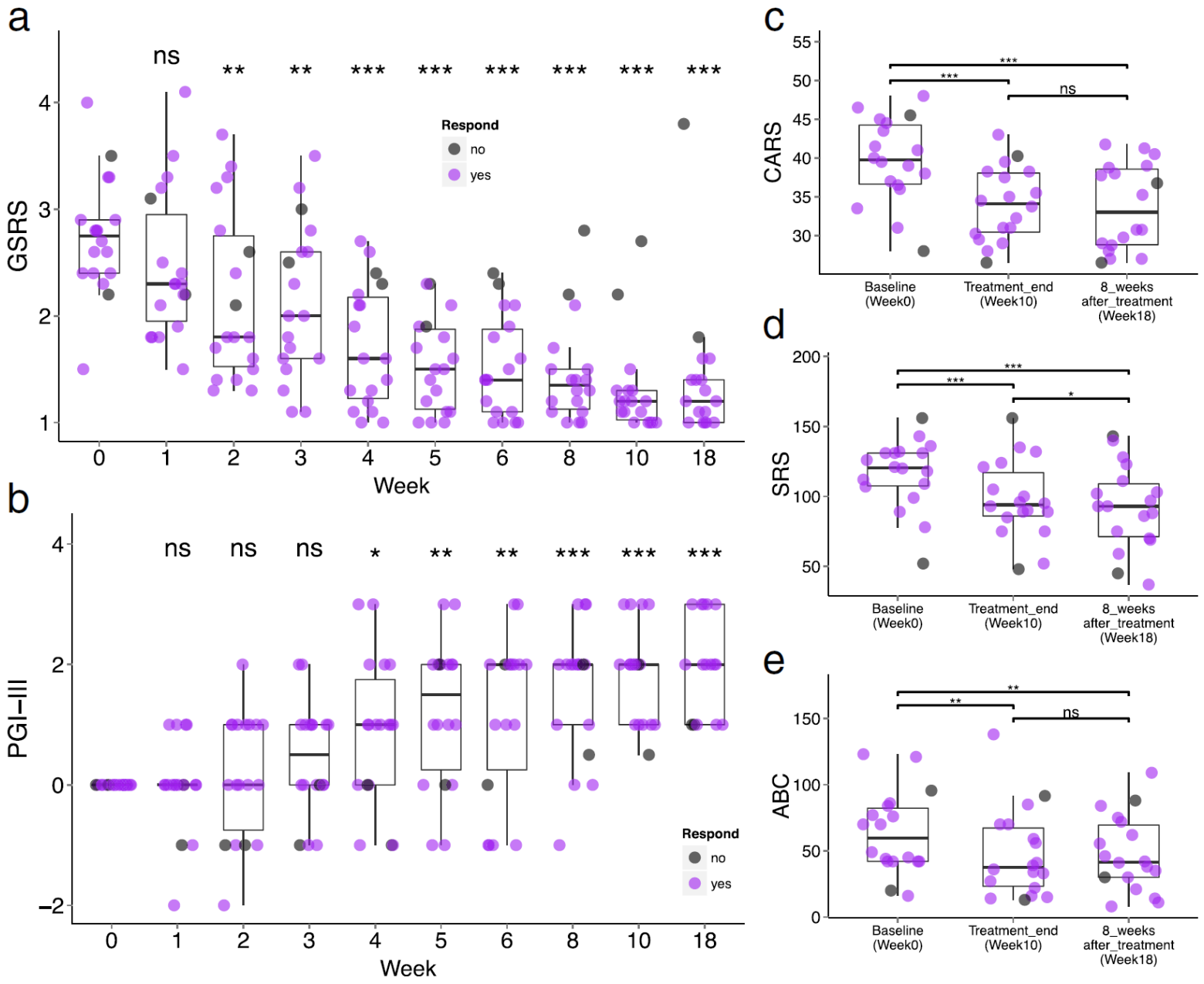
Kang *et al. Microbiome* (2017) 5:10
DOI 10.1186/s40168-016-0225-7

Microbiome

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 Borody[4], Lauren Chittick[5,15], Alessio Fasano[6], Alexander Khoruts[7,8,9], Elizabeth Geis[2], Juan Maldonado[1], Sharon McDonough-Means[10], Elena L. Pollard[2], Simon Roux[5,15], Michael J. Sadowsky[8,11], Karen Schwarzberg Lipson[12], 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

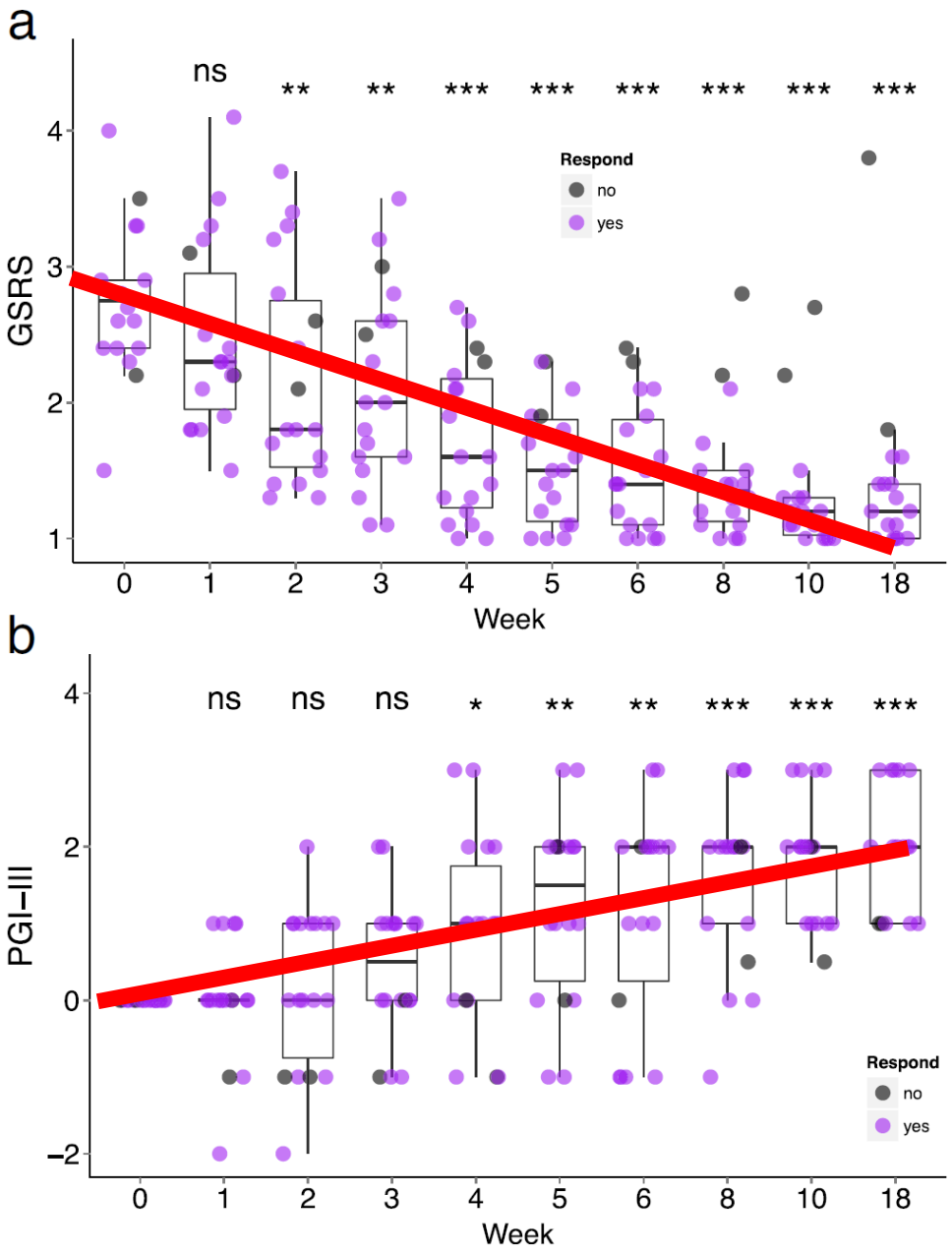
a) Gastrointestinal symptom rating scale

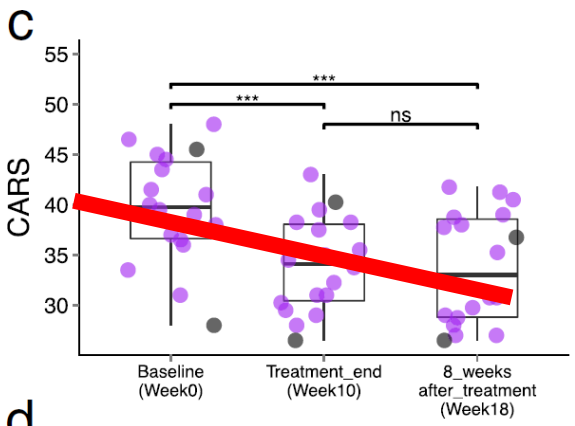
b) Parent global impressions-III

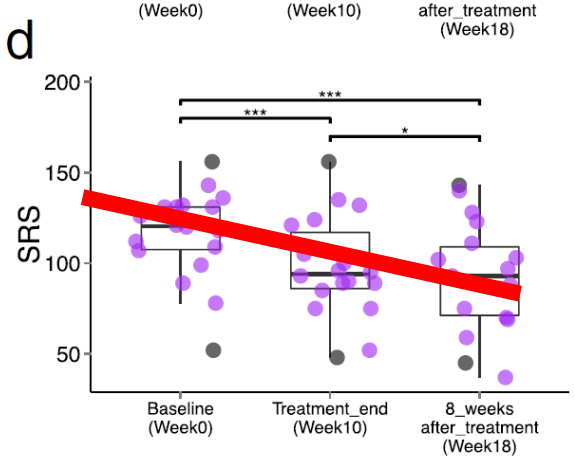
c) Childhood autism rating scale

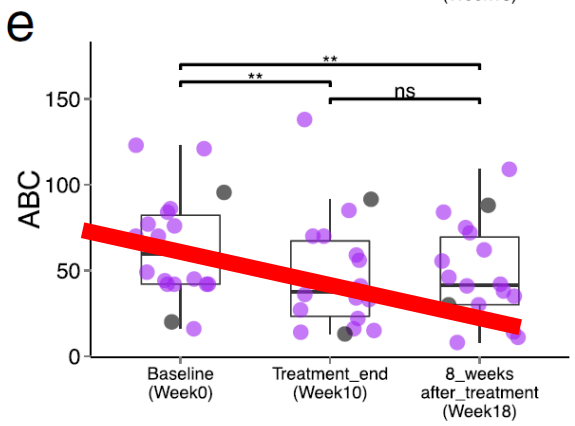
d) Social responsiveness scale

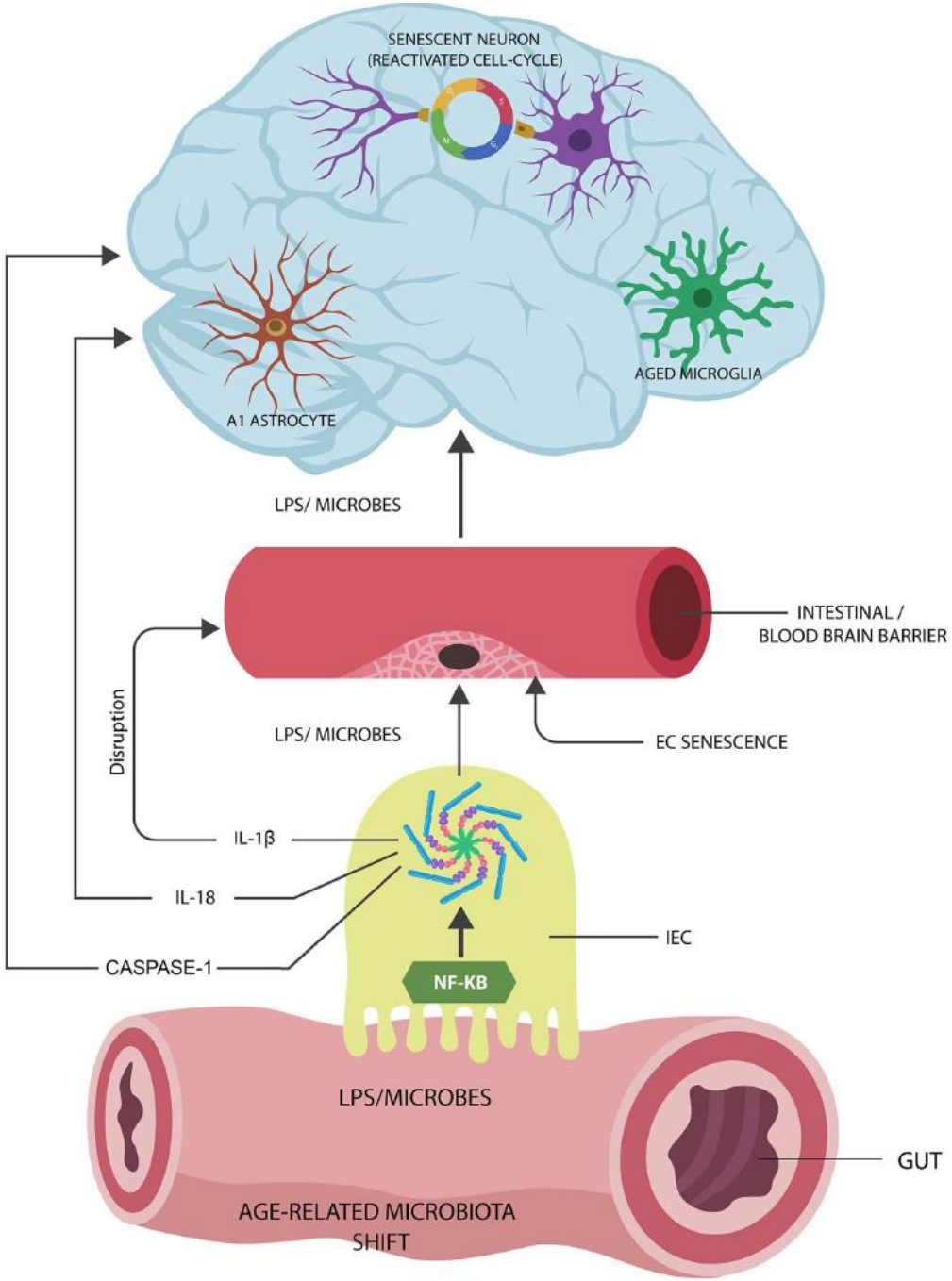
e) Aberrant behavior checklist











frontiers in Aging Neuroscience

REVIEW
published: 26 June 2019
doi: 10.3389/fnagi.2019.00143

Check for updates

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

Carolina Osorio[1], Tulasi Kanukuntla[2], Eddie Diaz[2], Nyla Jafri[2], Michael Cummings[2] 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 .

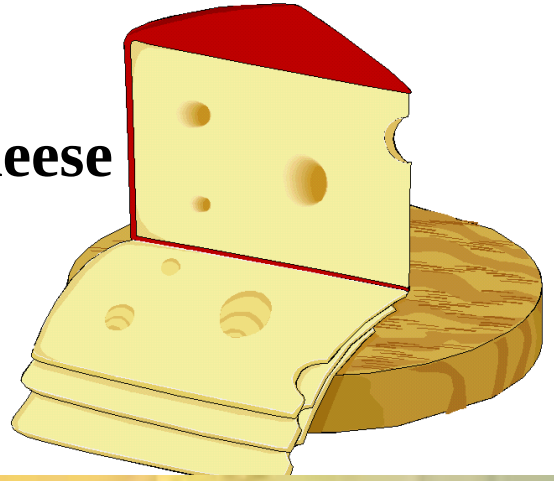
The history of probiotics: the untold story.
Ozen M, Dinleyici EC

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**.

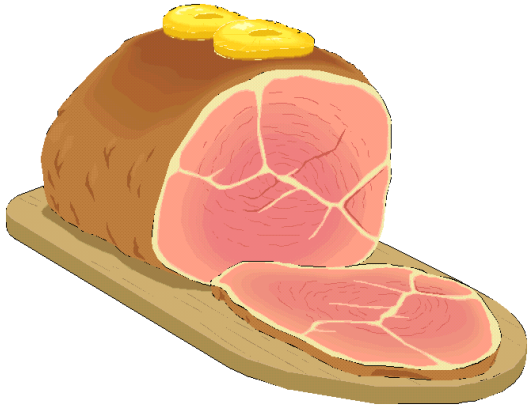
Cheese



Yogurt

Beer

Sauerkraut



Sourdough bread

cured ham

Salami and pickles

Vinegar

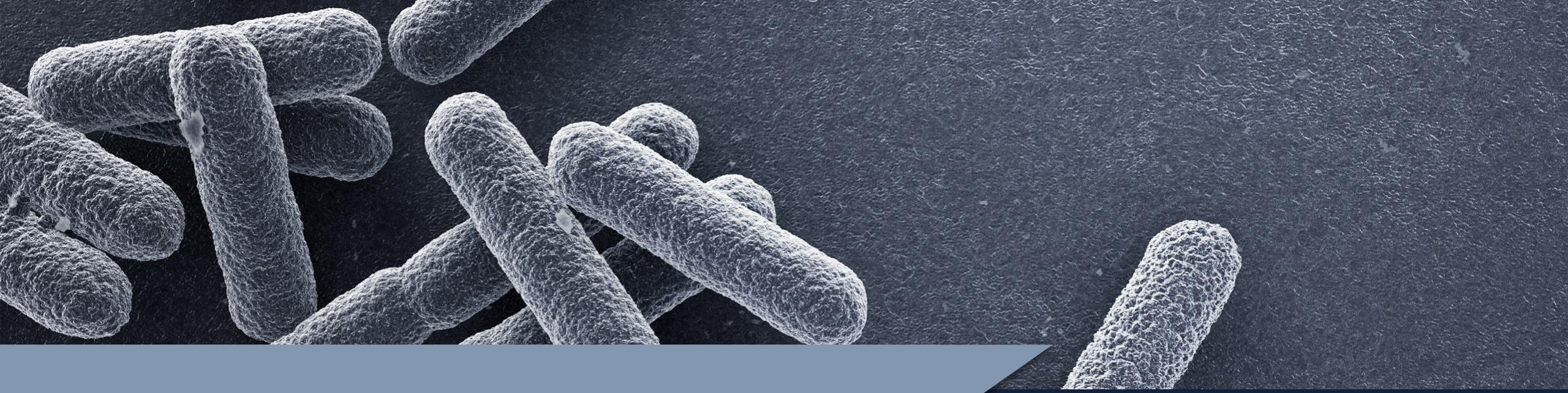
Poll 4 waar begint de spijsvertering?

- Mond
- Maag
- Lever
- Dunne darm

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

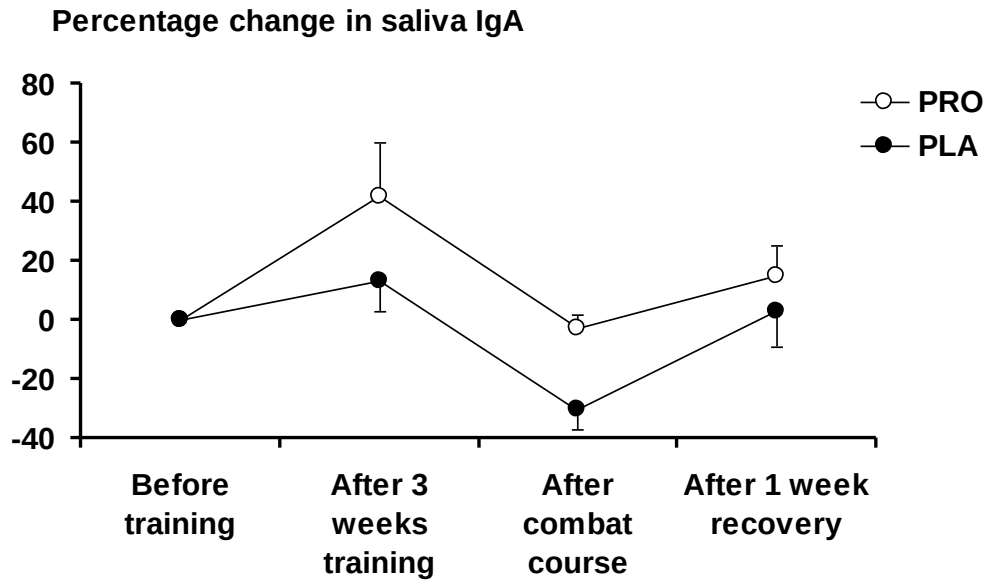
School of Sport, Exercise & Health Sciences
Loughborough University, UK

TEAM GB

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



Tiollier et al 2007 Military Med 172: 1006-1011

Environmental Health: A Global Access Science Source

BioMed Central

Research

Open Access

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

Py Tubelius[1], Vlaicu Stan[1] and Anders Zachrisson*[2]

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

Published: 07 November 2005

Environmental Health: A Global Access Science Source 2005, **4**:25 doi:10.1186/1476-069X-4-25

Received: 22 August 2005
Accepted: 07 November 2005

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**

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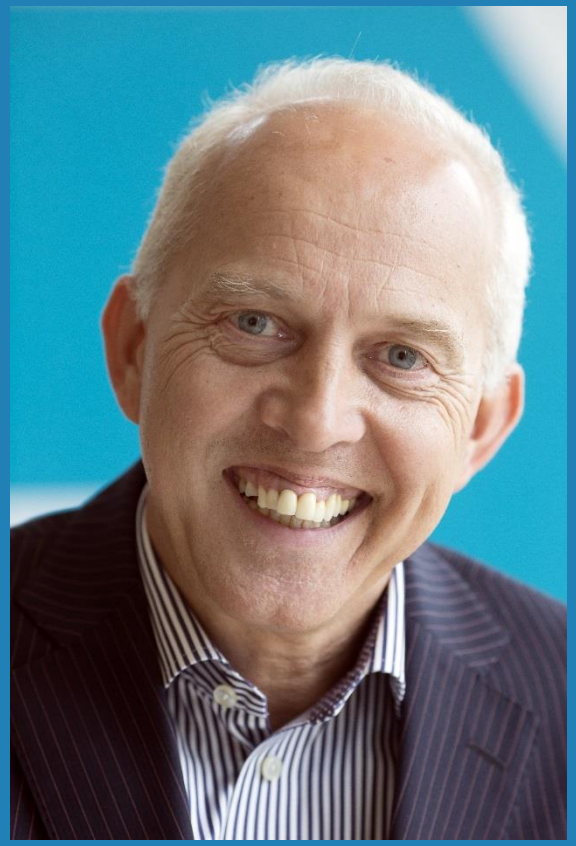

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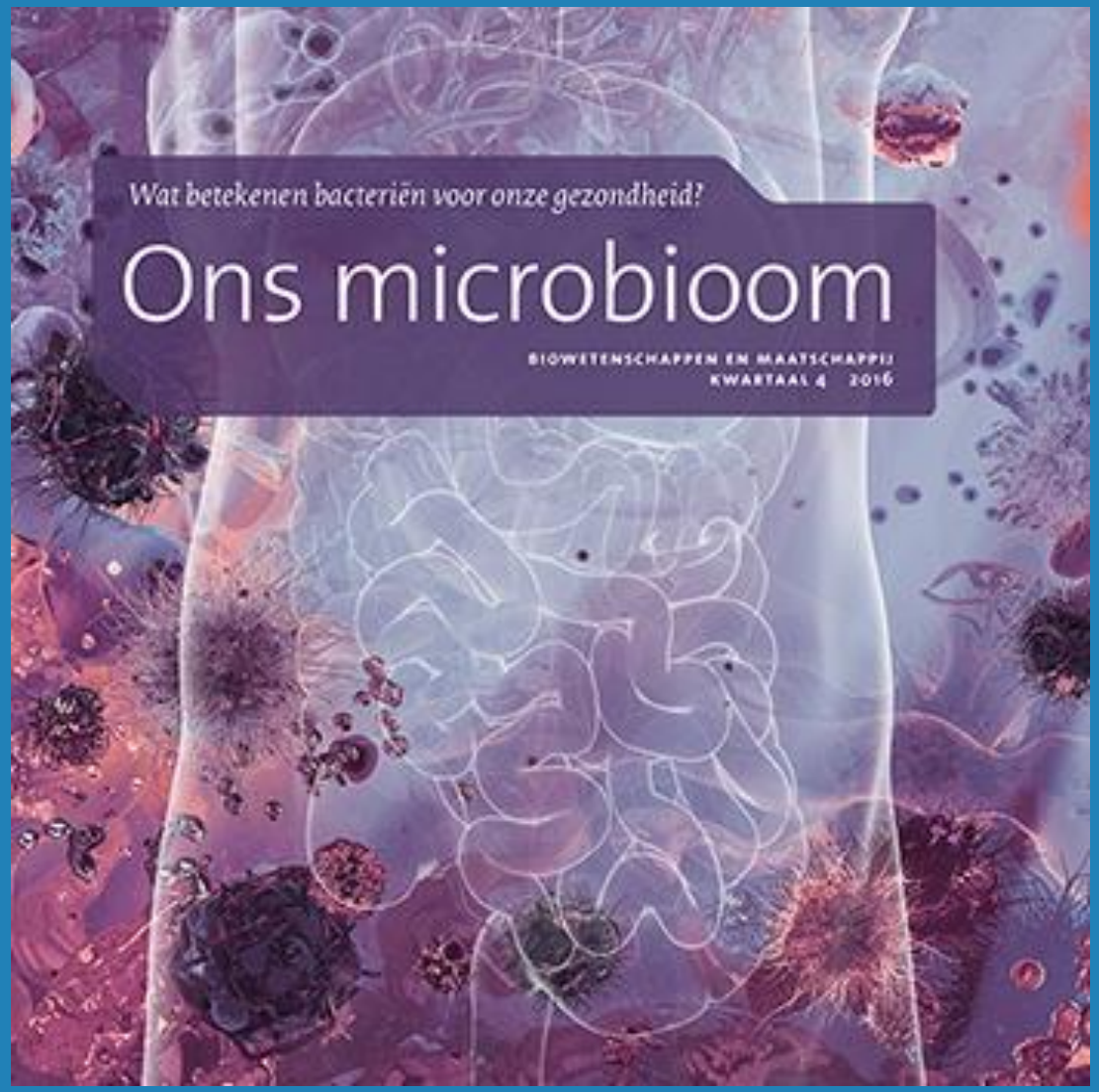
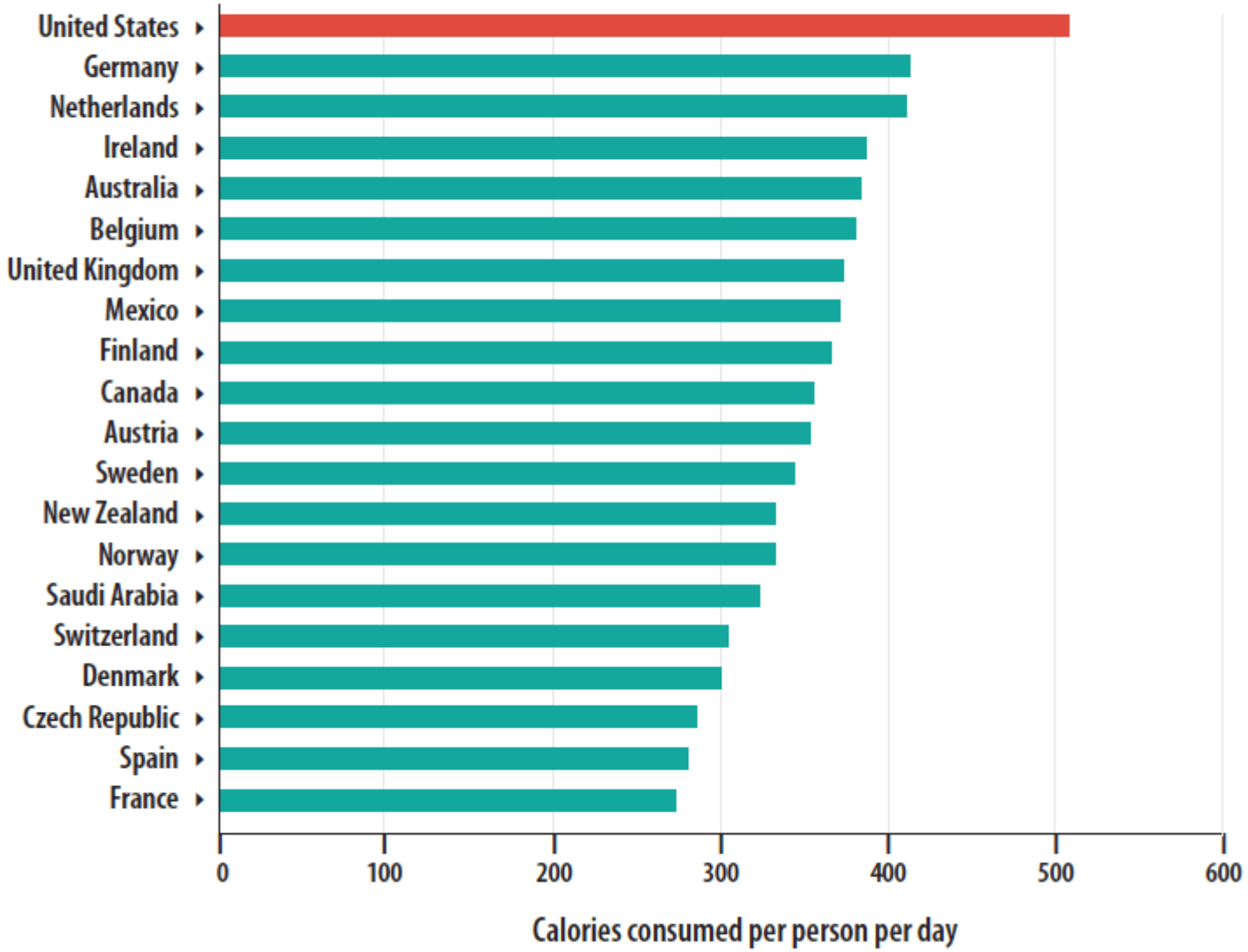
- Prof.eric.claassen@gmail.com
- tel: +31 6 20443098



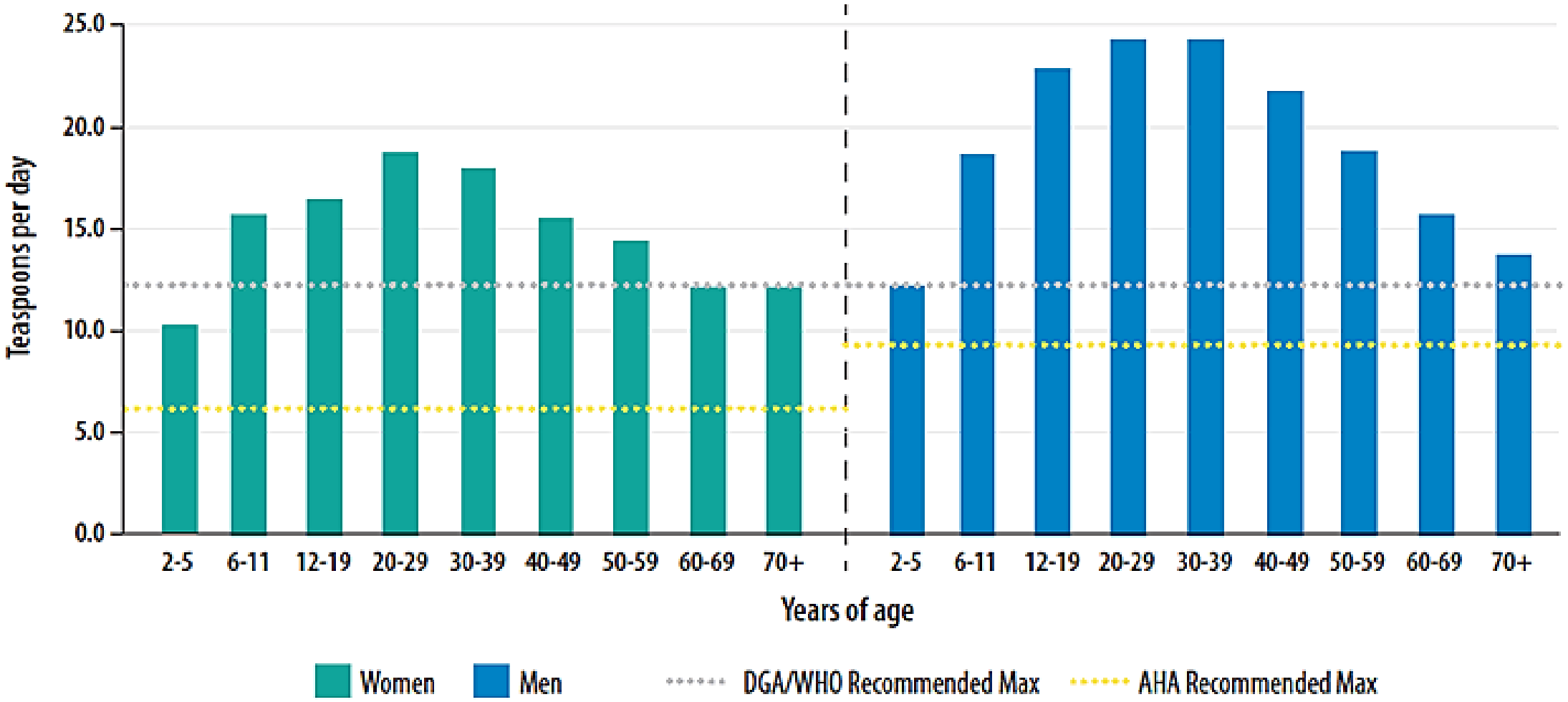
bio wetenschap + maatschappij

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

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