probiotika

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DSSO, October 8 2015

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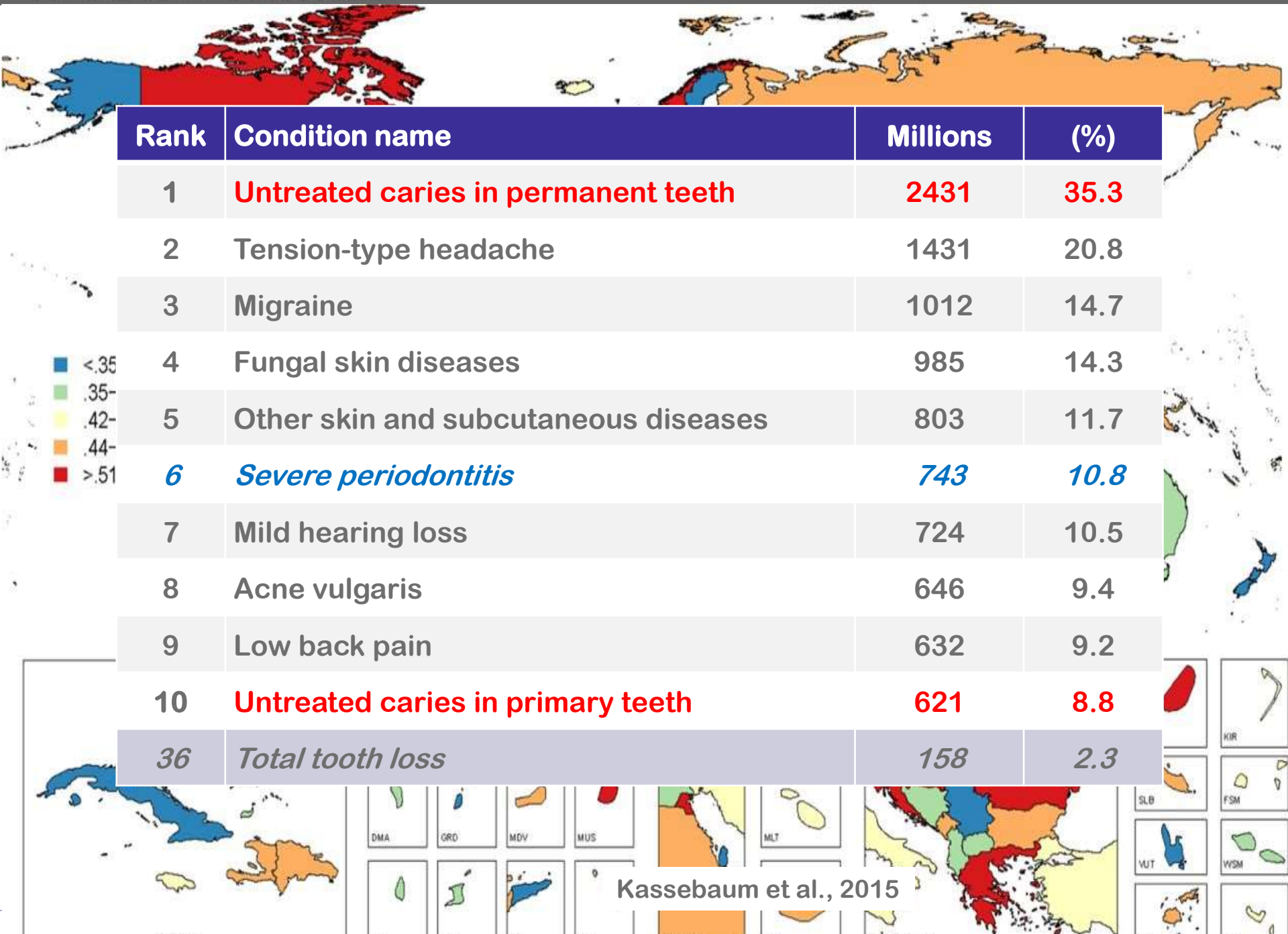
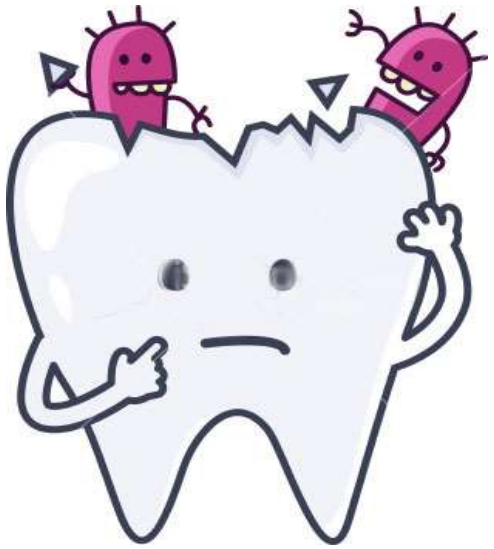
Rank	Condition name	Millions	(%)
1	Untreated caries in permanent teeth	2431	35.3
2	Tension-type headache	1431	20.8
3	Migraine	1012	14.7
4	Fungal skin diseases	985	14.3
5	Other skin and subcutaneous diseases	803	11.7
6	*Severe periodontitis*	*743*	*10.8*
7	Mild hearing loss	724	10.5
8	Acne vulgaris	646	9.4
9	Low back pain	632	9.2
10	Untreated caries in primary teeth	621	8.8
36	*Total tooth loss*	*158*	*2.3*



Kassebaum et al., 2015

caries is a biofilm-mediated disease

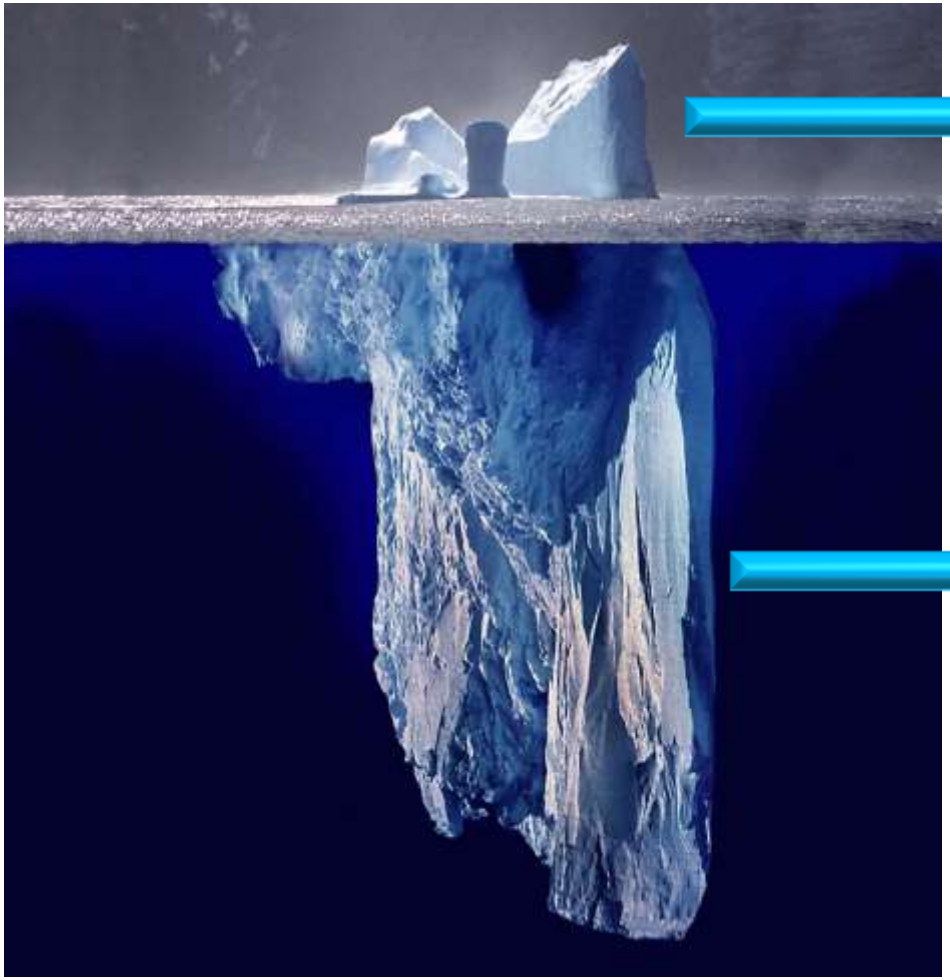


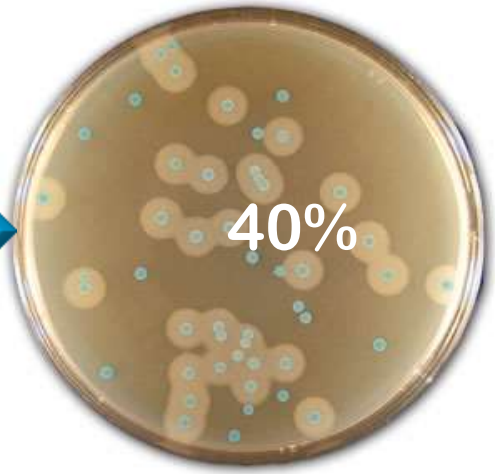
"…result from a complex interaction between the **commensal** microbiota, host susceptibility and environmental factors such as diet."

Wade, 2013

a non-communicable disease

an important role for oral health



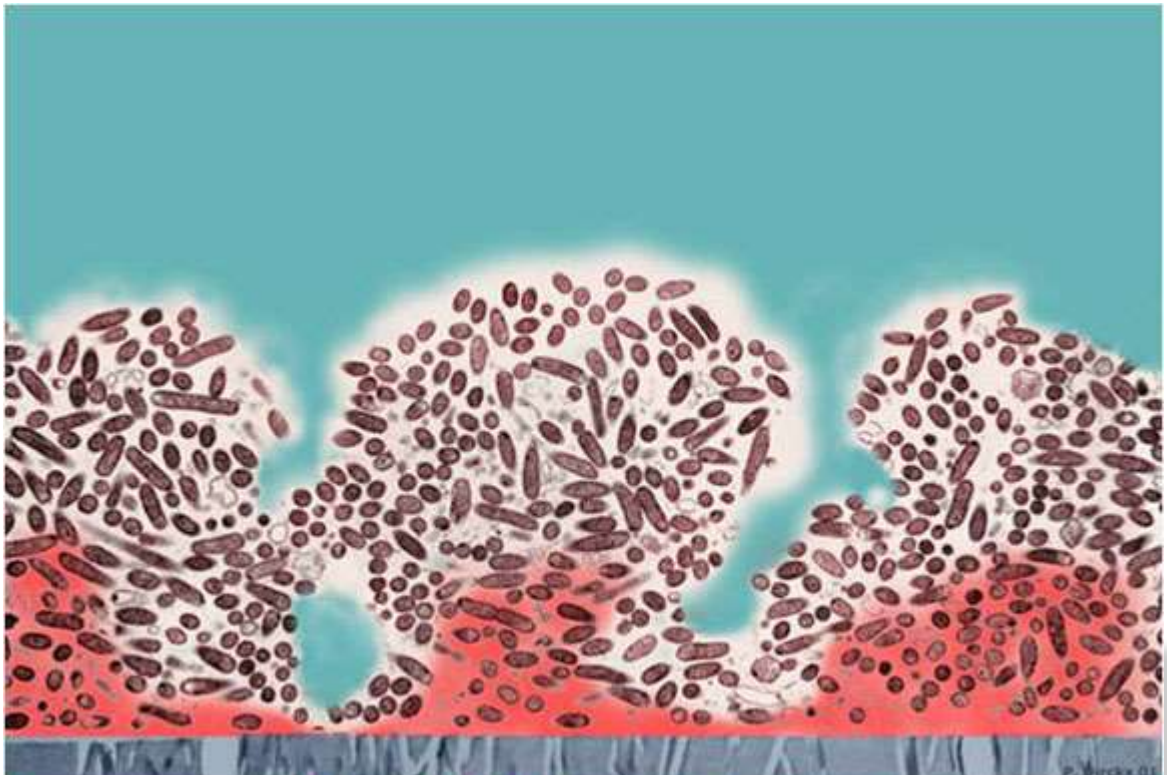


selective
non-selective
aerobic
anaerobic

molecular methods 60%

- 16s rRNA, cloning and sequencing
- pyrosequencing
- whole genome sequencing
- PCR
- quantitative PCR
- DNA-DNA hybridization
- microarray

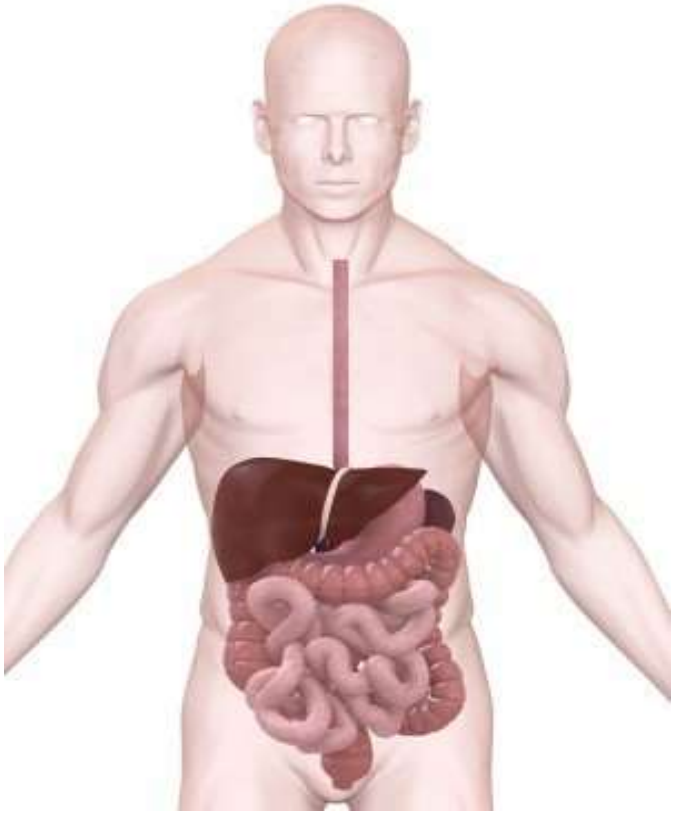
a **biofilm** is an aggregate or cluster of microorganisms in which cells adhere to each other on a surface that is protected



microorganisms in polysaccharide matrix

a crucial role in health

- break down food
- convert to energy
- excludes bacteria that are harmful
- **80% of our immune response located in the intestines**

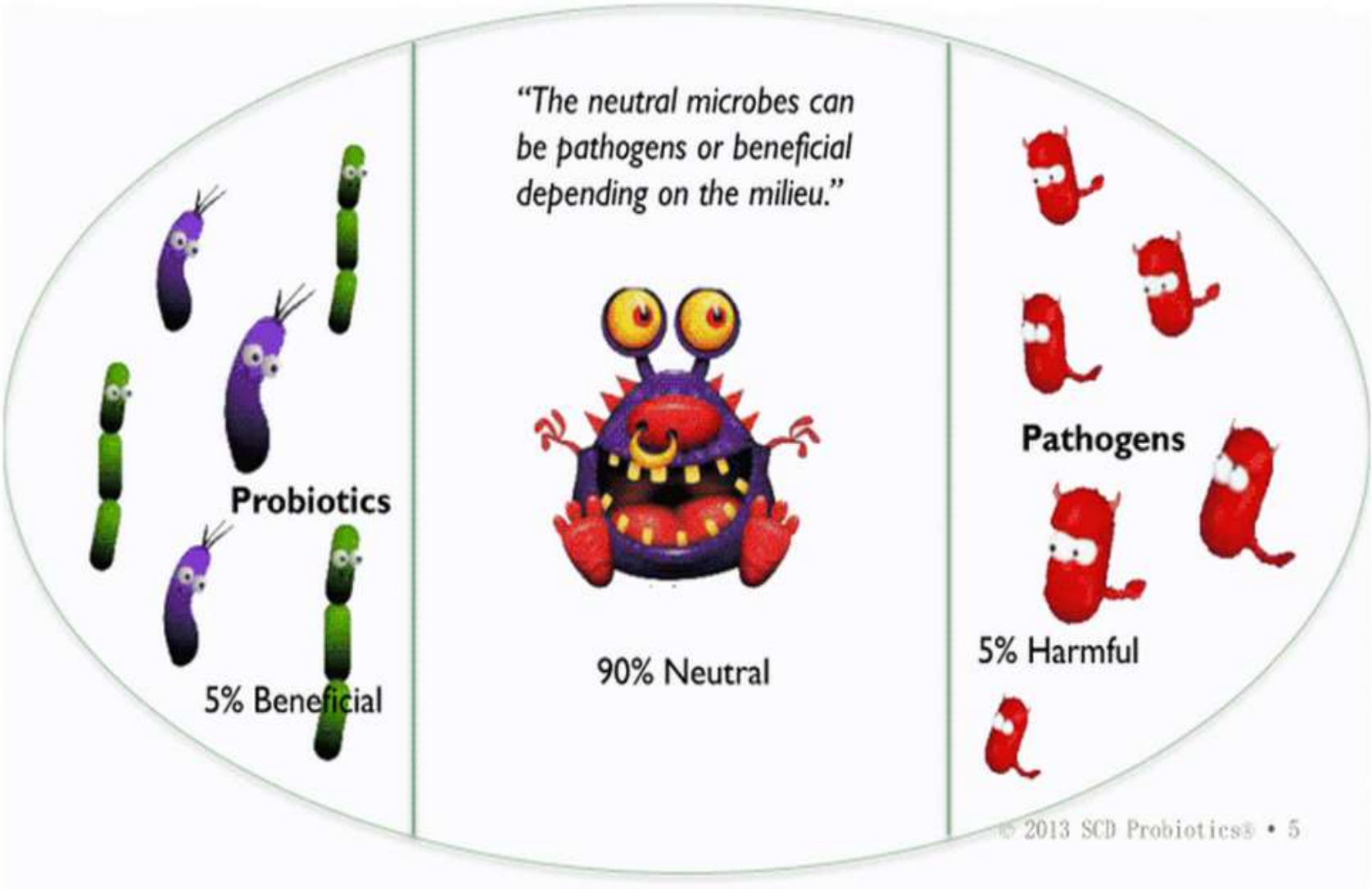


microbial diversity and stability associated with health

STRESSED, DESTABILIZED BIOFILM WITH REDUCED DIVERSITY ASSOCIATED WITH DISEASE

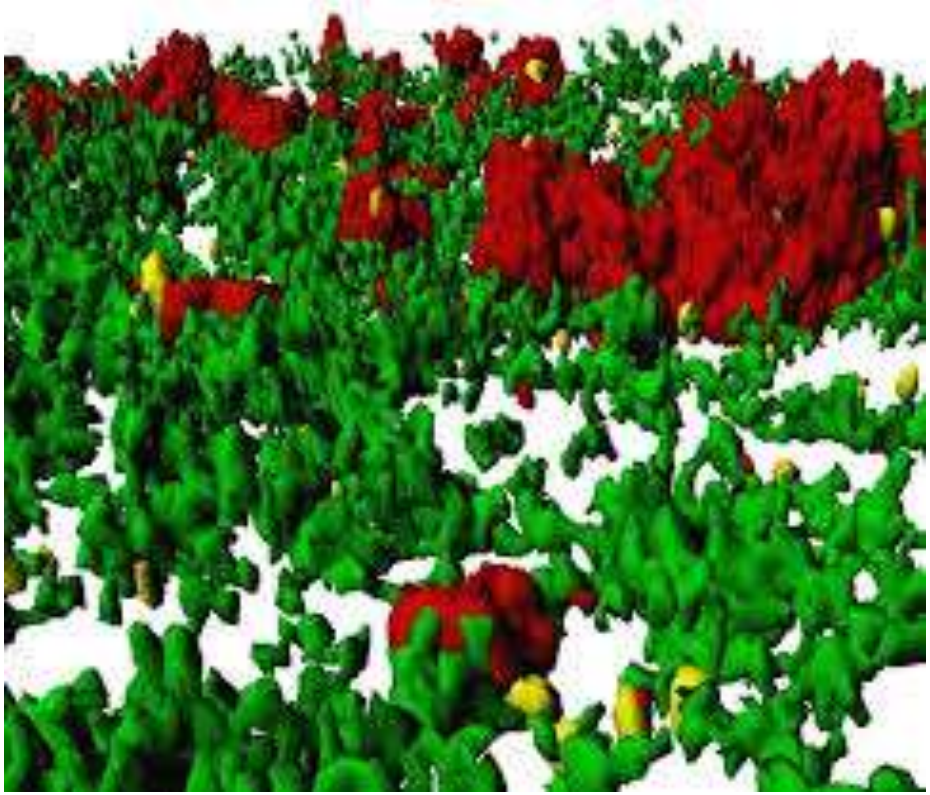
dysbiosis


The Human Oral Microbiome Database contains over 600 taxa and 13 phyla
(Dewhirst et al., 2010)
P intermedia


Probiotics
5% Beneficial
"The neutral microbes can be pathogens or beneficial depending on the milieu."
90% Neutral
Pathogens
5% Harmful
© 2013 SCD Probiotics® • 5

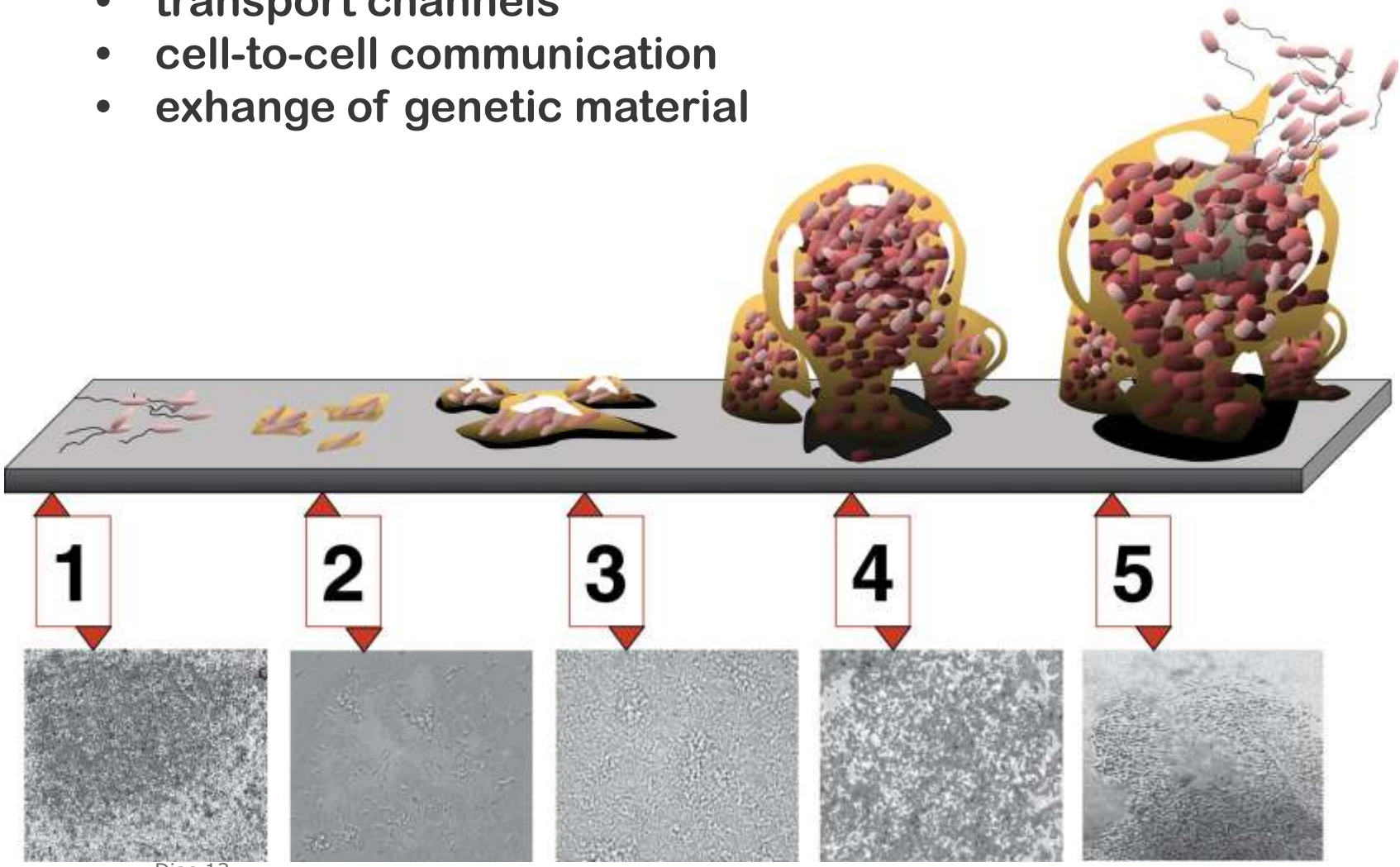
proposed genera in the core oral microbiome

Streptococcus
Veillonella
Granulicatella
Neisseria
Haemophilus
Corynebacterium
Rothia
Actinomyces
Prevotella
Capnocythophaga
Porphyromonas
Fusobacterium

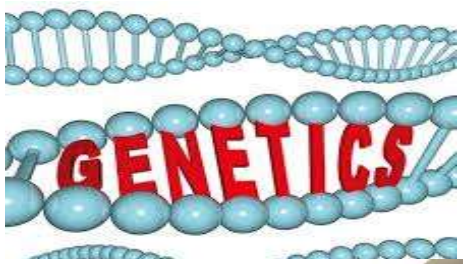


Zaura 2009, Marsh 2015

- co-aggregate
- metabolic exchange
- transport channels
- cell-to-cell communication
- exhange of genetic material



- genetics



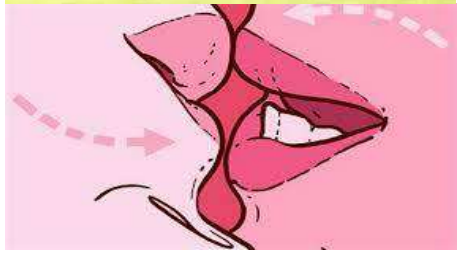
- location

- age

- diet

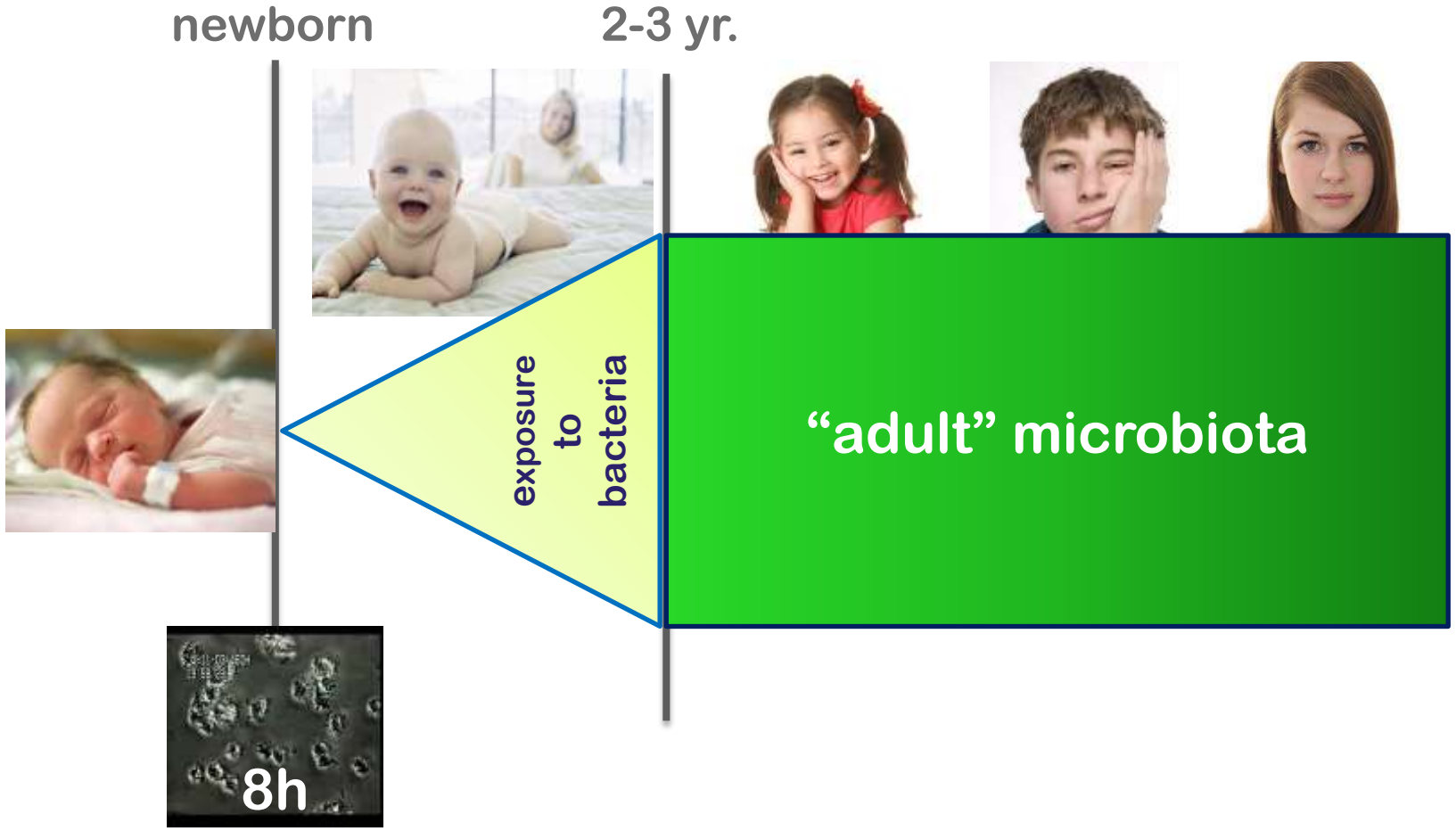
- sexual behavior

  80.000.000 cfu in one kiss



sequence and timing of exposure to microbes dictate the composition of the oral biofilm

"first come, first served"




with a vaginal
birth, you
get your
first
probiotics

the microbiota of the mouth differs between 3-month-old breast-fed and formula-fed infants

lactobacilli 0%

lactobacilli 28%

- more bifidobacteria
- greater diversity

Holgerson et al., 2013 J Pediatr Gastoenterol Nutr

“the oral microbiota does not play a passive role but actively contributes to the maintenance of health”

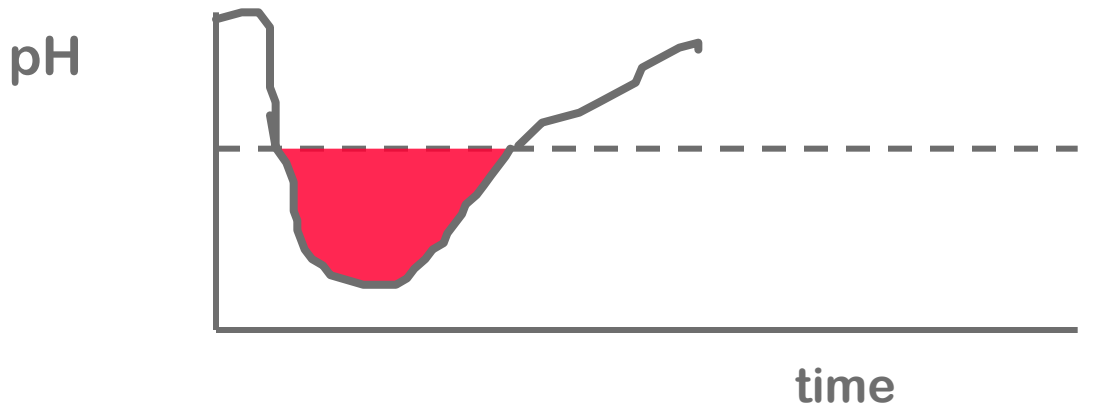
Devine and Marsh, 2009

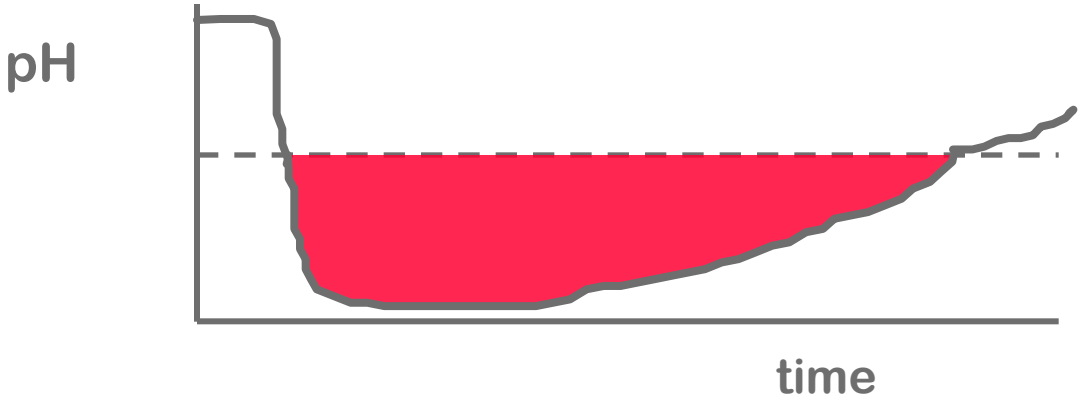
“the resident oral microbiota is diverse, natural and beneficial to the host”

Marsh, 2015

sucrose in diet is fueling the caries process

acid-tolerating bacteria



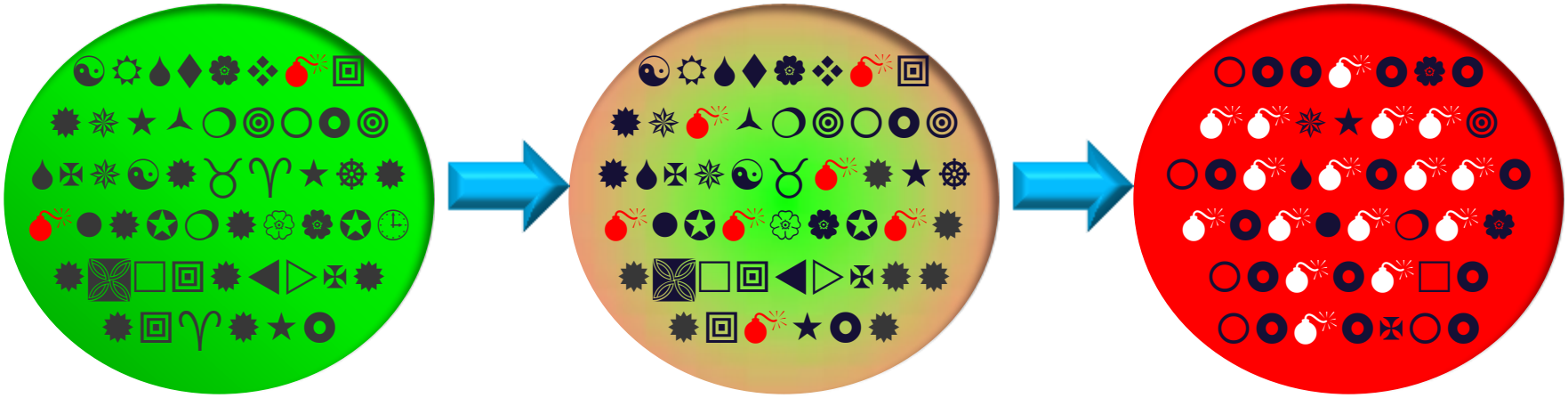


acid stress leads to microbial shift

stable and diverse

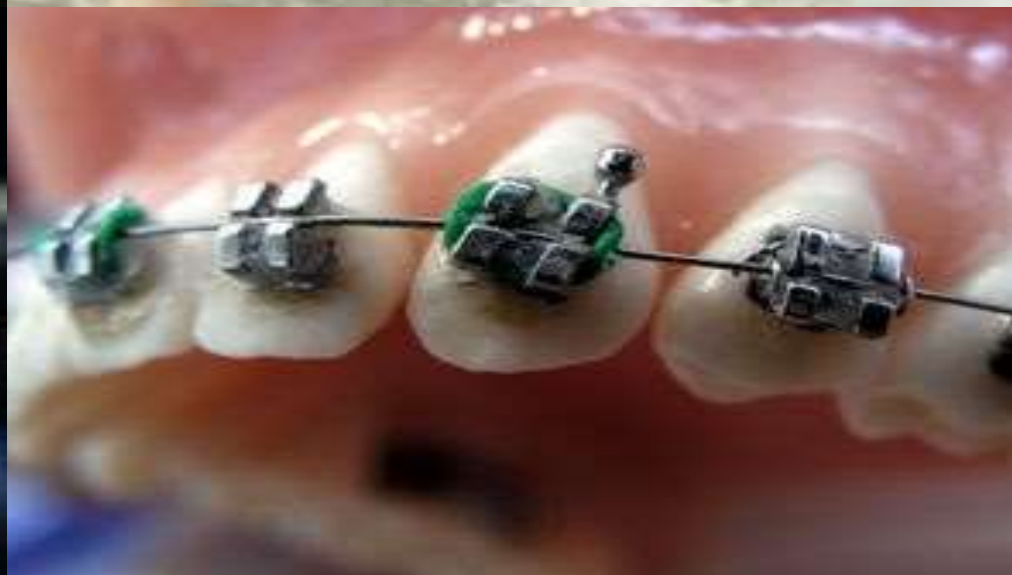
adaptation to low pH

overgrowth of aciduric bacteria, reduced diversity

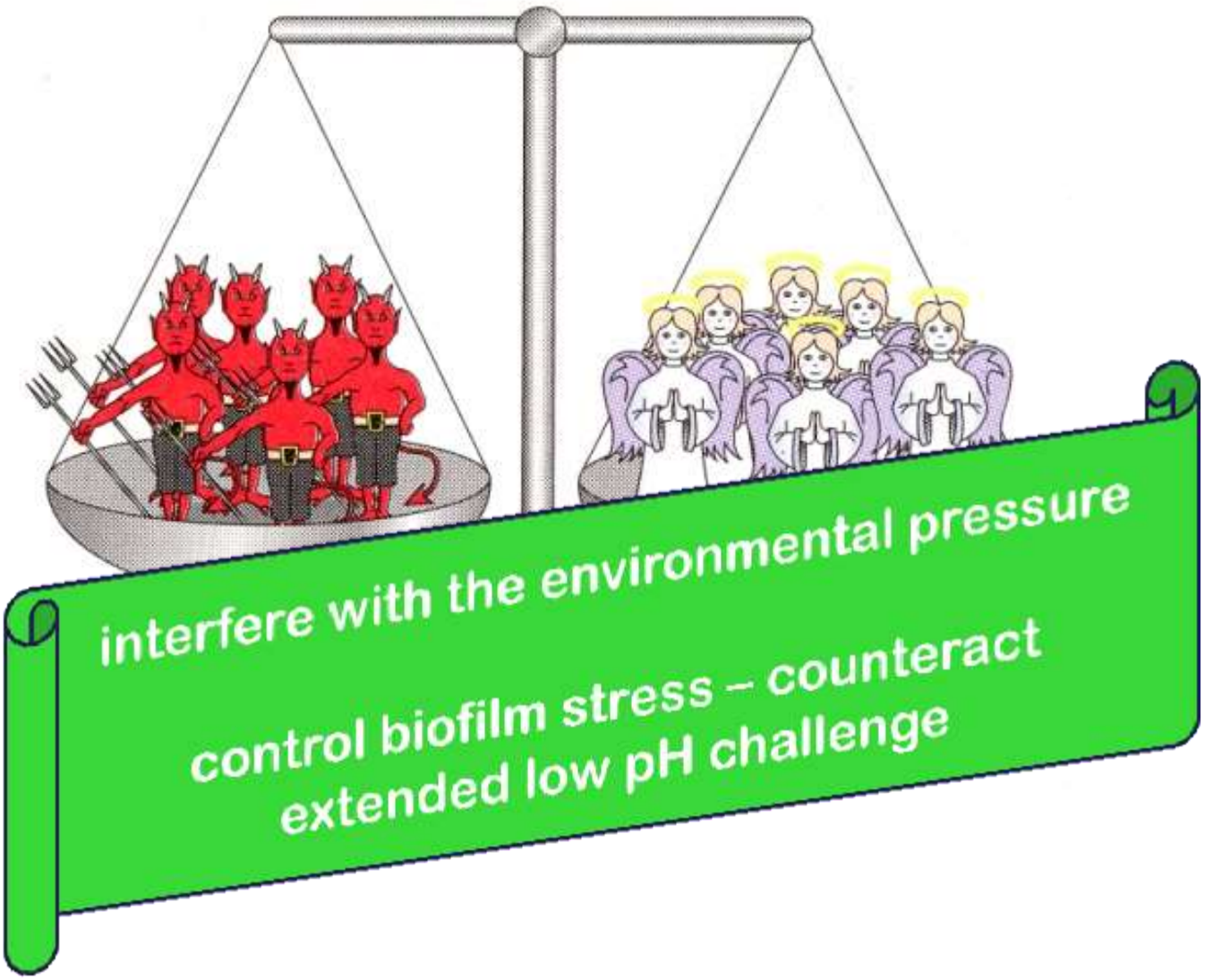


reversible

other examples of biofilm stress

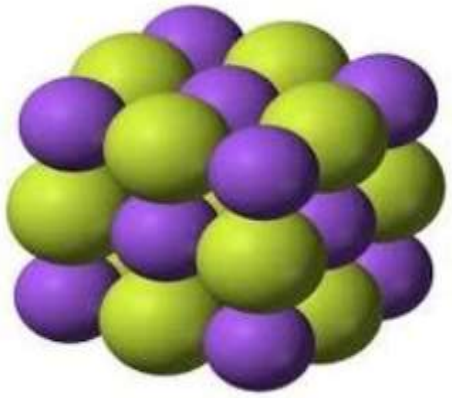


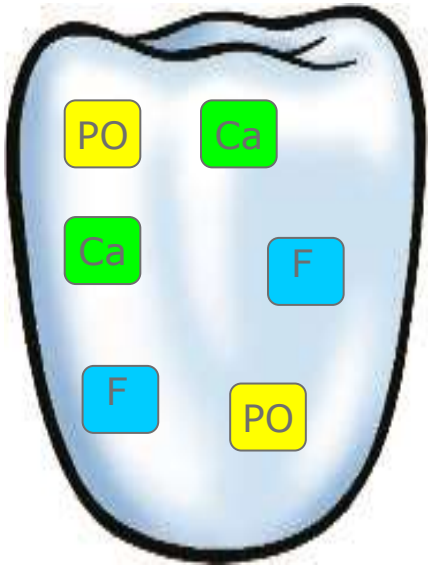
maintain or restore homeostasis



1) inhibition of biofilm acid production

- e.g. fluoride-containing products or metabolic inhibitors (xylitol)

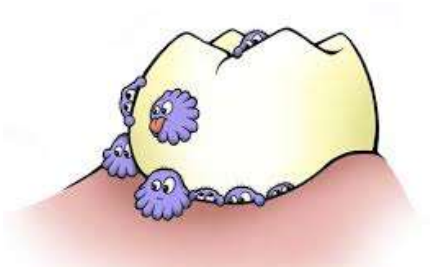




presence low [F] can inhibit the aciduric adaption of the biofilm and lower the critical pH

fluoride works locally in the biofilm/tooth interspace

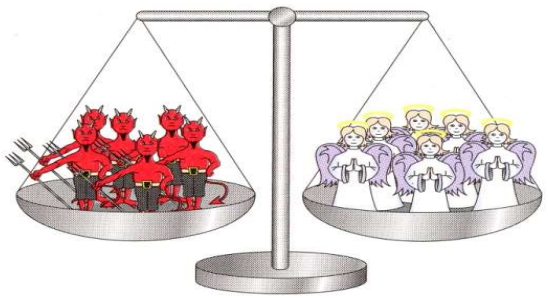
in very low concentrations
e.g. F milk, water F



stress adaption

in low concentrations
e.g. toothpaste

in high concentrations
e.g. F-varnish



metabolic inhibitor

2) mechanical plaque removal

- toothbrush
- flossing
- tooth sticks
- professional tooth cleaning

a ”healthy” biofilm

a stressed biofilm

good but not meticulous!

3) reduce sugar frequency

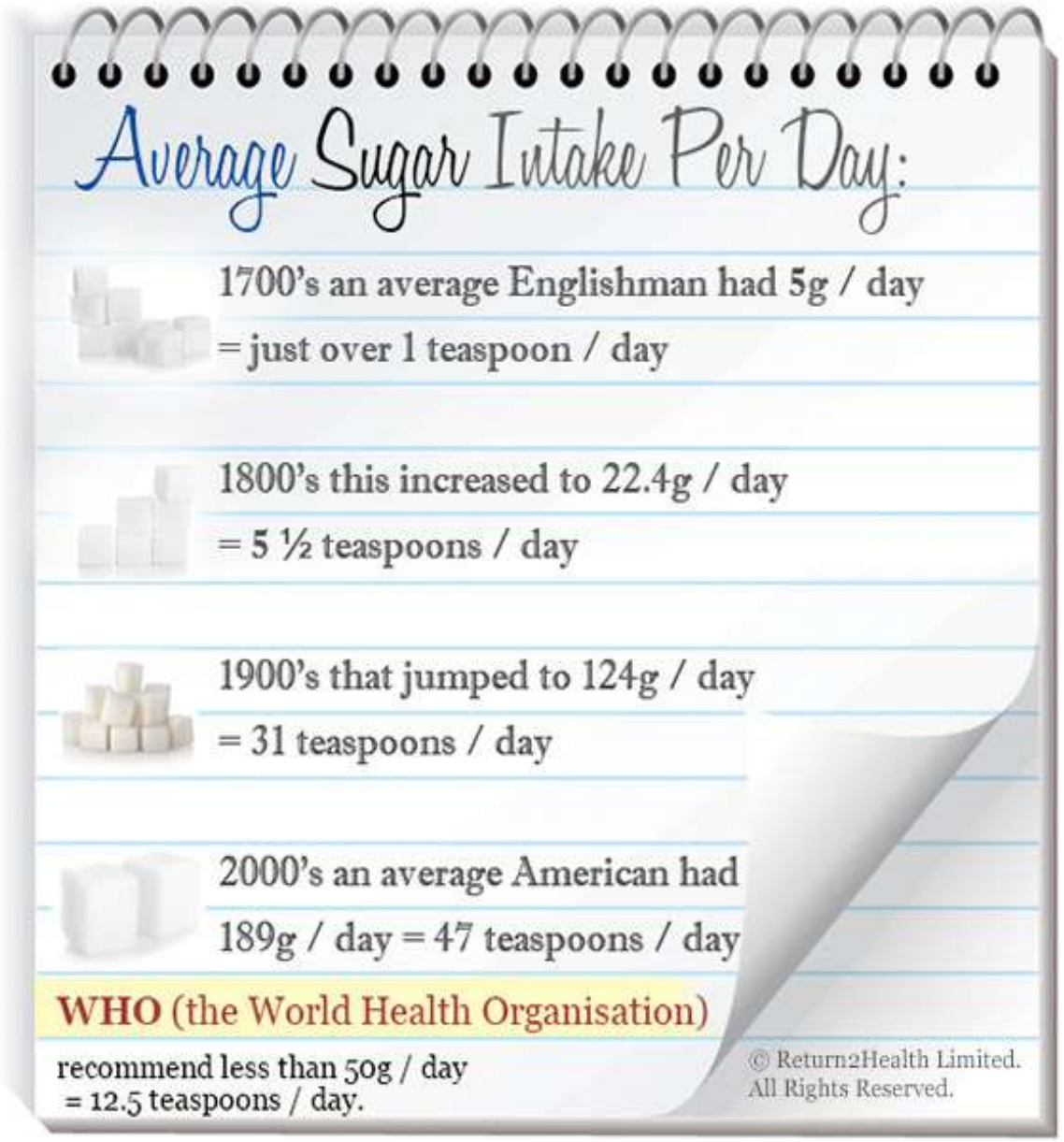
- reduction of repeated low-pH conditions

sugar amount =

obesity/overweight

sugar frequency =

caries



reduce free-sugar intake to < 10% E

Moynihan PJ, Kelly SA. J Dent Res. 2014 Jan;93:8-18.

4) stimulation of saliva flow after meals

- pH returns to resting levels more quickly

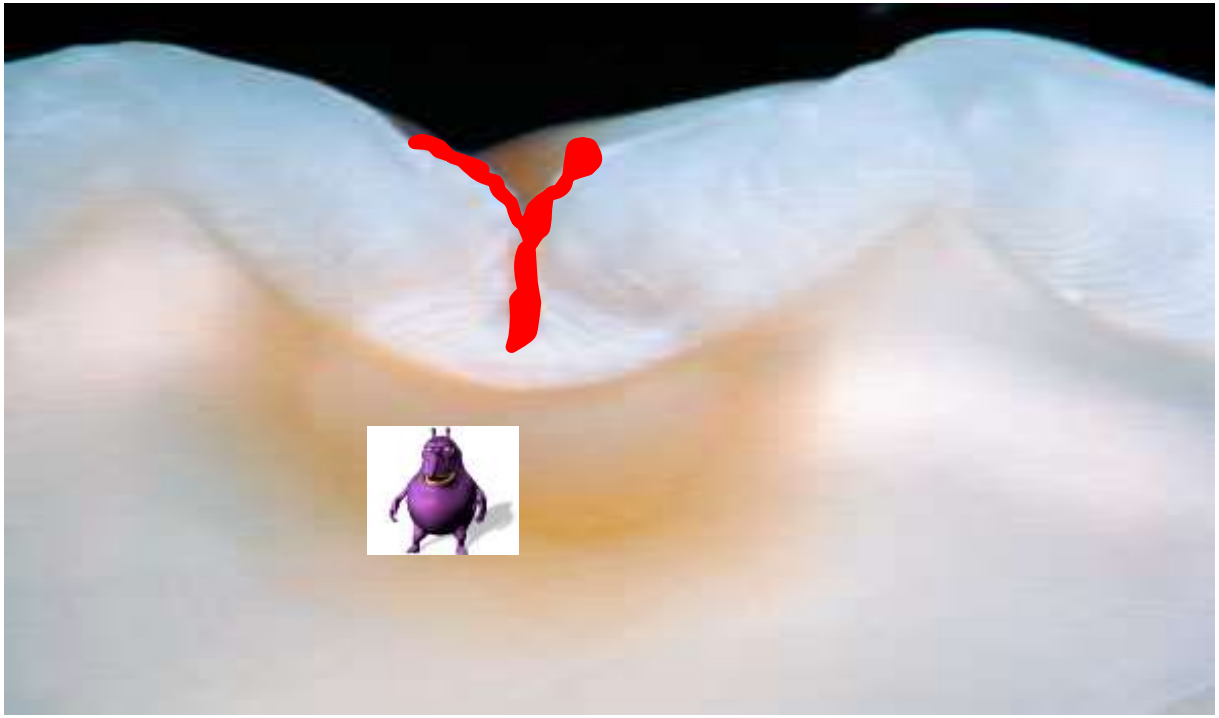
- 1.0-1.5 liter per 24h - clearance
- pH 6.5-6.9 - buffering capacity

- mucins, glycoproteins
- enzymes
- salt – electrolytes, minerals
- immunoglobulins, AMP

contributes to biofilm control

5) blocking of substrate

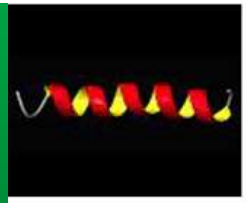
- ie. fissure sealants, ART

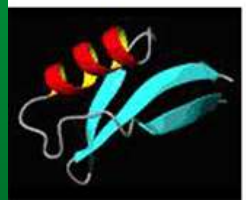
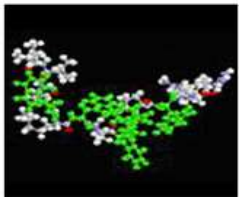


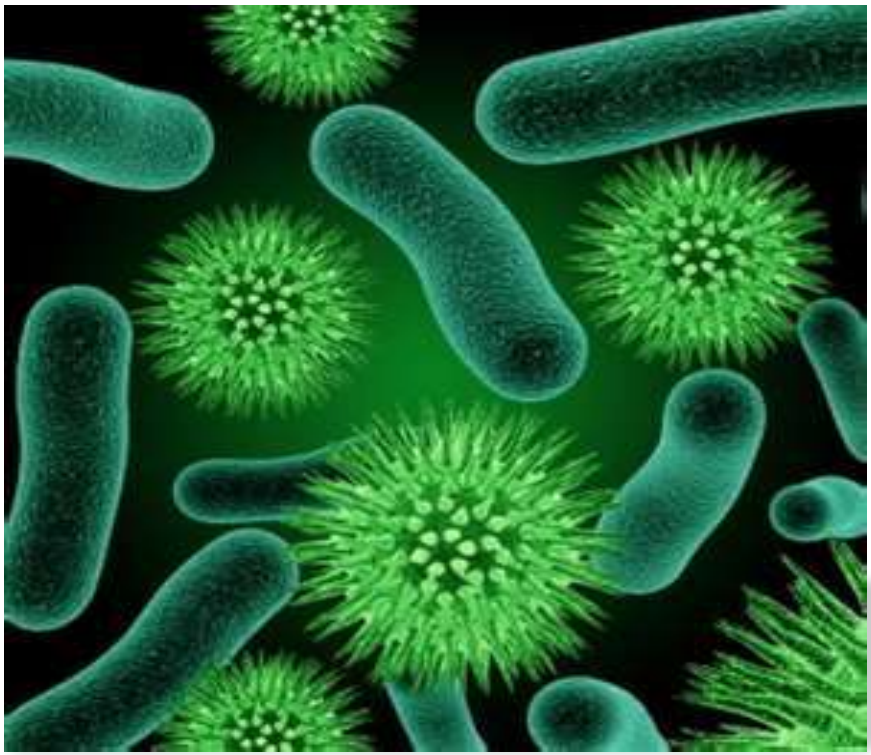
Beauchamp et al. 2008, Bakhshandeh, 2012, Zandona 2015

6) any other approach designed to maintain pH around neutrality

- e.g. bacteriotherapy (prebiotics, probiotics), antimicrobial agents, alkali supplements, targeted antimicrobial peptides

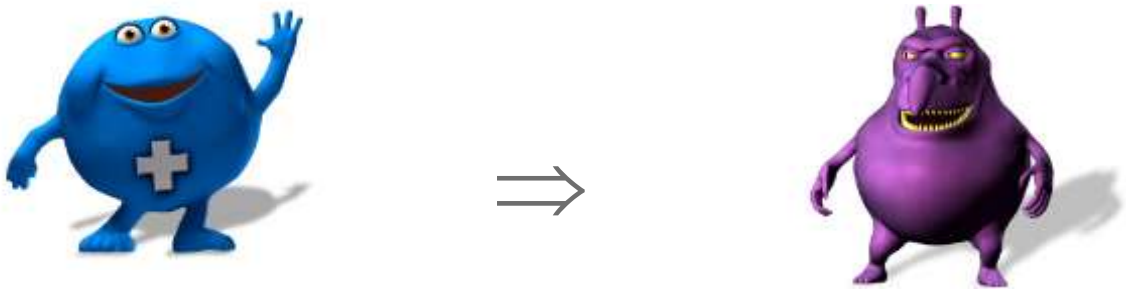




replacement/bacterio-/probiotic therapy

a harmless effector strain is implanted in the host's microflora to maintain or restore a natural microbiome by interference and/or inhibition of other microorganisms



Florey, 1946, Hillman, 1999

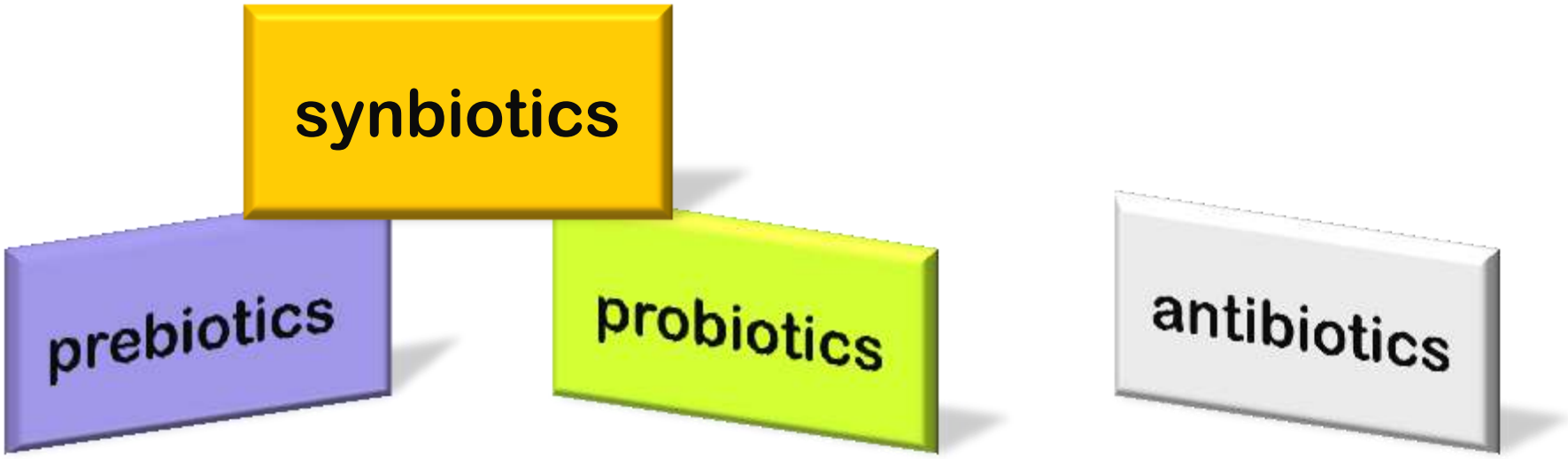
defense through diversity

daily addition of health-promoting bacteria

pro bios = for life

lactobacilli

bifidobacteria



FAO/WHO definition of probiotics (2001):

- "**live** microorganisms which when administered in adequate amounts confer a health benefit on the host"
- host benefits to probiotics are strain specific

pharmaceutical medicine and bioecological medicine

+

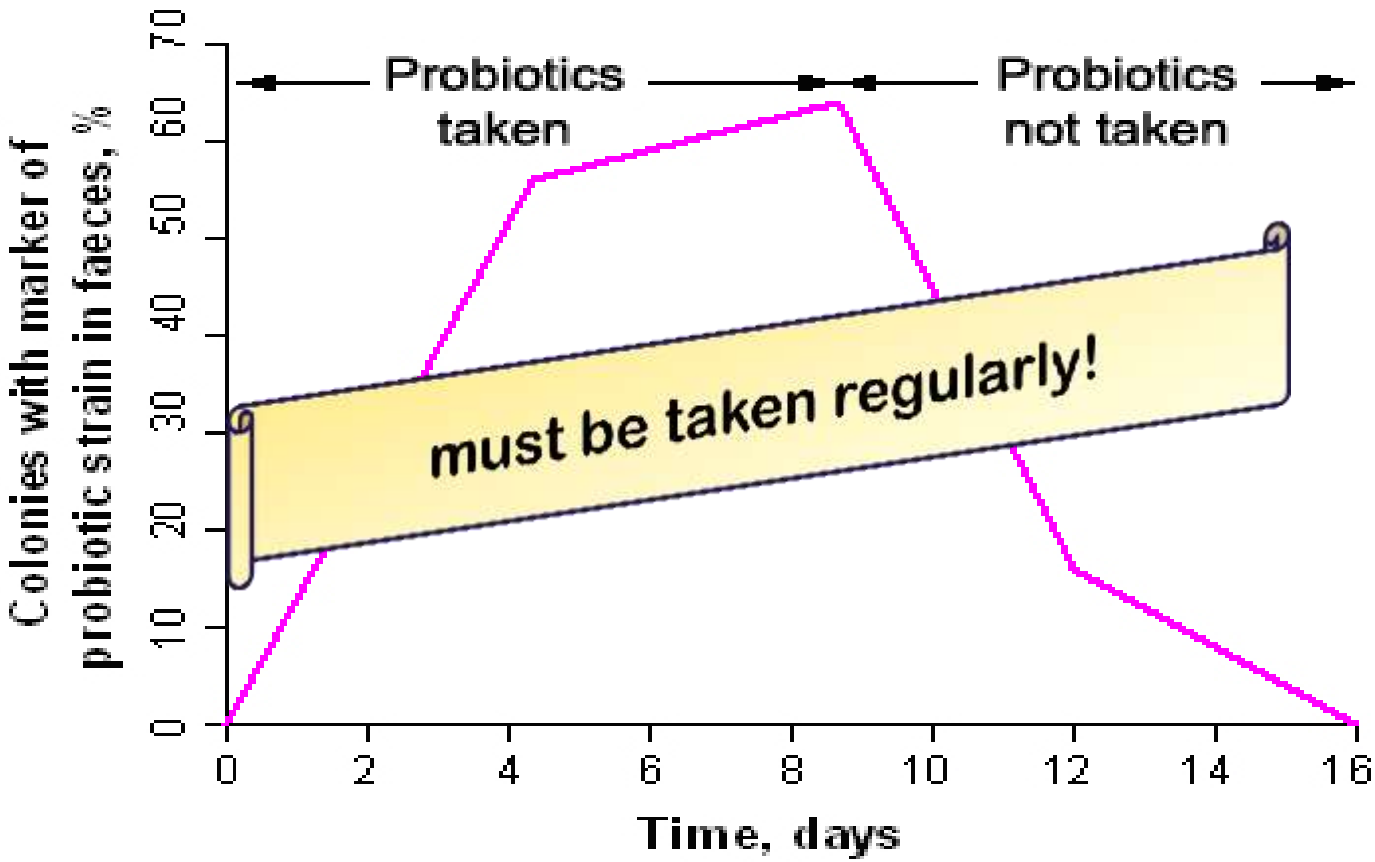
daily intake of 10^{8-9} probiotic cells (FAO/WHO, 2003)

1-2 dl yoghurt
- less costly
- Ca, P comes ”free”

1-2 tablets
- practical
- a mix of different strains
- less sugar

Fate of Ingested Probiotics

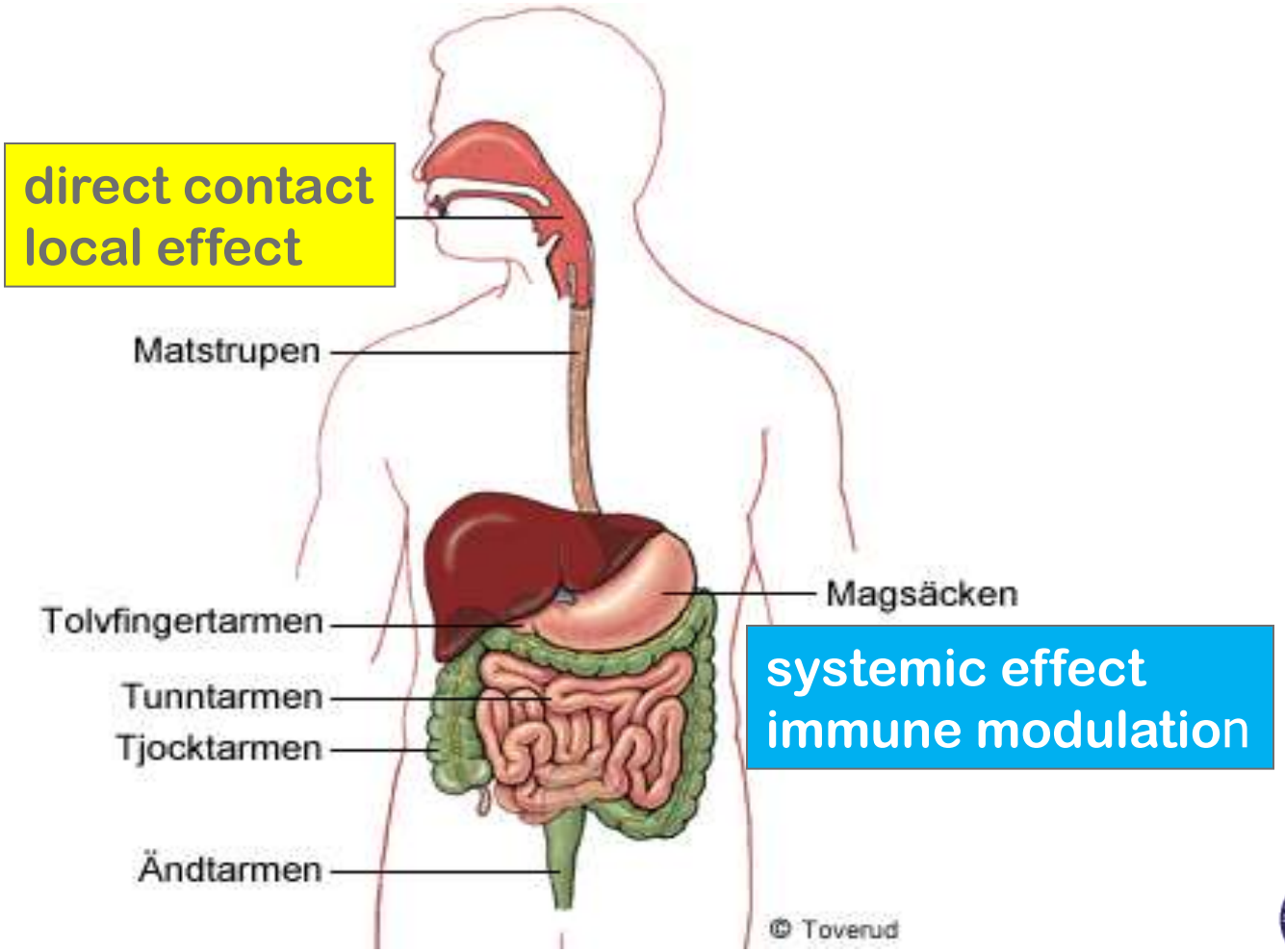
The appearance of ingested probiotics bacteria in faeces



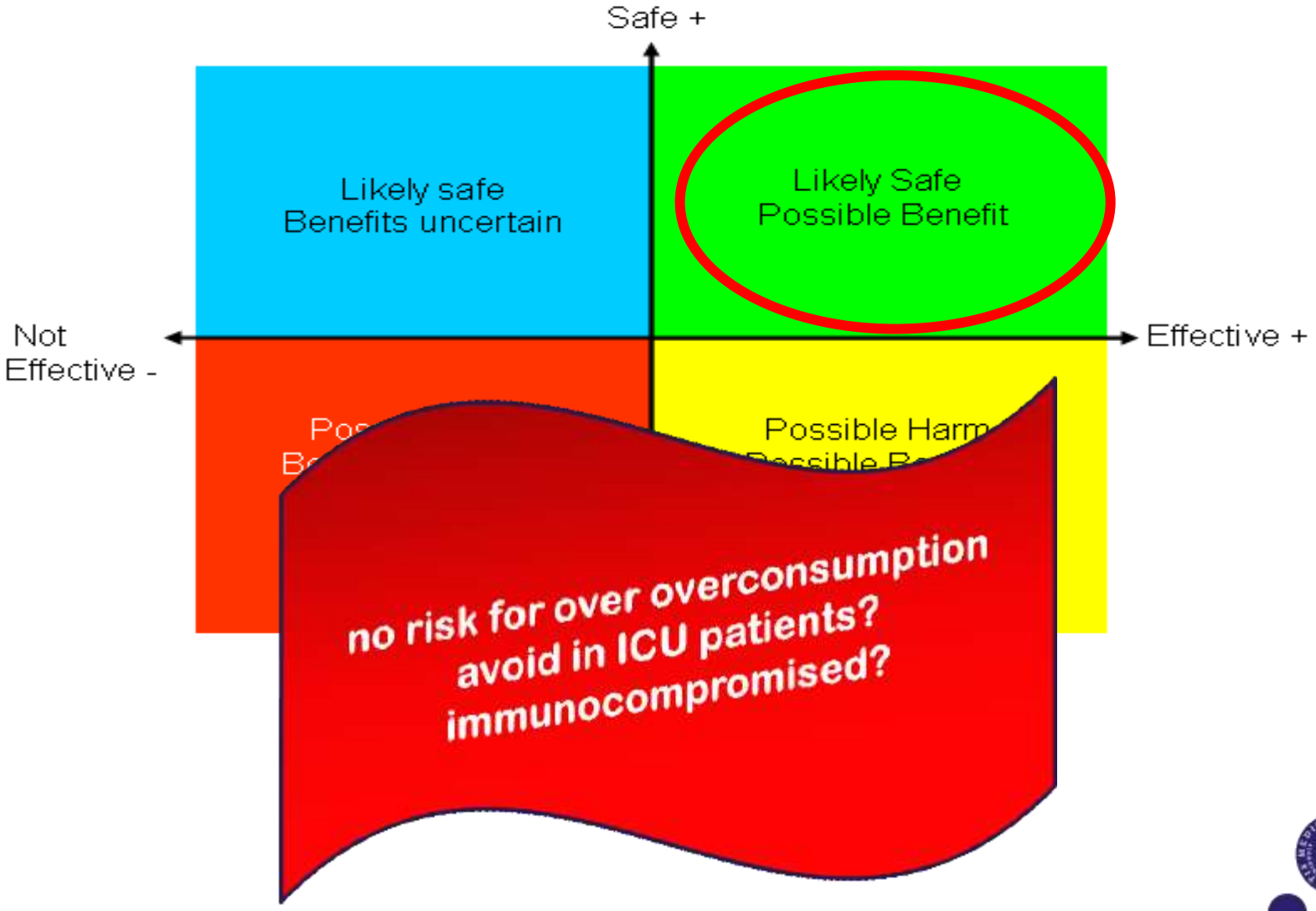
Yli-Knuuttila et al., 2006; Caglar et al., 2009

- early colonizers have an ecological advantage
- the earlier the start, the greater the chance of a persisting beneficial effect
- before 1 year

probiotics may affect oral cavity



GRAS = generally regarded as safe food additive



probiotics and oral health

caries

gingivitis, tooth loss
mucositis, candidosis

halithosis (bad breath)

tooth whitening

dry mouth

two systematic reviews

included: 23 papers

quality: 4 low risk of bias, 9 moderate, 10 high

conclusion: reduces *S. mutans* in plaque and saliva

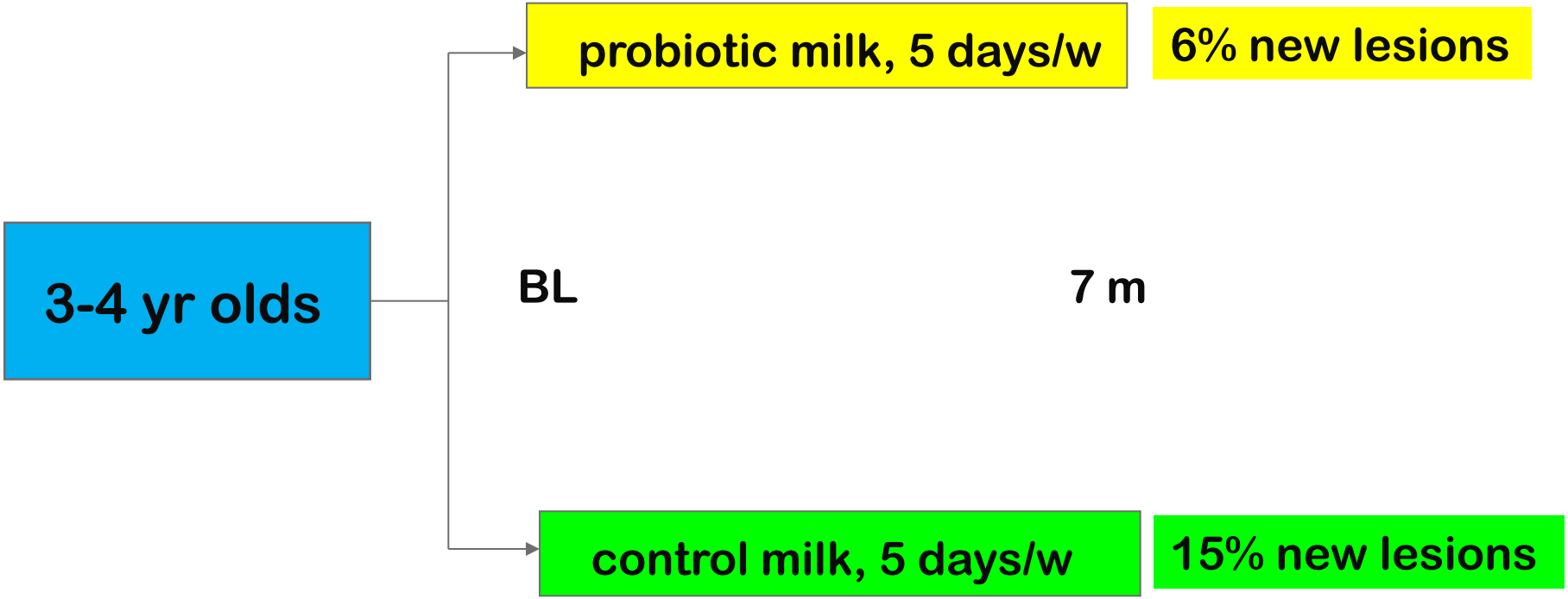
Cagetti et al., 2013 Nutritients

....it may be concluded that probiotics decrease the mutans streptococci counts. **This suggests that probiotics could have a positive effect in the prevention of caries**

Laleman et al., 2014 Clin Oral Invest

randomized double-blind placebo-controlled trial

L. rhamnosus GG



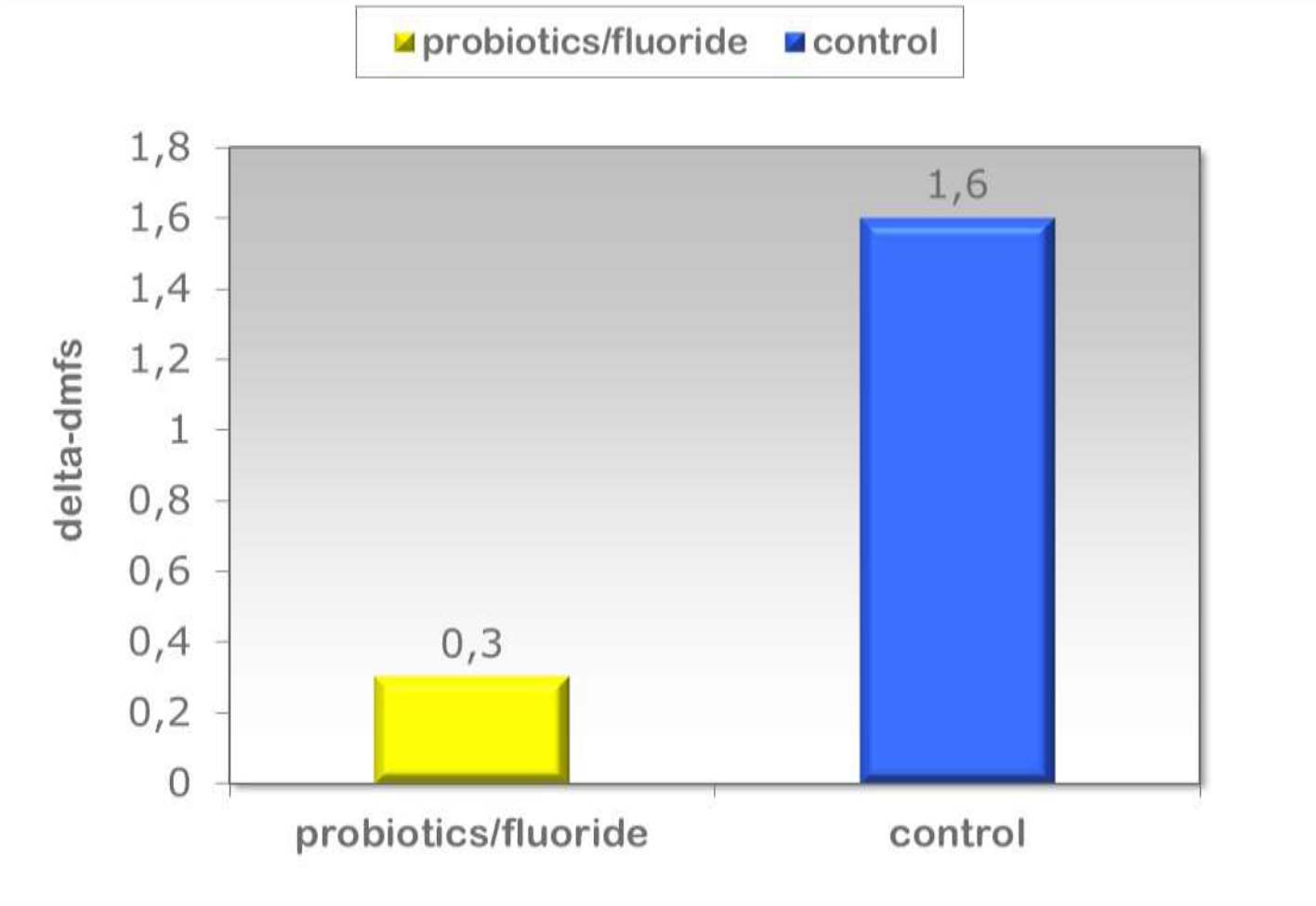
Näse et al., 2001

additional effects

- 16% less absence from daycare
- 17% reduction of URI
- 19% less antibiotics

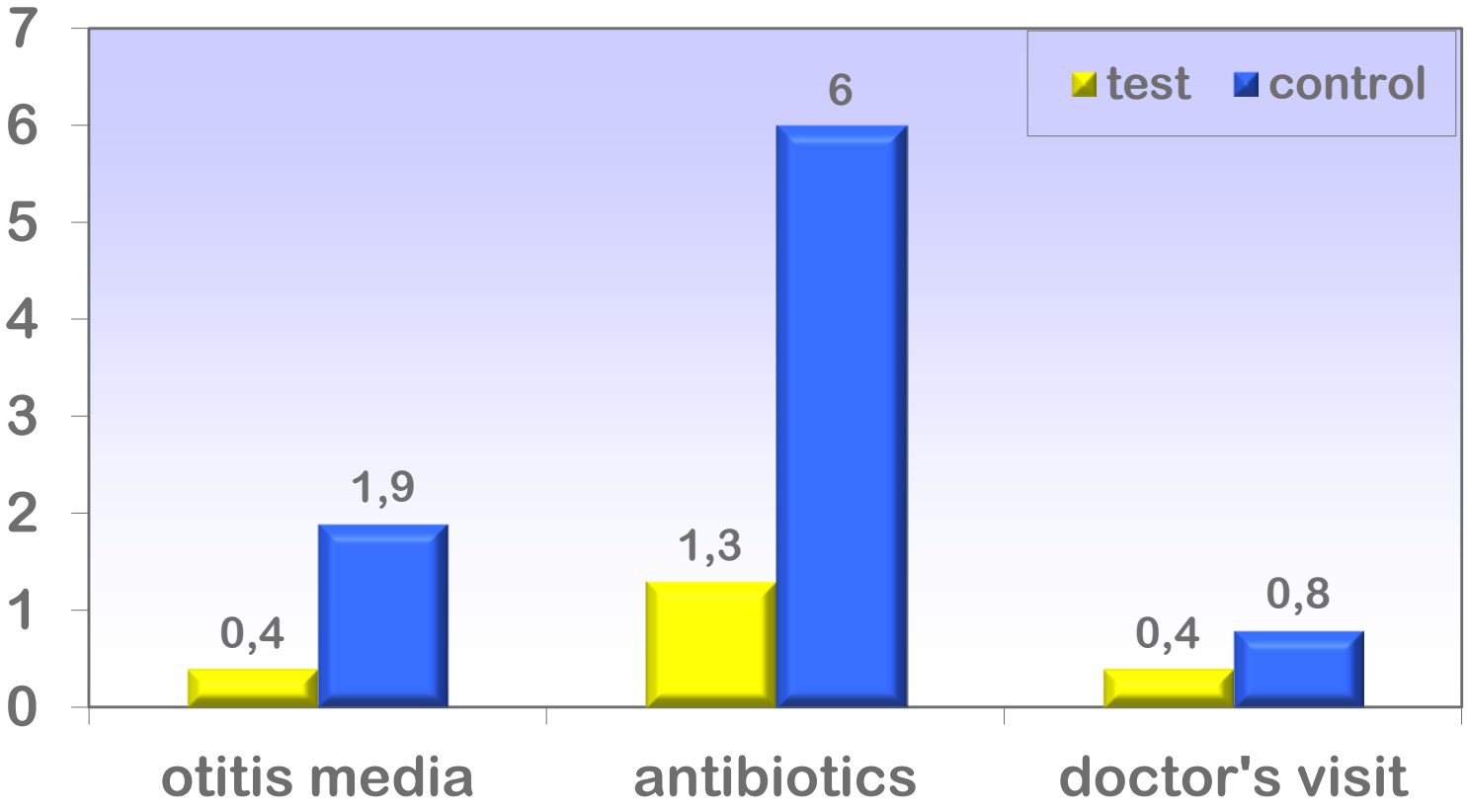
Hatakka et al., 2001 Br Med J

caries incidence after 21 months



Stecksen-Blicks et al., Caries Res 2009;43:374–81

effects on general health



Stecksen-Blicks et al., Caries Res 2009;43:374–81

metabolic domino effect
- link between oral and general health

oral health improvement

general health improvement

long-term effect on caries after probiotic supplements during infancy

birth

L. reuteri, 5 drops, 0-12 months

IgE-mediated eczema

placebo, 5 drops, 0-12 months

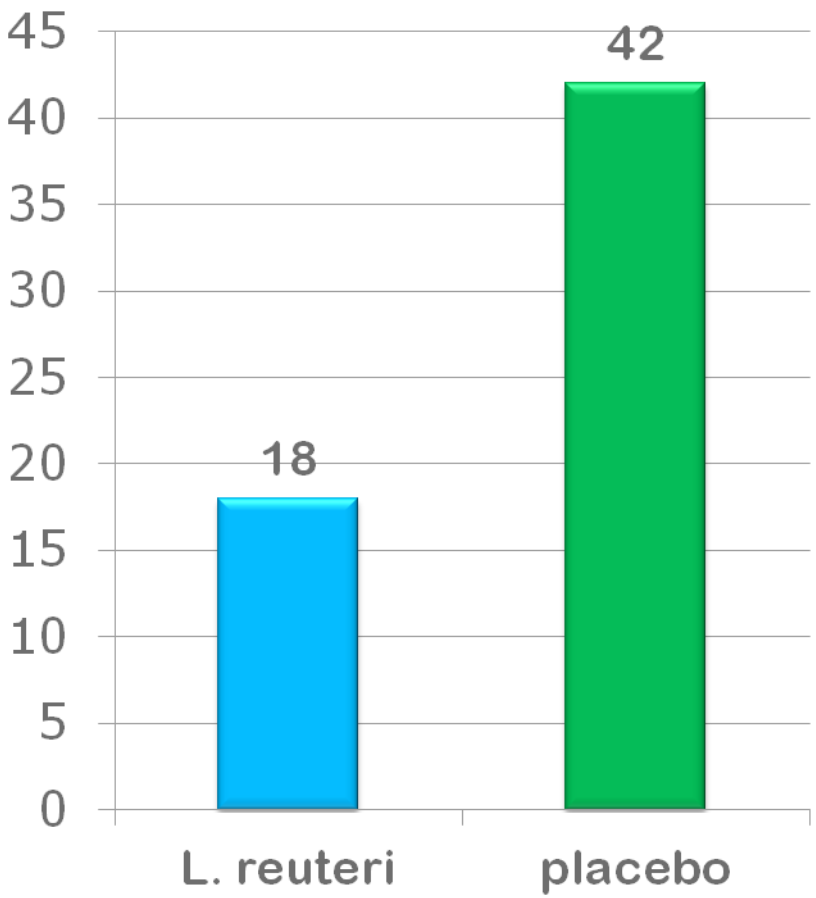
birth

caries 9 years

n=113

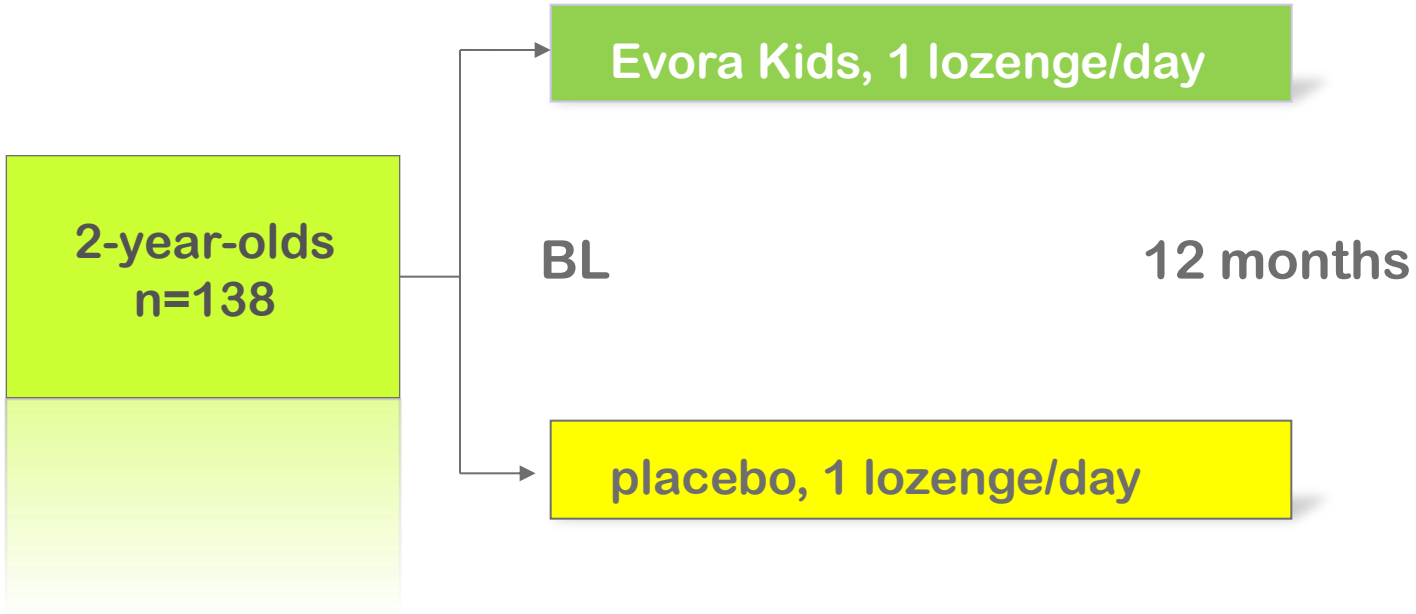
Stensson et al., 2013 Car Res

caries prevalence (dmf>0), 9 year



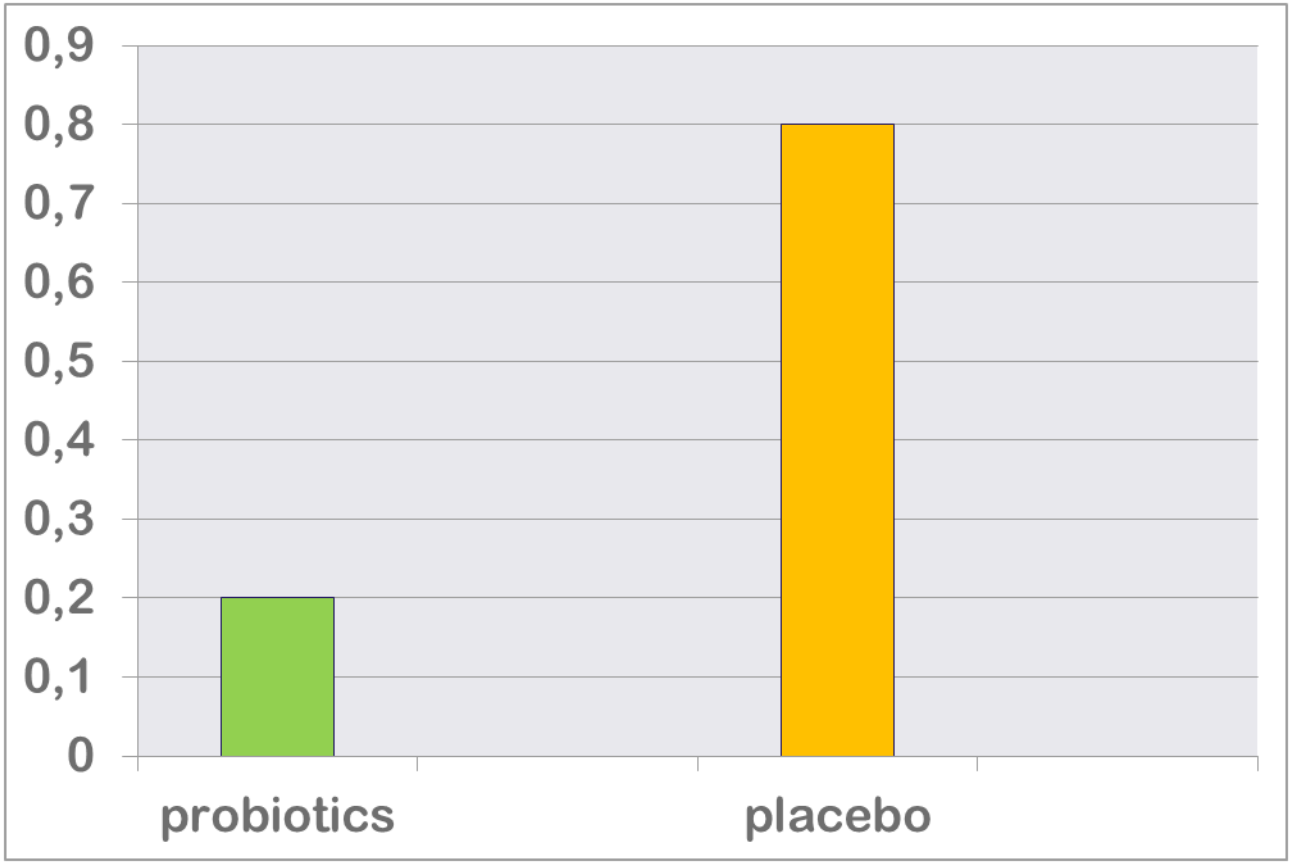
Stensson et al., 2013, Car Res

probiotic lozenges for toddlers



Hedayati-Hajikand et al., 2015

development of early childhood caries (∆dmfs) in 2-3 yr-old multicultural children – 1 year RCT



Twetman et al., 2015

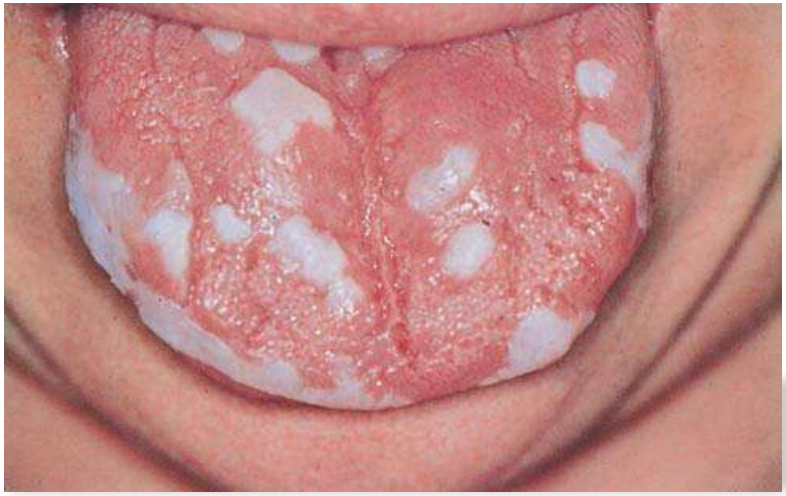
clinical trials with caries endpoint

First author, yr	design[a]	n; age (yr)	vehicle, time[b]	strain	caries test/ctr	PF[c] (%)
Näse, 2001	RCT	594; 1-6	milk, 7m	*L. rhamnosus* GG	15%/19%[d]	21%
		164; 3-4	milk, 7m	*L. rhamnosus* GG	10%/23%[d]	56%
Stecksén-B, 2009	CRCT	174; 1-5	milk, 21m	*L. rhamnosus* LB21 +2.5 ppm F	Δdmfs 0.4/1.6	75%
Petersson, 2011	RCT					65%
						55%
Taipele, 2013						5% (NS)
Hasslöf, 2013		180; 6	cereals	*L. paracasei* F19	CF 80%/74%	6% (NS)
Stensson, 2013	RCT	113;9	drops, 1st yr	*L. reuteri*	CF 82%/58%	29%
Teanpaisan, 2015	RCT	54; 14	milk powder, 1yr	*L. paracasei*	0.2/0.9	82%
H-Hajikand, 2015	RCT	150;2-4	tablets	Probiora[3]	0.2/0.8	75%

mean caries preventive fraction 45%

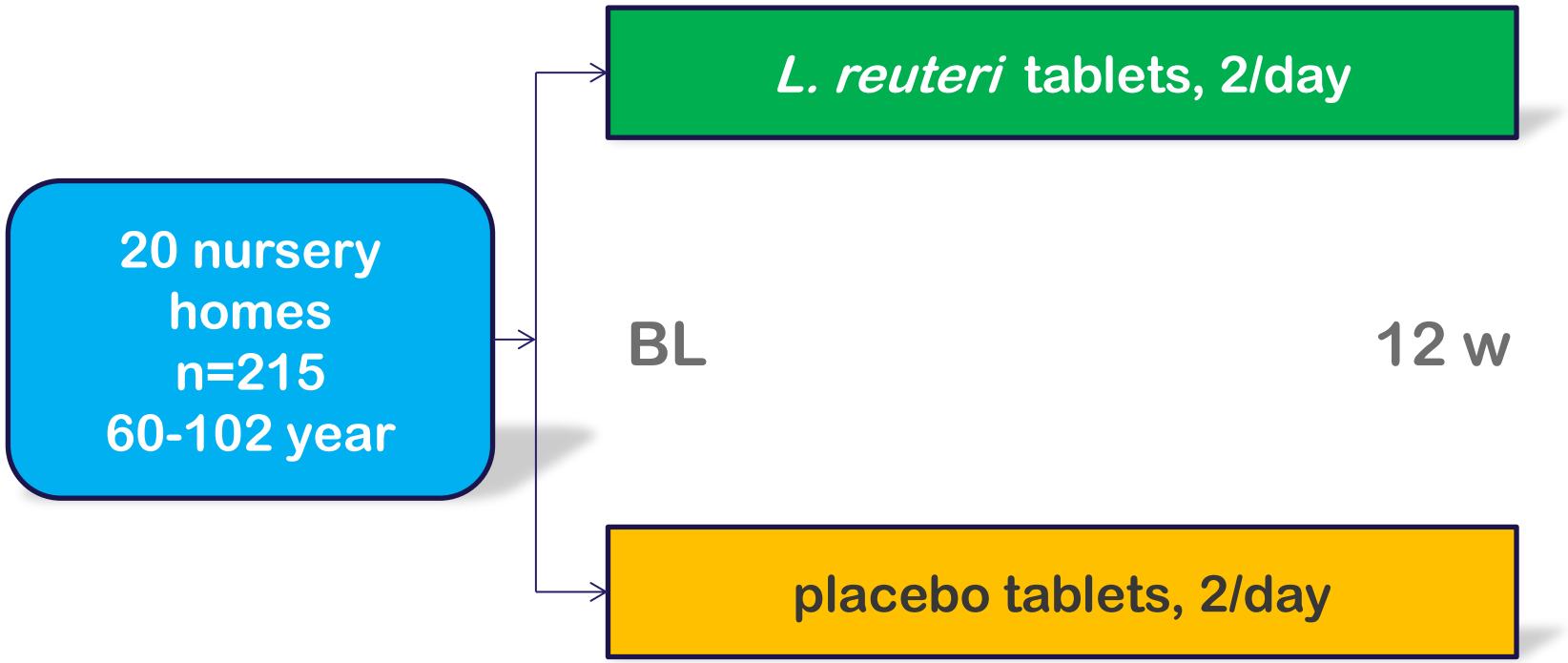
[a] RCT=randomized controlled trial; CRCT=cluster randomized controlled trial; [b]m=months; [c]PF=prevented fraction; [d]caries prevalence (%); [e] root caries reversals (%), CF= caries free

candidiasis



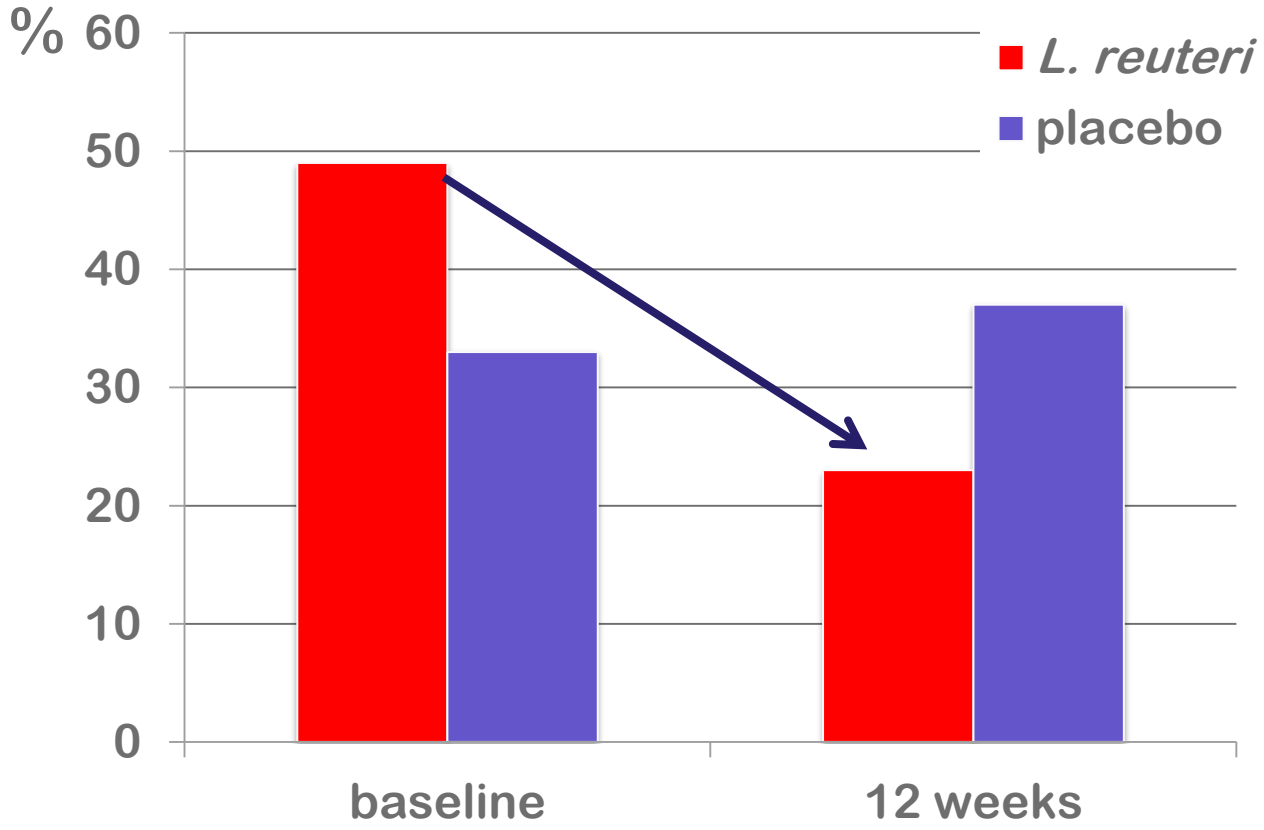
root caries

double-blind randomized placebo-controlled trial



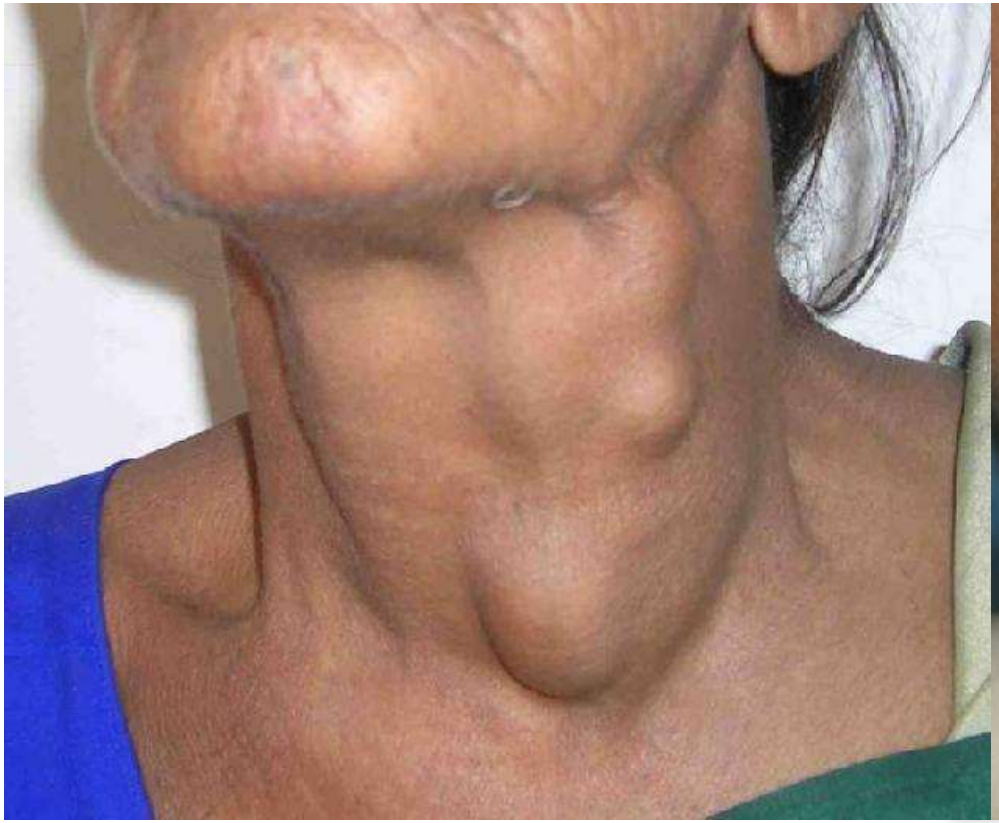
Kraft-Bodi et al 2015 JDR

high counts of salivary *C. albicans* after intake of *L. reuteri* tablets in elderly nursing home residents (n=227)

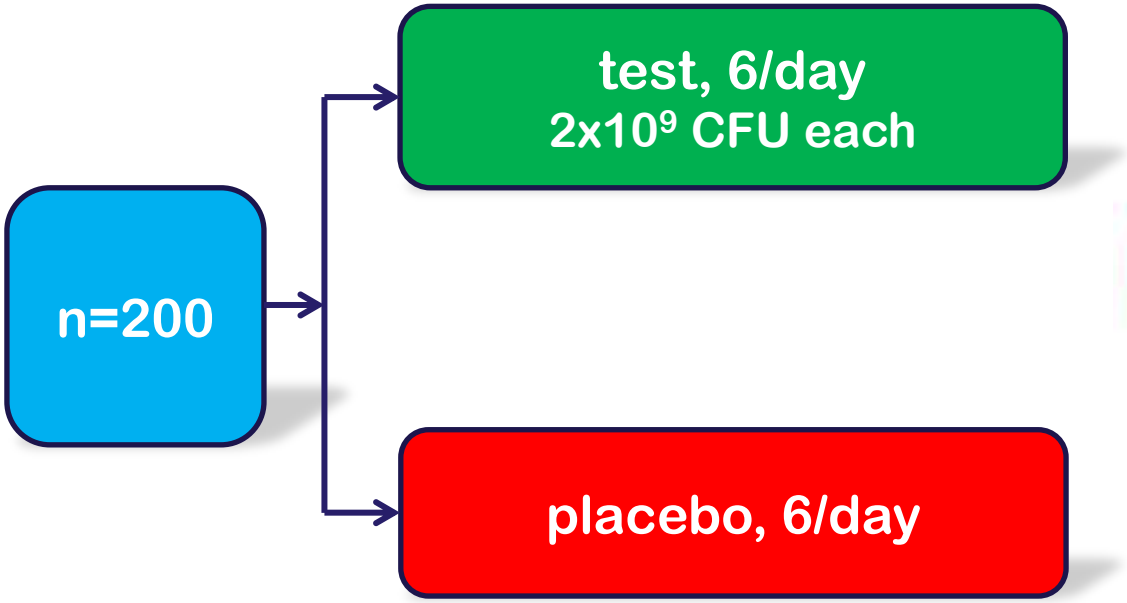


Kraft-Bodi et al., 2015 J Dent Res

probiotic supplements can relieve mucositis among patients with head- and neck cancer, treated with chemo and radiation

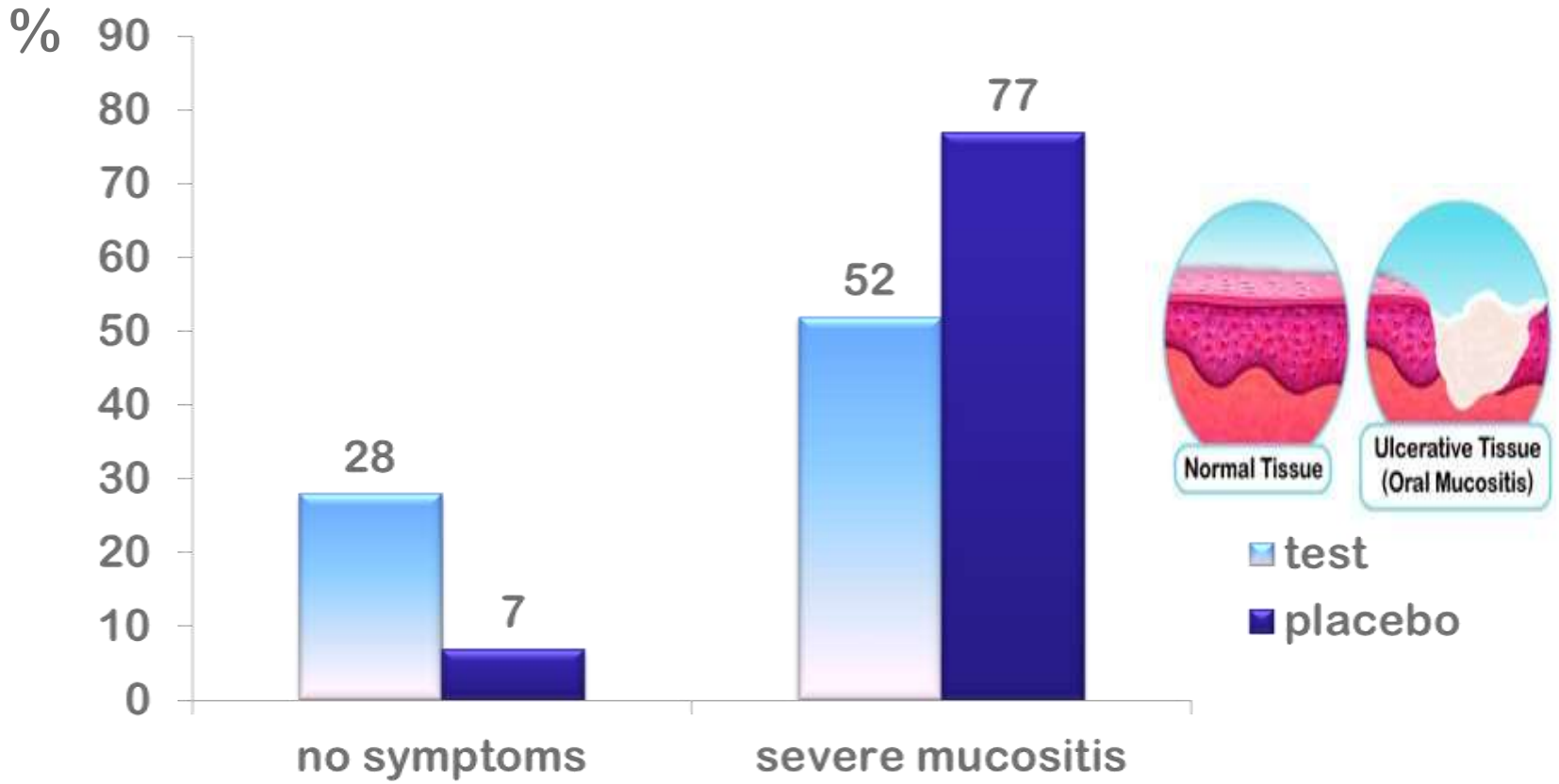


probiotic lozenges (*L. brevis)* and mucositis



Sharma et al., 2012

probiotic lozenges (*L. brevis)* and mucositis



Sharma et al., 2012

probiotic reduction of gingivitis – clinical observations

day 0

day 14

Krasse *et al.* Swed Dent J, 2006;30:55-60

after treatment with the probiotic *L. reuteri* in patients with implants presenting mucositis, the **clinical parameters improved**, and the **cytokine levels decreased** - in contraposition to the observations in the placebo group

Flichy-Fernandez et al., 2015 J Period Res

- early probiotic start may prevent caries
- a metabolic domino effect is obvious in childhood
- probiotics may reduce PI, GI, BOP and PPD
- probiotics beneficial to maintain oral balance in elderly
- probiotics supplements adjunct to fluoride and periodontal therapy

bad breath

volatile sulphur compounds (VSC) produced by oral bacteria i.e. *F. nucleatum*

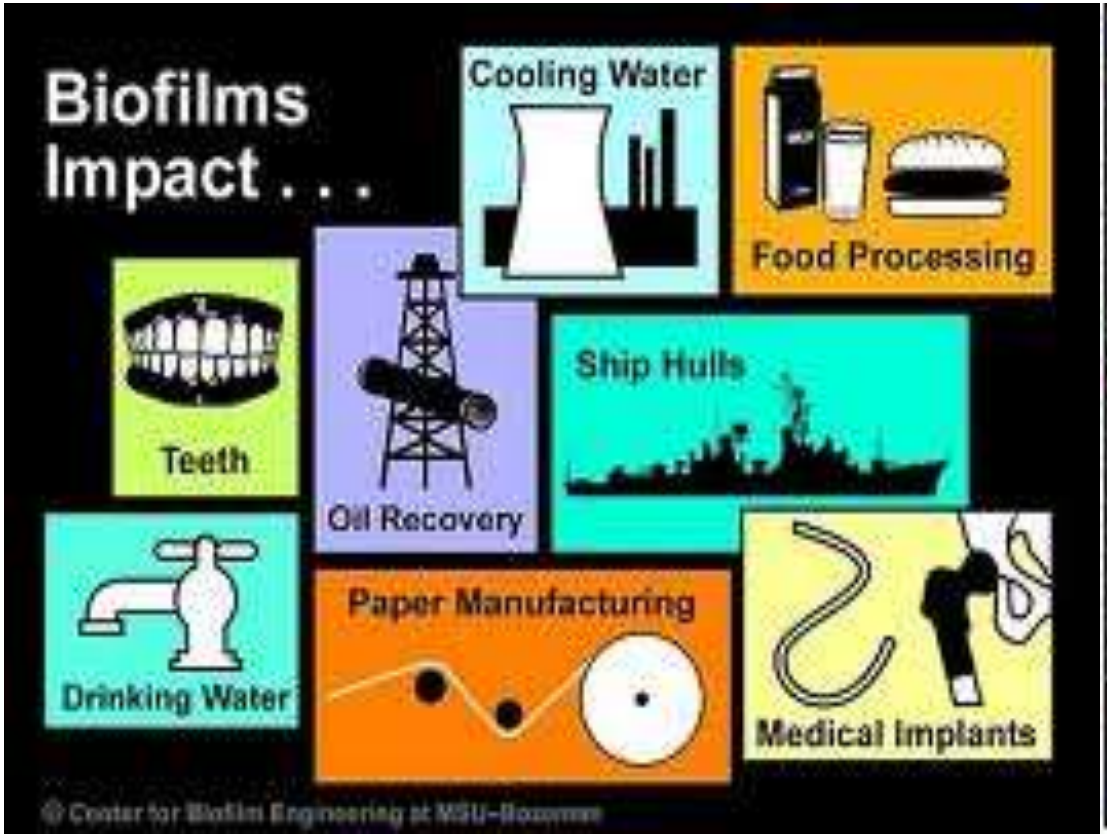
probiotics reduces VSC?

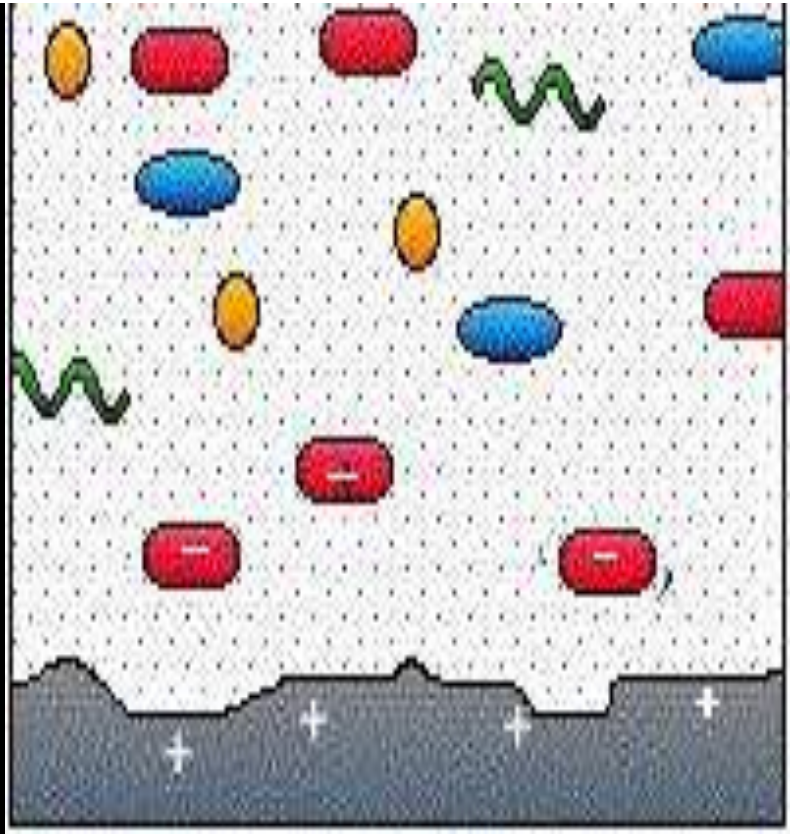
- use of tablets with *Streptococcus salivarius* K12 beneficial for long-term reduction of malodour
- similar findings for *Weissella cibaria*
- reduction of volatile sulphur compounds

(Burton et al., 2005; 2006; Kang et al., 2006).


• health by nature
• control biofilm rather than killing and eradication

future in preventive dentistry is biofilm control and biofilm engineering





examples of strategies to control biofilm stress