II Jornada del Grup de Nutrició de Farmacèutics d'Hospital de Catalunya

Introducció

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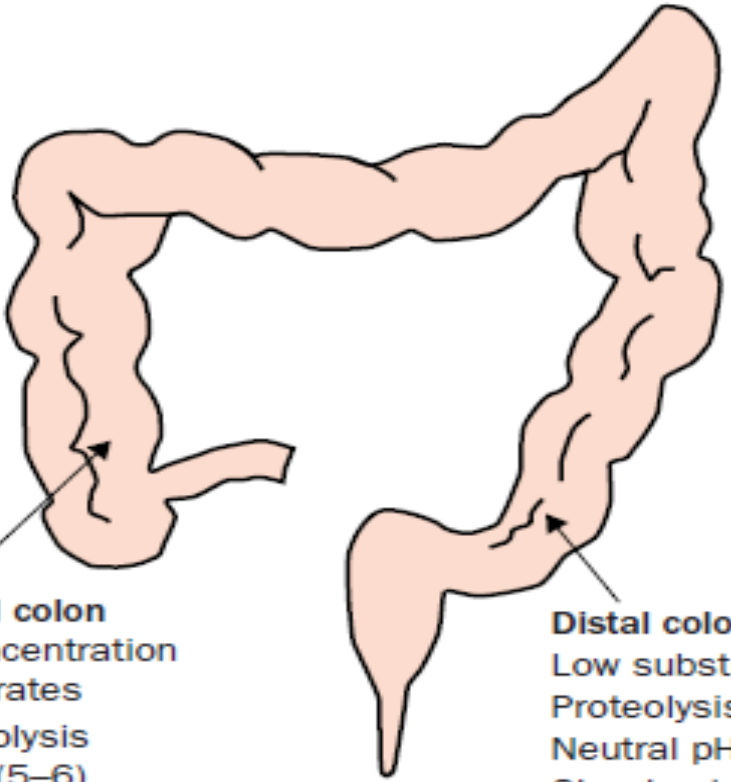
Physiological Role of the Human Colon

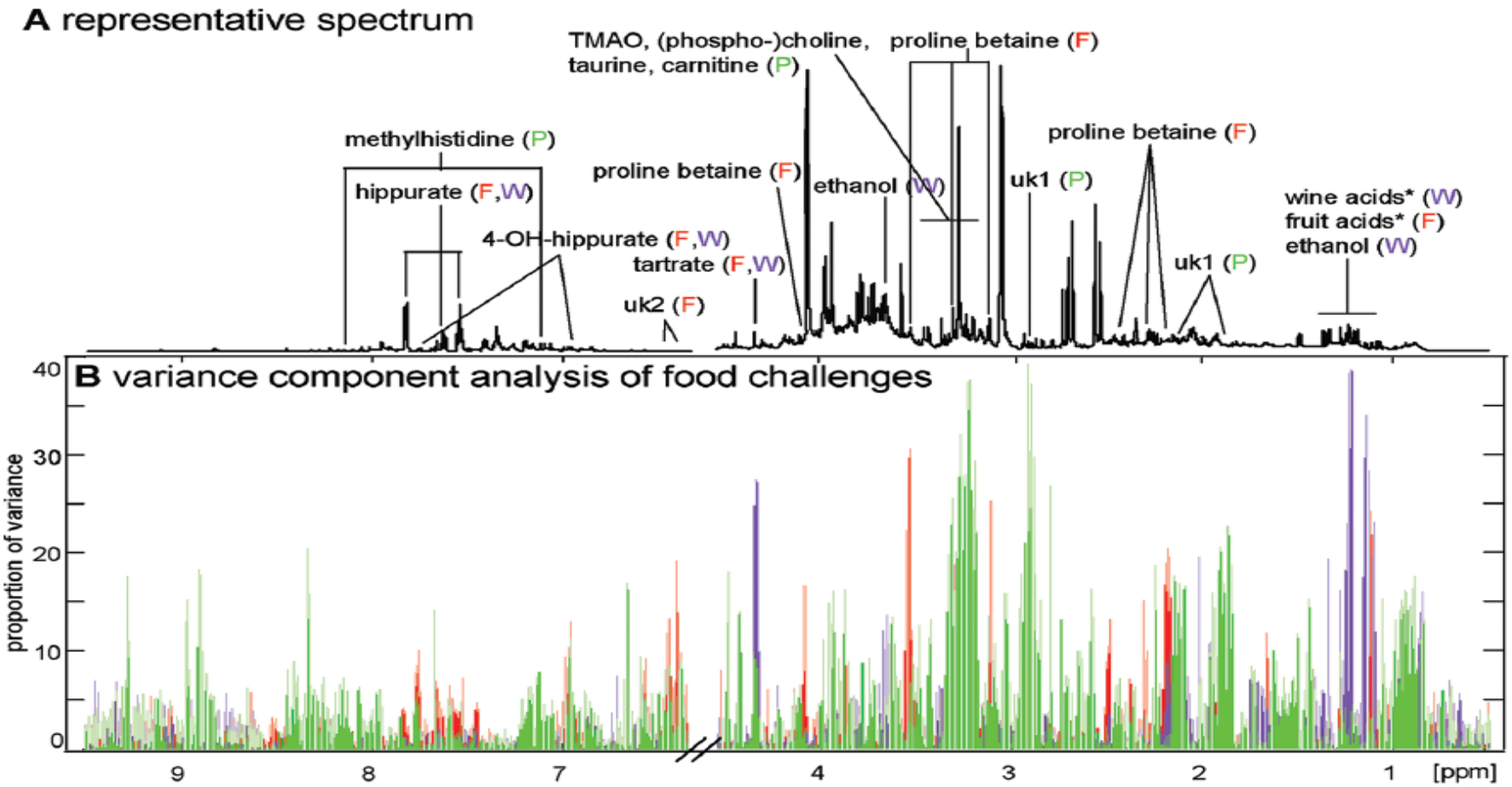


Proximal colon
High concentration of substrates
Saccharolysis
Acid pH (5–6)
Rapid bacterial growth

Distal colon
Low substrate availability
Proteolysis
Neutral pH
Slow bacterial growth

Guarner & Malagelada, Lancet 2003

Microbiota Impact on Human Metabolic Phenotype



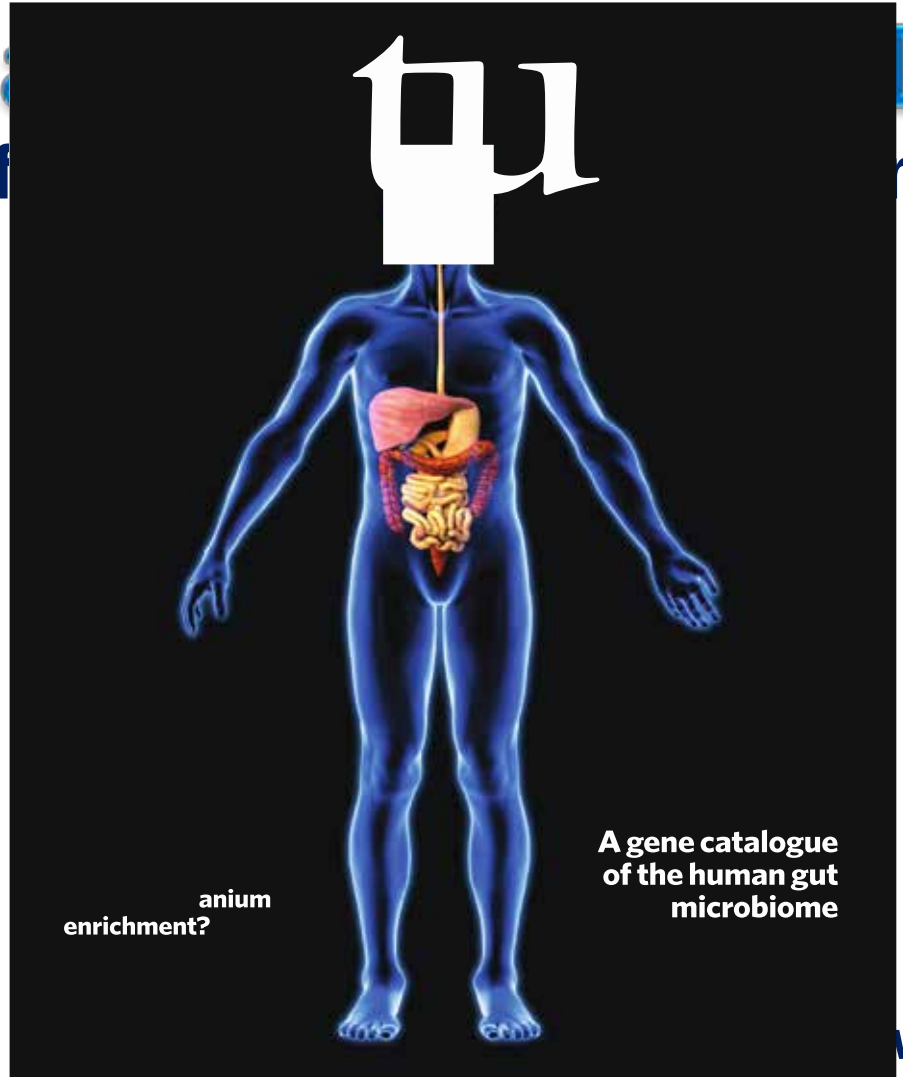
Heinzmann et al, J Proteome Res 2012

The Huma Database

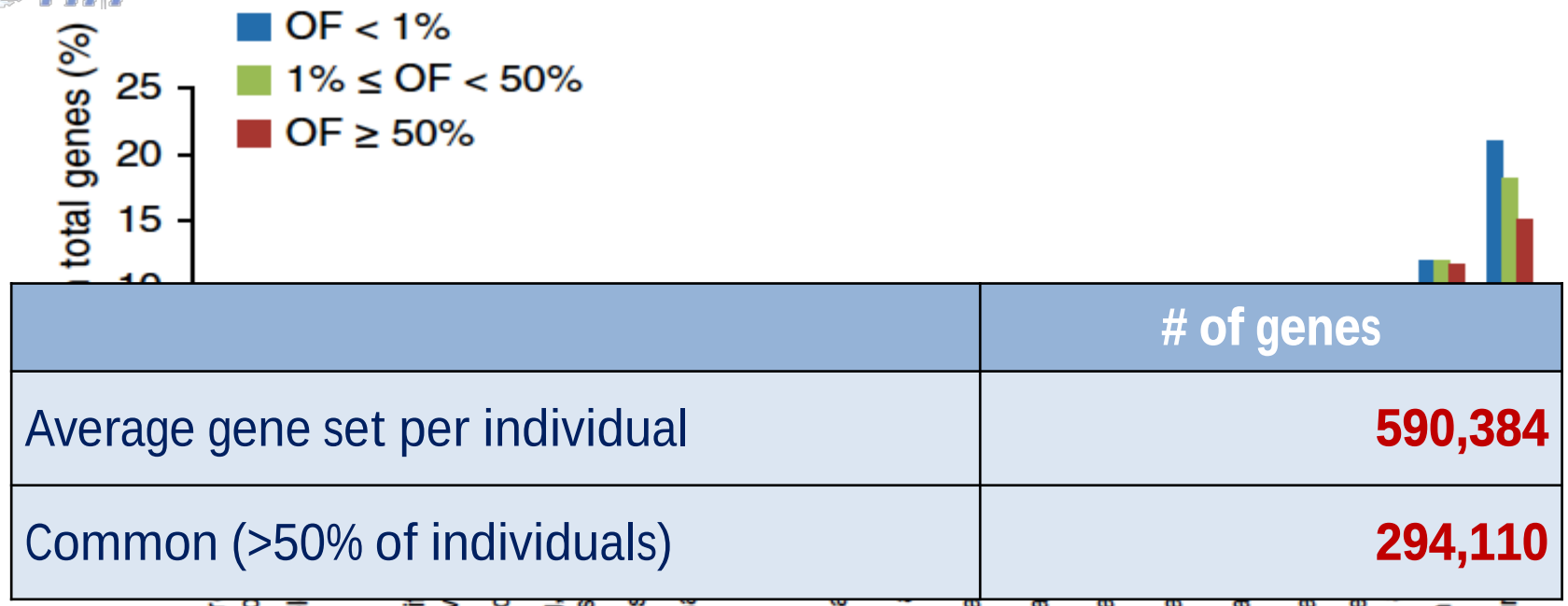
Number of man Fluids

Fluid	% Microbial origin
Blood	3,3
Saliva	4,8
Urine	5,2
CSF	8,0
Breast milk	8,3
Bile	27,8

www.hmdb.ca



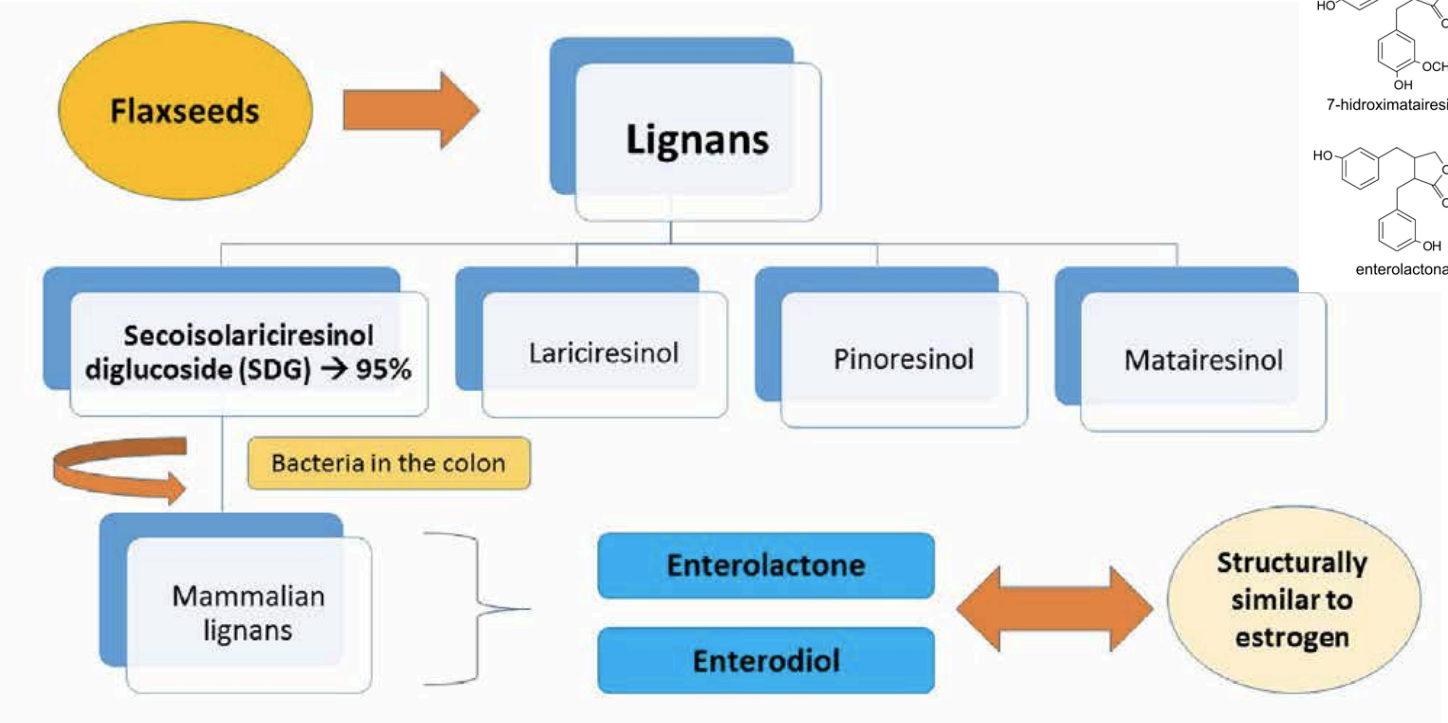
Gene Catalogue of the Human Gut Microbiome



	# of genes
Average gene set per individual	**590,384**
Common (>50% of individuals)	**294,110**

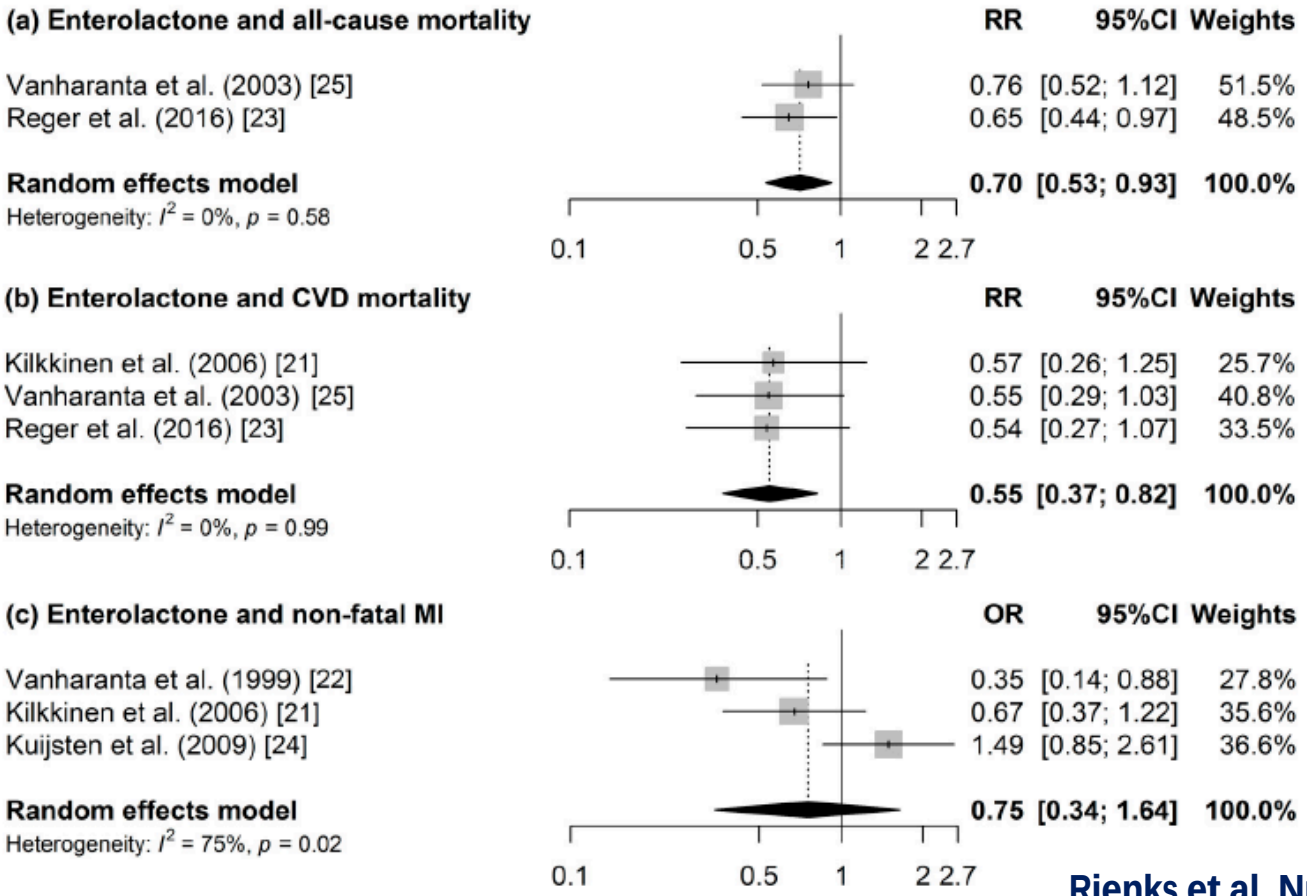
Li et al, Nat Biotech 2014

Flaxseeds have an important role in decreasing breast cancer risk



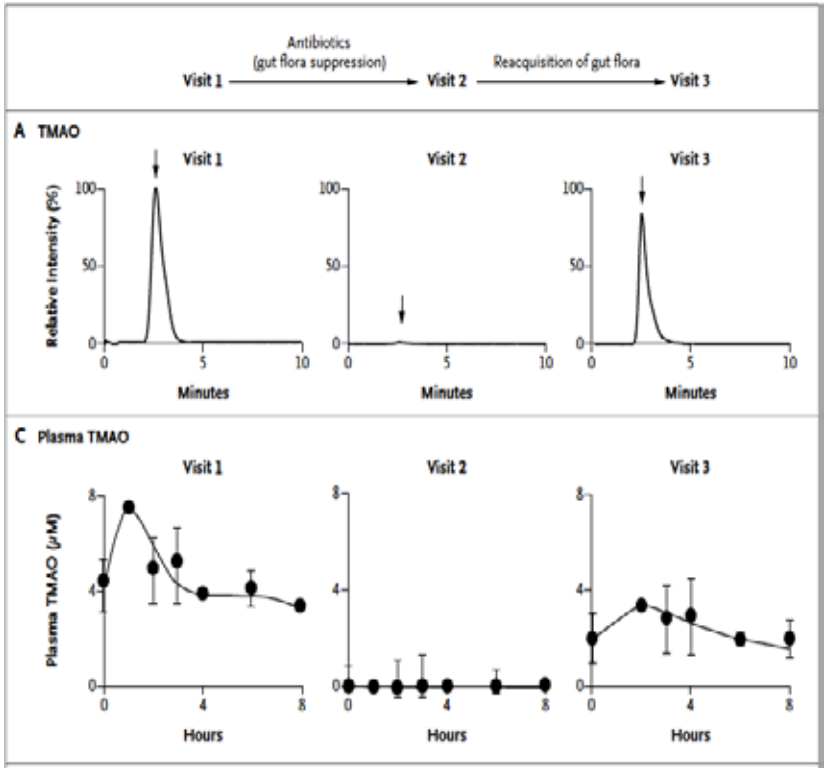
Calado A et al. The effect of flaxseed in breast cancer: a literature review. Front Nutr 2018

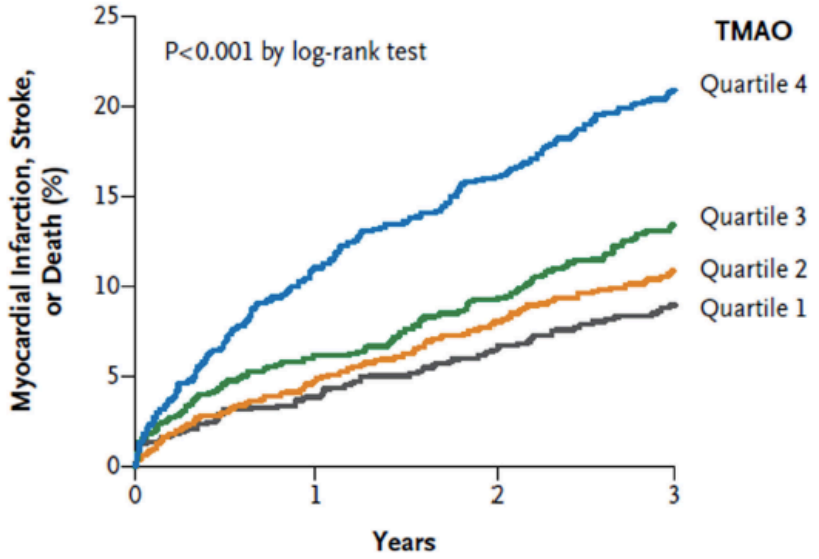
Polyphenol Biomarkers and Cardiovascular Disease and Mortality Risk



Rienks et al, Nutrients 2017

Microbial Metabolism of Phosphatidylcholine and Carnitine: Cardiovascular Risk and Mortality

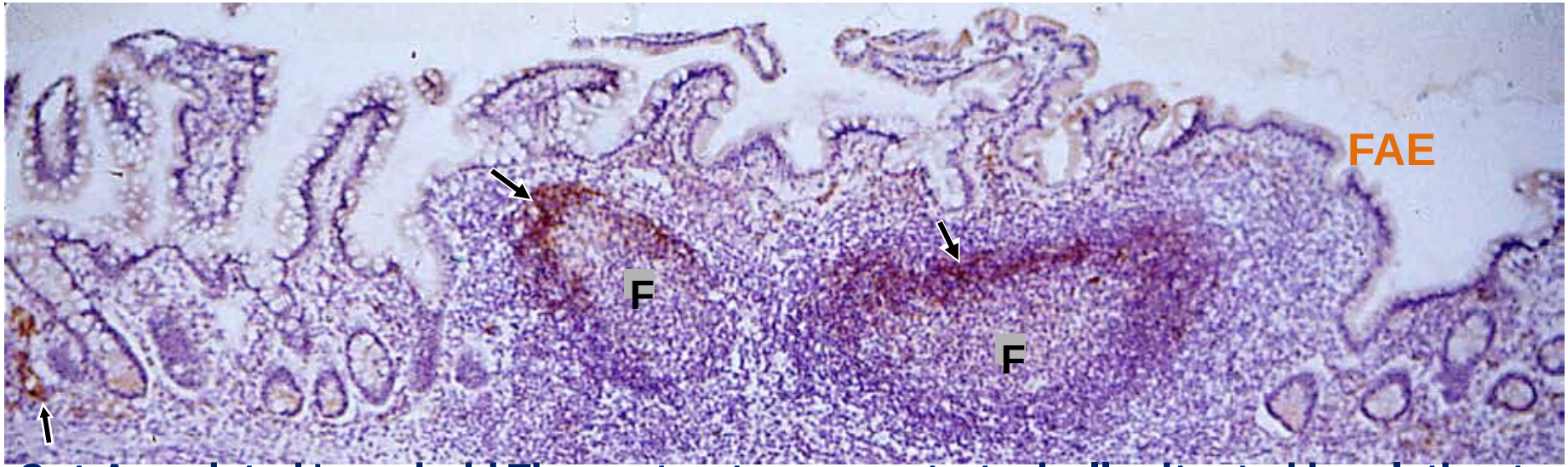




No. at Risk				
Quartile 1	1001	933	869	827
Quartile 2	998	940	884	843
Quartile 3	1003	938	888	835
Quartile 4	1005	913	849	791

Tang et al, NEJM 2013

Induction of Adaptive Immunity

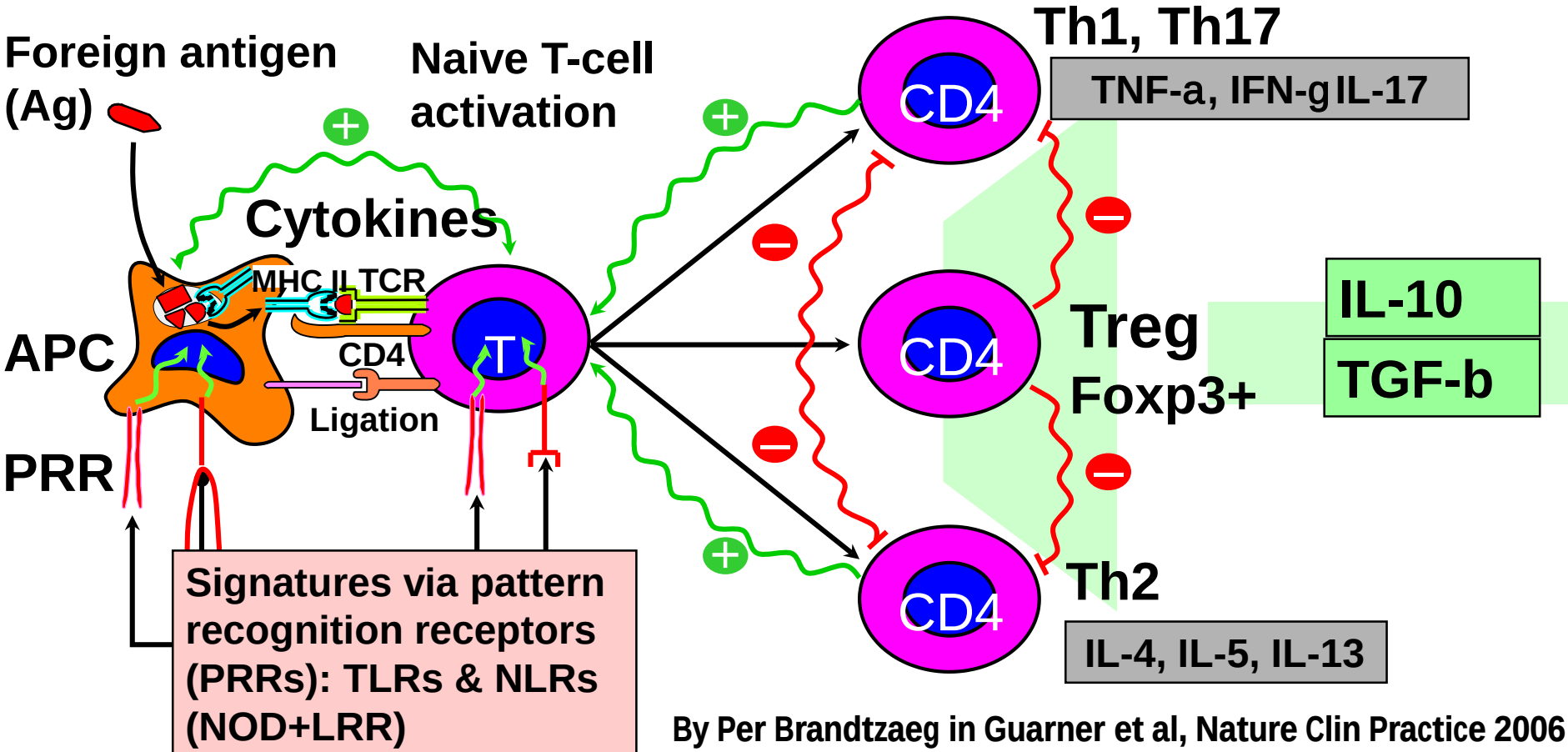


Gut-Associated Lymphoid Tissue structures are strategically situated in relation to the greatest concentration of microbiota

- **Peyer's patches:**
  distal ileum (nos. 100-250)
- **Isolated lymphoid follicles (ILFs):**
  large bowel (nos. ~ 30 000)

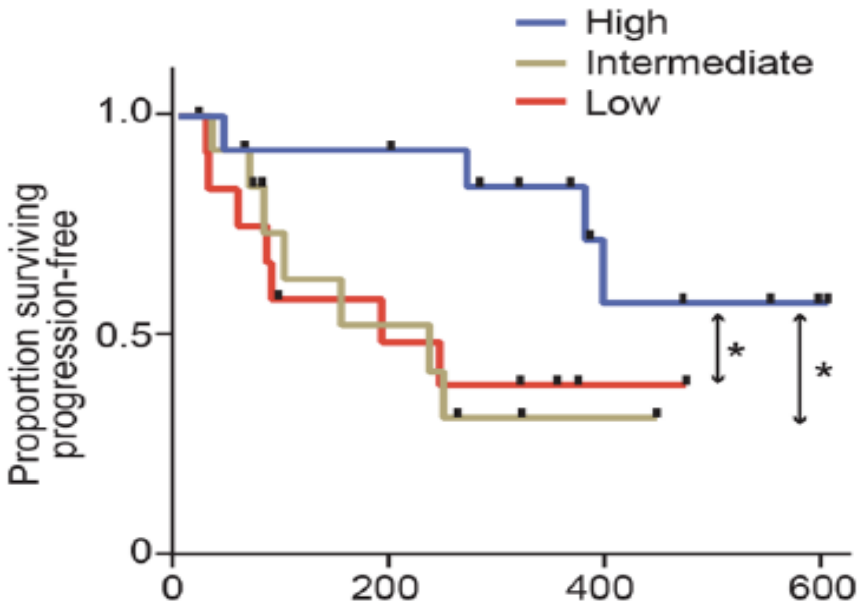
Brandtzaeg, Immunological Investigations 2010

Decision making in the adaptive (acquired) immune system is instructed by the microbial impact on APCs and T cells



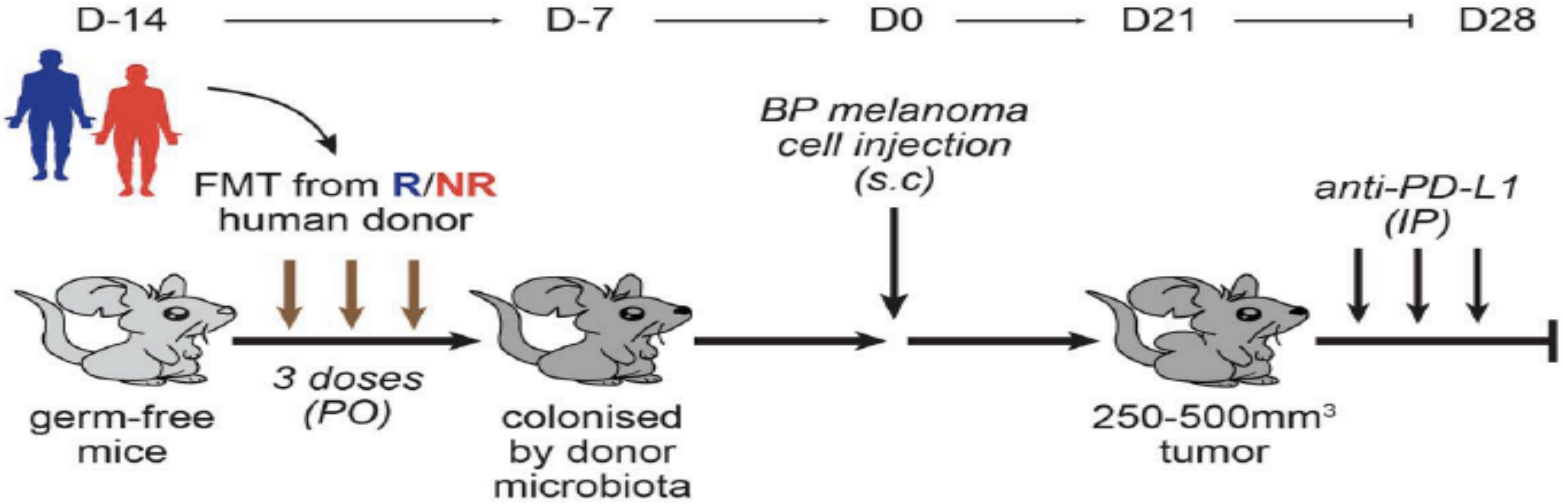
By Per Brandtzaeg in Guarner et al, Nature Clin Practice 2006

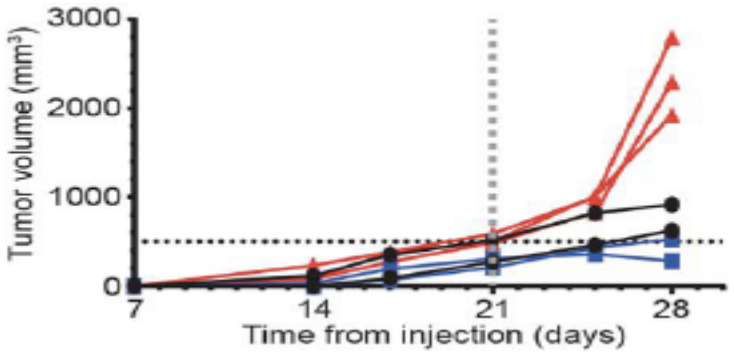
Gut microbes modulate response to immunotherapy in melanoma patients

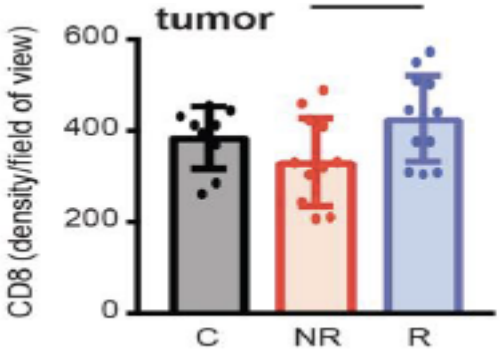


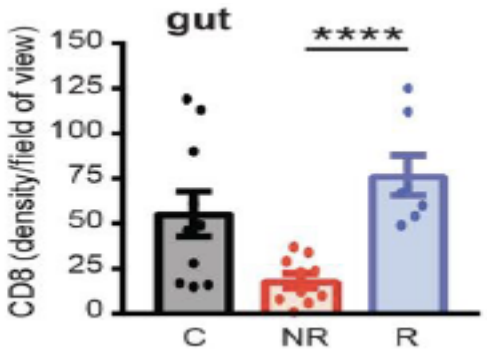
Gopalakrishnan et al, Science 2017

Gut microbes modulate response to immunotherapy in melanoma patients



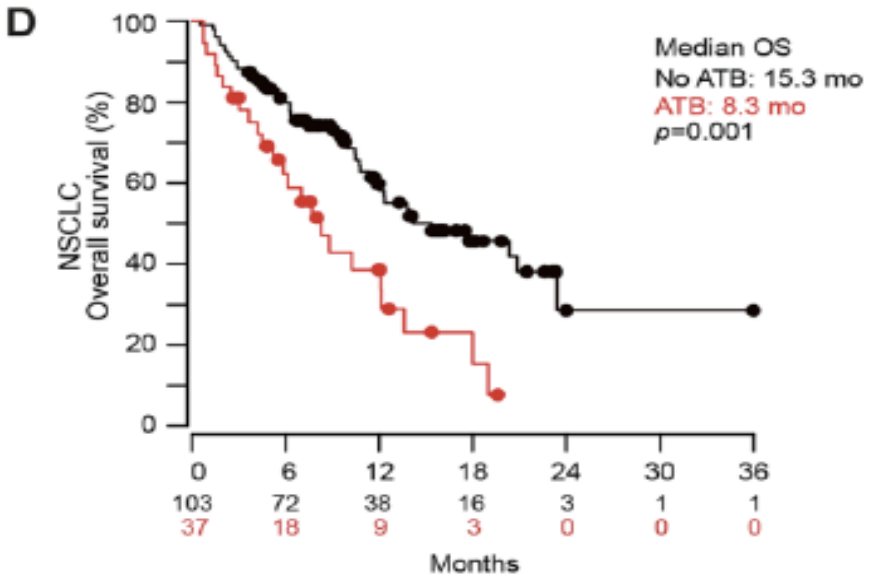


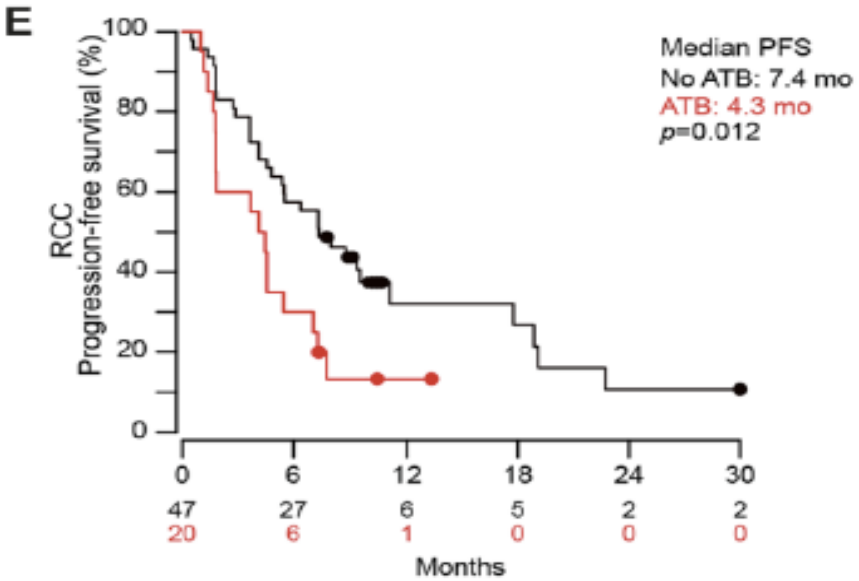




Gopalakrishnan et al, Science 2017

Gut microbes modulate response to Immunotherapy against epithelial tumors





Routy et al, Science 2017

Gut Microbiota Dysbiosis and Disease

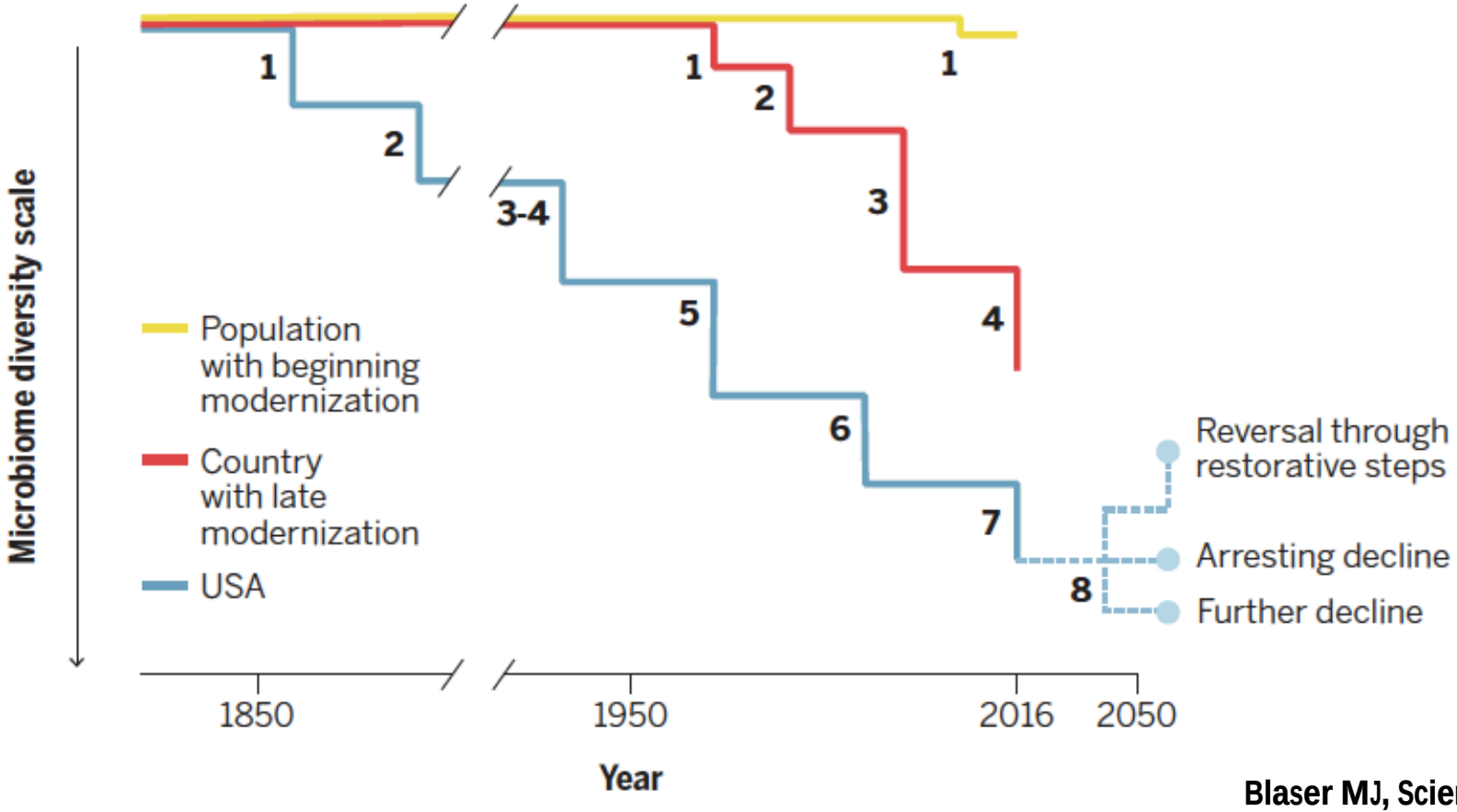
Disorders associated with altered composition of the gut microbiota:

- Nutrition-related disorders (obesity, type 2 diabetes and the metabolic syndrome)
- Inflammatory bowel diseases (UC and CD)
- Caeliac disease

Loss of microbial richness is a common feature of chronic non-communicable disease of modern society

- Certain allergies
- Certain mental and neuro-developmental conditions, such as autism spectrum disorders

Microbiota Changes in Different Societies



Blaser MJ, Science 2016

Antibiotic use and risk of early onset IBD

Table 2 Rate ratios of inflammatory bowel diseases according to antibiotic use among Danish children born 1995—2003 followed from birth until 1 January 2005

	Inflammatory bowel diseases			Crohn's disease			Ulcerative colitis		
	Number of cases	RR*	95% CI	Number of cases	RR*	95% CI	Number of cases	RR*	95% CI
Antibiotic use									
No courses	33	1	Reference	11	1	Reference	22	1	Reference
At least 1 course	84	1.84	(1.08 to 3.15)	39	3.41	(1.45 to 8.02)	45	1.21	(0.61 to 2.38)
Use in last 3 months	26	2.39	(1.36 to 4.19)	14	4.43	(1.88 to 10.44)	12	1.49	(0.69 to 3.19)
Use >3 months previously	58	1.42	(0.79 to 2.53)	25	2.27	(0.88 to 5.84)	33	1.04	(0.50 to 2.16)
Number of courses									
1—2	32	1.63	(0.92 to 2.91)	14	2.94	(1.18 to 7.31)	18	1.11	(0.54 to 2.32)
3—4	21	2.07	(1.03 to 4.18)	11	5.12	(1.69 to 15.53)	10	1.12	(0.45 to 2.80)
5—6	15	2.76	(1.27 to 5.97)	6	5.30	(1.49 to 18.87)	9	1.86	(0.71 to 4.87)
7+	16	2.93	(1.34 to 6.40)	8	7.32	(2.14 to 24.99)	8	1.59	(0.57 to 4.39)
Increase in RR per course		1.12	(1.04 to 1.21)		1.18	(1.06 to 1.32)		1.08	(0.97 to 1.19)

*Adjusted for age and calendar period.

Hviid et al, Gut 2011

ORIGINAL ARTICLE

Antibiotic and acid-suppression medications during early childhood are associated with obesity

Christopher M Stark,[1,2] Apryl Susi,[3] Jill Emerick,[2,3] Cade M Nylund[2,3]

Results 333 353 children met inclusion criteria, with 241 502 (72.4%) children prescribed an antibiotic, 39 488 (11.8%) an H2RA and 11 089 (3.3%) a PPI. Antibiotic prescriptions were associated with obesity (HR 1.26; 95% CI 1.23 to 1.28). This association persisted regardless of antibiotic class and strengthened with each

Conclusions Antibiotics, acid suppressants and the combination of multiple medications in the first 2 years of life are associated with a diagnosis of childhood obesity. Microbiota-altering medications administered in early childhood may influence weight gain.

Table 2 Total obese, incidence density, unadjusted and adjusted HRs of obesity for sex, caesarean section, military rank and those prescribed histamine-2 receptor antagonists (H2RAs), proton pump inhibitors (PPIs) and antibiotics

	Number of obese (%)	Incidence density (per 100 person-years)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
PPI prescription	1841 (16.6)	3.85	1.04 (1.03 to 1.05)	1.02 (1.01 to 1.03)
H2RA prescription	5955 (15.1)	3.64	1.03 (1.02 to 1.03)	1.01 (1.004 to 1.02)
Antibiotic class prescriptions	36 899 (15.3)	3.54	1.26 (1.23 to 1.28)	–
0	10 094 (11.0)	2.71	Ref	Ref
1	13 852 (13.3)	3.17	1.14 (1.11 to 1.17)	1.12 (1.09 to 1.15)
2	10 882 (15.4)	3.56	1.26 (1.23 to 1.30)	1.23 (1.20 to 1.26)
3	7457 (17.4)	3.93	1.38 (1.34 to 1.42)	1.33 (1.29 to 1.37)
4+	4708 (19.4)	4.27	1.48 (1.43 to 1.53)	1.42 (1.37 to 1.46)

Stark et al, Gut 2018

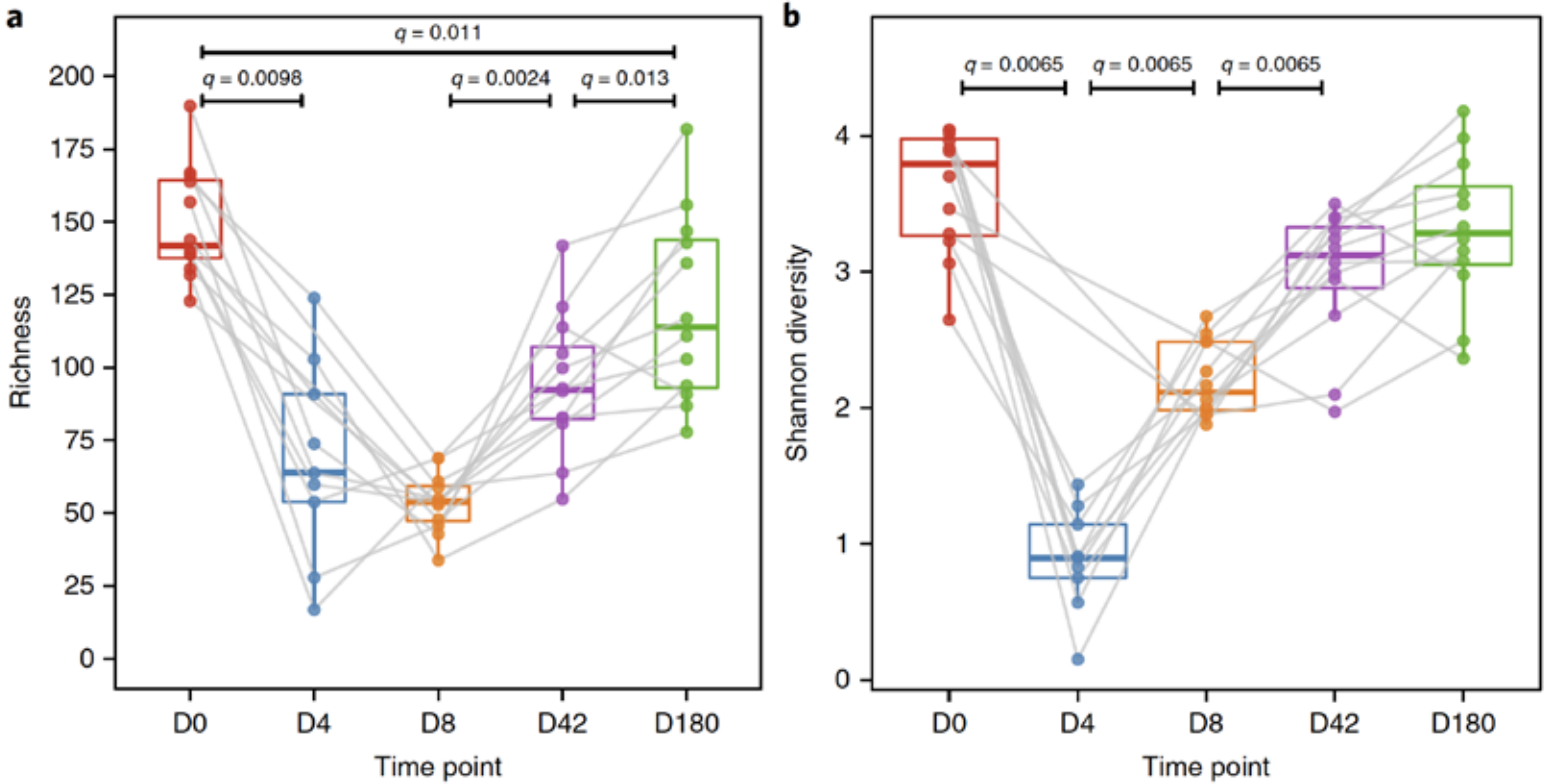
Antibiotic use and risk of colorectal Adenoma

Table 2 Antibiotic use at age 20–39 and risk of colorectal adenoma, Nurses' Health Study 2004–2010

	Antibiotic use at age 20–39				
	None	1–14 days	15 days to 2 months	2 months+	p_{trend}
Total adenoma					
No. of cases (n=1195)	141	653	296	105	
Age-adjusted* OR (95% CI)	1 (referent)	1.13 (0.93–1.37)	1.40 (1.13–1.74)	1.36 (1.04–1.79)	0.001
Multivariable† OR (95% CI)	1 (referent)	1.12 (0.92–1.36)	1.41 (1.13–1.75)	1.36 (1.03–1.79)	0.002
High risk‡					
No. of cases (n=436)	51	251	100	34	
Age-adjusted* OR (95% CI)	1 (referent)	1.25 (0.92–1.71)	1.40 (0.99–2.00)	1.35 (0.86–2.11)	0.22
Multivariable† OR (95% CI)	1 (referent)	1.23 (0.90–1.68)	1.43 (1.00–2.05)	1.37 (0.86–2.16)	0.14
Low risk					
No. of cases (n=630)	73	331	167	59	
Age-adjusted* OR (95% CI)	1 (referent)	1.08 (0.83–1.40)	1.47 (1.10–1.96)	1.40 (0.97–2.00)	0.002
Multivariable† OR (95% CI)	1 (referent)	1.08 (0.82–1.41)	1.47 (1.09–1.97)	1.42 (0.98–2.05)	0.002
Proximal					
No. of cases (n=709)	82	391	176	60	
Age-adjusted* OR (95% CI)	1 (referent)	1.18 (0.92–1.51)	1.46 (1.11–1.92)	1.36 (0.96–1.93)	0.02
Multivariable† OR (95% CI)	1 (referent)	1.17 (0.91–1.51)	1.46 (1.10–1.93)	1.43 (1.00–2.04)	0.01
Distal					
No. of cases (n=509)	67	271	128	43	
Age-adjusted* OR (95% CI)	1 (referent)	0.99 (0.75–1.30)	1.29 (0.94–1.76)	1.20 (0.81–1.79)	0.04
Multivariable† OR (95% CI)	1 (referent)	0.98 (0.74–1.30)	1.31 (0.96–1.81)	1.18 (0.78–1.78)	0.04

Cao et al, Gut 2017

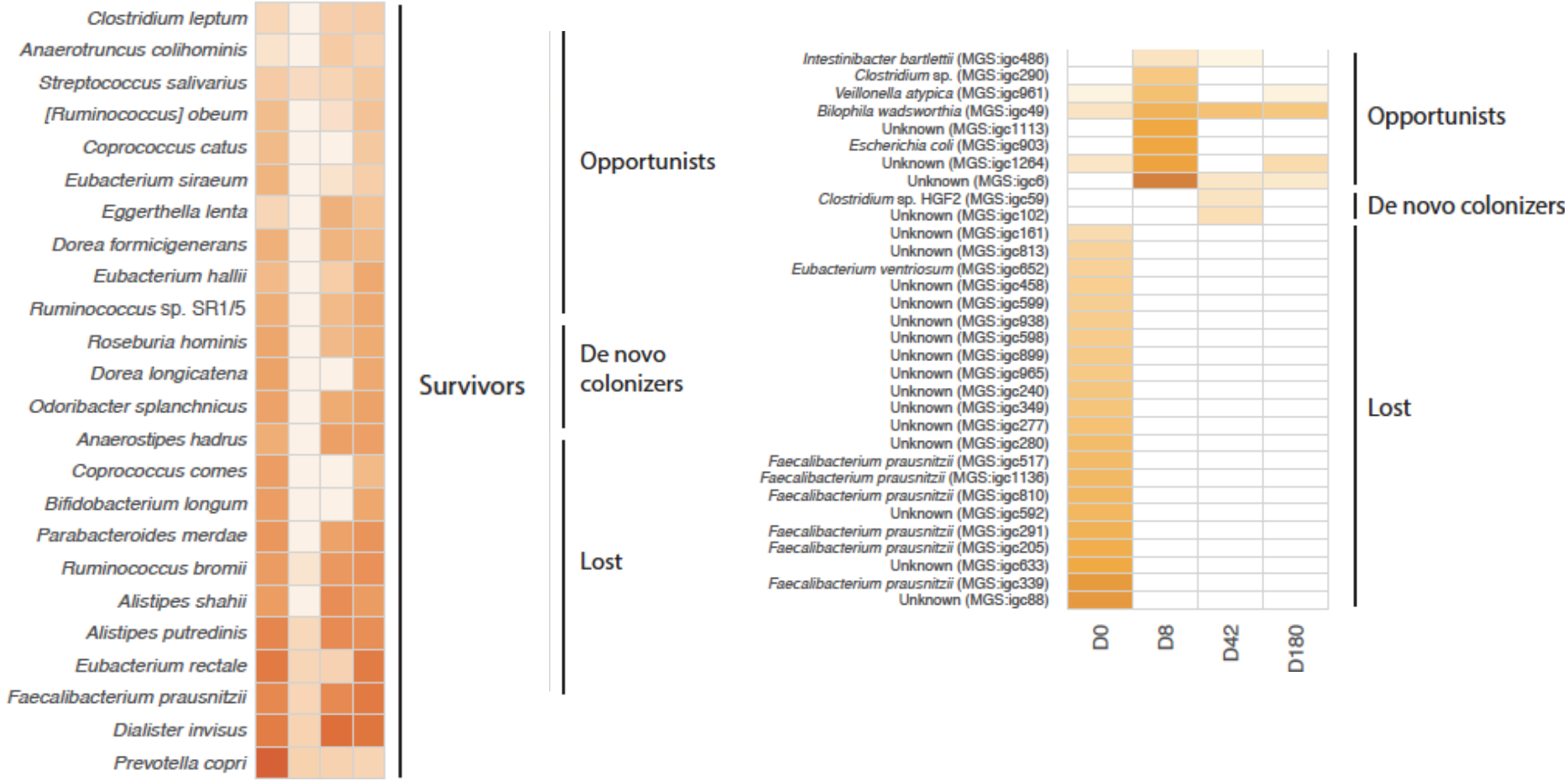
Recovery of Human Gut Microbiome after Antibiotic Exposure



Oral vancomycin, gentamicin and meropenem from D0 to D4

Palleja et al, Nat Microbiol 2018

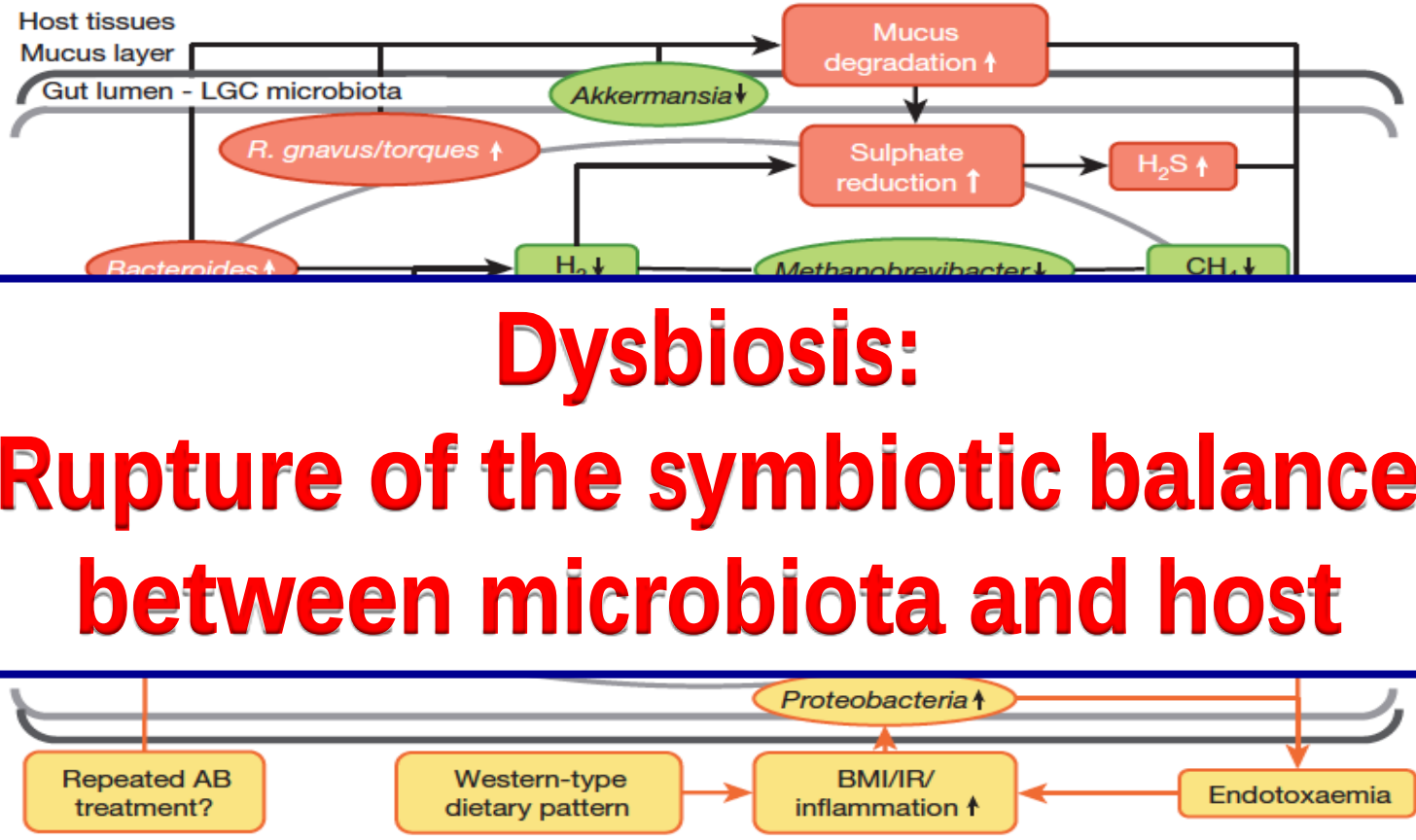
Different Recovery Capacities between Strains



Oral vancomycin, gentamicin and meropenem from D0 to D4

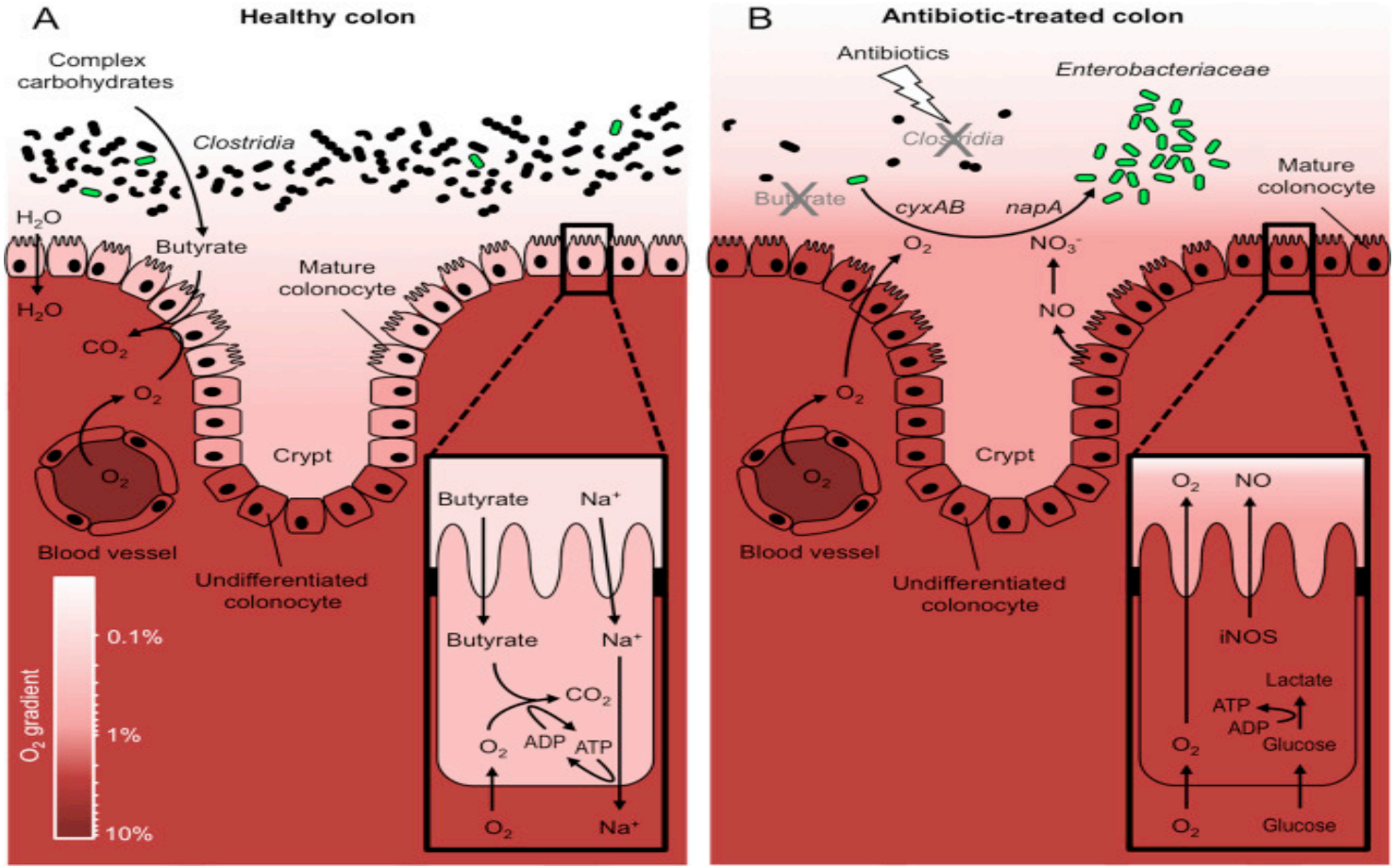
Palleja et al, Nat Microbiol 2018

Functional Dysbiosis



Dysbiosis:
Rupture of the symbiotic balance between microbiota and host

Le Chatellier et al, Nature 2013

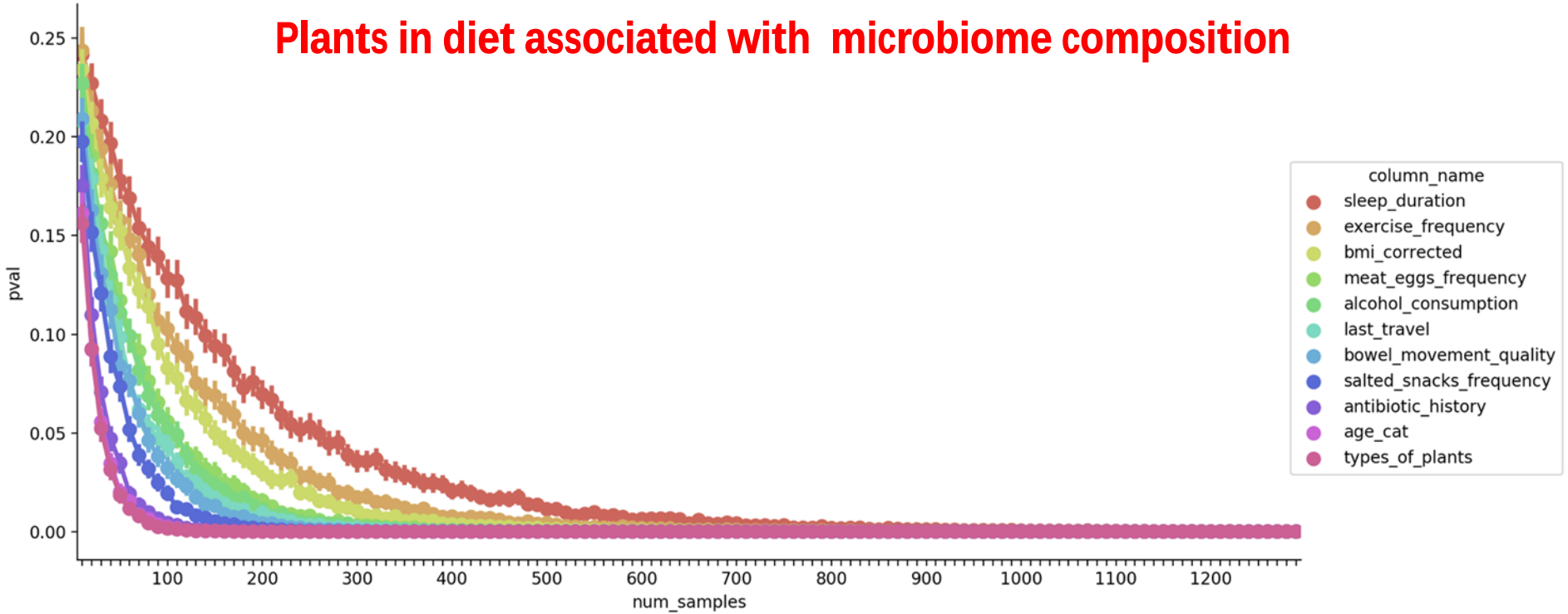


Oxygen as a driver of gut dysbiosis. Rivera-Chávez et al. Free Radic Biol

American Gut Project

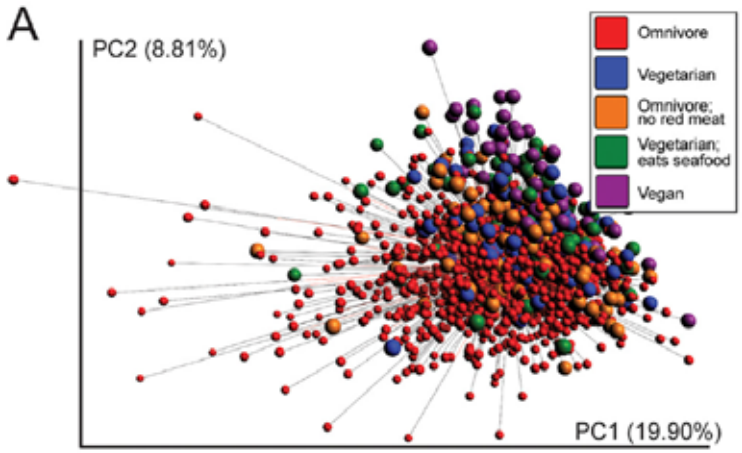
Microbial sequence data from 15,096 samples from 11,336 human participants

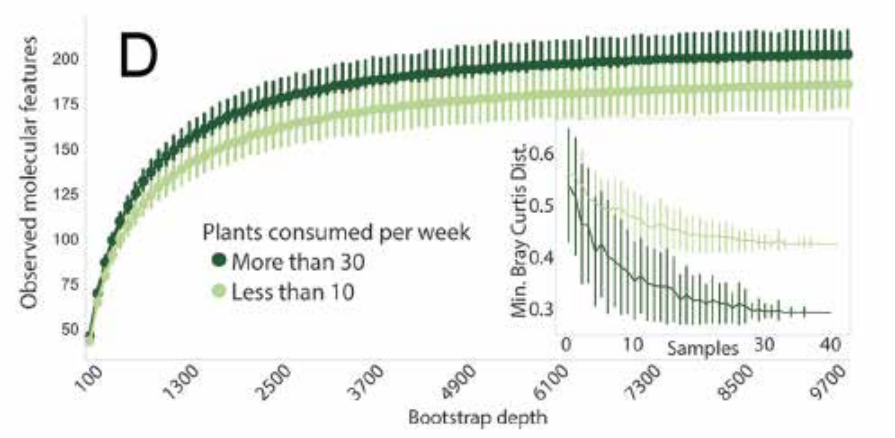
Plants in diet associated with microbiome composition

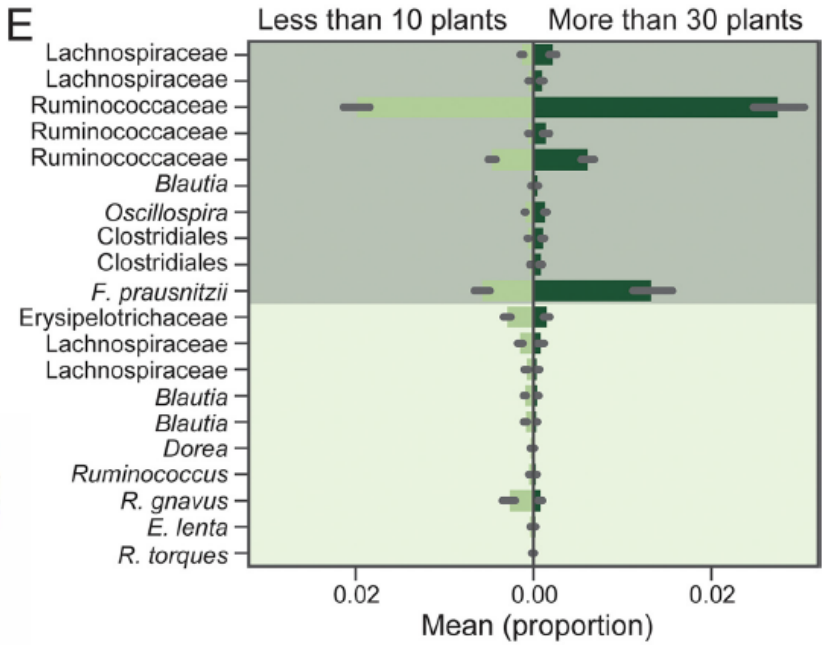


McDonald et al, mSystems 2018

Diversity of plants in diet associated with microbiome composition

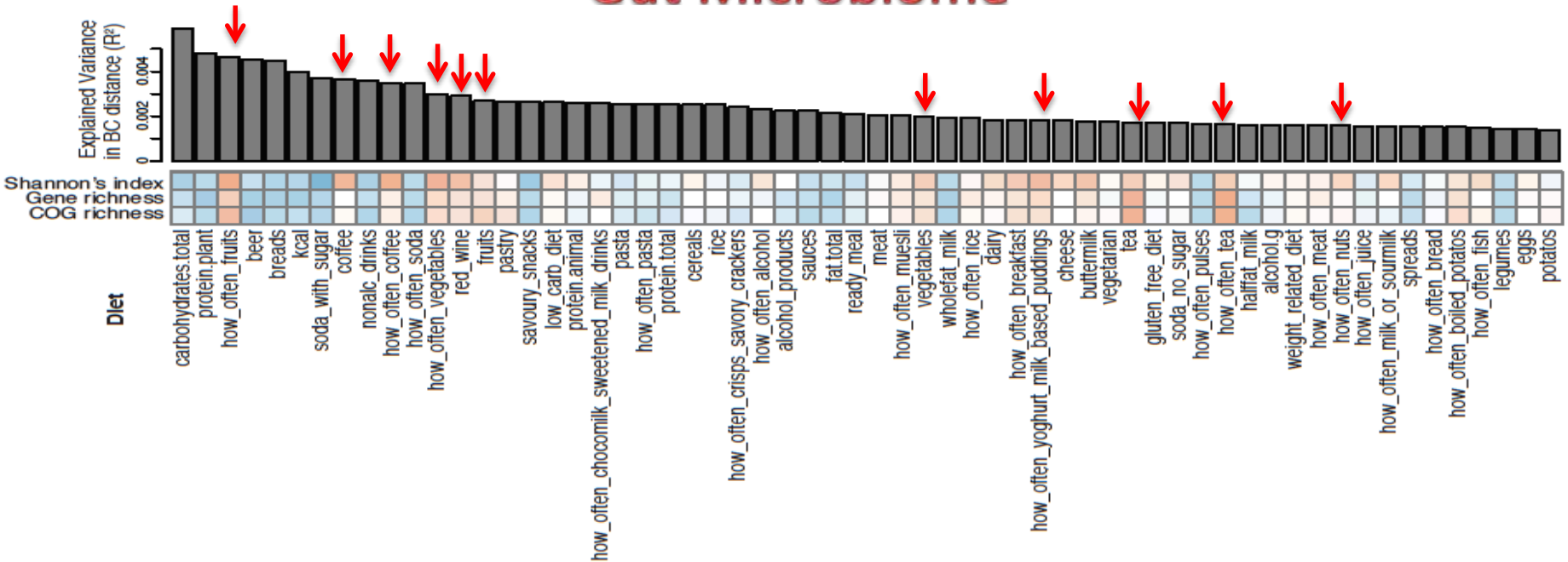






McDonald et al, mSystems 2018

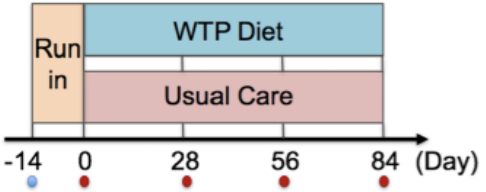
Dietary Factors associated with interindividual variation of Gut Microbiome

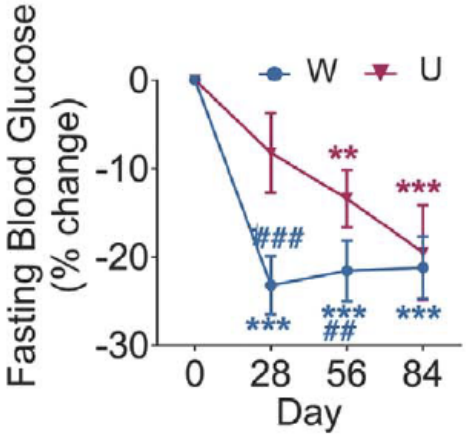


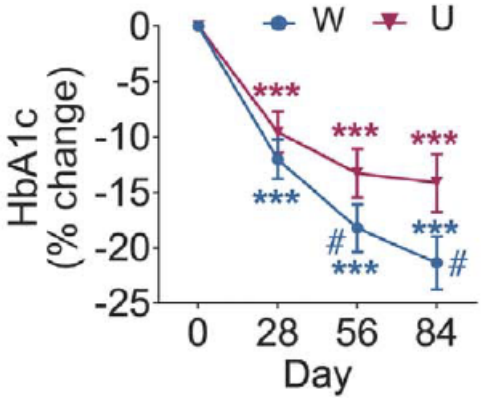
Zhernakova et al, Science 2016

Gut bacteria selectively promoted by dietary fibers alleviate type 2 diabetes

Group	Daily intake	Day 0	Day 84
W (*N*=24)	Total Energy (kcal)	1924.93±129.67	1874.87±71.10
	Fat (g)	63.48±4.57	58.32±4.04
	Fat %	31.03±1.86	27.54±1.07
	Protein (g)	81.52±5.90	74.58±3.67
	Protein %	16.94±0.63	15.88±0.49
	Total carbohydrate (g)	268.77±25.67	282.72±9.63
	Total carbohydrate %	52.03±2.16	56.58±1.09
	Total fiber (g)	12.12±1.24	37.10±1.90$^{***\#\#\#}$
	Soluble fiber (g)	4.59±0.47	14.61±0.69$^{***\#\#\#}$
U (*N*=14)	Total Energy (kcal)	2063.54±161.42	1954.48±142.80
	Fat (g)	70.44±8.30	62.41±5.14
	Fat %	30.70±2.39	29.16±1.57
	Protein (g)	87.31±9.14	79.32±9.00
	Protein %	16.65±0.88	15.76±0.86
	Total carbohydrate (g)	285.53±24.85	284.94±21.45
	Total carbohydrate %	52.65±2.44	55.08±1.63
	Total fiber (g)	15.43±2.43	16.06±1.95
	Soluble fiber (g)	5.85±0.92	6.09±0.74

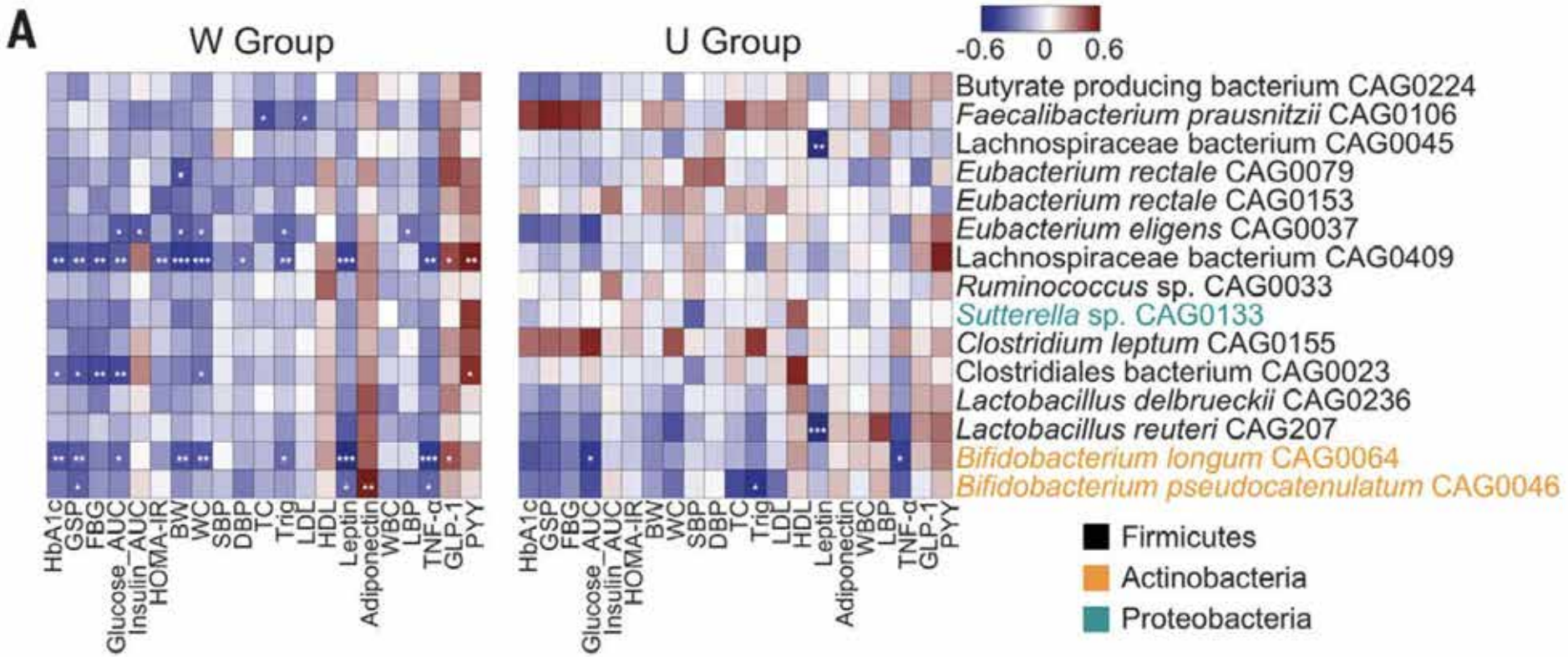






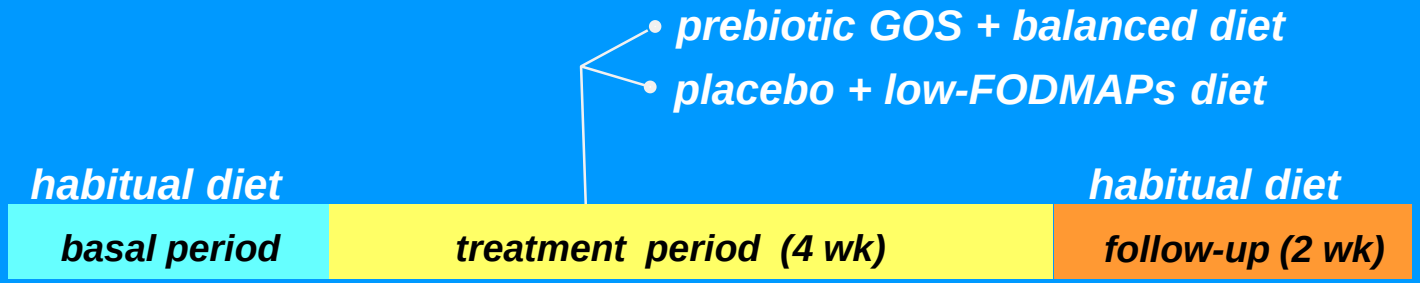
Zhao et al, Science 2018

Gut bacteria selectively promoted by dietary fibers alleviate type 2 diabetes



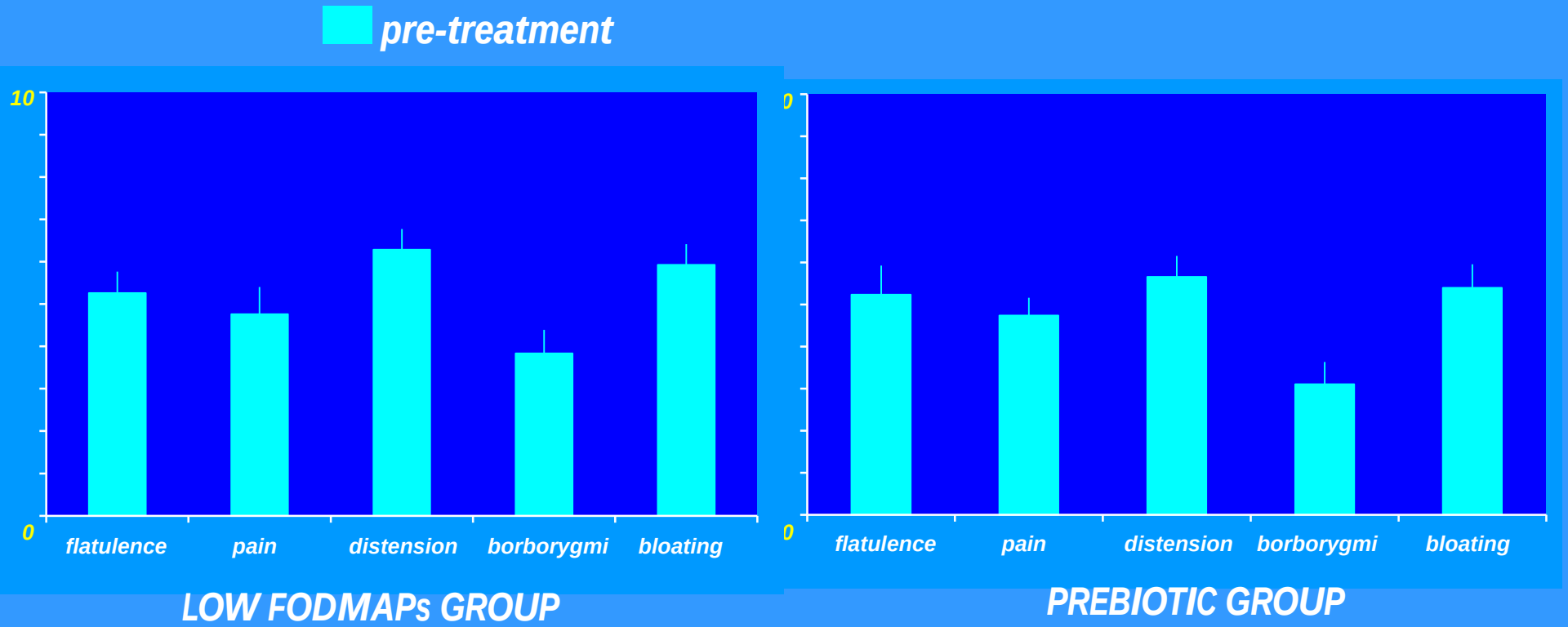
Zhao et al, Science 2018

Bimuno GOS versus low FODMAPs diet in patients with FGD complaining of excessive gas: experimental design



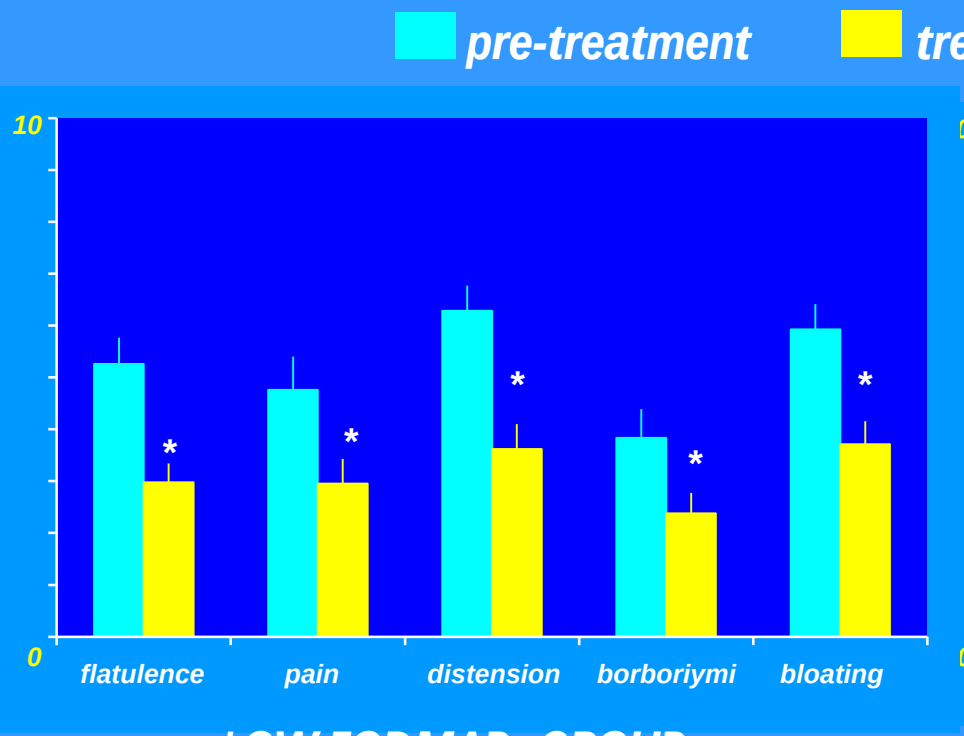
Huaman et al, Gastroenterology 2018

Digestive symptoms

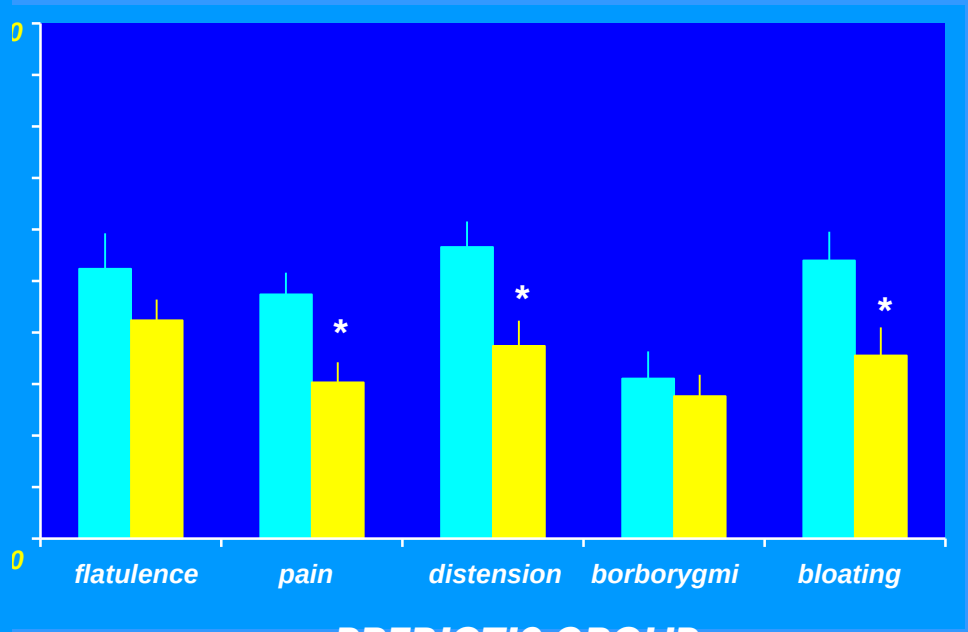


Huaman et al, Gastroenterology 2018

Digestive symptoms



LOW FODMAPs GROUP



PREBIOTIC GROUP

* p<0,05 vs basal

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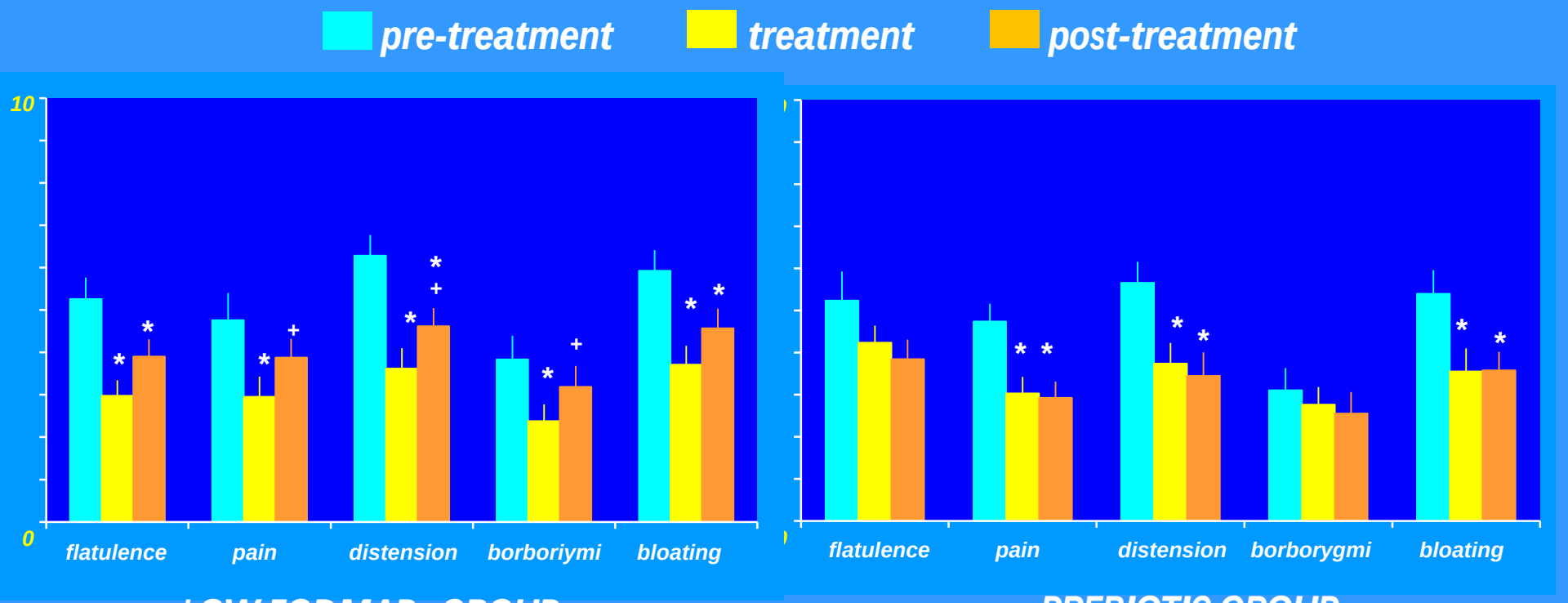
Digestive symptoms



* p<0,05 vs basal + p<0,05 vs treatment

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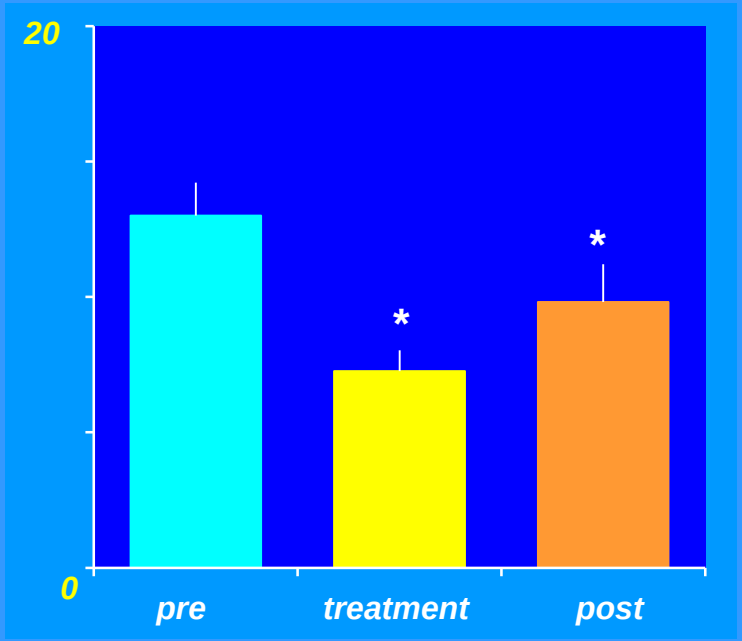
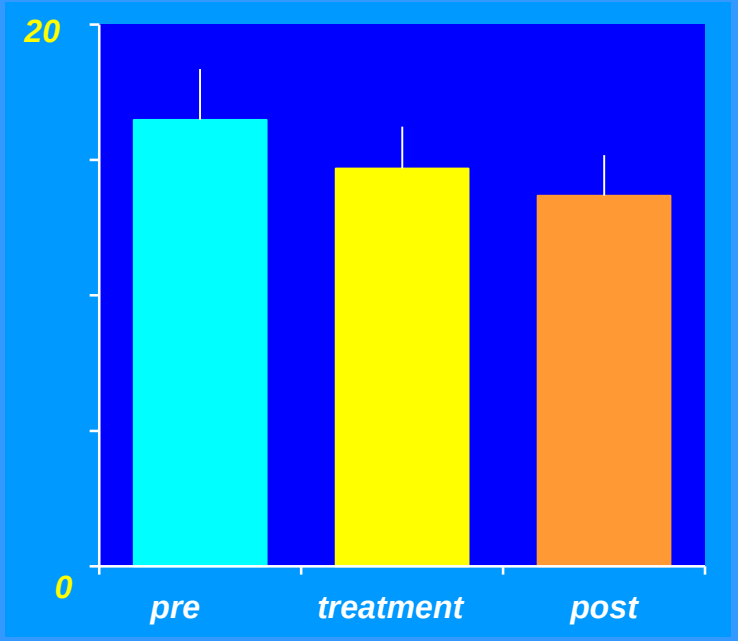
Number of daytime anal gas evacuation



LOW FODMAPs GROUP



PREBIOTIC GROUP

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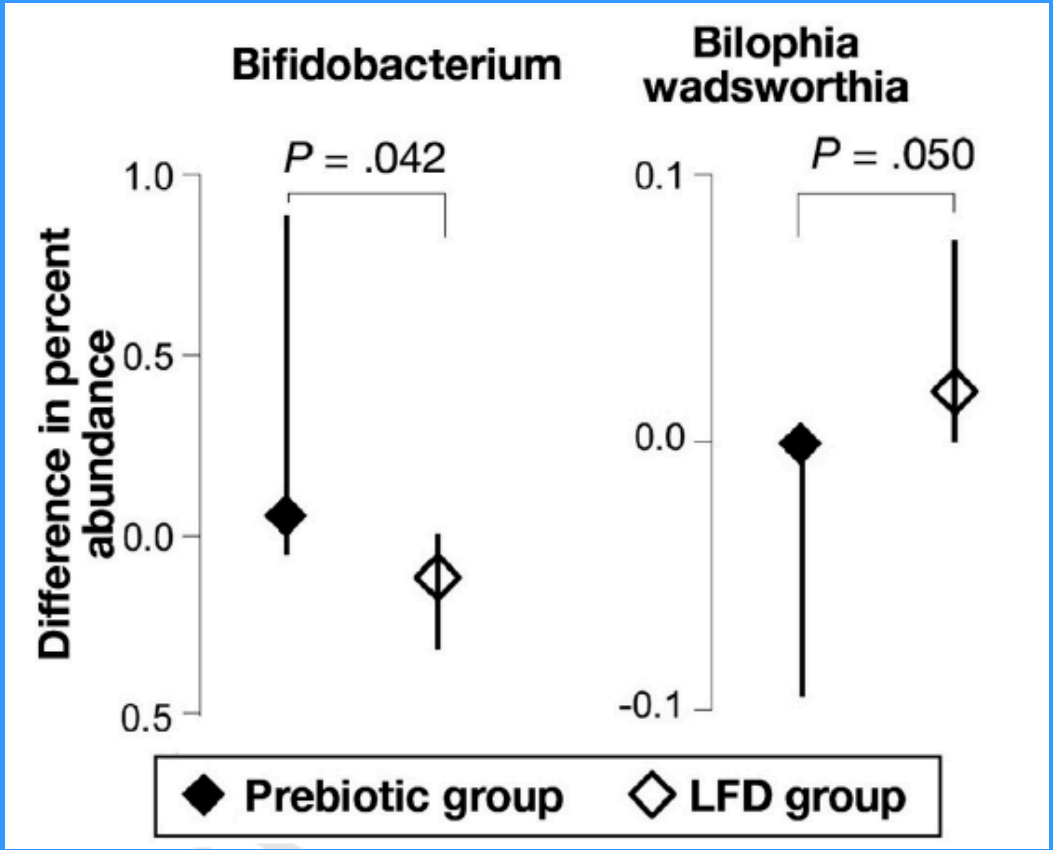
* p<0.05 vs pre-treatment

Changes in luminal bacteria during treatment



Huaman et al, Gastroenterology 2018

Functional gut symptoms: treatment strategies

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