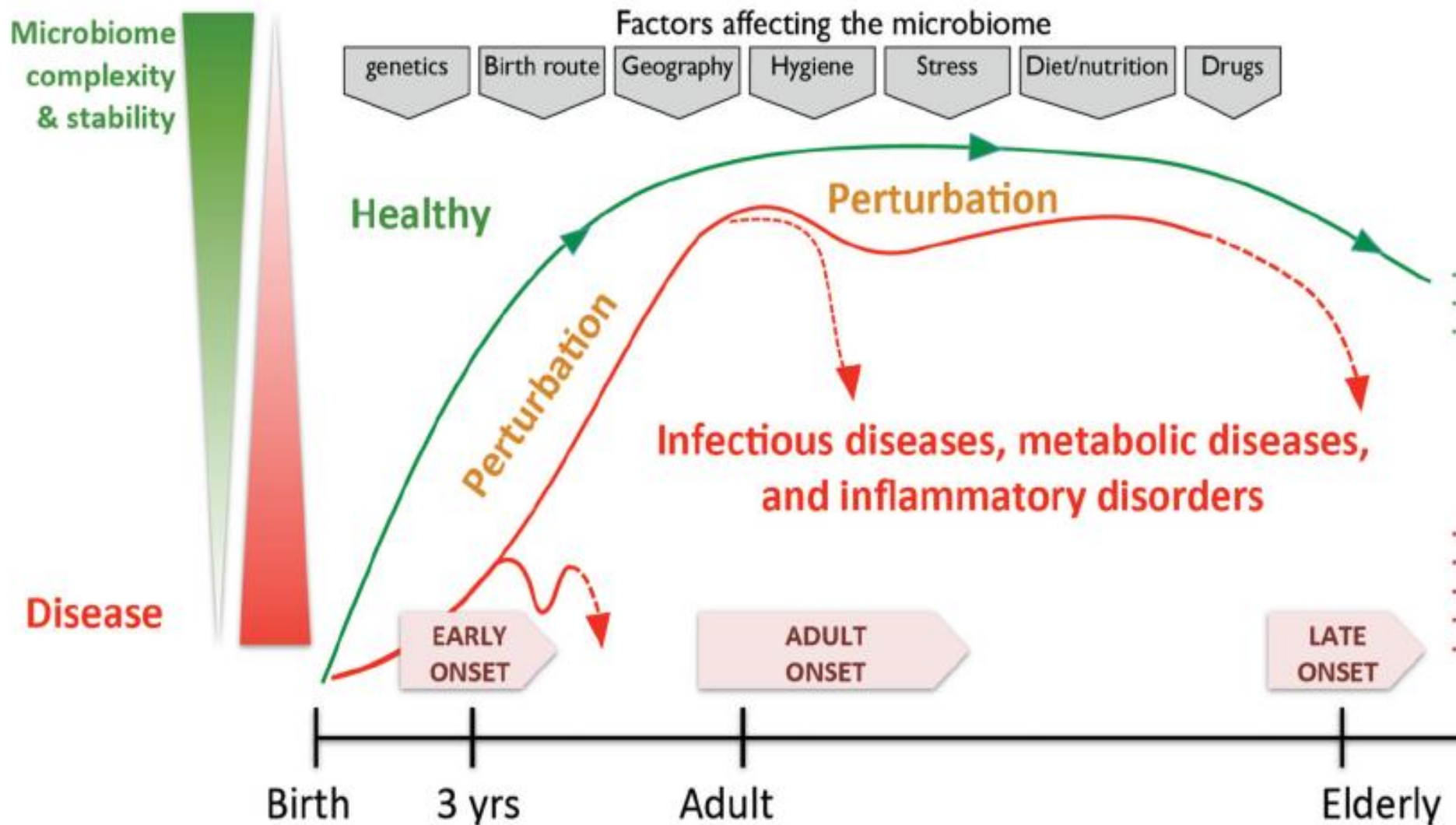


Patai Árpád

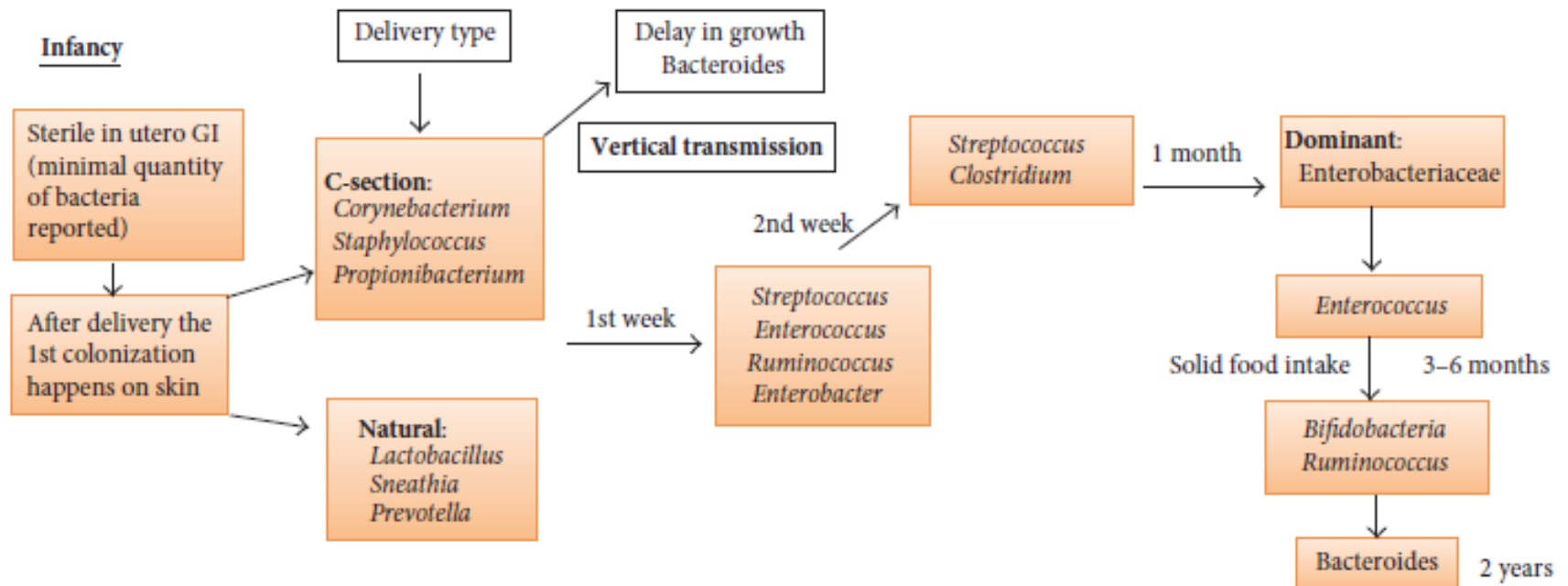
Antibioticummal összefüggő dysbiosis kezelése

A mikrobiom egészségesegekben és betegekben

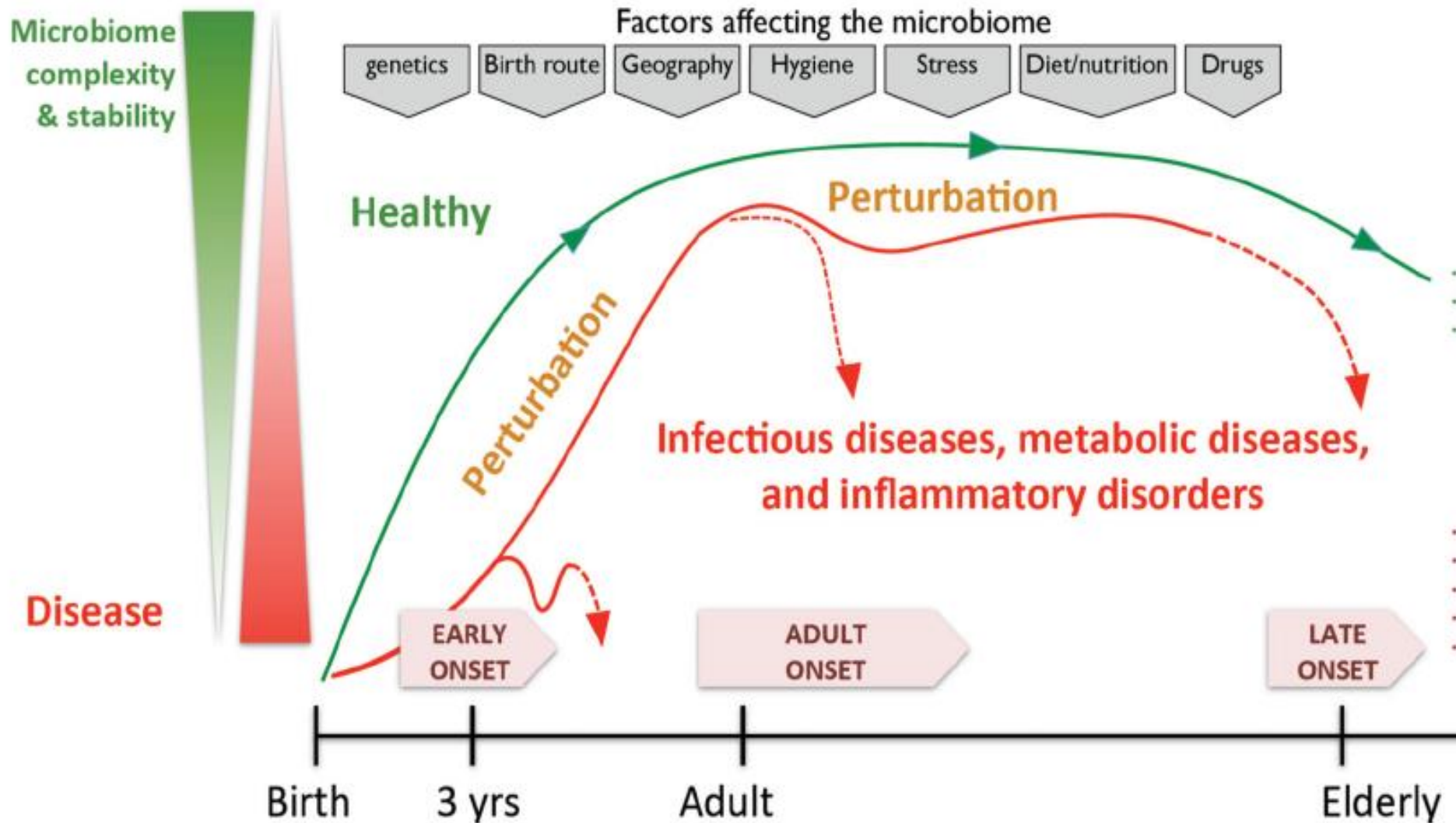


Gastroenterology. 2014 May ; 146(6): 1489–1499.

A bél mikrobiom kialakulása 2 éves korig

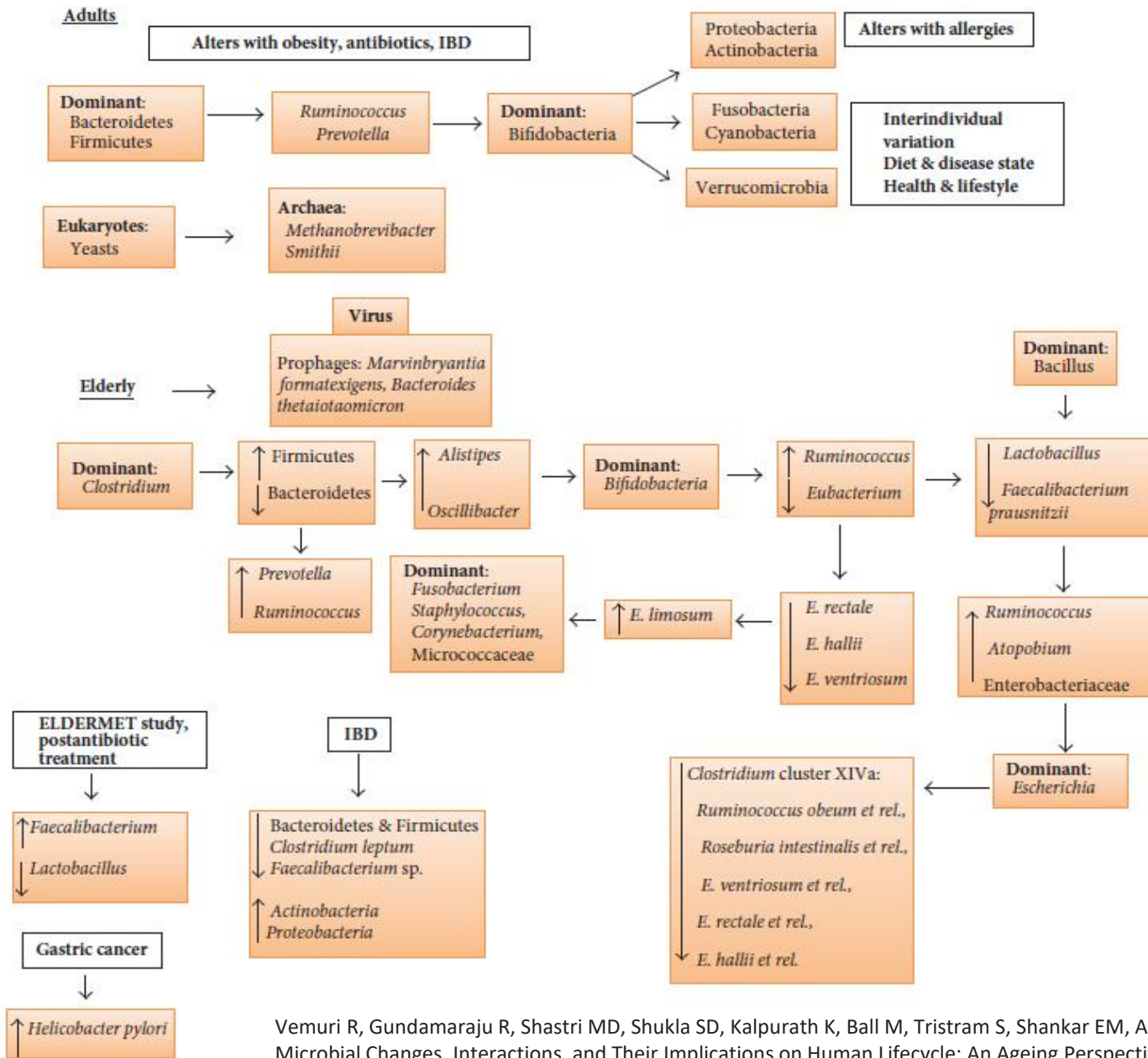


A mikrobiom egészségesebben és betegekben



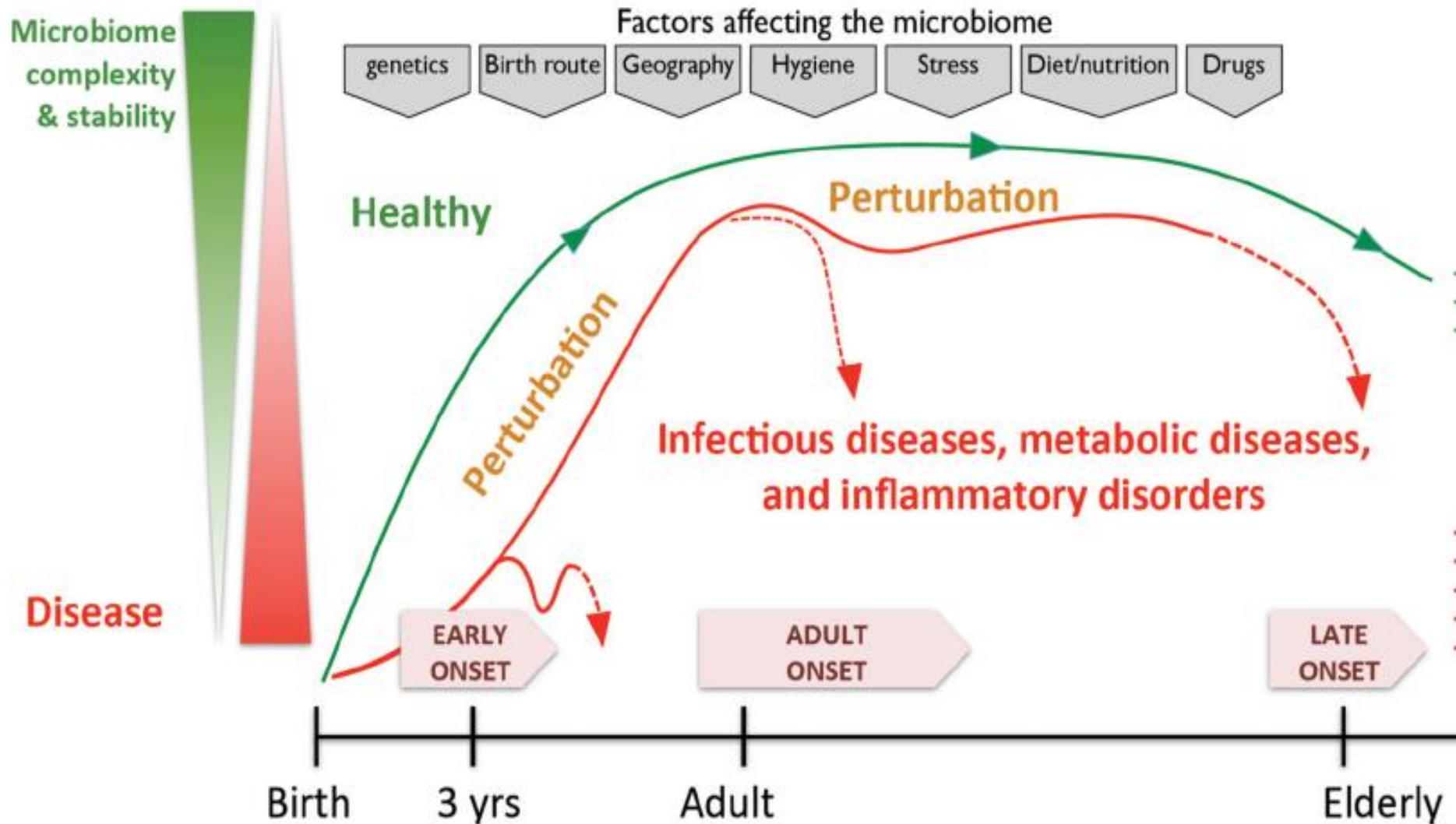
Gastroenterology. 2014 May ; 146(6): 1489–1499.

A bélmicrobiom felnőttkorban



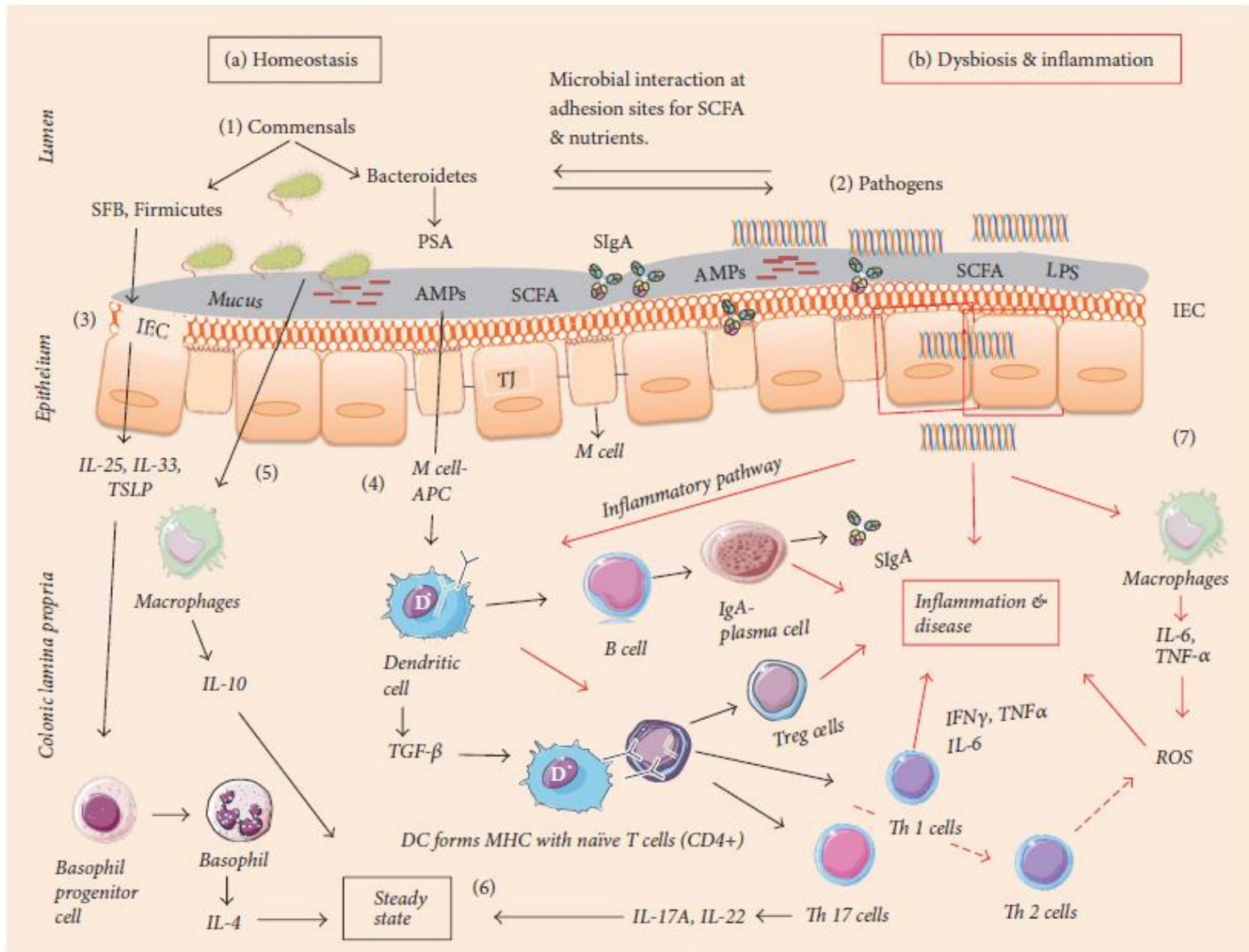
Vemuri R, Gundamaraju R, Shastri MD, Shukla SD, Kalpurath K, Ball M, Tristram S, Shankar EM, Ahuja K, Eri R. Gut Microbial Changes, Interactions, and Their Implications on Human Lifecycle: An Ageing Perspective. *Biomed Res Int*. 2018 Feb 26;2018:4178607. doi: 10.1155/2018/4178607. PMID: 29682542; PMCID: PMC5846367.

A mikrobiom egészségesebben és betegekben



Gastroenterology. 2014 May ; 146(6): 1489–1499.

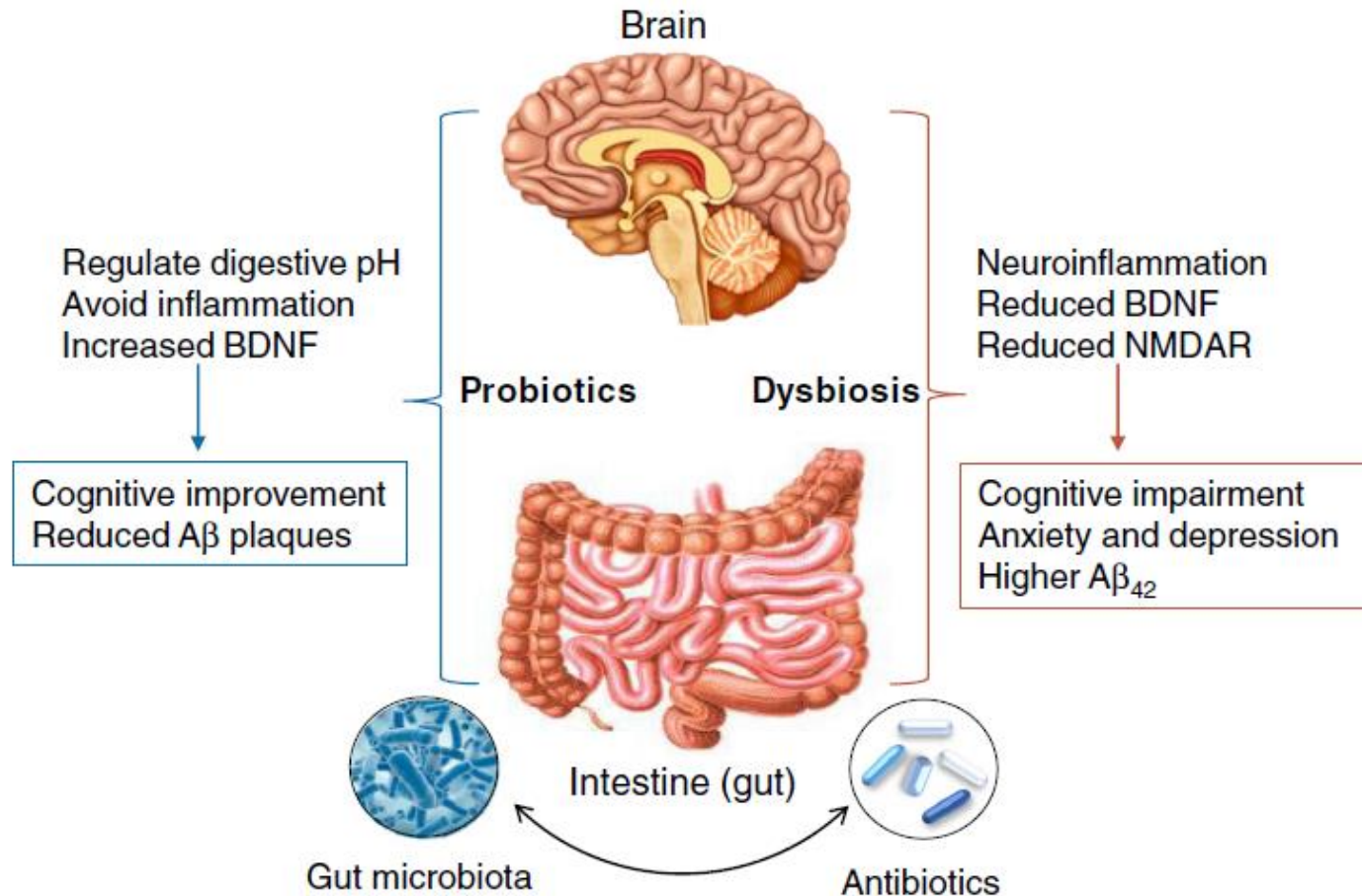
A bél mikrobiom és az immunrendszer kapcsolata



Gut Dysbiosis and Intestinal Barrier Dysfunction: Potential Explanation for Early-Onset Colorectal Cancer

*Siti Maryam Ahmad Kendong^{1,2}, Raja Affendi Raja Ali^{3,4},
Khairul Najmi Muhammad Nawawi^{3,4}, Hajar Fauzan Ahmad^{5,6}
and Norfilza Mohd Mokhtar^{1,4*}*

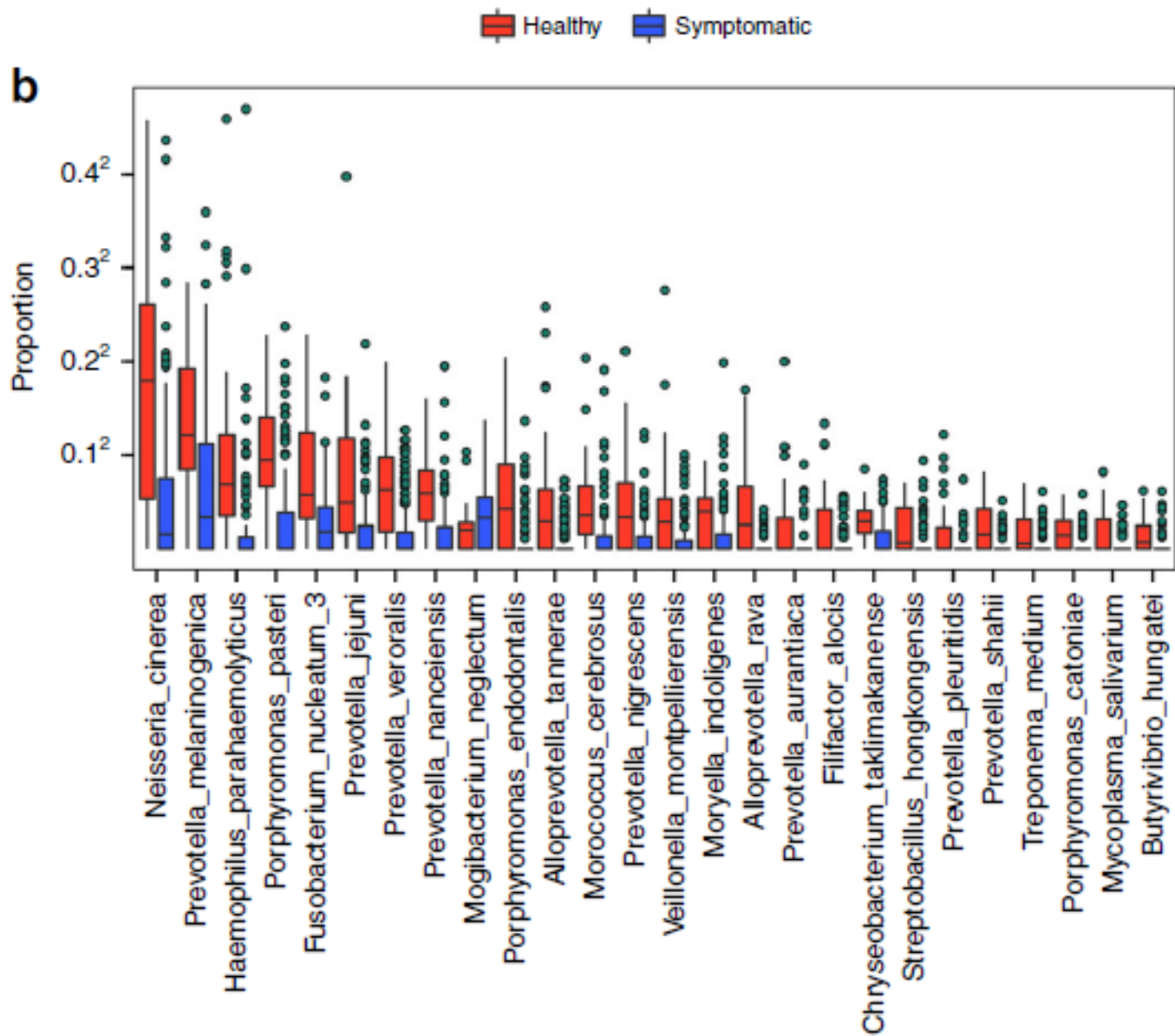
A vékonybél dysbiosis hatása a cognitív funkcióra, a szorongásra és a depresszióra



Antibacterialis kezelés hatása a microbiomra

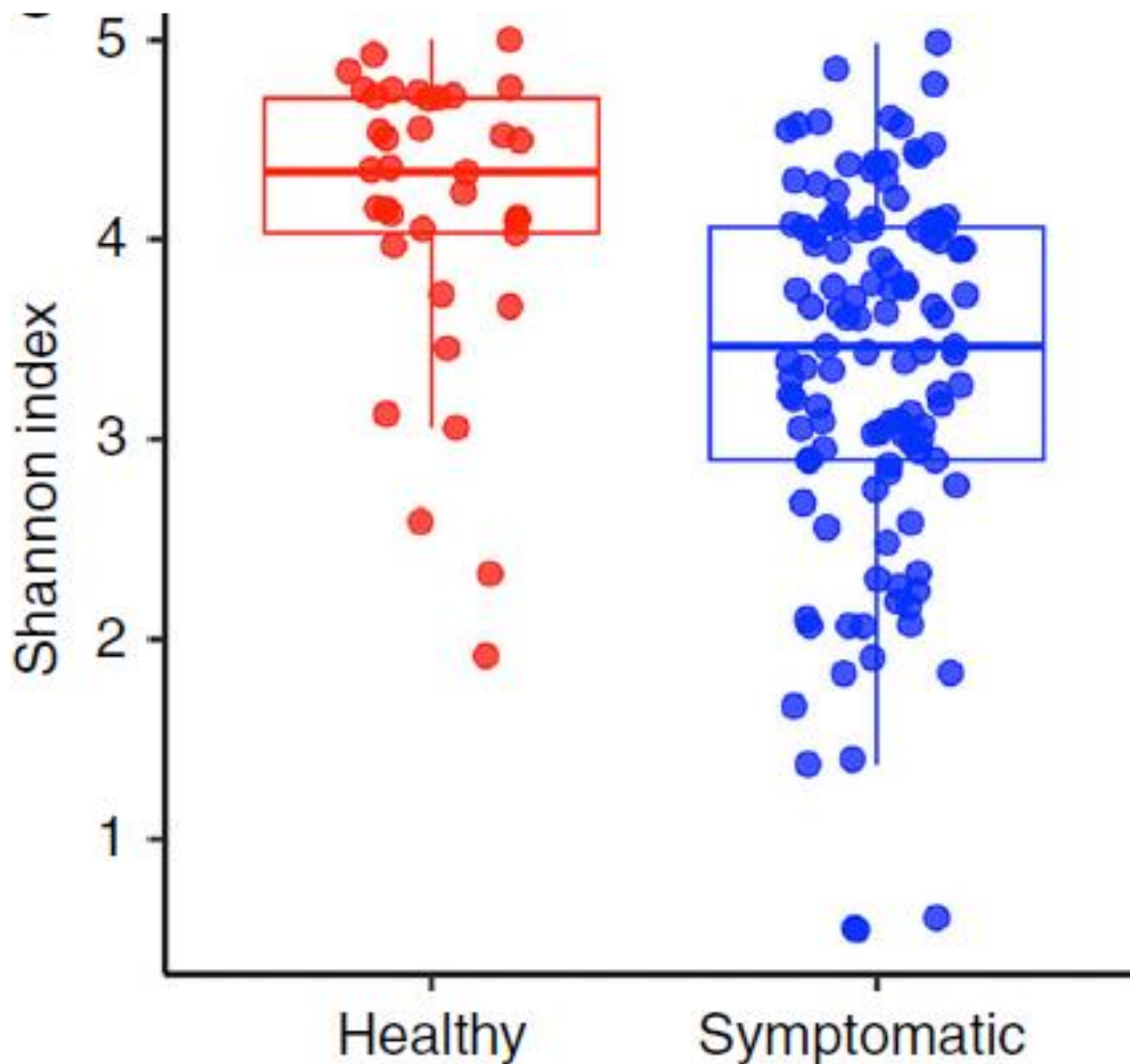
Study details	Sample details ¹	Methods	Outcome	Reference
Comparative study of faecal microbiota	n=94 – healthy = 35; – hospitalised = 38; – hospitalised + antibiotics = 21	16S rRNA gene sequencing, RT- PCR	profound changes in fecal microbiota were observed during antibiotic treatment in hospitalised and the opportunistic species <i>Enterococcus faecalis</i> proliferated	Bartosch <i>et al.</i> , 2004
Molecular-phylogentic characterisation of microbiota	n=190 – CD = 68; – UC = 61; – non-IBD controls = 61	16S rRNA analysis & clone-based sequencing	the findings indicate significant abnormalities in the microbiota of a subset of CD and UC individuals	Frank <i>et al.</i> , 2007
Comparative study on healthy adults with Ciprofloaxin treatment	n=3 adults	16S rRNA gene & 454 pyrosequencing	Ciprofloxacin reduced the diversity of the intestinal microbiota, with significant effects on about one-third of the bacterial taxa	Dethlefsen <i>et al.</i> , 2008
Observational study on hospitalised elderly with CDAD	n=292 – CDAD positive = 22; – controls =252; – asymptomatic CDAD = 18	16S rRNA gene sequencing	a marked reduction in microbial diversity at genus level was observed in patients who had been diagnosed with CDAD	Rea <i>et al.</i> , 2012
ELDERMET study (post-antibiotic therapy)	n=184	16S rRNA gene sequencing	the impact of antibiotic therapy on the intestinal microbiota in the elderly should be considered for long-term health effects	O'Sullivan <i>et al.</i> , 2013
Elderly on antibiotics (multi-omics study)	n=1	16S rRNA gene sequencing	the results demonstrated that antibiotics targeting specific pathogenic infections and diseases may alter gut microbial ecology	Pérez-Cobas <i>et al.</i> , 2013
Prospective cohort study	n=32 – Ciprofloxacin = 10; – Nitrofurantoin = 10; – Fosfomycin = 2; – control = 10	16S rRNA gene sequencing	this study supported the use of Nitrofurantoin over Fluoroquinolones for treatment of uncomplicated UTIs to minimise perturbation of intestinal microbiota	Stewardson <i>et al.</i> , 2015
Comparative study	n=43 – PPI = 26; – antibiotics = 17	16S rRNA gene & 454 pyrosequencing	PPIs appeared to attenuate the negative effects of antibiotics on the gut microbiome	O'Donoghue <i>et al.</i> , 2016

Vemuri RC, Gundamaraju R, Shinde T, Eri R. Therapeutic interventions for gut dysbiosis and related disorders in the elderly: antibiotics, probiotics or faecal microbiota transplantation? *Benef Microbes*. 2017;26;8(2):179-192. doi: 10.3920/BM2016.0115.



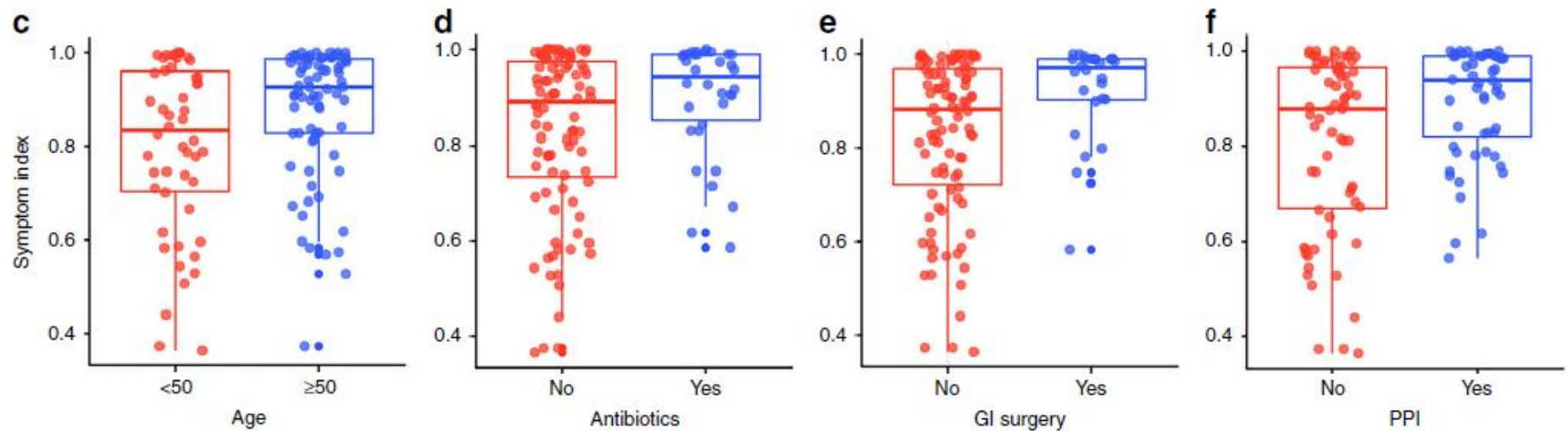
Saffouri GB, Shields-Cutler RR, Chen J, Yang Y, Lekatz HR, Hale VL, Cho JM, Battaglioli EJ, Bhattarai Y, Thompson KJ, Kalari KK, Behera G, Berry JC, Peters SA, Patel R, Schuetz AN, Faith JJ, Camilleri M, Sonnenburg JL, Farrugia G, Swann JR, Grover M, Knights D, Kashyap PC. Small intestinal microbial dysbiosis underlies symptoms associated with functional gastrointestinal disorders. Nat Commun. 2019 May 1;10(1):2012.

A mikrobiom diversitásának csökkenése tünetképző



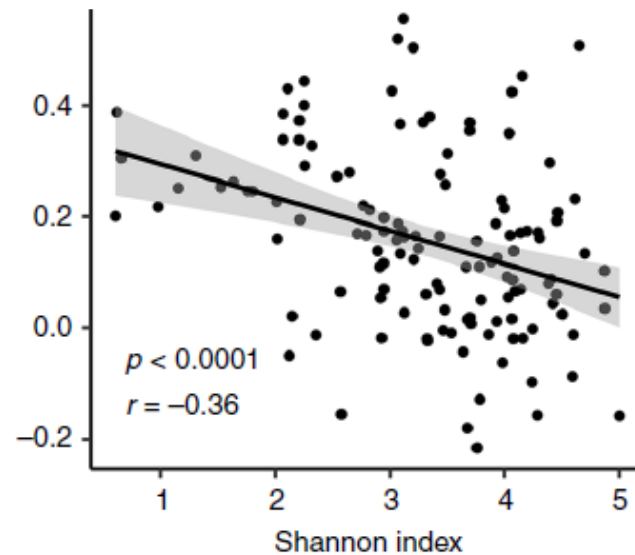
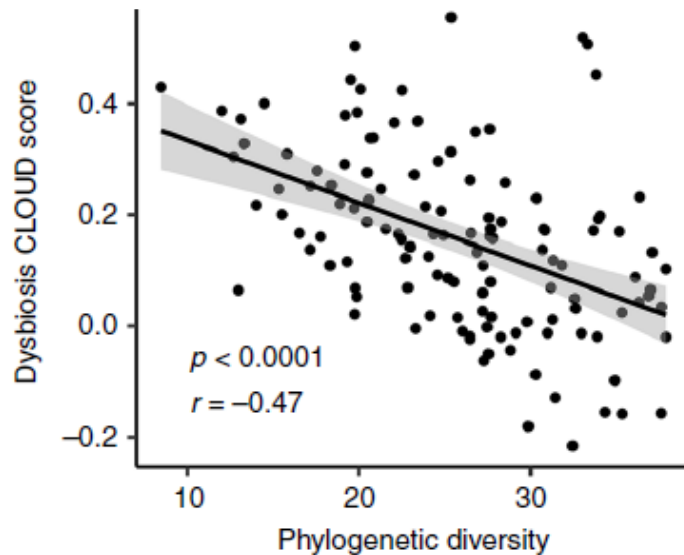
Saffouri GB, Shields-Cutler RR, Chen J, Yang Y, Lekatz HR, Hale VL, Cho JM, Battaglioli EJ, Bhattarai Y, Thompson KJ, Kalari KK, Behera G, Berry JC, Peters SA, Patel R, Schuetz AN, Faith JJ, Camilleri M, Sonnenburg JL, Farrugia G, Swann JR, Grover M, Knights D, Kashyap PC. Small intestinal microbial dysbiosis underlies symptoms associated with functional gastrointestinal disorders. *Nat Commun.* 2019 May 1;10(1):2012.

A functionális bélbetegségek tüneti scoreját befolyásoló hatások



Saffouri GB, Shields-Cutler RR, Chen J, Yang Y, Lekatz HR, Hale VL, Cho JM, Battaglioli EJ, Bhattarai Y, Thompson KJ, Kalari KK, Behera G, Berry JC, Peters SA, Patel R, Schuetz AN, Faith JJ, Camilleri M, Sonnenburg JL, Farrugia G, Swann JR, Grover M, Knights D, Kashyap PC. Small intestinal microbial dysbiosis underlies symptoms associated with functional gastrointestinal disorders. *Nat Commun.* 2019 May 1;10(1):2012.

A dysbiosis CLOUD score a vékonybél mikrobiom diversitásának növekedésével csökken



Saffouri GB, Shields-Cutler RR, Chen J, Yang Y, Lekatz HR, Hale VL, Cho JM, Battaglioli EJ, Bhattarai Y, Thompson KJ, Kalari KK, Behera G, Berry JC, Peters SA, Patel R, Schuetz AN, Faith JJ, Camilleri M, Sonnenburg JL, Farrugia G, Swann JR, Grover M, Knights D, Kashyap PC. Small intestinal microbial dysbiosis underlies symptoms associated with functional gastrointestinal disorders. Nat Commun. 2019 May 1;10(1):2012.

Patai Árpád

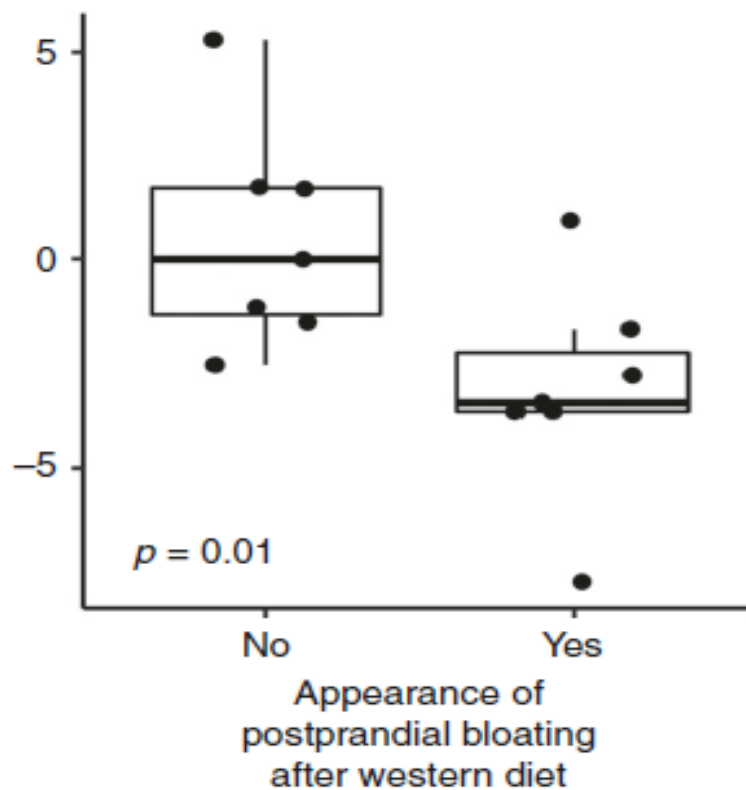
Antibioticummal összefüggő dysbiosis kezelése

Antibiosis mérlegelése

Antibiosis mérlegelése

Diéta

A „nyugati” diéta növeli a postprandialis puffadást



Saffouri GB, Shields-Cutler RR, Chen J, Yang Y, Lekatz HR, Hale VL, Cho JM, Battaglioli EJ, Bhattarai Y, Thompson KJ, Kalari KK, Behera G, Berry JC, Peters SA, Patel R, Schuetz AN, Faith JJ, Camilleri M, Sonnenburg JL, Farrugia G, Swann JR, Grover M, Knights D, Kashyap PC. Small intestinal microbial dysbiosis underlies symptoms associated with functional gastrointestinal disorders. Nat Commun. 2019 May 1;10(1):2012.

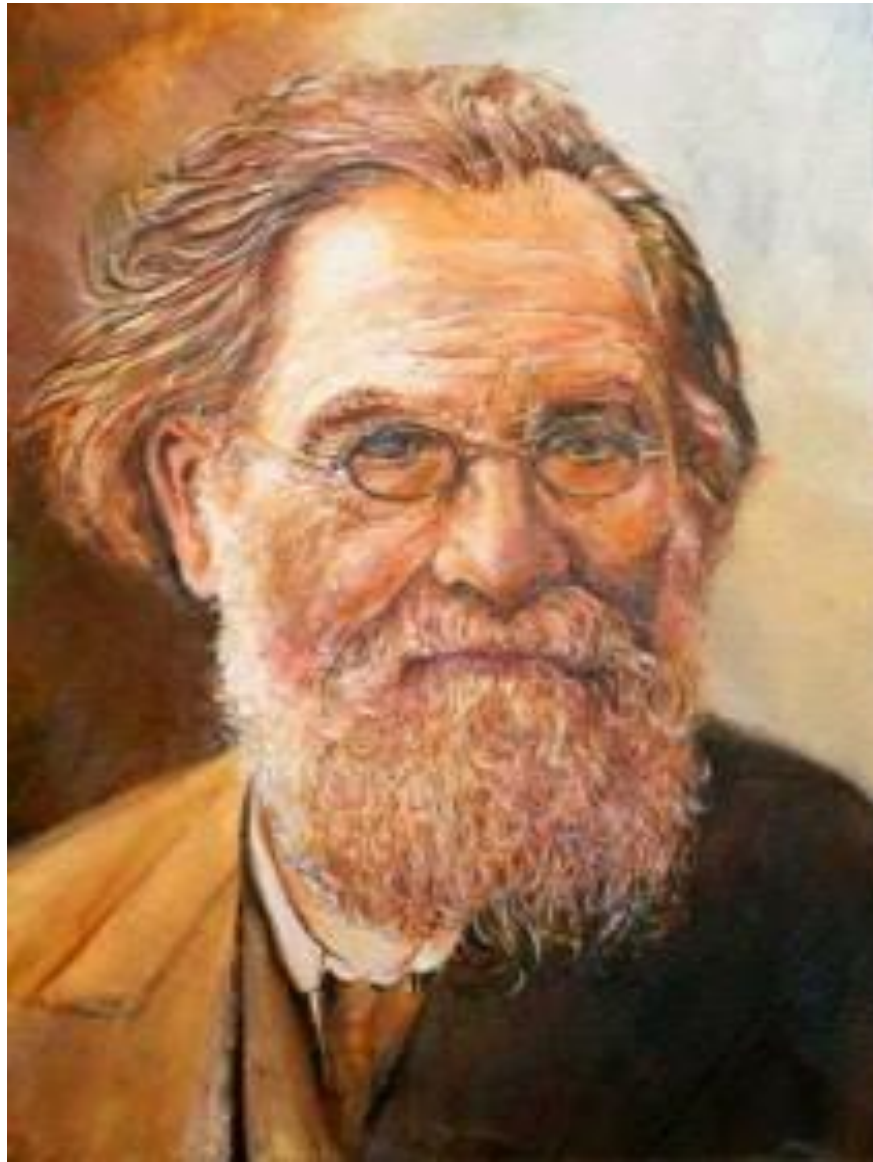
Butler MI, Bastiaanssen TFS, Long-Smith C, Berding K, Morkl S, Cusack AM, Strain C, Busca K,

Porteous-Allen P, Claesson MJ, Stanton C, Cryan JF, Allen D, Dinan TG. **Recipe**

for a Healthy Gut: Intake of Unpasteurised Milk

Is Associated with

Increased *Lactobacillus* Abundance in the Human Gut Microbiome. *Nutrients*. 2020 May 19;12(5):1468. doi: 10.3390/nu12051468. PMID: 32438623; PMCID: PMC7285075.



Ilja Iljics Mecsnyikov (1845-1916)

Antibiosis mérlegelése

Diéta

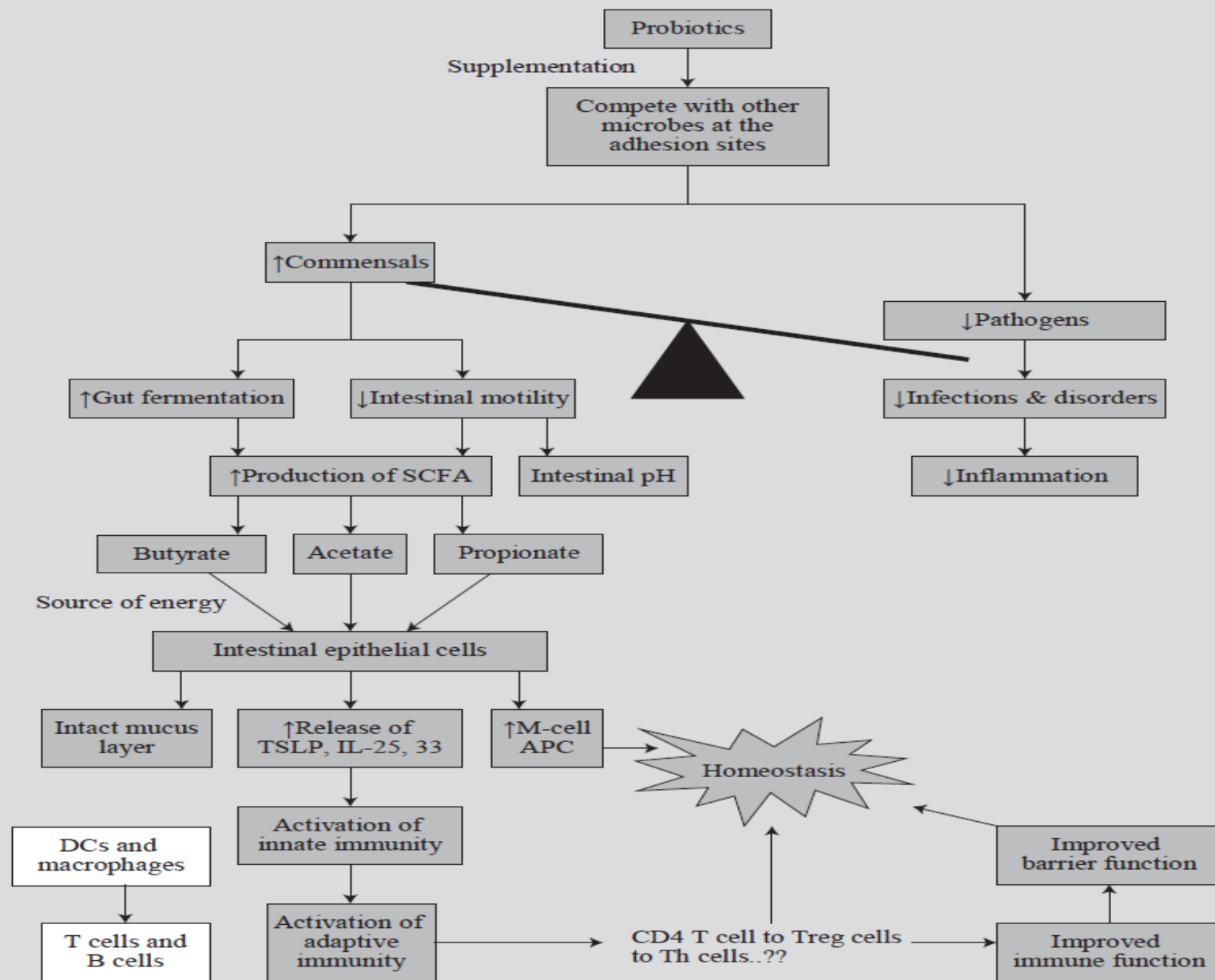
Bacteriotherapia

Bacteriotherapia / 1. Prebioticum

Prebiotics	Inulin	Lipid control, cardiovascular effects, cancer prevention
	Xylooligosaccharide	Lipid control, cancer prevention
	Oligofructose	Cancer prevention, treatment of recurrent CDI
	Fructooligosaccharide	Lipid control, cardiovascular effects, prevention of atopic dermatitis

Bacteriotherapia / 2. Probioticum

Probiotics	<i>Saccharomyces boulardii</i>	Prevention of AAD, prevention and treatment of infectious diarrhea, prevention of CDI, improvement in symptoms of IBS
	<i>Lactobacillus rhamnosus</i> GG	Prevention of AAD, CDI, and infectious diarrhea; treatment of IBS and prevention of atopic dermatitis
	<i>Lactobacillus reuteri</i> (strains SD2112 and RC14)	Treatment of functional bowel disease (eg, IBS) and treatment of vaginosis/vaginitis
	<i>Lactobacillus plantarum</i> 299V DSM 9843	Treatment of IBS
	<i>Lactobacillus acidophilus</i> (strain NCDO1748 and other strains)	Prevention of necrotizing enterocolitis, radiation enteritis, and vaginitis
	<i>Lactobacillus casei</i> DN-114001	Prevention of AAD, infectious diarrhea, and CDI
	<i>Lactobacillus rhamnosus</i> GR-1	Treatment of vaginosis/vaginitis
	<i>Lactobacillus gasseri</i> SBT2055	Associated with weight loss
	<i>Escherichia coli</i> DSM 17252	Treatment of IBS
	<i>Streptococcus faecalis</i>	Treatment of IBS
	<i>Bifidobacterium infantis</i> B5624	Treatment of IBS
	<i>Bifidobacterium bifidum</i> strain NCDO1463	Treatment of necrotizing enterocolitis
	<i>Bifidobacterium lactis</i>	Prevention of atopic dermatitis
	<i>Lactobacillus brevis</i> CD2	Reduce incidence of radiation- and chemotherapy-induced mucositis
	<i>Lactobacillus casei</i> , <i>Lactobacillus acidophilus</i> (Bio-K+ CL1285)	Prevention of AAD and CDI
	Eight probiotic strains (VSL#3) ^a	Management of IBS, IBD, and pouchitis; prevention of radiation-induced diarrhea



Probioticum hatása az antibiotist követő hasmenésre gyermekkorban

1.1.2 Incidence of Diarrhea: Placebo controlled trials

Arvola 1999	3	59	9	60	2.2%	0.34 [0.10, 1.19]
Esposito 2017	3	30	12	30	2.4%	0.25 [0.08, 0.80]
Fox 2015	0	34	6	36	0.6%	0.08 [0.00, 1.39]
Georgieva 2015	1	49	1	48	0.6%	0.98 [0.06, 15.22]
Jirapinyo 2002	3	8	8	10	3.0%	0.47 [0.18, 1.21]
King 2010	3	8	4	7	2.6%	0.66 [0.22, 1.97]
Kodadad 2013	2	33	8	33	1.7%	0.25 [0.06, 1.09]
Kolodziej 2018	14	123	8	124	3.5%	1.76 [0.77, 4.05]
Kotowska 2005	4	119	22	127	2.8%	0.19 [0.07, 0.55]
LaRosa 2003	14	48	31	50	5.0%	0.47 [0.29, 0.77]
Merenstein 2009	11	57	14	60	4.0%	0.83 [0.41, 1.67]
Olek 2017	6	218	9	220	2.8%	0.67 [0.24, 1.86]
Ruszczynski 2008	9	120	20	120	3.8%	0.45 [0.21, 0.95]
Saneeyan 2011	3	25	13	25	2.5%	0.23 [0.07, 0.71]
Sykora 2005	3	39	5	47	1.9%	0.72 [0.18, 2.84]
Szajewska 2009	2	34	6	30	1.7%	0.29 [0.06, 1.35]
Szymanski 2008	1	40	2	38	0.8%	0.47 [0.04, 5.03]
Tankanow 1990	10	15	16	23	5.2%	0.96 [0.61, 1.50]
Vanderhoof 1999	7	93	25	95	3.6%	0.29 [0.13, 0.63]
Subtotal (95% CI)		1152		1183	50.6%	0.50 [0.37, 0.67]

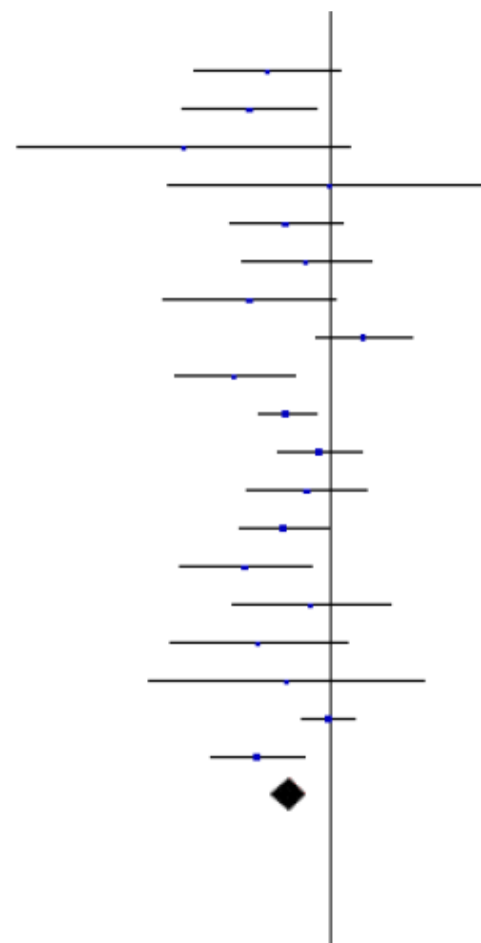
Total events

99

219

Heterogeneity: $\tau^2 = 0.18$; $\chi^2 = 32.50$, $df = 18$ ($P = 0.02$); $I^2 = 45\%$

Test for overall effect: $Z = 4.48$ ($P < 0.00001$)



Guo Q, Goldenberg JZ, Humphrey C, El Dib R, Johnston BC. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. Cochrane Database Syst Rev. 2019 Apr 30;4(4):CD004827. doi: 10.1002/14651858.CD004827.pub5. PMID: 31039287; PMCID: PMC6490796.

Guo Q, Goldenberg JZ, Humphrey C, El Dib R, Johnston BC.
Probiotics for the prevention of pediatric antibiotic-associated
diarrhea. Cochrane Database Syst Rev. 2019 Apr 30;4(4):CD004827.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Arvola 1999	+	?	+	-	?	+
Benhamou 1999	?	?	?	-	?	?
Conway 2007	+	+	-	?	?	+
Correa 2005	?	?	+	+	?	?
Destura unpublished	+	?	-	+	+	+
Dharani 2017	?	?	?	+	?	?
Erdeve 2004	+	?	?	-	?	?
Esposito 2017	?	?	?	+	?	?
Fox 2015	+	+	+	+	+	+
Georgieva 2015	+	+	+	?	+	-

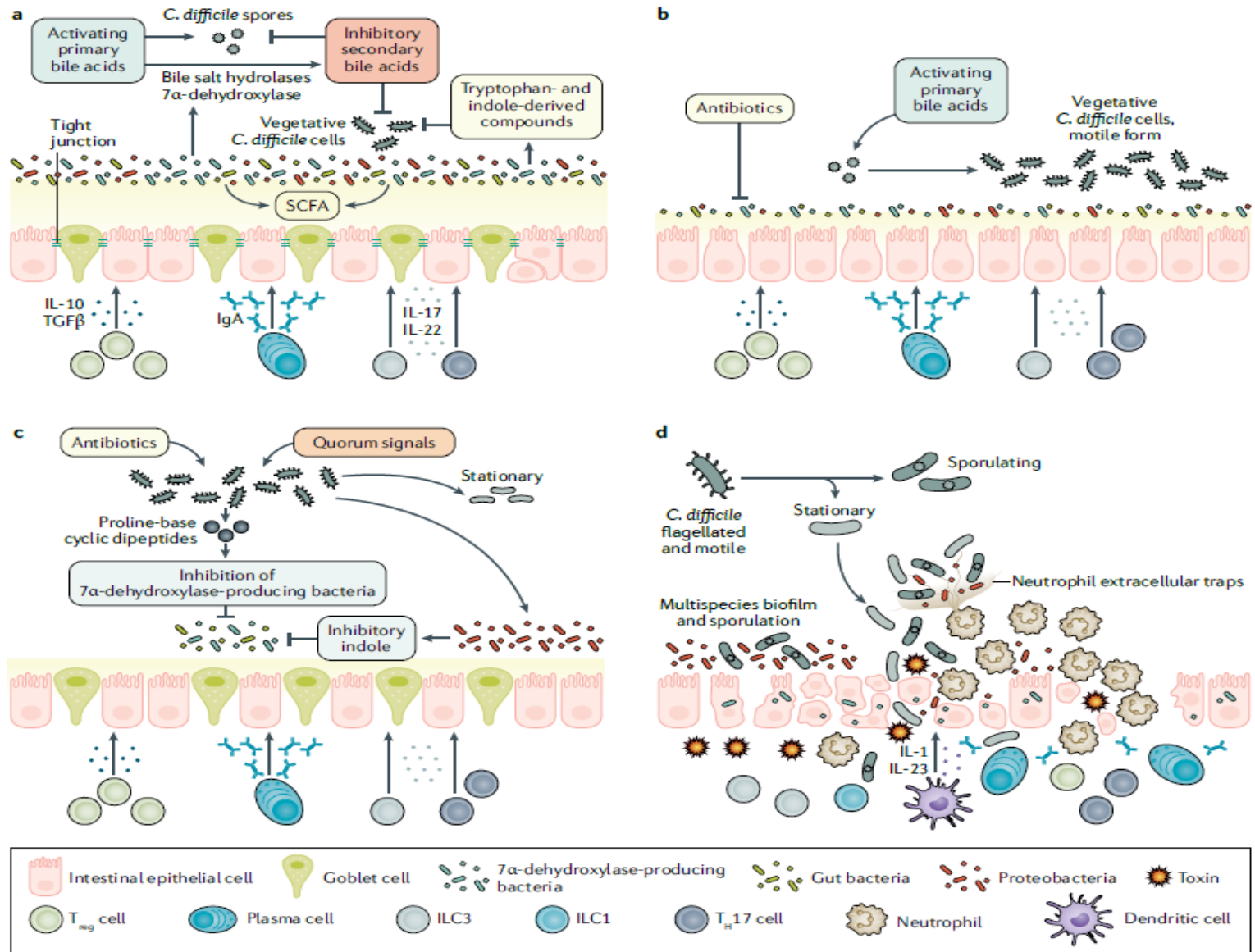
Probioticum hatása az antibiotist követő hasmenésre gyermekkorban

Intervention: Probiotics treatment with either *Bacillus spp.*, *Bifidobacterium spp.*, *Clostridium butyricum spp.*, *Lactobacilli spp.*, *Lactococcus spp.*, *Leuconostoc cremoris spp.*, *Saccharomyces spp.*, or *Streptococcus spp.*, alone or in combination

Outcomes	Anticipated absolute effects * (95% CI)			Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Baseline risk	Corresponding risk				
	Risk in Control	Risk with Probiotics	Risk Difference			
Incidence of AAD Follow-up: 5 days to 12 weeks	190 per 1000 ¹	86 per 1000 (68 to 106)	104 fewer AAD cases per 1000 (84 fewer to 122 fewer)	RR 0.45 (0.36 to 0.56)	6352 (33 studies)	 Moderate ^{2,3,4}

Guo Q, Goldenberg JZ, Humphrey C, El Dib R, Johnston BC. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. Cochrane Database Syst Rev. 2019 Apr 30;4(4):CD004827. doi: 10.1002/14651858.CD004827.pub5. PMID: 31039287; PMCID: PMC6490796.

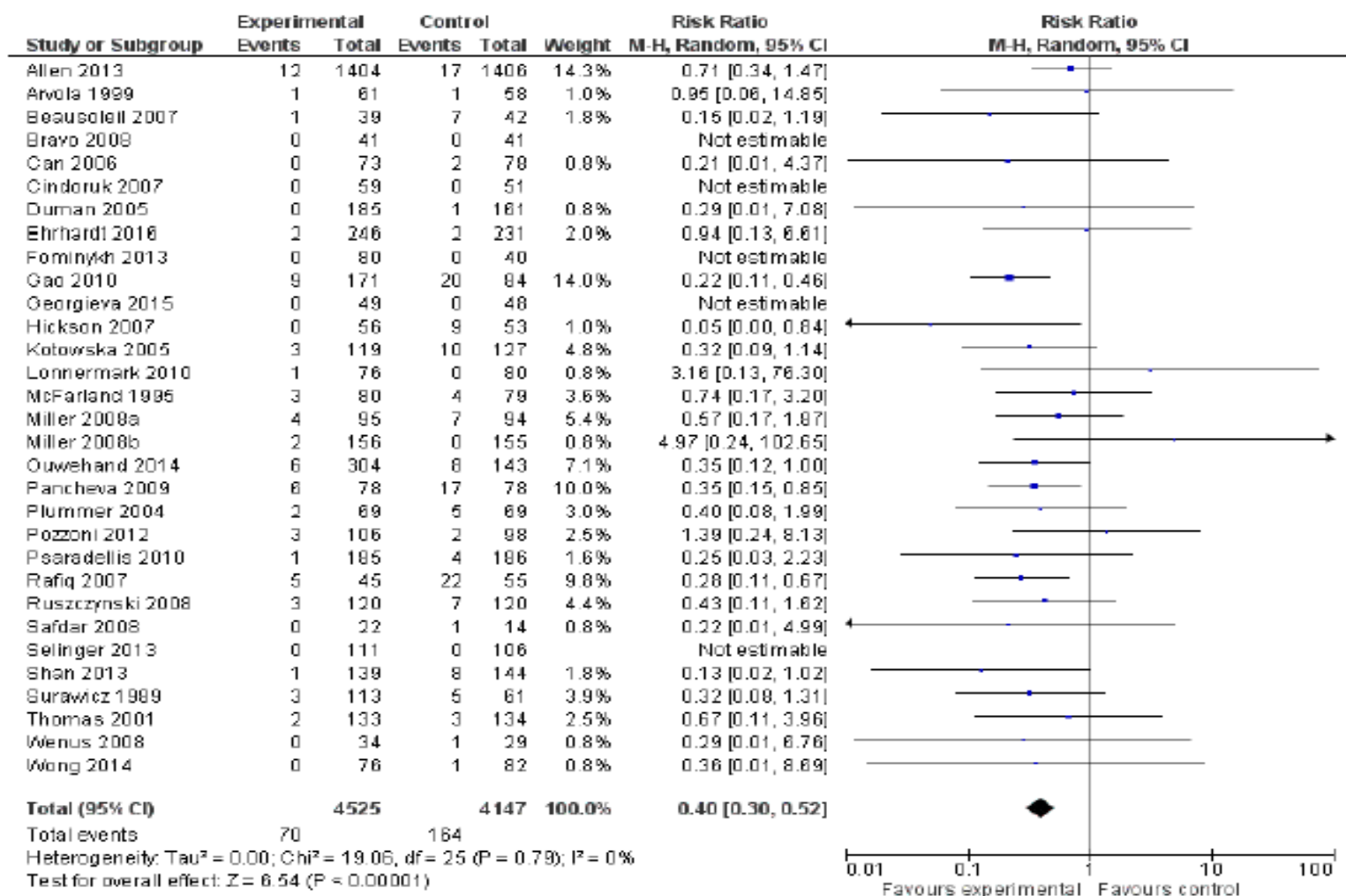
Clostridioides difficile



Khoruts A, Staley C, Sadowsky MJ. Faecal microbiota transplantation for *Clostridioides difficile*: mechanisms and pharmacology. *Nat Rev Gastroenterol Hepatol*. 2021 Jan;18(1):67-80. doi: 10.1038/s41575-020-0350-4. Epub 2020 Aug 25. PMID: 32843743.

Probioticum hatása a *C. difficile* asszociált hasmenésre

Figure 3. Forest plot of comparison: 1 *C. difficile* associated diarrhea, outcome: 1.1 Incidence CDAC complete case.



Probioticum hatása a *C. difficile* asszociált hasmenésre

There was a statistically significant test for subgroup difference when comparing the adult subgroup (RR 0.62, 95% CI 0.51 to 0.76, $I^2 = 59\%$, $n = 7036$) to the child subgroup (RR 0.38, 95% CI 0.29 to 0.49, $I^2 = 0\%$, $n = 1141$) for the AAD outcome ($P < 0.01$) but not for other outcomes.

Probioticum hatása a *C. difficile* asszociált hasmenésre

There was a statistically significant test for subgroup difference when comparing the adult subgroup (RR 0.62, 95% CI 0.51 to 0.76, $I^2 = 59\%$, $n = 7036$) to the child subgroup (RR 0.38, 95% CI 0.29 to 0.49, $I^2 = 0\%$, $n = 1141$) for the AAD outcome ($P < 0.01$) but not for other outcomes.

C. difficile in the stool. *C. difficile* detection was 15.5% (98/633) in the probiotics group compared to 17.0% (99/581) in the placebo or no treatment control group (RR 0.86, 95% CI 0.67 to 1.10;

Probioticum hatása a *C. difficile* asszociált hasmenésre

There was a statistically significant test for subgroup difference when comparing the adult subgroup (RR 0.62, 95% CI 0.51 to 0.76, $I^2 = 59\%$, $n = 7036$) to the child subgroup (RR 0.38, 95% CI 0.29 to 0.49, $I^2 = 0\%$, $n = 1141$) for the AAD outcome ($P < 0.01$) but not for other outcomes.

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A mellékhatásokban nem volt különbség a probioticummal kezelt és control csoport között

Bacteriotherapia / 3. Synbioticum

Synbiotics	<i>Lactobacillus acidophilus</i> , <i>Bifidobacterium bifidum</i> , and fructooligosaccharides	Increase HDL cholesterol and reduce fasting glycemia
	<i>Bifidobacterium</i> and fructooligosaccharides	Treatment of hepatic encephalopathy

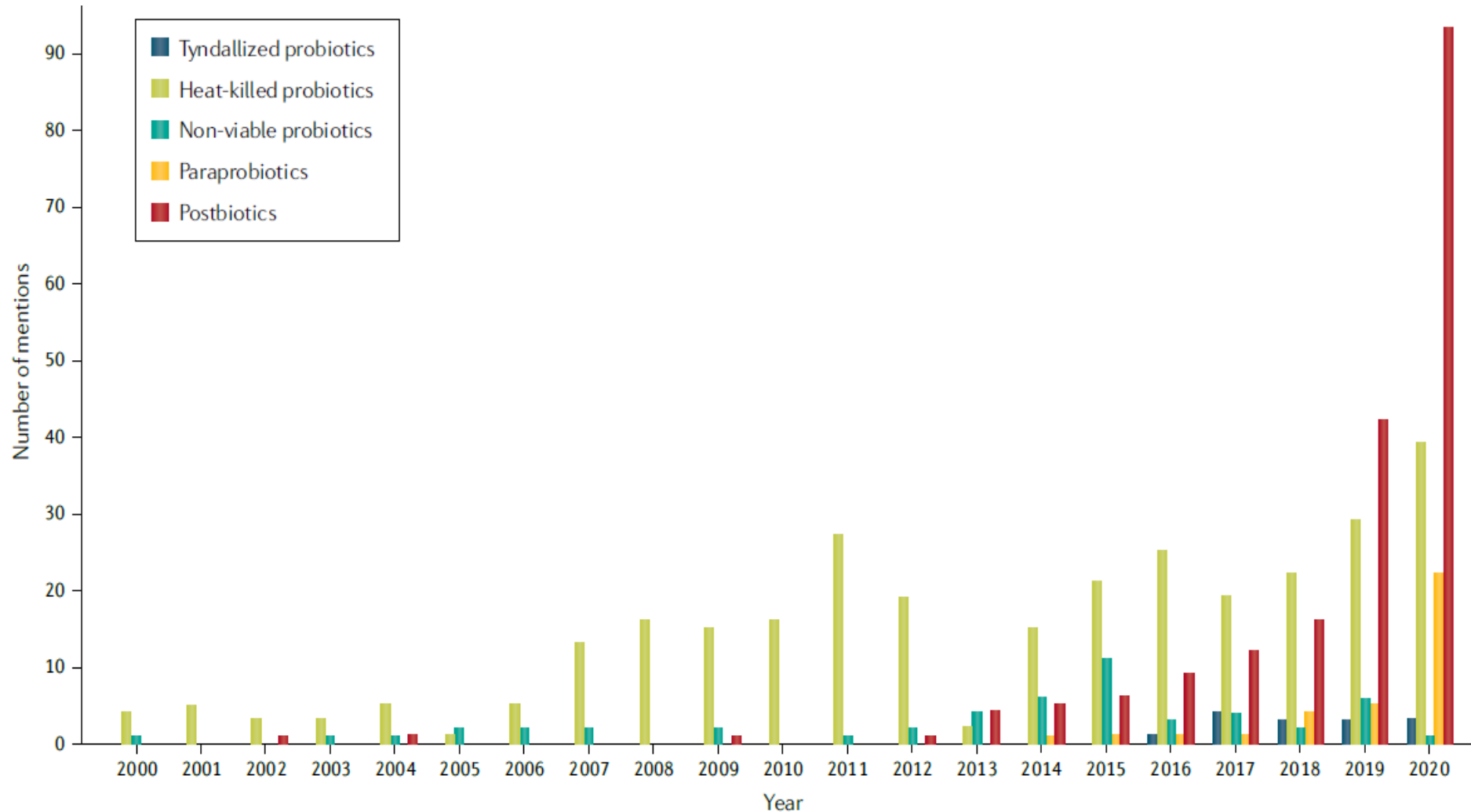
Target Condition	Synbiotic Agent	Study Outcome	Reference
Treatment of infectious diarrhea in children	<i>Bifidobacterium lactis</i> B94 plus inulin	Randomized, double-blind, placebo-controlled trial. N = 156. <i>B. lactis</i> B94 dose of 5×10^{10} CFU plus 900 mg inulin (Maflo sachet) was given once a day for 5 days. The duration of diarrhea was significantly reduced in the synbiotic group vs the placebo group (3.9 ± 1.2 d vs 5.2 ± 1.3 d, respectively; $P < .001$). The decrease was most pronounced in synbiotic-group cases of rotavirus diarrhea, (3.2 ± 1.3 d vs 5.2 ± 1.3 d, respectively; $P = .001$).	[115]
Constipation in adult women	<i>Lactobacillus</i> and <i>Bifidobacterium</i> strains plus FOS	Randomized, double-blind, placebo-controlled trial. N = 100. Each LACTOFOS sachet contained 6 g of FOS and 10^8 – 10^9 bacteria of <i>Lactobacillus paracasei</i> (Lpc-37), <i>Lactobacillus rhamnosus</i> (HN001), <i>Lactobacillus acidophilus</i> (NCFM), and <i>Bifidobacterium lactis</i> (HN019). Patients were given 2 daily doses of each for 30 days. Synbiotic group had increased frequency of evacuation, as well as stool consistency and shape nearer normal parameters than the placebo group, with significant benefits starting during the second and third weeks, respectively (interaction group/time, $P < .0001$).	[116]
Treatment of irritable bowel syndrome	<i>Bacillus coagulans</i> and FOS	Randomized, double-blind, placebo-controlled trial. N = 85. <i>B. coagulans</i> (15×10^7 CFU) and 100 g FOS (Lactol). Patients received synbiotic $3 \times /d$ for 12 weeks. After treatment, more reduction in abdominal pain frequency was observed with synbiotic vs placebo (score reduction 4.2 ± 1.8 vs 1.9 ± 1.5 ; $P < .001$). Diarrhea frequency was decreased in the synbiotic group, but not in the placebo group (score reduction 1.9 ± 1.2 vs 0.0 ± 0.5 ; $P < .001$).	[117]
Crohn disease	<i>Bifidobacterium longum</i> and inulin/oligofructose (Synergy 1)	Randomized, double-blind, placebo-controlled trial. N = 35. <i>B. longum</i> , 2×10^{11} CFU plus 6 g of Synergy 1 were taken 2x daily for 6 months. Significant improvements in clinical outcomes occurred with synbiotic consumption, with reductions in both Crohn disease activity indices ($P = .020$) and histological scores ($P = .018$). Significant reductions occurred in TNF- α expression in synbiotic patients at 3 months ($P = .041$). Mucosal bifidobacteria proliferated in synbiotic patients.	[118]
Treatment of ulcerative colitis	<i>Bifidobacterium longum</i> plus psyllium	Randomized controlled trial. N = 120. <i>B. longum</i> 2×10^9 CFU and 8 g doses of psyllium. The primary endpoint was scores on the IBD Questionnaire, which assesses health-related quality of life in IBD at 4 weeks. Results showed a statistically significant improvement in scores (168 to 176; $P = .03$) for the synbiotic group at the end of the study. Individual scores for synbiotics group—systemic and social functions ($P = .008$ and $P = .02$).	[119]
Treatment of ulcerative colitis	<i>Bifidobacterium breve</i> strain Yakult and GOS	Randomized controlled study. <i>B. breve</i> strain Yakult (10^9 CFU/g) $3 \times$ a day, and 5.5 g of GOS per day for 1 year. There was significantly improvement of endoscopic grading (Matts classification) in the synbiotic group vs the standard therapy group ($P < .05$).	[120]
Necrotizing enterocolitis in very low birth weight infants	<i>Bifidobacterium lactis</i> plus inulin	Randomized, double-blind, placebo-controlled trial. N = 400. 30 mg of <i>B. lactis</i> (5×10^9 CFU) plus 900 mg of inulin. One sachet per day with breast milk or formula for 8 weeks before discharge or death. The rate of NEC was lower in probiotic (2.0%) and synbiotic (4.0%) groups vs prebiotic (12.0%) and placebo (18.0%) groups ($P < .001$).	[121]
Weight gain in children with failure to thrive	<i>Bacillus coagulans</i> plus FOS	Randomized, triple-blinded, placebo-controlled. N = 84. <i>B. coagulans</i> (1.5×10^8 CFU) and 100 mg FOS. Synbiotic mixture were administered for 6 months. The increase in weight was significantly higher in synbiotics group than in controls ($P < .05$). At the beginning, the mean weights were 10.25 ± 0.20 kg and 10.750 ± 0.160 kg in intervention and control groups, respectively. After 6 months, the mean weights became 12.280 ± 0.190 and 11.760 ± 0.17 kg in intervention and control groups, respectively.	[122]
Diabetes	<i>Lactobacillus sporogenes</i> plus inulin	Randomized double-blind, crossover controlled trial. N = 62. <i>L. sporogenes</i> (1×10^7 CFU) plus 0.04 g inulin, packed in 9-g packages taken $3 \times$ a day for 6 weeks. There was a significant decrease in serum insulin levels (changes from baseline: -1.75 ± 0.60 vs 0.95 ± 1.09 mIU/mL; $P = .03$), a significant decrease in hs-CRP levels (-1057.86 ± 283.74 vs 95.40 ± 385.38 ng/mL; $P = 0.01$), a significant increase in plasma total GSH (319.98 vs 19.73 mmol/L; $P < 0.001$) and serum uric acid levels (0.7 vs 0.1 mg/dL; $P = .04$).	[123]
Nonalcoholic fatty liver disease	<i>Lactobacillus casei</i> , <i>Lactobacillus rhamnosus</i> , <i>Streptococcus thermophilus</i> , <i>Bifidobacterium breve</i> , <i>Lactobacillus acidophilus</i> , <i>Bifidobacterium longum</i> , and <i>Lactobacillus bulgaricus</i> and FOS (Protexin)	Randomized, double-blind, placebo-controlled trial. N = 52. Each Protexin capsule contained 2×10^8 CFU of probiotic mixture and FOS. The synbiotic mixture was supplemented $2 \times$ daily for 28 wk. There was a significant reduction of ALT in the synbiotic group. ALT, -25.1 (-26.2 , -24) vs -7.29 (-9.5 , -5.1) IU/L, $P < .001$; AST, -31.33 (-32.1 , -30.5) vs -7.94 (-11.1 , -4.8) IU/L, $P < .001$; gamma-glutamyltransferase, -15.08 (-15.5 , 214.7) vs -5.21 (-6.6 , -3.9) IU/L, $P < .001$; hs-CRP, -2.3 (-3 , -1.5) vs -1.04 (-1.5 , -0.6) mmol/L, $P < .05$; TNF- α , -1.4 (-1.7 , -1.1) vs -0.59 (-0.8 , -0.3) mmol/L, $P < .001$; total nuclear factor kB p65, -0.016 (-0.022 , -0.011) vs 0.001 (-0.004 , -0.007) mmol/L, $P < .001$; and fibrosis score as determined by transient elastography, -2.98 (-3.6 , -2.37) vs -0.77 (-1.32 , -0.22) kPa, $P < .001$.	[124]

Bacteriotherapia / 4. Postbioticum

Country/ region	Participants (n)	Intervention and control group	Duration of the intervention	Main conclusion	Ref.
Inactivated bacteria					
Italy	<i>Helicobacter pylori</i> -positive individuals (n = 120)	Triple therapy based on rabeprazole, clarithromycin and amoxicillin vs the same regimen supplemented with a lyophilized and inactivated culture of <i>L. acidophilus</i>	7 days	Eradication rates: triple therapy alone, 72%; triple therapy plus inactivated <i>L. acidophilus</i> , 87% ($P = 0.02$)	122
France	Patients with IBS with diarrhoea (n = 297)	Lacteol (inactivated <i>L. acidophilus</i> LB plus fermented culture medium), two capsules daily (no control)	1 month	Improved scores for pain, bloating, frequency of diarrhoea and quality of life	123
Germany	Patients with IBS (n = 443)	Non-viable, heat-inactivated <i>Bifidobacterium bifidum</i> MIMBb75 (SYN-HI-001) 1×10^9 daily vs placebo	8 weeks	Composite primary end point of $\geq 30\%$ improvement in pain and adequate relief of overall IBS symptoms in at least 4 of 8 weeks of treatment; primary end point achieved in 34% in active group vs 19% in the placebo group	25
China	Patients with chronic diarrhoea (n = 137)	Heat-killed <i>L. acidophilus</i> LB (Lacteol Fort), two capsules BID vs lacidophilin, five chewable tablets TID	4 weeks	Reduced stool frequency at weeks 2 and 4; overall symptoms improved at 4 weeks in Lacteol group	124
UK	Patients with obstructive jaundice (n = 25)	Oatmeal drink containing <i>Lactiplantibacillus plantarum</i> (formerly known as <i>Lactobacillus plantarum</i>) 299v (LP299v) vs oatmeal drink containing inactivated LP299v vs water	4 days	Measured intestinal permeability increased in water and inactivated groups; trend towards normalization in active group	126
Japan	Stress responses in undergraduate medical students taking a cadaver course (n = 32)	Heat-inactivated <i>L. gasseri</i> strain CP2305 in an acid beverage vs beverage alone	5 weeks	In male students, sleep quality was improved and diarrhoea prevented, but not in female students	155
Japan	Chronic stress responses in medical students (n = 60)	Heat-inactivated, washed and dried <i>L. gasseri</i> strain CP2305 (1×10^{10} bacterial cells per two tablets) vs placebo tablets once daily	24 weeks	Significant reduction ($P < 0.05$) in anxiety and sleep disturbance in CP2305 group accompanied by electroencephalogram changes, reduction in salivary chromogranin and resolution of stress-related microbiota changes	125
Israel	Responses to self-defence training in soldiers (n = 16)	Inactivated <i>Bacillus coagulans</i> 1×10^9 once daily vs placebo	2 weeks	No statistically significant effect on any inflammatory, endocrine or performance responses	127
Spain	Adults with and without latent tuberculosis (n = 51)	Preparation of heat-killed <i>Mycobacterium manresensis</i> in low (10^4) or high (10^5) dose vs placebo	2 weeks	Increased regulatory T cell response with both doses; well tolerated	128
China	Patients with moderate, persistent asthma	Inhaled inactivated <i>Mycobacterium phlei</i> vs salmeterol xinafoate and fluticasone propionate powder	5 days	Symptom scores and spirometry improved to the same extent in both groups	129
Australia	Patients with severe COPD (n = 38)	Inactivated, non-typable <i>H. influenzae</i> vs placebo	Three courses, each lasting 3 days on days 0, 28 and 56 and followed for up to 20 weeks	Reduced severe exacerbations by 63% and exacerbations requiring corticosteroid therapy by 56% and hospitalization by 90%	130

Salminen S, Collado MC, Endo A, Hill C, Lebeer S, Quigley EMM, Sanders ME, Shamir R, Swann JR, Szajewska H, Vinderola G. The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. *Nat Rev Gastroenterol Hepatol*. 2021 Sep;18(9):649-667. doi: 10.1038/s41575-021-00440-6.

A 'postbioticum' terminológia térhódítása



Salminen S, Collado MC, Endo A, Hill C, Lebeer S, Quigley EMM, Sanders ME, Shamir R, Swann JR, Szajewska H, Vinderola G. The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. *Nat Rev Gastroenterol Hepatol*. 2021 Sep;18(9):649-667. doi: 10.1038/s41575-021-00440-6.

A ,postbioticum' hatásai

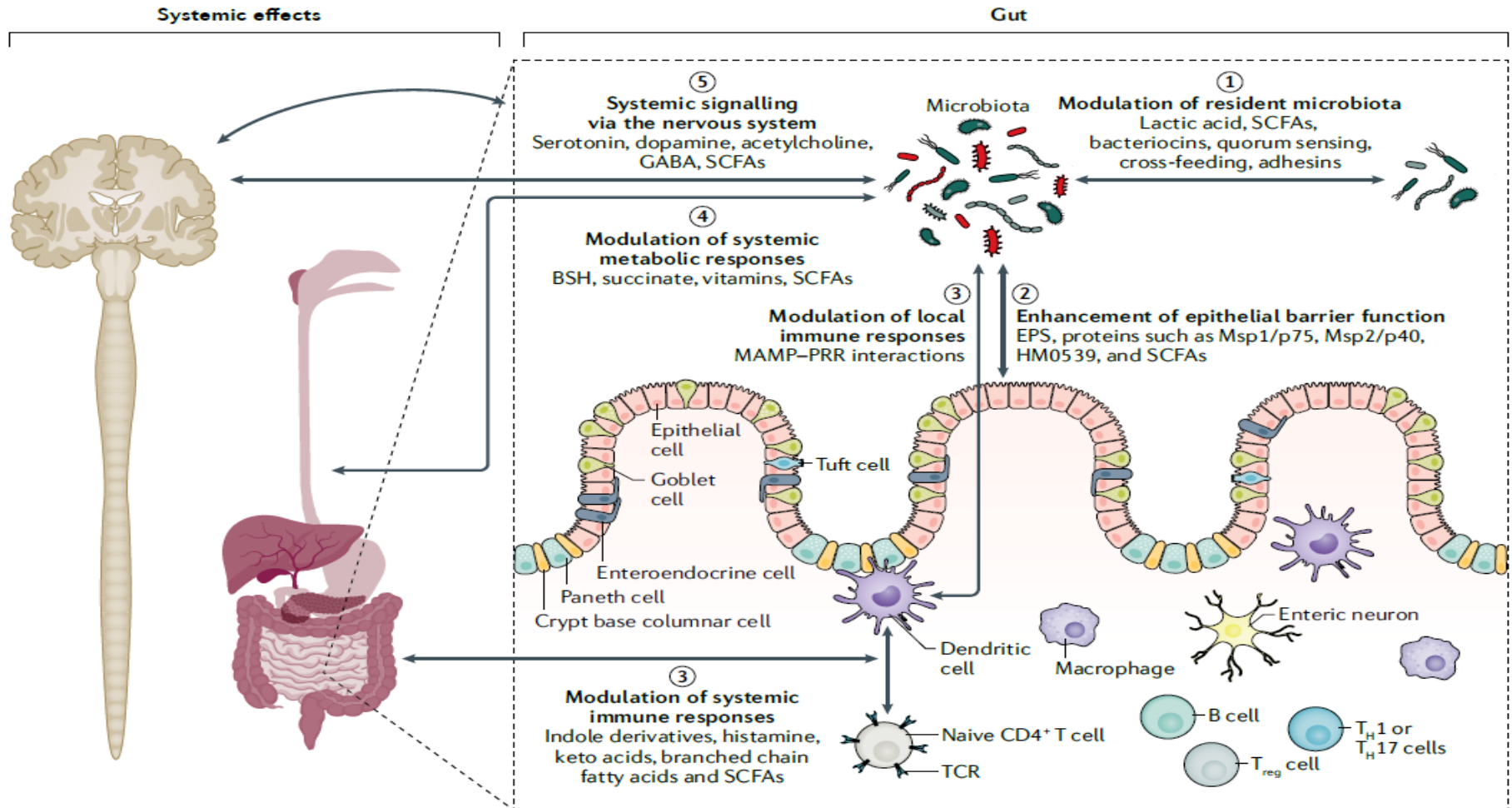
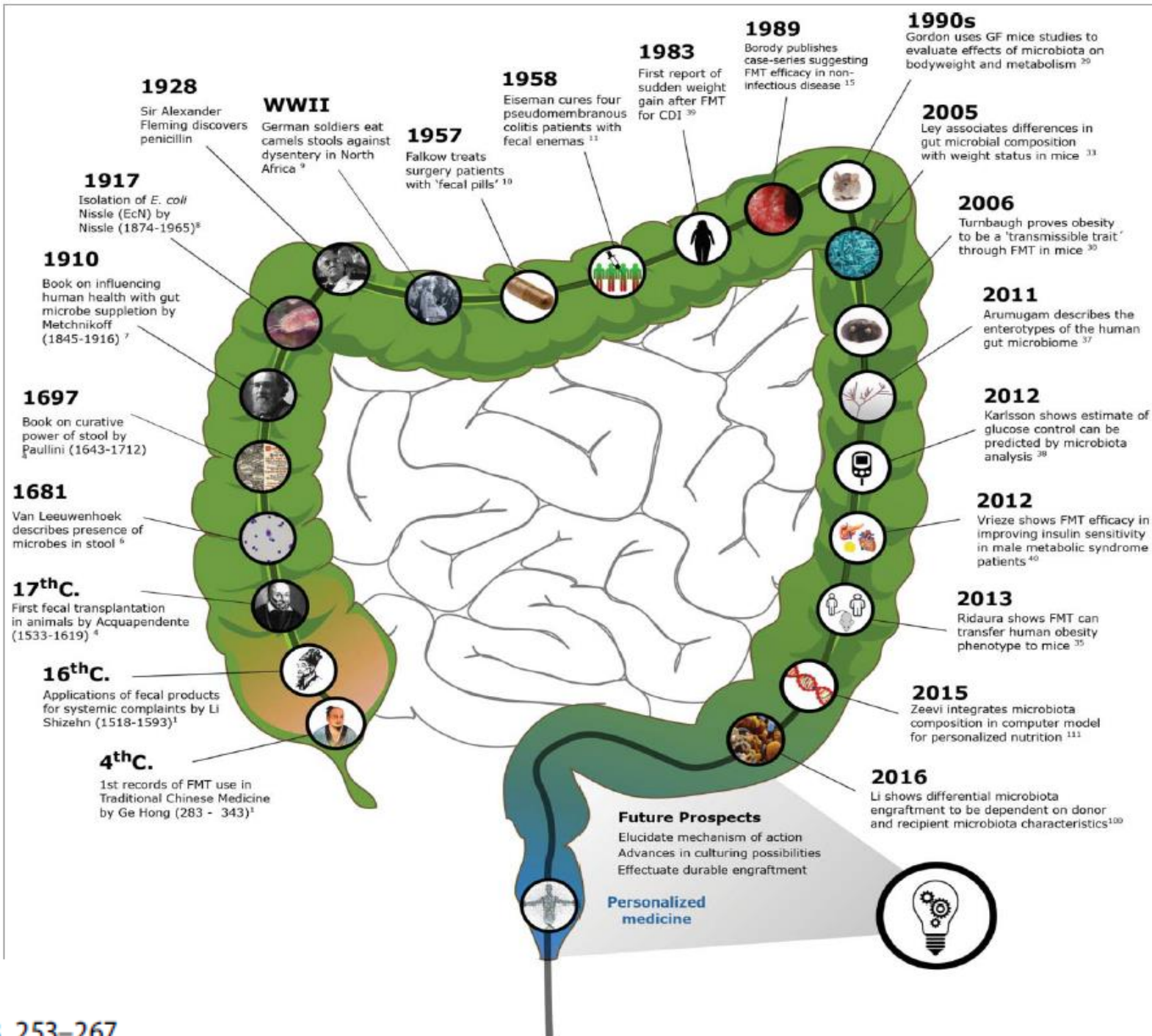


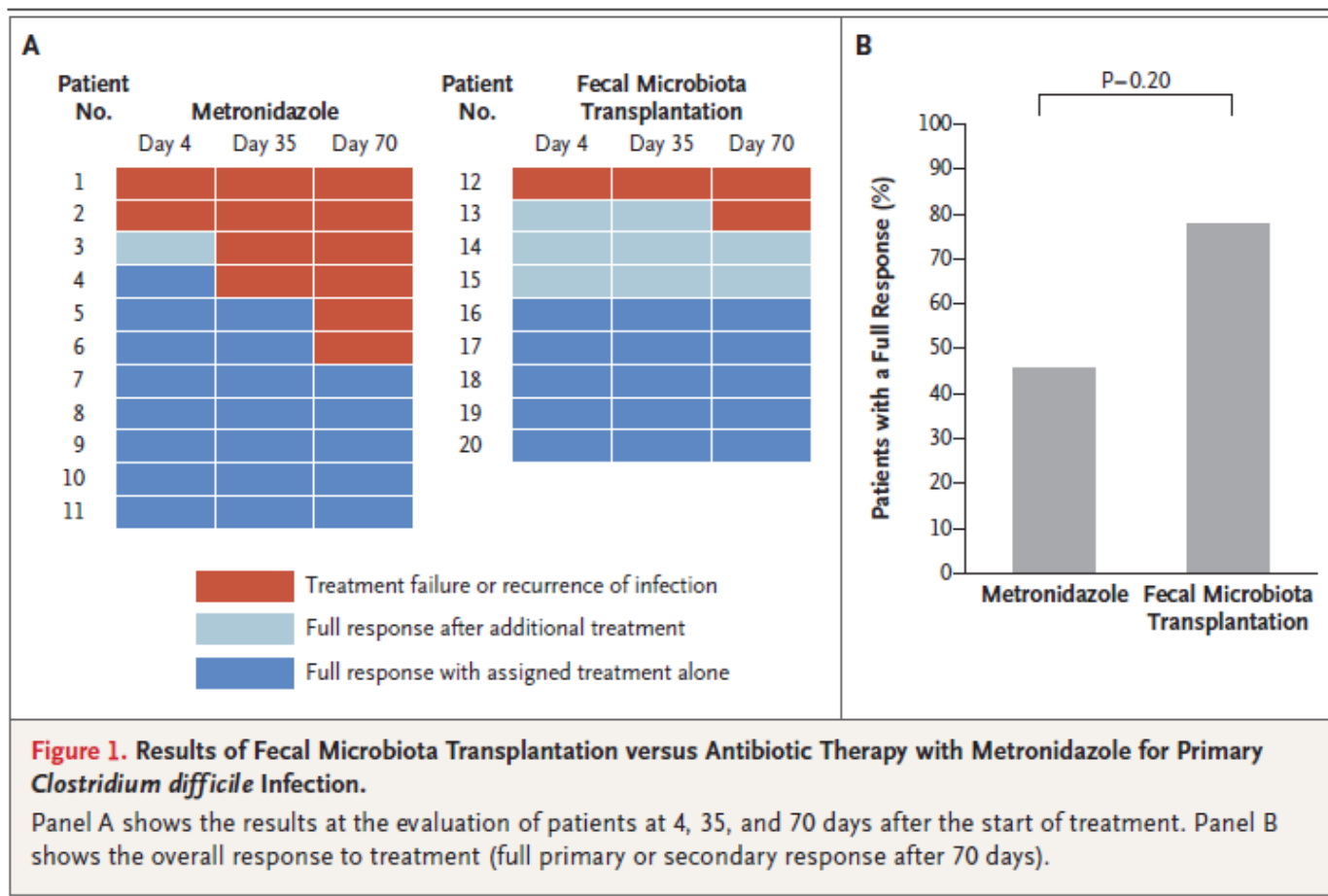
Fig. 4 | Postulated mechanisms of postbiotics and example effector molecules utilized by them. Five mechanisms

Salminen S, Collado MC, Endo A, Hill C, Lebeer S, Quigley EMM, Sanders ME, Shamir R, Swann JR, Szajewska H, Vinderola G. The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. *Nat Rev Gastroenterol Hepatol.* 2021 Sep;18(9):649-667. doi: 10.1038/s41575-021-00440-6.

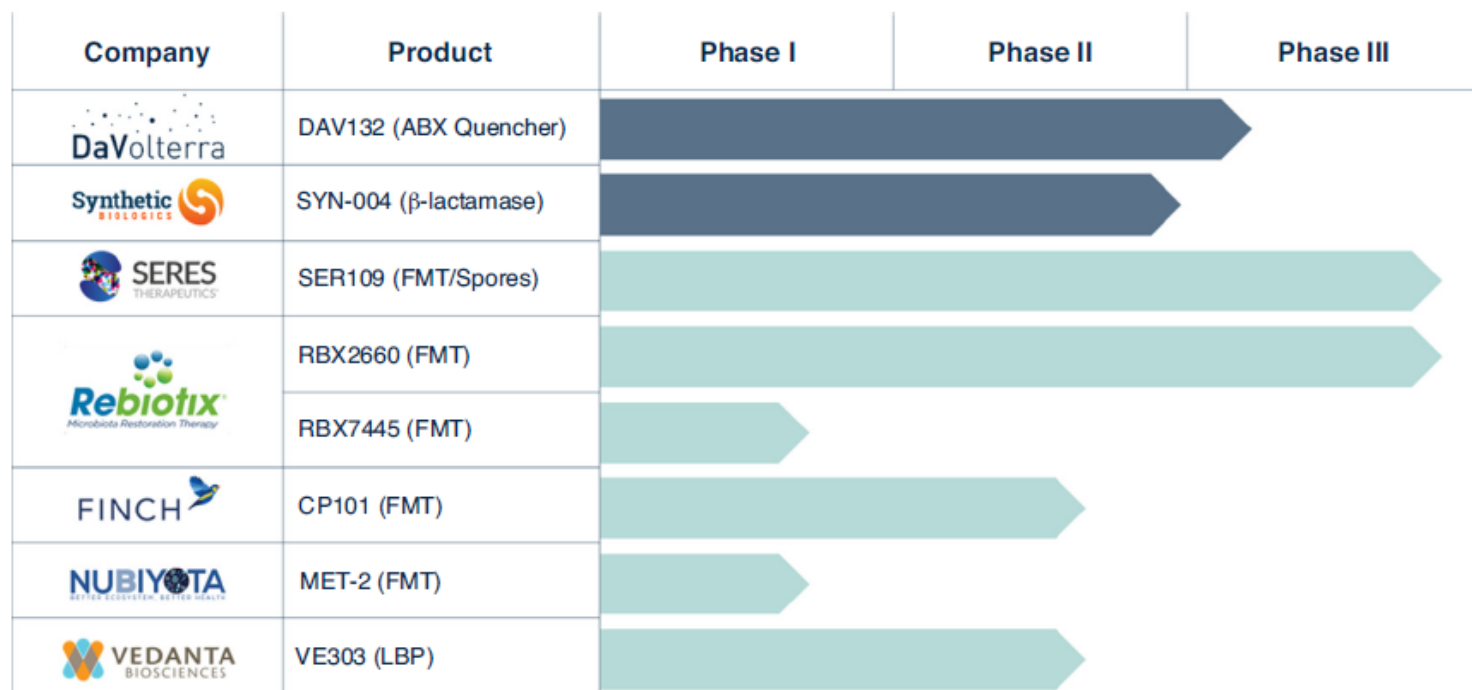
Széklettel történi kezelés története



Széklettranszplantatio C. difficile infectióban



Clostridioides difficile infectio / recurrentia megelőzése beta-lactam antibiotikumok alkalmazása esetén



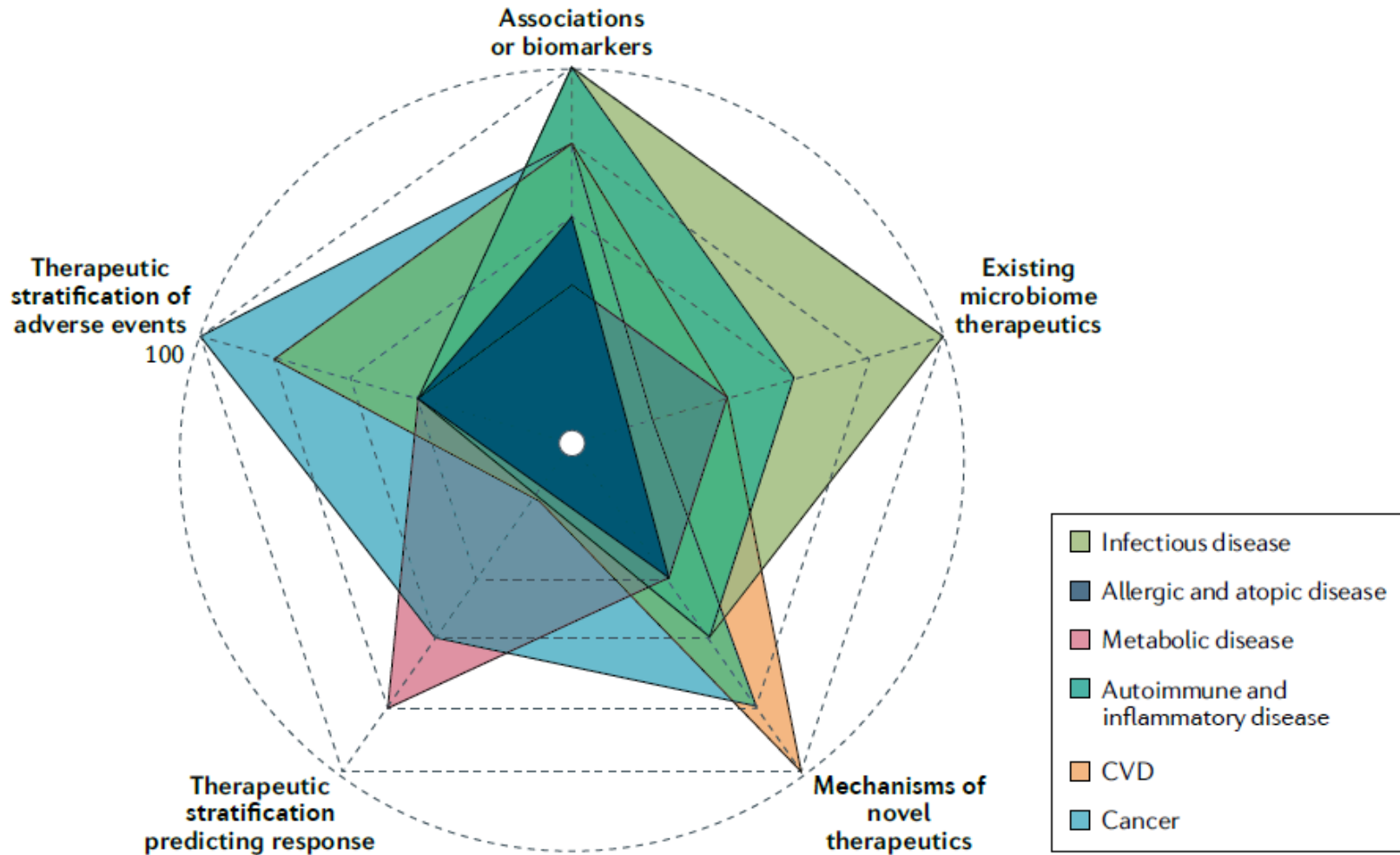
Drug Discovery Today

FIGURE 1

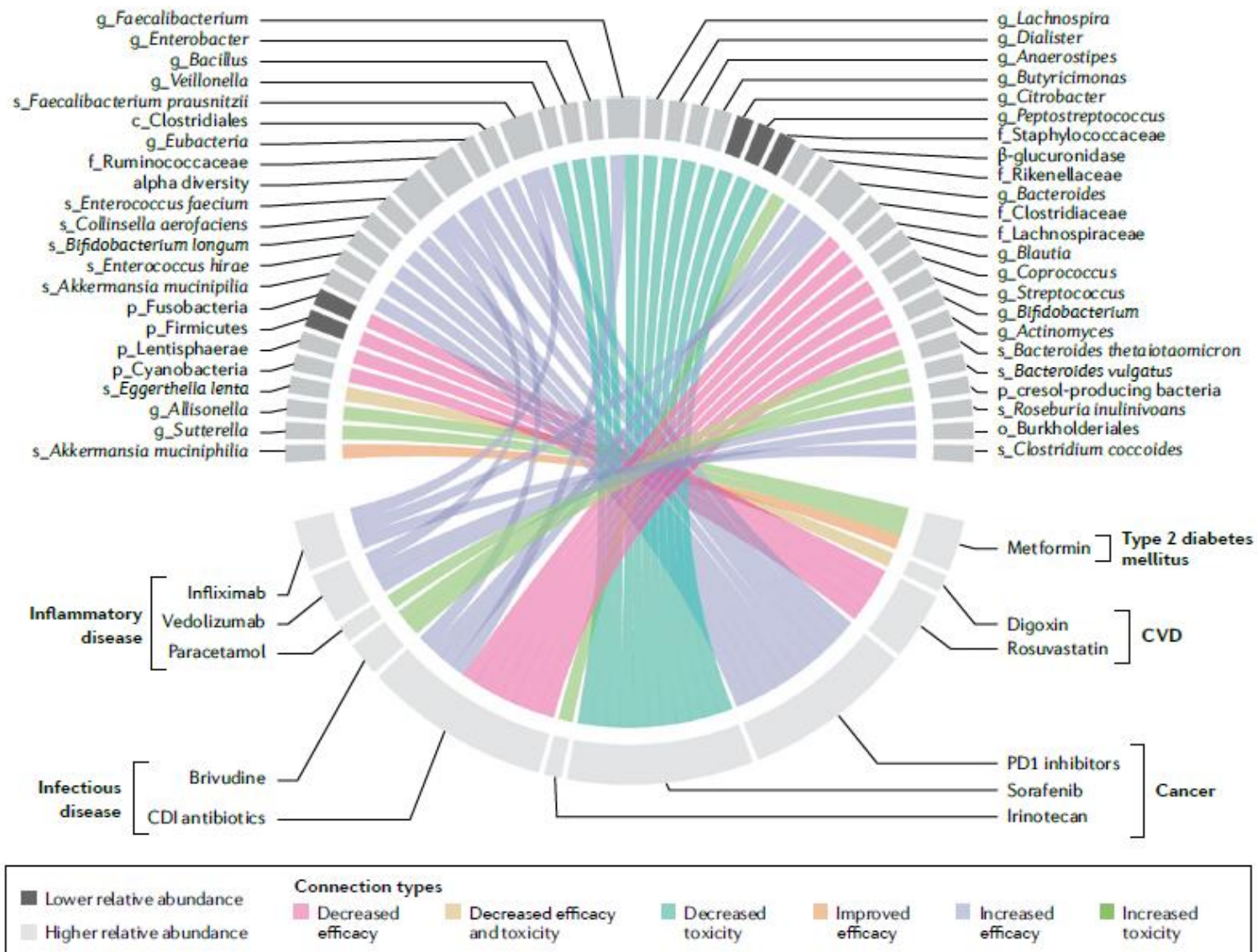
Main microbiome-based approaches in clinical development for the prevention of recurrent *Clostridioides difficile* infections (in green) and for the primary prevention of *C. difficile* infections (in blue). Abbreviations: ABX, antibiotic; FMT, fecal microbiota transplant [59]; LBP, live biotherapeutic product.

Andremont A, Cervesi J, Bandinelli PA, Vitry F, de Gunzburg J. Spare and repair the gut microbiota from antibiotic-induced dysbiosis: state-of-the-art. *Drug Discov Today*. 2021 Sep;26(9):2159-2163. doi: 10.1016

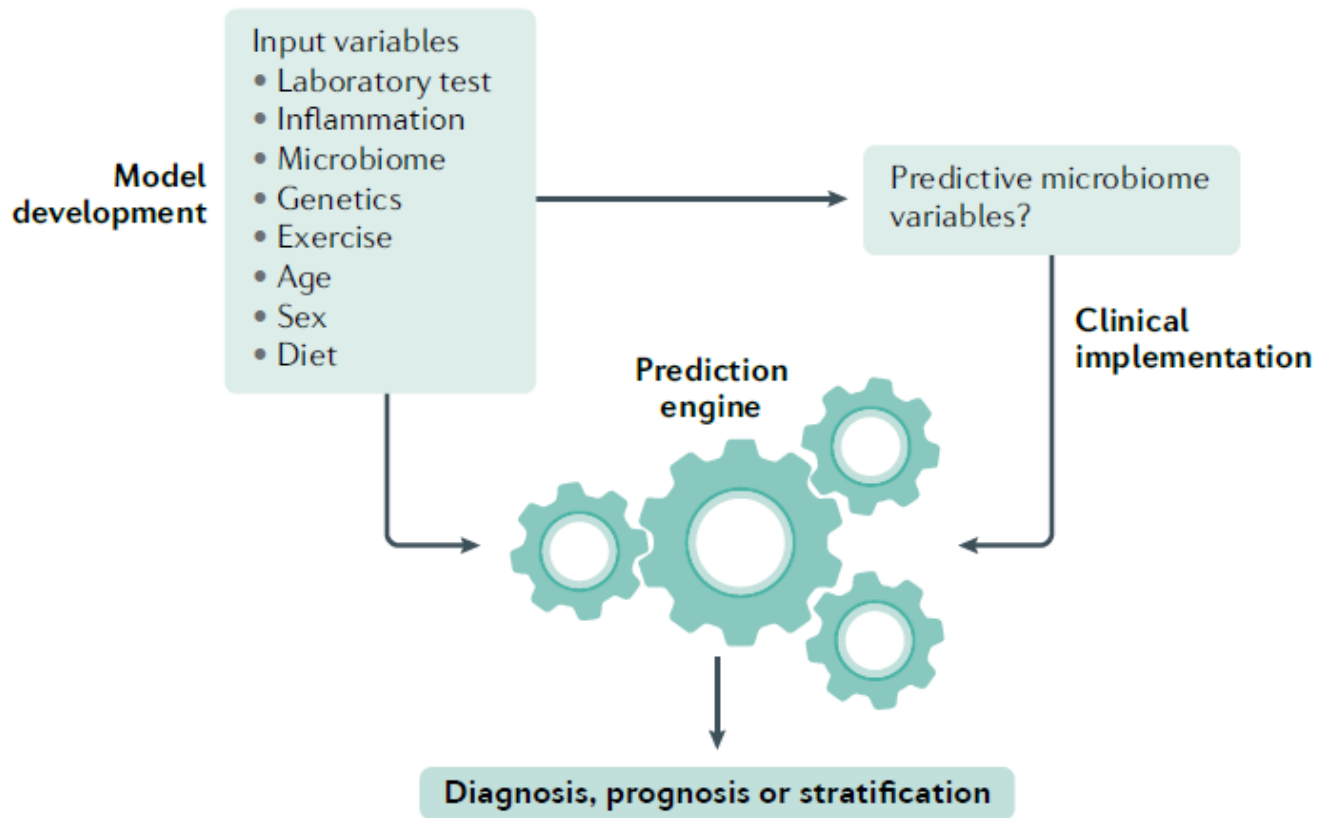
Személyre szabott antibiotikum



Személyre szabott antibiotis



Személyre szabott antibiotis



Schupack DA, Mars RAT, Voelker DH, Abeykoon JP, Kashyap PC. The promise of the gut microbiome as part of individualized treatment strategies. *Nat Rev Gastroenterol Hepatol*. 2022 Jan;19(1):7-25. doi: 10.1038/s41575-021-00499-1. Epub 2021 Aug 27. PMID: 34453142; PMCID: PMC8712374.

Köszönöm a figyelmet!

