Probiotici in Pediatria: moda o nuovo approccio terapeutico?

7 febbraio 2018
Ore 11.00-19.40

Auditorium SYNLAB-CAM Monza,
Via Martiri delle Foibe 1

Sergio Bernasconi

Professore Ordinario di Pediatria

GLI STUDI SUL MICROBIOTA/MICROBIOMA HANNO (IN MANIERA INIMMAGINABILE FINO A POCHI ANNI FA) STIMOLATO :

1) LA RICERCA IN VARI SETTORI DELLA MEDICINA.

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Microbial endocrinology: the interplay between the microbiota and the endocrine system

Hadar Neuman[1], Justine W. Debelius[2], Rob Knight[2,$] and Omry Koren[1,*]

FEMS Microbiology Reviews, 39, 2015, 509–521

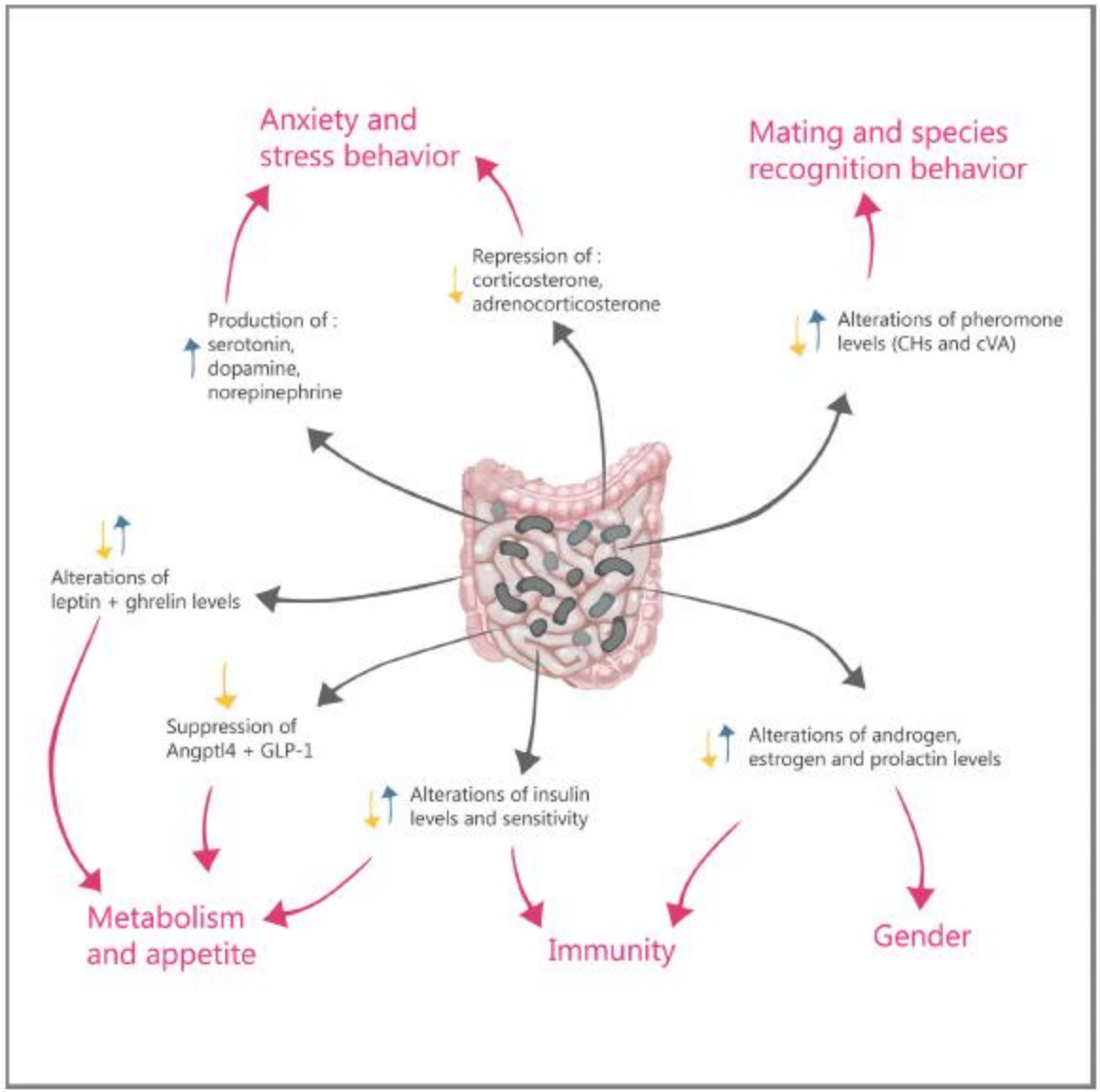

Figure 2. The effects of the gut microbiota on the host via hormones. Gray arrows and text refer to the effects of the gut microbiota on various hormone levels. Pink arrows and text refer to the effects of these hormonal alterations on host outcomes (e.g. behavior).

Microbial endocrinology: the interplay between the microbiota and the endocrine system

Hadar Neuman[1], Justine W. Debelius[2], Rob Knight[2,$] and Omry Koren[1,*]

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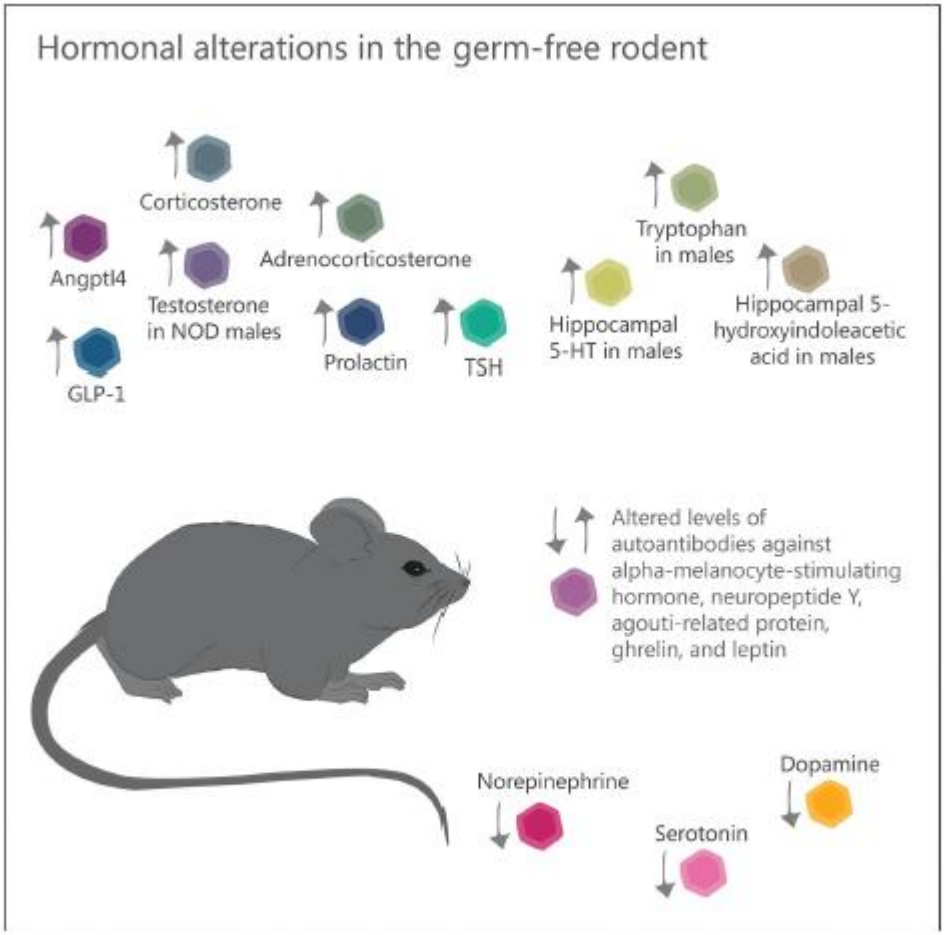

Figure 3. Hormonal alterations reported in GF rodents (Based on Wostmann 1996; Fetissov et al., 2008; Backhed 2009; Wikoff et al., 2009; Grenham et al., 2011; Asano et al., 2012; Clarke et al., 2013; Markle et al., 2013; Wichmann et al., 2013). The arrows refer to the hormone levels in GF compared to conventionally raised rodents.

The impact of probiotic supplementation during pregnancy on DNA methylation of obesity-related genes in mothers and their children

Sanna Vähämiko[1] · Asta Laiho[3] · Riikka Lund[3] · Erika Isolauri[2,4] · Seppo Salminen[1] · Kirsi Laitinen[5]

European Journal of Nutrition

Published online: 03 January 2018

Table 3 DNA methylation changes in the promoters of obesity and weight gain-associated risk genes in response to the intake of either a placebo or the probiotics. Positive fold change = less methylated in the probiotics group, negative fold change = more methylated in the probiotics group

Gene symbol	Mothers		Children		Genomic location
	Fold change	*p* value	Fold change	*p* value	
FTO	3.13	0.021	1.06	0.872	chr16:53,736,875-53,738,375
MC4R	3.47	0.007	1.89	0.107	chr18:58,039,501-58,041,001
MSRA	2.59	0.042	2.57	0.016	chr8:9,910,830-9,912,330
MTMR9	2.36	0.093	2.31	0.024	chr8:11,141,000-11,142,500
TNKS	1.90	0.180	2.76	0.012	chr8:9,412,445-9,413,945
CTNNBL1	1.63	0.221	2.19	0.044	chr20:36,321,434-36,322,934
BDNF	− 1.08	0.873	2.02	0.047	chr11:27,743,105-27,744,605

Role of the intestinal microbiome in health and disease: from correlation to causation

Willem M de Vos and Elisabeth AJ de Vos

doi:10.1111/j.1753-4887.2012.00505.x
Nutrition Reviews® Vol. 70(Suppl. 1):S45–S56

Table 1 **Intestinal microbiota-associated diseases, syndromes, or other aberrations, with summaries of multiple studies that support an association between the microbiota and the indicated aberration.**

Aberration	Most relevant observations and potential correlation	References
Crohn's disease	Diversity decrease – reduced *F. prausnitzii*	Kaser et al. 2010[51]; Sokol et al. 2009[52]; Willing et al. 2010[53]
Ulcerative colitis	Diversity decrease – reduced *A. muciniphila*	Png et al. 2010[54]; Kaser et al. 2010[51]; Lepage et al. 2011[55]
Irritable bowel syndrome	Global signatures – increased *Dorea* and *Ruminococcus*	Salonen et al. 2010[36]; Saulnier et al. 2011[56]; Rajilić-Stojanović et al. 2011[13]
Clostridium difficile infection	Strong diversity decrease – presence of *C. difficile*	Grehan et al. 2010[57]; Khoruts et al. 2010[58]
Colorectal cancer	Variation in *Bacteroides* spp. – increased fusobacteria	Sobhani et al. 2011[59]; Wang et al. 2012[60]; Marchesi et al. 2011[61]
Allergy/atopy	Altered diversity – specific signatures	Stsepetova et al. 2007[62]; Bisgaard et al. 2011[63]; Storrø et al. 2011[64]
Celiac disease	Altered composition, notably in small intestine	Nistal et al. 2012[65]; Di Cagno et al. 2011[66]; Kalliomäki et al. 2012[67]
Type 1 diabetes	Signature differences	Vaarela 2011[68]; Giongo et al. 2011[69]; Brown et al. 2011[70]
Type 2 diabetes	Signature differences	Larssen et al. 2010[71]; Wu et al. 2010[72]; Kootte et al. 2012[73]
Obesity	Specific bacterial ratios (*Bacteroidetes*/*Firmicutes*)	Ley et al. 2006[74]; Turnbaugh et al. 2009[10]; Musso et al. 2011[75]

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Table 2 **Indications for associations between the microbiota and health aberrations, provided as an alphabetical listing of the aberrations suggested to be associated with the intestinal microbiota, along with support for such an association.**

Disease or aberration	Type of support	Reference*
Alzheimer's disease	Microbiota in a mouse model of Alzheimer's disease	Karri et al. 2010[103]
Atherosclerosis	Analysis of plaques in humans	Koren et al. 2011[104]
Autistic spectrum disorders	Analysis of mucosa in children with autism spectrum disorders	Williams et al. 2011[105]
Chronic fatigue syndrome	Cultured microbiota in patients with chronic fatigue syndrome	Sheedy et al. 2009[106]
Colic babies	Longitudinal analysis of colic babies cohort	de Weerth et al. 2012 unpublished data
Cardiovascular disease	Cardiovascular-diseased mice and microbial metabolism	Wang et al. 2011[48]
Depression and anxiety	Probiotic intervention in stressed mice	Bravo et al. 2011[34]
Frailty	Analysis of elderly and high frailty scores	van Tongeren et al. 2005[107]
Graft-vs-host disease	Review of human data on graft-vs-host disease	Murphy et al. 2011[108]
Multiple sclerosis	Involvement of microbiota in mice with multiple sclerosis	Berer et al. 2011[109]
Nonalcoholic fatty liver disease	Effect of choline depletion in humans	Spencer et al. 2011[101]
Parkinson's disease	Role of enteric nervous system and review of Parkinson's disease development	Braak et al. 2003[110]
Rheumatoid arthritis	Microbiota as predisposing factor in rheumatoid arthritis	Scher and Abramson 2011[111]
Retrovirus infection	Mouse retrovirus infection relies on microbiota	Kane et al. 2011[112]
Poliovirus infection	Mouse microbiota promotes poliovirus infection	Kuss et al. 2011[113]

* The most recent single reference is given.

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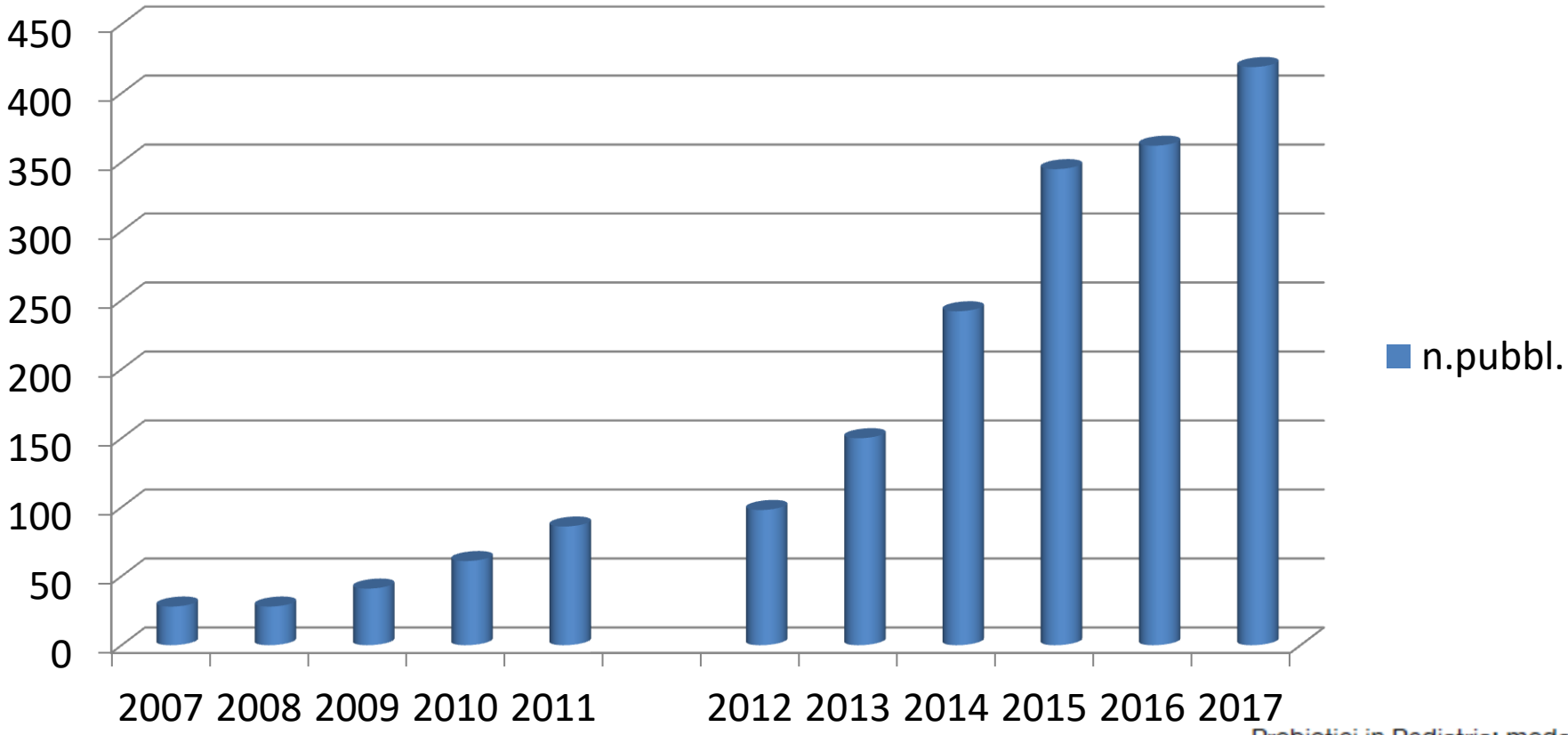
2) **LA RICERCA IN CAMPO PEDIATRICO**

Numero di pubblicazioni riportate su Pub Med alla voce “microbiota children”



Probiotici in Pediatria: moda o nuovo approccio terapeutico?
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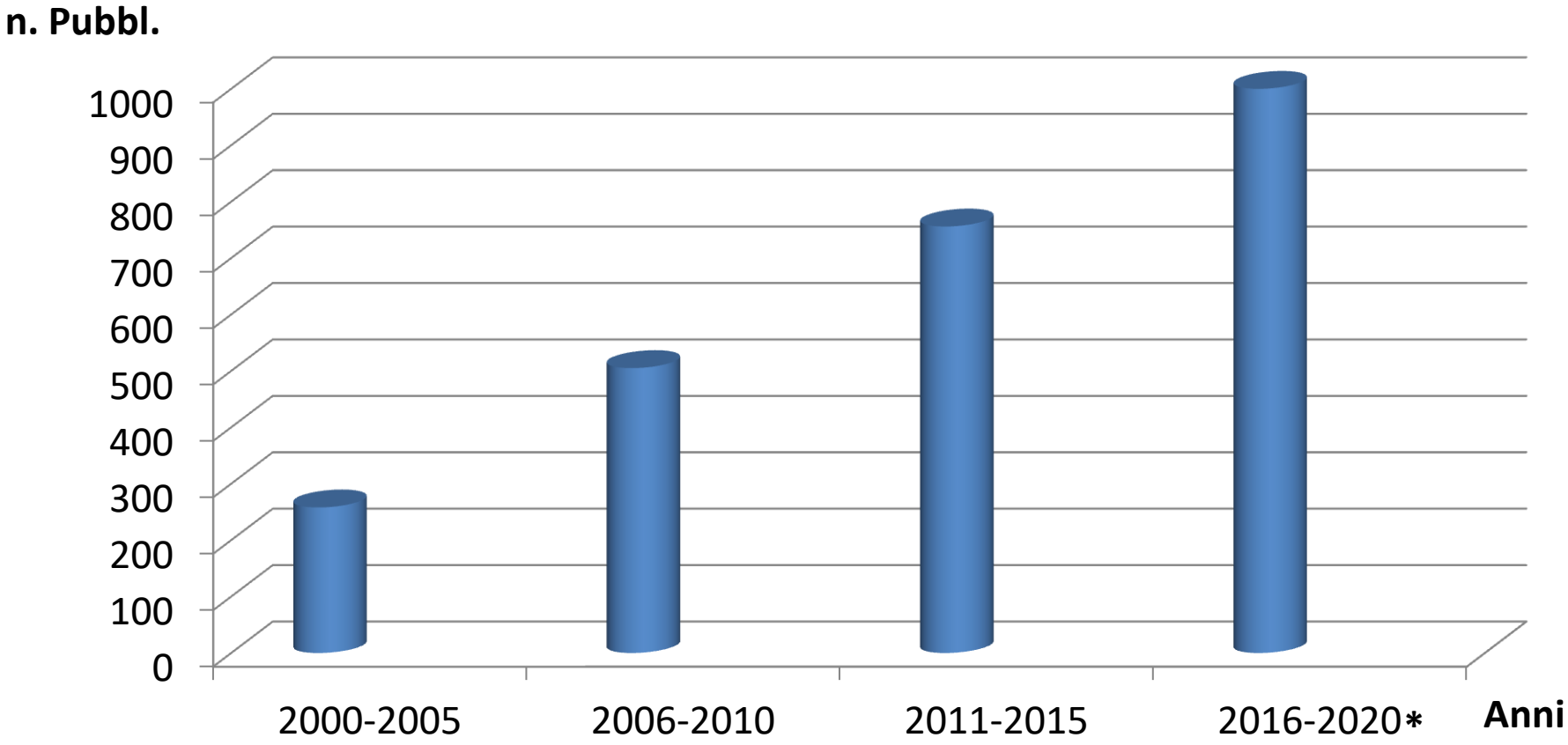
Numero di lavori da Pub Med : Probiotics children



*** Proiezione sui dati 2016-2017**

Probiotici in Pediatria: moda o nuovo approccio terapeutico?
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Building a Beneficial Microbiome from Birth

Esther Castanys-Muñoz,[3] Maria J Martin,[4] and Enrique Vazquez[4]*

Adv Nutr 2016;7:323–30;

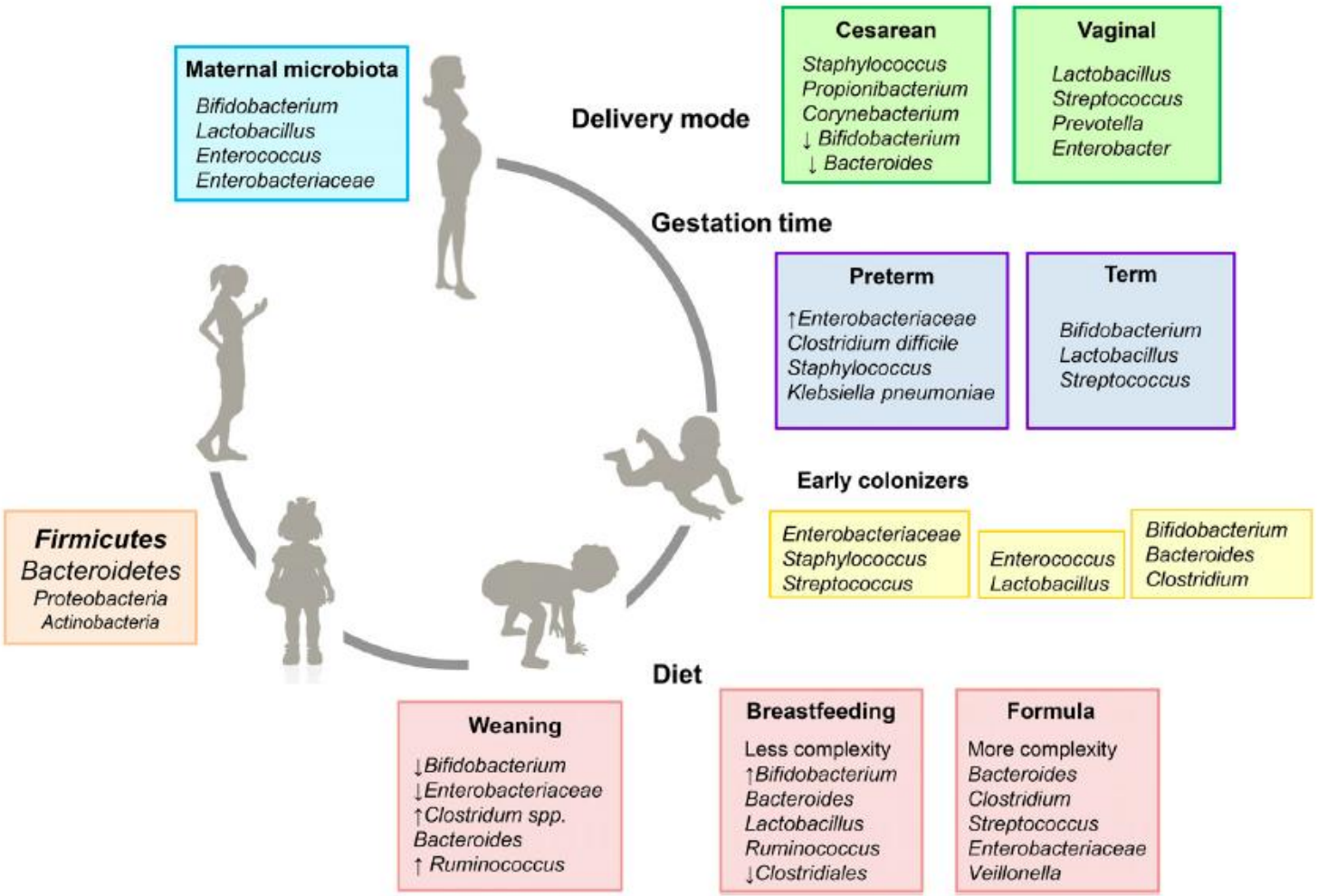

FIGURE 2 Evolution of the early-life gut microbiota and events influencing its composition. Factors such as the maternal microbiota, delivery mode, gestation time, and type of feeding strongly influence the microbiota. Colonization and expansion of the gut microbiota, shaped by diet, results in the establishment of an adult-like microbiota around 2–3 y of age, with firmicutes and bacteroidetes as the predominant phyla. Early life is a susceptible period when modifications in the gut microbiota compositio have long-term effects on health (5, 22).

The importance of the microbiome in pediatrics and pediatric infectious diseases

Curr Opin Pediatr 2017, 29:000–000

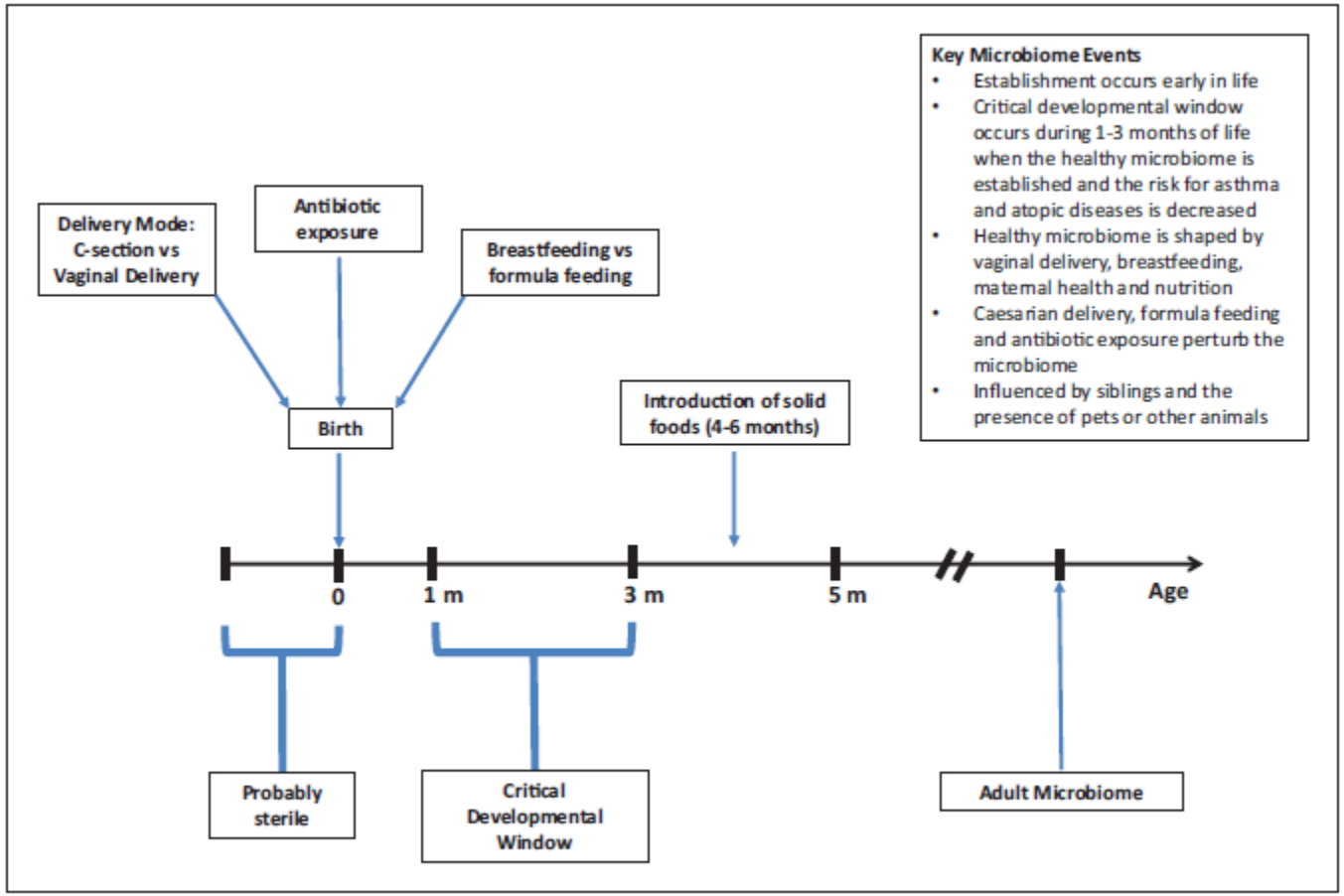

FIGURE 1. Timeline of key events in the development of the microbiome. C-section: Caesarean-section.

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3) **GLI INVESTIMENTI ECONOMICI**

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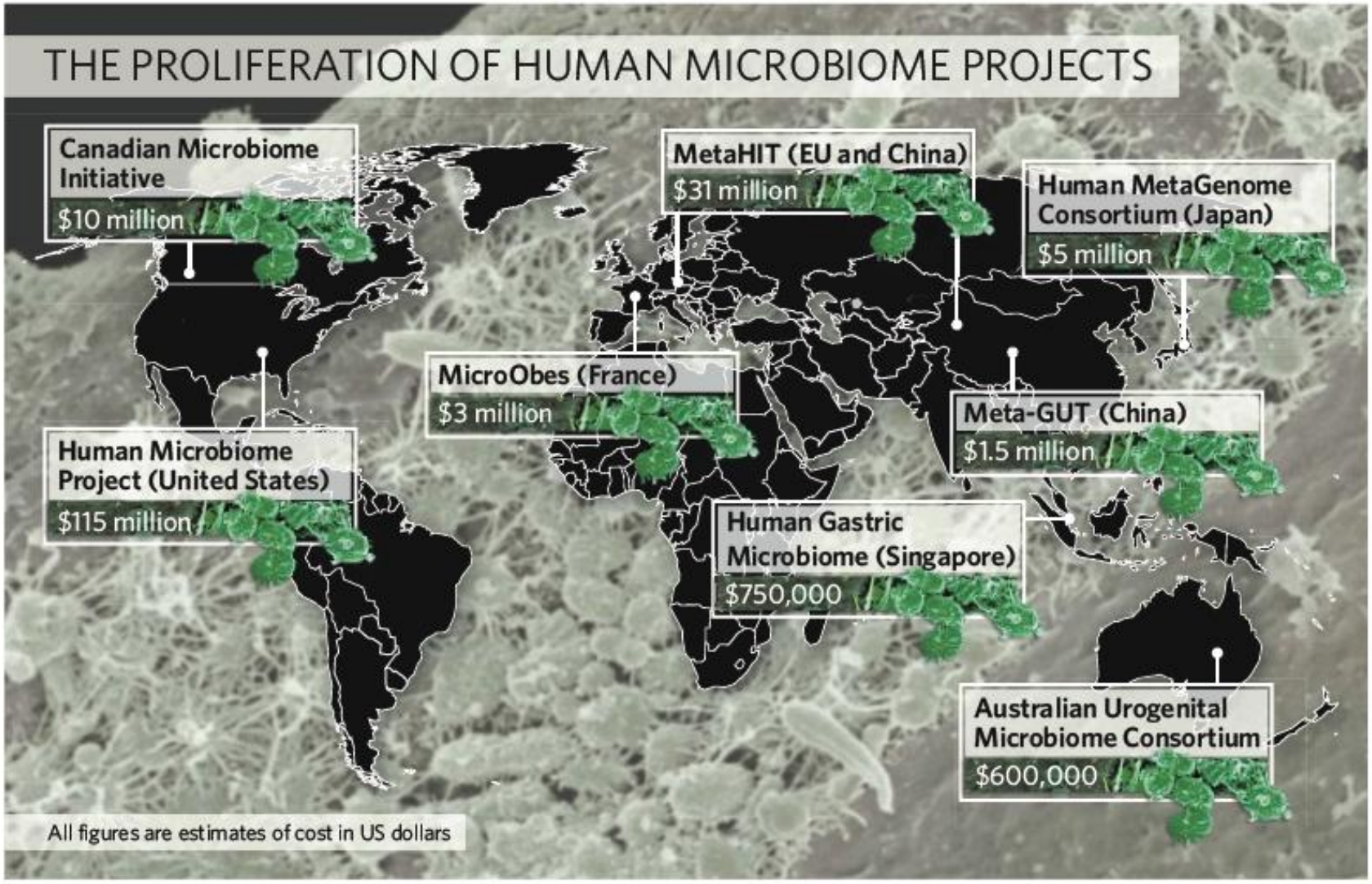
THE PROLIFERATION OF HUMAN MICROBIOME PROJECTS
Canadian Microbiome Initiative
$10 million
MetaHIT (EU and China)
$31 million
Human MetaGenome Consortium (Japan)
$5 million
MicroObes (France)
$3 million
Meta-GUT (China)
$1.5 million
Human Microbiome Project (United States)
$115 million
Human Gastric Microbiome (Singapore)
$750,000
Australian Urogenital Microbiome Consortium
$600,000
All figures are estimates of cost in US dollars

Market data reflect this sea change. According to *Nutrition Business Journal*, sales of probiotic supplements hit $1.6 billion in the U.S. in 2015, making the largest sector—22 percent—of the specialty supplements market.

Not Ist Super Sanità 2013;26(5):3-6

STUDI RELATIVI ALL'UTILIZZO DI INTEGRATORI ALIMENTARI IN ITALIA: IL CONTRIBUTO DELL'ISTITUTO SUPERIORE DI SANITÀ

Stefania Giammarioli[1], Concetta Boniglia[1], Brunella Carratù[1], Flavia Chiarotti[2] e Maurizio Mosca[1]
[1]*Dipartimento di Sanità Pubblica Veterinaria e Sicurezza Alimentare, ISS*
e, ISS

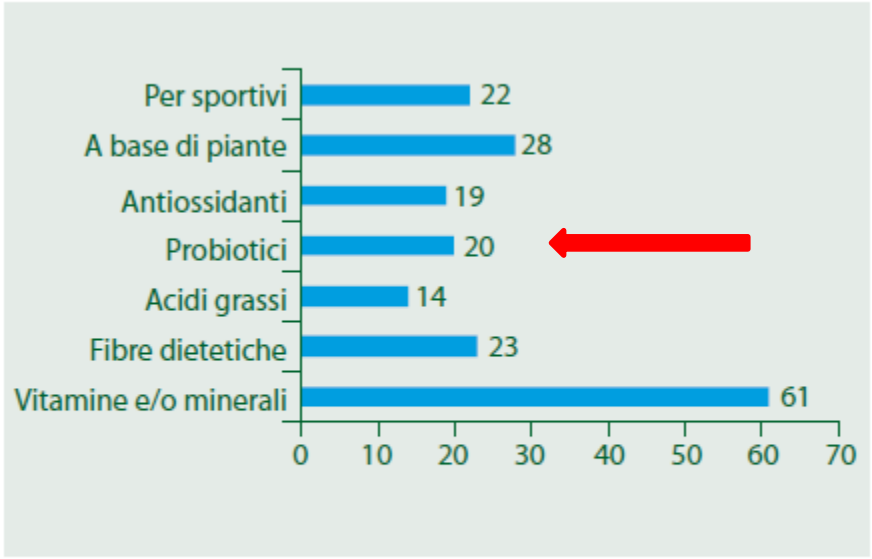

Figura 2 - Uso di differenti tipologie di integratori espresso in percentuale. I risultati sono relativi agli utilizzatori (Totale n. 840, di cui 313 uomini e 527 donne)

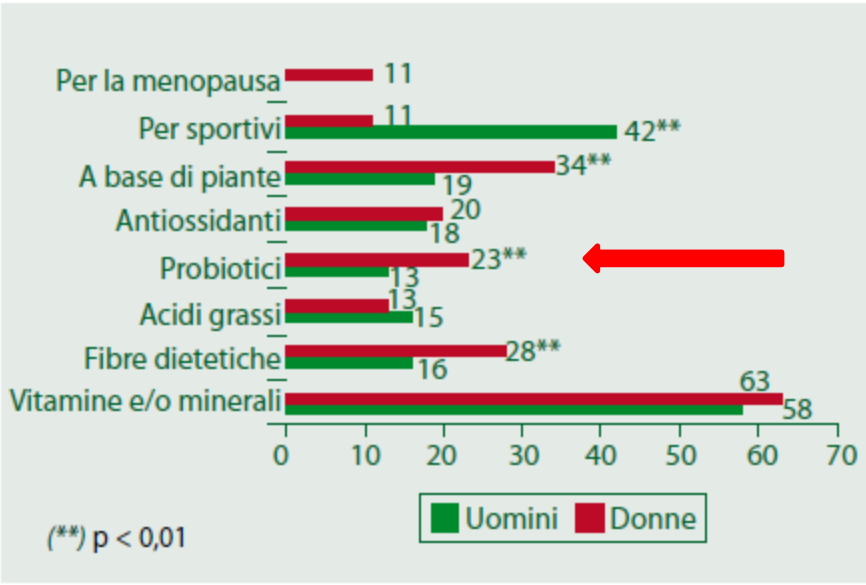

Figura 3 - Uso di differenti tipologie di integratori in funzione del sesso

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A LIVELLO CLINICO QUALI LE EVIDENZE REALI ?

Probiotici in Pediatria: moda o nuovo approccio terapeutico?
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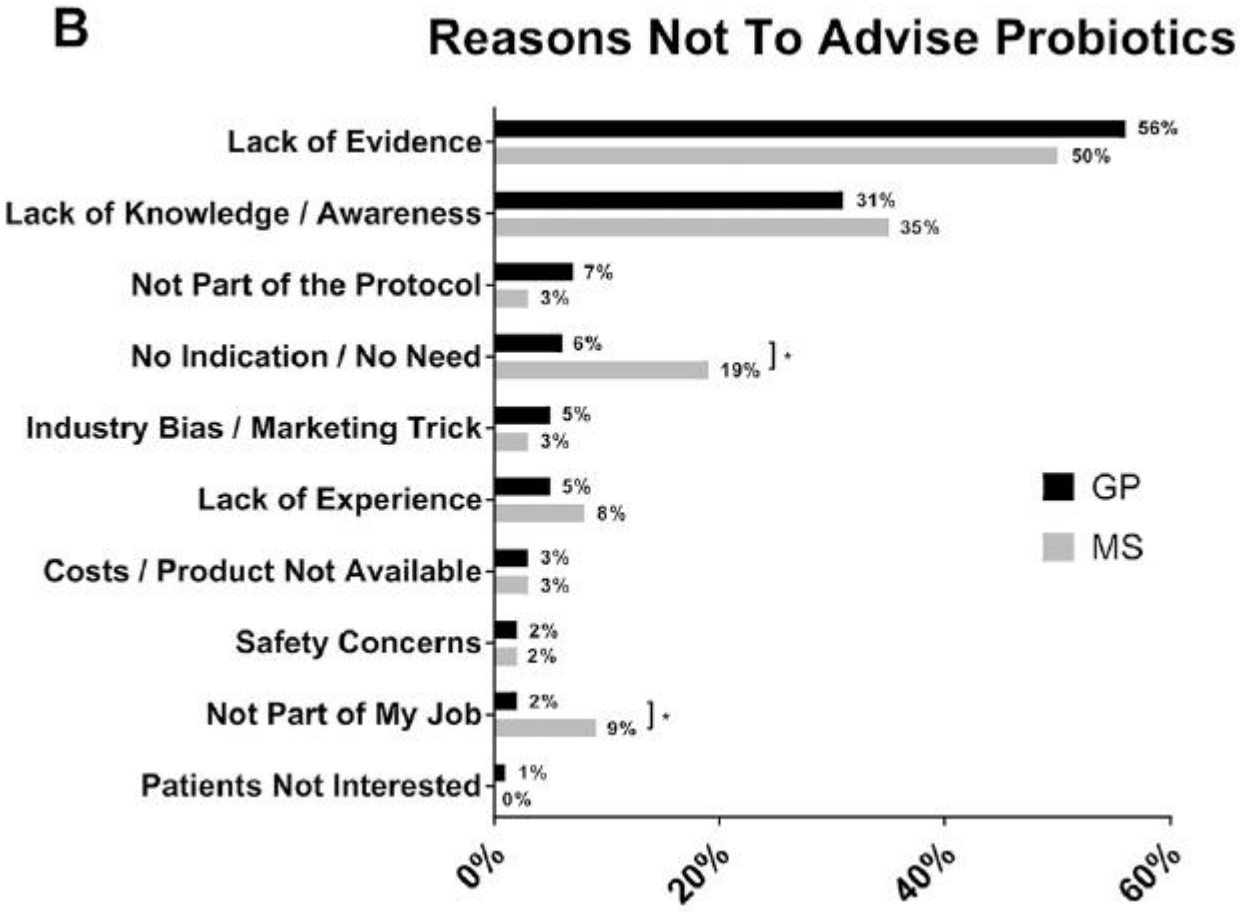
Medical doctors' perceptions on probiotics: Lack of efficacy data hampers innovation

J. Flach[a,b,*], A.S.M. Dias[a], S.H.M. Rademaker[a], M.B. van der Waal[a,b], E. Claassen[a], O.F.A. Larsen[a]

PharmaNutrition 5 (2017) 103–108



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Probiotics for gastrointestinal disorders: Proposed recommendations for children of the Asia-Pacific region

Donald Cameron, Quak Seng Hock, Musal Kadim, Neelam Mohan, Eell Ryoo, Bhupinder Sandhu, Yuichiro Yamashiro, Chen Jie, Hans Hoekstra, Alfredo Guarino

World J Gastroenterol 2017 December 7; 23(45): 7952-7964

Table 1 Recommendations for use of probiotics in childhood intestinal diseases by geographic region

Diseases		Europe[14,40]	United States[36]	Latin America[50]	World[51]
Acute gastroenteritis	T	*L. rhamnosus GG, S. boulardii, L reuteri*	*L. rhamnosus GG, S. boulardii*	*L. rhamnosus GG, S. boulardii, L. reuteri*	*S. boulardii, L. rhamnosus GG,* Indian Dahi
AAD	P	*L. rhamnosus GG, S. boulardii*	*L. rhamnosus GG, S. boulardii*	*L. rhamnosus GG, S. boulardii*	*S. boulardii; L. rhamnosus GG, , B. lactis* Bb12 + *S. thermophilus, L. rhamnosus* strains E/N, Oxy and Pen
CDAD	P	*S. boulardii*			
Nosocomial diarrhea	P	*L. rhamnosus GG*	*L. rhamnosus GG*	*L. rhamnosus GG, B. lactis Bb12, S. thermophilus, B. bifidum S. boulardii*	*L. rhamnosus GG, B. lactis Bb12 + S. Thermophilus*
Traveler's diarrhea	P				
Functional intestinal disorders (IBS)	T	Insufficient evidence		*L. rhamnosus GG,* VSL#3	*L. rhamnosus GG, L. reuteri DSM 17938*
Infant colic	T	*L. reuteri DSM 17938*		*L. reuteri DSM 17938*	*L. reuteri DSM 17938*
IBD (CD, UC, pouchitis)	T	*E. coli Nissle 1917,* VSL#3[1]		VSL#3[1]	VSL#3[2]
Helicobacter pylori infection	T			Not recommended	*L. casei DN-114 001*

[1]Available evidence supports use in UC but not CD or pouchitis; [2]For mildly active UC. T: Treatment; P: Prevention; AAD: Antibiotic-associated diarrhea; CDAD: *Clostridium difficile*-associated diarrhea; CD: Crohn's disease; IBD: Inflammatory bowel disease; IBS: Irritable bowel syndrome; UC: Ulcerative colitis; VSL#3: Proprietary mixture of eight probiotic strains.

Probiotics for gastrointestinal disorders: Proposed recommendations for children of the Asia-Pacific region

Donald Cameron, Quak Seng Hock, Musal Kadim, Neelam Mohan, Eell Ryoo, Bhupinder Sandhu, Yuichiro Yamashiro, Chen Jie, Hans Hoekstra, Alfredo Guarino

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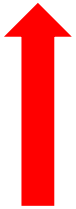
Diseases		Europe[14,40]	United States[36]	Latin America[50]	World[51]
Infant colic	T	*L. reuteri DSM 17938*		*L. reuteri DSM 17938*	*L. reuteri DSM 17938*



Treating infant colic with the probiotic *Lactobacillus reuteri*: double blind, placebo controlled randomised trial

BMJ 2014;348:g2107

Valerie Sung *paediatrician*[123], Harriet Hiscock *associate professor*[123], Mimi L K Tang *professor*[123], Fiona K Mensah *statistician*[123], Monica L Nation *honours student*[23], Catherine Satzke *research fellow*[23], Ralf G Heine *paediatric gastroenterologist/allergist*[123], Amanda Stock *paediatrician*[1], Ronald G Barr *professor*[4], Melissa Wake *professor*[123]

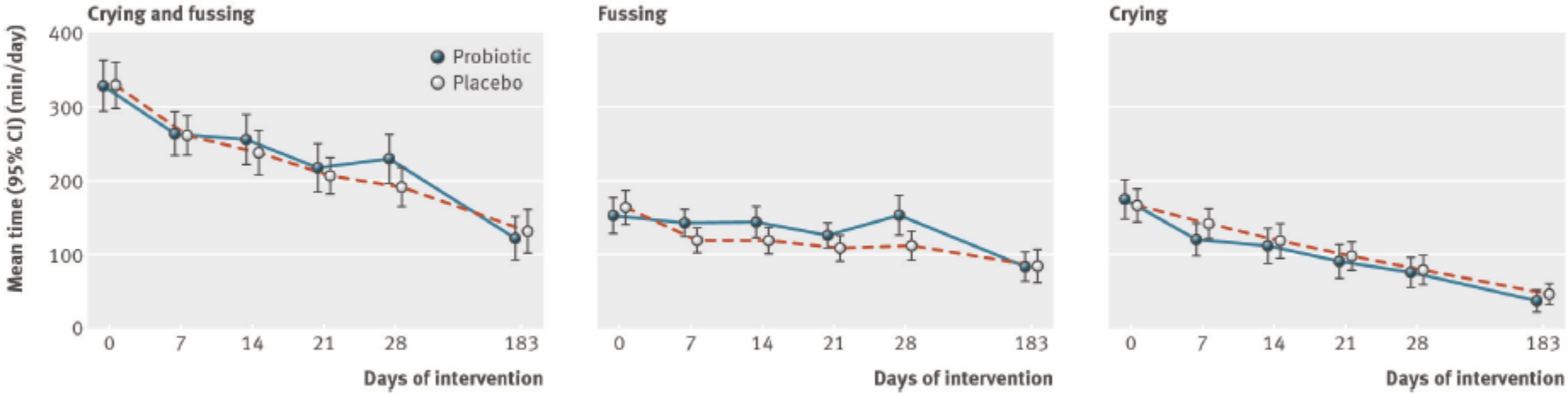


Fig 2 Daily duration of cry or fuss over study period and at 6 month follow-up. Day 28=1 month; day 183=6 months

What this study adds

L reuteri treatment did not reduce crying or fussing in infants with colic, nor was it effective in improving infant sleep, maternal mental health, family or infant functioning, or quality of life

Probiotics therefore cannot be routinely recommended for all infants with colic

Further research is needed to identify which subgroups of infants with colic may benefit from probiotics

Probiotics for Infantile Colic: A Randomized, Double-Blind, Placebo-Controlled Trial Investigating *Lactobacillus reuteri* DSM 17938

Kim Chau, MSc[1,2], Eddy Lau, MD[3,4,5], Saul Greenberg, MD[6], Sheila Jacobson, MD[2,6], Parvaneh Yazdani-Brojeni, MD[2]
Natasha Verma, MD[2], and Gideon Koren, MD[1,2,3,6,7]

(J Pediatr 2015;166:74-8).

Table II. Primary outcome: duration of crying and/or fussing times in the placebo and *L reuteri* DSM 17938 groups

	Duration of crying time, min/day, median (IQR)			Total crying/21 days, min, mean ± SD			
Time	Placebo (n = 28)	*L reuteri* (n = 24)	Median difference (95% CI)	Placebo (n = 28)	*L reuteri* (n = 24)	Mean difference (95% CI); RR (95% CI)	*P* value
Baseline	122 (163-88)	131 (149-84)	9 (−29 to 46)				.804*
Day 7	120 (149-91)	90 (129-53)	−30 (−65 to 5)				.032*
Day 14	103 (140-78)	75 (103-54)	−28 (−55 to 0)				.018*
Day 21	102 (148-61)	60 (99-35)	−42 (−74 to −10)				.045*
Total				2195 ± 764	1719 ± 750	477 (53-900); 0.78 (0.58-0.98)	.028†

RR, relative risk.
*Mann-Whitney *U* test.
†Student *t* test.

In conclusion, our findings support the beneficial effects of administering *L reuteri* DSM 17938 to treat infantile colic in breastfed Canadian infants with colic, as was previously reported in other geographical regions. Of particular importance, our study provides evidence from North America that supplementation of probiotics in early infancy is effective in managing colic symptoms. ■

Lactobacillus reuteri for Infants with Colic: A Double-Blind, Placebo-Controlled, Randomized Clinical Trial

Nicole Y. Fatheree, BBA[1], Yuying Liu, PhD[1], Christopher M. Taylor, PhD[2], Thomas K. Hoang, BS[1], Chunyan Cai, PhD[3,4], Mohammad H. Rahbar, PhD[3,4,5], Manouchehr Hessabi, MD, MPH[4], Michael Ferris, PhD[2], Valarie McMurtry, PhD[2], Christine Wong, PharmD, RPh[6], Ta Vu, PharmD, RPh, CCRP[6], Theresa Dancsak, RN, MSN[7], Ting Wang, MS[1], Wallace Gleason, MD[1], Vinay Bandla, MD[1], Fernando Navarro, MD[1], Dat Q. Tran, MD[1], and J. Marc Rhoads, MD[1]

(J Pediatr 2017;191:170-8).

Table IV. Summary statistics of baseline Barr diary and fecal calprotectin by treatment group

Measurements	*L reuteri* n = 13	Placebo n = 7	*P* value
Barry diary			
Visit 2 (baseline), median (IQR)			
Crying and fussing time, min	275 (267, 368)	283.5 (255, 612)	.66
Crying time, min	109.5 (70, 185)	96.0 (38, 140)	.43
Fussing time, min	170.0 (147, 217)	231.0 (187, 502)	.09
Barr diary			
Follow-up visits, adjusted means (95% CI)			
Crying and fussing time, min			
Visit 3 (day 21)	99 (42, 234)	164 (110, 246)	31
Visit 5 (day 92)	3 (1, 7)	5 (1, 22)	.55
Fussing time, min			
Visit 3 (day 21)	68 (28, 164)	111 (70, 177)	.38
Visit 4 (day 42)	58 (34, 100)	20 (5, 76)	.15
Visit 5 (day 92)	31 (14, 72)	22 (10, 49)	.56
Fecal calprotectin, μg/g, median (IQR)			
Visit 1 (baseline)	216 (132, 266)	148 (82, 192)	.19
Follow-up visits, adjusted means (95% CI)			
Visit 4 (day 42)	140 (78, 251)	103 (62, 172)	.50
Visit 5 (day 92)	75 (48, 118)	94 (58, 150)	.57

The adjusted geometric means and 95% CI of Barr diary data and fecal calprotectin data at follow-up visits are shown after we controlled for age and each individual baseline values. *P* values for baseline data are obtained by Wilcoxon rank sum test. For follow-up visits, longitudinal models were used as follows. Longitudinal model: (1). ln(Barr diary) = $\beta 0 + \beta 1$*visit3 + $\beta 2$*group + $\beta 3$*visit3*group + $\beta 4$*visit4 + $\beta 5$*group + $\beta 6$*visit4*group + $\beta 7$*(Age at baseline) + $\beta 8$*(Barr diary at baseline); Here, visit3and visit4 are dummy variables; visit3 = 1 if at visit 3, 0 otherwise; visit4 = 1 if at visit 4, 0 otherwise; group = 1 if in *L reuteri* strain DSM 17938 group, 0 otherwise; (2). ln(fecal calprotectin) = $\beta 0 + \beta 1$*visit4 + $\beta 2$*group + $\beta 3$*visit4*group + $\beta 4$*(age at baseline) + $\beta 5$*(fecal calprotectin at baseline); Here, visit4 is dummy variable; visit4 = 1 if at visit 4, 0 otherwise; group = 1 if in *L reuteri* strain DSM 17938 group, 0 otherwise.

Conclusions Daily administration of *L reuteri* strain DSM 17938 appears to be safe in newborn infants with colic, including those with neutropenia, which frequently coexists. A placebo response of 66% suggests that many infants with colic will have resolution within 3 weeks. *(J Pediatr 2017;191:170-8).*

Infant Colic—What works: A Systematic Review of Interventions for Breast-fed Infants

JPGN • Volume 62, Number 5, May 2016

*Tracy Harb, *Misa Matsuyama, †Michael David, and *Rebecca J. Hill

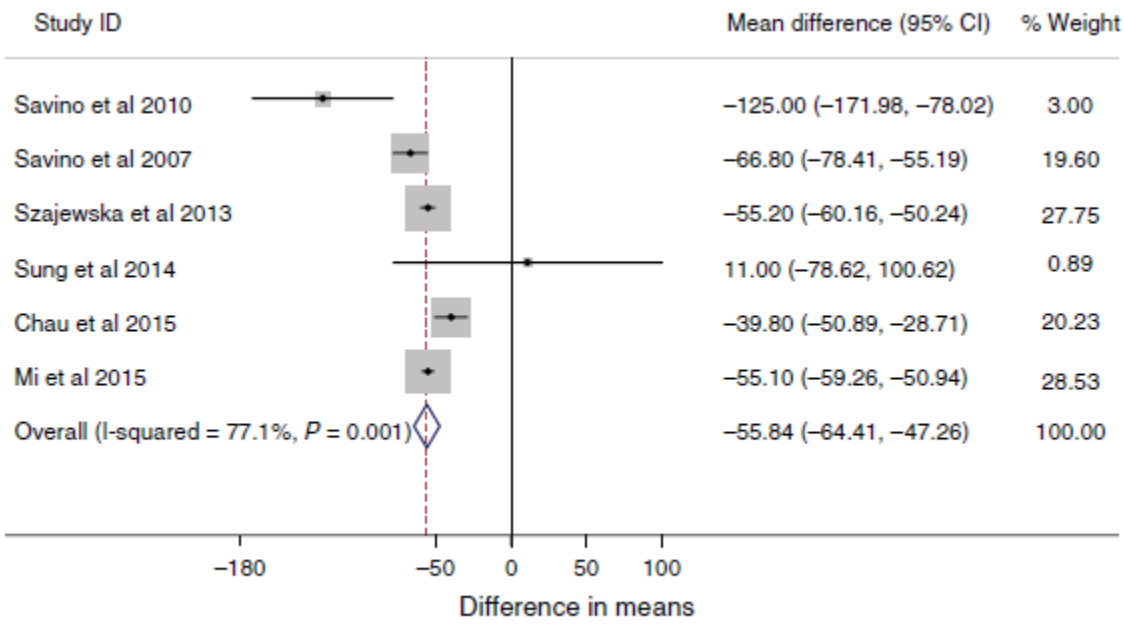


FIGURE 2. Subgroup meta-analysis of the effect of probiotics (*L reuteri*) at 21 days.

Infant Colic—What works: A Systematic Review of Interventions for Breast-fed Infants

*Tracy Harb, *Misa Matsuyama, †Michael David, and *Rebecca J. Hill

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Future Directions

Any future research methodology should seek to address the high levels of heterogeneity within the present body of research for infant colic.

This could be achieved by ensuring a standardised definition of colic, which could be based on the internationally agreed Rome III criteria. Data collection methods should also be standardised, this could include the use of validated tools that capture infant crying in real time, either paper-based or in electronic format to ensure consistency of the data, and ease of data collection for mothers participating in research.
Also, a consistent approach to measuring the rates of responding infants would ensure less heterogeneity, this could be achieved by researchers reaching consensus on defining what is meant by a "responder" to treatment by standardising the percentage of reduced crying time to either 25% and more or 50% and more, for example.

Infant Colic—What works: A Systematic Review of Interventions for Breast-fed Infants

JPGN • Volume 62, Number 5, May 2016

*Tracy Harb, *Misa Matsuyama, †Michael David, and *Rebecca J. Hill

- **In addition, standardised reporting of crying data in mean minutes per day, with standard deviations, would be useful to assist with comparisons across similar interventions.**

- **With regard to future research investigating maternal dietary interventions for colic, heterogeneity can be reduced by ensuring that the infants of participating mothers are exclusive or fully breast-fed, and that the mothers are subject to only 1 intervention, for example, a hypoallergenic diet or another type of diet, and that these diets are well managed by the inclusion of a clinical dietitian in the research team.**

EBM ?

- COLICHE “GASSOSE” LATTANTE

- GASTROENTERITE ACUTA

Probiotici in Pediatria: moda o nuovo approccio terapeutico?
S. Bernasconi

Probiotics for gastrointestinal disorders: Proposed recommendations for children of the Asia-Pacific region

Donald Cameron, Quak Seng Hock, Musal Kadim, Neelam Mohan, Eell Ryoo, Bhupinder Sandhu, Yuichiro Yamashiro, Chen Jie, Hans Hoekstra, Alfredo Guarino

World J Gastroenterol 2017 December 7; 23(45): 7952-7964

Table 1 Recommendations for use of probiotics in childhood intestinal diseases by geographic region

Diseases		Europe[14,40]	United States[36]	Latin America[50]	World[51]
Acute gastroenteritis	T	*L. rhamnosus GG, S. boulardii, L reuteri*	*L. rhamnosus GG, S. boulardii*	*L. rhamnosus GG, S. boulardii, L. reuteri*	*S. boulardii, L. rhamnosus GG,* Indian Dahi

Probiotics for Prevention and Treatment of Diarrhea

Alfredo Guarino, MD, Stefano Guandalini, MD,†*
*and Andrea Lo Vecchio, MD**

J Clin Gastroenterol • Volume 49, Supp. 1, November/December 2015

TABLE 5. Indications to the Use of Probiotics for Prevention and Treatment of Diarrhea

Condition	Level of Evidence in Support (– to + + +)	
	Prevention	**Treatment**
Acute infectious diarrhea	+ / –	+ + +
Acute infectious nosocomial diarrhea	+ +	+ + +
Antibiotic-associated diarrhea	+ + +	–
C. difficile-associated diarrhea	+ +	+ / –
C. difficile infection recurrence	–	+
Necrotizing enterocolitis	+ + +	–

Schnadower D, *et al. BMJ Open* 2017;**7**:e018115. doi:10.1136/bmjopen-2017-018115

However, the studies included in these analyses have had important methodological limitations such as small sample sizes, lack of probiotic quality control, outcomes that are of minimal relevance to patients and their families and unclear randomisation, allocation concealment and blinding and attrition biases.[12–15] Remarkably, few studies of probiotics have evaluated outpatients, a group that represents the preponderance of AGE episodes in the USA,[16–18] and only one small study has evaluated probiotics in children with AGE presenting to a US emergency department (ED), where no benefit was demonstrated.[19]

Given the lack of adequate efficacy and safety evidence, most guidelines do not endorse the use of probiotics in paediatric AGE.[12 15 20–23] However, the European Society of Pediatric Gastroenterology, Hepatology and Nutrition has offered a 'strong' recommendation in support of specific probiotics to treat previously healthy children with AGE, despite their acknowledgement of the 'low quality of the evidence'.[24] Furthermore, probiotic manufacturers aggressively market probiotics citing health claims that have not been supported by rigorous research,[25–28] and the US market for digestive health enzymes, prebiotics and probiotics was estimated at US$495 million in 2015 and was expected to grow at an annual rate of 13%.[29]

Schnadower D, *et al. BMJ Open* 2017;**7**:e018115. doi:10.1136/bmjopen-2017-018115

Despite these concerns about their value, and issues surrounding safety and regulatory oversight,[30–32] parents of patients with AGE often administer probiotics to their children without guidance from medical professionals.[9 22]

FEDER SALUS

Categorie protagoniste totale mercato
Vendite a valore (AT giugno 2015)

	Diff. % fatturato anno precedente	Diff. % fatturato 1° semestre 2015	Prezzo medio a confezione (AT GIU 2015)	Var% rispetto all'anno precedente
INTEGRATORI DI VITAMINE E SALI MINERALI	+3,5	+6,9	12,36	0,8
PROBIOTICI	+8,9	+7,9	13,34	1,0
PRODOTTI PER PATOLOGIE INVERNALI, GOLA E TOSSE	**+24,7**	**+26,3**	11,06	2,5
ENERGETICI	-0,0	+4,3	14,03	-1,1
COADIUVANTI NEL CONTROLLO DEL COLESTEROLO	**+17,8**	**+16,5**	15,79	1,6
COADIUVANTI NEL CONTROLLO DEL PESO	-3,7	-4,8	17,47	-2,3
COADIUVANTI DELLA FUNZIONE INTESTINALE	+3,4	+2,6	9,89	0,4
NUTRICOSMETICI	+5,6	+5,7	22,05	-0,1
ANTIOSSIDANTI	-2,9	-4,2	24,41	-2,5
PRODOTTI PER LA CIRCOLAZIONE	+0,4	+1,9	17,29	0,9
COADIUVANTI PER LA SALUTE DEGLI OCCHI	+0,8	+0,1	19,52	1,1
PRODOTTI PER LE ARTICOLAZIONI	+7,2	+6,3	20,55	1,3
COADIUVANTI DEL RIPOSO NOTTURNO E CALMANTI	+5,3	+8,7	11,67	1,0
COADIUVANTI LE FUNZIONI IMMUNITARIE	**+11,2**	**+14,5**	15,41	-0,4
PRODOTTI PER GRAVIDANZA E ALLATTAMENTO	+3,9	+0,9	18,15	1,9
COADIUVANTI DELLE FUNZIONI DELLE VIE URINARIE	+11,3	+6,0	17,34	2,4
PRODOTTI PER IL CICLO E LA MENOPAUSA	-1,4	-3,8	23,72	1,6
PRODOTTI PER MEMORIA E FUNZIONI COGNITIVE	+13,2	+15,4	17,46	0,6

Fonte: elaborazione dati New Line Ricerche di Mercato e IRi (anno terminante Giugno 2015)

EBM ?

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- GASTROENTERITE ACUTA
- **DERMATITE ATOPICA**

Probiotici in Pediatria: moda o nuovo approccio terapeutico?
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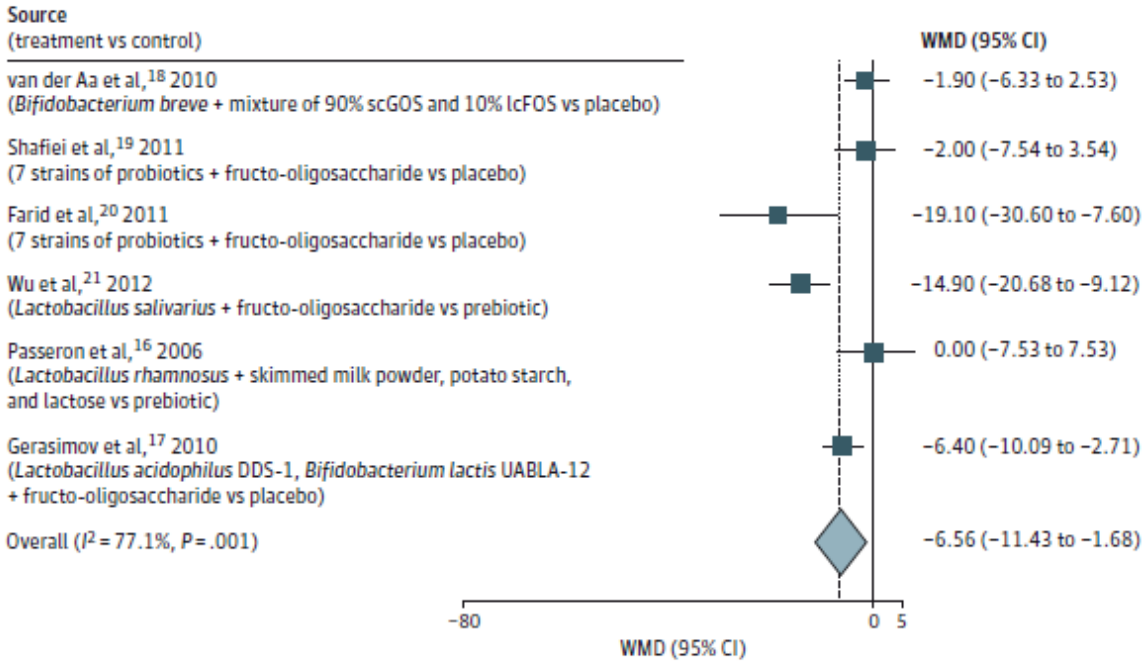
Synbiotics for Prevention and Treatment of Atopic Dermatitis
A Meta-analysis of Randomized Clinical Trials

JAMA Pediatrics March 2016 Volume 170, Number 3

Yung-Sen Chang, MD, MPH; Michelle K. Trivedi, MD, MPH; Ayan Jha, MBBS, MPH; Yen-Feng Lin, MD; Liezeel Dimaano, MD, MPH; Maria T. García-Romero, MD, MPH

Figure 2. Forest Plot for Weighted Mean Difference (WMD) in Change in Severity Scoring of Atopic Dermatitis (SCORAD) Index at 8 Weeks of Treatment With Synbiotics



Weights are from random-effects analysis. lcFOS indicates long-chain fructo-oligosaccharides; scGOS, short-chain galacto-oligosaccharides.

Synbiotics for Prevention and Treatment of Atopic Dermatitis
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Chang and colleagues performed a meta-analysis on randomized clinical trials evaluating synbiotics for the treatment and prevention of AD. The authors concluded that while there is insufficient evidence of effectiveness for prevention of AD, there is evidence to support synbiotic use in treatment of established AD, particularly for synbiotics containing mixtures of probiotics and in children aged 1 year or older. Meta-analysis of 6 treatment studies revealed a significant decrease in the weighted mean difference of Severity Scoring of Atopic Dermatitis (SCORAD) values in the synbiotics group compared with the control group after 8 weeks of treatment (weighted mean difference, −6.56; 95% CI, −11.43 to −1.68; $P = .008$; $I^2 = 77.1\%$) but not at 4 weeks. Longer duration of treatment (12 weeks) did not provide additional benefit.

Examining the Evidence for Using Synbiotics to Treat or Prevent Atopic Dermatitis

JAMA Pediatrics March 2016 Volume 170, Number 3

Mimi L. K. Tang, MBBS, PhD, FRACP, FRCPA; Caroline J. Lodge, MBBS, PhD

In summary, based on the current evidence, it is not appropriate to recommend synbiotics for the treatment of AD at this time.

The meta-analysis conducted by Chang and colleagues offers encouraging findings, but the small number of studies and the significant heterogeneity of those studies limit the quality of evidence and confidence in the findings.

Moreover, several issues around the practicalities of using synbiotics in the clinical setting are yet to be resolved.

Examining the Evidence for Using Synbiotics to Treat or Prevent Atopic Dermatitis

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Further studies are required
-to confirm reproducibility of beneficial effects with selected synbiotic combinations;
- to define the optimal combination of agents, dose of each component, duration of treatment, and age group of patients for clinical effectiveness;
- to clarify whether any chosen synbiotic combination is indeed more effective than its respective probiotic or prebiotic components as single interventions.

Examining the Evidence for Using Synbiotics to Treat or Prevent Atopic Dermatitis

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In addition, the clinical relevance of synbiotic use should be supported by studies to determine whether reduced eczema severity can be maintained during longer treatment periods and whether there is rebound of symptoms or continued benefit after treatment is discontinued.

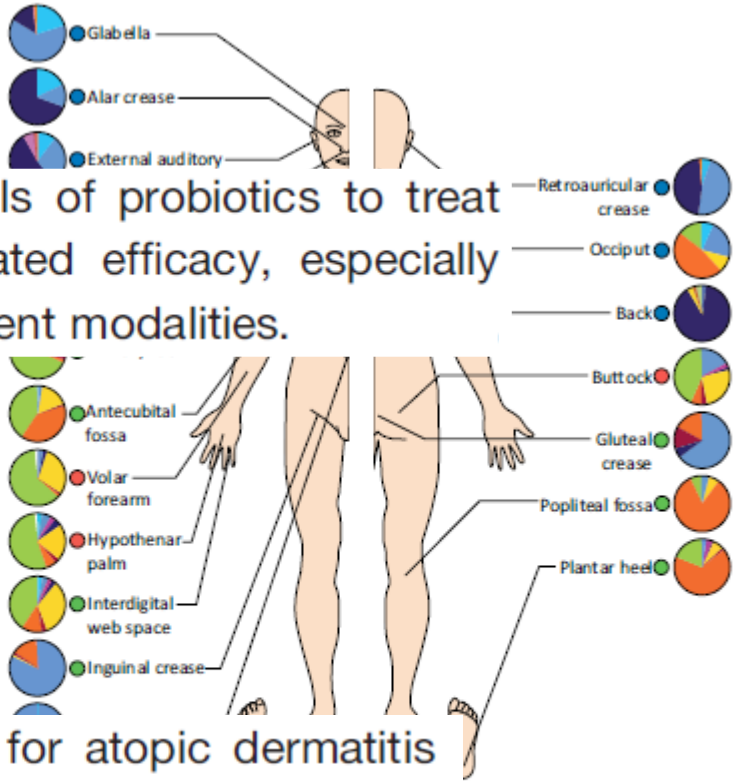
In relation to prevention of AD, there is insufficient evidence to confirm effectiveness of synbiotics.

Microbiome and pediatric atopic dermatitis

Journal of Dermatology 2015; **42**: 1137–1142

Claire E. POWERS,[1] Diana B. MCSHANE,[2] Peter H. GILLIGAN,[3] Craig N. BURKHART,[2] Dean S. MORRELL[2]

Randomized clinical trials of probiotics to treat atopic dermatitis have not demonstrated efficacy, especially when compared with traditional treatment modalities.



bacteria on skin sites.

Most probiotics for atopic dermatitis have only contained one or two microbes, which is in contrast to the normal skin that maintains a plethora of commensal organisms. Therefore, even if deemed effective, the exact composition, along with the route of administration and safety of an eventual probiotic treatment, must be determined.

EBM ?

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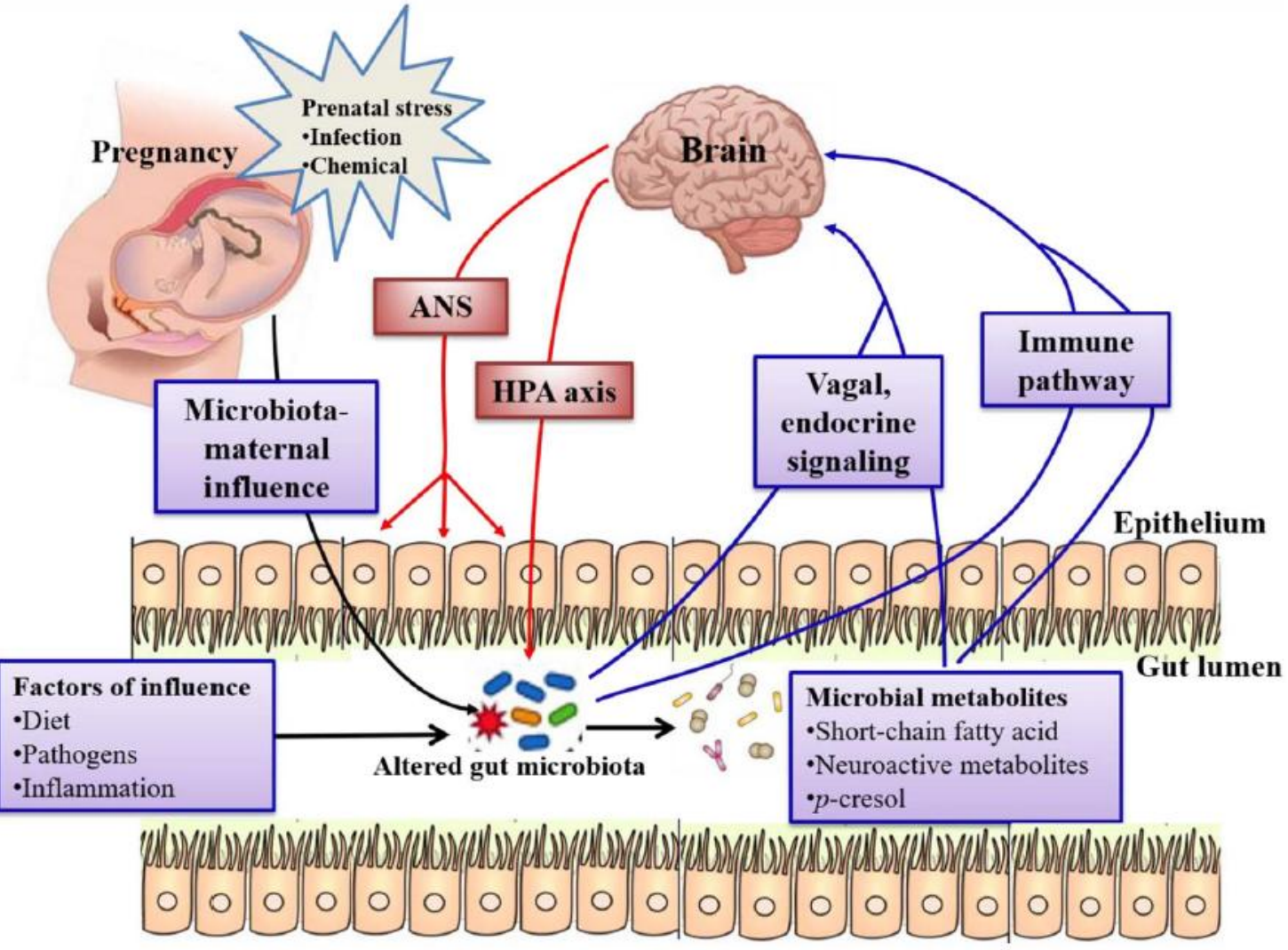
- DERMATITE ATOPICA
- **SPETTRO AUTISTICO**

Probiotici in Pediatria: moda o nuovo approccio terapeutico?
S. Bernasconi

Targeting gut microbiome: A novel and potential therapy for autism

Yongshou Yang[a,*], Jinhu Tian[b], Bo Yang[a]

Life Sciences 194 (2018) 111–119



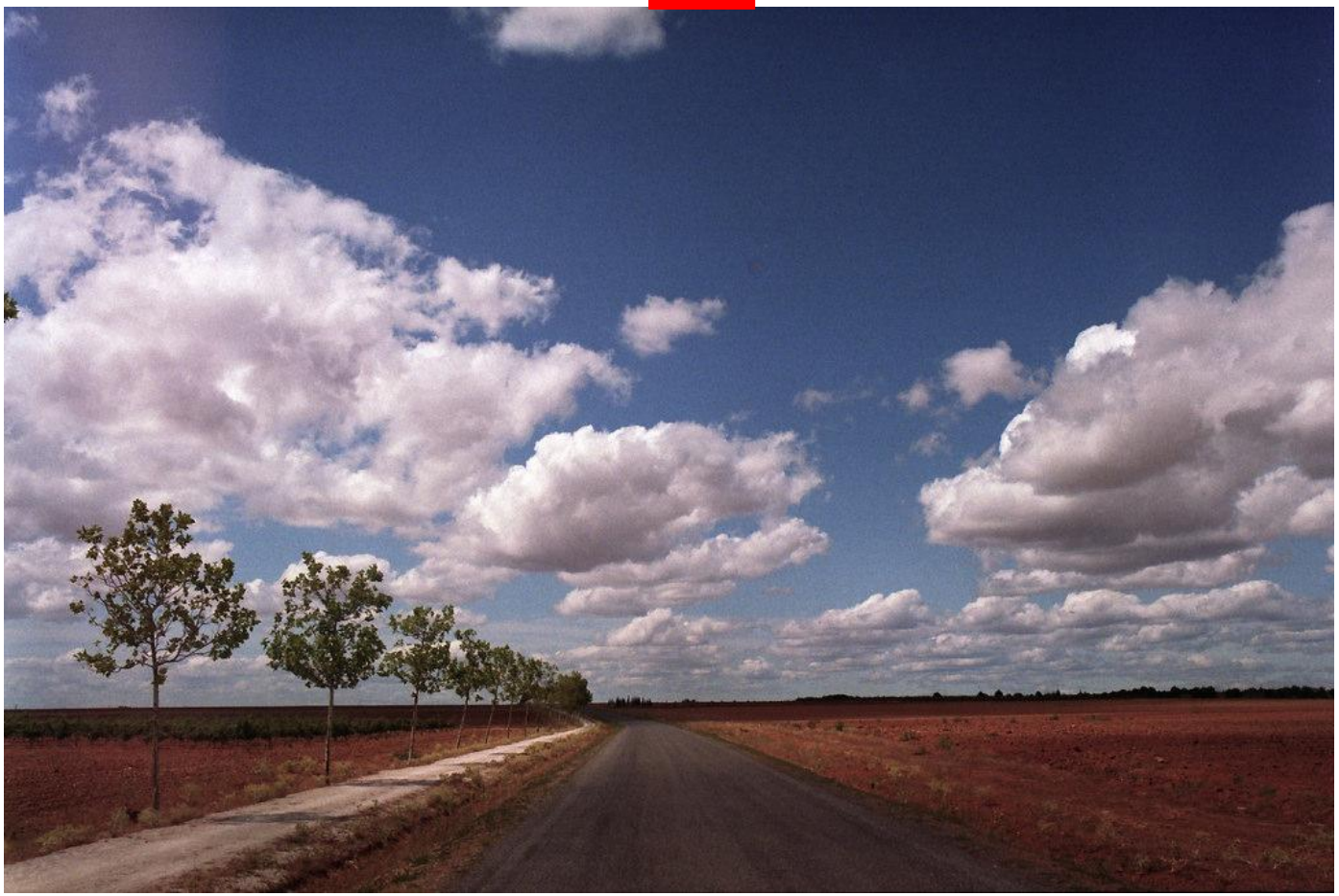
Targeting gut microbiome: A novel and potential therapy for autism

Yongshou Yang[a,*], Jinhu Tian[b], Bo Yang[a]

Life Sciences 194 (2018) 111–119

However, the detailed roles of gut microbiome in the pathology of ASD are still unclear, and thus studies investigating mechanisms, such as the contributions of immune, neural, and endocrine pathways in microbiome-brain communications, are significant. Moreover, the disputed microbial alterations seen in ASD patients need to be examined deeply. Additionally, caution should be taken in using the probiotics applied in animal models into human clinics. Finally, the effects of a large number of symbiotic species and their metabolites in the body of hosts remain unknown, and they may act as carriers for therapeutic substances. It is therefore crucial to elucidate their functions in the future.

EBM



Probiotici in Pediatria: moda o nuovo approccio terapeutico?
S. Bernasconi

Nutrition in Paediatric Inflammatory Bowel Disease:

A Position Paper on Behalf of The Porto IBD Group of ESPGHAN

*Erasmo **Miele**[1], Raanan **Shamir**[2], Marina **Aloi**[3], Amit **Assa**[2], Christian **Braegger**[4], Jiri **Bronsky**[5], Lissy **de Ridder**[6], Johanna C. **Escher**[6], Iva **Hojsak**[7], Sanja **Kolaček**[7], Sibylle **Koletzko**[8], Arie **Levine**[9], Paolo **Lionetti**[10], Massimo **Martinelli**[1], Frank **Ruemmele**[11], Richard K. **Russell**[12], Rotem **Sigall Boneh**[9], Johan **van Limbergen**[13], Gigi **Veereman**[14], Annamaria **Staiano**[1].*

Journal of Pediatric Gastroenterology and Nutrition, Publish Ahead of Print

High quality studies on the effect of probiotics in paediatric IBD are limited, with only three RCTs two in UC (228, 229) and one in CD (230). Some extrapolations can be made from adult data (231-242) but these have limited applicability in the paediatric population.

Probiotics in Newborns and Children

Mary W. Lenfestey, MD[a], Josef Neu, MD[b,*]

Pediatr Clin N Am 64 (2017) 1271–1289

Conclusioni

Overall, this is an area that does show great promise for certain conditions. Probiotic therapy should continue to be further investigated, with specific focus on the most useful strains and dosing for effect. As probiotics are used more and more for disease-altering purposes, it may also be time to classify them as medications or drugs to subjugate them to more stringent regulatory oversight.

Grazie per l'attenzione

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