

VII CONGRESSO NAZIONALE B&M 2018

I SESSIONE

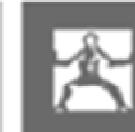


Dott. Sergio Riso

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Coordinatore Didattico Regionale SINPE



Microbiota: l'utilizzo dei probiotici

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S.C. Dietetica e Nutrizione Clinica
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Microbiota e patologie/sindromi

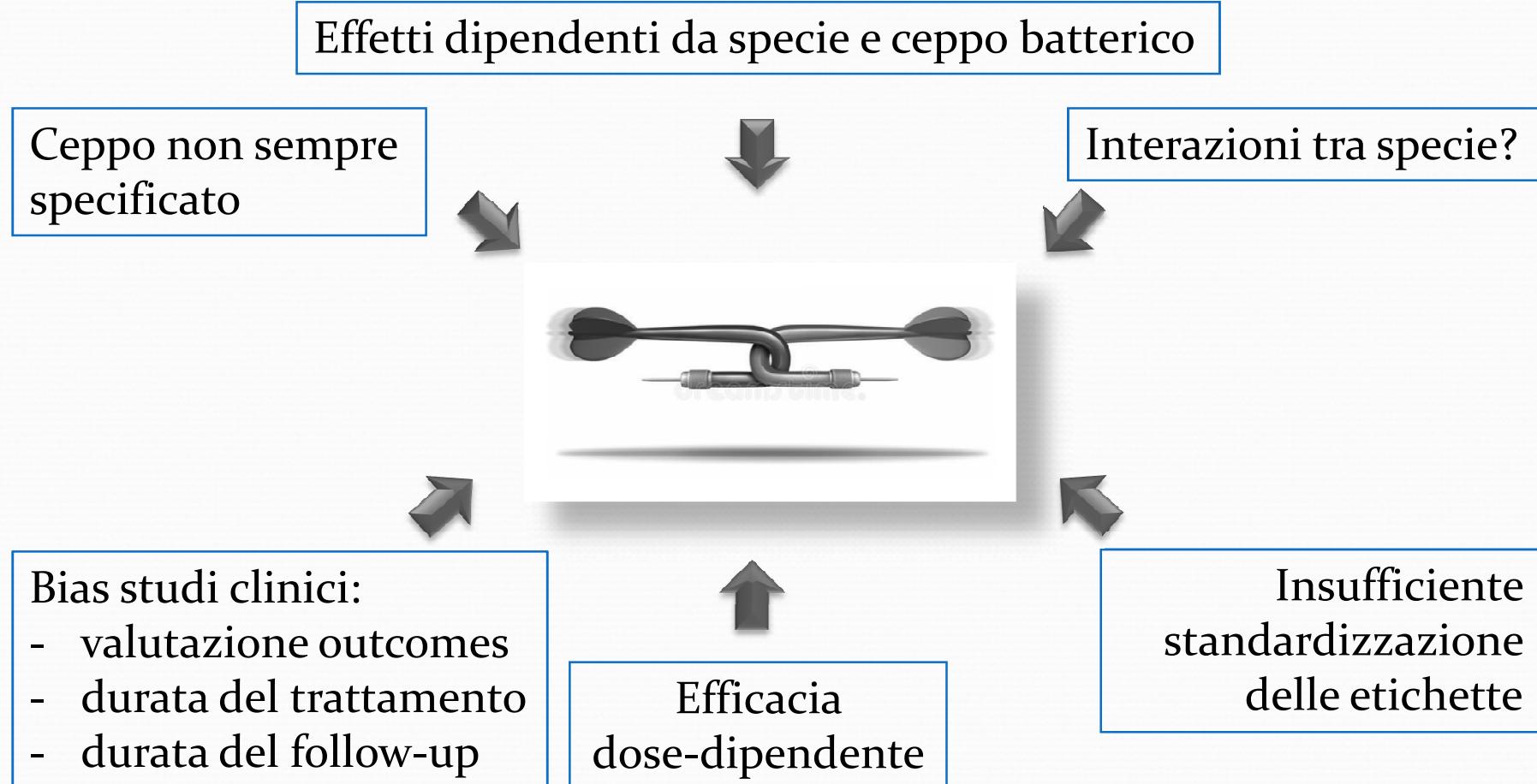
Crohn's disease
Ulcerative colitis
Irritable bowel syndrome
Clostridium difficile infection
Colorectal cancer
Allergy/atopy
Celiac disease
Type 1 diabetes
Type 2 diabetes
Obesity



Alzheimer's disease
Atherosclerosis
Autistic spectrum disorders
Chronic fatigue syndrome
Colic babies
Cardiovascular disease
Depression and anxiety
Frailty
Graft-vs-host disease
Multiple sclerosis
Nonalcoholic fatty liver disease
Parkinson's disease
Rheumatoid arthritis
Retrovirus infection
Poliovirus infection

de Vos WM. Nutr Rev 2012

Probiotici: evidenze eterogenee

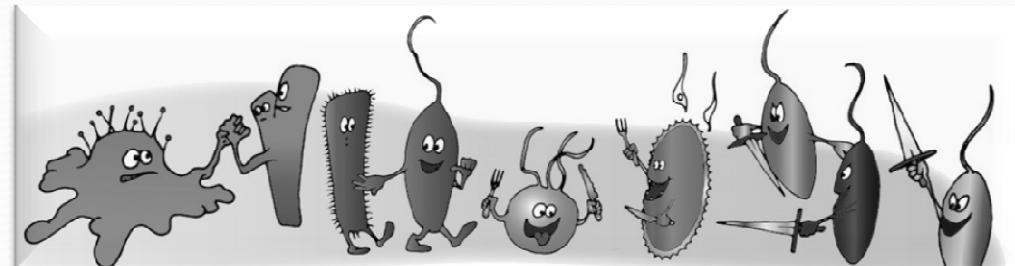


Inoltre ...

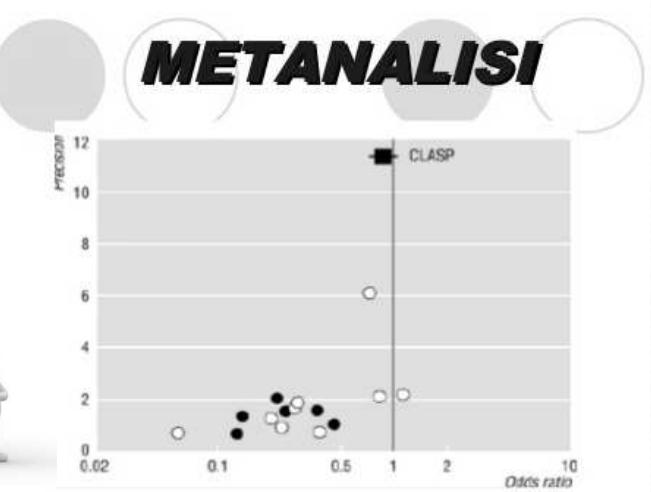
CORRESPONDENCE

Pooling data on different probiotics is not appropriate to assess the efficacy of probiotics

Hania Szajewska



Eur J Pediatr 2014

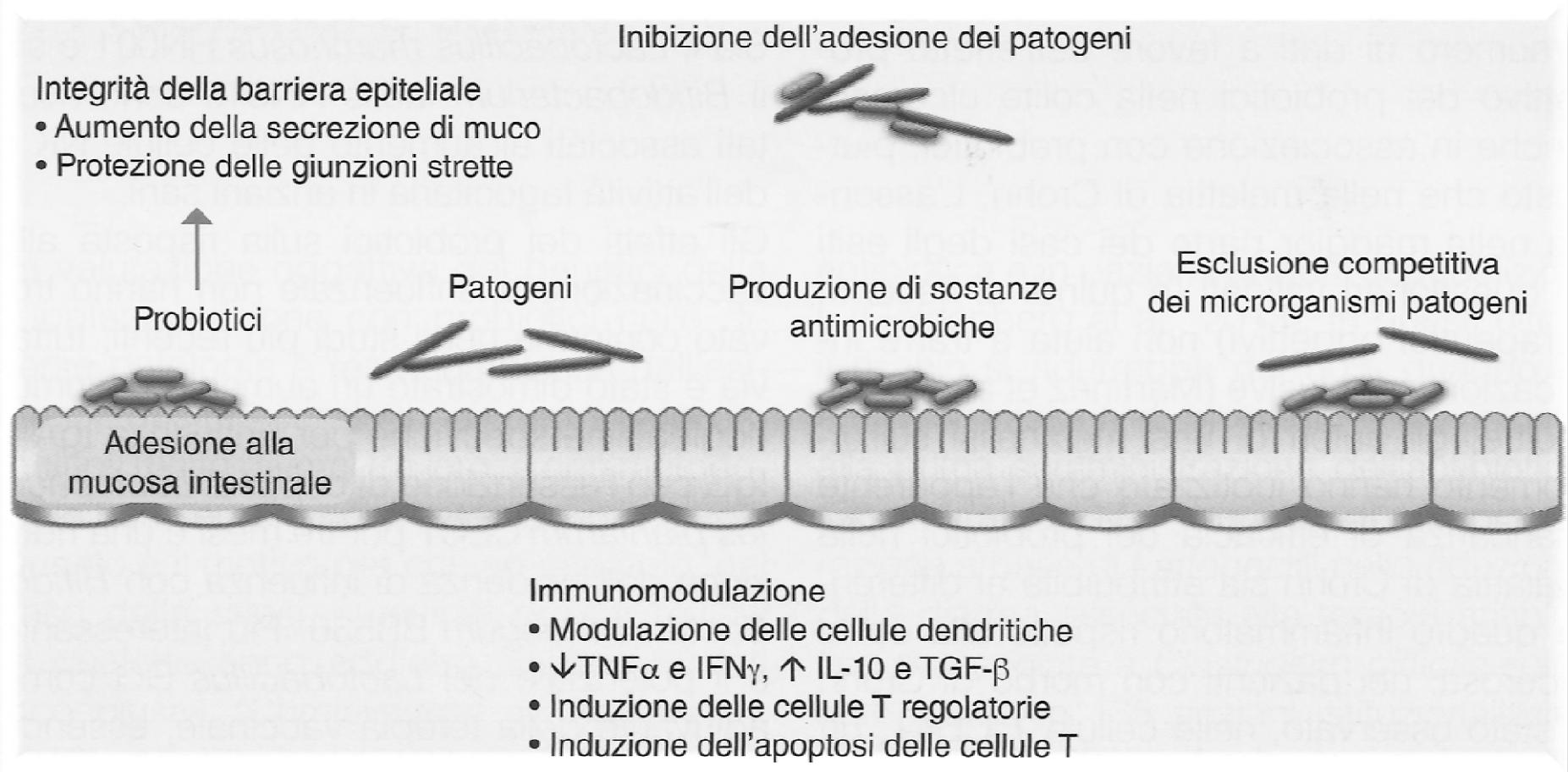


Principali specie e
ceppi di comune
impiego

Ghoshal UC. J
Gastroenterol
Hepatol 2018

<i>Bifidobacterium</i> spp.	<i>B. breve</i> SD5206 <i>B. bifidum</i> CUL20 <i>B. infantis</i> SD5220 <i>B. lactis</i> CUL34 <i>B. longum</i> SD5219 <i>B. longum infantis</i> 35624
<i>Escherichia</i> spp.	<i>E. coli</i> Nissle 1917
<i>Lactobacillus</i> spp.	<i>L. acidophilus</i> CL 1285, CUL21, CUL60, SD512 <i>L. bulgaricus</i> SD5210 <i>L. casei</i> LBC80R, SD5218 <i>L. helveticus</i> R0052 <i>L. paracasei</i> 8700:2 <i>L. plantarum</i> 299v, HEAL9, SD5209 <i>L. reuteri</i> ATCC 55730, ATCC PTA 5289, DSM 17938, NCIMB 30242 <i>L. rhamnosus</i> CLR2, GG, R0011 <i>S. boulardii</i> lyo <i>S. cerevisiae</i> I-3856
<i>Saccharomyces</i> spp.	<i>S. salivarius</i> K12
<i>Streptococcus</i> spp.	<i>S. thermophilus</i> SD5207

Probiotici: meccanismi d'azione



Evidence-based medicine



Diarrea da antibiotici



Cochrane Database of Systematic Reviews

Probiotics for the prevention of pediatric antibiotic-associated diarrhea (Review)

Goldenberg JZ, Lytvyn L, Steurich J, Parkin P, Mahant S, Johnston BC

2015

- 23 studi clinici (3938 partecipanti, tra 0 e 18 anni)
- Probiotici (*Lactobacilli spp.*, *Bifidobacterium spp.*, *Streptococcus spp.*, or *Saccharomyces boulardii*) da soli o in associazione, contemporaneamente alla terapia antibiotica (3-30 gg)

Outcomes	Anticipated absolute effects* (95% CI)		Effect size (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)
	Risk with control	Risk with Probiotics			
Incidence of diarrhea Follow up: range 1 week to 12 weeks	191 per 1000	88 per 1000 (67 to 116)	- 54%	3898 (22 RCTs)	⊕⊕⊕○ MODERATE ^{1,2}

Implications for practice



Moderate quality evidence suggests a **protective effect** of probiotics in preventing antibiotic-associated diarrhea (AAD)

Among the various probiotics evaluated, evidence suggests that **Lactobacillus rhamnosus or Saccharomyces boulardii** at 5 to 40 billion colony forming units/day may be appropriate in otherwise healthy children.

Serious adverse events have been observed in severely debilitated or immunocompromised children with underlying risk factors including central venous catheter use and disorders associated with bacterial/fungal translocation. Until further research has been conducted, probiotic use **should be avoided in pediatric populations at risk** for adverse events.

Diarrea da Clostridium difficile



**Cochrane
Library**

Cochrane Database of Systematic Reviews

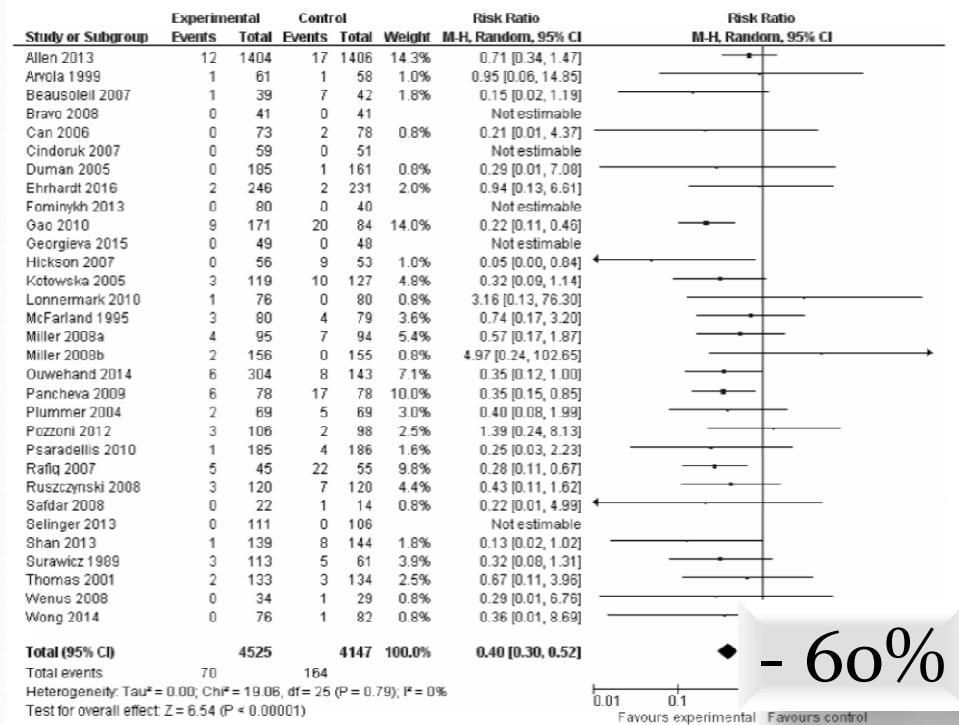
Probiotics for the prevention of Clostridium difficile-associated diarrhea in adults and children (Review)

Goldenberg JZ, Yap C, Lytvyn L, Lo CKF, Beardsley J, Mertz D, Johnston BC

2017

- 31 studi clinici (8672 partecipanti, adulti e bambini in terapia antibiotica)
- Durata del trattamento con probiotici (da soli o in associazione): almeno per tutta la durata della terapia antibiotica (in alcuni casi fino a 7 gg dopo)

Diarrea da Clostridium difficile



Implications for practice

- Moderate quality evidence supports a large **protective effect** for probiotics (e.g. *S. boulardii* or *L. acidophilus plus L. casei* at a dose of 10 to 50 billion CFUs per day) in preventing *Clostridium difficile* associated diarrhea.
- The short-term use of probiotics appear to be **safe and effective** when used as an **adjunct to antibiotics** in immunocompetent patients

Infezione da *Helicobacter pylori*

Guidelines

Management of *Helicobacter pylori* infection—the Maastricht V/Florence Consensus Report

P Malfertheiner,¹ F Megraud,² C A O'Morain,³ J P Gisbert,^{4,5} E J Kuipers,⁶ A T Axon,⁷ F Bazzoli,⁸ A Gasbarrini,⁹ J Atherton,¹⁰ D Y Graham,¹¹ R Hunt,^{12,13} P Moayyedi,¹⁴ T Rokkas,¹⁵ M Rugge,¹⁶ M Selgrad,¹⁷ S Suerbaum,¹⁸ K Sugano,¹⁹ E M El-Omar,²⁰ on behalf of the European Helicobacter and Microbiota Study Group and Consensus panel

Gut 2017

Statement 9: Only certain probiotics have been shown to be effective in reducing GI side effects caused by *H. pylori* eradication therapies. Specific strains should be chosen only upon the basis of a demonstrated clinical efficacy.

Level of evidence: moderate

Grade of recommendation: strong

- *Lactobacillus*
- *Saccharomyces boulardii*



per almeno 2 settimane
LV Z. Exp Ther Med 2015

Statement 10: Certain probiotics may have a beneficial effect on *H. pylori* eradication.

Level of evidence: very low

Grade of recommendation: weak

- *Lactobacillus*
- *Bifidobacterium*
- *Saccharomyces boulardii*

Efficacia correlata alla riduzione degli effetti collaterali (nausea, diarrea) della terapia eradicante, più che ad effetti diretti

Colon irritabile: disbiosi (un quadro proinfiammatorio)

Taxon	Percentage in IBS
<i>Enterobacteriaceae</i>	Higher
<i>Lactobacillus</i>	Lower
<i>Lactobacillus</i> genus or <i>Lactobacillales</i> order	Higher
<i>Bifidobacterium</i>	Lower
<i>Firmicutes/Bacteroides</i>	Higher
<i>Firmicutes/Bacteroides</i>	Lower

Taxon	Percentage in IBS
<i>Clostridiales</i>	
Ruminococcaceae or <i>Ruminococcus</i>	Higher
<i>Erysipelotrichaceae</i>	
<i>Methanogens</i>	Lower
<i>Veillonella</i>	Higher
<i>Faecalibacterium</i>	Lower

Rodinõ-Janeiro BK. Adv Ther 2018

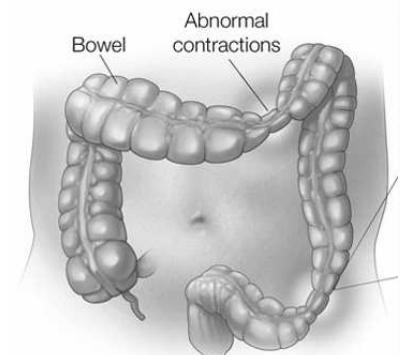
IBS: effetti dei probiotici

	No. of studies	Mantel–Haenszel risk ratio (95% CI) for any probiotic versus placebo	P-value
Persistence of symptoms	23	0.79 (0.70, 0.89)	< 0.0001
Global symptom or abdominal pain scores	25	−0.25 (−0.36, −0.14)	< 0.0000
Bloating scores	18	−0.15 (−0.27, −0.03)	0.01
Flatulence scores	10	−0.23 (−0.38, −0.07)	0.004

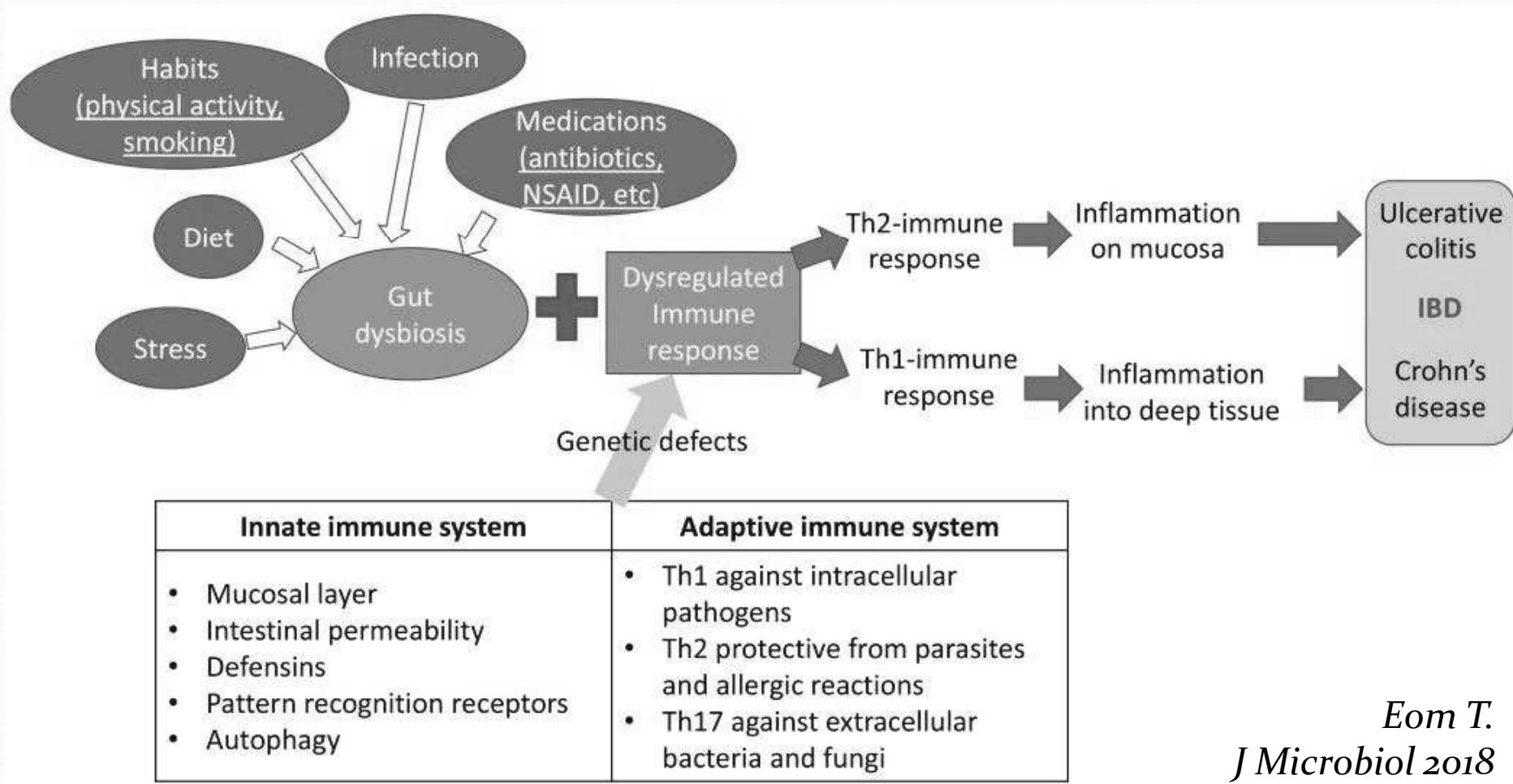
CI, confidence interval.

Ford AC. Am. J. Gastroenterol. 2014

- superiorità delle combinazioni rispetto a singoli probiotici
- effetti dei singoli probiotici:
 - *Lactobacillus* migliora flatulenza
 - *Bifidobacterium* migliora dolore addominale
 - *Escherichia* e *Streptococcus* riducono la persistenza dei sintomi
- non si conoscono dose e durata del trattamento ottimali



Malattie infiammatorie croniche intestinali: patogenesi



Eom T.
J Microbiol 2018

IBD: disbiosi

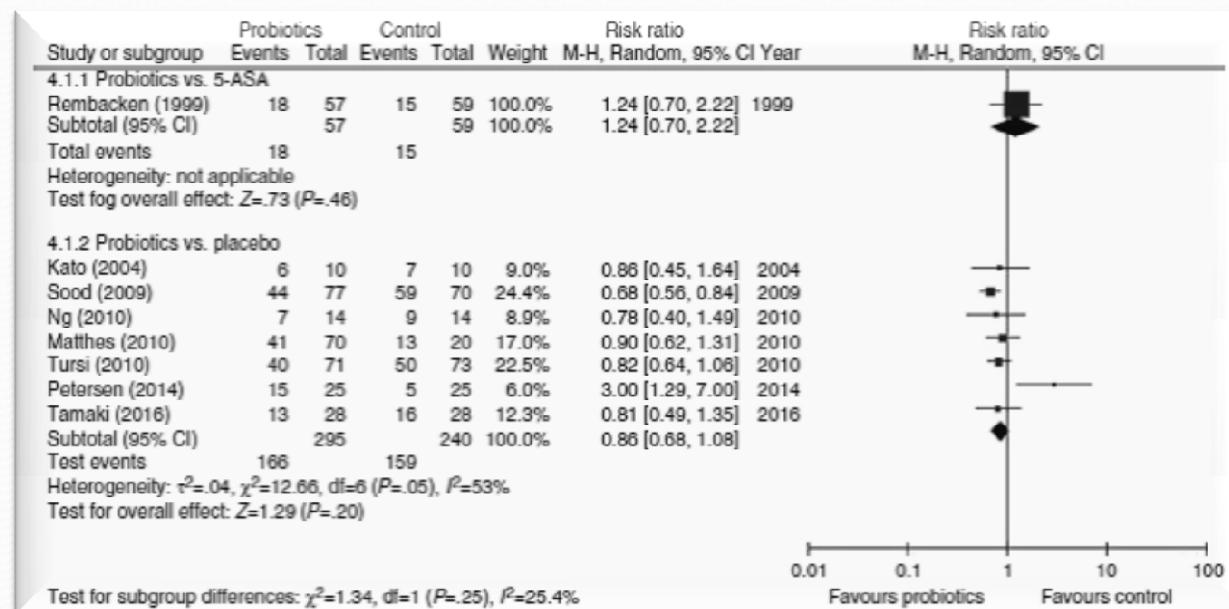
- Reduced diversity of the microbiota
(Decrease of Firmicutes)
- Decrease of SCFA-producing bacteria
(Decrease of *Clostridium* cluster IV, XIVa, XVII
and *Faecalibacterium prausnitzii*)
- Increase of mucolytic bacteria
(*Ruminococcus gnavas*, *Ruminococcus torques*)
- Increase of sulfate-reducing bacteria
(*Desulfovibrio*)
- Increase of pathogenic bacteria
(Adhesion/invasive *E. coli*)

Nishida A. Clin J Gastroenterol 2018

Systematic review with meta-analysis: the efficacy of probiotics in inflammatory bowel disease

Y. Derwa^{1,2,*} | D. J. Gracie^{1,2,*}  | P. J. Hamlin¹ | A. C. Ford^{1,2} 

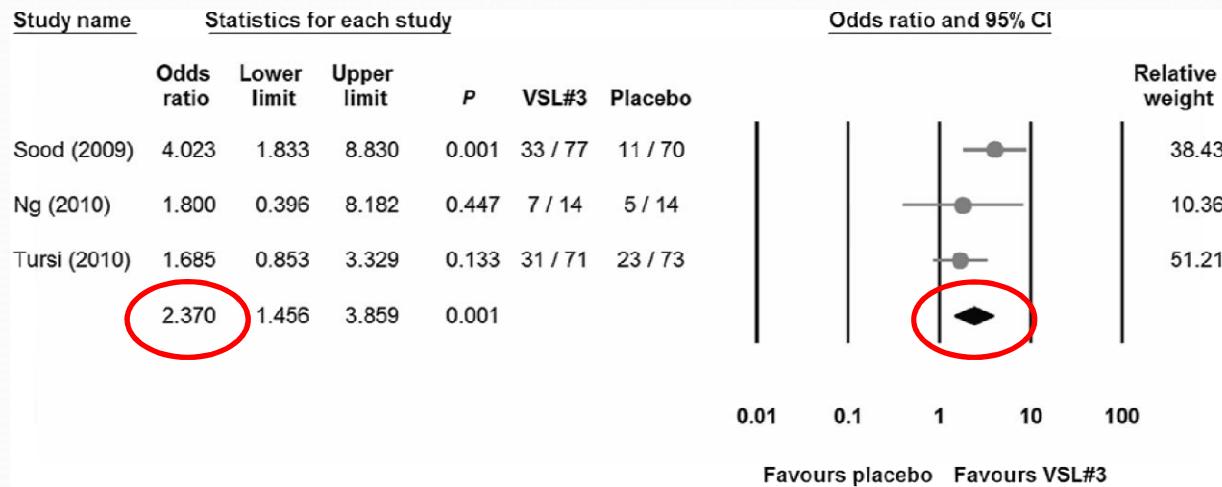
Aliment Pharmacol Ther. 2017



Nessuna efficacia nell'induzione della remissione nella RCU in fase attiva
(vs 5-ASA o placebo)

Probiotic Mix VSL#3 Is Effective Adjunctive Therapy for Mild to Moderately Active Ulcerative Colitis: A Meta-analysis

Mardini HE. Inflamm Bowel Dis 2014



VSL#3:
4 *Lactobacilli*
3 *Bifidobacteria*
1 *Streptococcus*

Efficacia di VSL#3 ad alte dosi (3.6×10^{12} CFU/d), ad integrazione del trattamento standard, sull'induzione della remissione clinica nelle forme di RCU di grado lieve-moderato: 43.8 % vs 24.8% (p=0.006)