

**top**  
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in gastroenterologia

9<sup>a</sup> E D I Z I O N E

2-3 MARZO 2018

BERGAMO Hotel Excelsior S. Marco  
Piazza della Repubblica, 6

# Probiotici come Profilassi e Terapia delle Malattie infettive

Relatore

Dr Giorgio Severgnini

Divisione di Medicina Generale

ASST-Bergamo EST Ospedale Bolognini di Seriate

# DI CHE COSA PARLEREMO?

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- Probiotici e HP
- Probiotici e tratto urinario
- Probiotici e terapia antibiotica
- Probiotici e diarrea del viaggiatore
- Probiotici ed HIV

Drug Design, Development and Therapy

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REVIEW

# Antibiotic susceptibility, heteroresistance, and updated treatment strategies in *Helicobacter pylori* infection

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Drug Design, Development and Therapy  
28 July 2017

# Antibiotic susceptibility, heteroresistance, and updated treatment strategies in *Helicobacter pylori* infection

Recommendation	Regimen	Definition
First line		
Recommended option	Bismuth quadruple (PBMT)	PPI + bismuth + metronidazole <sup>a</sup> + tetracycline
Recommended option	Concomitant non-bismuth quadruple (PAMC)	PPI + amoxicillin + metronidazole <sup>a</sup> + clarithromycin
Restricted option <sup>b</sup>	PPI triple (PAC, PMC, or PAM)	PPI + amoxicillin + clarithromycin PPI + metronidazole <sup>a</sup> + clarithromycin

Appl Microbiol Biotechnol (2018) 102:1–7  
DOI 10.1007/s00253-017-8535-7

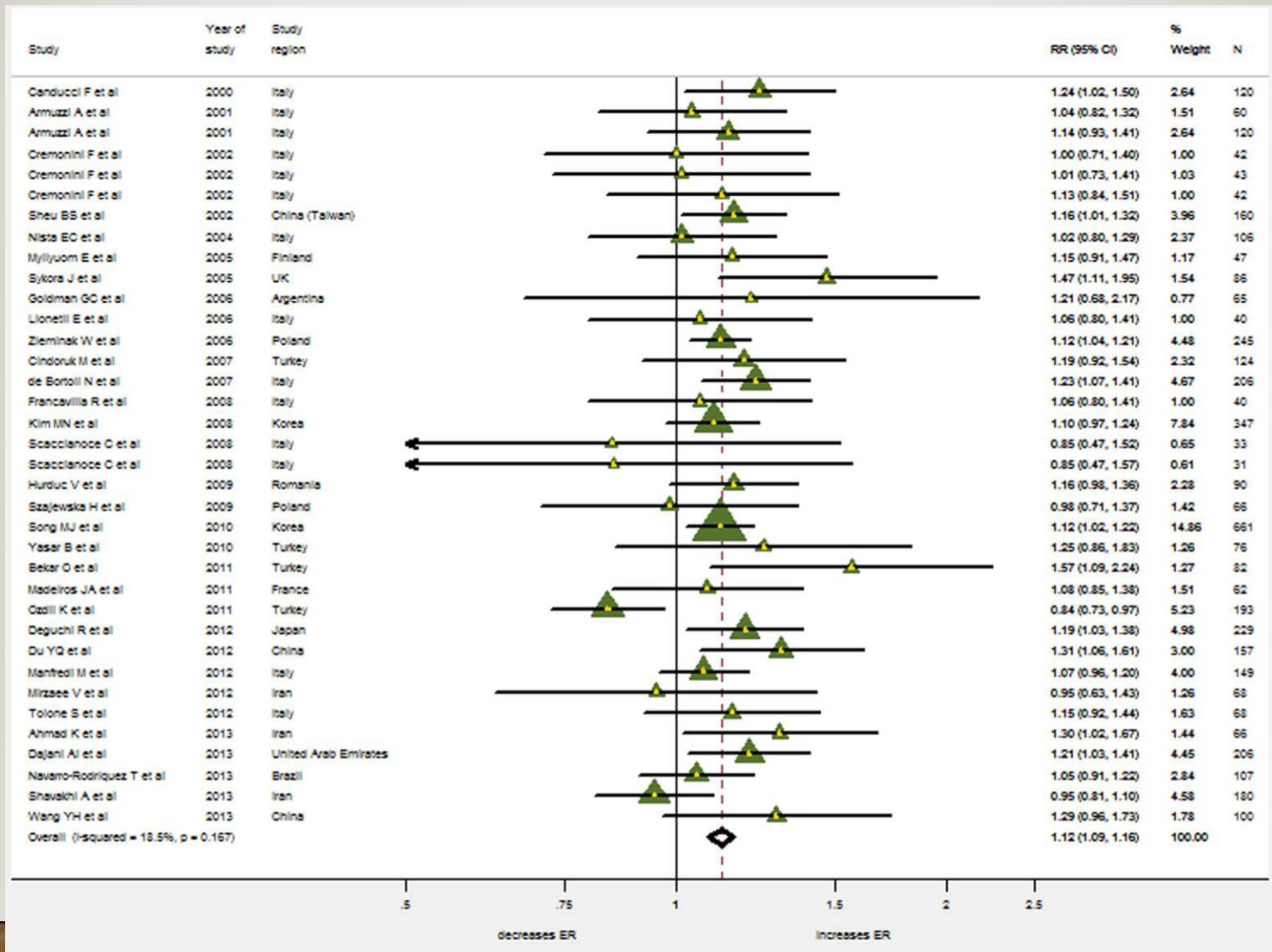


MINI-REVIEW

## *Helicobacter pylori* treatment: antibiotics or probiotics

Kamila Goderska<sup>1</sup>  • Sonia Agudo Pena<sup>1</sup> • Teresa Alarcon<sup>2</sup>

# Effetto della supplementazione con Probiotici nel tasso di eradicazione



## ***Helicobacter pylori* treatment: antibiotics or probiotics**

Kamila Goderska<sup>1</sup>  • Sonia Agudo Pena<sup>1</sup> • Teresa Alarcon<sup>2</sup>

Related to probiotics, probiotics could not be recommended to be used as a single agent for eradication therapy. However, their use associated to standard treatment as an adjunct will improve the eradication rates and decrease treatment-related side effects.

Review article

*European Journal of Microbiology and Immunology* 7 (2017) 3, pp. 158–167  
DOI: 10.1556/1886.2017.00016

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## **CHANGES OF THE INTESTINAL MICROBIOME–HOST HOMEOSTASIS IN HIV-INFECTED INDIVIDUALS – A FOCUS ON THE BACTERIAL GUT MICROBIOME**

**Ana Beatriz Dein Terra Mota Ribeiro, Markus M. Heimesaat\*, Stefan Bereswill**

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Received: June 28, 2017; Accepted: July 24, 2017



# Modificazioni del MI in pazienti con infezione da HIV<sub>4</sub>

**Table 1.** Summary of the main findings

Study details and study type	Study population	Type of sample analyzed	Microbiome analysis technique	Main findings (HIV+ compared to controls)
Nowak et al. 2015 (26)  Observational study with longitudinal components	31 HIV+ ART naive individuals (28 viremic patients, 3 elite controllers) 9 HIV- individuals	Stool and blood samples	16S rRNA sequencing	<p>Before ART:</p> <ul style="list-style-type: none"> <li>• ↓ <math>\alpha</math> diversity in untreated HIV+ patients</li> <li>• ↑ <math>\beta</math> diversity</li> </ul> <p>Elite controllers' gut microbiome composition resembles healthy controls' gut microbiome more than that of viremic patients</p> <ul style="list-style-type: none"> <li>• ↑ Bacteroidetes in elite controllers compared to viremic patients (<math>p = 0.02</math>)</li> <li>• ↑ Actinobacteria and Proteobacteria in viremic patients compared to elite controllers (<math>p = 0.02</math>)</li> </ul> <p>Viremic patients compared to HIV- individuals:</p> <p>Firmicutes:</p> <ul style="list-style-type: none"> <li>• ↑ <i>Lactobacillus</i></li> <li>• ↓ <i>Lachnobacterium</i> (<math>p = 0.018</math>)</li> <li>• ↓ <i>Faecalibacterium</i> (<math>p = 0.008</math>)</li> </ul> <p>Proteobacteria:</p> <ul style="list-style-type: none"> <li>• ↓ <i>Haemophilus</i> (<math>p = 0.04</math>)</li> </ul> <p>Viremic patients after ART introduction:</p> <ul style="list-style-type: none"> <li>• Further decrease of <math>\alpha</math> diversity (<math>p = 0.001</math>)</li> </ul> <p>Phyla:</p> <ul style="list-style-type: none"> <li>• ↓ Firmicutes (<i>Lachnospiraceae</i>)</li> <li>• ↓ Bacteroidetes (<i>Prevotella</i>) (<math>p = 0.0007</math>)</li> </ul>
Vázquez-Castellanos et al. 2015 (27)  Case-control study	15 HIV+ individuals on ART, 15 HIV- individuals	Stool samples	16S rRNA gene, metagenome sequencing	<ul style="list-style-type: none"> <li>• Healthy subjects cluster separately from positive subjects based on 16S rRNA sequencing.</li> <li>• HIV positive <ul style="list-style-type: none"> <li>↑ Bacteroidetes (<i>Prevotella</i>)</li> <li>↑ Proteobacteria (<i>Succinivibrio</i>, <i>Desulfovibrio</i>)</li> <li>↑ Firmicutes (<i>Catenibacterium</i>)</li> <li>↑ LPS biosynthesis</li> </ul> </li> <li>• HIV negative <ul style="list-style-type: none"> <li>↑ Bacteroidetes (<i>Bacteroides</i>)</li> <li>↑ Firmicutes (<i>Faecalibacterium</i>)</li> <li>↓ Starch and sucrose metabolism</li> <li>↓ Glycolysis/gluconeogenesis</li> </ul> </li> </ul>

Ribeiro et al.



*nutrients*



*Review*

# Microbiota and Probiotics in Health and HIV Infection

Chiara D'Angelo, Marcella Reale \* and Erica Costantini

Unit of Immunodiagnostic and Molecular Pathology, Department of Medical, Oral and Biotechnological Sciences, University "G. d'Annunzio" Chieti-Pescara, 66100 Chieti, Italy; chiara.dangelo@unich.it (C.D.); erica.costantini@unich.it (E.C.)

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Received: 26 January 2017; Accepted: 12 June 2017; Published: 16 June 2017

Review

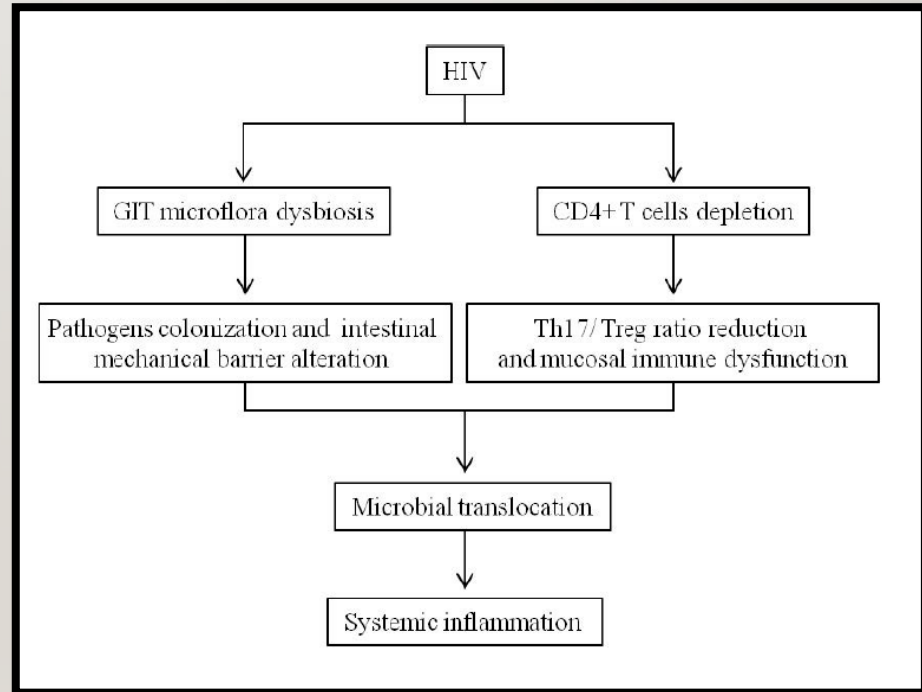
# Microbiota and Probiotics in Health and HIV Infection

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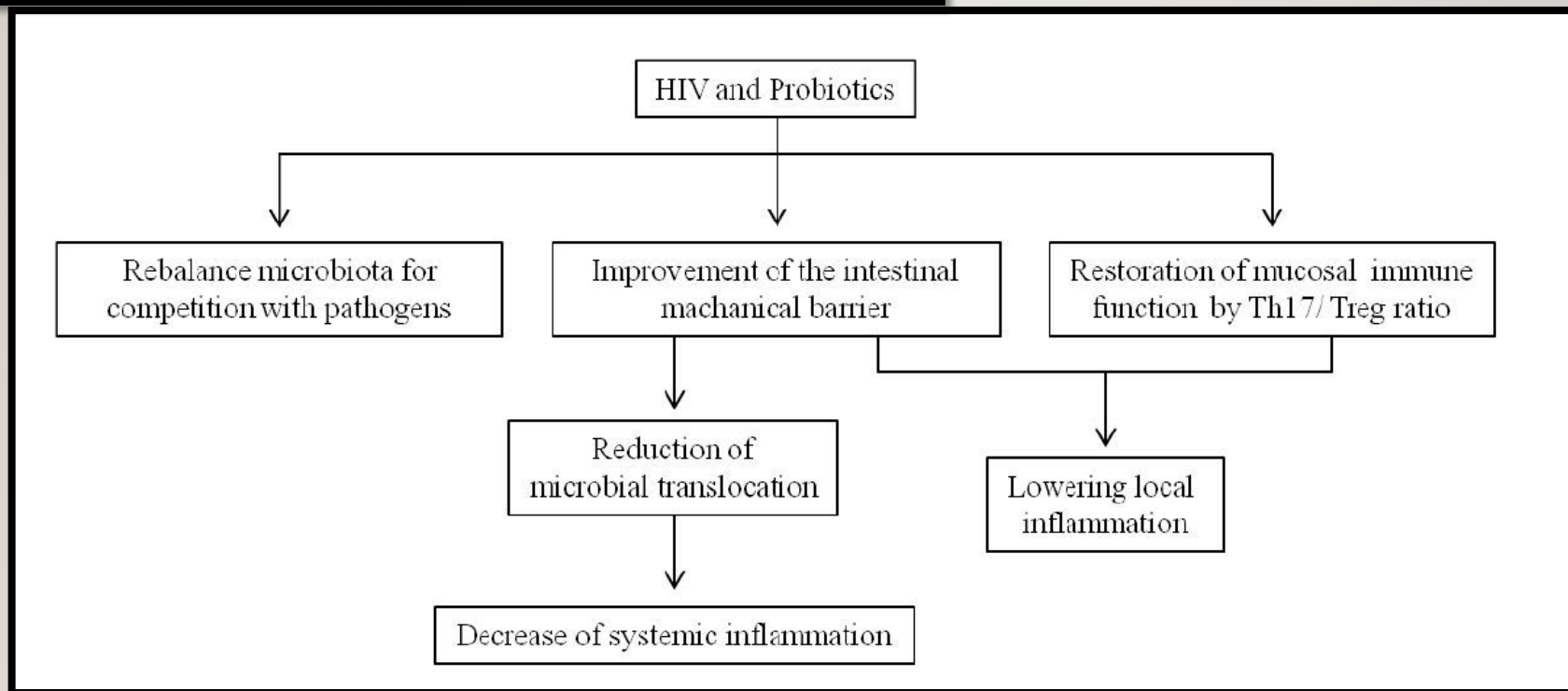
# Microbiota and Probiotics in Health and HIV Infection

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Received: 26 January 2017; Accepted: 12 June 2017; Published: 16 June 2017



*Open Forum Infectious Diseases*

REVIEW ARTICLE



# Probiotics in Human Immunodeficiency Virus Infection: A Systematic Review and Evidence Synthesis of Benefits and Risks

George M. Carter,<sup>1</sup> Aryan Esmaeili,<sup>2</sup> Hardikkumar Shah,<sup>2</sup> Debbie Indyk,<sup>3</sup> Matthew Johnson,<sup>4</sup> Michael Andreae,<sup>5</sup> and Henry S. Sacks<sup>3</sup>

<sup>1</sup>Foundation for Integrative AIDS Research, Brooklyn<sup>2</sup>Icahn School of Medicine at Mount Sinai<sup>3</sup>Department of Preventive Medicine, Icahn School of Medicine at Mount Sinai<sup>4</sup>Teachers College, Columbia University<sup>5</sup>Department of Anesthesiology, Albert Einstein College of Medicine, Bronx, New York

The data suggest possible benefits for CD4 count, recurrence or management of bacterial vaginosis, and diarrhea management.

We examined RCTs explicitly assessing sepsis in any patient population, and we found **zero** cases of supplement-associated bacteremia or fungemia in 39 randomized controlled trials comprising 9402 subjects. The estimated number needed to harm is 7369 in Bayesian approach.

# CMAJ OPEN

## Research

### ***Lactobacillus* probiotics in the prevention of diarrhea associated with *Clostridium difficile*: a systematic review and Bayesian hierarchical meta-analysis**

CMAJ Open 2016. DOI:10.9778/cmajo.20160087

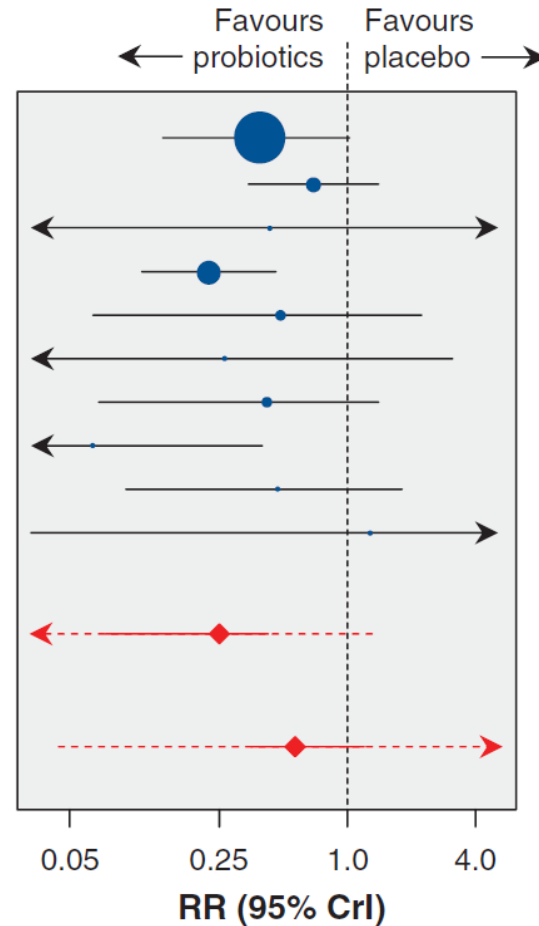
Alison Sinclair MD, Xuanqian Xie MSc, Lama Saab MSc, Nandini Dendukuri PhD

# Effetto dei Probiotici...

Study	RR (95% CrI)
Ouwehand et al. <sup>24</sup>	0.39 (0.14–1.03)
Allen et al. <sup>10</sup>	0.70 (0.35–1.39)
Selinger et al. <sup>25</sup>	0.43 (0.01–15.99)
Gao et al. <sup>20</sup>	0.23 (0.11–0.46)
Sampalis et al. <sup>26</sup>	0.48 (0.06–2.21)
Safdar et al. <sup>27</sup>	0.27 (0.01–3.13)
Beausoleil et al. <sup>28</sup>	0.42 (0.07–1.41)
Hickson et al. <sup>29</sup>	0.06 (0.00–0.40)
Plummer et al. <sup>30</sup>	0.47 (0.09–1.80)
Heimburger et al. <sup>31</sup>	1.29 (0.03–49.22)

Pooled RR with 95% credible and prediction intervals with vague prior distribution

Pooled RR with 95% credible and prediction intervals with skeptical prior distribution



Sinclair et al

# Conclusioni degli Autori

- The pooled risk ratio was highly statistically significant, at 0.25 (95% credible interval 0.08–0.47)
- However, owing to heterogeneity between studies, the beneficial effect of probiotics was more likely to be reported in studies with an increased risk of *C. difficile*-associated diarrhea in the control group.



# Timely Use of Probiotics in Hospitalized Adults Prevents *Clostridium difficile* Infection: A Systematic Review With Meta-Regression Analysis



Nicole T. Shen,<sup>1</sup> Anna Maw,<sup>2</sup> Lyubov L. Tmanova,<sup>3</sup> Alejandro Pino,<sup>4</sup> Kayley Ancy,<sup>4</sup> Carl V. Crawford,<sup>1</sup> Matthew S. Simon,<sup>5,6</sup> and Arthur T. Evans<sup>5</sup>

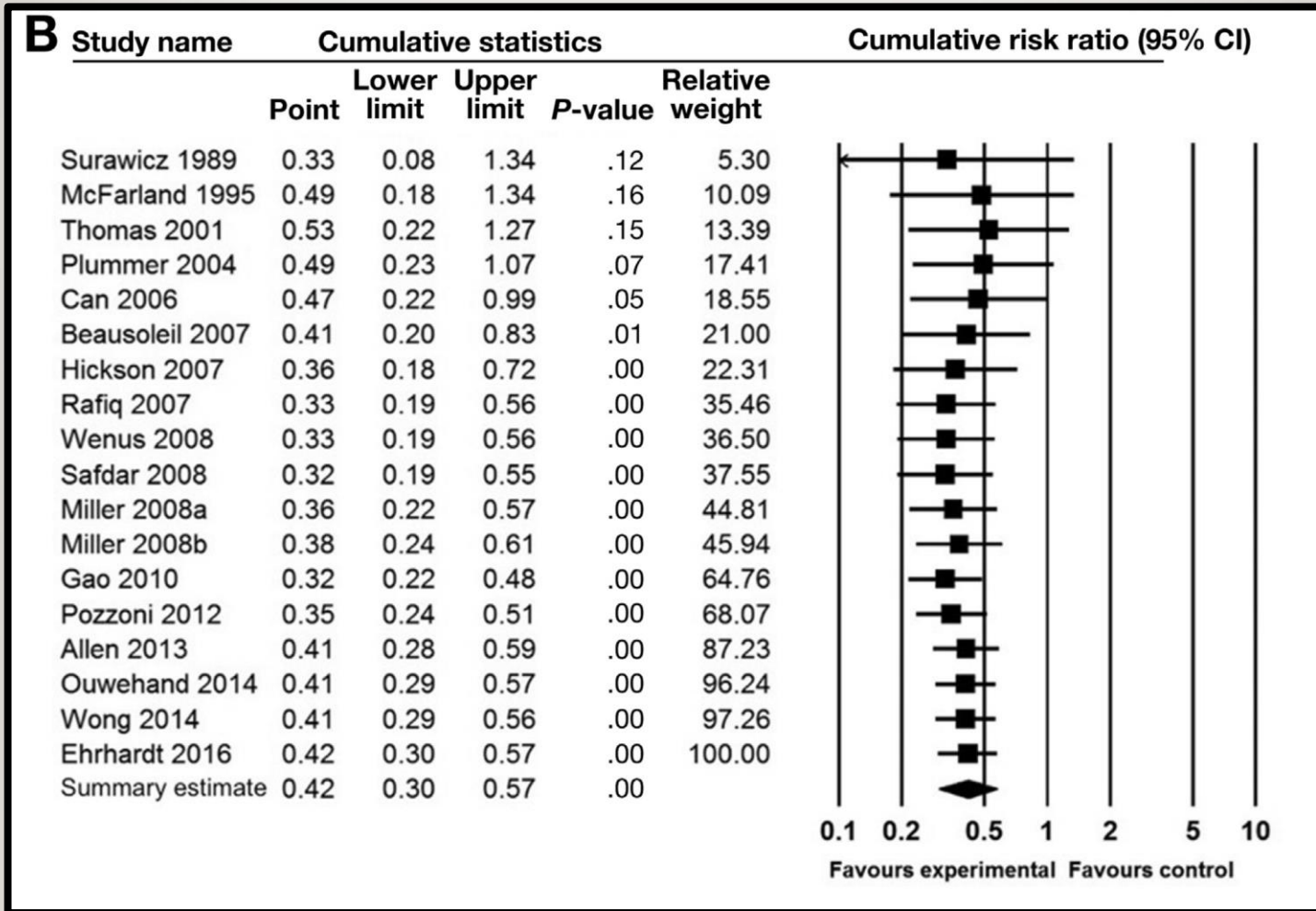
<sup>1</sup>Division of Gastroenterology and Hepatology, Weill Department of Medicine, Weill Cornell Medicine, New York, New York; <sup>2</sup>Hospitalist Medicine Section, Division of General Internal Medicine, Department of Medicine, University of Colorado, Denver, Colorado; <sup>3</sup>Samuel J. Wood Library and CV Starr Biomedical Information Center, Weill Cornell Medical College, New York, New York; <sup>4</sup>NewYork-Presbyterian-Weill Cornell Medical Center, New York, New York; <sup>5</sup>Section of Hospital Medicine, Division of General Internal Medicine, Weill Department of Medicine, Weill Cornell Medicine, New York, New York; and <sup>6</sup>Division of Infectious Diseases, Weill Department of Medicine, Weill Cornell Medicine, New York, New York

This article has a corresponding continuing medical education activity available for MOC credit on page e13. Learning Objective: Upon completion of this activity, you should be able to identify the relationship between the timing of probiotic administration and the risk of *Clostridium difficile* infection.

## BACKGROUND AND CONTEXT

Recently published guidelines, systematic reviews, and large randomized trials provided conflicting recommendations for use of probiotics in preventing *Clostridium difficile* infection (CDI) among hospitalized adults on antibiotics.

# Effetto dei Probiotici....



Shen et al

# Conclusioni degli Autori

- The incidence of CDI in the probiotic cohort, 1.6% (54 of 3277), was lower than of controls, 3.9% (115 of 2984) ( $P < .001$ ).
- The pooled relative risk of CDI in probiotic users was 0.42 (95% confidence interval, 0.30-0.57; I<sup>2</sup> ¼ 0.0%).
- Meta-regression analysis demonstrated that probiotics were significantly more effective if given closer to the first antibiotic dose, with a decrement in efficacy for every day of delay in starting probiotics ( $P$  ¼ .04)

# Conclusioni degli Autori

## NEW FINDINGS

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Timely use of probiotics was effective at preventing CDI in hospitalized adults receiving antibiotics, with the efficacy cut in half if probiotics were begun more than 2 days after antibiotics were started.

## LIMITATIONS

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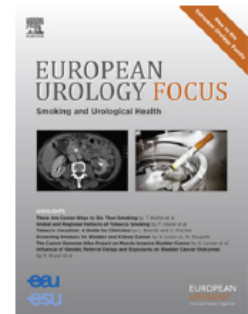
These findings may not apply to patients who were routinely excluded from studies. The optimal probiotic species and dose are still uncertain.

## IMPACT

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For hospitalized adults needing antibiotics, the concurrent prescription of probiotics might reduce the incidence of CDI by over 50%, preventing approximately 200,000 cases of CDI each year in the US.

available at [www.sciencedirect.com](http://www.sciencedirect.com)  
journal homepage: [www.europeanurology.com/eufocus](http://www.europeanurology.com/eufocus)



Review – Incontinence

## The Urinary Tract Microbiome in Health and Disease

Isabel M. Aragón<sup>a,†</sup>, Bernardo Herrera-Imbroda<sup>a,†</sup>, María I. Queipo-Ortuño<sup>b,c</sup>,  
Elisabeth Castillo<sup>a</sup>, Julia Sequeira-García Del Moral<sup>d</sup>, Jaime Gómez-Millán<sup>e</sup>,  
Gozde Yucel<sup>f</sup>, María F. Lara<sup>a,\*</sup>

<sup>a</sup>Department of Urology, Virgen de la Victoria University Hospital, Malaga, Spain; <sup>b</sup>Service of Endocrinology and Nutrition, Biomedical Research Institute, University of Malaga, Malaga, Spain; <sup>c</sup>Biomedical Research Networking Center for Pathophysiology of Obesity and Nutrition, Madrid, Spain; <sup>d</sup>Urology Unit, University Hospital Carlos Haya, Malaga, Spain; <sup>e</sup>Department of Radiation Oncology, University Hospital Virgen de la Victoria, Malaga, Spain; <sup>f</sup>Program in Epithelial Biology, School of Medicine, Stanford University, Stanford, CA, USA

# Probiotici e prebiotici usati nelle IVU

Probiotics/prebiotics/diet modification	Urinary diseases treated	Administration	Preventive effect against urinary disease	Refs.
Antimicrobial therapy and <i>Lactobacillus</i> suppositories	UTI	Vaginal	Yes	[59]
<i>Lactobacillus rhamnosus</i> GR-1 and <i>Lactobacillus reuteri</i> B-54	UTI	Vaginal	Yes	[60]
<i>Lactobacillus</i> GG and cranberry-lingonberry juice	UTI	Oral	No	[80]
<i>L. rhamnosus</i> GG	UTI in premature babies	Oral	Reduction in UTIs (nonsignificant differences)	[62]
<i>Lactobacillus</i> drinks and berry juice	UTI	Oral	Yes	[81]
<i>L. rhamnosus</i> GR-1 and <i>Lactobacillus fermentum</i> RC-14	UTI	Oral	Yes	[63]
Cranberries	UTI	Oral	No	[86]
Cranberry juice capsule	UTI after surgery	Oral	Yes	[83]
D-Mannose	UTI	Oral	Yes	[87]
Bacillus Calmette-Guérin immunotherapy	Bladder cancer	Intravesical	Yes (noninvasive [stage 0] or minimally invasive [stage 1] bladder cancer)	[44]
<i>Lactobacillus casei</i>	Bladder cancer	Oral	Yes (primary multiple tumors and recurrent single tumors)	[68,69]
<i>L. casei</i> strain Shirota	Bladder cancer	Oral	Yes	[70]
Lactic acid bacteria <sup>a</sup>	Urolithiasis	Oral	Yes	[71]
<i>L. casei</i> and <i>Bifidobacterium breve</i>	Urolithiasis	Oral	No	[72]
<i>Oxalabacter formigenes</i>	Urolithiasis	Oral	Yes	[76]
Commercially available probiotic	Urolithiasis	Oral	Yes	[77]
<i>O. formigenes</i>	Urolithiasis	Oral	No	[78]
Supplemental calcium	Urolithiasis	Oral	Yes	[88]
Diet low in sodium and animal protein	Urolithiasis	Oral	Yes	[89]

UTIs = urinary tract infections.

<sup>a</sup> *Lactobacillus acidophilus*, *Lactobacillus plantarum*, *Lactobacillus brevis*, *Streptococcus thermophilus*, *Bifidobacterium infantis*.

# Effetto dei probiotici sulle IVU

- Ceppi quali *L. Rhamnosus* GR1, *L. Reuteri* B-54, *L. Casei* ceppo Shirota hanno efficacia nel prevenire infezioni del tratto urinario

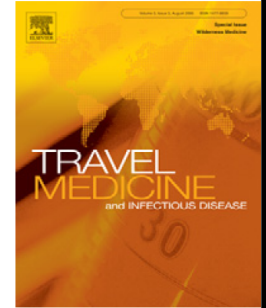


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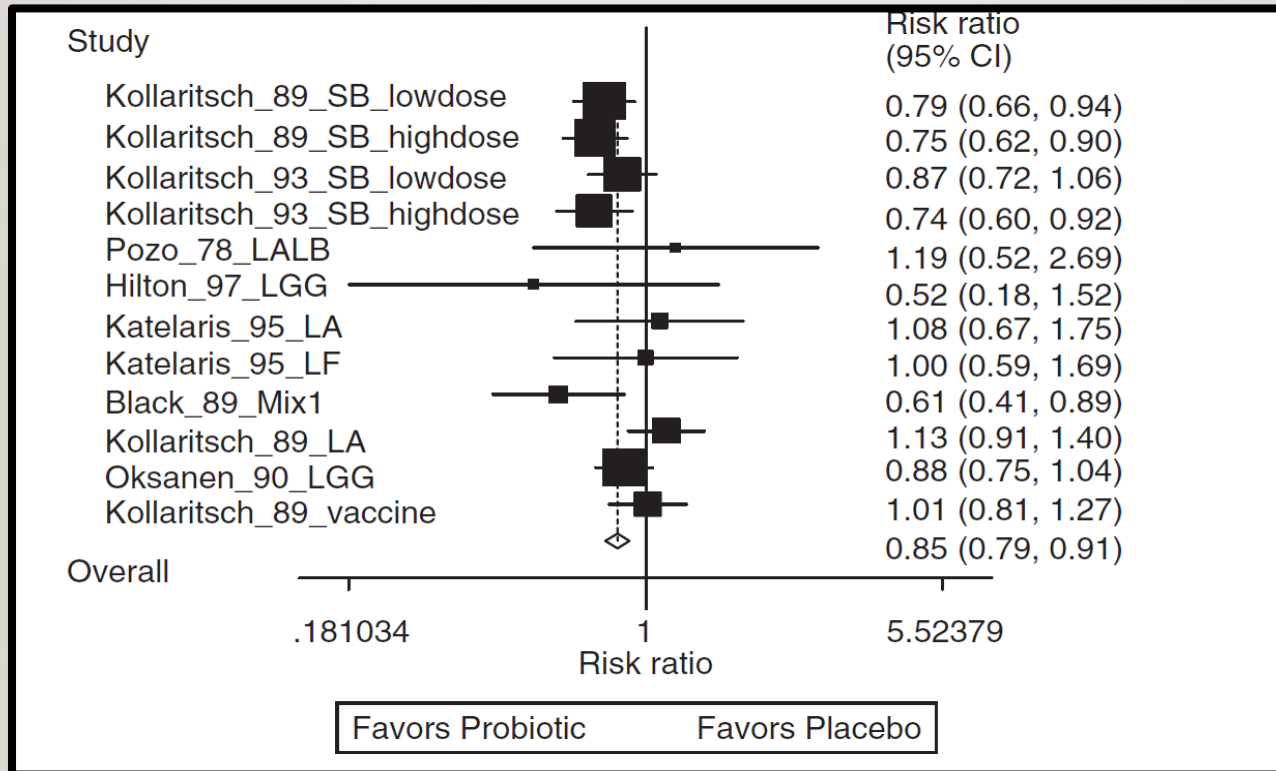


# Meta-analysis of probiotics for the prevention of traveler's diarrhea ☆

Lynne V. McFarland<sup>a,b,\*</sup>



# Effetto dei probiotici sulla diarrea del viaggiatore ....



# Conclusioni degli Autori

- The pooled relative risk indicates that probiotics significantly prevent TD (RR  $\frac{1}{4}$  0.85, 95% CI 0.79,0.91,  $p < 0.001$ ).
- Several probiotics (*Saccharomyces boulardii* and a mixture of *Lactobacillus acidophilus* and *Bifidobacterium bifidum*) had significant efficacy. No serious adverse reactions were reported in the 12 trials.



*antibiotics*

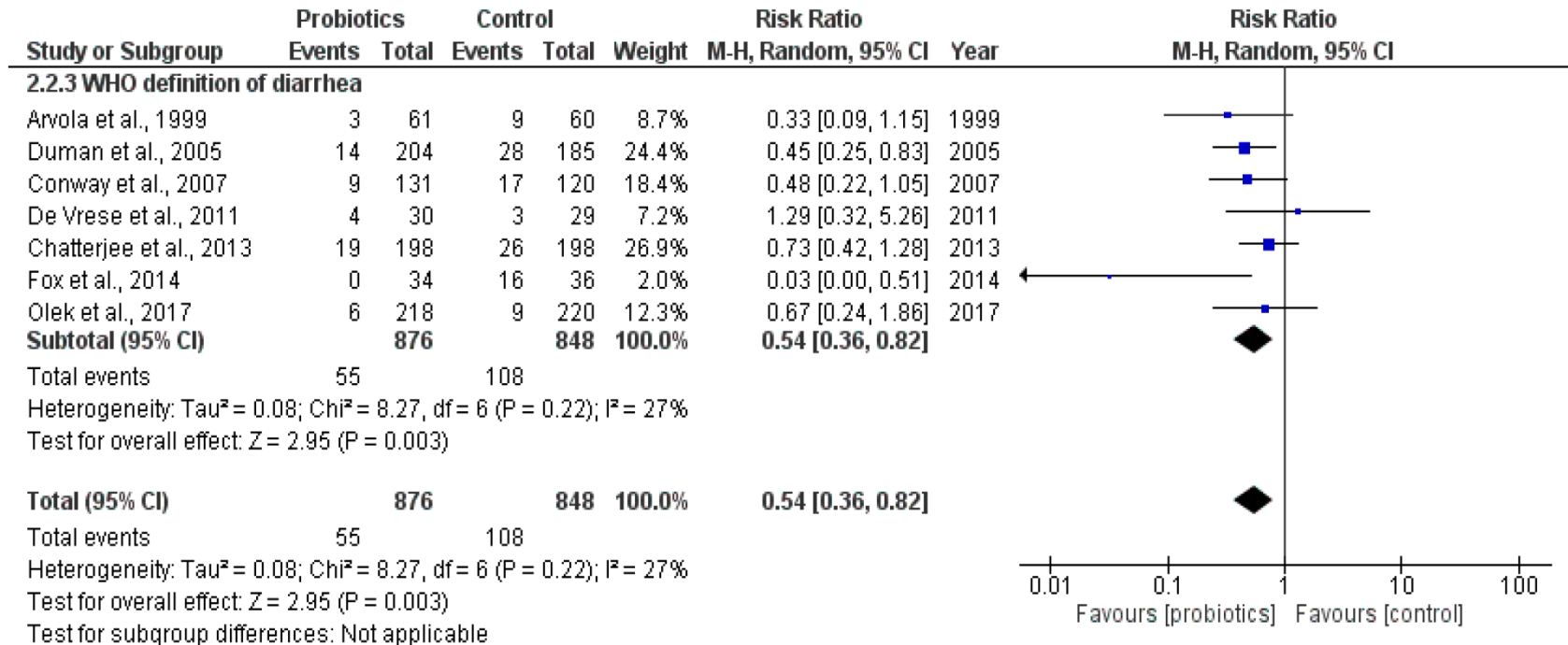


*Review*

# **Probiotics for the Prevention of Antibiotic-Associated Diarrhea in Outpatients—A Systematic Review and Meta-Analysis**

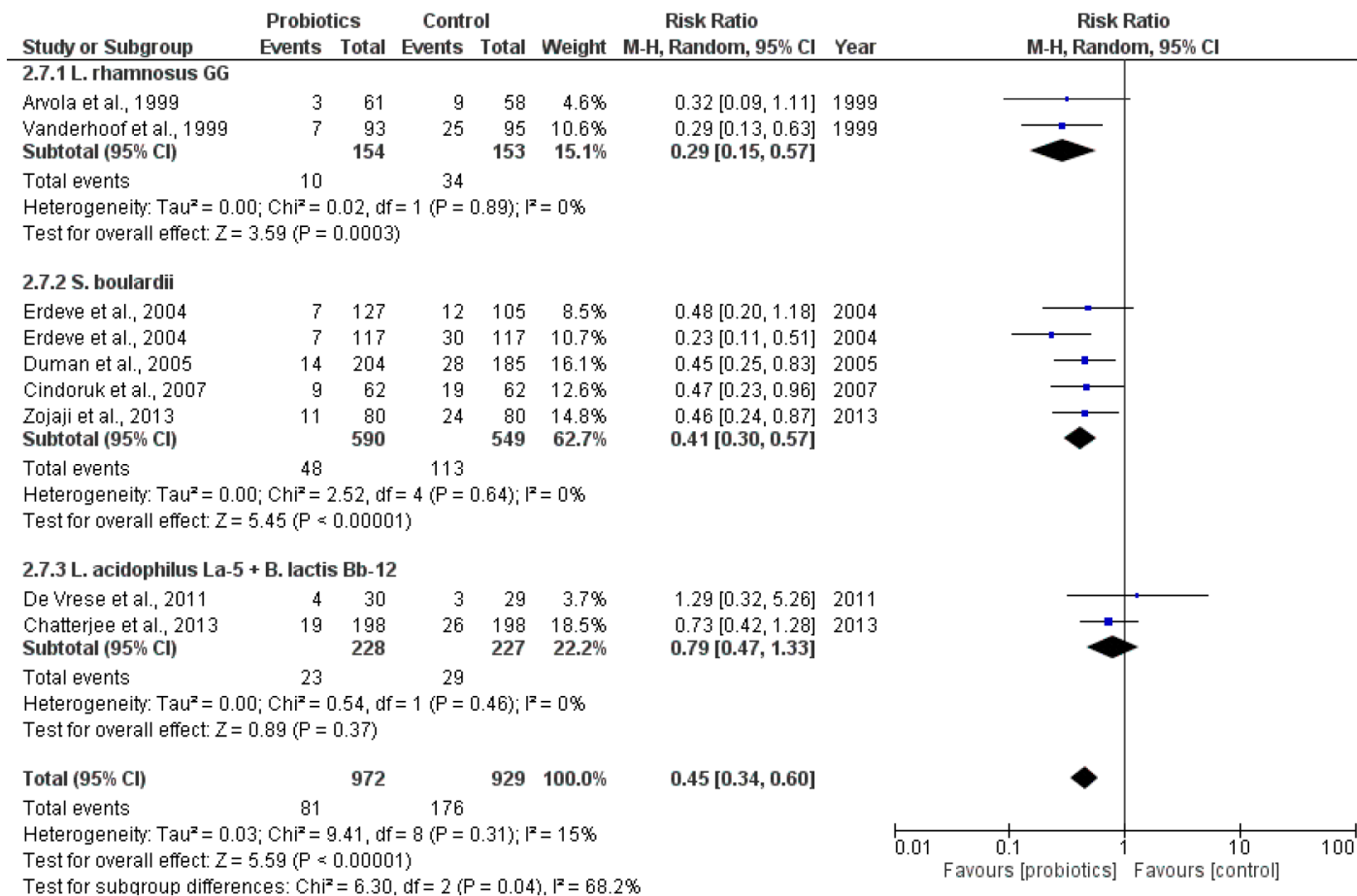
Sara Blaabjerg \*, Daniel Maribo Artzi \* and Rune Aabenhus \*

# Effetto dei probiotici sulla AAD definita secondo l'OMS



Blaabjerg et al.

# Effetto di 3 gruppi di probiotici sulla AAD



Blaabjerg

# Conclusioni degli Autori

- The pooled results found that AAD was present in 8.0% of the probiotic group compared to 17.7% in the control group (RR 0.49, 95% CI 0.36 to 0.66; I<sup>2</sup> = 58%), and the species-specific results were similar regarding the probiotic strains *L. rhamnosus* GG and *S. boulardii*.
- However, the overall quality of the included studies was moderate.
- no statistically significant differences in the incidence of adverse events between the intervention and control group

# Conclusioni

- Utili
- Sicuri
- Necessari dati di migliore qualità
- Differenze tra ceppi ?



Grazie per l'Attenzione !!

