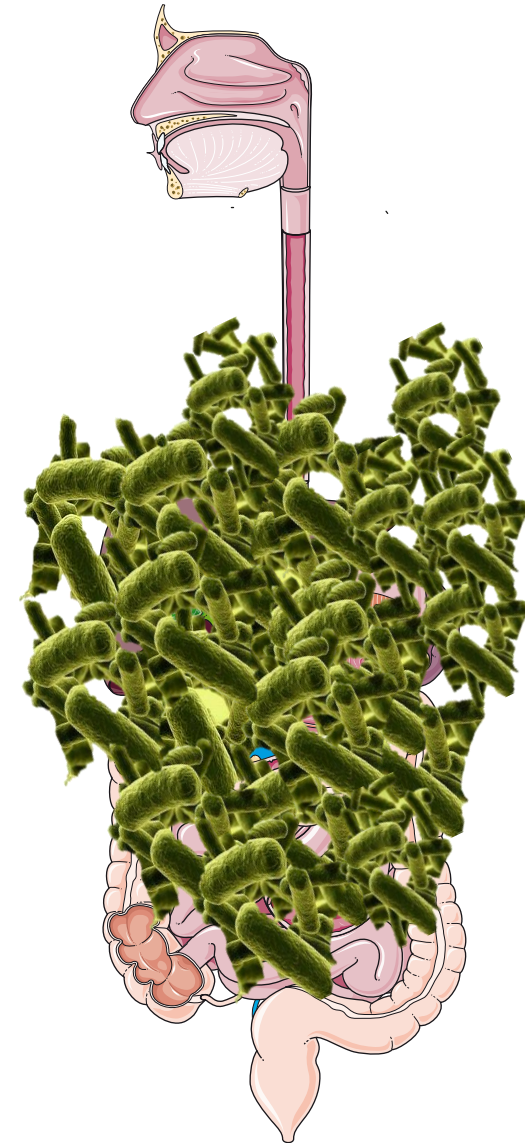


Probióticos en gastroenterología Cuál es la evidencia en 2022



William Otero R MD, FAGA, FACP
Profesor Titular de Medicina
Universidad Nacional de Colombia
Hospital Universitario Nacional de Colombia



Youtube “William otero gastroenterologo”

**Definición formal
FAO/OMS**

Probióticos



“Organismos vivos que al ser administrados en adecuadas cantidades Confieren beneficios para la salud del huésped”

FAO/WHO. Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria. <http://www.who.int/foodsafety/publications/fs>. [Accessed 1–4 October 2001]

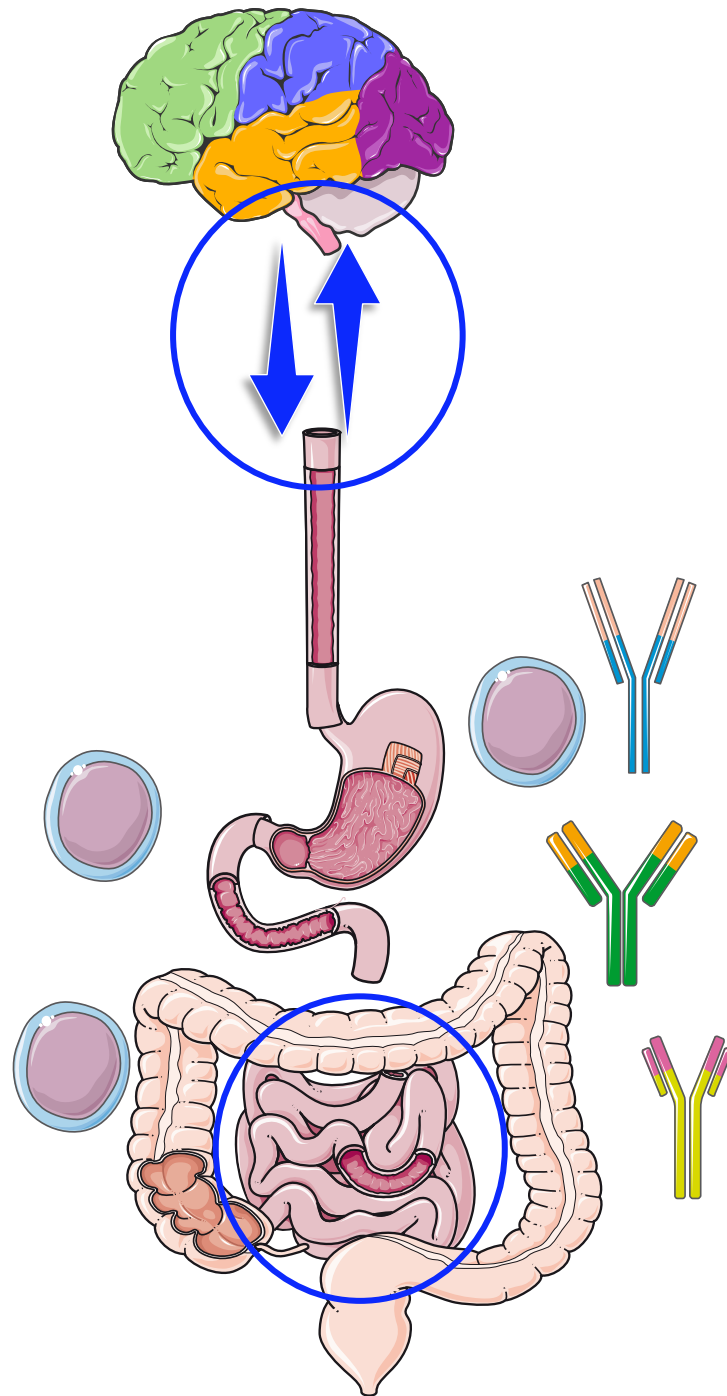
“Modulación de la microbiota alterada”

**2014, Consenso
Asociación Científica internacional
Prebióticos y probióticos”**

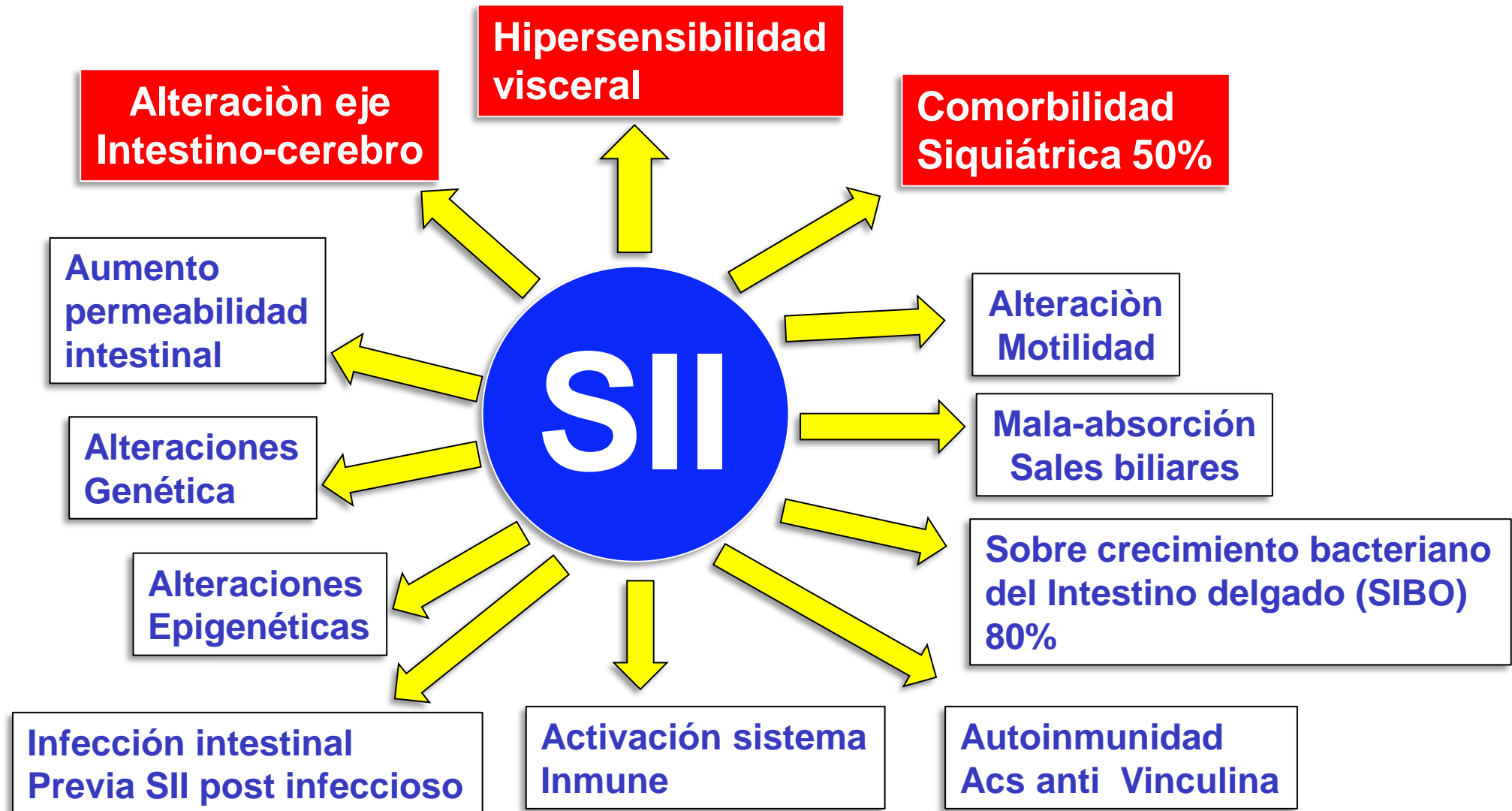
Probiòticos



Síndrome de Intestino Irritable

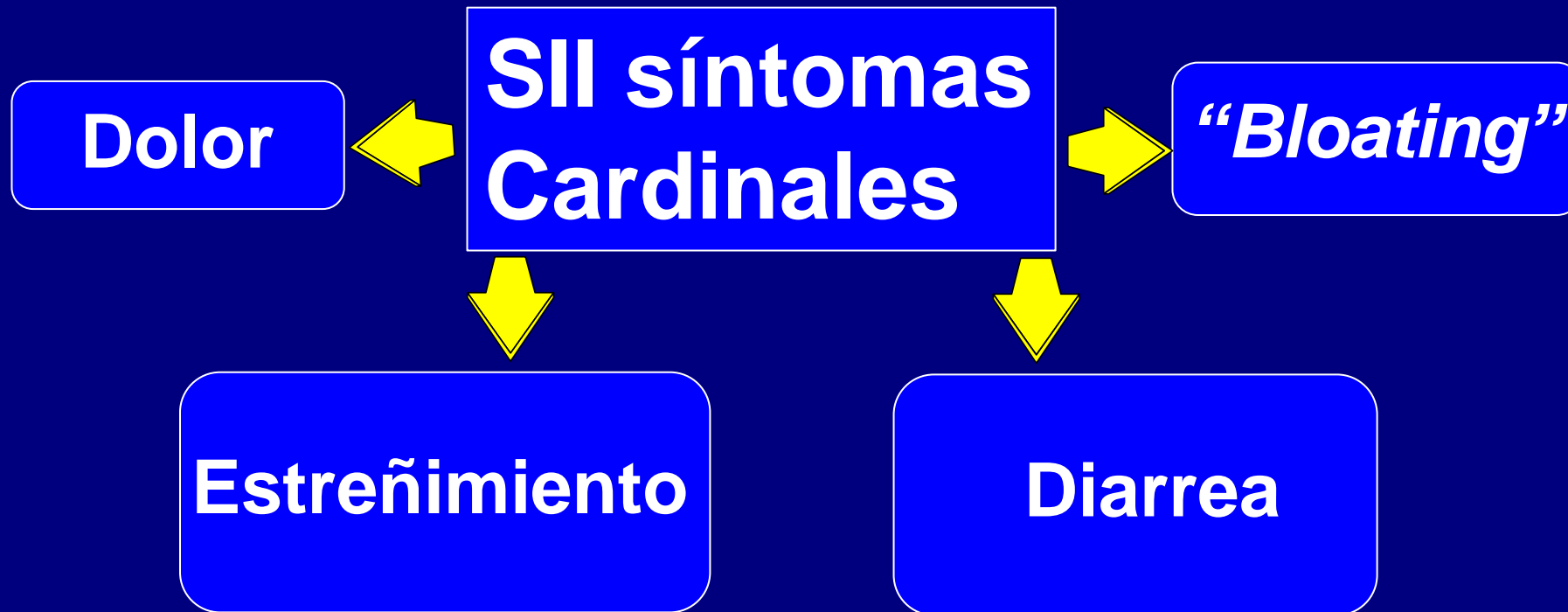


SII -Fisiopatología



Medicamentos

Múltiples alteraciones orgánicas
Autoinmunidad, eje intestino cerebro



Antibióticos

**Dieta baja
en FODMAP**

**Microbioma un
Blanco terapéutico**

**Trasplante
Fecal**

Probióticos

AGA Technical Review on the Role of Probiotics in the Management of Gastrointestinal Disorders



Geoffrey A. Preidis,¹ Adam V. Weizman,² Purna C. Kashyap,³ and Rebecca L. Morgan⁴

¹Section of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston, Texas; ²Division of Gastroenterology, Mount Sinai Hospital, Department of Medicine, University of Toronto, Toronto, Ontario, Canada; ³Enteric Neuroscience Program, Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, Minnesota; and ⁴Health Research Methods, Evidence and Impact, McMaster University, Hamilton, Ontario, Canada

The overall CoE across all critical outcomes for probiotics for the treatment of children and adults with IBS was Low.

Solamente en el contexto de ensayos clínicos

ACG Clinical Guideline: Management of Irritable Bowel Syndrome

Brian E. Lacy, PhD, MD, FACG¹, Mark Pimentel, MD, FACG², Darren M. Brenner, MD, FACG³, William D. Chey, MD, FACG⁴, Laurie A. Keefer, PhD⁵, Millie D. Long, MDMPH, FACG (GRADE Methodologist)⁶ and Baha Moshiree, MD, MSc, FACG⁷

Recommendation

We suggest against probiotics for the treatment of global IBS symptoms.

Conditional recommendation; very low level of evidence.

Save

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Sorted by: Most recent

Display options

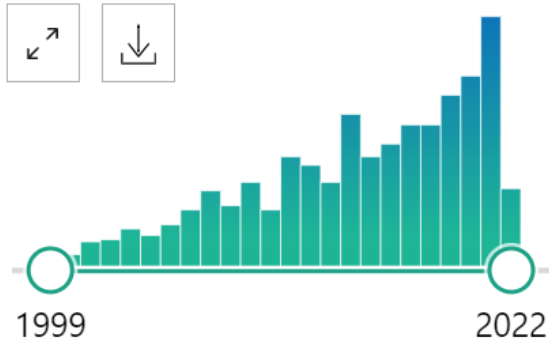
MY NCBI FILTERS

868 results

Mayo 5, 2022

Page 1 of 87

RESULTS BY YEAR



Association between intestinal microbiome and inflammatory bowel disease: Insights from bibliometric analysis.

1 Cite Share

Xu P, Lv T, Dong S, Cui Z, Luo X, Jia B, Jeon CO, Zhang J. Comput Struct Biotechnol J. 2022 Apr 7;20:1716-1725. doi: 10.1016/j.csbj.2022.04.006. eCollection 2022. PMID: 35495114 Free PMC article.

The most influential journal in this field is Gut with 13,359 citations. The co-citation analysis of references showed that the IBD-related topics with the highest focus are "gut microbiota," "metagenomics," "bacterial community," "fecal microbiota transplantation," "pr ...

TEXT AVAILABILITY

Abstract

Oral Administration of Lactobacillus paracasei N1115 on Neonatal Mice Prevents the Intestinal Inflammation in Adulthood.

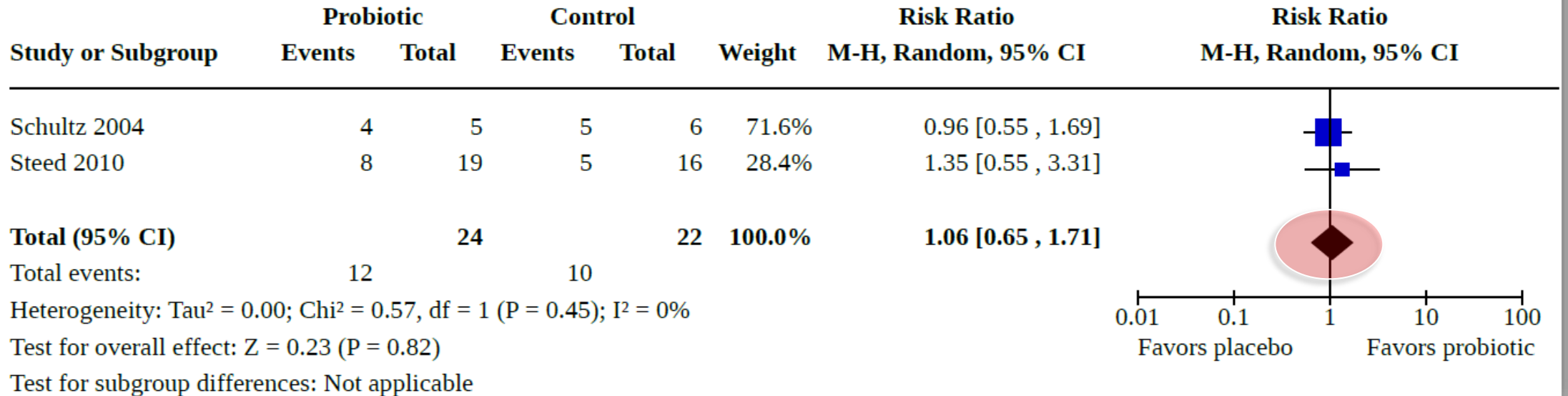
2







Probiotics for induction of remission in Crohn's disease (Review)

Limketkai BN, Akobeng AK, Gordon M, Adepoju AA

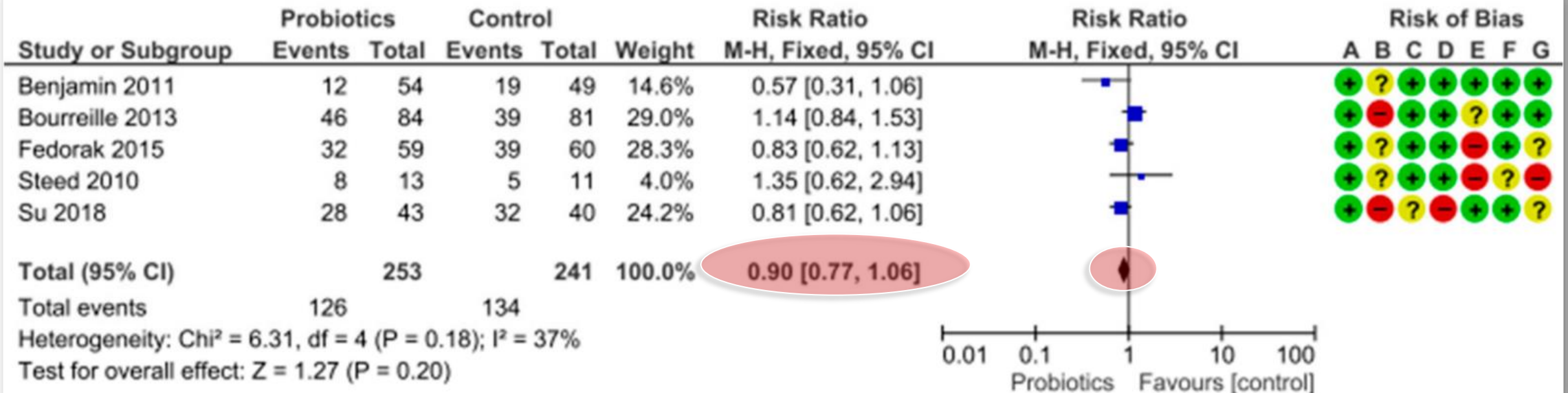
Figure 3. Forest plot of comparison: 1 Probiotics versus placebo, outcome: 1.1 Induction of remission.



Probiotics as a Coadjuvant Factor in Active or Quiescent Inflammatory Bowel Disease of Adults—A Meta-Analytical Study

Manuel Pabón-Carrasco ¹, Lucia Ramirez-Baena ^{1,*} , Samuel Vilar-Palomo ² , Aurora Castro-Méndez ³ , Raúl Martos-García ¹  and Isabel Rodríguez-Gallego ¹

Inducción de Remisión Enfermedad de Crohn





Cochrane
Library

Cochrane Database of Systematic Reviews

AMSTAR 11/11

Probiotics for maintenance of remission in Crohn's disease (Review)

Rolfe VE, Fortun PJ, Hawkey CJ, Bath-Hextall FJ. Probiotics for maintenance of remission in Crohn's disease.

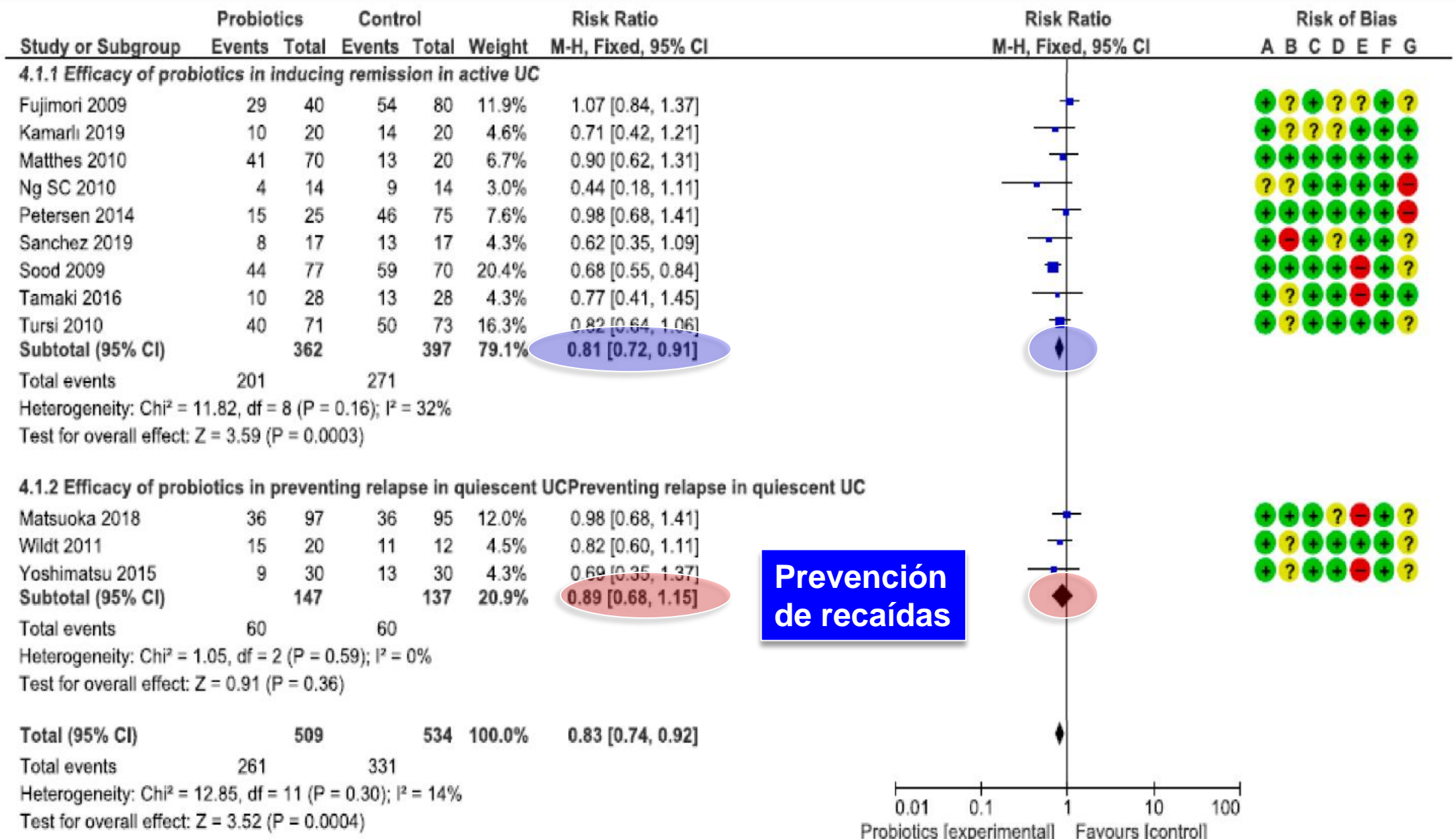
Cochrane Database of Systematic Reviews 2006, Issue 4. Art. No.:
CD004826. DOI: 10.1002/14651858.CD004826.pub2.

www.cochranelibrary.com

“Pequeños estudios con poco poder”

**No hay evidencia para
Recomendar pro-bióticos para
Mantener remisión en EC.
Se necesitan estudios más grandes
y con mejor calidad**

Colitis ulcerativa Inducción de remisión





**Probiotics for maintenance of remission in ulcerative colitis
(Review)**

Naidoo K, Gordon M, Fagbemi AO, Thomas AG, Akobeng AK.
Probiotics for maintenance of remission in ulcerative colitis.
Cochrane Database of Systematic Reviews 2011, Issue 12. Art. No
CD007443. DOI: 10.1002/14651858.CD007443.pub2.
www.cochranelibrary.com

**“Estudios con alto riesgo de sesgo”
Inadecuado cegamiento. Hubo pocos
pacientes, pocos eventos**

**Insuficiente evidencia para
Recomendar pro-bióticos para
Mantener remisión en CU.
Se necesitan estudios más grandes
y con mejor calidad**

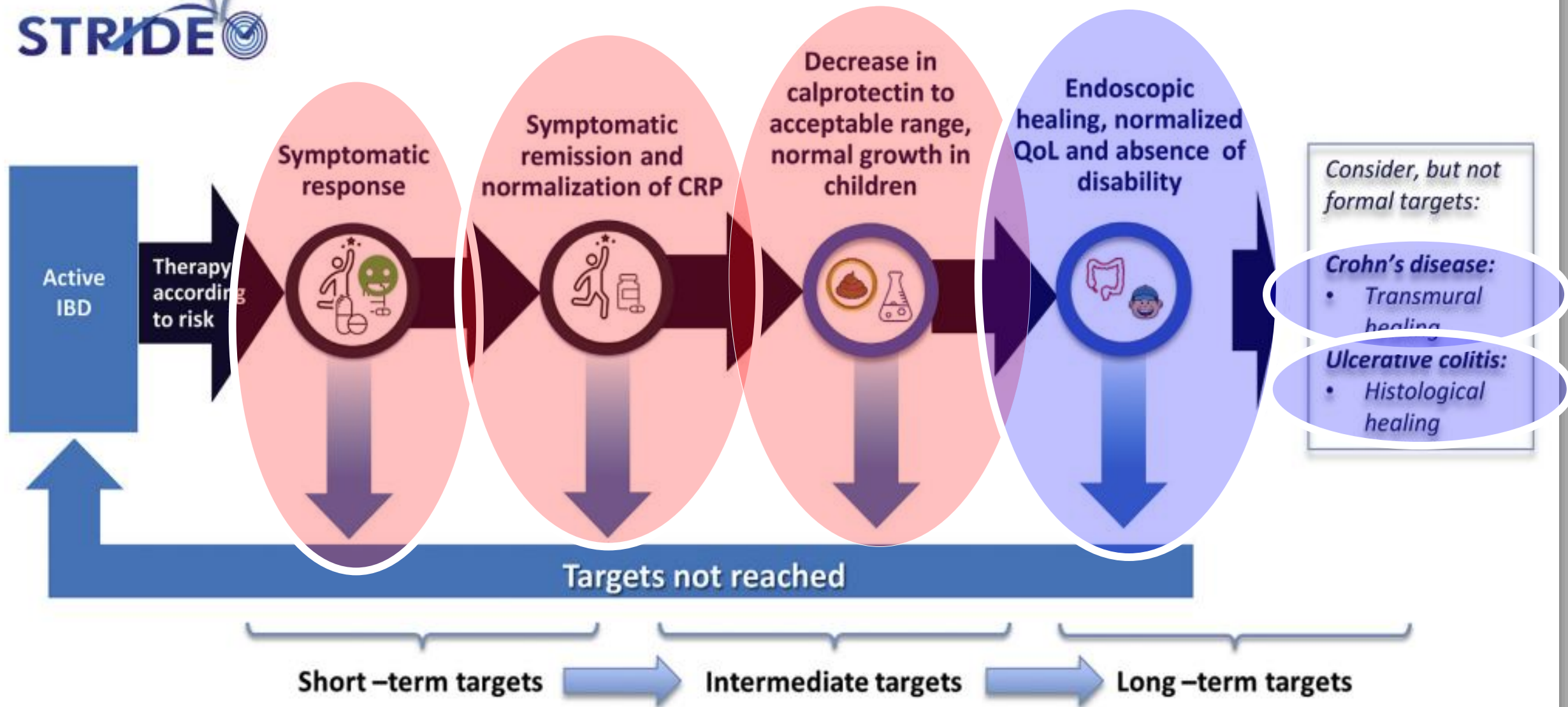


Figure 2. Treatment targets in CD and UC.

VSL #3

```
graph LR; VSL[VSL #3] -.-> Lactobacillus[Lactobacillus casei, plantarum, acidophilus, delbruekii (bulgaricus)]; VSL -.-> Bifidocateria[Bifidocateria longim, breve, infantis]; VSL -.-> Streptococcus[Streptococcus salivari (thermophilu)]; E_coli[E. coli Nissle 1917];
```

Lactobacillus

casei

plantarum

acidophilus

delbruekii (bulgaricus)

Bifidocateria

longim

breve

infantis

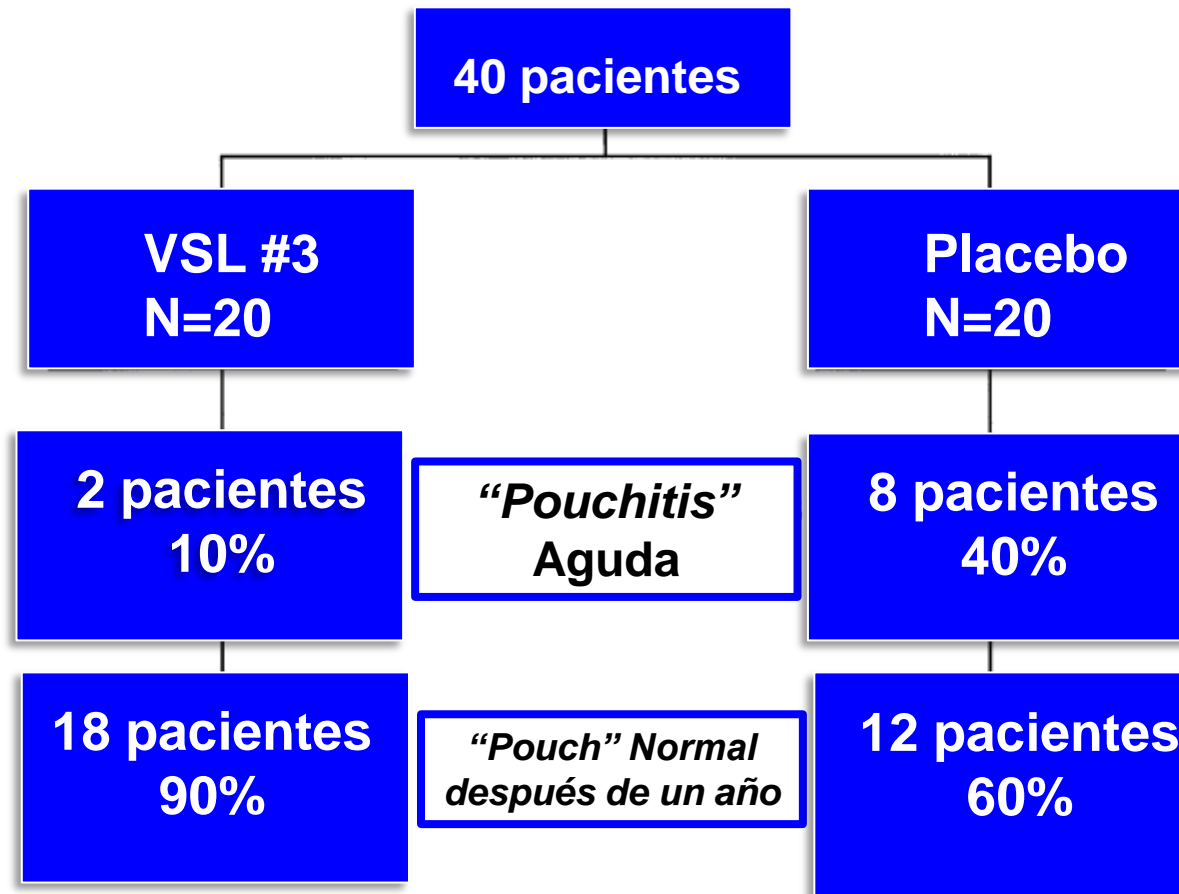
Streptococcus salivari

(thermophilu)

E. coli Nissle 1917

Prophylaxis of Pouchitis Onset With Probiotic Therapy: A Double-Blind, Placebo-Controlled Trial

PAOLO GIONCHETTI,* FERNANDO RIZZELLO,* ULF HELWIG,* ALESSANDRO VENTURI,*



Oral Bacteriotherapy as Maintenance Treatment in Patients With Chronic Pouchitis: A Double-Blind, Placebo-Controlled Trial

PAOLO GIONCHETTI,* FERNANDO RIZZELLO,* ALESSANDRO VENTURI,* PATRIZIA BRIGIDI,†

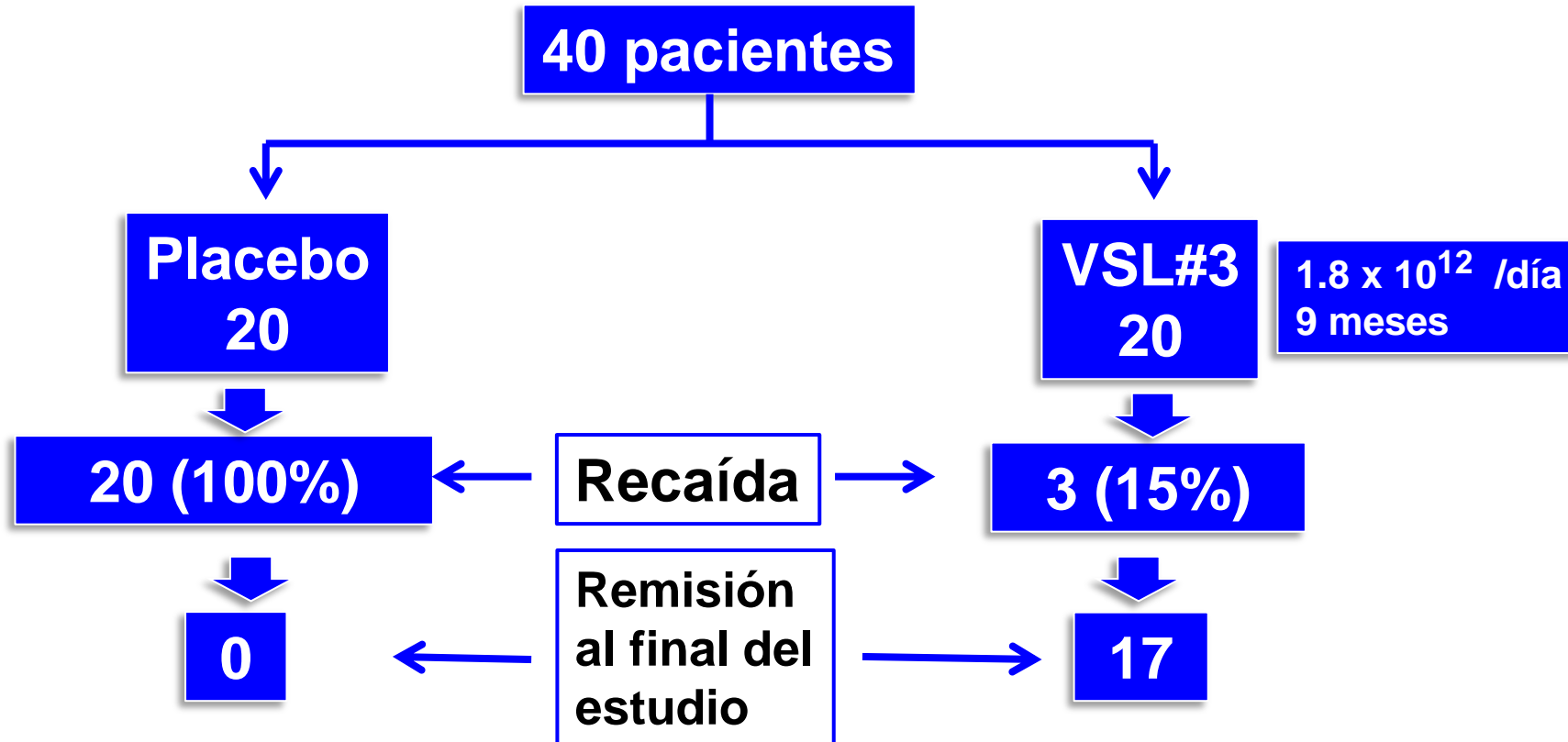
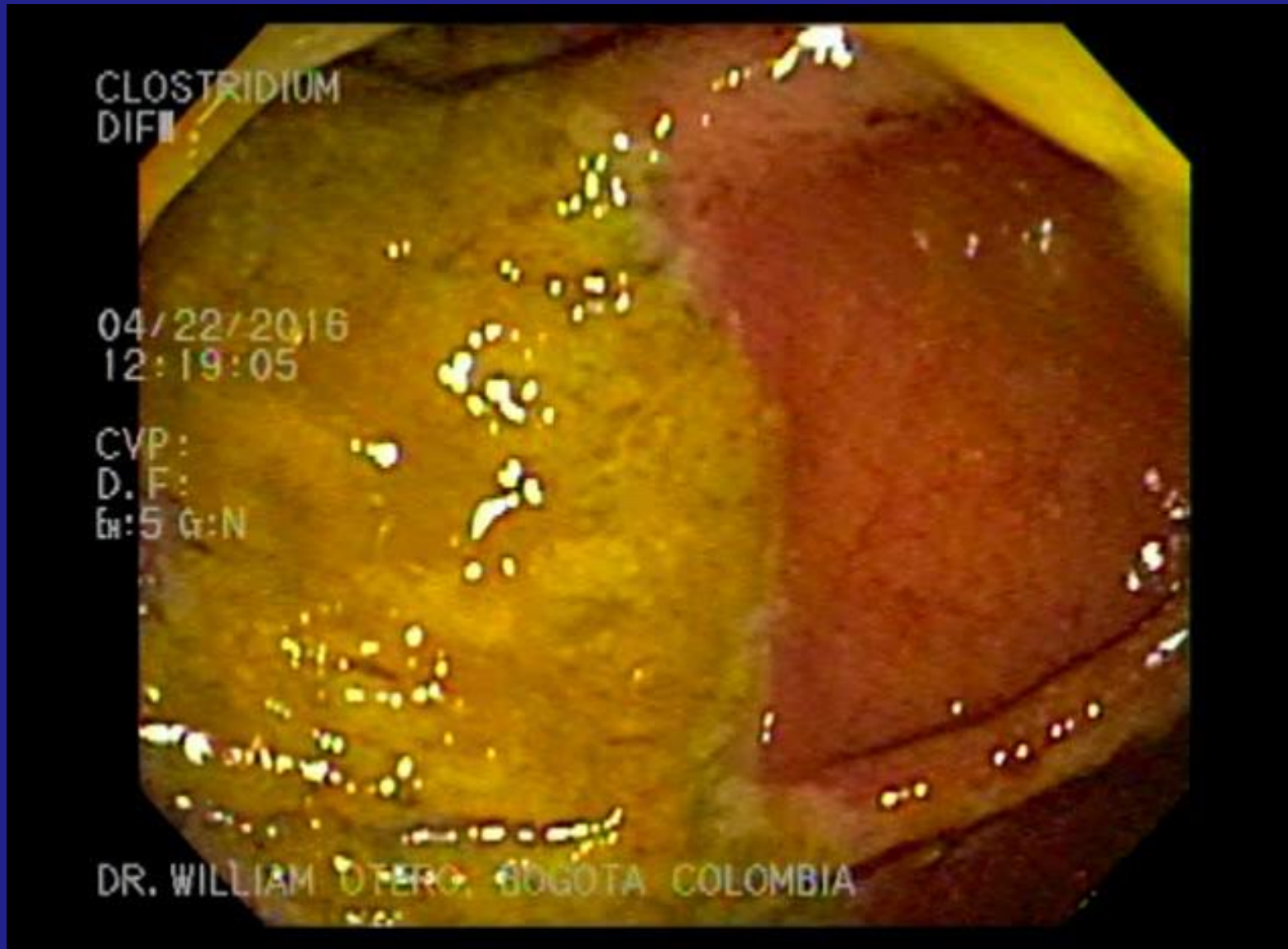


Table 3. Guidelines on the role of probiotics in IBD

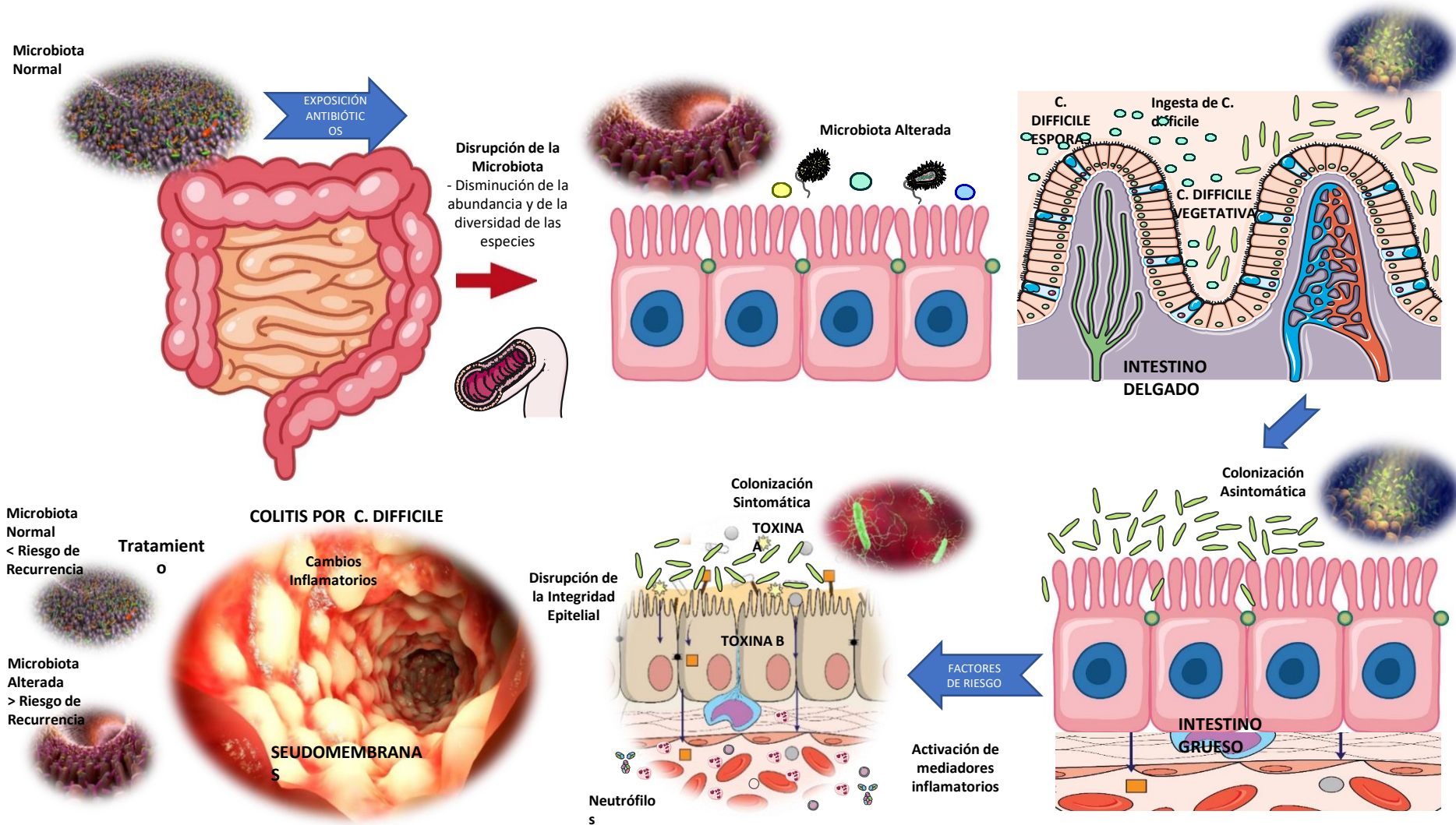
Source	Year	Recommendations	Strength of recommendation	Quality of evidence
Third European evidence-based consensus on diagnosis and management of UC	2017	<i>E. coli</i> Nissle 1917 is effective in inducing and maintaining remission in UC Harbord M, J <i>Crohn's Colitis</i> . 2017; 11: 769–84.	N/A	N/A
AGA clinical practice guidelines on the role of probiotics in the management of gastrointestinal disorders Su GL, <i>Gastroenterology</i> . 2020; 159: 697–705.	2020	In adults and children with CD, we recommend the use of probiotics only in the context of a clinical trial	No recommendations	Knowledge gap
		In adults and children with UC, we recommend the use of probiotics only in the context of a clinical trial	No recommendations	Knowledge gap
		In adults and children with pouchitis, we suggest the 8-strain combination of <i>L. paracasei</i> subsp <i>paracasei</i> , <i>L. plantarum</i> , <i>L. acidophilus</i> , <i>L. delbrueckii</i> subsp <i>bulgaricus</i> , <i>B longum</i> subsp <i>longum</i> , <i>B. breve</i> , <i>B. longum</i> subsp <i>infantis</i> , and <i>S. salivarius</i> subsp <i>thermophilus</i> over no or other probiotics	Conditional	Very low

Compare D, et al. *Dig Dis*. 2022;40:123-132.



***William Otero Regino MD Profesor Titular de Medicina,
Coordinador de Gastroenterología Universidad Nacional de Colombia***

Patogénesis de la infección por *C. difficile*



ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of *Clostridioides difficile* Infections

Colleen R. Kelly, MD, AGAF, FACG¹, Monika Fischer, MD, MSc, AGAF, FACG², Jessica R. Allegretti, MD, MPH, FACG³, Kerry LaPlante, PharmD, FCCP, FIDSA⁴, David B. Stewart, MD, FACS, FASCRS⁵, Berkeley N. Limketkai, MD, PhD, FACG (GRADE Methodologist)⁶ and Neil H. Stollman, MD, FACG⁷

PROBIOTICS

Recommendations

1. We recommend against probiotics for the prevention of CDI in patients being treated with antibiotics (primary prevention) (conditional recommendation, moderate quality of evidence).
2. We recommend against probiotics for the prevention of CDI recurrence (secondary prevention) (strong recommendation, very low quality of evidence).

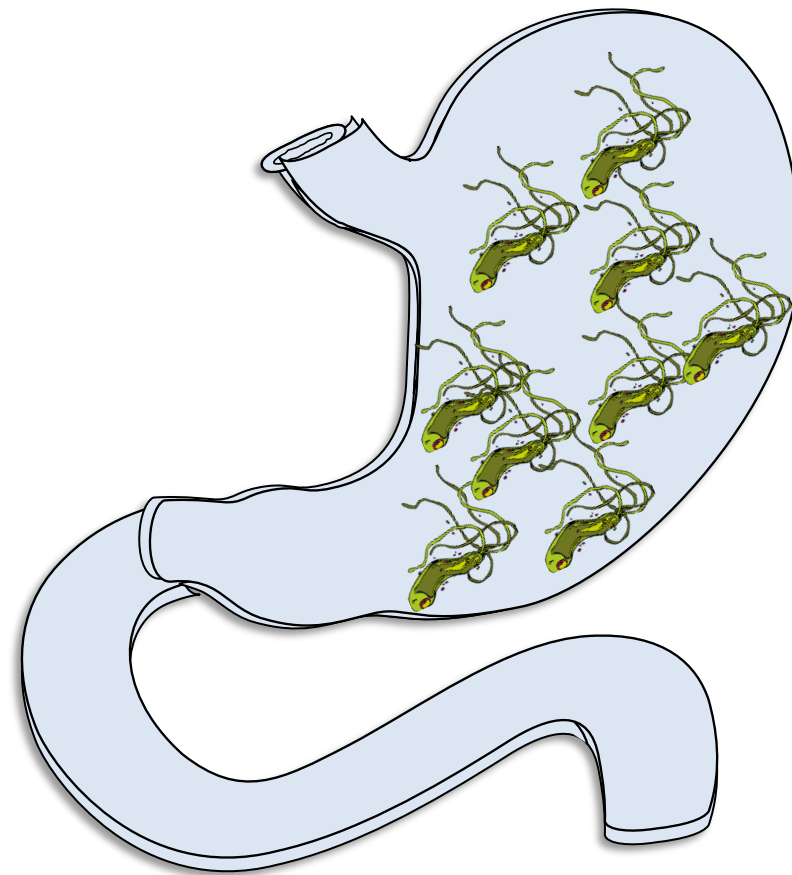
Probióticos en terapias Para curar H.pylori



*Aumentar
Eficacia*

*Disminuir
E. adversos*

*Restaurar
Microbiota*



Efectividad y seguridad del uso de probióticos como adyuvantes en la erradicación de *Helicobacter pylori*. Revisión sistemática y metaanálisis

Efficacy and safety of using probiotics as adjuvants in the eradication of *Helicobacter pylori*. Systematic review and meta-analysis

Título corto: Probióticos y *Helicobacter pylori*

Running title: Probiotics and *Helicobacter pylori*

Recibido: 22/07/2021 Aceptado: 06/04/2022

Gilberto Jaramillo-Trujillo¹, William Alberto Otero-Regino¹, Kelly Patricia Estrada-Orozco²

1 Universidad Nacional de Colombia - Sede Bogotá - Facultad de Medicina
- Departamento de Gastroenterología - Bogotá D.C. - Colombia.

2 Universidad Nacional de Colombia - Sede Bogotá - Facultad de Medicina
- Instituto de Investigaciones Clínicas - Bogotá D.C. - Colombia.

Correspondencia: William Alberto Otero-Regino. Departamento de Gastroenterología, Facultad de Medicina, Universidad Nacional de Colombia. Bogotá D.C. Colombia. Correo electrónico: waoteror@gmail.com.

William Alberto Otero-Regino: ORCID <https://orcid.org/0000-0002-6825->

**Jaramillo G, Otero W, Estrada K
Rev Fac Med 2022 On line Mayo 1**

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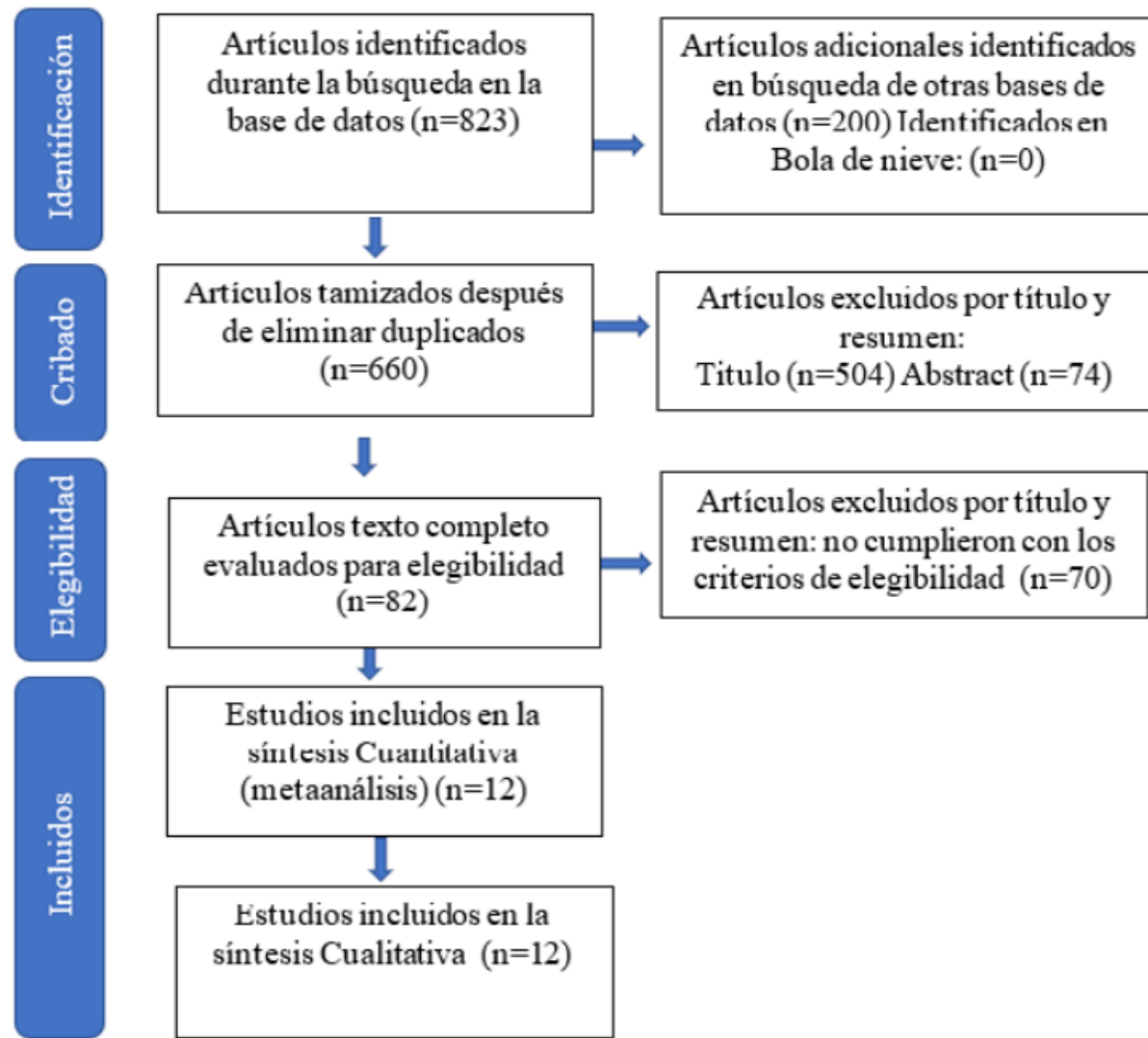


Figura 1. Flujograma de los estudios identificados y seleccionados.

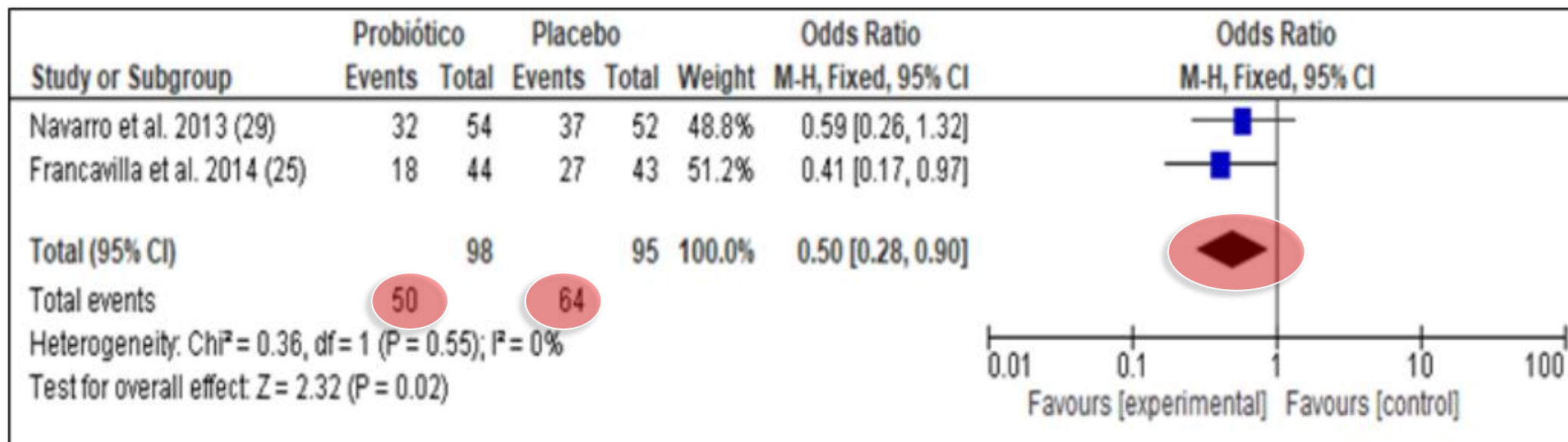
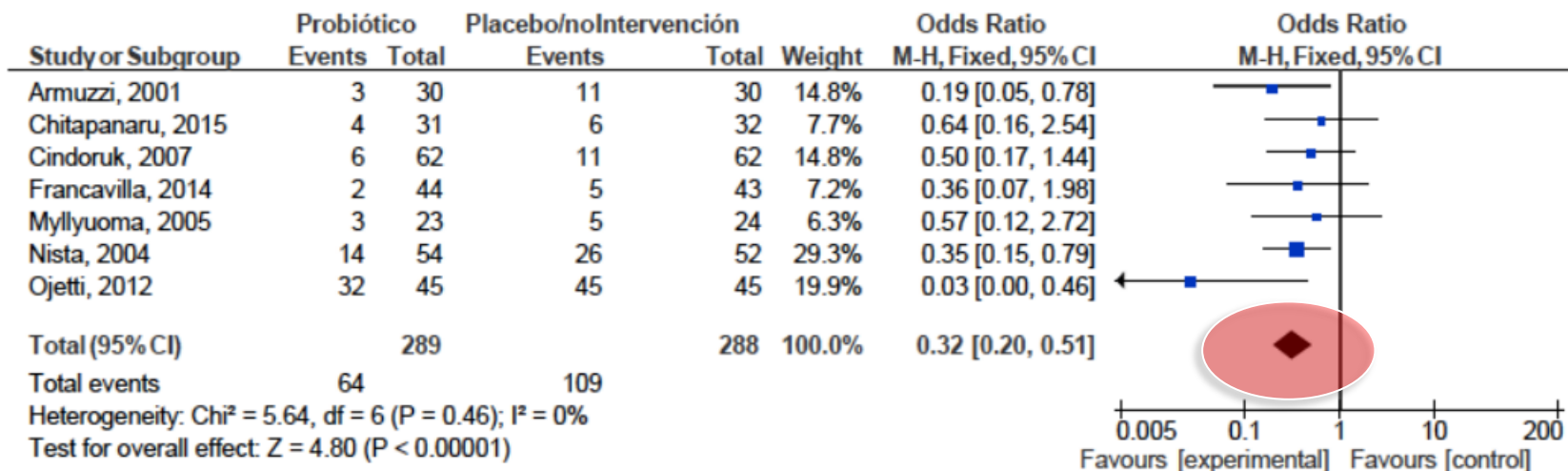


Figura 4. Eventos adversos con terapia triple.

FIGURA. Nauseas en terapia triple



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FIGURA. Diarrea en terapia triple

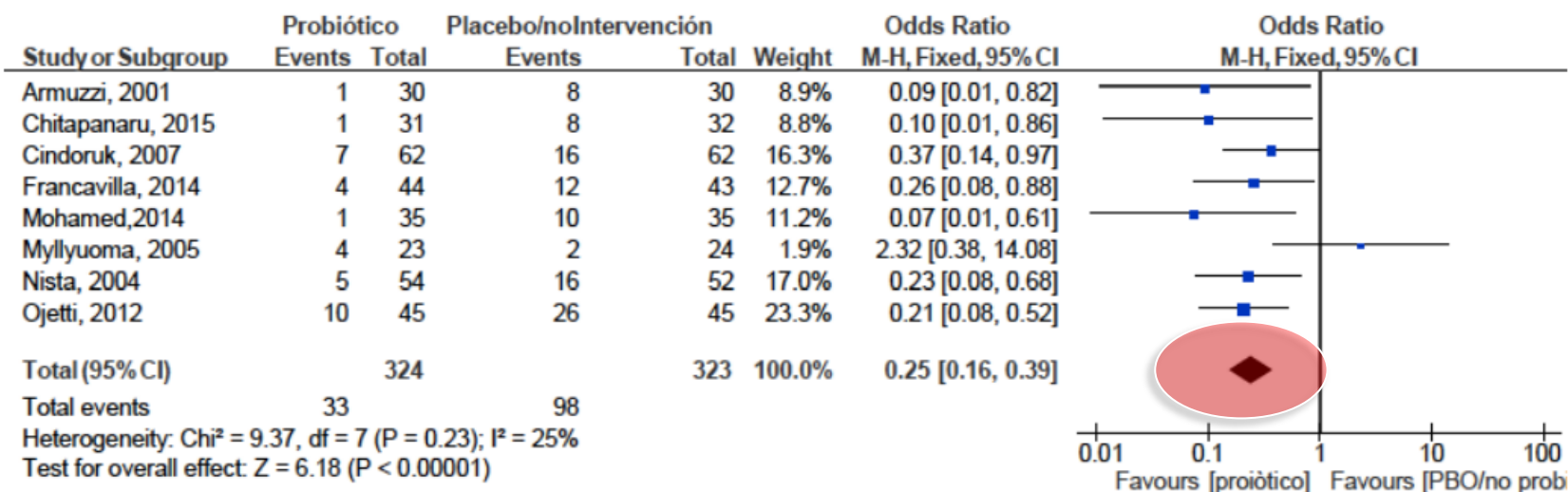


FIGURA. Dolor abdominal en terapia triple

Study or Subgroup	Probiótico		Placebo/no Intervención		Weight	Odds Ratio M-H, Fixed, 95% CI
	Events	Total	Events	Total		
Francavilla, 2014	4	44	11	43	47.9%	0.29 [0.08, 1.00]
Ojetti, 2012	29	45	31	45	52.1%	0.82 [0.34, 1.97]
Total (95% CI)		89		88	100.0%	0.57 [0.28, 1.14]
Total events	33		42			
Heterogeneity: $\text{Chi}^2 = 1.79$, $\text{df} = 1$ ($P = 0.18$); $I^2 = 44\%$						
Test for overall effect: $Z = 1.59$ ($P = 0.11$)						

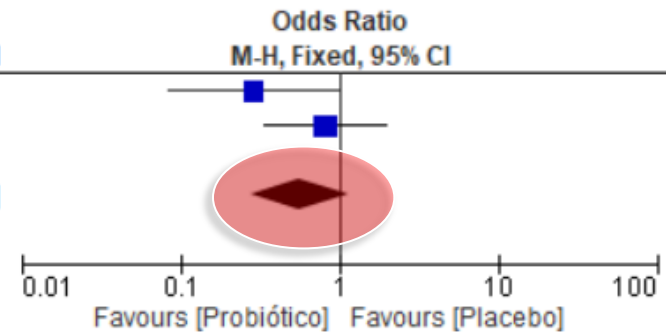


FIGURA. Anorexia en terapia triple

Study or Subgroup	Probiótico		Placebo		Weight	Odds Ratio M-H, Fixed, 95% CI
	Events	Total	Events	Total		
Armuzzi, 2001	2	30	4	30	12.0%	0.46 [0.08, 2.75]
Francavilla, 2014	1	44	2	43	6.4%	0.48 [0.04, 5.46]
Myllyuoma, 2005	2	23	3	24	8.6%	0.67 [0.10, 4.41]
Nista, 2004	9	54	19	52	51.8%	0.35 [0.14, 0.86]
Ojetti, 2012	36	45	33	45	21.2%	1.45 [0.54, 3.89]
Total (95% CI)		196		194	100.0%	0.63 [0.36, 1.11]
Total events	50		61			
Heterogeneity: $\text{Chi}^2 = 4.58$, $\text{df} = 4$ ($P = 0.33$); $I^2 = 13\%$						
Test for overall effect: $Z = 1.61$ ($P = 0.11$)						

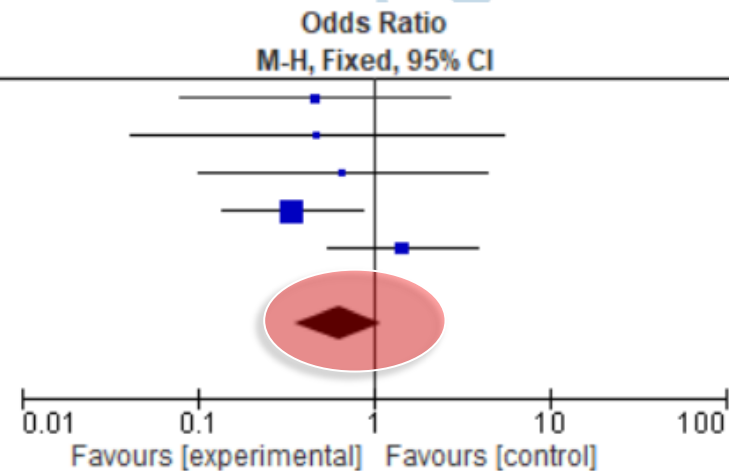
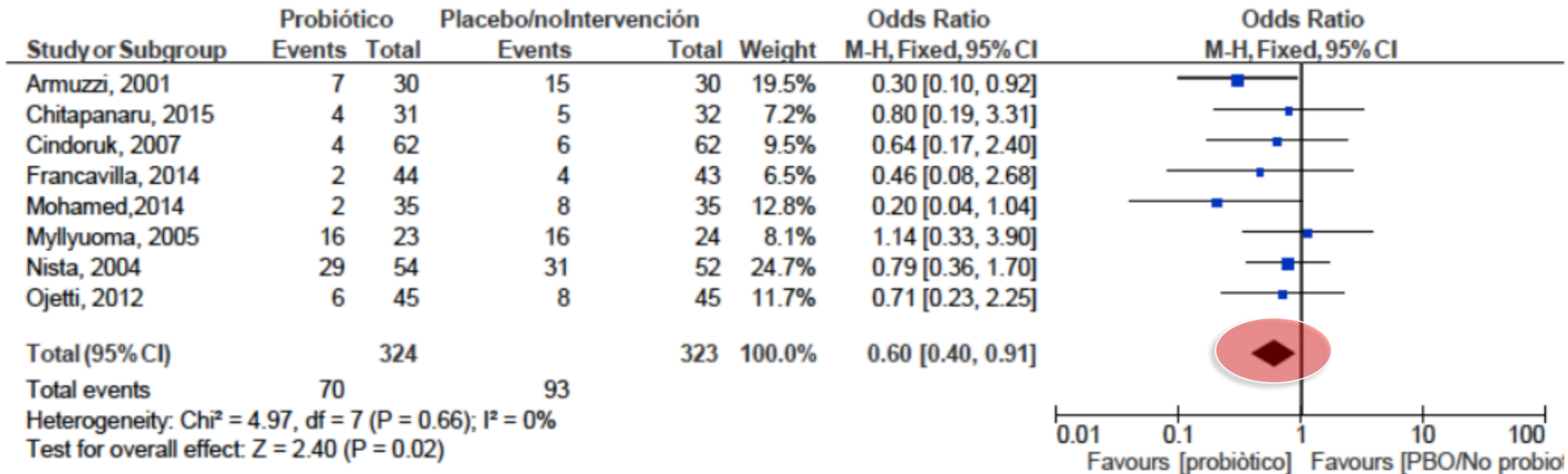
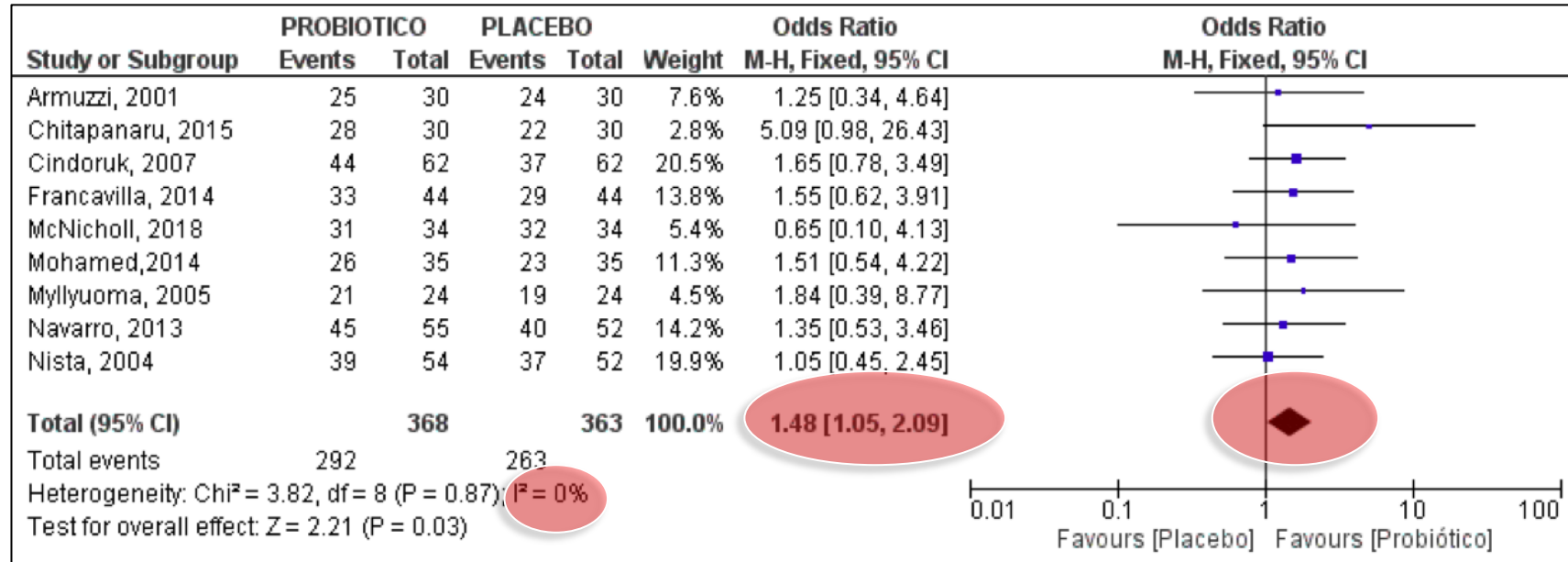


FIGURA. Alteración del gusto terapia triple



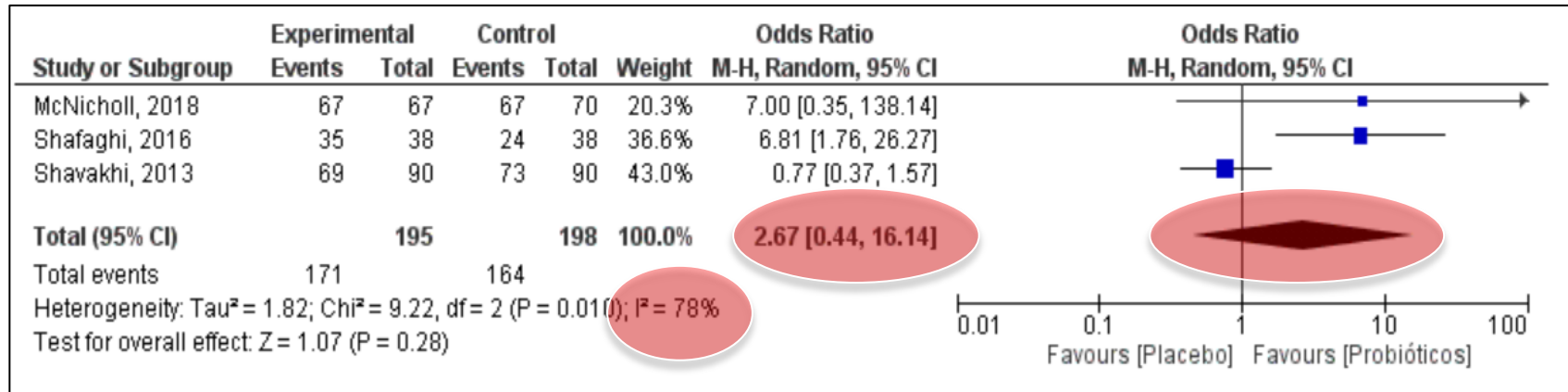
Jaramillo G, Otero W, Estrada K
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Curación de *H. pylori* en terapia triple



**Aumento de efectividad 8.3%
71.1%. Vs 79.4% NO logró 90-95%**

Erradicación de *H. pylori* terapia cuádruple



Jaramillo G, Otero W, Estrada K
 Rev Fac Med 2022 On line Mayo 1

The Toronto Consensus for the Treatment of *Helicobacter pylori* Infection in Adults



2016

Carlo A. Fallone,¹ Naoki Chiba,^{2,3} Sander Veldhuyzen van Zanten,⁴ Lori Fischbach, Javier P. Gisbert,⁶ Richard H. Hunt,^{3,7} Nicola L. Jones,⁸ Craig Render,⁹ Grigorios I. Leontiadis,^{3,7} Paul Moayyedi,^{3,7} and John K. Marshall^{3,7}

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

2017

P Malfertheiner,¹ F Megraud,² C A O'Morain,³ J P Gisbert,^{4,5} E J Kuipers,⁶ A T... F Bazzoli,⁸ A Gasbarrini,⁹ J Atherton,¹⁰ D Y Graham,¹¹ B Hunt,¹² S... T Rokkas,¹⁵ M Rugge,¹⁶ M Selgrad,¹⁷ S... on behalf of the European Society of Gastrointestinal Endoscopy

ACG Clinical Guideline for the Management of *Helicobacter pylori*

2021



Javier P. Gisbert¹, Javier Alcedo², Javier Amador³, Luis Bujanda⁴, Xavier Calvet⁵, Manuel Castro-Fernández⁶, Luis Fernández-Salazar⁷, Emili Gené⁸, Ángel Lanas⁹, Alfredo J. Lucendo¹⁰, Javier Molina-Infante¹¹, Olga P. Nyssen¹, A. Pérez-Aisa¹² e Ignasi Puig¹³

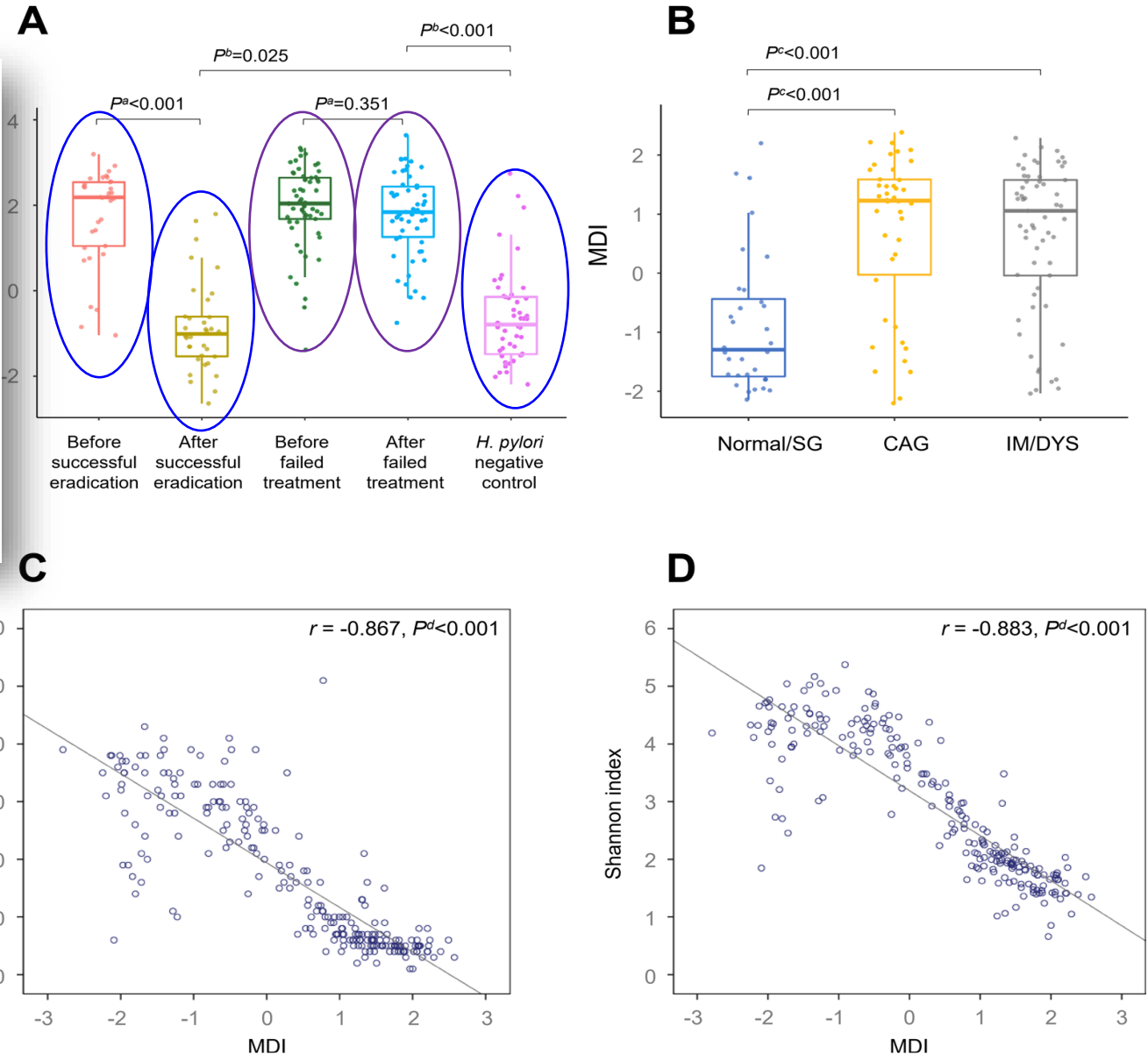
**Ninguna guía los
Recomienda por ahora**

Cura de *H.pylori* y microbiota

ORIGINAL RESEARCH

Effect of *Helicobacter pylori* on gastrointestinal microbiota: a population-based study in Linqu, a high-risk area of gastric cancer

Yang Guo,¹ Yang Zhang ^{1,2}, Markus Gerhard,^{2,3,4} Juan-Juan Gao,¹ Raquel Mejias-Luque,^{2,3,4} Lian Zhang,¹ Michael Vieth,^{2,5} Jun-Ling Ma,¹ Monther Bajbouj,^{2,6} Stepan Suchanek,^{2,7} Wei-Dong Liu,⁸ Kurt Ulm,^{2,9} Michael Quante ^{2,6}, Zhe-Xuan Li,^{1,2} Tong Zhou,¹ Roland Schmid,^{2,6} Meinhard Classen,^{2,6} Wen-Qing Li,^{1,2} Wei-Cheng You,^{1,2} Kai-Feng Pan,^{1,2}

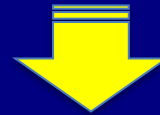


***Mundo
desarrollado***

USA Autolimitada rara vez letal
> 70.000 hospitalizaciones



Gastroenteritis aguda



***Mundo
Sub-desarrollado***

2004: 2600 millones,
2.2 millones/muertes,
2da causa de muerte en < 5 años
> Tasa mortalidad 8.5 veces
Desnutrición
Pobre acceso al servicio médico

World Health Organization. Diarrhoeal disease fact sheet. May 2017
(<http://www.who.int/mediacentre/factsheets/fs330/en/>).
Kotloff KL, Lancet 2013;382:209-22

Diarrea aguda

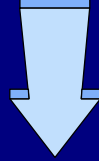
```
graph TD; A[Diarrea aguda] --> B[Bacteriana 10-20%]; A --> C[Viral 80-90%];
```

Bacteriana 10-20%
Salmonela,
Campylobacter
Shiguela, E.coli,
Yersinia

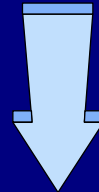
Viral 80-90%
Rotavirus (6m-4 años)
Vacunación Rotavirus
(Rotaris/RotaTed 2006)
Norovirus
Adenovirus, Astrovirus
Calicivirus,

Guarino A, JPGN 2014;59:132-52

***En la mayoría de los casos la diarrea
Aguda es de origen viral***



Autolimitada



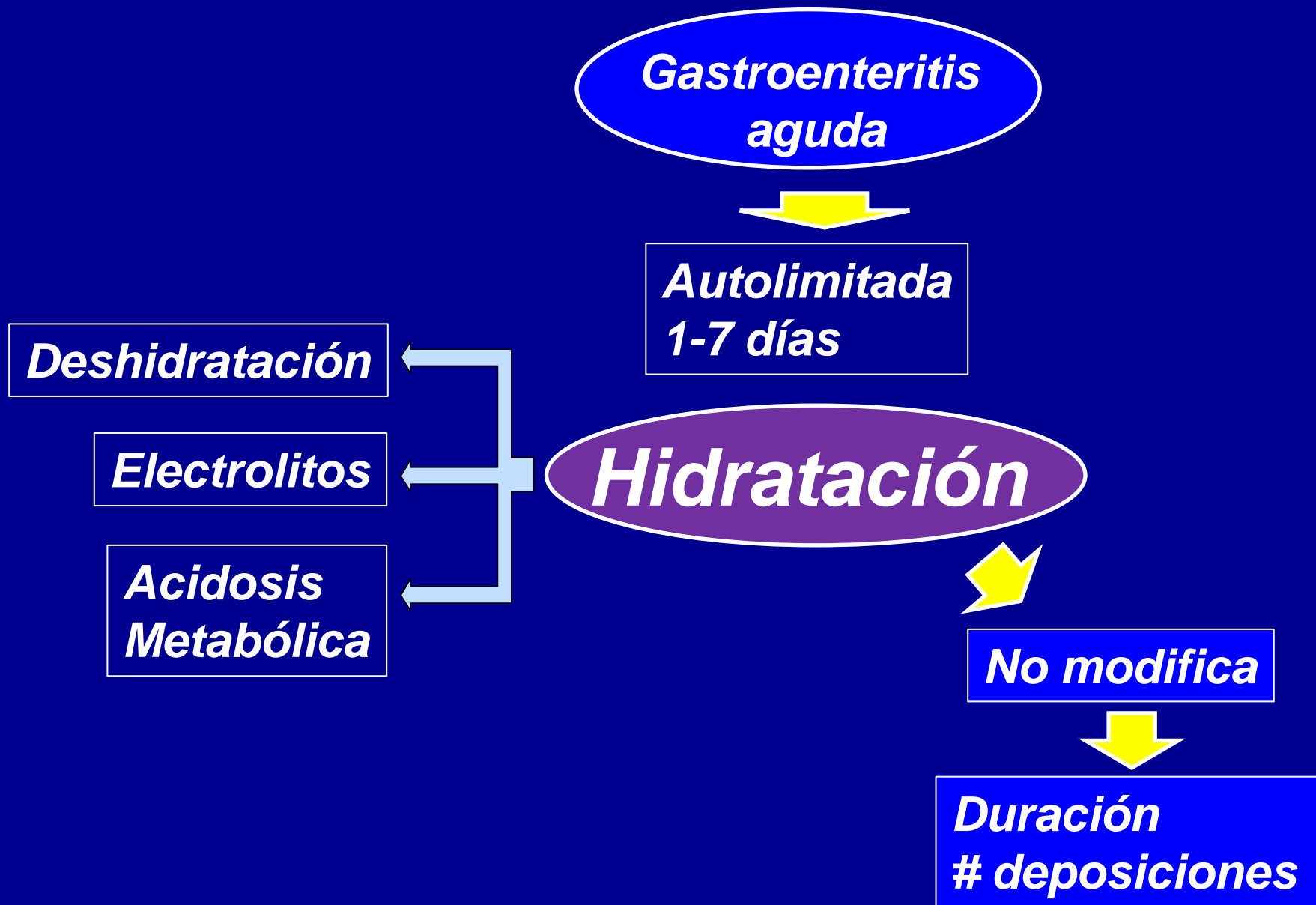
***Se podría intervenir para
Aligerar la recuperación ?***



**Altos costos en salud
y altos costos laborales**

Sufrimiento indescriptible de Muchas Personas





Diarrea aguda

En el pasado

Sólo hidratación
NO Utilización
Medicamentos

Temor de desplazar
La hidratación

Poca evidencia
Sobre eficacia



Hoy

Hidratación + Adyuvantes
Tempranamente

Evidencia sólida
Ensayos clínicos
Meta análisis
Guías GRADE

Probióticos

**Gèneros Màs conocidos
y estudiados**

Lactobacillus
Bifidobacterium

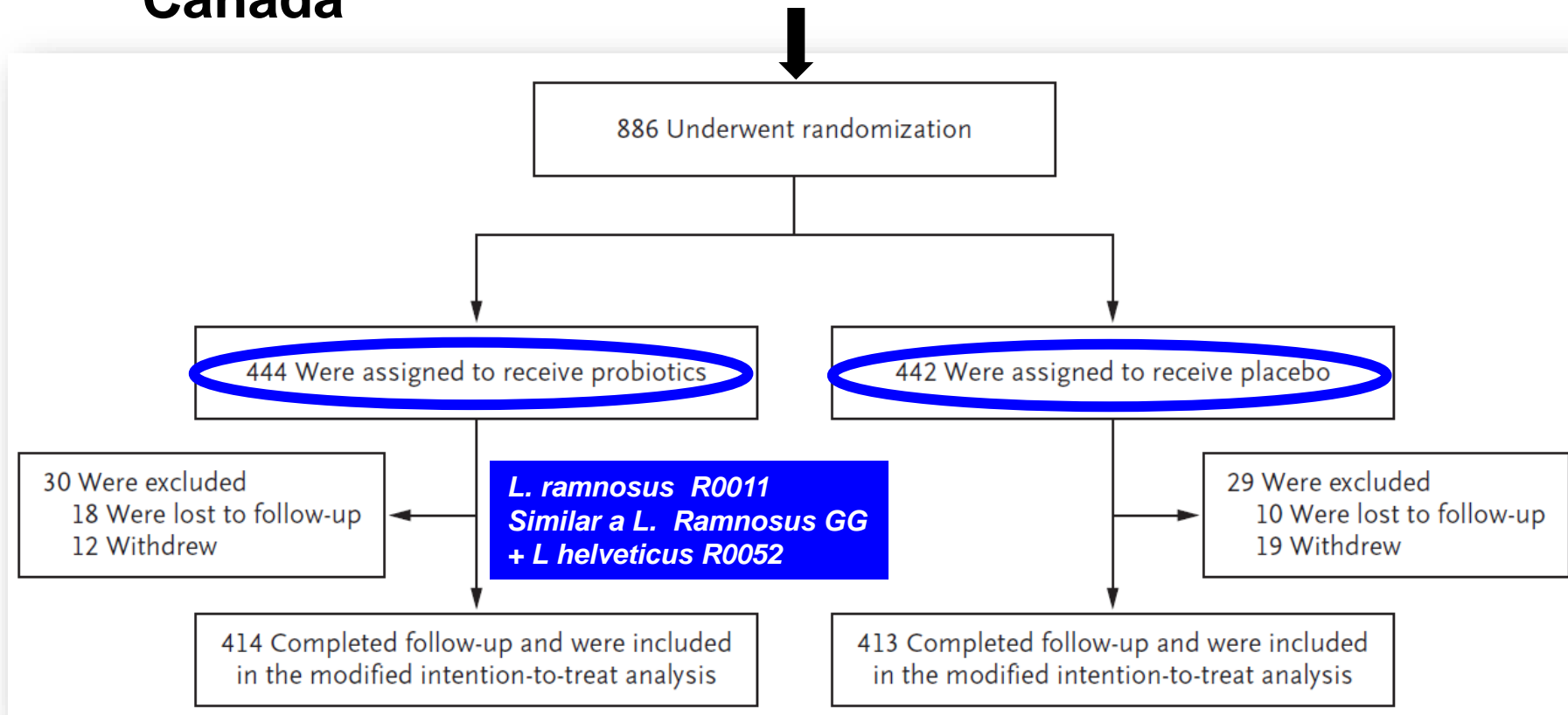
Jungersen M, Microorganisms 2014;2:92-100

Ensayos clínicos De impacto

Multicenter Trial of a Combination Probiotic for Children with Gastroenteritis

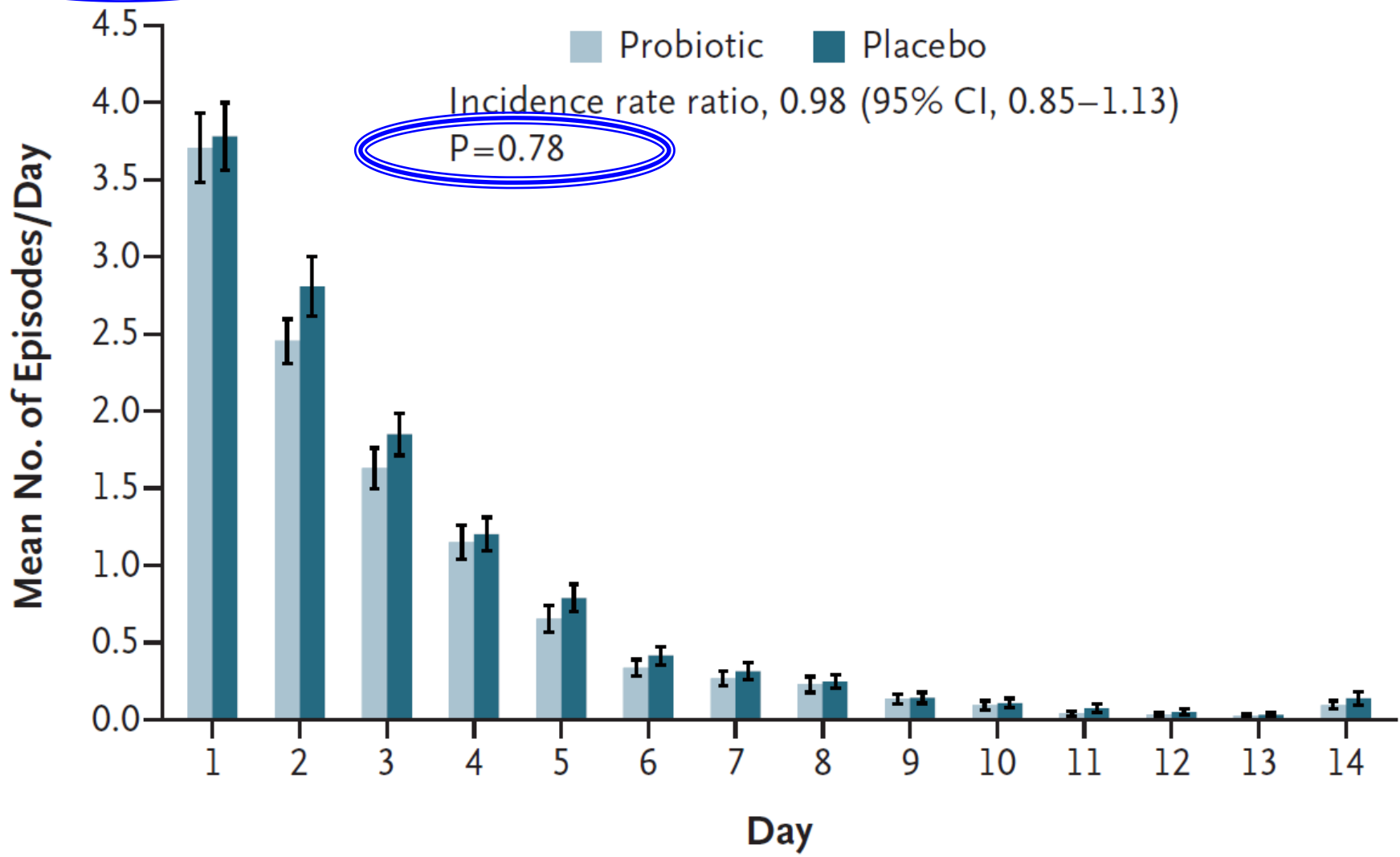
Stephen B. Freedman, M.D.C.M., Sarah Williamson-Urquhart, B.Sc.Kin.,
Ken J. Farion, M.D., Serge Gouin, M.D.C.M., Andrew R. Willan, Ph.D.,
Naveen Poonai, M.D., Katrina Hurley, M.D., Philip M. Sherman, M.D.,
Yaron Finkelstein, M.D., Bonita E. Lee, M.D., Xiao-Li Pang, Ph.D., Linda Chui, Ph.D.,
David Schnadower, M.D., M.P.H., Jianling Xie, M.D., M.P.H., Marc Gorelick, M.D.,
and Suzanne Schuh, M.D., for the PERC PROGUT Trial Group*

Canadá



Freedman SB, N Engl J Med 2018;379:2015-26.

Diarrhea



USA

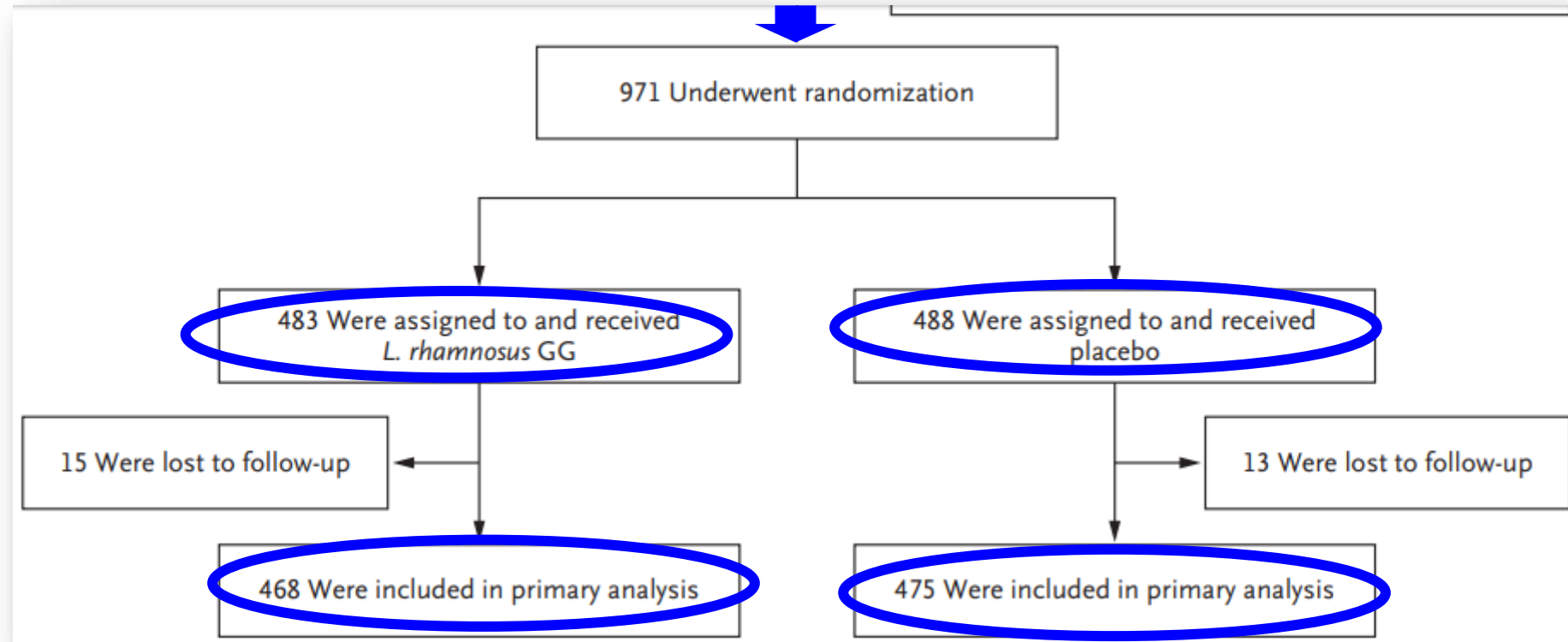
ORIGINAL ARTICLE

Lactobacillus rhamnosus GG versus Placebo for Acute Gastroenteritis in Children

David Schnadower, M.D., M.P.H., Phillip I. Tarr, M.D., T. Charles Casper, Ph.D.,
Marc H. Gorelick, M.D., M.S.C.E., J. Michael Dean, M.D., Karen J. O'Connell, M.D.,
Prashant Mahajan, M.D., M.P.H., Adam C. Levine, M.D., M.P.H.,
Seema R. Bhatt, M.D., Cindy G. Roskind, M.D., Elizabeth C. Powell, M.D.,
Alexander J. Rogers, M.D., Cheryl Vance, M.D., Robert E. Sapien, M.D.,
Cody S. Olsen, M.S., Melissa Metheney, B.S., R.N., Viani P. Dickey, A.B.,
Carla Hall-Moore, B.S., and Stephen B. Freedman, M.D.C.M.,
for the PECARN Probiotics Study Group

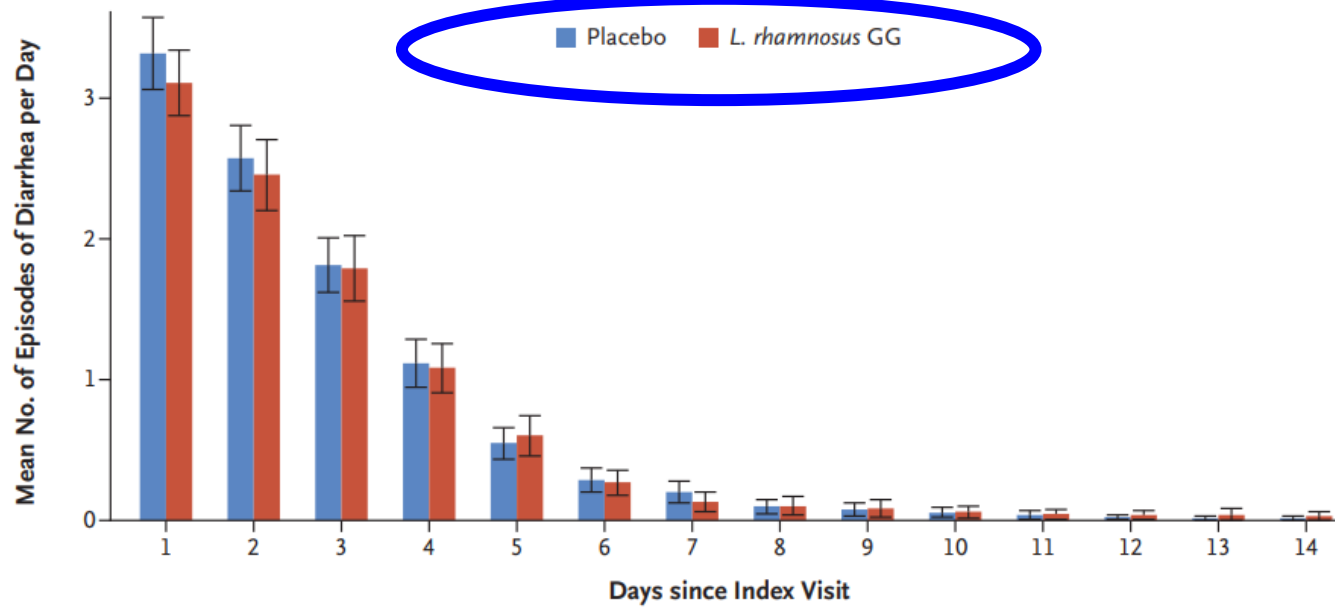
Schnasower D, N Engl J Med 2018;379:2002-14

USA

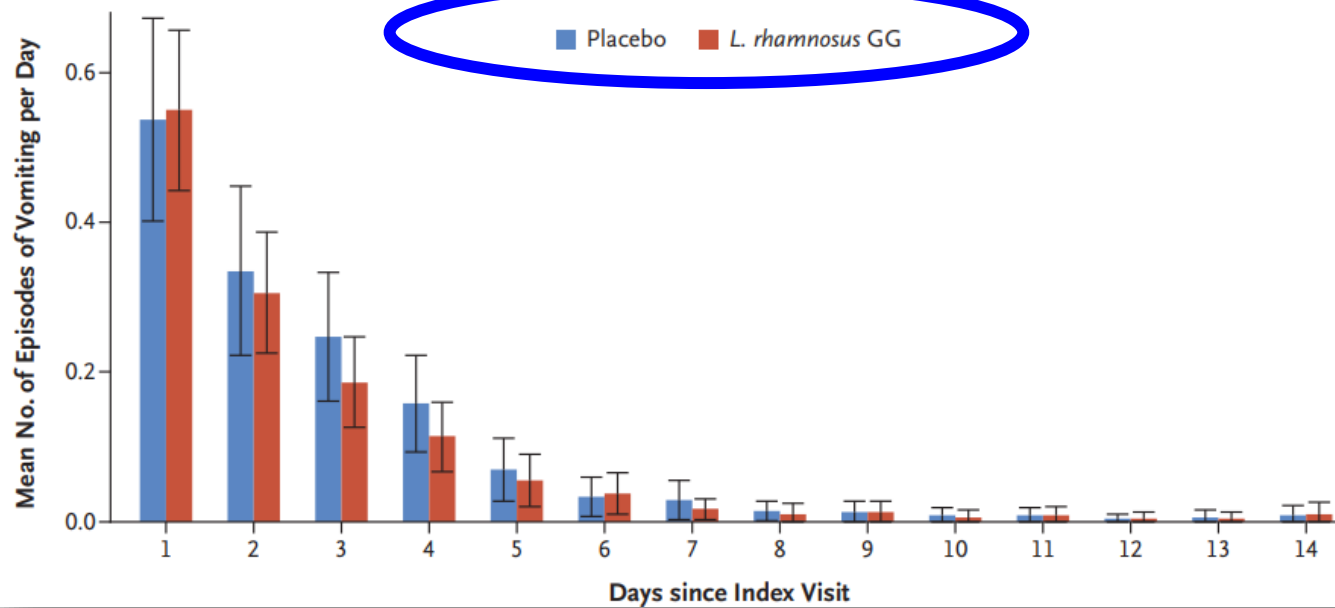


Schnadower D, N Engl J Med 2018;379:2002-14


A Diarrhea Episodes



B Vomiting Episodes



10 puntos de chequeo para evaluar un ensayo clínico

1. How was the allocation sequence generated, and was this adequately concealed?
2. Were participants and study personnel blinded? (enmascaramiento).
3. How many participants were lost to follow-up? (“Sesgo de desgaste”).
4. Was the study population well defined?. Was the intervention(s) administered correctly and appropriately?.
5. Were intervention groups comparable at baseline?.
6. Was the intervention(s) administered correctly and appropriately?
7. *Were outcome measures suitable and valid?* 
8. Was the sample size adequate and were the data analyzed properly? (What statistics have been used (and how do I interpret them?)
9. CONSORT: have the results been reported following these guidelines?
(CONSORT (CONsolidated Standards of Reporting Trials),
Creado en 1966: asegurar un correcto informe de los ECC, Actualizado en 2001, 2010
10. Were the conclusions properly drawn based on the results?

Multicenter Trial of a Combination Probiotic for Children with Gastroenteritis

Stephen B. Freedman, M.D.C.M., Sarah Williamson-Urquhart, B.Sc.Kin., Ken J. Farion, M.D., Serge Gouin, M.D.C.M., Andrew R. Willan, Ph.D., Naveen Poonai, M.D., Katrina Hurley, M.D., Philip M. Sherman, M.D., Yaron Finkelstein, M.D., Bonita E. Lee, M.D., Xiao-Li Pang, Ph.D., Linda Chui, Ph.D., David Schnadower, M.D., M.P.H., Jianling Xie, M.D., M.P.H., Marc Gorelick, M.D., and Suzanne Schuh, M.D., for the PERC PROGUT Trial Group*

Lactobacillus rhamnosus GG versus Placebo for Acute Gastroenteritis in Children

David Schnadower, M.D., M.P.H., Phillip I. Tarr, M.D., T. Charles Casper, Ph.D., Marc H. Gorelick, M.D., M.S.C.E., J. Michael Dean, M.D., Karen J. O'Connell, M.D., Prashant Mahajan, M.D., M.P.H., Adam C. Levine, M.D., M.P.H., Seema R. Bhatt, M.D., Cindy G. Roskind, M.D., Elizabeth C. Powell, M.D., Alexander J. Rogers, M.D., Cheryl Vance, M.D., Robert E. Sapien, M.D., Cody S. Olsen, M.S., Melissa Metheney, B.S., R.N., Viani P. Dickey, A.B., Carla Hall-Moore, B.S., and Stephen B. Freedman, M.D.C.M., for the PECARN Probiotics Study Group

Localización Geográfica: Canadá, USA.

Rotavirus vs Bacteriana invasiva vs Desconocida

Estudio USA (Schnadower) 2/3 vacunados contra rotavirus

Dosis $>10^{10}$ vs $<10^{10}$

Muchos había recibido antibióticos ❌

Ambos estudios iniciaron >72 horas diarrea ❌ ❌

Diarrea aguda remite espontáneamente después de 48 horas

Conclusiones correctas: Lactobacillus rhamnosus GG.

No es útil en países desarrollados si se administra

Después de 72 horas de diarrea

ORIGINAL ARTICLE

Multicenter Trial of a Combination Probiotic for Children with Gastroenteritis

Stephen B. Freedman, M.D.C.M., Sarah Williamson-Urquhart, B.Sc.Kin., Ken J. Farion, M.D., Serge Gouin, M.D.C.M., Andrew R. Willan, Ph.D., Naveen Poonai, M.D., Katrina Hurley, M.D., Philip M. Sherman, M.D., Yaron Finkelstein, M.D., Bonita E. Lee, M.D., Xiao-Li Pang, Ph.D., Linda Chui, Ph.D., David Schnadower, M.D., M.P.H., Jianling Xie, M.D., M.P.H., Marc Gorelick, M.D., and Suzanne Schuh, M.D., for the PERC PROGUT Trial Group*

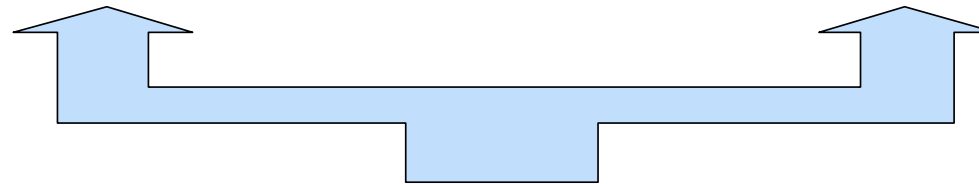
Freedman SB, N Engl J Med 2018;379:2015-26.

ORIGINAL ARTICLE

Lactobacillus rhamnosus GG versus Placebo for Acute Gastroenteritis in Children

David Schnadower, M.D., M.P.H., Phillip I. Tarr, M.D., T. Charles Casper, Ph.D., Marc H. Gorelick, M.D., M.S.C.E., J. Michael Dean, M.D., Karen J. O'Connell, M.D., Prashant Mahajan, M.D., M.P.H., Adam C. Levine, M.D., M.P.H., Seema R. Bhatt, M.D., Cindy G. Roskind, M.D., Elizabeth C. Powell, M.D., Alexander J. Rogers, M.D., Cheryl Vance, M.D., Robert E. Sapien, M.D., Cody S. Olsen, M.S., Melissa Metheney, B.S., R.N., Viani P. Dickey, A.B., Carla Hall-Moore, B.S., and Stephen B. Freedman, M.D.C.M., for the PECARN Probiotics Study Group

Schnasower D, N Engl J Med 2018;379:2002-14



**Prematuramente Negaron
beneficio de *L. rhamnosus* GG
En niños gastroenteritis aguda
En países diferentes a Canadá y USA**

CLINICAL PRACTICE GUIDELINES

AGA Clinical Practice Guidelines on the Role of Probiotics in the Management of Gastrointestinal Disorders






Grace L. Su,^{1,2} Cynthia W. Ko,³ Premysl Bercik,⁴ Yngve Falck-Ytter,^{5,6} Shahnaz Sultan,⁷ Adam V. Weizman,⁸ and Rebecca L. Morgan⁹

**In children with acute infectious gastroenteritis, we suggest against the use of probiotics.
*Conditional recommendation, moderate quality of evidence.***

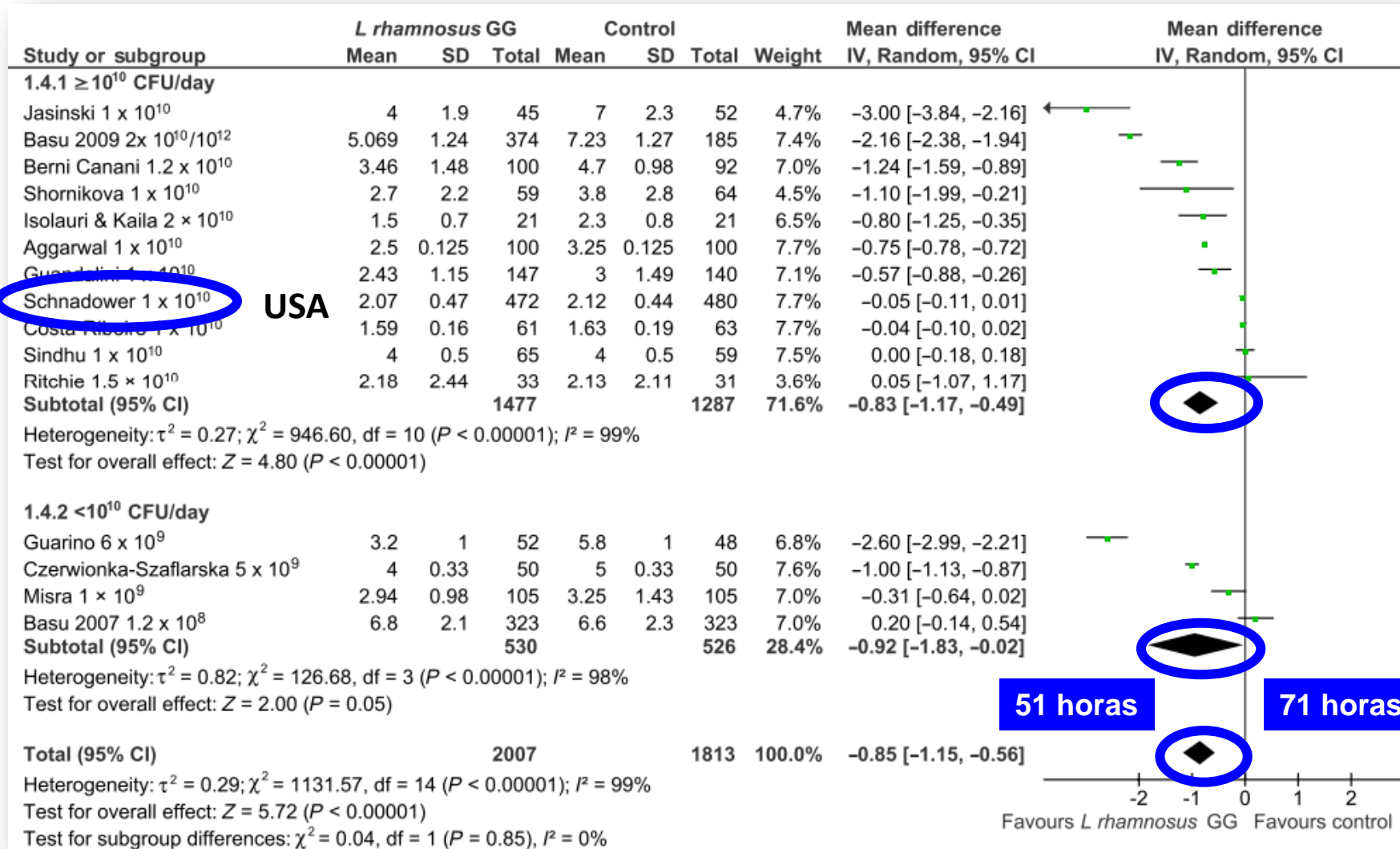
The AGA suggests against the use of probiotics in children with acute infectious gastroenteritis in the United States and Canada. The majority of the data supporting the use of probiotics in children with acute infectious gastroenteritis were from studies performed outside of United States and Canada, while 2 high-quality studies performed in the United States and Canada did not show any benefit.

Systematic review with meta-analysis: *Lactobacillus rhamnosus* GG for treating acute gastroenteritis in children – a 2019 update

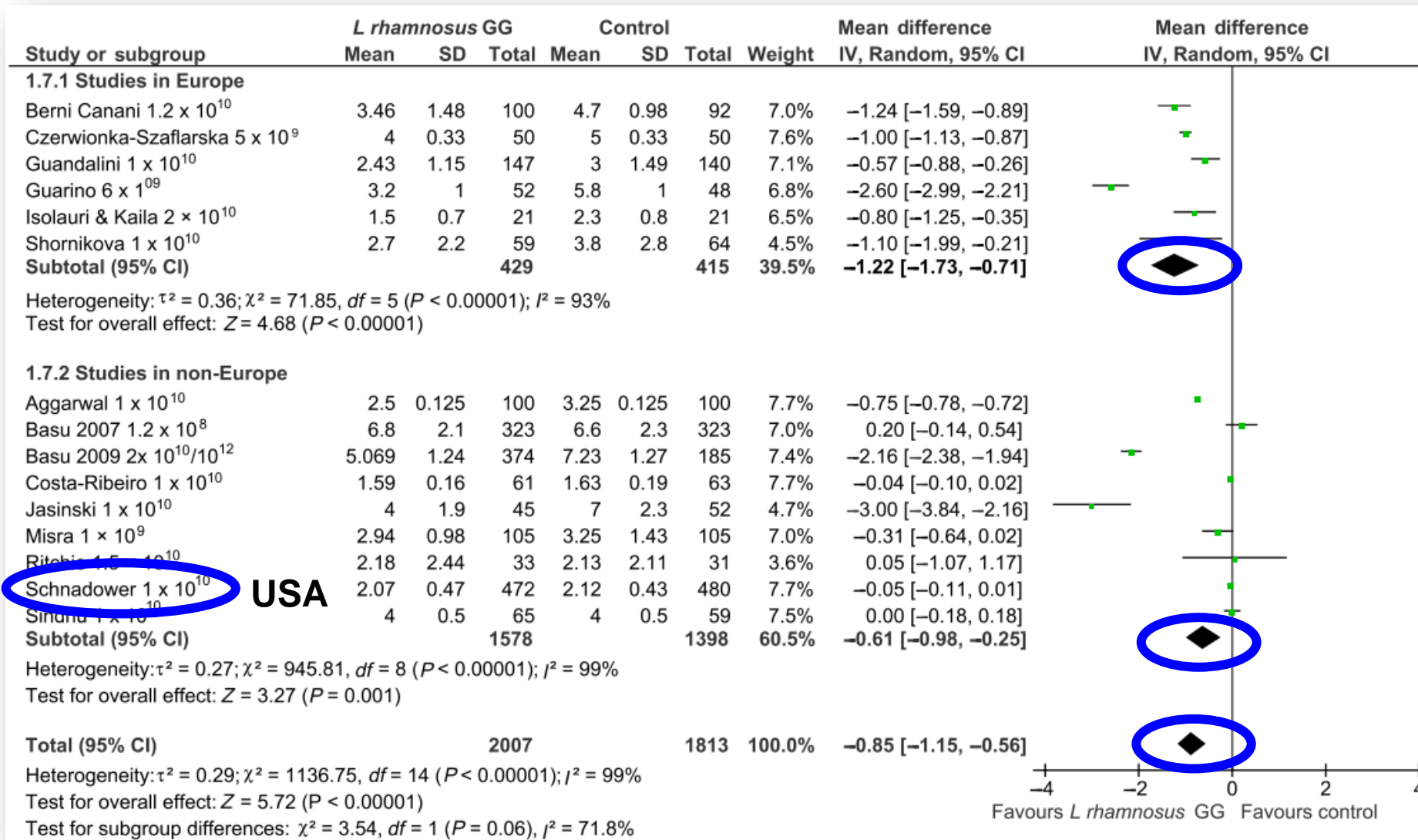
Hania Szajewska¹  | Maciej Kołodziej¹  | Dorota Gieruszczak-Białek¹ |
Agata Skórka¹  | Marek Ruszczyński¹ | Raanan Shamir²

8 ECC, 4.200 niños
Adición de LGG a hidratación estándar
Es benéfico si o no?

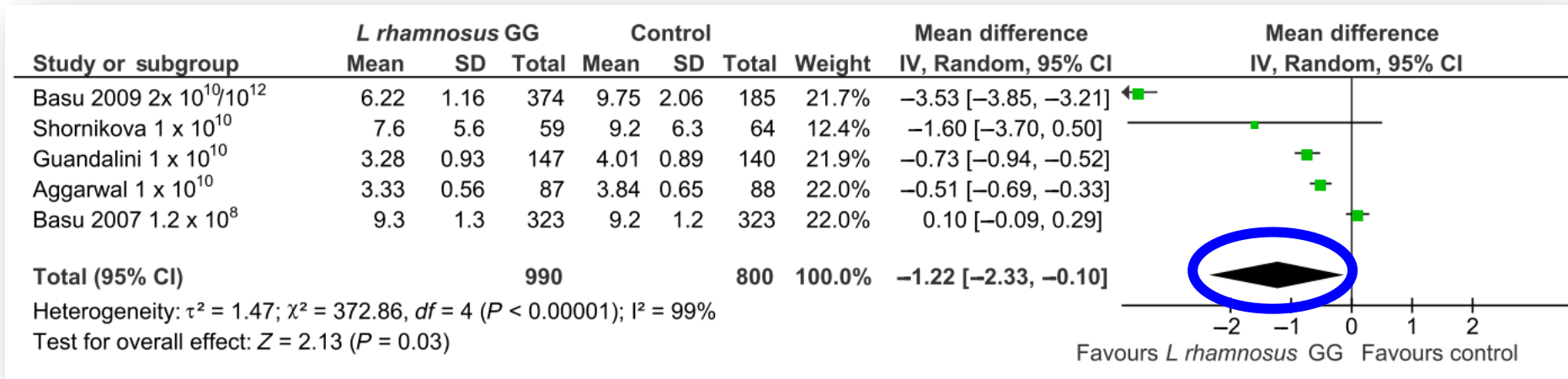
Control de gastroenteritis aguda: Altas dosis $\geq 1.4 \times 10^9$ UFC o Bajas dosis versus Placebo



Duración de la diarrea: Europa Versus Otros sitios






Duración Hospitalización



Disminuye 29 horas

Szajewska H, et al Aliment Pharmacol Ther 2019;49:1376-1384

Systematic review with meta-analysis: *Lactobacillus rhamnosus* GG for treating acute gastroenteritis in children – a 2019 update

Hania Szajewska¹  | Maciej Kołodziej¹  | Dorota Gieruszczak-Białek¹ |
Agata Skórka¹  | Marek Ruszczyński¹ | Raanan Shamir²

4.200 Niños LGG

Disminuye 20 horas duración diarrea

Disminuye hospitalización 29 horas

Mayor beneficio dosis alta $>10^9$ UFC Vs $<10^9$

Mejor en Europa vs Otros sitios



**Este meta-análisis respalda las
Recomendaciones de las guías de práctica clínica**



World Journal of
Gastroenterology

Submit a Manuscript: <https://www.f6publishing.com>

World J Gastroenterol 2019 September 7; 25(33): 4999-5016

DOI: [10.3748/wjg.v25.i33.4999](https://doi.org/10.3748/wjg.v25.i33.4999)

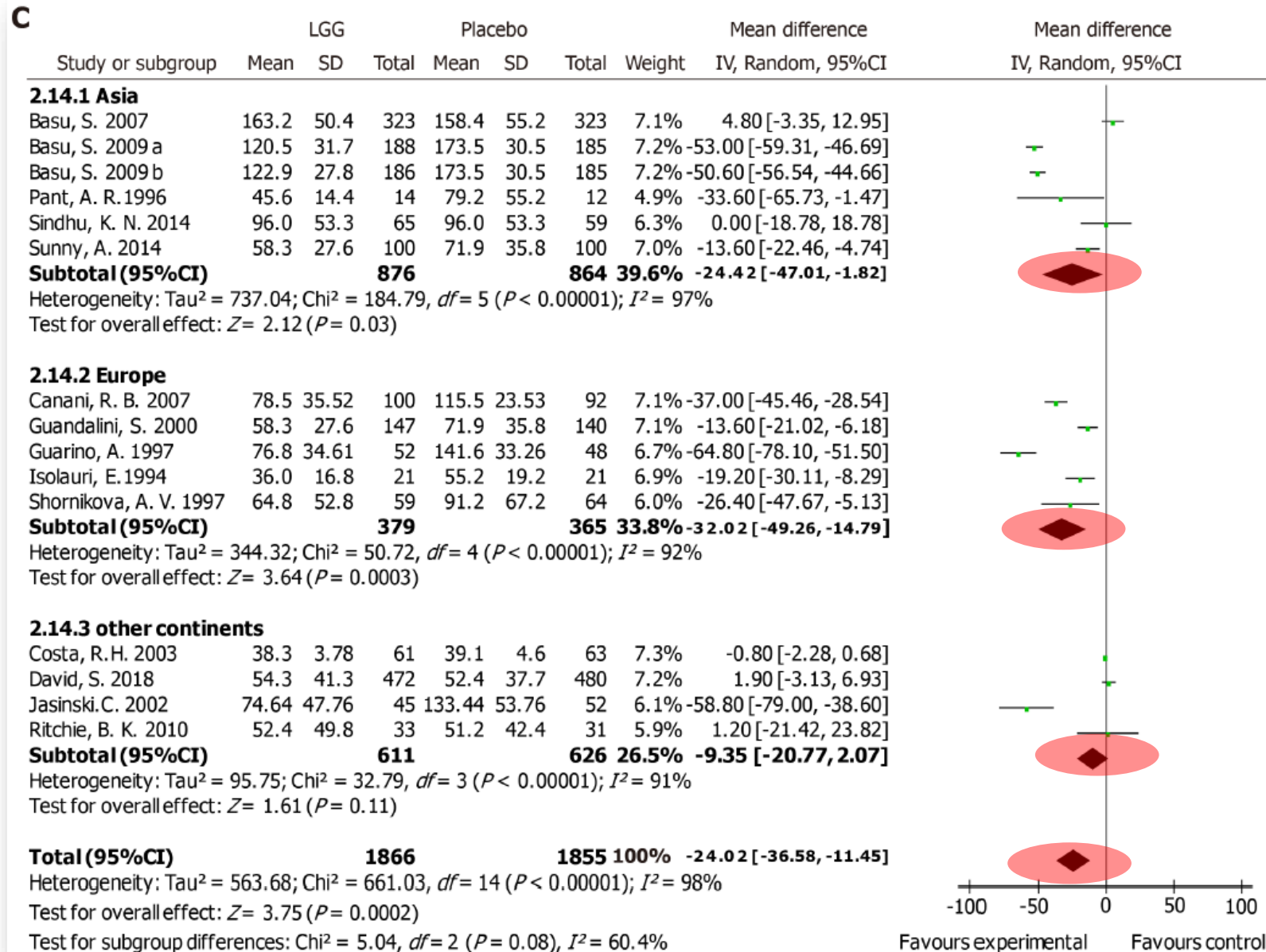
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

META-ANALYSIS

Efficacy of *Lactobacillus rhamnosus* GG in treatment of acute pediatric diarrhea: A systematic review with meta-analysis

Ya-Ting Li, Hong Xu, Jian-Zhong Ye, Wen-Rui Wu, Ding Shi, Dai-Qiong Fang, Yang Liu, Lan-Juan Li

Duración de la diarrea



Número deposiciones y consistencia heces

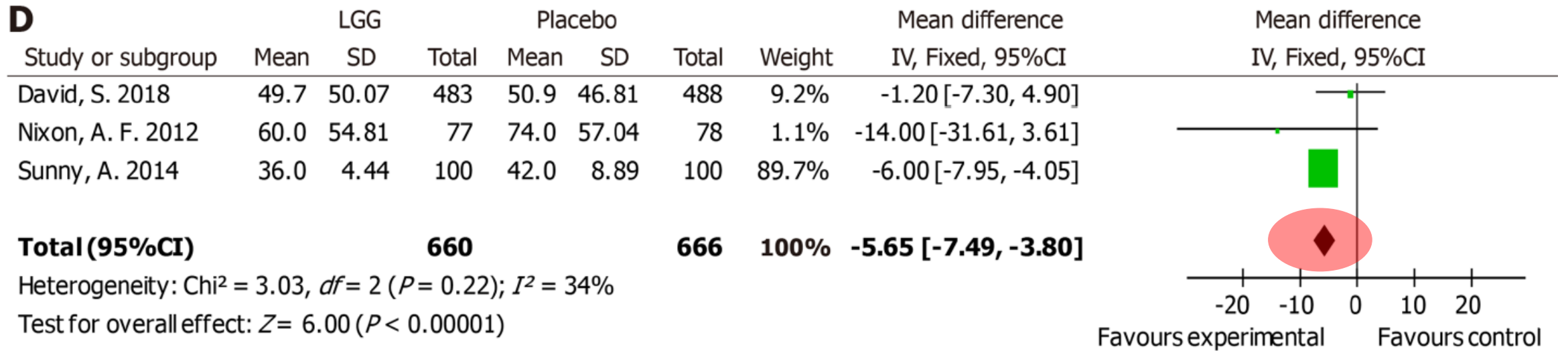
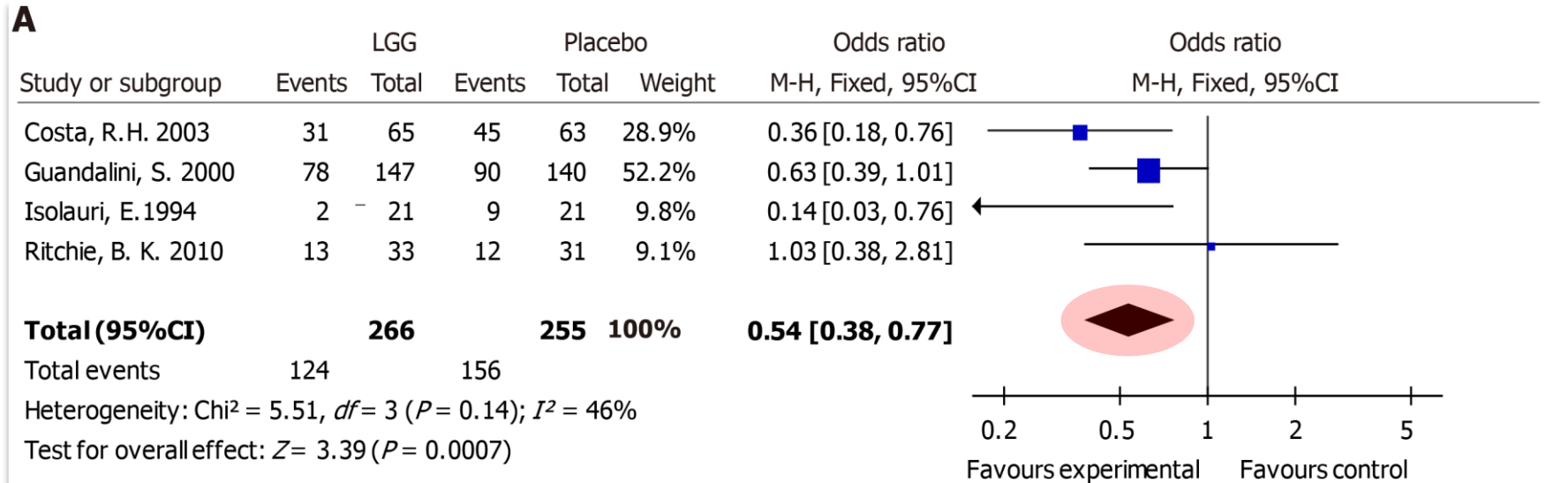


Figure 4 *Lactobacillus GG* vs control with regard to stool number and consistency. A: The average stool number per day (high dose and low dose); B: S frequency on day 2; C: Stool frequency on day 3; D: The mean time to improvement in stool consistency. LGG: *Lactobacillus rhamnosus GG*; CI: Confidence in SD: Standard deviation.

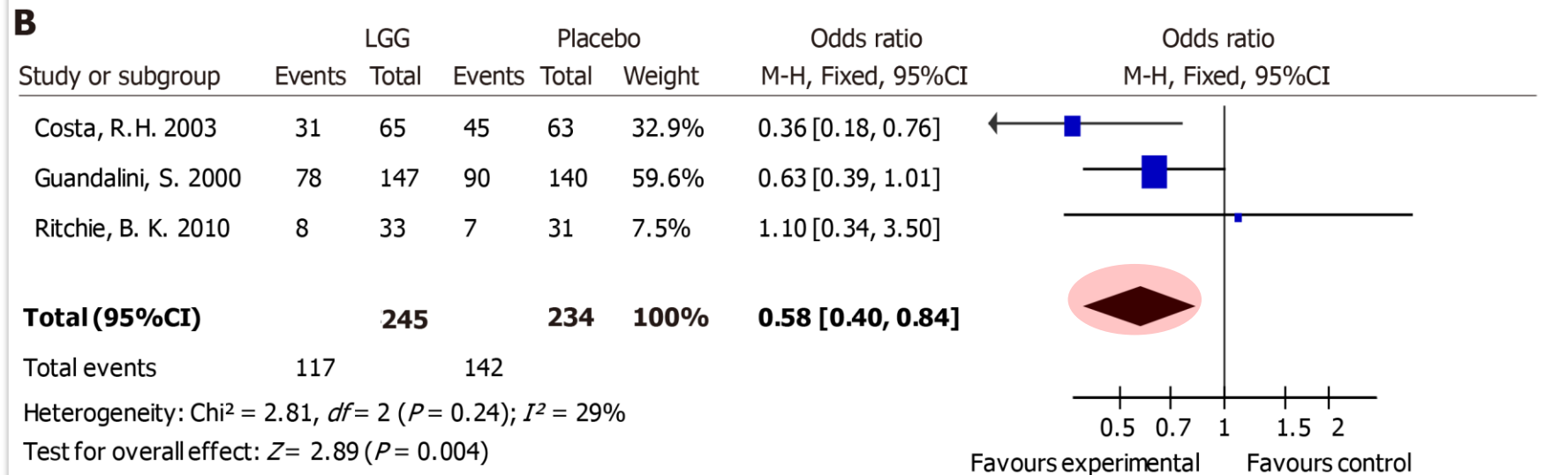
Li YT, World J Gastroenterol 2019; 25: 4999-5016

Lactobacillus GG vs Control

Diarrea > 3 días



Diarrea > 4 días



BMJ Open Probiotics for the prevention of antibiotic-associated diarrhoea: a systematic review and meta-analysis

Clare Goodman ¹, Georgia Keating,² Ekavi Georgousopoulou,
Charlotte Hespe ¹, Kate Levett ¹

Diarrea asociada a antibióticos

Goodman C, BMJ Open. 2021 Aug 12;11(8):e043054

Results Forty-two studies (11,305 participants) were included in this review. The pooled analysis suggests that co-administration of probiotics with antibiotics reduces the risk of AAD in adults by 37% (risk ratio (RR)=0.63 (95% CI 0.54 to 0.73), $p<0.00001$). The overall quality of the evidence using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) criteria was found to be moderate. In subgroup analyses, high dose compared with low dose of the same probiotic demonstrated a positive protective effect (RR 0.54 (95% CI 0.38 to 0.76), $p<0.01$), and only certain species, mainly of the lactobacillus and bifidobacteria genera, were found to be effective. Studies with a low baseline AAD risk did not show any difference in risk but studies with moderate or high baseline AAD risk demonstrated a significant risk reduction.

Conclusions Probiotics are effective for preventing AAD. Secondary analyses of higher dosages and certain species have shown increased effectiveness. Our results may not be applicable in clinical scenarios of lower baseline AAD risk.

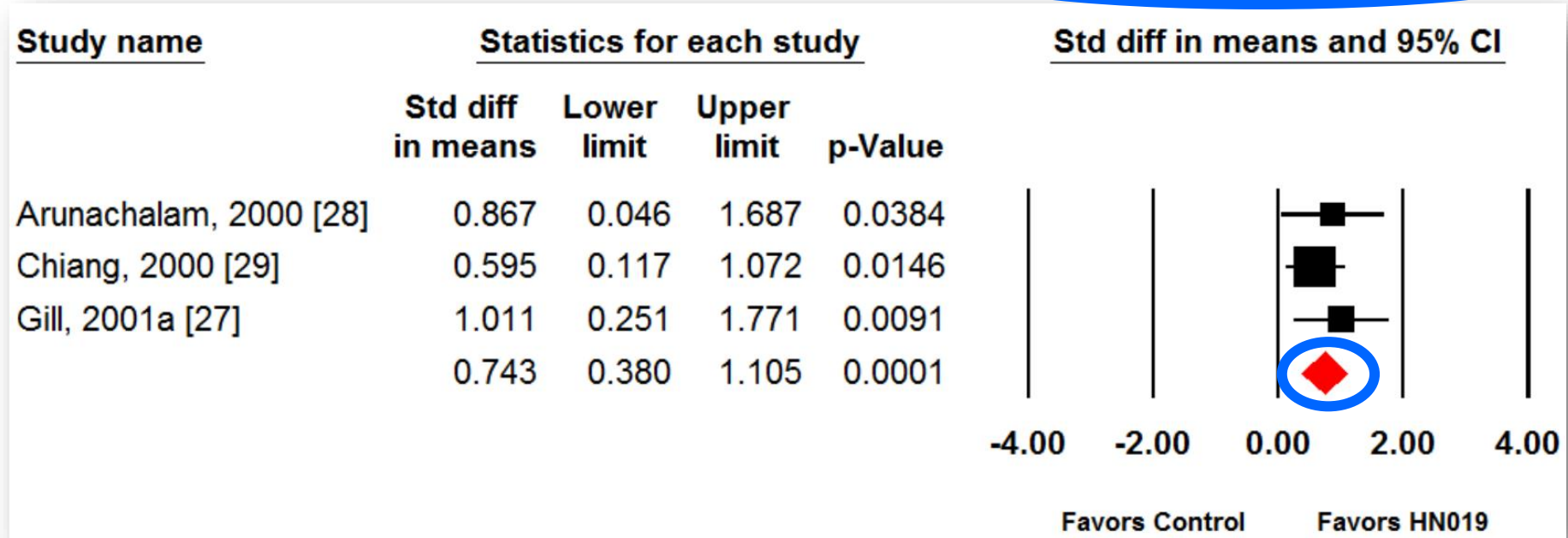
Bifidobacterium animalis (BB-12)
Múltiples investigaciones

Jungersen M, Microorganisms 2014;2:92-100

The Effect of *Bifidobacterium animalis* ssp. *lactis* HN019 on Cellular Immune Function in Healthy Elderly Subjects: Systematic Review and Meta-Analysis

Larry E. Miller ^{1,*}, Liisa Lehtoranta ² and Markus J. Lehtinen ²

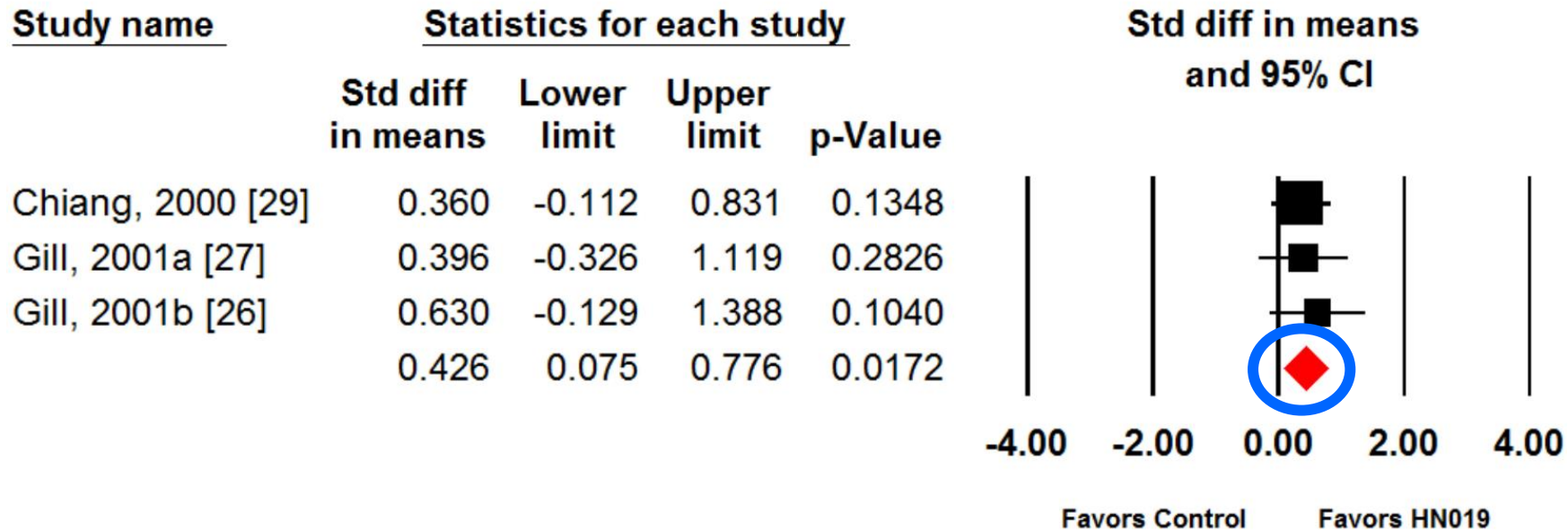
Capacidad fagocítica de PMN



The Effect of *Bifidobacterium animalis* ssp. *lactis* HN019 on Cellular Immune Function in Healthy Elderly Subjects: Systematic Review and Meta-Analysis

Larry E. Miller ^{1,*}, Liisa Lehtoranta ² and Markus J. Lehtinen ²

Tumoricida



Restitution of gut microbiota in Ugandan children administered with probiotics (*Lactobacillus rhamnosus* GG and *Bifidobacterium animalis* subsp. *lactis* BB-12) during treatment for severe acute malnutrition

Josué L. Castro-Mejía ¹, Sinéad O'Ferrall ¹, Łukasz Krych ¹, Elaine O'Mahony ¹, Hanifa Namusoke ², Betty Lanyero ³, Witold Kot ⁴, Nicolette Nabukeera-Barungi ⁵, Kim Fleischer Michaelsen ⁶, Christian Mølgaard ⁶, Henrik Friis ⁶, Benedikte Grenov ^{6*}, and Dennis S. Nielsen ^{6*}

Investigadores Daneses

Desnutrición

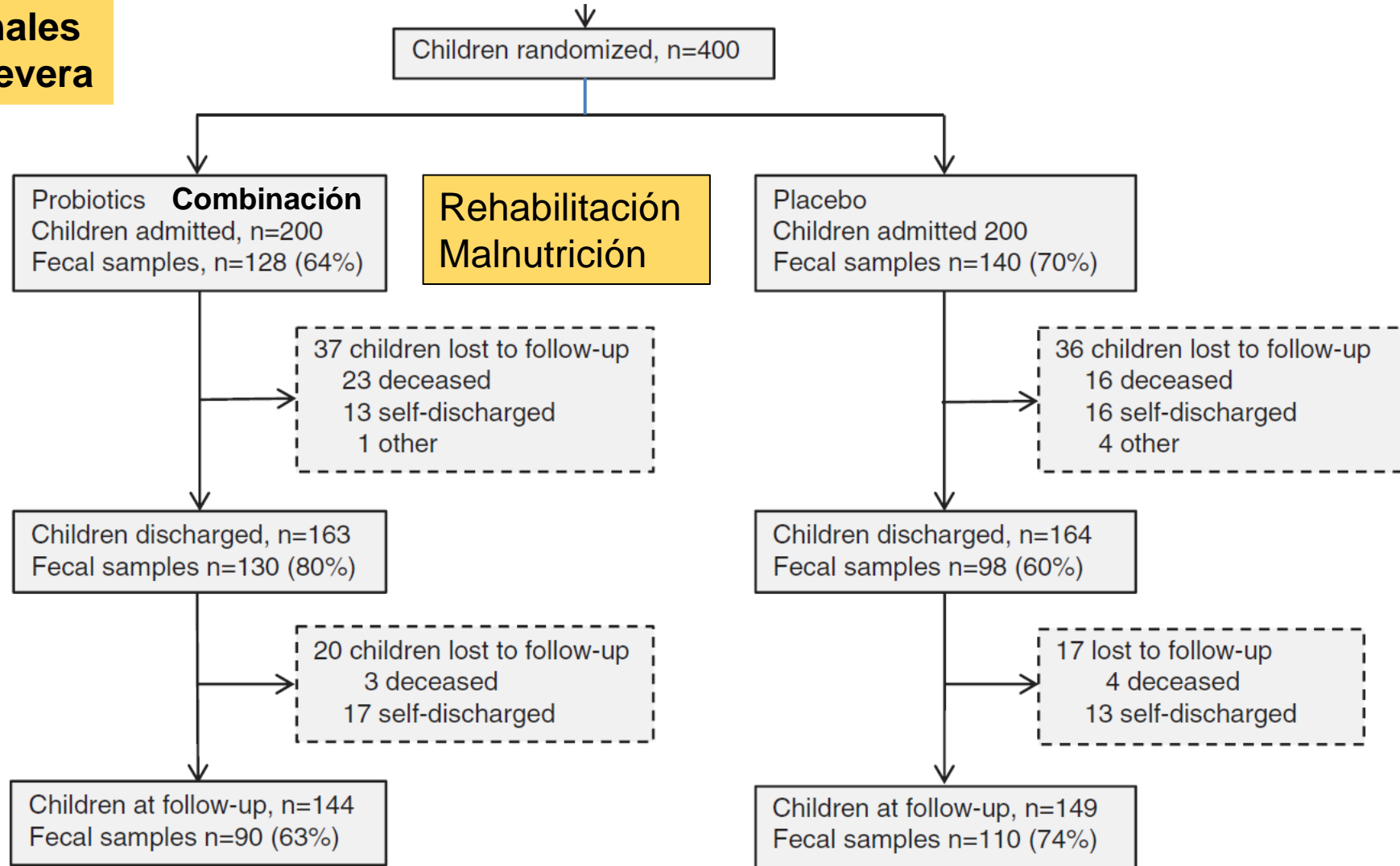
**Globalmente
45% muertes**

**Secuelas
Intelectuales
Productividad**

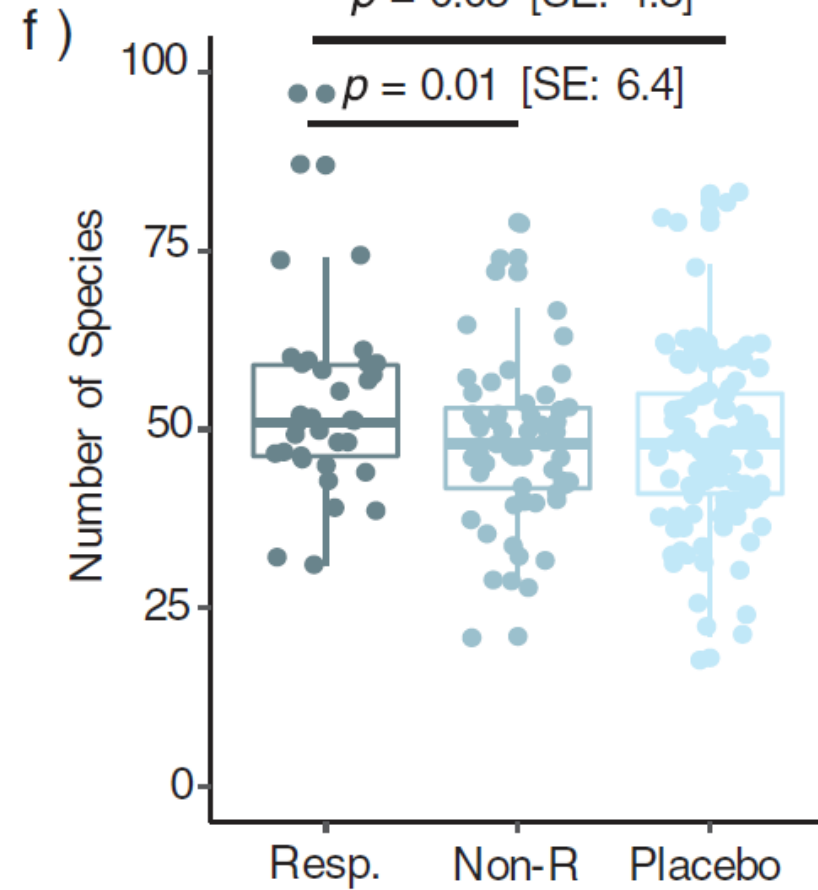
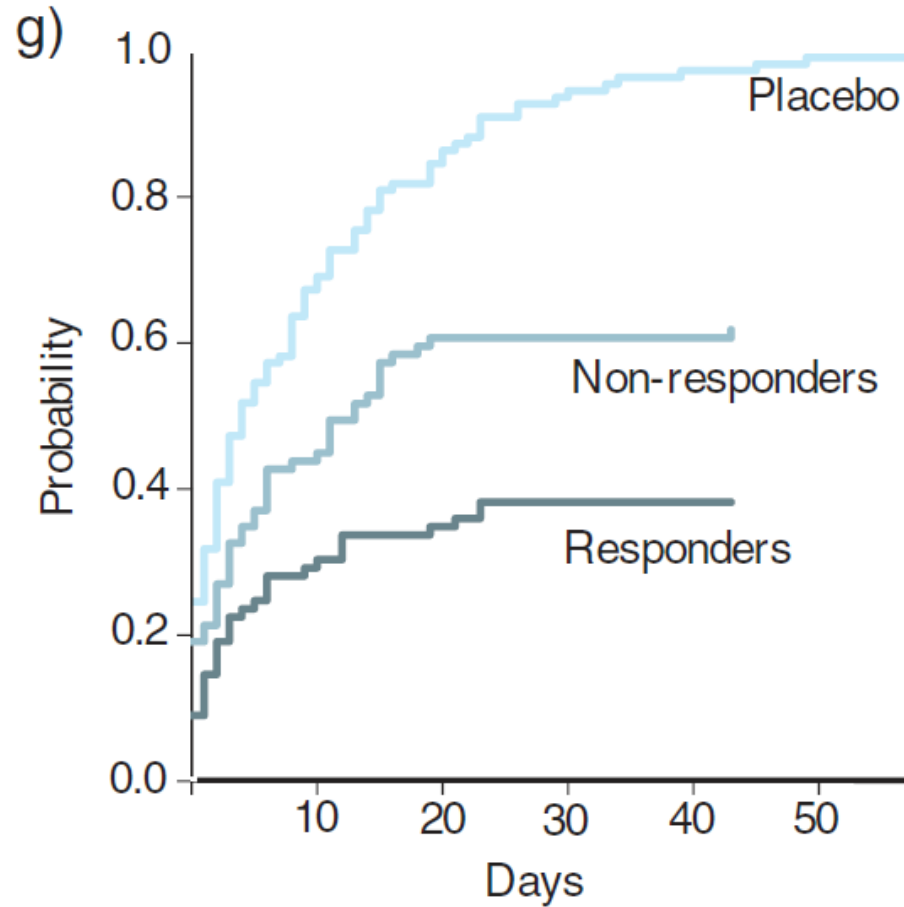
**Disbiosis: Desencadenar o
Mantener desnutrición aguda
Disminuye diversidad microbiota**



**Barrios marginales
Malnutrición severa**



Redujo la incidencia acumulativa de diarrea en el futuro



LGG +

Bifidobacterium animalis (BB-12)

>300 publicaciones,

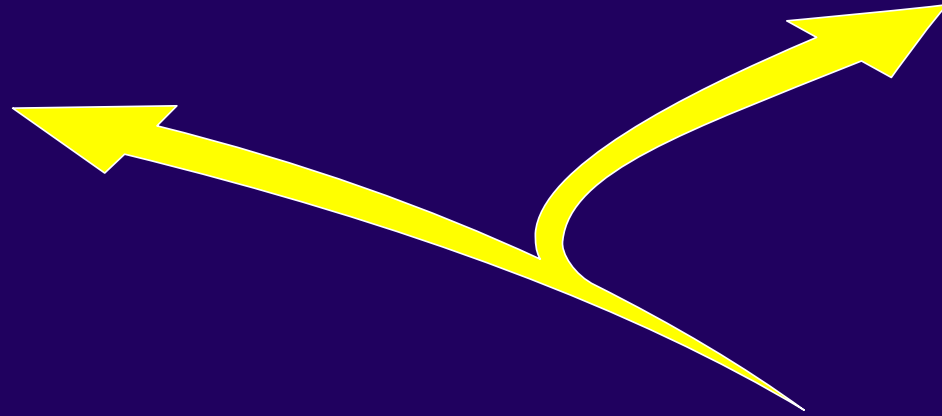
>130 estudios clínicos

Jungersen M, Microorganisms 2014;2:92-100

LGG probiótico más estudiado en EDA mundo

Probiótico mayor Adherencia /resistencia en el intestino

El BB12 más estudiado Fortalecer sistema inmune



Sinergismo



➤ Desplazamiento Patógenos

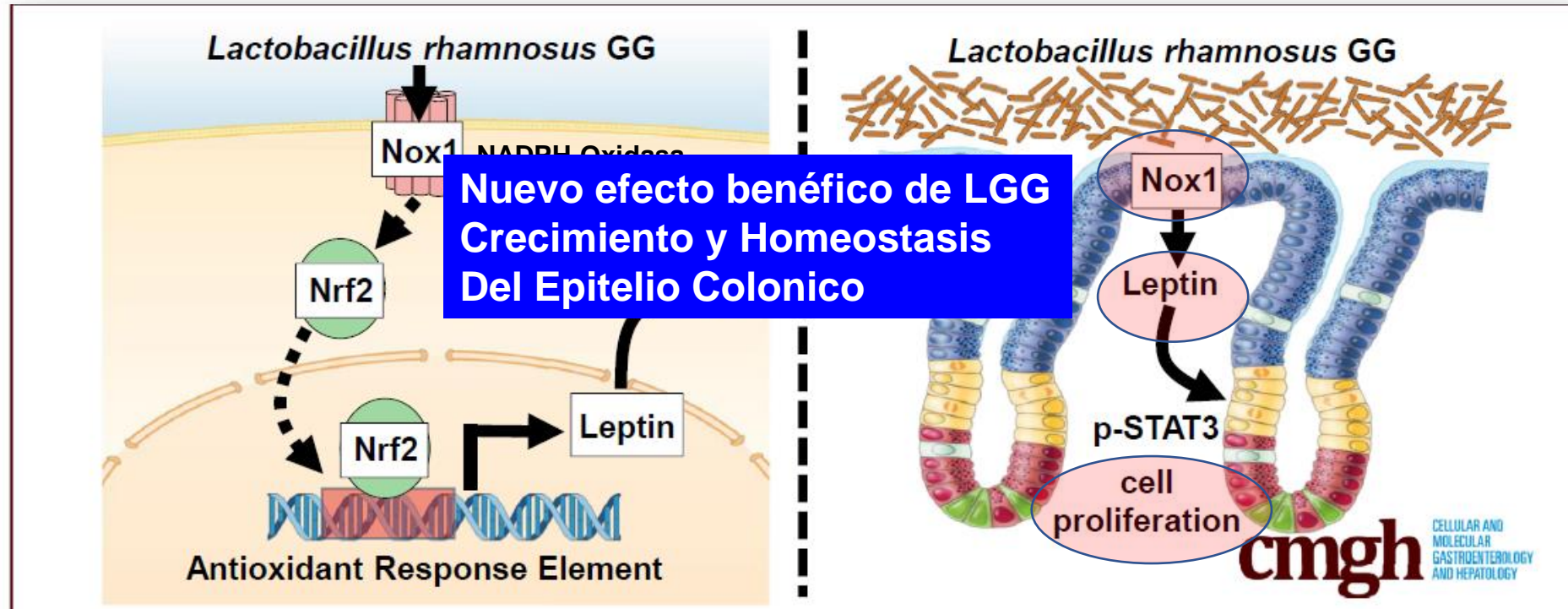
Efectos recientemente Identificados de LGG

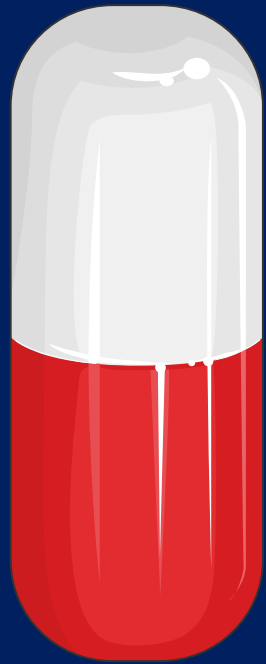
Lactobacillus rhamnosus GG–induced Expression of Leptin in the Intestine Orchestrates Epithelial Cell Proliferation

Trevor M. Darby,¹ Crystal R. Naudin,¹ Liping Luo,¹ and Rheinallt M. Jones^{1,2}

¹Division of Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, Emory University School of Medicine, Atlanta, Georgia; ²Emory Microbiome Research Center, Emory University School of Medicine, Atlanta, Georgia

Ratones ingestión oral de LGG





Lactobacillus rhamnosus GG
LGG, 3.25×10^9 UFC



Bifidocaterium animalis lactis
BB-12, 3.25×10^9 UFC

Diarrea aguda y asociada a Antibióticos

Dosis recomendada: 1×10^{10}

3 capsulas/día por 5-10 días o MAS ?(RN-99 años)

Profilaxis diarrea por antibióticos

Dosis recomendada: 1×10^9

1 cápsula diaria durante antibióticos 2h antes

GIGI12



Lactobacillus rhamnosus GG
LGG 3.25 x 10⁹ UFC



Bifidocaterium animalis lactis
BB-12 3.25 X 10⁹ UFC

Niños > 6 años 2-3 capsulas/d
< 6 años igual dosis
Abrir la cápsula



Inconvenientes

↑ **Materia Prima**
1-3 gr Vs 125 mg/C
Almidón de maíz,
Caseina, gelatina, lactosa



Alergias

Excipientes comunes

Almidón de Maíz
Fécula de Maíz
Lactosa
Proteína de leche
Carbonato de Magnesio
Gelatina

Añadidos a Ingrediente farmacológico Activo
Absorción, estabilidad
Sabor, apariencia,
resistencia manipulación

Table 1. List of critical inactive ingredients that can act as allergens or are potentially contaminated with allergens. Percentage occurrence refers to fraction of all formulations of medications (solid oral dosage forms) that contain the critical ingredient. PEG, polyethylene glycol.

Ingredient	Classification	Percentage occurrence in medications
Lactose	Food	44.82%
Corn starch	Food	36.54%
PEG	Polymer	36.03%
Povidone	Polymer	35.80%
Carboxymethylcellulose	Other	21.38%
Gelatin	Food	16.93%
Brilliant blue	Dye	14.47%
Sunset yellow FCF	Dye	12.27%
Allura red	Dye	11.20%
Propylene glycol	Other	11.14%
Indigo carmine	Dye	10.63%
Mannitol	Sugar	7.20%
Sucrose	Sugar	5.21%
Sodium benzoate	Other	1.72%
Parabens	Other	1.48%
Aspartame	Other	1.46%
Erythrosine	Dye	1.03%
Tartrazine	Dye	0.95%
Saccharin	Other	0.81%
Poloxamer	Polymer	0.76%
Soybean oil	Food	0.44%
Benzyl alcohol	Other	0.43%
Vanilla	Food	0.38%
Castor oil	Food	0.30%
Cetyl alcohol	Other	0.19%
Sulfite	Other	0.19%
PEG castor oils	Food	0.13%
Peanut oil	Food	0.08%
Benzoic acid	Other	0.07%
Corn syrup	Food	0.05%
Sesame oil	Food	0.05%
Starch wheat	Food	0.04%
Casein	Food	0.03%
Banana essence	Food	0.01%
Milk	Food	0.01%
Glucosamine	Food	0.00%
New coccine	Dye	0.00%
Stearyl alcohol	Other	0.00%

PHARMACOLOGY

“Inactive” ingredients in oral medications

Daniel Reker^{1,2,3*}, Steven M. Blum^{1,4,5*}, Christoph Steiger^{1,2,3}, Kevin E. Anger⁴,
Jamie M. Sommer⁶, John Fanikos⁶, Giovanni Traverso^{1,2,3,4,7†}



38 “compuestos inactivos”



Pueden dar alergias

Mensajes para la casa

No evidencia beneficio de Probioticos en
SII, EII, Cd, *H.pylori*.

En diarrea aguda Hidratación piedra angular
LGG administrado 1as 24-48 h

Acorta duración diarrea

Disminuye hospitalización

Evita diarrea antibióticos

LGG + BB-12: seguro eficaz

**Digestive
Diseases**

Nutrition and Probiotics: Review Article

Dig Dis

DOI: 10.1159/000516023

Compare D, et al. Dig Dis. 2022;40:123-132.

Probiotics in Gastrointestinal Diseases: All that Glitters Is Not Gold

Debora Compare Costantino Sgamato Olga Maria Nardone Alba Rocco
Pietro Coccoli Carmen Laurenza Gerardo Nardone

Department of Clinical Medicine and Surgery, Gastroenterology, University Federico II of Naples, Naples, Italy

Muchas gracias !