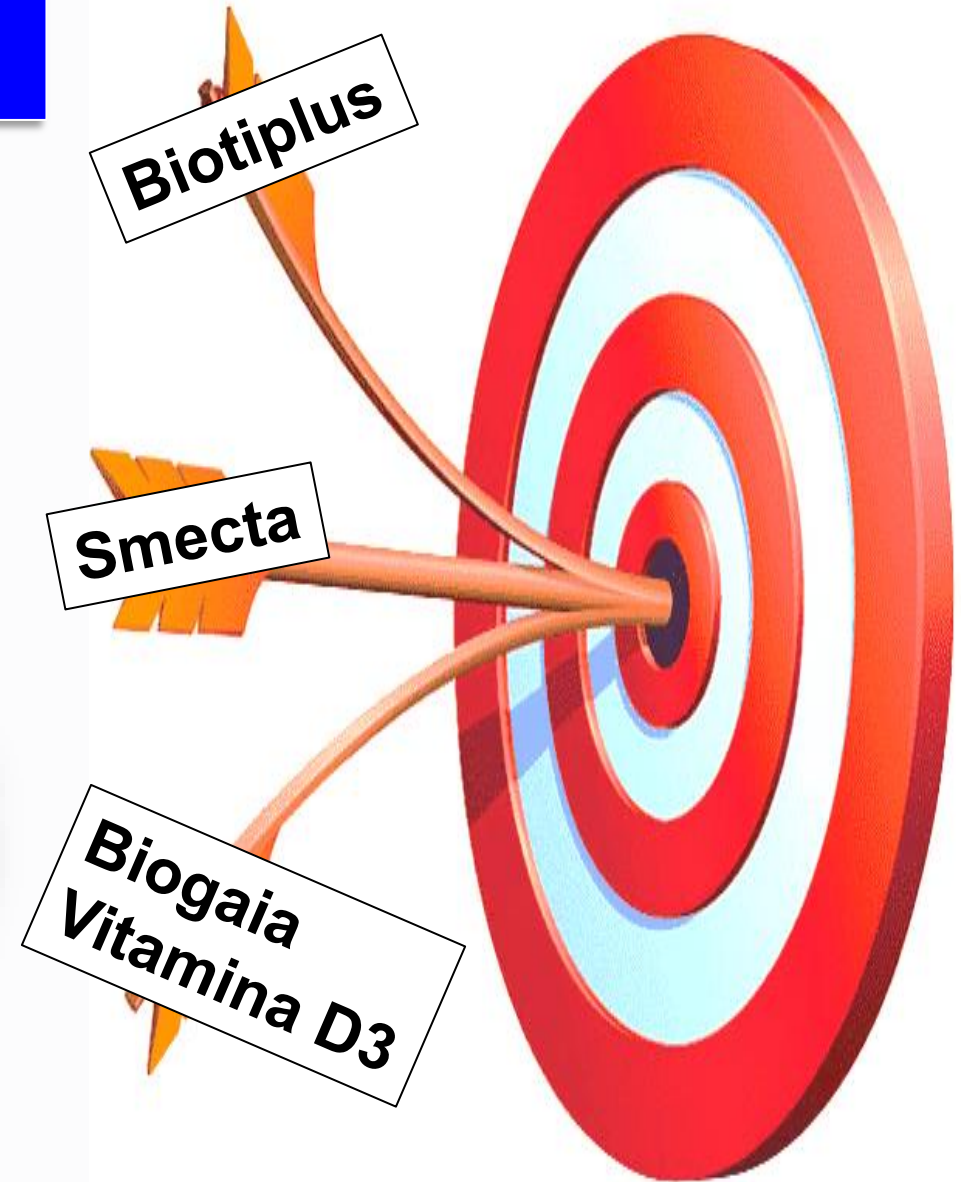


Jornadas Médicas de actualización integral JAMI
Quito julio 20, 2022

Diarrea aguda manejo en el 2022 ***Tres estrategias complementarias***



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



Canal YouTube "William Otero Gastroenterólogo"

Conflicto de intereses

Takeda Vedolizumab

Abbott Rifax, Izinova, Nedox, probióticos

Procaps Ezolium

Tecnoforma Nulytely, Contumax

Tecnoquímica,

Menarini Salofalk, spasmomen

Biotoscana

***Mundo
desarrollado***

USA Autolimitada rara vez letal
1.7 urgencias
> 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

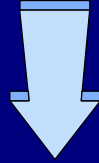
```
graph TD; A[Diarrea aguda] --> B[Bacteriana 10-20%]; A --> C[Viral 80-90%];
```

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

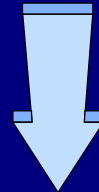
Viral 80-90%
Rotavirus (6m-4 años)
Vacunación Rotavirus
(Rotaris/RotaTed 2006)
Norovirus
Adenovirus, Astrovirus
Calicivirus,

Guarino A, JPGN 2014;59:132-52

***Mayoría de los casos
diarrea Aguda Viral***



Autolimitada



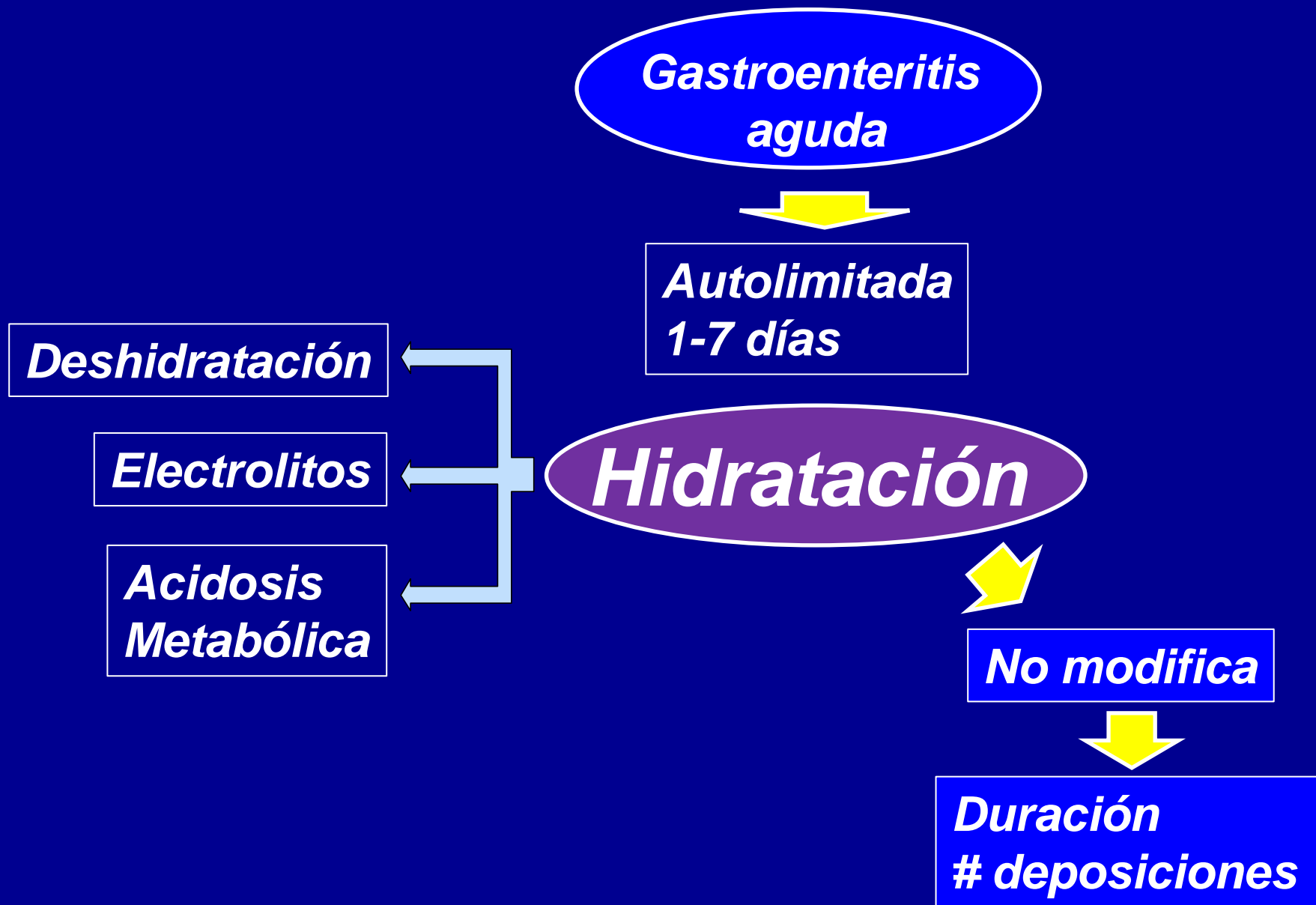
***Se podría intervenir para
Aligerar la recuperación ?***

Sufrimiento indescriptible de Muchas Personas





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



Diarrea aguda

En el pasado

Sólo hidratación
**NO Utilización
Medicamentos**

**Temor de desplazar
La hidratación**

**Poca evidencia
Sobre eficacia**



Hoy

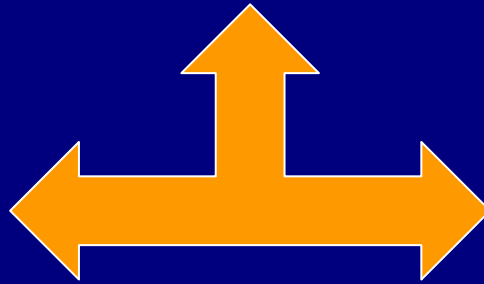
**Hidratación + Adyuvantes
Tempranamente**

*Evidencia sólida
Ensayos clínicos
Meta análisis
Guías GRADE*

Diarrea aguda

Estrategias adyuvantes

Esmectita



Probióticos



**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”

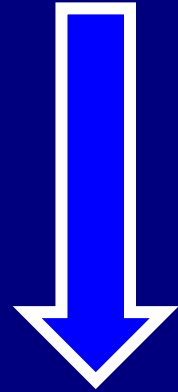
**2014, Consenso
Asociación Científica internacional
Prebióticos y probióticos”**

Probióticos



**No todos tienen la
Composición
y cantidad que
Anuncian**

Sansotta N, Curr Opin Pediatr 2019;31:661-9



**Evidencia
Su Utilidad
Contradictoria**



Probióticos

**Gèneros Màs conocidos
y estudiados**

Lactobacillus
Bifidobacterium

Jungersen M, Microorganisms 2014;2:92-100

Lactobacillus rhamnosus GG

Gram (+) Personas sanas

Aislado 1983, patentado 1985

Sherwood Gorbach, Barry Goldin

'GG'

Bifidobacterium animalis

Sub especie *lactis* BB-2

Lactobacillus rhamnosus GG

Bifidobacterium animalis lactis BB-12



**Existen beneficios
en diarrea aguda**

Probióticos

Adyuvancia en

diarrea aguda

Guías Mundiales de la Organización Mundial de Gastroenterología

Probióticos y prebióticos

Febrero de 2017



A Resource Sensitive Solution

Lactobacillus rhamnosus GG

Indicaciones	Dosis recomendada	Nivel Evidencia	Respaldo
Prevención diarrea asociada a antibióticos	1- 2 X10¹⁰ UFC	1	Szajewska H. Systematic review with meta-analysis Aliment Pharmacol Ther. 2015;42:1149–57. Szajewska H, J Pediatr Gastroenterol Nutr. 2016 ;62:495–506.
Prevención Diarrea nosocomial	10¹⁰-10¹¹ UFC dos veces al día	1	Szajewska H. Systematic review with meta-analysis Aliment Pharmacol Ther. 2015;42:1149–57.
Gastroenteritis aguda	≥ 10¹⁰ UFC/día 5–7 días	1	ESPGHAN Working Group for Probiotics and Prebiotics. J Pediatr Gastroenterol Nutr. 2014;58:531–9.
Infecciones en niños que asisten a guardería		1	Liu S, Meta-analysis. Indian Pediatr. 2013;50:377–81. Hojsak I, ECC Clin Nutr Edinb Scotl. 2010;29:312–6.

Use of Probiotics for Management of Acute Gastroenteritis: A Position Paper by the ESPGHAN Working Group for Probiotics and Prebiotics

**Hania Szajewska, †Alfredo Guarino, ‡Iva Hojsak, §Flavia Indrio, ‡Sanja Kolacek, ||Raanan Shamir, ¶Yvan Vandenplas, and #Zvi Weizman, on Behalf of the ESPGHAN Working Group for Probiotics and Prebiotics*

Recommendation. The use of *Lactobacillus* GG may be considered in the management of children with AGE as an adjunct to rehydration therapy.

QUALITY OF EVIDENCE: Low

RECOMMENDATION: Strong recommendation



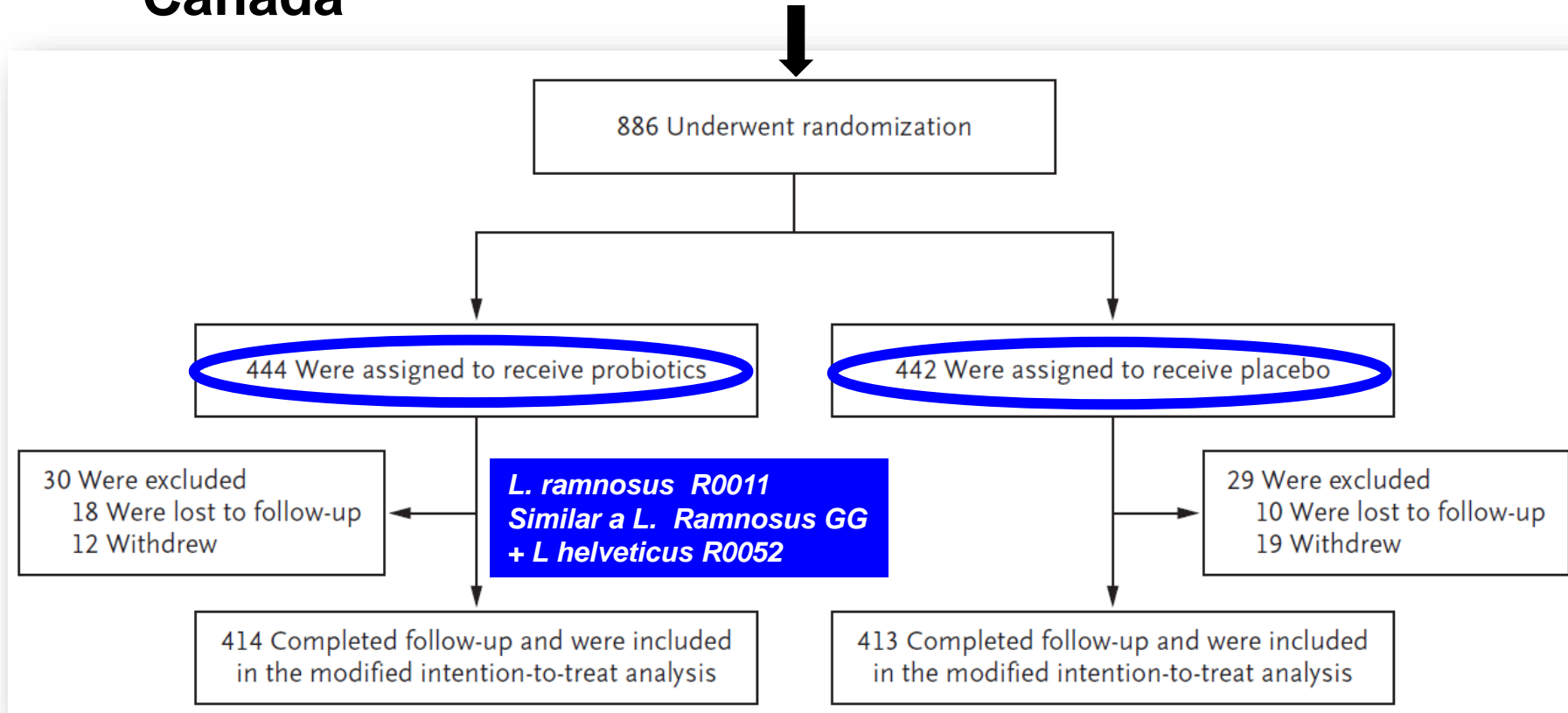
JPGN 2014;58: 531–539

Ensayos clínicos De impacto

Multicenter Trial of a Combination Probiotic for Children with Gastroenteritis

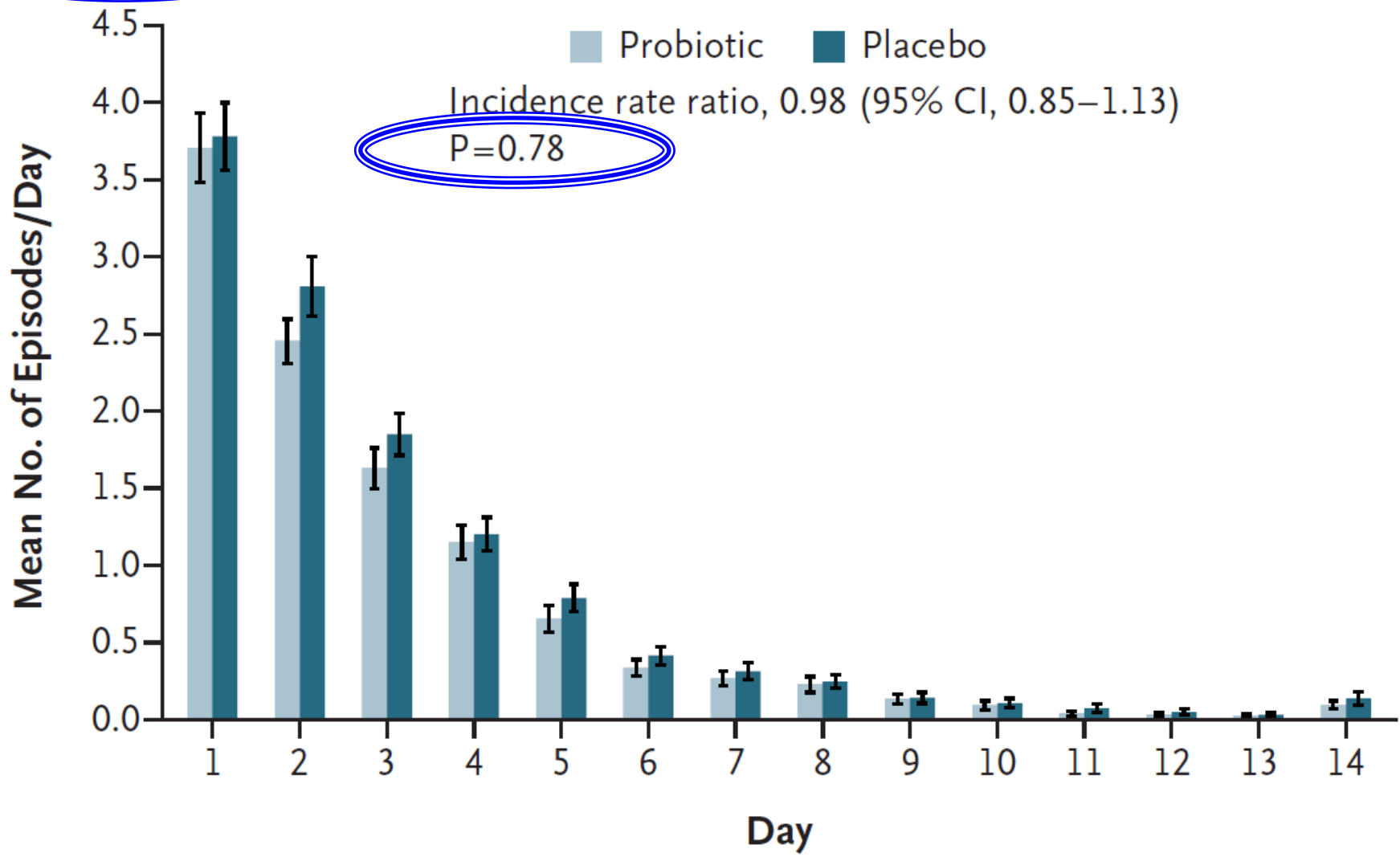
Stephen B. Freedman, M.D.C.M., Sarah Williamson-Urquhart, B.Sc.Kin.,
Ken J. Farion, M.D., Serge Gouin, M.D.C.M., Andrew R. Willan, Ph.D.,
Naveen Poonai, M.D., Katrina Hurley, M.D., Philip M. Sherman, M.D.,
Yaron Finkelstein, M.D., Bonita E. Lee, M.D., Xiao-Li Pang, Ph.D., Linda Chui, Ph.D.,
David Schnadower, 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

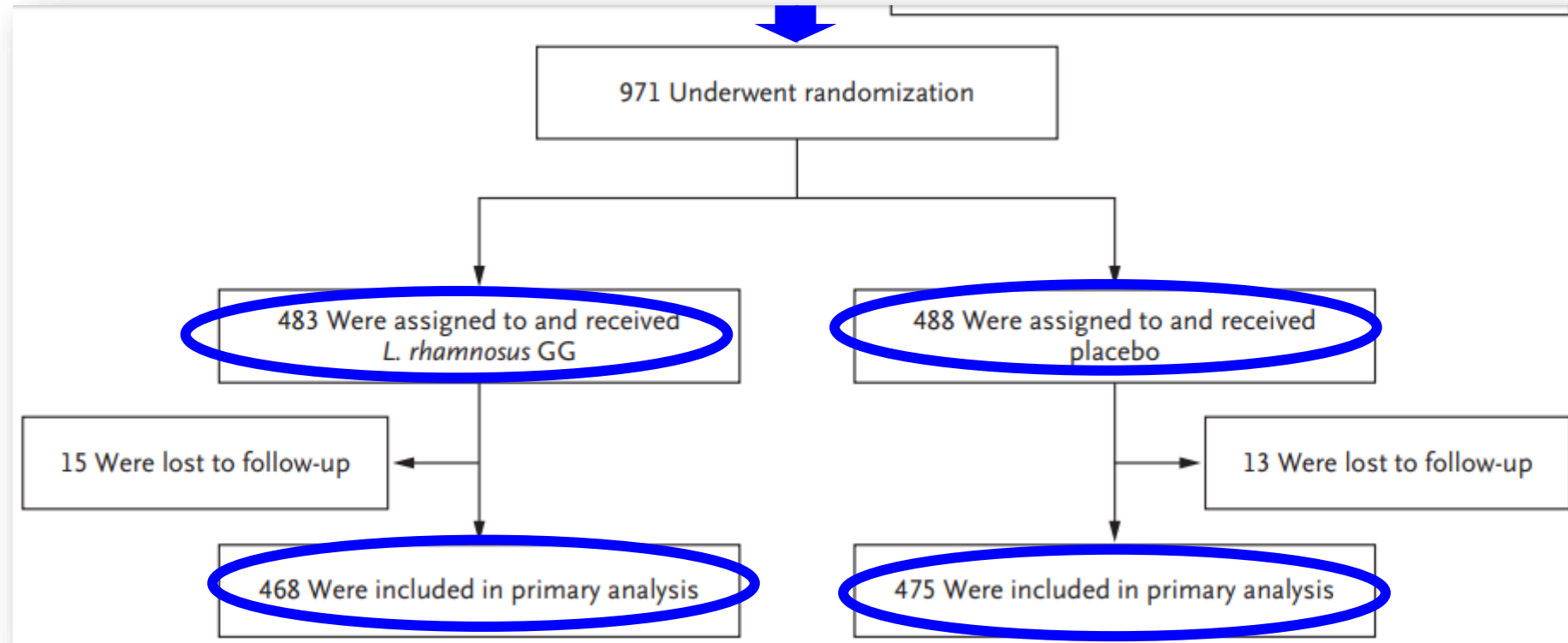
ORIGINAL ARTICLE

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.,
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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

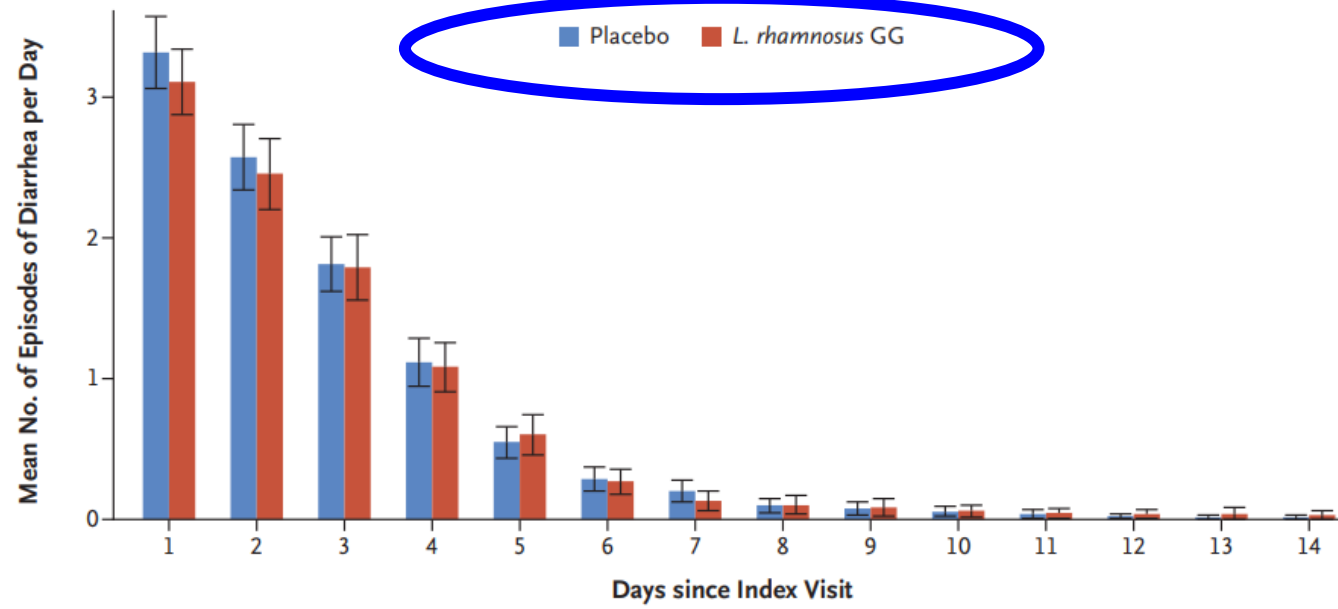
Schnasower D, N Engl J Med 2018;379:2002-14

USA

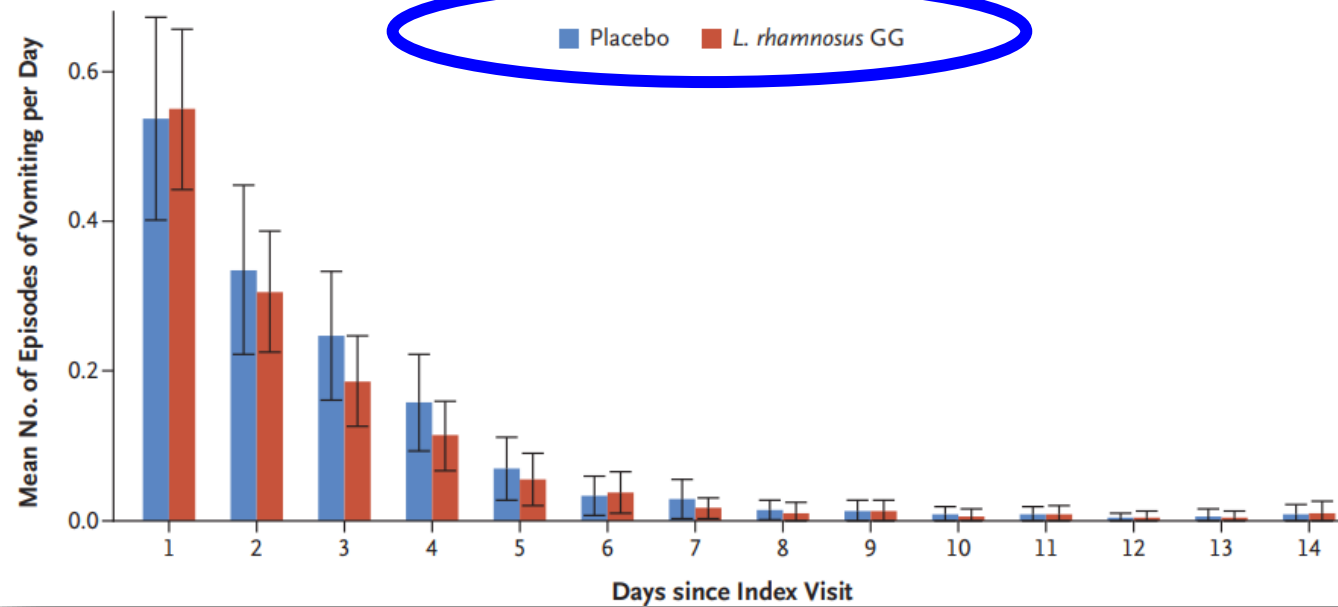


Schnadower D, N Engl J Med 2018;379:2002-14


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

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.

ORIGINAL ARTICLE

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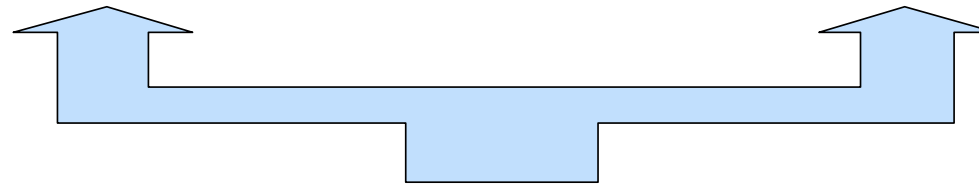
Freedman SB, N Engl J Med 2018;379:2015-26.

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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**

UpToDate®

Contenidos ▾ Calculadoras Interacciones de fármacos UpToDate Pathways

< Atrás

Approach to diarrhea in children in resource-rich countries

Author: [Gary R Fleisher, MD](#)
Section Editors: [Stephen J Teach, MD, MPH](#), [Teresa K Duryea, MD](#)
Deputy Editor: [James F Wiley, II, MD, MPH](#)

[Contributor Disclosures](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.
Literature review current through: **Jul 2021**. | This topic last updated: **Aug 05, 2021**.

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< Atrás

Approach to the child with acute diarrhea in resource-limited countries

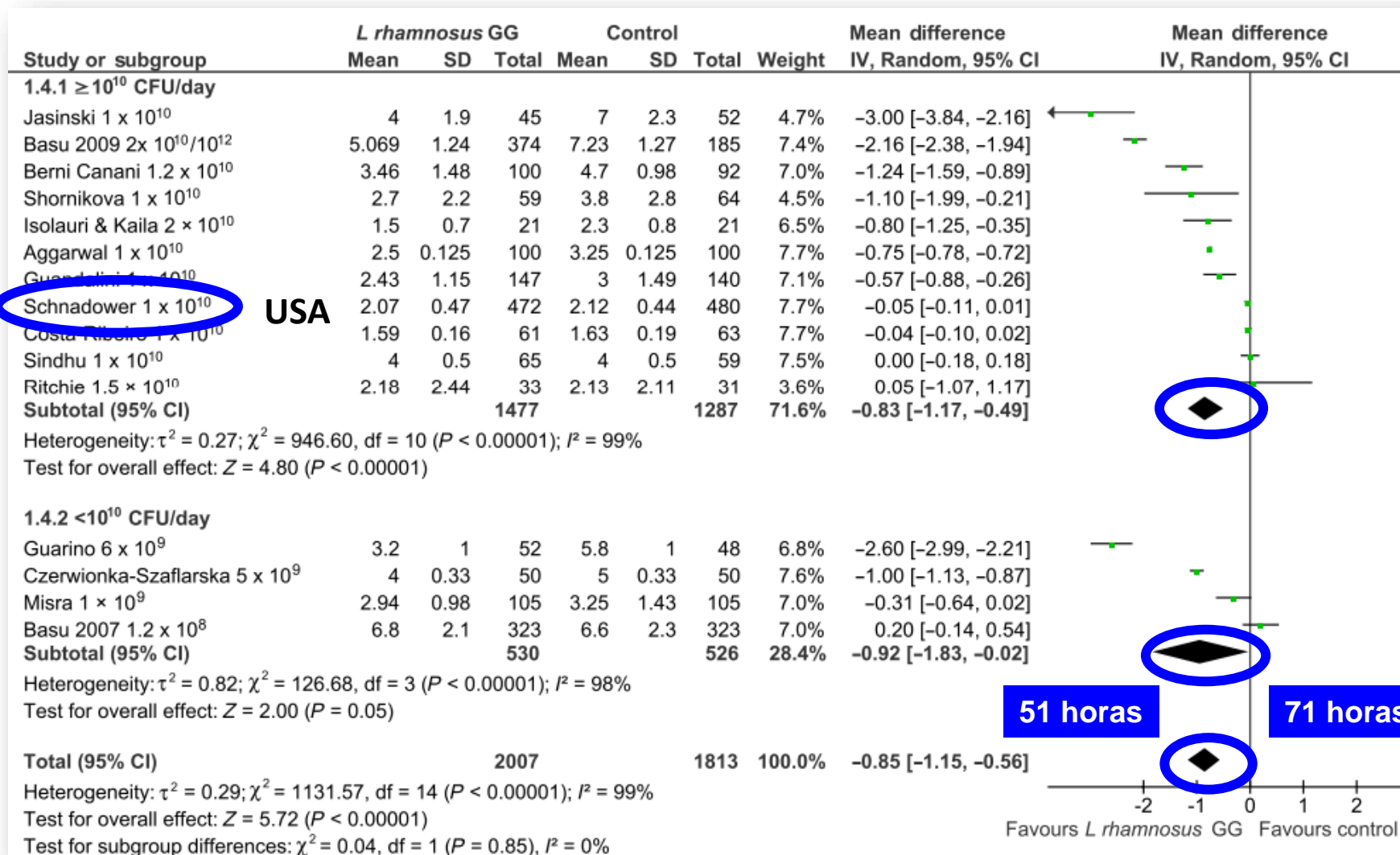
Authors: [Jason B Harris, MD, MPH](#), [Mark Pietroni, MA, FRCP, FFPH, DTM&H](#)
Section Editors: [Stephen B Calderwood, MD](#), [Morven S Edwards, MD](#)
Deputy Editor: [Allyson Bloom, MD](#)

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

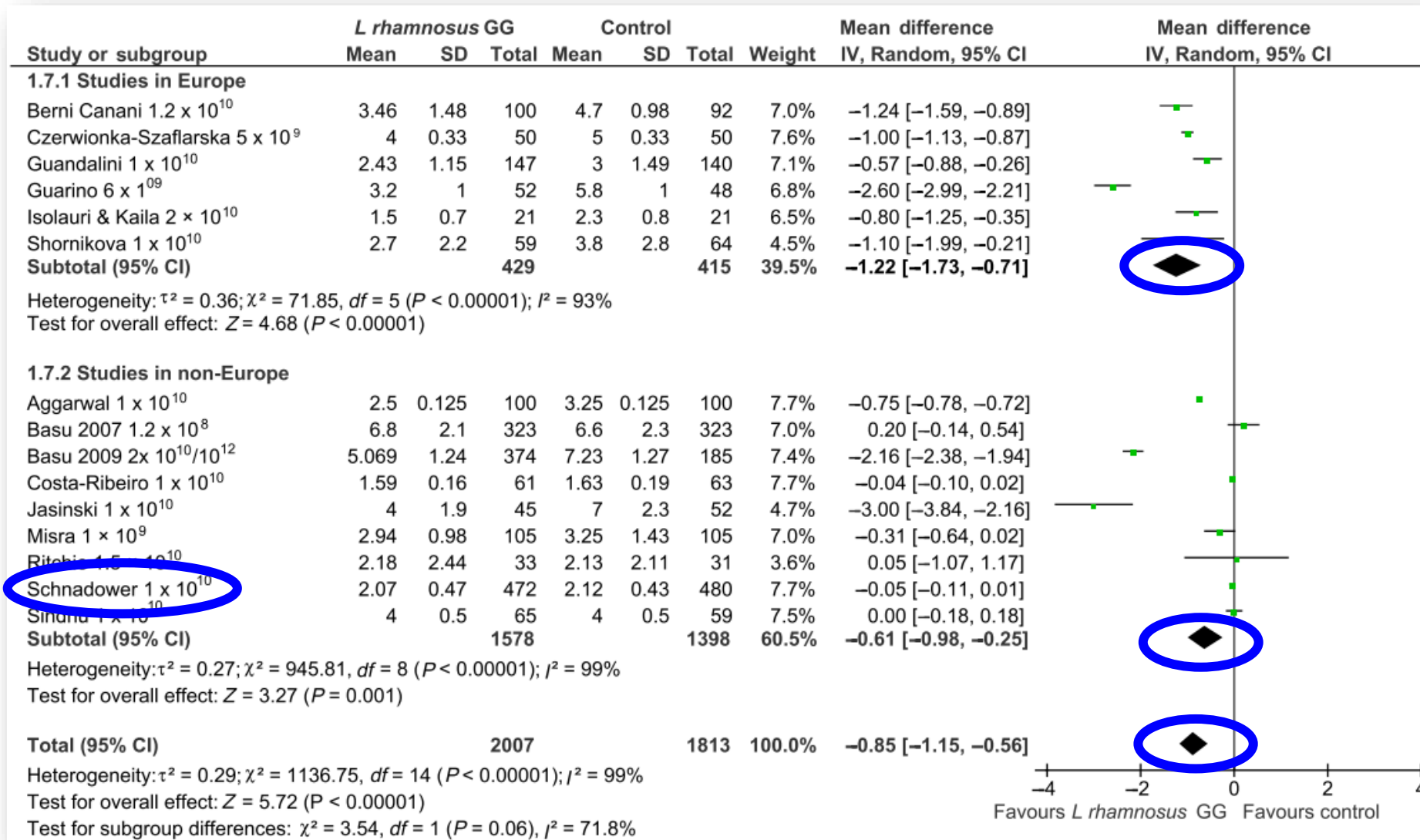
Hania Szajewska¹  | Maciej Kołodziej¹  | Dorota Gieruszczak-Białek¹ |
Agata Skórka¹  | Marek Ruszczyński¹ | Raanan Shamir²

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

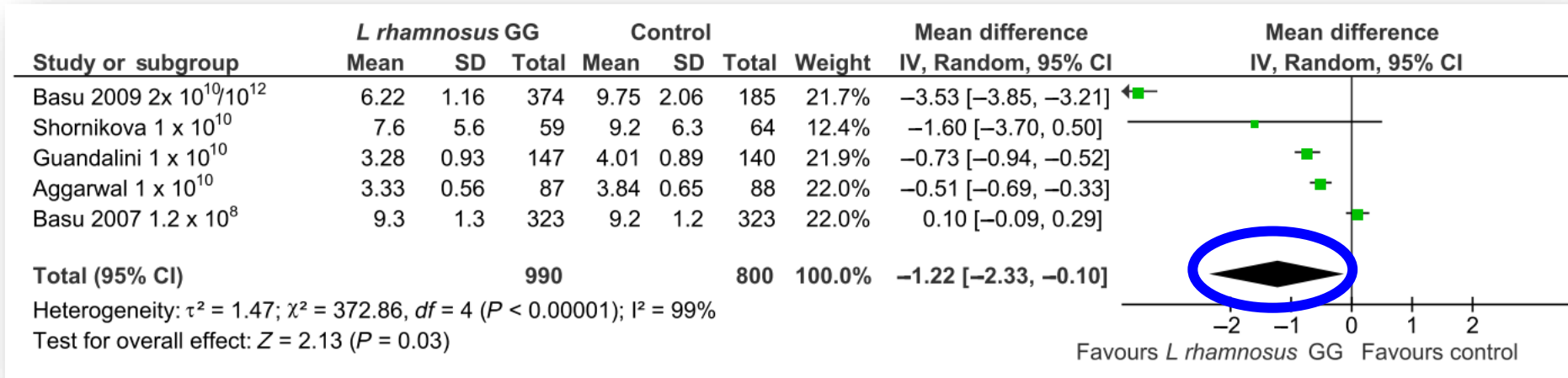
Control de gastroenteritis aguda: Altas dosis $\geq 1.4 \times 10^9$ UFC o Bajas dosis versus Placebo



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)

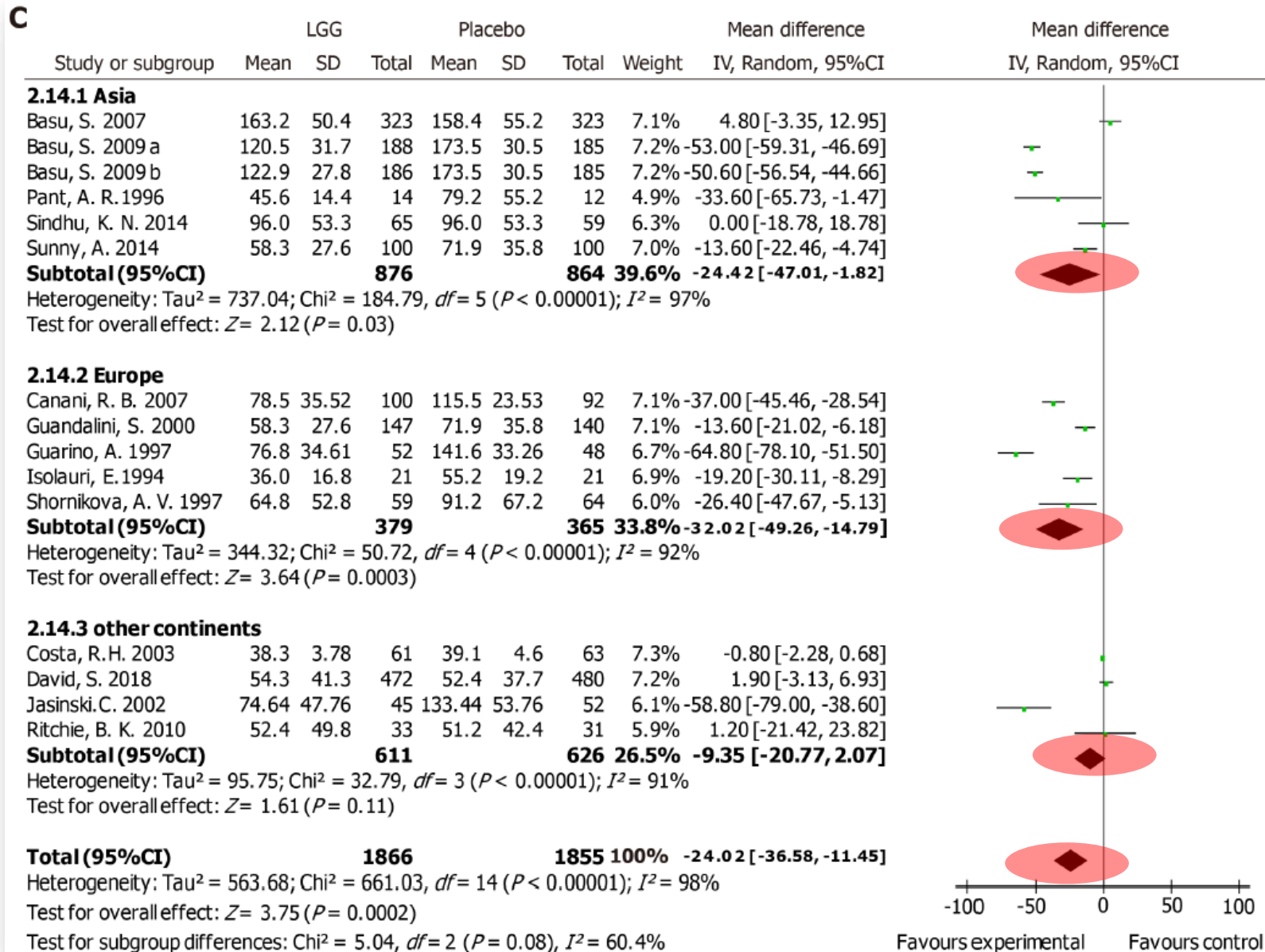
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

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

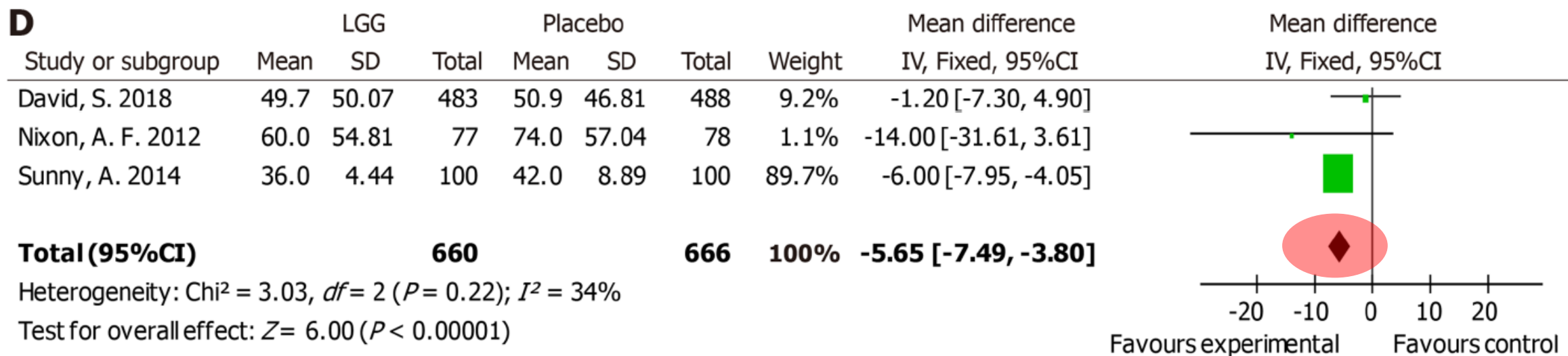
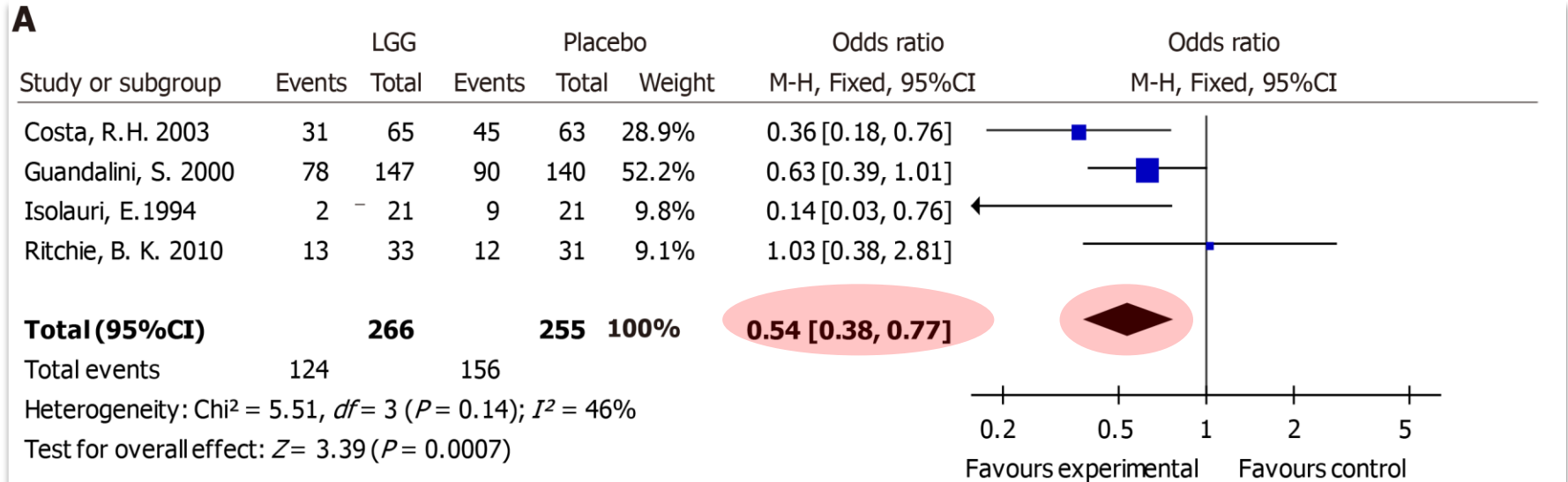


Figure 4 *Lactobacillus GG* vs control with regard to stool number and consistency. A: The average stool number per day (high dose and low dose); B: S frequency on day 2; C: Stool frequency on day 3; D: The mean time to improvement in stool consistency. LGG: *Lactobacillus rhamnosus GG*; CI: Confidence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

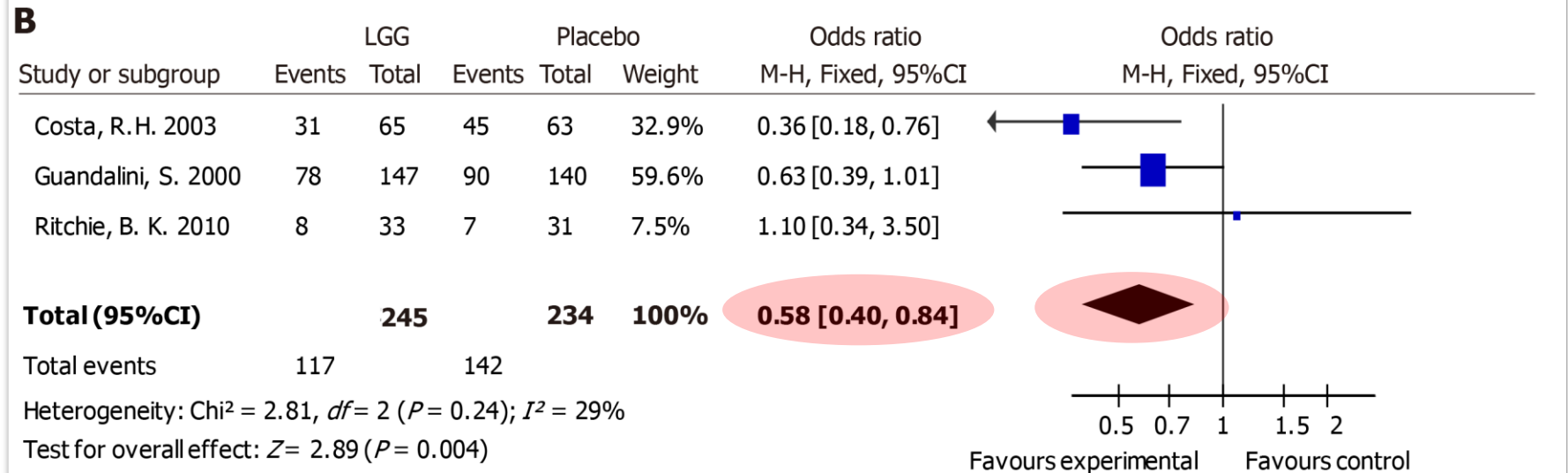
Li YT, World J Gastroenterol 2019; 25: 4999-5016

Lactobacillus GG vs Control

Diarrea > 3 días



Diarrea > 4 días



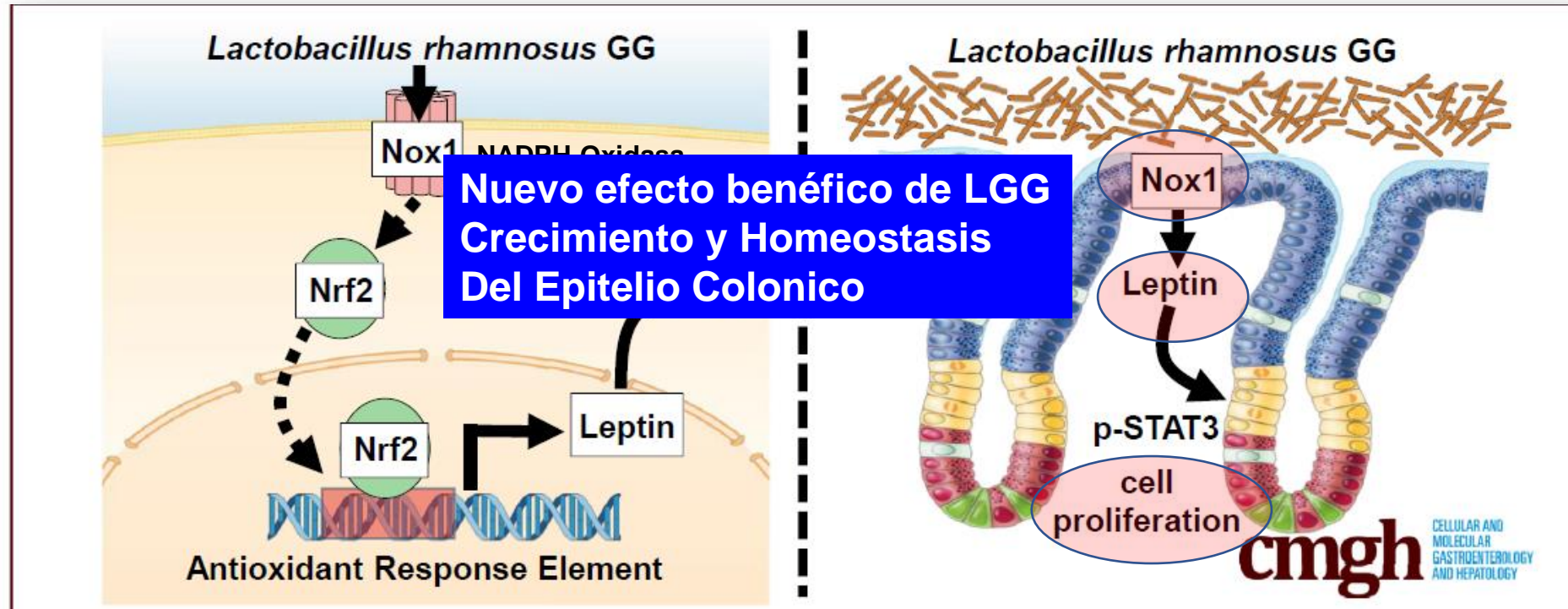
Efectos recientemente Identificados de LGG

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



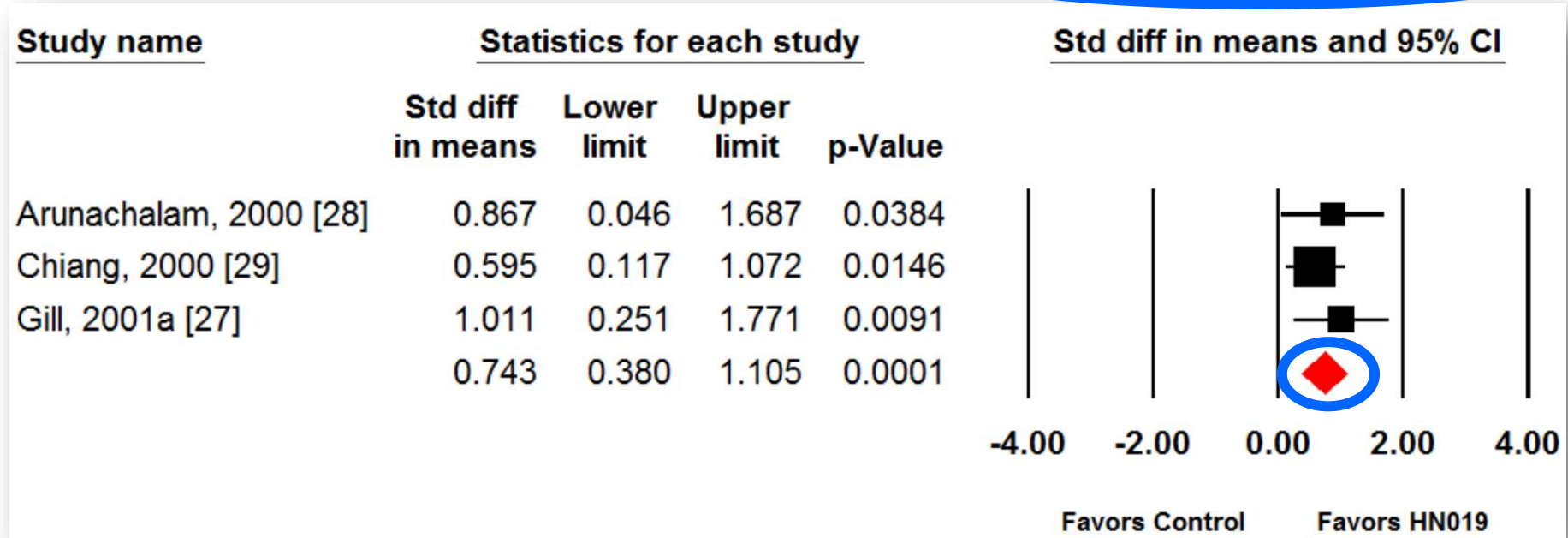
Bifidobacterium animalis (BB-12)
Múltiples investigaciones

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

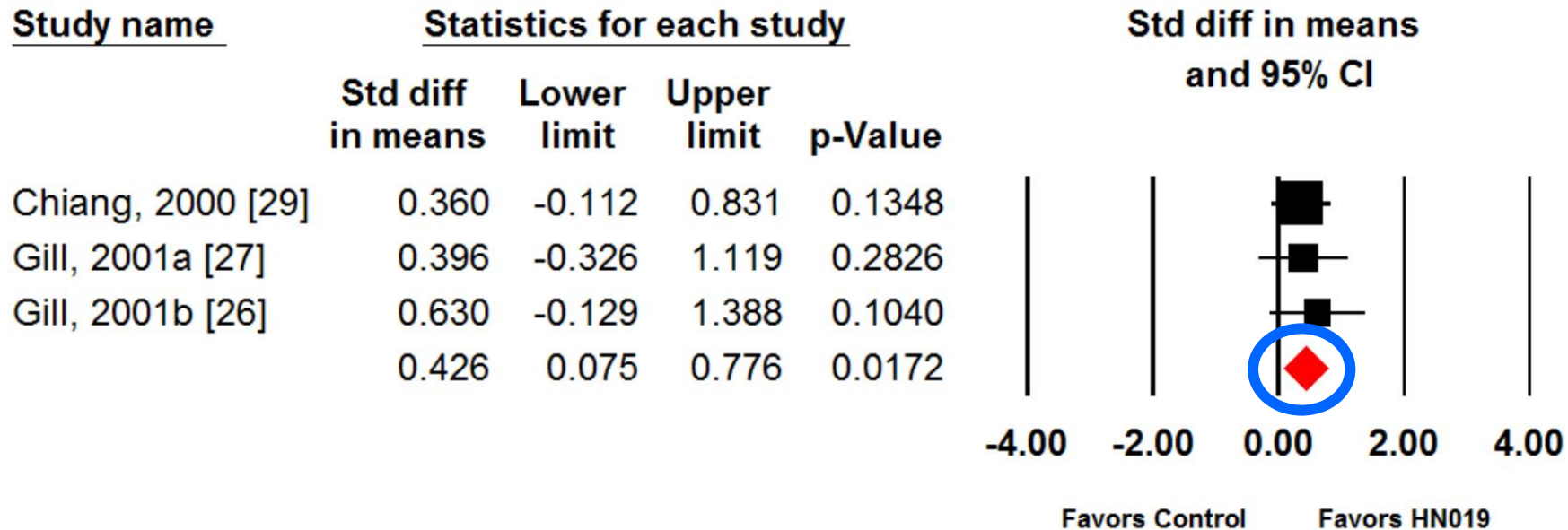
Capacidad fagocítica de PMN



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



LGG +






Bifidobacterium animalis (BB-12)

>300 publicaciones,

>130 estudios clínicos

Jungersen M, Microorganisms 2014;2:92-100

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 ^a, Sinéad O'Ferrall ^a, Łukasz Krych^a, Elaine O'Mahony^a, Hanifa Namusoke^b, Betty Lanyero ^b, Witold Kot^c, Nicolette Nabukeera-Barungi ^d, Kim Fleischer Michaelsen^e, Christian Mølgaard^e, Henrik Friis ^e, Benedikte Grenov^{e*}, and Dennis S. Nielsen^{a*}

Investigadores Daneses

Desnutrición

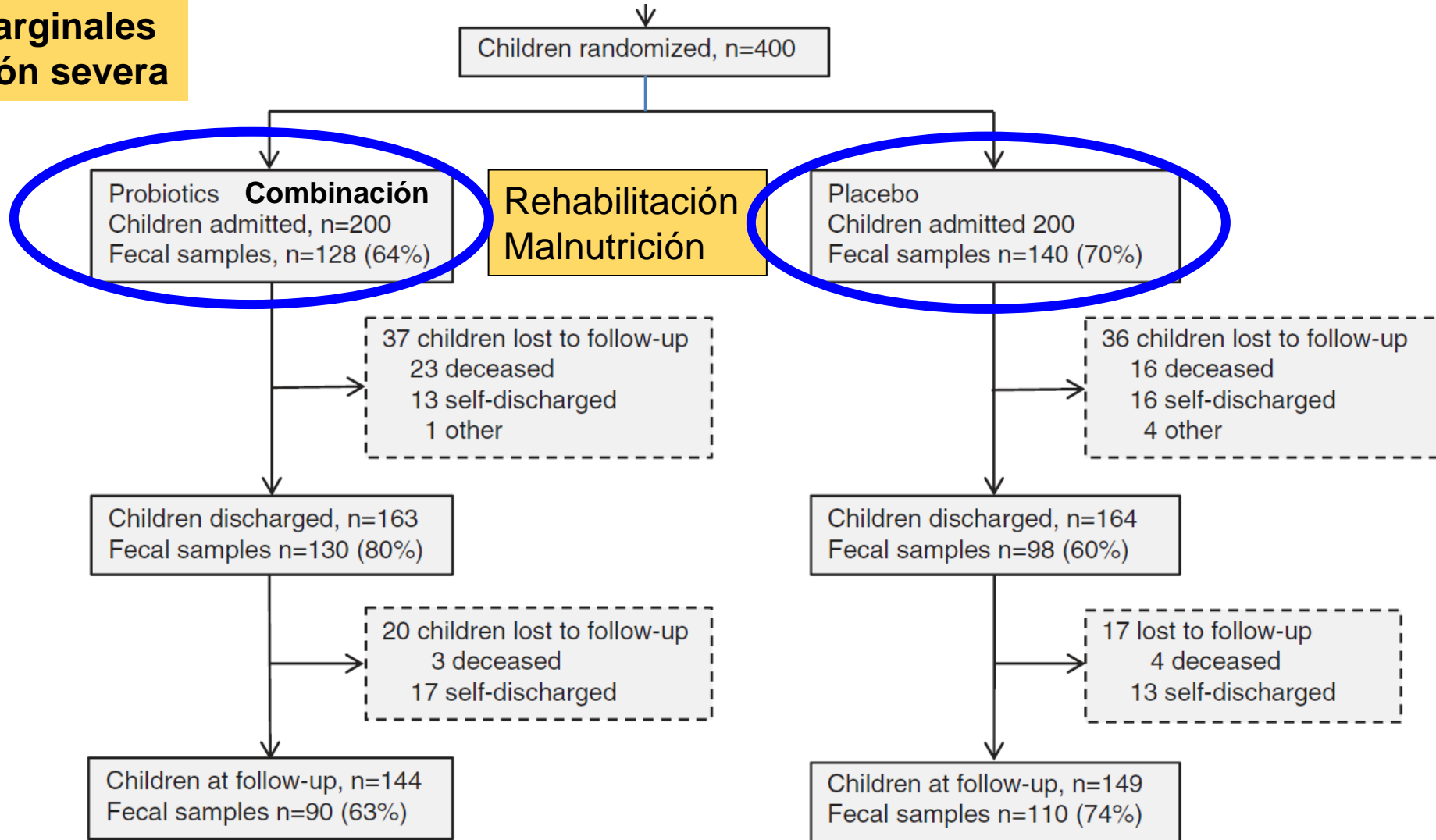
**Globalmente
45% muertes**

**Secuelas
Intelectuales
Productividad**

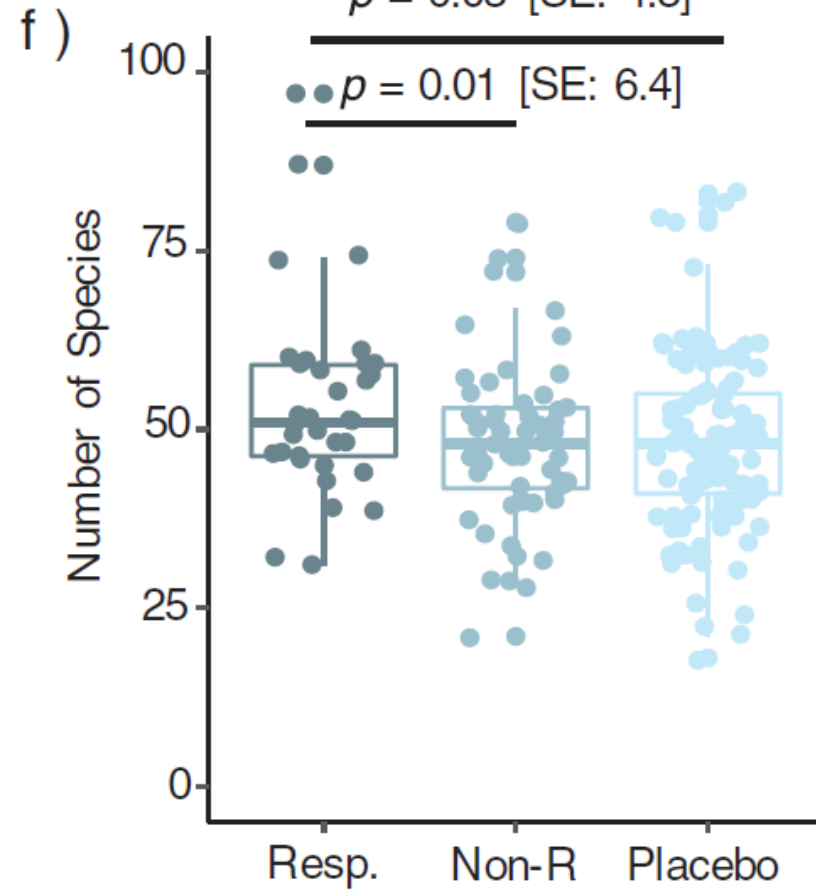
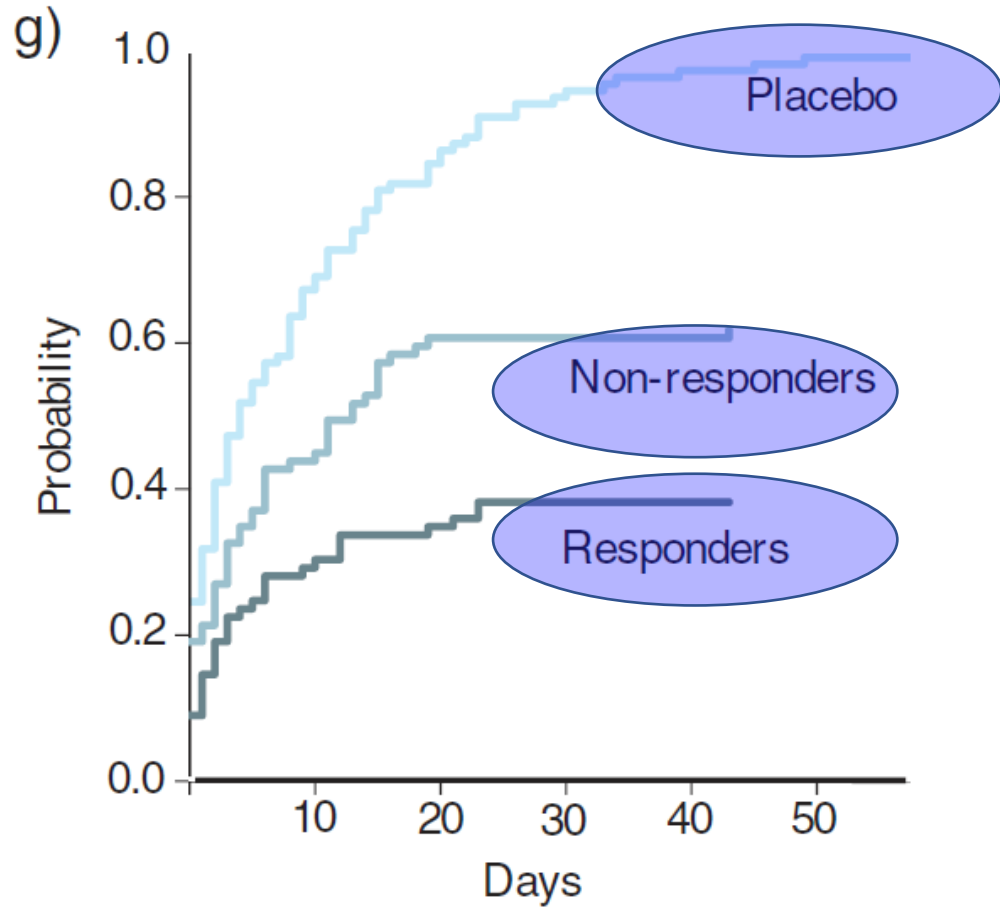
**Disbiosis: Desencadenar o
Mantener desnutrición aguda
Disminuye diversidad microbiota**

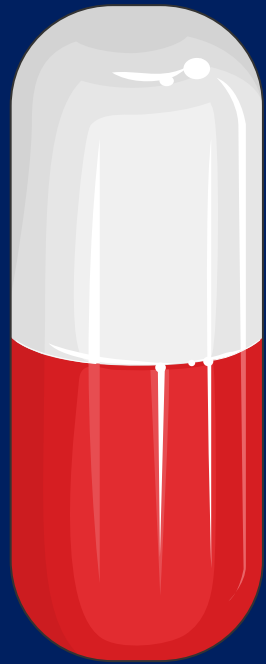


**Barrios marginales
Malnutrición severa**



Redujo la incidencia acumulativa de diarrea en el futuro





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

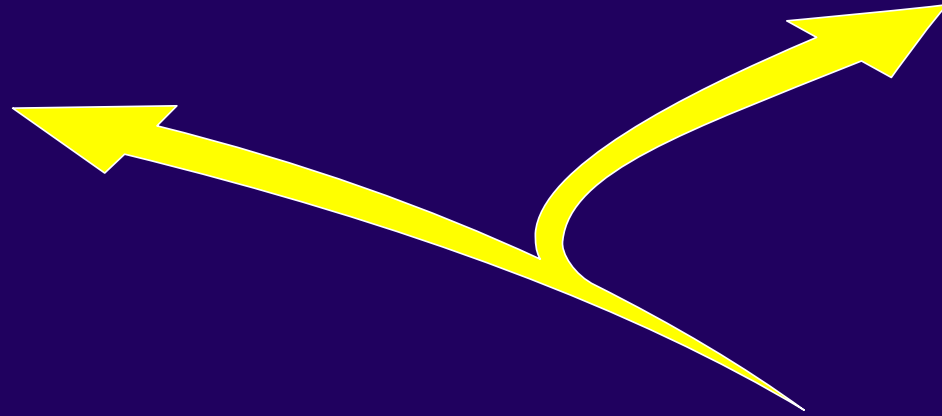
Dosis recomendada: 1×10^9

1 cápsula diaria durante antibióticos 2h antes

LGG probiótico más estudiado en EDA mundo

Probiótico mayor Adherencia /resistencia en el intestino

El BB12 más estudiado Fortalecer sistema inmune



Sinergismo



➤ Desplazamiento Patógenos

BIOTIPLUS



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%

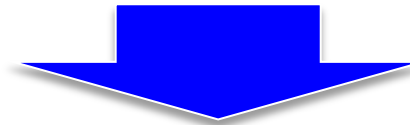
PHARMACOLOGY

“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”



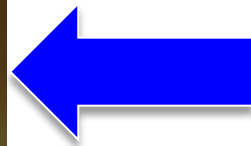
Pueden dar alergias

Diosmectita

Diosmectita = medicamento



Diosmectita = medicamento

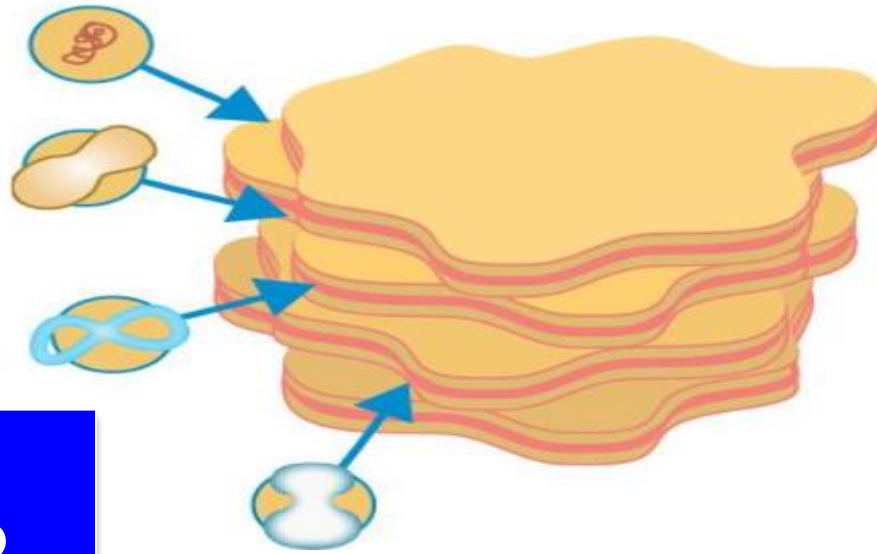


Diosmectita
purificada

Nov 1975

Diosmectita

**Adsorbe
Toxinas**



**Arcilla natural
Hojas finas de silicato
de Aluminio y magnesio**

**Fortalece la capa de moco
Destruída por patógenos**

**Impide llegada de toxinas
Células intestinales**

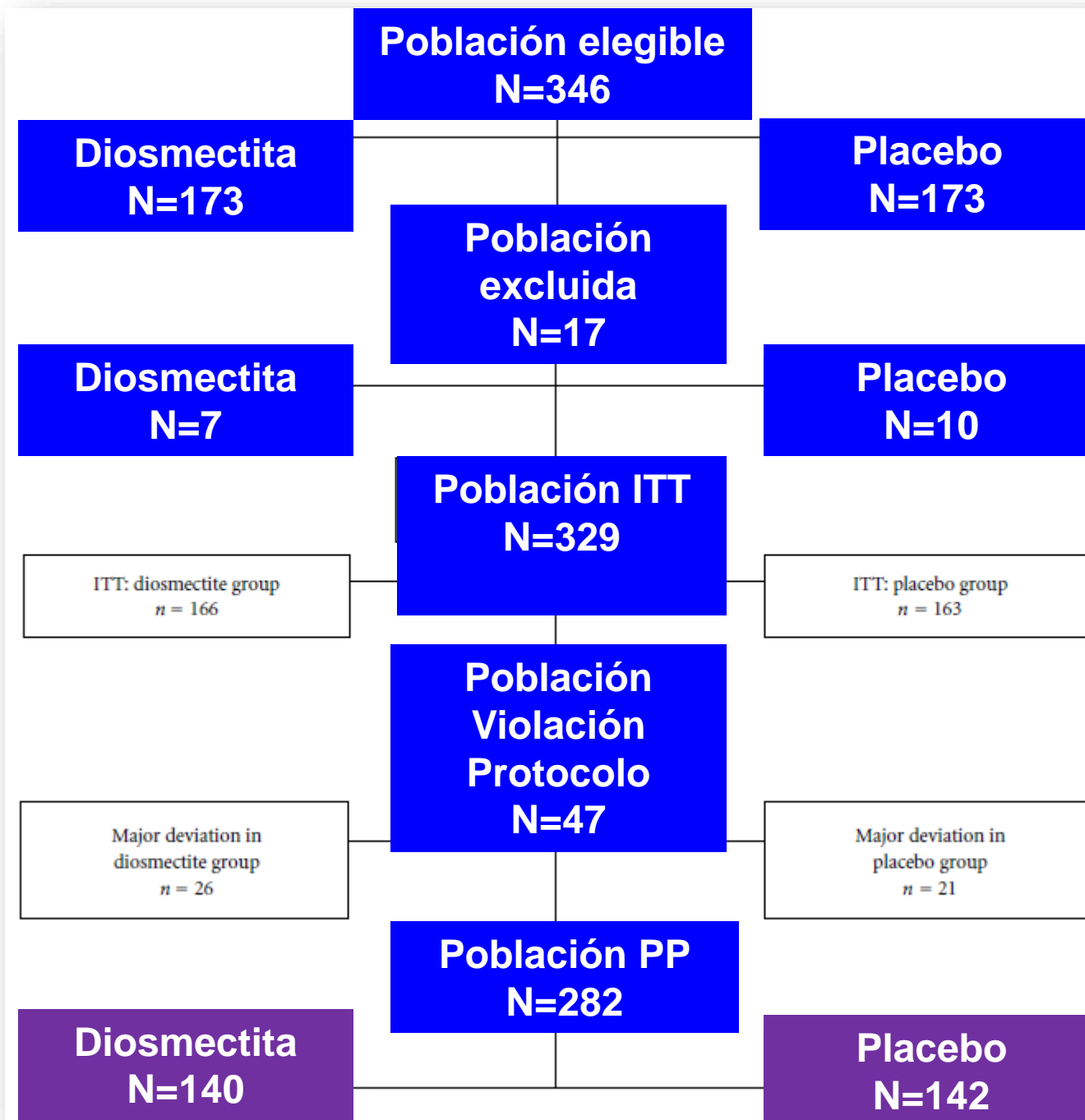


**Evita el estímulo para
Secreción H2O electrólitos**

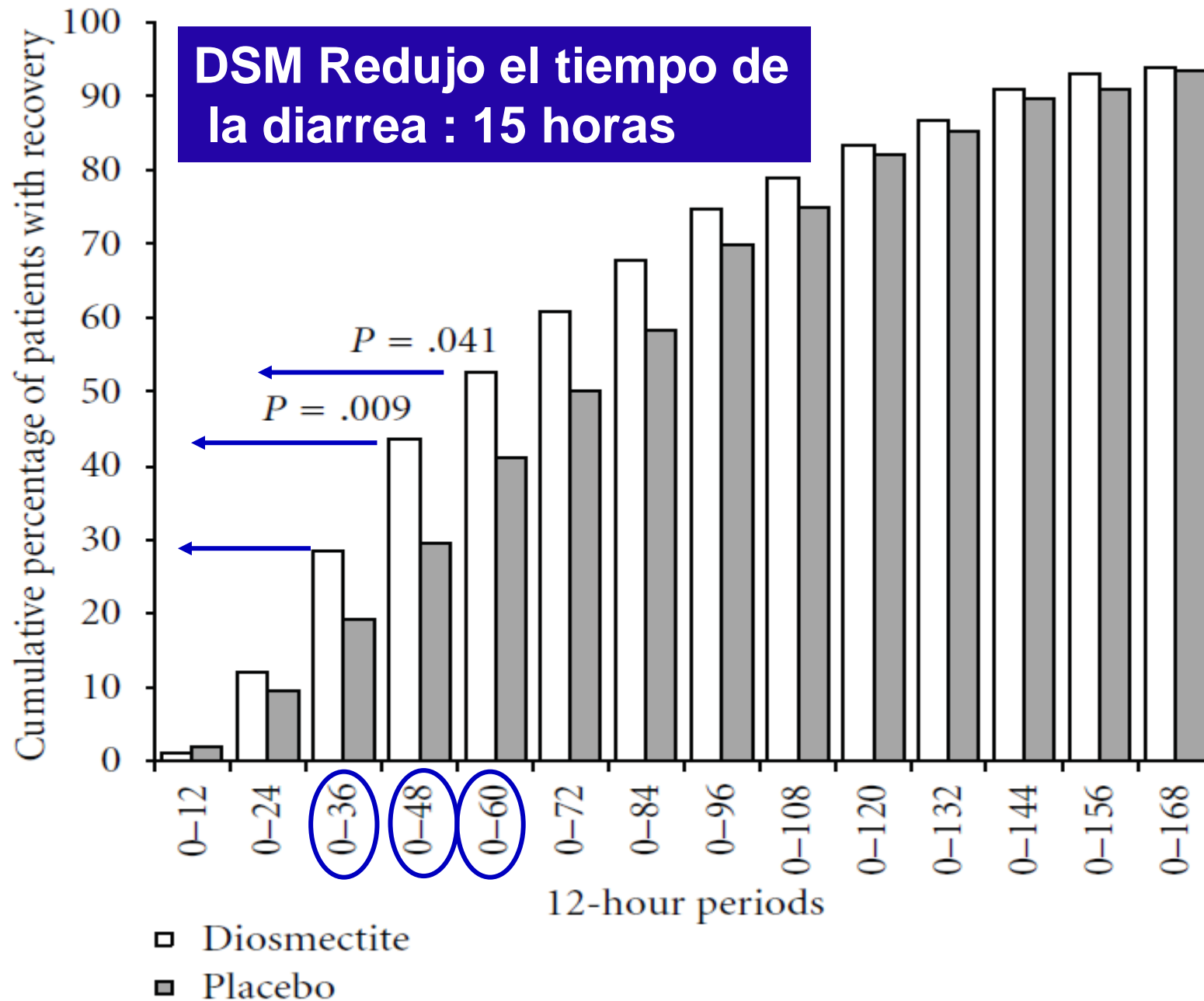
Research Article

Efficacy of Diosmectite (Smecta)[®] in the Treatment of Acute Watery Diarrhoea in Adults: A Multicentre, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study

Khediri F, Gastroenterol Res Pract 2011;ART ID 783196



% pacientes
Con recuperación



Oral Diosmectite Reduces Stool Output and Diarrhea Duration in Children With Acute Watery Diarrhea

CHRISTOPHE DUPONT,* JIMMY LEE KOK FOO,† PHILIPPE GARNIER,§ NICHOLAS MOORE,||
HÈLÈNE MATHIEX-FORTUNET,§ and EDUARDO SALAZAR-LINDO,¶ for the PERU AND MALAYSIA DIOSMECTITE
STUDY GROUPS

**Paris Descartes University, Cochin Saint-Vincent de Paul Hospital, Paris, France; †Kuala Terengganu Hospital, Kuala Terengganu, Malaysia; §Ipsen, Medical Department, Boulogne-Billancourt, Paris, France; ||INSERM U657, Bordeaux University & Hospital, Bordeaux, France; and ¶DS Consult, Surco, Lima, Peru*

Malasia	N (niños)	Perù
302		300

Intervenció: Hidratació oral + Placebo O Diosmectita

6 gr/dia: 1-12 meses: 3 días

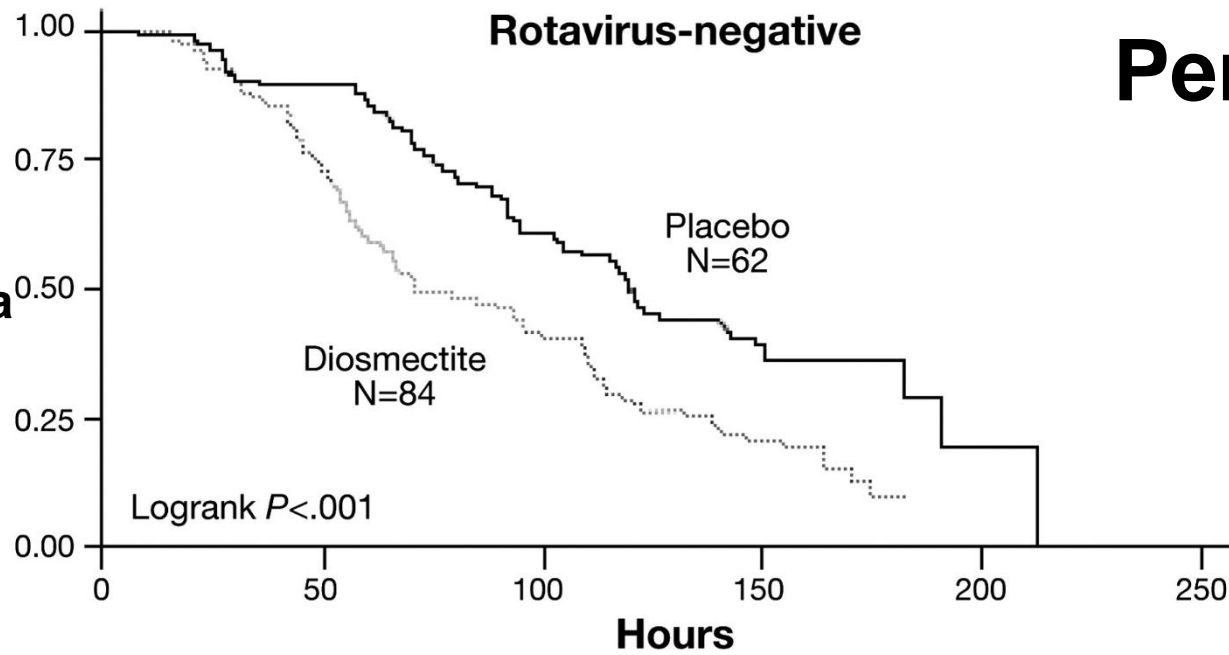
12 gr/dia: 12-36 meses: 3 días

Mitad de la dosis hasta la recuperación

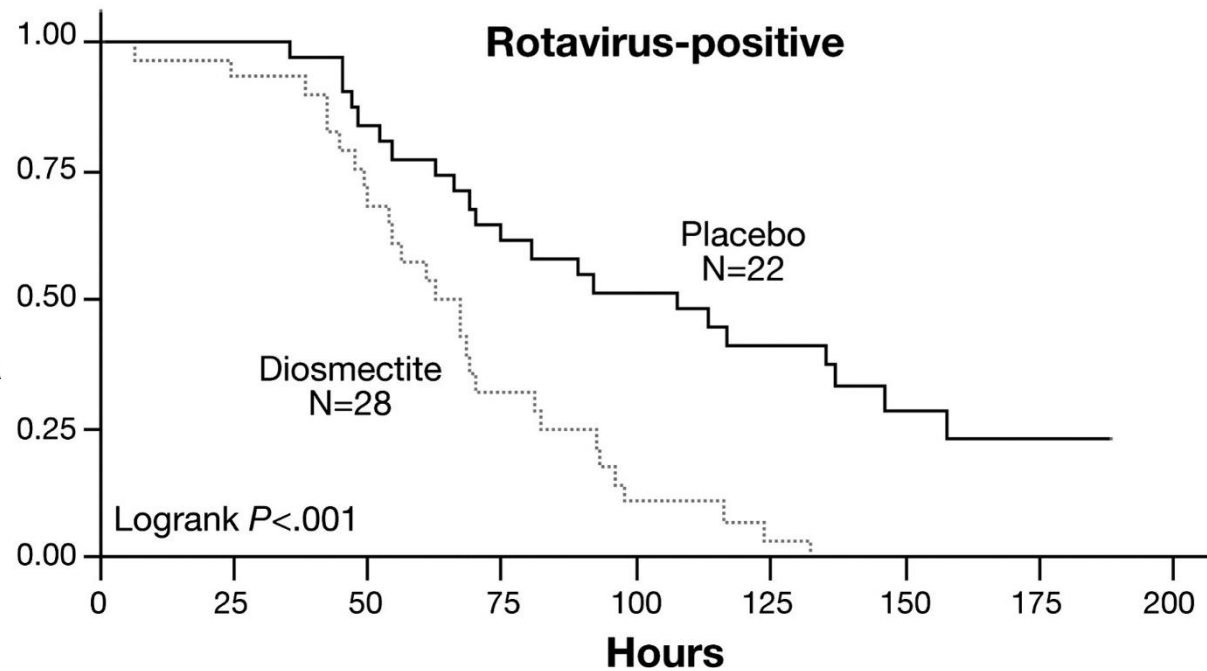
Clin Gastroenterol Hepatol 2009;7:456–462

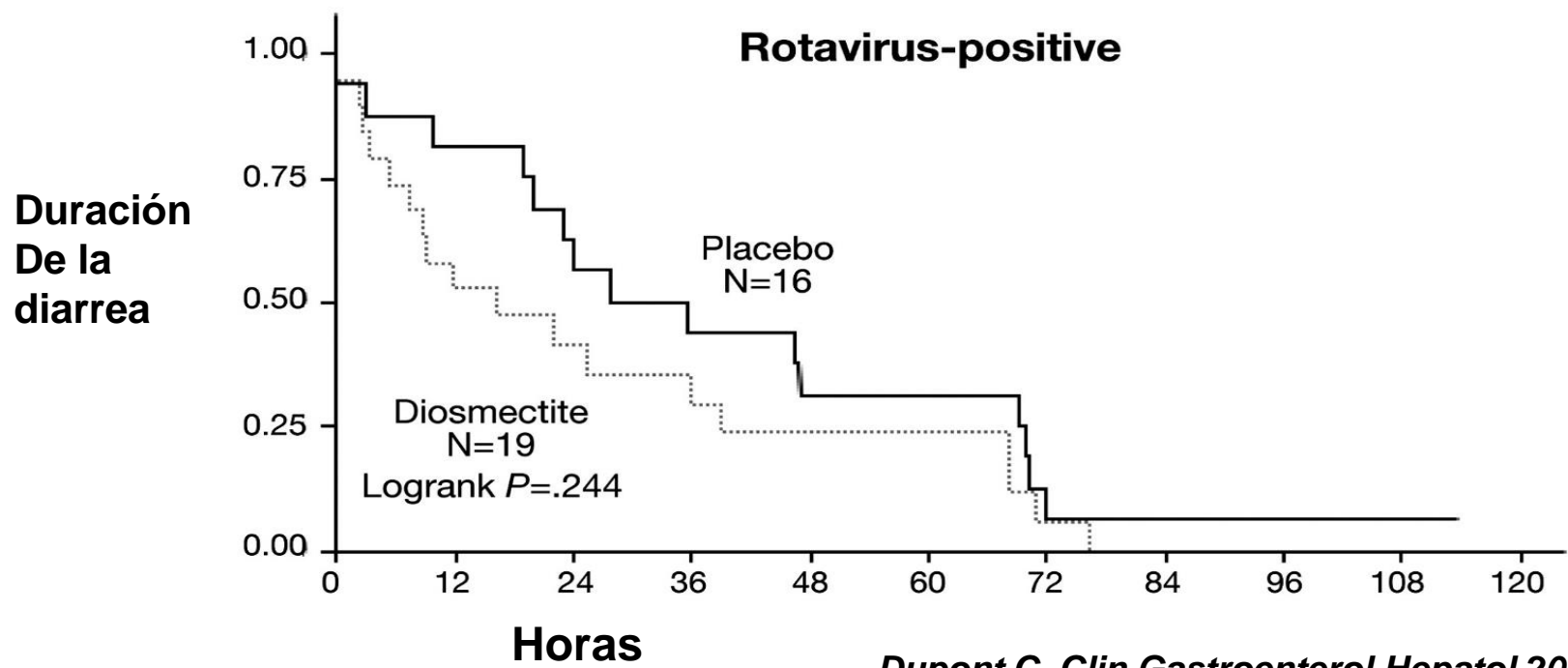
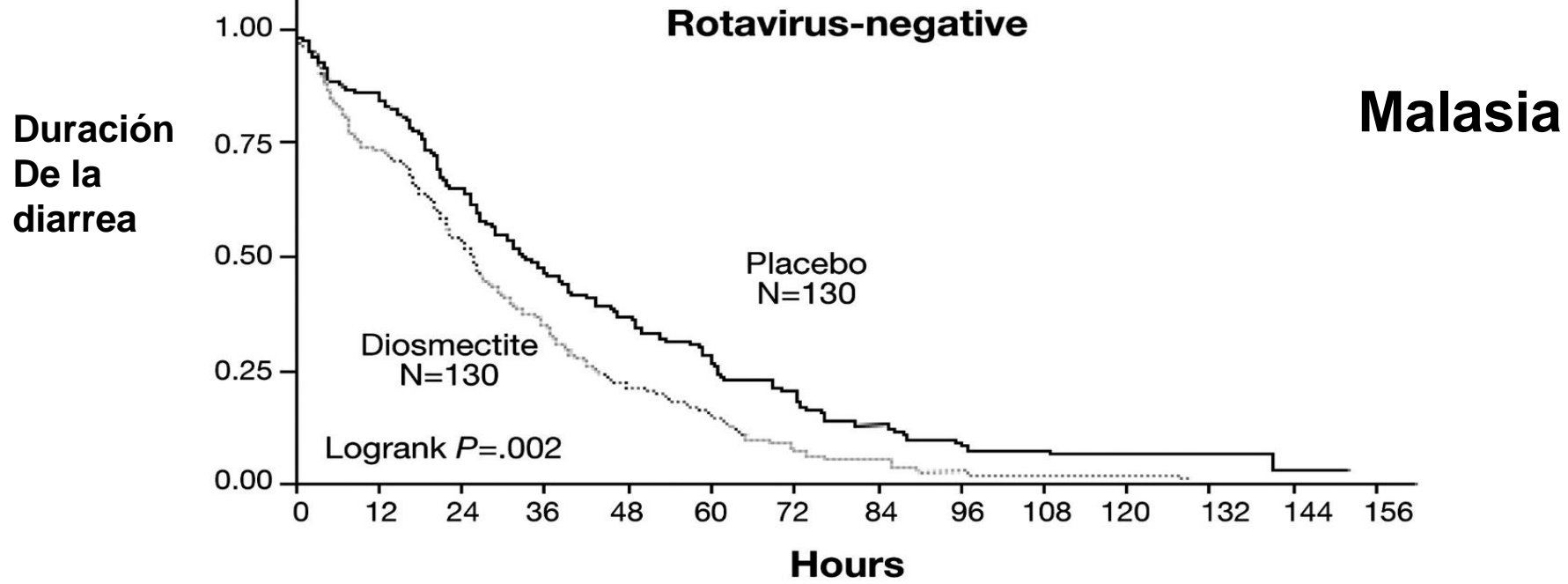
Perú

**Duración
De la diarrea**



**Duración
De la diarrea**





Diosmectita en Niños

Meta-anàlisis, 5 ECC

**Acortamiento
De la diarrea**

27.2 horas

Cura al día 3

OR 1.62 (IC95% 1.36-1.98)

NNT

4

Szajewska H Aliment Pharmacol Ther 2006; 23: 217-227



Cochrane
Library

Cochrane Database of Systematic Reviews

2018

Smectite for acute infectious diarrhoea in children (Review)

Pérez-Gaxiola G, Cuello-García CA, Florez ID, Pérez-Pico VM.

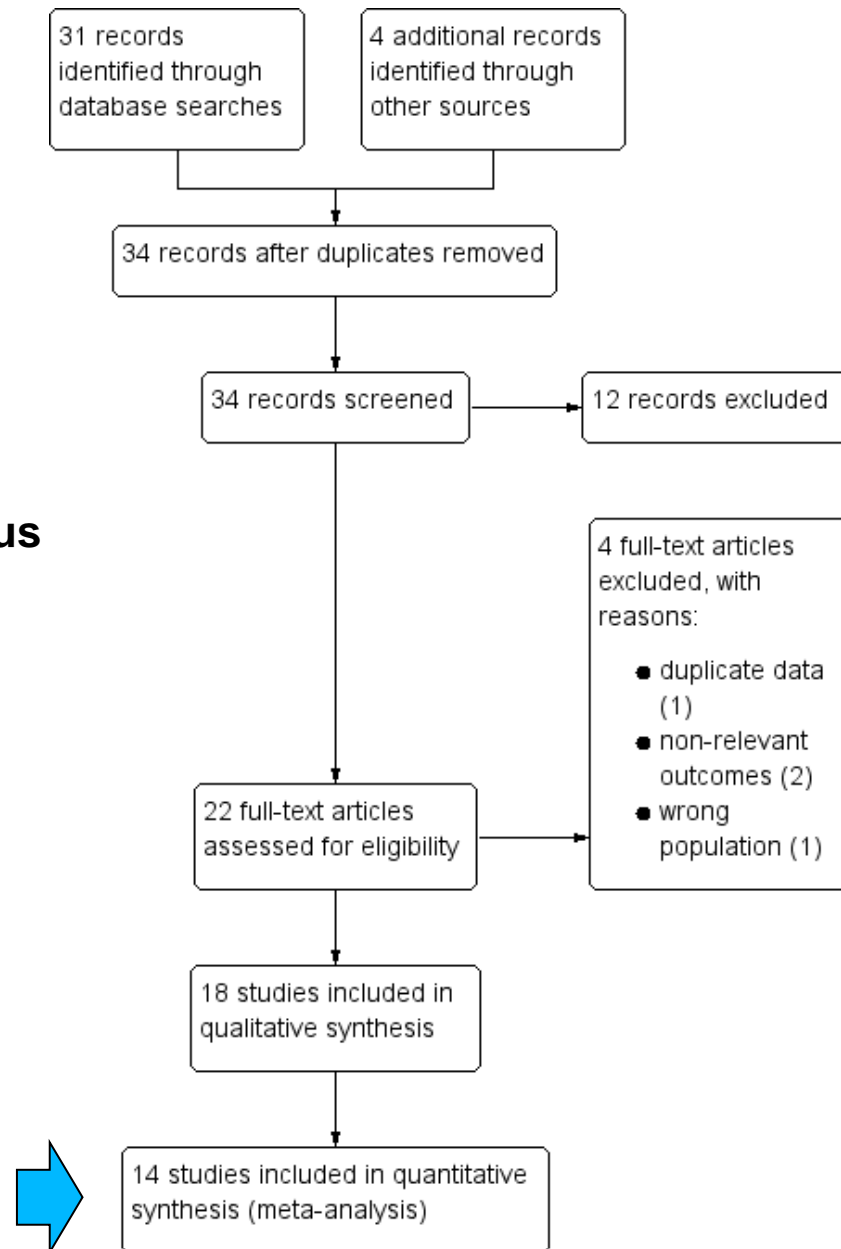
Smectite for acute infectious diarrhoea in children.

Cochrane Database of Systematic Reviews 2018, Issue 4. Art. No.: CD011526.

DOI: 10.1002/14651858.CD011526.pub2.

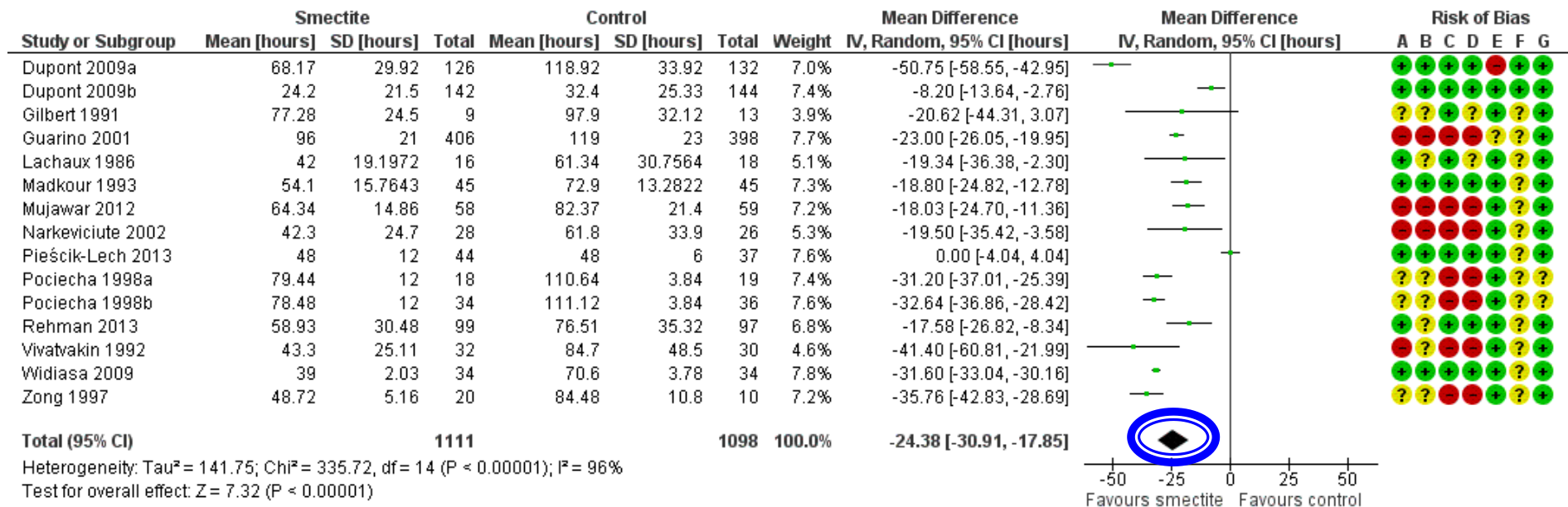
www.cochranelibrary.com

Smectite for acute infectious diarrhoea in children



Smectite for acute infectious diarrhoea in children

Duración promedio horas

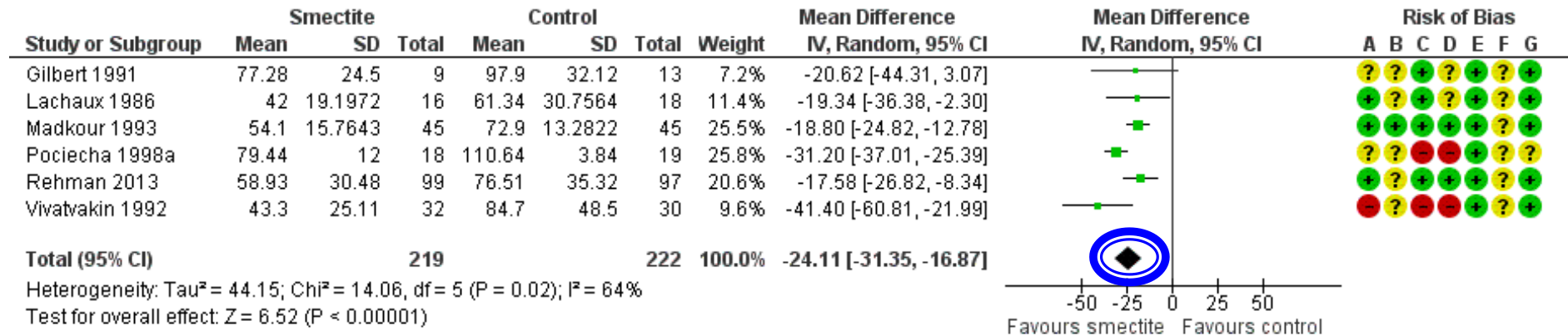


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Smectite para diarrea aguda infecciosa en niños < 2 años

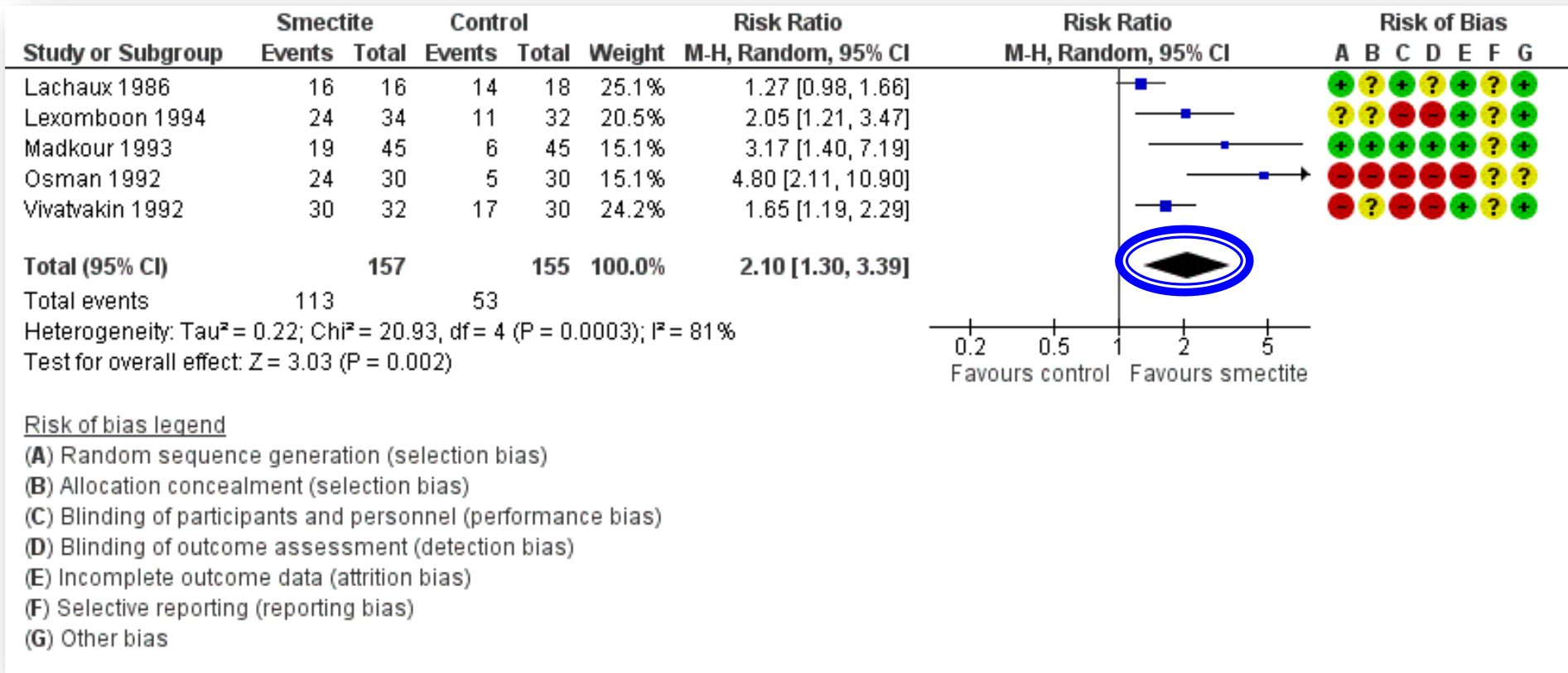
Duración



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Smectite para resolució clínic al Tercer dia de iniciar el tratamiento

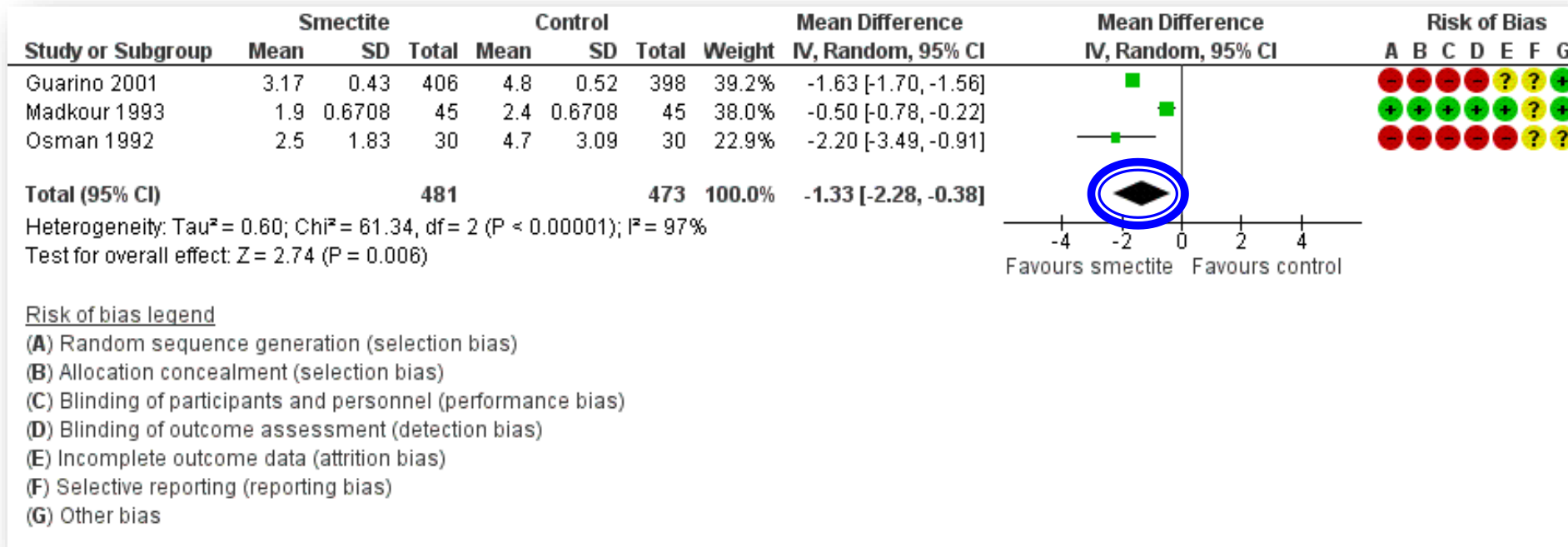


Cochrane Database of Systematic Reviews

25 APR 2018 DOI: 10.1002/14651858.CD011526.pub2

Smectite en diarrea infecciosa aguda en niños

Menor frecuencia de deposiciones al 3er día



Conclusión
 Reduce la diarrea 1 día (24.38 h)
 Aumenta la resolución al día 3
 Reduce el gasto fecal

Diosmectita

Mecanismos

RESEARCH

Open Access



Mechanisms of antidiarrhoeal effects by diosmectite in human intestinal cells

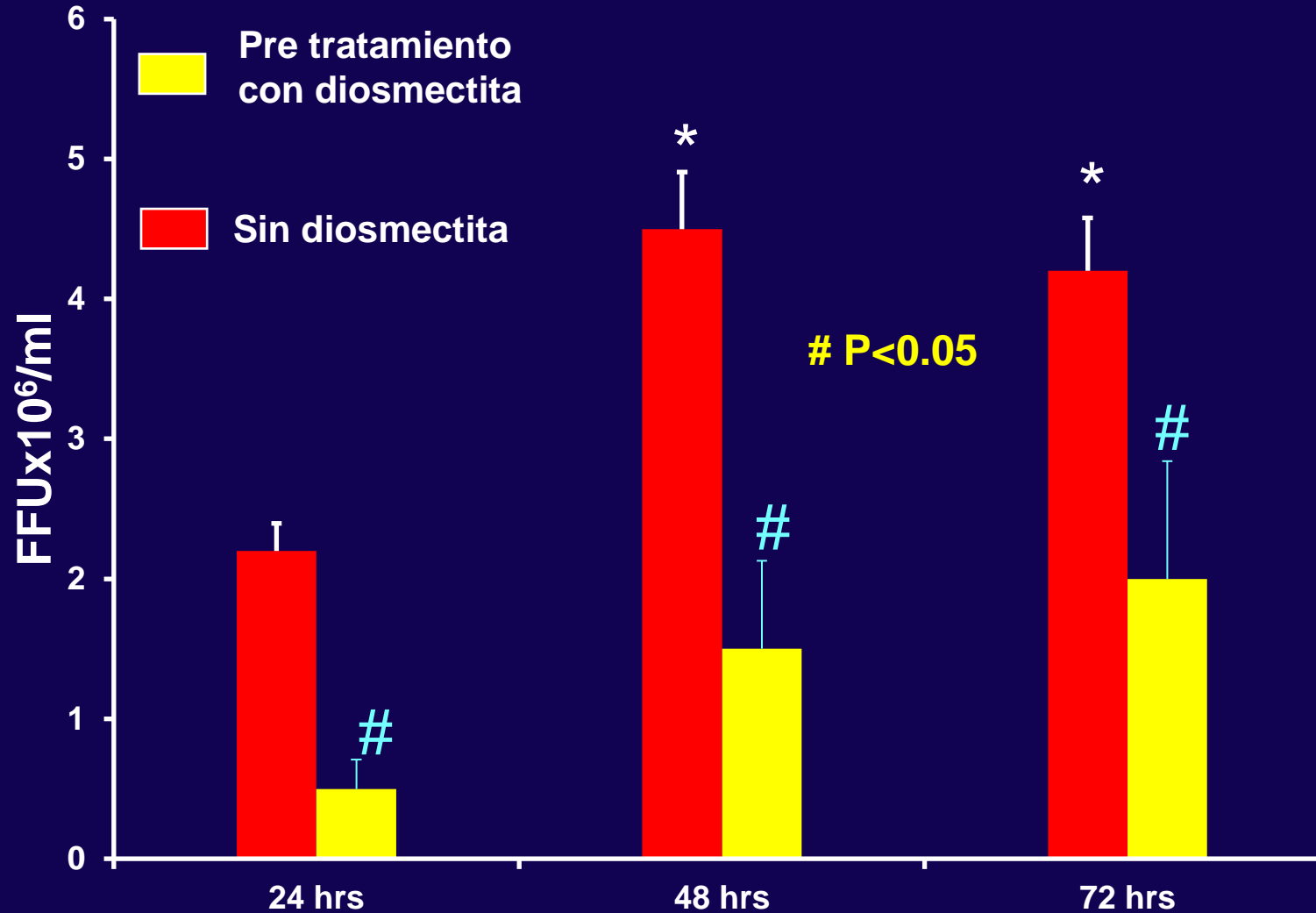
Vittoria Buccigrossi¹, Carla Russo¹, Amedeo Guarino¹, Maiara Brusco de Freitas² and Alfredo Guarino^{1*}

Pre incubación con DSM 100 mg/ml

Infectividad

Células humanas (caco-2) cultivadas con Rotavirus Virus intracecular

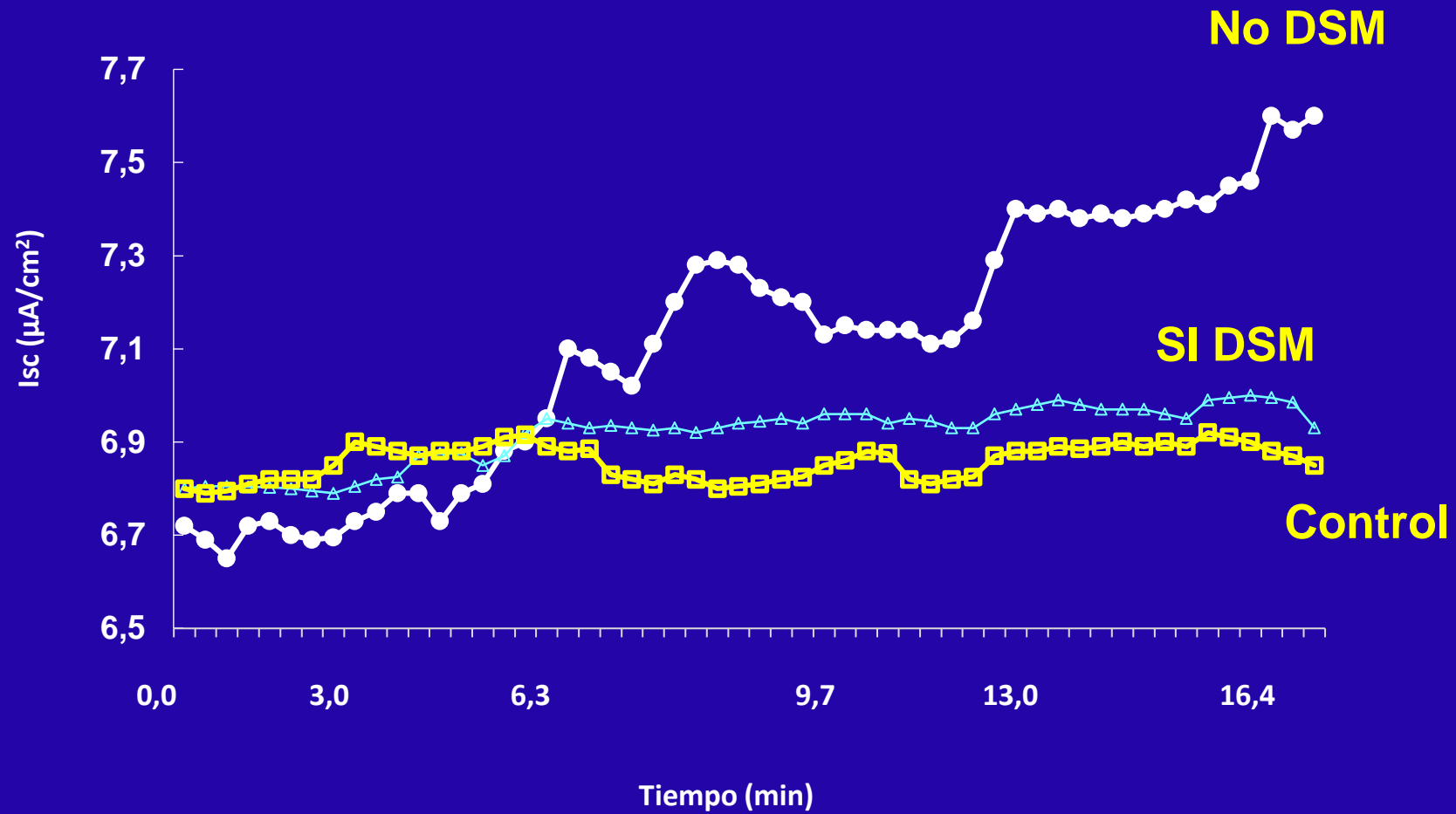
Se pueden diferenciar
En Enterocitos



Efectos enterotoxícos

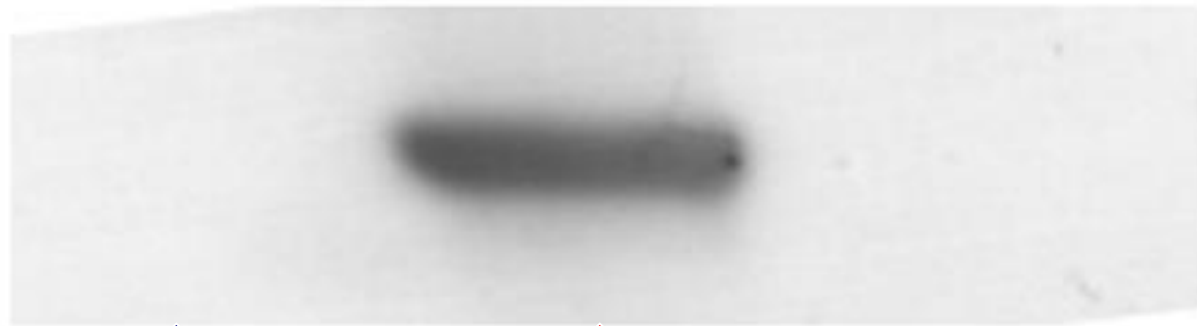
Efecto antisecretor

Secreción de Cloruro



DM inhibe completamente el efecto Secretor del rotavirus

CTRL RV DS+RV



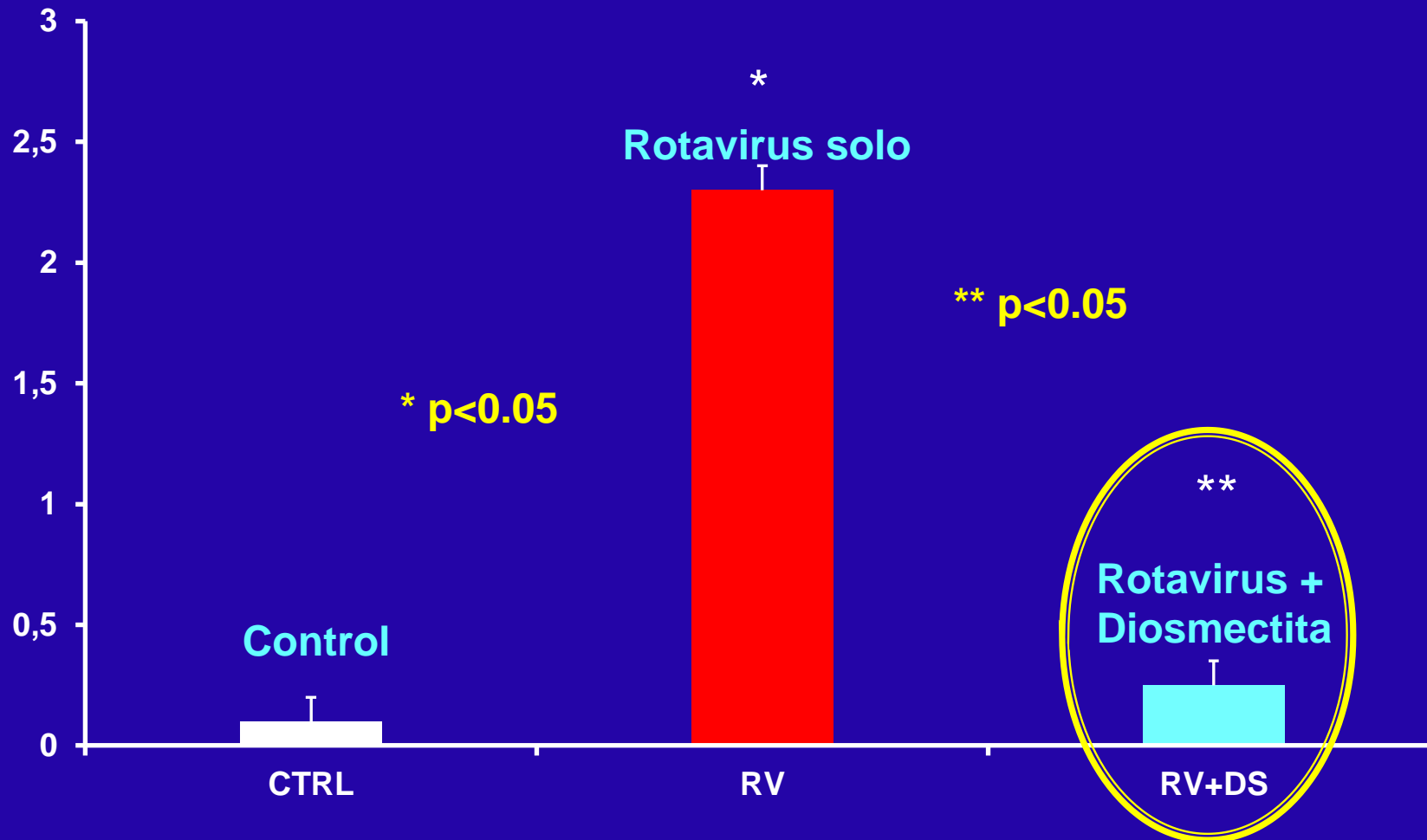
Expresión
Enterotoxina
viral



NSP4
(28kDa)

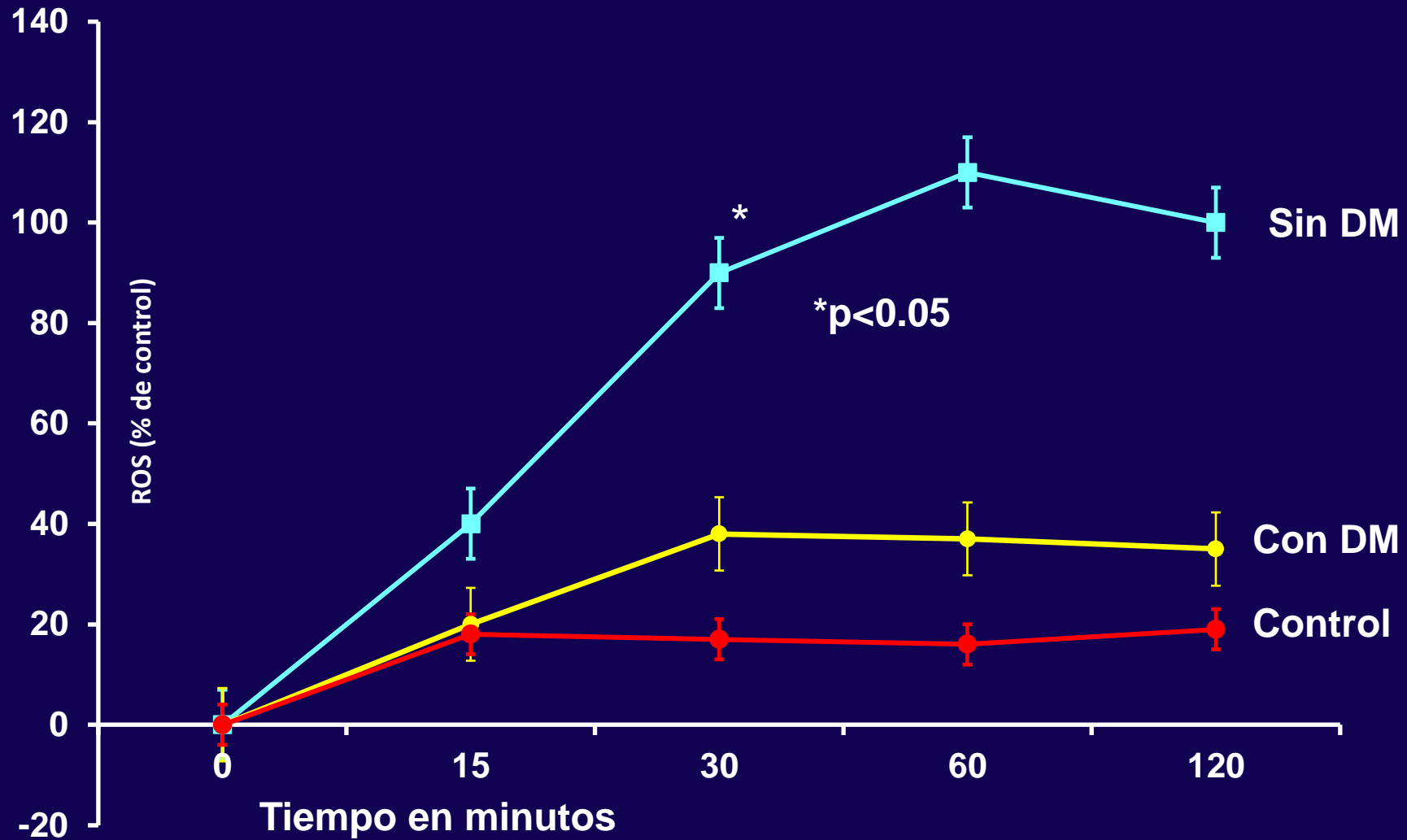
Citotoxicidad

Efecto citotóxico de Rotavirus

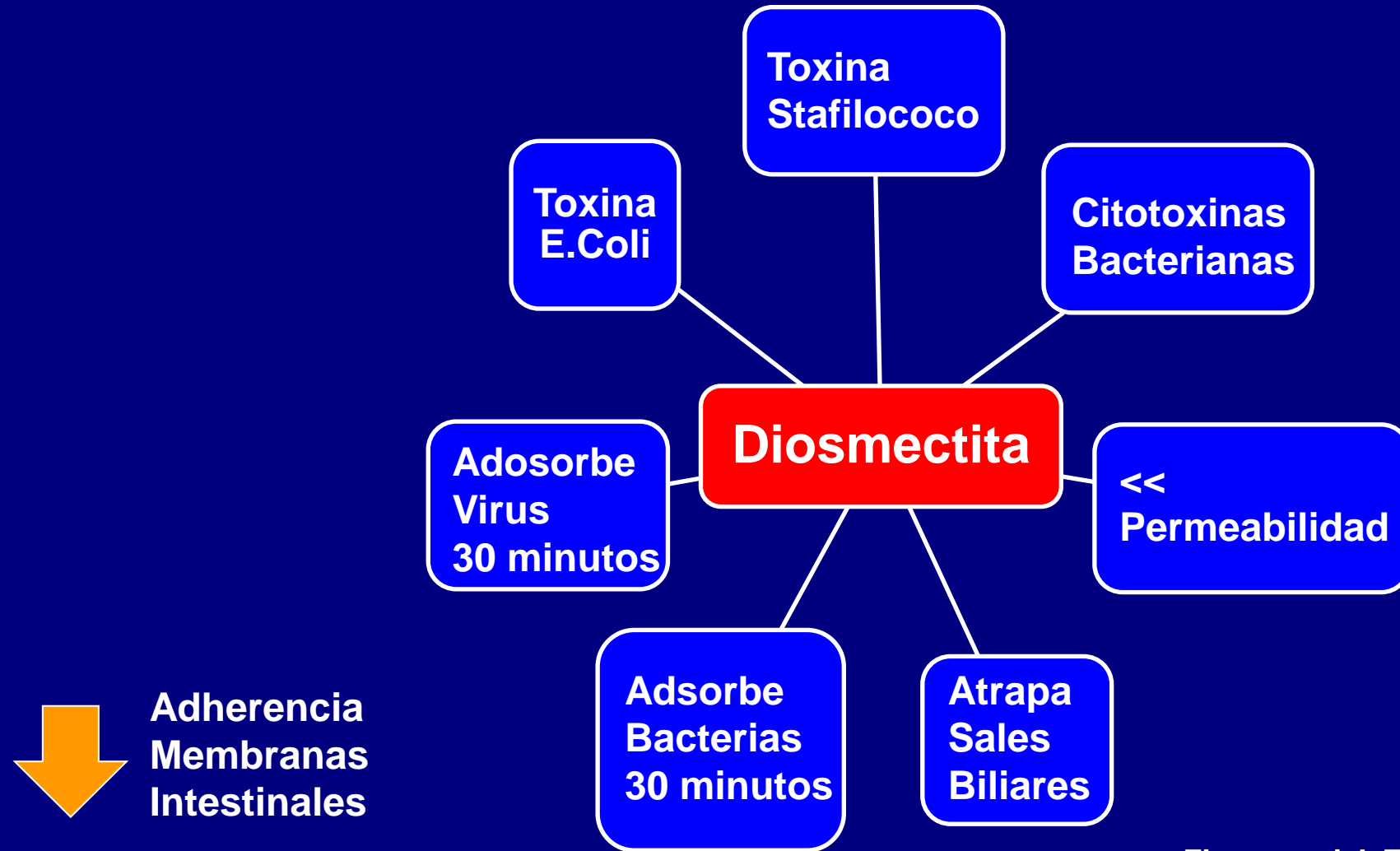


Estrés oxidativo

Estrés oxidativo con o sin pre incubación con DM

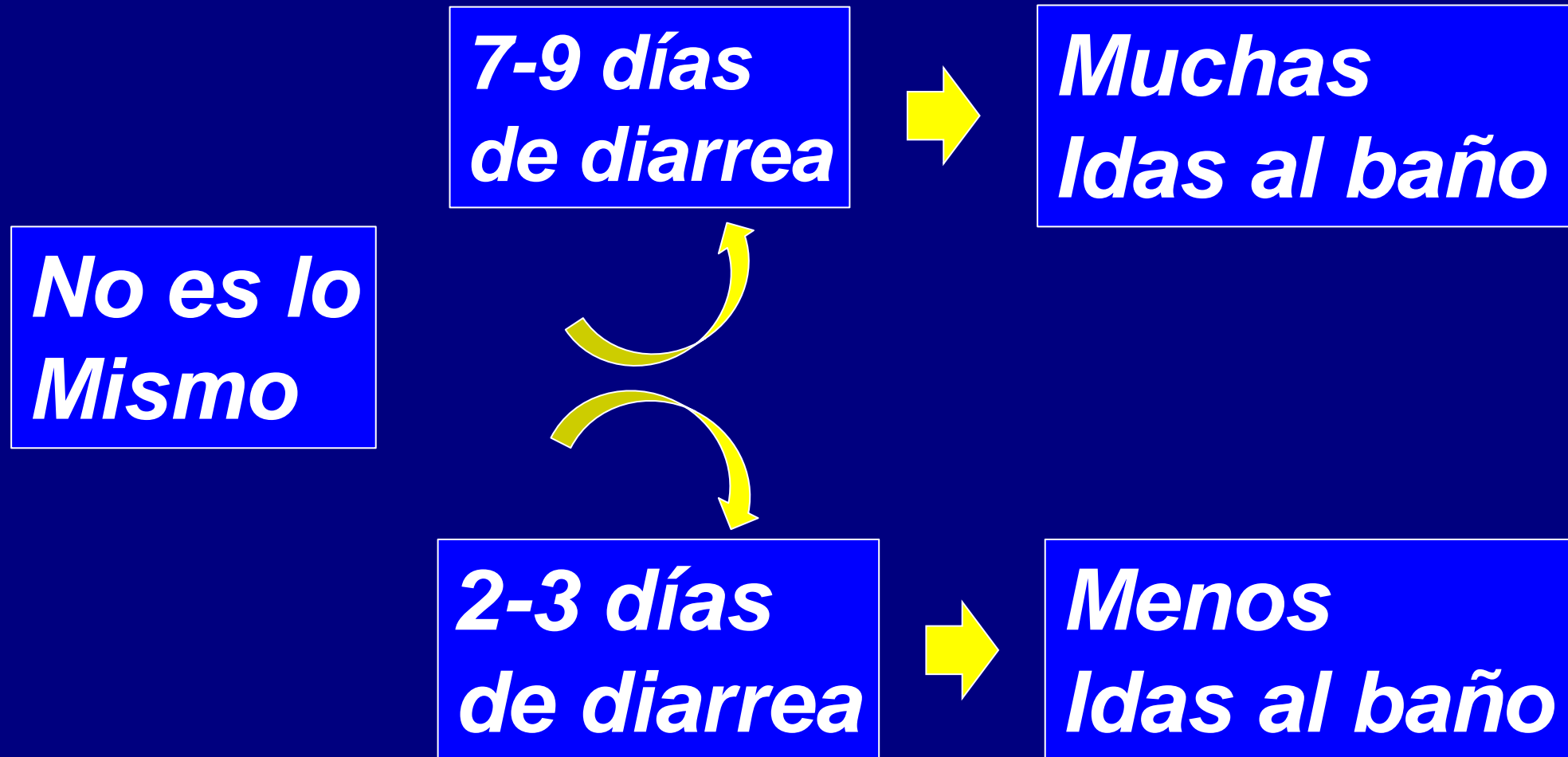


Mecanismos de acción de Diosmectita



Fioramonti J, Toxicol Letter 1987;36:227-32
Mahraoui L, Gut 1997;40:339-43
Morè J, Histochem J 1987;19:665-70

Diarrea aguda Diosmectita



Diosmectita-dosis

Niños < 1 año :

Dos sobres al inicio de la diarrea

Despuès 1 sobre al día (3 gr)/día

Niños > 1 año:

4 sobres al inicio de la diarrea

Despuès 2 sobres/día

Adultos:

6 sobres al inicio de la diarrea

Despuès 3 sobres/día (9 gr)

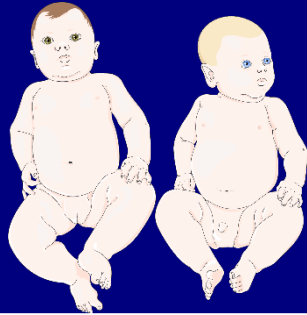
El contenido del
Sobre en 50 ml H₂O
Se consume en el día.

O Mezclado con
Alimentos líquidos
Compotas, puré etc

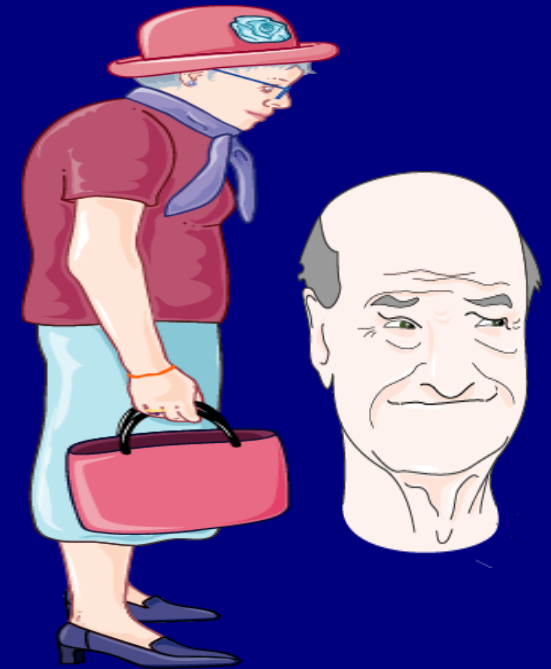
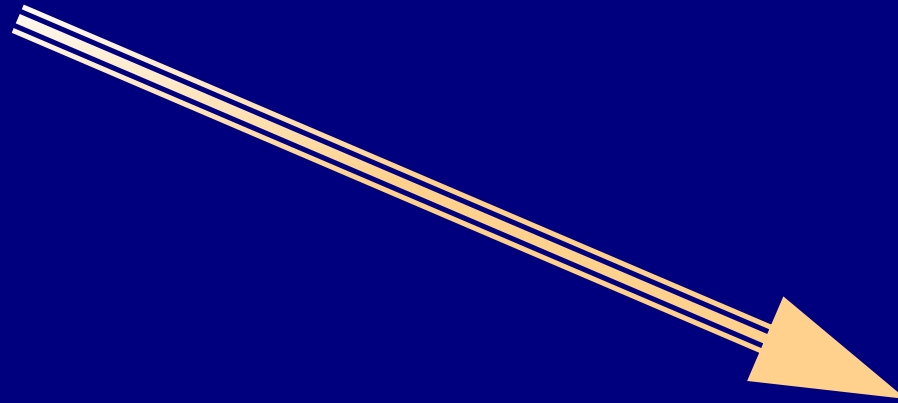
El contenido del
Sobre en MEDIO VASO
De H₂O: suspensión
Antes de consumirlo

Primero verter el polvo
Despuès el líquido

Diosmectita *Nueva clase de droga antidiarreica*



< 1 año



Adulto mayor

Seguridad

Ensayos clínicos

>6.300 niños

>11.800 adulto

Ningún efecto adverso serio

Estreñimiento infrecuente: 0.1%, <1%

Se alivia ajustando la dosis

Reportados: NO

FDA, WHO, French Agency

Interacción medicamentosa

Tomar otros medicamentos dos horas antes

Indicaciones

Niños:

Diarrea aguda: Incluyendo menores de 1 años
Asociada a hidratación oral

Adultos

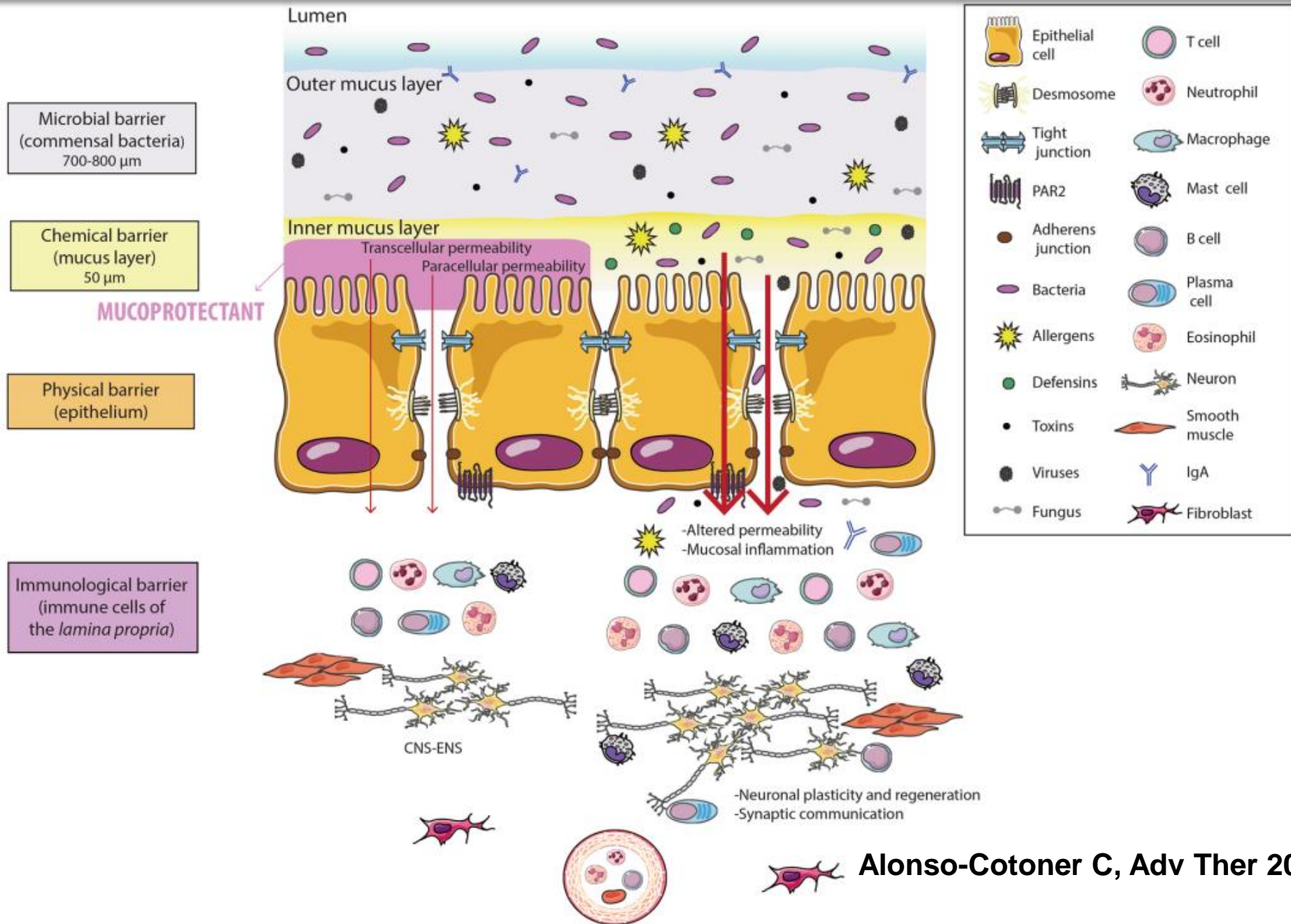
Diarrea aguda

Diarrea crónica funcional

Intestino irritable ?

Dolor asociado a trastornos GI Funcionales ?

Diosmectita/Mucoprotector



**Efectos recientemente
Identificados de la smectita**

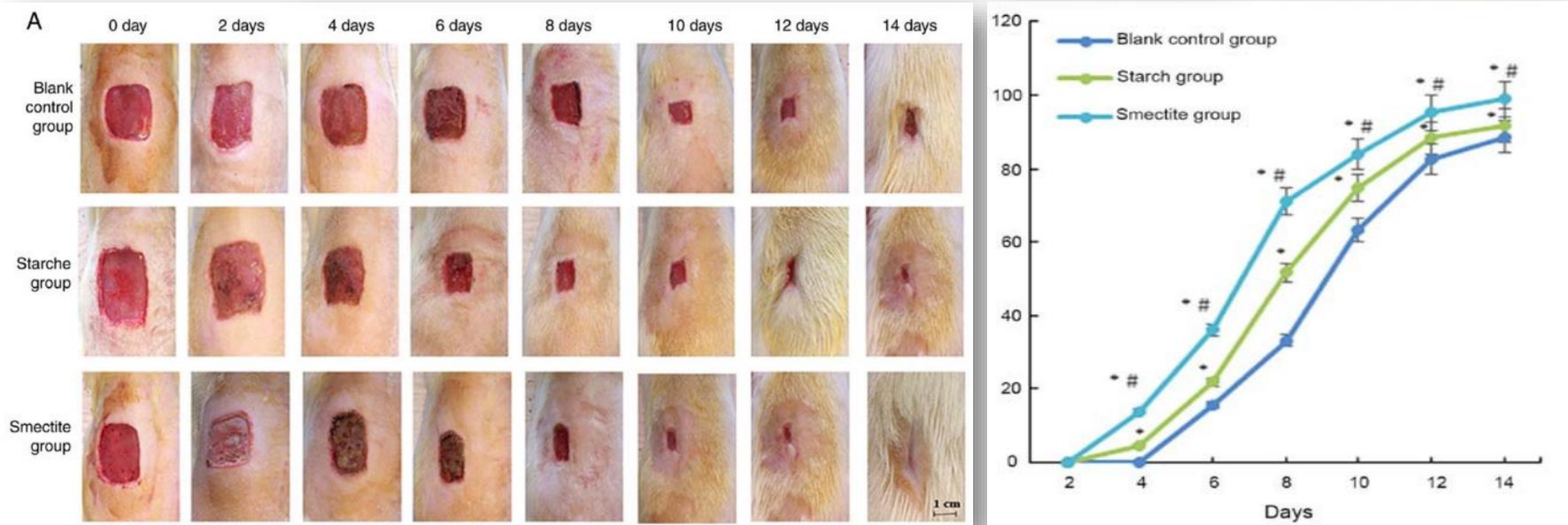
Diosmectite inhibits the interaction between SARS-CoV-2 and human enterocytes by trapping viral particles, thereby preventing NF-kappaB activation and CXCL10 secretion

**Marco Poeta¹, Valentina Cioffi¹, Vittoria Buccigrossi¹, Merlin Nanayakkara¹,
Melissa Baggieri², Roberto Peltrini³, Angela Amoresano⁴, Fabio Magurano² &
Alfredo Guarino¹✉**

Investigating the efficacy and safety of mineral smectite granules on wound healing

JIANKUN WANG*, MIN WANG*, LILI ZHAO, LI LIU, XIANG WANG and ZHINING FAN

Digestive Endoscopy Department and General Surgery Department, The First Affiliated Hospital with Nanjing Medical University and Jiangsu Province Hospital, Nanjing, Jiangsu 210029, P.R. China



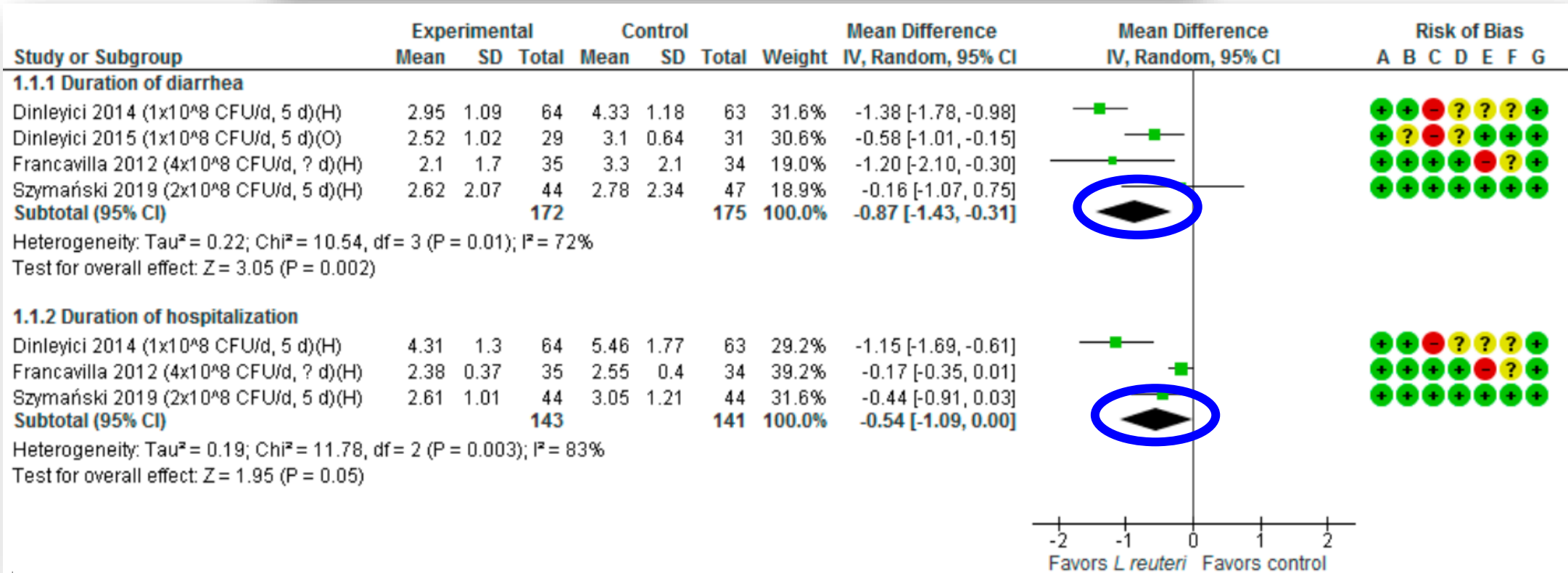
**Lactobacillus reuteri DSM 17938 +
Vitamina D3**

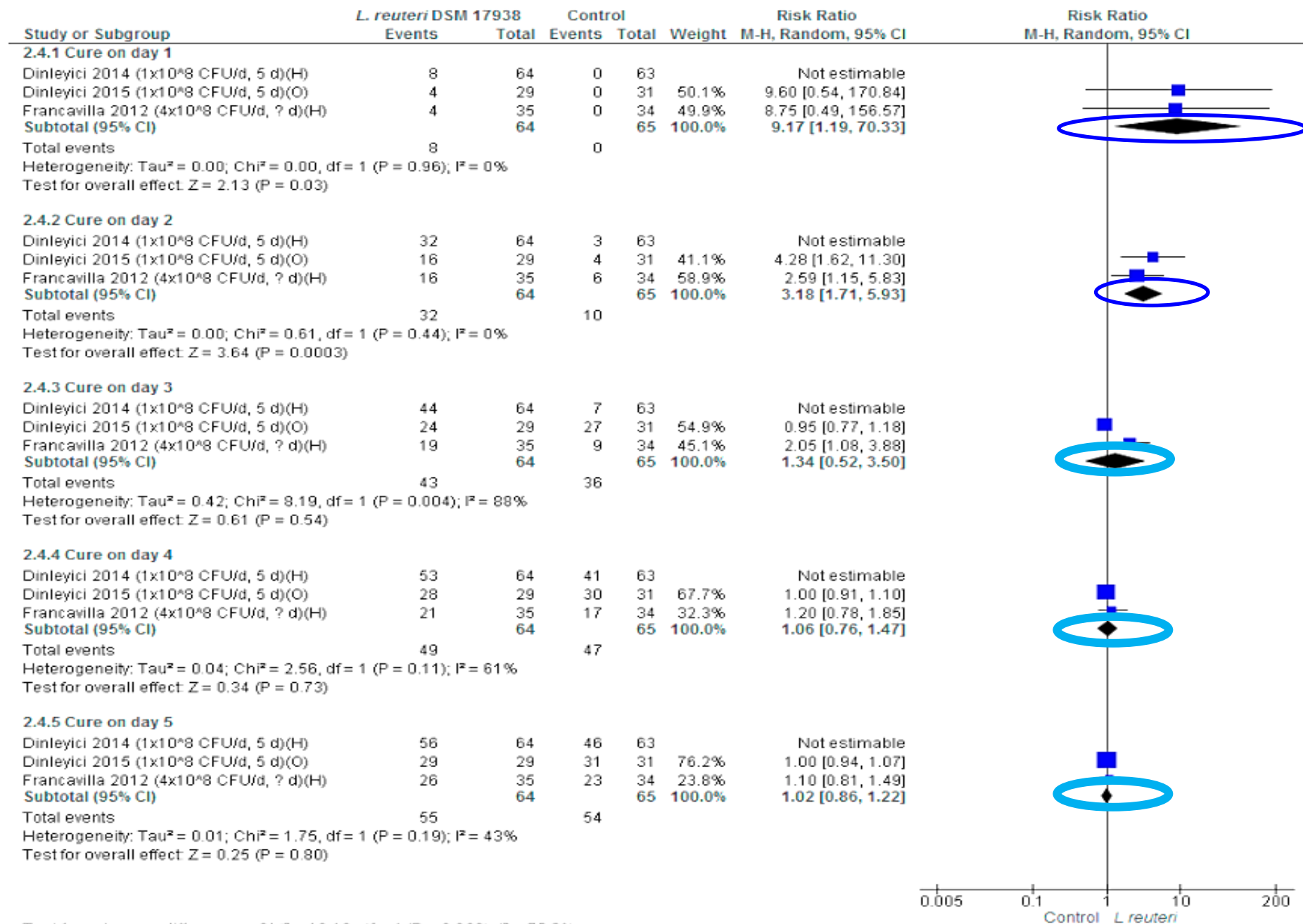


Review

Systematic Review with Meta-Analysis: *Lactobacillus reuteri* DSM 17938 for Treating Acute Gastroenteritis in Children. An Update

Bernadeta Patro-Gołąb and Hania Szajewska *





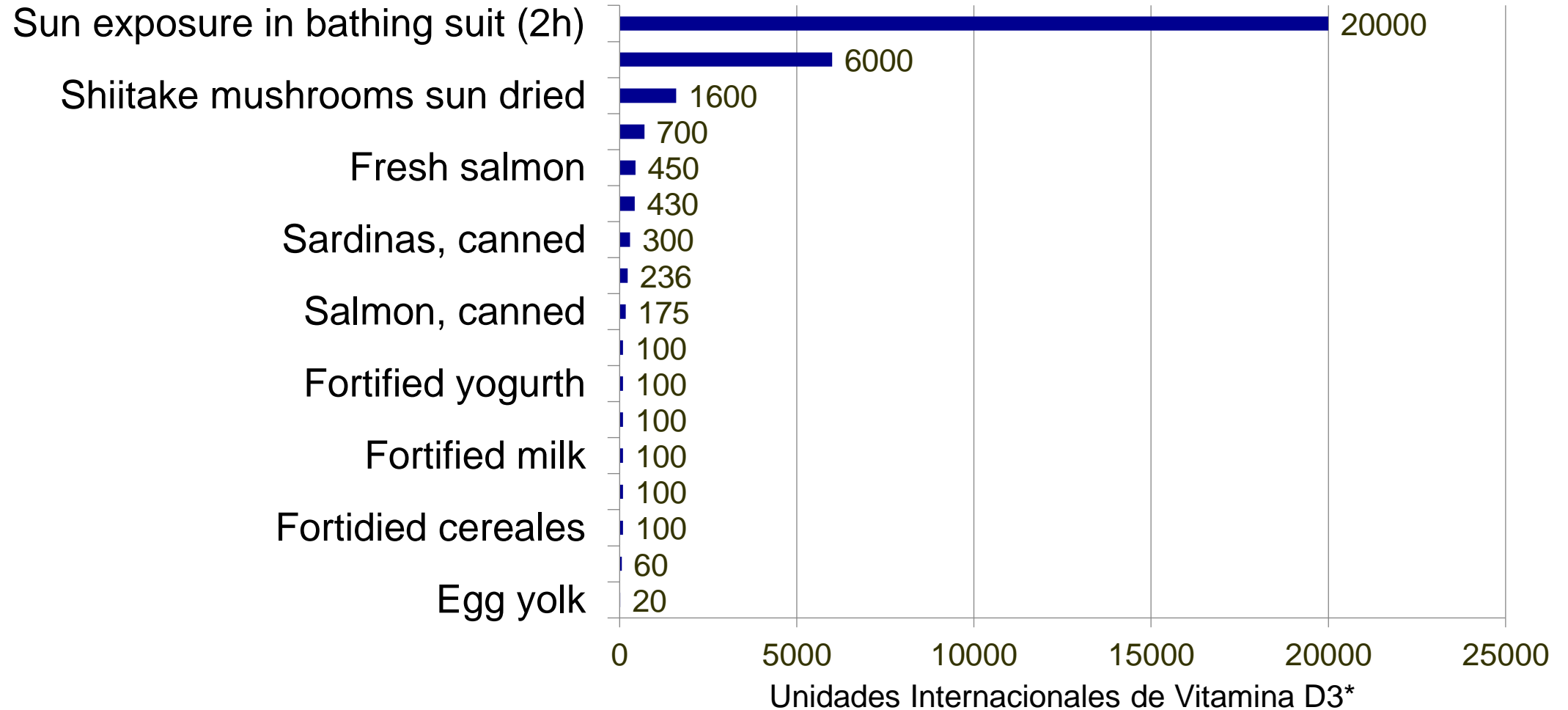
Test for subgroup differences: Chi² = 16.19, df = 4 (P = 0.003), I² = 75.3%

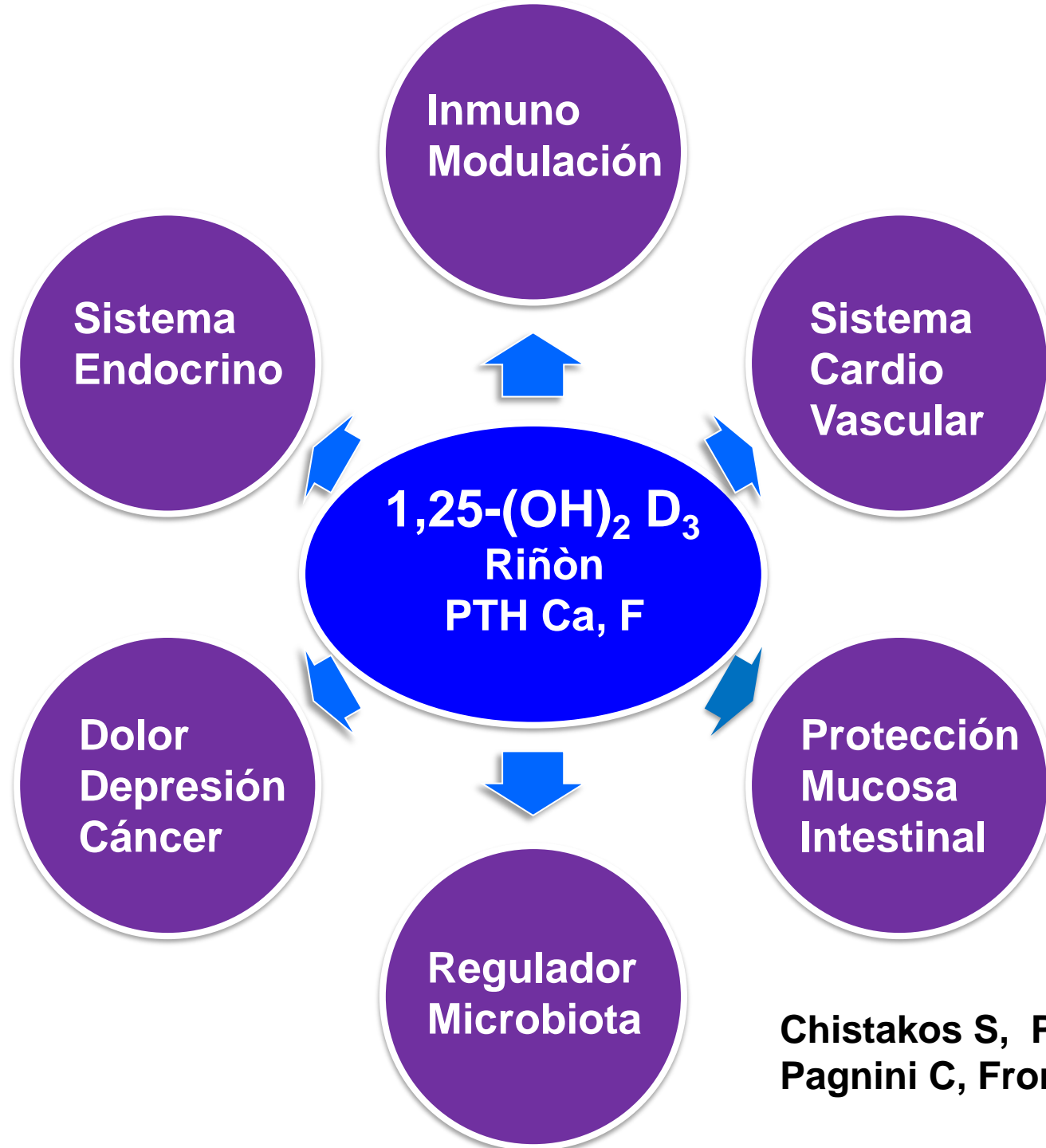
Vitamina D

D₃ Colecalciferol piel

D₂ Ergocalciferol plantas, hongos

Vitamina D: Fuente para los humanos





Chistakos S, Physiol Rev 2019;6:365-408
Pagnini C, Front Pharmacol 2021;12:747856

Probiotics and Vitamin D/Vitamin D Receptor Pathway Interaction: Potential Therapeutic Implications in Inflammatory Bowel Disease

Cristiano Pagnini^{1}, Maria Carla Di Paolo¹, Maria Giovanna Graziani¹ and Gianfranco Delle Fave^{2,3}*

Pagnini C, Front Pharmacol 2021;12: Article747856





Review

The Health Effects of Vitamin D and Probiotic Co-Supplementation: A Systematic Review of Randomized Controlled Trials

Myriam Abboud ^{1,*}, Rana Rizk ², Fatme AlAnouti ¹, Dimitrios Papandreou ¹, Suzan Haidar ³ and Nadine Mahboub ^{3,4}

Abboud M, Nutrients 2021;13:111

Table 1. Characteristics of included studies.

First Author, Year, Country	Study Design	Duration	Study Population	Intervention	Control	Co-Intervention	Compliance/Drop-out
Ghaderi, 2019, Iran [27]	Randomized, double-blind, placebo-controlled	12 weeks	n = 60, aged 25–65, 93.33% men, diagnosed with schizophrenia using DSM-IV-TR criteria with disease duration ≥2 years, PANSS score ≥55, treated with chlorpromazine	Vitamin D3 and probiotic supplement: - Vitamin D3: 50,000 IU every 2 weeks; DDE = 3571.4 IU - Probiotics: 8 × 10 ⁹ CFU/day containing <i>Lactobacillus acidophilus</i> , <i>Bifidobacterium bifidum</i> ,	Placebo similar shape and packaging	None	Compliance: >90% Drop out: I: 13.33% C: 13.33%
Jafarnejad, 2017, Iran [31]							Compliance 100% Drop out: 9% C: 5%
Jamilian, 2017, Iran [29]							Compliance: 100% Drop out: 7% C: 66% 0%
Ostadmohammadi, 2019, Iran [28]	placebo-controlled clinical trial	12 weeks	Rotterdam criteria with BMI: 17–34 kg/m ² and insulin resistance: 1.4–4	<i>Lactobacillus acidophilus</i> , <i>Bifidobacterium bifidum</i> , <i>Lactobacillus reuteri</i> and <i>Lactobacillus fermentum</i> (each 2 × 10 ⁹ CFU/g)	size, odor, taste and packaging	None	100%; No drop out
Raygan, 2018, Iran [30]	Randomized, double-blind, placebo-controlled clinical trial	12 weeks	n = 60, age 45–85 years, 50% men, with T2DM diagnosed based on the criteria of the ADA and with CHD diagnosed as per the AHA with 2- and 3-vessel CHD	Vitamin D3 and probiotic supplement: - Vitamin D3: 50,000 IU every 2 weeks; DDE = 3571.4 IU - Probiotics: 8 × 10 ⁹ CFU/g containing <i>Lactobacillus acidophilus</i> , <i>Bifidobacterium bifidum</i> , <i>Lactobacillus reuteri</i> , and <i>Lactobacillus fermentum</i> (each 2 × 10 ⁹ CFU/g)	Placebo similar in appearance, color, shape, size, odor, taste and packaging	None	Compliance > 90% Drop out: I: 13.33% C: 13.33% (Intention-to-treat analysis)

La combinación de probióticos mas vitamina D
Es un adyuvante en enfermedades crónicas

La combinación es superior a placebo y a cada uno por separado



Letter

Lactobacillus reuteri DSM 17938 plus vitamin D₃ as ancillary treatment in allergic children with asthma

Lactobacillus reuteri DSM 17938 más vitamina D₃ como tratamiento auxiliar en niños alérgicos con asma

Table 2

Clinical and Functional Data in Groups A and B at T0, T1, and T2^a

Variable	T0			T1		
	Group A	Group B	P Value ^b	Group A	Group B	P Value ^b

Conclusion

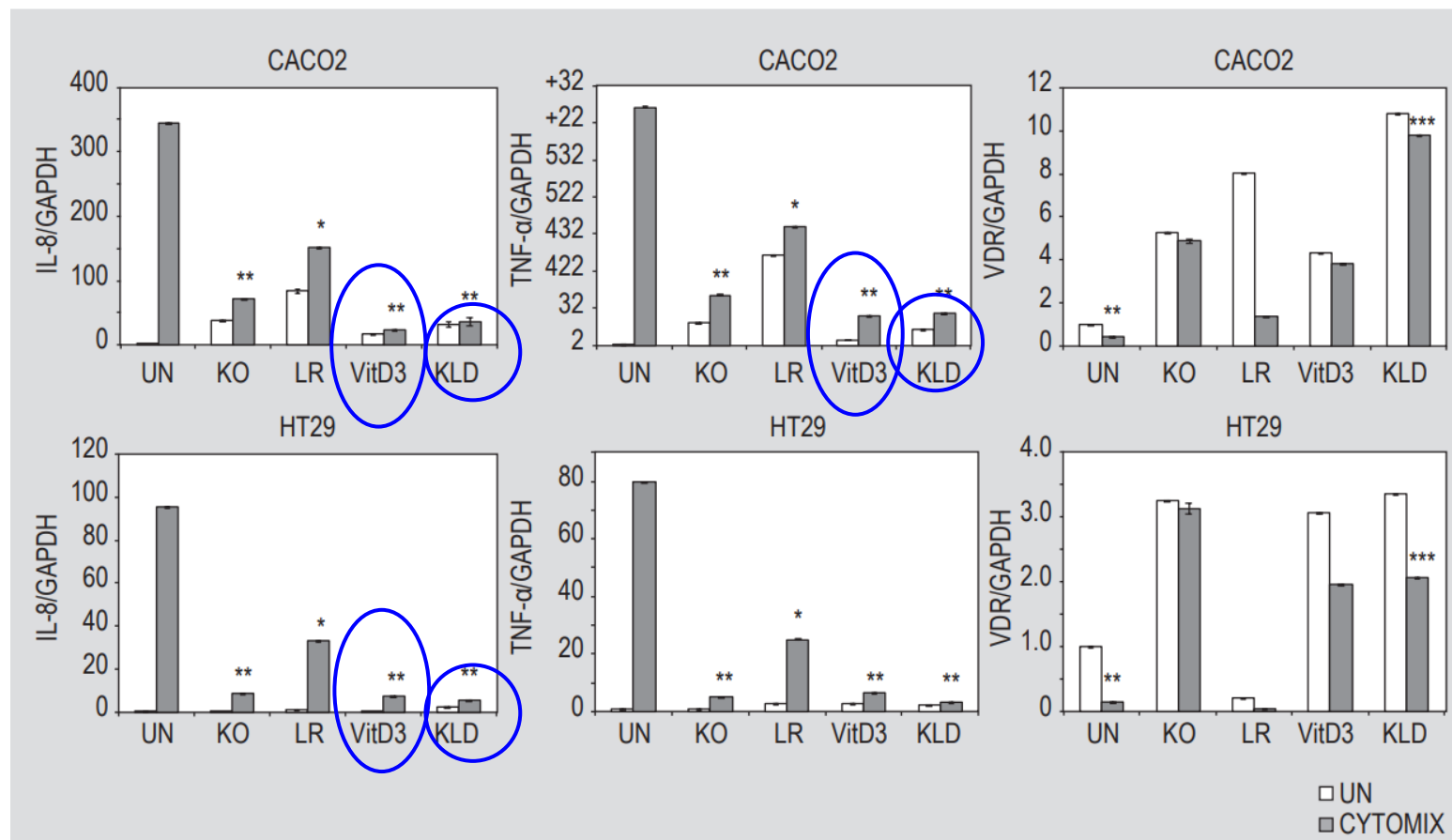
El estudio actual identificó que la suplementación con *L. reuteri* DSM 17938 (10⁸ CFU) y vitamina D₃ (400 IU) fue efectiva para reducir la inflamación bronquial. Además se observa un efecto positivo en el proceso de broncodilatación en los niños tratados con el principio activo.



Krill oil, vitamin D and *Lactobacillus reuteri* cooperate to reduce gut inflammation

M. Costanzo¹, V. Cesi², F. Palone¹, M. Pierdomenico¹, E. Colantoni¹, B. Leter¹, R. Vitali², A. Negroni², S. Cucchiara¹ and L. Stronati^{3*}

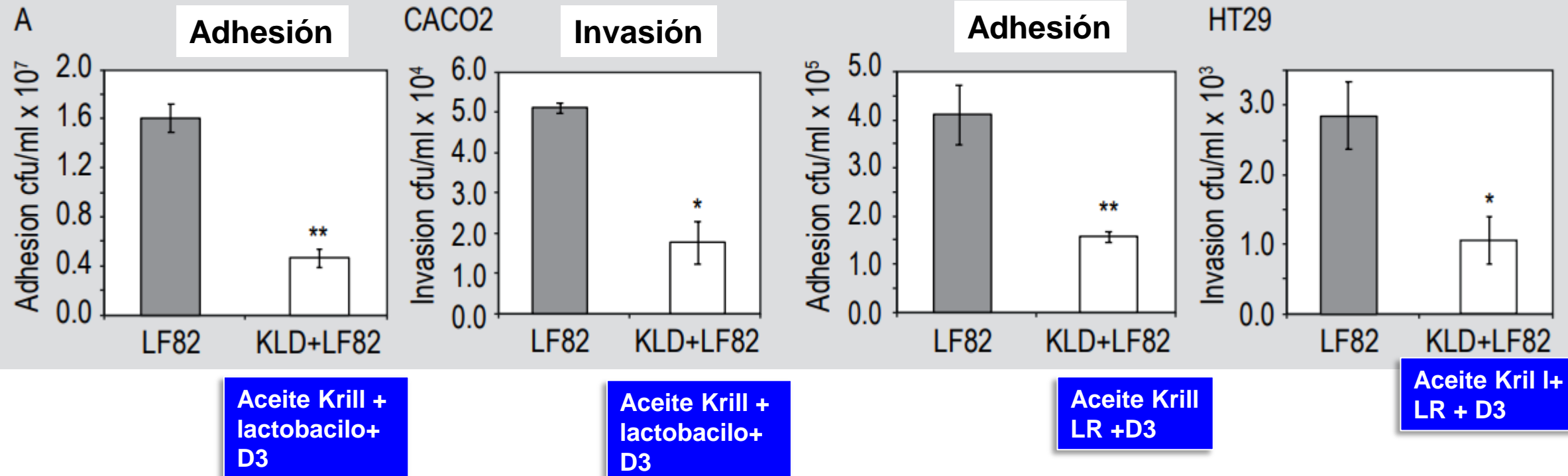
Colitis experimental con DDS (**Dextran Sulfato sódico** *Lactobacillus reuteri* (BioGaia Estocolmo, Suecia)



Krill oil, vitamin D and *Lactobacillus reuteri* cooperate to reduce gut inflammation

M. Costanzo¹, V. Cesi², F. Palone¹, M. Pierdomenico¹, E. Colantoni¹, B. Leter¹, R. Vitali², A. Negroni², S. Cucchiara¹ and L. Stronati^{3*}

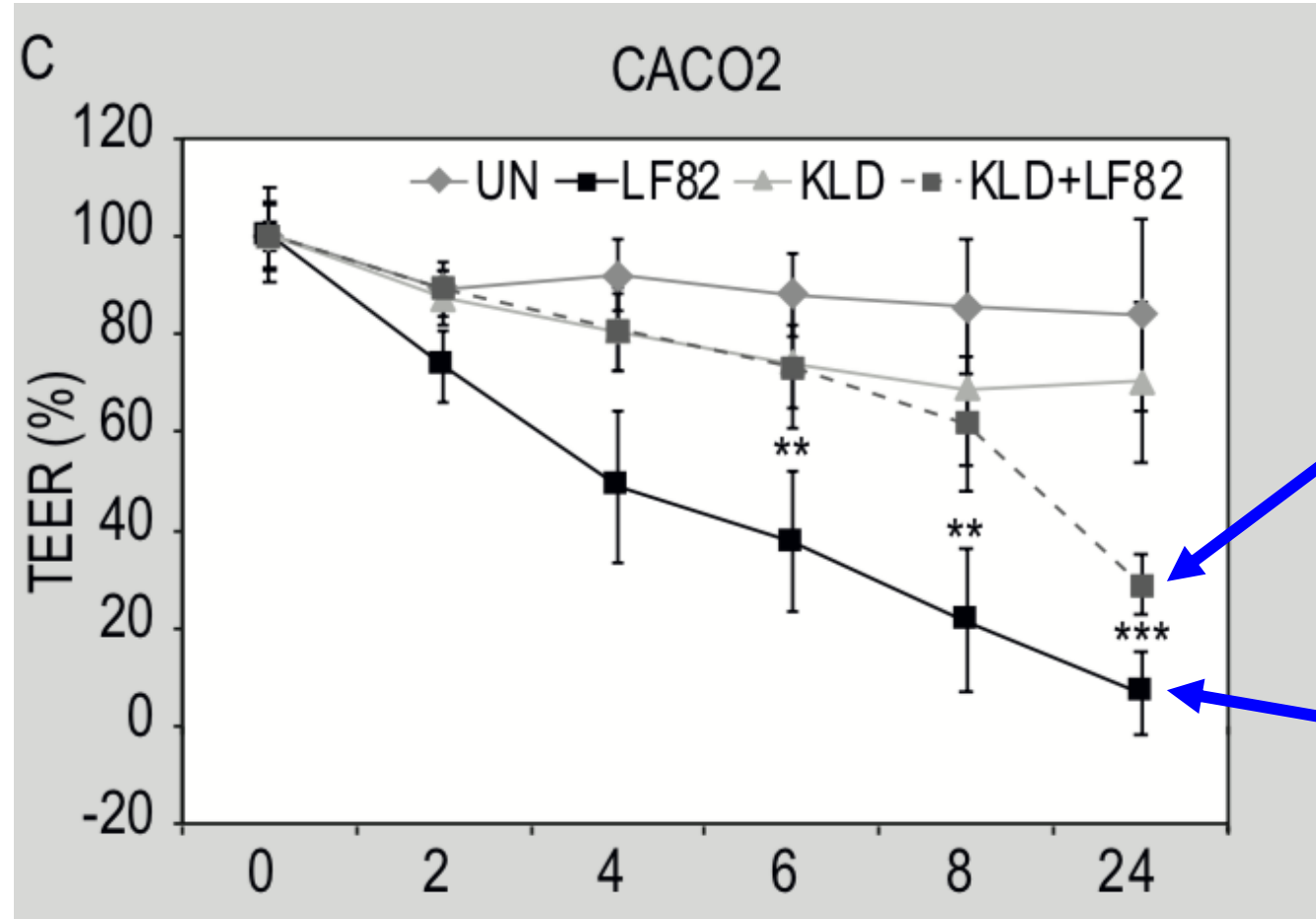
E. Coli enteroinvasiva LF82



Krill oil, vitamin D and *Lactobacillus reuteri* cooperate to reduce gut inflammation

M. Costanzo¹, V. Cesi², F. Palone¹, M. Pierdomenico¹, E. Colantoni¹, B. Leter¹, R. Vitali², A. Negroni², S. Cucchiara¹ and L. Stronati^{3*}

Resistencia Elèctrica Transepitelial



Recuperada por KLD

Reducida después Infección LF82 (E.Coli)

Krill oil, vitamin D and *Lactobacillus reuteri* cooperate to reduce gut inflammation

M. Costanzo¹, V. Cesi², F. Palone¹, M. Pierdomenico¹, E. Colantoni¹, B. Leter¹, R. Vitali², A. Negroni², S. Cucchiara¹ and L. Stronati^{3*}

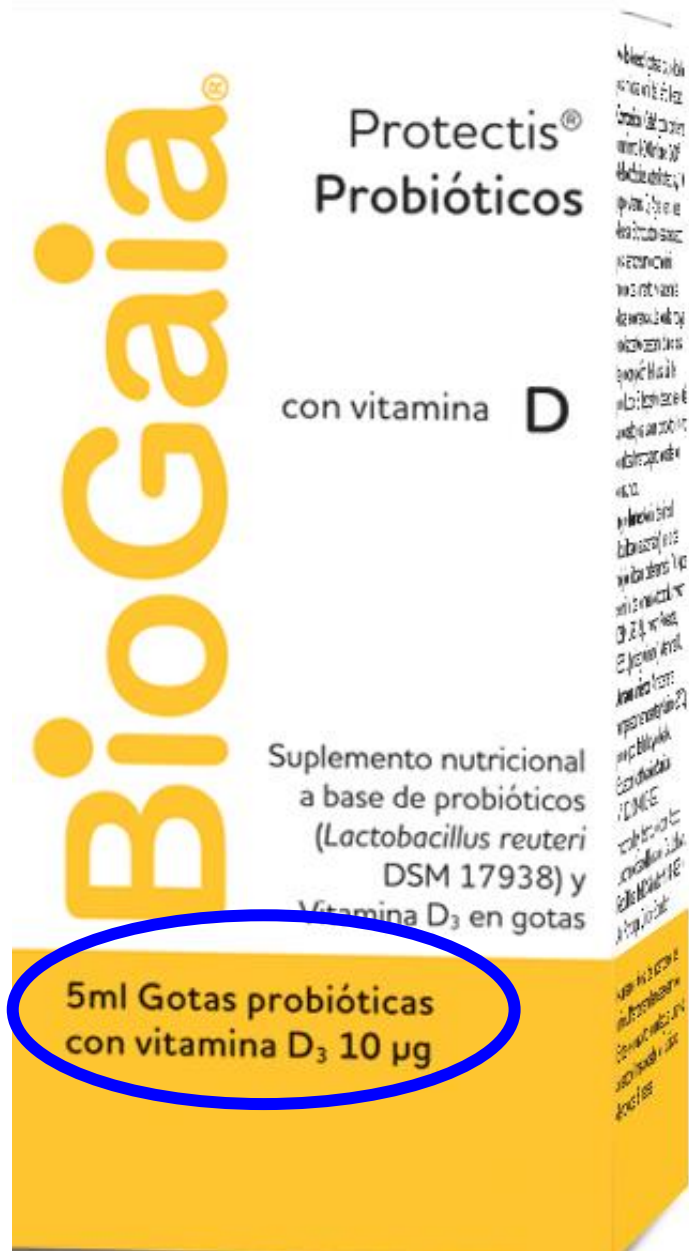
Aceite de Kril + LR+ D3

Disminuyó inflamación mucosa intestinal

Aumentó restitución epitelial

Redujo patogenicidad bacterias comensales peligrosas

Constanzo V, Benef Microbes 2018 ;9:389-399



7350012554798

Toxicidad de Vitamina D

La toxicidad de la vitamina D, poco frecuente pero potencialmente grave con cantidades excesivas de vitamina D

La toxicidad de la vitamina D se produce por grandes dosis de **suplementos** de vitamina D, no por la dieta o la exposición al sol

Hipercalcemia,: náuseas, vómitos, anorexia, debilidad, micción frecuente, nerviosismo hipertensión deshidratación daño renal, cálculos renales

60.000 UI/día varios meses causa toxicidad

Cortesía Pamela Ruiz, Abbott Ecuador
Dra Sylvia Cruchet M

Mensajes para la casa

Hidratación es la piedra angular

Zinc complementa hidratación

LGG administrado 1as 24-48 h

Acorta duración diarrea

Disminuye hospitalización

Evita diarrea antibióticos

LGG + BB-12: seguro eficaz

Diarrea aguda, asociada antibióticos

Evidencia respalda la combinación

Lactobacillus reuteri + vitamina D3

Combinación audaz

Diarrea aguda

Abanico de
Posibilidades

Explorar >



Muchas gracias !