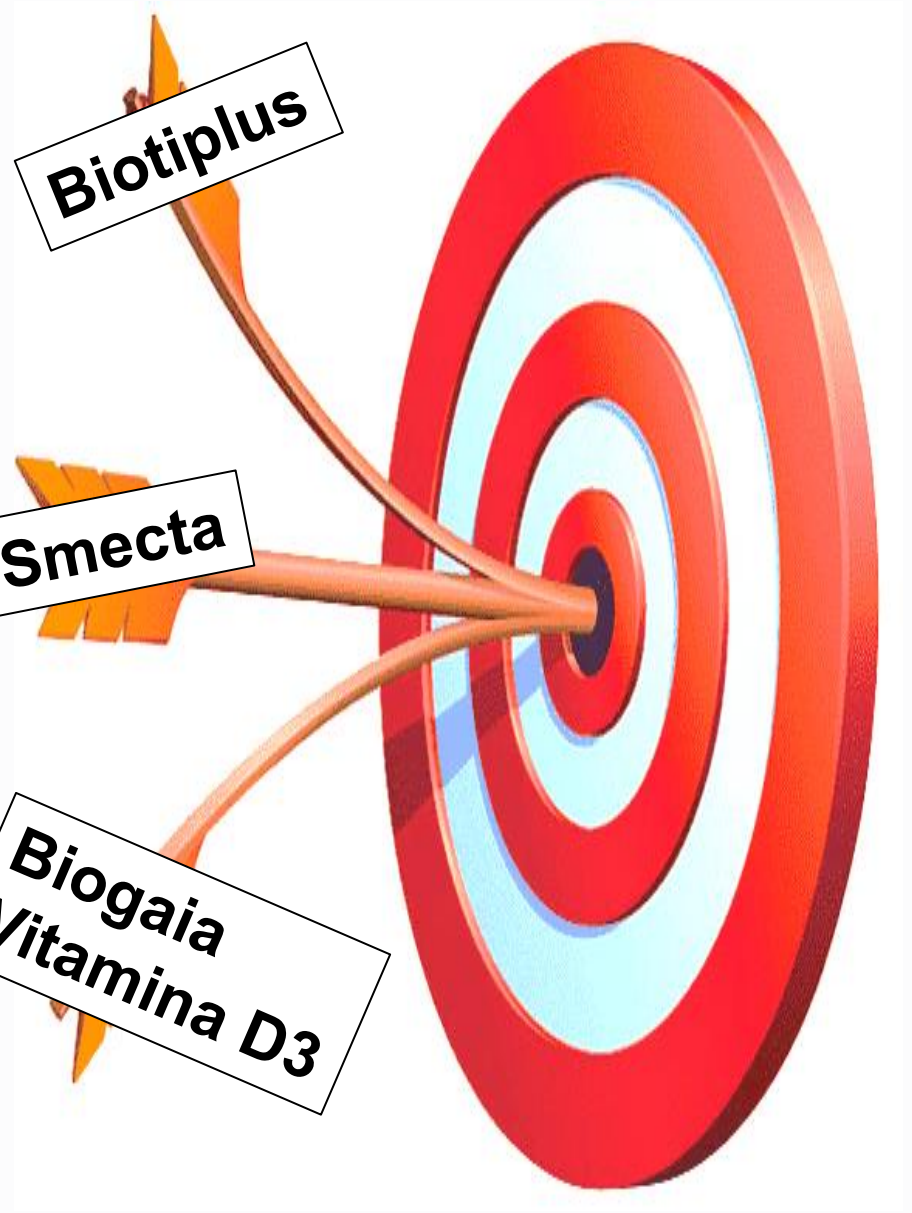
Jornadas Médicas de actualización integral JAMI
Quito julio 20, 2022

Diarrea aguda manejo en el 2022
Tres estrategias complementarias

William Otero R MD, FAGA, FACP
Profesor Titular de Medicina
Unidad 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, probioticos***
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

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

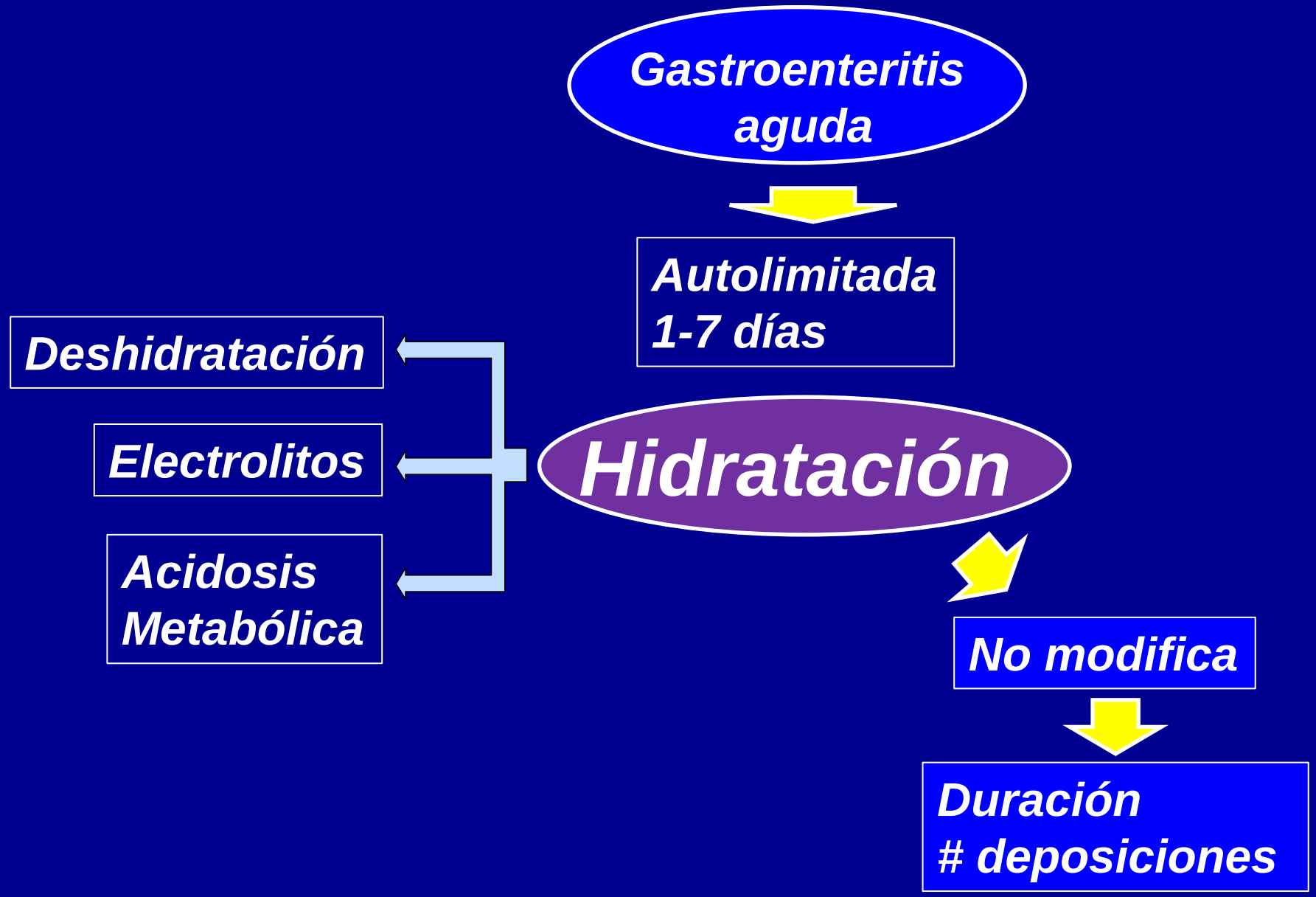
Mayoría de los casos diarrea Aguda Viral

Autolimitada

Se podría intervenir para Aligerar la recuperación ?

Sufrimiento indescriptible de Muchas Personas

Altos costos en salud y altos costos laborales


Gastroenteritis aguda
Autolimitada 1-7 días
Deshidratación
Electrolitos
Acidosis Metabólica
Hidratación
No modifica
Duración
deposiciones

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

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

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://wwwwhoint/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 *G*orbach, Barry *G*oldin
'GG'

Bifidobacterium animalis
Sub especie *lactis BB-2*

Lacbacillus rhamnosus GG
Bifidobacterium animales 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

Lactobacillus rhamnosus GG

Indicaciones	Dosis recomendada	Nivel Evidencia	Respaldo
Prevención diarrea asociada a antibióticos	1- 2 $X10^{10}$ 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	10^{10}-10^{11} UFC dos veces al día	1	Szajewska H. Systematic review with meta-analysis Aliment Pharmacol Ther. 2015;42:1149–57.
Gastroenteritis aguda	≥ 10^{10} 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.

OMGE Febrero 2017

MEDICAL POSITION PAPER

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

European Society for Paediatric Gastroenterology, Hepatology and Nutrition (**ESPGHAN**)

Ensayos clínicos De impacto

Canadá

ORIGINAL ARTICLE

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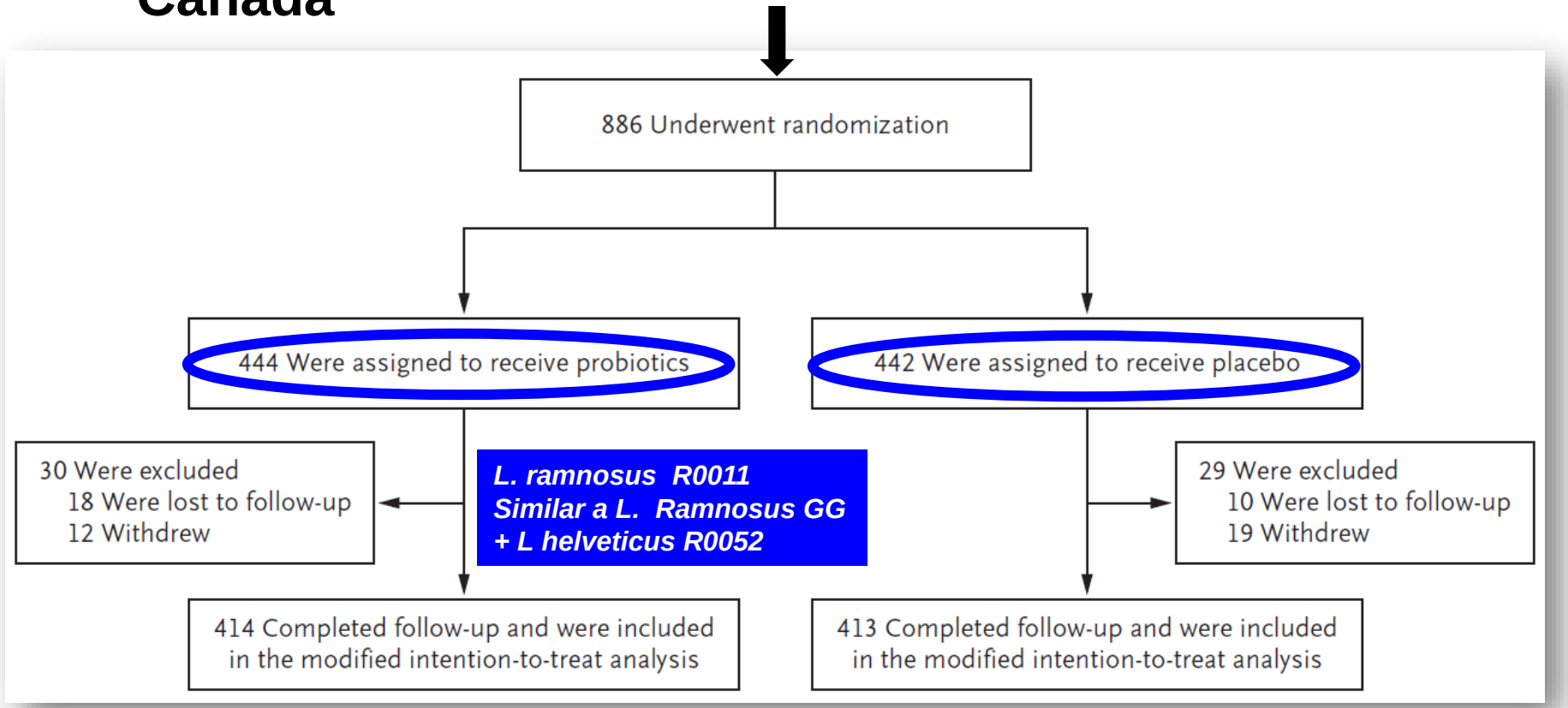
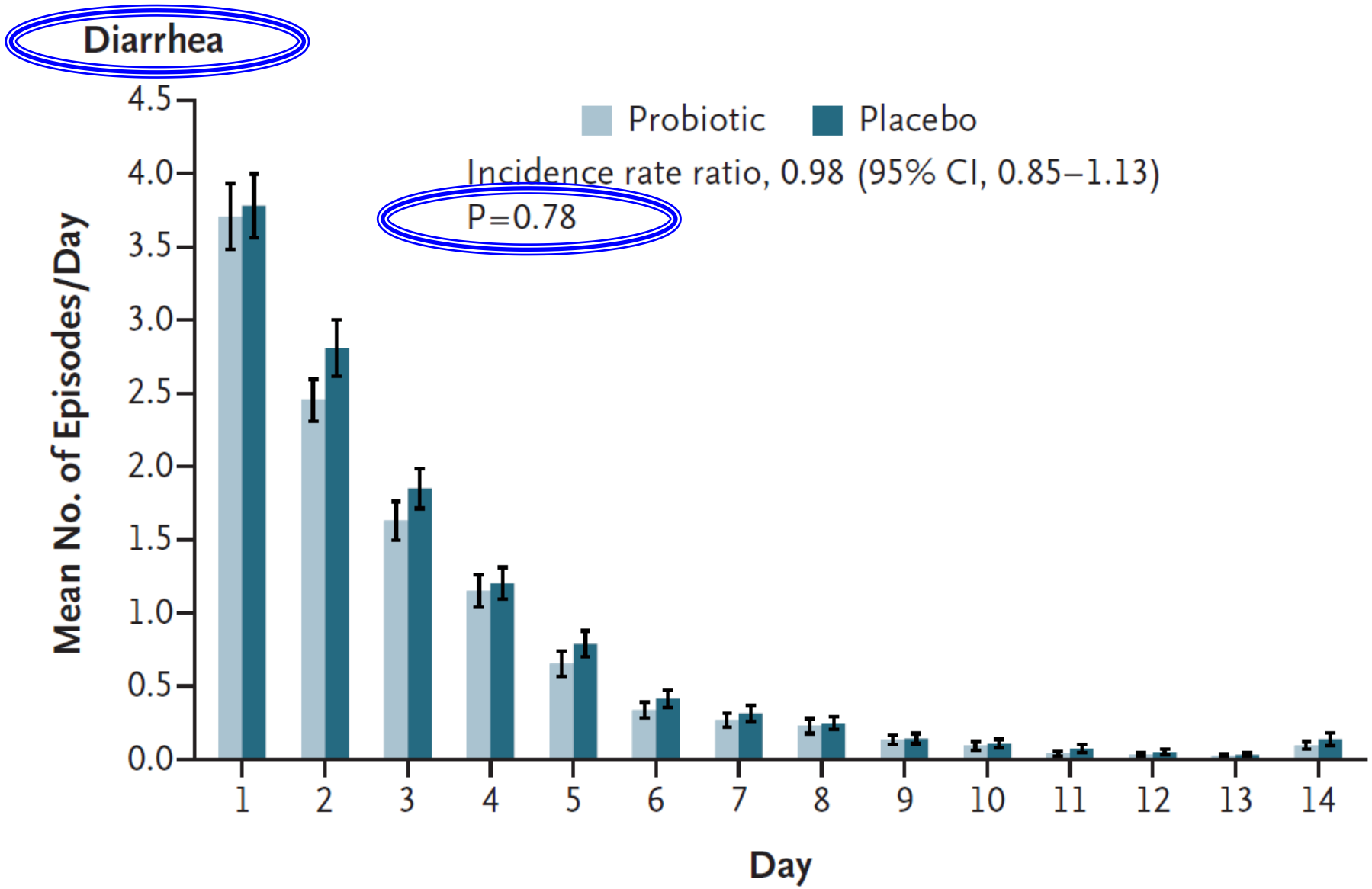
Freedman SB, N Engl J Med 2018;379:2015-26.

Canadá



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


Diarrhea
Probiotic
Placebo
Incidence rate ratio, 0.98 (95% CI, 0.85–1.13)
P=0.78
Mean No. of Episodes/Day
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Day

USA

ORIGINAL ARTICLE

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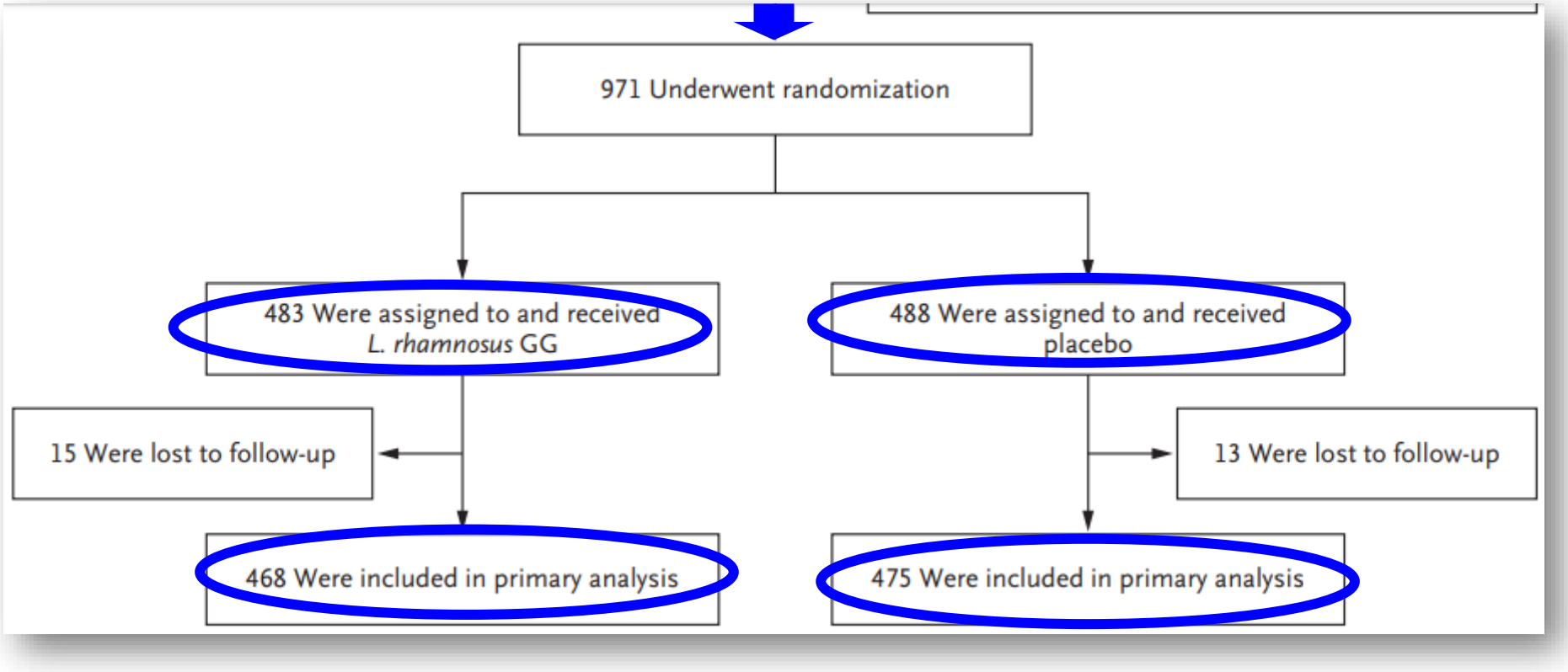
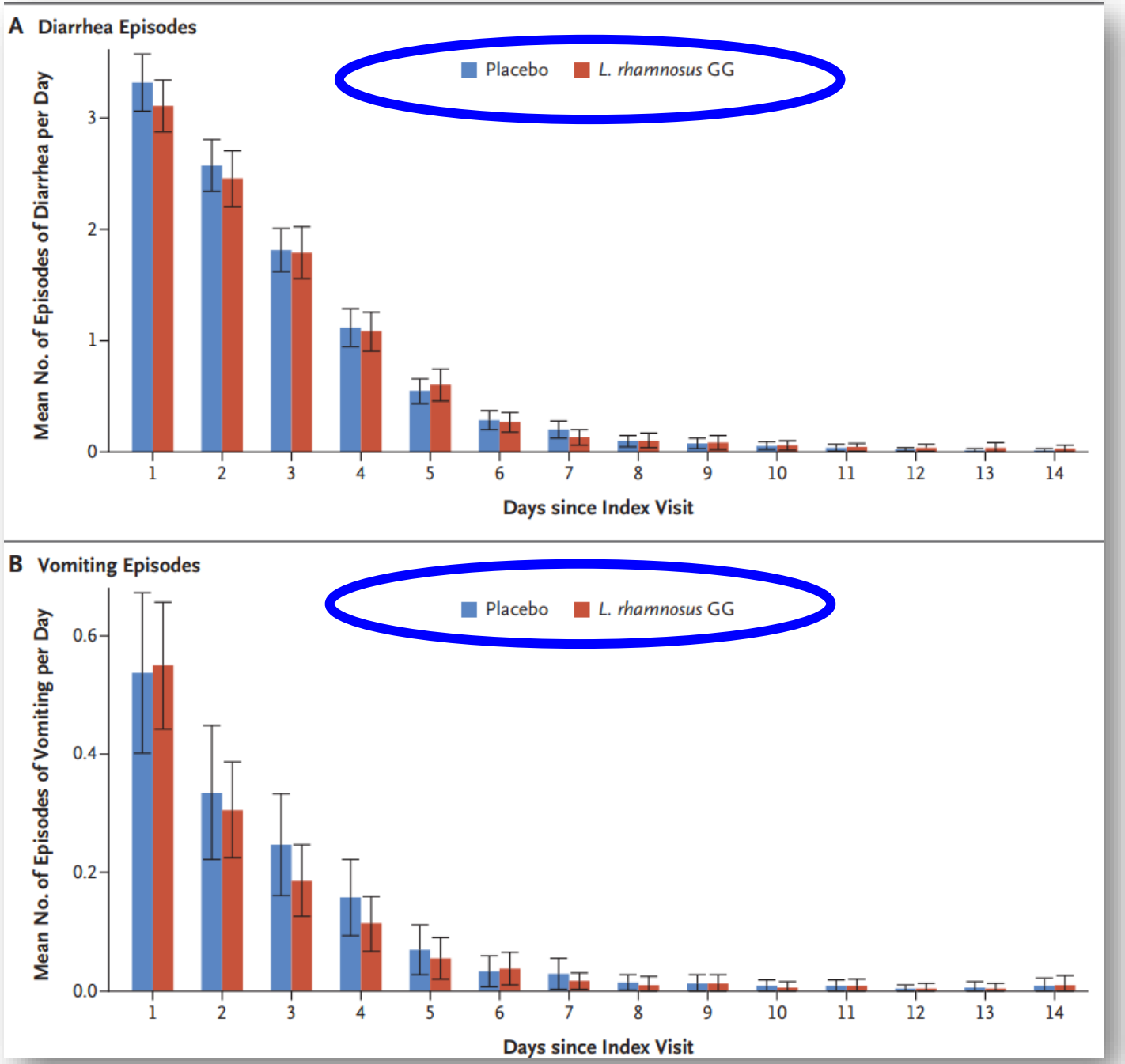
David Schnadower, M.D., M.P.H., Phillip I. Tarr, M.D., T. Charles Casper, Ph.D., Marc H. Gorelick, M.D., M.S.C.E., J. Michael Dean, M.D., Karen J. O'Connell, M.D., Prashant Mahajan, M.D., M.P.H., Adam C. Levine, M.D., M.P.H., Seema R. Bhatt, M.D., Cindy G. Roskind, M.D., Elizabeth C. Powell, M.D., Alexander 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

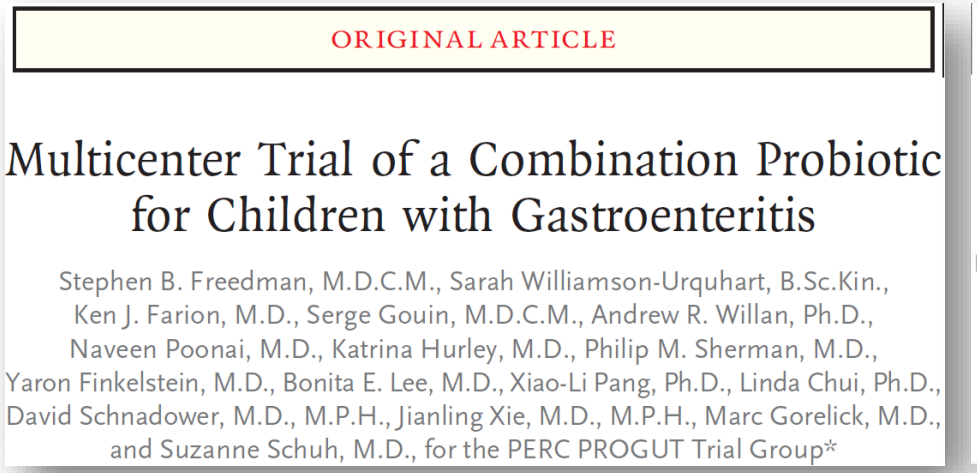


Schnadower D, N Engl J Med 2018;379:2002-14

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?

GI Epidemiology: Diseases and Clinical Methodology, 2th Edit. Edited Talley NJ. 2014 John Wiley & Sons, Ltd.pp 38-47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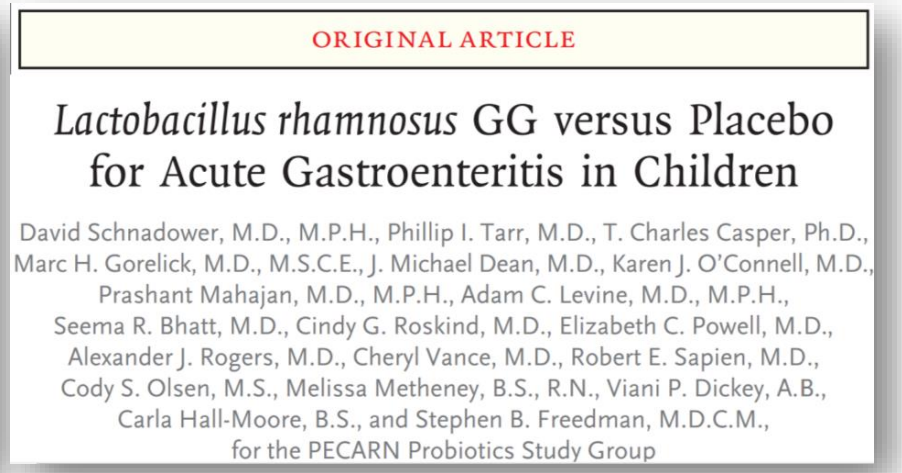
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Localización Geográfica: Canadá, USA.
Rotavirus vs Bacteriana invasiva vs Desconocida
Estudio USA (Schnadower) 2/3 vacunados contra rotavirus
Dosis $>10^{10}$ vs $<10^{10}$
Muchos había recibido antibióticos ✗
Ambos estudios iniciaron >72 horas diarrea ✗ ✗
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

Gastroenterology 2020;159:697–705

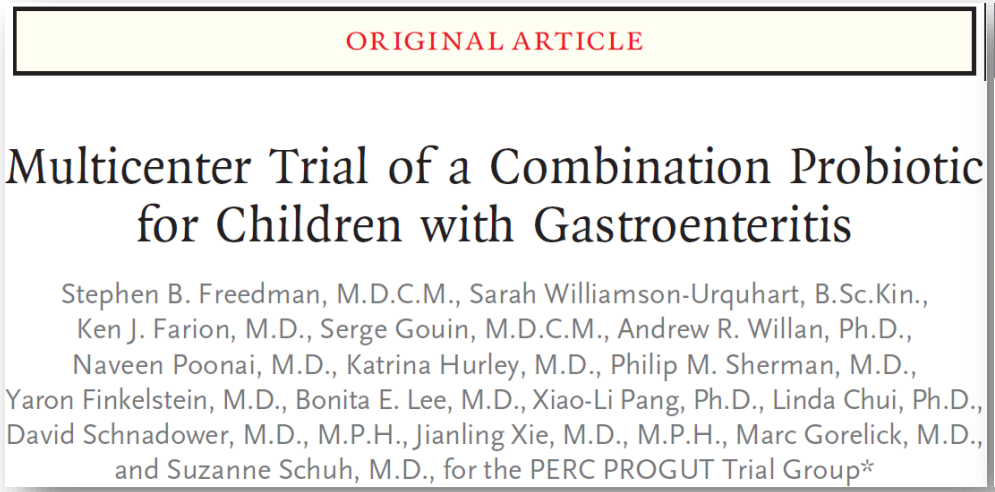
CLINICAL PRACTICE GUIDELINES

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. Morgan[9]

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.



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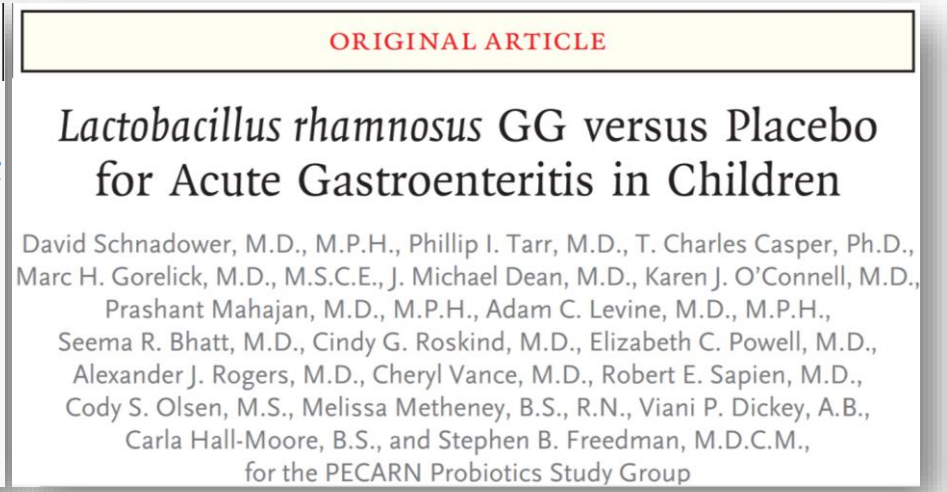

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Schnasower D, N Engl J Med 2018;379:2002-14

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


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diarrea
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

AP&T Alimentary Pharmacology & Therapeutics WILEY

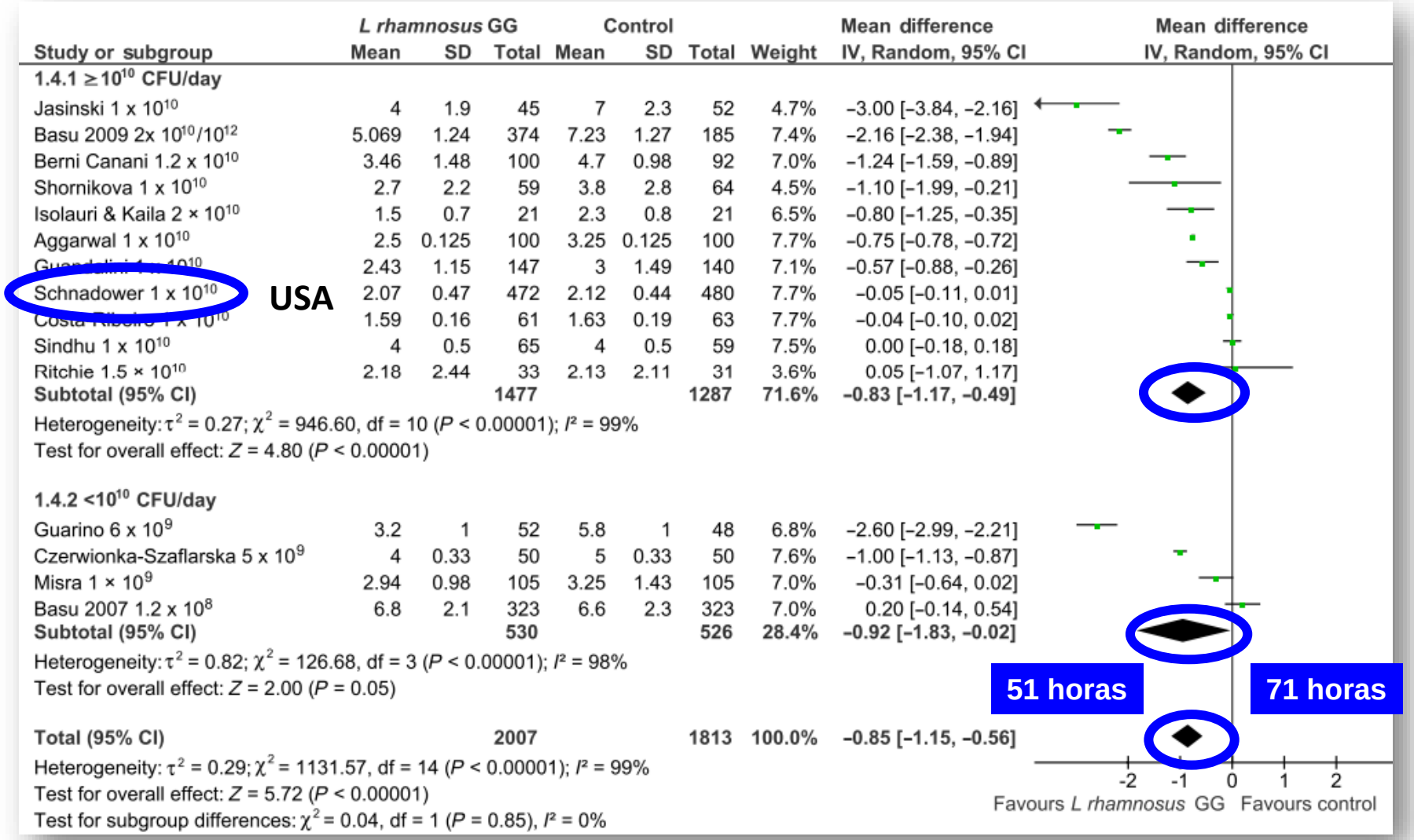
Systematic review with meta-analysis: *Lactobacillus rhamnosus* GG for treating acute gastroenteritis in children – a 2019 update

Hania Szajewska[1] | Maciej Kołodziej[1] | Dorota Gieruszczak-Białek[1] | Agata Skórka[1] | Marek Ruszczyński[1] | Raanan Shamir[2]

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

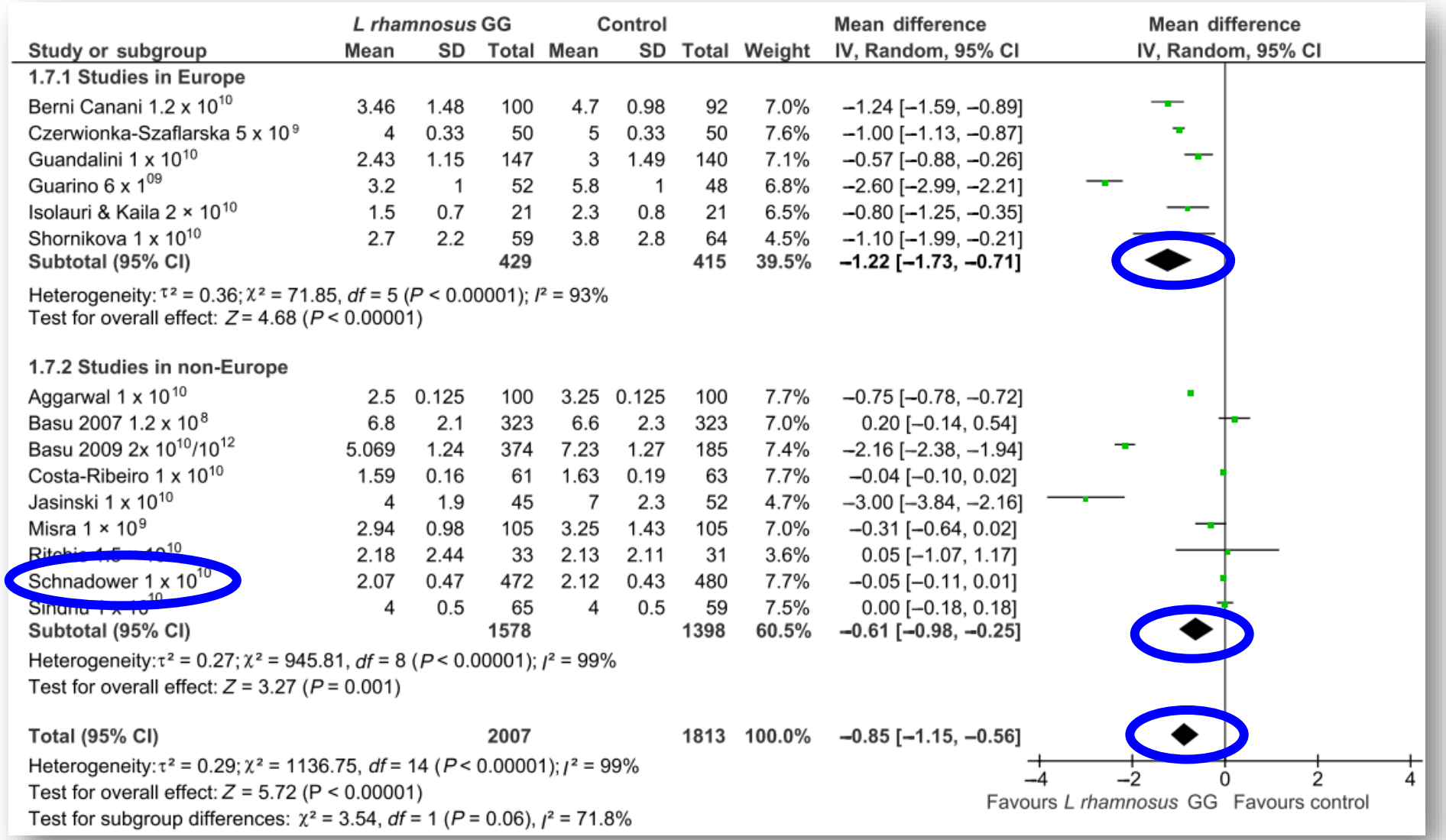
Aliment Pharmacol Ther 2019;49:1376-1384

Control de gastroenteritis aguda:
Altas dosis >/= 1.4 x 10^9 UFC o Bajas dosis versus Placebo



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

Duración de la diarrea: Europa Versus Otros sitios



Study or subgroup	*L rhamnosus* GG Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
1.7.1 Studies in Europe								
Berni Canani 1.2 x 10^{10}	3.46	1.48	100	4.7	0.98	92	7.0%	–1.24 [–1.59, –0.89]
Czerwionka-Szaflarska 5 x 10^{9}	4	0.33	50	5	0.33	50	7.6%	–1.00 [–1.13, –0.87]
Guandalini 1 x 10^{10}	2.43	1.15	147	3	1.49	140	7.1%	–0.57 [–0.88, –0.26]
Guarino 6 x 1^{09}	3.2	1	52	5.8	1	48	6.8%	–2.60 [–2.99, –2.21]
Isolauri & Kaila 2 × 10^{10}	1.5	0.7	21	2.3	0.8	21	6.5%	–0.80 [–1.25, –0.35]
Shornikova 1 x 10^{10}	2.7	2.2	59	3.8	2.8	64	4.5%	–1.10 [–1.99, –0.21]
Subtotal (95% CI)			**429**			**415**	**39.5%**	**–1.22 [–1.73, –0.71]**
Heterogeneity: $\tau^2 = 0.36$; $\chi^2 = 71.85$, $df = 5$ ($P < 0.00001$); $I^2 = 93\%$								
Test for overall effect: $Z = 4.68$ ($P < 0.00001$)								
1.7.2 Studies in non-Europe								
Aggarwal 1 x 10^{10}	2.5	0.125	100	3.25	0.125	100	7.7%	–0.75 [–0.78, –0.72]
Basu 2007 1.2 x 10^{8}	6.8	2.1	323	6.6	2.3	323	7.0%	0.20 [–0.14, 0.54]
Basu 2009 2x $10^{10}/10^{12}$	5.069	1.24	374	7.23	1.27	185	7.4%	–2.16 [–2.38, –1.94]
Costa-Ribeiro 1 x 10^{10}	1.59	0.16	61	1.63	0.19	63	7.7%	–0.04 [–0.10, 0.02]
Jasinski 1 x 10^{10}	4	1.9	45	7	2.3	52	4.7%	–3.00 [–3.84, –2.16]
Misra 1 × 10^{9}	2.94	0.98	105	3.25	1.43	105	7.0%	–0.31 [–0.64, 0.02]
Ritchi 1.5 10^{10}	2.18	2.44	33	2.13	2.11	31	3.6%	0.05 [–1.07, 1.17]
Schnadower 1 x 10^{10}	2.07	0.47	472	2.12	0.43	480	7.7%	–0.05 [–0.11, 0.01]
Sindhu 1 x 10^{10}	4	0.5	65	4	0.5	59	7.5%	0.00 [–0.18, 0.18]
Subtotal (95% CI)			**1578**			**1398**	**60.5%**	**–0.61 [–0.98, –0.25]**
Heterogeneity: $\tau^2 = 0.27$; $\chi^2 = 945.81$, $df = 8$ ($P < 0.00001$); $I^2 = 99\%$								
Test for overall effect: $Z = 3.27$ ($P = 0.001$)								
Total (95% CI)			**2007**			**1813**	**100.0%**	**–0.85 [–1.15, –0.56]**
Heterogeneity: $\tau^2 = 0.29$; $\chi^2 = 1136.75$, $df = 14$ ($P < 0.00001$); $I^2 = 99\%$								
Test for overall effect: $Z = 5.72$ ($P < 0.00001$)								
Test for subgroup differences: $\chi^2 = 3.54$, $df = 1$ ($P = 0.06$), $I^2 = 71.8\%$								

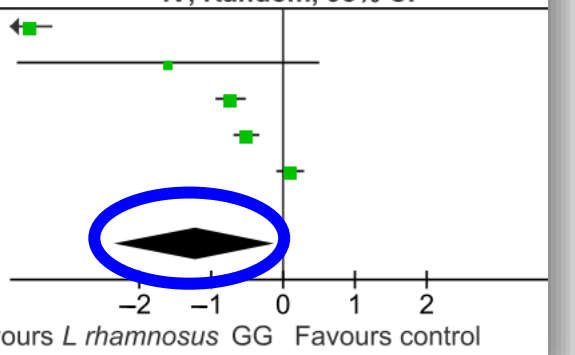
Szajewska H, et al Aliment Pharmacol Ther 2019;49:1376-1384

Duración Hospitalización

Study or subgroup	*L rhamnosus* GG Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
Basu 2009 2x 10^{10}/10^{12}	6.22	1.16	374	9.75	2.06	185	21.7%	–3.53 [–3.85, –3.21]
Shornikova 1 x 10^{10}	7.6	5.6	59	9.2	6.3	64	12.4%	–1.60 [–3.70, 0.50]
Guandalini 1 x 10^{10}	3.28	0.93	147	4.01	0.89	140	21.9%	–0.73 [–0.94, –0.52]
Aggarwal 1 x 10^{10}	3.33	0.56	87	3.84	0.65	88	22.0%	–0.51 [–0.69, –0.33]
Basu 2007 1.2 x 10^{8}	9.3	1.3	323	9.2	1.2	323	22.0%	0.10 [–0.09, 0.29]
Total (95% CI)			**990**			**800**	**100.0%**	**–1.22 [–2.33, –0.10]**

Heterogeneity: $\tau^2 = 1.47$; $\chi^2 = 372.86$, $df = 4$ ($P < 0.00001$); $I^2 = 99\%$

Test for overall effect: $Z = 2.13$ ($P = 0.03$)



Disminuye 29 horas

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

AP&T Alimentary Pharmacology & Therapeutics WILEY

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

Hania Szajewska[1] | Maciej Kołodziej[1] | Dorota Gieruszczak-Białek[1] | Agata Skórka[1] | Marek Ruszczyński[1] | Raanan Shamir[2]

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

Aliment Pharmacol Ther 2019;49:1376-1384

World Journal of Gastroenterology

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

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META-ANALYSIS

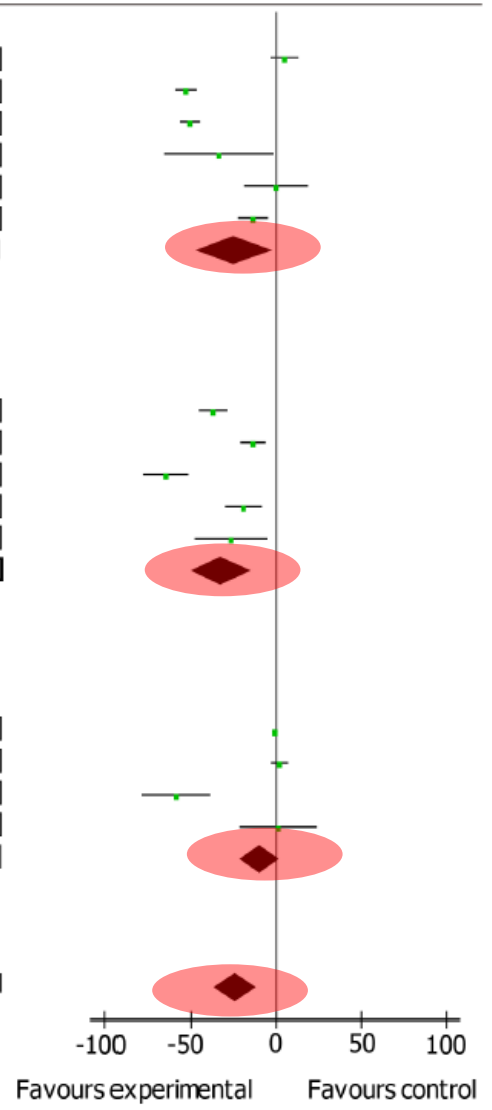
Efficacy of *Lactobacillus rhamnosus* GG in treatment of acute pediatric diarrhea: A systematic review with meta-analysis

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

C

Study or subgroup	LGG Mean	LGG SD	LGG Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean difference IV, Random, 95%CI
2.14.1 Asia								
Basu, S. 2007	163.2	50.4	323	158.4	55.2	323	7.1%	4.80 [-3.35, 12.95]
Basu, S. 2009 a	120.5	31.7	188	173.5	30.5	185	7.2%	-53.00 [-59.31, -46.69]
Basu, S. 2009 b	122.9	27.8	186	173.5	30.5	185	7.2%	-50.60 [-56.54, -44.66]
Pant, A. R. 1996	45.6	14.4	14	79.2	55.2	12	4.9%	-33.60 [-65.73, -1.47]
Sindhu, K. N. 2014	96.0	53.3	65	96.0	53.3	59	6.3%	0.00 [-18.78, 18.78]
Sunny, A. 2014	58.3	27.6	100	71.9	35.8	100	7.0%	-13.60 [-22.46, -4.74]
Subtotal (95%CI)			**876**			**864**	**39.6%**	**-24.42 [-47.01, -1.82]**
Heterogeneity: Tau² = 737.04; Chi² = 184.79, *df* = 5 (*P* < 0.00001); I^2 = 97%								
Test for overall effect: *Z* = 2.12 (*P* = 0.03)								
2.14.2 Europe								
Canani, R. B. 2007	78.5	35.52	100	115.5	23.53	92	7.1%	-37.00 [-45.46, -28.54]
Guandalini, S. 2000	58.3	27.6	147	71.9	35.8	140	7.1%	-13.60 [-21.02, -6.18]
Guarino, A. 1997	76.8	34.61	52	141.6	33.26	48	6.7%	-64.80 [-78.10, -51.50]
Isolauri, E. 1994	36.0	16.8	21	55.2	19.2	21	6.9%	-19.20 [-30.11, -8.29]
Shornikova, A. V. 1997	64.8	52.8	59	91.2	67.2	64	6.0%	-26.40 [-47.67, -5.13]
Subtotal (95%CI)			**379**			**365**	**33.8%**	**-32.02 [-49.26, -14.79]**
Heterogeneity: Tau² = 344.32; Chi² = 50.72, *df* = 4 (*P* < 0.00001); I^2 = 92%								
Test for overall effect: *Z* = 3.64 (*P* = 0.0003)								
2.14.3 other continents								
Costa, R. H. 2003	38.3	3.78	61	39.1	4.6	63	7.3%	-0.80 [-2.28, 0.68]
David, S. 2018	54.3	41.3	472	52.4	37.7	480	7.2%	1.90 [-3.13, 6.93]
Jasinski. C. 2002	74.64	47.76	45	133.44	53.76	52	6.1%	-58.80 [-79.00, -38.60]
Ritchie, B. K. 2010	52.4	49.8	33	51.2	42.4	31	5.9%	1.20 [-21.42, 23.82]
Subtotal (95%CI)			**611**			**626**	**26.5%**	**-9.35 [-20.77, 2.07]**
Heterogeneity: Tau² = 95.75; Chi² = 32.79, *df* = 3 (*P* < 0.00001); I^2 = 91%								
Test for overall effect: *Z* = 1.61 (*P* = 0.11)								
Total (95%CI)			**1866**			**1855**	**100%**	**-24.02 [-36.58, -11.45]**
Heterogeneity: Tau² = 563.68; Chi² = 661.03, *df* = 14 (*P* < 0.00001); I^2 = 98%								
Test for overall effect: *Z* = 3.75 (*P* = 0.0002)								
Test for subgroup differences: Chi² = 5.04, *df* = 2 (*P* = 0.08), I^2 = 60.4%								



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

Número deposiciones y consistencia heces

D

Study or subgroup	LGG Mean	LGG SD	LGG Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean difference IV, Fixed, 95%CI
David, S. 2018	49.7	50.07	483	50.9	46.81	488	9.2%	-1.20 [-7.30, 4.90]
Nixon, A. F. 2012	60.0	54.81	77	74.0	57.04	78	1.1%	-14.00 [-31.61, 3.61]
Sunny, A. 2014	36.0	4.44	100	42.0	8.89	100	89.7%	-6.00 [-7.95, -4.05]
Total (95%CI)			**660**			**666**	**100%**	**-5.65 [-7.49, -3.80]**

Heterogeneity: Chi² = 3.03, *df* = 2 (*P* = 0.22); I^2 = 34%

Test for overall effect: *Z* = 6.00 (*P* < 0.00001)

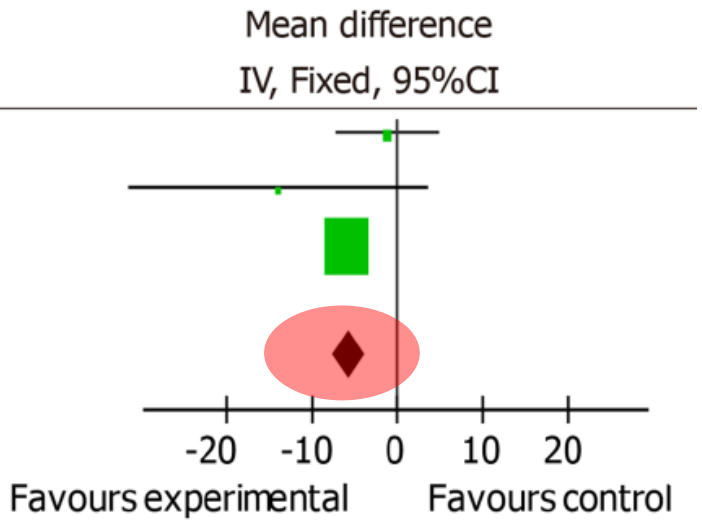


Figure 4 *Lactobacillus* GG *vs* control with regard to stool number and consistency. A: The average stool number per day (high dose and low dose); B: S frequency on day 2; C: Stool frequency on day 3; D: The mean time to improvement in stool consistency. LGG: *Lactobacillus rhamnosus* GG; CI: Confidence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

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

Lactobacillus GG vs Control

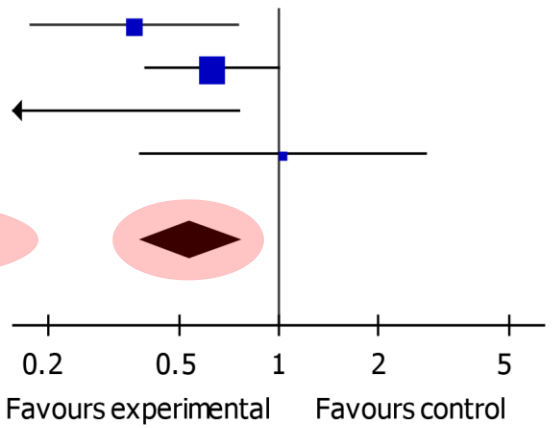
Diarrea > 3días

A

Study or subgroup	LGG Events	LGG Total	Placebo Events	Placebo Total	Weight	Odds ratio M-H, Fixed, 95%CI
Costa, R.H. 2003	31	65	45	63	28.9%	0.36 [0.18, 0.76]
Guandalini, S. 2000	78	147	90	140	52.2%	0.63 [0.39, 1.01]
Isolauri, E.1994	2	21	9	21	9.8%	0.14 [0.03, 0.76]
Ritchie, B. K. 2010	13	33	12	31	9.1%	1.03 [0.38, 2.81]
Total (95%CI)		**266**		**255**	**100%**	**0.54 [0.38, 0.77]**
Total events	124		156			

Heterogeneity: Chi² = 5.51, *df* = 3 (*P* = 0.14); I^2 = 46%

Test for overall effect: *Z* = 3.39 (*P* = 0.0007)



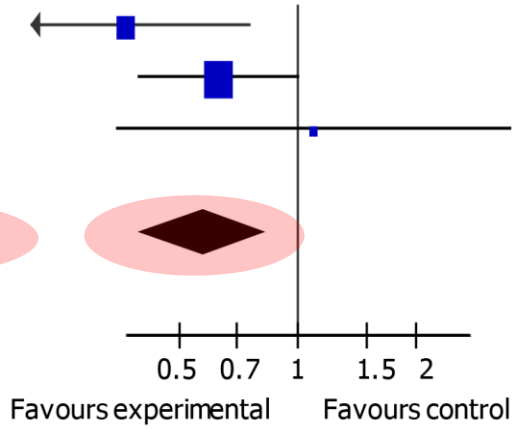
Diarrea > 4 días

B

Study or subgroup	LGG Events	LGG Total	Placebo Events	Placebo Total	Weight	Odds ratio M-H, Fixed, 95%CI
Costa, R.H. 2003	31	65	45	63	32.9%	0.36 [0.18, 0.76]
Guandalini, S. 2000	78	147	90	140	59.6%	0.63 [0.39, 1.01]
Ritchie, B. K. 2010	8	33	7	31	7.5%	1.10 [0.34, 3.50]
Total (95%CI)		**245**		**234**	**100%**	**0.58 [0.40, 0.84]**
Total events	117		142			

Heterogeneity: Chi² = 2.81, *df* = 2 (*P* = 0.24); I^2 = 29%

Test for overall effect: *Z* = 2.89 (*P* = 0.004)



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

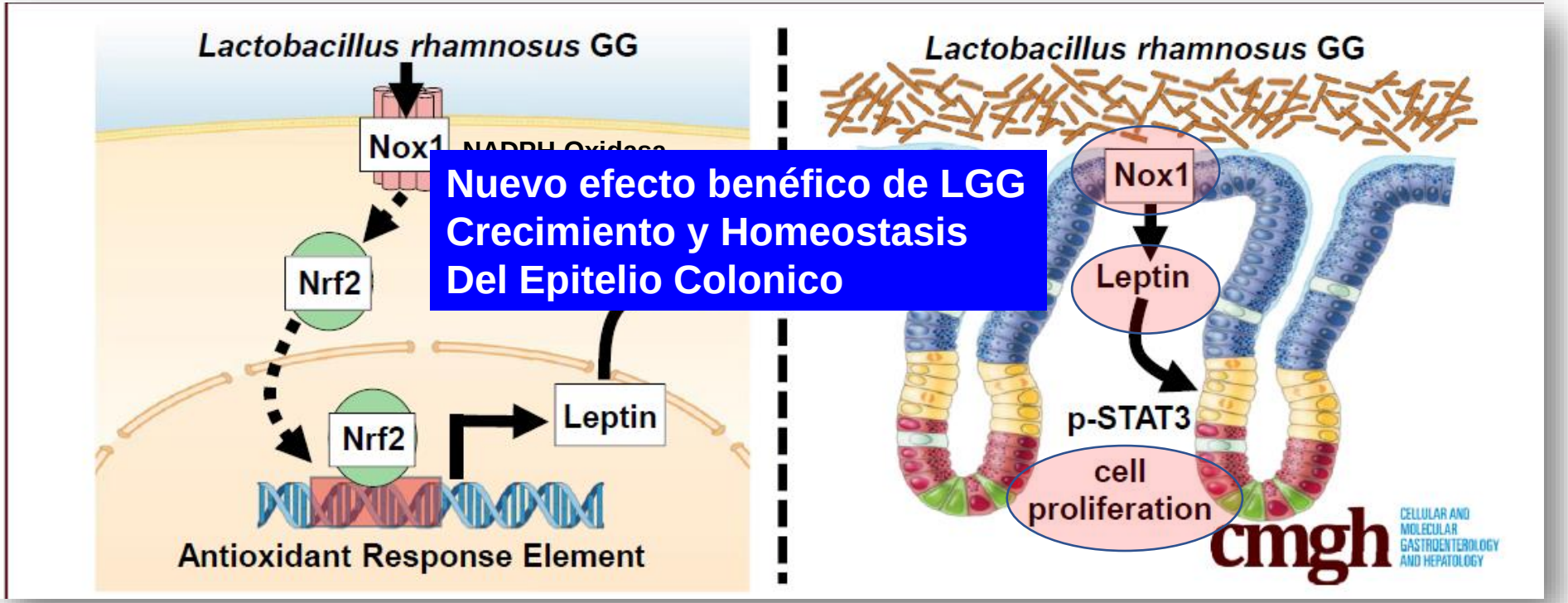
Efectos recientemente Identificados de LGG

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]

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

Ratones ingestión oral de LGG



Nuevo efecto benéfico de LGG
Crecimiento y Homeostasis
Del Epitelio Colonico

Cell Mol Gastroenterol Hepatol 2020;9:627–639

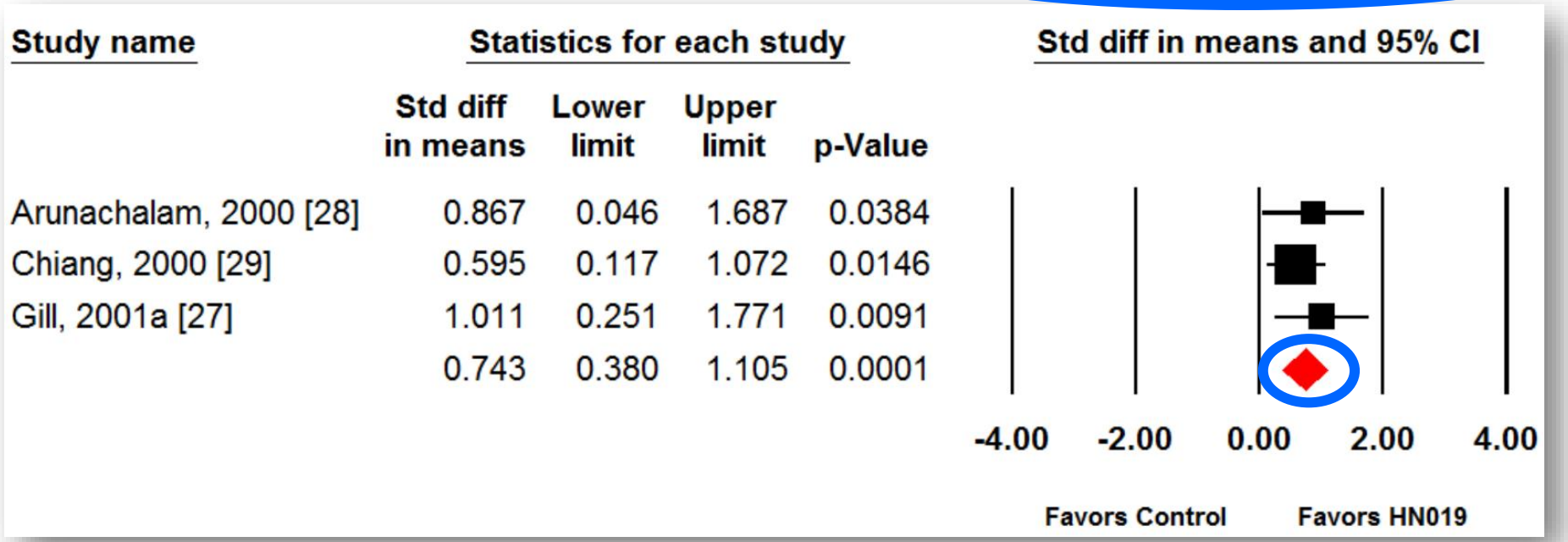
Bifidobacterium animalis (BB-12) Múltiples investigacionres

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



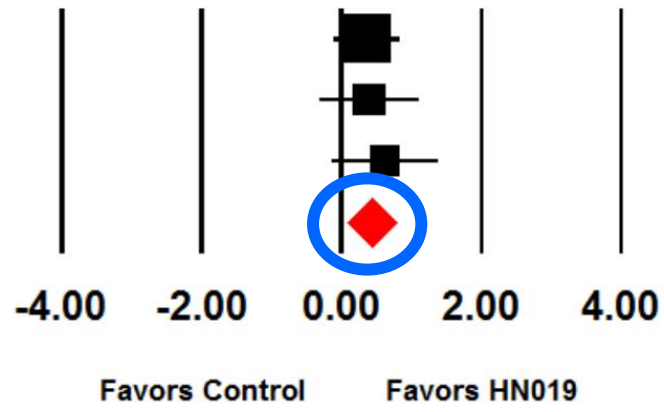
Nutrients 2017, 9, 191; doi:10.3390/nu9030191

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

Study name	Std diff in means	Lower limit	Upper limit	p-Value
Chiang, 2000 [29]	0.360	-0.112	0.831	0.1348
Gill, 2001a [27]	0.396	-0.326	1.119	0.2826
Gill, 2001b [26]	0.630	-0.129	1.388	0.1040
	0.426	0.075	0.776	0.0172



Nutrients 2017, 9, 191; doi:10.3390/nu9030191

LGG +
Bifidobacterium animalis (BB-12)
>300 publicaciones,
>130 estudios clínicos

Jungersen M, Microorganisms 2014;2:92-100

RESEARCH PAPER/REPORT

OPEN ACCESS Check for updates

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

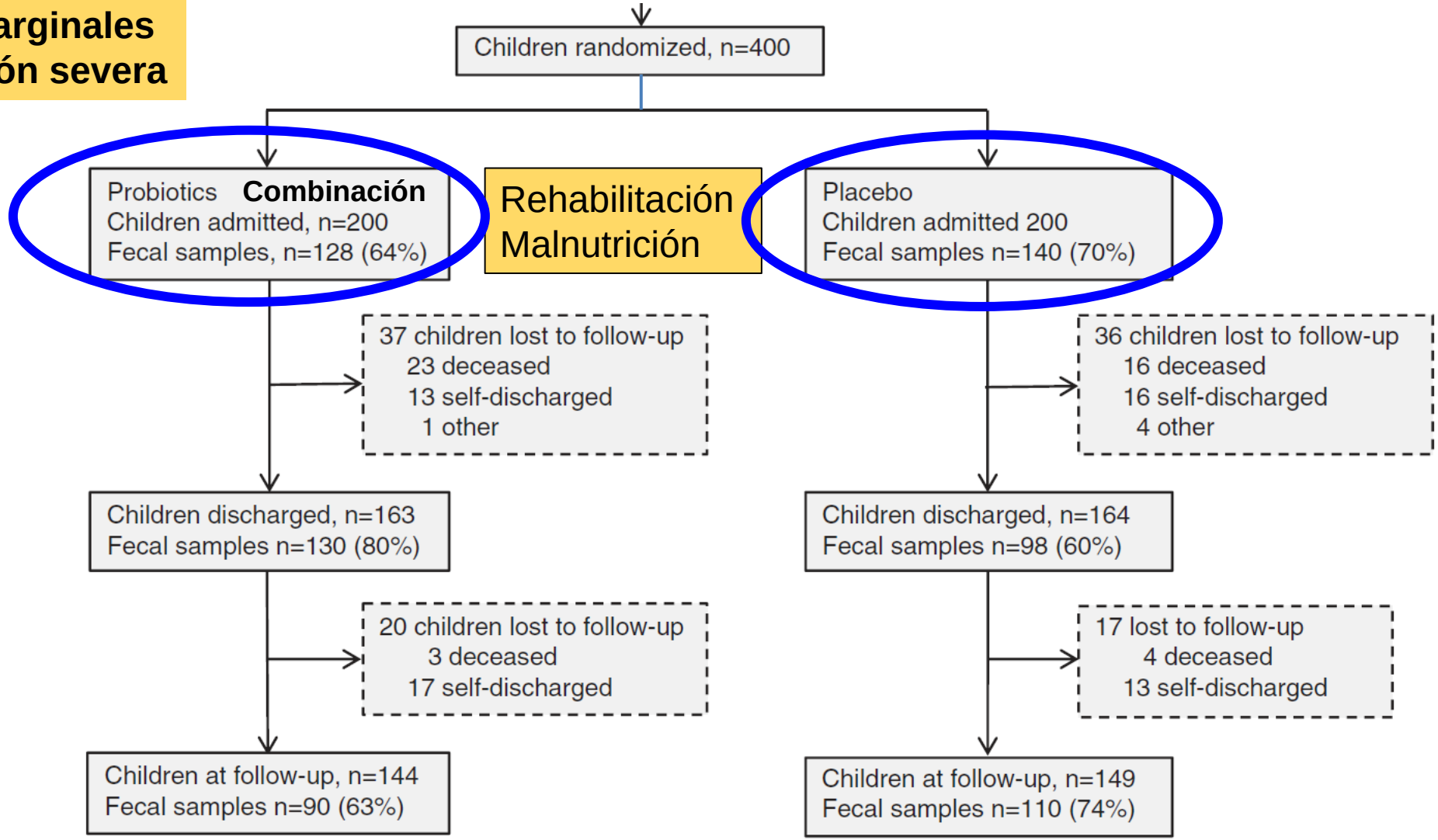
Globalmente 45% muertes

Secuelas Intelectuales Productividad

Disbiosis: Desencadenar o Mantener desnutrición aguda
Disminuye diversidad microbiota

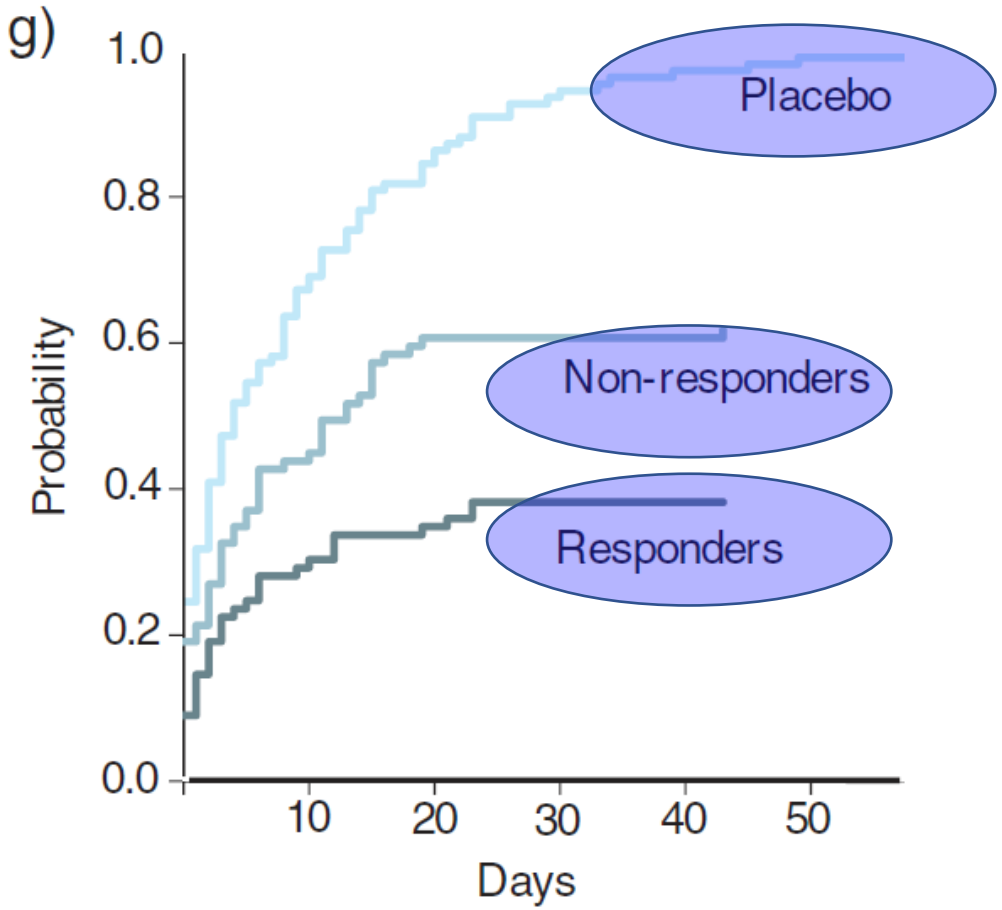
Gut Microbes 2020;11:855-67

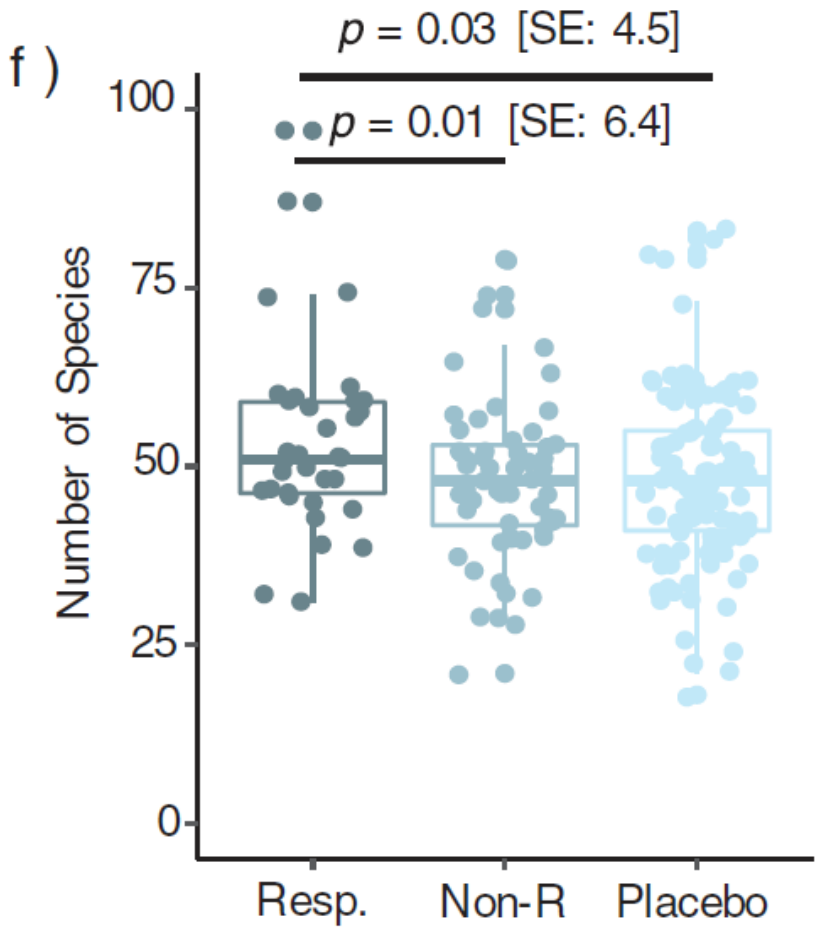
Barrios marginales
Malnutrición severa



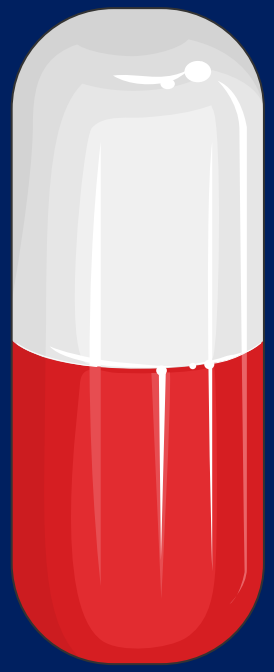
Castro-Mejía JL, et al, Gut Microbes 2020;11:855-67

Redujo la incidencia acumulativa de diarrea en el futuro





Castro-Mejía JL, et al, Gut Microbes 2020;11:855-67



Lactobacillus rhamnosus GG
LGG, 3.25 x 10^9 UFC

+

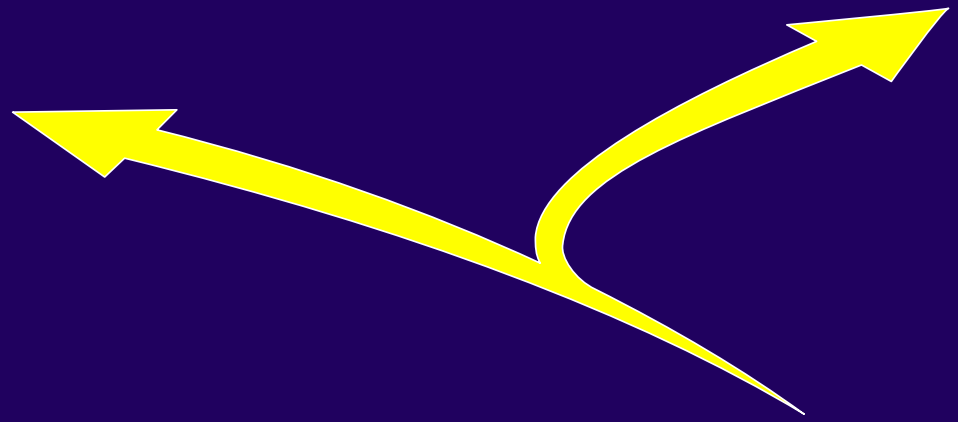
Bifidocaterium animalis lactis
BB-12, 3.25 X 10^9 UFC

Diarrea aguda y asociada a Antibióticos
Dosis recomendada: 1 x 10^{10}
3 capsulas/día por 5-10 días o MAS ?(RN-99 años)
Profilaxis diarrea por antibióticos
Dosis recomendada: 1 x 10^9
1cápsula diaria durante antibióticos 2h antes

LGG probiótico más estudiado en EDA mundo

El BB12 más estudiado Fortalecer sistema inmune

Probiótico mayor Adherencia /resistencia en el intestino



Sinergismo

➢ Desplazamiento Patógenos

BIOTIPLUS

Lactobacillus rhamnosus GG
LGG 3.25 x 10^9 UFC

+

Bifidocaterium animalis lactis
BB-12 3.25 X 10^9 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%

Reker D, et al, Sci Transl Med 2019;11:eaau6753

SCIENCE TRANSLATIONAL MEDICINE | PERSPECTIVE

PHARMACOLOGY

"Inactive" ingredients in oral medications

Daniel Reker[1,2,3]*, Steven M. Blum[1,4,5]*, Christoph Steiger[1,2,3], Kevin E. Anger[4], Jamie M. Sommer[6], John Fanikos[6], Giovanni Traverso[1,2,3,4,7]†

38 "compuestos inactivos"

Pueden dar alergias

Reker D, et al, Sci Transl Med 2019;11:eaau6753

Diosmectita

Diosmectita = medicamento

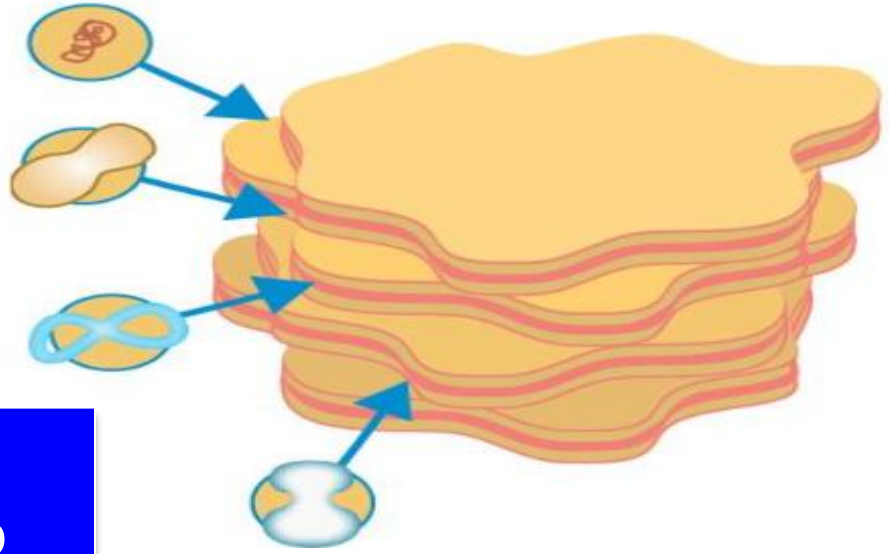
Diosmectita purificada

Diosmectita = medicamento

Nov 1975

Diosmectita

Adsorbe Toxinas



Arcilla natural
Hojas finas de silicato de Aluminio y magnesio

Fortalece la capa de moco Destruida por patógenos

Impide llegada de toxinas Células intestinales

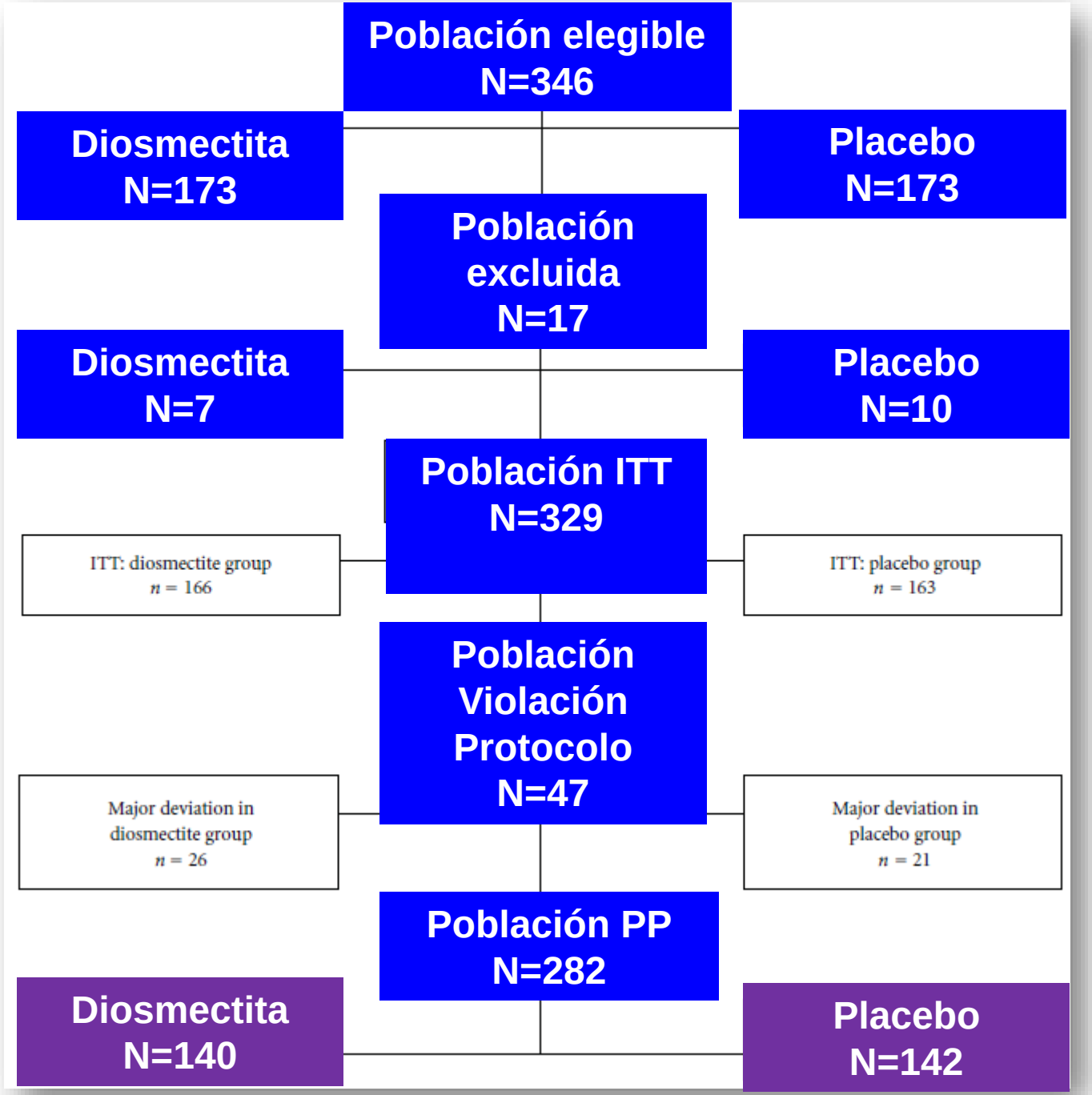
Evita el estímulo para Secreción H2O electrólitos

Dupont C, Ped Drugs 2009;11:89-99
Soares JA, J Anim Sci Biotechn 2013; 452

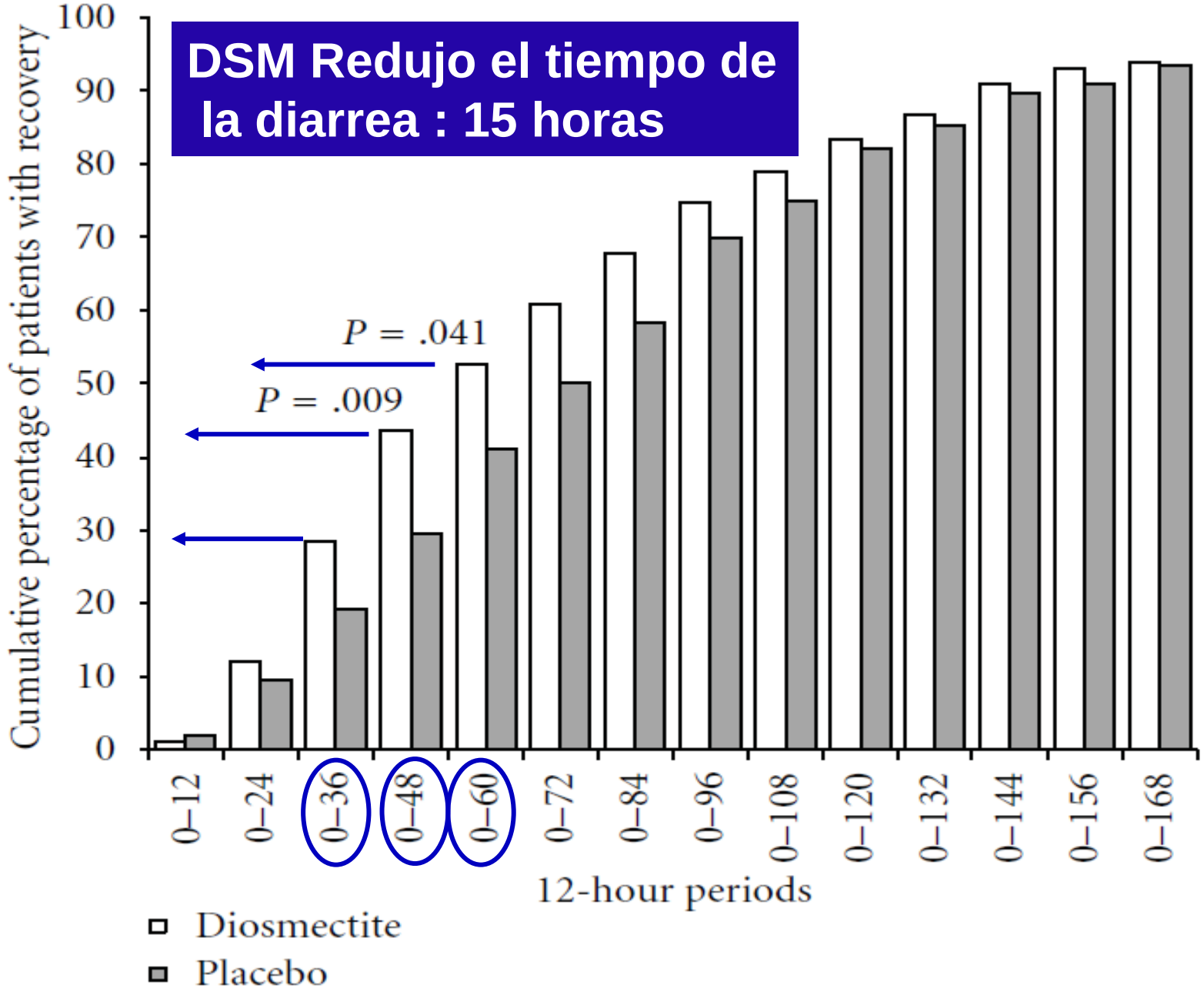
Research Article

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


Población elegible
N=346
Diosmectita
N=173
Placebo
N=173
Población
excluida
N=17
Diosmectita
N=7
Placebo
N=10
Población ITT
N=329
ITT: diosmectite group
n = 166
ITT: placebo group
n = 163
Población
Violación
Protocolo
N=47
Major deviation in
diosmectite group
n = 26
Major deviation in
placebo group
n = 21
Población PP
N=282
Diosmectita
N=140
Placebo
N=142

% 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**

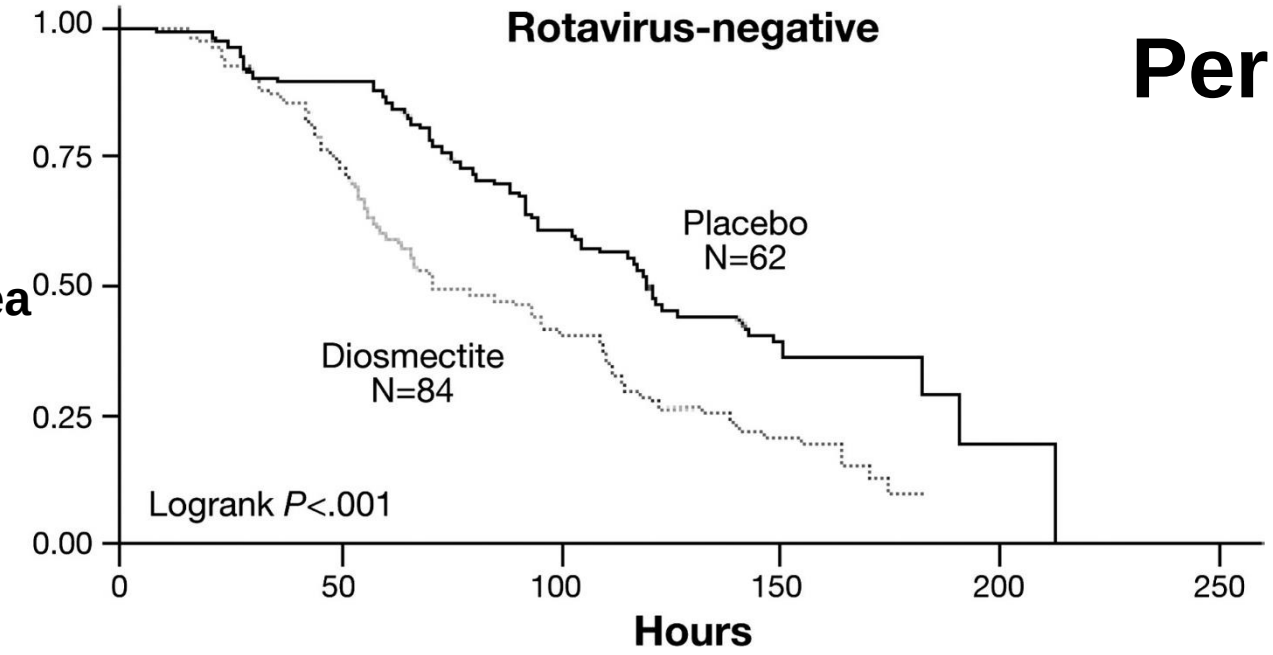
Intervenciòn: Hidrataciòn oral + Placebo O Diosmectita

6 gr/dìa: 1-12 meses: 3 dìas
12 gr/dìa: 12-36 meses: 3 dìas
Mitad de la dosis hasta la recuperaciòn

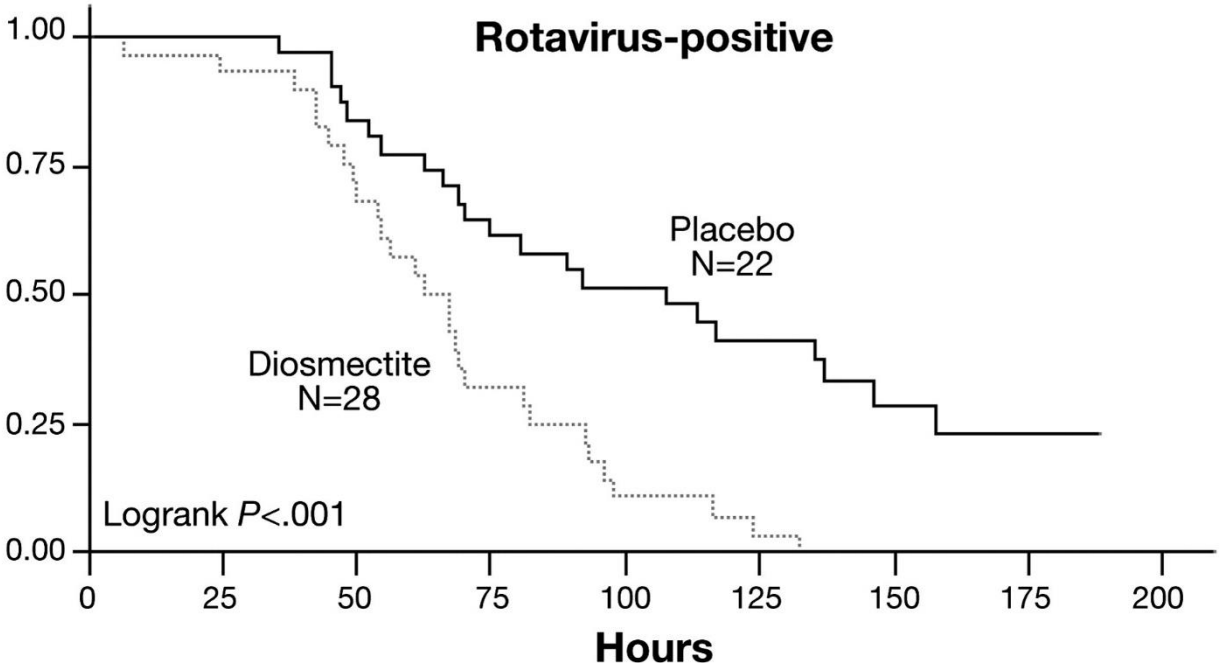
Clin Gastroenterol Hepatol 2009;7:456–462

Perú

Duración De la diarrea



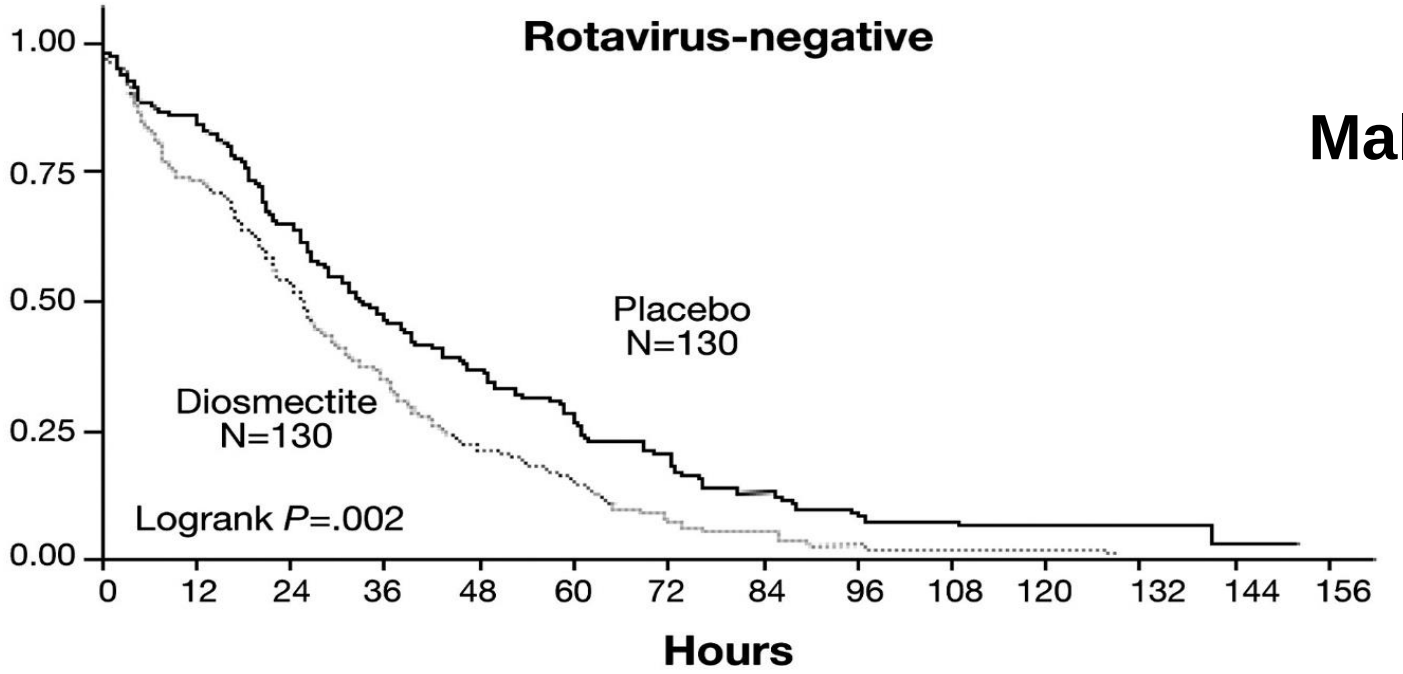
Duración De la diarrea



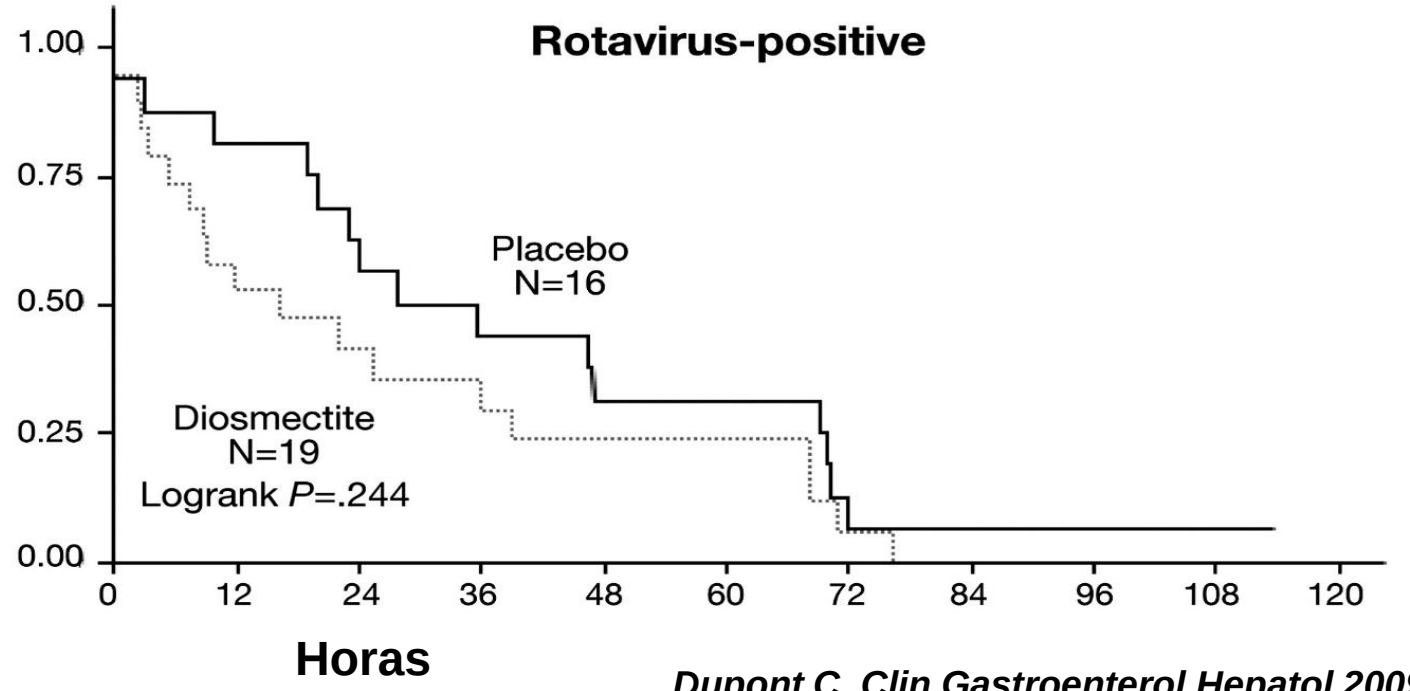
*Dupont C, Clin Gastroenterol Hepatol 2009;*7:456-462

Malasia

Duración De la diarrea



Duración De la diarrea



*Dupont C, Clin Gastroenterol Hepatol 2009;*7:456-462

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.

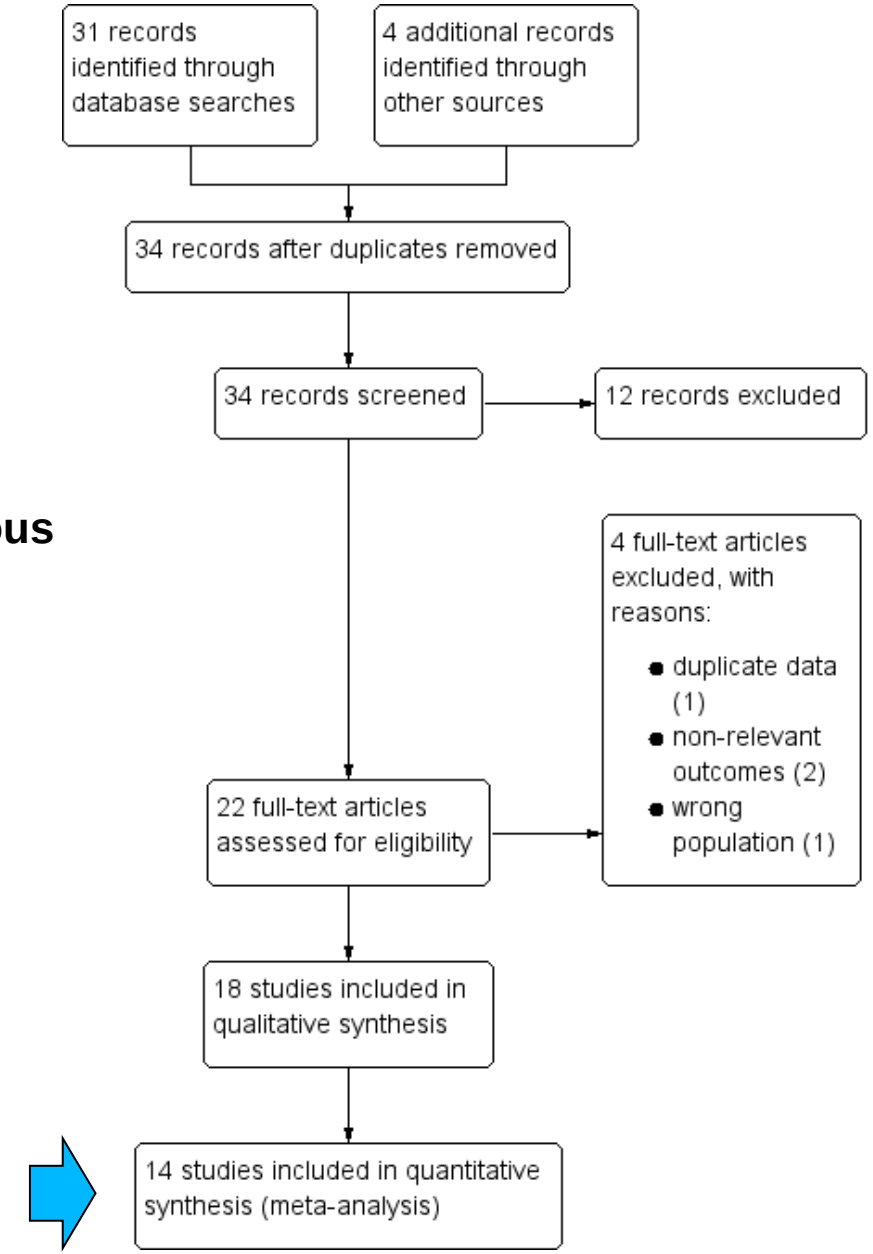
Smectite for acute infectious diarrhoea in children.

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



Cochrane Database of Systematic Reviews
25 APR 2018 DOI: 10.1002/14651858.CD011526.pub2

Smectite for acute infectious diarrhoea in children
Duraciòn promedio horas

	Smectite			Control				Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean [hours]	SD [hours]	Total	Mean [hours]	SD [hours]	Total	Weight	IV, Random, 95% CI [hours]	IV, Random, 95% CI [hours]	A B C D E F G
Dupont 2009a	68.17	29.92	126	118.92	33.92	132	7.0%	-50.75 [-58.55, -42.95]		+ + + + - + +
Dupont 2009b	24.2	21.5	142	32.4	25.33	144	7.4%	-8.20 [-13.64, -2.76]		+ + + + + + +
Gilbert 1991	77.28	24.5	9	97.9	32.12	13	3.9%	-20.62 [-44.31, 3.07]		? ? + ? + ? +
Guarino 2001	96	21	406	119	23	398	7.7%	-23.00 [-26.05, -19.95]		- - - - ? ? +
Lachaux 1986	42	19.1972	16	61.34	30.7564	18	5.1%	-19.34 [-36.38, -2.30]		+ ? + ? + ? +
Madkour 1993	54.1	15.7643	45	72.9	13.2822	45	7.3%	-18.80 [-24.82, -12.78]		+ + + + + ? +
Mujawar 2012	64.34	14.86	58	82.37	21.4	59	7.2%	-18.03 [-24.70, -11.36]		- - - - + ? +
Narkeviciute 2002	42.3	24.7	28	61.8	33.9	26	5.3%	-19.50 [-35.42, -3.58]		- - - - + ? +
Pieścik-Lech 2013	48	12	44	48	6	37	7.6%	0.00 [-4.04, 4.04]		+ + + + + ? +
Pociecha 1998a	79.44	12	18	110.64	3.84	19	7.4%	-31.20 [-37.01, -25.39]		? ? - - + ? ?
Pociecha 1998b	78.48	12	34	111.12	3.84	36	7.6%	-32.64 [-36.86, -28.42]		? ? - - + ? ?
Rehman 2013	58.93	30.48	99	76.51	35.32	97	6.8%	-17.58 [-26.82, -8.34]		+ ? + + + ? +
Vivatvakin 1992	43.3	25.11	32	84.7	48.5	30	4.6%	-41.40 [-60.81, -21.99]		- ? - - + ? +
Widiasa 2009	39	2.03	34	70.6	3.78	34	7.8%	-31.60 [-33.04, -30.16]		+ + + + + ? +
Zong 1997	48.72	5.16	20	84.48	10.8	10	7.2%	-35.76 [-42.83, -28.69]		? ? - - + ? +
Total (95% CI)			**1111**			**1098**	**100.0%**	**-24.38 [-30.91, -17.85]**		

Heterogeneity: Tau² = 141.75; Chi² = 335.72, df = 14 (P < 0.00001); I² = 96%
Test for overall effect: Z = 7.32 (P < 0.00001)

-50 -25 0 25 50
Favours smectite Favours control

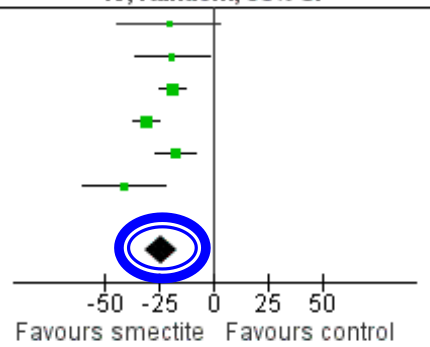
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective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

Cochrane Database of Systematic Reviews
25 APR 2018 DOI: 10.1002/14651858.CD011526.pub2

Smectite para diarrea aguda infeciosa en niños < 2 años
Duraciòn

Study or Subgroup	Smectite Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Gilbert 1991	77.28	24.5	9	97.9	32.12	13	7.2%	-20.62 [-44.31, 3.07]
Lachaux 1986	42	19.1972	16	61.34	30.7564	18	11.4%	-19.34 [-36.38, -2.30]
Madkour 1993	54.1	15.7643	45	72.9	13.2822	45	25.5%	-18.80 [-24.82, -12.78]
Pociecha 1998a	79.44	12	18	110.64	3.84	19	25.8%	-31.20 [-37.01, -25.39]
Rehman 2013	58.93	30.48	99	76.51	35.32	97	20.6%	-17.58 [-26.82, -8.34]
Vivatvakin 1992	43.3	25.11	32	84.7	48.5	30	9.6%	-41.40 [-60.81, -21.99]
Total (95% CI)			**219**			**222**	**100.0%**	**-24.11 [-31.35, -16.87]**

Heterogeneity: Tau² = 44.15; Chi² = 14.06, df = 5 (P = 0.02); I² = 64%
Test for overall effect: Z = 6.52 (P < 0.00001)



Risk of bias legend
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(**B**) Allocation concealment (selection bias)
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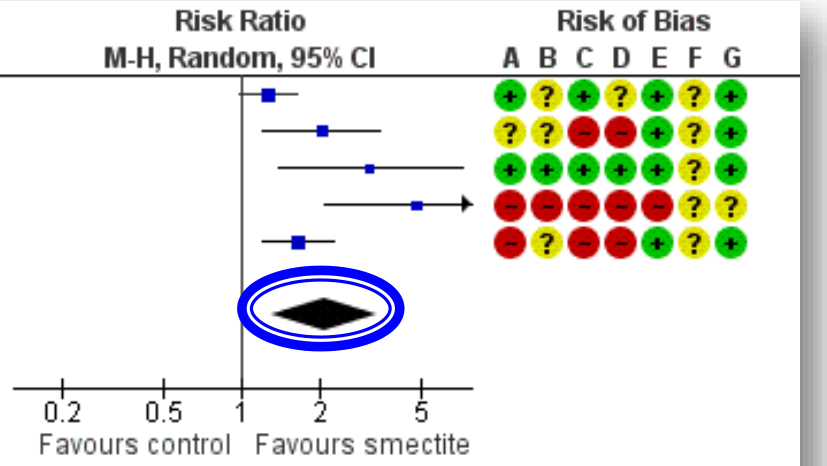
(**G**) Other bias

Cochrane Database of Systematic Reviews
25 APR 2018 DOI: 10.1002/14651858.CD011526.pub2

Smectite para resoluciòn clìnica al Tercer dìa de iniciar el tratamiento

Study or Subgroup	Smectite Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Lachaux 1986	16	16	14	18	25.1%	1.27 [0.98, 1.66]
Lexomboon 1994	24	34	11	32	20.5%	2.05 [1.21, 3.47]
Madkour 1993	19	45	6	45	15.1%	3.17 [1.40, 7.19]
Osman 1992	24	30	5	30	15.1%	4.80 [2.11, 10.90]
Vivatvakin 1992	30	32	17	30	24.2%	1.65 [1.19, 2.29]
Total (95% CI)		**157**		**155**	**100.0%**	**2.10 [1.30, 3.39]**
Total events	113		53			

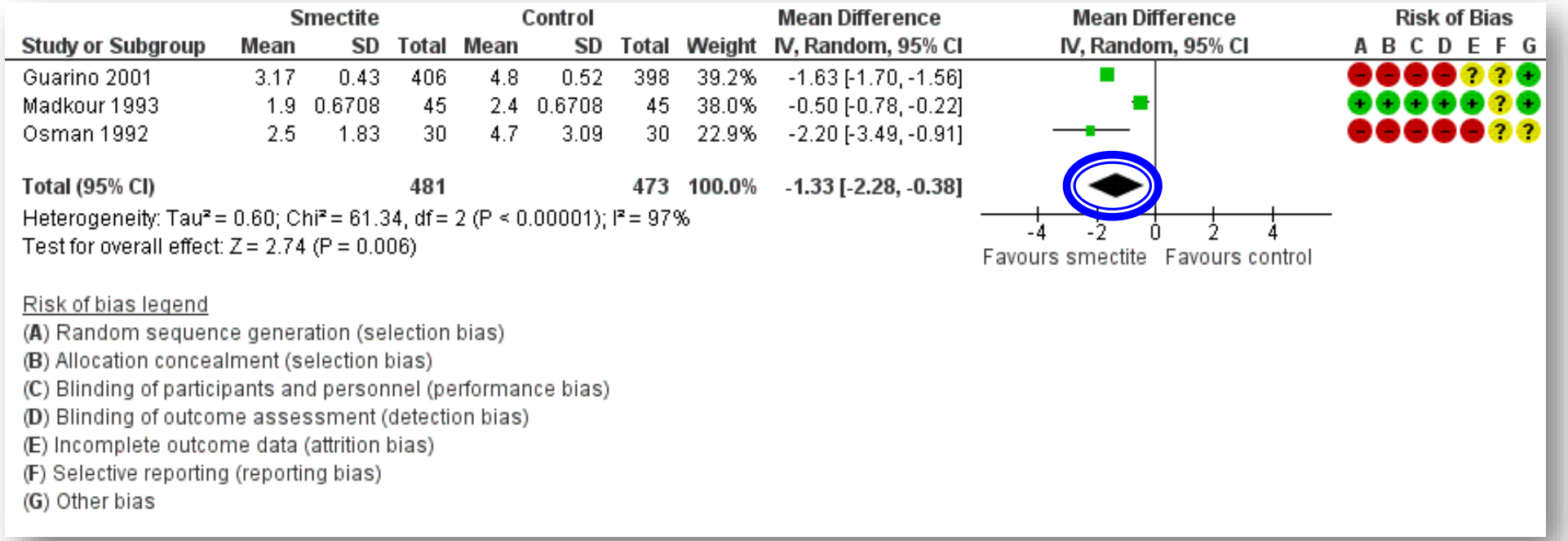
Heterogeneity: Tau² = 0.22; Chi² = 20.93, df = 4 (P = 0.0003); I² = 81%
Test for overall effect: Z = 3.03 (P = 0.002)



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

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 dìa



Study or Subgroup	Smectite Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Guarino 2001	3.17	0.43	406	4.8	0.52	398	39.2%	-1.63 [-1.70, -1.56]
Madkour 1993	1.9	0.6708	45	2.4	0.6708	45	38.0%	-0.50 [-0.78, -0.22]
Osman 1992	2.5	1.83	30	4.7	3.09	30	22.9%	-2.20 [-3.49, -0.91]
Total (95% CI)			**481**			**473**	**100.0%**	**-1.33 [-2.28, -0.38]**

Heterogeneity: Tau² = 0.60; Chi² = 61.34, df = 2 (P < 0.00001); I² = 97%
Test for overall effect: Z = 2.74 (P = 0.006)

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

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

Cochrane Database of Systematic Reviews
25 APR 2018 DOI: 10.1002/14651858.CD011526.pub2

Diosmectita
Mecanismos

Buccigrossi *et al. Gut Pathog (2017) 9:23*
DOI 10.1186/s13099-017-0172-2

Gut Pathogens

RESEARCH Open Access

Mechanisms of antidiarrhoeal effects by diosmectite in human intestinal cells

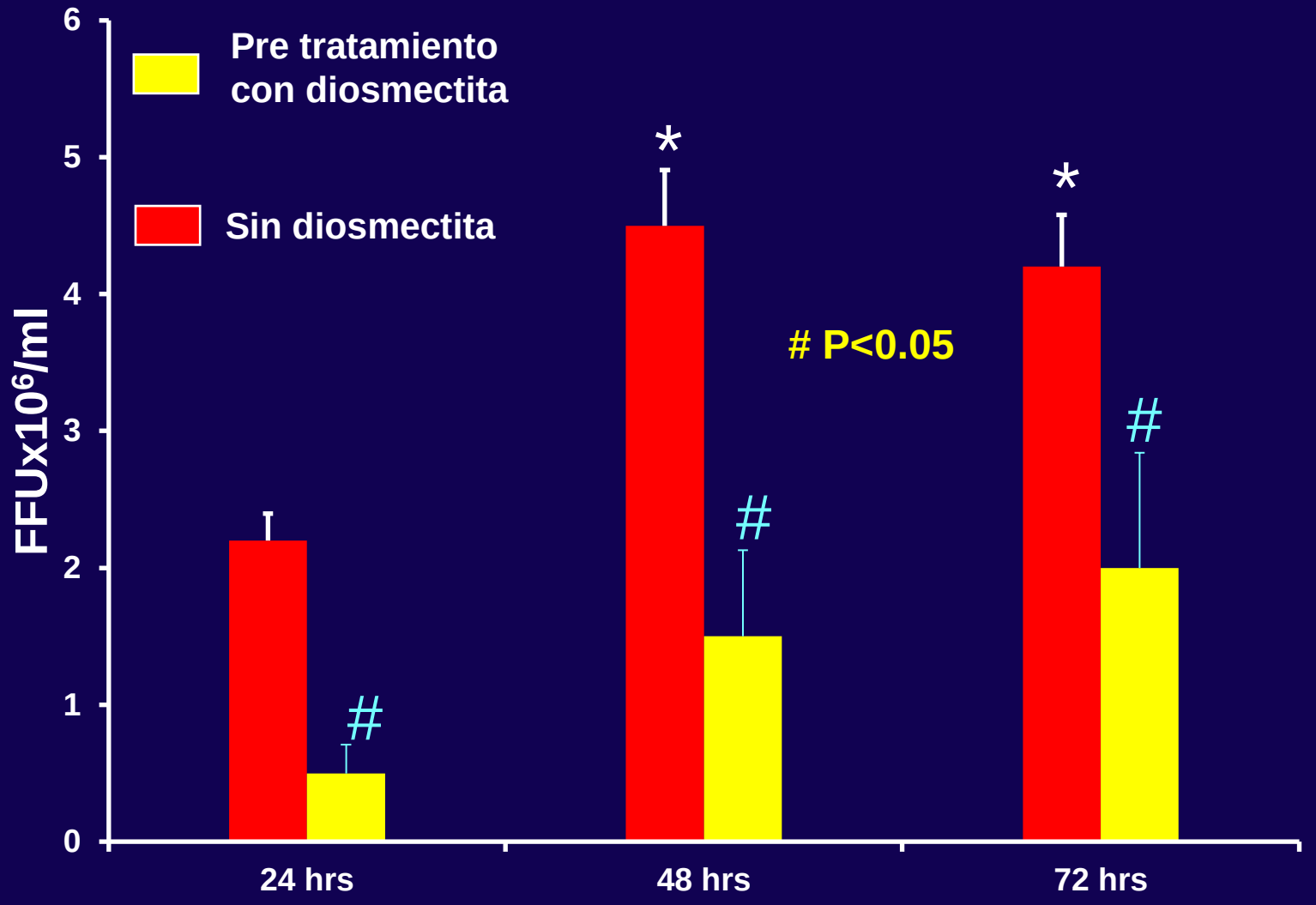
Vittoria Buccigrossi[1], Carla Russo[1], Amedeo Guarino[1], Maiara Brusco de Freitas[2] and Alfredo Guarino[1*]

Pre incubación con DSM 100 mg/ml

Infectividad

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

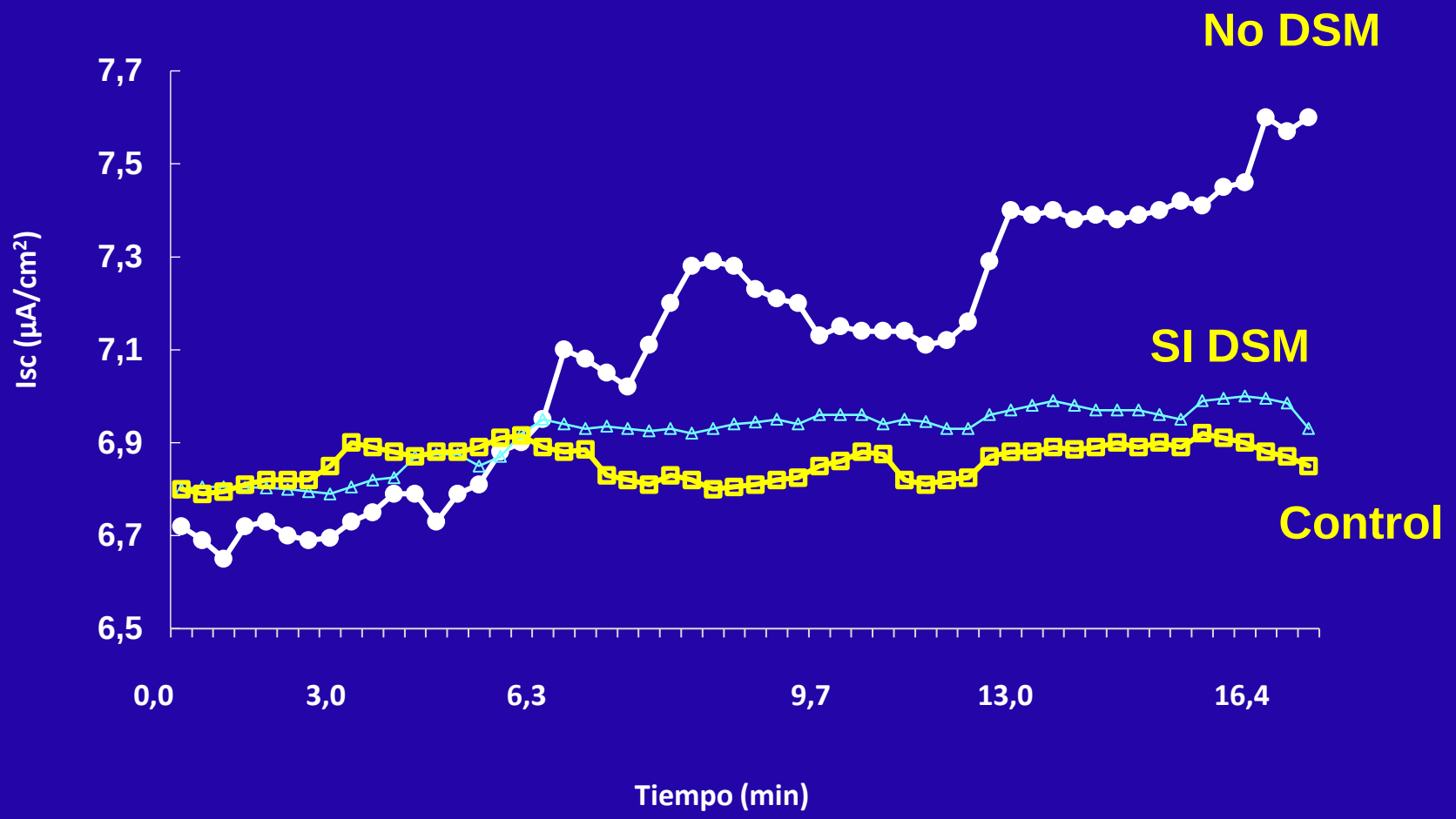
Se pueden diferenciar
En Enterocitos



Buccigrossi V, Gut Path 2017;9:23

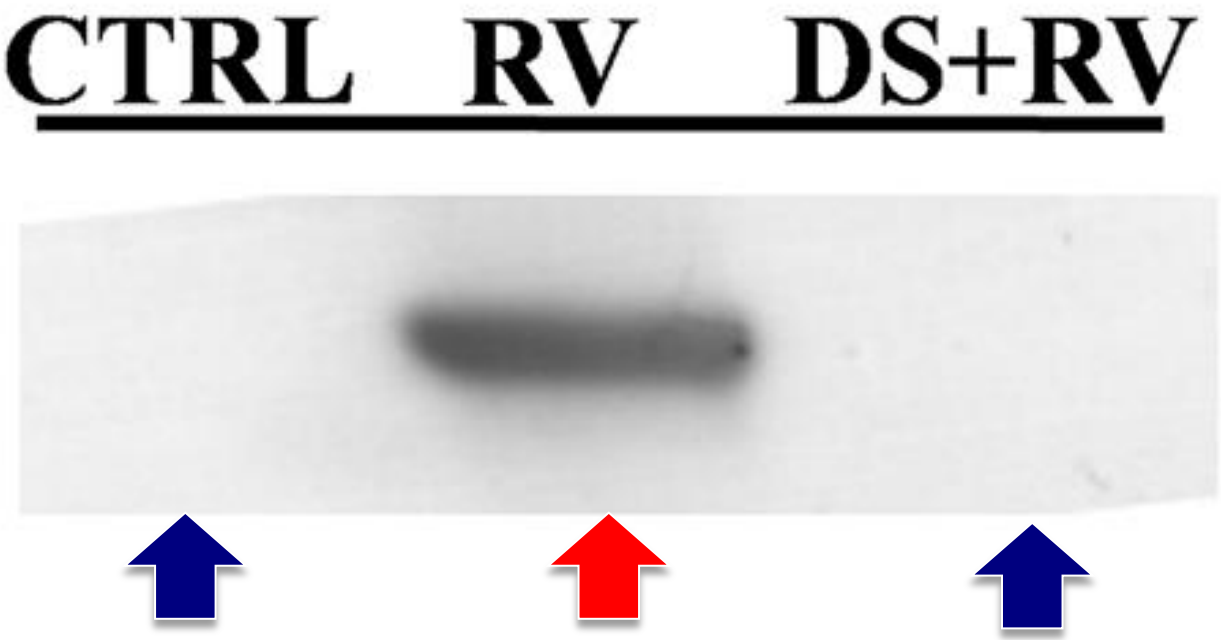
Efectos enterotoxicos
Efecto antisecretor

Secreción de Cloruro



Buccigrossi V, Gut Path 2017;9:23

DM inhibe completamente el efecto Secretor del rotavirus

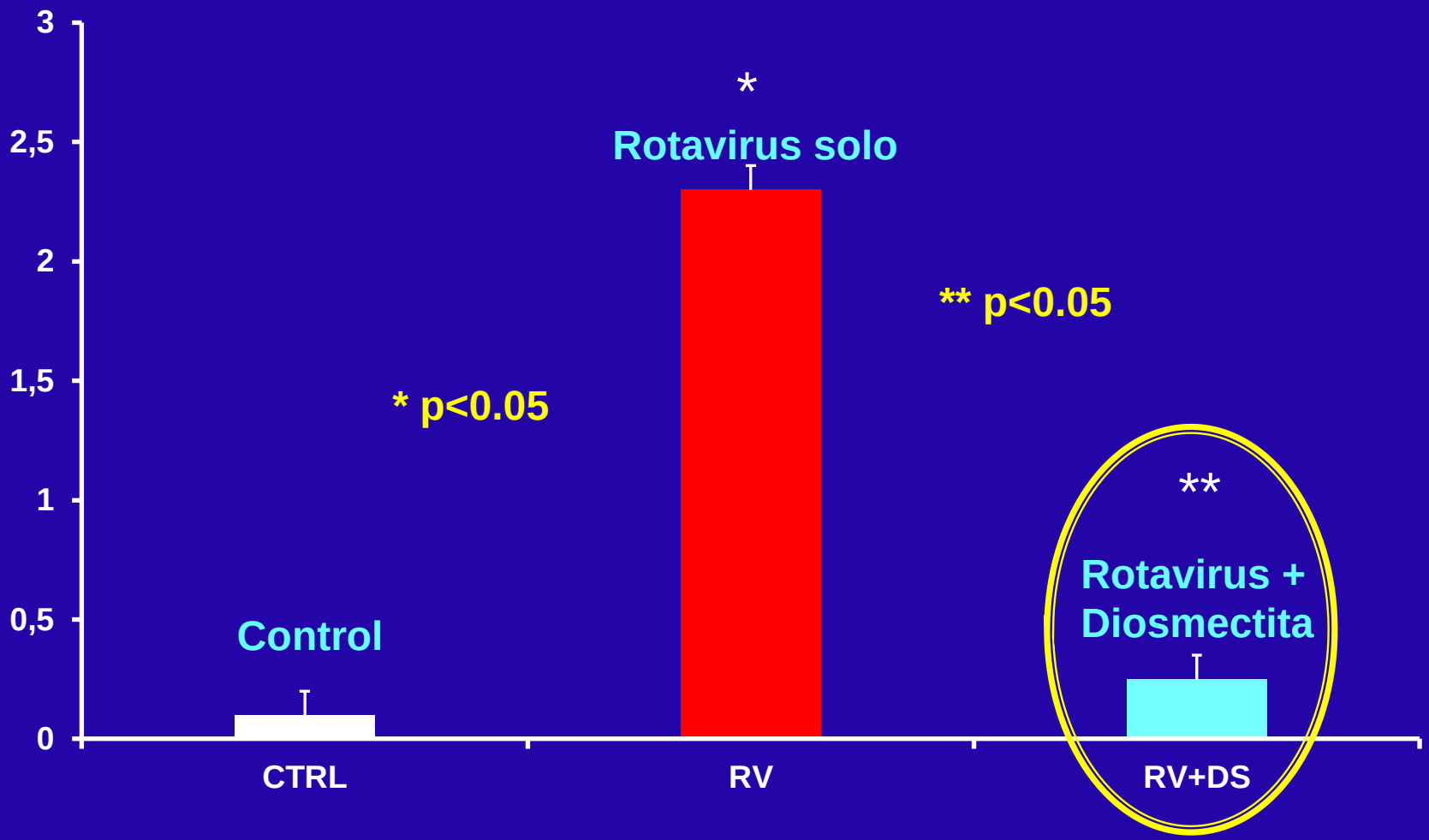


Expresión Enterotoxina viral

NSP4 (28kDa)

Citotoxicidad

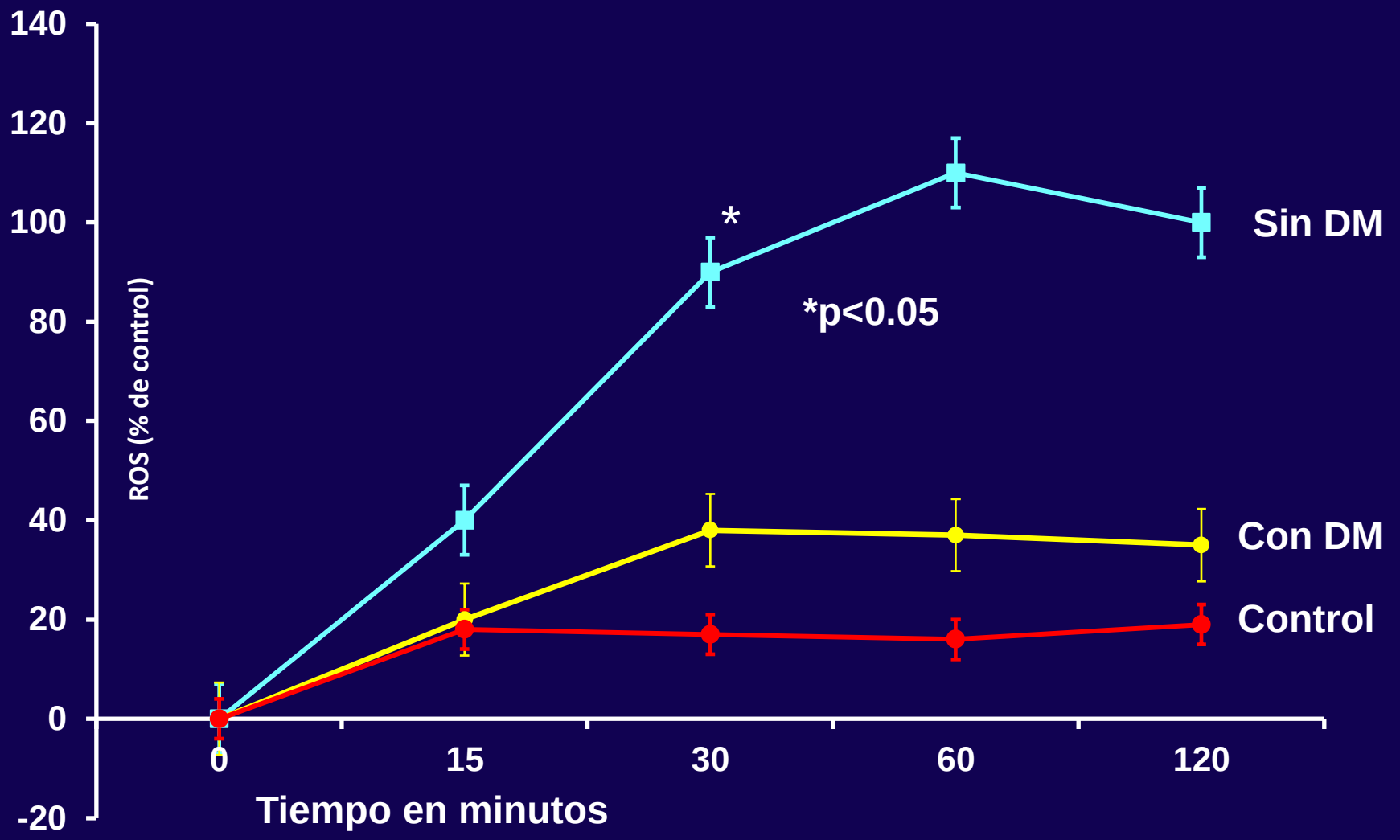
Efecto citotóxico de Rotavirus



Buccigrossi V, Gut Path 2017;9:23

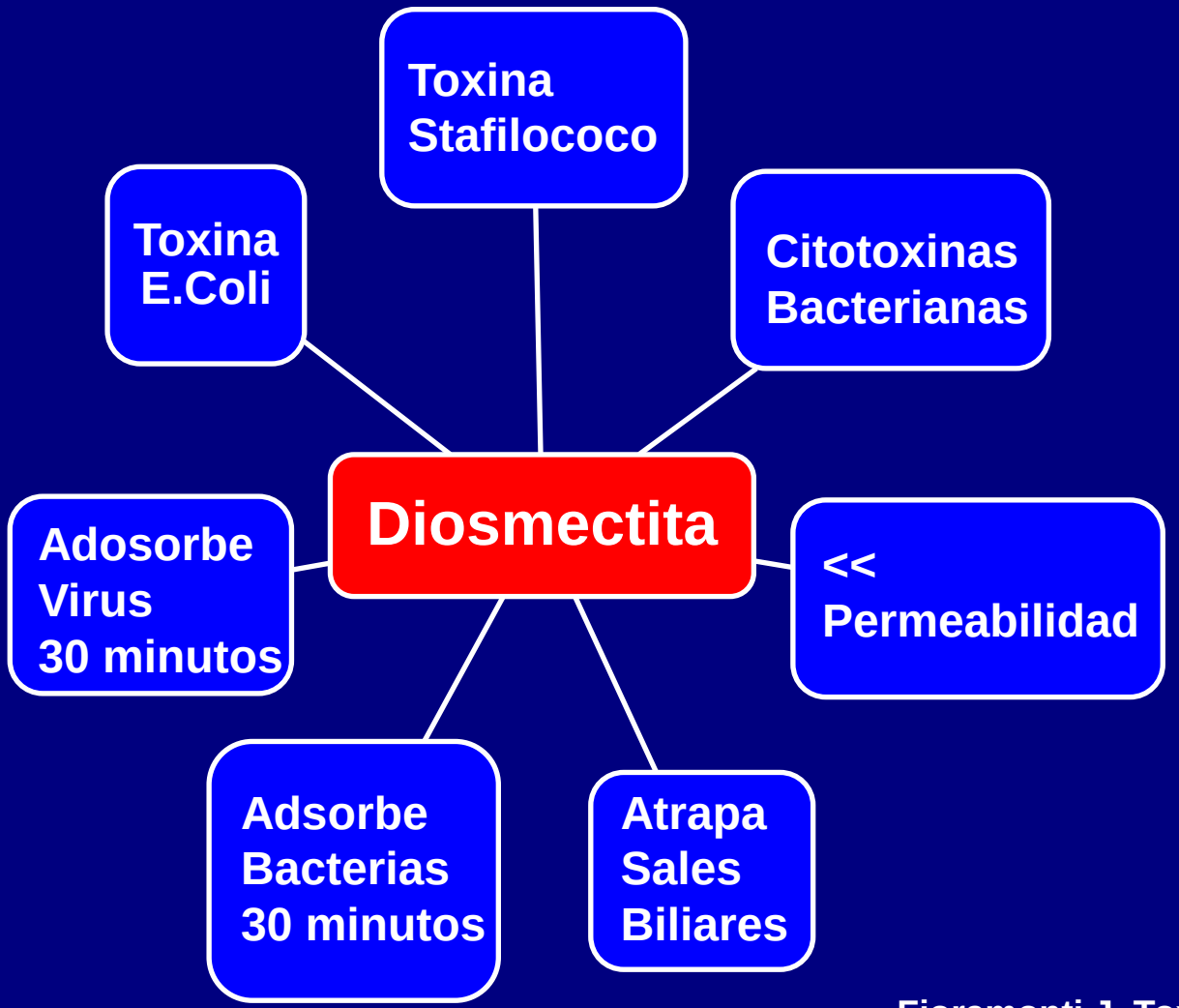
Estrés oxidativo

Estrés oxidativo con o sin pre incubación con DM



Buccigrossi V, Gut Path 2017;9:23

Mecanismos de acción de Diosmectita



Adherencia Membranas Intestinales

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

Diarrea aguda Diosmectita

No es lo Mismo

7-9 días de diarrea → ***Muchas Idas al baño***

2-3 días de diarrea → ***Menos Idas al baño***

Diosmectita-dosis

Niños < 1 año :
Dos sobres al inicio de la diarrea
Después 1 sobre al día (3 gr)/día

Niños > 1 año:
4 sobres al inicio de la diarrea
Después 2 sobres/día

Adultos:
6 sobres al inicio de la diarrea
Después 3 sobres/día (9 gr)

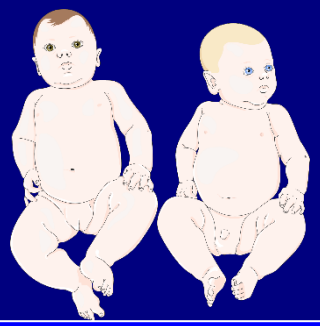
El contenido del Sobre en 50 ml H20 Se consume en el día.

O Mezclado con Alimentos lìquìdos Compotas, puré etc

El contenido del Sobre en MEDIO VASO De H20: suspensión Antes de consumirlo

Primero verter el polvo Después el líquido

Diosmectita *Nueva clase de droga antidiarreica*



< 1 año

Adulto mayor

Seguridad

Ensayos clinicos

>6.300 niños

>11.800 adulto

Ningùn efecto adverso serio

Estreñimieno infrecuente: 0.1%, <1%

Se alivia ajustando la dosis

Reportados: NO

FDA, WHO, French Agency

Interacción medicamentosa

Tomar otros medicamentos dos horas antes

Abbott 2018

Indicaciones

Niños:

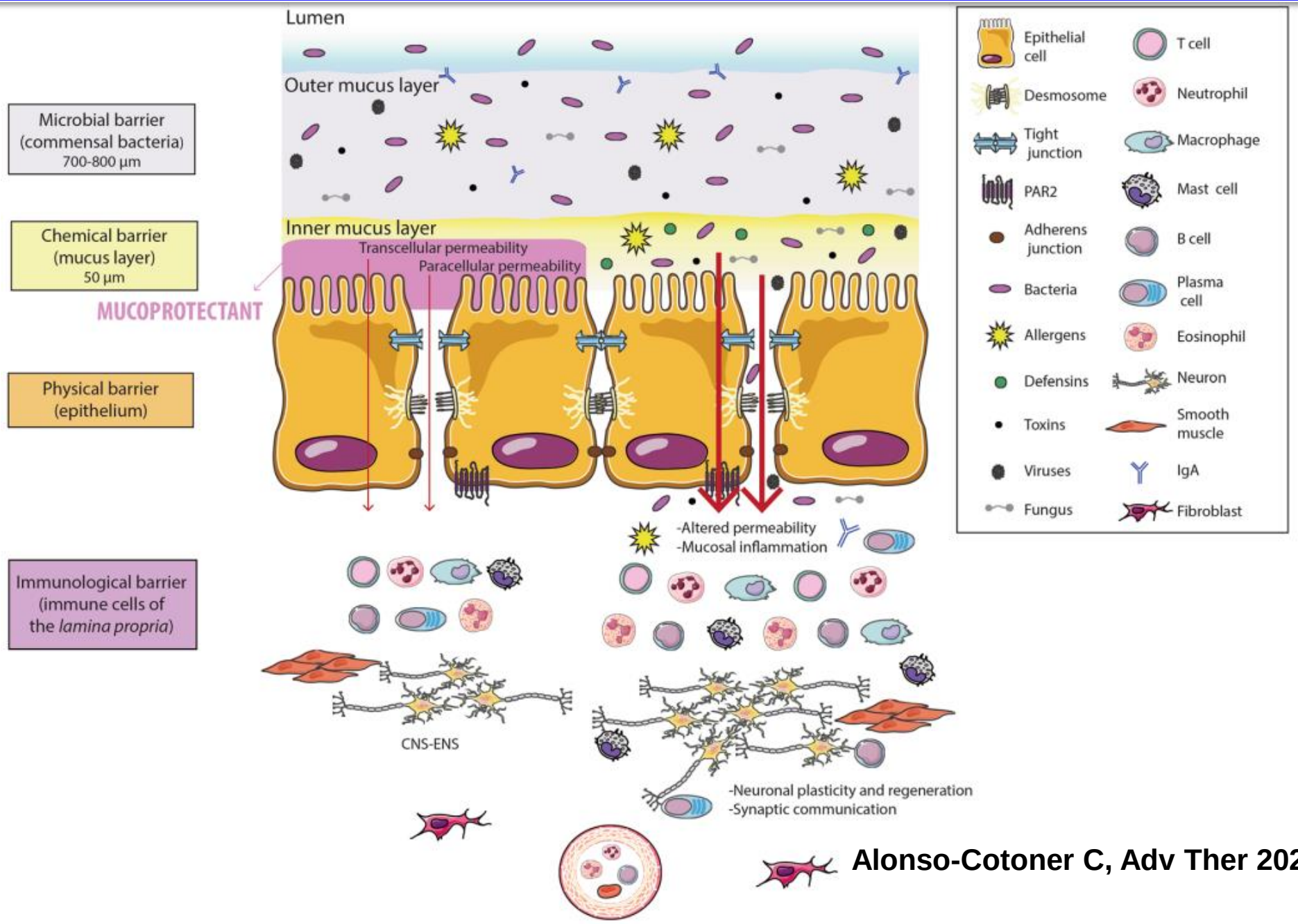
Diarrea aguda: Incluyendo menores de 1 años
Asociada a hidratación oral

Adultos

Diarrea aguda
Diarrea crónica funcional

Intestino irritable ?
Dolor asociado a trastornos GI Funcionales ?

Diosmectita/Mucoprotector



Alonso-Cotoner C, Adv Ther 2021; 38:2054–2076

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

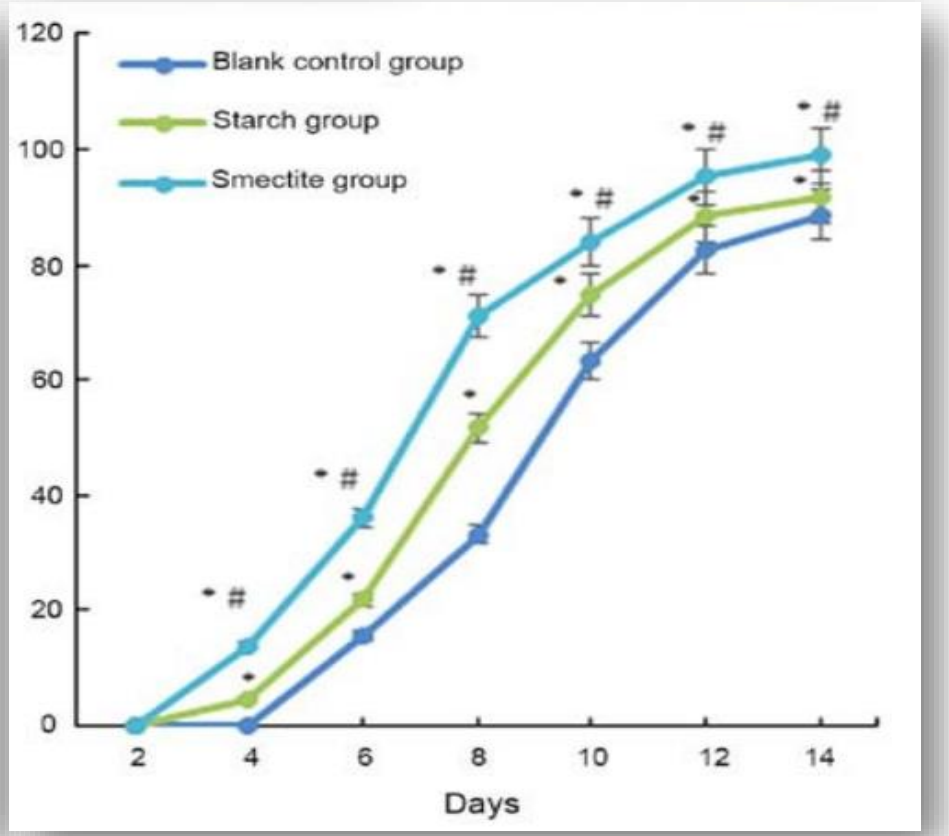
Marco Poeta[1], Valentina Cioffi[1], Vittoria Buccigrossi[1], Merlin Nanayakkara[1], Melissa Baggieri[2], Roberto Peltrini[3], Angela Amoresano[4], Fabio Magurano[2] & Alfredo Guarino[1]✉

Poeta M, Sci Rep. 2021;11:21725

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



Wang J, Exp Ther Med. 2021;21:160

Lactobacillus reuteri DSM 17938 + Vitamina D3

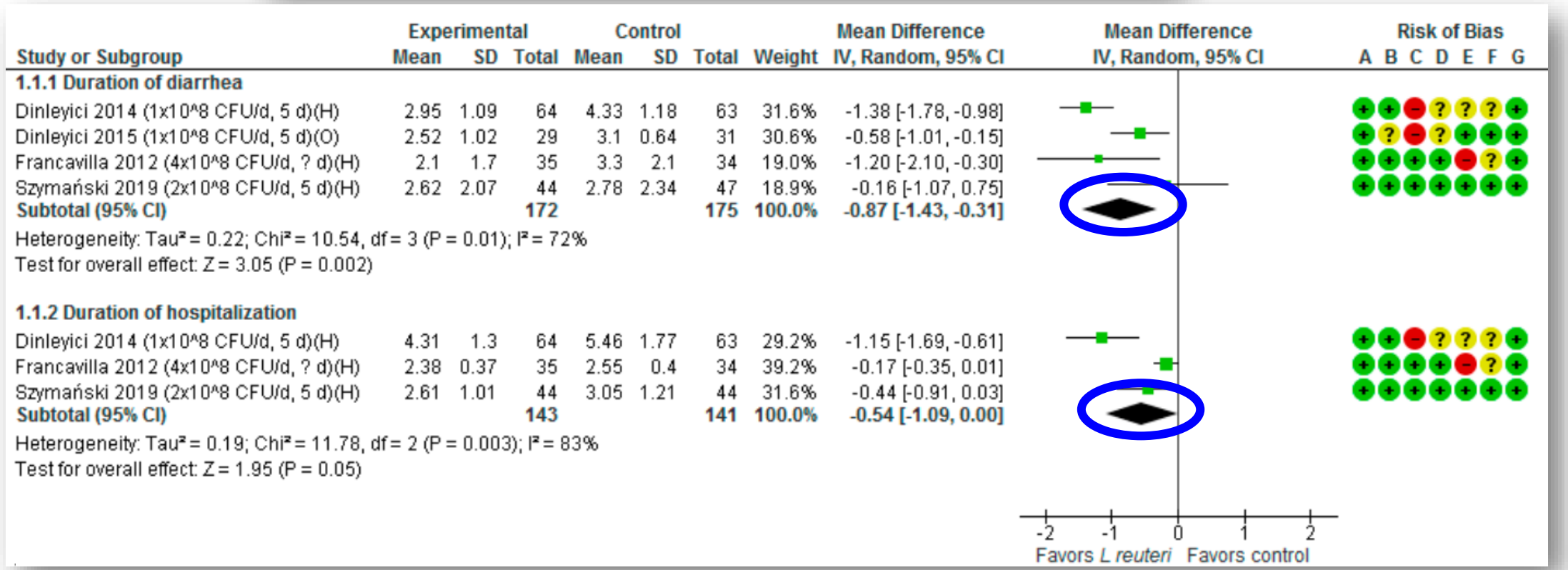
nutrients

MDPI

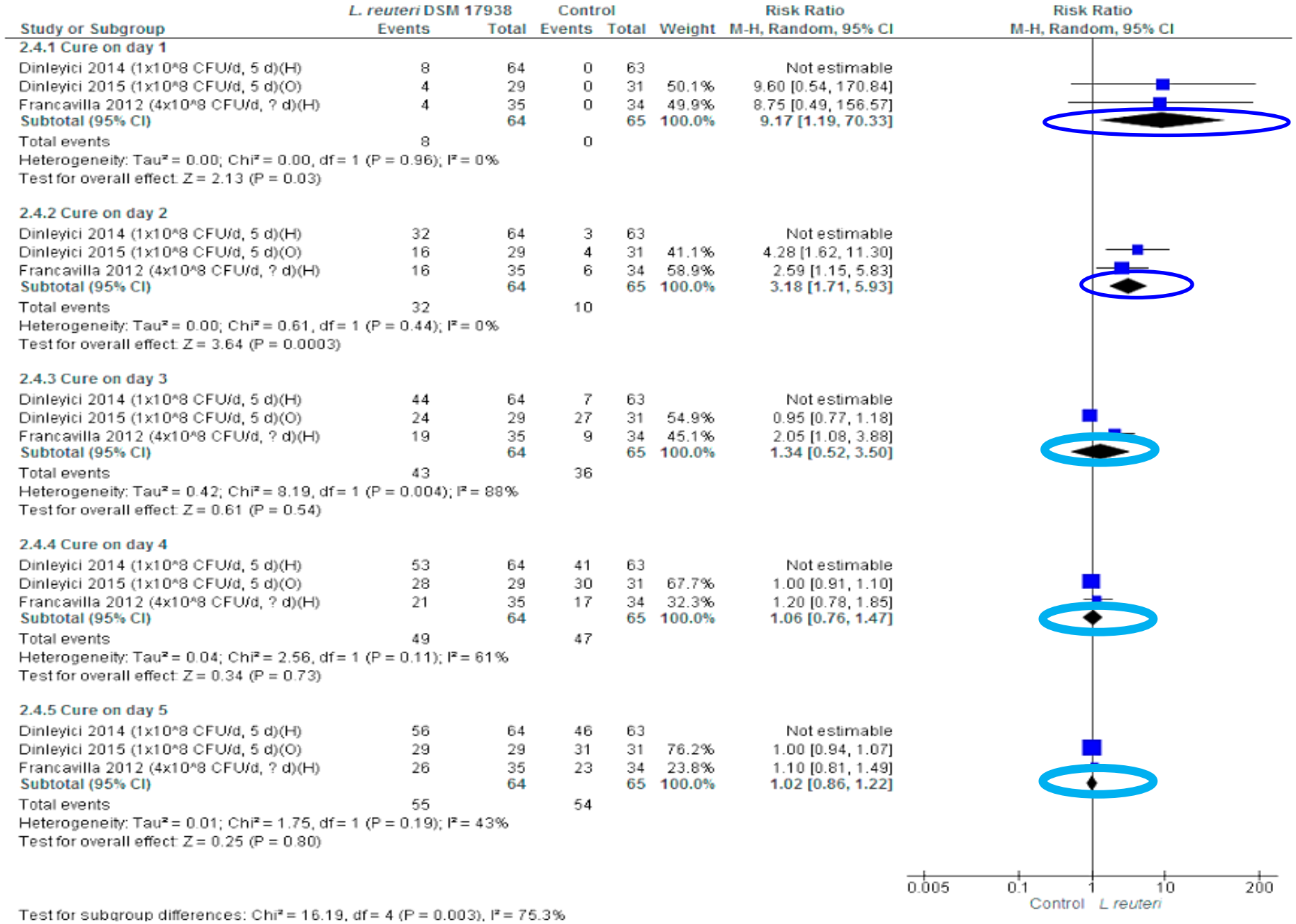
Review

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

Bernadeta Patro-Gołąb and Hania Szajewska *



Patro-Golab B, Nutrients. 2019;11:2762

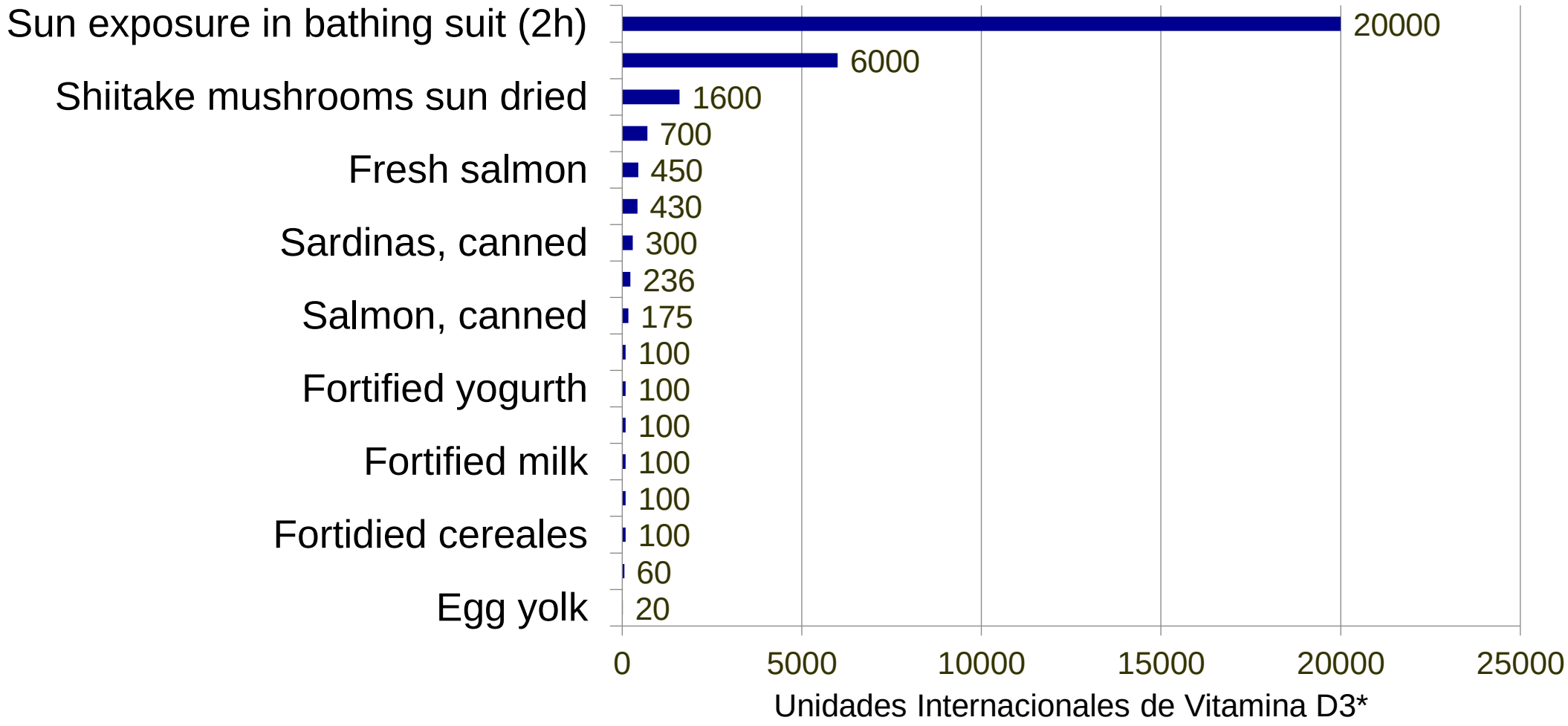


Patro-Golab B, Nutrients. 2019;11:2762

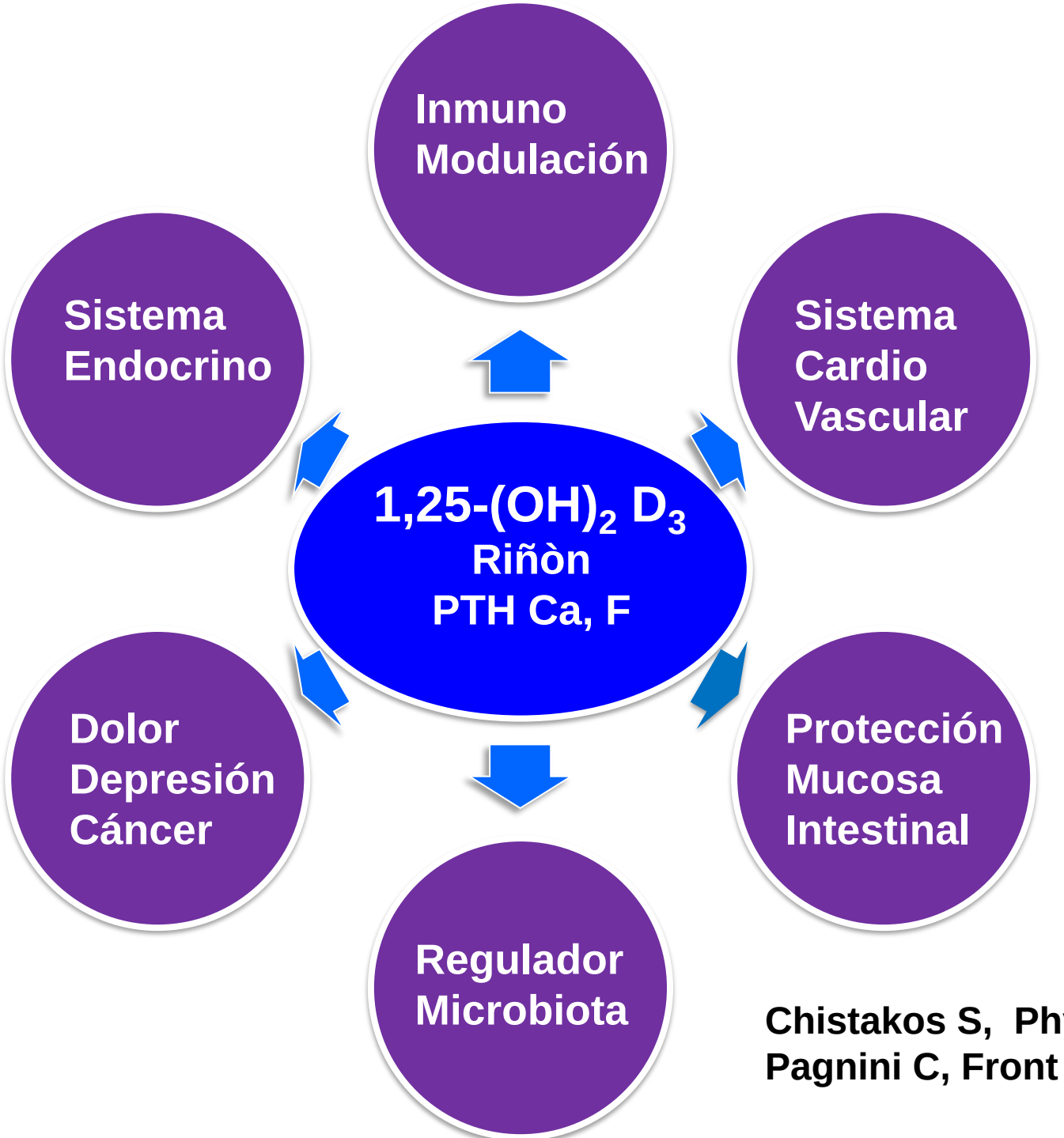
Vitamina D

D_3 Colecalciferol piel
D_2 Ergocalciferol plantas, hongos

Vitamina D: Fuente para los humanos



Wacker M, Nutrients 2013; 5:111-148



Chistakos S, Physiol Rev 20196:365-408
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 Paolo*[1], *Maria Giovanna Graziani*[1] and *Gianfranco Delle Fave*[2,3]

Pagnini C, Front Pharmacol 2021;12: Article747856

Pagnini C, Front Pharmacol 2021;12:747856

nutrients

MDPI

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

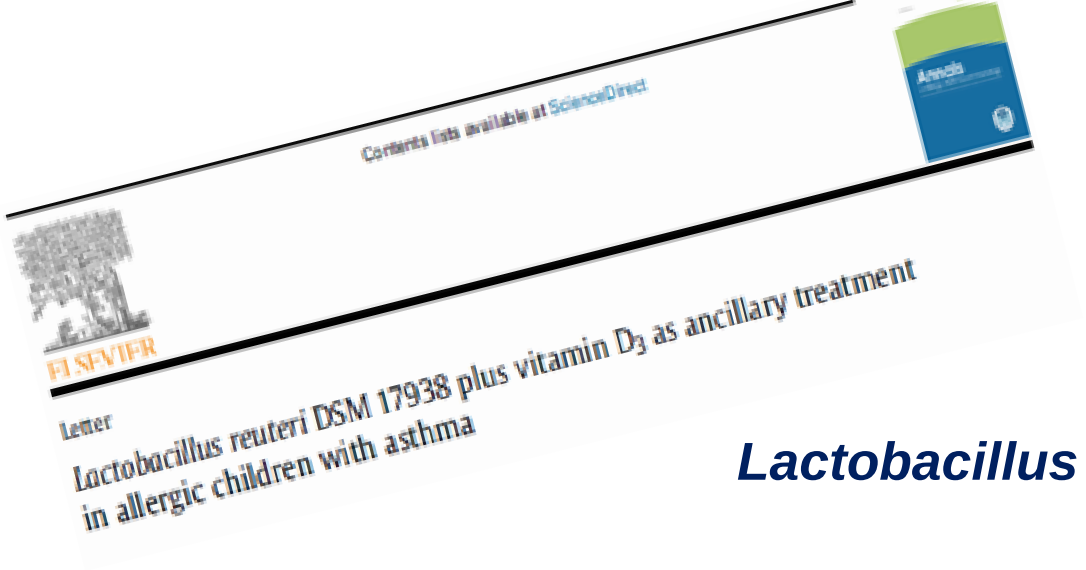
Table 1. Characteristics of included studies.

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 *Lactobacillus acidophilus, Bifidobacterium bifidum,*	Placebo similar shape and packaging	None	Compliance: >90%Drop out: I: 13.33% C: 13.33% -to-treat sis)
Jafarnejad, 2017, Iran [31]							ce 100% out: % %
Jamilian, 201 Iran [29]							ce: 100% out: % 66% 0%
Ostadmoham 2019, Iran [28]	placebo-controlled clinical trial	12 weeks	Rotterdam criteria with BMI: 17–34 kg/m^2 and insulin resistance: 1.4–4	*Lactobacillus acidophilus, Bifidobacterium bifidum, Lactobacillus reuteri* and *Lactobacillus fermentum* (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 *Lactobacillus acidophilus, Bifidobacterium bifidum, Lactobacillus reuteri,* and *Lactobacillus fermentum* (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 combinaciòn de probiòticos mas vitamina D
Es un adyuvante en enfermedades crònicas

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

Abboud M, Nutrients 2021;13:111


Contents lists available at ScienceDirect

Annals

ELSEVIER

Letter

Lactobacillus reuteri DSM 17938 plus vitamin D_3 as ancillary treatment in allergic children with asthma

Lactobacillus reuteri DSM 17938 más vitamina D_3 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

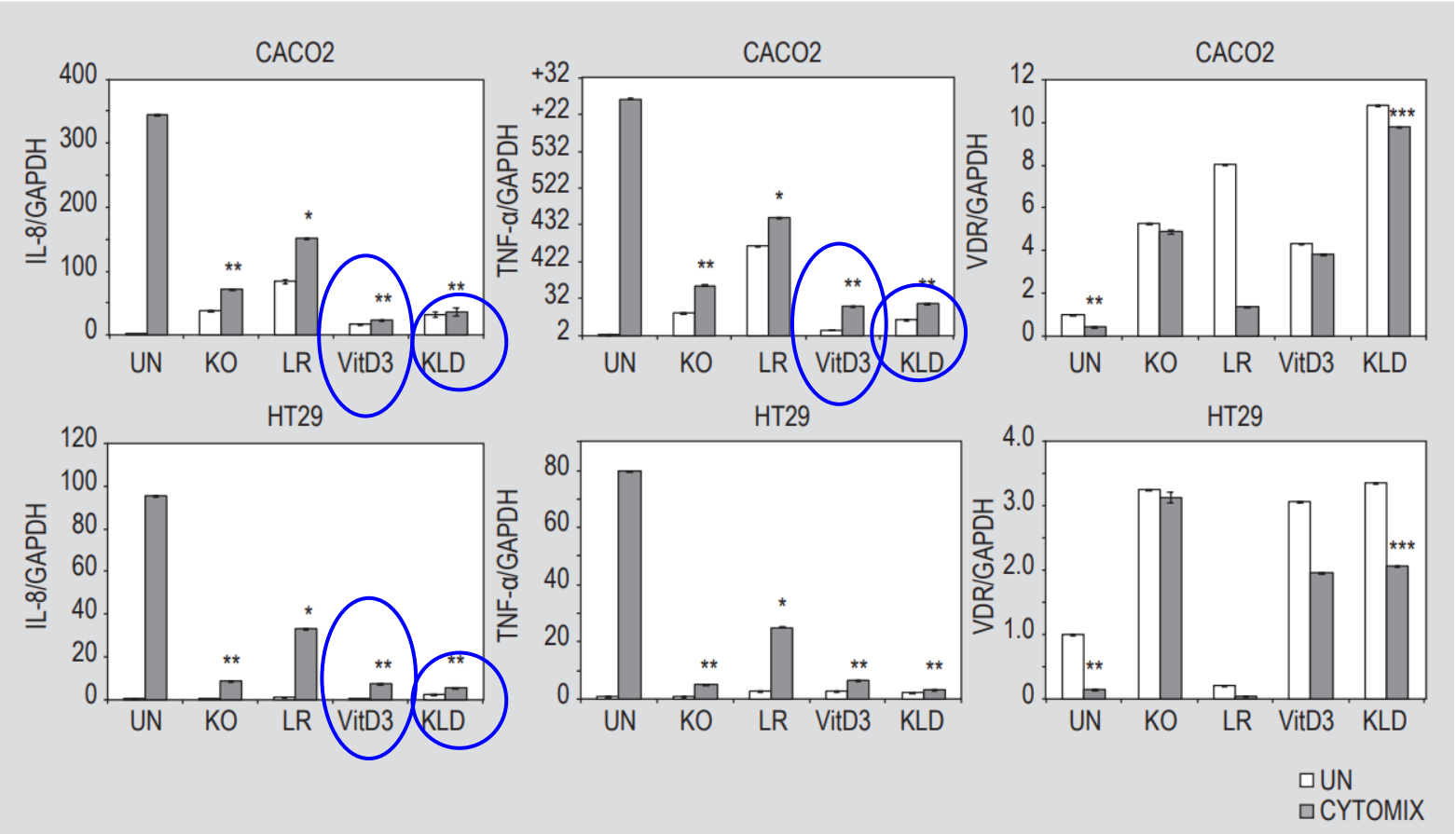
El studio actual identificó que la suplementación con *L. reuteri* DSM 17938 (10^8 CFU) y vitamina D_3 (400 IU) fue efectiva para reducir la inflamación bronquial. Además se observa un efecto positivo en el proceso de broncodilatación en los niños tratados con el principio activo.

Michele Miraglia del Giudice. Ann Allergy Asthma Immunol 2016;117:703-727

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

M. Costanzo[1], V. Cesi[2], F. Palone[1], M. Pierdomenico[1], E. Colantoni[1], B. Leter[1], R. Vitali[2], A. Negroni[2], S. Cucchiara[1] and L. Stronati[3*]

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

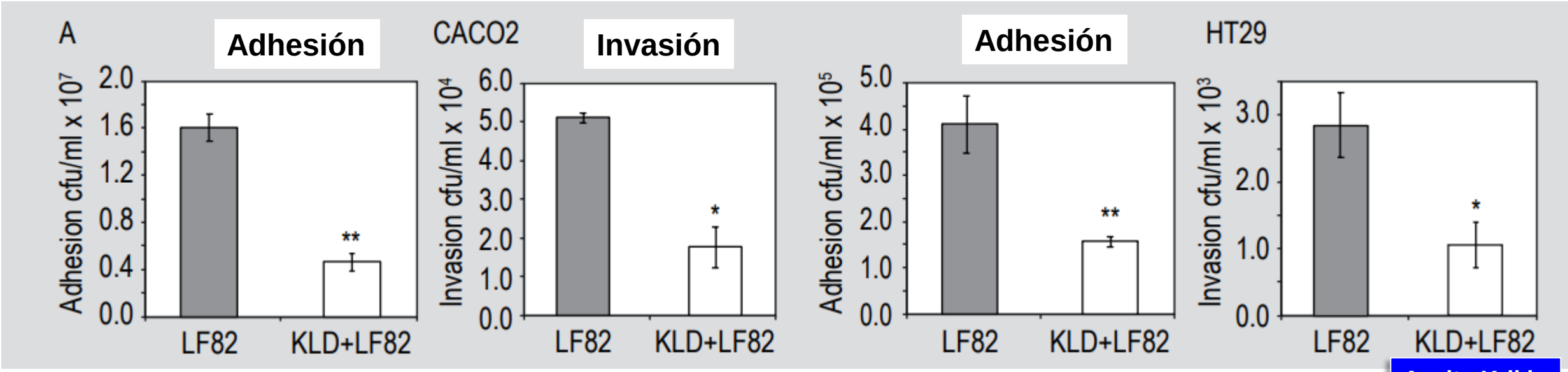


Constanzo V, Benef Microbes 2018 ;9:389-399

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

M. Costanzo[1], V. Cesi[2], F. Palone[1], M. Pierdomenico[1], E. Colantoni[1], B. Leter[1], R. Vitali[2], A. Negroni[2], S. Cucchiara[1] and L. Stronati[3*]

E. Coli enteroinvasiva LF82



Aceite Krill + lactobacilo+ D3

Aceite Krill + lactobacilo+ D3

Aceite Krill LR +D3

Aceite Kril l+ LR + D3

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

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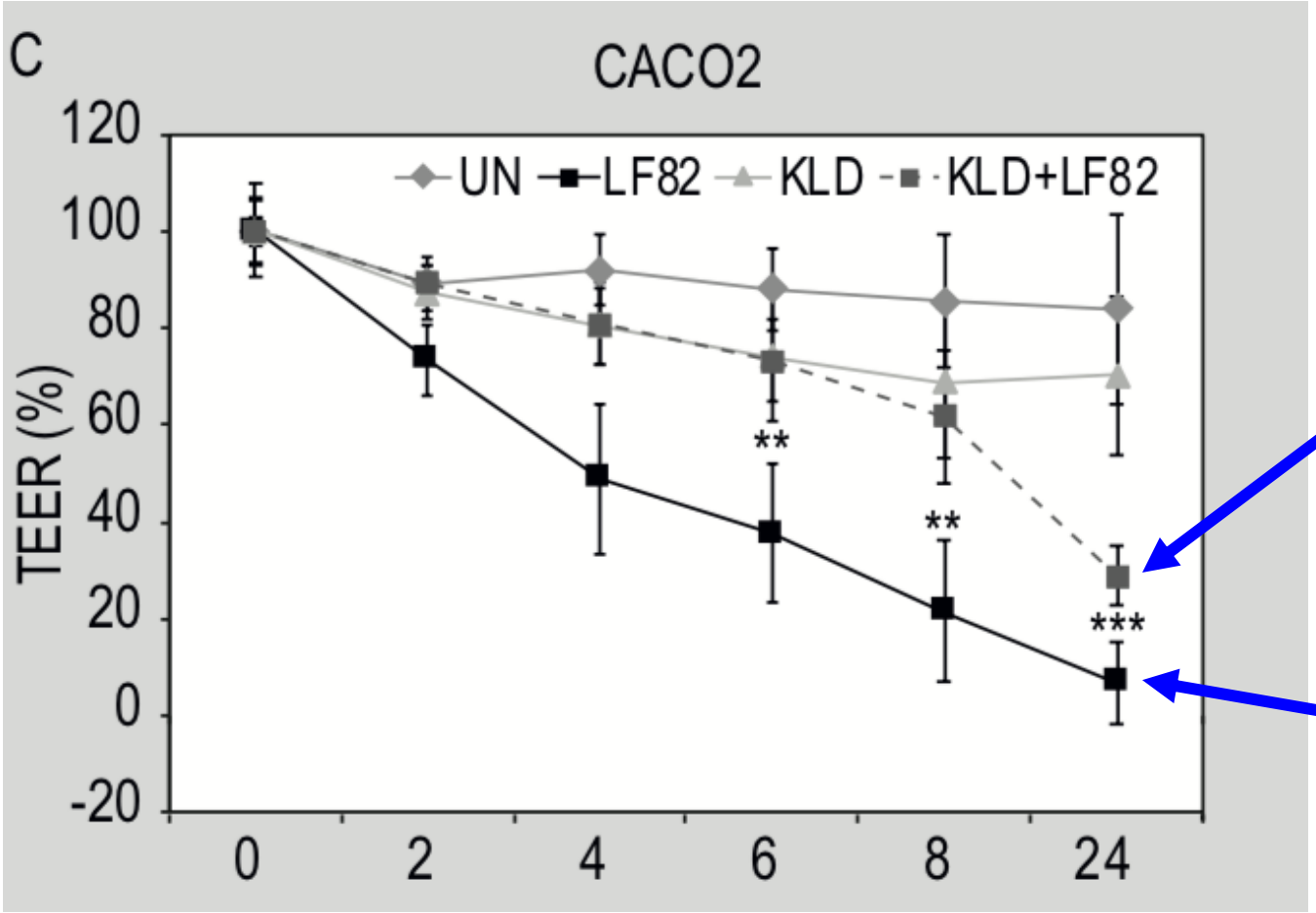
Resistencia Elèctrica Transepitelial



Recuperada por KLD

Reducida después Infecciòn LF82 (E.Coli)

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Aceite de Kril + LR+ D3
Disminuyó inflamación mucosa intestinal
Aumentò restitución epitelial
Redujo patogenicidad bacterias comensales peligrosas

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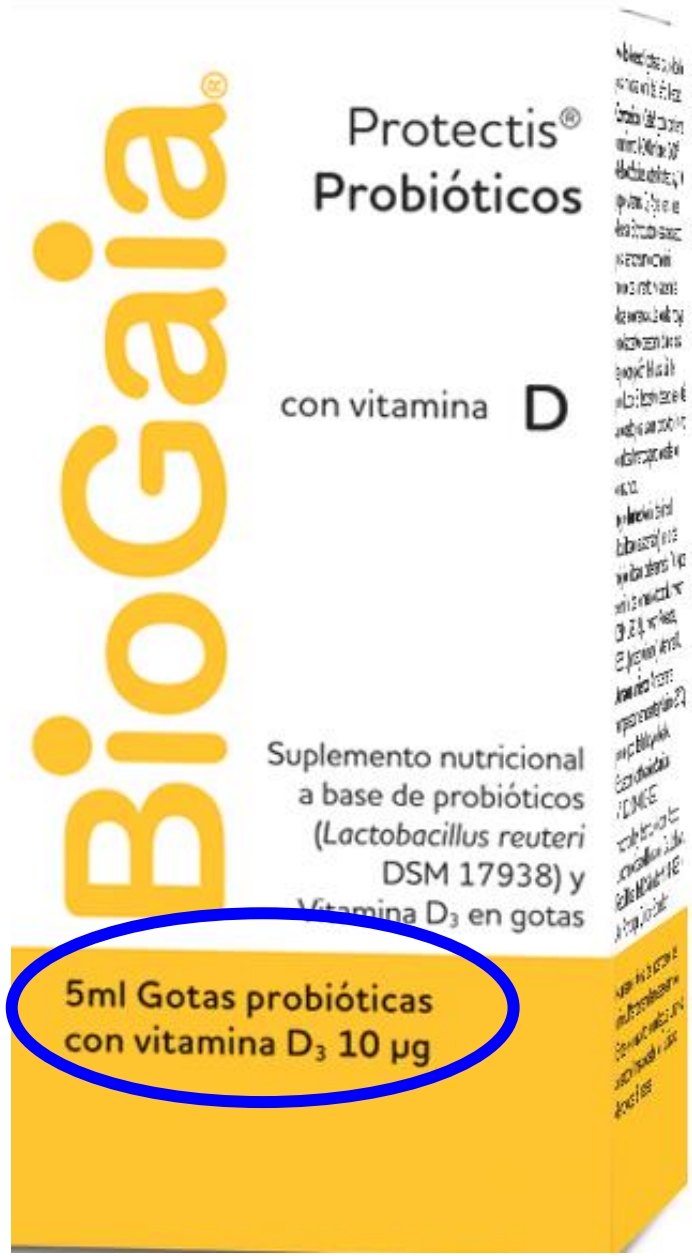

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Toxicidad de Vitamina D

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 hipertensiòn deshidrataciòn daño renal, càlculos enales

60.000 UI/dìa varios meses causa toxicidad

Cortesia Pammela Ruiz, Abbott Ecuador
Dra Sylvia Cruchet M

Mensajes para la casa

Hidratación es la piedra angular
Zinc complementa hidrataciòn
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 combinaciòn
Lactobacillus reuteri + vitamina D3
Combinaciòn audaz

Diarrea aguda

Abanico de Posibilidades

Muchas gracias !