EFICACIA DE PROBIÓTICOS EN ASMA, RINITIS ALÉRGICA Y SIBILANCIAS.

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1803

CONTEXTO

- Probióticos: microorganismos vivos
- LCG: *Lactobacillus rhamnosus*
- Afectan el metabolismo microbiano al modular los niveles de ácidos grasos de cadena corta
- Disminuir la inflamación y mejorar la función de barrera
- Microbioma se comunica con el sistema inmune a través de células epiteliales intestinales con las células dendríticas del intestino

- Modelos animales se ha demostrado que tratamiento preventivo con LGG resultan en una disminución del conteo de eosinófilos, IL5 e IL13 en el lavado bronco alveolar

CONTEXTO

- Microbiota colónica se ha asocia dado a la modulación de la respuesta inmune en edades tempranas incluyendo la gestación, parto, los primeros días y meses de vida.
- Exposición a la flora microbiana típica en la edad temprana es considerada como un incentivo efectivo para el balance el TH1 y TH2.
- Suplementación con probióticos se ha sugerido como una estrategia efectiva para la prevención de las alergias en muchos ensayos clínicos aleatorizados.

Numerosos estudios de la alteración en la colonización del colon con pre y probióticos.

Hasta ahora no había evidencia clara en sugerir el uso de probióticos para prevenir asma.

Se realizo un metaanálisis para determinar si la suplementación de probióticos en mujeres embarazadas y/o sus lactantes podría reducir la incidencia de asma y rinitis alérgica en niños.

Efficacy of probiotic supplementary therapy for asthma, allergic rhinitis, and wheeze: a meta-analysis of randomized controlled trials

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Estudio publicado en el 2019
Hunan, China
Sin conflictos de interés no financiado por laboratorios de probióticos y prebióticos.
Revista de allergy and asthma proceedings

MÉTODO

- Búsqueda para evaluar el efecto de la suplementación de probióticos para el asma, rinitis alérgica y sibilancias en el período pre y postnatal
- Pubmed, Web of science, Cochrane, Scopus, Chinese data bases
- Búsqueda por duplicado
- Límite de estudios en mandarín e ingles
- No se menciona literatura gris

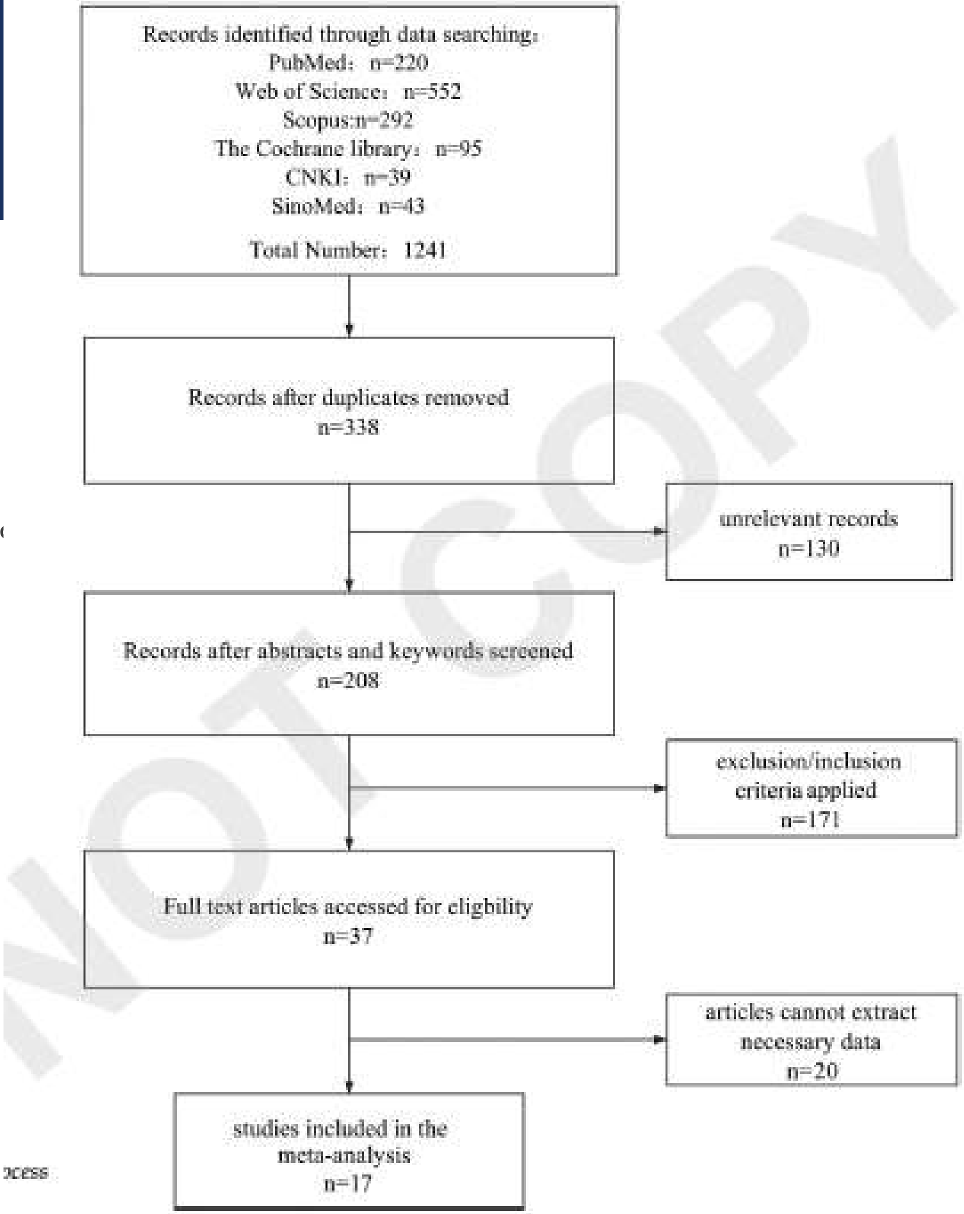
Resultado principal: diagnóstico de asma por un médico.

Resultados secundarios: sibilancias, rinitis alérgica, infecciones del tracto respiratorio inferior e IgE total.

MÉTODO

- Criterios de inclusión:
- 1. Cegamiento de los RCT
- 2. Niños sanos con o sin alto riesgo de desarrollar enferemdades alergicas
- 3. Suplementación de probióticos desde pre o periodo postnatal con mas de 3 meses de la intervención con
- Control: placebo
- 4. Descripción completa de la población
- 5. Todos los estudios aprobados por comité de ética

- Criterios de exclusión
- 1. Diseño de estudio inapropiado con una clara intervención comparación, resultado
- 2. Estudios en humanos
- 3. No fueran ensayos clínicos
- 4. Falta de medicion de HR RR CI



MÉTODO

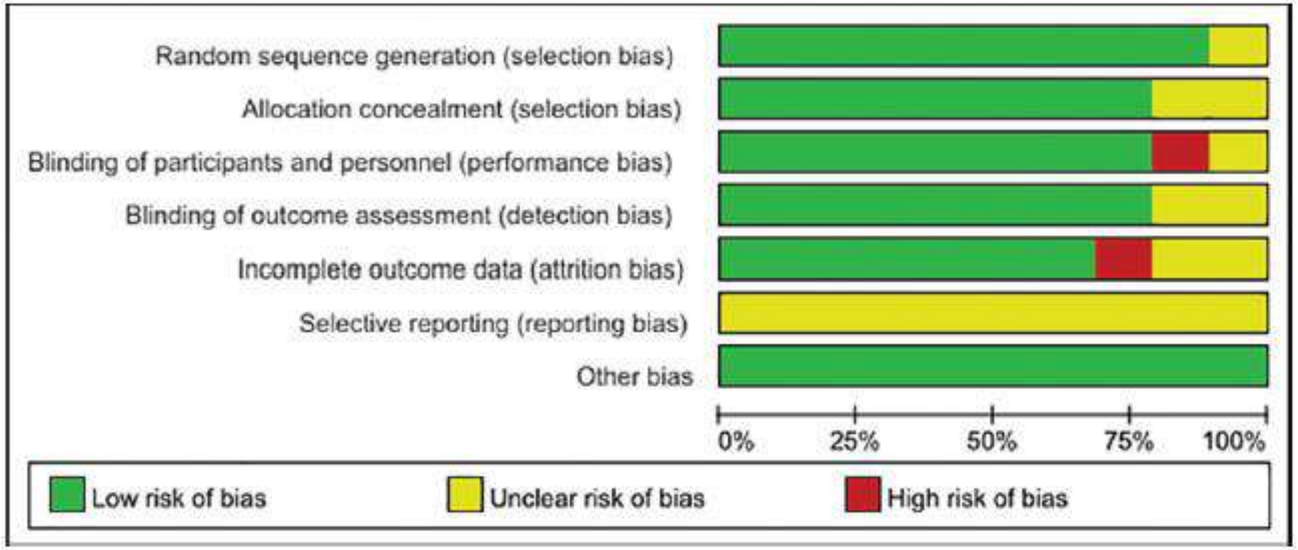


Figure 2. Quality assessment of randomized controlled trials (RCT) included in the meta-analysis by using the Cochrane Collaboration tool for assessing risk of bias.

MÉTODO

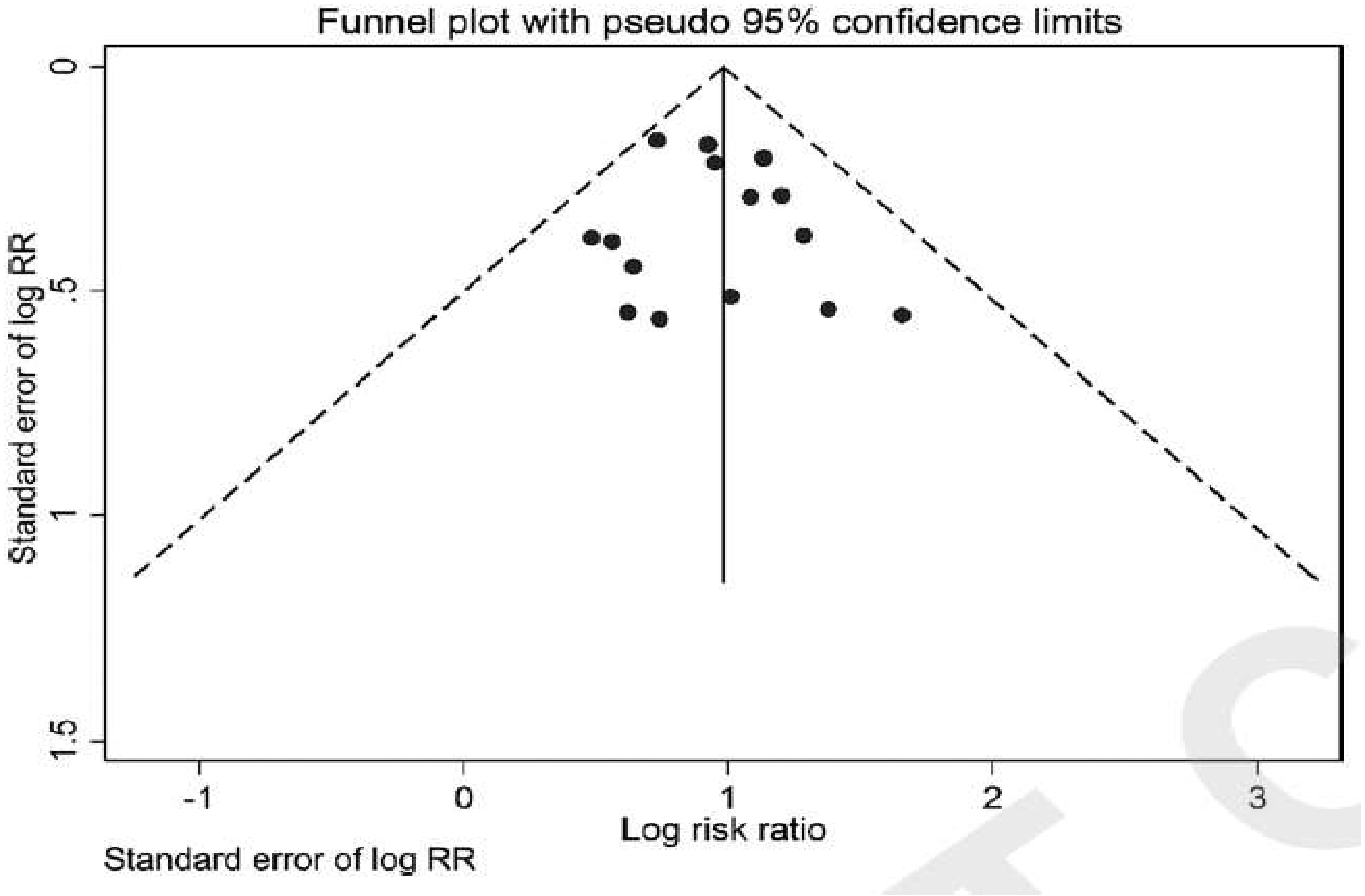

Funnel plot with pseudo 95% confidence limits
Standard error of log RR
0
.5
1
1.5
-1
0
1
2
3
Log risk ratio
Standard error of log RR

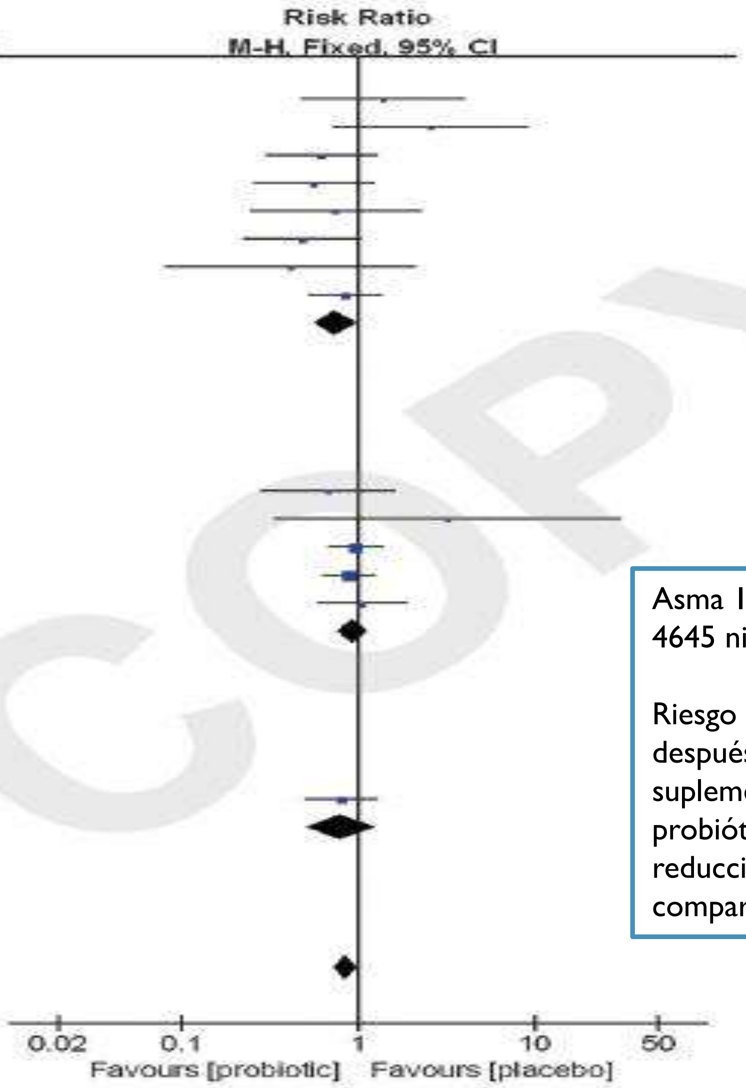
Table 1 Characteristics of RCTs included in the meta-analysis (quality score accessed by the Jadad scale)

Study	No. Participants/ High Risk	Pre- and/or Postnatal Intervention	Intervention/Dose $\times 10^8$ CFU/Duration	Placebo	Follow-up, y	AR/Wheeze/Positive Aeroallergen SPT Result	Quality Score
Lundelin et al[42], 2016	221/√	Pre- and postnatal	LGG, mixture/100/36 WG until delivery, first 6 mo	Not stated	4–5,10–15	—	5, 3, 4, 5 (4 studies)
Peldan et al[30], 2017	1223/√	Pre- and postnatal	Mixture/100/36 WG until delivery, first 6 mo	Not stated	10	AR	5
Melanie et al[29], 2015	215/√	Pre- and postnatal	Mixture/50/36 WG until delivery, first 6 mo	Not stated	6	Wheeze	4
Berni et al [34], 2016	193/√	Postnatal	LGG/unclear/first 12 mo	EHCF	3	—	4
Paula et al[31], 2014	796/√	Pre- and postnatal	Mixture/100/35 WG until delivery, first 6 mo	Not stated	3.5	—	3
Stephen J et al[37], 2014	454/×	Pre- and postnatal	Mixture/100/36 WG until delivery, first 6 mo	Maltodextrin	2	AR/wheeze/positive aeroallergen SPT result	5
Michael et al[35], 2017	184/√	Postnatal	LGG/100/first 6 mo	Inulin	2	—	4
Robert et al[36], 2011	250/√	Pre- and postnatal	LGG/180/36 WG until delivery, first 3 mo	Maltodextrin	1	Wheeze/postive aeroallergen SPT result	5
Dotterud et al[33], 2010	278/√	Pre- and postnatal	Mixture/1050/35 WG until delivery, first 3 mo	Not stated	2	—	5
Kalliomäki et al[41], 2007	116/√	Pre- and postnatal	LGG/100/36 WG until delivery, first 3 mo	Not stated	7–8	AR	4
Ou et al[39], 2012	191/√	Pre-and postnatal	LGG/100/24 WG until delivery, first 6 mo	Microcrystalline cellulose	3	Wheeze	2
Jensen et al[32], 2012	123/×	Postnatal	LGG/30/first 6 mo	Maltodextrin	5	AR/wheeze/postive aeroallergen SPT result	4
Prescott et al[40], 2008	105/√	Postnatal	LGG/30/first 6 mo	Not stated	2.5	Wheeze/postive aeroallergen SPT result	4
Taylor et al[32],	178/√	Postnatal	LGG/30/first 6 mo	Maltodextrin	6	Wheeze	4
Wickens et al[27], 2018a	278/√	Pre- and postnatal	LGG/60/35 WG until delivery, first 24 mo	Not stated	11	AR/wheeze	5
Wickens et al[27], 2018b	288/√	Pre- and postnatal	*Bifidobacterium*/90/35 WG until delivery, first 24 mo	Not stated	11	AR/wheeze	5

RESULTADOS ASOCIACIÓN DE PROBIÓTICOS Y ASMA

Lactobacillus Rhamnosus

Study or Subgroup	Probiotic Events	Probiotic Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 LGG						
Jensen MP	8	66	5	57	1.9%	1.38 [0.48, 3.99]
Kalliomäki M	9	62	3	53	1.1%	2.56 [0.73, 8.99]
Krista Lundelin	10	86	18	96	5.9%	0.62 [0.30, 1.27]
Michael D	9	92	16	92	5.6%	0.56 [0.26, 1.21]
Prescott SL	5	74	7	77	2.4%	0.74 [0.25, 2.24]
Roberto B	9	98	18	95	6.4%	0.48 [0.23, 1.02]
West CE	2	84	5	87	1.7%	0.41 [0.08, 2.08]
Wickens K(a)	24	108	30	114	10.2%	0.84 [0.53, 1.35]
Subtotal (95% CI)		**670**		**671**	**35.1%**	**0.75 [0.57, 0.99]**
Total events	76		102			
Heterogeneity: $Chi^2 = 7.86$, df = 7 (P = 0.35); $I^2 = 11\%$						
Test for overall effect: Z = 2.02 (P = 0.04)						
1.2.2 Mixture						
Dotterud CK	8	138	12	140	4.2%	0.68 [0.29, 1.60]
Melanie R	3	136	1	145	0.3%	3.20 [0.34, 30.38]
P. Kauppi	55	400	56	396	19.6%	0.97 [0.69, 1.37]
Päivi Peldan	58	395	66	399	22.9%	0.89 [0.64, 1.23]
Stephen J	23	217	20	199	7.3%	1.05 [0.60, 1.86]
Subtotal (95% CI)		**1286**		**1279**	**54.2%**	**0.94 [0.76, 1.16]**
Total events	147		155			
Heterogeneity: $Chi^2 = 2.01$, df = 4 (P = 0.73); $I^2 = 0\%$						
Test for overall effect: Z = 0.59 (P = 0.56)						
1.2.3 Other						
Wickens K(b)	25	118	30	114	10.6%	0.81 [0.51, 1.28]
Subtotal (95% CI)		**118**		**114**	**10.6%**	**0.81 [0.51, 1.28]**
Total events	25		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.92 (P = 0.36)						
Total (95% CI)		**2074**		**2064**	**100.0%**	**0.86 [0.73, 1.01]**
Total events	248		287			
Heterogeneity: $Chi^2 = 11.49$, df = 13 (P = 0.57); $I^2 = 0\%$						
Test for overall effect: Z = 1.89 (P = 0.06)						
Test for subgroup differences: $Chi^2 = 1.65$, df = 2 (P = 0.44), $I^2 = 0\%$						



Asma 14 estudios
4645 niños

Riesgo de desarrollar asma después de la suplementación con probióticos no mostro una reducción significativa comparado con placebo

ASMA Y LA DURACIÓN DE LA INTERVENCIÓN

Study or Subgroup	Probiotic Events	Probiotic Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 prenatal and postnatal						
Dotterud CK	8	138	12	140	4.2%	0.68 [0.29, 1.60]
Kalliomaki M	9	62	3	53	1.1%	2.56 [0.73, 8.99]
Krista Lundelin	10	86	18	96	5.9%	0.62 [0.30, 1.27]
Melanie R	3	136	1	145	0.3%	3.20 [0.34, 30.38]
P. Kauppi	55	400	56	396	19.6%	0.97 [0.69, 1.37]
Päivi Peldan	58	395	66	399	22.9%	0.89 [0.64, 1.23]
Stephen J	23	217	20	199	7.3%	1.05 [0.60, 1.86]
Wickens K(a)	24	108	30	114	10.2%	0.84 [0.53, 1.35]
Wickens K(b)	25	118	30	114	10.6%	0.81 [0.51, 1.28]
Subtotal (95% CI)		**1660**		**1656**	**82.1%**	**0.91 [0.77, 1.08]**
Total events	215		236			
Heterogeneity: Chi² = 6.16, df = 8 (P = 0.63); I² = 0%						
Test for overall effect: Z = 1.10 (P = 0.27)						
2.1.2 postnatal						
Jensen MP	8	66	5	57	1.9%	1.38 [0.48, 3.99]
Michael D	9	92	16	92	5.6%	0.56 [0.26, 1.21]
Prescott SL	5	74	7	77	2.4%	0.74 [0.25, 2.24]
Roberto B	9	98	18	95	6.4%	0.48 [0.23, 1.02]
West CE	2	84	5	87	1.7%	0.41 [0.08, 2.08]
Subtotal (95% CI)		**414**		**408**	**17.9%**	**0.63 [0.42, 0.96]**
Total events	33		51			
Heterogeneity: Chi² = 3.01, df = 4 (P = 0.56); I² = 0%						
Test for overall effect: Z = 2.18 (P = 0.03)						
Total (95% CI)		**2074**		**2064**	**100.0%**	**0.86 [0.73, 1.01]**
Total events	248		287			
Heterogeneity: = 11.49, df = 13 (P = 0.57); I² = 0%						
Test for overall effect: Z = 1.89 (P = 0.06)						
Test for subgroup differences: Chi² = 2.56, df = 1 (P = 0.11), I² = 60.9%						

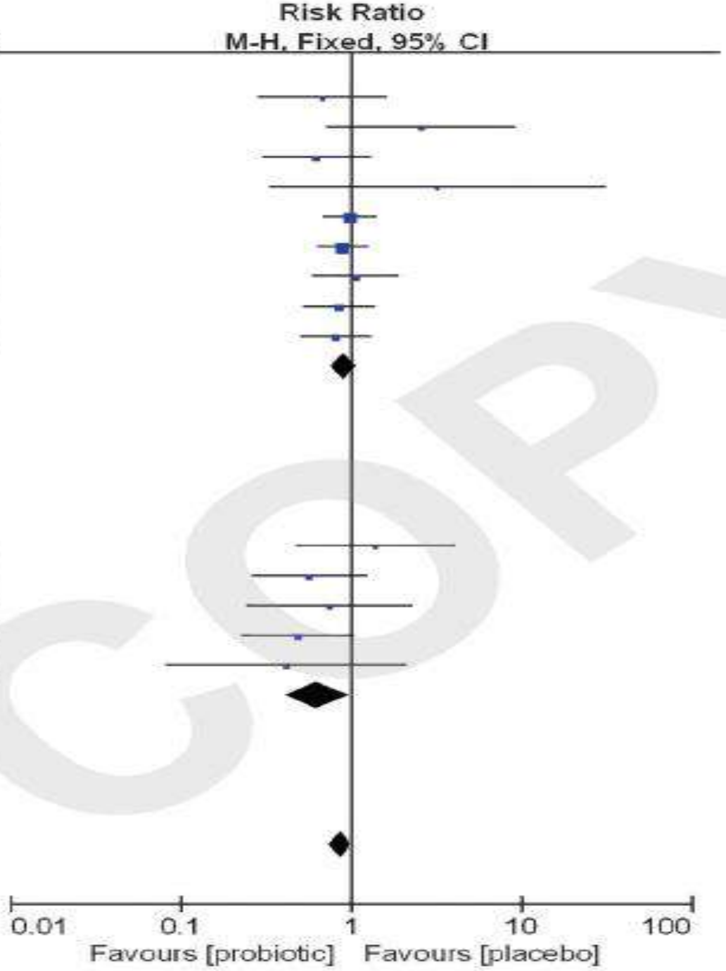


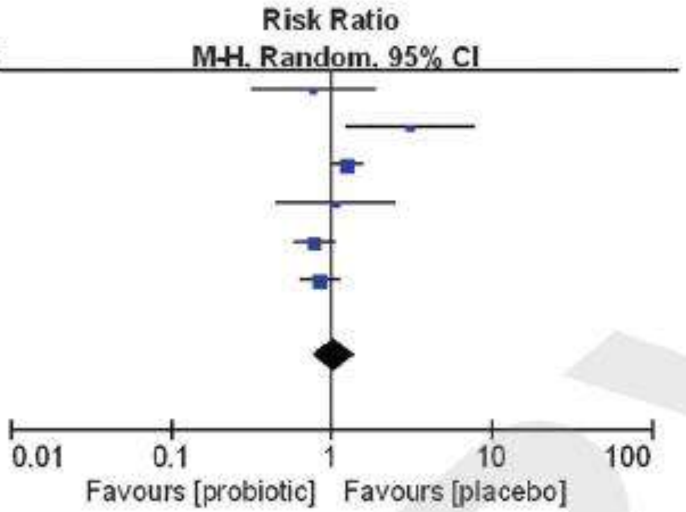
Figure 4. Forest plot, showing the comparison of probiotic supplementation versus placebo for asthma according to the period of intervention: (1) prenatal and postnatal, (2) postnatal.

RINITIS ALÉRGICA Y PROBIÓTICOS

A

	Probiotic		Placebo			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Jensen MP	8	58	9	50	8.3%	0.77 [0.32, 1.84]
Kalliomäki M	12	53	6	82	7.8%	3.09 [1.24, 7.74]
Päivi Peldan	148	406	116	400	27.0%	1.26 [1.03, 1.54]
Stephen J	10	190	10	201	8.6%	1.06 [0.45, 2.48]
Wickens K(a)	44	109	59	115	23.8%	0.79 [0.59, 1.05]
Wickens K(b)	51	118	59	115	24.4%	0.84 [0.64, 1.11]
Total (95% CI)		**934**		**963**	**100.0%**	**1.03 [0.77, 1.39]**
Total events	273		259			

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 15.41$, df = 5 (P = 0.009); $I^2 = 68\%$
Test for overall effect: Z = 0.22 (P = 0.83)



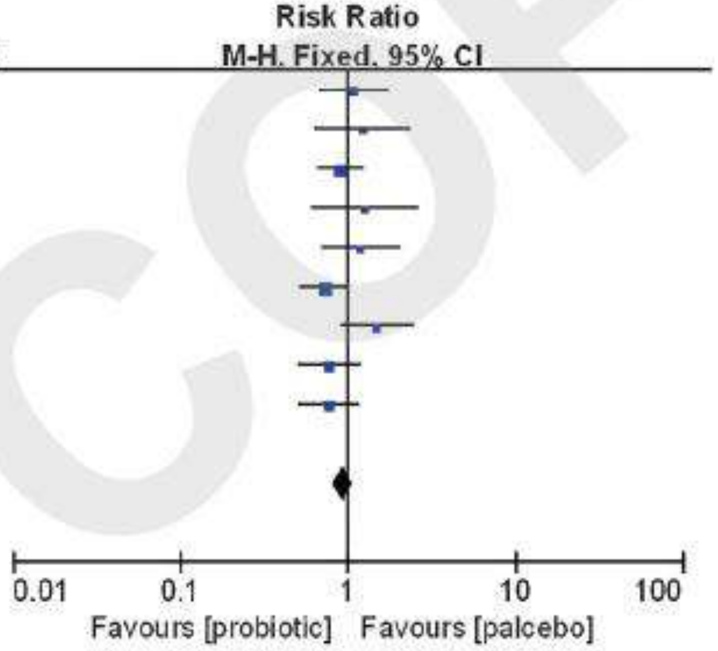
SIBILANCIAS Y PROBIÓTICOS

B

Study or Subgroup	Probiotic Events	Probiotic Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Boyle RJ	27	122	29	142	9.6%	1.08 [0.68, 1.73]
Jensen MP	17	66	12	57	4.6%	1.22 [0.64, 2.34]
Melanie R	46	132	55	142	19.0%	0.90 [0.66, 1.23]
Ou CY	14	65	11	64	4.0%	1.25 [0.62, 2.55]
Prescott SL	22	76	18	74	6.5%	1.19 [0.70, 2.03]
Stephen J	50	214	55	171	21.9%	0.73 [0.52, 1.01]
Taylor AL	30	88	20	87	7.2%	1.48 [0.92, 2.40]
Wickens K(a)	28	109	38	115	13.3%	0.78 [0.51, 1.17]
Wickens K(b)	30	118	38	115	13.8%	0.77 [0.51, 1.15]
Total (95% CI)		**990**		**967**	**100.0%**	**0.94 [0.81, 1.08]**
Total events	264		276			

Heterogeneity: $Chi^2 = 10.03$, df = 8 (P = 0.26); $I^2 = 20\%$

Test for overall effect: Z = 0.92 (P = 0.36)



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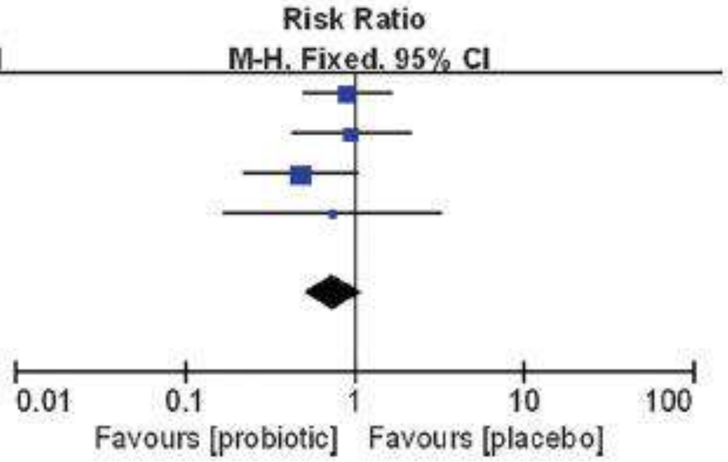
C

Study or Subgroup	Probiotic Events	Probiotic Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Boyle RJ	20	77	13	45	32.4%	0.90 [0.50, 1.63]
Jensen MP	11	118	11	112	22.3%	0.95 [0.43, 2.10]
Stephen J	9	171	19	173	37.3%	0.48 [0.22, 1.03]
Taylor AL	3	88	4	86	8.0%	0.73 [0.17, 3.18]
Total (95% CI)		**454**		**416**	**100.0%**	**0.74 [0.50, 1.09]**
Total events	43		47			

Heterogeneity: Chi² = 2.03, df = 3 (P = 0.57); I² = 0%

Test for overall effect: Z = 1.51 (P = 0.13)



CONCLUSIONES

CONCLUSIONES

Conclusion

We showed that probiotic supplementation may reduce the occurrence of asthma. In the subgroup analysis, LGG supplementation had a positive effect on the prevention of asthma. Moreover, there was no significant advantage of probiotic supplements on AR and other respiratory allergic symptoms. However, a larger sample size and well-designed RCTs need to be conducted to evaluate the exact role that probiotics play in the prevention of asthma in the future.

CONCLUSIONES

dence of childhood asthma. However, from the subgroup pooled analysis based on the sort of probiotic strains, Subgroup analysis of the comparison of probiotic supplementation versus placebo for asthma when using different probiotic strains showed that the risk of developing asthma was reduced in the LGG treatment group compared with the placebo group. Subgroup

Subtotal (95% CI)	670	671	35.1%	0.75 [0.57, 0.99]

Sin embargo en el análisis de subgrupos, la comparación de probióticos (LGG) con placebo mostro una reducción del riesgo de desarrollo de asma.

Suplementación con LGG facilita la prevención del asma

CONCLUSIONES

group compared with the placebo group. Subgroup analysis by duration time (pre- and postnatal, or post-natal only) showed that the postnatal-only group had a decrease in asthma occurrence. AR, wheeze, and pos-

Subtotal (95% CI)	414	408	17.9%	0.63 [0.42, 0.96]

- El subgrupo de suplementación postnatal tuvo una reducción en la ocurrencia de asma