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Effects of synbiotic supplementation on inflammatory and anti-inflammatory markers in adults: A GRADE-assessed systematic review and meta-analysis of randomized controlled trials

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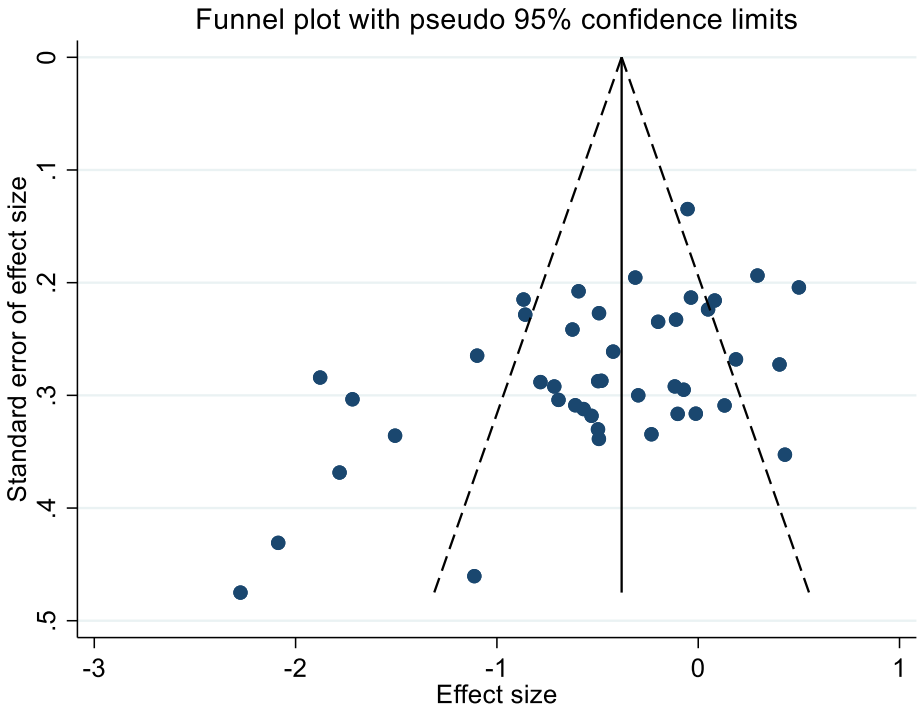
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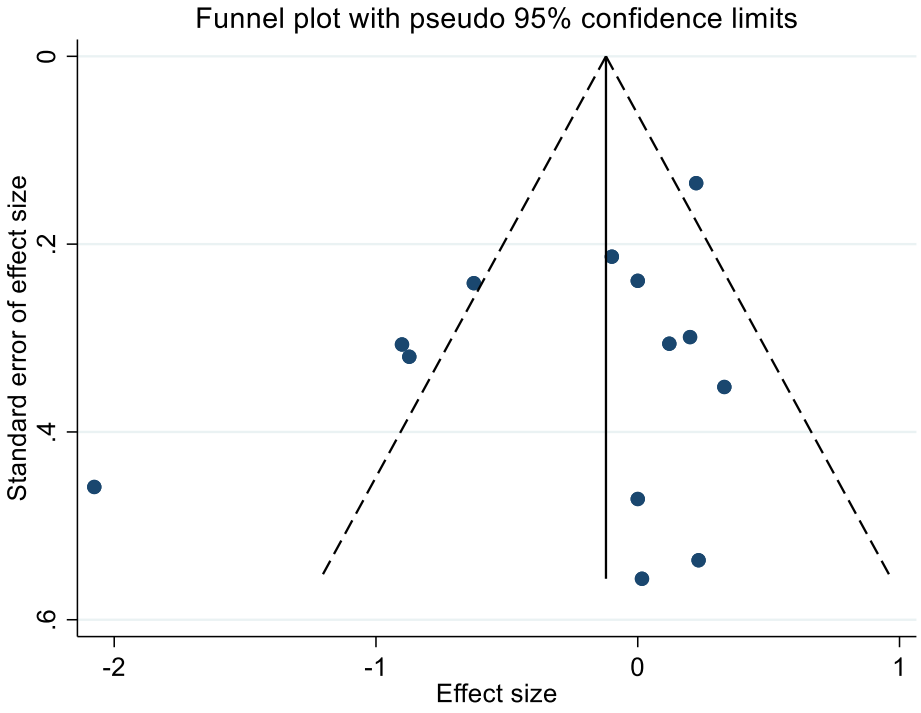
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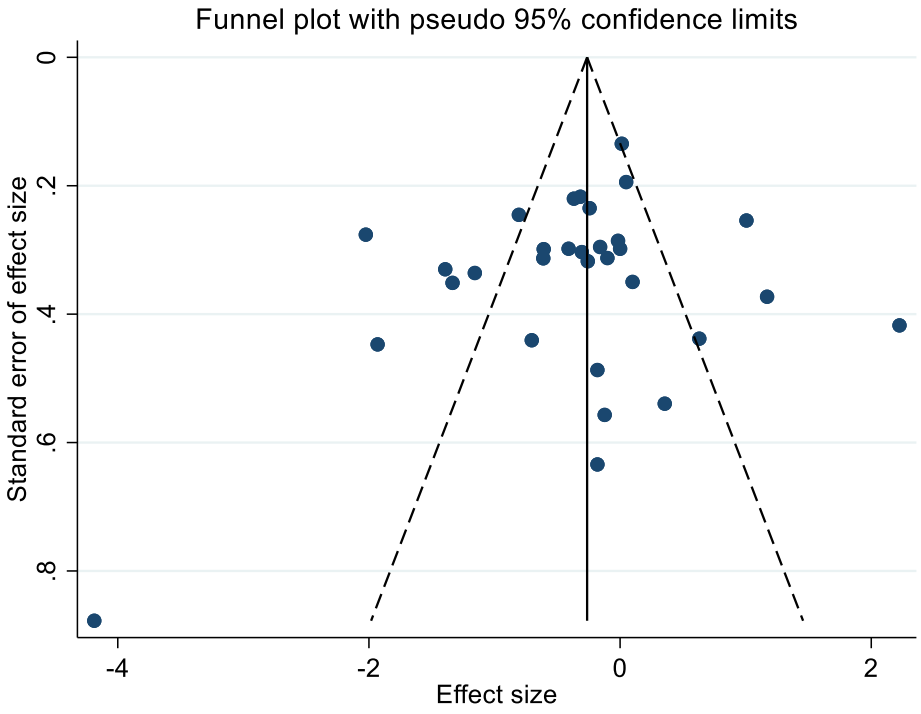
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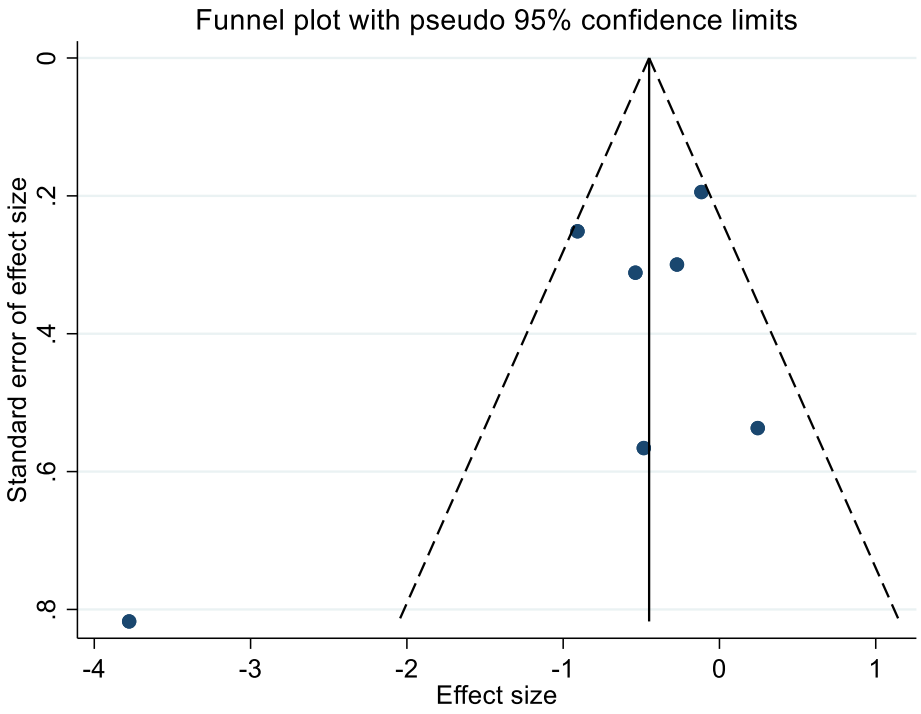
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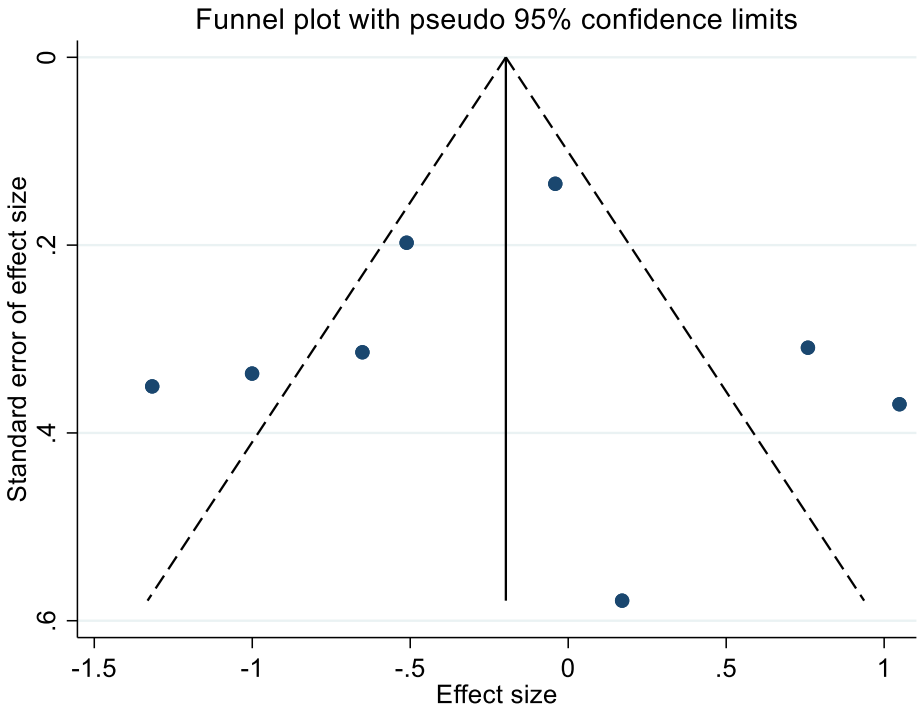
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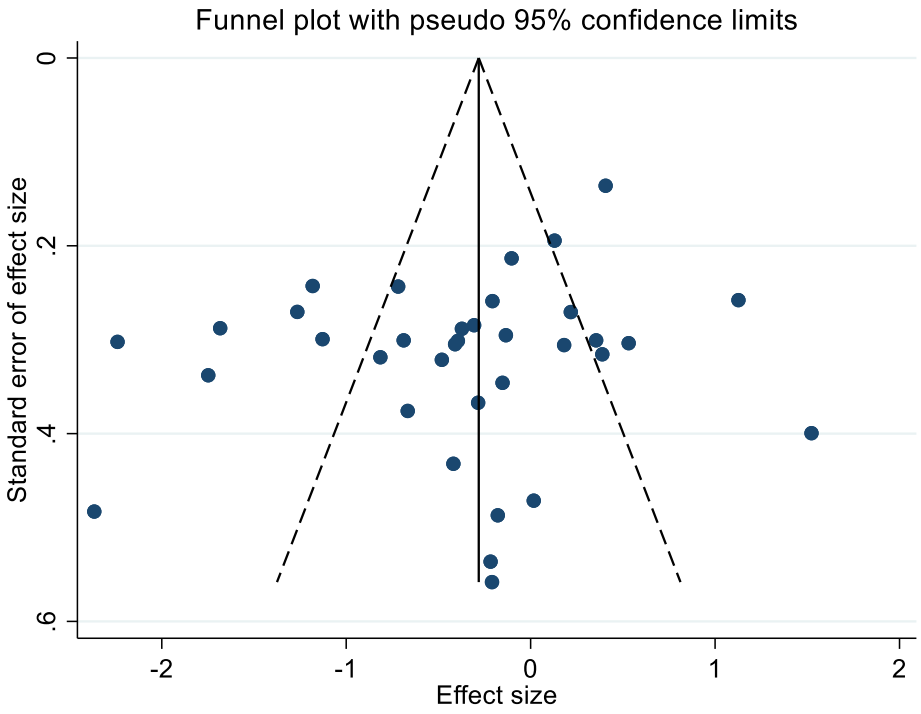
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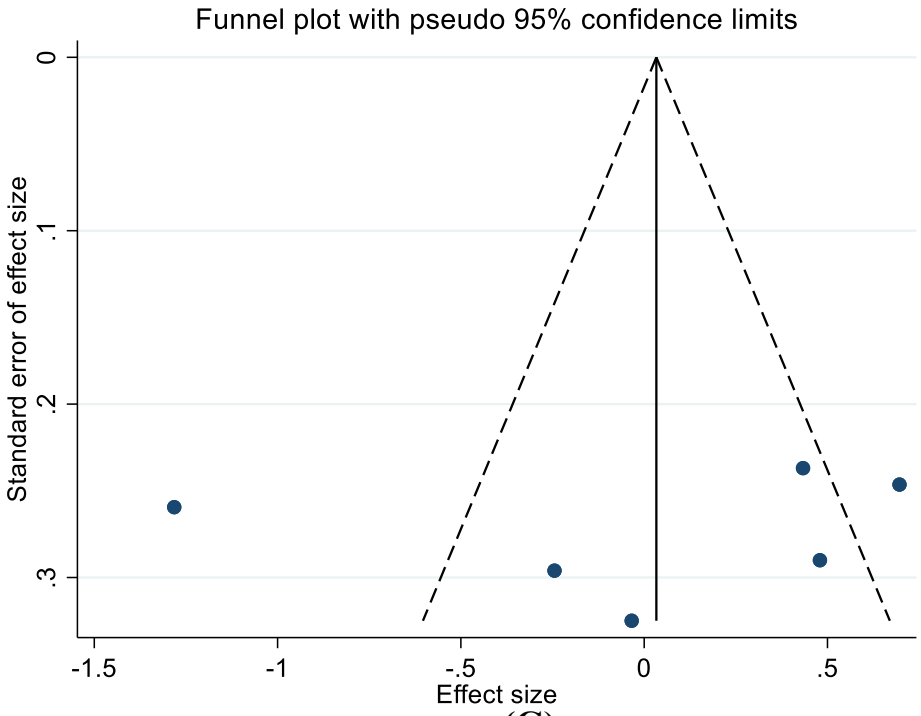
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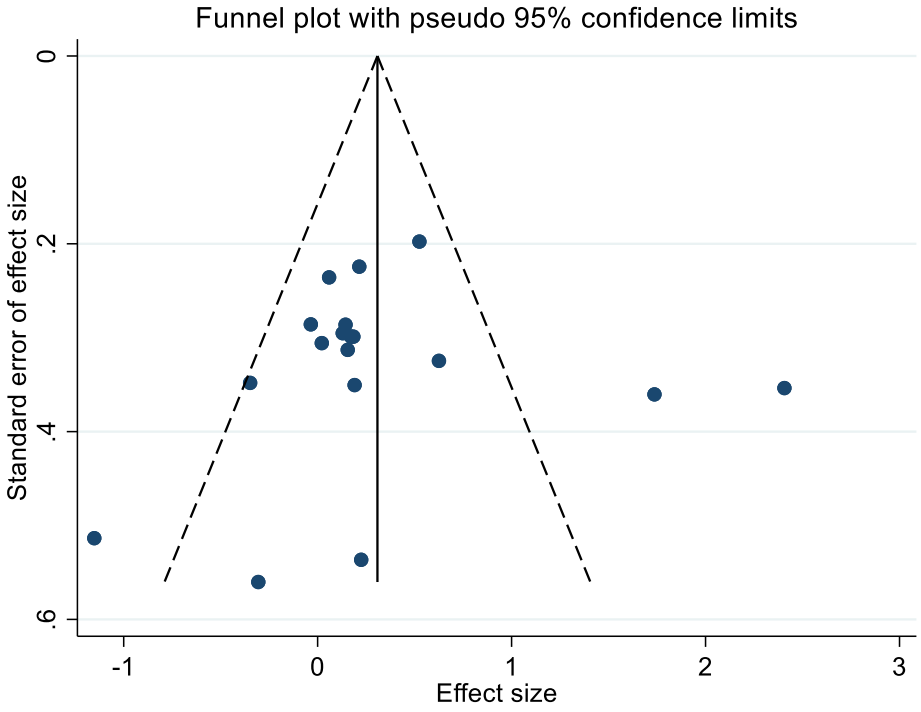
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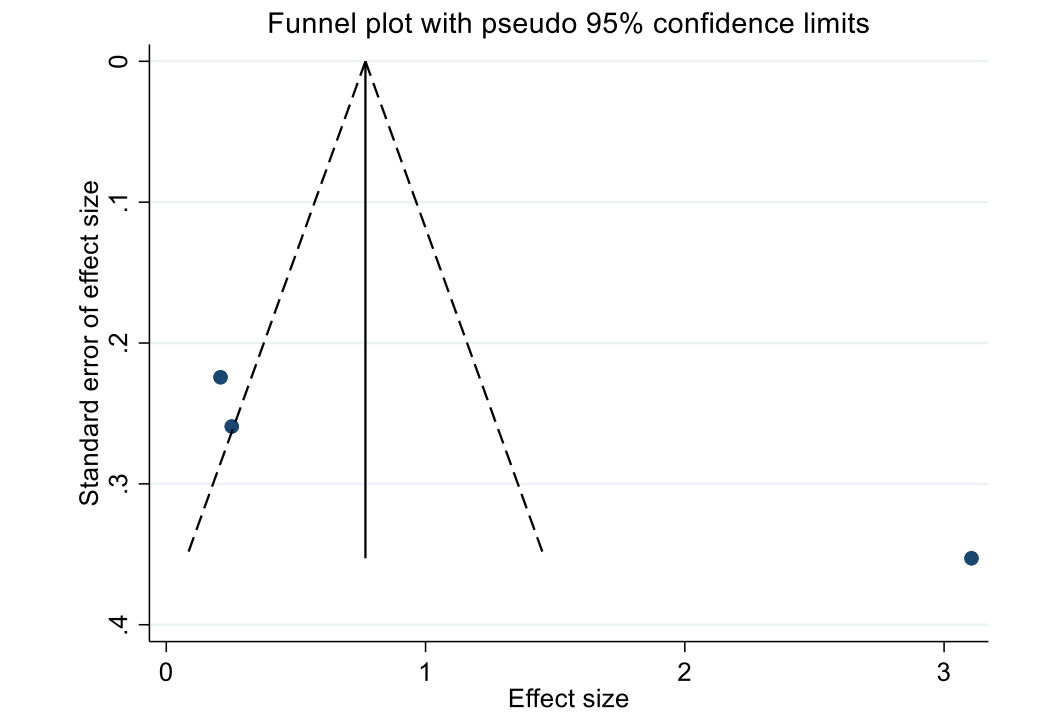

(I)

Figure S1. A-I. Assessment of publication bias in the impact of synbiotic supplementation on A: CRP, B: IL-1β, C: IL-6, D: IL-8, E: IFN-γ, F: TNF-α, G: LPS, H: IL-10, I: Adiponectin in adults.

Table S1. Characteristics of included studies in the meta-analysis.

Studies	Country	Study Design	Participant	Sample size and Sex	Sample size		Trial Duration (Week)	Means Age		Means BMI		Intervention	Features of Intervention				Control group
													Probiotics		Prebiotics		
					IG	CG		IG	CG	IG	CG		Type of colony	Dose of colony (CFU)	Type of prebiotis	Dosage (mg)	
Ogawa et al. (2006)	Japan	Rn/Db/ Pa	Healthy volunteers	12 B	6	6	4	40.71	40.14	NR	NR	Synbiotic powder	*Lactobacillus casei*	5×10^{9}	Dextran	1000	Placebo
Roller et al. (2007 A)	Ireland	Rn/Db/ Pa	Colon cancer patients	34 B	19	15	12	NR	NR	NR	NR	Synbiotic capsule	*Lactobacillus rhamnosus GG (LGG)* and *Bifidobacterium lactis Bb12 (Bb12)*	2×10^{10}	Inulin and oligofructose	10000	Maltodextrin
Roller et al. (2007 B)	Ireland	Rn/Db/ Pa	Polypectomised patients	40 B	19	21	12	NR	NR	NR	NR	Synbiotic capsule	*Lactobacillus rhamnosus GG (LGG)* and *Bifidobacterium lactis Bb12 (Bb12)*	2×10^{10}	Inulin and oligofructose	10000	Maltodextrin
Federico et al. (2009)	Italy	Rn/Db/ Pa	Patients with ulcerative colitis	18 B	9	9	8	46	48	NR	NR	Synbiotic powder	*Lactobacillus paracasei*	10×10^{9}	Arabinogalactan and xilo-oligosaccharides	500	Placebo
Nova et al. (2011)	Spain	Rn/Db/ Pa	Healthy adults	36 B	18	18	6	NR	NR	23.74	23.06	Synbiotic capsule	*L. acidophilus La5, B. animalis ssp. lactis Bb 12, Lactobacillus delbrueckii ssp. bulgaricus, Streptococcus thermophilus,* and *Lactobacillus paracasei ssp. paracasei*	2.4×10^{9}	FOS	1400	Placebo
González-Hernández et al. (2012)	Mexico	Rn/Db/ Pa	HIV-infected patients	10 B	5	5	16	26	30	23	24	Synbiotic gel formulation	*Lactobacillus rhamnosus HN001* plus and *Bifidobacterium lactis Bi-07*	2×10^{9}	FOS	10000	Placebo
Malaguarnera et al. (2012)	Italy	Rn/Db/ Pa	Non-Alcoholic	66 B	34	32	24	46.9	46.7	27.3	27.2	Synbiotic + lifestyle modification	*Bifidobacterium longum*	NR	FOS	NR	Placebo+ lifestyle modification

			Steatohepatitis													
Macfarlane et al. (2013)	UK	Rn/Db/Co	Older people	43 B	23	20	4	71.9	74	26.9	29.65	Synbiotic capsule	*Bifidobacterium longum*	4×10^{11}	Inulin and oligofructose	12000	Potato starch and 6 grams of powdered maltodextrose
Neto et al. (2013)	Brazil	Rn/Db/Pa	Older people	17 B	9	8	12	67.9	67	27.9	28.5	Synbiotic powder	*Lactobacillus paracasei*, *Lactobacillus rhamnosus*, *Lactobacillus acidophilus* and *Bifidobacterium lactis*	4×10^{9}	FOS	6000	Maltodextrin
Childs et al. (2014)	UK	Rn/Db/Co	Healthy adults	22 B	11	11	3	43	43	25	25	Synbiotic powder	*Bifidobacterium animalis subsp. lactis Bi-07*	1×10^{9}	xylo-oligosaccharide	8000	Maltodextrin
Eslamparast et al. (2014)	Iran	Rn/Db/Pa	Patients with NAFLD	52 B	26	26	28	46.35	45.69	32.1	31.3	Synbiotic capsule	*Lactobacillus casei,Lactobacillus rhamnosus, Streptococcus thermophilus, Bifidobacterium breve, Lactobacillus acidophilus, Bifidobacteriumlongum*, and *Lactobacillus bulgaricus*	4×10^{8}	FOS	197	Maltodextrin
Rajkumar et al. (2014)	India	Rn/Sb/Pa	Healthy young volunteers	30 B	15	15	6	NR	NR	22.23	22.72	Synbiotic capsule	*Lactobacillus salivarius UBL S22*	4×10^{9}	FOS	10000	Placebo
Peña et al. (2014)	Chile	Rn/Db/Pa	Obese Subjects	38 B	18	20	6	36.1	33.9	37	35.7	Synbiotic capsule	*Bifidobacterium lactis*	20×10^{9}	Oligofructose	16000	Placebo
Viramontes-Hörner et al. (2015)	Mexico	Rn/Db/Pa	HD patients	23 B	14	9	8	40.6	39	22.9	24	Nutritional counseling + Synbiotic gel	*Lactobacillus acidophilus* and *Bifidobacterium lactis Bi-07*	11×10^{6}	Inulin	2310	Nutritional counseling + placebo
Kooshki et al. (2015)	Iran	Rn/Db/Pa	Patients with T2DM	44 B	22	22	8	53.45	54.5	22.79	22.47	Synbiotic capsule	NR	NR	NR	NR	Placebo

Asgharian et al. (2016)	Iran	Rn/Db/ Pa	NAFLD patients	74 B	38	36	8	46.57	47.78	29.58	28.18	Synbiotic capsule	*Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus bulgaricus, Bifidobacterium breve, Bifidobacterium longum* and *Streptococcus thermophilus*	NR	FOS	NR	Starch
Stenman et al. (2016)	Finland	Rn/Db/ Pa	Overweight and Obese Adults	73 B	37	36	24	47.1	48.3	31.3	31	Synbiotic sachets	*Bifidobacterium animalis ssp. lactis*	10×10^{9}	Dietary fiber	12000	Placebo
Mofidi et al. (2017)	Iran	Rn/Db/ Pa	NAFLD patients	50 B	25	25	28	40.09	44.61	23.17	23.2	Synbiotic capsule	*Lactobacillus casei,Lactobacillus rhamnosus, Streptococcus thermophilus, Bifido-bacterium breve, Lactobacillus acidophilus, Bifidobacterium longum* and *Lactobacillus bulgaricus*	4×10^{8}	FOS	250	Maltodextrin
Ekhlasi et al. (2017 A)	Iran	Rn/Db/ Pa	NAFLD patients	30 B	15	15	8	NR	NR	27.28	27.84	Synbiotic capsule	*Lactobacillus casei, Lactobacillus rhamnosus, Stretococcus thermophilus, Bifidobacterium breve, Lactobacillus acidophilus, Bifidobacterium longum, Lactobacillus bulgaricus*	$7 \times 4 \times 10^{8}$	FOS	NR	Corn starch
Ekhlasi et al. (2017 B)	Iran	Rn/Db/ Pa	NAFLD patients	30 B	15	15	8	NR	NR	28.05	28.77	Synbiotic capsule+Alpha-tocopherol(400 IU)	*Lactobacillus casei, Lactobacillus rhamnosus, Stretococcus thermophilus, Bifidobacterium breve, Lactobacillus acidophilus, Bifidobacterium longum* and *Lactobacillus bulgaricus*	$7 \times 4 \times 10^{8}$	FOS	NR	Corn starch + Alpha-tocopherol (400 IU)

Mimura et al. (2017)	Brazil	Rn/Db/Pa	Recurrent aphthous stomatitis	45 B	22	23	16	36.6	38.3	NR	NR	Synbiotic sachets	*Lactobacillus paracasei Lpc-37 SD 5275*, *Lactobacillus rhamnosus HN001 SD 5675*, *Lactobacillus acidophilus NCFM SD 5221*, *Lactobacillus acidophilus NCFM SD 5221*, and *Bifidobacterium lactis*	8×10^{9}	FOS	12000	Maltodextrin
Xavier-Santos et al. (2018)	Brazil	Rn/Db/Pa	Patients with MetS	45 B	23	22	8	47	49.5	30.7	33.9	Synbiotic capsule	*Lactobacillus acidophilus La-5*	9.35×10^{10}	Inulin and FOS	4000	Placebo
Karimi et al. (2018)	Iran	Rn/Db/Pa	Women with PCOS	99 F	50	49	12	28.1	29	32.89	32	Synbiotic capsule	*Lactobacillus acidophilus*, *Lactobacillus casei*, *Lactobacillus bulgaricus*, *Lactobacillus rhamnosus*, *Bifidobacterium longum*, *Bifidobacterium breve* and *Streptococcus thermophilus*	123.6×10^{9}	FOS	NR	Starch and maltodextrin
Ghafouri et al. (2019 A)	Iran	Rn/Db/Pa	Patients with T2DM	50 B	25	25	8	54.92	54.6	26.39	27.04	Synbiotic bread	*Bacilluscoagulans*	1×10^{8}	Inulin	10000	Bread containing beta-glucan (3 g)
Ghafouri et al. (2019 B)	Iran	Rn/Db/Pa	Patients with T2DM	50 B	25	25	8	53.88	55	26.83	26.33	Synbiotic+lactic acid bread	*Bacilluscoagulans*	1×10^{8}	Inulin	10000	Lactic acid (4 g)
Rabiei et al. (2019)	Iran	Rn/Tb/Pa	Patients with MetS	40 B	20	20	12	57.1	60.8	32	32.7	Synbiotic capsule	*Lactobacillus casei, Lactobacillus rhamnosus, Streptococcus thermophilus, Bifidobacterium breve, Lactobacillus acidophilus, Bifidobacterium longum, Lactobacillus bulgaricus*	4×10^{8}	FOS	250	Maltodextrin

Soleimani et al. (2019)	Iran	Rn/Db/Pa	Diabetic Patients Undergoing HD	60 B	30	30	12	62.8	62.8	26.4	26.9	Synbiotic capsule	*Lactobacillus acidophilus strain T16 (IBRCM10785), L. casei strain T2 (IBRC-M10783)*, and *Bifidobacterium bifidum strain T1 (IBRC-M10771)*	6×10^9	Inulin	800	Corn starch
Kooshki et al. (2019)	Iran	Rn/Db/Pa	HD patients	46 B	23	23	8	62.92	62.83	23.45	23.6	Synbiotic capsule	*Lactobacillus coagulans*	NR	FOS	NR	Placebo
Altun et al. (2019)	Turkey	Rn/Pa	Ulcerative colitis	36 B	18	18	8	44.94	40	NR	NR	Synbiotic capsule	*Enterococcus faecium, Lactobacillus plantarum, Streptococcus thermophilus, Bifidobacterium lactis, Lactobacillus acidophilus, Bifido bacterium longum*	3×10^9	FOS	225	Placebo
Angelino et al. (2019)	Italy	Rn/Sb/Pa	Healthy sedentary overweight and obese	41 B	21	20	12	53	NR	30.6	31.3	Synbiotic Pasta	*Bacillus coagulans BC30*	7×10^9	Barley β-glucans	NR	Whole-grain
Louzada et al. (2020)	Brazil	Rn/Db/Pa	Healthy elders	49 B	25	24	24	77.2	77	NR	NR	Synbiotic capsule	*Lactobacillus paracasei*, *Lactobacillus rhamnosus*, *Lactobacillus acidophilus*, *Bifidobacterium lactis*	4×10^9	FOS	6000	Maltodextrin
Abhari et al. (2020)	Iran	Rn/Db/Pa	NAFLD patients	45 B	23	22	12	47.7	46.7	32.2	33.6	Synbiotic capsule	*Bifidobacterium coagulans (GBI-30)*	1×10^9	Inulin	400	Maltodextrin
Haghighat et al. (2020)	Iran	Rn/Db/Pa	HD Patients	42 B	23	19	12	48.04	45.47	23.85	23.38	Synbiotic powder	*Lactobacillus acidophilus T16, Bifidobacterium bifidum BIA-6, Bifidobacterium lactis BIA-6*, and *Bifidobacterium longum LAF-5*	10.8×10^7	5 g of FOS, 5 g of GOS, and 5 g of inulin.	15000	Maltodextrin
Bazyar et al. (2020)	Iran	Rn/Db/Pa	Patients with T2DM	47 B	23	24	8	48.6	50.1	24	25.5	Synbiotic capsule	Contained 7 viable and freeze-dried strains: *Lactobacillus*	23×10^9	FOS	100	Placebo

												acidophilus, *Lactobacillus casei*, *Lactobacillus rhamnosus*, *Lactobacillus bulgaricus*, *Bifidobacterium breve*, *Bifidobacterium longum* and *Streptococcus thermophilus*				
de Carvalho et al. (2020)	Brazil	Rn/Db/Pa	Elderly individuals	49 B	25	24	24	76.4	79.5	NR	NR	Synbiotic capsule	*Lactobacillus paracasei LPC-31*, *Lactobacillus rhamnosus HN001*, *Lactobacillus acidophilus NCFM*, and *Bifidobacterium lactis HN019*	4×10^9	FOS	6000	Maltodextrin
Mirzaeian et al. (2020)	Iran	Rn/Db/Pa	HD patients	42 B	21	21	8	58.3	69.74	24.81	24.62	Synbiotic capsule	*Lactobacillus casei*, *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus bulgaricus*, *Bifidobacterium breve*, *B. longum* and *Streptococcus thermophiles*	47×10^9	FOS	NR	Maltodextrin
Talebi et al. (2020)	Iran	Rn/Db/Pa	Patients with hypothyroidism	56 B	29	27	8	42.37	43.96	26.88	27.1	Synbiotic capsule	*Lactobacillus Casei*, *Lactobacillus Acidophilus*, *Lactobacillus Rhamnosus*, *lactobacillus Bulgaricus*, *Bifidobacterium Breve*, *Bifidobacterium Longum* and *Streptococcus Thermophilus*	52.7×10^9	FOS	500	Starch, lactose, magnesium stearate, silicon dioxide, and talc
Neto et al. (2020)	Brazil	Rn/Db/Pa	Elderly individuals	49 B	25	24	24	75.33	77.6	26.66	25.62	Synbiotic capsule	*Lactobacillus paracasei LCP-31*, *Lactobacillus rhamnosus HN001*, *Lactobacillus acidophilus NCFM* and *Bifidobacterium lactis HN019*	8×10^9	FOS	12000	Maltodextrin

Vafa et al. (2020)	Iran	Rn/Db/Pa	Breast cancer survivors	88 F	44	44	10	53.8	52.39	30.93	30.88	Synbiotic capsule	*Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus bulgaricus, Bifidobacterium breve, Bifidobacterium longum, Streptococcus thermophiles*	7×10^9	FOS	38.5	Placebo
Kanazawa et al. (2021)	Japan	Rn/Pa	Obese patients with T2Dm	86 B	44	42	24	61.1	55.9	29.5	29.1	Synbiotic powder	*Lacticaseibacillus paracasei YIT 9029*, *Bifidobacterium breve YIT 12272*	3×10^8	GOS	7500	Placebo
Chaiyasut et al. (2021)	Thailand	Rn/Db/Pa	Obese adults (BMI>25)	72 B	36	36	12	54.78	58.94	28.97	30.01	Synbiotic sachets	*Lactobacillus paracasei, Bifidobacterium longum, Bifidobacterium breve,*	5×10^{10}	Inulin and FOS	10000	Corn starch
Cicero et al. (2021)	Italy	Rn/Db/Pa	Elderly patients with diagnosis of MetS	60 B	30	30	8.6	72	71	27.4	27.3	Synbiotic liquid vial	*Lactobacillus plantarum PBS067, Lactobacillus acido-philus PBS066* and *Lactobacillus reuteri PBS072*	6×10^9	FOS	NR	Maltose
Raji Lahiji et al. (2021)	Iran	Rn/Tb/Pa	Overweight and obese breast cancer survivors	72 F	36	36	8	56.56	58.31	29.6	30	Synbiotic capsule	*Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus bulgaricus, Bifidobacterium breve, Bifidobacterium longum,* and *Streptococcus thermophiles*	10^9	FOS	35	Starch, lactose, magnesium stearate, and silicon dioxide
Ghavami et al. (2021)	Iran	Rn/Db/Pa	Participants with migraine	80 F	40	40	12	38.05	37.62	27.74	27.38	Synbiotic capsule	*Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus helveticus, Lactobacillus bulgaricus, Lactobacillus plantarum, Lactobacillus gasseri, Bifidobacterium breve, Bifidobacterium longum,*	2×10^9	FOS	42	Starch

												Bifidobacterium lactis, Bifidobacterium bifidum, and Streptococcus thermophilus,				
Quero et al. (2021 A)	Spain	Rn/Tb/ Pa	Sedentary students with low levels of physical activity (150 min/week)	14 M	7	7	4	23.04	24.31	NR	NR	Synbiotic sachets	*Bifidobacterium lactis CBP-001010, Lactobacillus rhamnosus CNCM I-4036* and *Bifidobacterium longum ES2*	1×10^9	FOS	200	Maltodextrin
Quero et al. (2021 B)	Spain	Rn/Tb/ Pa	Professional soccer players	13 M	7	6	4	20.66	21.9	NR	NR	Synbiotic sachets	*Bifidobacterium lactis CBP-001010, Lactobacillus rhamnosus CNCM I-4036* and *Bifidobacterium longum ES1*	1×10^9	FOS	200	Maltodextrin
Saneei Totmaj et al. (2022)	Iran	Rn/Db/ Pa	Obese and overweight breast cancer survivors women	80 F	41	39	10	53.8	52.39	30.93	30.88	Synbiotic capsule	*Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus bulgaricus, Bifidobacterium breve, Bifidobacterium longum* and *Streptococcus thermophiles*	1×10^9	FOS	38.5	Starch, lactose, magnesium stearate, and silicon dioxide
Rahimi et al. (2022)	Iran	Rn/Tb/ Pa	Patients with MetS	108 B	52	56	12	42.77	45.64	31.03	31.14	Synbiotic capsule	*Lactobacillus casei, Lactobacillus rhamnosus, Lactobacillus acidophilus, Lactobacillus bulgaricus, Bifidobacterium longum, Bifidobacterium breve,* and *Streptococcus thermophiles*	10^9	FOS	38500	Starch
Widhani et al. (2022)	Indonesia	Rn/Db/ Pa	Patients with Systemic Lupus Erythematosus	46 B	23	23	8.5	35	27	23.41	22.09	Synbiotic capsule	*Lactobacillus helveticus R0052* 60%, *Bifidobacterium infantis R0033* 20% and *Bifidobacterium bifidum R0071* 20%	3×10^9	FOS	80	Saccharum lactis

Shoaei Matin et al. (2022)	Iran	Rn/Db/ Pa	Patients with heart failure	80 B	41	39	10	50.54	50.1	25.51	26.53	Synbiotic capsule	*Lactobacillus casei*, *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus bulgaricus*, *Bifidobacterium breve*, *Bifidobacterium longum*, *Streptotus thermophilus*,	3.04×10^{10}	FOS	38.5	Placebo
Lyon et al. (2023 A)	India	Rn/Db/ Pa	Adults with overweight and obesity	95 B	46	49	12	41.13	41.74	31.15	29.89	Synbiotic capsule	*Lactobacillus gasseri BNR17*, *Lactobacillus salivarius Ls-33*, *Lactobacillus rhamnosus Lr-32*, *Lactobacillus paracasei Lpc-37*, *Lactobacillus plantarum Lp-115*, *Lactobacillus casei Lc-11*, *Lactobacillus fermentum*, *Lactobacillus reuteri, Bacillus subtilis MB40, Bifidobacterium bifidum Bb-06, Bifidobacterium lactis Bl-04, Bifidobacterium longum Bl-05, Streptococcus thermophilus St-21* and *Saccharomyces boulardii*	2×10^{10}	Inulin	315	Capsule contained inert rice hull concentrate
Lyon et al. (2023 B)	India	Rn/Db/ Pa	Adults with overweight and obesity	97 B	48	49	12	42.47	41.74	30.17	29.89	Synbiotic capsule	*Lactobacillus gasseri BNR17, Lactobacillus salivarius UALs-07, Lactobacillus rhamnosus GG, Lactobacillus paracasei UALpc-04, Lactobacillus plantarum UALp-05, Lactobacillus casei UALc-03, Lactobacillus fermentum SBS-1, Lactobacillus reuteri UALre-16, Bacillus subtilis DE111, Bifidobacterium bifidum UABb-10,*	2×10^{10}	Inulin	315	Capsule contained of inert rice hull concentrate

												Bifidobacterium lactis UABla-12, Bifidobacterium longum UABl-14 and *Streptococcus thermophilus*				
Li et al. (2023)	China	Rn/Db/Pa	Healthy adults	106 B	53	53	8	22.4	22.2	21.6	21.5	Synbiotic powder	*Bifidobacterium lactis HN019* and *Lactobacillus rhamnosus*	2.5×10^{8}	FOS	500	Maltodextrin
Mitrovic et al. (2023)	Serbia	Rn/Db/Pa	Non dialyzed chronic kidney disease patients	34 B	17	17	12	69	69	26.5	25.5	Synbiotic capsule	*Lactobacillus acidophilus CBT*, *Lactobacillus casei CBT LC5*, and *Bifidobacterium lactisCBT BL3*	32×10^{9}	Inulin	3200	Maltodextrin
Fallah et al. (2023)	Iran	Rn/Db/Pa	Obese patients	46 F	23	23	8	38.39	38	32.59	32.22	Synbiotic + L-Carnitine	*Lactobacillus casei PXN 37, Lactobacillus rhamnosus PXN 54, Lactobacillus acidophilus PXN 35, Lactobacillus bulgaricus PXN 39, Bifidobacterium breve PXN 25, Bifidobacterium longum PXN 30* and *Streptococcus thermophilus PXN 66*	1×10^{8}	FOS	175	Same amounts of L-carnitine+ Maltodextrin
Liu et al. (2023)	China	Rn/Db/Pa	Patients with coronary artery diseases	46 F	23	23	8	49.12	51.82	NR	NR	Synbiotic sachets	*Lactobacillus rhamnosus*	1.9×10^{9}	Inulin	15	Placebo
Mitrović et al. (2024)	Serbia	Rn/Db/Pa	Patients with MASLD	84 B	41	43	12	69	68	26.2	25.7	Synbiotic capsule	*Lactobacillus acidophilus CBT LA1*, *Lactobacillus casei CBT LC5* and *Bifidobacterium lactis CBT BL3*	64×10^{9}	Inulin	6400	Maltodextrin
Salamat et al. (2024)	Iran	Rn/Db/Pa	Adult men with dyslipidemia	56 M	28	28	12	43.2	41.7	30.1	28.7	Synbiotic sachets	*Lactobacillus acidophilus ATCC4356* , *Lactobacillus fermentum DSM14241* , *Lactobacillus plantarum ATCC14917*, *Bifidobacterium longum*	6×10^{10}	Inulin and FOS	5000	Corn starch

												BAA-999 , *Bifidobacterium lactis ATCC27536* and *Saccharomyces boulardii CNCM I-745*				
Yarahmadi et al. (2024)	Iran	Rn/Db/Pa	Patients with T2DM	47 B	23	24	8	48.6	50.1	24	25.5	Synbiotic capsule	*Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus rhamnosus, Lactobacillus bulgaricus, Bifidobacterium breve, Bifidobacterium longum, Streptococcus thermophilus*	23×10^9	FOS	100	Placebo
Stougaard et al. (2024)	Denmark	Rn/Db/Co	Type 1 diabetes and albuminuria	70 B	35	35	12	60	60	26	27	Synbiotic sachets	*Lactobacillus reuteri DSM 34531, Lactobacillus rhamnosus DSM 26357, Bifidobacterium lactis DSM 32269*	7.5×10^9	FOS	2856	Placebo
Hosseini et al. (2024)	Iran	Rn/Db/Pa	Patients with MetS	55 B	28	27	8	46.89	47.44	30/92	31.77	Synbiotic capsule	*Bifidobacterium coagulans SC- 208 and Bifidobacterium indicus HU36*	24×10^9	FOS	1000	Placebo
Tirgar et al. (2024 A)	Iran	Rn/Db/Pa	Patients with breast cancer	43 F	21	22	18	46.5	50	28.9	28.2	Synbiotic capsule	*Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus salivarius, Lactobacillus reuteri, Bifidobacterium lactis, Bifidobacterium longum, and Bifidobacterium bifidum*	8×10^9	FOS	38.5	Placebo
Tirgar et al. (2024 B)	Iran	Rn/Db/Pa	Patients with breast cancer	33 F	18	15	18	46.7	49.6	29.1	28.3	Synbiotic capsule	*Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus salivarius, Lactobacillus reuteri,*	8×10^9	FOS	38.5	Vitamin D

												Bifidobacterium lactis, Bifidobacterium longum, and Bifidobacterium bifidum				
Yazdani et al. (2025)	Iran	Rn/Tb/Pa	Patients with NAFLD and T2DM	40 B	20	20	12	56.75	55.5	29.62	29.99	Synbiotic capsule	*Lactobacillus acidophilus, Lactobacillus lactis, Lactobacillus rhamnosus, Lactobacillus casei Bifidobacterium longum, Bifidobacterium breve*	1×10^9	FOS	21	Placebo
Fasitasari et al. (2025)	Indonesia	Rn/Db/Pa	Patients with advanced Nasopharyngeal Cancer	34 B	14	20	6	45.8	47.9	23.7	21.9	Synbiotic capsule	*Lactobacillus plantarum,Streptococcus thermophiles, and Bifidobacterium bifidum*	1×10^9	FOS	NR	Placebo
Vijay et al. (2025)	UK	Rn/Pa	Healthy adults	40 B	20	20	6	50.17	46.10	26.9	26.85	Dairy	Kefir	170 millilitre	Inulin	10000	Placebo
Schott et al. (2025)	USA	Rn/Db/Pa	Early postmenopausal women	221 F	115	106	51	55	55	26	26	Synbiotic capsule	*Levilactobacillus brevis, Lactiplantibacillus plantarum, Leuconostoc mesenteroides, Pichia kudriavzevii*	95×10^9	Oligofructose	640	Placebo
Ramadan et al. (2025)	Egypt	Rn/Pa	Patients with Parkinson	66 B	33	33	12	56	55	NR	NR	Synbiotic sachets	*Lactobacillus acidophilus*	10×10^9	Inulin	3000	Placebo
Dinavari et al. (2026)	Iran	Rn/Db/Pa	Patients with MASLD	80 B	40	40	12	49.37	48.14	31.11	30.01	Synbiotic capsule	*Bifidobacterium breve and Bifidobacterium longum, Lacticaseibacillus rhamnosus and Lacticaseibacillus casei, Lactobacillus bulgaricus and Lactobacillus acidophilus, Streptococcus thermophilus*	2×10^9	FOS	1000	Placebo

Abbreviations: IG, intervention group; CG, control group; Db, double-blinded; Sb, single-blinded; Pa, Parallel; Co, Cross-Over; Rn, randomized; NR, not reported; F, Female; M, Male; B, Both gender; NR, not reported; CFU, Colony Forming Unit; FOS, Fructooligosaccharides; GOS, galactooligosaccharides; MetS, Metabolic syndrome; NAFLD, Non-alcoholic fatty liver disease; MASLD, Metabolic dysfunction-associated steatotic liver disease; T2DM, Type 2 diabetes mellitus; HD, Hemodialysis; PCOS,Polycystic Ovary Syndrome; Tb, Triple blind.

Table S2. Risk of bias assessment

Study	Random sequence generation	Allocation concealment	Selective reporting	Other sources of bias	Blinding (participants and personnel)	Blinding (outcome assessment)	Incomplete outcome data	General Quality
Ogawa et al. (2006)	L	U	U	U	U	U	U	Poor
Roller et al. (2007)	U	U	U	U	U	U	U	Poor
Federico et al. (2009)	U	U	L	U	U	U	U	Poor
Nova et al. (2011)	L	U	L	U	L	U	U	Good
González-Hernándezet al. (2012)	U	U	L	U	U	U	U	Poor
Malaguarnera et al. (2012)	L	L	U	U	U	U	U	Fair
Macfarlane et al. (2013)	L	L	L	L	L	L	L	Good
Neto et al. (2013)	H	L	U	U	U	U	U	Poor
Childs et al. (2014)	L	L	L	U	L	L	U	Good
Eslamparast et al. (2014)	L	L	L	U	L	L	L	Good
Rajkumar et al. (2014)	U	H	U	U	H	L	L	Poor
Peña et al. (2014)	H	U	L	L	U	U	L	Poor
Viramontes-Hörner et al. (2015)	U	L	U	U	U	L	U	Fair
Kooshki et al. (2015)	U	U	U	U	U	U	U	Poor
Asgharian et al. (2016)	L	L	U	U	U	U	L	Good
Stenman et al. (2016)	L	L	L	L	L	L	L	Good
Mofidi et al. (2017)	U	L	L	U	L	U	L	Good
Ekhlasi et al. (2017)	L	L	L	L	L	L	L	Good
Mimura et al. (2017)	L	L	L	U	L	L	U	Good
Louzada et al. (2018)	L	L	L	U	L	U	L	Good
Xavier-Santos et al. (2018)	U	L	L	U	L	L	L	Good

Karimi et al. (2018)	L	U	L	U	L	L	L	Good
Ghafouri et al. (2019)	L	L	L	U	L	L	H	Good
Rabiei et al. (2019)	L	L	L	L	L	L	L	Good
Soleimani et al. (2019)	L	L	L	U	L	L	L	Good
Kooshki et al. (2019)	L	L	U	U	U	U	U	Fair
Altun et al. (2019)	L	U	U	U	U	U	U	Fair
Angelino et al. (2019)	L	U	L	L	L	H	L	Poor
Abhari et al. (2020)	L	L	L	U	L	L	L	Good
Haghighat et al. (2020)	L	L	U	U	L	L	H	Good
Bazyar et al. (2020)	L	L	L	L	L	L	L	Good
de Carvalho et al. (2020)	L	L	U	U	L	L	U	Good
Mirzaeian et al. (2020)	L	L	L	U	L	L	U	Good
Talebi et al. (2020)	L	L	L	U	L	L	H	Good
Neto et al. (2020)	L	L	L	U	L	U	U	Good
Vafa et al. (2020)	L	L	L	U	L	L	L	Good
Kanazawa et al. (2021)	L	U	U	U	H	H	U	Poor
Chaiyasut et al. (2021)	L	U	L	U	L	U	U	Good
Cicero et al. (2021)	L	L	L	L	L	L	U	Good
Raji Lahiji et al. (2021)	L	L	L	U	L	L	L	Good
Ghavami et al. (2021)	L	L	L	U	L	L	H	Good
Quero et al. (2021)	L	U	L	U	L	L	L	Good
Saneei Totmaj et al. (2021)	L	L	L	L	L	L	L	Good
Rahimi et al. (2022)	L	L	L	U	U	U	L	Good
Widhani et al. (2022)	L	L	U	U	L	L	L	Good
Shoaei Matin et al. (2022)	L	L	L	L	L	L	L	Good
Lyon et al. (2023)	L	L	L	U	L	L	L	Good

Li et al. (2023)	L	L	L	L	L	L	L	Good
Mitrovic et al. (2023)	L	L	L	U	U	U	U	Good
Fallah et al. (2023)	L	L	L	L	L	L	L	Good
Liu et al. (2023)	L	L	L	U	U	U	U	Good
Mitrović et al. (2024)	L	L	L	L	L	L	U	Good
Salamat et al. (2024)	L	L	L	U	L	L	L	Good
Yarahmadi et al. (2024)	L	L	L	L	L	L	L	Good
Stougaard et al. (2024)	L	L	L	L	L	L	L	Good
Hosseini et al. (2024)	L	L	L	U	L	L	L	Good
Tirgar et al. (2024)	L	L	L	L	L	L	L	Good
Fasitasari et al. (2025)	U	L	L	L	L	L	L	Good
Yazdani et al. (2025)	L	L	L	L	L	L	L	Good
Vijay et al. 2025	L	U	L	L	H	H	U	Poor
Schott et al. 2025	U	L	L	L	L	L	L	Good
Ramadan et al. 2025	L	L	L	L	H	H	L	Poor
Dinavari et al. (2026)	L	L	L	L	L	L	L	Good

Abbreviations: L: low risk of bias; H: high risk of bias; U: unclear risk of bias.

Overall good quality: 2< Low risk of bias items

Overall fair quality: = 2 Low risk of bias items

Overall poor quality: < 2 Low risk of bias items

Table S3. Pooled estimates of the subgroup analyses.

	NO	SMD (95%CI)	P-value	Heterogeneity		
				P heterogeneity	I^2	P between sub-groups
Subgroup analyses of Synbiotic supplementation on CRP						
Overall effect	43	-0.49 (-0.67, -0.31)	**<0.001**	**<0.001**	79.7%	
Continents						
Asia	32	-0.44 (-0.65, -0.22)	**<0.001**	**<0.001**	81.7%	0.66
Europe	8	-0.70 (-1.05, -0.36)	**<0.001**	**0.004**	66.7%	
South America	1	-0.50 (-1.15, 0.15)	0.13	-	-	
North America	2	-0.49 (-1.51, 0.53)	0.35	**0.03**	79.5%	
Age						
<50	22	-0.35 (-0.57, -0.12)	**0.002**	**<0.001**	75.2%	0.29
>50	19	-0.60 (-0.88, -0.32)	**<0.001**	**<0.001**	82.4%	
NR	2	-1.23 (-3.23, 0.78)	0.23	**<0.001**	91.9%	
Trial duration (week)						
<12	23	-0.43 (-0.68, -0.19)	**<0.001**	**<0.001**	76.0%	0.55
≥12	20	-0.55 (-0.81, -0.28)	**<0.001**	**<0.001**	83.5%	
Type of prebiotics						
FOS	25	-0.34 (-0.58, -0.09)	**0.006**	**<0.001**	80.5	**0.04**
Inulin	9	-0.91 (-1.23, -0.59)	**<0.001**	**0.003**	66.0%	
Inulin + FOS	1	-0.63 (-1.10, -0.15)	**0.01**	**-**	-	
Others	8	-0.46 (-0.80, -0.11)	**0.009**	**0.001**	72.5%	
Type of colony						
L. casei, L. rhamnosus, S. thermophilus, B. breve, L. acidophilus, B. longum and L. bulgaricus	13	-0.17 (-0.48, 0.15)	0.30	**<0.001**	80.6%	0.08
B. coagulans	3	-0.50 (-0.83, -0.17)	**0.003**	0.61	0.0%	
B. longum	2	-0.86 (-1.38, -0.34	**0.001**	0.20	40.1%	
L. acidophilus, L. casei, and B. lactis	2	-1.42 (-2.62, -0.22)	**0.02**	**0.01**	84.2%	
B. lactis, and L. rhamnosus	1	-0.31 (-0.70, 0.07)	**0.11**	**-**	-	
Others	22	-0.59 (-0.83, -0.34)	**<0.001**	**<0.001**	78.3%	
Health status						
Healthy	11	-0.53 (-0.79, -0.26)	**<0.001**	**0.001**	67.6%	0.76
Unhealthy	32	-0.47 (-0.70, -0.25)	**<0.001**	**<0.001**	82.4%	
Sex						
Both sexes	37	-0.52 (-0.70, -0.33)	**<0.001**	**<0.001**	75.8%	0.50
Female	6	-0.32 (-0.86, 0.22)	0.25	**<0.001**	90.0%	
Baseline BMI (kg/m^2)						
Normal (18.5-24.9)	12	-0.67 (-1.06, -0.28)	**0.001**	**<0.001**	78.6%	0.11
Overweight (25-29.9)	17	-0.61 (-0.90, -0.31)	**<0.001**	**<0.001**	83.4%	
Obese (>30)	13	-0.20 (-0.46, 0.07)	0.14	**<0.001**	72.4%	
NR	1	-0.49 (-1.16, 0.17)	0.15	-	-	

Overall quality						
Good	36	-0.41 (-0.59, -0.23)	**<0.001**	**<0.001**	78.6%	**0.003**
Fair	2	-1.26 (-1.74, -0.77)	**<0.001**	0.05	59.0%	
Poor	5	-0.15 (-0.70, 0.41)	0.60	0.15	51.3%	
Subgroup analyses of Synbiotic supplementation on IL-1β						
Overall effect	13	-0.25 (-0.56, 0.07)	0.13	**<0.001**	73.5%	
Continents						
Asia	6	-0.65 (-0.18, -0.13)	**0.02**	**<0.001**	79.3%	**0.03**
Europe	5	0.06 (-0.26, 0.37)	0.73	0.99	0.0%	
South America	1	0.20 (-0.39, 0.79)	0.50	-	-	
North America	1	0.22 (-0.04, 0.49)	0.10	-	-	
Age						
<50	7	-0.19 (-0.63, 0.26)	0.40	**0.02**	58.9%	**<0.001**
>50	5	-0.06 (-0.36, 0.24)	0.70	**0.04**	59.3%	
NR	1	-2.08 (-2.98, -1.18)	**<0.001**	-	-	
Trial duration (week)						
<12	8	-0.31 (-0.79, 0.18)	0.21	**0.001**	73.0%	0.69
≥12	5	-0.17 (-0.62, 0.27)	0.44	**0.001**	77.3%	
Type of prebiotics						
FOS	8	-0.42 (-0.89, 0.006)	0.09	**<0.001**	75.8%	0.06
Inulin + FOS	2	-0.23 (-1.04, 0.58)	0.57	**0.03**	78.3%	
Others	3	0.19 (-0.04, 0.43)	0.11	0.87	0.0%	
Type of colony						
L. casei, L. rhamnosus, S. thermophilus, B. breve, L. acidophilus, B. longum and L. bulgaricus	2	-0.47 (-1.25, 0.31)	0.24	**0.03**	78.3%	0.67
B. lactis, L. rhamnosus, and B. longum	2	0.13 (-0.63, 0.89)	0.74	0.78	0.0%	
L.casei, L. acidophilus, L. rhamnosus, L. salivarius, L. reuteri, B.lactis, B.longum, and B. bifidum	2	-0.28 (-1.46, 0.90)	0.64	**0.01**	84.4%	
B. longum	1	0.12 (-0.48, 0.72)	0.69	-	-	
Others	6	-0.31 (-0.83, 0.22)	0.25	**<0.001**	83.4%	
Health status						
Healthy	6	-0.33 (-0.94, 0.28)	0.29	**<0.001**	83.3%	0.71
Unhealthy	77	-0.20 (-0.55, 0.15)	0.27	**0.02**	59.4%	
Sex						
Both sexes	7	-0.43 (-0.92, 0.07)	0.09	**<0.001**	77.9%	0.40
Male	2	0.13 (-0.63, 0.89)	0.74	0.78	0.0%	
Female	4	-0.08 (-0.52, 0.37)	0.74	**0.01**	72.9	
Baseline BMI (kg/m^2)						
Normal (18.5-24.9)	2	-1.44 (-2.59, -0.29)	**0.01**	**0.03**	0.78	0.12
Overweight (25-29.9)	6	-0.13 (-0.50, 0.25)	0.51	**0.003**	72.0%	
Obese (>30)	2	0.002 (-0.34, 0.34)	0.99	0.42	0.0%	
NR	3	0.08 (-0.51, 0.66)	0.80	0.94	0.0%	

Overall quality						
Good	11	-0.14 (-0.41, 0.13)	0.32	**0.003**	62.4%	**<0.001**
Fair	1	-2.08 (-2.98, -1.18)	**<0.001**	-	-	
Poor	1	0.00 (-0.92, 0.92)	0.99<	-	-	
Subgroup analyses of Synbiotic supplementation on IL-6						
Overall effect	31	-0.33 (-0.61, -0.05)	**0.02**	**<0.001**	85.2%	
Continents						
Asia	13	-0.69 (-1.05, -0.32)	**<0.001**	**<0.001**	81.9%	**0.005**
Europe	11	-0.32 (-0.86, 0.23)	0.26	**<0.001**	86.0%	
South America	4	0.49 (-0.51, 1.50)	0.37	**<0.001**	87.7%	
North America	3	0.06 (-0.19, 0.30)	0.65	0.38	0.0%	
Age						
<50	1	-0.45 (-0.89, -0.002)	**0.049**	**<0.001**	87.2%	**<0.001**
>50	12	-0.08 (-0.38, 0.23)	0.62	**<0.001**	75.8%	
NR	1	-1.93 (-2.81, -1.05)	**<0.001**	**-**	-	
Trial duration (week)						
<12	16	-0.44 (-0.89, 0.01)	0.06	**<0.001**	85.4%	0.48
≥12	15	-0.23 (-0.60, 0.13)	0.21	**<0.001**	85.8%	
Type of prebiotics						
FOS	13	-0.15 (-0.50, 0.19)	0.38	**<0.001**	71.7%	0.69
Inulin	5	-0.28 (-1.18, 0.63)	0.55	**<0.001**	89.8%	
Inulin + FOS	2	-0.42 (-1.21, -0.37)	0.30	**0.003**	77.0%	
Others	11	-0.54 (-1.10, 0.01)	0.06	**<0.001**	90.8%	
Type of colony						
L. paracasei, L. rhamnosus, L. acidophilus, and B. lactis	2	-0.06 (-0.54, 0.43)	0.81	0.77	0.0%	0.32
B. lactis, and L. rhamnosus	2	0.03 (-0.34, 0.39)	0.88	0.73	0.0%	
L. casei, L. rhamnosus, S. thermophilus, B. breve, L. acidophilus, B. longum and L. bulgaricus	4	-0.77 (-1.65, 0.11)	0.09	**<0.001**	89.2%	
B. lactis, L. rhamnosus, and B. longum	2	0.12 (-0.64, 0.88)	0.75	0.54	0.0%	
L. acidophilus, L. casei, and B. lactis	2	0.37 (-1.13, 1.88)	0.63	**<0.001**	92.1%	
L.casei, L. acidophilus, L. rhamnosus, L. salivarius, L. reuteri, B.lactis, B.longum, and B. bifidum	1	0.10 (-0.59, 0.79)	0.78	-	-	
B. longum	1	-0.61 (-1.23, 0.002)	0.05	-	-	
Others	17	-0.42 (-0.83, -0.01)	**0.045**	**<0.001**	88.4%	
Health status						
Healthy	14	-0.24 (-0.63, 0.14)	0.21	**<0.001**	82.4%	0.57
Unhealthy	17	-0.41 (-0.83, 0.008)	0.05	**<0.001**	87.3%	

Sex						
Both sexes	26	-0.40 (-0.74, -0.07)	**0.02**	**<0.001**	87.1%	0.13
Male	2	0.12 (-0.64, 0.88)	0.75	0.54	0.0%	
Female	3	-0.004 (-0.23, 0.22)	0.98	0.83	0.0%	
Baseline BMI (kg/m^2)						
Normal (18.5-24.9)	8	-0.48 (-0.95, -0.01)	**0.04**	**<0.001**	75.3%	0.51
Overweight (25-29.9)	11	-0.18 (-0.57, 0.21)	0.37	**<0.001**	83.1%	
Obese (>30)	7	-0.11 (-0.90, 0.69)	0.79	**<0.001**	92.2%	
NR	5	-0.91 (-2.00, 0.19)	0.11	**<0.001**	86.9%	
Overall quality						
Good	24	-0.24 (-0.55, 0.07)	0.12	**<0.001**	86.0%	0.47
Fair	3	-0.53 (-1.83, 0.78)	0.43	**<0.001**	88.4%	
Poor	4	-1.00 (-2.22, 0.22)	0.11	**<0.001**	84.2%	
Subgroup analyses of Synbiotics supplementation on IL-8						
Overall effect	7	-0.62 (-1.15, -0.09)	**0.02**	**<0.001**	76.0%	
Continents						
Asia	1	-0.12 (-0.50, 0.27)	0.55	**-**	-	0.23
Europe	5	-0.91 (-1.72, -0.09)	**0.03**	**0.001**	78.1%	
South America	1	-0.27 (-0.86, 0.32)	0.36	**-**	-	
Age						
<50	5	-0.63 (-1.43, 0.17)	0.12	**<0.001**	80.1%	0.77
>50	2	-0.76 (-1.15, -0.38)	**<0.001**	0.36	0.0%	
Type of prebiotics						
FOS	4	-0.37 (-0.90, 0.16)	0.17	0.05	60.8%	0.55
Inulin + FOS	1	-0.27 (-0.86,0.32)	0.36	-	-	
Others	2	-2.07 (-5.24, 1.10)	0.20	**<0.001**	92.7%	
Type of colony						
B. lactis, L. rhamnosus, and B. longum	2	-0.10 (-0.86, 0.66)	0.80	0.35	0.0%	0.20
B. lactis, and L. rhamnosus	1	-0.12 (-0.50, 0.27)	0.55	-	-	
B. longum	1	-0.54 (-1.15, 0.07)	0.08	-	-	
Others	3	-1.36 (-2.59, -0.14)	**0.03**	**<0.001**	87.9%	
Health status						
Healthy	4	-0.21 (-0.51, 0.08)	0.16	0.51	0.0%	0.08
Unhealthy	3	-1.36 (-2.59, -0.14)	**0.03**	**<0.001**	87.9%	
Sex						
Both sexes	5	-0.79 (-1.43, -0.14)	**0.02**	**<0.001**	82.8%	0.18
Male	2	-0.10 (-0.86, 0.66)	0.80	0.35	0.0%	
Baseline BMI (kg/m^2)						
Normal (18.5-24.9)	1	-0.12 (-0.50, 0.27)	0.55	**-**	-	0.10
Overweight (25-29.9)	2	-0.76 (-1.15, -0.38)	**<0.001**	0.36	0.0%	
Obese (>30)	1	-0.27 (-0.86, 0.32)	0.36	**-**	-	
NR	3	-1.25 (-3.35, 0.84)	0.24	**<0.001**	88.5%	
Overall quality						
Good	6	-0.39 (-0.71, -0.07)	**0.02**	0.15	37.8%	**<0.001**
Poor	1	-3.78 (-5.38, -2.18)	**<0.001**	**-**	-	

Subgroup analyses of Synbiotic supplementation on IL-10						
Overall effect	18	0.30 (0.002, 0.59)	**0.048**	**<0.001**	76.1%	
Continents						
Asia	7	0.72 (0.15, 1.29)	**0.01**	**<0.001**	87.5%	0.21
Europe	7	-0.04 (-0.42, 0.35)	0.85	0.11	42.7%	
South America	4	0.11 (-0.17, 0.40)	0.44	0.95	0.0%	
Age						
<50	10	0.45 (-0.09, 0.99)	0.10	**<0.001**	84.5%	0.50
>50	6	0.10 (-0.11, 0.32)	0.76	0.99	0.0%	
NR	2	0.15 (-0.81, 1.10)	0.76	**0.04**	76.1%	
Trial duration (week)						
<12	8	0.12 (-0.15, 0.40)	0.38	0.15	35.4%	0.19
≥12	10	0.50 (0.008, 0.98)	**0.046**	**<0.001**	84.4%	
Type of prebiotics						
FOS	10	0.32 (0.03, 0.61)	**0.03**	**0.01**	56.5%	0.25
Inulin + FOS	3	0.86 (-0.49, 2.21)	0.21	**<0.001**	94.0%	
Others	5	-0.06 (-0.54, 0.43)	0.82	**0.04**	59.9%	
Type of colony						
B. lactis, and L. rhamnosus	3	0.31 (-0.23, 0.84)	0.26	0.07	63.5%	0.91
L. paracasei, L. rhamnosus, L. acidophilus, and B. lactis	3	0.10 (-0.23, 0.42)	0.57	0.85	0.0%	
L. casei, L. rhamnosus, S. thermophilus, B. breve, L. acidophilus, B. longum and L. bulgaricus	2	0.18 (-0.17, 0.53)	0.30	0.82	0.0%	
L.casei, L. acidophilus, L. rhamnosus, L. salivarius, L. reuteri, B.lactis, B.longum, and B. bifidum	2	0.96 (-0.55, 2.48)	0.21	**0.002**	89.4%	
B. lactis, L. rhamnosus, and B. longum	2	-0.03 (-0.79, 0.73)	0.94	0.49	0.0%	
B. longum	1	0.02 (-0.58, 0.62)	0.94	-	-	
Others	5	0.35 (-0.59, 1.30)	0.46	**<0.001**	91.0%	
Health status						
Healthy	9	0.18 (-0.01, 0.37)	0.07	0.76	0.0%	0.36
Unhealthy	9	0.47 (-0.13, 1.06)	0.12	**<0.001**	87.1%	
Sex						
Both sexes	11	0.12 (-0.09, 0.33)	0.26	0.13	33.2%	0.39
Male	3	0.82 (-0.98, 2.61)	0.37	**<0.001**	90.9%	
Female	4	0.54 (-0.13, 1.22)	0.12	**0.001**	80.7%	
Baseline BMI (kg/m^2)						
Normal (18.5-24.9)	1	0.53 (0.14, 0.91)	**0.008**	**-**	-	0.22
Overweight (25-29.9)	5	0.37 (-0.21, 0.94)	0.22	**0.001**	79.2%	
Obese (>30)	5	0.60 (-0.16, 1.35)	0.12	**<0.001**	88.4%	
NR	7	0.30 (-0.39, 0.37)	0.97	**-**	-	

Overall quality						
Good	15	0.39 (0.07, 0.70)	**0.02**	**<0.001**	75.9%	0.23
Poor	3	-0.23 (-1.20, 0.73)	0.64	**0.008**	79.3%	
Subgroup analyses of Synbiotic supplementation on IFN-γ						
Overall effect	8	-0.21 (-0.69, 0.27)	0.39	<0.001	83.8%	
Continents						
Asia	2	-0.39 (-0.90, 0.13)	0.14	0.27	19.7%	**0.03**
Europe	4	-0.49 (-1.46, 0.49)	0.33	**<0.001**	88.2%	
South America	1	0.76 (0.15, 1.37)	**0.01**	-	-	
North America	1	-0.04 (-0.31, 0.22)	0.76	-	-	
Age						
<50	4	-0.25 (-1.11, 0.62)	0.58	**<0.001**	86.3%	0.96
>50	2	-0.28 (-0.86, 0.30)	0.35	0.07	68.7%	
NR	2	0.02 (-1.99, 2.03)	0.99	**<0.001**	94.0%	
Trial duration (week)						
<12	4	-0.66 (-1.11, -0.20)	**0.005**	0.11	51.0%	0.06
≥12	4	0.18 (-0.56, 0.91)	0.64	**<0.001**	86.8%	
Type of prebiotics						
FOS	2	0.10 (-1.14, 1.35)	0.87	**<0.001**	80.3%	**0.02**
Inulin	1	-1.32 (-2.00, -0.63)	**<0.001**	**-**	-	
Others	5	-0.12 (-0.73, 0.48)	0.69	**<0.001**	80.3%	
Type of colony						
B. lactis, and L. rhamnosus	3	-0.18 (-1.20, 0.85)	0.74	**<0.001**	89.3	**0.01**
L. paracasei, L. rhamnosus, L. acidophilus, and B. lactis	1	0.76 (0.15, 1.37)	**0.01**	-	-	
B. longum	1	-0.65 (-1.27, -0.04)	**0.04**	-	-	
Others	3	-0.42 (-1.33, 0.49)	0.37	**0.003**	83.3%	
Health status						
Healthy	5	-0.48 (-0.93, -0.03)	**0.04**	**0.004**	73.6%	0.27
Unhealthy	3	0.27 (-0.98, 1.51)	0.67	**<0.001**	90.6%	
Baseline BMI (kg/m^2)						
Normal (18.5-24.9)	1	-0.51 (-0.90, -0.12)	**0.01**	-	-	0.34
Overweight (25-29.9)	3	-0.62 (-1.38, 0.14)	0.11	**0.001**	84.9%	
NR	4	0.25 (-0.75, 1.24)	0.63	**<0.001**	85.8%	
Overall quality						
Good	5	-0.33 (-0.86, 0.20)	0.22	**<0.001**	84.4%	0.60
Poor	3	0.06 (-1.30, 1.43)	0.93	**<0.001**	88.2%	
Subgroup analyses of Synbiotic supplementation on TNF-α						
Overall effect	35	-0.38 (-0.65, -0.11)	**0.005**	**<0.001**	86.5%	
Continents						
Asia	17	-0.49 (-0.86, -0.12)	**0.009**	**<0.001**	86.1%	**0.02**
Africa	1	-1.27 (-1.80, -0.74)	**<0.001**	**-**	-	
Europe	10	-0.22 (-0.78, 0.33)	0.43	**<0.001**	85.3%	
South America	5	-0.28 (-1.08, 0.53)	0.50	**<0.001**	86.9%	
North America	1	0.10 (-0.69, 0.88)	0.81	0.07	69.9%	

Age						
<50	17	-0.22 (-0.57, 0.14)	0.24	**<0.001**	82.3%	0.36
>50	13	-0.46 (-0.95, -0.03)	0.06	**<0.001**	91.5%	
NR	5	-0.73 (-1.39, -0.08)	**0.03**	**0.003**	74.9%	
Trial duration (week)						
<12	17	-0.45 (-0.79, -0.11)	**0.009**	**<0.001**	79.9%	0.60
≥12	18	-0.31 (-0.72, 0.10)	0.14	**<0.001**	90.0%	
Type of prebiotics						
FOS	22	-0.39 (-0.77, -0.01)	**0.04**	**<0.001**	88.5%	0.83
Inulin	3	-0.73 (-1.35, -0.11)	**0.02**	0.06	64.0%	
Inulin + FOS	2	-0.20 (-1.25, -0.86)	0.72	**0.006**	87.0%	
Others	7	-0.26 (0.81, 0.29)	0.35	**<0.001**	85.9%	
NR	1	-0.41 (-1.01, 0.19)	0.18	-	-	
Type of colony						
L. casei, L. rhamnosus, S. thermophilus, B. breve, L. acidophilus, B. longum and L. bulgaricus	9	-0.90 (-1.42, -0.39)	**0.001**	**<0.001**	86.1%	**0.03**
L. paracasei, L. rhamnosus, L. acidophilus, and B. lactis	4	-0.44 (-1.42, 0.54)	0.38	**<0.001**	88.3%	
B. lactis, and L. rhamnosus	3	-0.09 (-0.46, 0.27)	0.61	0.25	27.1%	
B. longum	2	-1.26 (-2.11, -0.41)	**0.004**	**0.04**	75.6%	
B. lactis, L. rhamnosus, and B. longum	2	-0.21 (-0.97, 0.54)	0.58	0.99	0.0%	
Others	12	-0.09 (-0.47, 0.30)	0.67	**<0.001**	83.9%	
Health status						
Healthy	12	-0.33 (-0.70,0.05)	0.09	**<0.001**	80.4%	0.78
Unhealthy	23	-0.40 (-0.77, -0.04)	**0.03**	**<0.001**	88.3%	
Sex						
Both sexes	27	-0.46 (-0.74, 0.18)	**0.001**	**<0.001**	83.3%	0.59
Male	6	-0.21 (-0.97, 0.54)	0.58	0.99	0.0%	
Female	2	-0.07 (-0.86, 0.72)	0.86	**<0.001**	93.7%	
Baseline BMI (kg/m^2)						
Normal (18.5-24.9)	6	-0.32 (-0.62, -0.03)	**0.03**	0.18	34.4%	0.91
Overweight (25-29.9)	13	-0.53 (-1.14, 0.09)	0.09	**<0.001**	93.6%	
Obese (>30)	8	-0.25 (-0.68, 0.17)	0.25	**<0.001**	80.1%	
NR	8	-0.30 (-0.73, 0.14)	0.19	**0.004**	66.8%	
Overall quality						
Good	27	-0.34 (-0.65, -0.03)	**0.03**	**<0.001**	84.8%	0.33
Fair	4	-0.82 (-1.49, -0.16)	**0.02**	**0.009**	74.2%	
Poor	4	-0.25 (-0.63, 0.13)	0.20	0.82	0.0%	
Subgroup analyses of Synbiotic supplementation on LPS						
Overall effect	6	-0.01 (-0.60, 0.62)	0.97	**<0.001**	87.2%	
Continents						

Asia	2	-0.77 (-1.79, 0.24)	0.14	**0.008**	85.6%	**0.04**
Europe	2	0.56 (0.23, 0.89)	**0.001**	0.44	0.0%	
South America	2	0.24 (-0.26, 0.75)	0.34	0.24	28.0%	
Age						
<50	3	0.09 (-0.34, 0.51)	0.69	0.18	42.7%	0.85
>50	3	-0.04 (-1.29, 1.22)	0.96	**<0.001**	94.3%	
Trial duration (week)						
<12	2	-0.15 (-0.58, 0.62)	0.50	0.63	0.0%	0.65
≥12	4	0.08 (-0.81, 0.98)	0.86	**<0.001**	92.1%	
Type of prebiotics						
FOS	3	0.33 (-0.23, 0.88)	0.25	0.05	67.8%	**<0.001**
Inulin + FOS	1	-1.28 (-1.79, -0.77)	**<0.001**	-	-	
Others	2	0.25 (-0.19, 0.70)	0.28	0.25	26.0%	
Type of colony						
L. casei, L. rhamnosus, S. thermophilus, B. breve, L. acidophilus, B. longum and L. bulgaricus	1	-0.25 (-0.83, 0.34)	0.41	-	-	0.21
L. paracasei, L. rhamnosus, L. acidophilus, and B. lactis	1	0.48 (-0.09, 1.05)	0.10	-	-	
Others	4	-0.04 (-0.94, 0.85)	0.92	**<0.001**	91.6%	
Health status						
Healthy	4	-0.28 (-1.06, 0.50)	0.48	**<0.001**	86.0%	0.05
Unhealthy	2	0.56 (0.23, 0.89)	**<0.001**	0.44	0.0%	
Sex						
Both sexes	5	0.06 (-0.67, 0.79)	0.87	**<0.001**	89.5%	0.52
Female	1	-0.25 (-0.83, 0.34)	0.41	-	-	
Baseline BMI (kg/m^2)						
Overweight (25-29.9)	2	-0.29 (-2.23, 1.65)	0.77	**<0.001**	96.7%	0.49
Obese (>30)	3	0.09 (0.34, 0.51)	0.69	0.18	42.7%	
NR	1	0.48 (-0.09, 1.05)	0.10	-	-	
Subgroup analyses of Synbiotic supplementation on Adiponectin						
Overall effect	3	1.17 (-0.44, 2.78)	0.15	**<0.001**	96.3%	

Notes: The bold values highlight statistically significant results ($p < 0.05$), emphasizing key findings in the subgroup analyses. **Abbreviations:** CI, confidence interval; SMD, standardized mean differences; NO, number; NR, not reported; FOS: Fructooligosaccharides; BMI: body mass index; L, Lactobacillus; B, Bifidobacterium; S, Streptococcus; CRP: C-reactive protein; IL-1β: Interleukin-1 beta; IL-6: Interleukin-6; IL-8: Interleukin-8; IFN-γ: Interferon-gamma; TNF-α: Tumor necrosis factor-alpha; LPS: Lipopolysaccharide; IL-10: Interleukin-10.