

Probiotics/prebiotics/synbiotics and human neuropsychiatric outcomes: an umbrella review

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Table S1. The search strategies.

(A). Probiotics related search strategies.

Database	Search Strategies
PubMed	<p>#1 Search: " Probiotics "[Mesh] Sort by: Most Recent</p> <p>#2 Search: " Systematic review "[Mesh] Sort by: Most Recent</p> <p>#3 Search: " Meta-analysis "[Mesh] Sort by: Most Recent</p> <p>#4 Search: "<i>Lactobacillus</i>"[Title/Abstract] OR "<i>Bifidobacterium</i>"[Title/Abstract] OR "<i>Streptococcus thermophilus</i>"[Title/Abstract] OR "<i>Clostridium butyricum</i>"[Title/Abstract] OR "<i>Lactobacillus rhamnosus</i>"[Title/Abstract] OR "<i>Bifidobacterium animalis</i>"[Title/Abstract]</p> <p>#5 Search: #1 or #4</p> <p>#6 Search: #2 or #3</p> <p>#7 Search: #5 and #6</p>
Embase	<p>1 ' Probiotics '/exp</p> <p>2 ' Systematic review '/exp</p> <p>3 ' Meta-analysis '/exp</p> <p>4 '<i>Lactobacillus</i>': ab,ti OR '<i>Bifidobacterium</i>':ab,ti OR '<i>Streptococcus thermophilus</i>':ab,ti OR '<i>Clostridium butyricum</i>':ab,ti OR '<i>Lactobacillus rhamnosus</i>':ab,ti OR '<i>Bifidobacterium animalis</i>':ab,ti</p> <p>5 #1 OR #4</p> <p>6 #2 OR #3</p> <p>7 #5 AND #6</p>
Web of Science	<p>1 TS=(Probiotics) OR TS=(<i>Lactobacillus</i>) OR TS=(<i>Bifidobacterium</i>) OR TS= (<i>Streptococcus thermophilus</i>) OR TS= (<i>Clostridium butyricum</i>) OR</p>

TS=(*Lactobacillus rhamnosus*) OR TS=(*Bifidobacterium animalis*)

2 TS= (Systematic review) OR TS=(Meta-analysis)

3 #1 and #2

(B). Prebiotics related search strategies.

Database	Search Strategies
PubMed	#1 Search: " Prebiotics "[Mesh] Sort by: Most Recent #2 Search: " Systematic review "[Mesh] Sort by: Most Recent #3 Search: " Meta-analysis "[Mesh] Sort by: Most Recent #4 Search: " Lactulose "[Title/Abstract] OR " Inulin "[Title/Abstract] OR " Galactose "[Title/Abstract] OR " Oligofructose "[Title/Abstract] #5 Search: #1 or #4 #6 Search: #2 or #3 #7 Search: #5 and #6
Embase	1 ' Prebiotics '/exp 2 ' Systematic review '/exp 3 ' Meta-analysis '/exp 4 'Lactulose': ab,ti OR 'Inulin':ab,ti OR 'Galactose':ab,ti OR 'Oligofructose': ab,ti 5 #1 OR #4 6 #2 OR #3 7 #5 AND #6
Web of Science	1 TS=(Prebiotics) OR TS=(Lactulose) OR TS=(Inulin) OR TS= (Galactose) OR TS=(Oligofructose) 2 TS= (Systematic review) OR TS=(Meta-analysis) 3 #1 and #2

(C). Synbiotics related search strategies.

Database	Search Strategies
PubMed	#1 Search: " Synbiotics "[Mesh] Sort by: Most Recent #2 Search: " Systematic review "[Mesh] Sort by: Most Recent #3 Search: " Meta-analysis "[Mesh] Sort by: Most Recent

	#4 Search: #2 or #3
	#5 Search: #1 and #4
Embase	1 ' Synbiotics '/exp
	2 ' Systematic review '/exp
	3 ' Meta-analysis '/exp
	4 #2 OR #3
	5 #1 AND #4
Web of	1 TS=(Synbiotics)
Science	2 TS= (Systematic review) OR TS=(Meta-analysis)
	3 #1 and #2

Table S2. Associations between probiotics, prebiotics, or synbiotics consumption and neuropsychiatric outcomes.

Outcomes	First author, year of publication	Populations	Type and dose of intervention	Duration of intervention or follow-up	Outcome comparison	No. of studies in MA	Study design	No. of intervention or observation/total	Effects mode	Metric of MA	Estimated summary effect (95% CI)	I ² %	Publication biases
Neuropsychological test outcomes													
Risk of no improvement in neuropsychological tests	Luo, M. 2011 ^[1]	Patients with MHE	lactulose, NR	2-24 weeks	Lactulose versus no treatment / placebo	9	RCT	228/434	Fixed	RR	0.52 (0.44 to 0.62)	0	No significant publication bias
The mean number of abnormal neuropsychological tests	Luo, M. 2011 ^[1]	Patients with MHE	lactulose, NR	2-24 weeks	Lactulose versus no treatment / placebo	4	RCT	107/203	Fixed	MD	-1.76 (-1.96 to -1.56)	34	NR
Results of psychometric testing	Zucker, D.M. 2019 ^[2]	Patients with MHE	lactulose, 30–60 ml in two to three divided doses per day	Mean 1-3 months	Lactulose versus usual care/ l-ornithine-l-aspartate	2	RCT	63/130	Fixed	SM D	-0.99 (-1.38 to -0.61)	95	NR
Number connection test	Cao, Q. 2018 ^[8]	Cirrhotic patients with MHE	Probiotic, 1*10 ⁹ -1.1*10 ¹¹ CFU/d	4 weeks	Probiotic versus placebo/no treatment	2	RCT	54/104	Random	MD	-30.25 (-49.85 to -10.66)	55	NR
SIP(psychosocial dimension)	Zhao, L.-N. 2015 ^[20]	Patients with MHE or OHE	Probiotic, NR	8-12 weeks	Probiotic versus placebo/no treatment	2	RCT	48/95	Fixed	MD	-3.50 (-4.91 to -2.08)	0	NR

SIP(psychosocial dimension)	Dalal, R. 2017 ^[22]	Patients with HE	Probiotic, no uniform standard	8 weeks to 3 months	Probiotic versus placebo/no treatment	2	RCT	48/95	Random	MD	-3.54 (-4.95 to -2.12)	0	NR
Hepatic encephalopathy outcomes													
Reversal of MHE	Viramontes Hörner, D. 2017 ^[6]	Adult (18 years old or older) patients with hepatic cirrhosis.	Probiotic, 3*10 ⁶ -5*10 ¹³ CFU/d	1-6 months	Probiotic versus placebo/no treatment	9	RCT	262/570	Random	RR	1.53 (1.14 to 2.05)	59	NR
Improvement in MHE	Cao, Q. 2018 ^[8]	Cirrhotic patients with MHE	Probiotic, 3*10 ⁶ CFU/d	4 weeks	Probiotic versus placebo/no treatment	2	RCT	26/33	Random	OR	0.18 (0.07 to 0.47)	0	No significant publication bias
Improvement in MHE	Saab, S. 2016 ^[21]	Patients with HE	Probiotic, no uniform standard	1-6 months	Probiotic versus placebo/no treatment	7	Cohort study/RCT	174/352	Fixed	OR	3.91 (2.25 to 6.80)	33	NR
Risk of no improvement of MHE	Shukla, S. 2011 ^[32]	Patients with MHE or SHE	Probiotic/prebiotic/synbiotic, no uniform standard	2-24 weeks	Probiotic/prebiotic/synbiotic versus placebo	9	RCT	422/698	Fixed	RR	0.40 (0.32 to 0.50)	21.7	No significant publication bias
Risk of no improvement of MHE	Shukla, S. 2011 ^[32]	Patients with MHE or SHE	Lactulose, NR	2-24 weeks	Lactulose versus placebo	5	RCT	204/340	Fixed	RR	0.34 (0.24 to 0.47)	34.5	No significant publication bias
Improvement in HE	Holte, K. 2012 ^[18]	Patients with HE	Probiotic, no uniform standard	10 d-16 weeks	Probiotics/synbiotics versus placebo	6	RCT	171/333	Random	RR	1.40 (1.05 to 1.86)	5	NR

[illegible]

MMSE score	Meng, H.Y.H. 2022 ^[3]	Age-related dementia	Probiotic, 4×10^8 - 5×10^{10} CFU/d	12-28 weeks	Probiotic versus placebo	5	RCT/ open-label, single-arm study	161/316	Random	MD	0.92 (-0.05 to 1.89)	94.8	0.1671
MMSE score	Zhu, G. 2021 ^[12]	Individuals diagnosed with Alzheimer disease or mild cognitive impairment	Probiotic, no uniform standard	12 weeks	Probiotic/ synbiotics versus usual care/placebo/ other interventions without any probiotics/prebiotic/symbiotic supplementation	4	RCT	116/230	Random	SM D	0.59 (-0.44 to 1.63)	93	NR
MMSE score	Li, X. 2021 ^[13]	Patients with mild cognitive impairment and Alzheimer disease	Probiotic, NR	12 weeks	Probiotic versus no probiotic interventions	3	RCT	118/234	Random	WM D	1.08 (-0.34 to 2.50)	92.6	NR
Non-MMSE score	Den, H. 2020 ^[33]	Adults with Alzheimer's disease or mild cognitive impairment	Probiotic, 3×10^9 - 1×10^{10} CFU/d	12 weeks	Probiotic versus placebo	2	RCT	NR/140	Fixed	SM D	0.16 (-0.17 to 0.50)	0	0.54

Global cognition	Marx, W. 2020 ^[4]	No restrictions	Probiotic, Total Dose: 6 million CFU - 900 billion CFU	4-12 weeks	Probiotic versus placebo	11	RCT/ Cross-over	285/562	Random	Hedges' g	0.115 (-0.041 to 0.270)	0	> 0.1
Global cognition	Marx, W. 2020 ^[4]	No restrictions	Prebiotic, 3.375-10 g/d	2 h-24 weeks	Prebiotic versus placebo	5	RCT/ Cross-over	274/324	Random	Hedges' g	0.077 (-0.091 to 0.246)	0	> 0.1
Global cognition	Lv, T. 2021 ^[34]	Healthy individuals or individuals with cognitive impairment	Probiotic, NR	8-12 weeks	Probiotic versus no probiotic interventions	4	RCT	93/182	Random	MD	0.17 (-0.12 to 0.46)	0	NR
Cognitive function	Zhu, G. 2021 ^[12]	Individuals diagnosed with Alzheimer disease	Probiotic, no uniform standard	12 weeks	Probiotic/synbiotics versus usual care/placebo/other interventions without any probiotics/prebiotic/synbiotic supplementation	4	RCT	114/234	Random	MD	0.34 (-0.66 to 1.34)	93	0.205
Cognitive function	Krüger, J.F. 2021 ^[16]	Individuals with Alzheimer's	Probiotic, no uniform standard	12 weeks	Probiotic versus placebo	3	RCT	82/161	Random	MD	0.56 (-0.06 to 1.18)	73	NR

		disease											
Cognitive function	Lv, T. 2021 ^[34]	Healthy individuals	Probiotic, NR	12 weeks	Probiotic versus no probiotic interventions	2	RCT	40/76	Random	MD	0.15 (-0.30 to 0.60)	0	NR
Cognitive function	Upadhyay, R.P. 2020 ^[35]	Preterm infants	Probiotic/prebiotic, no uniform standard	28.7-47.9 d	Probiotic/prebiotic versus no probiotic/prebiotic interventions	4	RCT	700/1388	NR	MD	0.20 (-1.42 to 1.83)	0	No significant publication bias
Risk of cognitive impairment	Upadhyay, R.P. 2020 ^[35]	Preterm infants	Probiotic/prebiotic, no uniform standard	28.7-47.9 d	Probiotic/prebiotic versus no probiotic/prebiotic interventions	4	RCT	700/1388	NR	RR	0.98 (0.75 to 1.27)	0	No significant publication bias
Attention / Vigilance	Marx, W. 2020 ^[4]	No restrictions	Probiotic, NR	NR	Probiotic versus placebo	6	RCT/ Cross-over	NR	Random	Hedges' g	0.068 (-0.120 to 0.256)	0	NR
Attention / Vigilance	Marx, W. 2020 ^[4]	No restrictions	Prebiotic, NR	NR	Prebiotic versus placebo	2	RCT	NR	Random	Hedges' g	-0.007 (-0.208, 0.194)	0	NR
Working Memory	Marx, W. 2020 ^[4]	No restrictions	Probiotic, NR	NR	Probiotic versus placebo	4	RCT	NR	Random	Hedges' g	-0.036 (-0.260 to 0.188)	0	NR
Working Memory	Marx, W. 2020 ^[4]	No restrictions	Prebiotic, NR	NR	Prebiotic versus placebo	3	RCT	NR	Random	Hedges' g	0.198 (-0.134 to 0.530)	0	NR
Memory - Accuracy	Marx, W. 2020 ^[4]	No restrictions	Probiotic, NR	NR	Probiotic versus placebo	4	RCT	NR	Random	Hedges' g	0.191 (-0.025 to 0.66.334)	66.334	NR

										g	0.406)		
Memory - Accuracy	Marx, W. 2020 ^[4]	No restrictions	Prebiotic, NR	NR	Prebiotic versus placebo	3	RCT	NR	Random	Hedges' g	-0.045 (-0.288 to 0.197)	26.195	NR
Memory Efficiency	Marx, W. 2020 ^[4]	No restrictions	Probiotic, NR	NR	Probiotic versus placebo	2	RCT	NR	Random	Hedges' g	0.168 (-0.099 to 0.435)	0	NR
Memory Efficiency	Marx, W. 2020 ^[4]	No restrictions	Prebiotic, NR	NR	Prebiotic versus placebo	2	RCT	NR	Random	Hedges' g	-0.100 (-0.301 to 0.101)	0	NR
Psychomotor Speed	Marx, W. 2020 ^[4]	No restrictions	Probiotic, NR	NR	Probiotic versus placebo	7	RCT/ Cross-over	NR	Random	Hedges' g	0.084 (-0.097 to 0.265)	0	NR
Psychomotor Speed	Marx, W. 2020 ^[4]	No restrictions	Prebiotic, NR	NR	Prebiotic versus placebo	2	RCT	NR	Random	Hedges' g	-0.003 (-0.204 to 0.198)	0	NR
Executive Function	Marx, W. 2020 ^[4]	No restrictions	Probiotic, NR	NR	Probiotic versus placebo	5	RCT/ Cross-over	NR	Random	Hedges' g	0.189 (-0.129 to 0.507)	49.737	NR
Instant Memory Score	Liu, C. 2022 ^[14]	Individuals diagnosed with Alzheimer disease	Probiotic/probiotic combined with other drug, NR	8 weeks-12 months	Probiotic/probiotic combined with other drug versus nonprobiotic	2	RCT	49/98	Fixed	MD	3.24 (3.09 to 3.40)	93	NR
RBANS	Ruiz-Gonzalez, C.	Patients with mild cognitive	Bifidobacterium breve A1	12-16 weeks	Probiotic versus other	2	RCT	99/196	Random	MD	-6.02 (-16.68 to	99	NR

	2021 ^[15]	impairment	Capsules, 2*10 ¹⁰ CFU		interventions						4.64)		
Depressive symptoms													
Depressive symptoms related scores	Goh, K.K. 2019 ^[5]	General population or clinical population	Probiotic, 3*10 ³ -2*10 ¹⁰ CFU/d	4 weeks-6 months	Probiotic versus placebo	19	RCT	1030/1901	Random	SM D	−0.31 (−0.56 to −0.07)	82	No significant publication bias
Depressive symptomatology related scores	Chao, L. 2020 ^[10]	Participants (age ≥16 years)who had no medication history within the 3 months or during the study	Probiotic, 1*10 ⁹ -1.8*10 ¹⁰ CFU/g	8-24 weeks	Probiotic versus placebo	7	RCT	204/404	Random	SM D	-0.48 (-0.71 to -0.26)	21	No significant publication bias
Depressive symptomatology related scores	Liu, R.T. 2019 ^[23]	Medical and/or community population	Probiotic, NR	4-45 weeks	Probiotic versus placebo	23	Controlled clinical trial	NR/2418	Random	SM D	-0.24 (-0.36 to -0.12)	48.2	0.08
Depressive symptomatology related scores	Zagórska, A. 2020 ^[27]	Healthy volunteers and people suffering from psychiatric disorders	Probiotic, no uniform standard	4-24 weeks	Probiotic versus placebo	16	RCT	NR/1774	Random	SM D	-0.35 (-0.59 to -0.12)	79	No significant publication bias
Depressive symptomatology	Le Morvan de	Adults, either	Probiotic,	4-24 weeks	Probiotic versus	15	RCT	551/1092	Rando	SM	-0.37	48	NR

related scores	Sequeira, C. 2022 ^[28]	healthy or with a specified functional CNS or psychiatric disorder	6*10 ⁶ -3*10 ¹⁰ CFU/d		placebo				m	D	(-0.55 to -0.20)		
Depressive symptomatology related scores	Zhu, H. Y. 2022 ^[41]	Adults	Probiotic, 8*10 ⁷ -5*10 ¹⁰ CFU/d	4-20 weeks	Probiotic versus placebo	19	RCT	675/1345	Random	SM D	0.19 (0.01 to 0.37)	59.67	0.688
Depressive symptomatology related scores	Misera,A. 2021 ^[42]	Clinical diagnosis of MDD	Probiotic, 2*10 ⁸ -2*10 ¹⁰ CFU	28 d-2 months	Probiotic versus placebo	6	RCT	150/306	Random	SM D	-0.292(-0.577 to -0.007)	45.63	0.32
Depressive symptomatology related scores	Nikolova, V.L. 2021 ^[43]	Patients with depression	Probiotic, no uniform standard	6-8 weeks	Probiotic versus placebo	7	RCT	202/404	Random	SM D	0.58 (0.19 to 0.97)	73	NR
Depressive symptomatology related scores	Sanada, K. 2020 ^[44]	Patients with depression	Probiotic /synbiotic, NR	6-10 weeks	Probiotic /synbiotic versus no probiotic /synbiotic interventions	5	RCT	128/254	NR	SM D	-1.618 (-2.732 to -0.505)	93.25	NR
Depressive symptomatology related scores	Hofmeister, M. 2021 ^[45]	Populations without depression	Probiotic, NR	4-52 weeks	Probiotic versus placebo	35	RCT	1569/2988	Random	SM D	0.31 (0.15 to 0.46)	74.4	No significant publication bias
Depressive symptomatology related scores	Hofmeister, M. 2021 ^[45]	Populations with depression	Probiotic, NR	6-12.9 weeks	Probiotic versus placebo	9	RCT	273/544	Random	SM D	0.78 (0.19 to 1.37)	89.9	No significant publication bias

Depressive symptomatology related scores	Hofmeister, M. 2021 ^[45]	Populations with depression	Prebiotic, NR	8 weeks	Prebiotic versus placebo	3	RCT	92/184	Random	SM D	0.39 (0.04 to 0.73)	26.6	NR
Depressive symptomatology related scores	Hofmeister, M. 2021 ^[45]	Populations without depression	Synbiotic, NR	6-24 weeks	Synbiotic versus placebo	6	RCT	151/307	Random	SM D	0.68 (0.36 to 1.00)	44.0	No significant publication bias
Depressive symptomatology related scores	Huang, R. 2016 ^[46]	Healthy or depressed population	Probiotic, 3×10^3 - 2×10^{10} CFU/g	4-20 weeks	Probiotic versus placebo	5	RCT	183/365	Fixed	SM D	-0.30 (-0.51 to -0.09)	0	No significant publication bias
BDI total scores	Jiang, J. 2021 ^[7]	Patients with multiple sclerosis	Probiotic, 2×10^9 - 1×10^{10} CFU/g	6-16 weeks	Probiotic versus placebo	3	RCT	86/173	Random	SM D	-1.58 (-3.03 to -0.12)	94	NR
BDI total scores	Mirashrafi, S. 2021 ^[17]	Relapsing-remitting multiple sclerosis patients	Probiotic, 2×10^9 - 4×10^9 CFU/d	12-24 weeks	Probiotic versus placebo	3	RCT	86/173	Random	WM D	-3.22 (-4.38 to -2.06)	90.6	0.123
BDI total scores	El Dib, R. 2021 ^[40]	Patients with depression and/or anxiety and/or stress	Probiotic, NR	8 weeks	Probiotic versus placebo	3	RCT	129/256	Random	MD	-3.20 (-5.91 to -0.49)	21	No significant publication bias
HAMD total scores	Amirani, E. 2020 ^[9]	Patients with neurological or	Probiotic, 60-1000mg/d or	6-12 weeks	Probiotic/synbiotic versus	4	RCT	90/180	Random	WM D	-9.60 (-10.08 to -	99.7	NR

		psychiatric disorders	2*10 ¹⁰ CFU/d		placebo							9.11)		
Anxiety symptoms														
Anxiety symptomatology related scores	Chao, L. 2020 ^[10]	Participants (age ≥16 years)who had no medication history within the 3 months or during the study	Probiotic,1*10 ⁹ -1.8*10 ¹⁰ CFU/g or 100 ml/d	6-24 weeks	Probiotic versus placebo	7	RCT	258/511	Fixed	MD	0.00 (-0.41 to 0.41)	26	No significant publication bias	
Anxiety symptomatology related scores	Liu, B. 2018 ^[24]	No restrictions	Probiotic, 2*10 ⁸ -3*10 ¹⁰ CFU/d	4-24 weeks	Probiotic versus placebo	12	RCT	871/1551	Random	MD	-0.12 (-0.28 to 0.04)	51	0.139	
Anxiety symptomatology related scores	Reis, D.J. 2018 ^[25]	No restrictions	Probiotic, 1*10 ⁹ -1*10 ¹¹ CFU	14 d-1 year	Probiotic versus other interventions	14	RCT	NR/1527	Random	MD	-0.12 (-0.29 to 0.05)	61.76	0.146	
Anxiety symptomatology related scores	Zagórska, A. 2020 ^[27]	Healthy volunteers and people suffering from psychiatric disorders	Probiotic, no uniform standard	4-24 weeks	Probiotic versus placebo	14	RCT	NR/1830	Random	MD	0.08 (-0.21 to 0.38)	87	No significant publication bias	

Anxiety symptomatology related scores	Le Morvan de Sequeira, C. 2022 ^[28]	Adults, either healthy or with a specified functional CNS or psychiatric disorder	Probiotic, 6×10^6 - 1×10^{11} CFU/d	4-24 weeks	Probiotic versus placebo	17	RCT	728/1378	Random	MD	-0.30 (-0.60 to 0.01)	86	NR
STAI-6 anxiety score	Desai, V. 2021 ^[37]	Participants scoring above cut-off in STAI-6 anxiety scores in the perinatal period	Probiotic, 6×10^9 - 6.5×10^9 CFU/d	12-36 weeks	Probiotic versus placebo	2	RCT	279/543	Random	OR	0.65 (0.23 to 1.85)	59	NR
DASS(Anxiety Scale) score	El Dib, R. 2021 ^[40]	Patients with depression and/or anxiety and/or stress	Probiotic, NR	8 weeks	Probiotic versus placebo	2	RCT	111/221	Random	MD	0.49 (-4.05 to 5.02)	74	No significant publication bias
BAI score	El Dib, R. 2021 ^[40]	Patients with depression and/or anxiety and/or stress	Probiotic, NR	8 weeks	Probiotic versus placebo	2	RCT	89/181	Random	MD	-3.21 (-6.50 to 0.08)	0	No significant publication bias
Stress symptoms													
Stress symptomatology related scores	Zagórska, A. 2020 ^[27]	Healthy volunteers and people suffering from psychiatric	Probiotic, no uniform standard	4-12 weeks	Probiotic versus placebo	5	RCT	NR/605	Random	MD	0.03 (0.23 to 0.17)	25	No significant publication bias

		disorders											
PSS score	Le Morvan de Sequeira, C. 2022 ^[28]	Adults, either healthy or with a specified functional CNS or psychiatric disorder	Probiotic, 1×10^8 - 1.75×10^{10} CFU/d	4-24 weeks	Probiotic versus placebo	5	RCT	297/582	Random	SM D	-0.17 (-0.33 to -0.00)	0	NR
Subjective stress levels	Zhang, N. 2020 ^[39]	Healthy volunteers	Single-strain probiotic, no uniform standard	6-24 weeks	Single-strain probiotic versus placebo	4	RCT	614/939	Fixed	SM D	-0.12 (-0.26 to 0.02)	0	NR
Subjective stress levels	Zhang, N. 2020 ^[39]	Healthy volunteers	Multi-strain probiotic, no uniform standard	30 d-12 weeks	Multi-strain probiotic versus placebo	2	RCT	51/104	Fixed	SM D	-0.32 (-0.71 to 0.07)	55	NR
DASS(Stress Scale) score	El Dib, R. 2021 ^[40]	Patients with depression and/or anxiety and/or stress	Probiotic, NR	8 weeks	Probiotic versus placebo	2	RCT	111/221	Random	MD	0.84 (-2.64 to 4.33)	34	No significant publication bias
Mood States and Psychiatric Distress													
POMS score	Le Morvan de Sequeira, C. 2022 ^[28]	Adults, either healthy or with a specified functional CNS or psychiatric disorder	Probiotic, 2×10^9 - 3×10^{10} CFU/d	4-20 weeks	Probiotic versus placebo	4	RCT	2268/3486	Random	SM D	0.17 (0.10 to 0.24)	0	NR

Mood symptoms	Ng, Q.X. 2018 ^[11]	Individuals with mild-moderate depressive symptoms	Probiotic, 2* 10 ⁹ -1*10 ¹⁰ CFU/g	8-10 weeks	Probiotic versus placebo	3	RCT	NR/163	Randomized	SM D	-0.684 (-1.296 to -0.0712)	NR	0.5496
Psychiatric distress symptom outcomes	Le Morvan de Sequeira, C. 2022 ^[28]	Adults, either healthy or with a specified functional CNS or psychiatric disorder	Probiotic, 5*10 ⁸ -1.5*10 ¹⁰ CFU/d	4-24 weeks	Probiotic versus placebo	8	RCT	360/680	Random	SM D	-0.33 (-0.53 to -0.13)	36	NR
Schizophrenic symptoms													
Total PANSS score	Ng, Q.X. 2019 ^[26]	Patients with at least moderately severe psychotic symptoms, aged 18–65 years	Probiotic, NR	14 weeks	Probiotic versus placebo	3	RCT	NR/172	Fixed	SM D	-0.0884 (-0.380 to 0.204)	0	NR
Total PANSS score	Zagórska, A. 2020 ^[27]	Healthy volunteers and people suffering from psychiatric disorders	Probiotic, no uniform standard	12-14 weeks	Probiotic versus placebo	4	RCT	NR/255	Random	SM D	-0.16 (-0.43 to 0.12)	13	No significant publication bias

Overall mental health													
GHQ scores	Jiang, J. 2021 ^[7]	Patients with multiple sclerosis	Probiotic, 2×10^9 - 1×10^{10} CFU/g	6-16 weeks	Probiotic versus placebo	3	RCT	86/173	Fixed	SM D	-0.71 (-1.02 to -0.40)	0	NR
GHQ scores	Mirashrafi, S. 2021 ^[17]	Relapsing-remitting multiple sclerosis patients	Probiotic, 2×10^9 - 4×10^9 CFU/d	12-24 weeks	Probiotic versus placebo	3	RCT	86/173	Random	WM D	-4.37 (-6.43 to -2.31)	0	0.111
Subclinical psychological symptoms	McKean, J. 2017 ^[38]	Healthy volunteers and people suffering from psychiatric disorders	Probiotic, no uniform standard	21-56 d	Probiotic versus placebo	7	RCT	394/785	Random	SM D	0.34 (0.07 to 0.61)	67	NR
Neurological function													
EDSS score	Jiang, J. 2021 ^[7]	Patients with multiple sclerosis	Probiotic, 2×10^9 - 1×10^{10} CFU/g	6-16 weeks	Probiotic versus placebo	3	RCT	86/173	Random	SM D	-1.22 (-2.40 to -0.03)	92	NR
EDSS score	Mirashrafi, S. 2021 ^[17]	Relapsing-remitting multiple sclerosis patients	Probiotic, 2×10^9 - 4×10^9 CFU/d	12-24 weeks	Probiotic versus placebo	3	RCT	86/173	Random	WM D	-0.43 (-0.65 to -0.20)	7.2	0.934

BDNF													
BDNF	Foshati, S. 2022 ^[29]	Healthy or unhealthy adults aged 18 years old or above	Probiotic/syn- biotic, 0.2*10 ⁹ - 10*10 ⁹ CFU/d	42-180 d	Probiotic/synbio- tic versus placebo	10	RCT	387/713	Rando- m	WM D	0.20 (0.06 to 0.34)	86. 6	NR
Other neuropsychiatric outcomes													
NIHSS score	Zhong, D.-Y. 2021 ^[30]	Patients with stroke	Probiotic, NR	14-21 d	Probiotics combined with EN and life support treatment versus EN and life support treatment	2	RCT	105/210	Rando- m	MD	-1.11 (-7.92 to 5.70)	93	NR
Frequency of migraine headaches	Parohan, M. 2022 ^[31]	Adult patients (≥18 years old)	Probiotic, 4*10 ⁹ -5*10 ⁹ CFU/d	8-14 weeks	Probiotic versus placebo/current preventive drug	3	RCT	94/179	Rando- m	WM D	-2.54 (-5.31 to 0.22)	98. 1	0.249
Severity of migraine headaches	Parohan, M. 2022 ^[31]	Adult patients (≥18 years old)	Probiotic, 4*10 ⁹ -5*10 ⁹ CFU/d	8-14 weeks	Probiotic versus placebo/current preventive drug	3	RCT	94/179	Rando- m	WM D	-1.23 (-3.37 to 0.92)	98. 5	0.199
Risk of NDI	Upadhyay, R.P. 2020 ^[35]	Preterm infants	Probiotic/pre- biotic, no uniform standard	28.7-47.9 d	Probiotic/prebiot- ic versus no probiotic/prebiot- ic interventions	5	RCT	866/1637	NR	RR	0.90 (0.75 to 1.09)	9.9	No significant publication bias
Risk of cerebral palsy	Upadhyay,	Preterm infants	Probiotic/pre	28.7-47.9 d	Probiotic/prebiot	4	RCT	700/1388	NR	RR	1.33 (0.84	0	No significant

	R.P. 2020 ^[35]		biotic, no uniform standard		ic versus no probiotic/prebiotic interventions						to 2.11)		publication bias
PSQI score	Irwin, C. 2020 ^[36]	Adults >18 years of age	Probiotic/paraprobiotic, 1*10 ⁹ -9*10 ¹¹ CFU	3-24 weeks	Probiotic/paraprobiotic versus placebo	8	RCT	181/356	Random	MD	0.780 (0.395 to 1.166)	0	NR
Subjective sleep ratings	Irwin, C. 2020 ^[36]	Adults >18 years of age	Probiotic/paraprobiotic, 1*10 ⁹ -9*10 ¹¹ CFU	3-24 weeks	Probiotic/paraprobiotic versus placebo	5	RCT	135/267	Random	SM D	0.081 (-0.135 to 0.297)	36	NR
Sleep efficiency	Irwin, C. 2020 ^[36]	Adults >18 years of age	Probiotic/paraprobiotic, NR	3-11 weeks	Probiotic/paraprobiotic versus placebo	3	RCT	137/453	Random	MD	0.019 (-1.207 to 1.244)	0	NR
Sleep latency	Irwin, C. 2020 ^[36]	Adults >18 years of age	Probiotic/paraprobiotic, NR	3-11 weeks	Probiotic/paraprobiotic versus placebo	4	RCT	151/467	Random	MD	0.693 (-1.364 to 2.750)	0	NR
Severity of ASD symptoms	Song, W. 2022 ^[47]	Patients with ASD	Probiotic/prebiotic, NR	4 weeks to 6 months	Probiotic/prebiotic versus placebo	3	RCT	74/144	Fixed	SM D	-0.23 (-0.56 to 0.11)	0	NR

MA meta-analysis, CI confidence interval, OR odds ratios, RR relative risks, SMD standardized mean differences, MD mean differences, WMD weighted mean difference, d day, CFU Colony-Forming Unit, RCT randomized controlled trial, MMSE Mini-Mental State Examination, MHE minimal hepatic encephalopathy, OHE overt hepatic encephalopathy, HE hepatic encephalopathy, SHE subclinical hepatic encephalopathy, BDI Beck Depression Inventory, BAI Beck Anxiety Inventory, GHQ general health questionnaire, HAMD Hamilton Depression Rating Scale, RBANS Repeatable Battery for the Assessment of Neurophychological Status, TYM Test Your Memory, EDSS Expanded Disability Status Scale, SIP sickness impact profile, PANSS Positive and Negative Syndrome Scale, POMS Profile of Mood States, PSS Perceived Stress scale, NIHSS national institutes of health stroke scale, NDI neurodevelopment impairment, PSQI Pittsburgh Sleep Quality Index, STAI-6 State-trait anxiety inventory-6, DASS Depression Anxiety Stress Scale, MDD Major Depressive Disorder, ASD autism spectrum disorder, CNS central nervous system, BDNF brain-derived neurotrophic factor, EN Enteral nutrition, NR not reported.

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