Zhuang *et al. Nutrition Journal* (2025) 24:147
https://doi.org/10.1186/s12937-025-01218-1

Nutrition Journal

RESEARCH **Open Access**

Effects of probiotics, prebiotics, and synbiotics on gut microbiota in older adults: a systematic review and meta-analysis of randomized controlled trials

Kai Zhuang[1,2,3], Huanhuan Luo[1,2,3], Muhuang Zeng[4], Sze Chun Leo CHAN[5,6], Meiting Gong[5,6] and Yunhan Wang[7,8*]

Abstract

Background There is a lack of evidence on microbial compositions and associated metabolic changes in probiotics, prebiotics, or synbiotics (PPS) in older adults.

Objective This meta-analysis aims to evaluate the effects of PPS on gut microbiota composition, short-chain fatty acids (SCFAs), and inflammatory markers in older adults.

Methods PubMed, Embase, Cochrane Library, and Scopus databases were searched for randomized controlled trials (RCTs) published up to May 2025. RCTs were included if they examined microbiome-related outcomes in individuals aged ≥ 60 years following PPS interventions. The Cochrane Risk of Bias Tool was adopted for Quality appraisal. Meta-analysis was performed in RevMan 5.3, with standardized mean difference (SMD) as effect measures.

Results 29 RCTs were included, involving 1,633 participants. PPS supplementation notably increased *Bifidobacterium* abundance (prebiotics: SMD = 1.09; probiotics: SMD = 0.40), whereas synbiotics showed no overall effect but enhanced the abundance of specific strains (B. angulatum, B. longum, B. breve). Probiotic supplementation enhanced microbial diversity (Shannon index: SMD = 0.76), while synbiotics increased *Lactobacillus casei* abundance (SMD = 0.75) and reduced *Pseudomonas* levels (SMD = -0.55). For inflammatory markers, prebiotics increased IL-10 levels (SMD = 0.61) and reduced IL-1β (SMD = -0.39), whereas synbiotics reduced TNF-α (SMD = -0.36). Synbiotic supplementation enhanced valeric acid (SMD = 0.50) and acetic acid levels (SMD = 0.62).

Conclusion PPS interventions demonstrated potential benefits for older adults by increasing beneficial bacteria such as *Bifidobacterium* and *Lactobacillus casei*, reducing harmful genera like *Pseudomonas*, improving anti-inflammatory responses, and enhancing the production of SCFAs.

Keywords Older adults, Gut microbiota, Probiotics, Prebiotics, Synbiotics, Meta-analysis, RCT

---

*Correspondence:
Yunhan Wang
wangyunhan@gzucm.edu.cn

Full list of author information is available at the end of the article

This study followed the PRISMA statement and was preliminarily registered on PROSPERO (CRD42022357834).

Introduction

Over the past decades, population aging has accelerated significantly [1]. The aging process is frequently correlated with surgical trauma, tumors, cognitive dysfunction, insulin resistance, and chronic inflammation [2–6]. To address the socioeconomic challenges posed by an aging population, extensive research has been conducted to explore various strategies for managing healthcare demands and mitigating the broader socioeconomic impacts of aging [7].

During aging, the gastrointestinal microbiota plays a crucial role in various pathophysiological processes, and it may contribute to the age-related chronic, sterile, and low-grade inflammation, known as inflammaging [8]. Alpha diversity is commonly used to describe the richness and evenness of species within a sample, whereas beta diversity is often used to compare the similarity between two or more communities [9, 10]. Compared to young individuals, older adults appear to have enhanced alpha diversity and different beta diversity [11]. Increased abundance of potentially harmful bacteria such as *Enterobacteriaceae*, along with reduced levels of beneficial genera like *Bifidobacterium*, possibly reinforces the pro-inflammatory state caused by inflammaging [12].

Aging can also reduce the production of short-chain fatty acids (SCFAs) and exacerbate chronic inflammation [13]. SCFAs represent the primary end products of intestinal microbiota fermentation of indigestible carbohydrates [14]. In older adults, supplementation with probiotics, prebiotics, or synbiotics (PPS) may help enhance SCFA production, thus exerting anti-inflammatory effects and improving glucose and lipid metabolism [15, 16]. Given the complex etiology of older adults, the combined use of PPS often yields better therapeutic outcomes by improving gut microbiota homeostasis [17]. Moreover, PPS can greatly enhance SCFA production and relieve inflammatory responses in older adults [18–21].

Currently, many studies have focused on the efficacy of microbiome products in enhancing health outcomes in older adults, but the results remain contradictory [22, 23]. Supplementation with the same probiotic in similar populations has yielded opposing results in microbial diversity, composition shifts, and disease outcomes [24, 25]. Furthermore, existing systematic reviews and meta-analyses regarding the impact of microbiome products on older adults primarily focus on host physiology rather than associated changes in the microbiome and SCFAs [26, 27]. Therefore, this research intends to evaluate the effects of microbiome-based interventions on gut microbiota, SCFAs, and inflammatory markers in older adults. In addition, we hope to further understand the impacts of microbial formulations on the gut microenvironment in older adults, uncover correlations and causality, and ultimately provide support for clinical interventions to improve and prevent age-related diseases.

Table 1 Inclusion criteria based on PICOS principles

Domain	Criteria
P(Participants)	Older adults aged ≥60 years
I(Interventions)	Supplementation with any type of probiotics, prebiotics, or synbiotics (PPS).
C(Comparators)	Control groups: Placebo or no PPS intervention.
O(Outcomes)	Gut microbiota-related outcomes (e.g., composition, diversity, and SCFA (include the rest))
S(Study design)	Randomized controlled trials

Methods

This study followed the PRISMA statement and was preliminarily registered on PROSPERO (CRD42022357834).

Search strategy

PubMed, Embase, Cochrane, and Scopus databases were comprehensively searched up to May 2025. The major terms used in the search strategy included “elderly”, “old”, “microbiota”, “prebiotics”, “probiotics”, and “synbiotics”. The detailed search strategy is presented in Additional Table 1. No more limitations were set.

Literature screening

Two independent reviewers separately screened the literature and discussed the results to solve the disagreements. The inclusion and exclusion criteria were preliminarily set based on PICOS principles. Inclusion criteria covered: (1) Studies investigating patients who reported gut microbiota outcomes; (2) The control group consisted of individuals who either did not receive PPS supplementation or those who were administered a placebo; (3) Randomized controlled trials (RCTs); (4) Analysis of the link between the intake of prebiotics, probiotics, or synbiotics and the microbiome. (5) Participants aged ≥ 60 years. Exclusion criteria were: (1) Data missing or unreported; (2) reports of studies cannot be retrieved. Details are provided in the PICOS table (Table 1).

Quality appraisal and data extraction

The Cochrane Risk of Bias 2.0 (RoB 2) tool was used to assess the methodological quality of the included RCTs. The risk of bias was evaluated independently by two reviewers across five domains: (a) bias arising from the randomization process; (b) bias due to deviations from intended interventions; (c) bias due to missing outcome data; (d) bias in outcome measurement; and (e) bias in the selection of the reported result. Each domain was judged as having a low risk of bias, some concerns, or a high risk of bias. Any disagreements were resolved through discussion with a third reviewer to reach a consensus.

Statistical analysis

Data analyses were performed in RevMan 5.3. Standard mean difference (SMD) and 95% confidence interval (CI) were effect estimates for continuous variables. Differences in means and standard deviations were estimated based on the methods recommended in the Cochrane Handbook for Systematic Reviews of Interventions. When only the sample size, median, range, and/or interquartile range were reported, the online tool available at https://www.math.hkbu.edu.hk/~tongt/papers/median2mean.html was used to estimate the sample mean and standard deviation. For subgroup data that required pooling, we performed the combination using the calculator at https://www.statstodo.com/CombineMeansSDs.php. Data that could not be reliably estimated were excluded from the analysis. Heterogeneity was quantitatively determined by I^2. If little or no heterogeneity ($P > 0.1$, $I^2 \leq 50\%$) was found, a fixed-effect model was selected. In the presence of significant heterogeneity ($P \leq 0.1$, $I^2 > 50\%$), the source of heterogeneity was further tested, and the random-effect model was selected after excluding the source of heterogeneity. Sensitivity analysis was performed using the leave-one-out method to assess the sources of heterogeneity and their impact on the overall results. Publication bias was evaluated only when a single outcome included more than 10 studies, as assessments based on fewer studies may yield unreliable results.

Results

Literature retrieval

3174 records were retrieved from electronic databases. After eliminating duplications, we read the titles and abstracts of the remaining 2272 documents, and then we excluded 2061 reports. The remaining 211 were read in full texts, while 71 of them were excluded for not being RCTs. Additionally, 67 studies were excluded for focusing on non-old populations, 29 for not aligning with the related interventions, and 15 for not meeting the specified outcomes. Finally, 29 RCTs were enrolled. The screening process is displayed in Fig. 1.

Risk of bias and demographic characteristics of included trials

Detailed information regarding the risk of bias is displayed in Fig. 2. All RCTs specified their methods of random allocation. Only 3 RCTs were rated as high risk for missing outcome data [28–30]. In addition, 3 RCTs were judged as high risk for the randomization process [30–32]. Each item was manifested as a percentage, which implied the proportion of risk levels (Fig. 2). To ensure comprehensive data coverage and minimize the influence of subjective selection bias, we included the above-mentioned studies in this systematic review and meta-analysis although they were considered to have a high risk of bias.

1,633 old individuals were included, with 864 in the intervention group and 769 in the control group. In the probiotic group, one study each was conducted in Denmark, New Zealand, UK, Finland, USA, and Italy. Additionally, two RCTs were carried out in China and three RCTs were carried out in Japan. A multicenter study included patients from Italy, France, and Germany. In the prebiotic group, one study each was conducted in Japan, China, the Netherlands, and Germany, while two RCTs each were from the UK and USA. In the synbiotic group, two RCTs each were in Finland, Japan, Brazil, and UK. Among the probiotic studies, three RCTs (Rubin, 2022; Ouwehand, 2008; Kwak, 2020) reported changes in relative abundance of gut microbiota rather than absolute abundance [28, 33, 34]. Similarly, one prebiotic study (Konstanti, 2022) focused on relative abundance [35]. Consequently, these RCTs were not considered when assessing the extent of microbiota changes. Detailed study characteristics are listed in Table 2.

Meta-analysis

Primary outcomes

Twenty-nine RCTs reported various interventions involving PPS and their impacts on the gut microbiota of older adults. A notable increase was found in the abundance of Bifidobacterium in the prebiotics (SMD = 1.09, 95% CI, 0.31 to 1.86, $p < 0.001$) (Fig. 3 and Additional Fig. 1) and probiotics (SMD = 0.40, 95% CI, 0.06 to 0.75, $p < 0.05$) groups (Fig. 3 and Additional Fig. 2). In addition, the abundance of *Bifidobacterium longum subsp. longum* also increased significantly following probiotic supplementation (Fig. 3 and Additional Fig. 3). Specific strains of *Bifidobacterium*, such as *Bifidobacterium angulatum* (SMD = 1.69, 95% CI, 1.01 to 2.38, $p < 0.001$) (Fig. 3 and Additional Fig. 4), *Bifidobacterium longum* (SMD = 0.99, 95% CI, 0.39 to 1.59, $p < 0.01$) (Fig. 3 and Additional Fig. 5), and *Bifidobacterium breve strain Ya* (SMD = 0.95, 95% CI, 0.47 to 1.44, $p < 0.001$) (Fig. 3 and Additional Fig. 6) were substantially enhanced after synbiotic supplementation. However, the increase in Bifidobacterium abundance was not statistically significant ($P = 0.17$). Furthermore, old individuals in the probiotics groups exhibited a significant increase in the gut Shannon index (SMD = 0.76, 95% CI, 0.47 to 1.05, $p < 0.001$) (Fig. 3 and Additional Fig. 7), suggesting enhanced gut microbial diversity. In the synbiotics group, total microbial abundance (SMD = 0.44, 95% CI: 0.19 to 0.69, $p < 0.001$) was greatly elevated (Fig. 3 and Additional Fig. 8), particularly in *Lactobacillus casei strain Shirota* (SMD = 0.75, 95% CI: 0.27 to 1.23, $p < 0.01$)

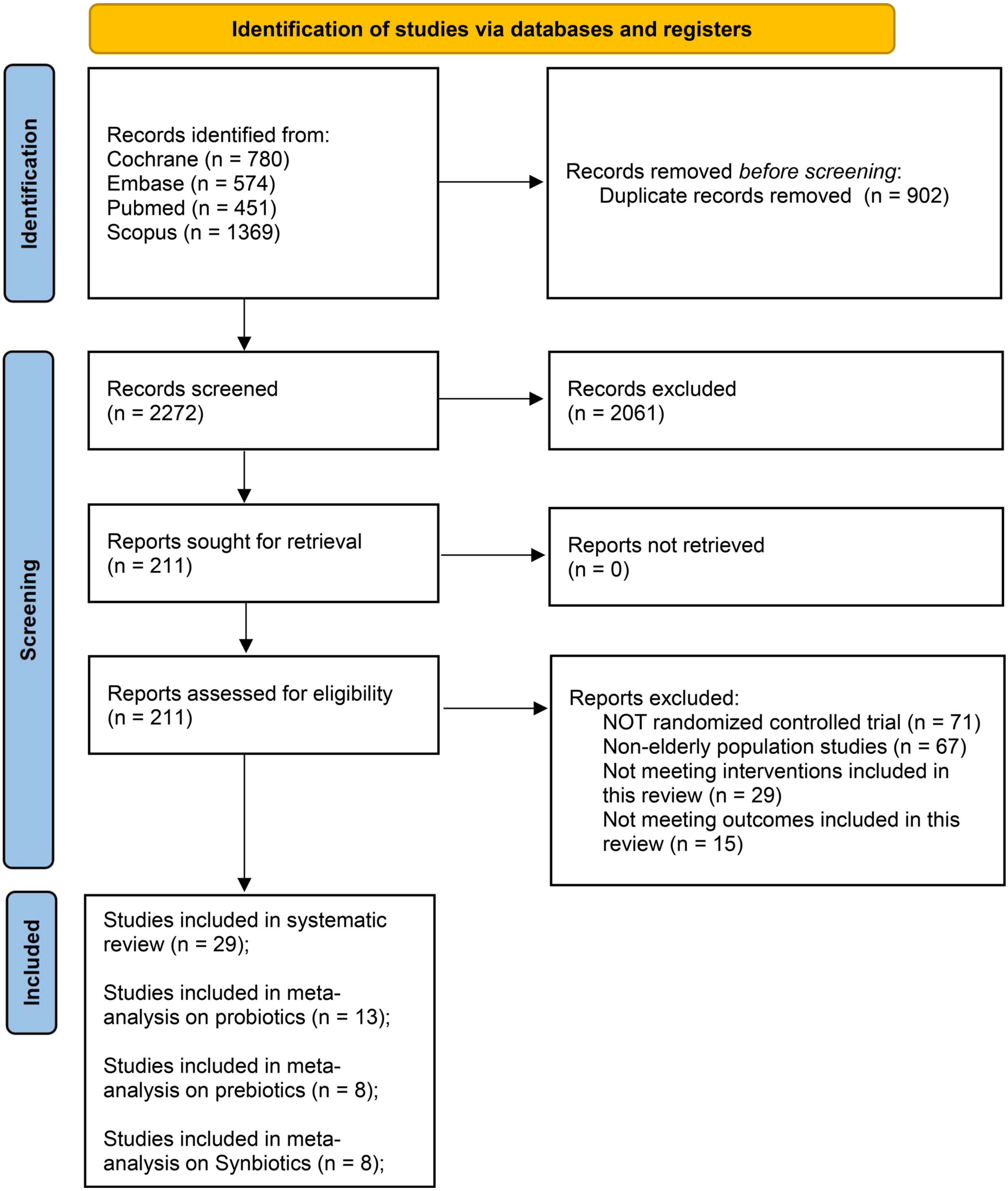
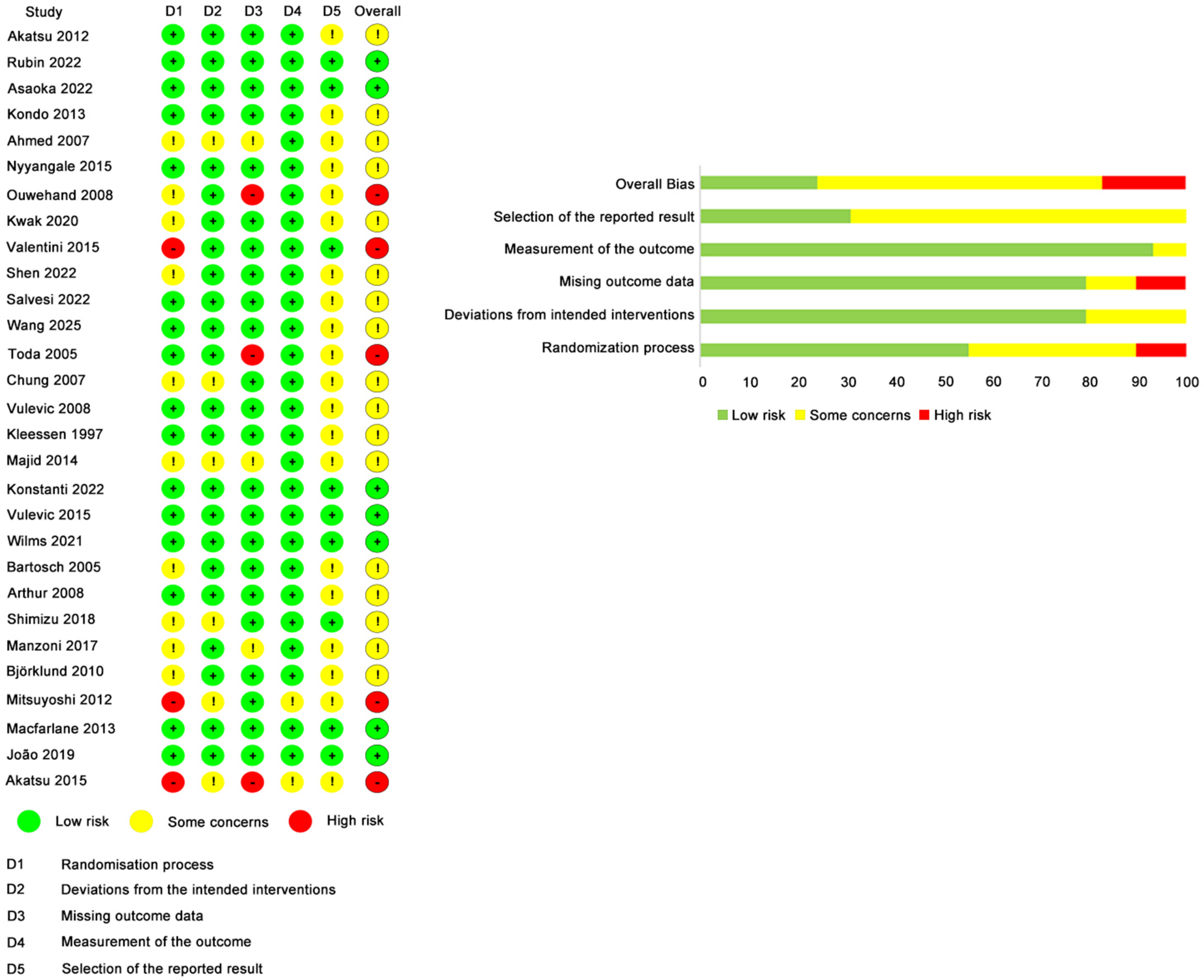


Fig. 1 PRISMA search flowchart



Study	D1	D2	D3	D4	D5	Overall
Akatsu 2012	+	+	+	+	!	!
Rubin 2022	+	+	+	+	+	+
Asaoka 2022	+	+	+	+	+	+
Kondo 2013	+	+	+	+	!	!
Ahmed 2007	!	!	!	+	!	!
Nyyangale 2015	+	+	+	+	!	!
Ouwehand 2008	!	+	-	+	!	-
Kwak 2020	!	+	+	+	!	!
Valentini 2015	-	+	+	+	+	-
Shen 2022	!	+	+	+	!	!
Salvesi 2022	+	+	+	+	!	!
Wang 2025	+	+	+	+	!	!
Toda 2005	+	+	-	+	!	-
Chung 2007	!	!	+	+	!	!
Vulevic 2008	+	+	+	+	!	!
Kleessen 1997	+	+	+	+	!	!
Majid 2014	!	!	!	+	!	!
Konstanti 2022	+	+	+	+	+	+
Vulevic 2015	+	+	+	+	+	+
Wilms 2021	+	+	+	+	+	+
Bartosch 2005	!	+	+	+	!	!
Arthur 2008	+	+	+	+	!	!
Shimizu 2018	!	!	+	+	+	!
Manzoni 2017	!	+	!	+	!	!
Björklund 2010	!	+	+	+	!	!
Mitsuyoshi 2012	-	!	+	!	!	-
Macfarlane 2013	+	+	+	+	+	+
João 2019	+	+	+	+	+	+
Akatsu 2015	-	!	-	!	!	-

Fig. 2 Risk of bias details

(Fig. 3 and Additional Fig. 9). Furthermore, synbiotic supplementation considerably reduced the abundance of the opportunistic pathogen *Pseudomonas* (SMD = -0.55, 95% CI: -0.91 to -0.18, p < 0.01) (Fig. 3 and Additional Fig. 10).

Secondary outcomes

Old individuals exhibited significantly increased interleukin-10 (IL-10) levels (SMD = 0.61, 95% CI, 0.30 to 0.93, $p < 0.001$) (Fig. 3 and Additional Fig. 11) after probiotic supplementation, while IL-1β levels were greatly decreased (SMD = −0.39, 95% CI, −0.7 to 0.08, $p < 0.05$) (Fig. 3 and Additional Fig. 12). TNF-α was also lowered after synbiotic supplementation (SMD= −0.36, 95% CI, −0.69 to −0.02, $p < 0.05$) (Fig. 3 and Additional Fig. 13). Additionally, valeric acids (SMD = 0.5, 95% CI, 0.16 to 0.84, $p < 0.01$) (Fig. 3 and Additional Fig. 14) and acetic acids (SMD = 0.62, 95% CI, 0.22 to 1.03) (Fig. 3 and Additional Fig. 15) were greatly elevated after synbiotic supplementation.

Sensitivity analysis

Sensitivity analyses were conducted for outcomes with substantial heterogeneity (I^2 >50%) and where more than three studies were included. Notable heterogeneity was observed in several outcomes, such as *Bifidobacterium* abundance (prebiotics) and acetic acid abundance (synbiotics). When any single study was excluded, the overall effect size and statistical significance remained largely unchanged, indicating that the results were stable and not unduly influenced by any individual study.

However, in the analysis of *Bifidobacterium* abundance (probiotics), the pooled results were not statistically significant when individual studies such as Akatsu 2012, Salvesi 2022, Toda 2005, or Valentini 2015 were excluded [29, 32, 36, 37]. Similarly, for *Bifidobacterium longum subsp. longum* abundance (probiotics), the pooled

Table 2 Characteristics of the included RCTs

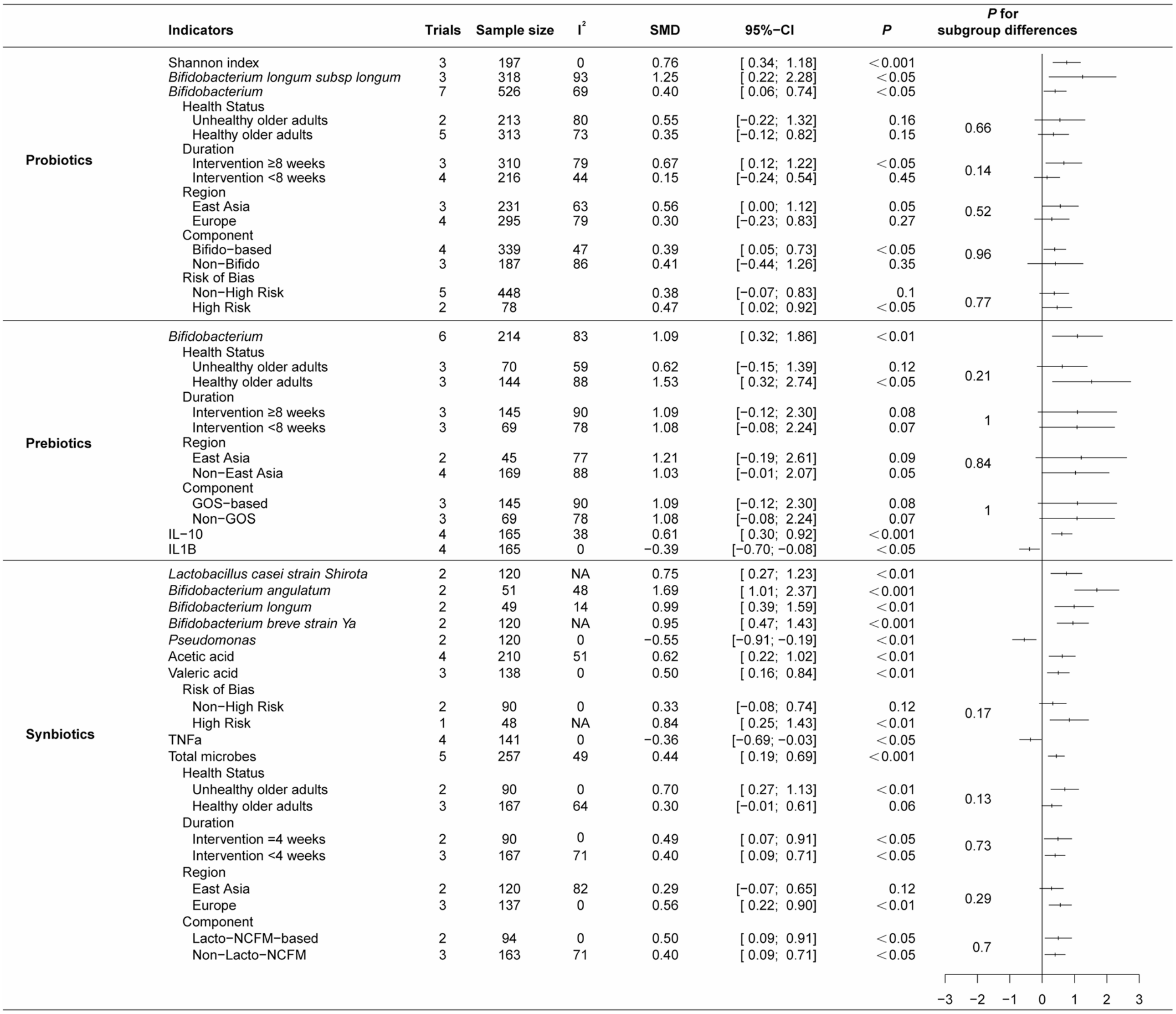
Study	Trial registration number	Country	Group	Sample size	Age (years)	Intervention	Dosage	Disease characteristics	Duration
Probiotics									
Akatsu 2012	NA	Japan	**Control**	22	81.0 ± 9.7	Dextrin	2 g/day	Older adult - patients receiving enteral feeding	12 Weeks
			Trial	23	82.5 ± 7.9	BB536	5*10^10 CFU, b.i.d.		
Rubin 2022	NCT03560700	Denmark	**Control**	27	74 (64.5–82.5)	Placebo	2 capsules/day	VREfm-positive patients	4 Weeks
			Trial	21	76 (71–82)	LGG	3*10^10 CFU, b.i.d.		
Asaoka 2022	UMIN000031507	Japan	**Control**	60	78.9 ± 4.3	Maize starch	1 sachet/day	Older adults with mild cognitive impairment	8 Weeks
			Trial	55	77.2 ± 5.8	B. breve MCC1274	2*10^10 CFU/day		
Kondo 2013	NA	Japan	**Control**	64	83.3 ± 8.5119	Dextrin	2 g/day	Long-term tube-fed older adults	16 Weeks
			Trial	104	84.8577 ± 8.0847	BB536	2.5*10^10 – 5*10^10 CFU/day		
Ahmed 2007	NA	New Zealand	**Control**	20	Mean: 69	Reconstituted skim milk	250 mL/day (no CFU)	Healthy older adults	4 Weeks
			Trial	60	Mean: 69	Reconstituted skim milk + B. lactis HN019	250 mL, 6.5*10^7 – 5*10^9 CFU/day		
Nyangale 2015	NA	UK	**Control**	36	65–80	Microcrystalline cellulose	1 capsule/day	Healthy older adults	4 Weeks
			Trial	36		BC30	1*10^9 CFU/day		
Ouwehand 2008	NA	Finland	**Control**	18	84.3 ± 0.98	Product without any added probiotic	NA	Healthy older adults	12 Weeks
			Trial	18		Product contain B. animalis ssp. lactis BB-12	1*10^9 CFU/day		
Kwak 2020	NCT02299570	USA	**Control**	21	Mean: 63	Normal saline and formulation solution	NA	Patients with recurrent *clostridioides difficile* infection	4 Weeks
			Trial	23	Mean: 68	RBX2660	≥ 1*10^7 – 2*10^7 live organisms/day		
Valentini 2015	NCT01069445-NCT01179789	Italy, France, Germany	**Control**	30	70.1 ± 3.9	RISTOMED diet alone	NA	Healthy older adults	8 Weeks
			Trial	30		Food combined with VSL#3 bacterial blend	2.24*10^11 CFU/day		
Shen 2022	NA	China	**Control**	80	64.95 ± 4.347	Traditional intestinal preparation	NA	Patients with colorectal cancer	1 Weeks
			Trial	80	66.85 ± 4.05	Traditional intestinal preparation + bifidobacteria triplex viable capsules	2.0 g per dose, t.i.d.		
Salvesi 2022	NA	Italy	**Control**	38	81.5 ± 8.9	Maltodextrin	NA	Healthy older adults	24 Weeks
			Trial	59	81.3 ± 10.1	Synbio®	5*10^9 CFU/day		
Wang 2025	NA	China	**Control**	52	77.61 ± 15.32	Placebo	1.5 g per dose, t.i.d.	Older adults with depression	4 Weeks
			Trial	53	75.72 ± 12.65	L. plantarum HEAL9 + L. paracasei 8702 + P. pentosaceus HH-LP56 + B. longum R0175	1.5 g per dose, t.i.d.		
Toda 2005	NA	Japan	**Control**	9	67.1 ± 4.8	Placebo	NA	Healthy older adults	8 Weeks
			Trial	9		L. lactis subsp. cremoris FC	1.5*10^9 CFU/day		
Prebiotics									

Table 2 (continued)

Study	Trial registration number	Country	Group	Sample size	Age (years)	Intervention	Dosage	Disease characteristics	Duration
Probiotics									
Akatsu 2015	NA	Japan	**Control**	11	84.5 ± 7.5	Meibalance	NA	Stroke bed-ridden patients	10 Weeks
			Trial	12	77.8 ± 9.6	Fibren YH + GOS + BGS	NA/4 g/0.4 g/day		
Chung 2007	NA	China	**Control**	9	79.8 ± 6.6	sucrose	4 g/day	Healthy older adults	3 Weeks
			Trial	13	77.5 ± 6.7	XOS	4 g/day		
Vulevic 2008	NA	USA	**Control**	41	69.3 ± 4.0	Maltodextrin	5.5 g/day	Healthy older adults	10 Weeks
			Trial	41		B-GOS	5.5 g/day		
Kleessen 1997	NA	germany	**Control**	15	76.4 (68–89)	lactose	40 g/day	Female constipated patients	19 Days
			Trial	10		Inulin	40 g/day		
Majid 2014	ISRCTN06446184	UK	**Control**	12	71.2 ± 10.6	Maltodextrin	7 g/day	Gastrointestinal patients	2 Weeks
			Trial	10	70.6 ± 8.9	Synergy-1	7 g/day		
Konstanti 2022	NCT03026244	Netherlands	**Control**	13	74 (69–85)	Maltodextrin	NA	Healthy older adults	6 Weeks
			Trial	12	74 (70–84)	BLF + GOS	1 g/2.64 g/day		
Vulevic 2015	NCT01303484	UK	**Control**	20	70.4 ± 3.8	Maltodextrin	5.5 g/day	Healthy older adults	10 Weeks
			Trial	20		B-GOS	5.5 g/day		
Wilms 2021	NCT03077529	USA	**Control**	10	74.3 ± 3.7	Maltodextrin	21.6 g/day	Healthy older adults	4 Weeks
			Trial	10		B-GOS	21.6 g/day		
Synbiotics									
Bartosch 2005	NA	UK	**Control**	9	71 (63–85)	MOS + gelatin capsule	6 g/day	Healthy older adults	8 Weeks
			Trial	9	73 (68–90)	Raftilose Synergy1 + B. bifidum strain BB-02 + B. lactis BL-01	6 g/3.5*10^10 CFU/day		
Arthur 2008	NA	Finland	**Control**	23	71.7 ± 6.2	Sucrose	5 g, b.i.d.	Older NSAID users	4 Weeks
			Trial	24	70.3 ± 7.2	Lactitol + L.acidophilus NCFM	Total: 2*10^9 CFU/g; 5–5.5 g, b.i.d.		
Shimizu 2018	UMINR000007633	Japan	**Control**	37	74 (64–81)	No-Synbiotics	NA	Septic older adults	2 Weeks
			Trial	35	74 (64–82)	Yakult BL Seichoyaku + GOS	3 g/10 g/day		
Manzoni 2017	NA	Brazil	**Control**	15	Mean: 71	Saussurea + soy extracts supplemented	150 mL/day	Healthy older adults	4 Weeks
			Trial	14	Mean: 67	Saussurea + soy extracts supplemented + BB-12	1.5*10^10 CFU, 150 mL/day		
Björklund 2010	NA	Finland	**Control**	24	70.3 ± 7.2	Saccharose	10 g/day	Healthy older adults	2 Weeks
			Trial	23	71.7 ± 6.2	Lactitol + L.acidophilus NCFM	10 g/2*10^10 cells/day		
Mitsuyoshi 2012	NA	Japan	**Control**	23	78 (70–92)	No-Synbiotics	NA	Older adults with gastrointestinal and hepatobiliary cancers	2 Weeks
			Trial	25	79 (70–87)	Biolactis powder + BBG-01 + GOS	1 g/1 g/15 g/day		
Macfarlane 2013	NCT01226212	UK	**Control**	20	71.9 ± 5.4	Potato starch + maltodextrose	6 g, b.i.d.	Healthy older adults	4 Weeks
			Trial	23		Synergy I + B. longum	6 g/2*10^11 CFU, b.i.d.		

Table 2 (continued)

Study	Trial registration number	Country	Group	Sample size	Age (years)	Intervention	Dosage	Disease characteristics	Duration
Probiotics									
João 2019	RBR-6qr9xx	Brazil	**Control**	10	77.60 ± 7.22	Maltodextrin	6 g, b.i.d.	Frail older adults	24 Weeks
			Trial	12	75.33 ± 6.85	FOS + L.paracasei LPC-31 + L.rhamnosus HN001 + L. acidophilus NCFM + B. lactis HN019	6 g/1*10^8 – 1*10^9 CFU, b.i.d.		



	Indicators	Trials	Sample size	I^2	SMD	95%−CI	*P*	*P* for subgroup differences
Probiotics	Shannon index	3	197	0	0.76	[0.34; 1.18]	< 0.001	
	Bifidobacterium longum subsp longum	3	318	93	1.25	[0.22; 2.28]	< 0.05	
	Bifidobacterium	7	526	69	0.40	[0.06; 0.74]	< 0.05	
	Health Status							
	Unhealthy older adults	2	213	80	0.55	[−0.22; 1.32]	0.16	0.66
	Healthy older adults	5	313	73	0.35	[−0.12; 0.82]	0.15	
	Duration							
	Intervention ≥8 weeks	3	310	79	0.67	[0.12; 1.22]	< 0.05	0.14
	Intervention <8 weeks	4	216	44	0.15	[−0.24; 0.54]	0.45	
	Region							
	East Asia	3	231	63	0.56	[0.00; 1.12]	0.05	0.52
	Europe	4	295	79	0.30	[−0.23; 0.83]	0.27	
	Component							
	Bifido−based	4	339	47	0.39	[0.05; 0.73]	< 0.05	0.96
	Non−Bifido	3	187	86	0.41	[−0.44; 1.26]	0.35	
	Risk of Bias							
	Non−High Risk	5	448		0.38	[−0.07; 0.83]	0.1	0.77
	High Risk	2	78		0.47	[0.02; 0.92]	< 0.05	
Prebiotics	*Bifidobacterium*	6	214	83	1.09	[0.32; 1.86]	< 0.01	
	Health Status							
	Unhealthy older adults	3	70	59	0.62	[−0.15; 1.39]	0.12	0.21
	Healthy older adults	3	144	88	1.53	[0.32; 2.74]	< 0.05	
	Duration							
	Intervention ≥8 weeks	3	145	90	1.09	[−0.12; 2.30]	0.08	1
	Intervention <8 weeks	3	69	78	1.08	[−0.08; 2.24]	0.07	
	Region							
	East Asia	2	45	77	1.21	[−0.19; 2.61]	0.09	0.84
	Non−East Asia	4	169	88	1.03	[−0.01; 2.07]	0.05	
	Component							
	GOS−based	3	145	90	1.09	[−0.12; 2.30]	0.08	1
	Non−GOS	3	69	78	1.08	[−0.08; 2.24]	0.07	
	IL−10	4	165	38	0.61	[0.30; 0.92]	< 0.001	
	IL1B	4	165	0	−0.39	[−0.70; −0.08]	< 0.05	
Synbiotics	*Lactobacillus casei strain Shirota*	2	120	NA	0.75	[0.27; 1.23]	< 0.01	
	Bifidobacterium angulatum	2	51	48	1.69	[1.01; 2.37]	< 0.001	
	Bifidobacterium longum	2	49	14	0.99	[0.39; 1.59]	< 0.01	
	Bifidobacterium breve strain Ya	2	120	NA	0.95	[0.47; 1.43]	< 0.001	
	Pseudomonas	2	120	0	−0.55	[−0.91; −0.19]	< 0.01	
	Acetic acid	4	210	51	0.62	[0.22; 1.02]	< 0.01	
	Valeric acid	3	138	0	0.50	[0.16; 0.84]	< 0.01	
	Risk of Bias							
	Non−High Risk	2	90	0	0.33	[−0.08; 0.74]	0.12	0.17
	High Risk	1	48	NA	0.84	[0.25; 1.43]	< 0.01	
	TNFa	4	141	0	−0.36	[−0.69; −0.03]	< 0.05	
	Total microbes	5	257	49	0.44	[0.19; 0.69]	< 0.001	
	Health Status							
	Unhealthy older adults	2	90	0	0.70	[0.27; 1.13]	< 0.01	0.13
	Healthy older adults	3	167	64	0.30	[−0.01; 0.61]	0.06	
	Duration							
	Intervention =4 weeks	2	90	0	0.49	[0.07; 0.91]	< 0.05	0.73
	Intervention <4 weeks	3	167	71	0.40	[0.09; 0.71]	< 0.05	
	Region							
	East Asia	2	120	82	0.29	[−0.07; 0.65]	0.12	0.29
	Europe	3	137	0	0.56	[0.22; 0.90]	< 0.01	
	Component							
	Lacto−NCFM−based	2	94	0	0.50	[0.09; 0.91]	< 0.05	0.7
	Non−Lacto−NCFM	3	163	71	0.40	[0.09; 0.71]	< 0.05	

Fig. 3 Forest plot of significant indicators in older adults taking PPS

estimates were also not statistically significant when the study by Akatsu 2012 or Wang 2025 was excluded. Nevertheless, the overall direction of the effect remained consistent, suggesting the moderate robustness of the findings (Additional Table 2).

In this study, five RCTs were rated as high risk of bias, including Ouwehand 2008, Valentini 2015, Toda 2005, Mitsuyoshi 2012, and Akatsu 2015 [28–32]. After excluding these studies in a sensitivity analysis, the previously significant effects on *Bifidobacterium* abundance (probiotics) and valeric acid levels (synbiotics) became non-significant (Additional Table 3). This change indicates that the above outcomes are highly sensitive to specific studies, suggesting limited robustness of the pooled results. Nevertheless, to preserve data completeness and minimize subjective judgment, all eligible RCTs were included in this meta-analysis regardless of their risk of bias. However, these findings should be interpreted with caution, and further validation is warranted through rigorously designed RCTs with a low risk of bias.

Subgroup analysis

To explore the potential sources of heterogeneity, we conducted subgroup analyses for PPS based on participants' health status and intervention duration. When stratified by health status (healthy vs. unhealthy older adults), no statistically significant differences were observed in the abundance of *Bifidobacterium* following probiotic (Fig. 3, Additional Fig. 16) or prebiotic (Fig. 3, Additional Fig. 17) supplementation, nor in total microbial abundance following synbiotic supplementation (Fig. 3, Additional Fig. 18).

Similarly, when stratified by intervention duration, no significant subgroup differences were found. For probiotics (Fig. 3, Additional Figs. 19) and prebiotics (Fig. 3, Additional Figs. 20), *Bifidobacterium* abundance did not differ significantly between interventions lasting < 8 weeks and those ≥ 8 weeks. For synbiotics, total microbial abundance showed no significant difference between interventions < 4 weeks and those ≥ 4 weeks (Fig. 3, Additional Fig. 21).

When stratified by the type of probiotic supplemented (*Bifido*-based vs. Non-*Bifido*), no statistically significant difference was observed in *Bifidobacterium* abundance (Fig. 3, Supplementary Fig. 22), suggesting that the observed increase in *Bifidobacterium* abundance may not be solely attributable to the direct supplementation of *Bifidobacterium* strains. Similarly, for prebiotics, subgroup analysis of GOS-based vs. Non-GOS interventions revealed no significant difference in *Bifidobacterium* abundance (Fig. 3, Supplementary Fig. 23). For synbiotics, a subgroup analysis of *Lacto-NCFM*-based formulations vs. non-*Lacto-NCFM* ones also showed no statistically significant difference in total microbial abundance (Fig. 3, Supplementary Fig. 24). For probiotics (Fig. 3, Supplementary Fig. 25) and prebiotics (Fig. 3, Supplementary Fig. 26), the pooled estimates demonstrated no significant regional differences in *Bifidobacterium* abundance between studies conducted in East Asia and those conducted elsewhere. Similarly, for synbiotics, no significant differences in total microbial abundance were observed between studies conducted in East Asia and Europe (Fig. 3, Supplementary Fig. 27).

Discussion

PPS is pivotal in reshaping the gut microenvironment and alleviating intestinal inflammation [38]. This meta-analysis evaluated the effects of PPS supplementation on gut microbiota, related metabolic products, and inflammatory markers in older adults. The pooled results indicated that PPS increased the abundance of beneficial gut bacteria in this population. Additionally, synbiotic supplementation enhanced the production of SCFAs, such as acetic acid and valeric acid, and reduced the abundance of harmful bacteria, including Pseudomonas, whereas these effects were not observed with probiotics or prebiotics alone. Furthermore, prebiotic and synbiotic interventions exerted anti-inflammatory effects, which were not evident in the probiotic-only group.

This study showed that PPS supplementation upregulated *Bifidobacterium* abundance, consistent with findings reported in the literature [24]. *Bifidobacterium* abundance gradually declines with aging [39], and a high abundance of *Bifidobacterium* is considered a hallmark of longevity and extreme longevity [40]. Furthermore, *Bifidobacterium* not only improves chronic constipation and cognitive function in older adults but also alleviates colitis and maintains microbial homeostasis [41–43]. As a well-known beneficial bacterium, *Bifidobacterium* maintains gut barrier integrity and mitigates age-related cognitive decline [44, 45]. *Lactobacillus casei strain Shirota* is widely recognized for its anti-inflammatory and antioxidant properties [46]. In this study, we also found that synbiotic supplementation increased the abundance of this bacteria.

Additionally, the opportunistic pathogen *Pseudomonas* was reduced following synbiotic intervention in two RCTs of patients with critical diseases (sepsis and cancer) [31, 47]. This finding suggests that synbiotic or probiotic supplementation may help reduce pathogenic bacteria in older individuals with underlying diseases, potentially alleviating disease progression.

After prebiotic supplementation, IL-1β was lowered and IL-10 was elevated. In contrast, following synbiotic supplementation, TNF-α levels were reduced. Excessive production of inflammatory cytokines can lead to gut barrier dysfunction, characterized by downregulated tight junction proteins and increased intestinal permeability [48]. This compromised intestinal integrity allows the translocation of microbes and lipopolysaccharide, further contributing to systemic damage in older individuals [49]. Beneficial bacteria, including *Lactobacillus* and *Bifidobacterium*, can reduce Gram-negative bacteria and gut-derived lipopolysaccharide-induced inflammatory factors, such as TNF-α and IL-1β [50, 51]. IL-10 is crucial in suppressing excessive inflammation and is increased in response to beneficial bacteria like *Lactobacillus* and *Bifidobacterium* [52]. Therefore, supplementation with prebiotics and synbiotics may help improve gut function and alleviate chronic inflammation in older adults, which is significant for preventing age-related diseases. Ouwehand et al. found no significant changes in inflammatory cytokine levels following probiotic intervention [28]. Consistently, we did not observe significant effects on inflammatory cytokines in the probiotic group.

Gut microbiota influences the production of gastrointestinal metabolites, especially SCFAs, which are generated through the fermentation of complex polysaccharides. A reduction in SCFAs-producing species has been reported in older adults [53]. SCFAs cover butyric acids, propionic acids, acetic acids, and valeric acids. Acetic acids and valeric acids are energy sources for gut-resident microbiota that protect the intestinal mucosal barrier and alleviate inflammation [54]. However, this study observed a more pronounced effect of synbiotics in improving SCFA production, whereas such effects were not seen in probiotic or prebiotic interventions alone. By combining probiotics and prebiotics, synbiotics may provide a more favorable environment for SCFAs-producing microbiota, thereby promoting the efficient conversion of prebiotics into SCFAs.

The RCTs included in this study involved older adults with different baseline health conditions, with more than 50% of participants diagnosed with chronic diseases. Subgroup analyses were performed for outcomes reported in more than five RCTs, and the results indicated that neither intervention duration nor participants' health status significantly influenced *Bifidobacterium* abundance (probiotics and prebiotics) or total microbial abundance (synbiotics). Similarly, no significant subgroup differences were observed based on the type of PPS used or the geographic region. These findings suggest that the above factors may not substantially affect the impact of PPS on gut microbiota in older adults. Although we intended to explore the impact of different dosages on outcomes, the substantial variability and a lack of standardization in the doses used prevented us from conducting any relevant subgroup analyses or meta-regression. Such variability in dosage may represent one of the major sources of heterogeneity. In addition, individual-level factors, such as sex, underlying disease types, and medication history, may also confound the intervention effects. These confounding factors were difficult to control in this study and may have affected the accuracy and interpretability of the results. Moreover, the wide variability in disease types may influence gut microecology through different mechanisms, contributing to substantial inter-individual differences in response to PPS interventions. Future trials should consider stratified designs based on participants' health status to elucidate the differential efficacy of PPS in specific disease conditions or health states.

In the present meta-analysis, *Bifidobacterium* levels consistently increased following PPS interventions. *Bifidobacterium* interventions can improve various common conditions among older adults, including hypertension, coronary heart disease, diabetes, and cognitive impairment [45, 55, 56]. Therefore, future research should focus on evaluating the effects of *Bifidobacterium* at different doses, in various formulations, and in combination with other microbial strains in older populations, to optimize the benefits of *Bifidobacterium*-based interventions. The limited number of studies included and small sample sizes for certain outcomes, such as the *Lactobacillus casei strain Shirota*, may compromise the reliability and generalizability of the findings. Additional well-designed, large-scale trials are warranted to validate these preliminary observations.

During the literature screening process, studies that reported only relative abundance were excluded due to difficulties in data standardization and extraction. Most of these studies presented microbial composition in stacked bar chart without providing specific numerical values. Such Qualitative data are not suitable for meta-analysis, which requires standardized Quantitative measures. Nevertheless, we acknowledge the potential value of such studies in providing broader contextual insights. As the number of included studies for each outcome was fewer than 10, key reliability assessments—such as Egger's test for publication bias—could not be performed. Although funnel plots appeared generally symmetrical (Additional Figs. 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41 and 42), it may not be sufficient to rule out publication bias, especially when the number of studies is small. Therefore, the possibility of publication bias cannot be excluded. Under such circumstances, all findings should be considered exploratory and interpreted with caution.

Moreover, the effects of different probiotic strains and prebiotic types vary, and the optimal combination of probiotics and prebiotics remains unclear. Future research should prioritize large-scale, rigorously designed RCTs to ascertain the long-term effects of PPS on gut microbiota composition and metabolism in older adults. Given the variability in individual health status and gut microbiota characteristics, future studies should also explore personalized probiotic, prebiotic, and synbiotic interventions to optimize their effectiveness in the older population.

Conclusion

PPS may serve as an effective dietary intervention to improve gut microbiota homeostasis and regulate chronic inflammation in older adults. Our findings provide preliminary evidence to support the use of PPS to modulate gut microecology in older adults, which could offer a theoretical and practical foundation for future nutritional or clinical interventions targeting age-related microbial dysbiosis and inflammation. Specific supplementation of PPS may promote the production of beneficial metabolites, such as SCFAs, further enhancing the intestinal environment and potentially improving health outcomes. However, due to limitations such as small sample sizes and heterogeneity in intervention protocols, further well-designed, large-scale RCTs are necessary. Future research should standardize outcome measures and more comprehensively assess gut microbial and metabolic markers to confirm the clinical benefits of PPS in aging populations.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12937-025-01218-1.

Supplementary Material 1.

Supplementary Material 2: Additional Table 1 Search Strategy Additional Table 2 Sensitivity Analyses for High-Heterogeneity Outcomes Additional Table 3 Sensitivity Analyses for High-risk Outcomes.

Supplementary Material 3: Additional Figure 1 Forest Plots of***Bifidobacterium*** Abundance in Older Adults with Prebiotic Supplementation Compared with Non-Supplemented Individuals. Additional Figure 2 Forest Plots of***Bifidobacterium*** Abundance in Older Adults with Probiotic Supplementation Compared with Non-Supplemented Individuals. Additional Figure 3 Forest Plots of***Bifidobacterium longum subsp. longum*** Abundance in Older Adults with Probiotic Supplementation Compared with Non-supplemented Individuals. Additional Figure 4 Forest Plots of***Bifidobacterium angulatum*** Abundance in Older Adults with Synbiotics Supplementation Compared with Non-Supplemented Individuals. Additional Figure 5 Forest Plots of***Bifidobacterium longum*** Abundance in Older Adults with Synbiotics Supplementation Compared with Non-supplemented Individuals. Additional Figure 6 Forest Plots of***Bifidobacterium breve strain Ya*** in Older Adults with Synbiotics Supplementation Compared with Non-supplemented Individuals. Additional Figure 7 Forest Plots of Shannon Diversity Index in Older Adults with Probiotics Supplementation Compared with Non-supplemented Individuals. Additional Figure 8 Forest Plots of Total Microbial Abundance in Older Adults with Synbiotics Supplementation Compared with Non-supplemented Individuals. Additional Figure 9 Forest Plots of***Lactobacillus casei strain Shirota*** Abundance in Older Adults with Synbiotics Supplementation Compared with Non-supplemented Individuals. Additional Figure 10 Forest Plots of***Pseudomonas*** Abundance in Older Adults with Synbiotics Supplementation Compared with Non-Supplemented Individuals. Additional Figure 11 Forest Plots of IL-10 Levels in Older Adults with Prebiotic Supplementation Compared with Non-Supplemented Individuals. Additional Figure 12 Forest Plots of IL-1β Levels in Older Adults with Prebiotic Supplementation Compared with Non-Supplemented Individuals. Additional Figure 13 Forest Plots of TNFα Levels in Older Adults with Synbiotics Supplementation Compared with Non-Supplemented Individuals. Additional Figure 14 Forest Plots of Valeric Acid Levels in Older Adults with Synbiotics Supplementation Compared with Non-Supplemented Individuals. Additional Figure 15 Forest Plots of Acetic Acid Levels in Older Adults with Synbiotics Supplementation Compared with Non-Supplemented Individuals. Additional Figure 16 Forest Plots from Subgroup Analyses of ***Bifidobacterium*** Abundance in Older Adults with Probiotic Supplementation Compared with Non-supplemented Individuals, Stratified by Health Status. Additional Figure 17 Forest Plots from Subgroup Analyses of ***Bifidobacterium*** Abundance in Older Adults with Prebiotic Supplementation Compared with Non-Supplemented Individuals, Stratified by Health Status. Additional Figure 18 Forest Plots from Subgroup Analyses of Total Microbial Abundance in Older Adults with Synbiotic Supplementation Compared with Non-Supplemented Individuals, Stratified by Health Status. Additional Figure 19 Forest Plots from Subgroup Analyses of Bifidobacterium Abundance in Older Adults with Probiotic Supplementation Compared with Non-Supplemented Individuals, Stratified by Intervention Duration (<8 Weeks vs. ≥8 Weeks). Additional Figure 20 Forest Plots from Subgroup Analyses of Bifidobacterium Abundance in Older Adults with Prebiotic Supplementation Compared with Non-Supplemented Individuals, Stratified by Intervention Duration (<8 Weeks vs. ≥8 Weeks). Additional Figure 21 Forest Plots from Subgroup Analyses of Total Microbial Abundance in Older Adults with Synbiotic Supplementation Compared with Non-Supplemented Individuals, Stratified by Intervention Duration (<4 Weeks vs. ≥4 Weeks). Additional Figure 22 Forest Plots from Subgroup Analyses of Bifidobacterium Abundance in Older Adults with Probiotic Supplementation, Stratified by Probiotic Type (Bifido-based vs. Non-Bifido). Additional Figure 23 Forest Plots from Subgroup Analyses of Bifidobacterium Abundance in Older Adults with Prebiotic Supplementation, Stratified by Prebiotics Type (GOS-based vs. Non-GOS). Additional Figure 24 Forest Plots from Subgroup Analyses of Total Microbial Abundance in Older Adults with Synbiotic Supplementation, Stratified by Synbiotic Type (Lacto-NCFM-Based vs. Non-Lacto-NCFM). Additional Figure 25 Forest Plots from Subgroup Analyses of Bifidobacterium Abundance in Older Adults with Probiotic Supplementation, Stratified by Geographic Region (East Asia vs. Europe). Additional Figure 26 Forest Plots from Subgroup Analyses of Bifidobacterium Abundance in Older Adults with Prebiotic Supplementation, Stratified by Geographic Region (East Asia vs. Non-East Asia). Additional Figure 27 Forest Plots from Subgroup Analyses of Total Microbial Abundance in Older Adults with Synbiotic Supplementation, Stratified by Geographic Region (East Asia vs. Europe). Additional Figure 28 Funnel Plot Assessing Potential Publication Bias for ***Bifidobacterium*** Abundance in Older Adults with Prebiotic Supplementation. Additional Figure 29 Funnel Plot Assessing Potential Publication Bias for ***Bifidobacterium*** Abundance in Older Adults with Probiotic Supplementation. Additional Figure 30 Funnel Plot Assessing Potential Publication Bias for ***Bifidobacterium longum subsp. longum*** Abundance in Older Adults with Probiotic Supplementation. Additional Figure 31 Funnel Plot Assessing Potential Publication Bias for ***Bifidobacterium angulatum*** Abundance in Older Adults with Synbiotic Supplementation. Additional Figure 32 Funnel Plot Assessing Potential Publication Bias for ***Bifidobacterium longum*** Abundance in Older Adults with Synbiotic Supplementation. Additional Figure 33 Funnel Plot Assessing Potential Publication Bias for ***Bifidobacterium breve Strain Ya*** Abundance in Older Adults with Synbiotic Supplementation. Additional Figure 34 Funnel Plot Assessing Potential Publication Bias for Shannon Diversity Index in Older Adults with Probiotic Supplementation. Additional Figure 35 Funnel Plot Assessing Potential Publication Bias for Total Microbial Abundance in Older Adults with Synbiotic Supplementation. Additional Figure 36 Funnel Plot Assessing Potential Publication Bias for ***Lactobacillus casei Strain Shirota*** Abundance in Older Adults with Synbiotic Supplementation. Additional Figure 37 Funnel Plot Assessing Potential Publication Bias for ***Pseudomonas*** Abundance in Older Adults with Synbiotic Supplementation. Additional Figure 38 Funnel Plot Assessing Potential Publication Bias for IL-10 Levels in Older Adults with Prebiotic Supplementation. Additional Figure 39 Funnel Plot Assessing Potential Publication Bias for IL-1β Levels in Older Adults with Prebiotic Supplementation. Additional Figure 40 Funnel Plot Assessing Potential Publication Bias for TNFα Levels in Older Adults with Synbiotic Supplementation. Additional Figure 41 Funnel Plot Assessing Potential Publication Bias for Valeric Acid Levels in Older Adults with Synbiotic Supplementation. Additional Figure 42 Funnel Plot Assessing Potential Publication Bias for Acetic Acid Levels in Older Adults with Synbiotic Supplementation.

Acknowledgements

Not applicable.

Authors' contributions

KZ designed research; KZ, HL, MG conducted research; KZ, HL, MG analyzed data; and KZ, HL, SC, MG and YW wrote the paper. KZ, HL, SC and MG had primary responsibility for final content. All authors read and approved the final manuscript.

Funding

This work was supported by the National Natural Science Foundation of China (82174244).

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]State Key Laboratory of Traditional Chinese Medicine Syndrome, Guangzhou University of Chinese Medicine, Guangzhou 510006, China
[2]Chinese Medicine Guangdong Laboratory, Zhu Hai 519031, China
[3]School of Basic Medical Sciences, Guangzhou University of Chinese Medicine, Guangzhou 510006, China
[4]Shantou Hospital of Traditional Chinese Medicine, Shantou, China
[5]Department of Microbiology and Immunology, and Immunology Translational Research Programme, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore
[6]Immunology Programme, The Life Science Institute, National University of Singapore, Singapore, Singapore
[7]School of Pharmaceutical Sciences, Guangzhou University of Chinese Medicine, Guangzhou 510006, Guangdong, China
[8]Key Laboratory of Chinese Medicinal Resource from Lingnan, Guangzhou University of Chinese Medicine, No.232, Outer Ring East Road, Guangzhou, Guangdong Province, China

Received: 22 April 2025 / Accepted: 1 September 2025

References

1. Division UP. World Population Prospects 2022: Data sources. p. 245 2022:245.
2. Zhang Y, Baldyga K, Dong Y, Song W, Villanueva M, Deng H, et al. The association between gut microbiota and postoperative delirium in patients. Transl Psychiatry. 2023;13:156.
3. Xu Y, He C, Xi Y, Zhang Y, Bai Y. Gut microbiota and Immunosenescence in cancer. Semin Cancer Biol. 2024;104–105:32–45.
4. Garcez FB, Garcia de Alencar JC, Fernandez SSM, Avelino-Silva VI, Sabino EC, Martins RCR, Franco LAM, Lima Ribeiro SM, Possolo de Souza H, Avelino-Silva TJ. Association between gut microbiota and delirium in acutely ill older adults. J Gerontol Biol Sci Med Sci. 2023;78:1320–7.
5. Zhao L, Fang J, Tang S, Deng F, Liu X, Shen Y, et al. PM2.5 and serum metabolome and insulin resistance, potential mediation by the gut microbiome: a population-based panel study of older adults in China. Environ Health Perspect. 2022;130:27007.
6. Ferrucci L, Fabbri E. Inflammageing: chronic inflammation in ageing, cardiovascular disease, and frailty. Nat Rev Cardiol. 2018;15:505–22.
7. Global fertility. In 204 countries and territories, 1950–2021, with forecasts to 2100: a comprehensive demographic analysis for the global burden of disease study 2021. Lancet. 2024;403:2057–99.
8. Franceschi C, Garagnani P, Parini P, Giuliani C, Santoro A. Inflammaging: a new immune-metabolic viewpoint for age-related diseases. Nat Rev Endocrinol. 2018;14:576–90.
9. Badal VD, Vaccariello ED, Murray ER, Yu KE, Knight R, Jeste DV, et al. The gut microbiome, aging, and longevity: a systematic review. Nutrients. 2020. https://doi.org/10.3390/nu12123759
10. Odamaki T, Kato K, Sugahara H, Hashikura N, Takahashi S, Xiao JZ, et al. Age-related changes in gut microbiota composition from newborn to centenarian: a cross-sectional study. BMC Microbiol. 2016;16:90.
11. Li J, Si H, Du H, Guo H, Dai H, Xu S, Wan J. Comparison of gut microbiota structure and actinobacteria abundances in healthy young adults and elderly subjects: a pilot study. BMC Microbiol. 2021;21:13.
12. Paul W, O'Toole MJC. Gut microbiota: changes throughout the lifespan from infancy to elderly. Int Dairy J. 2010;20:281–91.
13. Cătoi AF, Corina A, Katsiki N, Vodnar DC, Andreicuţ AD, Stoian AP, Rizzo M, Pérez-Martínez P. Gut microbiota and aging-A focus on centenarians. Biochim Biophys Acta Mol Basis Dis. 2020;1866:165765.
14. Lee J, d'Aigle J, Atadja L, Quaicoe V, Honarpisheh P, Ganesh BP, et al. Gut microbiota-derived short-chain fatty acids promote poststroke recovery in aged mice. Circ Res. 2020;127:453–65.
15. Warman DJ, Jia H, Kato H. The potential roles of probiotics, resistant starch, and resistant proteins in ameliorating inflammation during aging (Inflammaging). Nutrients. 2022. https://doi.org/10.3390/nu14040747.
16. McLoughlin RF, Berthon BS, Jensen ME, Baines KJ, Wood LG. Short-chain fatty acids, prebiotics, synbiotics, and systemic inflammation: a systematic review and meta-analysis. Am J Clin Nutr. 2017;106:930–45.
17. Ale EC, Binetti AG. Role of probiotics, prebiotics, and synbiotics in the elderly: insights into their applications. Front Microbiol. 2021;12:631254.
18. Wilms E, An R, Smolinska A, Stevens Y, Weseler AR, Elizalde M, et al. Galacto-oligosaccharides supplementation in prefrail older and healthy adults increased faecal bifidobacteria, but did not impact immune function and oxidative stress. Clin Nutr. 2021;40:3019–31.
19. Ouwehand AC, Tiihonen K, Saarinen M, Putaala H, Rautonen N. Influence of a combination of *Lactobacillus acidophilus* NCFM and lactitol on healthy elderly: intestinal and immune parameters. Br J Nutr. 2009;101:367–75.
20. Macfarlane S, Cleary S, Bahrami B, Reynolds N, Macfarlane GT. Synbiotic consumption changes the metabolism and composition of the gut microbiota in older people and modifies inflammatory processes: a randomised, double-blind, placebo-controlled crossover study. Aliment Pharmacol Ther. 2013;38:804–16.
21. Nyangale EP, Farmer S, Cash HA, Keller D, Chernoff D, Gibson GR. *Bacillus coagulans* GBI-30, 6086 modulates *Faecalibacterium prausnitzii* in older men and women. J Nutr. 2015;145:1446–52.
22. Tran TTT, Cousin FJ, Lynch DB, Menon R, Brulc J, Brown JR, et al. Prebiotic supplementation in frail older people affects specific gut microbiota taxa but not global diversity. Microbiome. 2019;7:39.
23. Qu H, Zhang Y, Chai H, Gao ZY, Shi DZ. Effects of microbiota-driven therapy on inflammatory responses in elderly individuals: a systematic review and meta-analysis. PLoS ONE. 2019;14:e0211233.
24. Lai H, Li Y, He Y, Chen F, Mi B, Li J, Xie J, Ma G, Yang J, Xu K, et al. Effects of dietary fibers or probiotics on functional constipation symptoms and roles of gut microbiota: a double-blinded randomized placebo trial. Gut Microbes. 2023;15:2197837.
25. Cheng J, Gao C, Ala-Jaakkola R, Forssten SD, Saarinen M, Hibberd A, et al. Eight-week supplementation with *bifidobacterium lactis* HN019 and functional constipation: a randomized clinical trial. JAMA Netw Open. 2024;7:e2436888.
26. Miller LE, Lehtoranta L, Lehtinen MJ. Short-term probiotic supplementation enhances cellular immune function in healthy elderly: systematic review and meta-analysis of controlled studies. Nutr Res. 2019;64:1–8.
27. Kou J, Kang H, Hu L, Wang D, Wang S, Wang Q, et al. Evaluation of improvement of cognitive impairment in older adults with probiotic supplementation: a systematic review and meta-analysis. Geriatr Nurs. 2023;54:155–62.
28. Ouwehand AC, Bergsma N, Parhiala R, Lahtinen S, Gueimonde M, Finne-Soveri H, et al. *Bifidobacterium* microbiota and parameters of immune function in elderly subjects. FEMS Immunol Med Microbiol. 2008;53:18–25.
29. Toda T, Kosaka H, Terai M, Mori H, Benno Y, Yamori Y. Effects of fermented milk with <i>lactococcus lactis subsp. <i>cremoris FC on defecation frequency and fecal microflora in healthy elderly volunteers</i>. Nippon Shokuhin Kagaku Kogaku Kaishi. 2005;52:243–50.
30. Akatsu H, Nagafuchi S, Kurihara R, Okuda K, Kanesaka T, Ogawa N, et al. Enhanced vaccination effect against influenza by prebiotics in elderly patients receiving enteral nutrition. Geriatr Gerontol Int. 2016;16:205–13.
31. Okazaki M, Matsukuma S, Suto R, Miyazaki K, Hidaka M, Matsuo M, Noshima S, Zempo N, Asahara T, Nomoto K. Perioperative synbiotic therapy in elderly patients undergoing gastroenterological surgery: a prospective, randomized control trial. Nutrition. 2013;29:1224–30.
32. Valentini L, Pinto A, Bourdel-Marchasson I, Ostan R, Brigidi P, Turroni S, et al. Impact of personalized diet and probiotic supplementation on inflammation, nutritional parameters and intestinal microbiota - the RISTOMED project: randomized controlled trial in healthy older people. Clin Nutr. 2015;34:593–602.
33. Lee S, You H, Lee Y, Baik H, Paik J, Lee H, et al. Intake of MPRO3 over 4 weeks reduces glucose levels and improves gastrointestinal health and metabolism. Microorganisms. 2021. https://doi.org/10.3390/microorganisms10010088.

34. Kwak S, Choi J, Hink T, Reske KA, Blount K, Jones C, et al. Impact of investigational microbiota therapeutic RBX2660 on the gut microbiome and resistome revealed by a placebo-controlled clinical trial. Microbiome. 2020;8:125.
35. Konstanti P, van Splunter M, van den Brink E, Belzer C, Nauta A, van Neerven RJJ, et al. The effect of nutritional intervention with lactoferrin, galactooligosacharides and vitamin D on the gut microbiota composition of healthy elderly women. Nutrients. 2022. https://doi.org/10.3390/nu14122468.
36. Akatsu H, Iwabuchi N, Xiao JZ, Matsuyama Z, Kurihara R, Okuda K, et al. Clinical effects of probiotic *bifidobacterium longum* BB536 on immune function and intestinal microbiota in elderly patients receiving enteral tube feeding. J Parenter Enteral Nutr. 2013;37:631–40.
37. Salvesi C, Silvi S, Fiorini D, Scortichini S, Sagratini G, Palermo FA, De Leone R, Egidi N, Fatone L, Cifani C, et al. Impact of a probiotic diet on well-being of healthy senior: THE PROBIOSENIOR PROJECT. J Appl Microbiol. 2022;133:2941–53.
38. Kerri L, Glassner BPA, Eamonn MM, Quigley. The Microbiome and inflammatory bowel disease. J Allergy Clin Immunol. 2020;145:16–27.
39. Ma J, Hong Y, Zheng N, Xie G, Lyu Y, Gu Y, et al. Gut microbiota remodeling reverses aging-associated inflammation and dysregulation of systemic bile acid homeostasis in mice sex-specifically. Gut Microbes. 2020;11:1450–74.
40. Biagi E, Franceschi C, Rampelli S, Severgnini M, Ostan R, Turroni S, et al. Gut microbiota and extreme longevity. Curr Biol. 2016;26:1480–5.
41. Takeda T, Asaoka D, Nojiri S, Yanagisawa N, Nishizaki Y, Osada T, et al. Usefulness of *bifidobacterium longum* BB536 in elderly individuals with chronic constipation: a randomized controlled trial. Am J Gastroenterol. 2023;118:561–8.
42. Shi S, Zhang Q, Sang Y, Ge S, Wang Q, Wang R, et al. Probiotic *bifidobacterium longum* BB68S improves cognitive functions in healthy older adults: a randomized, double-blind, placebo-controlled trial. Nutrients. 2022. https://doi.org/10.3390/nu15010051.
43. Cao F, Jin L, Gao Y, Ding Y, Wen H, Qian Z, et al. Artificial-enzymes-armed bifidobacterium longum probiotics for alleviating intestinal inflammation and microbiota dysbiosis. Nat Nanotechnol. 2023;18:617–27.
44. Qi Y, He J, Zhang Y, Ge Q, Wang Q, Chen L, Xu J, Wang L, Chen X, Jia D, et al. Heat-inactivated bifidobacterium adolescentis ameliorates colon senescence through Paneth-like-cell-mediated stem cell activation. Nat Commun. 2023;14:6121.
45. Yang X, Yu D, Xue L, Li H, Du J. Probiotics modulate the microbiota-gut-brain axis and improve memory deficits in aged SAMP8 mice. Acta Pharm Sin B. 2020;10:475–87.
46. Matsuzaki T. Immunomodulation by treatment with Lactobacillus casei strain Shirota. Int J Food Microbiol. 1998;41:133–40.
47. Shimizu K, Yamada T, Ogura H, Mohri T, Kiguchi T, Fujimi S, Asahara T, Yamada T, Ojima M, Ikeda M, Shimazu T. Synbiotics modulate gut microbiota and reduce enteritis and ventilator-associated pneumonia in patients with sepsis: a randomized controlled trial. Crit Care. 2018;22:239.
48. Li H, Fan L, Yang S, Tan P, Lei W, Yang H, Gao Z. Lactobacillus acidophilus 6074 fermented jujube juice ameliorated DSS-induced colitis via repairing intestinal barrier, modulating inflammatory factors, and gut microbiota. Mol Nutr Food Res. 2025;69:e202400568.
49. Gomes JMG, Costa JA, Alfenas RCG. Metabolic endotoxemia and diabetes mellitus: A systematic review. Metabolism. 2017;68:133–44.
50. Rodes L, Khan A, Paul A, Coussa-Charley M, Marinescu D, Tomaro-Duchesneau C, et al. Effect of probiotics *Lactobacillus* and *Bifidobacterium* on gut-derived lipopolysaccharides and inflammatory cytokines: an in vitro study using a human colonic microbiota model. J Microbiol Biotechnol. 2013;23:518–26.
51. Liu Y, Zhang H, Xie A, Sun J, Yang H, Li J, Li Y, Chen F, Mei Y, Liang Y. Lactobacillus rhamnosus and L. plantarum combination treatment ameliorated colitis symptoms in a mouse model by altering intestinal microbial composition and suppressing inflammatory response. Mol Nutr Food Res. 2023;67:e2200340.
52. Ma X, Shin YJ, Jang HM, Joo MK, Yoo JW, Kim DH. Author correction: *Lactobacillus rhamnosus* and *bifidobacterium longum* alleviate colitis and cognitive impairment in mice by regulating IFN-γ to IL-10 and TNF-α to IL-10 expression ratios. Sci Rep. 2023;13:735.
53. DeJong EN, Surette MG, Bowdish DME. The gut microbiota and unhealthy aging: disentangling cause from consequence. Cell Host Microbe. 2020;28:180–9.
54. Van den Abbeele P, Belzer C, Goossens M, Kleerebezem M, De Vos WM, Thas O, et al. Butyrate-producing *clostridium* cluster XIVa species specifically colonize mucins in an in vitro gut model. ISME J. 2013;7:949–61.
55. Tang J, Wei Y, Pi C, Zheng W, Zuo Y, Shi P, Chen J, Xiong L, Chen T, Liu H, et al. The therapeutic value of bifidobacteria in cardiovascular disease. NPJ Biofilms Microbiomes. 2023;9:82.
56. Gurung M, Li Z, You H, Rodrigues R, Jump DB, Morgun A, et al. Role of gut microbiota in type 2 diabetes pathophysiology. EBioMedicine. 2020;51:102590.

Publisher's Note