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Review article

Impact of probiotics on cognition and constipation in the elderly: A meta-analysis

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ABSTRACT

Cognitive decline and constipation are common complications in the elderly. Probiotics are potential therapeutic agents to ameliorate cognitive impairment through gut-brain axis. Several clinical studies have investigated the beneficial effects of probiotics on cognitive impairment and constipation in elderly. However, a quantitative meta-analysis is required to evaluate the efficacy of probiotics on cognitive function and constipation. Thirteen clinical studies were included in this meta-analysis. We examined the risk of bias assessment and heterogeneity of eight studies for cognition and five studies for constipation, followed by group and subgroup meta-analyses using a random-effects model to evaluate the potential of probiotic supplements on cognition function and constipation in aged people. The results of the pooled meta-analysis revealed that probiotic supplementation did not improve the cognitive rating scale assessment for all studies (estimate = 0.13; 95%CI [-0.18, 0.43]; $p = 0.41$; $I^2 = 83.51\%$). However, subgroup analysis of single strain supplementation showed improved cognitive function in elderly people (estimate = 0.35; 95%CI [0.02, 0.69]; $p = 0.039$; $I^2 = 19.19\%$) compared to multiple strains. Probiotics also enhanced defecation frequency in constipated patients (estimate = 0.27; 95%CI [0.05, 0.5]; $p = 0.019$; $I^2 = 67.37\%$). Furthermore, probiotic supplementation resulted in higher fecal *Lactobacillus* counts than placebo (estimate = 0.37; 95%CI [0.05, 0.69]; $p = 0.026$; $I^2 = 21.3\%$). Subgroup analysis indicated that a probiotic intervention period of $\geq$4 weeks was more effective (estimate = 0.35; 95%CI [0.01, 0.68]; $p = 0.044$; $I^2 = 0\%$) in reducing constipation symptoms than a short intervention duration. Based on these results, probiotic supplementation could be a potential intervention to reduce constipation symptoms in the elderly population. The heterogeneity between studies is high, and limited trials are available to evaluate the cognitive function of aged individuals using probiotics. Therefore, further studies are required to determine the effect of probiotics on cognition.

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1. Introduction

Cognitive decline and constipation are more prevalent in older adults, affecting their quality of life. In the United States, 22% of people above 71 years of age have cognitive impairment without dementia and 12% of those with progress to dementia [1]. The World Health Organization (WHO) estimated that more than 50 million people were living with dementia worldwide, and this was expected to triple by 2050 [2]. The incidence of constipation was higher (33%) in individuals aged >60 years than in adults (16%) [3]. The prevalence of constipation has increased (55%–67%) in elderly people living in institutional geriatric-care settings [4,5]. Commonly, laxatives are prescribed to treat constipation; however, they are associated with various adverse effects and are an economic burden on individuals [6]. In North America, spending on laxatives reaches approximately $500 million annually [7]. Hence, researchers have focused on non-pharmacological management strategies to improve quality of life as well as lower healthcare costs for older people.

Constipation is a general term that describes when a person experience difficulties in defecation and less frequency of bowel movements. Health providers define constipation as defecation frequency of less than 3 times per week [8]. The incidence of constipation increases with increasing age and more frequent in elder people. Probiotics are live microorganisms and have been recognized as safe and helpful bacteria for their beneficial effects to the host, such as modulation of gut microbial composition, intestinal immune function, and epithelial barrier function [9–11]. Probiotic therapy is an effective alternative approach to treat several gastrointestinal disorders and increasingly being used in elderly care. Probiotics also able to improve cognitive functions through the regulation of the gut-brain axis [12]. The gut-brain axis is a bidirectional communication between the gut and the brain, which integrates the intestinal function with cognitive centers of the brain [13,14]. Gut microbiota play a major role in cognitive and neuronal function via gut-brain axis. The imbalance of gut microbial composition may associated with many neurodevelopment and cognitive dysfunction [15,16]. Probiotics are effective in modulating gut microbiota-gut-brain axis [12,17,18]. *Lactobacillus plantarum* DP189 intervention prevented the cognitive dysfunction and development of Alzheimer's disease via regulating microbiota-gut-brain axis [19]. Several studies have investigated the beneficial effects of probiotics on constipation and cognitive impairment [20–23]. These previous studies indicated that probiotics might be a nonpharmacological alternative intervention strategy to reduce age-related cognitive decline and constipation. However, quantitative form of literature review regarding probiotic benefits on cognition and constipation in elderly people is limited. Therefore, the aim of the current study was to provide an updated systematic and meta-analysis of clinical studies since the year of 2000 in the elderly people.

2. Methods

2.1. Literature search strategy

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) guidelines [24]. Studies were identified through multiple electronic databases and reference lists of relevant publications, which were screened manually to identify additional studies. Electronic databases, such as Web of Science, EMBASE, and PubMed, were used through different search terms (Supplementary File S1). The following advanced search filters were used in all databases: time filter (studies from 2000 to 2022), article type (clinical trial, randomized controlled trial), species (humans), language (English only), and age filter (middle aged (45–64 years), aged 65+ years, aged 80+ years). The corresponding authors of the articles were not contacted

Table 1
Inclusion and exclusion criteria to select studies for meta-analysis.

		Inclusion criteria	Exclusion criteria
Cognition	Study type	Human studies with randomized controlled trials (RCTs)	Animal studies Single case reports, studies without control/placebo
	Study period	Published 2000–2022 Published in English	<2000 Non-English publications
	Population	Total population ≥20 in each trial Elder people (mean age ≥60 y)	<20 Infants, children, adults under 60 y
	Outcomes	Outcomes reported using at least one cognitive rating scale among Mini-Mental State Examination (MMSE), Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), Digit Symbol Test (DST), Block Design Test (BDT), Test Your Memory (TYM), and Japanese version of the Montreal Cognitive Assessment (JMCIS)	Other outcomes than mentioned
Constipation	Study type	Human studies with randomized controlled trials	Animal studies Single case reports, studies without control/placebo
	Study period	Published 2000–2022 Published in English	<2000 Non-English
	Population	Total population ≥20 in each trial Elder people (mean age ≥60 y)	<20 Infants, children, adults under 60 y
	Outcomes	Outcomes related to constipation and fecal microflora after intervention	N/A

Abbreviation: N/A, not applicable.

to provide missing data and additional data. Grey literature was not searched and the review articles were excluded.

2.2. Study selection and data extraction

All identified records were screened, and duplications were removed. Studies for meta-analysis were selected based on inclusion and exclusion criteria that strictly met the population, intervention, comparison, outcome, and study (PICOS) strategy (Table 1). The titles and abstracts of the remaining records were screened, and ineligible studies were excluded. The full texts of the remaining studies were accessed and screened for the final selection. Two independent reviewers examined the abstracts and titles of all citations using defined criteria. The PRISMA flow diagram was generated using 'metagear' package in R statistical program version 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria). The following parameters were extracted from the final included studies: basic information of the study (first author, publication year, study conducted country, and study type), participant characteristics (total sample number, sex, age range, mean age, and health status of participants), intervention details (supplemented strain type, duration of intervention, and form of supplementation), outcome assessments (type of cognition rating scale for cognition, defecation frequency, gut transit time, constipation rating scale, and fecal microbial counts for constipation), and outcome data extraction for meta-analysis (sample number for placebo and treatment groups, mean values of placebo and treatment groups at baseline and post-intervention period, standard deviation (SD) values for placebo and treatment groups, and other available data).

2.3. Studies quality check

The revised Cochrane risk-of-bias tool for randomized trials (RoB 2) was used to check the quality of the included studies [25]. The tool has five bias domains, with several questions in each domain to assess the risk of bias (Supplementary File S2). We (Neeraja Recharla and Pradeep Puligundla) gave each study a rating as "high," "low" or "some concerns" based on judging the category according to questions in each domain. And disagreements were resolved with another author (Jihee Choi). Summary plots for risk-of-bias assessment were generated using 'robvis' package in R program (R Foundation for Statistical Computing, Vienna, Austria).

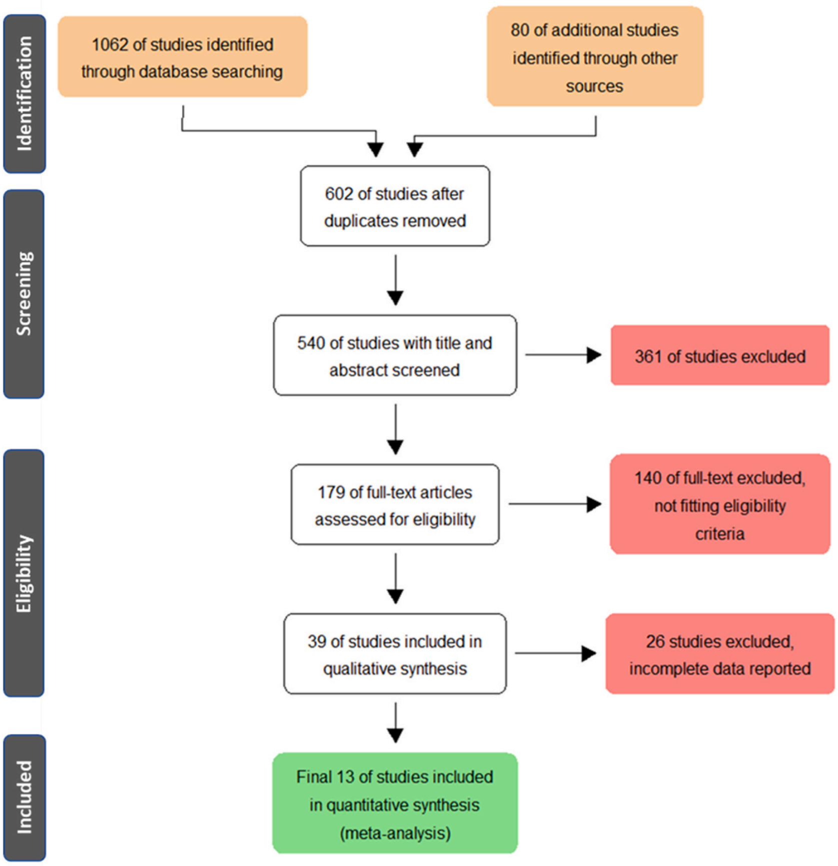

Fig. 1. PRISMA flow diagram of the literature search.

Table 2
Characteristics of final included studies for constipation.

Study	Author	Region	Participants	Strains	Strain name	Method of probiotics delivery	Age range (mean ± SD)	Place	Diagnosis	Other diagnosis
1	Ouwehand et al. [29]	Finland	28	Single	*L. reuteri* ING1	Juice	70–96	Nursing home	Difficulties in defecation	NA
2	Aoki et al. [30]	Japan	118	Single	*Lactobacillus casei* strain Shirota	Fermented milk	64 ± 9	NA	Abnormal defecation	Gastrectomized subjects
3	Kondo et al. [21]	Japan	66	Single	*Bifidobacterium longum* BB536 (2.5 × 10^{10} cfu)	powder in drinking water	67-101 (85.8 ± 7.3)	Hospital	NA	Enteral tube feeding
4	Yeun and Lee [31]	Korea	40	Multiple	*Bifidobacterium bifidum, B. lactis, B. longum, Lactobacillus acidophilus, L. rhamnosus*, and *Streptococcus thermophilus*	Lyophilized powder in capsule	82.45 ± 9.36	Nursing home	Functional constipation	NA
5	Kondo et al. [21]	Japan	102	Single	*Bifidobacterium longum* BB536 (2.5 × 10^{10} and 5 × 10^{10} cfu)	Powder in drinking water	65-102 (85.8 ± 7.3)	Hospital	NA	Enteral tube feeding
6	Ibrahim et al. [32]	Malaysia	48	Multiple	*Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus lactis, Bifidobacterium infantis, and Bifidobacterium longum*	Powder in drinking water	69 ± 7.83	Outpatient clinic	Functional constipation	Parkinson's disease

Table 3
Characteristics of final included studies for cognition.

Study	Author	Region	Age	Strains	Strain name	Method of probiotics delivery	Participants	Diagnosis	Duration (wk)	Assessment
1	Kobayashi et al. [33]	Japan	50–80	Single	*Bifidobacterium breve* A1	Powder	121	Memory complaints	12	RBANS, MMSE
2	Ohsawa et al. [34]	Japan	50–70	Single	*Lactobacillus helveticus*	Liquid	60	Healthy-self-identified forgetfulness	8	RBANS
3	Akbari et al. [22]	Iran	70–85	Multiple	*Lactobacillus acidophilus, Lactobacillus casei, Bifidobacterium bifidum, and Lactobacillus fermentum*	Liquid	60	AD	12	MMSE
4	Xiao et al. [23]	Japan	50–79	Single	*Bifidobacterium breve*	Powder	79	Mild cognitive impairment	16	RBANS, JMCIS
5	Agahi et al. [35]	Iran	65–90	Multiple	*Lactobacillus* and *Bifidobacterium*	Capsule	48	AD	12	TYM
6	Bajaj et al. [36]	USA	18–65	Single	*Lactobacillus* GG	NA	37	Cirrhosis	8	BDT, DST
7	Tamtaji et al. [37]	Iran	55–100	Multiple	*Lactobacillus acidophilus, Bifidobacterium bifidum, and Bifidobacterium longum*	NA	90	AD	12	MMSE
8	Inoue et al. [38]	Japan	66–78	Multiple	*B. longum* BB536, *B. infantis* M − 63, *B. breve* M − 16V and *B. breve* B-3	NA	38	Healthy	12	MoCA-J

2.4. Data synthesis and meta-analysis

The primary group analysis was performed by calculating standard mean differences (SMDs) with 95% confidence intervals (CIs) based on defecation frequency for constipation and cognitive rating scale for cognition using 'metafor' package in R statistical program (R Foundation for Statistical Computing, Vienna, Austria). We used a random effects model and performed subgroup analysis by SMDs of mean change from baseline to post-intervention in the control and treatment groups. Subgroup analysis to assess the effect of probiotics on constipation was performed for the frequency of defecation (based on the duration of intervention and strains) and fecal bacterial counts (based on the type of bacteria and strains). The effects of probiotics on cognition were measured by subgroup analysis of cognition rating scales (MMSE, RBANS, and others) and types of strains (single and multiple strains). Statistical heterogeneity between the studies was tested using the I^2 statistic. An I^2 value ranging between 0% and 100% measures the degree of inconsistency of the studies in a meta-analysis. I^2 values of 25%, 50%, and 75% indicate low, moderate, and high heterogeneity, respectively [26]. *The P*-value for the heterogeneity test was $\geq$0.1 considered as no heterogeneity and $<$0.1 considered as heterogeneity. Baujat plots were produced to identify heterogeneity-contributing studies [27]. Forest plots were generated using 'metafor' package to illustrate the SMDs and CIs for the individual study outcome. Publication bias was quantitatively measured using Egger's test, and funnel plots were generated to visualize publication bias for both constipation and cognition studies [28]. Meta-analysis data provided as effect size estimates with 95% CIs and *p* values $\leq$ 0.05 were considered statistically significant for the treatment effect.

3. Results

3.1. Study selection and characteristics

A total of 1062 studies were identified for both constipation and cognition function through a database search, and 80 additional studies were identified through the manual search of reference lists of reviews and other relevant publications. Among these, 602 duplicate studies were removed, and 540 remaining studies were screened by the title and abstract. Of these, 361 studies were

Fig. 2. Summary plots for risk-of-bias assessment for constipation studies.

excluded after title and abstract screening and 179 full-text articles were assessed for eligibility. Among the full-text articles, 140 were excluded because they did not fit the eligibility criteria, and 39 studies were included for qualitative synthesis, of which 26 were excluded due to incomplete data. Thirteen studies (five for constipation and eight for cognition function) were included in the final meta-analysis (Fig. 1).

The characteristics of the included studies on constipation are presented in Table 2. All five studies were published between 2000 and 2020. All the trials were performed in Asian and European countries. Among the five studies, two were performed and published in one study article using *Bifidobacterium longum* BB536 probiotic strain with two different doses [21]. A total of six trials were conducted: four trials used single strain supplementation, and the other two trials used multiple strains. Most of these trials were conducted in hospitals or nursing homes. The participants were older than 60 years in all trials. Among the five studies, one study participant was gastrectomized and another study participant was diagnosed with Parkinson's disease. Table 3 shows the characteristics of the studies on cognition function. As shown in this table, eight studies were performed in different regions of the world and all studies were published between 2010 and 2020. Four of the eight studies used single strain supplementation, and the remaining four studies used multiple strain supplementation in capsule or liquid form. The intervention duration for all these studies was ≥8 weeks. Three of the eight studies were diagnosed with Alzheimer's disease (AD), one study was diagnosed with cirrhosis, and the remaining study participants complained of memory issues. The cognitive rating scales used in the included studies were the MMSE (3 studies), RBANS (3 studies), JMCIS (1 study), MoCA-J (1 study), TYM, BDT, and DST screening tests.

3.2. Results of the risk-of-bias assessment

The risk-of-bias assessment results for constipation are summarized in Fig. 2. Among the five included studies, one did not provide

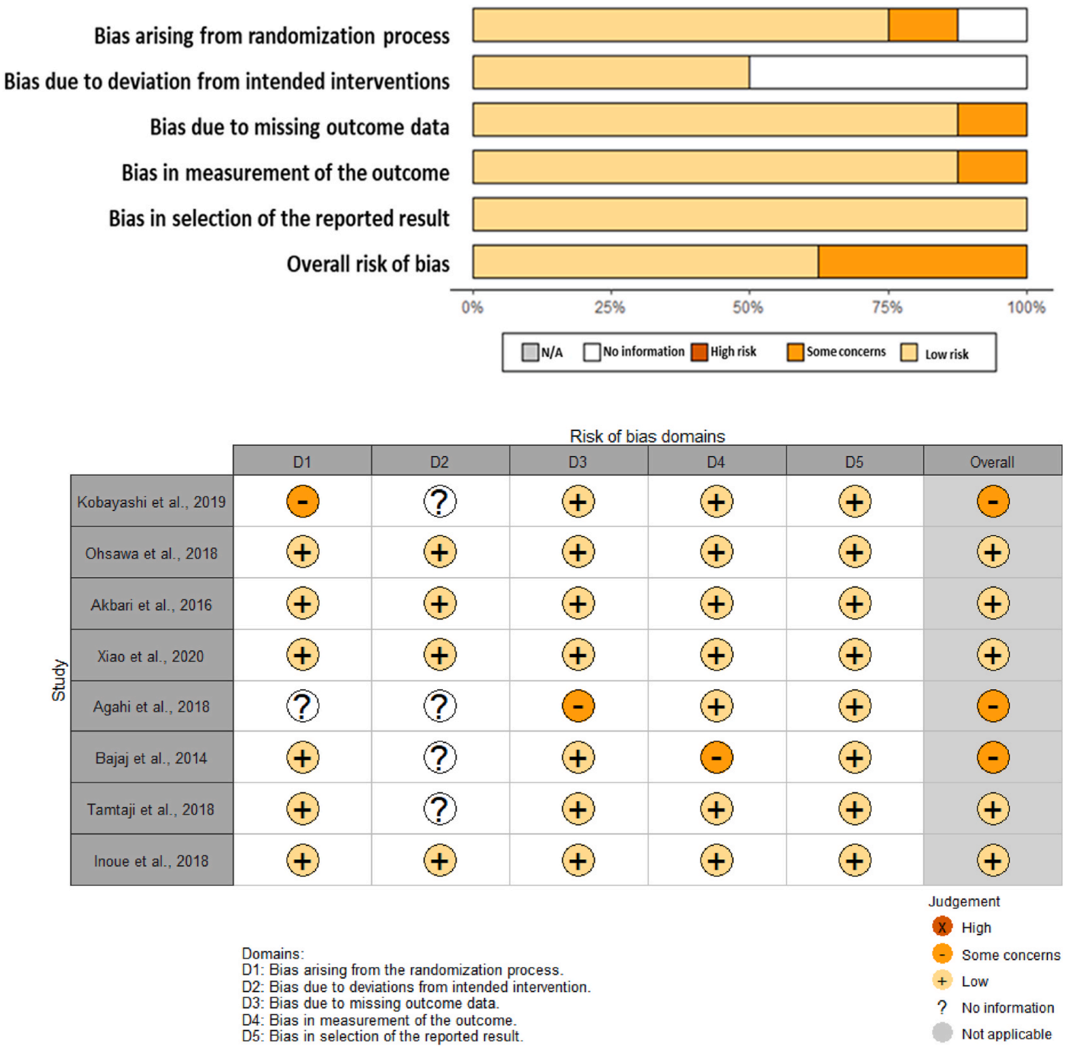

Fig. 3. Summary plots for risk-of-bias assessment for cognition studies.

information about the randomization process and intervention concealment [29]. Another study also failed to provide information on intervention concealment to participants and people delivering the intervention [31]. There was no risk of missing outcome data, measurement of the outcome, or selection of the reported results for all included studies. Overall, the included studies had a low risk of bias except for one study which found some concerns.

A summary of the risk-of-bias assessment for cognitive studies is shown in Fig. 3. One study had concerns regarding the randomization process due to significant baseline differences between the control and intervention groups [33]. Another study failed to provide information regarding allocation sequence concealment [35]. Four studies had no information on intervention concealment for participants or caregivers [33,35–37]. Missing data or concerns in measuring outcome data were found in two studies [35,36]. Overall, three studies had concerns [33,35,36]. However, no high risk-of-bias was observed in any of the included studies.

3.3. *Meta-analysis results*

3.3.1. *Effect of probiotics on constipation*

Five publications on constipation were included in this quantitative meta-analysis. In each publication, the researchers reported the results of probiotic interventions for constipation in different intervention periods and various assessment methods (For more information at https://data.mendeley.com/datasets/j33zk8wkd6/1). A meta-analysis was performed for all comparisons between the probiotics and control groups (Fig. 4). The results of the meta-analysis showed a significant improvement in constipation after probiotic supplementation (estimate = 0.27; 95%CI [0.05, 0.5]; $p = 0.019$). However, moderate heterogeneity was observed ($I^2 = 67.37\%$; $p = < .0001$). The effect size and standard error for each study are shown in a funnel plot (Fig. 5). As shown, most studies showed a positive effect size; however, overall, the dataset appears to have an asymmetrical distribution due to the high standard error and high variance of a few studies, which indicates some publication bias. Funnel plot asymmetry was quantitatively confirmed by Egger's regression test, using standard error ($p = 0.0003$) and sampling variance ($p = 0.0004$) as predictors (Supplementary Fig. S1). The trim-and-fill method was used to estimate the missing data (Supplementary Fig. S2).

Subgroup analyses were performed based on intervention duration and type of strains for defecation frequency assessment and fecal bacterial counts using a random-effects model meta-analysis. The results of the heterogeneity and meta-analysis of subgroup analyses are summarized in Table 4. As shown in the table, there was no heterogeneity between the studies for all subgroup analyses. Probiotic intervention did not influence the defecation frequency in constipated participants during the 3-week intervention period (estimate = 0.06; 95%CI [−0.38, 0.5]; $p = 0.787$), but the defecation frequency significantly improved with increased intervention duration from 4 to 8 weeks (estimate = 0.35; 95%CI [0.01, 0.68]; $p = 0.044$) and above 8 weeks (estimate = 0.46; 95%CI [0.08, 0.83]; $p = 0.016$). Based on the number of probiotic strains, single-strain supplementation (estimate = 0.49; 95%CI [0.11, 0.88]; $p = 0.013$) was more effective in reducing constipation symptoms than multiple-strain supplementation (estimate = 0.48; 95%CI [−0.12, 1.08]; $p = 0.117$). Fecal bacterial counts were higher in single-strain-supplemented participants (estimate = 0.21; 95%CI [0.01, 0.4]; $p = 0.035$) and *Lactobacillus* counts were significantly increased in probiotic-supplemented participants (estimate = 0.37; 95%CI [0.05, 0.69]; $p = 0.026$), while *Bifidobacterium* counts did not change significantly (estimate = 0.12; 95%CI [−0.10, 0.35]; $p = 0.286$).

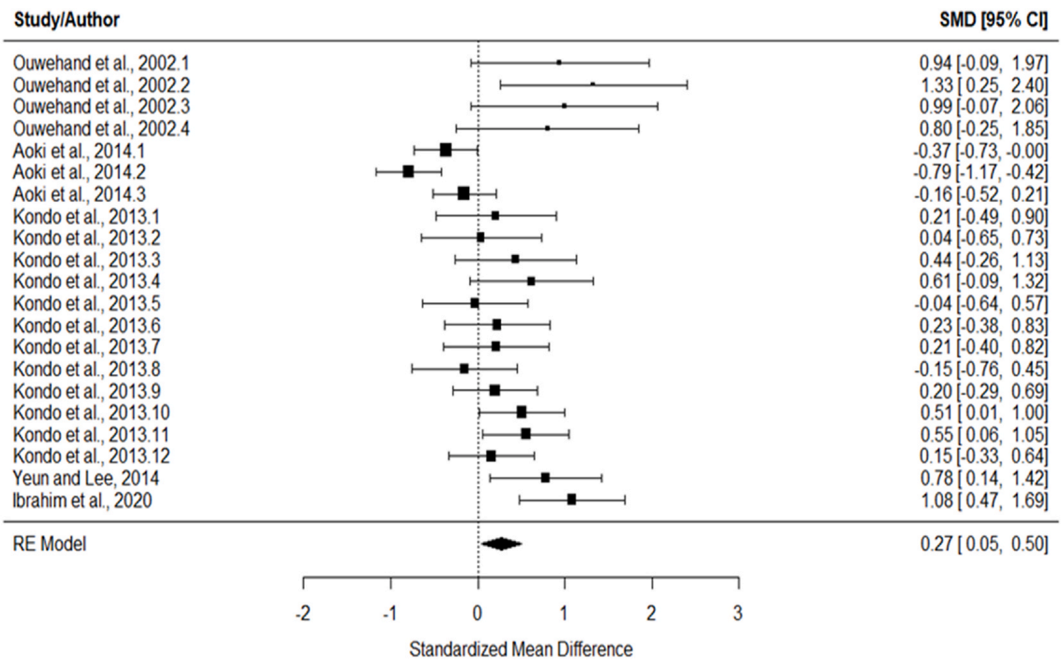

Fig. 4. Forest plot of random effect model meta-analysis for overall trials in constipated older individuals.

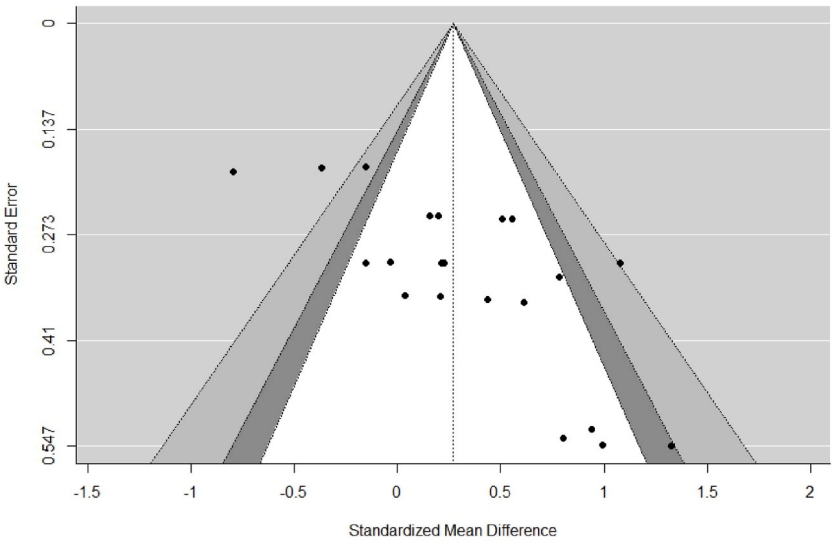

Fig. 5. Funnel plot illustrating publication bias in constipation studies. White, dark grey, and light grey represent 90%, 95%, and 99% confidence intervals, respectively.

Table 4
Summary of subgroup meta-analyses on constipation.

Subgroups	Participants	Meta-analysis estimate (95% CI)	Heterogeneity		Study *p*-value
			I^2 (%)	*p*-value	
1. Frequency of defecation					
1.1. Based on duration (weeks)					
1.1.1. ≤ 3	158	0.06 (−0.38, 0.5)	0	0.341	0.787
1.1.2.4–8	362	0.35 (0.01, 0.68)	0	0.974	0.044
1.1.3. ≥9	280	0.46 (0.08, 0.83)	0	0.517	0.016
1.2. Based on strains					
1.2.1. Single	243	0.49 (0.11, 0.88)	0	0.477	0.013
1.2.2. Multiple	120	0.48 (−0.12, 1.08)	0	0.963	0.117
2. Fecal bacteria counts					
2.1. Based on type of bacteria					
2.1.1. *Lactobacillus*	394	0.37 (0.05, 0.69)	21.3	0.346	0.026
2.1.2. *Bifidobacterium*	608	0.12 (−0.10, 0.35)	0	0.995	0.286
2.2. Based on strains					
2.2.1. Single	842	0.21 (0.01, 0.4)	0	0.547	0.035
2.2.2. Multiple	160	0.28 (−0.16, 0.73)	0	0.997	0.211

3.3.2. Effect of probiotics on cognition

Meta-analysis was performed for eight publications with 17 comparisons using a random-effects model for cognition assessment. The forest and funnel plots are shown in Figs. 6 and 7, respectively. The SMD of all cognition rating scales was not significantly influenced by probiotic supplementation (estimate = 0.13; 95%CI [−0.18, 0.43]; $p = 0.41$), and the included studies showed high heterogeneity ($I^2 = 83.51\%$; $p = < .0001$). Akbari et al. [22] study lied in the upper quadrant of baujat scatter plot which indicating this study has highest contribution to overall heterogeneity among all studies (Fig. 8). The effect size of the dataset was distributed symmetrically around the summary effect in the funnel plot, and there was no publication bias associated with the small sample size. Egger's regression test was conducted using standard error ($p = 0.494$) and sampling variance as predictors ($p = 0.864$), and the regression lines were illustrated in a funnel plot (Supplementary Fig. S3). Sub-group analyses for the type of cognitive rating scale and strain numbers are summarized in Table 5. The results of the meta-analysis indicated that probiotic supplementation did not improve the MMSE (estimate = 0.62; 95%CI [−0.49, 1.74]; $p = 0.274$), RBANS (estimate = 0.35; 95%CI [−0.16, 0.86]; $p = 0.184$), or other (estimate = 0.23; 95%CI [−0.16, 0.62]; $p = 0.24$) scores. However, single-strain supplementation (estimate = 0.35; 95%CI [0.02, 0.69]; $p = 0.039$) showed more significant changes in cognition than multiple-strain supplementation (estimate = 0.83; 95%CI [−0.07, 1.72]; $p = 0.07$).

4. Discussion

Worldwide, constipation is a common affliction. The pathophysiology of constipation is complex and may result from abnormal

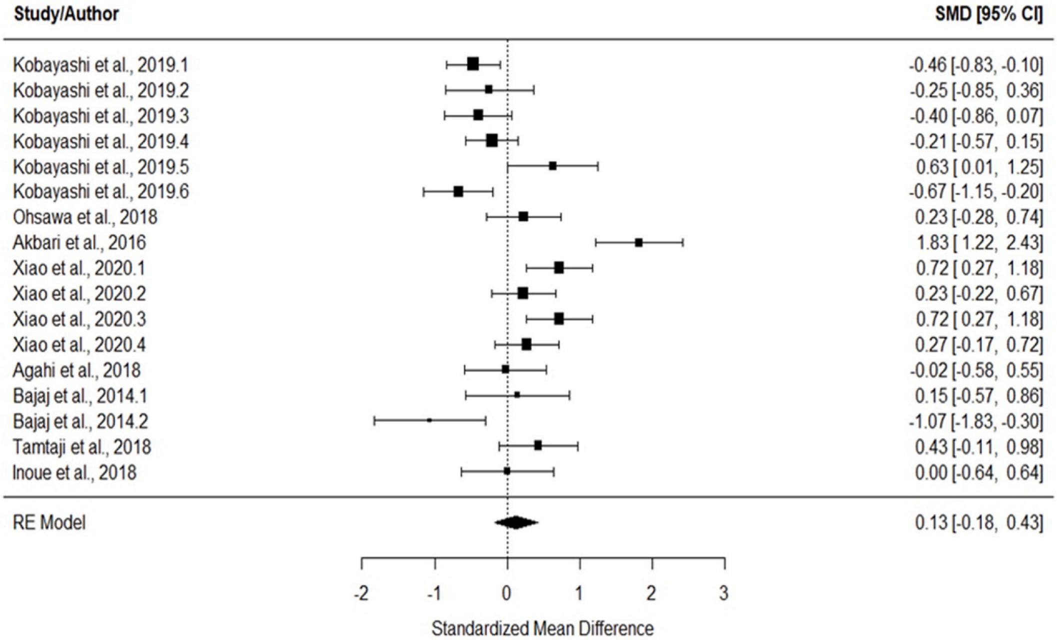

Fig. 6. Forest plot of random effect model meta-analysis for overall trials on cognition.

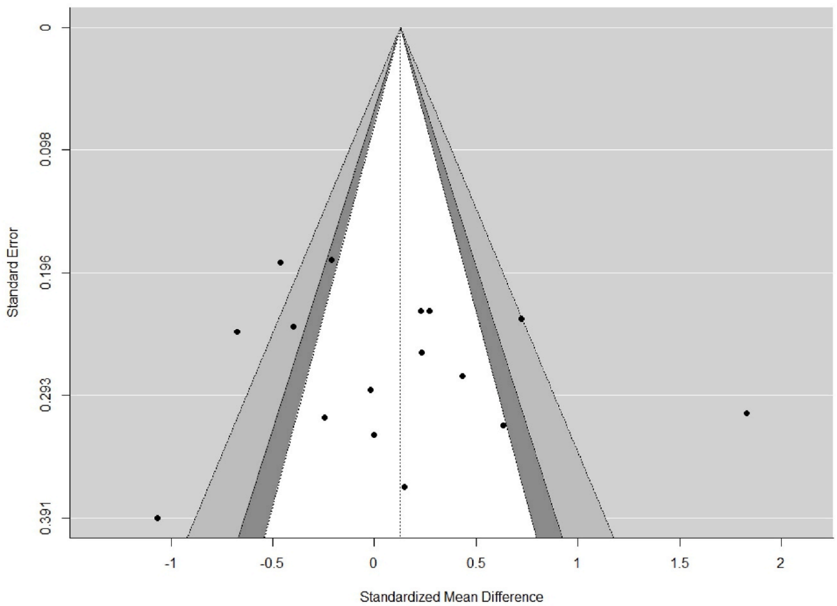

Fig. 7. Funnel plot for the assessment of publication bias. White, dark grey, and light grey represent 90%, 95%, and 99% confidence intervals, respectively.

intestinal motility caused by impaired colonic motor function and impaired defecation due to pelvic floor dysfunction or anorectal disorders [39]. These are associated with several factors, including poor dietary habits, dehydration, lack of physical activity, emotional stress, and the side effects of prolonged medication. Other causes of constipation include age-related changes in the gut microbiota that lead to dysbiosis, which influences immune system function [40]. Accumulating evidence suggests that modulation of the gut microbiota with beneficial microbial strains may ameliorate constipation symptoms. Furthermore, modulation of the intestinal microbiota may improve colonic motor function through the microbiota-gut-brain axis. Long-term administration of probiotics can reduce the colon transit time and promote intestinal peristalsis by increasing short-chain fatty acid (SCFAs) levels and regulating the

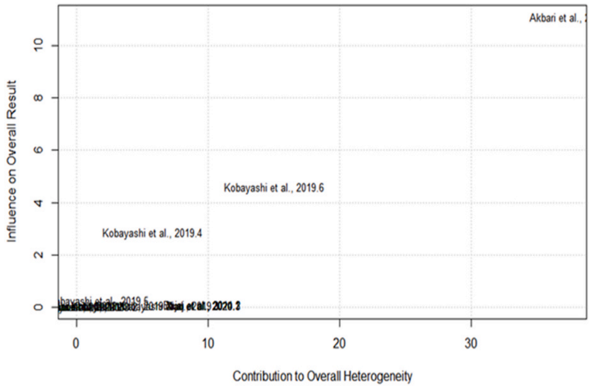

Fig. 8. Baujat plot visualizing heterogeneity contributed studies.

Table 5
Summary of subgroup meta-analyses on cognition.

Subgroups	Participants	Trials	Meta-analysis estimate (95% CI)	Heterogeneity		Study *p*-value
				I^2 (%)	*p*-value	
1. Based on cognitive rating scale						
1.1. MMSE	230	3	0.62 (−0.49, 1.74)	85.01	0.001	0.274
1.2. RBANS	256	3	0.35 (−0.16, 0.86)	45.02	0.166	0.184
1.3. Others	225	5	0.23 (−0.16, 0.62)	0	0.877	0.24
2. Based on strains						
2.1. Single	439	4	0.35 (0.02, 0.69)	19.19	0.31	0.039
2.2. Multiple	161	4	0.83 (−0.07.1.72)	70.23	0.03	0.07

concentrations of brain-derived neurotropic factor (BDNF) and 5-hydroxytryptamine (5-HT) neurotransmitters [41–43].

Cognitive impairment is also a common condition among older adults. Many factors can cause cognitive deficits, including stress, depression, and chronic metabolic disorders. Previous studies have reported that probiotics improve cognitive function by modulating gut microbiota and neurotransmitters through the microbiome-gut-brain axis [15,44].

Despite the administration of probiotics for the treatment of constipation and cognition, the efficacy of probiotics in improving symptoms needs to be evaluated quantitatively. The aim of this study was to quantitatively evaluate the efficacy of probiotic intervention on constipation and cognition in the elderly. To the best of our knowledge, this is the first meta-analysis to summarize the available RCTs data regarding constipation and probiotics in older people. Some researchers performed meta-analyses in adults and children, but no meta-analysis has investigated the effects of probiotics on constipation in elderly people [45–48].

Although the included studies for cognition function had no high risk of bias, a significant heterogeneity indicating variation in data was found between studies. Hence, the results showed no significant effects. Similarly, previous meta-analyses have also reported high heterogeneity in cognition studies and probiotic outcomes [49,50]. Subgroup meta-analysis for the RBANS cognition rating scale showed moderate heterogeneity, but probiotic supplements not significantly improved cognition function. Similar to these results, a systematic review and meta-analysis also reported that there was no difference in cognitive function between probiotic supplemented and placebo group participants with AD [51]. Our findings suggest that based on cognition rating scale such as RBANS and MMSE probiotics did not influence the cognitive function in elderly people. Similarly, Tahmasbi et al. [52] reported in a meta-analysis that probiotic supplementation did not alter the cognition function in elderly. However, subgroup analysis of single strain supplementation improved cognitive function compared to multiple strains, but there was a lack of uniformity in cognitive testing tools.

The results of this meta-analysis reveal that probiotic supplementation significantly improved the frequency of defecation, specifically with single-strain supplementation and in long-term consumption of probiotics in elderly. The positive effects of probiotics on stool frequency in constipated adults were also reported in a meta-analysis [45]. However, a systematic review reported that probiotic interventions did not influence defecation frequency in children [53]. The composition of the gut microbiota may change in hospitalized or less physically active older adults. Constipation is associated with gut dysbiosis including imbalance or low abundance of beneficial gut microbiota. The abundance of *Firmicutes* and *Proteobacteria* decreased in functionally constipated elderly patients compared to normal individuals, whereas the abundance of the *Bacteroidetes* phylum increased [54]. At the genus level, the abundance of *Lactobacillus* and *Bifidobacterium* was lower in chronically constipated patients, while that of pathogenic bacteria increased [55]. Probiotics may modify the microbial communities in the gut and reduce constipation. The findings of this meta-analysis indicate that the intake of probiotics may increase beneficial bacterial counts in the intestine. Furthermore, supplementation with a single strain, such as *L. reuteri* ING1, *L. casei* Shirota, and *Bifidobacterium longum*, increased fecal *Lactobacillus* counts in constipated participants. The present meta-analysis provides evidence that the duration of probiotic intervention is important in alleviating constipation. The results of this meta-analysis revealed that probiotics need to supplement for a minimum of four weeks and above to relieve constipation. Aoki et al. [30] reported that continuous consumption of *Lactobacillus casei* strain Shirota-fermented milk improved bowel movements than two weeks consumed patients. Single strain supplementation showed significant effects than multiple strain supplementations on defecation frequency in constipated patients. This is consistant with previous review report about the effectiveness of single-strain intervention in various medical conditions [56]. *Lactobacillus reuteri*, *Lactobacillus casei* strain Shirota and *Bifidobacterium longum* starins were used as single strain supplementation in 3 studies among 5 papers used for constipation. A recent randomized controlled trail in elderly nursing home residents reported that supplementation of multispecies liquid probiotic formulation consisting of *Lactobacillus acidophilus* LA3, *Lactobacillus casei* BGP93 and *Bifidobacterium animalis* subsp. *lactis* BLC1 showed significant improvement after prolonged treatment (after the 75th day) for functional constipation [57]. It indicating that long-term intake of multi-strain probiotics also has the potential effect on constipation. However, further clinical trials are needed to confirm this effect in elderly. Fecal *Lactobacillus* counts were significantly improved than other fecal microbial counts in probiotic supplemented groups. Similarly, other studies were also reported increased fecal *Lactobacillus* levels after probiotics administration [58,59].

5. Limitations

Limitations of this meta-analysis for cognition are as follows: 1) high variability shown in assessed methods. 2) Few cognition rating scales such as RBANS and MMSE only used for this analysis to reduce heterogeneity. 3) Even though, this study mainly focused on cognitive impairment, one study participants were diagnosed with cirrhosis which may influence the outcomes the analysis. There were also several limitations for constipation including moderate heterogeneity and publication bias which indicating variations between the estimates of probiotic intervention. Hence, sub-group analysis was performed to reduce heterogeneity and publication bias due intervention duration. Probiotic supplementation showed significant improvement in defecation frequency, however, constipated related other symptoms were not reported in all included studies and therefore meta-analysis did not perform for other variables. One of key limitation for both cognition and constipation studies are the type of strains that used for intervention. Each study used different type of probiotic strains. Some studies used *Lactobacillus* strains and others used *Bifidobacterium* strains. The results can be applicable for only these two types of bacteria and cannot be generalized to other probiotics.

6. Conclusions and future prospects

Despite the limitations, we believe our study has a number of strengths as this meta-analysis used all randomized controlled trails which had low risk-of-bias, sufficient sample size and there are not much meta-analyses reported on probiotic intervention in elderly. This meta-analysis provided quantitative outcomes regarding the impact of probiotics on cognitive function and constipation. Our meta-analysis suggests that long-term intake of probiotics including *Lactobacillus* and *Bifidobacterium* strains could improve constipation symptoms while increasing the beneficial microbiota in the intestine. However, it is difficult to get more studies investigated on same type of probiotic strains and similar condition of all participants involved in all papers for both constipation and cognition. It would be helpful in future studies use same type of single strain supplementation and similar condition of participants for constipation in order to get more reliable data. Further clinical trials using standard methodological approaches are needed to confirm the effectiveness of treatments.

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Author contribution statement

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Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e18306.

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