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Review

Effect of Probiotic Supplementation on Body Fat, Skeletal Muscle Mass, and Body Mass Index in Individuals ≥45 Years Old: A Systematic Review

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Abstract

Background/Aim: Probiotics are living microorganisms that confer health benefits when administered in adequate amounts. Several studies have shown the positive effects on body fat, muscle mass, and body mass index (BMI) in young adults and athletes; however, the results in adults aged ≥45 years are not conclusive.

Materials and Methods: A systematic review was conducted in accordance with the PRISMA guidelines, analyzing studies up to December 10, 2024, from nine databases (PubMed, Scopus, Web of Science, LILACS, SciELO, Springer, Redalyc, Cochrane Library and TESIUNAM). Mean differences (MD) were estimated using RevMan V 5.4.1. software.

Results: Six hundred and sixty-six studies were identified, of which 15 met the eligibility criteria. A statistically significant decrease in fat mass (%) was found in two studies and in fat mass (kg) in another two studies. Likewise, one study reported a statistically significant increase in skeletal muscle mass.

Conclusion: Probiotic supplementation may have a beneficial effect on reducing body fat mass and increasing or preventing skeletal muscle mass loss in adults ≥45 years old; however, further clinical trials are needed to determine the optimal types, doses, and duration of probiotic treatment for best results.

Keywords: Probiotics, muscle mass, body fat, body mass index, aging, review.

Introduction

Human aging is characterized by physiological, biochemical, molecular, and phenotypic changes that manifest in body composition. Among the most important modifications is a decrease in skeletal muscle mass (SMM) between 3 and 8% per decade from the age of 30 (1). Likewise, after the age of 60, there is an annual decrease of 0.5% in weight, a loss of

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one cm of height for each decade of life, and an increase in fat mass, which favors the appearance of sarcopenic obesity (2), which is characterized by a progressive and generalized decrease in SMM due to aging, reduction in physical activity, an inadequate nutritional contribution or inflammation related to aging (3). Anthropometric and body composition measurements, such as weight, body mass index (BMI), waist circumference, waist/hip index, as well as the percentage of adipose tissue and fat-free mass, including SMM, are fundamental clinical indicators for determining health status (4, 5).

One of the emerging issues in healthy aging is the role of microbiota. The dysbiosis has been recognized as a hallmark of aging (5), since it has been observed that the changes in the intestinal bacterial microsystem are related to the presence and lack of control of various non-communicable chronic diseases (NCDs), including type 2 diabetes mellitus, obesity, Parkinson's disease, and sarcopenia (6, 7). Microbiota changes with age, and it is observed that a healthy microbiota prevents frailty and increases longevity (8). For this reason, nutritional supplementation with probiotics has been proposed as a strategy to prevent or defer sarcopenia, fragility, and other geriatric syndromes (9, 10).

Probiotics are living microorganisms that, when administered in adequate quantities, confer a benefit to the health of the host by improving the function and composition of the intestinal barrier, the production of mucus and short-chain fatty acids, the regulation of the immune system, and the modulation of anti-inflammatory functions and metabolic balance (11). Probiotics can promote anabolism through greater absorption of amino acids and the negative regulation of skeletal muscle catabolism by competing with pathogenic intestinal bacteria involved in the stimulation of pro-inflammatory pathways through the systemic increase in the levels of interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), so a positive effect has been reported on the decrease of body fat, muscle mass, and strength (12).

Although there is no consensus regarding the age of onset of human aging, our research group has established a cut-off point of the age of onset of human aging at 45 years (fifth decade of life) since, at this stage of life, evident physiological and bodily changes are presented, which mark the beginning of the human aging process, linked to the hallmarks of aging including oxidative stress (OxS), inflammaging and dysbiosis (13-15). For this reason, we assumed this age cut-off point for this study. However, the results in people aged ≥45 years are inconsistent since the positive effect of probiotic consumption on muscle mass and strength has been reported in young adults (13, 16). In this framework, this systematic review aims to present a synthesis of knowledge regarding whether supplementation with probiotics affects body fat, skeletal muscle mass, and BMI in adults aged ≥45 years.

Materials and Methods

A systematic review was carried out according to the methodology established by Preferred Reporting Items Systemic Reviews and Meta-analysis (PRISMA). The protocol was registered prospectively in INPLASY (17), which specifies the components of the acronym PICO (Population, intervention, comparator, outcomes), the scientific article platforms consulted, the inclusion and exclusion criteria, and the search strategy carried out independently by two reviewers (J.G-N & V.M.M-N) until December 10, 2024.

Outcomes. The outcomes were fat mass, skeletal muscle mass, and BMI.

Data collection. All selected studies were analyzed considering the following data: (i) authors, (ii) year of publication, (iii) study design, (iv) study population (age, state of health, and/or metabolic condition), (v) sample size, (vi) pre-treatment results with probiotics, (vii) post-treatment results with probiotics, (viii) type and doses of probiotics (colony-forming units, CFU) and (ix) duration of the intervention.

Data were extracted from the means ($\bar{X}$) and standard deviations (SD) of the selected articles, and the study group estimated the pre- and post-treatment mean differences

(MD) according to the formulas proposed in the Cochrane Handbook for Systematic Reviews of Interventions (18). In addition, the Cochrane Collaboration's RoB2 risk of bias assessment tool was used to determine the methodological quality of the studies (19).

Results

A total of 660 articles were identified from the search in the following databases: PubMed (n=35); Scopus (n=74); Web Of Science (n=67); LILACS (n=2); SciELO; (n=6); Springer (n=364); Redalyc (n=8); Cochrane (n=104); TESISUNAM (n=0) and from other sources (n=10). Subsequently, duplicates were eliminated, and after the review of titles and abstracts, forty-six studies that met the inclusion criteria were selected to be reviewed in full text, of which thirty-one were eliminated for various reasons. Finally, fifteen met the eligibility criteria for systematic review (Figure 1 and Table I).

Regarding assessment of the risk of bias, the domain observed most frequently was "blinding of outcome assessment". The studies of Hric (21), Karim (23, 24), and Nilsson (34) showed the most methodological limitations (Figure 2).

Of the fifteen randomized clinical trials, thirteen were double-blind placebo (19, 21-28, 30-33) and two single-blind randomized clinical trials (21, 29). The number of participants included in the selected studies was from a minimum of 22 (21) to a maximum of 127 (30). Likewise, in eight studies, females and males were included (20, 22, 25-27, 29, 30, 32), in four only females (21, 28, 31, 33) and in three only males (23, 24, 30). The total sample size of the experimental group of the systematic review was 523, while the control group was 489, between 40 and 76 years old. The duration of the interventions was 56 weeks in one study (28), 16 weeks in two studies (23, 30), 12 weeks in eight studies (20, 22, 24-26, 31-33), 10 weeks in two studies (27, 29), four and three weeks in one study (21, 31) (Table I).

The analysis of this systematic review shows high variability regarding the characteristics of the population, as well as the effect of time, type, and dose of probiotic supplementation on some parameters of body composition, and a high variability of population characteristics (Table I).

The intervention was carried out in a healthy population in three studies (20-22). However, in six clinical trials, the treatment was administered to an overweight or obese population (25, 26, 31-34), of which one had hypertension in addition to obesity (31). Likewise, two studies were carried out in a population with metabolic syndrome (27, 29), one in patients with chronic obstructive pulmonary disease (23), one in people with chronic heart failure (24), one in subjects with low bone mineral density (34), and one in people with sarcopenia (30).

In the studies in which the effect on fat mass was reported, ten presented the results as fat mass percentage (%) (20-24, 26, 29, 30, 32, 34) and six as absolute fat mass (Kg) (25, 27-29, 31, 33), whereas one reported both parameters (29). Likewise, fourteen clinical trials measured the effect on muscle mass: four presented the results as changes in muscle mass (%) (20, 21, 32, 34), seven as muscle mass (Kg) (28, 31, 32, 34, 35, 37, 39) and two as appendicular skeletal mass (kg) (23, 24). Likewise, one study reported fat free mass (kg) (27). BMI was reported in thirteen studies (20-27, 29-31, 33, 34).

The treatment duration of the ten studies reporting the effect on fat mass percentage (%) was highly variable, ranging from four (21) to 16 weeks (30). The type, dose, and combination of probiotics tested in the studies was very different; however, *Bifidobacterium breve* and *Bifidobacterium longum* were the most used in six trials (20-24, 26, 30).

Of the ten studies that measured the effect of probiotic treatment on fat mass percentage (%), only two clinical trials reported a statistically significant decrease, the one conducted by Chaiyasut *et al*. (2022) in healthy subjects [MD=−4.82, 95% confidence interval (CI)=−6.06 to −3.58, $p<0.001$] (20) and the other carried out in overweight Japanese adults, who consumed *Bifidobacterium breve* B-3 5×10^{10} CFU (1 capsule per/day) for 12 weeks (MD=−1.00, 95%CI=−2.99 to 0.99, $p<0.05$) (26) (Table I).

Likewise, the treatment duration of the six studies that reported the effect on absolute fat mass (kg) was also very

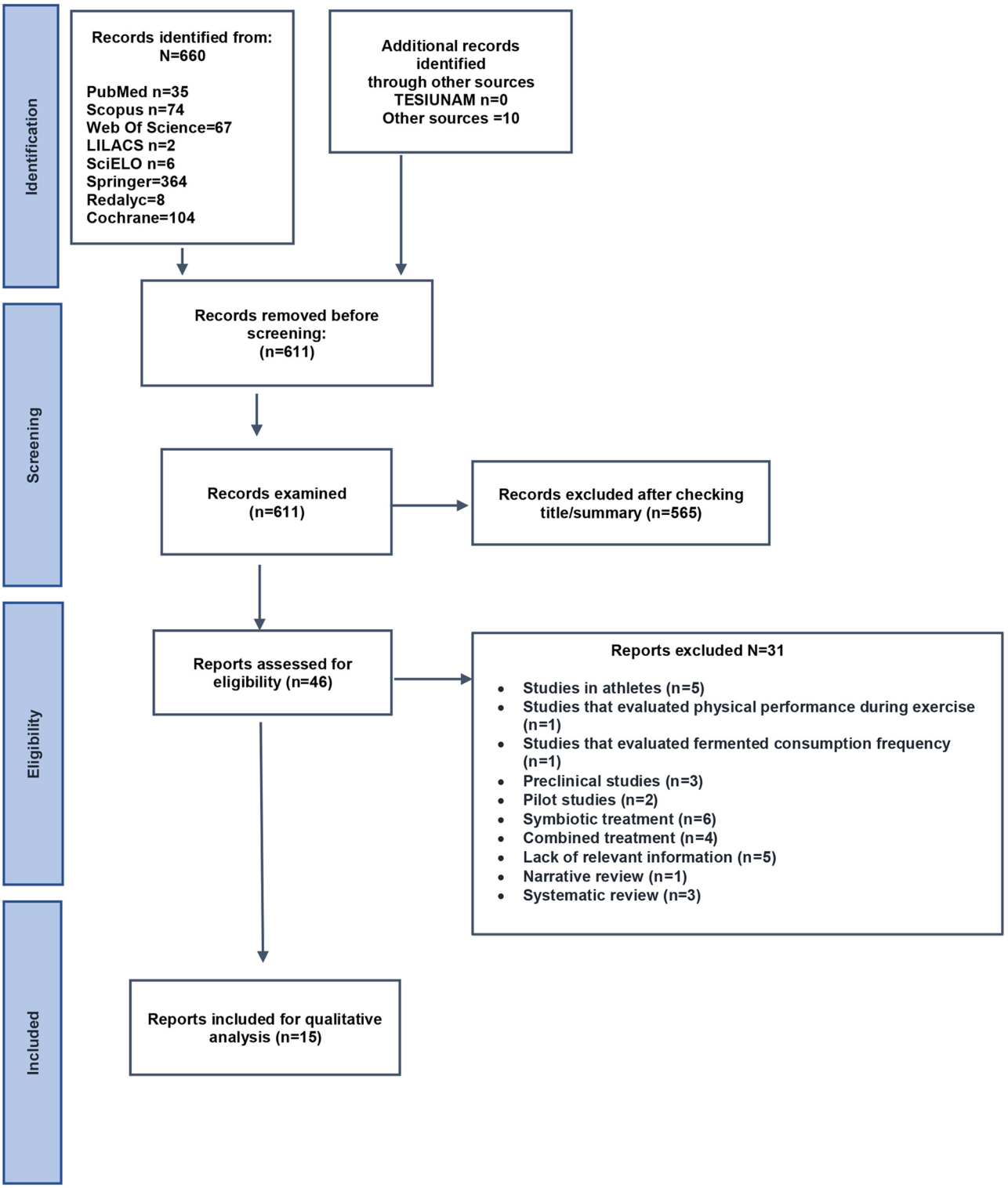

Figure 1. *PRISMA flow diagram on the selection of studies included.*

variable, from three weeks (31) to 56 weeks (28). The type, dose, and combination of probiotics tested in the studies were very different. However, the most used was *Lactobacillus plantarum* in three clinical trials (29, 31, 33).

The treatment duration of the four studies that reported the effect on muscle mass (%) was variable, from four weeks (21) to 12 weeks (20, 32, 34). The type, dose, and combination of probiotics were very different. Of the four studies that measured the effect of probiotic treatment on muscle mass (%), only in the study carried out by Chaiyasut *et al*. (2022), a statistically significant difference was found (MD=3.99, 95%CI=3.38-4.60, p<0.001) (20). It is important to note that the increase with treatment in the experimental group was marginal (0.79±0.60); however, in the placebo group, a significant decrease was observed (–3.12±1.41), so the most important effect is on the prevention of muscle mass loss and not on gain (20) (Table I).

The seven studies that reported the effect on absolute muscle mass (kg) showed very different durations, types, doses, and combinations of probiotics tested, and none reported statistically significant differences (Table I).

The treatment duration of the two trials reporting the effect on appendicular skeletal mass (kg) was 12 weeks (23) and 16 weeks (24). The type, dose, and combination of probiotics differed between the studies, and neither study had statistically significant differences observed between the experimental and placebo groups (Table I). Only in the study conducted by Mohammdi-Sartang *et al.* (2018) (27), the effect of probiotics on fat free mas was reported. They administered Fortified Yogurt (FY) (500 g/day) three gr of inulin as a prebiotic, initiators of *S. Thermophiles* and *L. Bulgaricus* enriched with at least 10^7 CFU/g of *bifidobacterium lactis* Bb12 for 10 weeks, observing a significantly greater decrease in the comparison group (low-fat plain yogurt) (change, –2.0±2.7) compared to the FY group (change, –0.9±3.5) (Table I). However, the measurement of this parameter does not allow evaluation of the specific effect on muscle mass.

The type, dose, and combination of probiotics in the thirteen studies reporting BMI were very different. However, the most used probiotics were *Bifidobacterium breve* and *Bifidobacterium longum* in five trials (20, 22-24, 26). Furthermore, only two trials reported a statistically significant decrease, one by Pan *et al.* (2020) (MD=–1.97, 95%CI=–3.47 to –0.47, p<0.01) (29), and the other by Sharafedtinov *et al.* (2013) (MD=–0.80, 95%CI=–2.10 to –1.10, p<0.05) (31) (Table I).

Discussion

Clinical studies on the effect of microbiota on health have re-emerged as preventive and therapeutic options for various diseases, including gastrointestinal, liver, metabolic, chronic inflammatory, neurological, and NCDs, through different strategies or types of therapeutic interventions, such as prebiotics, probiotics, symbiotics, and postbiotics (35, 36). Likewise, interest has arisen in studying the effect of probiotic consumption on body composition in people aged ≥45 years to prevent or control NCDs linked to aging, such as obesity and sarcopenia (37).

In our systematic review, it was impossible to carry out a meta-analysis due to the high variability of the types of probiotics tested, the time of administration, and the characteristics of the population studied. Although there are similarities in some of the parameters of body composition reported in some selected studies, the inconsistency of the types and duration of treatment, as well as the characteristics of the population, did not allow us to present the sum of data from at least two studies through a forest plot.

It has been shown that genetics, lifestyle (diet, sedentary lifestyle, and psychological stress), environment, and age are determining factors of the type of microbiota of people. The increase in body fat mass and, consequently, obesity is linked to gut dysbiosis, causing different alterations, including decreased mucus production, decreased capacity of the intestinal epithelium to repair, and alterations in regulating short-chain fatty acid (SCFA) production. In addition, there is an increase in pro-inflammatory bacteria and metabolic alterations that cause increased appetite (38).

Table I. *Characteristics and results of studies on the effect of the consumption of probiotics on fat and muscle mass.*

Author (Ref) & Location	Design	Population	Age (m±SD) & Comorbidity	Duration	Probiotic type/Doses	Parameters & Methods	Outcomes
Chaiyasut *et al.* (2022) (20) Thailand	RCT-PAR-DB-P	N=48 PG: n=24 F: n=17 M: n=7 EG: n=24 F: n=3 M: n=21	PG: 58.79±1.21 EG: 61.63±0.84 Healthy	12 weeks	PG: 10 g of corn starch in a similar package of probiotics. EG: 2.0×1010 CFU of *Lactobacillus paracasei* HII01; 2.0×10^{10} CFU of *Bifidobacterium breve*; 1.0×10^{10} CFU of *Bifidobacterium longum*	Fat mass Muscle mass BMI Picooc®, Model S1 Pro Weight Height	Fat mass (%) Mean difference: −4.82 [95%CI=−6.06 to −3.58, $p<0.001$] Muscle mass (%) Mean difference: 3.99 [95%CI=3.38 to 4.60, $p<0.001$] BMI (kg/m^2) Mean difference: 0.03 [95%CI=−0.34 to 0.40, $p>0.05$]
Hric *et al.* (2021) (21) Slovakia	RCT	N=22 Females CG: n=9 EG: n=13	CG: 44±13 EG: 51±12.6 Healthy	4 weeks	CG: low-calorie diet (45% carbohydrates, 30% fats and 25% proteins) and vigorous aerobic exercise. EG: low-calorie diet (45% carbohydrates, 30% fats and 25% proteins), vigorous aerobic exercise and 30 g of probiotic sheep cheese "Bryndza" contains (*Lactococcus*, *Streptococcus*, *Lactobacillus* and *Enterococcus*).	Fat mass Muscle mass Body weight BMI Omron 511BF Weight Height	Fat mass (%) Mean difference: 1.80 [95%CI=−1.67 to 5.27, $p>0.05$] Muscle mass (%) Mean difference: −1.20 [95%CI=−2.67 to 0.27, $p>0.05$] BMI (kg/m^2) Mean difference: −0.20 [95%CI=−3.16 to 2.76, $p>0.05$]
Inoue *et al.* (2018) (22) Japan	RCT-DB-P	N=38 PG: n=18 F: n=11 M: n=7 EG: n=20 F: n=13 M: n=7	PG: 70.9±3.2 EG: 69.9±3.0 Healthy	12 weeks	PG: Water (preferably after breakfast) EG: Lyophilized powder of *B. longum* BB536, *B. infantis* M-63, *B. breve* M-16V and *B. breve* B-3 (approximately 1.25×1010 CFU each; Morinaga Milk Industry Co., Ltd., Kanagawa, Japan)	Fat mass Muscle mass Body weight BMI InBody S10, BioSpace, Seoul, Korea Weight Height	Fat mass (%) Mean difference: −0.10 [95%CI=−2.66 to 2.46, $p>0.05$] Muscle mass (kg) Mean difference: −0.30 [95%CI=−3.00 to 2.40, $p>0.05$] BMI (kg/m^2) Mean difference: −0.30 [95%CI=−1.42 to 0.82, $p>0.05$]

Table I. *Continued*

Table I. *Continued*

Author (Ref) & Location	Design	Population	Age (m±SD) & Comorbidity	Duration	Probiotic type/Doses	Parameters & Methods	Outcomes
Karim *et al.* (2022a) (23) Pakistan	RCT-PAR-DB-P	N=92 Males PG: n=48 EG: n=44	PG: 68.7±4.2 EG: 67.1±3.4 COPD	16 weeks	PG: Inactive agents in similar capsules. EG: Vivomix 112 billion (bifidobacteria (*B. longum* DSM 24736, *B. breve* DSM 24732, DSM 24737), lactobacilli (DSM 24735, DSM 24730, DSM 24733, *L. delbrueckii subsp. bulgaricus* DSM 24734) and thermophilic Streptococcus (DSM 24731 1 capsule/day)	Fat mass Appendicular skeletal mas BMI RENPHO Weight Height	Fat mass (%) Mean difference: −0.15 [95%CI=−1.17 to 0.87, p>0.05] Appendicular skeletal mass (kg) Mean difference: 0.24 [95%CI=−0.48 to 0.96, p>0.05] BMI (kg/m^2) Mean difference: 0.26 [95%CI=−0.47 to 0.99 p>0.05]
Karim *et al.* (2022b) (24) Pakistan	RCT-PAR-DB-P	N=100 Males PG: n=53 EG: n=47	PG: 65.2±5.6 EG: 67.6±4.9 CHF	12 weeks	PG: Inactive agents in similar capsules. EG: Vivomix 112 billion live bacteria (Streptococcus thermophilus DSM 24731, bifidobacteria (*B. longum* DSM 24736, *B. breve* DSM 24732, DSM 24737), lactobacilli (DSM 24735, DSM 24730, DSM 24733, *L. delbrueckii subsp. bulgaricus* DSM 24734) along with maltose, anti-caking agent: silicon dioxide (Vivomix*, UAE). 1 capsule/day	Fat mass Appendicular skeletal mass BMI RENPHO Weight Height	Fat mass (%) Mean difference: 0.08 [95%CI=−1.04 to 1.208, p>0.05] Appendicular skeletal mass (kg) Mean difference: 0.51 [95%CI=−0.31 to 1.33, p>0.05] BMI (kg/m^2) Mean difference: 0.76 [95%CI=0.02 to 1.50, p>0.05]
Lim *et al.* (2020) (25) Korea	RT-DB-P	N=95 PG: n=48 F: n=31 M: n=17 EG: n=47 F: n=33 M: n=14	PG: 47.2±11.2 EG: 46.4±12.2 Overweight or obesity	12 weeks	PG: Equivalent vehicle EG: *L. sakei* (CJLS03) 5×10^9 CFU. This strain was grown in de Man–Rogosa–Sharpe broth, a specific broth for Lactobacillus (Difco Laboratories, Detroit, MI, USA) and prepared for oral intake. It was grown for 7 hours to reach the late log phase, collected (16,000×g, 5 minutes, 4°C), and washed twice with phosphate-buffered saline.	Fat mass Total muscle mass Body weight BMI DXA for muscle mass, Inbody 720 for fat dough Weight Height	Fat mass (kg) Mean difference: −0.80 [95%CI=−2.22 to 0.62, p>0.05] Total muscle mass (kg) Mean difference: −0.10 [95%CI=−2.26 to 2.06, p>0.05] BMI (kg/m^2) Mean difference: −0.40 [95%CI=−1.04 to 0.24, p>0.05]

Table I. *Continued*

Table I. *Continued*

Minami *et al.* (2015) (26) Japan	RT-DB-P	N=44 PG: n=25 F: n=14 M: n=11 EG: n=19 F: n=13 M: n=6	PG: 61.9±1.9 EG: 58.9±2.0 Overweight	12 weeks	PG: Capsule only included an internal matrix (mainly maize starch). EG: *Bifidobacterium breve* B-3 5×10^{10} CFU. The capsules of B-3 contained lyophilized powder of B. breve. B-3, a strain originating from a healthy infant, and had mainly maize starch as the carrier in an acid-protective gelatin capsule (1/day).	Fat mass Muscle mass Body weight BMI Inbody 3.0 Weight Height	Fat mass (%) Mean difference: −1.00 [95%CI=−2.99 to 0.99, $p<0.05$] Muscle mass (kg) Mean difference: 1.20 [95%CI=−2.35 to 4.75, $p>0.05$] BMI (kg/m^2) Mean difference: 0.00 [95%CI=−0.97 to 0.97, $p>0.05$]
Mohammdi-Sartang *et al.* (2018) (27) Iran	RT-DB-P	N=87 PG: n=43 F: n=26 M: n=17 EG: n=44 F: n=27 M: n=17	PG: 45.6±8.7 EG: 45.4±8.9 Metabolic syndrome	10 weeks	PG: Plain yogurt (PY) contained the starter cultures of *S. Thermophiles* and *L. bulgaricus* EG: Fortified yogurt (FY) (500 g/day) 3 g of inulin as a prebiotic, initiators of *S. Thermophiles* and *L. Bulgaricus* enriched with at least 10^7 cfu/g of *bifidobacterium lactis Bb12*.	Fat mass Muscle mass Body weight BMI Inbody S10 Weight Height	Fat mass (kg) Mean difference: −1.70 [95%CI=−3.26 to −0.14 $p<0.05$] Fat free mass (kg) Mean difference: 1.15 [95%CI=0.21 to 2.41, $p<0.05$] BMI (kg/m^2) Mean difference: −0.30 [95%CI=−0.86, 0.26, $p>0.05$]
Nilsson *et al.* (2018) (28) Sweden	RT-DB-P	N=68 Females PG: n=36 EG: n=32	PG: 76.3±1.1 EG: 76.4±1.0 Low bone mineral density	56 weeks	PG: Maltodextrin dust EG: *L. reuteri* 6475 (BioGaia AB, Stockholm, Sweden) in doses of $5x10^9$ CFU mixed with maltodextrin powder, filled in stick packs, and was taken twice daily, yielding a total daily dose of 1×10^{10} CFU day.	Fat mass Muscle mass DXA	Fat mass (kg) Mean difference: 0.56 [95%CI=4.67 to 5.79, $p>0.05$] Muscle mass (kg) Mean difference: 0.44 [95%CI=1.69 to 2.57, $p>0.05$]
Pan *et al.* (2020) (29) China	RT-DB-P	N=31 PG: n=16 F: n=8 M: n=8 EG: n=15 F: n=8 M: n=7	PG: 57.60±6.10 EG: 53.60±6.77 Metabolic syndrome	10 weeks	PG: Whole wheat noodles not fermented. (500 g total wheat flour) EG: Whole wheat noodles not fermented. (300 g wheat flour and 200 g fermented barley flour by *Lactobacillus plantarum*).	Fat mass Muscle mass Body weight Tanita	Fat mass (%) Mean difference: −0.06 [95%CI=−3.76 to 3.64, $p>0.05$] Fat mass (kg) Mean difference: −1.65 [95%CI=−4.82

Table I. *Continued*

Table I. *Continued*

					About 75 g noodles per day for female and 90 g noodles per day for men were calculated *via* the formula of daily noodles requirement from dietary guidelines for Chinese residents		to 1.52, $p>0.05$] Muscle mass (kg) Mean difference: −1.68 [95%CI=−5.21 to 1.85, $p>0.05$] BMI (kg/m^2) Mean difference: −1.97 [95%CI=−3.47 to −0.47, $p<0.01$]
Qaisar *et al.* (2024) (30) Pakistan	RT-DB-P:	N=123 Males PG: 63 EG: 60	PG: 71.4±3.9 EG: 73±4.1 Sarcopenia	16 weeks	A capsule of Vivomix 112 included bifidobacteria (*B. longum* DSM 24736, *B. breve* DSM 24732, DSM 24737), *Streptococcus thermophilus* DSM 24731, and *lactobacilli* (DSM 24735, DSM 24730, DSM 24733, *L. delbrueckii subsp. bulgaricus* DSM 24734)	Fat mass BM SMI RENPHO	Fat mass (%) Mean difference: −0.45 [95%CI=−0.81, −0.09, $p<0.05$] BMI (kg/m^2) Mean difference: 0.14 [95%CI=0.08 to 0.20, $p>0.05$]
Sharafedtinov *et al.* (2013) (31) Estonia	RT-DB-P	N=40 PG: n=15 F: n=11 M: n=4 EG: n=25 F: n=16 M: n=9	PG: 51.7±12.1 EG: 52.0±10.9 Obesity Hypertension	3 weeks	PG: Cheeses prepared on the basis of regular Edam-type cheese with a starter C92 (CSK Food Enrichment, Netherlands). EG: Cheese Edam type containing *L. plantarum* TENSIA (1.5×10^{11} CFU/g was developed at E-Piim Production in Estonia under the trademark Harmony™ 50 gr/cheese day (175 kcal)	Fat mass Muscle mass Body weight Inbody720	Fat mass (kg) Mean difference: −4.82 [95%CI=−6.06 to −3.58, $p<0.001$] Muscle mass (kg) Mean difference: 0.20 [95%CI=−2.71 to 3.11, $p>0.05$] BMI (kg/m^2) Mean difference: −0.40 [95%CI=−2.10 to 1.30, $p>0.05$]
Skrypnik *et al.* (2019) (32) Poland	RT-RB-P	N=73 Females PG: n=24 EG1: n=26 EG2: n=23	PG: 60.46±6.92 EG1: 56.88±6.41 EG2: 56.00±6.56 Obesity	12 weeks	PG: Received the excipient alone (maize starch and maltodextrins) packed in the identical sachets. EG1: Daily dose of 2.5×10^9 CFU. (*Bifidobacterium bifidum* W23, *B. Lactis* W51, *B. Lactis* W52, *Lactobacillus Acidophilus* W37, *L. Brevis* W63, *L. Casei* W56, *L. Salivarius* W24, *Lactococcus Lactis* W19, and *Lc. Lactis* W58) EG2: Daily dose of 2.5×1010 CFU. (*Bifidobacterium bifidum* W23, *B. Lactis* W51,	Fat mass Muscle mass Body weight Bioscan 920-2, Maltron International, Essex, UK	Fat mass (%) G1 Mean difference: 2.14 [95%CI=−0.06 to 4.34, $p>0.05$] G2 Mean difference: 1.22 [95%CI=−1.50 to 3.94, $p>0.05$] Muscle mass (%) G1 Mean difference: −2.15 [95%CI=−4.35

Table I. *Continued*

Table I. *Continued*

					B. Lactis W52, *Lactobacillus Acidophilus* W37, *L. Brevis* W63, *L. Casei* W56, *L. Salivarius* W24, *Lactococcus Lactis* W19, and *Lc. Lactis* W58)		to 0.05, $p>0.05$] G2 Mean difference: −1.08 [95%CI=−3.79 to 1.63, $p>0.05$]
Sohn *et al.* (2022) (33) Korea	RCT-DB-P	N=71 PG: n=36 F: n=22 M: n=14 EG: n=35 F: n=21 M: n=14	PG: 45.5±10.0 EG: 47.8±11.7 Overweight or obesity	12 weeks	PG: Microcrystalline capsules with texture, color, and odor identical at the vehicle probiotic was used. EG: Probiotic capsules were composed of Lactobacillus plantarum and microcrystalline cellulose powder, named CKDB156, including 4×10^9 CFU	Fat mass Muscle mass Body weight BMI DXA Weight Height	Fat mass (kg) Mean difference: −1.50 [95%CI=−2.66 to −0.34, $p<0.05$] Muscle mass (kg) Mean difference: −0.90 [95%CI=−3.16 to 1.36, $p>0.05$] BMI (kg/m^2) Mean difference: −0.30 [95%CI=−0.77 to 0.17, $p>0.05$]
Szulińska *et al.* (2018) (34) Poland	RCT-DB-P	N=71 Females PG: n=24 EG1: n=24 EG2: n=23	PG: 58.72±7.25 EG1: 56.38±6.55 EG2: 55.16±6.87 Obesity	12 weeks	PG: corn and maltodextrin starch. EG1: Low-dose probiotic contained nine bacterial strains: *Bifidobacterium bifidum* W23, *Bifidobacterium lactis* W51, *Bifidobacterium lactis* W52, *Lactobacillus acidophilus* W37, *Lactobacillus brevis* W63, *Lactobacillus casei* W56, *Lactobacillus salivarius* W24, *Lactococcus lactis* W19, and *Lactococcus lactis* W58. (2.5×10^9 CFU per day). EG2: High-dose probiotic contained nine bacterial strains: *Bifidobacterium bifidum* W23, *Bifidobacterium lactis* W51, *Bifidobacterium lactis* W52, Lactobacillus acidophilus W37, *Lactobacillus brevis* W63, *Lactobacillus casei* W56, *Lactobacillus salivarius* W24, *Lactococcus lactis* W19, and *Lactococcus lactis* W58. (2.5×10^{10} CFU per day).	Fat mass Muscle mass Body weight BMI Bioscan 9202 Weight Height	Fat mass (%) G1 Mean difference: 0.36 [95%CI=−1.90 to 2.62, $p>0.05$] G2 Mean difference: 0.10 [95%CI=−2.64 to 2.84, $p>0.05$] Muscle mass (%) G1 Mean difference: −0.93 [95%CI=−3.52 to 1.66, $p>0.05$] G2 Mean difference: −0.51 [95%CI=−3.38 to 2.36, $p>0.05$] BMI (kg/m^2) G1 Mean difference: −0.43 [95%CI=−2.14 to 1.28, $p>0.05$] G2 Mean difference: −0.29 [95%CI=−2.30 to 1.72, $p>0.05$]

M: Males; F: females; CFU: colony-forming units; PG: placebo group; EG: experimental group; CG: control group; EG1: experimental group 1; EG2: experimental group 2; RCT: randomized controlled trial; RCT-DB-P: randomized, double-blind, placebo-controlled clinical trial; RCT-PAR-DB-P: randomized, parallel, double-blind, placebo-controlled clinical trial; RT-DB-P: randomized, double-blind placebo clinical trial; RT-SB-P: Randomized clinical trial, blind with placebo; COPD: chronic obstructive pulmonary disease; CHF: chronic heart failure; DXA: dual energy X-ray absorptiometry; BMI: body mass index.

In our systematic review, only four clinical trials found a statistically significant decrease in fat mass after probiotic consumption, two in percentage (%) (20, 26) and two in absolute weight (kg) (27, 33). In contrast, Pontes *et al*. conducted two meta-analyses, one of which included eight studies that reported changes in fat mass (%) and observed a statistically significant decrease. Likewise, in the other meta-analysis on thirteen studies, the authors reported a decrease in fat mass (kg), with a greater effect when the probiotics consumed were of a single species, dose $\geq 10^{10}$ (CFU/day), and duration ≥8 weeks (39). These results are not entirely reliable since the authors grouped and added data from all the studies without considering the heterogeneity regarding the type, dose, and treatment time of the probiotics. Therefore, further studies are needed, taking into consideration the homogeneity of the probiotic species, doses, and time that have demonstrated greater efficacy to perform reliable meta-analyses that determine not only the statistical significance but also the clinical relevance.

In addition, Wang *et al.* carried out a systematic review of overweight and obese adults over 18 years of age. They found a greater decrease in fat mass (Kg) with high dosage probiotics $\geq 10^{10}$ (CFU/day), a greater decrease with single strain probiotics compared to multiple strain probiotics, and a greater decrease with administration probiotics in the form of food (40). In this regard, homogeneity regarding the type, dose, and duration of treatment was not considered either since the authors established arbitrary categories of dose (low and high) and type (single *vs*. multiple strain probiotics). Therefore, the meta-analysis results are not entirely reliable. However, they point out the most effective doses and types of probiotics to reduce fat mass. However, Hamed Riveros *et al.* (2024), who evaluated the effect of *Bifidobacterium* consumption in a meta-analysis of seven studies, observed a significant decrease in body fat percentage and fat mass (kg) (41). Although the results presented are specific to the type of probiotic, we must consider the effect size to determine the clinical relevance.

The mechanisms of the beneficial effects of probiotics on body adiposity are not yet clear. However, it has been pointed out that probiotics could increase SCFA-producing bacteria and promote the recovery of epithelial cell barrier, thus decreasing intestinal permeability, preventing the translocation of bacteria and decreasing tissue inflammation derived from lipopolysaccharides (42). Likewise, it has been shown that the reduction of chronic inflammation increases insulin sensitivity in the hypothalamus, increasing satiety and reducing food intake, which results in loss of weight and total fat mass (38).

Therefore, although some isolated studies from the published meta-analyses suggest that probiotic treatment significantly reduces body fat mass, the overall results of the meta-analysis presented in the forest plots are unreliable due to the high heterogeneity. Therefore, it is necessary to carry out more studies, taking note of the species, doses, and duration that have shown greater efficacy.

With aging, there is a chronic increase in the levels of inflammatory biomarkers such as IL-6, C-reactive protein (CRP), and TNF-α, a process termed "inflammaging" (43). In this regard, systemic inflammation has been shown to decrease the net balance of muscle proteins by suppressing the anabolic pathways and promoting the catabolic pathways, which leads to reductions in skeletal muscle mass and quality (44). A study carried out in animal models supplemented with Lactobacillus strains showed that probiotics regulate the levels of proinflammatory cytokines such as IL-6 and TNF-α and increase muscle amount, strength, and function (45). Although anabolic responses to supplementation with probiotics are mediated, in part, by anti-catabolic responses that suppress systemic inflammation, it is currently unknown if this is sufficient to suppress the loss of muscle mass in older populations.

In this framework, it has been pointed out that older individuals exhibit a reduced response of muscle protein synthesis to anabolic stimuli compared to younger adults, a phenomenon termed anabolic resistance (46). Therefore, treatment with probiotics could be a good means to prevent, maintain or recover muscle mass.

The mechanisms related to the effect of probiotic consumption on the prevention and recovery of skeletal muscle mass loss related to aging that causes sarcopenia

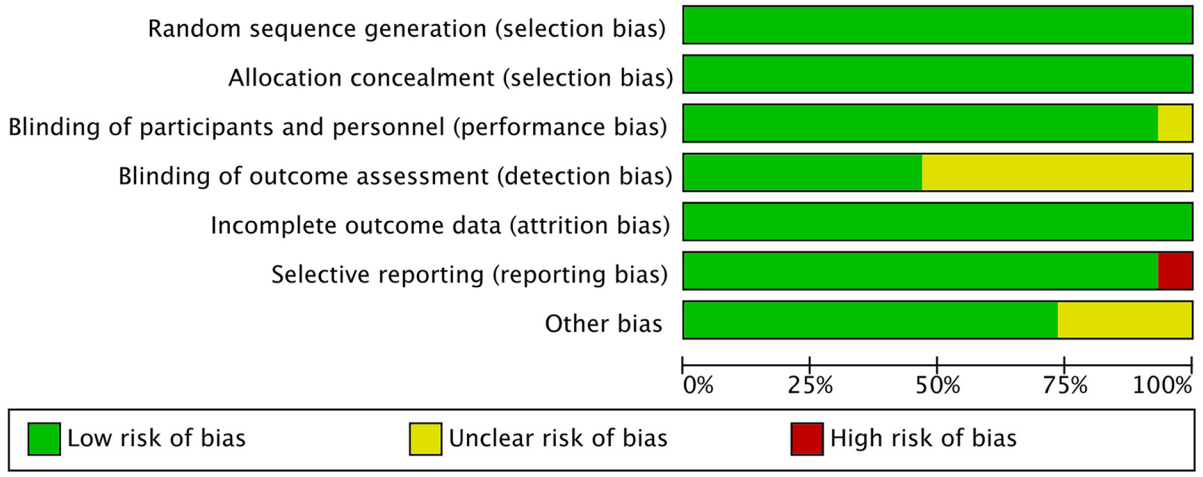

Figure 2. *Continued*

are not precisely known. In this regard, it has been noted that probiotics have anti-inflammatory and antioxidant effects, improve insulin function, and consequently increase muscle mass and strength (9, 47, 48).

In our systematic review, four studies measured the effect of probiotic consumption on muscle mass (%) (20, 21, 32, 34). Of these, only the study conducted by Chaiyasut *et al*. (2022) found a statistically significant difference (20). However, the increase in the experimental group was marginal. Therefore, the usefulness of probiotic consumption on muscle mass could be preventive or adjuvant to other therapeutic options, such as increased protein consumption and physical strength effect.

The effect of probiotics on muscle mass (kg) from seven selected studies (22, 25, 26, 28, 29, 31, 33) and two on appendicular skeletal mass (kg) (23, 24) was also analyzed; no study reported statistically significant differences between the groups that consumed probiotics compared to the placebo groups. Another included study that evaluated fat-free mass (27) reported statistically significant differences, although this parameter does not allow us to assess whether the effect was on muscle mass. In this regard, a systematic review and meta-analysis of 10 studies carried out in adults over 18 years of age by Prokopidis *et al.* revealed a significant increase in muscle mass, but in subgroup analyses, no statistically significant effect on muscle mass was observed in overweight or obese individuals. However, a significant increase was found in those <50 years. Although the results of this systematic review are interesting and suggest that the best effect of probiotics on muscle mass can be observed in non-obese subjects <50 years old, it is important to note that the authors carried out the meta-analysis without considering the high heterogeneity in the type and doses of probiotics, the health status of the population and treatment duration (12). Likewise, Besora-Moreno *et al.*, conducted a meta-analysis of four studies in older people, reporting a positive effect of probiotic consumption on muscle strength, physical performance and function by gait speed. However, they also did not respect the homogeneity criteria regarding the type, dose, and duration of treatment (49). Therefore, it is necessary to carry out more clinical trials, considering the probiotics' type, dose, and duration, which have shown greater efficacy on muscle mass.

Scientific evidence suggests the use of probiotic strains to improve the digestion of proteins and the absorption of amino acids that can reduce the dose of protein required to stimulate the synthesis of muscle proteins; however, considering anabolic resistance during aging, its impact on skeletal muscle mass is questionable in older populations (50). Therefore, one way to prevent muscle

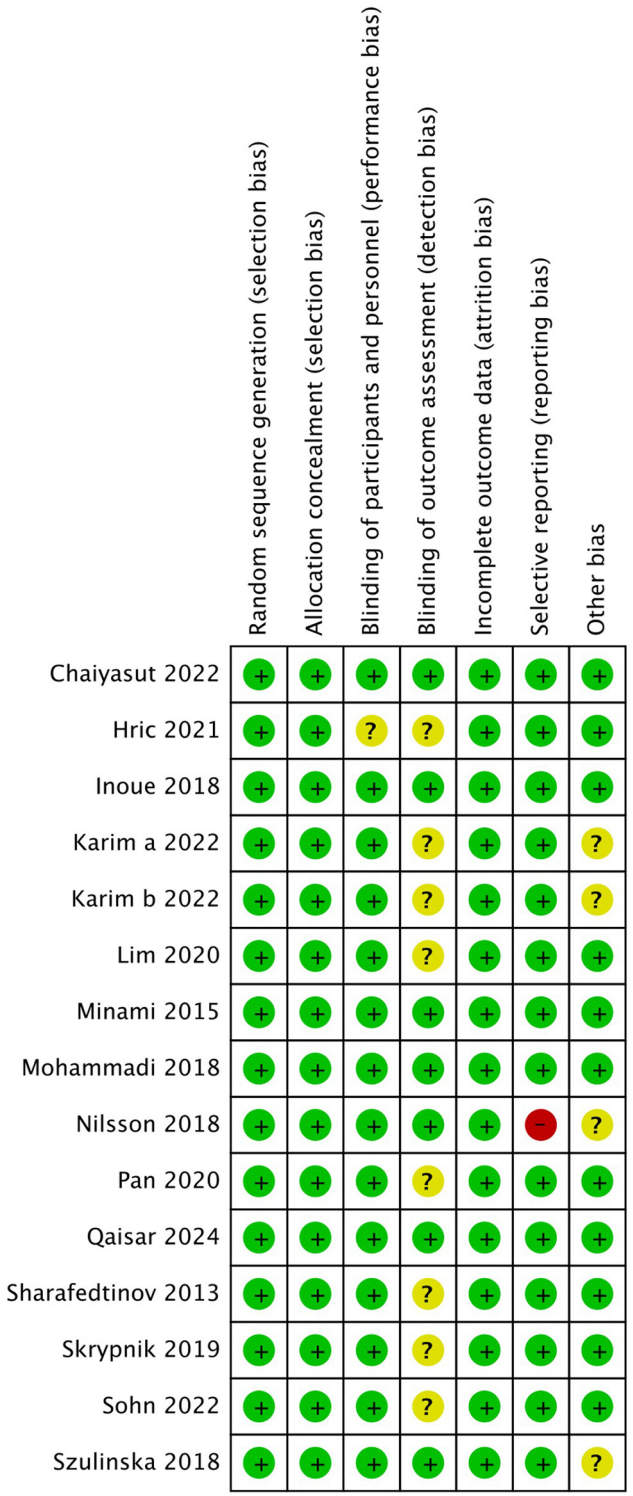

Figure 2. *Risk analysis of bias and methodological quality per domain and author.*

mass loss during aging would be to increase protein intake combined with physical exercise, higher doses, and longer probiotic treatment. In this regard, it is necessary to conduct more controlled clinical trials with different doses and duration of different types of probiotic treatment, alone and in combination with other interventions in people over 50 years of age considering the effect by age, sex, and health status.

BMI is also a widely used anthropometric parameter for assessing and detecting health problems. However, like body weight, it is very nonspecific and must be interpreted comprehensively with the other clinical data.

In this systematic review, thirteen articles reported the effect of probiotic consumption on BMI (20-27, 29-34). Of these, only two found statistically significant differences between the groups (35, 37). In contrast, Pontes *et al.* (2021), who conducted a meta-analysis, reported a decrease in BMI (kg/m^2) in the group that consumed probiotics compared to the control (39). However, the authors did not meet the criteria of homogeneity of the studies in terms of type, dose, and treatment duration of probiotics, which justifies their inclusion in a meta-analysis.

Likewise, in the meta-analysis carried out by Peckmezian *et al.*, no statistically significant decrease in BMI (kg/m^2) was found in the group that consumed probiotics (51). However, the authors also did not meet the criteria of homogeneity. In addition, one of the studies included represents 59.2% and another 29.5% of the meta-analysis's weight, so the authors should not have carried out the forest plot.

In this regard, it has been noted that BMI measurement has low reliability as an indicator of fat and muscle mass (52, 53), so the inconsistencies reported in meta-analyses limit its clinical usefulness.

Strengths and limitations. This is the first systematic review that is carried out to evaluate the effect of probiotic supplementation on fat mass, muscle mass, and BMI in adults ≥45 years old. The selected clinical trials were conducted in different countries, and most studies included male and female individuals. The effects of

different types and presentations of probiotics and doses and duration of consumption were also included. The homogeneity criteria of the probiotic treatment and its effect on fat mass, muscle mass, and body mass index were carefully analyzed to avoid the error of performing a meta-analysis with the heterogeneity detected in the treatment as occurs in other published studies.

Among the most important limitations, we can point out the scarcity of clinical trials and the high heterogeneity of the studies regarding the type of probiotics administered and the duration of administration.

Clinical implications. The comprehensive and differentiated analysis of the synthesis of knowledge on the effect of probiotic supplementation on body fat and skeletal muscle mass in individuals ≥45 years old indicates that there is not enough scientific evidence to suggest probiotics as a single therapeutic option for the treatment of overweight, obesity, and sarcopenia.

Finally, further clinical trials are needed to determine the use of certain probiotic strains selected based on age, doses and duration of treatment, and evaluate the results before and after treatment, considering the intervening variables of age, sex, and health status.

Conclusion

Supplementation with probiotics may have a beneficial effect on reducing fat mass; however, further clinical trials are needed considering the types, doses, and duration that have shown the best results. Regarding their effect on skeletal muscle mass, there is no scientific evidence to support their efficacy. Therefore, additional studies should be carried out to complement the treatment with probiotics with increased protein intake, caloric restriction, and physical exercise.

Conflicts of Interest

The Authors declare that there are no conflicts of interest regarding this study. The funders had no role in study design, data collection and analysis, publication decision, or manuscript preparation.

Authors' Contributions

J G-N: Writing – review & editing, Resources, Investigation; VM M-N, Conceptualization. Oliver Micke: Writing – review & editing.

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