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Impact of probiotics on weight loss, glucose and lipid metabolism in overweight or obese women: A meta-analysis of randomized controlled trials

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ABSTRACT

Our meta-analysis aimed to assess the effectiveness of probiotics in weight loss and glucose and lipid metabolism in overweight or obese women. PubMed, EMBASE, Cochrane Library, and Web of Science were used from inception until March 2024 to identify randomized controlled trials (RCT's) literature. Finally, 11 RCTs were included. Following critical appraisal, a meta-analysis was conducted using the fixed effects model and the random effects model found that probiotic consumption significantly decreased waist circumference (WC) (SMD = −0.39 cm, 95% CI: −0.60, −0.18 cm, $P < 0.00001$, $I^2 = 33\%$), insulin (SMD = −0.45 mcU/ml; 95% CI: −0.72, −0.18 mcU/ml; $P = 0.04$, $I^2 = 40\%$) and low-density lipoprotein cholesterol (LDL-C) levels (SMD = −0.51 mmol/L; 95% CI: −0.92, −0.11 mmol/L; $P = 0.02$, $I^2 = 75\%$) in overweight or obese women. Moreover, subgroup analyses revealed that the effects of probiotic supplementation were significantly influenced by the intervention duration and diet and/or exercise intervention. This meta-analysis suggested that probiotic supplementation has a moderate and statistically significant effect on weight loss and glucose and lipid metabolism in overweight and obese women.

1. Introduction

As complex and chronic diseases, overweight and obesity continue to pose a serious threat to global health(Perdomo et al., 2023). In 2022, the number of adults affected by overweight and obesity reached 2.5 billion worldwide(World Health Organization, n.d.). Despite regional variations in BMI, the prevalence of obesity increased in every country between 1975 and 2016(Li et al., 2023; NCD Risk Factor Collaboration (NCD-RisC), 2017; Zhang et al., 2023). It is imperative to take effective measures to prevent the rise in the prevalence of overweight and obesity to prevent and treat these diseases as well as associated comorbidities such as diabetes, dyslipidemia, and cardiovascular disease (CVD)(Bray et al., 2017; "Roth et al., 2020: Update From the GBD, 2019 Study - PubMed," n.d.; Ruze et al., 2023).

Overweight and obesity present significant differences between men and women, both in terms of prevalence and the way they manifest. Data from 1975 to 2014 indicate that the prevalence of obesity has increased from 3.2% to 10.8% in men and from 6.4% to 14.9% in women on a global scale. It is projected that 18% of men and 21% of women worldwide will be affected by obesity by 2025(NCD Risk Factor Collaboration (NCD-RisC), 2016). While there has been a narrowing of the gap in overweight and obesity prevalence between men and women, severe obesity is more prevalent in women than men(Cooper et al., 2021; Hales et al., 2020, pp. 2017–2018; NCD Risk Factor Collaboration (NCD-RisC), 2017; Regensteiner and Reusch, 2022). In the manifestations of obesity, pre-menopausal women tend to have higher peripheral fat depots(Zore et al., 2018), while menopause and the subsequent decline in estrogen levels lead to a redistribution of adipose tissue to the visceral adipose depots in women. This redistribution is associated with an increased risk of cardiovascular disease (CVD). Meanwhile, women

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have a higher fat mass than men(Regensteiner and Reusch, 2022). Finally, obesity affects gonadotropin hormones in women, leading to reduced fecundity and increased adverse pregnancy rates. Despite these differences, sex-related differences have rarely been considered in previous studies on obesity treatment.

Studies conducted on both human populations and animals have consistently established a correlation between the gut microbiota and various health issues, such as overweight/obesity, diabetes, and dyslipidemia(Sun et al., 2018; Zhao, 2013). Dysbiosis of the gut microbiota can activate the lipopolysaccharide/toll-like receptor 4 signaling pathway and trigger downstream inflammatory responses, thereby contributing to the development of obesity, diabetes, and dyslipidemia by inducing insulin resistance and promoting lipid synthesis and storage (Canfora et al., 2019; Cheng et al., 2022; de Aguiar Vallim et al., 2013; Koh et al., 2018; Sun et al., 2018). Additionally, gut microbiota metabolites such as short-chain fatty acids (SCFAs)(Canfora et al., 2019) and trimethylamine-N-oxide(Brown and Hazen, 2017) play crucial roles in the development of obesity, diabetes, and dyslipidemia.

Probiotics are live microorganisms that provide health benefits when consumed in adequate amounts(Ma et al., 2023; Suez et al., 2019). Probiotics have shown promising results in the prophylactic, mitigating, or curative treatment of certain metabolic diseases when used as nutrient supplements or adjunctive therapy. Specifically, they have been found to enhance intestinal homeostasis, intestinal barrier function, host immunity, gut microbiome, and metabolome modulation(Ma et al., 2023). Recent meta-analyses have also shown that probiotic intake can have health-promoting effects on body adiposity and glycemic and lipid levels in overweight or obesity(Mayta-Tovalino et al., 2023; Perna et al., 2021; Pontes et al., 2021; Tomé-Castro et al., 2021). However, sex-specific clinical guidelines for the treatment of overweight/obesity in women are lacking, as most recommendations are based on findings in the general population.

Several randomized controlled trials (RCTs) have been conducted to explore the impact of probiotic supplementation on weight loss and glucose and lipid metabolism in overweight or obese women, but the findings have been inconclusive. Therefore, we performed a meta-analysis of all relevant randomized control trials (RCTs) with the main focus on the efficacy of probiotics on the weight loss and glucose and lipid metabolism in overweight or obese women, with a view to providing evidence-based scientific and medical findings for probiotic claims for women.

2. Methods

The present systematic review and meta-analysis were performed in accordance with The PRISMA 2020 statement: an updated guideline for reporting systematic reviews (Page et al., 2021). The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (registration No. CRD42024552620).

2.1. Literature search

Two authors (Ning Cao and Feiyan Zhao) independently performed comprehensive literature searches using different databases: PubMed, EMBASE, Cochrane Library, and Web of Science (as of March 2024). Search terms included “Probiotic” or “Probiotics,” “*Lactococcus*,” “*Bifidobacterium*,” “*Saccharomyces*,” “*Streptococcus*” and “Overweight" or “Obesity” in combination with “Women" or “Female”. The full search strategy used for the four databases is shown in Supplementary Tables S1–4.

2.2. Inclusion and exclusion criteria

Studies were selected for inclusion by two independent authors (Ning Cao and Feiyan Zhao), subjected to the approval by a third author (Zhihong Sun). The study selection procedure is illustrated in Fig. 1. The inclusion criteria were as follows: (1) subjects: overweight or obese women; (2) intervention: probiotics as the primary active intervention, no restriction on the form of probiotic supplementation and interventions period; (3) study design: randomized controlled trial (RCT); (4) study included ≥1 of the following outcomes: body weight (BW), body mass index (BMI), waist circumference (WC), waist-to-hip ratio

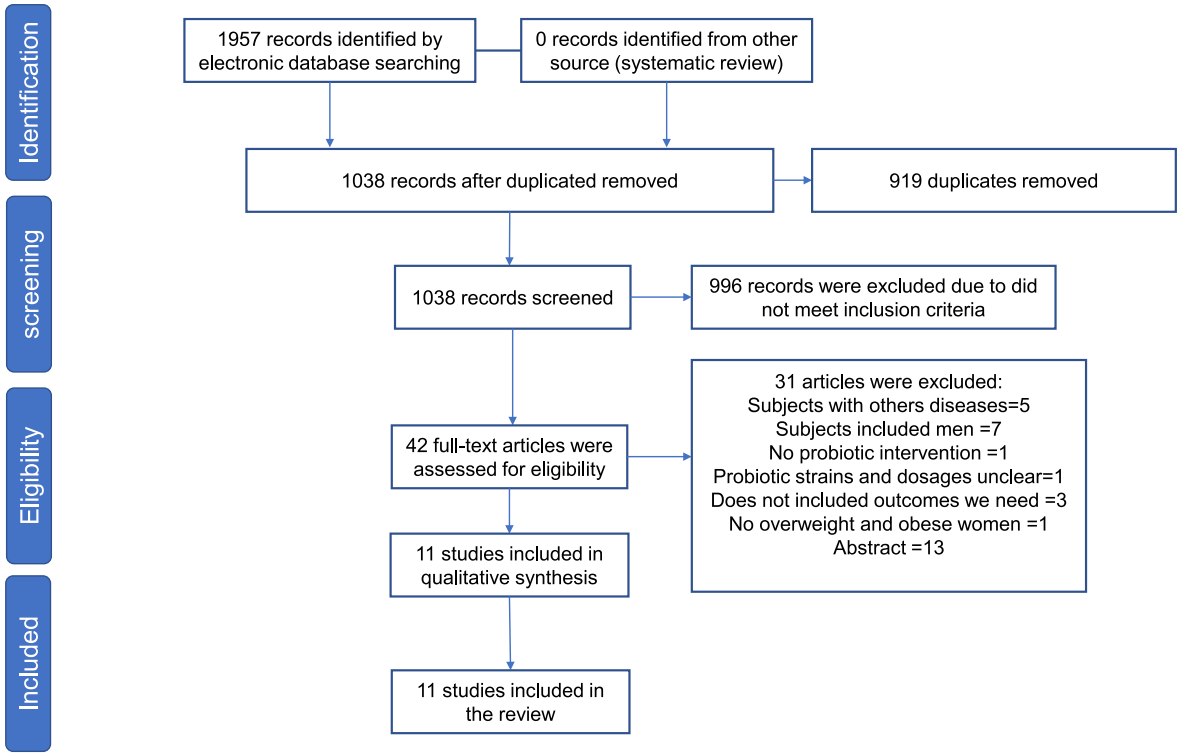

Fig. 1. Flow chart depicting the literature search and selection strategy.

(WHR), fat mass, fasting blood glucose (FBG), insulin, homeostasis model assessment-insulin resistance (HOMA-IR), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), or a combination of any of the above parameters.

We excluded studies that were: (1) categorized as review papers, letters, or conference abstracts; (2) conducted animal studies; (3) involved subjects with other diseases, such as gastrointestinal disorders, diabetes, hypertension, heart disease, renal or hepatic dysfunction, non-alcoholic fatty liver disease, and cancer; (4) performed on children, adolescents, or pregnant women; and (5) did not report the mean and standard deviation (SD) of outcome variables at baseline and/or the treatment endpoint (or mean changes) in the intervention and/or the control group(s).

2.3. Data extraction

Data extraction was independently performed by two reviewers (Ning Cao and Feiyan Zhao). The following information was collected from each study: the first author, publication year, study design, country, sample size, demographic characteristics of the subjects, including age, the characteristics of probiotics used, including species/strains, dose, and mode of administration; whether additional dietary and/or exercise interventions were implemented; and outcome measures. If there were discrepancies between the reviewers, the original article was reevaluated jointly by both reviewers.

Two independent reviewers evaluated the quality of each study based on the Cochrane risk of bias tool(Higgins et al., 2011). The following criteria were considered: (1) random sequence distribution generation, (2) allocation concealment, (3) subjects and personnel blinding, (4) outcome assessment blinding, (5) selective reporting, (6) incomplete outcome data, and (7) other bias(es). Each study was classified as having low, unclear, or high risk of bias.

2.4. Statistical analysis

Changes in outcome variables, including mean and SD in outcome variables (from baseline to endpoint) in both the probiotic and control groups of all selected studies were used for the meta-analysis according to the Cochrane Handbook for Systematic Reviews of Interventions (version 6.3). The studies were required to report the mean and SD values at both the baseline and the endpoint. The following formula was used to calculate the changes in the mean and SD values based on the data provided.

Changes in mean = (measured at endpoint) – (measured at baseline)

$$SD^2 = SD^2_{baseline} + SD^2_{endpoint} - 2 \times r \times SD_{baseline} \times SD_{endpoint}$$

(r was calculated from other studies in the meta-analysis)

For studies reporting the standard error (SE) rather than the standard deviation (SD), the SD was estimated using the formula ($SD = SE \times \sqrt{n}$), where n is the number of subjects. For studies reporting 95% confidence intervals (CI), the SD was estimated by using the formula $SD = \sqrt{n} \times$ (upper limit - lower limit)/3.92.

FBG levels were measured in mmol/L, which was converted from mg/dL to mmol/L when necessary. Similarly, insulin levels were measured in mcU/mL, which was converted from pmol/L to mcU/mL when necessary. Total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were also measured in mmol/L, which were converted from mg/dl to mmol/L when necessary.

A meta-analysis was conducted using the fixed effects model and the random effects model to evaluate the weighted mean difference (SMD) with 95% confidence intervals (CI) for continuous outcomes. Cochran's Q statistic and the I-square (I^2) statistic were used to assess the statistical heterogeneity in the meta-analysis. If the data were homogeneous ($P > 0.05$), a fixed effect model meta-analysis was performed; if the data were heterogeneous ($P < 0.05$), a random effects model meta-analysis was performed. The I^2 statistic was used to assess the heterogeneity between studies, with low, moderate, and high degrees of heterogeneity, defined as I^2 values ranging from 0 to 25%, 26–75%, and 76–100%, respectively (Higgins et al., 2003). Funnel plots and Egger's tests were used to evaluate publication bias in each analysis. In addition, sensitivity analysis was performed on each study to assess the impact of individual factors on the overall meta-analysis results. Data analysis was conducted using Stata version 17.0 (Stata Corporation, College Station, TX, USA) and Review Manager software (RevMan version 5.4).

3. Results

3.1. Search results

Our initial search generated 1957 pertinent publications, of which 919 were excluded because of duplicate records. Subsequently, 1038 records were excluded based on the title/abstract review, and 42 publications remained for screening based on full-text information. After a thorough examination of the full text of these articles, 31 records were further removed for the following reasons: subjects with other diseases (5), inclusion of male subjects (7), absence of a probiotic intervention (1), unclear probiotic strains and dosages (1), absence of the desired outcomes (3), absence of overweight and obese women (1), and abstract articles (13). Finally, 11 studies(Brahe et al., 2015; Fathi et al., 2016, 2017; Gomes et al., 2017; Lee et al., 2014; Madjd et al., 2016; Majewska et al., 2020; Orak et al., 2023; Razmpoosh et al., 2020; Skrypnik et al., 2019; Szulińska et al., 2018) that satisfied the inclusion criteria were selected for the meta-analysis (Fig. 1).

3.2. Overview of the included studies

The 11 studies included were published between 2014 and 2023 and were conducted in six different countries, including South Korea (Lee et al., 2014), Denmark(Brahe et al., 2015), Brazil(Gomes et al., 2017), Turkey(Orak et al., 2023), Poland(Majewska et al., 2020; Skrypnik et al., 2019; Szulińska et al., 2018), and Iran(Fathi et al., 2016, 2017; Madjd et al., 2016; Razmpoosh et al., 2020). One study was unblinded (Razmpoosh et al., 2020), two were single-blinded(Brahe et al., 2015; Madjd et al., 2016), and the remaining were double-blinded. The duration of the intervention ranged from 6 to 12 weeks. The studies focused on obesity, with three studies specifically on this topic (Majewska et al., 2020; Skrypnik et al., 2019; Szulińska et al., 2018), whereas the remaining studies focused on both obesity and overweight. The ages of the subjects ranged from 18 to 70 years. The number of probiotic strains used in the studies varied, with two studies not specifying the number of strains(Fathi et al., 2016, 2017), one study used a single-species probiotic(Brahe et al., 2015), and the remaining studies used multi-species probiotics. The daily dose of probiotics ranged from 8.95×10^7 to 9.4×10^{10} CFU/day. Probiotics were administered in the form of kefir, Kashk, or powder in capsules or sachets. Six studies were performed with additional diet and/or exercise interventions (Fathi et al., 2016, 2017; Gomes et al., 2017; Madjd et al., 2016; Orak et al., 2023; Razmpoosh et al., 2020). A summary of the characteristics of the included studies is shown in Table 1.

3.3. Risk of bias assessment

The results of the risk of bias assessment are presented in Fig. 2A and B. Generally, two of the included studies were classified as having a low risk of bias(Gomes et al., 2017; Szulińska et al., 2018), whereas eight were considered to have an unclear risk of bias(Brahe et al., 2015; Fathi et al., 2016, 2017; Lee et al., 2014; Majewska et al., 2020; Orak et al., 2023; Razmpoosh et al., 2020; Skrypnik et al., 2019). Finally, one studies were found to have a high risk of bias(Madjd et al., 2016). The

Table 1
Studies included in this meta-analysis.

Author/year	Study design	Country	Duration	Population	Age (years)	Probiotic(s)	Dose (CFU/day)	Vehicle	Control	Dietary and/or exercise intervention	Main outcomes
Lee et al., 2014(Lee et al., 2014)	DB, PC	Korea	8 weeks	Women with overweight or obesity	19~65	*S.thermophiles (KCTC 11870BP), L. plantarum (KCTC 10782BP), L. acidophilus (KCTC 11906BP), L. rhamnosus (KCTC 12202BP), B. lactis (KCTC 11904BP), B. longum (KCTC 12200BP), and B.breve (KCTC 12201BP)*	ND	capsules	*Bofutsushosan*	No	BW, BMI, WC, BF, LIP
Brahe et al., 2015(Brahe et al., 2015)	SB, PC	Denmark	6 weeks	Women with obesity	40~70	*L. paracasei* F19	9.4×10^{10}	Sachet	Maltodextrin	No	FBG, INS, HOMA-IR, LIP
Fathi et al., 2016 (Fathi et al., 2016)	DB, PC	Iran	8 weeks	Women with overweight or obesity	25~45	ND	ND	Kefir	Low-fat dairy product	Yes	BW, BMI, WC
Madjd et al., 2016(Madjd et al., 2016)	SB, PC	Iran	12 weeks	Women with overweight and obesity	18~50	*L. acidophilus* LA5 and *B. lactis* Bb12	2×10^{7}	Yogurt	Yogurt	Yes	BW, BMI, WC, FBG, INS, HOMA-IR, HbA1C, LIP,
Fathi et al., 2017 (Fathi et al., 2017)	DB, PC	Iran	8 weeks	Women overweight or obesity	25~45	ND	ND	Kefir	Low-fat dairy product	Yes	LIP
Gomes et al., 2017(Gomes et al., 2017)	DB, PC	Brazil	8 weeks	Women with overweight or obesity	20~59	*L.acidophilus* LA-14, *L. casei* LC-11, *L. lactis* LL-23, *B. bifidum* BB-06, and *B. lactis* BL-4	2×10^{10}	sachet	maltodextrin, modified starch, xylitol, and silicium dioxide	Yes	BW, BMI, WC, BF, HBA1C, LIP
Szulińska et al., 2018(Szulińska et al., 2018)	DB, PC	Poland	12 weeks	Women with obesity	45~70	*B. bifidum* W23, *B. lactis* W51, *B. lactis* W52, *L. acidophilus* W37, *L. brevis* W63, *L. casei* W56, *L. salivarius* W24, *Lc. Lactis* W19, and *Lc. lactis* W58.	1×10^{10} 2.5×10^{9}	Sachet	Maize starch and maltodextrins	No	BW, BMI, WC, BF, AF, FBG, INS, HOMA-IR, BP, LIP
Skrypnik et al., 2019(Skrypnik et al., 2019)	DB, PC	Poland	12 weeks	Women with obesity	40~70	*B. bifidum* W23, *B. lactis* W51, *B. lactis* W52, *L. acidophilus* W37, *L. brevis* W63, *L. casei* W56, *L. salivarius* W24, *Lc. lactis* W19, and *Lc. lactis* W58	1×10^{10} 2.5×10^{9}	Sachet	ND	No	BF
Majewska et al., 2020(Majewska et al., 2020)	DB, PC	Poland	12 weeks	Women with obesity	45~70	*B. bifidum* W23, *B. lactis* W51, *B. lactis* W52, *L. a cidophilus* W37, *L. brevis* W63, *L. casei* W56,	1×10^{10}	Sachet	ND	ND	LIP

(*continued on next page*)

Table 1 (*continued*)

Author/year	Study design	Country	Duration	Population	Age (years)	Probiotic(s)	Dose (CFU/day)	Vehicle	Control	Dietary and/or exercise intervention	Main outcomes
						L. salivarius W24, *Lc. Lactis* W19 and *Lc. lactis* W58.					
Razmpoosh et al., 2020(Razmpoosh et al., 2020)	PC	Iran	8 weeks.	Women with overweight or obesity	20–60	*L. acidophilus* La5, *B. lactis* Bb12	9.25×10^7 for *L. acidophilus* La5, 8.95×10^7 *for B. lactis* Bb12	Kashk	a low energy diet,	Yes	BMI, WC, BF, FBG, LIP
Orak et al. (2023)	DB, PC	Turkey	8weeks	Women with overweight or obesity	19–50	*E.faecium CBT EF4, L. plantarum CBT LP3, S.thermophilus CBT ST3, B. lactis CBT BL3, L. CBT LA1 and B.longum CBT BG7*	3×10^9	capsule	a weight-loss diet and an exercise program	Yes	BW, BMI, WHR

BW, body weight; BMI: Body mass index; BF: Body fat; CFU: Colony-forming units; DB: Double-blind; FBG, glucose; HOMA-IR: Homeostasis model assessment-insulin resistance; HbA1C: Glycated hemoglobin; INS: Insulin; LIP: Lipid profile; ND, not differentiated. PC: Placebo controlled; SB: Single-blind; UB: Unblinded; WC: Waist circumference; WHR: Waist-to-hip ratio.
Probiotic strain: *B: Bifidobacterium; E: Enterococcus*; *L: Lactobacillus*; *Lc: Lactococcus*; *S: Streptococcus*.

most frequent reason for studies categorized as having an unclear risk of bias was insufficient description of methods for random sequence generation, allocation concealment, or outcome assessment blinding. On the other hand, the primary reason for studies being categorized as having a high risk of bias was the failure to carry out blinded subjects and personnel.

3.4. Effects of probiotic intake on body weight, BMI, WC and fat mass

To assess the effects of probiotic supplementation on BW, BMI, WC, and fat mass in overweight or obese women, data were extracted from eligible studies. The effect of probiotic intake on BW was reported in 7 intervention studies ($N = 405$). The results of subsequent meta-analysis revealed a non-significant effect of probiotic use on BW in women with overweight/obesity (SMD = −0.18 kg; 95% CI: −0.61, 0.26 kg; $P = 0.43$), with a high level of heterogeneity ($I^2 = 78\%$, $P < 0.0001$; Fig. 3A). The effect of probiotic intake on BMI was reported in 7 intervention studies ($N = 400$), and the results showed a non-significant effect of probiotic use in reducing BMI in overweight/obese women (SMD = −0.31; 95% CI: −0.75, 0.14; $P = 0.18$), with a moderate level of heterogeneity ($I^2 = 79\%$, $P < 0.0001$; Fig. 3B). Five studies ($N = 336$) reported data on fat mass change, and the analysis of the pooled estimate showed a non-significant effect of probiotic supplementation in reducing the fat mass compared to controls (SMD = −0.14 kg; 95% CI: −0.35, 0.08 kg; $P = 0.21$), without significant heterogeneity ($I^2 = 0\%$, $P = 0.50$; Fig. 3C). Six studies ($N = 366$) examined changes in WC after probiotic intake, and the results revealed a significant reduction in WC when probiotics were given, with an SMD of −0.39 cm between the probiotic and control groups (95% CI: −0.60, −0.18 cm, $P = 0.0003$), without a moderate heterogeneity ($I^2 = 33\%$, $P = 0.18$; Fig. 3D). Two studies ($N = 77$) assessed changes in the waist-to-hip ratio (WHR). Analysis after data pooling detected a non-significant reduction in WHR after probiotic intervention (SMD = −0.28; 95% CI: −0.73, 0.17; $P = 0.23$), without a low heterogeneity ($I^2 = 16\%$, $P = 0.28$) as shown in Fig. 3E.

3.5. Effect of probiotic intake on glucose metabolism

The effect of probiotic supplementation on glucose metabolism was assessed by analyzing data extracted from eligible studies pertaining to FBG, insulin, and HOMA-IR. The effect of probiotic intake on FBG was evaluated in five interventions ($N = 319$), and the results of the meta-analysis indicated a non-significant effect of probiotic use on FBG levels (SMD = −0.06 mmol/L; 95% CI: −0.28, 0.16 mmol/L; $P = 0.58$; Fig. 4A), with a moderate level of heterogeneity among the included trials ($I^2 = 28\%$, $P = 0.23$). Three studies involving 218 subjects measured the changes in insulin levels, and the results of the meta-analysis showed a significant decrease in insulin in the intervention group compared with the control group (SMD = −0.45 mcU/ml; 95% CI: −0.72, −0.18 mcU/ml; $P = 0.001$; Fig. 4B), with a moderate degree of heterogeneity among the included trials ($I^2 = 40\%$, $P = 0.17$). The effect of probiotic intake on HOMA-IR was analyzed in the three interventions, and no significant difference was observed between the probiotic and control groups (SMD = −0.35; 95% CI: −0.83, 0.13; $P = 0.16$; Fig. 4C), with a moderate level of heterogeneity among the studies ($I^2 = 66\%$, $P = 0.03$).

3.6. Effect of probiotic intake on lipid metabolism

To investigate the impact of probiotic supplementation on lipid metabolism, data on TC, TG, HDL-C, and LDL-C levels were extracted from relevant studies. The effects of probiotic intake on TC, TG, and HDL-C were reported in eight interventions (N = 450), while the effects of probiotic intake on LDL-C were reported in seven interventions ($N = 414$). After analyzing the pooled estimate, it was revealed that probiotic supplementation significantly reduced LDL-C levels (SMD = −0.51 mmol/L; 95% CI: −0.92, −0.11 mmol/L; $P = 0.01$), compared to control group (Fig. 5D), with a moderate level of heterogeneity ($I^2 = 75\%$, $P = 0.0002$). However, the pooled effect of probiotics on TC (SMD = −0.30 mmol/l; 95% CI: −0.63, 0.03 mmol/l; $P = 0.07$; Fig. 5A), TG (SMD = −0.11 mmol/l; 95% CI: −0.30, 0.08 mmol/l; $P = 0.24$; Fig. 5B) and HDL-C (SMD = 0.16 mmol/l; 95% C I: −0.07, 0.35 mmol/l; $P = 0.09$; Fig. 5C) were non-significant, with moderate heterogeneity for TC ($I^2 = 66\%$, $P = 0.003$; Fig. 5A), TG ($I^2 = 31\%$, $P = 0.17$; Fig. 5B), and HDL-C ($I^2 = 39\%$, $P = 0.11$; Fig. 5C).

3.7. Subgroup analysis of indicators of weight, glucose and lipid metabolism of overweight or obese women

Subgroup analyses were performed for body weight, BMI, fat mass,

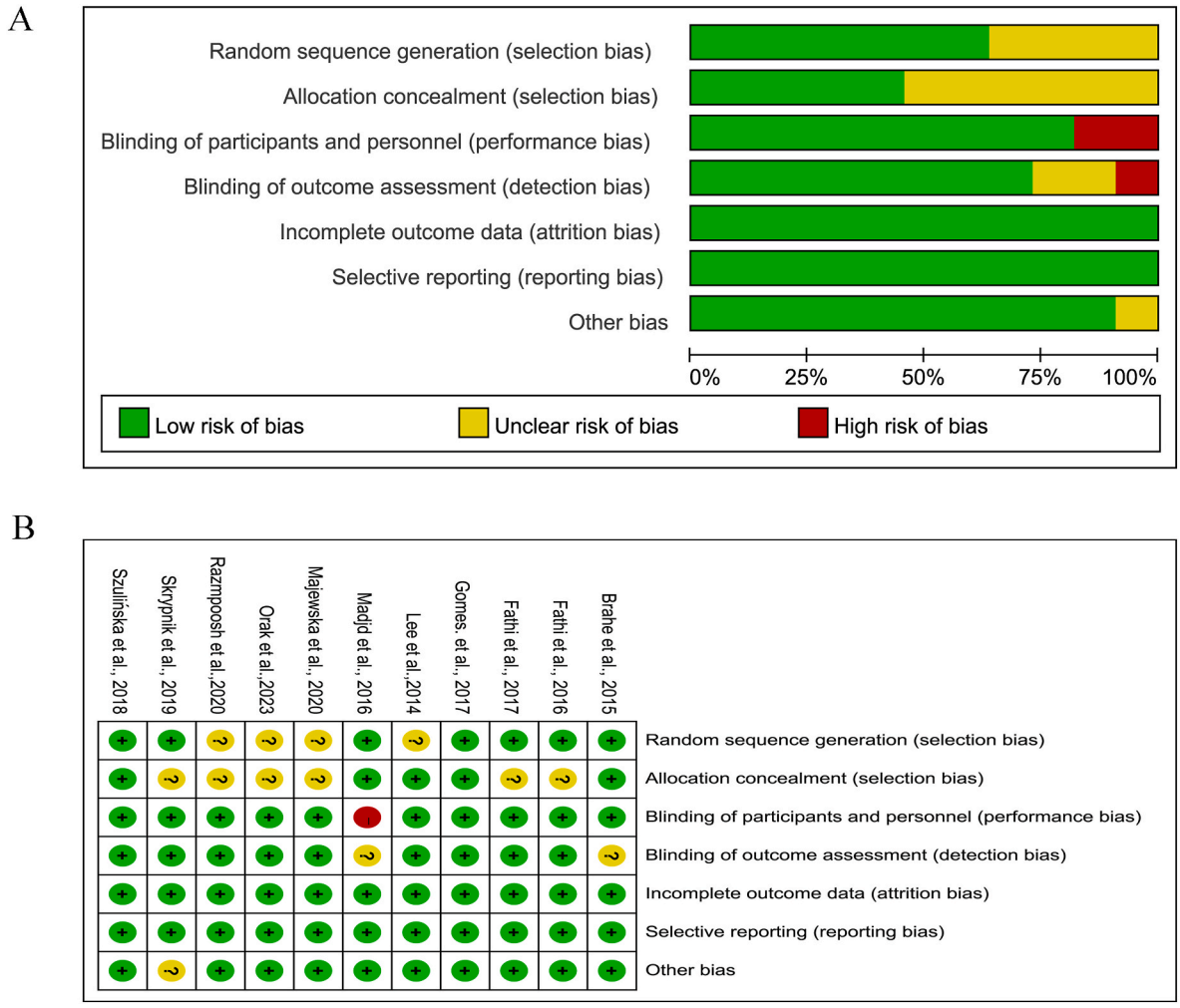

Fig. 2. Summary of results of risk of bias analysis. The risk of bias analysis of each of the 39 included studies. "+" in green circle, "-" in red circle, and "?" in yellow circle represent low, high, and unclear risk of bias, respectively (A). The risk of bias distribution across all included studies (B). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

WC, FBG, insulin, TC, TG, HDL-C, and LDL-C levels (Table 2). Initially, the effects of probiotic intake in trials with shorter interventions were compared (<12 weeks) with those in trials with longer interventions (≥12 weeks). The results showed that WC was significantly reduced following a shorter (<12 weeks) intervention period ($P < 0.05$), insulin was significantly reduced following a longer (≥12 weeks) interventions ($P < 0.05$). Furthermore, a significant decrease in LDL-C was observed in both shorter and longer intervention periods. Meanwhile, we observed that TC was significantly reduced following a longer intervention (≥12 weeks) ($P < 0.05$). Subsequently, this study examined whether dietary and/or exercise interventions influenced these parameters. WC and LDL-C was significantly lower in studies with or without diet and/or exercise interventions, whereas insulin was only lower in studies without dietary interventions ($P < 0.05$). Meanwhile, we observed that fat mass was significantly reduced with dietary interventions ($P < 0.05$). Additionally, meta-regression analysis was performed to determine the potential sources of heterogeneity. The results demonstrated that the duration of intervention and were not contributing factors affecting the heterogeneity observed in these studies,.

3.8. Publication bias and sensitivity analysis

We examined publication bias by generating funnel plots (Supplementary Fig. S1) and performing Egger's test. For the probiotic supplementation improves glycemic control, our analysis revealed a significant difference publication bias in insulin ($P = 0.045$, Table 3). However, no significant differences in publication bias were observed for the other outcomes ($P > 0.05$). Finally, to further examine the sensitivity of the results, sensitivity analyses were performed on the ten parameters that demonstrated significant publication bias. The results of these analyses indicate that the removal of any study involving these parameters would not affect the overall results.

4. Discussion

This meta-analysis is the first to assess the impact of probiotic supplementation among overweight and obese adult women based on sex-specific criteria. This meta-analysis described and evaluated 11 RCTs studies, and the results showed that probiotic intervention is effective in promoting weight loss and glucose and lipid metabolism in overweight or obese women. Probiotic intake resulted in a significant decrease in

WC and insulin and LDL-C levels. Given the high prevalence of overweight/obesity and CVD, the meta-analysis findings support that probiotic supplementation is an important health management strategy for women with overweight or obesity, as it can lower some weight, glucose, and lipid metabolism parameters. Furthermore, the impact of probiotics in overweight/obese adult women in this study differed from earlier meta-analyses of probiotics in all adults. It implies that sex may play a crucial role in the effects of probiotics on weight loss, glucose and

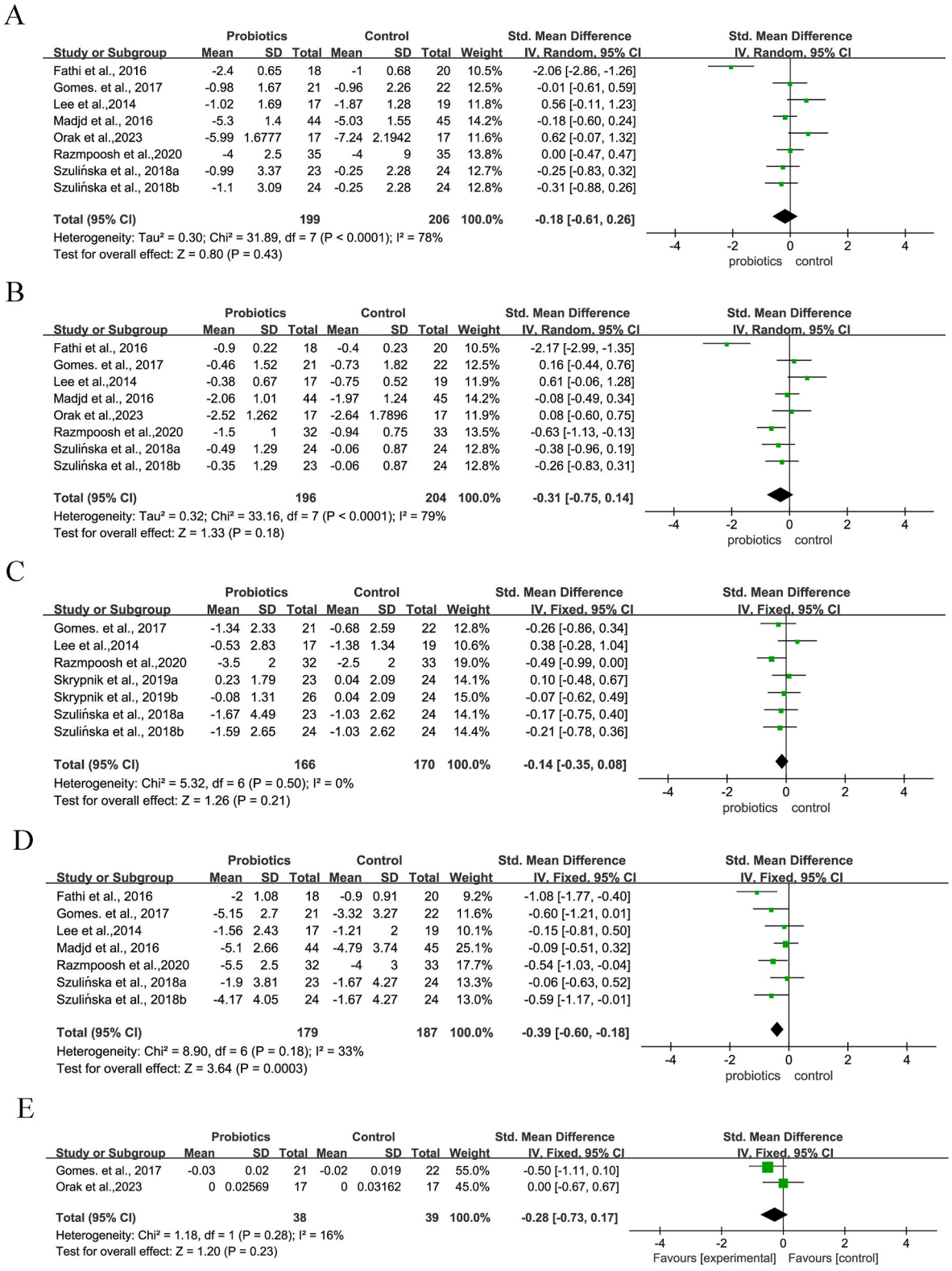

Fig. 3. Forest plots of the effects of probiotics on body weight (A), body mass index (B), fat mass (C), waist circumference (D), and waist-to-hip ratio (E). Skrypnik et al., 2019, dose (CFU/day) of probiotic = 1×10^{10}, Skrypnik et al., 2019, dose (CFU/day) of probiotic = 2.5×10^{9}; Szulińska et al. (2018) a, dose (CFU/day) of probiotic = 1×10^{10}, Szulińska et al. (2018) b, dose (CFU/day) of probiotic = 2.5×10^{9}.

lipid metabolism in overweight/obese women. In future probiotic applications, we may need take sex into account.

Several meta-analyses have evaluated the effects of probiotics on body adiposity in overweight or obese adults; however, the results obtained are inconsistent(Borgeraas et al., 2018; Mayta-Tovalino et al., 2023; Perna et al., 2021; Pontes et al., 2021; Tomé-Castro et al., 2021). This variability may be due to the different sex composition of the participants in the included studies. This meta-analysis found that probiotic supplementation could not reduce body weight, BMI, and fat mass in women with overweight or obesity based on pooled data from the literature (7studies, as of April 2024), which is consistent with previous studies on postmenopausal women(Li et al., 2023). It is probably related to the higher fat mass in women(Kapoor et al., 2019; Regensteiner and Reusch, 2022). Moreover, the fat distribution varies by sex, with men having larger central adiposity and women (particularly before menopause) having greater peripheral fat depots(Bray et al., 2018; Milionis et al., 2023; Zore et al., 2018). This may also have contributed to the non-significant effects of probiotic supplementation. Consequently, the meta-analysis findings suggest that probiotics may be more effective for weight management in adults with central obesity. The fact that probiotic intake significantly decreased WC in women with overweight/-obesity in this meta-analysis supports this claim.

Furthermore, the distribution of body fat that varies between males and females, is influenced by the composition of the gut microbiome (Min et al., 2019; Valeri and Endres, 2021). Generally, data from both animal and human studies has demonstrated that obesity and metabolic syndrome are associated with microbial imbalances, or dysbiosis(Geng et al., 2022; Gomes et al., 2018). Probiotics have been shown to restore healthier gut microbiota from a disease-linked state, suggesting a potential anti-obesity mechanism that may involve the modulation of an imbalanced gut microbiota in adults(Sivamaruthi et al., 2019). Some probiotic strains have been reported to increase the abundance of beneficial bacteria, such as *Bifidobacterium* and *Lactobacillus*, (Sivamaruthi et al., 2019). These bacteria produce specific beneficial metabolites such as short-chain fatty acids (SCFAs)(Butt and Volkoff, 2019; Seimon et al., 2014). However, the relationship between these beneficial bacteria and fat mass distribution varied between men and women. Studies have shown that certain strains of *Lactobacillus* and *Ruminococcus* genera exhibit a negative association with the gynoid fat ratio in women but not in men. Meanwhile, different taxa from the *Holdemanella* genus, *Erysipelotrichaceae* family, exhibited a negative association with android fat ratio in women but a positive association in men(Min et al., 2019). This evidence suggests that differences in the application of probiotics for weight management of overweight and obese individuals may need to consider sex differences in the future.

This meta-analysis demonstrated that probiotic supplementation enhanced only the insulin level among the glucose metabolism indicators but not the FBG or HOMA-IR in overweight or obese women. These findings indicated that probiotics may improve insulin sensitivity in women. Although insulin sensitivity differs between men and women (Regensteiner and Reusch, 2022), our results are consistent with those of previous meta-analyses that did not differentiate between the sexes (Pontes et al., 2021). A possible mechanism is that probiotics increase the production of SCFA, which activate G protein-coupled receptors (FFAR2 and FFAR3) on gut enteroendocrine L cells. This leads to a reduction in inflammatory factors, an increase in glucagon-like peptide-1 release, and an improvement in insulin resistance(Byrne et al., 2015; Drucker, 2018). Additionally, the results of the meta-analysis showed that probiotics did not significantly improve the insulin sensitivity index and HOMA-IR. This may be attributed to the absence of a significant reduction in FBG levels. Although some recent meta-analyses of patients with type 2 diabetes have demonstrated that probiotics can significantly improve FBG (Liang et al., 2021; Naseri et al., 2022; Yao et al., 2017), this benefit was not observed in overweight or obese women in this study. This discrepancy might be attributable to the lower FBG levels of the women in this study compared to those of the diabetic

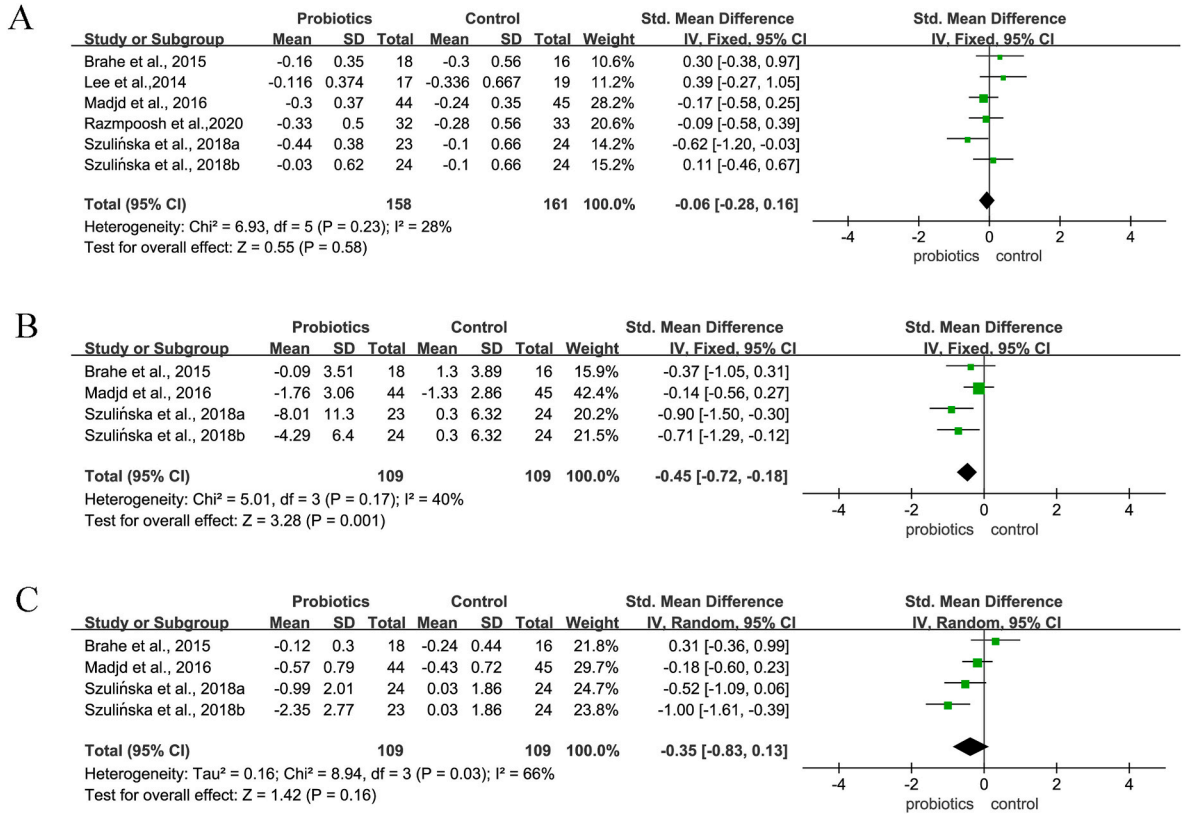

Fig. 4. Forest plots of the effects of probiotics on glucose (A), insulin (B) and glycated hemoglobin, HbA1C (C). Szulińska et al. (2018) a, dose (CFU/day) of probiotic $= 1 \times 10^{10}$, Szulińska et al. (2018) b, dose (CFU/day) of probiotic $= 2.5 \times 10^{9}$.

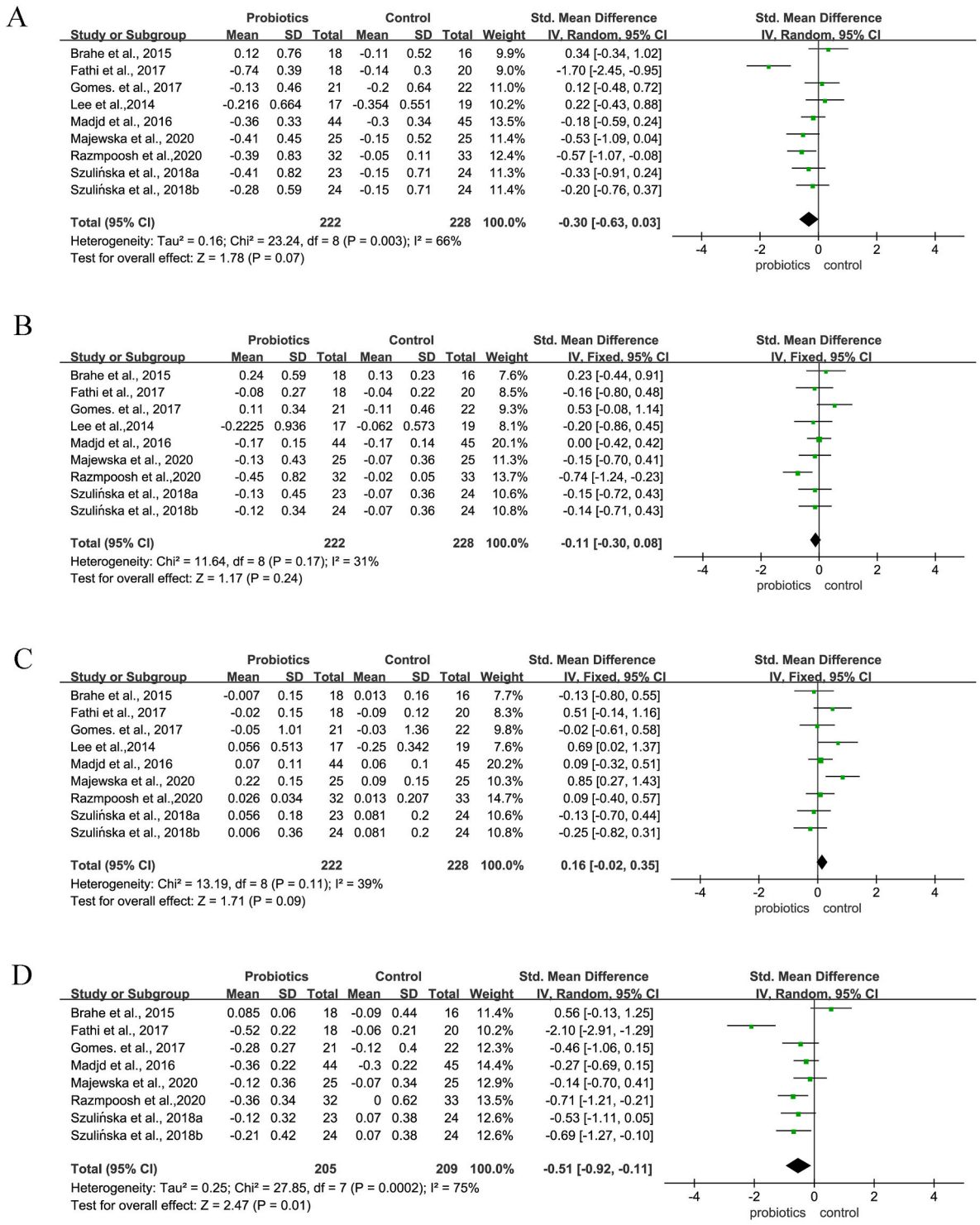

Fig. 5. Forest plots of the effects of probiotics on total cholesterol (A), triglycerides (B), high-density lipoprotein cholesterol (C), and low-density lipoprotein cholesterol (D). Szulińska et al. (2018) a, dose (CFU/day) of probiotic $= 1 \times 10^{10}$, Szulińska et al. (2018) b, dose (CFU/day) of probiotic $= 2.5 \times 10^{9}$.

patients.

Obesity and being overweight frequently contribute to abnormal lipid metabolism. This study revealed that probiotics can reduce LDL-C levels in overweight or obese women, suggesting that probiotics may enhance lipid metabolism in women under these conditions. Elevated LDL-C is a significant risk factor for CVD(DiRienzo, 2014; Grundy, 2008). The primary objective of lipid-lowering therapy is to employ safe, cost-effective, and non-pharmacological measures to reduce LDL-C levels, and probiotics may be a viable approach to achieve this goal. Previous meta-analyses have shown that probiotics have a modulating effect on lipid levels in people with type 2 diabetes, overweight/obesity and other high-risk groups for CVD (Borgeraas et al., 2018; DiRienzo, 2014; Mayta-Tovalino et al., 2023; Pontes et al., 2021; Yan et al., 2019; Yao et al., 2017). Several factors could be involved in the mechanism of action of probiotics in lowering LDL-C levels. First, probiotics may decrease serum cholesterol levels by inhibiting the expression of intestinal Niemann-pick C1 like 1(NPC1L1), a key protein involved in cholesterol absorption(Bhat and Bajaj, 2020; Yoon et al., 2013). Second,

Table 2
Subgroup analysis of indicators of weight, glucose and lipid metabolism of overweight or obese women.

Indicator	Subgroup	Subgroup parameter parameter parameter	*n*	Weighted mean difference (95% CI)	I^2 (%)	P^a	P^b	P^c
Body weight	Duration of intervention	<12 weeks	5	−0.15 (−0.94, 0.63)	87	0.70	<0.0001	0.85
		≥12 weeks	2	−0.23(-0.52, 0.06)	0	0.12	0.94	
	Dietary and/or exercise intervention	No	3	−0.49 (−1.41, 0.43)	88	0.30	<0.0001	0.29
		Yes	4	0.03 (−0.26, 0.33)	22	0.82	0.28	
Body mass index	Duration of intervention	<12 weeks	5	−0.37 (−0.18, 0.44)	88	0.37	<0.0001	0.71
		≥12 weeks	2	−0.39 (−0.93, 0.15)	0	0.17	0.68	
	Dietary and/or exercise intervention	No	3	−0.53 (−1.50, 0.44)	89	0.29	<0.0001	0.47
		Yes	4	−0.15 (−0.49, 0.20)	41	0.41	0.17	
Fat mass	Duration of intervention	<12 weeks	3	−0.16 (−0.66, 0.34)	54	0.53	0.11	0.80
		≥12 weeks	2	−0.09 (−0.37, 0.19)	0	0.54	0.68	
	Dietary and/or exercise intervention	No	3	−0.02 (−0.28, 0.25)	0	0.91	0.71	0.10
		Yes	2	−0.40 (−0.78, −0.02)	0	0.04	0.56	
Waist circumference	Duration of intervention	<12 weeks	4	−0.58(-0.87, −0.28)	19	0.0002	0.29	0.12
		≥12 weeks	2	−0.21 (−0.52, 0.10)	11	0.16	0.33	
	Dietary and/or exercise intervention	No	3	−0.44(-0.75, −0.13)	51	0.005	0.11	0.66
		Yes	3	−0.35 (−0.63, −0.06)	24	0.02	0.27	
Fasting blood glucose	Duration of intervention	<12 weeks	3	0.13 (−0.21, 0.47)	0	0.44	0.44	0.16
		≥12 weeks	2	−0.23 (−0.61, 0.15)	38	0.23	0.20	
	Dietary and/or exercise intervention	No	3	−0.01 (−0.32, 0.30)	56	0.95	0.08	0.58
		Yes	2	−0.13 (−0.45, 0.18)	0	0.40	0.83	
Insulin	Duration of intervention	<12 weeks	1	−0.37 (−1.05, 0.31)	–	0.29	–	0.79
		≥12 weeks	2	−0.47 (−0.77, −0.17)	60	0.002	0.08	
	Dietary and/or exercise intervention	No	2	−0.68 (−1.04, −0.32)	0	0.002	0.52	0.05
		Yes	1	−0.14 (−0.56, 0.27)	–	0.50	–	
Total cholesterol	Duration of intervention	<12 weeks	5	−0.08 (−0.37,0.22)	81	0.61	0.0003	0.30
		≥12 weeks	3	−0.29 (−0.54, −0.03)	0	0.03	0.78	
	Dietary and/or exercise intervention	No	5	−0.18(-0.44, 0.09)	72	0.18	0.003	0.27
		Yes	3	−0.02(-0.15, 0.10)	0	0.92	0.55	
Triglyceride	Duration of intervention	<12 weeks	5	−0.03 (−0.14, 0.08)	69	0.61	0.01	0.78
		≥12 weeks	3	−0.01 (−0.32, 0.29)	0	0.69	0.88	
	Dietary and/or exercise intervention	No	5	−0.11 (−0.35, 0.14)	0	0.40	0.95	0.95
		Yes	3	−0.12 (−0.40, 0.17)	81	0.42	0.005	
High-density lipoprotein cholesterol	Duration of intervention	<12 weeks	5	0.21 (−0.06, 0.48)	18	0.13	0.30	0.68
		≥12 weeks	3	0.13 (−0.13, 0.39)	65	0.34	0.04	
	Dietary and/or exercise intervention	No	5	0.24 (−0.01, 0.50)	60	0.06	0.03	0.36
		Yes	3	0.07 (−0.21, 0.35)	0	0.64	0.95	
Low-density lipoprotein cholesterol	Duration of intervention	<12 weeks	4	−0.59 (−0.90, −0.28)	88	0.0002	<0.0001	0.30
		≥12 weeks	3	−0.38 (−0.64, −0.12)	0	0.004	0.51	
	Dietary and/or exercise intervention	No	5	−0.48 (−0.76, −0.20)	85	0.0009	<0.0001	0.91
		Yes	3	−0.45 (−0.74, −0.17)	0	0.002	0.42	

CI: confidence interval.
[a] *P* value for subgroup differences between groups and $P < 0.05$, indicate a significant difference within each subgroup.
[b] *P* value for intra-subgroup heterogeneity and $P < 0.05$, indicating a significant difference.
[c] *P* value for the inter-subgroup meta-regression and $P < 0.05$, indicated that this factor may be one of the reasons for heterogeneity.

probiotics can diminish the rate of liver cholesterol synthesis and serum cholesterol levels by inhibiting the expression of 3-hydroxy-3-methyl glutaryl coenzyme A reductase (HMGCR), a key rate-limiting enzyme in cholesterol synthesis(Kumar et al., 2013). Additionally, gut microbial metabolites, such as SCFAs, can inhibit cholesterol synthesis(Park et al., 2018). Finally, the effect of probiotics on blood lipid levels may also be related to leptin levels. Probiotics showed modulatory effects only on LDL-C and not on other lipid markers in this study of overweight or obese women, which differed from studies on overweight or obese adults (Pontes et al., 2021; Yan et al., 2019). Leptin is positively correlated with LDL-C levels (Holven and Roeters Van Lennep, 2023). Women, including newborn girls, typically have higher fat mass and leptin levels than men (Volberg et al., 2013). Previous meta-analyses also found that probiotics can lower leptin levels(Noormohammadi et al., 2023), potentially through the involvement of SCFAs(Gabriel and Fantuzzi, 2019).

In subgroup analyses, the duration of probiotic intervention and the presence of dietary and/or exercise interventions influenced these indicators. Firstly, a shorter duration of probiotic use was effective in reducing WC. A longer (≥12 weeks) intervention could significantly decrease insulin levels, however, the number of studies was modest and may have been under-represented. Based on these findings, we believe that WC is a relatively easy indicator to decrease, and even with a short duration of probiotic treatment, a significant benefit can be achieved. However, additional systematic studies are required to determine the appropriate intervention time for different diseases. Moreover, a longer (≥12 weeks) intervention could significantly decrease TC levels, while in a shorter duration of probiotic use was ineffective in reducing TC. This suggests that if the primary goal is to reduce cholesterol levels in overweight or obese women, it may be necessary to supplement them with a longer (≥12 weeks) intervention. Secondly, the influence of dietary

Table 3
Evaluation of clinical parameters using Egger's test.

Parameter	Subject no., *n*	*β*	SE	*t*	*P*
Body weight	7	−4.87	5.100	−0.96	0.376
Body mass index	7	1.09	1.102	0.99	0.361
Fat mass	6	0.21	1.713	0.12	0.909
Waist circumference	6	−0.14	0.851	−0.16	0.880
Fasting blood glucose	5	1.16	2.006	0.58	0.595
Insulin	3	−2.34	0.703	−3.33	0.045
Homeostasis model assessment-insulin resistance	3	1.72	1.983	0.87	0.449
Total cholesterol	8	2.02	1.780	1.14	0.293
Triglyceride	8	0.01	0.549	0.01	0.989
High-density lipoprotein cholesterol	8	0.35	0.782	0.45	0.666
Low-density lipoprotein cholesterol	7	−0.33	3.140	−0.11	0.919

and/or exercise interventions to these indicators was different. insulin was only lower in studies without dietary interventions, however, fat mass was significantly reduced with dietary interventions. This suggests that the effects of dietary and/or exercise interventions on weight loss and glucose metabolism in overweight/obese women may be complicated and require additional research.

The current study had several limitations. Initially, certain outcomes exhibited considerable heterogeneity and publication biases. Second, different probiotic strains (s) were employed in the studies, complicating the precise evaluation and direct comparison of the efficacies of individual strains. Finally, only English-language studies were included in this meta-analysis, which may have resulted in some degree of language bias.

5. Conclusion

In conclusion, the results of this systematic review and meta-analysis indicate that probiotic supplementation has a moderate and statistically significant effect on weight loss and glucose and lipid metabolism in overweight and obese women. Generally, the duration of probiotic interventions and the presence of dietary and/or exercise interventions influence these indicators. Future clinical trials should consider the duration and implementation of diet or exercise intervention when using probiotics to manage body weight, glucose, and lipid metabolism indicators in overweight/obese women.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent for publication

Not applicable.

CRediT authorship contribution statement

Ning Cao: Conceptualization, Methodology, Data curation, Formal analysis, Writing – original draft, Visualization, Writing – review & editing. **Feiyan Zhao:** Data curation, Formal analysis. **Lai-Yu Kwok:** Writing – review & editing, Conceptualization. **Huan Wang:** Methodology. **Zhihong Sun:** Conceptualization, Methodology, Supervision.

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.

Data availability

The authors do not have permission to share data.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.crfs.2024.100810.

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