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Effects of pro-/synbiotic supplementation on anthropometric and metabolic indices in overweight or obese children and adolescents: A systematic review and meta-analysis

Hamed Mohammadi[a], Abed Ghavami[a], Amir Hadi[b,*], Gholamreza Askari[c], Michael Symonds[d], Maryam Miraghajani[e,d,**]

[a] Student Research Committee, Department of Clinical Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran
[b] Halal Research Center of IRI, FDA, Tehran, Iran
[c] Food Security Research Center, Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran
[d] The Early Life Research Unit, Academic Division of Child Health, Obstetrics and Gynaecology, and Nottingham Digestive Disease Centre and Biomedical Research Centre, The School of Medicine, University of Nottingham, Nottingham, NG7 2UH, Iran
[e] Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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ABSTRACT

Background & aims: Existing evidence on the possible effects of pro-/synbiotics on overweight or obese children and adolescents has not been fully established. Therefore, the present review was undertaken to evaluate the overall effects of pro-/synbiotics supplementation on anthropometric indices and metabolic indices in overweight or obese children and adolescents.

Methods: A systematic computerized literature search of PubMed, Scopus, ISI Web of science and Google Scholar databases was conducted up to November 2018. All RCTs using pro-/synbiotics supplements in overweight or obese children and adolescents included in this systematic review and meta-analysis.

Results: Overall 9 randomized trials including 410 subjects were identified for the present meta-analysis. Pooled analysis did not illustrate any significant changes in BMI z-score, waist circumference, weight, body fat, fasting blood sugar and lipid profiles (triglyceride, total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol) after supplementation with pro-/synbiotics for 4–16 weeks. However, subgroup analysis by intervention type revealed a significant reduction of BMI z-score in synbiotic subgroups.

Conclusion: Based on our findings, modulation of gut microbiota composition through pro-/ synbiotic supplements did not have favorable effects to manage overweight or obese children and adolescents. Further large-scale studies are warranted to confirm present findings.

1. Introduction

Overweight and obesity among children and adolescents has become one of the most important public health problems that is rising in parallel with lifestyle transitions around the world. [1,2] It is widely recognized that obesity during childhood and adolescence can lead to the development of obesity and non-communicable diseases, such as diabetes and cardiovascular diseases in adults. [3] Moreover, obese children and adolescents are at risk of psychosocial complications including poor self-esteem and depression. [4] Reducing the risk of these health concerns, through a reduction of obesity could have beneficial effects on cognitive and educational performance. [5] Although, numerous factors attribute to overweight and obesity, calorie restriction and exercise remain the primary treatment of obesity, [6,7] but their efficacy remains low. [8–10] Therefore, alternative strategies of weight management are required.

Due to the role of gut microbiota in energy homeostasis and secretion of appetite suppressing hormones, modulating its composition is a potential target to prevent obesity. [11–14] Growing evidence suggests that adverse changes in this complex ecosystem, i.e. gut dysbiosis, contribute to the development and progression of obesity. [15] In this context, pro-/synbiotics have attracted a great deal of attention. [14] According to the Food and Agriculture Organization of the United States (FAO), probiotics are defined as a culture of living

* Corresponding author at: Halal Research Center of IRI, FDA, PO Box 81745, Tehran, Iran.
** Corresponding author at: Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
E-mail addresses: amirhadi.vnt@gmail.com, Hadi@halal.ac.ir (A. Hadi), Maryam.sadatmiraghajani@nottingham.ac.uk (M. Miraghajani).

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microorganisms that when consumed in adequate amounts and duration, can have health benefits for the host. [16] "Synbiotic" refers to nutritional supplements combining probiotic and prebiotic synergistically. Prebiotics contain a group of fermentable dietary fibers that benefit the host by stimulating the growth and survival of probiotics. [17] Pro-/synbiotics both influence the abundance and functions of gut microbiota that could prevent obesity. [18]

Substantial evidence suggests that pro-/synbiotics supplementation may improve anthropometric and metabolic indices by modulating the form and/or function of the gut microbiota. [2,19] However, existing evidence on the possible effects of pro-/synbiotics on overweight or obese children and adolescents, [20–28] and its optimal role in the clinical management has not been fully established. Therefore, the present review was undertaken to evaluate the overall effect of pro-/synbiotics supplementation on anthropometric indices (i.e. body mass index (BMI), waist circumference (WC), weight, body fat), fasting blood glucose (FBS) and lipid profiles (triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C)) in overweight or obese children and adolescents.

2. Methods

2.1. Search strategy

This systematic and meta-analysis was performed based on the Preferred Reporting Item for Systematic Review and meta-analysis (PRISMA) guideline. A systematic computerized literature search of PubMed, Scopus, ISI Web of science and Google Scholar databases was conducted up to November 2018 using following search terms: ("probiotics" OR "synbiotics" OR "symbiotics" OR "Fermented Foods" OR "Lactobacillus" OR "Bifidobacterium") AND ("children" OR "adolescents" OR "Teenager" OR "Youth") AND ("Intervention Studies" OR "intervention" OR "controlled trial" OR "randomized" OR "randomised" OR "random" OR "randomly" OR "placebo" OR "assignment"). In addition, the reference lists of all eligible papers were further checked to find relevant studies not found from computerized search.

2.2. Eligibility criteria

Relevant articles were included if they: 1) applied a clinical trial design; 2) examined the effects of pro-/synbiotics on anthropometric or metabolic indices; 3) provided sufficient information on anthropometric indices in both treatment and control groups; 4) were conducted on overweight or obese children and adolescents (2–18 years); 5) administered pro-/synbiotics for at least 4 weeks. Studies were excluded if they: 1) were uncontrolled studies; 2) used a mixture of pro-/synbiotic with other substances; 3) reported duplicate data; 4) were reviews, letters, editorial articles, or case reports.

2.3. Quality assessment

Two authors (A.G and A.H) independently evaluated the quality of selected articles using Cochrane Collaboration's tool [29] including six domains as follows: 1) random sequence generation; 2) allocation concealment; 3) blinding of participants and personnel; 4) blinding of outcome assessment; 5) incomplete outcome data; and 6) selective reporting. Each domain was classified to three categories i.e. low risk of bias, high risk of bias and unclear risk of bias. Any disagreements during the quality assessment process were resolved by panel discussions.

2.4. Data extraction

Two independent investigators (H.M and A.H) extracted relevant data. Any controversy with study selections were discussed and eventually resolved by a third reviewer (M.M). The relevant data were extracted including: first author, year of publication, target population, number and mean age of participants, study location, study design, intervention duration and supplement dosage. Also, mean and standard deviation (SD) of anthropometric and metabolic indices at baseline and end of intervention were extracted.

2.5. Data synthesis and statistical analysis

For each parameter the mean and SD at baseline and post-intervention in pro-/synbiotic and control groups was used. If the SD was not reported it was calculated with the following formula: $SD^2 = [(SD\ baseline^2 + SD\ final^2) - (2 \times R \times SD\ baseline \times SD\ final)]$ where correlation coefficient (R) was considered as 0.5. [30] To make sure that our meta-analysis is not sensitive to the selected correlation coefficient (R = 0.5), all the analyses was repeated by the use of correlation coefficient of 0.2 and 0.8. To calculate pooled effect size we used random effects model. Between-study heterogeneity was evaluated using I-square (I^2) test. To find the potential sources of between-study heterogeneity, a pre- planned subgroup analysis based on type of supplementation (probiotics or synbiotics) and duration of supplementation (equivalent or below 8 weeks/ above 8 weeks) was undertaken. The proportion of each study on the overall effect was assessed using a sensitivity analysis. Begg's rank correlation test and Egger's regression asymmetry test evaluated publication bias. Statistical analysis was performed using STATA11.2 software (StataCorp, College Station, Texas, USA).

3. Results

3.1. Selection and identification of studies

We identified 4313 records in a combined search of electronic databases. Of these, 1592 citations were found to be duplicates and therefore removed. In the title and abstract screening, 2708 publications were excluded. We identified 4313 records in a combined search of electronic databases. Of these, 1592 citations were found to be duplicates and therefore removed. In the title and abstract screening, 2708 publications were excluded [20–28] met the eligibility criteria and were included in systematic review and meta-analysis. The PRISMA flow diagram for the study selection process is presented in Fig. 1.

3.2. Study characteristics

Included studies were published between 2011 and 2017 and reported data on 410 subjects (215 subjects in intervention group and 195 in the control group). All studies were performed on overweight or obese children. Two studies were conducted on obese children with non-alcoholic fatty liver disease. [20,21] Included trials were conducted in Iran, [21,25,26] Italy, [20,28] Turkey, [23] Denmark, [22] Spain, [27] USA. [24] The duration of intervention ranged from 4 to 16 weeks. Of the 9 included RCTs, 6 used probiotics, [20–22,24,27,28] and 3 used synbiotics.[23,25,26] A blinding design was reported in all studies except for one. [23] Basic characteristics of these trials are summarized in Table 1.

3.3. Risk of bias assessment

Random allocation of participants was mentioned in all included trials. Nevertheless, only five trials described the method of random sequence generation, [20–22,27,28] Seven trials, [20–22,25–28] reported allocation concealment. Most of the included studies had low/unclear risk of bias in blinding of participants, personnel and outcome assessors, except Ipar's[23] study, which applied an open label design. Most studies showed low/unclear risk of bias based on incomplete outcome data and selective outcome reporting. Details of risk of bias assessment are presented in Table 2.

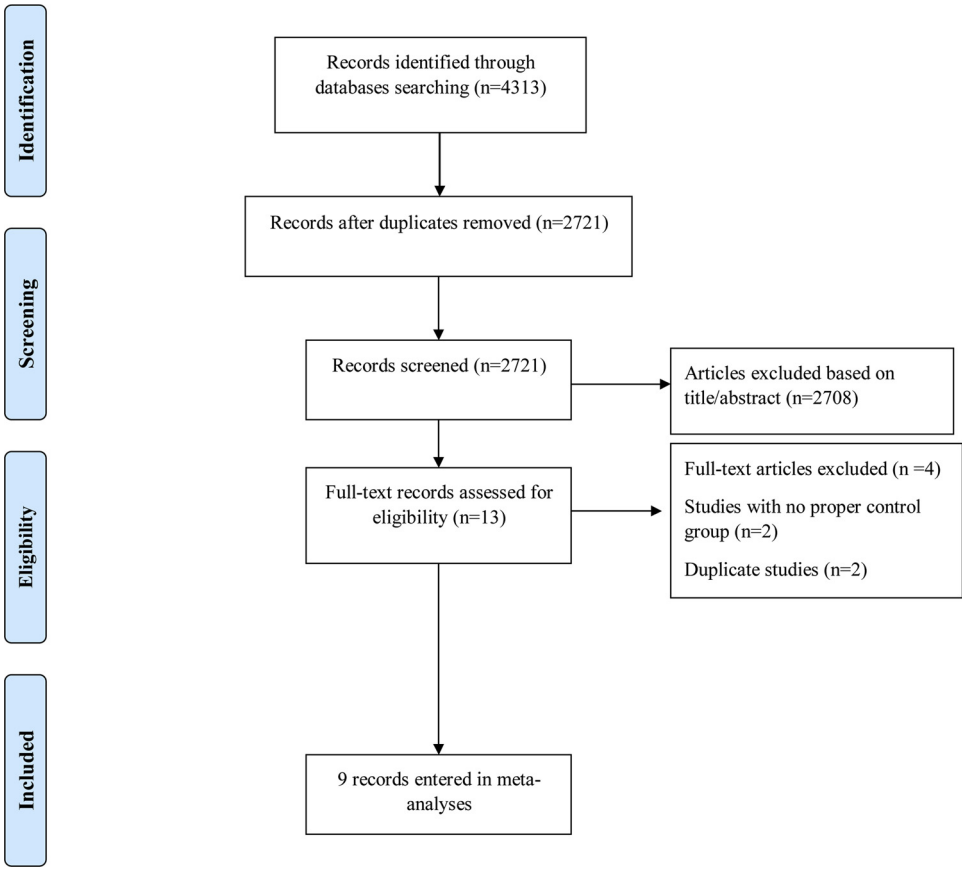

Fig. 1. PRISMA flow diagram of study selection process.
Flow chart of the process of the study selection.

*3.4. The effect of pro-/synbiotics on anthropometric indices (BMI z-score, WC, weight, **body fat**)*

The pooled mean difference of 6 studies [20,22,25–28] for the effects of pro-/synbiotics on BMI z-score was (WMD: -0.09 z-score; 95% CI: -0.23, 0.05, P = 0.19) with significant heterogeneity (I^2 = 85.0%, P < 0.001) (Fig.2a). When the meta-analysis was sub-grouped by study duration and intervention type, heterogeneity was attenuated in studies that used synbiotics (I^2 = 0.0%, P = 0.72) and studies with < 8 weeks duration (I^2 = 34.1%, P = 0.21) (Table 3). Also, subgroup analysis by intervention type revealed a significant reduction of BMI z-score in synbiotic subgroups. The sensitivity analysis revealed that exclusion of Alisi's study [20] from the analysis altered the overall effect (WMD: -0.06 z-score; 95% CI: -0.09, -0.04). Begg's (P = 0.85) and Egger's test (P = 0.81) suggested no publication bias.

Seven trials reported the data on WC. [21–27] Pooled effect size showed no effect of pro-/synbiotics supplementation on WC (WMD: -0.62 cm; 95% CI: -1.73, 0.48, P = 0.26) and no heterogeneity (I^2 = 10.7%, P = 0.34) (Fig.2b). When the meta-analysis was sub-grouped by study duration and intervention type the result remained insignificant among all subgroups (Table 3). The sensitivity analysis revealed that exclusion of the Jones study [24] from the analysis modified the overall effect (WMD: -0.92 cm; 95% CI: -1.76, -0.08). Also, Begg's (P = 0.17) and Egger's test (P = 0.12) suggested no evidence of publication bias.

The pooled mean difference of four trials [22,23,25,27] showed no effects of pro-/synbiotics on weight (WMD: 0.70 kg; 95% CI: -1.07, 2.47, P = 0.43) with no significant heterogeneity (I^2 = 0.0%, P = 0.97) (Fig.2c). When the meta-analysis was sub-grouped by intervention type the result remained insignificant among all subgroups (Table 3). Sensitivity analysis showed that no study prominently affected the overall effects, and Begg's (P = 0.85) and Egger's test (P = 0.81) suggested no evidence of publication bias.

The effect of pro-/synbiotics on body fat percent was examined in 4 clinical trials [22,24,25,27] and showed no effect on body fat content (WMD: 0.41%; 95% CI: -1.70, 2.51, P = 0.70) (Fig.2d). There was a significant heterogeneity between studies (I^2 = 78.1%, P = 0.003). Findings from the sensitivity analysis revealed that the exclusion of any single study from the analysis did not alter the overall effect. Begg's (P = 1.00) and Egger's test (P = 0.53) suggested no publication bias.

3.5. The effect of pro-/synbiotics on fasting blood glucose

Four studies reported the data on FBS, [22,24,26,27] and the meta-analysis showed no effect of pro-/synbiotics supplementation (WMD: -0.03 mg/dL; 95% CI: -2.20, 2.14, P = 0.98) with no heterogeneity (I^2 = 22.2%, P = 0.27) (Fig. 3). When the meta-analysis was sub-grouped by intervention type the result remained insignificant among all subgroups (Table 3). Findings from the sensitivity analysis revealed that the exclusion of any single study from the analysis did not alter the overall effect. Also, Begg's (P = 0.49) and Egger's test (P = 0.35) suggested no evidence of publication bias.

3.6. The effect of pro-/synbiotics on lipid profiles (LDL-C, HDL-C, TC, TG)

Overall, the effect of pro-/synbiotics supplementation on TC, LDL-C, HDL-C, and TG was assessed in 5, 5, 5 and 6 trials, respectively. Meta-analysis showed no effect of pro-/synbiotics supplementation on plasma concentrations of TC (WMD: -3.37 mg/dL, 95% CI: -8.51, 1.78, P = 0.20; Fig. 4a), LDL-C (WMD: -1.73 mg/dL, 95% CI: - 4.27, 0.80, P = 0.18; Fig. 4b), HDL-C (WMD: -0.04 mg/dL, 95% CI: -2.80, 2.71, P = 0.79; Fig. 4c), and TG (WMD: -6.41 mg/dL, 95% CI: -17.26, 4.43,

Table 1
Characteristics of included studies.

First author (publication year)	Country	Sample size (M/F)	Target Population	Mean Age	RCT design (Blinding)	Duration (wks)	Intervention of experimental group	Intervention of control group	Investigated outcomes
Vajro (2011)	Italy	20 (18/2)	Obese children	10	Parallel (yes)	8	Lactobacillus rhamnosus Strain GG 12×10^8 CFU	Placebo	BMI z score
Gobel (2012)	Denmark	50 (ND)	Obese adolescents	13	Parallel (yes)	12	L salivarius 10^{10} CFU	Placebo	BMI z-score, Fat mass, Weight, WC, TG, TC, LDL-C, HDL-C
Safavi (2013)	Iran	56 (ND)	overweight and obese children	10	Parallel (yes)	8	Lactobacillus Casei, Lactobacillus Rhamnosus, Streptococcus, Thermophilus, Bifidobacterium Breve, Lactobacillus Acidophilus, Bifidobacterium Longum and Lactobacillus Bulgaricus 2.0×10^8 CFU + frocto oligosaccharides	Placebo	BMI z-score, WC, TG, TC, LDL-C, HDL-C
Alisi (2014)	Italy	44 (24/20)	Obese children with NAFLD	10	Parallel (yes)	16	VSL#3	Placebo	BMI z-score, TG
Ipar (2015)	Turkey	77 (33/44)	Obese children	12	Parallel (No)	4	Lifestyle modification + Lactobacillus acidophilus 4.3×10^8 cfu/sachet, Lactobacillus rhamnosus 4.3×10^8 CFU, Bifidobacterium bifidum 4.3×10^8 CFU, Bifidobacterium longum 4.3×10^8 CFU, Enterococcus faecium 8.2×10^8 CFU + fructo-oligosaccharydes, lactulose	Lifestyle modification	Weight, WC, TG, TC, LDL-C, HDL-C
Famouri (2017)	Iran	64 (ND)	Obese children with NAFLD	12	Parallel (yes)	12	Lactobacillus acidophilus 3×10^9 CFU, Bifidobacterium lactis 6×10^9 CFU, Bifidobacterium bifidum 2×10^9 CFU, Lactobacillus rhamnosus 2×10^9 CFU	Placebo	WC, TG, TC, LDL-C, HDL-C
Kianifar (2018)	Iran	31 (ND)	Overweight or obese children	10	Parallel (yes)	12	Lactobacillus casei, L rhamnosus, Streptococcus thermophilus, Bifidobacterium breve, L acidophilus, B infantis, L bulgaricus 10×10^7 CFU + fructooligosaccharides	Placebo	BMI z score, Fat mass, Weight, WC
Sanchis-Chorda (2018)	Spain	48 (24/24)	Obese children	7-16	Parallel (yes)	13	Bifidobacterium pseudocatenulatum CECT 7765	Placebo	BMI z score, Fat mass, Weight, WC, TG, TC, LDL-C, HDL-C
Jones (2018)	USA	20 (8/12)	Obese Hispanic adolescents	14.4	Parallel (yes)	16	VSL#3	Placebo	Fat mass, WC

M, male; F, female; ND, no data, NAFLD, non-alcoholic fatty liver disease; CFU, colony forming units; WC, waist circumference; FBS, fasting blood sugar; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC; total cholesterol; TG, triacylglyceride.

Table 2
Risk of bias assessment for included randomized controlled clinical trials.

First author (publication year)	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting
Vajro (2011)	+	+	+	?	+	?
Gobel (2012)	+	+	+	+	+	?
Safavi (2013)	?	+	+	+	+	?
Alisi (2014)	+	+	+	+	+	?
Ipar (2015)	?	?	–	–	+	?
Famouri (2017)	+	+	+	+	+	?
Kianifar (2018)	?	+	+	+	+	?
Sanchis-Chorda (2018)	+	+	+	+	+	?
Jones (2018)	?	?	+	?	+	?

P = 0.16; Fig. 4d). There were no evidence of heterogeneity for TC, LDL-C and TG. However, significant heterogeneity was found for HDL-C (I^2 = 63.2%, P = 0.02). When the meta-analysis was stratified by intervention type and study duration the result remained insignificant among all subgroups (Table 3). No evidence of publication bias was found for TC (P = 0.62, Begg's test and P = 0.62, Egger's test), LDL-C (P = 1.00, Begg's test and P = 0.38, Egger's test), HDL-C (P = 0.32, Begg's test and P = 0.17, Egger's test), and TG (P = 0.85, Begg's test and P = 0.93, Egger's test).

4. Discussion

Historical evidence suggests that an imbalance within the gut microbiome could contribute to overweight and obesity. [2] Although, the pathogenesis and mechanisms underlying excess adiposity are complex, manipulation of the bacteria in the gastro-intestinal system to ensure a non-dysbiotic state, offers a potential therapy for overweight and obesity. [2] There are several potential mechanisms for the effectiveness of pro-/synbiotic supplementation to prevent excess weight gain. It may reduce inflammation, [31] strengthen the intestinal epithelial barrier, [32,33] and modulate the action of intestinal enzymes, [15] as well as neuroendocrine, immune functions, [34,35] thereby impacting on energy storage, [36,37] energy expenditure [37] and food intake. [35] Also, the beneficial influence of pro-/synbiotic on lipid profile and FBS might be due to the inhibition of dietary cholesterol absorption, or the suppression of bile acid reabsorption in the small intestine, [38] and reduction of intestinal inflammatory activity index, respectively. [39] However, the balance between obesity and microbiota is complex, not only affecting susceptibility to obesity, as changes in the hosts environment with obesity further influence the presence and properties of microbiota. [18,40]

As far we are aware, this is the first meta-analysis of randomized controlled trials specifically considered to evaluate the effects of pro-/synbiotic supplementation on anthropometric indices (BMI z-score, WC, weight, body fat), FBS and lipid profiles (LDL-C, HDL-C, TC, TG) in overweight or obese children and adolescents. Our goal was to determine whether pro-/synbiotic supplementation could be recommended as a public health policy to improve overweight or obese indices among children and adolescents. Our analysis of 9 randomized trials did not illustrate any significant changes in BMI z-score, WC, weight, body fat, FBS and lipid profiles after supplementation with probiotics /symbiotic for 4–16 weeks. However, subgroup analysis revealed a significant reduction of BMI z-score in with synbiotic supplementation. This is not in line with our previous meta-analysis that assessed the effects of synbiotic supplementation on anthropometric indices among participants with overweight or obesity. [2] Previous findings revealed that mentioned supplementation was effective on the body weight and WC but not on the BMI, and body fat. Interestingly, another meta-analysis illustrated weight loss among adults and minor weight gains among children and infants taking mainly Lactobacillus probiotic supplements. [41] Supplementation with a multispecies probiotic also had beneficial effects on the lipid profile and glucose, in a

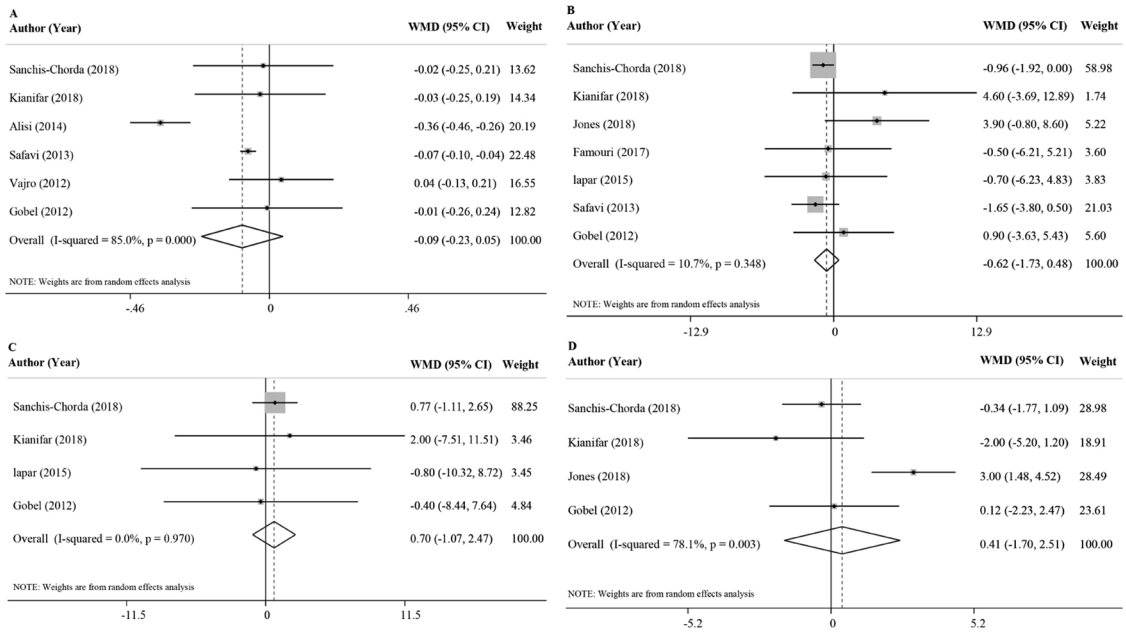

Fig. 2. Forest plot of the effect of pro-/synbiotic supplementation on anthropometric indices (BMI z-score, WC, weight, body fat).

Table 3
Subgroup analysis to assess the effect of pro/synbiotic supplementation on anthropometric and metabolic indices.

Sub-grouped by	No. of trials	Effect size[1]	95% CI	I^2 (%)	P for heterogeneity
BMI z-score					
Intervention type					
Probiotic	4	−0.10	−0.34, 0.14	86.3	< 0.001
Synbiotic	2	−0.07	−0.10, -0.04	0.0	72
Duration					
> 8 weeks	4	−0.12	−0.34, 0.10	81.2	< 0.001
≤ 8 weeks	2	−0.05	−0.13, 0.03	34.1	0.21
WC					
Intervention type					
Probiotic	4	−0.10	−1.95, 2.14	32.4	0.21
Synbiotic	3	−1.12	−3.23, 1.00	3.8	0.35
Duration					
> 8 weeks	5	0.44	−1.67, 2.56	33.1	0.20
≤ 8 weeks	2	−1.52	−3.53, 0.48	0.0	0.75
Weight					
Intervention type					
Probiotic	2	0.71	−1.12, 2.54	0.0	0.78
Synbiotic	2	0.60	−6.12, 7.33	0.0	0.68
FBS					
Intervention type					
Probiotic	2	0.28	−3.33, 3.89	0.0	0.78
Synbiotic	2	0.58	−3.58, 5.03	0.0	0.68
TC					
Intervention type					
Probiotic	3	−2.98	−11.53, 5.57	0.0	0.65
Synbiotic	2	−3.59	−10.03, 2.86	0.0	0.44
Duration					
> 8 weeks	3	−2.98	−11.53, 5.57	0.0	0.65
≤ 8 weeks	2	−3.59	−10.03, 2.86	0.0	0.44
LDL-C					
Intervention type					
Probiotic	3	−3.67	−12.17, 4.83	0.0	0.88
Synbiotic	2	−1.55	−4.20, 1.11	0.0	0.97
Duration					
> 8 weeks	3	−3.67	−12.17, 4.83	0.0	0.88
≤ 8 weeks	2	−1.55	−4.20, 1.11	0.0	0.97
HDL-C					
Intervention type					
Probiotic	3	1.75	−0.93, 4.43	11.6	0.32
Synbiotic	2	−2.10	−7.72, 3.51	69.2	0.07
Duration					
> 8 weeks	3	1.75	−0.93, 4.43	11.6	0.32
≤ 8 weeks	2	−2.10	−7.72, 3.51	69.2	0.07
TG					
Intervention type					
Probiotic	4	−4.34	−17.73, 9.05	0.0	0.76
Synbiotic	2	−10.65	−30.84, 9.54	15.4	0.27
Duration					
> 8 weeks	4	−4.34	−17.73, 9.05	0.0	0.76
≤ 8 weeks	2	−10.65	−30.84, 9.54	15.4	0.27

BMI: body mass index, WC, waist circumference; FBS, fasting blood sugar; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC; total cholesterol; TG, triacylglycerid.
[1] Calculated by Random-effects model.

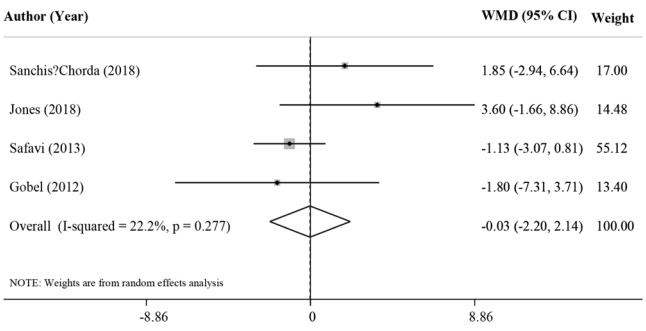

Fig. 3. Forest plot of the effect of pro-/synbiotic supplementation on FBS.

dose-dependent manner, in obese postmenopausal women. [42]

The underlying reason for the divergence in the results described here are likely to be the difference in participant characteristics, probiotic strain, dosages, antibiotic consumption, study duration, ethnic origin, and dietary context that will affect the proliferation and survival of probiotics, and the timing of exposure. [16,43,44] In addition, the discrepancy in the context of intra-individual strain differences and genotype of individuals can affect the response. [16,43,44]

The primary limitation of our meta-analyses is heterogeneity in some indices that still remained, although the results were analyzed by sensitivity and subgroup analysis. Subgrouping the studies by type of supplementation (probiotics or synbiotics) and duration of supplementation (equivalent or below 8 weeks/ above 8 weeks) did not reduce the heterogeneity except in the indices of BMI. In addition, a diversity of probiotic's strains were employed between studies, each with a different predicted impact on the microbiota. [45] This is important, as only certain strains of probiotics may regulate body weight. [45] Due to small number of studies, we could not subgroup the studies by probiotic strain. Furthermore, the effects of confounding variables including, dietary patterns and life styles, intra-individual strain differences, and genotype of individuals on the efficacy of pro-/synbiotic supplements remains unclear.

The strength of the current study was the subgroup analysis and assessment of the type of supplementation and duration of supplementation. Moreover, existence of homogeneity for WC, weight and FBS values were reported. Furthermore, we searched, screened, conducted and reported the review carefully with minimizing biases in this process by adhering to the PRISMA guidelines.

5. Implications for practice

The evidence from our meta-analysis suggests that only giving synbiotic supplements to overweight or obese children and adolescents may have beneficial effects on BMI. However, we are still unable to provide guidelines for clinical application due to the complex nature of obesity and its effect on gut microbiota. Moreover, a particular concern about using the synbiotic/probiotic products in children with serious medical conditions and a possible increase in infectious complications among them should be considered. [46]

6. Implications for research

As, there are some deficiencies in the quality of literature which impact on the final results, we stress the importance of larger, randomized multi-centre studies without attrition bias and selective reporting. These would allow more accurate evidence-based conclusions and practical applications. The next challenge is to establish the appropriate safe dose of pro-/synbiotic for improving obesity for target age groups. Although they are known to be safe for human consumption, there is a risk of antibiotic resistance, [47] and gastrointestinal disorders. [48]

7. Conclusion

Based on our findings, modulation of gut microbiota composition through pro-/ synbiotic supplements did not have favorable effects to manage overweight or obese children and adolescents. Further large-scale studies are warranted to confirm present findings.

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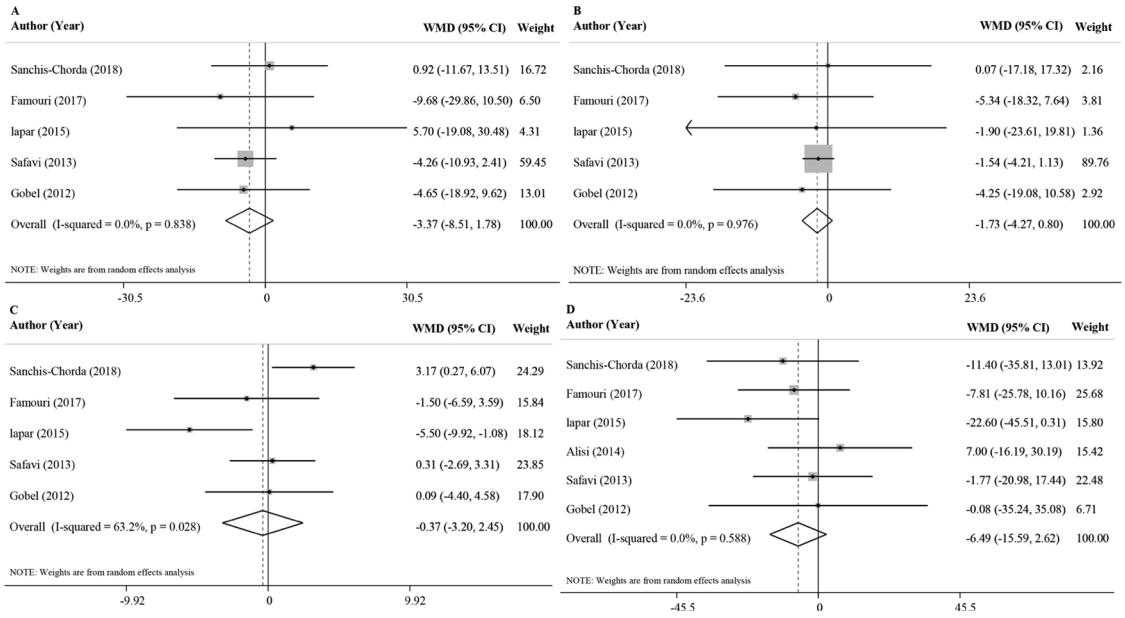

Fig. 4. Forest plot of the effect of pro-/synbiotic supplementation on lipid profiles (LDL-C, HDL-C, TC, TG).

Conflict of interest

None.

Acknowledgments

None.

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