ORIGINAL ARTICLE

Effectiveness of probiotics in type 2 diabetes: a meta-analysis

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KEY WORDS

diabetes, gut microbiota, meta-analysis, metabolism, probiotics

ABSTRACT

INTRODUCTION An increasing number of studies suggest that the use of probiotics may have a beneficial effect in patients with type 2 diabetes.

OBJECTIVES The aim of the study was to assess the ability of probiotics to modify selected cardiometabolic risk factors in subjects with type 2 diabetes.

METHODS PubMed, Embase, Cochrane Library, and Scopus databases were thoroughly reviewed up to January 2015 to search for randomized controlled trials (RCTs) that examined the effect of probiotics on selected modifiable cardiometabolic parameters in patients with type 2 diabetes. The following endpoints were considered: fasting plasma glucose (FPG), insulin concentration, insulin resistance, hemoglobin A_{1c} (HbA_{1c}), as well as the levels of total cholesterol, triglycerides, low-density and high-density lipoprotein cholesterols, and C-reactive protein (CRP). A total of 571 RCTs were initially identified, of which 8 trials with 438 individuals were selected for meta-analysis. The effects of probiotics were calculated for each parameter.

RESULTS The meta-analysis showed a significant effect of probiotics on reducing HbA_{1c} levels (standardized mean difference [SMD], –0.81; confidence interval [CI], –1.33 to –0.29, $P = 0.0023$; $I^2 = 68.44\%$; $P = 0.0421$ for heterogeneity) and HOMA-IR (SMD, –2.10; CI –3.00 to –1.20, $P < 0.001$; $I^2 = 82.91\%$; $P = 0.0029$ for heterogeneity). Supplementation with probiotics did not have a significant effect on FPG, insulin, and CRP levels as well as the lipid profile.

CONCLUSIONS Our meta-analysis suggests that probiotic supplementation might improve, at least to some extent, metabolic control in subjects with type 2 diabetes. However, larger well-designed, long-term RCTs are needed to confirm any potentially beneficial relationship between the use of probiotics and modifiable cardiometabolic risk factors in patients with type 2 diabetes.

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INTRODUCTION For centuries, one of the most effective methods of maintaining the balance of the intestinal microbiome was the use of probiotics defined as "live microorganisms which when administered in adequate amounts confer a health benefit on the host".[1] Products containing probiotic bacteria have been increasingly applied to prevent or treat numerous disorders such as irritable bowel syndrome, inflammatory bowel disease, chronic idiopathic constipation, obesity, allergic and pulmonary diseases, and various types of diarrhea.[2] It has also been suggested that probiotic supplementation alone or foods supplemented with probiotics may positively modify the metabolic disturbances associated, directly or indirectly, with chronic hyperglycemia.

While the human body comprises approximately 60 trillion somatic cells, the gut microbiota consists of hundreds of trillions (over 100×10^{18}) of bacteria, mainly Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria.[3] It was found that lean and obese individuals have different ratios of Bacteroidetes and Firmicutes.[4-6] Interestingly, other analyses of intestinal microbiota have shown that patients with type 2 diabetes have a significantly lower number of bacteria that produce butyrate (Roseburia, *Faecalibacterium prauznitzii*), when compared with healthy people.[7,8] Butyrate, a short-chain fatty acid (SCFA), is an important source of energy for intestinal cells.[9] Several studies have demonstrated that SCFAs serve as substrates for gluconeogenesis

and lipogenesis, and affect the proliferation, differentiation, and modulation of gene expression.[10] SCFAs bind to G protein-coupled receptors and exert various biological effects, including the regulation of glucagon-like peptide 1, which is associated with the improvement of insulin secretion and thus, with lower glucose levels.[11] Additionally, SCFAs affect metabolism via interaction with histone deacetylases, which in turn influences the expression of genes, including those related to metabolism.[12] It has also been suggested that SCFAs may directly prevent the low-grade inflammatory response, a condition closely associated with type 2 diabetes, through maintaining intestinal integrity. As a result, probiotics may prevent the translocation of proinflammatory lipopolysaccharides into the bloodstream, associated with a decrease in inflammatory-related Toll-like 4 receptor signaling.[11,13] Interestingly, recent clinical trials have revealed an increased number of butyrate-producing bacteria in insulin-resistant men with metabolic syndrome after infusion of feces from lean donors, accompanied by beneficial metabolic effects.[14] Thus, the appropriate balance of gut microbiota may be of great importance for glucose, lipid, and protein metabolism. Since a growing body of evidence suggests an association between probiotic consumption and metabolic profile in subjects with type 2 diabetes, we aimed to assess the effect of probiotic supplementation on selected modifiable cardiometabolic risk factors in type 2 diabetes using a meta-analysis of existing research.

PATIENTS AND METHODS

Data extraction and selection criteria The present study was performed according to PRISMA guidelines.[15] The PubMed, Embase, Cochrane Library, and Scopus databases were searched using the terms "probiotics" and "diabetes" connected via the logical (Boolean) operator "AND", which restricted the search to trials focusing on both aspects at the same time. The search was last updated in January 2015 and involved only full-text articles published in English. Both authors were equally involved in the process of study selection, starting with the initial verification of abstracts followed by the assessment of full texts as well as quality assessment and data extraction. Any disagreements were resolved by compromise. Only randomized controlled trials (RCTs) were taken into consideration. Concerning the population, only adults with type 2 diabetes assessed in the original study were included in the meta-analysis. Furthermore, interventions of the included studies covered specified probiotic, probiotic mixes, synbiotics, or dairy products containing probiotic bacteria compared with placebo in the form of identically looking capsules, tablets, or liquids.

After establishing the most relevant endpoints, the obtained data were extracted from the studies and collated in a computer spreadsheet in the form of a table. The tables, individual for each single endpoint, included the number of subjects in the study and control groups, and values of tested parameters before and after the administration of probiotic or placebo. The outcomes of interest were fasting plasma glucose (FPG), insulin concentration, insulin resistance estimated using the homeostatic model assessment (HOMA-IR), hemoglobin A_{1c} (HbA_{1c}), and the levels of total cholesterol (TC), triglycerides, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and C-reactive protein (CRP). Subsequently, all collected data were transferred into a statistical software.

Quality and risk of bias The quality of the methodology of the included RCTs was assessed using the Jadad criteria,[16] as performed recently in another meta-analysis, which we considered as a model for our study.[17] While assessing the number of points,we considered the quality of randomization, correctness of blinding, and reason for subject withdrawal from a specific study. Each RCT was granted a score from 0 to 5 with a higher score indicating higher credibility. Moreover, the allocation concealment and intention-to-treat analysis as well as the risk of bias were evaluated.

Statistical analysis A statistical analysis was conducted with STATISTICA version 10 (StatSoft Inc., Tulsa, Oklahoma, United States; Statsoft Polska, Kraków, Poland). All endpoints of interest constituted continuous data. Therefore, the *t* test for mean difference between 2 independent groups with 95% confidence interval (95% CI) using the random-effects model, implying variation between single effects resulting from normal distribution, was used for the calculation. Effect size (standardized mean difference [SMD] defined in the software as Cohen's *d*) was calculated as the difference in the mean outcome between the groups divided by a standard deviation of outcome among participants.[18] SMD is usually interpreted as a relative "small" (0.2–0.3), "medium" (~0.5), and "large" (0.8 to ∞) effect.[19] Combining groups (if reasonable) and missing data were calculated using methods described in the Cochrane Handbook for Systematic Reviews of Interventions.[19] Heterogeneity across the included studies was assessed using the I^2 statistics, representing the percentage of actual variation in relation to total variation.[20] Additionally, sensitivity analyses were performed.

RESULTS

A total of 8 RCTs with 438 subjects met the inclusion criteria and were included in the meta-analysis (TABLE 1). The detailed process of study identification and selection is presented in FIGURE 1. All studies were small-scale, recruiting between 20 and 108 participants, and had diversified quality. The quality of studies selected for the meta-analysis is described in detail in Supplementary material online, *Table S1*. Sensitivity analyses corresponding to attached forest plots may be also found in Supplementary material online (*Figures S1–S6*).

TABLE 1 Characteristics of randomized controlled trials assessing the metabolic effects of probiotics in subjects with type 2 diabetes included in the meta-analysis

Trial	Type	Participants	Intervention	Duration	Effects	Follow- up	Jadad score, AC, ITT
Andreasen[21]	DB-RCT	45 adult patients (18 with type 2 diabetes, 5 with impaired glucose tolerance, 22 with normal glucose tolerance)	*L. acidophilus* NCFM	4 weeks	insulin sensitivity, inflammatory markers	no	4 ✓ –
Asemi[22]	DB-RCT	54 adult diabetic patients	7 viable and freeze-dried strains: *L. acidophilus* (2×10^9 CFU), *L. casei* (7×10^9 CFU), *L. rhamnosus* (1.5×10^9 CFU), *L. bulgaricus* (2×10^8 CFU), *B. breve* (2×10^{10} CFU), *B. longum* (7×10^9 CFU), *S. thermophilus* (1.5×10^9 CFU), and 100 mg fructo-oligosaccharide	8 weeks	metabolic profiles, hs-CRP, biomarkers of oxidative stress	no	4 ✓ –
Asemi[23]	DB-RCT	62 adult diabetic patients	probiotic viable and heat-resistant *L. sporogenes* (1×10^7 CFU), 0.04 g insulin (HPX) as prebiotic with 0.38 g isomalt, 0.36 g sorbitol and 0.05 g stevia as sweetener per 1 g	6 weeks	metabolic profiles, hs-CRP, biomarkers of oxidative stress	no	4 ✓ –
Ejtahed[24]	DB-RCT	60 adult diabetic patients	300 g/d of probiotic yogurt containing *L. acidophilus* La5 and *B. lactis* Bb12	6 weeks	fasting blood samples, 24-hour dietary recalls, and anthropometric measurements	no	5 ✓ –
Judiono[25]	RCT	108 adult diabetic patients	clear kefir	30 days	HbA_{1c}, FBG, PBG, insulin, C-peptide	no	1 ✓ ?
Mahboobi[26]	DB-RCT	55 adult prediabetic patients	7×10^9 CFU *L. casei*, 2×10^9 CFU *L. acidophilus*, 1.5×10^9 CFU *L. rhamnosus*, 2×10^8 CFU *L. bulgaricus*, 2×10^{10} CFU *B. breve*, 7×10^9 CFU *B. longum*, 1.5×10^{10} CFU *S. thermophilus*, fructooligosaccharide (as prebiotic), B-group vitamins, maltodextrin, lactose, and magnesium stearate	8 weeks	lipid profile, blood pressure	no	5 ✓ –
Mazloom[27]	SB-CT	34 adult diabetic patients	*L. acidophilus*, *L. bulgaricus*, *L. bifidum*, and *L. casei*	6 weeks	glucose, insulin, TG, TC, LDL-C, HDL-C, malondialdehyde, hs-CRP, and IL-6	no	3 ✓ –
Moroti[28]	DB-RCT	20 adult diabetic patients	synbiotic shake containing 10^8 CFU/ml *L. acidophilus*, 10^8 CFU/ml *B. bifidum and* 2 g oligofructose	30 days	standard lipid profile (TC, TG, HDL-C) and glycemia, or blood sugar levels	no	5 ✓ –

Abbreviations: AC, allocation concealment; CFU, colony-forming unit; DB-RCT, double-blind randomized controlled trial; FBG, fasting blood glucose; HbA_{1c}, hemoglobin A_{1c}; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; IL-6, interleukin 6; ITT, intention-to-treat; LDL-C, low-density lipoprotein cholesterol; PBG, postprandial blood glucose; SB-CT, single-blind controlled trial; TC, total cholesterol; TG, triglycerides

Probiotics and fasting plasma glucose levels Of 6 RCTs,[22-25,27,28] 5 showed a significant decrease of FPG after the consumption of probiotics, while only 1 did not.[23] A random-effects meta-analysis did not show the effect of supplementation with probiotics on FPG levels (SMD, –1.05; CI, –2.66 to 0.56; $P = 0.2017$; FIGURE 2). The included studies showed highly significant heterogeneity ($I^2 = 97.66\%$; $P < 0.001$).

Probiotics and hemoglobin A_{1c} levels HbA_{1c} is a marker of average blood glucose levels over prolonged time periods, which reflects the adequacy of metabolic control.[29] A pooled analysis of 3

FIGURE 1 Flowchart demonstrating the selection of trials assessing the metabolic effect of probiotics in subjects with type 2 diabetes

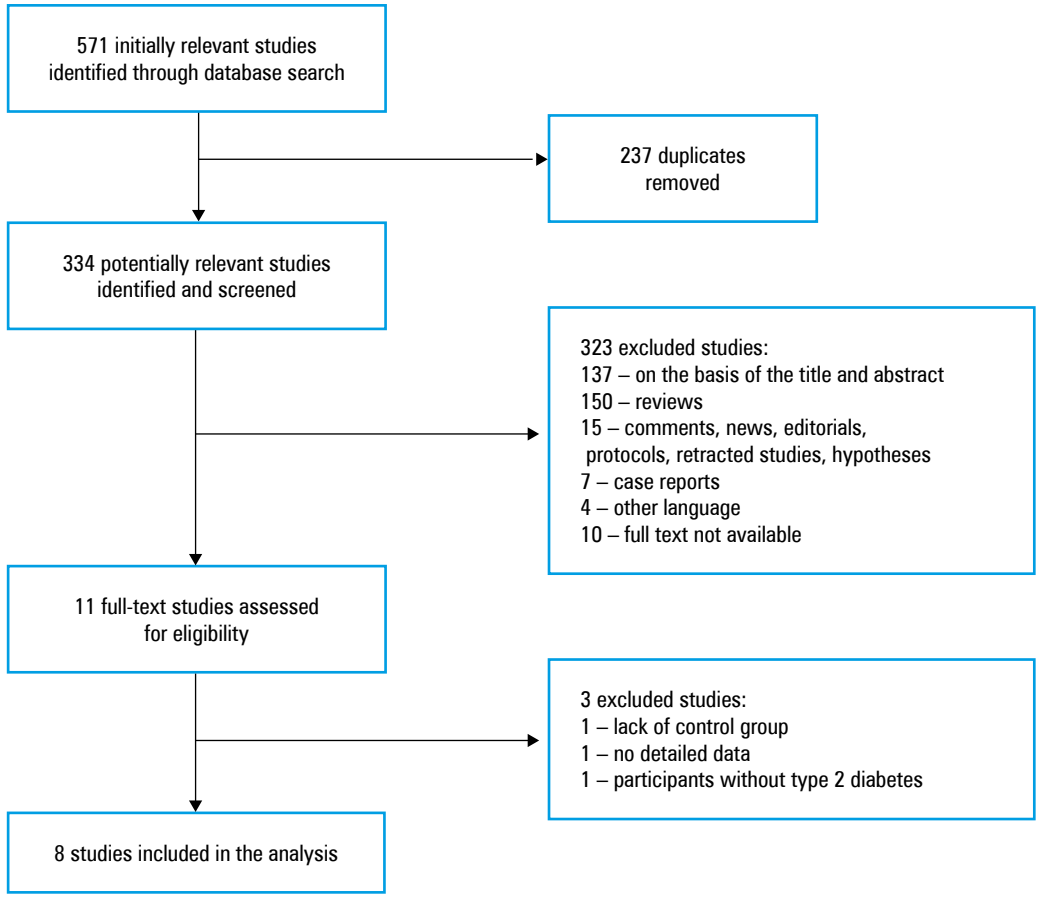
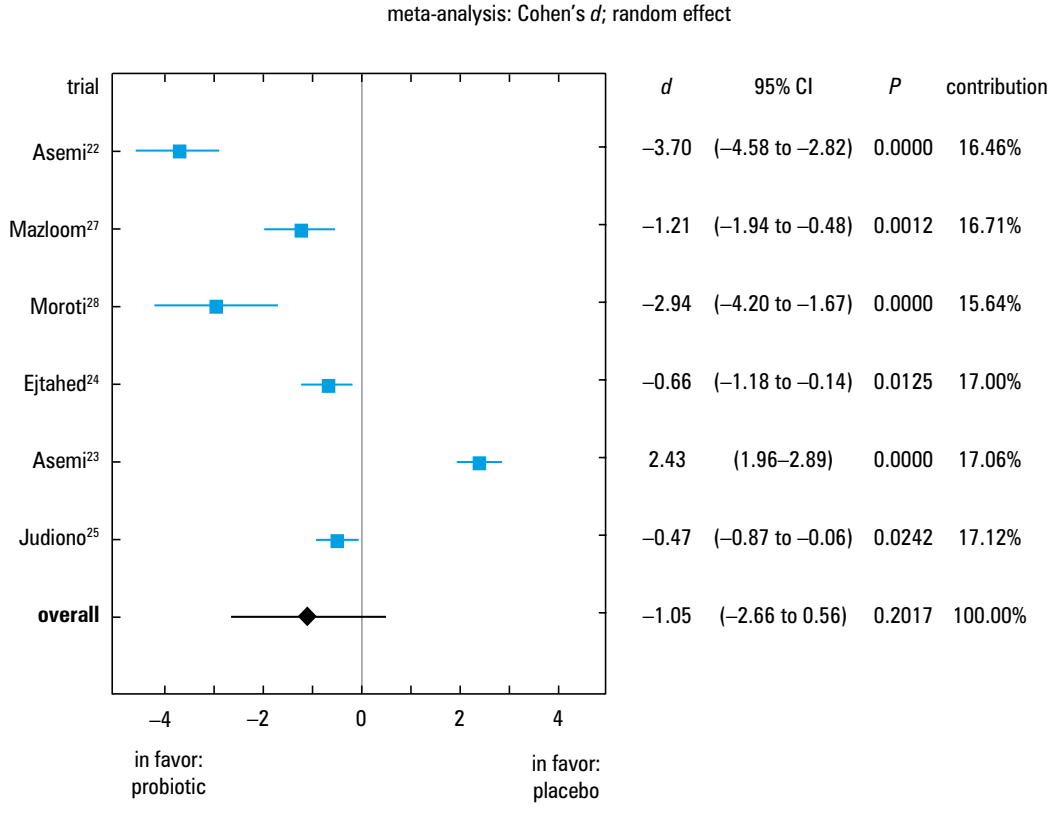


FIGURE 2 Forest plot of the association between probiotic use and fasting plasma glucose levels. The shaded squares indicate the effect of probiotics in a particular study. The horizontal lines represent 95% confidence intervals (CIs). The diamond data marker indicates the pooled effect.



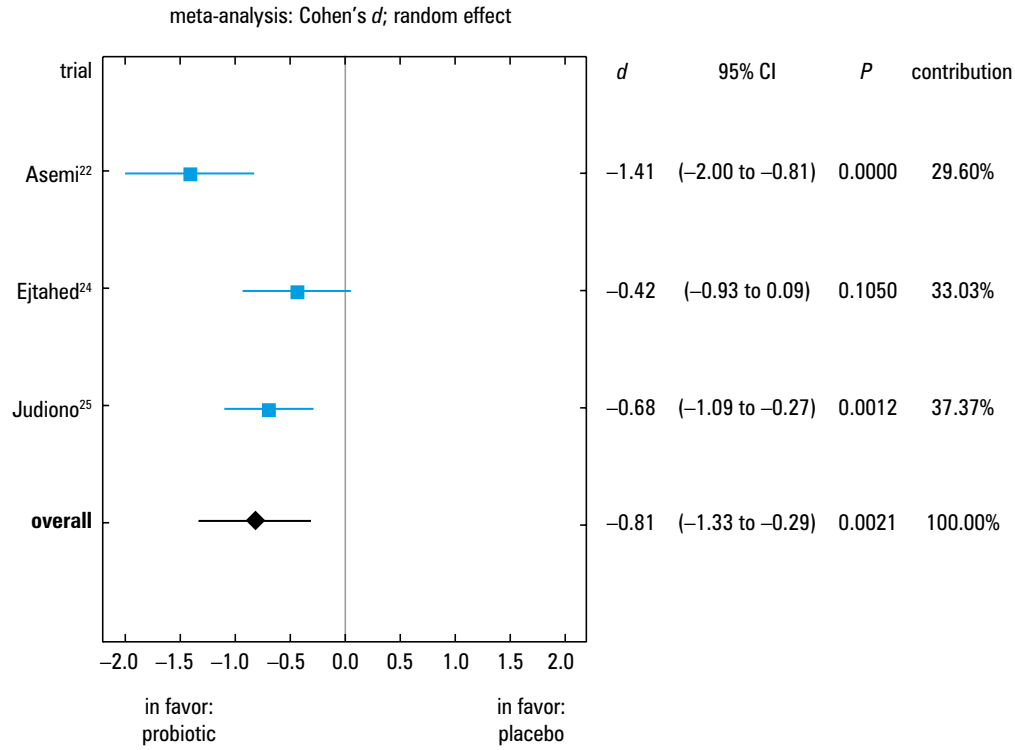


FIGURE 3 Forest plot of the association between probiotic use and hemoglobin A_{1c} levels. The shaded squares indicate the effect of probiotics in a particular study. The horizontal lines represent 95% confidence intervals (CIs). The diamond data marker indicates the pooled effect.

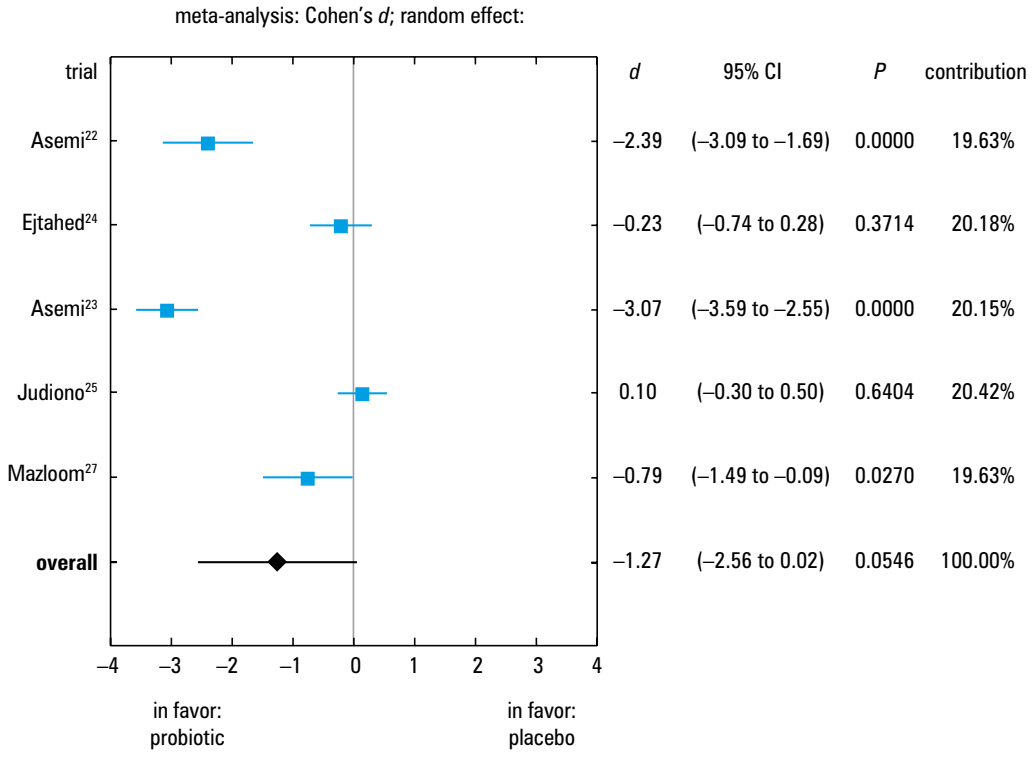


FIGURE 4 Forest plot of the association between probiotic use and insulin levels. The shaded squares indicate the effect of probiotics in a particular study. The horizontal lines represent 95% confidence intervals (CIs). The diamond data marker indicates the pooled effect.

RCTs[22,24,25] showed a significant decrease in HbA_{1c} levels in diabetic patients receiving probiotics compared with those receiving placebo (SMD, –0.81; CI, –1.33 to –0.29; $P = 0.0021$; FIGURE 3). The heterogeneity of the included studies was moderate ($I^2 = 68.44\%$; $P = 0.0421$).

Probiotics and insulin levels Three of five studies[22,23,27] included in the analysis[22-25,27] showed a significant decrease in insulin levels after probiotic consumption. However, no significant difference in mean insulin levels was observed between probiotic and placebo users, based on a pooled estimate (SMD, –1.27; CI, –2.56 to 0.02, $P = 0.0546$; $I^2 = 96.49\%$; $P < 0.001$ for heterogeneity; FIGURE 4).

Probiotics and insulin resistance A pooled analysis of 3 RCTs[22,23,27] demonstrated a significant decrease of HOMA-IR after the use of probiotics

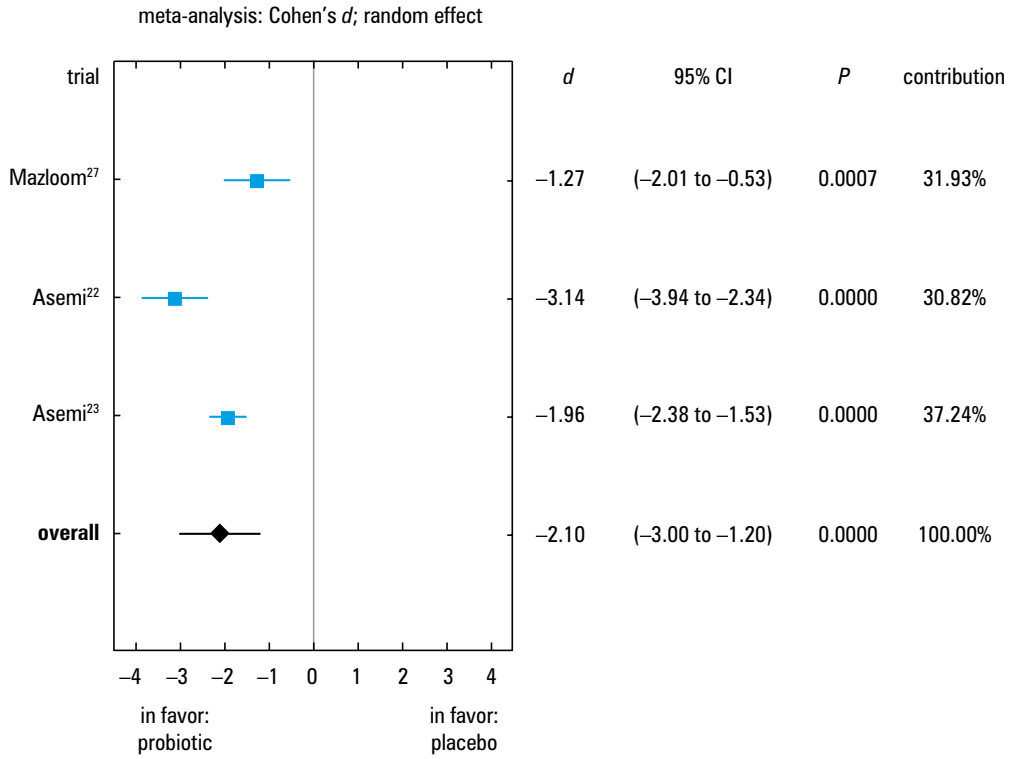


FIGURE 5 Forest plot of the association between probiotics use and HOMA-IR. The shaded squares indicate the effect of probiotics in a particular study. The horizontal lines represent 95% confidence intervals (CIs). The diamond data marker indicates the pooled effect.

(SMD, –2.10; CI, –3.00 to –1.2; P <0.001; I^2 = 82.91%; P = 0.0029 for heterogeneity; FIGURE 5).

Probiotics and total cholesterol levels Only 2[22,28] of 5 RCTs included in this analysis[20,23,26-28] showed a significant decrease in TC levels after the administration of probiotic formulas. A pooled effect was found to be nonsignificant (SMD, 0.12; CI, –1.32 to 1.57; P = 0.8664; I^2 = 96.48%; P <0.001 for heterogeneity).

Probiotics and triglyceride levels Five RCTs were included in this analysis.[22,23,26-28] Of these, 3 studies[22,27,28] showed a significant decrease in triglyceride levels after the administration of probiotic formulas. Nevertheless, a nonsignificant association was found between the supplementation of probiotics and placebo in subjects with type 2 diabetes (SMD, –0.27; CI, –2.04 to 1.50; P = 0.7655; I^2 = 97.43%; P <0.001 for heterogeneity).

Probiotics and low-density lipoprotein cholesterol levels Of 4 RCTs included in this analysis,[22,23,26,27] only 1 study[22] showed a significant decrease in LDL cholesterol levels after the administration of probiotics. The total effect was found to be nonsignificant (SMD, 0.37; CI, –0.69 to 1.43; P = 0.4947, I^2 = 93.68%; P <0.001 for heterogeneity).

Probiotics and high-density lipoprotein cholesterol levels Only 2[23,26] of 5 RCTs[22,23,26-28] included in this analysis demonstrated a significant increase in HDL cholesterol levels after the administration of probiotics. However, no significant overall association was found between the use of probiotics and HDL cholesterol levels (SMD, 0.73; CI, –0.50 to 1.96; P = 0.2472; FIGURE 6). The included studies were highly heterogeneous (I^2 = 95.22%; P = 0.0003).

Probiotics and C-reactive protein levels CRP levels indicate an inflammatory state considered as an integral element of type 2 diabetes.[30] Two[22,23] of four RCTs[21-23,27] showed a significant decrease in CRP levels after probiotic intake. However, the overall effect was nonsignificant (SMD, –1.73; CI, –3.54 to 0.08; P = 0.0617; FIGURE 7). The included studies were highly heterogeneous (I^2 = 96.85%; P <0.001).

Risk of bias All of the included studies were RCTs. Allocation concealment was provided in original evidence. Random and blinded assignment to study and control groups as well as blinded performance of trials and outcome assessment limit the probability of cumulative risk of bias. However, the studies analyzed only outcome data of patients who completed the study. There were no data on patients who were withdrawn during the study (mostly for reasons not related to the intervention, for example, the need for therapy change). Details on quality assessment may be found in Supplementary material online.

As the included studies reported both beneficial effects of intervention as well as the lack of beneficial effects of intervention, the risk of publication bias may be assessed as low. Furthermore, the studies reported both statistically significant and nonsignificant results of intervention; therefore, the risk of selective outcome-reporting bias is also reduced.

Only 4 papers were written in a language other than English. However, on the basis of an abstract in English, we assessed these studies as not

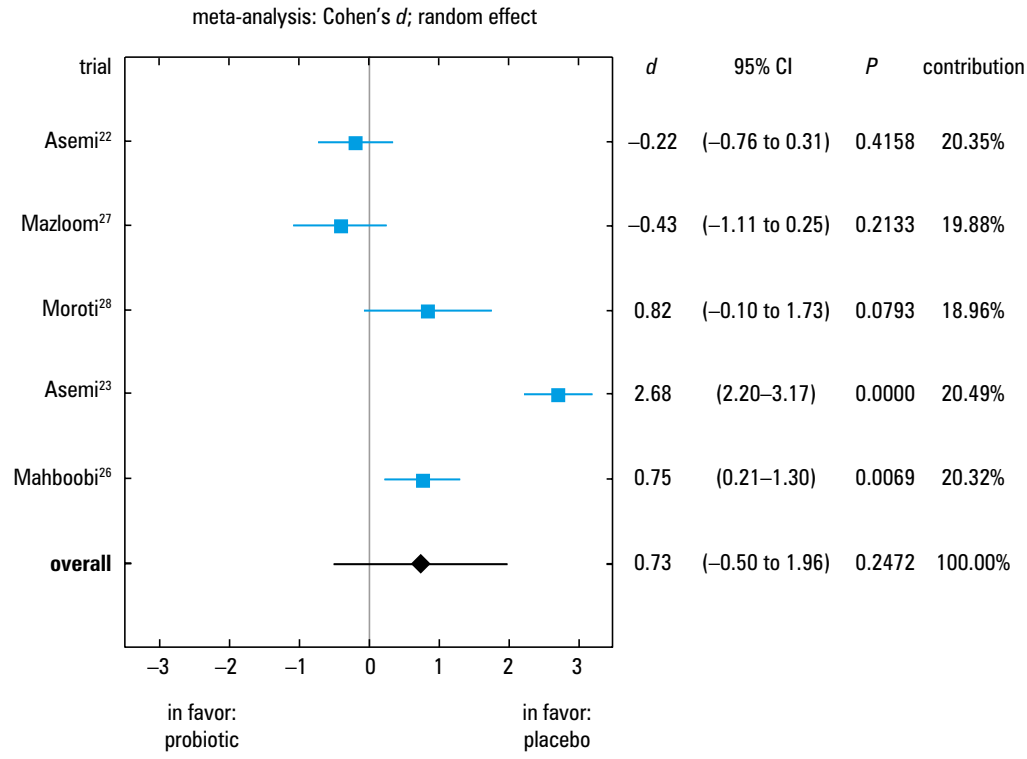


FIGURE 6 Forest plot of the association between probiotic use and high-density lipoprotein cholesterol levels. The shaded squares indicate the effect of probiotics in a particular study. The horizontal lines represent 95% confidence intervals (CIs). The diamond data marker indicates the pooled effect.

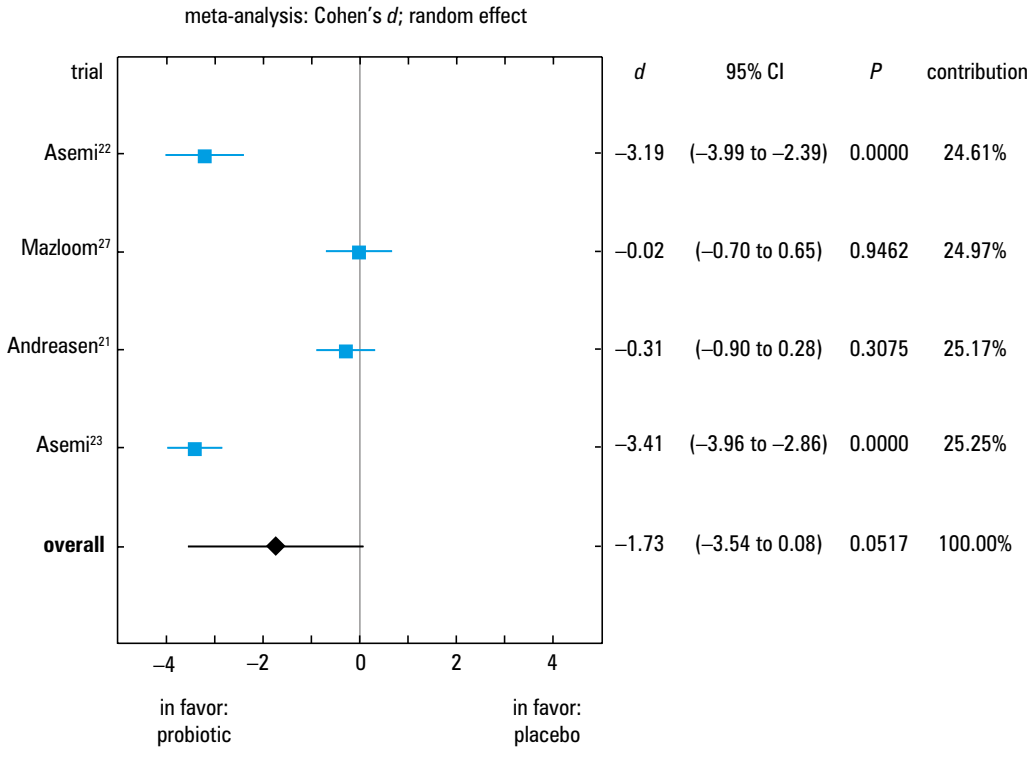


FIGURE 7 Forest plot of the association between probiotic use and C-reactive protein levels. The shaded squares indicate the effect of probiotics in a particular study. The horizontal lines represent 95% confidence intervals (CIs). The diamond data marker indicates the pooled effect.

fulfilling the eligibility criteria. Therefore, we considered the risk of language bias as low. Additionally, the risk of multiple-publication bias as well as citation bias may be also considered as nonsignificant. Unfortunately, owing to a low number of the included studies, it was impossible to assess the risk of bias on the funnel plot.

DISCUSSION To the best of our knowledge, this is the first meta-analysis assessing the effect of probiotics on modifiable cardiometabolic risk factors in subjects with type 2 diabetes. Although individual studies have reported that probiotic use has varied effects on these parameters, the present meta-analysis indicates that they have a significant impact only on HbA_{1c} and HOMA-IR in subjects with type 2 diabetes when compared with placebo, indicating a potential effect of probiotics on glycemia-related parameters. However, importantly, Ejtahed et al[24] reported a nonsignificant

effect of probiotics on HbA_{1c} levels (FIGURE 3). Furthermore, all of the studies included in our analysis, except 1, showed a substantial decrease in blood glucose levels in subjects with diabetes after the use of probiotics. Only Asemi et al[23] reported a significant increase in glycemia in the intervention group in comparison with subjects receiving placebo. Interestingly, studies by Asemi et al[22,23] show notably different results from the remaining studies. Also, sensitivity analyses (presented in supplementary material online) highlight the significant effect of those studies on the total effect. It is difficult to tell the reason for such discrepancies. This might have been caused by the longer duration of the trials (8 and 6 weeks, respectively). Additionally, it seems that using high-dose multispecies probiotic supplements or synbiotic may be more effective than single-strain supplement. The analysis of the association between probiotic intake and insulin levels also demonstrated inconsistent findings. It cannot be excluded that the differences between the results of these studies are caused by the use of different protocols.

It has been reported that probiotic supplementation is associated with reduced adipose tissue mass and body mass index and that these changes may play a role in the prevention of type 2 diabetes.[31,32] Hulston et al[33] reported that probiotic consumption has a positive effect on blood glucose concentrations and insulin sensitivity in healthy subjects on obesogenic diet. Furthermore, studies have demonstrated that probiotics may have potential benefits for the prevention of other diabetes-related changes,[34-37] which has been confirmed, at least partially, by our meta-analysis.

The beneficial effects of probiotics on glycemia--related parameters are not fully understood. It has been suggested that probiotics may increase glucagon-like peptide 1 secretion from enteroendocrine L-cells to improve carbohydrate metabolism, decrease glucotoxicity, and increase insulin sensitivity of target cells.[11] Probiotic intake affects the structure of the gut flora, which might improve the integrity of the intestinal epithelium, weaken the immune responses, and diminish the Toll-like receptor 4 pathway, which in turn reduces proinflammatory signaling and enhances insulin sensitivity.[11,38]

Our findings did not show probiotics to have any significant effects on other cardiometabolic risk factors, including lipid profile components and CRP levels; this may have been caused by the use of various probiotic strains and short duration of studies. An elevated HDL cholesterol level is generally regarded as a factor reducing the risk of cardiovascular disease. Interestingly, it is also considered as a protective factor in metabolic disorders, including diabetes.[39] Our study did not show a significant effect of probiotics on HDL cholesterol levels. However, several previous RCTs have shown a significant increase in HDL cholesterol levels after the administration of probiotic-containing products to nondiabetic subjects.[40,41] Importantly, reports on the association between other lipid parameters and probiotic consumption are also inconsistent.[31,40,42]

The present meta-analysis failed to confirm that probiotics have any effect on lowering triglyceride, TC, or LDL levels. In contrast to our findings, previous meta-analyses reported that probiotics effectively reduced the levels of TC and LDL cholesterol in subjects with originally high or normal lipid levels.[43,44] This discrepancy may result from the characteristics of the study group (healthy or obese subjects in previous analyses vs subjects with diabetes in our meta-analysis), the length of intervention, or the choice of probiotic strain.

The anti-inflammatory properties of bacteria are known to be strain-specific, and these properties are determined by the antigens present on the bacterial wall.[45,46-48] Therefore, the variable effectiveness of probiotic bacteria in reducing an inflammatory state, assessed by measuring CRP levels after the use of probiotics, may be associated with the use of various probiotic preparations and differences in strain-specific efficacy. However, as the efficacy of probiotics is suggested to be beneficial in other inflammatory disorders, they may also appear an effective tool in the treatment of diabetes.[49,50]

Limitations Our meta-analysis has several limitations. Firstly, several other search strategies for probiotics and diabetes may be used. There are many synonyms for probiotics, comprising designations of different probiotic species. Likewise, there is a variety of synonyms for diabetes. However, we believe that adding subsequent probiotic strains into the searching query might in fact lead to the exclusion of other probiotic types, especially those which are used less frequently. In our opinion, using only 2 expressions—probiotics and diabetes—expands the number of results because these terms are commonly used as keywords. The number of identified RCTs that met the inclusion criteria was relatively low. This could be associated to a low popularity of this issue: the first reports investigating the effect of probiotics on modifiable cardiometabolic risk factors in diabetics have been published only recently. This low number of RCTs implies a relatively low number of enrolled subjects, which reduces the credibility of the meta--analysis. Furthermore, the low number of RCTs and their diversified settings make it impossible to assess the effect of a particular probiotic strain on all analyzed metabolic parameters. The majority of analyzed studies exploited probiotic mixes or dairy products containing several probiotic strains; only 1 study[21] assessed the effect of a single probiotic strain. Therefore, no subgroup analysis to estimate which probiotic preparations could be more effective in improving metabolic parameters in diabetic patients was possible. Another important limitation is that the analyzed RCTs only had a maximum length of 8 weeks and had no follow--up. It

is widely believed that a substantially longer period of probiotic consumption is needed for its true effect to be demonstrated on various glucose and lipid metabolism markers. Furthermore, significant heterogeneity was observed between trials within the meta-analysis. Sensitivity analyses highlighted how the effect of potential exclusion of a study would affect the total effect. Furthermore, they show that studies affect the standard error differently and it is mostly associated with the number of subjects enrolled to a study. However, to avoid reducing reliability and giving rise to bias, despite the fact that the experimental exclusion of extreme results considerably increases experimental homogeneity, all of the studies were included in the analysis, while factors possibly affecting their homogeneity were noted. Most probably, the reason for this heterogeneity is the diversified setting of the included RCTs. Firstly, interventions in considered trials involved different probiotic formulas including a specified single probiotic strain, a multispecies probiotic preparation, synbiotic, or dairy product containing probiotic bacteria. Secondly, the duration of intervention across the studies varied considerably. Finally, the low number of studies also increases the heterogeneity of the analyses. All of these issues greatly reduce the clarity and explicit nature of the conclusions. Nevertheless, the results of our meta-analysis may indicate a trend that requires further scientific research.

In conclusion, this meta-analysis of available RCTs suggests that probiotic supplementation has a beneficial effect on selected cardiometabolic parameters in patients with type 2 diabetes. However, before they can be recommended for use in supportive treatment of type 2 diabetes, larger well-designed studies are needed to determine the true relationship between probiotic supplementation and modifiable cardiometabolic risk factors.

Contribution statement MK conceived the idea for the study. Both authors contributed to the design of the research. Both authors were independently involved in data collection, selection, and quality assessment. Both authors analyzed the data. Both authors edited and approved the final version of the manuscript.

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Supplementary material online Supplementary material is available with the online version of the article at www.pamw.pl.

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Skuteczność probiotyków w terapii cukrzycy typu 2 – metaanaliza

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SŁOWA KLUCZOWE

cukrzyca, metaanaliza, metabolizm, mikrobiota jelitowa, probiotyki

STRESZCZENIE

WPROWADZENIE Rosnąca liczba badań sugeruje, że stosowanie probiotyków może mieć korzystny wpływ na stan zdrowia osób z cukrzycą typu 2.

CELE Celem badania była ocena zdolności probiotyków do modyfikowania wybranych czynników ryzyka sercowo-metabolicznego u osób z cukrzycą typu 2.

METODY Bazy PubMed, Embase, Cochrane Library i Scopus poddano dokładnemu przeglądowi do stycznia 2015 w celu wyszukania randomizowanych kontrolowanych badań (*randomized controlled trials* – RCTs) oceniających wpływ probiotyków na wybrane modyfikowalne parametry sercowo-metaboliczne u osób z cukrzycą typu 2. Brano pod uwagę następujące punkty końcowe: stężenie glukozy na czczo (*fasting plasma glucose* – FPG) i stężenie insuliny, insulinooporność, hemoglobinę A_{1c} (HbA_{1c}), a także poziom cholesterolu całkowitego, triglicerydów, lipoprotein o niskiej gęstości, lipoprotein o wysokiej gęstości oraz białka C-reaktywnego (*C-reactive protein* – CRP). Z początkowo zidentyfikowanych 571 RCT do metaanalizy włączono 8 badań przeprowadzonych na 438 osobach. Efekt stosowania probiotyków obliczano dla każdego parametru.

WYNIKI Metaanaliza wykazała istotny wpływ probiotyków na spadek poziomu HbA_{1c} (standaryzowana średnia różnic [*standardized mean difference* – SMD] –0,81; CI od –1,33 do –0,29; $p = 0,0023$; niejednorodność: $I^2 = 68,44\%$, $p = 0,0421$) i HOMA-IR (SMD –2,10; CI od –3,00 do –1,20; $p < 0,001$; niejednorodność: $I^2 = 82,91\%$, $p = 0,0029$). Suplementacja probiotyków nie miała istotnego wpływu na stężenie FPG, insuliny, CRP oraz profil lipidowy.

WNIOSKI Wyniki naszej metaanalizy sugerują, że suplementacja probiotyków może – przynajmniej do pewnego stopnia – poprawić kontrolę metaboliczną u osób z cukrzycą typu 2. Potrzebne są jednak większe, dobrze zaplanowane, długoterminowe badania kliniczne w celu potwierdzenia korzystnego wpływu probiotyków na modyfikowalne czynnika ryzyka sercowo-metabolicznego u osób z cukrzycą typu 2.

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