Special Article

NUTRITION REVIEWS

Fiber intake and glycemic control in patients with type 2 diabetes mellitus: a systematic review with meta-analysis of randomized controlled trials

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This systematic review with meta-analysis of randomized controlled trials (RCT) aimed to analyze the effect of fiber intake on glycemic control in patients with type 2 diabetes. Databases were searched up to November 2012 using the following medical subject headings: diabetes, fiber, and randomized controlled trial. Absolute changes in glycated hemoglobin and fasting plasma glucose were reported as differences between baseline and end-of-study measures. Pooled estimates were obtained using random-effects models. Of the 22,046 articles initially identified, 11 (13 comparisons; range of duration, 8–24 weeks) fulfilled the inclusion criteria, providing data from 605 patients. High-fiber diets, including diets with foods rich in fiber (up to 42.5 g/day; four studies) or supplements containing soluble fiber (up to 15.0 g/day; nine studies), reduced absolute values of glycated hemoglobin by 0.55% (95% CI –0.96 to –0.13) and fasting plasma glucose by 9.97 mg/dL (95% CI –18.16 to –1.78). In conclusion, increased fiber intake improved glycemic control, indicating it should be considered as an adjunctive tool in the treatment of patients with type 2 diabetes.

INTRODUCTION

Over 345 million people worldwide have diabetes, and it is projected that diabetes will be the seventh leading cause of death by 2030.[1] Achieving glycemic control close to the non-diabetic range may reduce both micro-[2,3] and macrovascular diabetic complications.[3,4] Despite the fact that drug therapy is mandatory for most patients,[5,6] lifestyle interventions such as physical exercise[7] and dietary modifications[8–10] are essential in diabetes management.

The main role of diet in glucose control is to decrease the postprandial glucose response, because this is an important contributor to glycated hemoglobin (HbA1c)[11] and it may also be an independent risk factor for cardiovascular disease in patients with diabetes.[12] In this sense, carbohydrates that are rich in fiber and also have a low glycemic index, such as whole grains, vegetables, and fruits, have been recommended to improve glucose control and should be encouraged for people with diabetes.[8,13]

It is hypothesized that dietary fibers form a viscous solution in the stomach that delays gastric emptying and physically inhibits the absorption of macronutrients at the lumen of the small intestine.[14] These effects decrease the rate of glucose absorption and, consequently, can reduce the postprandial plasma glucose increase.[15–17] However, the glucose-lowering effect of fiber intake has not been consistently demonstrated in the literature, indicating that the effect may depend on the fiber type, amount, and/or source.

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A substantial number of clinical trials have investigated the effects of fiber intake on the glycemic profile of patients with diabetes, but the results have not been consistent.[18–28] This lack of consistency may be due to variations in the trials' sample size and intervention duration, in addition to the type of intervention and composition of the control diet. Although this subject has been reviewed previously,[14,16] the magnitude of a possible favorable effect of fiber intake on glycemic control is still uncertain. Therefore, the present systematic review was conducted to analyze the effect of dietary fiber (type and amount) on glycemic control in patients with type 2 diabetes.

METHODS

This systematic review was carried out using a protocol constructed according to the Cochrane recommendations[29] and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[30]

Search strategy

The Medline, Embase, Scopus, and Cochrane electronic databases were searched for the period 1950 to November 21, 2012 to identify reports of RCTs that reported the effect of fiber intake on the glycemic control (glycated hemoglobin [HbA1c] and fasting plasma glucose) of patients with diabetes.

The initial search comprised the following MESH terms: diet, dietary therapy, dietary fiber, carbohydrates, diabetes; these terms were accompanied by related entry terms associated with a high-sensitivity strategy for the search of RCTs (available at http://www.sign.ac.uk/methodology/filters.html#random). The complete Medline search strategy is presented in Appendix S1, available in the Supporting Information for this article online. The same terms were used to search the database of clinical studies maintained by the National Institutes of Health (www.clinicaltrials.gov) and all published abstracts from the annual meetings of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) between 2007 and 2012. All potentially eligible studies were considered for review, regardless of the language of publication. A manual search of the reference lists of the included articles and of two previous systematic reviews on this topic was also performed.[14,16]

Inclusion and exclusion criteria

RCTs that evaluated the effect of dietary fiber (foods or supplements) on the glycemic control of patients with type 2 diabetes and that lasted for at least 8 weeks were eligible for inclusion. This duration was chosen because changes in HbA1c can be better detected after 2–3 months of intervention.[9] Outcomes included changes in HbA1c and fasting plasma glucose from baseline to the end of study.

In studies that evaluated the effect of dietary fiber, the intervention diet was defined as the diet with the highest total fiber content and the control diet was the diet with lowest fiber content. In studies that evaluated the effect of a fiber supplement, the intervention was defined as the usual diet plus a soluble fiber supplement and the control diet was defined as the usual diet or the usual diet plus a placebo or another type of fiber.

Studies were excluded if they were not randomized or if they included children or pregnant women or patients with type 1 diabetes and did not report the chosen outcomes or the means and standard deviations (SD) of them. Crossover RCTs without a washout period between diets were also excluded.

Study selection and data extraction

Two investigators (FMS and CKK) independently analyzed the title and abstract of each paper retrieved from the initial literature search in order to identify potentially eligible studies. All articles that did not meet the inclusion criteria were excluded. The full text of the remaining papers was obtained for further examination. Disagreements regarding inclusion were resolved by a third investigator (JCA).

The data of included studies were independently extracted by two reviewers (FMS and TS) using a standardized data extraction form. Disagreements were resolved by a third reviewer (JCA). Extracted data included the following: first author's name, year of publication, number of participants, details of the study design (i.e., crossover or parallel design, duration of the washout period, and randomization method), trial duration, and patient characteristics (i.e., age, body mass index, duration of diabetes, gender, diabetes treatment). Total energy, macronutrients, fiber content, and any evaluation of dietary compliance were extracted from descriptions of the intervention and control diets. Baseline and end-of-study means and statistical dispersion for HbA1c and fasting plasma glucose were extracted.

Assessment of bias and quality of studies and body of evidence

Two reviewers (FMS and TS) independently assessed the sources of bias in the included RCTs, following the Cochrane guidelines.[29] Biases were classified into six domains: selection, performance, detection, attrition,

reporting, and other.[29,31] The "other" domain included the assessment of dietary compliance. The risk of bias with regard to each domain was classified as high, low, or unclear. Regarding dietary compliance, the risk of bias was classified as "low" if the study described the method of dietary compliance evaluation.

The quality of the body of evidence was assessed using the GRADE approach.[32] This evaluation included factors that may decrease the quality of body of evidence (e.g., methodological quality, directness of evidence, heterogeneity, precision of effect estimates, risk of publication bias) and factors that may increase it (e.g., large magnitude of effect, reduction or spurious effect due to plausible confounding factors, dose-response gradient). Each evaluated factor was rated as high, moderate, low, or very low.[29,32]

Statistical analyses

Changes in fasting plasma glucose and HbA1c levels were reported as absolute differences between mean values at baseline and end-of-study. HbA1c changes were also expressed as percentages of the calculated differences from baseline to the end-of-study. This additional strategy was adopted because the method of measurement of HbA1c was not the same in all studies. Changes between baseline and final SD values for fasting plasma glucose and HbA1c were directly extracted from the articles or calculated assuming a correlation of 0.5 between the baseline and final measures within each group, according to the formula of Follmann et al.,[33] as proposed in the Cochrane guidelines.[29] Equal variance was assumed among trials and between intervention and controls.

The heterogeneity among studies was evaluated using Cochran's test (Q test) and a P for trend of ≤ 0.10 was considered statistically significant. The I^2 test was also performed to evaluate the magnitude of heterogeneity. The pooled estimates of the weighted mean differences (WDM) between high-fiber-diet and control-diet groups were calculated using the random effects model (DerSimonian-Laird method)[34] since significant heterogeneity among studies was identified in preliminary models. This approach also provided a more conservative assessment of the average effect size.

Potential sources of heterogeneity among trials were investigated by meta-regression analyses. Covariates were chosen based on biological relevance before the meta-analyses were undertaken. The selected covariates were as follows: source of fiber (foods rich in fiber or fiber supplements), difference in dietary fiber content between intervention and control groups, study duration and design. Quantitative covariates were categorized as binary variables considering the mean values of these variables in all included studies (≥mean value and <mean value). Thereafter, sensitivity analyses (subgroup analyses) were conducted and the variables with a positive R-adjusted square on meta-regression analyses were included; this revealed how much of the between-study difference could be explained by these variables.[29]

The possibility of publication bias was assessed visually with funnel plot asymmetry and statistically with Begg's and Egger's tests; a significant publication bias was considered if the P value was <0.10.[35–37] The trim-and-fill computation was also used to estimate the effect of publication bias on the interpretation of results if visual asymmetry in the funnel plot suggested the presence of publication bias.[38]

All statistical analyses were performed using Stata 11.0 software (Stata, College Station, TX, USA). Significance was set at $P < 0.05$ and 95% confidence intervals are quoted throughout.

RESULTS

From the initial search strategy, 22,046 studies were identified (Figure 1). Based on titles and abstracts, 45 studies were selected for full-text examination. In addition, 15 studies were identified in the references lists of the included studies and in the two previously published systematic reviews on the topic. None of the studies identified at www.clinicaltrials.gov ($n = 51$) and in the published ADA ($n = 325$) and EASD ($n = 26$) meeting abstracts fulfilled the inclusion criteria for the current review. Thus, 60 studies underwent full-text evaluation.

Among these 60 studies, 11[18–28] fulfilled the inclusion criteria. One study report[20] was included as three independent reports because data were described according to the type of diabetes treatment (i.e., diet only, insulin, or oral antidiabetic drugs); thus, a total of 13 comparisons were included in the analyses (Figure 1). All of the included studies evaluated HbA1c changes and eight also reported fasting plasma glucose as an outcome.[19–22,24,26–28]

Study characteristics

The essential features of the individual studies are summarized in Table 1. The total sample size of all studies comprised 605 patients with type 2 diabetes, with a mean age of 62.0 years and diabetes duration ranging from 3.0 to 9.4 years. Eight studies were parallel RCTs.[18,20,21,23,25–28] Three RCTs had a crossover controlled design[19,22,24] with a washout period varying from 4 to 8 weeks. The trial duration ranged from 8 to 24 weeks.

In studies in which the intervention was comprised of foods rich in fiber[18,22,24,27] the difference in dietary fiber content between intervention and control groups ranged from 3.0 to 22.5 g/day. In studies that evaluated fiber

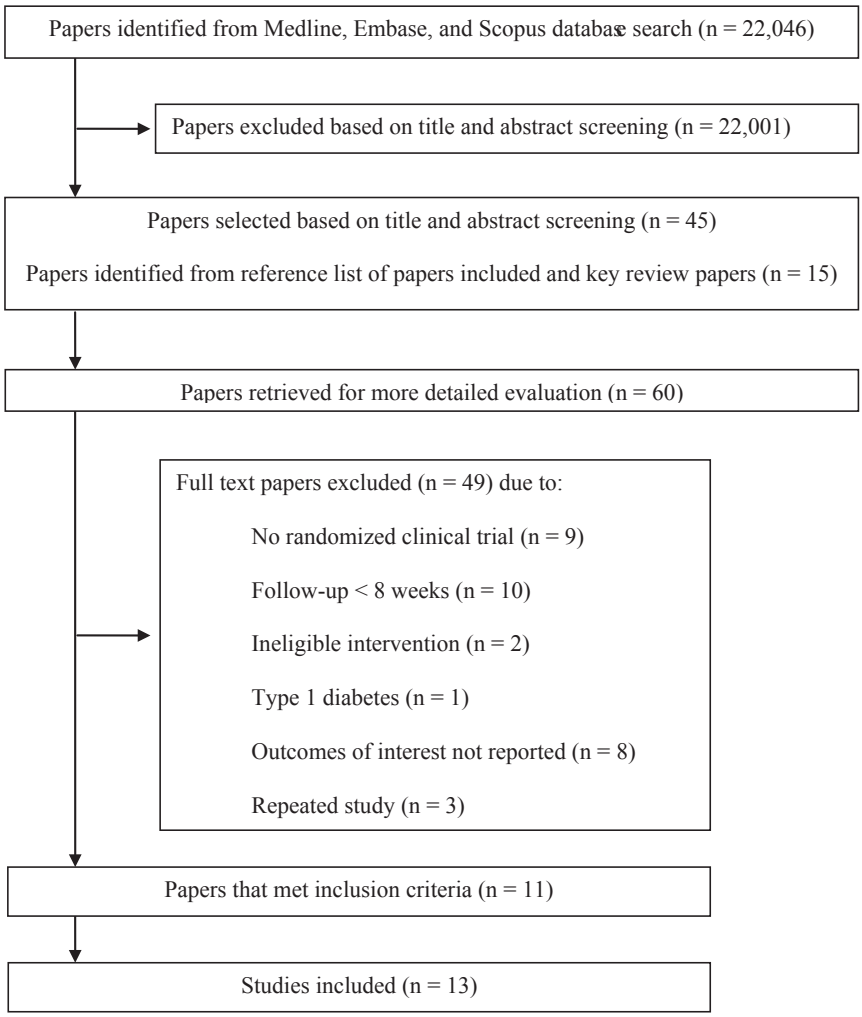

Figure 1 **Flow chart of article selection process.**

supplements (3.5–16.5 g/day), guar-gum was used in four studies,[19–21,25] psyllium in two,[23,26] and β-glucan in one.[28] Total energy and dietary macronutrients composition was not described in five[19,20,25,26,28] of the seven studies that evaluated the effect of a supplement. All studies[18,22,24,27] that analyzed the effect of high-fiber diets showed differences in the dietary content between the intervention and control groups. Just one study[27] described the glycemic index (GI) (Table 1).

Diabetes treatments did not differ between the intervention and control groups in the studies for which it was reported, but this information was not provided for three of the studies.[22,23,25] Six studies[20,22–25,28] described the weight of patients at the beginning of the trial (range, 74.0–88.4 kg). Regarding weight change during follow-up, in six studies[18–20,22,27,28] the weight of the patients was not modified and in three studies[21,24,26] these data were not described. In another two studies[23,25] weight loss was greater in the intervention group than in the control group.[22,24] In the majority (78.5%) of the reports it was unclear if the participants received recommendations about physical activity.[18–22,25–28]

Risk of bias, quality of studies, and quality of body of evidence

The risk of bias in the included studies is summarized in Table 2. The risk of selection bias was low in all trials taking into account the presence of random sequence generation, although the allocation concealment was unclear in most studies. In general, performance bias was low (83.3% of the patients and 58.3% of the researchers were blinded). Information about blinding of outcome assessors was described in only two studies. Regarding attrition bias, rates of dropout and/or withdrawal were lower than 20% in seven studies. Dietary compliance was evaluated in the majority of studies.

The quality of the body of evidence of the current systematic review is described in Table 3. The methodological quality, as evaluated by within-study risk of bias,

Table 1 **Characteristics of studies examining the effect of increased fiber intake in glycemic control of patients with type 2 diabetes.**

Reference	Study design and duration	No. of patients; % male; mean age; (diabetes treatment)	Diabetes duration (years)	Method of HbA1c measurement	Baseline HbA1c (% as means ± standard deviation)		Baseline fasting plasma glucose (mg/dL)		Group characteristics		Fiber difference between groups (g)	Possible dietary confounders
					Intervention	Control	Intervention	Control	Intervention	Control		
Dodson et al. (1984)[18]	Parallel 8 weeks	50 50% 56.8 y (oral agents)	6.8	Chromatography	12.4 ± 3.1	10.7 ± 3.3	NR		Diet of high-fiber (40–45 g/day), high-unrefined-carbohydrate (50% of energy) and low-fat content (25% of energy)	Diet of low-carbohydrate (26% of energy), low-fiber (20g/day), and high-fat content (40% of energy)	22.5	Total energy carbohydrate fat protein
Niemi et al. (1988)[19]	Crossover 12 weeks	22 27.3% male 63.0 y (diet or oral agents)	NR	Electrophoresis	12.1 ± 2.3	11.4 ± 2.1	210.6 ± 46.8	223.3 ± 48.6	Usual diet plus 5 g of guar gum granules 3 times a day	Usual diet plus 5 g of microcrystalline cellulose 3 times a day	15	Composition of diet not reported
Uusitupa et al. (1989)[20]	Parallel 12 weeks	39 33.3% male 60.5 y (oral agents)	9.4	HPLC	8.9 ± 1.4	9.4 ± 1.5	220.1 ± 42.7	230.4 ± 46.8	Usual diet plus 5 g of guar gum granules 3 times a day before the main meals	Usual diet plus 5 g of placebo granules (wheat flour) 3 times a day before the main meals	15.0	Composition of diet not reported
Calvo-Rubio et al. (1989)[21]	Parallel 12 weeks	9 62.5% male 62.5 y (diet only)	2.5	Chromatography	8.3 ± 0.6	9.3 ± 0.4	140.4 ± 10.8	124.2 ± 16.2	Usual diet plus 5 g of guar gum granules three times a day before the main meals	Usual diet (55% of energy from carbohydrate, 25% from fat and 20% from protein) without supplement	15.0	None
Calvo-Rubio et al. (1989)[21]		15 60% male 60.8 y (oral agents)	3.0	Chromatography	9.7 ± 0.8	10.1 ± 0.9	172.8 ± 14.4	151.2 ± 9.0				
Calvo-Rubio et al. (1989)[21]		10 80% male 67.5 y (insulin)	4.0	Chromatography	9.8 ± 1.3	9.7 ± 0.7	178.2 ± 30.6	156.6 ± 12.6				
Walker et al. (1995)[22]	Crossover 12 weeks	24 37.5% male 69.1 y (diabetes treatment not reported)	NR	HPLC	6.4 ± 0.3	6.8 ± 0.4	153 ± 10.8	172.8 ± 14.4	High-carbohydrate and low-fat diet: 21% of energy from fat and 59% of energy from fiber-rich carbohydrate (34 g of fiber/day).	Modified-fat diet: 40% of energy from fat and 40% of energy from carbohydrate (25 g of fiber/day)	9.0	Total energy carbohydrate fat
Anderson et al. (1999)[23]	Parallel 8 weeks	34 100% male 62.9 y (diabetes treatment not reported)	NR	NR	0.073 ± 0.003	0.075 ± 0.002	180.4 ± 10.4	193.3 ± 10.1	Psyllium group: traditional weight-maintaining diabetes exchange diet plus an orange-flavored, sugar-free product (Metamucil: two doses with 5.1 g of psyllium in each)	Placebo group: traditional weight-maintaining diabetes exchange diet plus an insoluble fiber, microcrystalline cellulose (two doses of 5.1g).	10.2	Total energy fat protein
Jenkins et al. (2002)[24]	Crossover 12 weeks	65 69.6% male 63.0 y (diet only or oral agents)	NR	HPLC	7.0 ± 0.2	7.3 ± 0.3	131.4 ± 5.4	133.2 ± 7.2	Wheat-bran diet(21.3 g/1,000 kcal of fiber) providing high-wheat-bran bread and breakfast cereal	Control diet (11.7 g/1,000 kcal of fiber) providing white bread and low-fiber breakfast cereal	16.1	Total energy protein
Hesse et al. (2004)[25]	Parallel 8 weeks	25 32% male 58.9 y (diabetes treatment not reported)	NR	Turbidimetry	8.7 ± 0.9	8.3 ± 0.9	221.4 ± 41.4	230.4 ± 41.4	Fiber group: 5.5 g of fiber 3 times a day (16% of guar gum)	Placebo group: 5.5 g of cellulose 3 times a day	16.5	Composition of diet not reported
Ziai et al. (2005)[26]	Parallel 8 weeks	49 Gender not reported 56.2 y (diet only or diet and oral agents)	NR	HPLC	10.5 ± 0.7	9.1 ± 0.5	208.2 ± 12.7	179.1 ± 10.8	Psyllium group: 5.1 g of psyllium twice daily	"Placebo group": 5.1 g of microcrystalline cellulose twice daily	10.2	Composition of diet not reported
Jenkins et al. (2008)[27]	Parallel 24 weeks	210 61% male 60.5 y (oral agents)	7.8	HPLC	7.1 ± 0.5	7.1 ± 0.6	141.2 ± 29.3	138.8 ± 29.3	Diet with 18.7 g/1,000 kcal of fiber and GI equal to 69.6 (defined as low-GI diet)	Diet with 15.7 g/1,000 kcal of fiber and GI equal to 83.5 (defined as high-fiber diet)	3.0	Carbohydrate fat protein glycemic index
Cugnet-Anceau et al. (2010)[28]	Parallel 8 weeks	53 Gender not reported 61.8 y (insulin and/or oral agents and/or diet)	NR	HPLC	7.3 ± 0.9	7.5 ± 1.3	159.1 ± 38.0	150.5 ± 41.0	Diet with one portion/day of ready-to-eat soups enriched with3.5g of β-glucan	Diet with one portion/day of ready-to-eat soups enriched with 3.5g of maltodextrin	3.5	Composition of diet not reported

Abbreviations: kcal, calories; HPLC, high performance liquid chromatography; NR, not reported.

Table 2 **Assessment of bias and study quality for studies included in the present systematic review.**

Reference	Selection bias		Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Dietary compliance assessed
Dodson et al. (1984)[18]	Low	Unclear	Low	Unclear	Low	Low	High
Niemi et al. (1988)[19]	Low	Unclear	Low	Unclear	Low	Low	High
Uusitupa et al. (1989)[20]	Low	Unclear	Low	Unclear	Low	Low	Low
Calvo-Rubio et al. (1989)[21]	Low	Unclear	High	Unclear	Low	Low	Unclear
Walker et al. (1995)[22]	Low	Unclear	Low	Unclear	Low	Low	Low
Anderson et al. (1999)[23]	Low	Unclear	Low	Low	Low	Low	Low
Jenkins et al. (2002)[24]	Low	Unclear	Low	Unclear	High	Low	Low
Hesse et al. (2004)[25]	Low	Unclear	Low	Unclear	Low	Low	Unclear
Ziai et al. (2005)[26]	Low	Unclear	Low	Unclear	High	Low	Low
Jenkins et al. (2008)[27]	Low	Low	Low	Low	High	Low	Low
Cugnet-Anceau et al. (2010)[28]	Low	Unclear	Low	Unclear	High	Low	Low

was classified as moderate. The precision of the main effect estimates of interest was high. The analyses were highly heterogeneous and no dose-response effect could be established. Risk of publication bias was not identified in the analyses performed and for the major outcome (HbA1c changes) a clinically relevant effect of great magnitude was demonstrated. Overall, the quality of the body of evidence of this systematic review was classified as moderate.

Publication bias was assessed by visually examining a funnel plot, with asymmetry being formally assessed by the Egger regression test. No significant asymmetry was demonstrated for either HbA1c ($P = 0.135$; Figure 2) or fasting plasma glucose ($P = 0.466$; Figure 3). Trim-and-fill computation for HbA1c pooled data did not demonstrate any missing study (data not presented).

Analyses of summary estimates

HbA1c change. Data from studies that assessed HbA1c were pooled. HbA1c absolute values decreased by 0.55% (−0.96 to −0.13; $I^2 = 94.1\%$; $P < 0.001$) in patients who consumed high-fiber diets as compared to control diets (Figure 4). Thirteen comparisons were included in this analysis because one study presented only the percent change of HbA1c rather than the absolute values.[23] The percent reduction in HbA1c values (14 comparisons) was −4.75% (95% CI:−9.35 to −0.15; $I^2 = 93.5\%$; $P < 0.001$). The observed reduction in HbA1c, both in absolute values and in percentage, was achieved with dietary fiber intakes ranging from 37.4 to 42.6 g/day (considering a 2,000 kcal/day diet) or with 3.5 to 15 g/day of fiber supplements. These results did not change when a trim-and-fill computation was performed.

The heterogeneity observed in HbA1c analysis (absolute values) was explored by meta-regression analysis (Table 4). The proportion of between-study variance explained by each predefined covariate is shown. Study follow-up was the only variable that individually influenced the heterogeneity (adjusted R-square = 35.62%). A subgroup analysis of HbA1c including the follow-up as a binary variable was not significant: follow-up ≤12 weeks ($n = 4$; WMD = −1.488; 95% CI −3.139 to 0.164; I square = 95.9%) in comparison with follow-up >12 weeks ($n = 8$; WMD = −0.037; 95% CI −0.330 to 0.256; I square = 83.9%).

Fasting plasma glucose change. Eight studies (10 comparisons) described data on fasting plasma glucose. Pooled data showed a mean glucose reduction of −9.97 mg/dL (95% CI −18.16 to −1.78; $I^2 = 95.5\%$; $P < 0.001$) in patients who consumed high-fiber diets compared with control diets (Figure 5).

The observed heterogeneity was explored using univariate meta-regression analyses (Table 4). Variability in

Table 3 **Assessment of the quality of the body of evidence for studies included in the present systematic review.**

Factor	Quality	Support for judgment
Within-study risk of bias (methodological quality)	Moderate	All trials included a random sequence generation, although allocation bias was unclear in the majority of studies. The risk of performance bias was low. In general, the blinding of outcome assessment was unclear and about one-third of trials had a high risk of incomplete data outcomes due to a dropout/withdrawal rate >20%. Selective reporting bias was low.
Directness of evidence	High	Direct comparisons of an intervention diet with a control diet were performed in all trials.
Heterogeneity	Low	High heterogeneity was observed in the analyses of HbA1c and fasting plasma glucose. This heterogeneity was partially explained by the duration of follow-up and patient age, respectively.
Precision of effect estimates	High	The confidence interval for HbA1c changes was not large, but the CI for fasting plasma glucose was large; values did not have clinical relevance.
Risk of publication bias	High	No significant asymmetry was demonstrated by the funnel plot; the Egger regression test and the trim-and-fill computation did not demonstrate any missing study.
Large magnitude effect	High	The magnitude of effect observed for HbA1c reduction, which was the main clinically relevant outcome, was large.
Effect of confounding factors	Moderate	The good glycemic control demonstrated by patients in up to half of the included trials could have led to an underestimation of the expected fiber effects. On the other hand, differences in diet composition between intervention and control diets (besides dietary fiber content) could have influenced the trials results.
Dose-response gradient	Very low	A dose-response effect of fiber intake on glycemic control could not be established.

the age of the patients explained 63.56% of the observed heterogeneity. Study design, period of follow-up, quality score of study, type of intervention, and difference in fiber content did not explain the heterogeneity. In the sensitivity analyses, age was included as a binary variable according to the mean age of the patients studied. However, only one study of fasting plasma glucose included patients with a mean age <59.4 years and the reduction observed in that study was −89.70 (95% CI −105.27 to −74.13).[26] In the group of studies that included patients older than 59.4 years, the effect of fiber was not significant (WMD = −0.88 [95% CI −6.78, 5.02]; I square = 89.5%; $P < 0.001$).

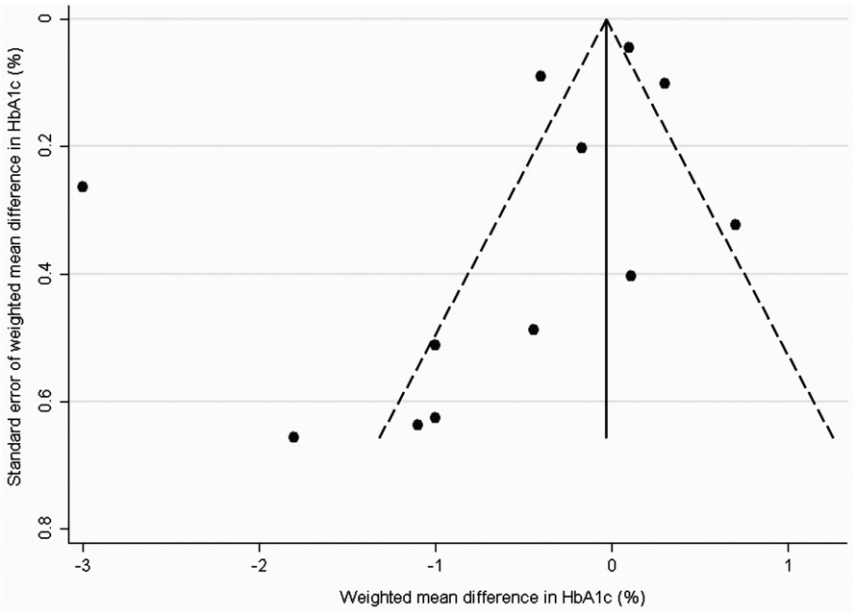

Figure 2 **Funnel plot diagram of publication bias in RCTs evaluating HbA1c.**

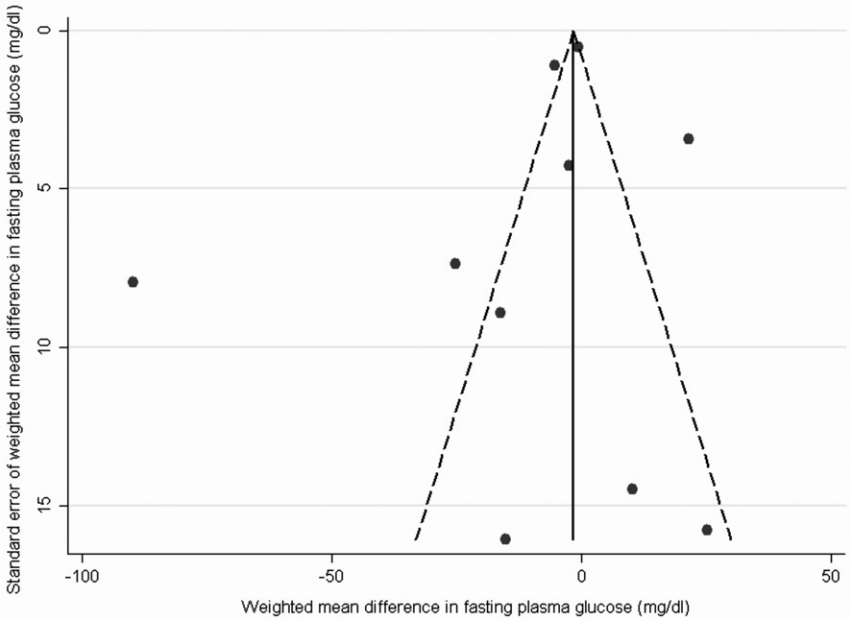

Figure 3 **Funnel plot diagram of publication bias in RCTs evaluating fasting plasma glucose.**

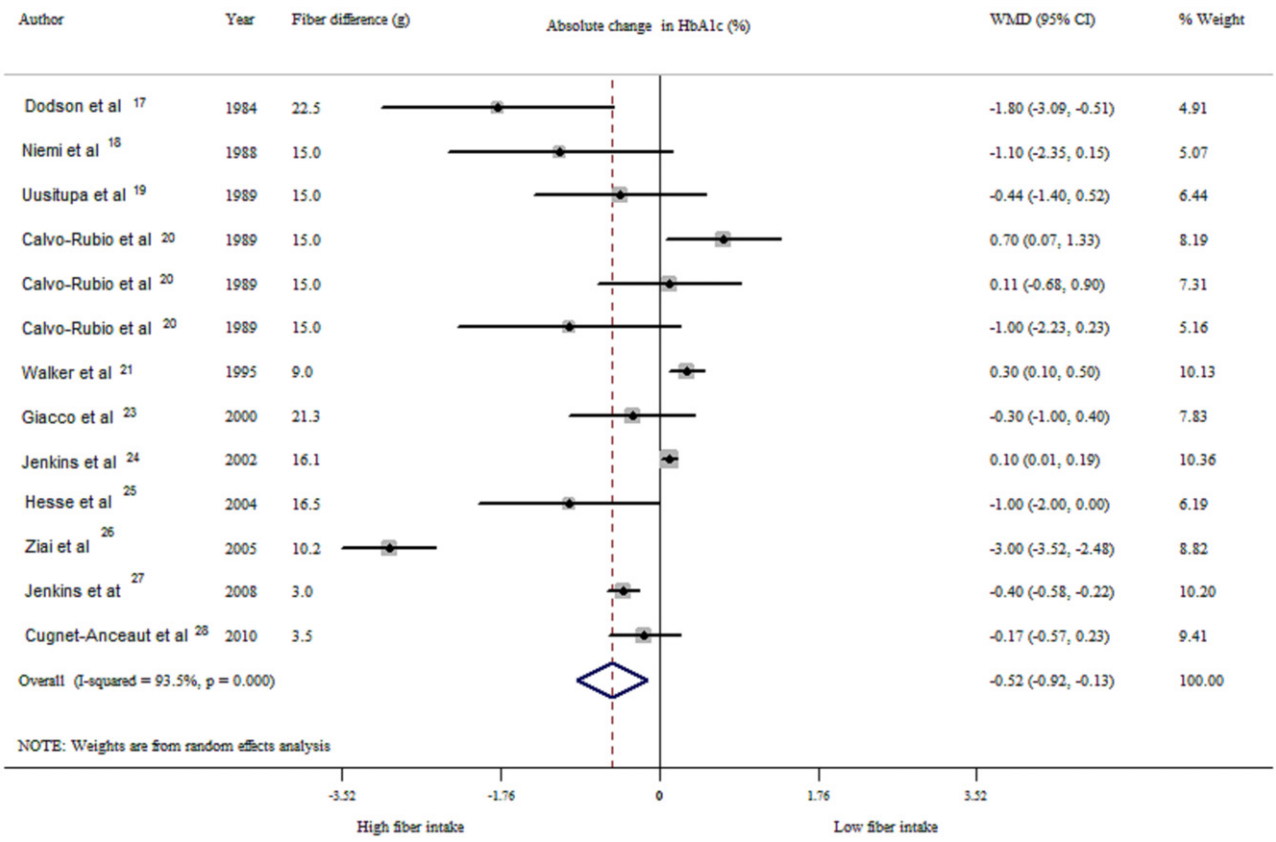

Figure 4 **Forest plot diagram of the effect of fiber intake on HbA1c.**

Table 4 **Univariate meta-regression analysis of the effect of increased fiber intake on absolute HbA1c and fasting plasma glucose changes.**

Covariate	HbA1c (%)		Fasting plasma glucose (mg/dL)	
	Adjusted R-square (%)	$P > \|t\|$	Adjusted R-square (%)	$P > \|t\|$
Study design[a]	−1.17	0.860	−335.69	0.235
Study follow-up[b]	35.62	0.034	−6.29	0.787
Age of patients[c]	5.31	0.280	63.56	0.001
Type of intervention[d]	−5.36	0.570	−348.53	0.324
Fiber difference between groups[e]	−7.76	0.480	−287.22	0.657

[a] Parallel or crossover.
[b] > or ≤12 weeks.
[c] > or ≤59.4 years.
[d] Foods or supplement.
[e] > or ≤13.0 g/day.

DISCUSSION

In this systematic review with meta-analyses, the effect of dietary fiber on glycemic control of patients with type 2 diabetes was evaluated through an analysis of 11 pooled RCTs (13 comparisons) of at least 8 weeks' duration. Diets with foods rich in fiber or fiber supplements caused an absolute reduction of 0.55% in HbA1c (corresponding to an average reduction of 4.75% and an absolute reduction of 10 mg/dL in fasting plasma glucose values.

In a systematic review published in 2004, diets with low fiber and moderate carbohydrate content were compared with diets that were high in fiber and carbohydrates in patients with diabetes.[15] Diets rich in fiber and carbohydrate were associated with reductions in HbA1c (6 trials; weighted average percent change, −6%) and fasting, postprandial, and average plasma glucose; however, the search strategy, the selection criteria for inclusion, and the study quality were not described.[15] Another systematic review, without a meta-analysis, evaluated the effects of psyllium supplementation on glycemic control of patients with type 2 diabetes.[39] Two of the four RCTs included in that review (also included in the present systematic review) compared the effect of psyllium with placebo on HbA1c; the other two studies evaluated the acute postprandial glucose effects only.

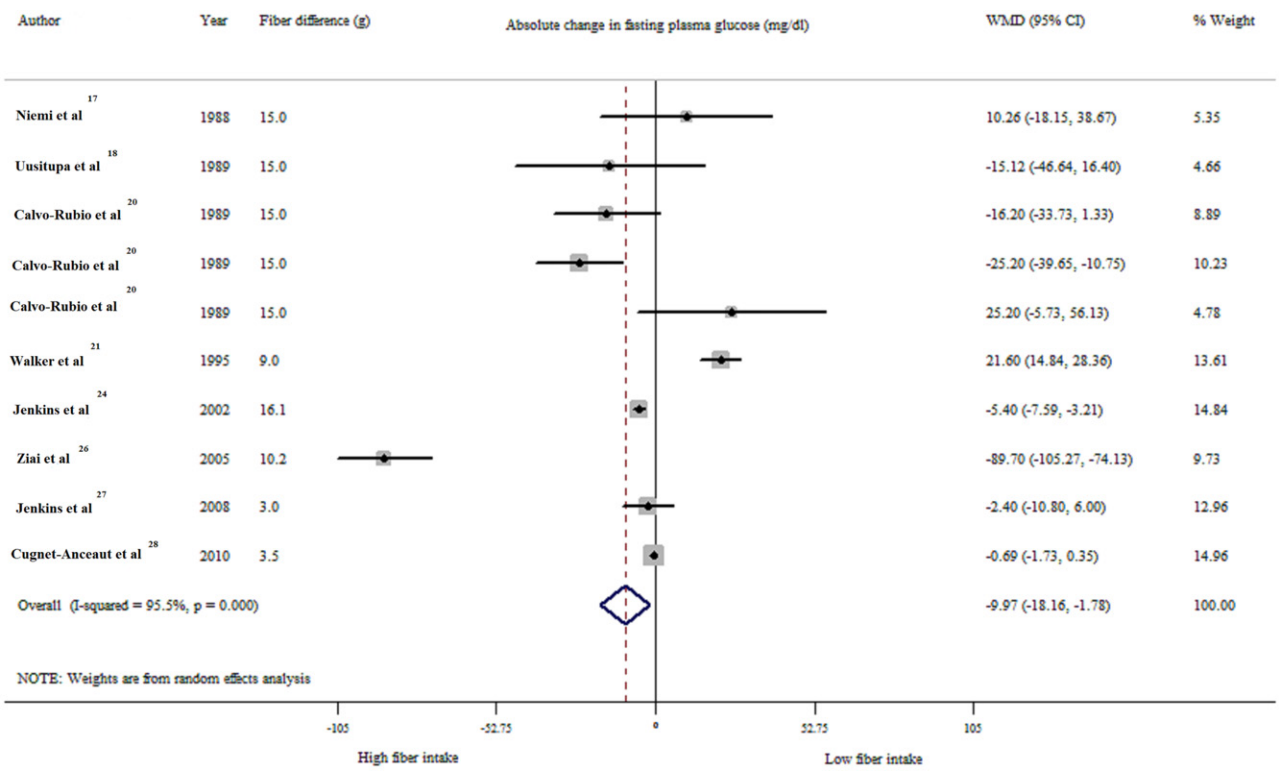

Figure 5 **Forest plot diagram of the effect of fiber intake on fasting plasma glucose.**

The authors concluded that psyllium supplementation may be effective for improving glycemic control.[39] Recently, another systematic review including 15 clinical trials evaluated the effect of fiber intake on glycemic control of patients with type 2 diabetes. A decrease of 0.26% (absolute value) in HbA1c and 15.3 mg/dL in fasting plasma glucose was demonstrated.[17] The following aspects of that study preclude comparison of results with the present meta-analysis: 5 of the 15 included studies lasted less than 8 weeks; the method for HbA1c measurement in each trial was not described; and HbA1c values at baseline were not included in the analysis – instead, the authors compared the final HbA1c values of the intervention and control groups. Furthermore, nine of the RCTs in the present meta-analysis also fulfilled the selection criteria for the prior review but were not included.

In the present meta-analyses, a high level of heterogeneity was detected for HbA1c and fasting plasma glucose. Therefore, a random effects model was used instead of a fixed model, since the random effects model involves an assumption that the effects being estimated in the different studies are not identical.[29] The age of the patients was the only identified variable that partially explained the heterogeneity of fasting plasma glucose changes, according to meta-regression and sensitivity analyses; however, just one study included patients younger than 59.4 years and a definitive conclusion about the influence of age on fasting plasma glucose reduction by increased fiber intake cannot be established. In the analyses of HbA1c, patient age was not associated with heterogeneity.

The high heterogeneity of the models in the present review could not be fully explained. Some differences in the composition of the intervention and control diets (e.g., macronutrients – especially carbohydrate content, glycemic index, and energy restriction; and the sources of dietary fiber) used in the RCTs might have influenced the confidence values in the final results, thereby contributing to the heterogeneity; however, these aspects could not be investigated as potential sources of heterogeneity because most studies did not report them. Physical activity as well as changes in weight and types of diabetes treatment could also be possible sources of heterogeneity, since these variables can influence glycemic control. However, data on these variables were absent or incomplete in most reports and could not be included in the present analyses.

The influence of dietary fiber on glucose metabolism has been attributed particularly to soluble rather than insoluble fiber. Soluble fiber physiologically modulates the postprandial glycemic response through its effects on the stomach and small bowel. These effects include the following: delayed gastric emptying; modification of gastrointestinal myoelectrical activity and delayed small bowel transit; reduced glucose diffusion through the unstirred water layer; and reduced accessibility of α-amylase to its substrates due to increased viscosity of gut contents.[16] In addition, both soluble and insoluble fiber intake can improve glycemic control by increasing the insulin sensitivity.[40,41] The mechanisms associated with this last beneficial effect have not yet been completely established.

The results of the current meta-analysis pointed to an average reduction of 0.55% in HbA1c absolute values (relative reduction of 4.75%) due to diets containing foods rich in fiber or fiber supplements. A reduction of 5% in HbA1c is clinically relevant and comparable to the decrease achieved through some medications for type 2 diabetes.[42] Lastly, it is meaningful that the improvement of glycemic control achieved with fiber intake occurs without relevant adverse effects, especially hypoglycemia, that are often associated with anti-diabetic medications.[6] Furthermore, in the general population, high dietary fiber intake provides many health benefits, including enhancement of weight loss and reduction of cardiovascular risk.[43] These effects can be especially relevant in patients with type 2 diabetes.

The present systematic review and meta-analysis were conducted in accordance with the Cochrane[29] and PRISMA[30] guidelines. All relevant studies were included, regardless of language. In addition, the inclusion of studies with at least 8 weeks of follow-up allowed the detection of actual HbA1c changes.[9] Using the GRADE approach, the quality of the body of evidence in the current review was classified as moderate.

A possible limitation of this systematic review was the inclusion of studies with a small sample size; most of the studies (64%) included fewer than 50 patients. There was also high variability in the duration of study follow-up (8–24 weeks). A further limitation could be related to the methods of HbA1c measurement, since these were not uniform among the RCTs evaluated. For that reason, HbA1c reduction was described in terms of percentage of change in addition to changes in absolute values. This approach confirmed the beneficial effect of high-fiber diets in HbA1c. Another potential limitation is the inability to demonstrate an independent effect of soluble and insoluble fiber, since the majority of studies reported only the total fiber content. In fact, a recent review revealed that studies in this field have generally paid insufficient attention to providing detailed descriptions of the characteristics of dietary fibers.[43] Furthermore, in some studies, the control group received insoluble fiber as placebo, and this can be a confounder since insoluble fibers can influence the postprandial glucose response.[16] Finally, as expected due to the parameters of this systematic review, the benefit of fiber intake

on glucose control cannot be extrapolated to patients with type 1 diabetes.

CONCLUSION

The results of the meta-analysis presented here support the recommendation to increase dietary fiber intake in patients with type 2 diabetes in order to decrease HbA1c and fasting plasma glucose levels. Thus, these patients should be encouraged to include in their daily diet foods that are rich in fiber, such as whole grains, vegetables, and fruits, or to use fiber supplements. However, considering the different types and sources of fibers (soluble and/or insoluble fibers provided by foods and/or supplements), RCTs should be performed to explore the best sources and amounts of dietary fiber necessary to improve glycemic control in patients with type 2 diabetes.

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Declaration of interest. The authors have no relevant interests to declare.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix S1 **Complete Medline search strategy.**