See corresponding editorial on page 921.

Low-glycemic index diets as an intervention for diabetes: a systematic review and meta-analysis

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ABSTRACT

Background: Low-glycemic index (GI) diets are thought to reduce postprandial glycemia, resulting in more stable blood glucose concentrations.

Objective: We hypothesized that low-GI diets would be superior to other diet types in lowering measures of blood glucose control in people with type 1 or type 2 diabetes, or impaired glucose tolerance.

Methods: We searched PubMed, the Cochrane Library, EMBASE, and clinical trials registries for published and unpublished studies up until 1 March, 2019. We included 54 randomized controlled trials in adults or children with impaired glucose tolerance, type 1 diabetes, or type 2 diabetes. Continuous data were synthesized using a random effects, inverse variance model, and presented as standardized mean differences with 95% CIs.

Results: Low-GI diets were effective at reducing glycated hemoglobin (HbA1c), fasting glucose, BMI, total cholesterol, and LDL, but had no effect on fasting insulin, HOMA-IR, HDL, triglycerides, or insulin requirements. The reduction in fasting glucose and HbA1c was inversely correlated with body weight. The greatest reduction in fasting blood glucose was seen in the studies of the longest duration.

Conclusions: Low-GI diets may be useful for glycemic control and may reduce body weight in people with prediabetes or diabetes. *Am J Clin Nutr* 2019;110:891–902.

Keywords: glycemic index, diabetes, low-GI diets, HbA1c, blood glucose, BMI, body fat, blood lipids

Introduction

People with prediabetes, type 1 diabetes, or type 2 diabetes are, by definition, unable to successfully control their postprandial blood glucose concentrations in the absence of medical care. First developed by Jenkins et al. (1), the glycemic index (GI) of a food represents the effect on postprandial blood glucose concentrations that the carbohydrate portion of a food has compared with glucose or white bread. The glycemic load calculates the amount that the whole food raises blood glucose postprandially (2). Low-GI foods, such as fructose, lower peak postprandial blood glucose excursions (3) and have been shown to have a positive effect on glucose control (4). A recent network meta-analysis including 56 trials showed that various dietary types lowered both glycated hemoglobin (HbA1c) and fasting blood glucose (FBG) compared with a control diet (5), and another meta-analysis of 18 trials showed similar results when comparing low-GI diets with high-GI diets (6).

We recently showed in a systematic review and meta-analysis that low-GI diets improve body weight, BMI, total cholesterol (TC), and LDL in people with overweight and obesity, but had no effect on FBG (7). Evans et al. demonstrated the strongest positive effects on postprandial glucose and FBG of fructose consumption in people with diabetes (3). We hypothesized that low-GI diets would lower both FBG and HbA1c in these populations. We thus undertook a systematic review and meta-analysis according to Cochrane principles (8) of randomized controlled trials (RCTs) comparing low-GI diets with any other diet type in people with impaired glucose tolerance, type 1 diabetes, or type 2 diabetes.

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Supplemental Table 1 and Supplemental Figures 1–34 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/ajcn/.

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Abbreviations used: FBG, fasting blood glucose; FBI, fasting blood insulin; GI, glycemic index; HbA1c, glycated hemoglobin; RCT, randomized controlled trial; SMD, standardized mean difference; TC, total cholesterol.

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Methods

Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and review registration

This systematic review and meta-analysis was prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions (9). The review was registered in the PROSPERO International Prospective Register of Systematic Reviews (CRD42017057306).

Review question [PICOTS – Population (P), Intervention (I), Comparison (C), Outcome (O), Time (T), Study (S)]

Our study asked the question: in children, adolescents, or adults with impaired glucose tolerance, type 1 diabetes, or type 2 diabetes (P), do low-index (GI) or load (GL) diets (I), compared with high-GI, low-fat, low-carbohydrate, conventional weight loss diets or specialty diets (C) lower measures of blood glucose control and body weight (O) over a period of ≥1 wk (T) in RCTs (S)?

Primary and secondary outcomes

As stated in CRD42017057306, the primary outcome of interest for this analysis was HbA1c. Secondary outcomes were FBG, fasting blood insulin (FBI), HOMA-IR, postprandial blood glucose, and BMI.

Data sources and search strategy

A comprehensive search strategy was designed for Entrez-PubMed and modified for use in other databases. The search strategy was:

((“glycemic index” OR “glycaemic index”) OR (“glycemic load” OR “glycaemic load”) OR “Low GI” OR “high GI”)

AND

(“child” OR “children” OR “adolescent” OR “adolescence” OR “adult” OR “elderly”)

AND

(“diabetes” OR “pre-diabetes” OR “impaired glucose tolerance” OR “glucose” OR “HbA1c” OR “body weight” OR “obesity” OR “BMI” OR “weight loss”)

AND

(“diet” OR “dietary”).

We searched PubMed, the Cochrane Library, EMBASE, clinicaltrials.gov, and the WHO clinical trials database. We did not restrict our search results by time or language. The final search was carried out on 1 March, 2019.

Eligibility criteria

Studies were included if they met the PICOTS criteria: RCTs of 1 wk or longer in duration; in people with impaired glucose tolerance, type 1 diabetes, or type 2 diabetes; with a comparison of a low-GI or low-glycemic load diet with a high-GI, low-fat, low-carbohydrate, conventional weight loss diet or specialty diet; measuring markers of blood glucose control or body weight.

Study selection

Abstracts and full text articles were included or excluded by 2 authors, using the double-blind coding assignment function of EPPI-Reviewer 4 (10). Disagreements were resolved by consensus, or by reference to a third author.

Study quality

Study quality was determined independently by 2 authors using the Cochrane Collaboration’s tool for assessing the risk of bias in randomized trials (11). Disagreements were resolved by consensus, or by reference to a third author.

Data extraction

Data extraction was done by one author and checked by a second author. Data extracted included study characteristics, outcomes of interest, and study quality. If data were present only in figures, we used WebPlotDigitizer to extract the mean and error (12). SEs were converted to SDs using the equation: $SD = SEM \times \sqrt{N}$, where N is the number in the study arm.

Data synthesis and analysis

Data from included studies were meta-analyzed with Review Manager 5.3 (13) using a random effects, inverse variance model. A random effects model was chosen to account for differences in effects sizes that were influenced by factors other than chance (e.g., sex, baseline BMI, glucose tolerance, delivery of the intervention, and others). As outcomes were reported in different ways, we used a standardized mean difference (SMD) calculation with 95% CI to retain maximum information. To convert SMDs to example mean differences, we multiplied the SMD by the mean SD of studies reporting the outcome of choice. Where SDs were missing, these were imputed by taking the mean of the other studies reporting the same outcome using the same method. Where a study had >2 arms, and 1 arm was used twice in a single analysis, the population number for that arm was halved to avoid double-counting.

Heterogeneity was calculated in Review Manager 5.3 and reported as Tau^2, Chi^2, and I^2. A funnel plot analysis was undertaken to test for publication bias.

Additional analyses

We prespecified the following subgroup analyses: subgroup by control diet type, subgroup by diabetes status, subgroup by body weight. We performed a posthoc sensitivity analysis by length of intervention.

Results

Study selection

We uploaded 2405 citations to EPPI-Reviewer 4 (10) (**Figure 1**). Of these, 777 were duplicates, leaving 2328 abstracts.

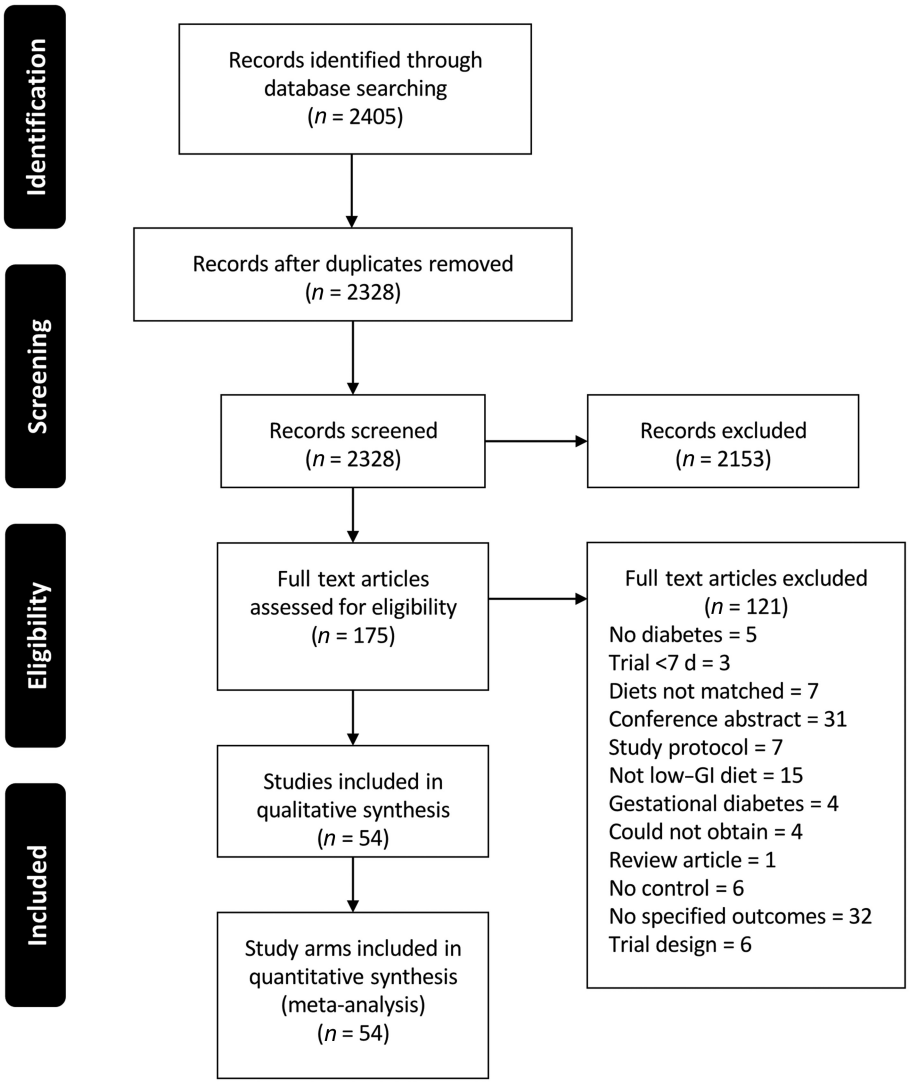

FIGURE 1 PRISMA flow diagram. Of an initial 2328 independent records, 2153 were excluded at the title/abstract level. The remaining 175 full text articles were assessed for inclusion, resulting in 54 included articles. Data from all 54 articles was included in the meta-analyses.

These were then subjected to inclusion or exclusion at the title and abstract level. This left 175 full text articles, which were then subjected to inclusion or exclusion by application of the full text inclusion criteria. We included 54 individual articles (**Supplementary Table 1**) (14–67).

Study characteristics

Studies varied in length from 1 wk to 12 mo. The diets that were compared against low-GI diets included carbohydrate exchange, diabetes diets, habitual diets, healthy diets, high-fat diets, high-fiber diets, high-GI diets, hypertensive diets, and low-fat diets. Outcomes extracted included HbA1c, FBG, FBI, HOMA-IR, insulin requirements, body weight, BMI, and blood lipids. All studies involved people with impaired glucose tolerance, type 1 diabetes, or type 2 diabetes. The majority of studies included participants who were obese (25 studies) or overweight (14 studies).

Quality of included studies

The quality of the included studies was determined with reference to the Cochrane Collaboration's tool for assessing the risk of bias in randomized trials (11). The risk of bias was substantial, mostly due to the general difficulty of blinding (**Supplementary Figure 1**). The method of randomization was rarely reported.

Glycemic and insulinemic control

As stated previously, low-GI diets have been suggested to be effective in achieving long-term glycemic control (14). We found a statistically significant lowering of HbA1c (36 studies, 2077 participants) (SMD = −0.19; 95% CI: −0.28, −0.11; P <0.0001) (**Figure 2**) and FBG (46 studies, 2602 participants) as a result of low-GI diets (SMD = −0.15; 95% CI: −0.26, −0.03; P = 0.01) (**Supplementary Figure 2**), which equates to a reduction in HbA1c of ∼0.15 points and FBG of ∼1.67 mg/dL.

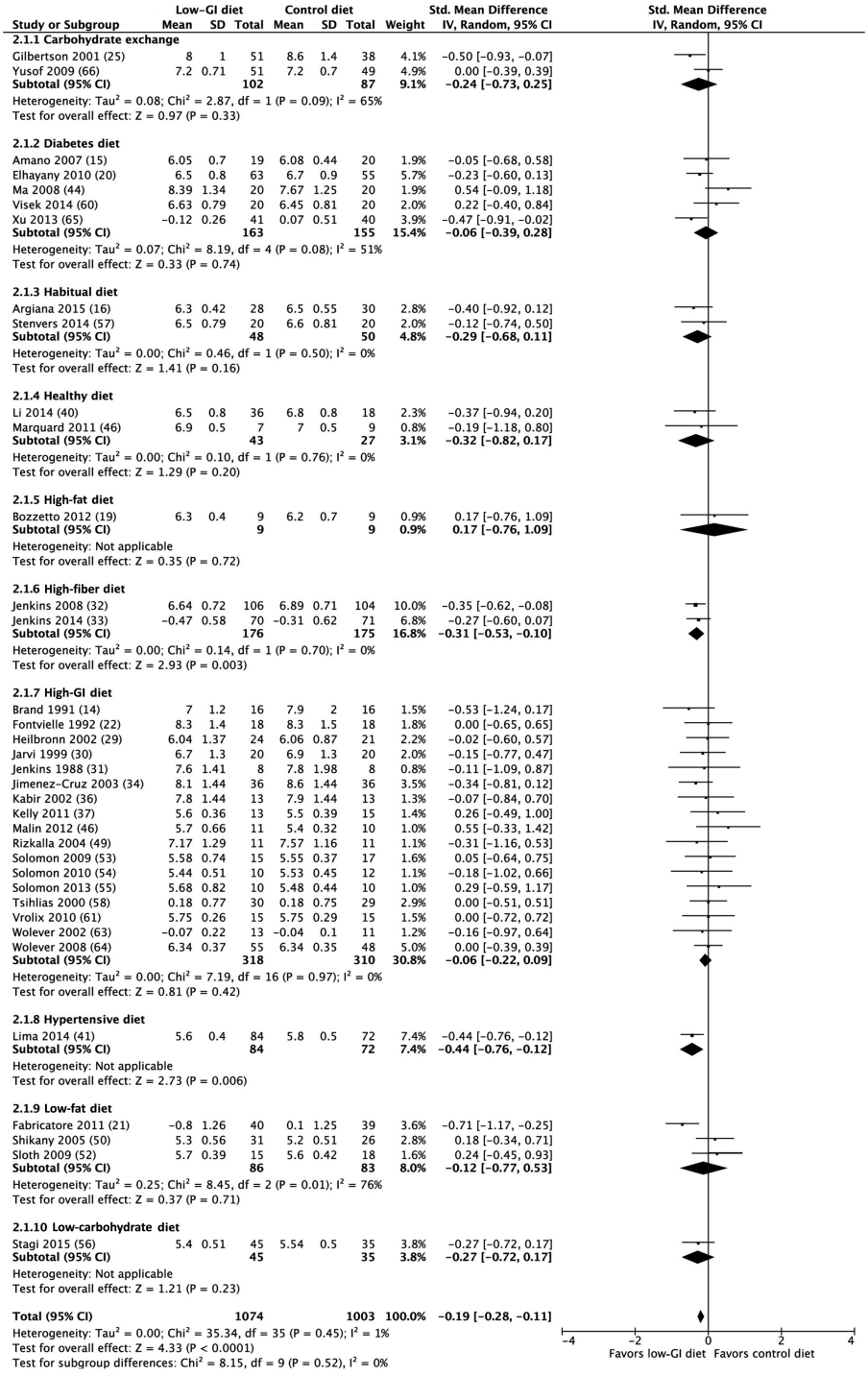

FIGURE 2 Subgroup meta-analysis of HbA1c by control diet. Data are presented as standardized mean differences with 95% CIs.

In terms of specific control diets, the low-GI diet lowered FBG significantly more than habitual diets, a healthy diet, an antihypertensive diet, and a low-carbohydrate diet.

In our analysis of studies reporting on FBI (28 studies, 1512 participants), HOMA-IR (13 studies, 647 participants), or insulin requirements for people with type 1 diabetes (4 studies, 147 participants), we did not find any overall differences between low-GI diets and control diets (**Table 1**, **Supplementary Figures 3–5**).

Because many studies failed to achieve a meaningful difference in GI between the low-GI and control arms, we undertook a subgroup meta-analysis only of studies achieving a reduction in GI of 20 points or more. In these subgroups, HbA1c was significantly lower in people consuming a low-GI diet than a

control diet (SMD = −0.19; 95% CI: −0.34, −0.04; $P = 0.01$ – equivalent to 0.15 points), but no other glycemic or insulinemic outcomes were statistically significant.

In order to see if low-GI diets were more effective in people with impaired glucose tolerance, type 1 diabetes, or type 2 diabetes, we undertook subgroup analyses by diabetes status (Table 1). There were no differences between subgroups, except in FBG, where people with type 2 diabetes had a greater reduction in FBG on low-GI diets than on control diets (SMD = −0.17; 95% CI: −0.27, −0.07; $P = 0.0009$) (**Supplementary Figure 6**). This is equivalent to a reduction in FBG of ∼1.7 mg/dL. In both HbA1c and FBG, people with type 1 diabetes showed a larger reduction on low-GI diets than people with other forms of diabetes. However, a lack of studies, combined with very small sample sizes, meant that these subgroups failed to reach statistical significance ($P = 0.05$, $P = 0.07$, respectively). There were no significant differences in hypoglycemia between low-GI diets and carbohydrate exchange diets, or a high-GI diet (**Supplementary Figure 7**).

We also analyzed HbA1c, FBG, FBI, and HOMA-IR by the obesity status of the participants (Table 1, **Supplementary Figures 8–11**, respectively). Although no differences in FBI were apparent between people of healthy weight, overweight, or obesity, stark differences were apparent in both HbA1c and FBG. In both analyses, the greatest improvement in glycemic control was in people of healthy body weight, which decreased in a "dose response" fashion as obesity increased. For example, whereas people of healthy body weight experienced a decrease in FBG of ∼4.3 mg/dL (SMD = −0.39; 95% CI: −0.71, −0.08; $P = 0.02$), this decreased to ∼2.4 mg/dL in people who were overweight ($P = 0.02$) and to 0.4 mg/dL in people with obesity ($P = 0.59$). A similar pattern was observed in HbA1c measurements, and to a lesser extent, HOMA-IR.

Body weight

Overall, the 42 studies included in the analysis failed to show a significant difference between low-GI diets and control diets in lowering body weight (SMD = −0.08; 95% CI: −0.16, 0.00; $P = 0.07$), and the low-GI diets were not superior to any individual control diet (Table 1, **Supplementary Figure 12**). An analysis of all 22 studies that reported BMI showed a reduction in BMI associated with low-GI diets (SMD = −0.16; 95% CI: −0.28, −0.04; $P = 0.01$) (**Supplementary Figure 13**). This is equivalent to a reduction in BMI of ∼0.6 kg/m^2. A subgroup analysis of the studies that achieved a reduction in GI of 20 points or more failed to show any significant differences for either body weight or BMI (**Supplementary Figures 14** and **15**), nor did a subgroup analysis of studies with energy restriction as an aim (**Supplementary Figures 16** and **17**). Similarly, a subgroup analysis of these studies by diabetes status failed to show any reduction in body weight (**Supplementary Figure 18**) but did show a significant overall reduction in BMI (**Supplementary Figure 19**).

In contrast, an analysis of body weight and BMI by obesity status produced interesting insights. Whereas people of healthy weight and those who were overweight did not show any significant decrease in body weight from a low-GI diet, people with obesity were the only group that showed a significant reduction in body weight (SMD = −0.14; 95% CI: −0.24, −0.04; $P = 0.007$) (Table 1, **Supplementary Figure 20**). This is equivalent to a reduction in body weight of ∼1.8 kg. A similar pattern was seen in our analysis of BMI by obesity status (**Supplementary Figure 21**).

Blood lipids

Overall, low-GI diets were significantly superior to control diets in lowering TC (Table 1, **Supplementary Figure 22**). This reduction (SMD = −0.14; 95% CI: −0.23, −0.05; $P = 0.003$) is equivalent to ∼4.5 mg/dL (0.14 mmol/L). A similar reduction [equivalent to ∼6.4 mg/dL (0.20 mmol/L)] was seen in a subgroup of studies achieving a 20 point or greater reduction in dietary GI (**Supplementary Figure 23**). This reduction was driven by studies in people with impaired glucose tolerance, as low-GI diets in studies involving people with type 1 or type 2 diabetes did not reduce TC significantly compared with control diets.

Similarly, LDL cholesterol was significantly lower in people consuming low-GI diets compared with control diets (SMD = −0.18; 95% CI: −0.28, −0.07; $P = 0.001$) (Table 1, **Supplementary Figure 24**). This difference is equivalent to ∼5.5 mg/dL. This effect was even greater in the studies achieving a reduction in dietary GI of 20 points or greater (SMD = −0.26; 95% CI: −0.42, −0.11; $P = 0.0007$ – equivalent to 8.0 mg/dL) (**Supplementary Figure 25**). There was a numerically larger reduction in LDL in people with impaired glucose tolerance compared with those with type 2 diabetes (**Supplementary Figure 26**), but the difference between the subgroups was not statistically significant (test for subgroup differences: $P = 0.17$). There were no significant differences in HDL or triglycerides (**Supplementary Figures 27** and **28**).

Sensitivity analyses

There was considerable variation in the length of study intervention periods. We undertook a subgroup analysis of FBG by length of intervention (**Table 2**, **Supplementary Figure 29**). Although we found an increase in the effect of low-GI diets on FBG over time, none of the subgroups reached statistical significance.

We also undertook a sensitivity analysis of the effect of blinding on study outcomes. We analyzed the 8 studies that were either double-blind or blinded to outcome assessors (Table 2, **Supplementary Figure 30**). There were no significant differences between low-GI diets and control diets in this analysis.

We undertook a sensitivity analysis to identify individual studies that substantially change the heterogeneity of our analyses. Heterogeneity was generally nonexistent to low overall; however, we examined all outcomes that had both an I^2 of 50% or greater and >3 studies in the analysis. In this analysis, the removal of Xu et al. 2013 from the triglyceride analysis resulted in the low-GI diet becoming statistically significantly superior to the diabetes diet but did not change the overall significance of the comparison. Furthermore, the removal of Klemsdal et al. 2010 or Wolever et al. 2008 from the analysis of studies longer than 6 mo in duration resulted in a statistically significant difference between low-GI diets and control diets.

TABLE 1 Outcomes of meta-analyses (SMD [95% CI])[1]

Outcome	Subgroup	Studies	Participants	Effect estimate (SMD [95% CI])	Representative conversion (unit [95% CI])
HbA1c SMD; %HbA1c	Control diet	36	2077	−0.19 [−0.28, −0.11]	−0.15 [−0.23, −0.09]
	Carbohydrate exchange	2	189	−0.24 [−0.73, 0.25]	−0.19 [−0.59, 0.20]
	Diabetes diet	5	318	−0.06 [−0.39, 0.28]	0.05 [−0.32, 0.23]
	Habitual diet	2	98	−0.29 [−0.68, 0.11]	−0.23 [−0.55, 0.09]
	Healthy diet	2	70	−0.32 [−0.82, 0.17]	−0.26 [−0.66, 0.14]
	High-fat diet	1	18	0.17 [−0.76, 1.09]	0.14 [−0.62, 0.88]
	High-fiber diet	2	351	−0.31 [−0.53, −0.10]	−0.25 [−0.43, −0.08]
	High-GI diet	17	628	−0.06 [−0.22, 0.09]	−0.05 [−0.18, 0.07]
	Anti-hypertensive diet	1	156	−0.44 [−0.76, −0.12]	−0.36 [−0.62, −0.10]
	Low-fat diet	3	169	−0.12 [−0.77, 0.53]	−0.10 [−0.62, 0.14]
	Low-carbohydrate diet	1	80	−0.27 [−0.72, 0.17]	−0.22 [−0.58, 0.14]
	Diabetes status	36	2077	−0.19 [−0.28, −0.11]	−0.15 [−0.23, −0.09]
	Impaired glucose tolerance	12	584	−0.12 [−0.31, 0.07]	−0.10 [−0.25, 0.06]
	Type 1 diabetes	3	141	−0.33 [−0.67, 0.00]	−0.27 [−0.54, 0.00]
	Type 2 diabetes	21	1352	−0.20 [−0.30, −0.09]	−0.16 [−0.24, −0.07]
	Obesity status	36	2077	−0.19 [−0.28, −0.11]	−0.15 [−0.23, −0.09]
	Healthy weight	5	234	−0.29 [−0.55, −0.03]	−0.23 [−0.45, −0.02]
	Overweight	8	380	−0.16 [−0.37, 0.04]	−0.13 [−0.30, 0.03]
	Obesity	22	1307	−0.14 [−0.26, −0.01]	−0.11 [−0.21, −0.01]
	Mixed	1	156	−0.44 [−0.76, −0.12]	−0.36 [−0.62, −0.10]
	GI difference >19	14	692	−0.19 [−0.34, −0.04]	−0.15 [−0.28, −0.03]
Fasting blood glucose SMD; mg/dL	Control diet	46	2602	−0.15 [−0.26, −0.03]	−1.67 [−2.89, −0.33]
	Carbohydrate exchange	1	100	−0.16 [−0.55, 0.23]	−1.78 [−6.11, 2.55]
	Diabetes diet	5	329	−0.30 [−0.61, 0.02]	−3.33 [−6.77, 0.22]
	Habitual diet	3	201	−0.29 [−0.57, −0.01]	−3.22 [−6.33, −0.11]
	Healthy diet	1	54	−0.75 [−1.34, −0.17]	−8.33 [−14.87, −11.88]
	High-fat diet	2	52	−0.04 [−0.59, 0.51]	−0.44 [−6.55, 5.66]
	High-fiber diet	2	351	−0.21 [−0.42, 0.00]	−2.33 [−4.66, 0.00]
	High-GI diet	25	875	−0.03 [−0.20, 0.14]	−0.33 [−2.22, 1.55]
	Anti-hypertensive diet	1	156	−0.64 [−0.97, −0.32]	−7.10 [−10.77, −3.55]
	Low-fat diet	5	404	0.08 [−0.13, 0.28]	0.89 [−1.44, 3.11]
	Low-carbohydrate diet	1	80	−0.93 [−1.40, −0.47]	−10.32 [−15.54, −5.22]
	Diabetes status	46	2602	−0.15 [−0.26, −0.03]	−1.67 [−2.89, −0.33]
	Impaired glucose tolerance	17	959	−0.05 [−0.34, 0.23]	−0.56 [−3.77, 2.55]
	Type 1 diabetes	3	70	−0.44 [−0.91, 0.04]	−4.88 [−10.10, 0.44]
	Type 2 diabetes	26	1573	−0.17 [−0.27, −0.07]	−1.89 [−3.00, −0.78]
	Obesity status	46	2602	−0.15 [−0.26, −0.03]	−1.67 [−2.89, −0.33]
	Healthy weight	5	163	−0.39 [−0.71, −0.08]	−4.33 [−7.88, −0.89]
	Overweight	14	588	−0.22 [−0.41, −0.03]	−2.44 [−4.55, −0.33]
	Obese	25	1665	−0.04 [−0.20, 0.11]	−0.44 [−2.22, 1.22]
	Mixed	2	186	−0.53 [−0.92, −0.15]	−5.88 [−10.21, −1.67]
	GI difference >19	18	864	−0.03 [−0.25, 0.19]	−0.33 [−2.78, 2.11]
Fasting blood insulin SMD; pmol/L	Control diet	28	1512	−0.00 [−0.15, 0.15]	0.00 [−8.00, 8.00]
	Carbohydrate exchange	1	100	0.48 [0.08, 0.88]	25.59 [4.27, 46.92]
	Diabetes diet	2	157	−0.13 [−0.45, 0.18]	−6.93 [−23.99, 9.60]
	Habitual diet	3	201	−0.30 [−0.58, −0.02]	−16.00 [−30.93, −1.07]
	Healthy diet	1	54	−0.56 [−1.13, 0.02]	−29.86 [−60.25, 1.07]
	High-fat diet	2	52	0.27 [−0.92, 1.47]	14.40 [−49.05, 78.38]
	High-GI diet	14	497	0.19 [−0.02, 0.40]	10.13 [−1.07, 21.33]
	Low-fat diet	4	371	−0.04 [−0.25, 0.16]	−2.13 [−68.25, −19.20]
	Low-carbohydrate diet	1	80	−0.82 [−1.28, −0.36]	−43.72 [−68.25, −19.20]
	Diabetes status	28	1524	−0.00 [−0.15, 0.15]	0.00 [−8.00, 8.00]
	Impaired glucose tolerance	14	681	0.03 [−0.23, 0.29]	1.60 [−12.26, 15.46]
	Type 2 diabetes	14	843	−0.03 [−0.21, 0.15]	−1.60 [−11.20, 8.00]
	Obesity status	28	1524	−0.00 [−0.15, 0.15]	0.00 [−8.00, 8.00]
	Healthy weight	2	93	−0.22 [−0.90, 0.45]	−11.73 [−47.99, 23.99]
	Overweight	7	288	0.13 [−0.17, 0.44]	6.93 [−9.06, 23.46]
	Obese	19	1143	−0.02 [−0.20, 0.15]	−1.07 [−10.66, 8.00]
	GI difference >19	11	356	0.32 [0.11, 0.54]	17.06 [5.87, 28.79]

(*Continued*)

TABLE 1 (*Continued*)

Outcome	Subgroup	Studies	Participants	Effect estimate (SMD [95% CI])	Representative conversion (unit [95% CI])
HOMA–IR SMD; units	Control diet	13	647	−0.09 [−0.34, 0.16]	−0.17 [−0.66, 0.31]
	Carbohydrate exchange	1	100	0.37 [−0.03, 0.77]	0.71 [−0.06, 1.49]
	Diabetes diet	1	118	−0.32 [−0.68, 0.05]	v0.62 [−1.31, 0.10]
	Habitual diet	1	58	−0.42 [−0.94, 0.11]	−0.81 [−1.81, 0.21]
	Healthy diet	1	54	−0.83 [−1.42, −0.24]	−1.60 [−2.74, −0.46]
	High-fat diet	2	52	0.34 [−0.21, 0.90]	0.66 [−0.41, 1.74]
	High-GI diet	5	106	0.03 [−0.46, 0.52]	0.06 [−0.89, 1.00]
	Low-fat diet	1	79	−0.02 [−0.46, 0.42]	−0.04 [−0.89, 0.81]
	Low-carbohydrate diet	1	80	−0.37 [−0.82, 0.07]	−0.71 [−1.58, 0.14]
	Diabetes status	13	647	−0.09 [−0.34. 0.16]	−0.17 [−0.66, 0.31]
	Impaired glucose tolerance	7	255	−0.16 [−0.57, 0.26]	−0.31 [−1.10, 0.50]
	Type 2 diabetes	6	392	−0.03 [−0.35, 0.29]	−0.06 [−0.68, 0.56]
	Obesity status	13	647	−0.09 [−0.35, 0.18]	−0.17 [−0.66, 0.31]
	Healthy weight	1	54	−0.83 [−1.42, −0.24]	−1.60 [−2.74, −0.46]
	Overweight	3	152	0.36 [0.04, 0.68]	0.69 [0.08, 1.31]
	Obese	8	421	−0.17 [−0.42, 0.08]	−0.33 [−0.81, 0.15]
	GI difference >19	3	58	0.49 [−0.04, 1.02]	0.95 [−0.08, 1.97]
Insulin requirement (type 1 diabetes) SMD; units per day	Control diet	4	147	0.17 [−0.16, 0.49]	2.24 [−2.10, 6.44]
	Carbohydrate exchange	1	89	0.33 [−0.09, 0.75]	4.34 [−1.18, 9.86]
	High-GI diet	3	58	−0.08 [−0.59, 0.44]	−1.05 [−7.76, 5.79]
Hypoglycemia SMD; episodes per month	Control diet	2	122	0.17 [−0.19, 0.52]	0.70 [−0.66, 2.01]
	Carbohydrate exchange	1	104	0.18 [−0.21, 0.56]	0.74 [−0.86, 2.30]
	High-GI diet	1	18	0.13 [−0.79, 1.06]	0.53 [−3.24, 4.35]
Body weight	Control diet	42	2361	−0.08 [−0.16, 0.00]	−1.02 [−2.05, 0.00]
	Carbohydrate exchange	1	100	0.17 [−0.23, 0.56]	2.17 [−2.94, 7.16]
	Diabetes diet	6	369	−0.18 [−0.38, 0.03]	−2.30 [−4.86, 0.38]
	Habitual diet	3	201	−0.32 [−0.71, 0.06]	−4.09 [−9.08, 0.77]
	Healthy diet	1	54	0.14 [−0.43, 0.70]	1.79 [−5.50, 8.95]
	High-fat diet	2	52	0.02 [−0.59, 0.63]	0.26 [−7.55, 8.06]
	High-fiber diet	2	351	−0.13 [−0.34, 0.08]	−1.66 [−4.35, 1.02]
	High-GI diet	22	731	−0.00 [−0.15, 0.14]	0.00 [−1.92, 1.92]
	Anti-hypertensive diet	1	156	−0.03 [−0.34, 0.29]	−0.38 [−4.35, 3.71]
	Low-fat diet	4	347	−0.04 [−0.25, 0.18]	−0.51 [−3.20, 2.30]
	Diabetes status	42	2361	−0.08 [−0.16, 0.00]	−1.02 [−2.05, 0.00]
	Impaired glucose tolerance	16	821	−0.05 [−0.19, 0.09]	−0.64 [−0.19, 0.09]
	Type 1 diabetes	1	16	−0.00 [−0.98, 0.98]	0.00 [−12.53, 12.53]
	Type 2 diabetes	24	1488	−0.09 [−0.19, 0.01]	−1.15 [−2.43, 0.13]
	Mixed type 1 and type 2 diabetes	1	36	−0.02 [−0.67, 0.63]	−0.26 [−8.57, 8.06]
	Obesity status	42	2361	−0.08 [−0.16, 0.00]	−1.02 [−2.05, 0.00]
	Healthy weight	5	175	0.06 [−0.24, 0.37]	0.77 [−3.07, 4.73]
	Overweight	10	440	0.15 [−0.04, 0.34]	1.92 [−0.51, 4.35]
	Obese	25	1509	−0.14 [−0.24, −0.04]	−1.79 [−3.07, −0.51]
	Mixed overweight/obese	1	156	−0.03 [−0.34, 0.29]	−0.38 [−4.35, 3.71]
	GI difference >19	12	342	−0.05 [−0.26, 0.16]	−0.64 [−3.33, 2.05]
	Energy restriction in diets	11	710	−0.03 [−0.17, 0.12]	−0.38 [−2.17, 1.53]
BMI SMD; kg/m^2	Control diet	23	1094	−0.16 [−0.28, −0.04]	−0.62 [−1.09, −0.16]
	Carbohydrate exchange	1	100	0.04 [−0.35, 0.43]	0.16 [−1.37, 1.68]
	Diabetes diet	4	278	−0.22 [−0.45, 0.02]	−0.86 [−1.76, 0.08]
	Habitual diet	2	161	−0.46 [−1.09, 0.17]	−1.79 [−4.25, 0.66]
	Healthy diet	1	54	0.08 [−0.49, 0.64]	0.31 [−1.91, 2.50]
	High-GI diet	11	298	−0.04 [−0.27, 0.19]	−0.16 [−1.05, 0.74]
	Low-fat diet	3	123	−0.00 [−0.36, 0.36]	0.00 [−1.40, 1.40]
	Low-carbohydrate diet	1	80	−0.34 [−0.79, 0.10]	−1.33 [−3.08, 0.39]
	Diabetes status	23	1094	−0.16 [−0.28, −0.04]	−0.62 [−1.09, −0.16]
	Impaired glucose tolerance	12	496	−0.15 [−0.33, 0.03]	−0.59 [−1.29, 0.12]
	Type 2 diabetes	11	598	−0.16 [−0.33, 0.02]	−0.62 [−1.29, 0.08]
	Obesity status	23	1094	−0.16 [−0.28, −0.04]	−0.62 [−1.09, −0.16]
	Healthy weight	2	93	0.09 [−0.33, 0.51]	0.35 [−1.29, 1.99]
	Overweight	6	323	−0.10 [−0.32, 0.12]	−0.39 [−1.25, 0.47]

(*Continued*)

TABLE 1 (*Continued*)

Outcome	Subgroup	Studies	Participants	Effect estimate (SMD [95% CI])	Representative conversion (unit [95% CI])
	Obese	15	678	−0.22 [−0.37, −0.07]	−0.86 [−1.44, −0.27]
	GI difference >19	7	193	−0.06 [−0.35, 0.22]	−0.23 [−1.37, 0.86]
	Energy restriction in diets	7	374	−0.05 [−0.26, 0.15]	−0.20 [−1.01, 0.59]
Total cholesterol SMD; mg/dL	Control diet	42	2387	−0.14 [−0.23, −0.05]	−4.50 [−7.40, −1.61]
	Carbohydrate exchange	1	100	−0.30 [−0.70, 0.09]	−9.62 [−22.52, 2.90]
	Diabetes diet	5	329	0.14 [−0.12, 0.40]	4.50 [−3.86, 12.87]
	Habitual diet	2	98	−0.26 [−0.66, 0.14]	−8.36 [−21.23, 4.50]
	Healthy diet	1	54	−0.23 [−0.79, 0.34]	−7.40 [−25.41, 10.94]
	High-fat diet	2	52	−0.48 [−1.14, 0.18]	−15.44 [−36.67, 5.79]
	High-fiber	2	351	−0.40 [−0.84, 0.05]	−12.87 [−27.02, 1.61]
	High-GI diet	23	796	−0.04 [−0.18, 0.10]	−1.29 [−5.79, 3.22]
	Anti-hypertensive diet	1	156	−0.64 [−0.96, −0.32]	−20.59 [−30.88, −10.29]
	Low-fat diet	4	371	−0.12 [−0.32, 0.08]	−3.86 [−10.29, 2.57]
	Low-carbohydrate diet	1	80	−0.11 [−0.55, 0.33]	−3.54 [−17.69, 10.62]
	Diabetes status	42	2387	−0.14 [−0.23, −0.05]	−4.50 [−7.40, −1.61]
	Impaired glucose tolerance	15	863	−0.18 [−0.33, −0.03]	−5.79 [−10.62, −9.65]
	Mixed type 1 and type 2 diabetes	1	36	0.12 [−0.53, 0.78]	3.86 [−17.05, 25.09]
	Type 1 diabetes	1	16	0.00 [−0.98, 0.98]	0.00 [−31.53, 31.53]
	Type 2 diabetes	25	1472	−0.12 [−0.25, 0.00]	−3.86 [−8.04, 0.00]
	GI difference >19	16	785	−0.20 [−0.34, −0.06]	−6.43 [−10.94, −1.93]
HDL SMD; mg/dL	Control diet	37	2199	0.02 [−0.06, 0.11]	0.20 [−0.61, 1.11]
	Carbohydrate exchange	1	100	−0.22 [−0.61, 0.18]	−2.23 [−6.18, 1.82]
	Diabetes diet	6	369	0.25 [0.05, 0.46]	2.53 [0.51, 4.66]
	Habitual diet	2	98	−0.26 [−0.66, 0.14]	−2.63 [−6.69, 1.42]
	Healthy diet	1	54	−0.25 [−0.81, 0.32]	−2.53 [−8.21, 3.24]
	High-fat diet	2	52	−0.30 [−1.06, 0.46]	−3.04 [−10.74, 4.66]
	High-fiber diet	2	351	−0.02 [−0.26, 0.21]	−0.2 [−2.63, 2.13]
	High-GI diet	19	681	0.01 [−0.14, 0.16]	0.10 [−1.42, 1.62]
	Anti-hypertensive diet	1	156	0.16 [−0.16, 0.47]	1.62 [−1.62, 4.76]
	Low-fat diet	3	338	0.04 [−0.18, 0.25]	0.41 [−1.82, 2.53]
	Diabetes status	37	2199	0.02 [−0.06, 0.11]	0.20 [−0.61, 1.11]
	Impaired glucose tolerance	12	723	0.04 [−0.11, 0.19]	0.41 [−1.11, 1.92]
	Mixed type 1 and type 2 diabetes	1	36	0.28 [−0.38, 0.94]	2.84 [−3.85, 9.52]
	Type 1 diabetes	1	16	−0.19 [−1.17, 0.79]	−1.92 [−11.85, 8.00]
	Type 2 diabetes	23	1424	0.01 [−0.09, 0.12]	0.10 [−0.91, 1.22]
	GI difference >19	12	688	0.12 [−0.03, 0.27]	1.22 [−0.30, 2.74]
LDL	Control diet	36	2246	−0.18 [−0.28, −0.07]	−5.53 [−8.60, −2.15]
	Carbohydrate exchange	1	100	−0.29 [−0.68, 0.10]	−8.90 [−20.88, 3.07]
	Diabetes diet	6	369	0.10 [−0.28, 0.48]	3.07 [−8.60, 14.74]
	Habitual diet	2	98	−0.07 [−0.46, 0.33]	−2.15 [−14.12, 10.13]
	Healthy diet	1	54	−0.21 [−0.77, 0.36]	−6.45 [−23.64, 11.05]
	High-fat diet	2	52	−0.73 [−1.98, 0.52]	−22.41 [−60.79, 15.96]
	High-fiber diet	2	351	−0.26 [−0.47, −0.05]	−7.98 [−14.43, −1.54]
	High-GI diet	17	648	−0.16 [−0.31, −0.00]	−4.91 [−9.52, 0.00]
	Anti-hypertensive diet	1	156	−0.64 [−0.96, −0.32]	−19.65 [−29.47, −9.82]
	Low-fat diet	3	338	−0.10 [−0.35, 0.15]	−3.07 [−10.75, 4.61]
	Low-carbohydrate diet	1	80	−0.13 [−0.57, 0.31]	−3.99 [−17.50, 9.52]
	Diabetes status	36	2246	−0.18 [−0.28, −0.07]	−5.53 [−8.60, −2.15]
	Impaired glucose tolerance	13	810	−0.30 [−0.52, −0.07]	−9.21 [−15.96, −2.15]
	Type 2 diabetes	23	1436	−0.13 [−0.23, −0.02]	−3.99 [−7.06, −0.61]
	GI difference >19	12	673	−0.26 [−0.42, −0.11]	−7.98 [−12.89, −3.38]
Triglycerides	Control diet	43	2413	−0.04 [−0.14, 0.05]	−2.50 [−8.74, 3.12]
	Carbohydrate exchange	1	100	0.22 [−0.17, 0.61]	13.73 [−10.61, 38.08]
	Diabetes diet	5	329	−0.38 [−0.80, 0.04]	−23.72 [−49.94, 2.50]
	Habitual diet	3	201	−0.11 [−0.40, 0.19]	−6.87 [−24.97, 11.86]
	Healthy diet	1	54	0.04 [−0.53, 0.60]	2.50 [−33.09, 37.46]
	High-fat diet	2	52	0.47 [−0.09, 1.03]	29.34 [−5.62, 64.30]
	High-fiber	2	351	−0.06 [−0.27, 0.15]	−3.75 [−16.86, 9.36]
	High-GI diet	22	686	0.09 [−0.06, 0.24]	5.62 [−3.75, 14.98]

(*Continued*)

TABLE 1 (*Continued*)

Outcome	Subgroup	Studies	Participants	Effect estimate (SMD [95% CI])	Representative conversion (unit [95% CI])
	Anti-hypertensive diet	1	156	−0.40 [−0.71, −0.08]	−24.97 [−44.33, −4.99]
	Low-fat diet	5	404	−0.06 [−0.25, 0.14]	−3.75 [−15.61, 8.74]
	Low-carbohydrate diet	1	80	0.18 [−0.26, 0.62]	11.24 [−16.23, 38.71]
	Diabetes status	43	2413	−0.04 [−0.14, 0.05]	−2.50 [−8.74, 3.12]
	Impaired glucose tolerance	16	889	0.04 [−0.10, 0.18]	2.50 [−6.24, 11.24]
	Mixed type 1 and type 2 diabetes	1	36	−0.41 [−1.07, 0.25]	−25.60 [−66.80, 15.61]
	Type 1 diabetes	1	16	−0.36 [−1.35, 0.63]	−22.47 [−84.28, 39.33]
	Type 2 diabetes	25	1472	−0.09 [−0.22, 0.04]	−5.62 [−13.73, 2.50]
	GI difference >19	15	764	−0.03 [−0.18, 0.12]	−1.87 [−11.24, 7.49]

[1]GI, glycemic index; HbA1c, glycated hemoglobin; SMD, standardized mean difference.

In order to test for publication bias, we created funnel plots for FBG, HbA1c, FBI, and body weight (**Supplementary Figures 31–34**, respectively). All plots appeared to be symmetrical, with no obvious publication bias.

Discussion

Our analysis of 54 studies demonstrated that low-GI diets have benefits over other diet types for people with impaired glucose tolerance or diabetes in the reduction of HbA1c, FBG, BMI, and blood lipids. Although these changes appear small, even pharmacological interventions only have small effects on FBG in people with impaired glucose tolerance (68–72). People must eat, and therefore low-GI diets do have the potential to positively affect measures of blood glucose control, in combination with appropriate and effective pharmacological and lifestyle interventions. Indeed, the improvements seen in FBG and HbA1c suggest a possible improvement in insulin sensitivity, a significant achievement for a dietary intervention.

The observed effects of low-GI diets on blood lipids were not unexpected. We previously showed that in people with overweight and obesity, both TC and LDL were lowered by low-GI diets (7), and a 2013 meta-analysis found a similar outcome (73). These changes in cholesterol from low-GI diets are similar to those seen from the consumption of oat bran and whole oats (74), an outcome that has led at least one independent body to recommend including oats in the diet (75).

In our previous analysis of low-GI diets as an intervention for obesity, we found that low-GI diets were only effective for weight loss in people with normal glucose tolerance (7). In concordance with that analysis, our current analysis failed to find an effect of low-GI diets on body weight in people with impaired glucose tolerance, type 1 diabetes, or type 2 diabetes. This outcome could be explained from the lack of satiety experienced by people with decreased insulin sensitivity, as shown in Verdich et al. 2001 (76). Thus, our previous and current work show that low-GI diets, although effective in many aspects of diabetes, may not be effective in achieving weight loss in people with impaired glucose tolerance or type 2 diabetes.

However, our analysis of BMI did show a significant difference between low-GI diets and other diets (Supplementary Figure 14). This is hard to explain, as without a change in height, the only other variable in BMI is weight. We speculate that because BMI is a ratio between height and weight, it will produce a smaller variance, and will thus be more likely to achieve statistical significance. This may therefore suggest that low-GI diets may be effective for weight loss in this population. Clearly, high-quality studies that achieve meaningful differences in GI are required in order to fully establish the effect of low-GI diets in people with impaired glucose tolerance or diabetes.

We hypothesized that the duration of the study may affect the success of the intervention. In fact, our sensitivity analysis failed to show any statistical difference between the studies, regardless of duration, although in an absolute sense, the effect size increased as the study duration increased. In addition, no differences were evident from the blinded studies; however, this is likely due to the very small number of studies that used even a single-blind methodology.

Strikingly, there were very few studies on dietary glucose control in people with type 1 diabetes. Given the early onset of this disease, the lifelong nature of its course, and its potential for poor outcomes, we find the lack of research into this extremely important condition disappointing. The lack of studies in people

TABLE 2 Sensitivity analyses[1]

Outcome	Subgroup	Studies	Participants	Effect estimate (SMD [95% CI])	Conversion of SMD to FBG (mmol/L [95% CI])	Conversion of SMD to FBG (mg/dL [95% CI])	*P* value
Fasting blood glucose	Length of study	46	2602	−0.15 [−0.26, −0.03]	−0.30 [−0.52, −0.06]	−5.4 [−9.37, 1.08]	0.01
	Under 4 wk	6	168	−0.04 [−0.34, 0.27]	−0.08 [−0.68, 0.54]	−1.44 [−12.25, 9.73]	0.81
	4 wk to 6 mo	33	1561	−0.12 [−0.26, 0.02]	−0.24 [−0.52, 0.04]	−4.32 [−9.37, 0.72]	0.10
	Longer than 6 mo	7	873	−0.29 [−0.59, 0.02]	−0.58 [−1.18, 0.04]	−10.45 [−21.26, 0.72]	0.07
	Single- or double- blind	8	594	−0.00 [−0.21, 0.20]	0.00 [−0.42, 0.40]	0.00 [−7.57, 7.21]	0.98

[1]FBG, fasting blood glucose; SMD, standardized mean difference.

with type 1 diabetes means that subgroup analysis, or even general conclusions are impossible to draw for this group of people. This is a limitation of our study.

Our data show that a low-GI diet can be useful for glycemic control and blood lipids, particularly for people with type 2 diabetes. However, it is currently unclear whether low-GI diets are effective in lowering body weight, and further studies should be undertaken to resolve this question.

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The authors' contributions were as follows—MIZ and KEM: conceived the topic, designed the review questions and PICOTS, designed the search strategy, analyzed the data, interpreted the results, and wrote the manuscript; JZ, AR, and SQH: performed systematic searches on the bibliographic databases to retrieve the literature; JZ and LG: performed the data extraction; MIZ and AR performed the quality assessment of the included studies; LLC resolved all issues related to data procurement, quality assessment, and did the critical review and revision of the scientific content of the manuscript; and all authors: approved the final manuscript. None of the authors reported a conflict of interest related to this study.

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