See corresponding editorial on page 453.

Systematic review and meta-analysis of different dietary approaches to the management of type 2 diabetes[1–3]

Olubukola Ajala, Patrick English, and Jonathan Pinkney

ABSTRACT

Background: There is evidence that reducing blood glucose concentrations, inducing weight loss, and improving the lipid profile reduces cardiovascular risk in people with type 2 diabetes.

Objective: We assessed the effect of various diets on glycemic control, lipids, and weight loss.

Design: We conducted searches of PubMed, Embase, and Google Scholar to August 2011. We included randomized controlled trials (RCTs) with interventions that lasted ≥6 mo that compared low-carbohydrate, vegetarian, vegan, low–glycemic index (GI), high-fiber, Mediterranean, and high-protein diets with control diets including low-fat, high-GI, American Diabetes Association, European Association for the Study of Diabetes, and low-protein diets.

Results: A total of 20 RCTs were included (n = 3073 included in final analyses across 3460 randomly assigned individuals). The low-carbohydrate, low-GI, Mediterranean, and high-protein diets all led to a greater improvement in glycemic control [glycated hemoglobin reductions of −0.12% (P = 0.04), −0.14% (P = 0.008), −0.47% (P < 0.00001), and −0.28% (P < 0.00001), respectively] compared with their respective control diets, with the largest effect size seen in the Mediterranean diet. Low-carbohydrate and Mediterranean diets led to greater weight loss [−0.69 kg (P = 0.21) and −1.84 kg (P < 0.00001), respectively], with an increase in HDL seen in all diets except the high-protein diet.

Conclusion: Low-carbohydrate, low-GI, Mediterranean, and high-protein diets are effective in improving various markers of cardiovascular risk in people with diabetes and should be considered in the overall strategy of diabetes management. *Am J Clin Nutr* 2013;97:505–16.

INTRODUCTION

There is good evidence that complex interventions, including dietary changes, can prevent the progression of impaired glucose tolerance to diabetes (1, 2). However, there is limited evidence on the optimal dietary approach to control hyperglycemia in type 2 diabetes (T2D)[4]. It is clear that weight loss and reduced total calorie intake are important in the obtainment of good glycemic control (3–7), but the ideal proportion of the 3 main food components (carbohydrate, fat, and protein) that should be recommended remains unclear.

Several trials (8–10) have documented the potential benefits of carbohydrate restriction and low–glycemic index (GI) and Mediterranean diets on glycemic control and weight loss that are maintained long term (9, 11–14).

Epidemiologic data showed a relation between a high intake of saturated fat and raised glycated hemoglobin (Hb A_{1c}) (15), but randomized studies have failed to corroborate these findings (3–8). Systematic reviews and meta-analyses have shown that low-GI, high-fiber, and Mediterranean diets improve glucose metabolism (16–18).

The British Diabetes Association, European Association for the Study of Diabetes (EASD), American Diabetes Association (ADA), American Heart Association, Canadian Diabetes Association, International College of Nutrition, groups from South Africa and Japan, and the National Cholesterol Education Panel (Adult Treatment Panel 3) (19–27) have various recommendations for the optimal diet in people with T2D (summarized in **Table 1**). Most of these authorities recommend a carbohydrate intake of 50–60% of total energy intake, total fat intake ≤30% of energy (with moderate polyunsaturated fat and restriction of saturated and *trans* fat intake). However, there is insufficient evidence to justify these recommendations. To our knowledge, there is no systematic review or meta-analysis that has compared the effects of different categories of dietary intervention on glycemic control, weight loss, and lipids in T2D. This systematic review was conducted to provide a succinct but robust evidence base to guide clinicians and patients on the most suitable dietary intervention to induce weight loss and improve glycemic control and the lipid profile.

METHODS

Search strategy and study selection

Electronic searches of PubMed, Embase, and Google Scholar for randomized controlled trials (RCTs), systematic reviews, and

[1] From the Department of Diabetes and Endocrinology, Peninsula College of Medicine and Dentistry, Plymouth, United Kingdom.

[2] No funding was received for this study.

[3] Address correspondence to O Ajala, Department of Diabetes and Endocrinology, Peninsula Medical School, University Medicine, Level 7, Derriford Hospital, Plymouth PL6 8DH. E-mail: olubukola.ajala@nhs.net.

[4] Abbreviations used: ADA, American Diabetes Association; EASD, European Association for the Study of Diabetes; GI, glycemic index; Hb A_{1c}, glycated hemoglobin; RCT, randomized controlled trial; T2D, type 2 diabetes; WMD, weighted mean difference.

Received May 9, 2012. Accepted for publication November 14, 2012.
First published online January 30, 2013; doi: 10.3945/ajcn.112.042457.

meta-analyses were undertaken up to July 2011. References of included studies and key review and guideline reports were checked for additional studies. Key search terms included diabetic, atherogenic, carbohydrate restricted, low carbohydrate, ketogenic, fat restricted, low fat, Mediterranean, protein restricted, low protein, vegetarian, and glycemic index (GI). Studies were considered eligible for inclusion if they were RCTs carried out in adults (≥18 y of age) with an intervention that lasted ≥6 mo that compared low- and high-carbohydrate, high-protein, vegetarian and vegan, low-glycemic, high-fiber, and Mediterranean diets with any control diet in people with T2D.

Outcome measures

Outcomes of interest were Hb A_{1c}, which was used as the measure of glycemic control, difference in weight lost, and changes in HDL cholesterol, LDL cholesterol, and triglycerides.

Quality measures

The quality of each included trial was assessed based on specific criteria outlined in the Cochrane handbook for systematic reviews of interventions and included minimization of selection bias, attrition bias, detection bias, reporting bias and blinding of outcome assessment (**Figure 1**; *see* "Supplemental data" in the online issue).

Statistical analysis

A meta-analysis was undertaken for each dietary-intervention subgroup when appropriate (16 of 20 trials) with Revman 5 software (Cochrane Information Management System) when data were available for more than one trial and were of sufficient quality. The fixed-effect inverse-variance model was used to calculate the weighted mean difference (WMD) and was expressed in terms of the 95% CI and level of statistical significance. Outcomes were extracted by comparing means of the intervention compared with control diets and the SEM at follow-up.

RESULTS

Study selection

A total of 1801 records were identified from the initial electronic search, with an additional 64 records from other sources (references of reviews and other articles). From the abstracts of these records, we identified 55 articles for examination of full texts. Thirty-five studies were excluded either because the intervention lasted <6 mo or the studies were not randomized trials (**Figure 2**).

Studies were excluded from the meta-analysis but included in the results section (**Table 2**) if required data were not available or provided after correspondence from the authors (28), if only one study was available in that subgroup that made comparisons impossible (5, 29, 30), and if the study was carried out in both patients with diabetes and nonpatients with diabetes with separate data not available for the diabetic group (31). One study (32) had separate data for change in Hb A_{1c} in patients with diabetes, ant thus, this outcome was included in the meta-analysis; another study (33) was included in the quantitative analysis

TABLE 1
Recommendations for medical nutrition therapy for people with diabetes[1]

Variables	BDA (19)	ADA (22)	EASD (21)	CDA (20)	Japan (24)	South Africa (25)	India (23)	AHA (26)	NCEP (27)
Carbohydrates (%)	50–55	50–60	45–60	50–60	60	55–60	>65	45–55	50–60
GI (%)	—	Not recommended for general use	Recommended	Recommended	Recommended	Recommended	—	—	—
Fiber	<30 g/d	No specific amount	Increase with low-GI foods	25–35 g/d	1 fruit, 400 g vegetables	40 g/d	No specific amount	≥25 g/d	20–30 g/d
Protein (%)	10–15	15–20	10–20	11	15–20	12–20	No specific amount	15	15
Fat (%)	30–35	25–35	≤35	≤30	20–25	<30	<21	<30	25–35

[1] ADA, American Diabetes Association; AHA, American Heart Association; BDA, British Diabetic Association; CDA, Canadian Diabetes Association; EASD, European Association for the Study of Diabetes; GI, glycemic index; NCEP, National Cholesterol Education Program.

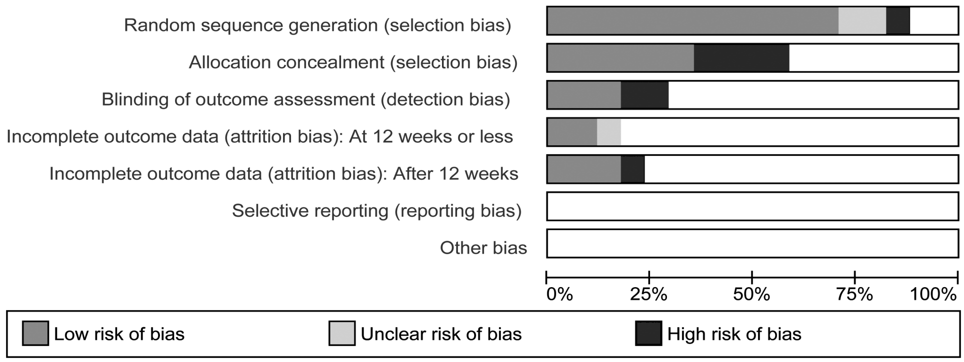


FIGURE 1. Risk-of-bias graph. The review of judgments of authors about each risk-of-bias item is presented as percentages across all included studies.

despite not having separate data for the diabetic group because >80% of the study population had diabetes.

The 16 studies included in the quantitative analysis were RCTs with dietary interventions that ranged from 6 mo (30, 32, 34, 35, 42) to 4 y (36). Two of the studies included in the meta-analysis compared 3 separate diets (37, 38). These arms were treated in isolation. Wolever et al (38) compared a low-GI diet compared with a high-GI diet compared with a low-carbohydrate diet. The low-carbohydrate arm was compared with the low-GI arm and labeled Wolever-1, whereas the low-GI arm was compared with high-GI arm and labeled Wolever-2. Elhayany et al (37) compared a low-carbohydrate Mediterranean diet compared with a traditional Mediterranean diet compared with an ADA diet, and thus, the low-carbohydrate Mediterranean arm was compared with the traditional Mediterranean arm in the subgroup "low-carbohydrate compared with other diets." This comparison was labeled Elhayany-1. The traditional Mediterranean diet was compared with the ADA diet in the "Mediterranean compared with other diets" subgroup, and this comparison was labeled Elhayany-2.

Quality of studies

None of the included trials reported any significant differences in characteristics of participants in the intervention or treatment arm. Except for 3 studies (8, 35, 37), all other studies reported the method of random assignment, 10 studies reported the method of allocation concealment, and 6 studies were analyzed on an intention-to-treat basis (7, 32, 34, 36, 39, 40).

Participants

The 20 studies included 3460 patients with final analyses in 3073 patients. Four of the studies (31–33, 41) included patients with and without diabetes, and one of these studies (32) provided data on the change in glycemic control in the diabetic group, and another study (33) was included in quantitative analysis despite not having separate data for the diabetic group because >80% of the study population had diabetes. All participants were ≥18 y old, and all but one study (35) included both sexes.

Intervention

Nine studies compared a low-carbohydrate diet to a variety of control diets including low-fat, low-GI, and traditional Mediterranean diets (compared with a low-carbohydrate Mediterranean diet) (7, 8, 32, 37, 38, 43). Four studies (31, 35–37) compared Mediterranean diets with low fat and the ADA diet, 3 studies (34, 38, 39) compared a low-GI diet with the ADA, high-GI, and high-fiber diets, respectively, and 2 studies (40, 44) compared a high-protein diet with low-protein and high-carbohydrate diets, respectively. Other studies compared vegan with ADA diets (29), vegetarian with EASD diets (30), high-carbohydrate with high-MUFA diets (5), and high-fiber with low-fat diets (28). Control diets are described in more detail in Table 2 (summary of trials).

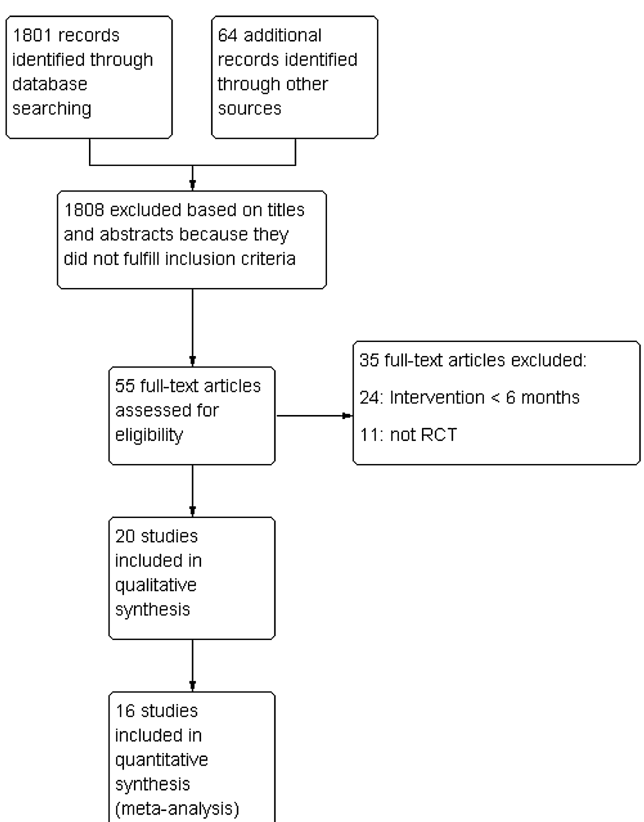


FIGURE 2. Study-flow diagram showing the number of studies screened, assessed for eligibility, and included in the review. RCT, randomized controlled trial.

TABLE 2
Summary of trials[1]

First author, year of publication (reference)	Participants	*n*	Intervention	Duration	Relevant variables	Significant outcome measures
Low-carbohydrate compared with other diets						
Samaha, 2003 (32)	Severely obese adults; 39% with T2D	51 with diabetes	Low-carbohydrate diet: 37% carbohydrates, 22% protein, 41% fat Control diet (low fat): 51% carbohydrates, 16% protein, 33% fat	6 mo	Weight, lipids, FPG, Hb A_{1c}	Higher weight loss (−3.9 kg),** lower triglycerides (−0.35 mmol/L),** FPG (−1.16 mmol/L), and* Hb A_{1c} (−0.6%)[NS]
Stern, 2004 (33)	Obese adults; 83% with T2D	109 with diabetes	Low-carbohydrate diet: 120 g carbohydrates, 73 g protein, 93 g fat Control diet (conventional): 230 g carbohydrate, 74 g protein, 69 g fat	1 y	Weight, Hb A_{1c}, lipids	No significant difference in weight loss, lower Hb A_{1c} (−0.6%),* better lipid profile triglycerides (−0.6 mmol/L)* and HDL (+0.37 mmol/L)*
Westman, 2008 (42)	Obese adults with T2D	97 (50 completers)	Low-carbohydrate diet: 13% carbohydrates, 28% protein, 59% fat Control diet (low GI): 44% carbohydrates, 20% protein, 36% fat	6 mo	Weight, Hb A_{1c}, FPG, lipids,	Higher weight loss (−4.2 kg)* and HDL (+0.14 mmol/L),* lower Hb A_{1c} (−1%)*
Wolever-1, 2008 (38)	Adults with T2D managed by diet only	162 (156 analyzed)	Low-carbohydrate diet: 40% fat, 40% carbohydrates, 60% GI Low-GI diet: 25% fat, 50% carbohydrates, 55% GI	1 y	Weight, lipids, Hb A_{1c}	No significant difference in glycemic control and weight, better lipid profile in the low-carbohydrate group
Haimoto, 2008 (8)	Adults with T2D	133 (127 with data at 1 y)	Low-carbohydrate diet: 45% carbohydrates, 33% fat, 18% protein Control diet (low fat): 57% carbohydrates, 26% fat, 16% protein	2 y (results at 1 y used for meta-analysis)	Weight, lipids, Hb A_{1c}	Higher weight loss (−1.2 kg),** lower Hb A_{1c} (−0.6%),** lower LDL (−0.44 mmol/L)**
Davis, 2009 (7)	Overweight adults with T2D	105	Low-carbohydrate diet: 20–25 g carbohydrates/d with 5-g increments/wk Control diet (low fat): 25% of energy from fat	1 y	Weight, lipids, Hb A_{1c}	Higher HDL (+0.1 mmol/L),** no other significant differences
Elhayany-1, 2010 (37)	Overweight adults with T2D	174 (124 completers)	Low-carbohydrate diet (Mediterranean): 35% low-GI carbohydrates, 45% fat rich in MUFAs, 15–20% protein Traditional Mediterranean diet: 50–55% low-GI carbohydrates, 30% fat rich in MUFAs, 15–20% protein	1 y	Weight, Hb A_{1c}, lipids	Higher HDL (+0.13mmol/L),** no other significant differences

(Continued)

TABLE 2 (*Continued*)

First author, year of publication (reference)	Participants	*n*	Intervention	Duration	Relevant variables	Significant outcome measures
Yancy, 2010 (41)	Overweight adults 32% with T2D	146 (45 with diabetes)	Low-carbohydrate diet: 50–60 g carbohydrates, 50–60 g fat, 50–55 g protein Low-fat diet: 190 g carbohydrates, 35–40 g fat, 120 mg orlistat 3 times/d, 73–80 g protein	1 y	Weight, lipids, FPG, Hb A_{1c}	No significant difference in weight lost or glycemic control in entire study population
Iqbal, 2010 (43)	Obese adults with diabetes	144 (77 assessed at 1 y)	Low-carbohydrate diet: 35 g carbohydrate, 20 g protein, 40 g fat Control diet (low fat): 40 g carbohydrate, 23 g protein, 34 g fat	2 y (results at 1 y used for meta-analysis)	Weight, Hb A_{1c}, lipids	No significant difference in weight lost or change in glycemic control
Vegan and vegetarian compared with other diets						
Barnard, 2009 (29)	Overweight adults with T2D	99	Vegan diet: 10% fat, 15% protein, 75% carbohydrates Control diet (ADA): 15–20% protein, 60–70% carbohydrates and MUFAs	74 wk	Weight, lipids, Hb A_{1c}	Lower TC (−0.53 compared with −0.18 mmol/L)*, LDL (−0.35 compared with −0.09 mmol/L),* and Hb A_{1c} (−0.4 compared with 0.01%)*
Kahleova, 2011 (30)	Adults with T2D	74	Vegetarian diet: 60% carbohydrates, 15% protein, 25% fat Control diet (EASD): 50% carbohydrates, 20% protein, <30% fat	6 mo	Weight, lipids, Hb A_{1c}	Reduced diabetes medication (43% compared with 5% of participants),** higher weight loss (−3 kg)**
Low-GI compared with other diets						
Ma, 2008 (39)	Adults with poorly controlled T2D	40	Low-GI diet: 37% carbohydrates, 76 GI, 42% fat, 20% protein ADA diet: 38% carbohydrate, 80 GI, 43% fat, 20% protein	10 mo	Weight, Hb A_{1c}, lipids	Reduction in the use of diabetic medication in the low-GI group with equivalent Hb A_{1c} Lower LDL in the ADA group (−0.42 mmol/L)*
Wolever-2, 2008 (38)	Adults with T2D managed by diet only	162	Low-GI diet: 20% protein, 25% fat, 50% carbohydrates with 55% high GI High-GI diet: 20% protein, 30% fat, 45% carbohydrates with 63% high GI	1 y	Weight, FPG, 2HPPG, triglycerides, HDL	Lower postprandial glucose, no other significant differences
Jenkins, 2008 (34)	Overweight adults with T2D	210 (155 completers)	Low-GI diet: 69.6 GI, 33% fat, 21% protein High-fiber cereal diet: 83.5 GI, 30.5% fat, 21% protein	6 mo	Weight, FPG, Hb A_{1c}, lipids	Lower Hb A_{1c} with high fiber (−0.32%)** Higher HDL (+2 mmol/L)** in low-GI group
Mediterranean compared with other diets						
Toobert, 2003 (35)	Postmenopausal women with T2D	279 (245 completers)	Mediterranean lifestyle program compared with usual care	6 mo	Hb A_{1c}, lipids, BMI	Lower Hb A_{1c} (−0.36% compared with 0.02%)* and BMI (−0.37 compared with +0.2)*

(*Continued*)

TABLE 2 (*Continued*)

First author, year of publication (reference)	Participants	*n*	Intervention	Duration	Relevant variables	Significant outcome measures
Salas-Salvadó, 2008 (31)	Adults at high risk of cardiovascular disease	1224, 819 of whom were diabetic	Mediterranean diet + olive oil: 50 g olive oil/d, 15 g nuts, 9.8 MedDiet Score, 41% fat compared with Mediterranean diet + nuts: 28 g olive oil/d, 39 g nuts, 9.9 MedDiet Score, 43% fat compared with Control diet (low fat): 8.7 MedDiet score, 38% fat	12 mo	Weight, waist circumference, triglycerides, blood pressure	Greater reduction in triglycerides in MedDiet + nuts group*
Esposito, 2008 (36)	Overweight adults with newly diagnosed T2D	215	Mediterranean diet: <50% of energy from carbohydrates, rich in vegetables and whole grains, and low in red meat Control diet (low-fat ADA): <30% of energy from fat	4 y (results at 1 y used for meta-analysis)	Time to introduction of antidiabetic medication, weight, FPG, Hb A_{1c}, lipids	Fewer patients needed antidiabetic medication at 4 y (44% compared with 70%)** Higher HDL (+0.07 mmol/L),* lower triglycerides (−0.35 mmol/L)*
Elhayany-2, 2010 (37)	Overweight adults with T2D	174 (118 completers)	Mediterranean diet: 50–55% low-GI carbohydrates, 30% fat rich in MUFAs, 15–20% protein Control diet (ADA): 15–20% protein, <7% saturated fat, 60–70% carbohydrates	1 y	Weight, FPG, Hb A_{1c}, lipids	Lower triglycerides (−0.58 mmol/L)**
High-protein compared with other diets						
Brinkworth, 2004 (44)	Obese adults with T2D	66 (38 completers)	High-protein diet: 30% protein, 40% carbohydrates, 30% fat, with extra 21 g protein after 2 mo Low-protein diet: 15% protein, 55% carbohydrates, 30% fat, with extra 7 g protein after 2 mo	12 mo	Weight, lipids, Hb A_{1c}, FPG	No significant differences
Larsen, 2011 (40)	Overweight/obese adults with T2D	108 (99 completers)	High-protein diet: 26.5% protein, 45% carbohydrates, 31% fat Control diet (high carbohydrates): 19% protein, 48% carbohydrates, 32% fat	12 mo	Weight, lipids, Hb A_{1c}	No evidence of superior benefit in either diet
High-carbohydrate compared with high-MUFA diets						
Brehm, 2009 (5)	Overweight/obese adults with T2D	124 (95 completers)	High-carbohydrate diet: 54% carbohydrate, 15% protein, and 28% fat (9% MUFAs) Control diet (high MUFAs): 46% carbohydrates, 15% protein, and 38% fat (14% MUFAs)	12 mo	Weight, Hb A_{1c}, lipids	No significant difference in any measured variables

(*Continued*)

TABLE 2 (*Continued*)

First author, year of publication (reference)	Participants	n	Intervention	Duration	Relevant variables	Significant outcome measures
High-fiber compared with low-fat diets						
Milne, 1994 (28)	Adults with T2D	70	High-carbohydrate and -fiber diet compared with low-fat diet	18 mo	Weight, lipids, Hb A_{1c}	No significant differences

[1] Wolever et al (38) compared a low-GI diet compared with a high-GI diet compared with a low-carbohydrate diet. The low-carbohydrate arm was compared with the low-GI arm and labeled Wolever-1, whereas the low-GI arm was compared with the high-GI arm and labeled Wolever-2. Elhayany et al (37) compared a low-carbohydrate Mediterranean diet compared with a traditional Mediterranean diet compared with an ADA diet, and thus, the low-carbohydrate Mediterranean arm was compared with the traditional Mediterranean arm and labeled Elhayany-1. The traditional Mediterranean diet was compared with the ADA diet and labeled Elhayany-2. *$P < 0.05$; ** $P < 0.001$; $^{ns}P > 0.05$. ADA, American Diabetes Association; FPG, fasting plasma glucose; GI, glycemic index; Hb A_{1c}, glycated hemoglobin; HDL, HDL cholesterol; LDL, LDL cholesterol; MedDiet Score, 14-point score of adherence to the Mediterranean diet; TC, total cholesterol; 2HPPG, 2-hour postprandial glucose.

Meta-analyses

Glycemic control

Low-carbohydrate compared with other diets (**Figure 3**). Data from 8 studies (7, 8, 32, 33, 38, 39, 43, 44) were pooled and compared low-carbohydrate with a variety of control diets. There was a significant decrease in the percentage of Hb A_{1c} in subjects who consumed low-carbohydrate compared with other diets (WMD: −0.12%; 95% CI: −0.24%, −0.00%; P = 0.04, I^2 = 75%).

Low-GI compared with other diets. Data from the 3 studies that compared low-GI with other diets (34, 38, 39) showed a −0.14% decrease in Hb A_{1c} in subjects who consumed low-GI compared with control diets (95% CI: −0.23%, −0.03%; P = 0.008, I^2 = 80%).

Mediterranean compared with other diets. The 3 studies that compared Mediterranean with other diets (35–37) showed a WMD in Hb A_{1c} of −0.47% in favor of the Mediterranean diet (95% CI: −0.64%, −0.30%; $P < 0.00001$, I^2 = 82%).

High-protein compared with other diets. Data pooled from 2 studies that compared high-protein with other diets (40, 44) showed a significant decrease in the percentage of Hb A_{1c} in subjects who consumed high-protein diets (WMD: −0.28%; 95% CI: −0.38%, −0.18%; $P < 0.00001$, I^2 = 60%).

Weight loss

Low-carbohydrate compared with other diets. There was no significant difference in weight loss when low-carbohydrate diets were compared with control diets (WMD: −0.69 kg; 95% CI: −1.77, 0.39 kg; P = 0.21).

Low-GI compared with other diets. There was no significant difference in weight loss with low-GI compared with control diets (+1.39 kg; 95% CI: −1.58, 4.36 kg; P = 0.36).

Mediterranean compared with other diets. The Mediterranean diet was more effective in achieving weight loss that control diets were with a WMD in weight loss of −1.84 kg (95% CI: 2.54, −1.15 kg; $P < 0.00001$).

High-protein compared with other diets. Data pooled from 2 studies showed no benefit of high-protein diet compared with control diets for achieving weight loss (WMD: +0.44 kg; 95% CI: –0.96, 1.84; P = 0.54).

Change in lipids

Low-carbohydrate compared with other diets. Low-carbohydrate diets appeared to be beneficial in increasing HDL (WMD +0.08 mmol/L; 95% CI: 0.05, 0.11 mmol/L; $P < 0.00001$) with no significant reduction in LDL (WMD: −0.03 mmol/L; 95% CI: −0.12, 0.07 mmol/L; P = 0.57) or triglycerides (WMD: −0.04 mmol/L; 95% CI: −0.15, 0.07 mmol/L; P = 0.47).

Low-GI compared with other diets. Low-GI diets were effective in increasing HDL (WMD: +0.05 mmol/L, 95% CI: 0.02, 0.07 mmol/L; $P < 0.0001$), but the reductions in LDL and triglycerides were not significant compared with those for control diets (for low-GI diets, WMD: −0.07 mmol/L; 95% CI: −0.16, 0.02 mmol/L; P = 0.15; for control diets, WMD: −0.01 mmol/L; 95% CI: −0.04, 0.03 mmol/L; P = 0.69).

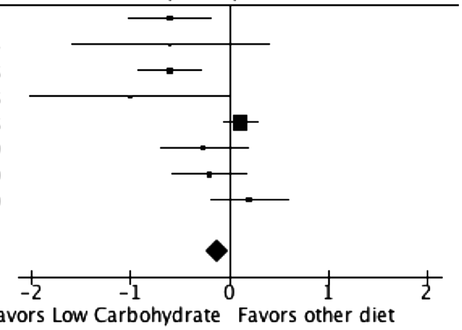
Mediterranean compared with other diets. The Mediterranean diet significantly reduced triglycerides (WMD: −0.21 mmol/L; 95% CI: −0.29, −0.14 mmol/L; $P < 0.00001$) and increased

A Difference in Hb A_{1c} low-carbohydrate versus other diets

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI	Year
Samaha 2003 [32]	−0.6	0.2133	8.1%	−0.60 [−1.02, −0.18]	2003
Stern 2004 [33]	−0.6	0.5102	1.4%	−0.60 [−1.60, 0.40]	2004
Haimoto 2008 [8]	−0.6	0.1611	14.1%	−0.60 [−0.92, −0.28]	2008
Westman 2008 [42]	−1	0.5173	1.4%	−1.00 [−2.01, 0.01]	2008
Wolever-1 2008 [38]	0.11	0.0868	48.6%	0.11 [−0.06, 0.28]	2008
Davis 2009 [7]	−0.26	0.2254	7.2%	−0.26 [−0.70, 0.18]	2009
Elhayany-1 2010 [37]	−0.2	0.191	10.0%	−0.20 [−0.57, 0.17]	2010
Iqbal 2010 [43]	0.2	0.2	9.2%	0.20 [−0.19, 0.59]	2010
Total (95% CI)			**100.0%**	**−0.12 [−0.24, −0.00]**	

Heterogeneity: $Chi^2 = 27.86$, df = 7 (P = 0.0002); $I^2 = 75\%$
Test for overall effect: Z = 2.02 (P = 0.04)

Mean Difference IV, Fixed, 95% CI



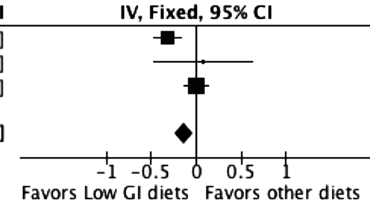
Difference in low carbohydrate vs. 'other' diets. 'Other' diets compared were low fat (Samaha [32], Haimoto [8], Davis [7] and Iqbal [43]), Low GI (Westman [42] and Wolever-1[38]), Mediterranean (Elhayany-1[37]) and conventional high CHO (Stern [33])
Wolever-1 [38] is the comparison between the low-CHO and low-GI arms of the study.
Elhayany-1 [37] is the comparison between the traditional Mediterranean and low-CHO arms of the study.

B Difference in low-GI versus other diets

Study or Subgroup	Mean Difference	SE	Low GI Total	Other diets Total	Weight	Mean Difference IV, Fixed, 95% CI
Jenkins 2008 [34]	−0.32	0.0784	106	104	43.3%	−0.32 [−0.47, −0.17]
Ma 2008 [39]	0.08	0.28	20	20	3.4%	0.08 [−0.47, 0.63]
Wolever-2 2008 [38]	0	0.0707	55	48	53.3%	0.00 [−0.14, 0.14]
Total (95% CI)			**181**	**172**	**100.0%**	**−0.14 [−0.24, −0.03]**

Heterogeneity: $Chi^2 = 9.80$, df = 2 (P = 0.007); $I^2 = 80\%$
Test for overall effect: Z = 2.63 (P = 0.008)

Mean Difference IV, Fixed, 95% CI



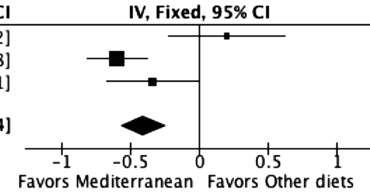
Difference in low-GI vs. 'other' diets. 'Other' diets compared were high fiber (Jenkins [35]), high GI (Wolever-2 [38]), ADA (Ma [39]).
Wolever-2 [38] is the comparison between the low-GI and high-GI arms of the study.

C Difference in Hb A_{1c} Mediterranean versus other diets

Study or Subgroup	Mean Difference	SE	Mediterranean Total	Other diets Total	Weight	Mean Difference IV, Fixed, 95% CI
Elhayany-2 2010 [37]	0.2	0.2164	63	65	15.8%	0.20 [−0.22, 0.62]
Esposito 2008 [36] (1)	−0.6	0.1124	108	107	58.5%	−0.60 [−0.82, −0.38]
Toobert 2003 [35]	−0.34	0.1693	137	108	25.8%	−0.34 [−0.67, −0.01]
Total (95% CI)			**308**	**280**	**100.0%**	**−0.41 [−0.58, −0.24]**

Heterogeneity: $Chi^2 = 10.97$, df = 2 (P = 0.004); $I^2 = 82\%$
Test for overall effect: Z = 4.73 (P < 0.00001)

Mean Difference IV, Fixed, 95% CI



(1) For Esposito 2008, data for outcome at 1 year

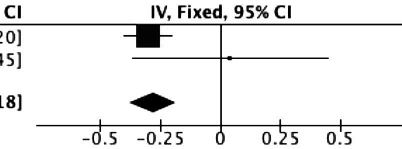
Difference in Mediterranean vs. 'other' diets. 'Other' diets were 'usual care' (Toobert [36]), ADA (Esposito [36] and Elhayany-2 [37]).
Elhayany-2 [37] is the comparison between the traditional Mediterranean and ADA arms of the study.

D Difference in Hb A_{1c} high-protein versus other diets

Study or Subgroup	Mean Difference	SE	High Protein Total	Other diets Total	Weight	Mean Difference IV, Fixed, 95% CI
Brinkworth 2004 [44]	−0.3	0.051	19	19	94.4%	−0.30 [−0.40, −0.20]
Larsen 2011 [40]	0.04	0.2092	53	46	5.6%	0.04 [−0.37, 0.45]
Total (95% CI)			**72**	**65**	**100.0%**	**−0.28 [−0.38, −0.18]**

Heterogeneity: $Chi^2 = 2.49$, df = 1 (P = 0.11); $I^2 = 60\%$
Test for overall effect: Z = 5.67 (P < 0.00001)

Mean Difference IV, Fixed, 95% CI



Difference in high protein vs. 'other' diets. 'Other' diets compared were low protein (Brinkworth [44]) and high carbohydrate (Larsen [40]).

FIGURE 3. Forest plots that show differences in Hb A_{1c} between low-carbohydrate and other diets (A), low-GI and other diets (B), Mediterranean and other diets (C), and high-protein and other diets (D). A meta-analysis was done with Revman 5 software (Cochrane Information Management System). A fixed-effect inverse-variance model was used to calculate the weighted mean difference and expressed in terms of 95% CIs and level of significance. ADA, American Diabetes Association; CHO, cholesterol; GI, glycemic index; Hb A_{1c}, glycated hemoglobin; IV, inverse variance.

HDL (WMD: +0.04 mmol/L; 95% CI: 0.01, 0.07 mmol/L; P = 0.004). One of the 3 studies did not provide data on the change in LDL cholesterol (49), but pooled data from the other studies showed no significant reduction in LDL (WMD: −0.08 mmol/L; 95% CI; −0.24, 0.08 mmol/L; P = 0.34).

High-protein compared with other diets. High-protein diets had no effects on markers of the lipid profile (LDL WMD: −0.16 mmol/L; 95% CI: −0.41, 0.09 mmol/L; P = 0.22; triglyceride WMD: −0.11 mmol/L; 95% CI: −0.56, 0.33 mmol/L; P = 0.61; HDL WMD: +0.01 mmol/L; 95% CI: −0.08, 0.10 mmol/L; P = 0.89).

Studies excluded from meta-analyses

Six studies were excluded from meta-analyses; 4 of these studies had no other studies for comparison within their subgroup (5, 28–30), and 2 studies included participants with and without diabetes with no separate data provided for subjects with diabetes (31, 41).

Barnard et al (36) compared a vegan diet with the low-fat ADA diet and showed a significantly greater reduction in total cholesterol, LDL, and Hb A_{1c} in the vegan group after 74 wk. A similar-sized study (30) that compared a vegetarian diet with the EASD diet showed greater weight loss and reduced requirements for diabetes medication in the vegetarian arm. No significant benefit was shown in studies that compared high-carbohydrate with high-MUFA diets (5) and high-fiber with low-fat diets (28).

Yancy et al (32) compared a low-carbohydrate diet with a low-fat diet in 146 patients, 45 of whom had diabetes. There was no significant difference in the amount of weight loss or glycemic control in the whole group (41). Salas-Salvadó et al (31) compared 2 variations of the Mediterranean diet with a low-fat diet in 1224 participants with high cardiovascular risk. Approximately two-thirds of participants had diabetes, and the major significant finding was a greater reduction in triglycerides in the group who consumed the Mediterranean diet with nut supplementation.

DISCUSSION

This review provides evidence that modifying the amount of macronutrients can improve glycemic control, weight, and lipids in people with diabetes. Low-carbohydrate, low-GI, Mediterranean, and high-protein diets reduced Hb A_{1c} by 0.12–0.5% compared with comparison or control diets. These Hb A_{1c} reductions were significant, with a reduction of 0.5% that was similar to that achieved by using medication (44, 45) and associated with lower risk of microvascular complications (46).

Low-carbohydrate, low-GI ,and Mediterranean diets led to significant improvements in the lipid profile with up to a 4–10% increase in HDL (4% in Mediterranean, 5% in low-GI, and 10% in low-carbohydrate diets), 1–4% reduction in LDL (1% in low-carbohydrate, 3% in low-GI, and 4% in Mediterranean diets), and 9% reduction in triglycerides.

Low-carbohydrate diets restrict carbohydrate intake to 20–60 g/d. The studies in this review compared diets low in carbohydrates with low-fat and low-GI diets. The low-carbohydrate diets appeared to provide superior weight loss, glycemic control, and lipid profile compared with low-fat diets and, in one of 2 studies (42), was superior to the low-GI diet for all 3 variables. However, the carbohydrate content of these diets was as low as 20g carbohydrates/d and ranged from 13–45% of the daily energy intake. In contrast, international authorities recommend a carbohydrate intake from 45 to >65% of total energy/d.

A recently published review by Wheeler et al (47) that looked at literature between 2001 and 2010 also showed that low-carbohydrate diets appeared to improve markers of glycemic control with nonsignificant improvements in lipoproteins.

A vegetarian diet includes mainly cereal products, nuts, seeds, fruit, and vegetables and, occasionally, dairy products and eggs. Vegans avoid dairy products, eggs, or any other foods derived from animals.

The study that compared a vegan diet to the low-fat ADA diet showed significantly lower total cholesterol, LDL, and Hb A_{1c} in the vegan arm (29). These differences were attributed to the weight-loss effect of the diet. Additional analysis at 18 mo (29) showed an advantage of vegetarian diets in terms of glycemic control and lipid profile but not in weight loss (48).

Kahleova et al (30) randomly assigned a similar number of participants to receive either a vegetarian or EASD diet and showed significant reductions in diabetes medication, greater weight loss, and increased insulin sensitivity in the vegetarian arm but no significant difference in Hb A_{1c}.

Therefore, there is a suggestion that vegan and vegetarian diets might be beneficial in improving glycemic control and inducing weight loss. However, there is a need for more studies to support the wider use of these diets in people with diabetes.

The GI is a way of ranking foods according to their glycemic effect. It is defined as the area under the 2-hour blood glucose response curve (AUC) after the ingestion of 50 g carbohydrates. The AUC of the test food is divided by the AUC of the standard (usually glucose or white bread) and multiplied by 100 (49, 50).

The definition of low GI in these trials was variable. Ma et al (39) defined low GI as "choosing predominantly low-GI foods," which translated to foods that had, on average, a 3-point lower GI than those in the control arm (the ADA diet); in the study of Wolever et al (38), the low-GI group had 8% less high-GI foods than the high-GI group did, whereas the low-GI group in the study of Jenkins et al (34) consisted of foods with a GI that was, on average, 14 points less than in the control arm (high-fiber diet).

Low-GI diets resulted in a lower Hb A_{1c} and higher HDL but no significant difference in weight loss (34, 38, 39). The Hb A_{1c} reduction was only 0.14% and might not have been clinically relevant.

Anderson et al (51) performed a meta-analysis that compared low-GI with high-GI diets and showed significant benefits in terms of glycemic control and lipid profile. However, these studies included subjects those with type 1 diabetes and children and enrolled a mean of just 14 participants for an average of 33 d per trial, which made it difficult to extrapolate the findings to the prevalently older T2D population and made it impossible to predict if these benefits would be sustained over time. The findings of Wheeler et al (47) were similar to ours with only little differences in glycemic control between low- and high-GI and other diets.

The Mediterranean diet is rich in olive oil, legumes, unrefined cereals, fruit, and vegetables, low in meat and meat products, and with moderate contents of dairy products (mostly cheese and yogurt), fish, and wine. The total fat in this diet is typically 25–35% of calories, with saturated fat at ≤8% of calories (52, 53).

The 3 trials included in the meta-analysis compared a Mediterranean diet with a conventional diet (ie, no change to the current diets of participants) and ADA diet (35–37) and showed better glycemic control, greater weight loss, and a more-favorable lipid profile in the Mediterranean-diet arm.

An important difference between the Mediterranean and ADA diets is likely to be the content of MUFAs, which has been shown to have an impact on the lipd profile (54, 55), insulin sensitivity (56–58), and postprandial glucose concentrations (59). Our conclusion regarding the Mediterranean diet is similar to that in a review by Esposito et al (60), which showed improved glycemic control, and Kastorini et al (61), whose meta-analysis showed an association between the Mediterranean diet and improved lipid profile and lower blood glucose.

High-protein diets are diets in which 20–30% or more of the total daily calories come from proteins (62). Of 2 studies, one study compared a high-protein diet with a low-protein diet (44), and the other study compared a high-protein diet with a high-carbohydrate diet (40). Neither study showed any significant differences in weight, glycemic control, or lipids, but pooled data showed significantly lower Hb A_{1c} concentrations in the high-protein–diet group. This impact on glycemic control might have been due to previous suggestions that protein has effects on appetite suppression (63) and insulin sensitivity (64–68). The concern of the development of diabetic nephropathy (69) with a high-protein diet was not substantiated by Brinkworth et al (44) who showed no change in urinary albumin excretion in either the high- or low-protein–diet arms. These data suggest a possible role for high-protein diets, but additional studies are probably required to examine the long-term effects in patients with renal disease.

The studies that compared a diet high in carbohydrates to one high in MUFAs and high-fiber with low-fat diets showed no significant differences in weight, glycemic control, and lipid profile (5, 28).

There are significant confounders in performing a meta-analysis of such varied interventions. The control diets were different in terms of the specific macronutrient composition, study participants sometimes had different baseline characteristics (eg, weight and Hb A_{1c}), the duration of the studies ranged between 6 mo and 4 y (although we performed the meta-analysis by using data at 6 mo or 1 y), and, although all studies included in the meta-analysis were RCTs, some studies failed to report on allocation concealment and assessor blinding. Thus, all of these features introduced heterogeneity and confounding effects in the analysis. Additional research should involve large trials that compared all of these diets in participants with similar characteristics for the same duration. The favorable results from the Mediterranean and high-protein categories should be interpreted with caution, particularly because few studies were analyzed.

Another major confounder was the independent effect of weight change on the other measured variables (glycemic control and lipid profile). It is difficult to isolate the effect of weight change on these markers of cardiovascular risk, and thus, these benefits could be falsely attributed to the change in quantity of a macronutrient when the change was due to the impact of weight loss alone. This possibility might be of particular relevance when the effect of low-carbohydrate diets is interpreted. Future studies that aim to keep weight constant or ensure an equal caloric intake in all study arms would be useful to help clarify this issue.

In conclusion, our review of the existing literature on low-carbohydrate, low-GI, Mediterranean, and high-protein diets suggests that these diets may be effective in improving various markers of cardiovascular risk in people with diabetes and could have a wider role in the management of diabetes. Dietary behaviors and choices are often personal, and it is usually more realistic for a dietary modification to be individualized rather than to use a one-size-fits-all approach for each person. The diets reviewed in this study show that there may be a range of beneficial dietary options for people with T2D.

We are grateful to Rod Taylor for his expert statistical advice and Suzanne Swift for her help with database searches.

The authors' responsibilities were as follows—OA: collection and analysis of data; and all authors: design and writing of the manuscript. None of the authors had a conflict of interest.

REFERENCES

1. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, Keinänen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343–50.
2. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393–403.
3. Kirk JK, Graves DE, Craven TE, Lipkin EW, Austin M, Margolis KL. Restricted-carbohydrate diets in patients with type 2 diabetes: a meta-analysis. J Am Diet Assoc 2008;108:91–100.
4. Cao Y, Mauger DT, Pelkman CL, Zhao G, Townsend SM, Kris-Etherton PM. Effects of moderate (MF) versus lower fat (LF) diets on lipids and lipoproteins: a meta-analysis of clinical trials in subjects with and without diabetes. J Clin Lipidol 2009;3:19–32.
5. Brehm BJ, Lattin BL, Summer SS, Boback JA, Gilchrist GM, Jandacek RJ, D'Alessio DA. One-year comparison of a high monounsaturated fat diet with a high-carbohydrate diet in type 2 diabetes. Diabetes Care 2009;32:215–20.
6. Kodama S, Saito K, Tanaka S, Maki M, Yachi Y, Sato M, Sugawara A, Totsuka K, Shimano H, Ohashi Y, et al. Influence of fat and carbohydrate proportions on the metabolic profile in patients with type 2 diabetes: a meta-analysis. Diabetes Care 2009;32:959–65.
7. Davis NJ, Tomuta N, Schechter C, Isasi CR, Segal-Isaacson CJ, Stein D, Zonszein J, Wylie-Rosett J. Comparative study of the effects of a 1-year dietary intervention of a low-carbohydrate diet versus a low- fat diet on weight and glycemic control in type 2 diabetes. Diabetes Care 2009;32:1147–52.
8. Haimoto H, Iwata M, Wakai K, Umegaki H. Long-term effects of a diet loosely restricting carbohydrates on HbA1c levels, BMI and tapering of sulfonylureas in type 2 diabetes: a 2-year follow-up study. Diabetes Res Clin Pract 2008;79:350–6.
9. Nordmann AJ, Nordmann A, Briel M, Keller U, Yancy WS Jr, Brehm BJ, Bucher HC. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials. Arch Intern Med 2006;166:285–93.
10. Arora SK, McFarlane SI. The case for low carbohydrate diets in diabetes management. Nutr Metab (Lond) 2005;2:16.
11. Lejeune MP, Kovacs EM, Westerterp-Plantenga MS. Additional protein intake limits weight regain after weight loss in humans. Br J Nutr 2005; 93:281–9.
12. Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, Greenberg I, Golan R, Fraser D, Bolotin A, Vardi H, et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. N Engl J Med 2008;359: 229–41.
13. Nielsen JV, Joensson EA. Low-carbohydrate diet in type 2 diabetes: stable improvement of bodyweight and glycemic control during 44 months follow-up. Nutr Metab (Lond) 2008;5:14.
14. Thomas DE, Elliott EJ. The use of low-glycaemic index diets in diabetes control. Br J Nutr 2010;104:797–802.

15. Harding AH, Sargeant LA, Welch A, Oakes S, Luben NR, Bingham S, Day EN, Khaw K, Wareham N. Fat consumption and HbA(1c) levels: the EPIC-Norfolk study. Diabetes Care 2001;24:1911–6.
16. Wolfram T, Ismail-Beigi F. Efficacy of high-fiber diets in the management of type 2 diabetes mellitus. Endocr Pract 2011;17:132–42.
17. Serra-Majem L, Roman B, Estruch R. Scientific evidence of interventions using the Mediterranean diet: a systematic review. Nutr Rev 2006;64:S27–47.
18. Brand-Miller J, Hayne S, Petocz P, Colagiuri S. Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials. Diabetes Care 2003;26:2261–7.
19. Nutrition Committee of the British Diabetic Association's Professional Advisory Committee. Dietary recommendations for people with diabetes: an update for the 1990s. Diabet Med 1992;9:189–202.
20. National Nutrition Committee CDA. Guidelines for the nutritional management of diabetes mellitus in the new millennium: a position statement by the Canadian Diabetes Association. Can J Diabetes Care 1999;23:56–69.
21. Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD). 1. Recommendations for the nutritional management of patients with diabetes mellitus. Diabetes Nutr Metab 1995;8:186–9.
22. American Diabetes Association. Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. Diabetes Care 2002;25:202–12.
23. Singh RB, Rastogi SS, Rao PV, Das S, Madhu SV, Das AK, Sahay BK, Fuse SM, Beegom R, Sainani GS, et al. Diet and lifestyle guidelines and desirable levels of risk factors for the prevention of diabetes and its vascular complications in Indians: a scientific statement of the International College of Nutrition. J Cardiovasc Risk 1997;4:201–8.
24. Kitamura S. Diet therapy and food exchange lists for diabetic patients. Diabetes Res Clin Pract 1994;24(suppl):S233–40.
25. Silvis N. Nutrition recommendations for individuals with diabetes mellitus. S Afr Med J 1992;81:162–6.
26. Krauss RM, Eckel RH, Howard BV, Appel LJ, Daniels SR, Deckelbaum RJ, Erdman JW Jr, Kris-Etherton P, Goldberg IJ, Kotchen TA, et al. AHA Guidelines Revision 2000: A statement for healthcare professionals from the Nutrition Committee of the American Heart Association. Circulation 2000;102:2284–99.
27. Expert Panel on Detection, Valuation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285:2486–97.
28. Milne RM, Mann JI, Chisholm AW, Williams SM. Long-term comparison of three dietary prescriptions in the treatment of NIDDM. Diabetes Care 1994;17:74–80.
29. Barnard ND, Cohen J, Jenkins DJ, Turner-McGrievy G, Gloede L, Jaster B, Seidl K, Green AA, Talpers S. A low-fat vegan diet improves glycemic control and cardiovascular risk factors in a randomized clinical trial in individuals with type 2 diabetes. Diabetes Care 2006; 29:1777–83.
30. Kahleova H, Matoulek M, Malinska H, Oliyarnik O, Kazdova L, Neskudla T, Skoch A, Hajek M, Hill M, Kahle M, et al. Vegetarian diet improves insulin resistance and oxidative stress markers more than conventional diet in subjects with type 2 diabetes. Diabetes Med 2011; 28:549–59.
31. Salas-Salvadó J, Fernández-Ballart J, Ros E, Martinez-Gonzalez MA, Fitó M, Estruch R, Corella D, Fiol M, Gómez-Gracia E, Arós F, et al. Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status: one-year results of the PREDIMED randomized trial. Arch Intern Med 2008;168:2449–58.
32. Samaha FF, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, Williams T, Williams M, Gracely EJ, Stern L. A low-carbohydrate as compared with a low-fat diet in severe obesity. N Engl J Med 2003; 348:2074–81.
33. Stern L, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, Williams M, Gracely EJ, Samaha FF. The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one year follow-up of a randomized trial. Ann Intern Med 2004;140:778–85.
34. Jenkins DJ, Kendall CW, McKeown-Eyssen G, Josse RG, Silverberg J, Booth GL, Vidgen E, Josse AR, Nguyen TH, Corrigan S, et al. Effect of a low-glycemic index or a high-cereal fiber diet on type 2 diabetes: a randomized trial. JAMA 2008;300:2742–53.
35. Toobert DJ, Glasgow RE, Strycker LA, Barrera M Jr, Radcliffe JL, Wander RC, Bagdade JD. Biologic and quality-of-life outcomes from the Mediterranean Lifestyle Program: a randomized clinical trial. Diabetes Care 2003;26:2288–93.
36. Esposito K, Maiorino MI, Ciotola M, Di Palo C, Scognamiglio P, Gicchino M, Petrizzo M, Saccomanno F, Beneduce F, Ceriello A, et al. Effects of a Mediterranean-style diet on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes: a randomized trial. Ann Intern Med 2009;151:306–14.
37. Elhayany A, Lustman A, Abel R, Attal-Singer J, Vinker S. A low carbohydrate Mediterranean diet improves cardiovascular risk factors and diabetes control among overweight patients with type 2 diabetes mellitus: a 1-year prospective randomized intervention study. Diabetes Obes Metab 2010;12:204–9.
38. Wolever TM, Gibbs AL, Mehling C, Chiasson JL, Connelly PW, Josse RG, Leiter LA, Maheux P, Rabasa-Lhoret R, Rodger NW, et al. The Canadian Trial of Carbohydrates in Diabetes (CCD), a 1-y controlled trial of low-glycemic-index dietary carbohydrate in type 2 diabetes: no effect on glycated hemoglobin but reduction in C-reactive protein. Am J Clin Nutr 2008;87:114–25.
39. Ma Y, Olendzki BC, Merriam PA, Chiriboga DE, Culver AL, Li W, Hébert JR, Ockene IS, Griffith JA, Pagoto SL. A randomized clinical trial comparing low-glycemic index versus ADA dietary education among individuals with type 2 diabetes. Nutrition 2008;24:45–56.
40. Larsen RN, Mann NJ, Maclean E, Shaw JE. The effect of high-protein, low-carbohydrate diets in the treatment of type 2 diabetes: a 12 month randomised controlled trial. Diabetologia 2011;54:731–40.
41. Yancy WS Jr, Westman EC, McDuffie JR, Grambow SC, Jeffreys AS, Bolton J, Chalecki A, Oddone EZ. A randomized trial of a low-carbohydrate diet vs orlistat plus a low-fat diet for weight loss. Arch Intern Med 2010;170:136–45.
42. Westman EC, Yancy WS, Mavropoulos JC, Marquart M, McDuffie JR. The effect of a low-carbohydrate, ketogenic diet versus a lowglycemic index diet on glycemic control in type 2 diabetes mellitus. Nutr Metab (Lond) 2008;5:36.
43. Iqbal N, Vetter ML, Moore RH, Chittams JL, Dalton-Bakes CV, Dowd M, Williams-Smith C, Cardillo S, Wadden TA. Effects of a low-intensity intervention that prescribed a low-carbohydrate vs. a low-fat diet in obese. Obesity (Silver Spring) 2010;18:1733–8.
44. Brinkworth GD, Noakes M, Parker B, Foster P, Clifton PM. Longterm effects of advice to consume a high-protein, low-fat diet, rather than a conventional weight-loss diet, in obese adults with type 2 diabetes: one-year follow-up of a randomised trial. Diabetologia 2004; 47:1677–86.
45. United Kingdom Prospective Diabetes Study Group. UKPDS 13: relative efficacy of randomly allocated diet, sulphonylureas, insulin or metformin in patients with newly diagnosed non-insulin dependent diabetes followed for three years. BMJ 1995;310:83–8.
46. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, Hadden D, Turner RC, Holman RR. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 2000;321:405–12.
47. Wheeler ML, Dunbar SA, Jaacks LM, Karmally W, Mayer-Davis EJ, Wylie-Rosett J, Yancy WS. Macronutrients, food groups, and eating patterns in the management of diabetes: a systematic review of the literature, 2010. Diabetes Care 2012;35:434–45.
48. Barnard ND, Gloede L, Cohen J, Jenkins DJ, Turner-McGrievy G, Green AA, Ferdowsian H. A low-fat vegan diet elicits greater macronutrient changes, but is comparable in adherence and acceptability, compared with a more conventional diabetes diet among individuals with type 2 diabetes. J Am Diet Assoc 2009;109:263–72.
49. Jenkins DJ, Wolever TM, Taylor RH, Barker H, Fielden H, Baldwin JM, Bowling AC, Newman HC, Jenkins AL, Goff DV. Glycemic index of foods: a physiological basis for carbohydrate exchange. Am J Clin Nutr 1981;34:362–6.
50. Brouns F, Bjorck I, Frayn KN, Gibbs AL, Lang V, Slama G, Wolever TM. Glycemic index methodology. Nutr Res Rev 2005;18:145–71.
51. Anderson JW, Randles KM, Kendall CWC, Jenkins DJ. Carbohydrate and fiber recommendations for individuals with diabetes: a quantitative assessment and meta-analysis of the evidence. J Am Coll Nutr 2004;23: 5–17.
52. Willett W, Skerrett PJ, Giovannucci EL, Callahan M. Eat, drink, and be healthy: the Harvard Medical School guide to healthy eating. New York, NY: Free Press, 2005.

53. Willett WC, Sacks F, Trichopoulou A, Drescher G, Ferro-Luzzi A, Helsing E, Trichopoulos D. Mediterranean diet pyramid: a cultural model for healthy eating. Am J Clin Nutr 1995;61:1402S–6S.
54. Rodríguez-Villar C, Perez-Heras A, Mercade I, Casals E, Ros E. Comparison of a high-carbohydrate and a high-monounsaturated fat, olive oil-rich diet on the susceptibility of LDL to oxidative modification in subjects with type 2 diabetes mellitus. Diabet Med 2004;21:142–9.
55. Garg A, Bantle JP, Henry RR, Coulston AM, Griver KA, Raatz SK, Brinkley L, Chen YD, Grundy SM, Huet BA, et al. Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus.. JAMA 1994;271:1421–8.
56. Esposito K, Marfella R, Ciotola M, Di Palo C, Giugliano F, Giugliano G, D'Armiento M, D'Andrea F, Giugliano D. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. JAMA 2004;292:1440–6.
57. Schwenke DC. Insulin resistance, low-fat diets, and low-carbohydrate diets: time to test new menus. Curr Opin Lipidol 2005;16:55–60.
58. Lara-Castro C, Garvey WT. Diet, insulin resistance, and obesity: zoning in on data for Atkins dieters living in South Beach. J Clin Endocrinol Metab 2004;89:4197–205.
59. O'Keefe JH, Gheewala NM, O'Keefe JO. Dietary strategies for improving post-prandial glucose, lipids, inflammation, and cardiovascular health. J Am Coll Cardiol 2008;51:249–55.
60. Esposito K, Maiorino MI, Ceriello A, Giugliano D. Prevention and control of type 2 diabetes by Mediterranean diet: A systematic review. Diabetes Res Clin Pract 2010;89:97–102.
61. Kastorini CM, Milionis HJ, Esposito K, Giugliano D, Goudevenos JA, Panagiotakos DB. The effect of Mediterranean diet on metabolic syndrome and its components: a meta-analysis of 50 studies and 534,906 individuals. J Am Coll Cardiol 2011;57:1299–313.
62. Academy of Nutrition and Dietetics. Available from: http://www.eatright.org/Foundation/ (cited 1 May 2012).
63. Weigle DS, Breen PA, Matthys CC, Callahan HS, Meeuws KE, Burden VR, Purnell JQ. A high-protein diet induces sustained reductions in appetite, ad libitum caloric intake, and body weight despite compensatory changes in diurnal plasma leptin and ghrelin concentrations. Am J Clin Nutr 2005;82:41–8.
64. Gannon MC, Nuttall F, Saeed A, Jordan K, Hoover H. An increase in dietary protein improves blood glucose response in persons with type 2 diabetes. Am J Clin Nutr 2003;78:734–41.
65. Seino Y, Seino S, Ikeda M, Matsukura S, Imura H. Beneficial effects of a high protein diet in the treatment of mild diabetes. Hum Nutr Appl Nutr 1983;37A:226–30.
66. Nielsen J, Jönsson E, Nilsson AK. Lasting improvement of hyperglycaemia and bodyweight: low-carbohydrate diets in type 2 diabetes. A brief report. Ups J Med Sci 2005;109:179–84.
67. Parker B, Luscombe N, Noakes M, Clifton P. Effect of a high protein, high-monounsaturated fat weight loss diet on glycemic control and lipid levels in type 2 diabetes. Diabetes Care 2002;25:425–30.
68. Brinkworth GD, Noakes M, Keogh JB, Luscombe ND, Wittert GA, Clifton PM. Long-term effects of a high-protein, low carbohydrate diet on weight control and cardiovascular risk markers in obese hyperinsulinemic subjects. Int J Obes Relat Metab Disord 2004;28:661–70.
69. Pijls LT, de Vries H, Donker AJ, van Eijk JT. The effect of protein restriction on albuminuria in patients with type 2 diabetes mellitus: a randomized trial. Nephrol Dial Transplant 1999;14:1445–53.