American Dietetic Association

Review

RESEARCH

Meets Learning Need Codes 5000, 5190, 9000, and 9020. To take the Continuing Professional Education quiz for this article, log in to ADA's Online Business Center at www.eatright.org/obc, click the "Journal Article Quiz" button, click "Additional Journal CPE Articles," and select this article's title from a list of available quizzes.

The Evidence for Medical Nutrition Therapy for Type 1 and Type 2 Diabetes in Adults

MARION J. FRANZ, MS, RD; MARGARET A. POWERS, PhD, RD; CAROLYN LEONTOS, MS, RD; LEA ANN HOLZMEISTER, RD; KARMEEN KULKARNI, MS, RD; ARLENE MONK, RD; NAOMI WEDEL, MS, RD; ERICA GRADWELL, MS, RD

ABSTRACT

This article reviews the evidence and nutrition practice recommendations from the American Dietetic Association's nutrition practice guidelines for type 1 and type 2 diabetes in adults. The research literature was reviewed to answer nutrition practice questions and resulted in 29 recommendations. Here, we present the recommendations and provide a comprehensive and systematic review of the evidence associated with their development. Major nutrition therapy factors reviewed are carbohydrate (intake, sucrose, non-nutritive sweeteners, glycemic index, and fiber), protein intake, cardiovascular disease, and weight management. Contributing factors to nutrition therapy reviewed are physical activity and glucose monitoring. Based on individualized nutrition therapy client/patient goals and lifestyle changes the client/patient is willing and able to make, registered dietitians can select appropriate interventions based on key recommendations that include consistency in day-to-day carbohydrate intake, adjusting insulin doses to match carbohydrate intake, substitution of sucrose-containing foods, usual protein intake, cardioprotective nutrition interventions, weight management strategies, regular physical activity, and use of self-monitored blood glucose data. The evidence is strong that medical nutrition therapy provided by registered dietitians is an effective and essential therapy in the management of diabetes.
J Am Diet Assoc. 2010;110:1852-1889.

M. J. Franz is a nutrition consultant, Nutrition Concepts by Franz, Inc, Minneapolis, MN. M. A. Powers is a research scientist, and A. Monk is a research clinician, International Diabetes Center at Park Nicollet, Minneapolis, MN. C. Leontos is a professor emeritus, University of Nevada Cooperative Extension, Las Vegas, NV. L. A. Holzmeister is a pediatric nutritionist, Phoenix Children's Hospital, Phoenix, AZ. K. Kulkarni is director, Scientific Affairs, Abbott Diabetes Care, Salt Lake City, UT. N. Wedel is a clinical specialist, Roche Diagnostics, Madison, WI. E. Gradwell is a lead evidence analyst/independent contractor, American Dietetic Association, Arvada, CO.

Address correspondence to: Marion J. Franz, MS, RD, Nutrition Concepts by Franz, Inc, 6635 Limerick Dr, Minneapolis, MN 55439. E-mail: MarionFranz@aol.com

Manuscript accepted: May 6, 2010.

0002-8223/$36.00
doi: 10.1016/j.jada.2010.09.014

In 2008 the American Dietetic Association (ADA) published evidence-based nutrition practice guidelines (EBNPGs) for ambulatory adults with type 1 and type 2 diabetes in the Evidence Analysis Library (EAL) (1). Type 1 diabetes is primarily a disease of insulin deficiency, whereas type 2 diabetes is a progressive disease that results from defects in insulin action (insulin resistance) and insulin secretion (insulin deficiency). Although the etiology of type 1 and type 2 diabetes differs, medical nutrition therapy (MNT) goals for both are similar. MNT plays a critical role in managing diabetes and reducing the potential complications related to poor glycemic, lipid, and blood pressure control (2). The need to provide patients with evidence-based nutrition care is essential to providing optimum diabetes care.

The development of an EBNPG begins with an expert panel identifying key questions and research criteria, followed by a review of the evidence and writing of summary statements. Based on this evidence, recommendations are made and integrated into the Nutrition Care Process. This review summarizes the research reviewed and used to write the recommendations, reviews research published after the completion of the recommendations, states the evidence-based nutrition practice recommendations, and identifies limitations and gaps in knowledge that require further research. Summarizing the EAL findings provides for access by a broader audience.

METHODS

In 2005, an expert panel was appointed by the ADA Evidence-Based Practice Committee to update the diabe-

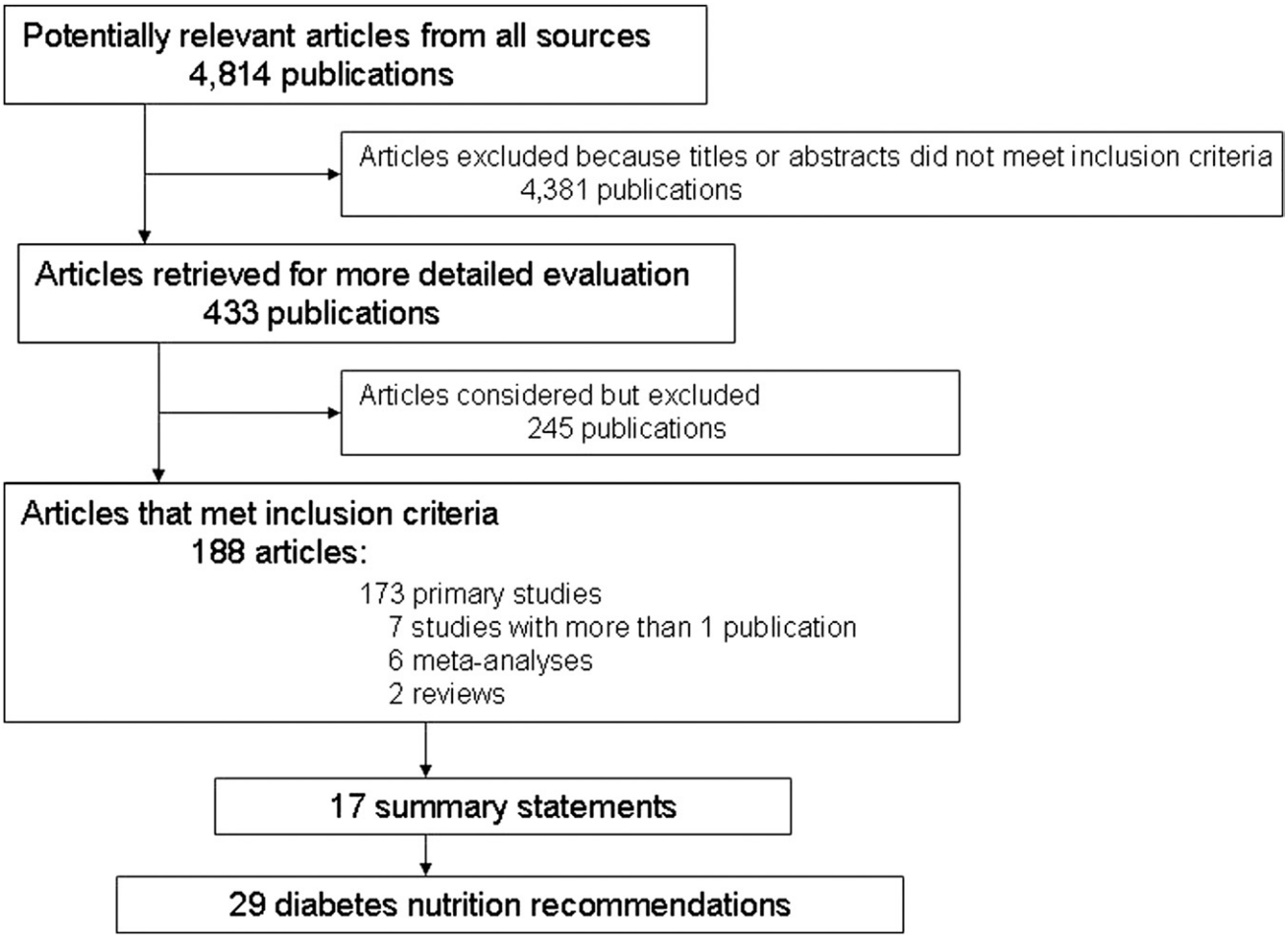

Figure. Flow chart of article selection for the development of diabetes nutrition recommendations. The literature search based on predetermined criteria resulted in a review of 173 primary studies from which summary statements and recommendations were written.

tes nutrition practice guidelines originally published in 2001 (3). The expert panel identified questions that address major nutrition therapy factors for diabetes, including carbohydrate (amount and distribution of intake, sucrose, non-nutritive sweeteners, glycemic index, and fiber), protein intake, prevention and treatment of cardiovascular disease (CVD), and weight management; contributing factors to diabetes nutrition therapy, including physical activity and glucose monitoring; and effectiveness of medical nutrition therapy for diabetes.

The literature search criteria for each question were determined and the search conducted using PubMed MEDLINE, the Database of Abstracts of Reviews of Effects, and the Agency for Healthcare Research and Quality (1). Additional articles were identified from reference lists and personal communication. Search criteria included: human participants with diabetes, English language articles, sample size $\geq$10 in each treatment group, and dropout rate $<$20%. In addition, studies for prevention of CVD and weight management had to be 1 year or longer in duration. Study design preferences were randomized controlled trials or clinical controlled studies, large nonrandomized observational studies, or cohort, case-control studies. Articles included for macronutrients were published between 2001 and February 2007, for sucrose, glycemic index, and fiber between 1980 and February 2007, and for nonnutritive sweeteners between 1985 and March 2006. For protein, weight management, and glucose monitoring between 2001 and May 2006, for physical activity between 2001 and June 2006, for effectiveness of diabetes MNT and CVD between 2001 and July 2006. Topics that extend back before 2001 were not adequately covered in the 2001 guidelines. Studies reviewed after the completion of the recommendations were published between the dates cited above for each topic and July 2009.

Key information was extracted and summarized by trained analysts according to prescribed guidelines developed by the ADA (4). A total of 173 primary studies, six meta-analyses, and two reviews (188 articles [seven primary studies had more than one publication]) were analyzed and graded based on the quality of the research. The Figure illustrates the study selection process. Using an expert consensus method, the panel then wrote 17 summary statements. Table 1 lists the articles reviewed for each factor, the summary statements, and grade. The summary statements were used to formulate the 29 diabetes nutrition practice recommendations.

The panel also developed a clinical algorithm based on

Table 1. Number of articles in patients with diabetes and graded summary statements used to write the recommendations in the *Nutrition Practice Guidelines for Type 1 and Type 2 Diabetes Mellitus* (3)

Factors	No. of primary studies [No. of articles] (reference)	No. of meta-analyses or review articles (reference)	No. of new studies, meta-analyses, or review articles added after initial review [No of articles] (reference)	Summary statements	Grade
Carbohydrate Intake	9 [9] (5-13)	0	9 studies; 2 meta-analyses [12] (14-25)	Adjusting mealtime insulin doses to match planned carbohydrate intake in persons with type 1 diabetes results in improved glycemic control. Consistency in carbohydrate intake also improves glycemic control.	I
	11 [12] (6,7,10-13,96,98-102)		0	Evidence for differing percentages of carbohydrate and macronutrients in the food/meal plan is inconclusive.	I
Sucrose	15 [15] (27-41)	0	0	Sucrose intakes of 10%-35% of total energy do not have a negative effect on glycemic or lipid responses when sucrose is substituted for isocaloric amounts of starch.	I
Non-nutritive sweeteners	8 [8] (31,43-49)	0	2 studies; 1 review (50-52)	Studies conducted outside the United States report children and adults with diabetes have higher intakes of non-nutritive sweeteners compared to controls but intakes do not exceed the Acceptable Daily Intake in most instances.	III
Glycemic index	11 [13] (5,53-58,61-66)	1 meta-analysis (59); 1 review (60)	4 studies; 1 meta-analysis [7] (18,67-72)	Studies comparing high- vs low-Glycemic Index diets report mixed effects on HbA1c[a] levels.	II
Fiber	15 [15] (40,75-88)	0	0	The evidence is inconclusive that increasing dietary fiber will influence glycemic outcomes; however, there is conclusive evidence that higher-fiber diets will lower total cholesterol compared to lower-fiber diets.	I
Protein Intake	6 [7] (90-96)	0	0	The amount of protein consumed has minimal influence on glycemic or lipid responses, and shows no long-term effect on insulin requirements.	II
	9 [9] (97-105)		4 studies; 2 meta-analysis (106-111)	In persons with diabetic nephropathy, improvements in albumin excretion rate are reported with protein intake <1 g/kg/d, but no improvements in glomerular filtration rate Malnutrition has been reported with a protein intake of $\sim$0.7 g/kg/d.	II
Cardiovascular disease	11 [12] (8,114-116,118-125)	1 meta-analysis (117)	4 (126-129)	Cardioprotective nutrition interventions reduce HbA1c, blood pressure, body weight, and improve serum lipid profiles, all of which reduce the risk of CVD[b].	I
	20 [20] (11,54,92,130-146)	0	7 (19,147-152)	In persons with diabetes and CVD, cardioprotective nutrition interventions improve endothelial health, lipid profiles, and blood pressure.	I
Weight management	19 [20] (94,125,153-166,168-171)	1 meta-analysis (167)	11 [12] (127,172-180)	In weight loss randomized controlled trials, approximately half report improvements in HbA1c values with weight loss, whereas approximately half report no improvement in HbA1c values despite fairly similar weight losses. Randomized controlled trials using weight loss medications report consistent modest improvement in HbA1c.	II
Physical activity	10 [12] (182-190,192-194)	1 meta-analysis (191); 1 review (181)	3 studies, 2 meta-analyses (200-204)	In persons with type 2 diabetes, 90-150 min of weekly physical activity (both aerobic and resistance/strength training) reduces HbA1c, improves insulin sensitivity, and decreases risk for all-cause mortality.	I
	4 [5] (181,195-1999)	0	1 study, 2 reviews (205-207)	In persons with type 1 diabetes, glycemic control generally does not improve in response to ongoing participation in physical activity alone.	II
Blood glucose monitoring	3 [3] (8,9,208)	0	1 (236)	In persons with type 1 diabetes, interventions that included self-management training adjustment of insulin doses based on SMBG[c] improves glycemic control compared to control groups; more frequent SMBG is associated with better glycemic control.	I
	12 [12] (208-212,215-221)	2 meta-analyses (213, 214)	3 studies; 1 meta-analysis; 1 review (236-240)	In persons with type 2 diabetes, SMBG, compared to non-SMBG, is associated with greater improvement in HbA1c when it is part of a structured education program where persons use the information to make changes in their management program; evidence on frequency and duration on SMBG is inconclusive.	II

(continued)

Table 1. Number of articles in patients with diabetes and graded summary statements used to write the recommendations in the *Nutrition Practice Guidelines for Type 1 and Type 2 Diabetes Mellitus* (3) (continued)

Factors	No. of primary studies [No. of articles] (reference)	No. of meta-analyses or review articles (reference)	No. of new studies, meta-analyses, or review articles added after initial review [No of articles] (reference)	Summary statements	Grade
	14 [14] (222-235)	0	4 studies; 1 review (241-245)	Continuous glucose monitoring studies report improvements in glycemic control and in hyper- and hypoglycemic ranges. However, it is unclear whether using the data derived from continuous glucose monitoring will improve glycemic outcomes more than use of data derived from SMBG.	II
Effectiveness of MNT[d]	18 [18] (1)	0		Medical nutrition therapy resulted in reductions in HbA1c, ranging from 0.25%-2.9%, depending on the type and duration of diabetes. Multiple encounters and a variety of nutrition therapy interventions were employed. Also reported are improvements in other outcomes, such as lipids, blood pressure, weight management, decreased need for medications and reduced risk for onset and progression of comorbidities.	I

[a]HbA1c = glycosylated homoglobin.
[b]CVD = cardiovascular disease.
[c]SMBG = self-monitoring of blood glucose.
[d]MNT = medical nutrition therapy.

the ADA's Nutrition Care Process of Nutrition Assessment, Diagnosis, Intervention, and Monitoring and Evaluation to illustrate how each recommendation can be used within the management process. The guideline was then reviewed internally and externally. The external reviewers consisted of an interdisciplinary group of health professionals. The expert panel preformed their work via regularly scheduled conference calls, shared Internet workspace, and a 2-day workshop.

CARBOHYDRATE INTAKE EVIDENCE AND RECOMMENDATIONS

Carbohydrate intake and available insulin are the primary determinants of postprandial glucose levels. Managing carbohydrate intake is, therefore, a primary strategy for achieving glycemic control. To develop recommendations on the amount and distribution of carbohydrate intake in persons with type 1 and type 2 diabetes, a total of nine studies meeting the predetermined criteria were reviewed (Table 2).

Research Reviewed

Three studies showed that day-to-day consistency in distribution of carbohydrate intake resulted in improved glycemic control (5-7). Wolever and colleagues (5), in a descriptive study of patients with type 1 diabetes, reported that consistency in the amount and source of carbohydrate was associated with improved glycemic control. However, they also noted that this conclusion might not apply to persons on intensified insulin therapy who adjust their insulin doses based on their carbohydrate intake at each meal. Two studies in patients with type 1 diabetes who adjusted mealtime (prandial) insulin to match planned carbohydrate intake reported improved glycemic control (8,9).

Of five studies evaluating differing percentages of carbohydrate intake, the evidence was not conclusive (6,10-13). Two of these studies substituted monounsaturated fats (MUFA) for carbohydrate and reported mixed results on glycemia and lipids (10,11), Two other studies reported benefits, two from a lower-carbohydrate (20%) diet vs a higher-carbohydrate diet (6,12) and in contrast, the other from a high-carbohydrate (80%) diet vs a standard-carbohydrate (55%) diet (13).

Research Published after Completion of the Initial Recommendations

No new studies have been published regarding consistency in carbohydrate intake since completion of the literature review in February 2007. Two studies were published supporting adjustment of mealtime insulin based on planned carbohydrate intake. A prospective observational study in Australia of patients with type 1 and type 2 diabetes taught to match their insulin dose to their carbohydrate intake reported improvements in average glycosylated hemoglobin (HbA1c) at 1 year (14). Bergenstal and colleagues (15) compared use of carbohydrate counting vs a simplified algorithm for weekly adjustments of mealtime insulin doses in patients with type 2 diabetes who used basal and bolus insulin regimens with regular blood glucose testing. Both groups used the results of the patient's blood glucose tests to make adjust-

Table 2. Studies reporting on carbohydrate: Amount and distribution of intake

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
DCCT[a] Research Group, 1993 (8)	n=1,398 patients with type 1 diabetes/6.5 y	Conventional therapy or intensive therapy, monthly clinic visits including registered dietitian visits (RCT[b])	Intensive diabetes therapy reduced the overall risk for onset and progression of diabetic retinopathy, nephropathy, and neuropathy by ~50%
Garg, 1994 (10)	n=42 adults with type 2 diabetes/6 wk on each diet	High CHO[c] (55% CHO, 30% fat) vs high MUFA[d] (45% fat, 40% CHO) (RCT)	High CHO: ↑ fasting TG[e] by 24% ($P<0.0001$) and plasma TG by 10% ($P=0.03$), glucose by 12% ($P<0.0001$), and insulin by 9% ($P=0.02$); other lipids unchanged
Wolever, 1999 (5)	n=272 adults with type 1 diabetes/cross-sectional	2, 3-d food records during run-in for drug trial (descriptive study)	Neither kcal or nutrient composition related to HbA1c[f]; day-to-day variation of CHO ($P=0.0097$), starch ($P=0.0016$), and Glycemic Index ($P=0.033$) positively related to HbA1c; consistency in amount and source of day to day CHO associated with improved blood glucose control
Komiyama, 2002 (13)	n=24 adults with type 2 diabetes/7 d on each diet	55% CHO diet vs 80% high CHO diet (nonrandomized trial)	High CHO: ↓ insulin resistance ($P=0.04$) and ↓ fasting plasma glucose ($P=0.04$)
DAFNE[g] Study Group, 2002 (9)	n=136 adults with type 1 diabetes/6 mo	Participants taught to adjust mealtime insulin based on planned CHO intake vs control (RCT)	Treatment group vs control: HbA1c ↓ 1.0%, 9.4%→8.4% ($P<0.0001$) and quality of life improved ($P<0.01$); severe hypoglycemia, lipids, and weight unchanged
Gerhard, 2004 (11)	n=11 patients with type 2 diabetes/6 wk on each diet	High CHO ad libitum (60% CHO, 20% fat) vs ad libitum high MUFA (25% MUFA, 45% CHO) (RCT)	High CHO vs high MUFA: greater weight loss (1.53 kg; $P<0.001$); TG, glycemic control, and insulin sensitivity did not differ between diets
Nielsen, 2005 (7)	n=24 adults with type 1 diabetes/12 mo	Low CHO (20% CHO, 30% protein, 50% fat) (nonrandomized trial)	HbA1c ↓ 7.5%→6.4% ($P<0.001$); meal insulin requirements ↓ 21→12 units/d ($P<0.001$)
Nielsen, Jonsson, Nilsson, 2005 (12)	n=31 adults with type 2 diabetes/24 wk	Low CHO (20% CHO, 30% protein, 50% fat) vs control (60% CHO, 15% protein, 25% fat (nonrandomized trial)	Low CHO vs control showed lower FPG and HbA1c; *P* values not reported
Boden, 2005 (6)	n=10 obese adults with type 2 diabetes/7 d on control diet followed by 14 d on low CHO diet	Low CHO (21 g CHO, 3,111→2,164 kcal/d) vs control (usual diet, 309 g CHO, 3,111 kcal) (nonrandomized trial)	Low CHO: ↓ kcal → weight loss of 1.65 kg completely accounted for by reduced kcal; fasting plasma glucose ↓ ($P=0.025$); HbA1c ↓ ($P=0.006$), and insulin sensitivity improved by ~75% ($P=0.008$)
Xu, 2007 (22)	n=1,284 American Indians with diabetes for ≥1 y at second examination of the Strong Heart Study	Dietary intake assessed by a 24-h recall (cross-sectional association)	Lower CHO intake (<35%-40% of energy), higher fat intake (>25%-30% of energy), saturated fat (>13% of energy), and MUFA (>10% of energy) were associated with poor glycemic control ($P<0.01$).
Wolever, 2008 (18)	n=162 adults with type 2 diabetes managed by diet alone/1 y	High CHO diets (47%, 52%) vs low-CHO, high MUFA diet (RCT)	NS[h] differences in HbA1c, lipids, or body weight between diets
Lowe, 2008 (14)	n=82 patients with type 1 and 55 patients with type 2 diabetes/1 y	CHO counting, insulin dose adjustment, and other self-care skills taught by a registered dietitian (observational study)	HbA1c ↓ from to 8.7% to 8.1% ($p=0.0002$); patients with HbA1c <8% ↑ from 48.9% to 62.8% ($P=0.0005$); quality of life ($P=0.05$) and problem-solving skills ($P>0.00001$) also improved
Bergenstal, 2008 (15)	n=273 with type 2 diabetes on basal/bolus insulin regimen/ 24 wk	Mealtime insulin adjusted using CHO counting vs simple algorithm of set mealtime doses (RCT)	CHO counting vs algorithm: HbA1c 6.54% vs 6.7% (NS); mean HbA1c ↓ from baseline, −1.46% and −1.59%, respectively ($P=0.70$ for both).
Nielsen, 2008 (21)	n=31 with type 2 diabetes/ 44 mo	Low CHO diet (20%) vs higher CHO, low-fat diet (55%-60%, 15% respectively (retrospective observational study)	Low CHO group: weight ↓ 7.5 kg; HbA1c ↓ 1.2% (both $P<0.001$); 7 of 15 controls switched to the low CHO diet at 6 mo. No sign of a negative cardiovascular effect in low CHO group.
Kirk (2008) (24)	13 studies with 263 participants with type 2 diabetes/3 to 26 wks	Lower CHO diets (4% to 45% kcal) vs higher CHO (40% to 70%) diets (meta-analysis)	HbA1c ($P=0.013$) and TG ($P<0.001$) lower on lower CHO diets; weight was equivocal (NS); conclusion: insufficient evidence to recommend CHO <130 g/d
Barnard, 2009 (16) and Turner-McGrievy, 2008 (17)	n=99 adults with type 2 diabetes/22 wk (74 wks in 2009 study)	Vegan diet (75% CHO, 15% protein, 10% fat), energy intake and CHO unrestricted vs control (60%-75% CHO and MUFA, <7% saturated fat), energy deficits of 500-1,000 kcal if body mass index >25 (RCT)	Vegan vs control: HbA1c ↓ 1.23% vs 0.38 ($P=0.01$); body weight ↓ 6.5 kg vs 3.1 kg ($P<0.001$); LDL ↓ 21.2% vs 10.7% ($P=0.02$). At wk 22, Alternate Healthy Eating Index improved in vegan ($P<0.0001$) while control did not, between groups ($P<0.0001$). At 74 wks, 33 of vegan and 22 of control reported adherence to diet criteria ($P=0.019$)
Delahanty (2009) (23)	n=532 in the intensive-treatment group of DCCT followed ≥5 y	Diet-composition goals at onset: 45%-55% CHO, 10%-25% protein, 30%-35% fat, diet consistency and regular meals, variety of meal planning approaches (cross-sectional)	CHO intake ~45.5%, total fat 35.8%, saturated fat 12.7%, protein 18% of energy, total energy ↓ from 2,496±1,036 to 2,144±707 ($P<0.0001$); lower CHO intake ($P=0.01$), and higher saturated ($P=0.002$), monounsaturated ($P=0.02$), and total fat ($P=0.004$) intakes, and higher insulin dose ($P<0.0001$) associated with higher HbA1c independent of exercise and body mass index; substitution of fat for CHO associated with higher HbA1c ($P=0.01$).
Brehm, 2009 (19)	n=124 overweight/obese patients with type 2 diabetes/1 y	High MUFA (45% CHO, 40% fat [20% MUFA]) diet vs high-CHO (60% CHO, 25% fat) diets with ↓ 200-300 kcal/d (RCT)	NS differences in beneficial effects on weight loss (−3.9 kg), blood pressure, high-density lipoprotein cholesterol, HbA1c, glucose, and insulin between groups at 1 y.
Kodama, 2009 (25)	19 studies with 306 patients with type 2 diabetes/1.4 to 12 wk	LFHC[i] (ave. 58% CHO 24% fat) vs HFLC[j] (40% fat, 40% CHO) diets (meta-analysis)	HbA1c, total cholesterol, low-density lipoprotein cholesterol: (NS between groups); LFHC vs HFLC: ↑ fasting insulin ($P=0.02$) and TG ($P<0.001$), ↓ high-density lipoprotein cholesterol ($P<0.001$); ↓ total energy intake and type of fat more important than C:F[k] for ↓ TG

(continued)

Table 2. Studies reporting on carbohydrate: Amount and distribution of intake (continued)

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Davis, 2009 (20)	n=105 overweight adults with type 2 diabetes/1 y	Low CHO diet (modeled after Atkins diet) vs low-fat diet (25% of energy needs) (RCT)	NS difference in weight loss (−3.1 kg), HbA1c, blood pressure, total cholesterol, TG, low-density lipoprotein cholesterol between groups, all NS from baseline; high-density lipoprotein cholesterol ↑ in low CHO group (P=0.002).

[a]DCCT=Diabetes Control and Complications Trial.
[b]RCT=randomized controlled trial.
[c]CHO=carbohydrate.
[d]MUFA=monounsaturated fatty acids.
[e]TG=triglycerides.
[f]HbA1C=glycosylated hemoglobin.
[g]DAFNE=Dose Adjustment for Normal Eating.
[h]NS=non-significant.
[i]LFHC=low-fat high-carbohydrate.
[j]HFLC=high-fat low-carbohydrate.
[k]C:F=carbohydrate-to-fat ratio.

ments in insulin doses, which resulted in similar improvements in HbA1c from both interventions.

Five studies (16-21) reported on differing percentages of carbohydrate intake. In individuals with type 2 diabetes, Barnard and colleagues (16,17) compared a low-fat vegan diet to a diet following the 2003 American Diabetes Association guidelines (72% vs 48% carbohydrate intake at Week 22 and 67% vs 48% carbohydrate at Week 74, respectively). At 22 weeks, both diets improved glycemic and lipid control, but the improvements were greater in the low-fat vegan group.

A 1-year study comparing two higher-carbohydrate diets (47% and 52%) to a lower-carbohydrate (39%), high-MUFA diet showed no impact from the amount of carbohydrate intake on glycemic control, HbA1c, lipid levels, and body weight (18). Similarly, in another 1-year study comparing a high-carbohydrate, low-fat diet (60% carbohydrate, 25% fat) to a high-MUFA, moderate-carbohydrate diet (45% carbohydrate, 40% fat [20% MUFA]) with prior energy intake reduced by 200 to 300 kcal/day in all three groups, weight loss was similar over 1 year (~3.9 kg) and improvements in body fat, waist circumference, diastolic blood pressure, high-density lipoprotein cholesterol, HbA1c, and fasting glucose and insulin were comparable (19). Another 1-year weight loss study reported similar effects on weight and HbA1c from a low-carbohydrate diet compared to a low-fat diet for weight loss (20). In contrast, another study reported improvements in body weight and glycemic control at 44 months from a low-carbohydrate reduced-energy diet vs a low-fat/low-energy diet (21).

The association of macronutrient intake and HbA1c in 1,284 American Indian adults with diabetes was examined in the Strong Health Study. A lower intake of carbohydrate and higher consumption of total fat and saturated and monounsaturated fatty acids were associated with poorer glycemic control (22). Similarly, in patients with type 1 diabetes receiving intensive treatment in the Diabetes Control and Complications Trial, diets lower in carbohydrate and higher in total and saturated fats were associated with worse glycemic control, independent of exercise and body mass index (BMI) (23).

A meta-analysis on restricted-carbohydrate diets in patients with type 2 diabetes reported that weight loss was similar, but HbA1c, fasting glucose, and triglyceride levels improved with lower carbohydrate-content diets compared to the higher-carbohydrate diets (24). The carbohydrate content in the restricted-carbohydrate diets ranged from 4% to 45% of total energy intake and in the higher carbohydrate diets from 40% to 70% of total energy. Interpretation of these data is difficult due to the overlap in the definitions of low- and high-carbohydrate intake. Four of the trials met ADA criteria and are included in Table 2 (2,6,10,11). A second meta-analysis of low-fat, high carbohydrate (24%/58%) compared to high-fat, low carbohydrate (40%/40%) diets found no significant differences in reduction in HbA1c and total and low-density lipoprotein (LDL) cholesterol; however, the low-fat, high-carbohydrate diet increased fasting insulin and triglyceride levels and lowered high-density lipoprotein cholesterol levels when energy intake was isocaloric, but did not increase triglyceride levels when a reduced-energy diet was prescribed (25). Only one of the trials met ADA criteria and is included in Table 2 (10). Of interest, most individuals with diabetes do not eat a low- or high-carbohydrate diet, but rather report eating a moderate intake of carbohydrate (~44% of total energy in individuals with type 2 diabetes [26] and ~46% in individuals with type 1 diabetes [23]).

Recommendations for Carbohydrate Intake

In persons receiving either MNT alone, glucose-lowering medications, or fixed insulin doses, meal and snack carbohydrate intake should be consistently distributed throughout the day on a day-to-day basis, as consistency in carbohydrate intake has been shown to result in improved glycemic control. Diets too low in carbohydrate may eliminate too many foods that are important sources of vitamins, minerals, fiber, and energy.

In persons with type 1 (or type 2) diabetes who adjust their mealtime insulin doses or who are on insulin pump therapy, insulin doses should be adjusted to match carbohydrate intake (insulin-to-carbohydrate ratios). This can be accomplished by comprehensive nutrition education and counseling on interpretation of blood glucose

patterns, nutrition-related medication management, and collaboration with the health care team. Adjusting insulin doses based on planned carbohydrate intake has been shown to improve glycemic control and quality of life without any adverse effects. However, protein and fat content (total energy intake) cannot be ignored as excessive energy intake may lead to weight gain.

Registered dietitians (RDs) should encourage consumption of macronutrients based on the Dietary Reference Intakes for healthy eating as research does not support any ideal percentage of energy from macronutrients in meal plans for persons with diabetes. Research published after the completion of the EBNPG also provides support for this position (16-21,24,25).

Limitations of Current Research and Additional Research Needed for Carbohydrate Intake

Studies examining consistency vs inconsistency of carbohydrate distribution are limited in number. Conclusions are, therefore, drawn from studies in which carbohydrate intake was kept consistent, although this was not always the primary study question. The majority of the studies examining differing percentage of carbohydrate intake are of short duration, have small sample sizes, and are predominately nonrandomized trials. They frequently have no assessment of actual dietary intake and vary in definitions of low and high carbohydrate intakes. Studies published after the completion of the EBNPG tend to be of a higher quality and longer duration but report conflicting outcomes (16-21). Additional research is warranted.

SUCROSE EVIDENCE AND RECOMMENDATIONS

To evaluate the relationship between sucrose intake and metabolic outcomes in persons with type 1 and type 2 diabetes, a total of 15 studies examining the effect of sucrose when substituted for isocaloric amounts of starch on glycemic control met the predetermined criteria and were evaluated (Table 3).

Research Reviewed

Research consistently reported that the total amount of carbohydrate consumed at meals, regardless of whether the source is sucrose or starch, is the primary determinant of postprandial glucose levels. Eleven studies, ranging in length from 2 days to 4 months and sucrose intake ranging from 19 to 42 g/day (5% to 35% of daily energy), showed no effect of sucrose intake on glycemic control compared to a lower sucrose intake when total carbohydrate is similar (27-37). Similar results were found from two one-meal studies (38,39) and one cross-sectional study (40). Three studies also observed no effects on lipids from the high sucrose diets (27,28,36). However, one 15-day study comparing 16% to 1% sucrose concluded that the addition of sucrose resulted in increased hyperglycemia and serum lipid levels (41).

Research Published after Completion of the Initial Recommendations

No studies meeting inclusion criteria published after February 2007 were found.

Recommendations for Sucrose

If persons with diabetes choose to eat foods containing sucrose, the sucrose-containing foods can be substituted for other carbohydrate foods. Sucrose intakes of 10% to 35% of total energy do not have a negative effect on glycemic or lipid level responses when substituted for isocaloric amounts of starch.

Limitations of Current Research and Additional Research Needed for Sucrose

Available research substituted isocaloric amounts of sucrose for starches. It is unknown whether individuals will substitute excessive amounts of sucrose for starches that will contribute to inadequate intake of foods contributing essential nutrients or if sucrose-containing foods habitually added to usual intake will lead to excessive energy intake.

NON-NUTRITIVE SWEETENERS (NNS) EVIDENCE AND RECOMMENDATIONS

Five NNS (sometimes called artificial sweeteners) are approved by the US Food and Drug Administration (FDA): aspartame, saccharin, acesulfame K, neotame, and sucralose. They are regulated as food additives and, therefore, must be approved as safe before being marketed. Studies in animals are the predominate type of research used in the approval process; very few human studies are available. The FDA also sets a sweetener Acceptable Daily Intake (ADI)—the level a person can safely consume on average every day over a lifetime without risk (42). In December 2008, the FDA stated that the stevia-derived sweetener rebaudioside A is generally recognized as safe as a food additive. To evaluate the role of NNS in the management of diabetes and their glycemic response and to determine what is the intake of NNS in persons with diabetes, eight studies that met predetermined criteria were evaluated (Table 4).

Research Reviewed

In a limited number of human studies, NNS intake had no effect on the glycemic responses and plasma lipid levels in adults with diabetes when NNS were added to diets as compared to control diets (31,43,44). One study reported a decrease in plasma glucose with the use of sucralose (45). In an examination of cross-sectional data from the third National Health and Nutrition Examination Survey, higher HbA1c levels in adults with diabetes were found in those who drank one or more drinks of diet soda per day compared to those who drank none (46).

In a limited number of studies conducted outside the United States, children and adults with diabetes compared to controls were found to have higher intakes of NNS, which in most cases did not exceed the ADI (47,48). An exception was Swedish children's intake of acesulfame-K and saccharin, which was greater than the ADI when worst case estimates were used (49).

Research Published after Completion of the Initial Recommendations

Two studies evaluated the effect of steviol glycoside (rebaudioside A) from the plant *Stevia rebaudiana* com-

Table 3. Studies reporting on sucrose substituted for isocaloric amounts of starch on glycemic control[e]

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Bantle, 1983 (38)	n=32 (12 adults with type 1 diabetes, 10 adults with type 2 diabetes, 10 adults without diabetes)/1 breakfast meal per variant per subject	5 breakfasts, 42 g CHO[a] from potato starch, wheat starch, sucrose, glucose, or fructose (nonrandomized crossover trial)	Sucrose did not produce a more rapid glucose rise, peak glucose increment, or greater glucose area increment compared to potato or wheat starch
Chantelau, 1985 (27)	n=10 patients with type 1 diabetes and on insulin pump/4 wk each period	Sucrose (24±13 g/d) vs cyclamate (randomized crossover trial)	NS[b] differences in HbA1c[c], random plasma glucose, lipids, or body weight
Coulston, 1985 (41)	n=11 adults with type 2 diabetes/15 d on each diet	16% of kcal from sucrose vs 1% of kcal from sucrose (nonrandomized crossover trial)	Addition of sucrose ↑ day-long postprandial hyperglycemia ($P<0.05$), fasting and postprandial TG[d] ($P<0.05$), and fasting total cholesterol ($P<0.001$)
Peterson, 1986 (28)	n=12 adults with type 1 diabetes and 11 adults with type 2 diabetes/6 wk on each diet	45 g starch replaced with 45 g sucrose vs control (randomized crossover trial)	NS differences in glucose profiles or lipids
Bantle, 1986 (29)	n=12 adults with type 1 diabetes and 12 adults with type 2 diabetes/8 d on each diet	Sucrose diet (23%) vs starch diet (<5% from sucrose and fructose) vs fructose diet (21%) (randomized crossover trial)	Sucrose vs starch diets: NS differences on all measures of glucose values; glucose values ↓ on fructose diet vs other diets ($P<0.1$)
Buysschaert, 1987 (30)	n=10 with diabetes treated with insulin/3 mo on each diet	Sucrose-enriched diet (12% of starch replaced with 19 g/d sucrose vs no added sucrose diet	Sucrose intake had no clinical or metabolic effects
Cooper, 1988 (31)	n=17 adults with type 2 diabetes/6 wk on each diet	Usual diet+28 g sucrose vs +saccharin and starch equal to 28 g sucrose (randomized crossover trial)	NS differences in meal glycemic responses
Santacroce, 1990 (32)	n=12 with type 1 diabetes/2 mo on each diet	Sucrose diet (16%) vs control diet (randomized crossover trial)	NS difference in metabolic control between diets
Loghmani, 1991 (33)	n=10 children with type 1 diabetes/2 d on each diet	10 g sucrose/d (2% of kcal) vs 52 g sucrose/d (10% of kcal) (randomized crossover trial)	NS differences in glucose responses
Bantle, 1993 (34)	n=12 adults with type 2 diabetes/28 d on each diet	High sucrose diet (19%) vs starch diet (<3% kcal from sucrose) (randomized crossover trial)	NS differences in fasting or postprandial glucose
Shimakawa, 1993 (40)	n=136 adults with type 1 diabetes/not applicable	Mean sucrose intake: 6.4%±4.1% for men; 7.1%±14.1% for women (cross-sectional study)	Sucrose intake did not show any association with HbA1c
Schwingshandl, 1994 (35)	n=28 adolescents with type 1 diabetes/ 83 d for sucrose group, 77 d for conventional group	Sucrose (5% sucrose) vs sucrose completely restricted diet (nonrandomized clinical trial)	NS differences in HbA1c between groups
Malerbi, 1996 (36)	n=16 adults with well-controlled type 2 diabetes/28 d on each diet	Sucrose diet (19%) vs fructose diet (20%) vs control diet (5% of kcal from sugars) (nonrandomized crossover trial)	NS effects of CHO sources on blood glucose control, lipids, or insulin levels
Nadeau, 2001 (37)	n=48 adults with type 2 diabetes/4 mo	Taught how to use sugar choices vs taught to avoid concentrated sweets) (RCT[e])	NS differences in HbA1c or other metabolic outcomes between groups
Rickard, 2001 (39)	n=10 adolescents with type 1 diabetes/ 4-h study of each diet	High sucrose diet (35%) vs moderate sucrose (17%) (RCT)	NS difference in glycemic response to diets

[a]CHO=carbohydrate.
[b]NS=non-significant.
[c]HbA1C=glycosylated hemoglobin.
[d]TG=triglycerides.
[e]RCT=randomized controlled trial.

Table 4. Studies reporting on non-nutritive sweeteners metabolic responses and intake in persons with diabetes

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Cooper, 1988 (31)	n=17 adults with type 2 diabetes/6 wk on each diet	Usual diet+28 g sucrose vs +saccharin and starch equal to 28 g sucrose (randomized crossover trial)	NS[a] differences in meal glycemic responses
Mezitis, 1996 (43)	n=13 adults with type 1 diabetes and 13 adults with type 2 diabetes/2 meal tests	1,000 mg sucralose vs cellulose placebo in 350 kcal liquid breakfast (RCT[b])	NS difference in plasma glucose or C-peptide between groups
Garnier-Sagne, 2001 (47)	n=227 children with diabetes/not applicable	Consumption of 3 most commonly consumed sweeteners compared to relevant average Acceptable Daily Intake (cross-sectional)	Although children with diabetes in France have median intakes of sweeteners which exceed the 90th percentile of the general population, intake did not exceed Acceptable Daily Intake
Ilback, 2003 (49)	n=790 individual with diabetes of various ages/not applicable	Estimation of intake of artificial sweeteners in Sweden (cross-sectional)	In adults intakes of non-nutritive sweeteners did not exceed the Acceptable Daily Intake
Reyna, 2003 (45)	n=16 adults with type 2 diabetes/4 wks	Experimental group, 2 starch servings of 3 cookies made with sucralose and a fat replacer vs C[f] group (RCT)	Both groups: NS difference in ↓ of HbA1c[c] from baseline, total cholesterol, and low-density lipoprotein cholesterol
Grotz, 2003 (44)	n=128 adults with type 2 diabetes/ 3-mo on each diet	667 mg sucralose supplement vs placebo (RCT)	NS difference in HbA1c between groups; sucralose group vs placebo had a ↓ in fasting plasma glucose (P=0.02)
Cullen, 2004 (48)	n=85 adults with type 1 diabetes and 85 matched controls/1 wk	Total intense sweetness index in participants with diabetes who were high users of intense sweeteners compared to matched control (observational study)	Diabetes group vs control had a higher total intense sweetness intake index and use level of intense sweeteners (2.5 vs 1.4/d; P=0.0001)
Mackenzie, 2006 (46)	n=1,024 persons with diabetes from third National Health and Nutrition Examination Survey data/not applicable	Association between type of beverage consumed and glucose control (cross-sectional association)	HbA1c positively associated with consumption of diet soda (r=0.14; P=0.025) but not regular soda (r=0.08; P>0.10)
Renwick, 2006 (52)	Not applicable	Intake of intense sweeteners (review)	Average and 95th percentile intakes of acesulfame-K, aspartame, cyclamate, and saccharin by adults are below Acceptable Daily Intake values.
Barriocanal, 2008 (50)	n=16 patients with type 1 diabetes, 30 with type 2 diabetes, 30 without diabetes/3 mo	Steviol glycoside stevioside (250 mg three daily servings) from the plant *Stevia rebaudiana* vs placebo (RCT)	Steviol glycoside groups: NS blood pressure glucose, and HbA1c from baseline; no side effects observed
Maki, 2008 (51)	n=122 adults with type 2 diabetes/ 16 wk	Rebaudioside A, a steviol glycoside (1,000 mg) vs placebo (RCT)	Between groups: NS HbA1c, blood pressure, body weight, lipids; from baseline: NS changes for both groups in fasting plasma glucose and insulin

[a]NS=non-significant.
[b]RCT=randomized controlled trial.
[c]HbA1c=glycosylated hemoglobin.

pared to a placebo in persons with diabetes (50,51). Both reported no effects on glucose, HbA1c, blood pressure, or body weight from the sweetener. A review of intense sweeteners intake reported that the average and 95th percentile intakes of acesulfame-K, aspartame, cyclamate, and saccharin by adults were below ADI values, and no significant changes in the intake of sweeteners has occurred in recent years (52).

Recommendations for NNS

If persons with diabetes choose to consume products containing FDA-approved NNS at levels that do not exceed the ADIs, the RD should advise that some of these products might contain energy and carbohydrate from other sources that needs to be accounted for. However, research reports that NNS intake does not effect changes in glycemic responses.

Limitations of Current Research and Additional Research Needed for NNS

The number of studies examining the safety and use of NNS in persons with diabetes is limited—only five studies were identified. However, these products are widely tested and proven to be safe in animal studies before being marketed. The FDA determines their safety and ADI. Additional studies are needed to monitor long-term metabolic outcomes and effects on appetite in humans, especially in adults and children with diabetes, and to determine amounts consumed.

GLYCEMIC INDEX (GI) EVIDENCE AND RECOMMENDATIONS

Although the balance between total carbohydrate intake and available insulin is the primary determinant of postprandial glucose response, research studies have identified a number of other factors that influence the glycemic response to food. The GI compares the relative area under the postprandial glucose curve of 50 g digestible carbohydrate with 50 g reference food, either glucose or white bread. When bread is the reference food, the GI value for the food is multiplied by 0.7 to obtain the GI value with glucose as the reference food. Problems such as the intra- and intervariability of glucose responses have been reported and the use of the GI in clinical practice has been questioned. To determine the relationship between GI and metabolic outcomes in persons with type 1 and type 2 diabetes, 14 studies (15 articles) that met predetermined criteria were evaluated (Table 5).

Research Reviewed

Two studies reported benefit from lower-GI diets compared to higher-GI diets on either HbA1c or fructosamine values (53,54) and one study reported benefits from a low GI breakfast compared to a high-GI breakfast (55). Four cohort or descriptive studies (5,56-58), one meta-analysis (59), and one review (60) also reported a beneficial association between HbA1c and lower-GI diets. Six of the trials in the meta-analysis met ADA criteria and are included in Table 5 (53-55,61,64,65). The review was written in 1991 before much of the research on the GI was published. In one study, a low-GI value also was reported to be inversely related to simple sugar intake (58).

Four studies reported no positive effects on HbA1c from lower- vs higher-GI diets (61-66), although two of the studies reported benefit on fructosamine values (64,65) and one study changed the GIs of breakfast only (66).

Research Published after Completion of the Initial Recommendations

Two trials, 1 year in duration, reported no significant differences in HbA1c levels from low- vs high-GI diets (18,67) or American Diabetes Association diets (68) at study end. However, one study (18) reported improvement in C-reactive protein values from a low-GI diet compared to a high-GI diet and the possibility that a low-GI diet can increase the disposition index, an index of beta cell function, compared to a low-carbohydrate diet (67). The other study reported less use of diabetes medications from low- compared to high-GI diets (68). Another study based on low- vs high- GI Japanese foods reported similar decreases in HbA1c values from baseline to study end in both groups (69). A 1-day study in youth with type 1 diabetes using continuous glucose monitoring reported lower daytime mean and area >180 mg/dL (9.99 mmol/L) glucose values, but no differences in daytime glucose area <70 mg/dL (3.89 mmol/L) or in nighttime glucose values from low- compared to high-GI diets (70,71).

A Cochrane review included studies lasting 4 weeks or longer (72). Five of the trials met ADA criteria and are included in Table 5 (53-55,61,65). Unfortunately, the two recent 1-year studies reviewed above were not included in the review (18,68).

Recommendations for GI

If the use of GI is proposed as a method of meal planning, RDs should advise on the conflicting evidence of effectiveness of this strategy. Studies comparing high- vs low-GI diets report mixed effects on HbA1c levels. These studies are complicated by differing definitions of high-GI or low-GI diets or quartiles, as well as possible confounding dietary factors.

Limitations of Current Research and Additional Research Needed for GI

Definitions of low- vs high-GI diets vary widely. In the studies reviewed, GIs in the low-GI diets range from 38% to 77% and in the high-GI diets from 63% to 98%. Other problems include the variability of GI responses from carbohydrate-containing foods within and among individuals (73,74). Variability problems in determining the GI of foods also need to be addressed. When reported, it appears that persons with diabetes already consume a moderate-GI diet (54), and it is unknown whether moving the usual GI down a few units will result in improved glycemic control.

Of the 15 studies reviewed, 12 are of a short duration, lasting less than 3 months, with a limited number of participants. Three studies were of 1-year duration. At study end, one study reported no difference in actual GI between the low-GI and carbohydrate-counting groups (61) and two studies reported no differences in HbA1c

Table 5. Studies reporting on the relationship between the glycemic index value of foods/diets and metabolic outcomes[c]

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Wolever, 1991 (60)	Patients with type 1 or type 2 diabetes/not applicable	Not applicable (narrative review)	Diets with reduced GI[a] results in modest improvements in overall glucose control; no criteria for studies given
Wolever, 1992 (55)	n=15 patients with type 2 diabetes/2 wk on each diet	Low-GI (60) vs high-GI (87) diets (RCT[b])	Low- vs high-GI diet: breakfast postprandial blood glucose less (47±6 vs 67±6 mg/dL, $P<0.001$)
Fontvieille, 1992 (65)	n=18 patients with type 1 or type 2 diabetes/5 wk on each diet	Low-GI (38±5) vs high-GI (64±2) diets (RCT)	Low-GI vs high-GI: NS[c] difference in HbA1c[d]; fructosamine (3.9±0.9 vs 3.4±0.4 mmol/L, $P<0.05$); and 2-h postprandial blood glucose (208.8±52.2 vs 187.2±45.0 mg/dL, $P<0.02$)
Frost, 1994 (53)	n=51 patients with type 2 diabetes/12 wk	Low-GI (77) vs high-GI (82) diets (RCT)	Correlation between low GI and ↓ in fructosamine ($r=0.54$, $P<0.01$), fasting blood glucose ($r=0.41$, $P<0.05$)
Wolever, 1994 (58); 1999 (5)	n=272 adults with type 1 diabetes/not applicable	Low GI (70) vs high GI (98) (descriptive study)	Day-to-day variation of CHO[e] ($P=0.0097$), starch ($P=0.0016$), and GI ($P=0.033$) positively related to HbA1c
Jarvi, 1999 (64)	n=20 adults with type 2 diabetes/3 wk on each diet	Low GI (57) vs high GI (83)/(RCT)	HbA1c between groups: NS; fructosamine lower in low-GI group ($P<0.05$)
Gilbertson, 2001 (61); 2003 (62)	n=104 children with type 1 diabetes/12 mo	Low GI (target 65-70) vs CHO-counting group; actual GI was NS between groups (RCT)	Low GI: lower HbA1c (8.15 vs 8.6, $P=0.05$); dietary quality or more limited food choices did not differ between groups
Buyken, 2001 (56)	n=2,810 patients with type 1 diabetes/3-d food records at assessment	Median GI for lowest quartile (75) vs median GI for highest GI (89) (cohort study)	Lower GI related to lower HbA1c ($P=0.0001$)
Heilbronn, 2002 (63)	n=56 overweight adults with type 2 diabetes/8 wk	Low-GI (43) vs high-GI (75) diets (RCT)	Fasting glucose, area under the curve or HbA1c: NS between groups
Kabir, 2002 (66)	n=13 adult men with type 2 diabetes/4 wk on each diet	Low-GI breakfast (40) vs high-GI breakfast (64) (RCT)	HbA1c, fasting blood glucose, and insulin not affected by chronic changes in type of breakfast
Rizkalla, 2004 (54)	n=12 men with type 2 diabetes/4 wk on each diet	Low-GI (39) vs high-GI (71) diets (RCT)	Low GI vs high GI: HbA1c ↓ 0.4% ($P<0.05$) and fasting blood glucose ↓ 9 mg/dL, $P<0.05$)
Brand-Miller, 2003 (59)	N=14 studies with 356 participants with diabetes/studies' duration 12 d to 12 mo	Low-GI (53-77) vs high-GI (79-106) diets (meta-analysis)	Low-GI vs high-GI diets: ↓ HbA1c by 0.43% (confidence interval 0.72-0.13)
Burani, 2006 (57)	n=21 adults with type 1 or type 2 diabetes, who had completed 2 h of medical nutrition therapy (low-GI diet)/ single interview	Mean GI of meals reduced from a mean of 59 to 44 (cohort study)	Of 199 patients seen only 21 met study criteria (ie, were successful); HbA1c ↓ 19.4% between initial counseling and interview ($P<0.0005$)
Amano, 2007 (69)	n=40 adults with type 2 diabetes or impaired fasting glucose/3 mo	Low-GI (62) vs conventional (68) diets (RCT)	HbA1c ↓ from baseline in both groups ($P<0.001$), but NS between groups
Wolever, 2008 (18); 2008 (67)	n=162 adults with type 2 diabetes managed by diet alone/1 y	Low-GI (55) vs high- GI (63) vs low-CHO, high–monounsaturated fatty acid diets (RCT)	Between groups: HbA1c (NS); low-GI diet: fasting glucose higher ($P=0.04$) but 2-h postprandial blood glucose lower ($P=0.01$), mean C-reactive protein ↓ 0.8 mg/L ($P=0.0078$); follow-up analysis suggested that a low-GI diet ↑ disposition index, an index of beta cell function compared to low-CHO diet ($P<0.05$)
Ma, 2008 (68)	n=40 adults with type 2 diabetes/1 y	Low-GI (76) vs American Diabetes Association diet (RCT)	HbA1c ↓ from baseline in both groups ($P<0.001$, but NS at any time point); intervention group less likely to add or increase diabetes medications (odd ratio 0.26, $P=0.01$)
Nansel, 2008 (70), Rovner, 2009 (71)	n=20 youths with type 1 diabetes using continuous glucose monitoring/1 d	Low GI (40) vs high GI (64) diets (crossover trial)	Low- vs high-GI diet: lower daytime mean blood glucose ($P<0.001$) and blood glucose area >180 mg/dL ($P=0.001$) but NS blood glucose area <70 mg/dL; 1-d low GI vs 1-d usual meals, more fiber ($P<0.007$) and less fat ($P<0.005$)
Thomas, 2009 (72)	11 studies with 402 participants, whose diabetes was not optimally controlled/1 to 12 mo	Low-GI vs high-GI diets (Cochrane review)	Low vs high GI: HbA1c –0.5% ($P=0.02$) (review same studies as in 59; did not include two 1-y studies (18,68)

[a]GI=glycemic Index.
[b]RCT=randomized controlled trial.
[c]NS=non-significant.
[d]HbA1c=glycosylated hemoglobin.
[e]CHO=carbohydrate.

between the low-GI groups and control groups (18,68). Wolever and colleagues (18) in their year-long trial found a nonsignificant trend toward a temporary reduction in HbA1c at approximately 6 weeks from the low-GI diet that was not sustained for 1 year.

FIBER EVIDENCE AND RECOMMENDATIONS

Controversy exists regarding the effect dietary fiber may have on glycemic and lipid level outcomes in people with diabetes. To evaluate the relationship between fiber and metabolic outcomes in persons with type 1 and type 2 diabetes, a total of 15 studies that met the predetermined criteria were reviewed (Table 6).

Research Reviewed

There is inconclusive evidence that increasing dietary fiber will influence glycemic outcomes in people with diabetes. Five studies compared high-fiber (40 to 60 g) to low-fiber (10 to 20 g) diets with similar macronutrient percentages of energy. Two studies showed no sig-

Table 6. Studies reporting on the effect of fiber intake on glycemic and lipid outcomes

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Kinmonth,1982 (78)	n=10 adolescents with type 1 diabetes/8 wk on each diet	HF[a] (60 g) vs LF[b] (20 g) (RCT[c])	HF vs LF: ↓ 24-h area under the curve ($P<0.01$), pre- ($P<0.01$) and postprandial blood glucose ($P<0.001$)
Lindsay, 1984 (86)	n=12 adolescents with type 1 diabetes/24 d	Control (22 g fiber) for 10 d; HF CHO[d] (64 g fiber) for 14 d (time series)	Fasting blood glucose and serial blood glucose after lunch and dinner: NS[e]
McCulloch, 1985 (86)	n=34 adults with type 1 diabetes/4-6 mo	HF CHO: (32 g achieved) vs LF CHO (29 g) vs control (20 g) (RCT)	HF CHO and LF CHO: ↓ HbA1c[f] vs control ($P<0.05$)
Riccardi, 1984 (84)	n=14 patients with type 1 and type 2 diabetes/10 d on each diet	HF CHO (53 g) vs LF (16 g) vs LF CHO (20 g) (RCT)	HF CHO vs LF: ↓ 2-h postprandial blood glucose ($P<0.01$), MPG[g] ($P<0.005$), low-density lipoprotein cholesterol ($P<0.001$) and high-density lipoprotein cholesterol ($P<0.001$); fasting blood glucose and TG[h] (NS)
Story, 1985 (85)	n=17 patients with type 1 and 2 diabetes/ average of 4-y	Control (20 g fiber) for 7-10 d; HF CHO (65 g fiber) for 2 wks; HF CHO maintenance (40-50 g/d) (time series)	HF CHO maintenance vs control: ↓ total cholesterol ($P<0.05$) and TG ($P<0.05$); fasting blood glucose (NS)
Simpson, 1988 (87)	n=13 adults with type 2 diabetes/5 wk	LF CHO (21 g fiber) for 3 d; HF CHO (56 g fiber) for 3 wks; LF CHO for 2 wk (time series)	HF CHO vs LF CHO: ↓ FBG ($P<0.01$), total cholesterol ($P<0.001$), high-density lipoprotein cholesterol ($P<0.05$)
Del Toma, 1988 (79)	n=10 adults with type 2 diabetes/1 meal	High soluble fiber (32 g) vs high insoluble fiber (34 g) vs LF (7 g) (randomized crossover trial)	HSF vs other 2 meals: ↓ postprandial blood glucose ($P<0.001$)
Hagander, 1988 (76)	n=14 adults with type 2 diabetes/8 wks on each diet	HF (44 g) vs LF (16 g) (RCT)	HF vs LF: ↓ fasting blood glucose ($P<0.01$), total cholesterol ($P<0.025$), low-density lipoprotein cholesterol ($P<0.025$); high-density lipoprotein cholesterol, TG, HbA1c: NS
Anderson, 1991 (81)	n=11 adults with type 1 diabetes/4 wk on each diet	HF CHO (72 g/d [25 g/d achieved]) vs LF CHO (11g/d) (RCT)	HF CHO vs LF CHO: ↓ total cholesterol and high-density liporotein cholesterol ($P<0.001$ for both); HbA1c: NS
Shimakawa, 1993 (40)	n=136 adults with type 1 diabetes/not applicable	Previous 12 mo fiber intake: 8-11 g/1,000 kcal) (cross-sectional)	No relationship between fiber and HbA1c
Milne, 1994 (80)	n=64 adults with type 2 diabetes/18 mo	HF CHO: >30 g/d (21 g achieved) vs moderate lipid (21 g) vs control (17 g) (RCT)	HF CHO vs moderate lipid vs control: HbA1c: NS; lipids: no lasting differences between groups
Buyken, 1998 (88)	n=3,250 patients with type 1 diabetes/not applicable	Total fiber (18 g/d [2.6-53.4]) (cross-sectional)	Total fiber inversely related to HbA1c ($P=0.02$)
Stevens, 1985 (82)	n=52 adults with type 2 diabetes/6 wks	HF: 20-30 g (19 g achieved) vs HF+oatbran (50 g) vs American Diabetes Association (14 g) vs control (8 g) (RCT)	HF vs control: HbA1c ↓ ($P<0.05$); HF and HF+oatbran vs American Dietetic Association and control: total cholesterol ↓ ($P<0.05$)
Chandalia, 2000 (75)	n=13 adults with type 2 diabetes/6 wk	HF (50 g) vs MF[i] (24 g) (RCT)	HF vs MF: ↓ 24-h AUC ($P=0.02$), total cholesterol ($P=0.02$), TG ($P<0.02$); HbA1c: NS
Giacco, 2000 (77)	n=63 patients with type 1 diabetes/24 wk	HF (50 g) vs LF (15 g) (RCT)	HF vs LF: HbA1c ↓ 2% in compliant HF group ($P<0.01$), no change in intent-to-treat group; MPG ↓ 9%-15% in both groups ($P<0.05$); lipids NS in both groups

[a]HF=high fiber.
[b]LF=low fiber.
[c]RCT=randomized controlled trial.
[d]CHO=carbohydrate.
[e]NS=non-significant.
[f]HbA1c=glcosylated hemoglobin.
[g]MPG=mean (daily) plasma glucose.
[h]TG=triglycerides.
[i]MF=moderate fiber.

nificant differences between diets on HbA1c (75,76); one study showed a 2% reduction in HbA1c only in participants compliant with the 50-g fiber diet (77). Three studies found 24-hour glycemic profiles lower on the higher fiber compared to lower-fiber diets (75,77,78) and one study of differing fiber content of meals showed lower postprandial glucose levels after the higher-fiber meals (79).

Another five studies compared high-fiber (30 to 53 g) to lower-fiber (5 to 20 g) diets with differing macronutrient percentages of energy. Two studies showed no differences in HbA1c between diets (80,81), while two studies showed improvements in HbA1c with the high-fiber compared to the low-fiber diet (82,83). Three studies found no change in fasting blood glucose between diets (84-86), whereas one study found significant improvement in fasting blood glucose in the higher- vs the lower-fiber diet (87). One cross-sectional study found that fiber intake was inversely related to HbA1c (88) and another study showed no relationship (40).

There appears to be conclusive evidence that higher-fiber diets will lower total cholesterol significantly compared to lower-fiber diets. In eight of the above studies lipid levels were measured outcomes. Seven studies showed a significant decrease in total cholesterol in the higher-fiber compared to the lower-fiber group (75,76,81,82,84,85,87) and one showed no change (80). Three of the eight studies reported significantly lower

high-density lipoprotein cholesterol values from high-fiber compared to low-fiber diets (81,84,87).

Research Published after Completion of the Initial Recommendations

No studies examining the relationship of dietary fiber intake in persons with diabetes on glycemic or lipid level outcomes published after February 2007 to July 2009 and meeting inclusion criteria were found.

Recommendations for Fiber

Recommendations for fiber intake for people with diabetes are similar to the recommendation for the general public (Dietary Reference Intake: 14 g/1,000 kcal). While diets containing 44 to 50 g fiber daily are reported to improve glycemia in persons with diabetes, more usual fiber intakes (up to 24 g/day) have not shown beneficial effects on glycemia.

It is recommended that persons with diabetes include foods containing 25 to 30 g fiber per day, with special emphasis on soluble fiber sources (7 to 13 g). Studies in participants without diabetes show that diets high in total and soluble fiber, as part of cardioprotective nutrition therapy, can further reduce total cholesterol by 2% to 3% and LDL cholesterol up to 7% (89).

Limitations of Current Research and Additional Research Needed for Fiber

Consuming diets high in total dietary fiber and their association with decreased risk of CVD have primarily been done in participants who do not have diabetes. Studies in patients with diabetes warrant further research. Studies determining the actual effects (potential decreases in total and LDL cholesterol) from consuming diets high in total and soluble fiber as part of a cardioprotective diet also have primarily been conducted in persons without diabetes. Research is needed to determine if the same benefits are experienced in persons with diabetes. Also of interest is determining if high-fiber diets (44 to 50 g/day) shown to improve glycemic control can be sustained in a free-living environment.

PROTEIN INTAKE EVIDENCE AND RECOMMENDATIONS

In the management of diabetes, the original focus of protein intake was to preserve lean body mass; however, recent research has examined a role for dietary protein in the management of hyperglycemia and body weight. To evaluate the relationship between protein intake and metabolic outcomes in persons with type 1 and type 2 diabetes, six studies (seven articles) meeting predetermined criteria were available (Table 7). Several of these studies also contributed to the macronutrient percentages recommendation (90,92-96).

Research Reviewed

Two single-meal studies (90,91) reported acute insulin and glucagon responses to ingestion of protein with minimal postprandial glycemic or lipid responses. Three

Table 7. Studies reporting on the relationship between protein intake and metabolic outcomes

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Nordt, 1991 (90)	n=24 patients with type 2 diabetes/ 1 meal	Group 1: Isocaloric meals, control (15% protein, 60% CHO[a]) vs LP[b] (0% protein) vs HP[c] (40% protein) Group 2: control (25% protein, 50% CHO, 10% fat) vs reduced fat (1% fat) vs high fat (20% fat) (RCT[d])	Group 1: Insulin after 120 min was highest after HP and lowest after LP (478±164 pmol/L, $P=0.05$). Group 2: NS[e] differences in insulin responses
Gannon, 2001 (91)	n=10 patients with type 2 diabetes/ 8 h	HP (50 g beef protein) vs control (water) (RCT)	HP: no ↑ in glucose response over 8 h; insulin response 3-fold ↑ ($P\leq0.01$); no insulin response in control
Parker, 2002 (92)	n=54 patients with type 2 diabetes/ 12 wk on each diet	HP (28% protein, 42% CHO, 28% fat) vs control (16% protein, 55% CHO, 26% fat); 8 wk energy restriction and 4 wk energy balance (RCT)	Weight loss: 5.2±1.8 kg NS difference; HP: ↓ total cholesterol and low-density lipoprotein cholesterol (13.5 mg/dL, $P<0.01$; 7.4 mg/dL, $P<0.01$, respectively); no difference in other lipid, insulin, or glycemic parameters
Luscombe, 2002 (93)	n=32 patients with type 2 diabetes/ 12 wk on each diet	HP (28% protein, 42% CHO, 28% fat) vs control (16% protein, 55% CHO, 26% fat); 8 wk energy restricted and 4 wk energy balance (RCT)	Weight loss: 4.6±0.4 kg NS difference; resting energy expenditure and thermic effect of food ↓ similarly with each of the diets ($P=0.02$ and $P<0.001$, respectively)
Nuttall, 2003 (95) and Gannon, 2003 (96)	n=12 patients with type 2 diabetes/ 5 wk on each diet	HP (30% protein, 40% CHO, 30% fat) vs control (15% protein, 55% CHO, 30% fat); weight stable (RCT)	HP: 24-h integrated glucose area response ↓ 40% ($P<0.05$), HbA1c ↓ 0.8% ($P<0.05$), fasting triglycerides ↓ 38 mg/dL ($P<0.03$)
Brinkworth, 2004 (94)	n=38 obese patients with type 2 diabetes/64-wk	HP (30% protein, 40% CHO) vs LP (15% protein, 55% CHO) (RCT)	HP vs LP: weight ↓ 3.7±1.0 vs 2.2±1.1 kg ($P<0.01$ from baseline for both groups, no diet effect); HbA1c, triglyceride, total cholesterol, blood pressure: NS compared to baseline in both groups

[a]CHO=carbohydrate.
[b]LP=low protein.
[c]HP=high protein.
[d]RCT=randomized controlled trial.
[e]NS=non-significant.

studies lasting 5 to 12 weeks comparing high-protein diets (30%) to lower-protein diets (15%) showed no significant difference in longer-term insulin response despite the acute insulin responses (92-96).

Two 12-week energy restriction (1,600 kcal) studies comparing a higher vs usual protein diets (28% vs 16%) reported similar weight loss from both diets (92,93). A 64-week study reported significantly lower body weight at study end compared to baseline (high-protein diet −3.7 kg; low-protein diet −2.2 kg) but no significant effect from diet (94). A 5-week study in which participants remained weight stable compared a high- vs usual-protein diet (30% vs 15%) and showed a decrease in glycated hemoglobin from the higher-protein diet; however, carbohydrate intake was also decreased (95,96).

Research Published after Completion of the Initial Recommendations

There have been no studies examining the effects of protein on diabetes-related outcomes in patients with diabetes published since the completion of the literature search in May 2006.

Recommendations for Protein Intake

In persons with type 1 or type 2 diabetes with normal renal function, RDs should advise that usual protein intake of approximately 15% to 20% of daily energy intake does not need to be changed. Although protein intake has an acute effect on insulin secretion, usual protein intake in longer-term studies has minimal effects on glucose, lipid levels, and insulin concentrations. Exceptions for change in protein intake are in persons who consume excessive protein choices high in saturated fatty acids, in those who have a protein intake less than the Recommended Dietary Allowance, or in patients with diabetic nephropathy.

Limitations of Current Research and Additional Research Needed for Protein Intake

The number of studies on protein intake in persons with diabetes and normal renal function is limited, the number of participants is small, and the duration of the studies are short. As percentage of energy from protein intake changes, if energy intake remains constant, either carbohydrate or fat percentages also change making it difficult to determine which change contributes to effects on metabolic outcomes. In addition, studies on protein intake are often conducted in research centers, and it is unknown whether free-living patients can change usual protein intake long term. Longer-term studies that are adequately powered are needed to verify the effects of protein ingestion in persons with diabetes on metabolic outcomes.

PROTEIN AND TREATMENT OF DIABETIC NEPHROPATHY EVIDENCE AND RECOMMENDATIONS

In the management of diabetic nephropathy, recent research has focused on the effect of low-protein diets (usually defined as <0.8 g both plant and animal protein/kg/day) on risk reduction for the development of end-stage renal disease. To determine the effectiveness of protein restriction in the treatment of diabetic nephropathy, nine studies meeting the predetermined criteria were reviewed (Table 8).

Research Reviewed for Protein and Treatment of Diabetic Nephropathy

In patients with earlier diabetic nephropathy (persistent microalbuminuria [30 to 299 mg/24 hours; chronic kidney disease stages 1 and 2, defined as hyperfiltration to glomerular filtration rate [GFR] 60 mL/minute/1.73 m^2 body surface area), two studies were able to compare protein levels >1 g/kg/day to protein levels of 0.8 g/kg/day or lower and reported that the lower protein intakes reduced albuminuria, but had no effect on GFR (97,98). However, two other studies found no benefit from a lower protein intake on either albuminuria or GFR (99,100).

In patients with later diabetic nephropathy (macroalbuminuria, defined as >300 mg/34 hours; chronic kidney disease stages 3 through 5, defined as GFR <60 mL/minute/1.73 m^2 body surface area), two studies reported that an actual protein intake of 0.7 to 0.9 g/kg/day vs a protein intake of 1.2 to 1.4 g/kg/day improved albumin excretion rate (AER) but again not GFR (101,102), whereas one study reported no benefit on either AER or GFR from a lower-protein diet (103). Of concern, hypoalbuminemia, a marker of malnutrition, was associated with a decrease in protein intake to ~0.7 g/kg/da, but not at a protein intake of ~0.9 g/kg/day (101,102). A cross-sectional study reported that protein intake was not associated with change in GFR (104) and a small study reported a decrease in proteinuria from a low-protein diet containing soy protein compared to animal protein (105).

Research Published after Completion of the Initial Recommendations

Four studies have been published evaluating the role of protein intake and diabetic nephropathy (106-109). A 2-year study in patients with type 1 and type 2 diabetes and incipient and overt nephropathy reported no significant changes in GFR or AER from a lower protein compared to a usual protein diet (106). A 4-month study reported improvements in AER and GFR in patients with macroalbuminuria from a lower protein diet (0.8 g/kg/day), but no changes in AER or GFR in patients with normo- or microalbuminuria (107). Long-term consumption of soy protein compared to no soy protein in low-protein diets (0.8 g/kg/day) led to improvements in kidney-related biomarkers (proteinuria and urinary creatinine) and cardiovascular risk factors (108). A cross-sectional study reported that patients with microalbuminuria compared to patients with normoalbuminuria consumed more total protein (20.5% vs 19.0% total energy) (109).

Of interest are a Cochrane Review and a meta-analysis of low-protein diets for diabetic nephropathy (110,111). The Cochrane Review (110) included 12 studies. Seven studies were published before the start date of this review and the other five met ADA criteria and are included in Table 8 (98,99,101-103). The authors concluded that reducing protein intake appears to slightly slow progres-

Table 8. Studies reporting on the effectiveness of protein restriction in the treatment of diabetic nephropathy

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Earlier diabetic nephropathy (persistent microalbuminuria [30-299 mg/24 h] or CKD[a] Stages 1 and 2 [hyperfiltration to GFR[b] 60 mL/min/1.73 m^2 body surface area])			
Raal, 1994 (98)	n=22 patients with type 1 diabetes and proteinuria/6 mo	LP[c] (0.8 g/kg/d prescribed, 0.87 g/kg/d achieved) vs control (unrestricted protein, 2.0 g/kg/d) (RCT[d])	LP vs control: ↓ AER[e] (mg/24 h) 884→815 (P=0.036 from baseline) vs ↑ 1,167→1,475 (P=0.036 from baseline); change in GFR (mL/min/1.73 m^2) 50→53 vs 66→58 (P=0.01 from baseline)
Hansen, 1999 (97)	n=29 patients with type 1 diabetes and diabetic nephropathy/4 wk followed by 4 wk of usual diet	LP (0.6 g/kg/d prescribed, 0.8 g/kg/d achieved) vs control (usual protein, 1.1 g/kg/d) (RCT)	LP vs control: ↓ AER 397→283 vs 438→438 (P<0.05); NS[f] change in GFR 94→85.4 vs 92→89.5; During 4 wk recovery: protein intake +0.3 vs 0 (P<0.0001); AER 25% ↑ vs 2.9% ↑ (NS); GFR +5.9 vs −2.9 (P<0.01)
Pijls, 2001 (100)	n=335 patients with type 2 diabetes	Not applicable (cross-sectional)	Total daily protein intake was not associated with albuminuria
Pijls, 2002 (99)	n=160 patients with type 2 diabetes and microalbuminuria/24 mo	LP (0.8 g/kg/d prescribed, 1.11 g/kg/d achieved) vs control (usual protein, 1.07 g/kg/d) (RCT)	LP vs control: NS change in AER 21.2→16 vs 20.5→14; NS change in GFR 82→74 vs 85→75
Dussol, 2005 (106)	n=63 patients with type 1 and type 2 diabetes/2 yr (incipient and overt nephropathy)	LP (0.8 g/kg/d prescribed, actual 16%±3%) vs control (usual protein, actual 19%±4%); 24-h urinary urea excretion did not differ between groups (RCT)	LP vs control: NS 2-y change in GFR 7±11 vs 5±15; 2-y change in AER did not increase in either group during follow-up
Almeida, 2008 (109)	119 NORMO[g] and 62 MICRO[h] patients with type 2 diabetes	Not applicable (cross-sectional)	MICRO vs NORMO: consumed more protein 20.5% vs 19.0% (P=0.01) and a higher animal source 14.5% vs 12.9% (P=0.015); also a lower intake of polyunsaturated fatty acids
Later diabetic nephropathy (macroalbuminuria [>300 mg/24 h]/CKD Stages 3-5 [GFR <60 mL/min/1.73 m^2 body surface area])			
Stojceva-Taneva, 2001 (104)	n=67 patients with type 2 diabetes and diabetic nephropathy	0.6 g protein/kg/d prescribed, actual intake not reported (cross-sectional)	Protein intake not associated with change in GFR
Meloni, 2002 (101)	n=32 patients with type 1 diabetes; n=37 patients with type 2 diabetes/ 12 mo	LP (0.6 g/kg/d prescribed, actual 0.68 g/kg/d) vs control (unrestricted protein, 1.38 g/kg/d) (RCT)	LP vs control: change in AER 2,400→1,300 vs 2,600→2,400 (P<0.01); NS change in GFR 43.9→38.8 vs 45.0→39.3; change in serum albumin (g/L) 4.7→ 3.7 vs 4.1→4.3 (P<0.01) (indicating malnutrition in a portion of the LP group)
Hansen, 2002 (103)	n=82 patients with type 1 diabetes, MACRO[i] and GFR 67-69/4 y or death	LP (0.6 g protein/kg/d prescribed, actual 0.89 g/kg/d) vs control (unrestricted protein, 1.02 g/kg/d) (RCT)	LP vs control: change in AER 690→542 vs 721→614 (P<0.01); change in GFR 69→43.8 vs 67→41.4 (NS between groups, P<0.005 from baseline in both groups); end-stage renal disease/death: LP 10% vs control 27% (P=0.01)
Azadbakht, 2003 (105)	n=14 patients with type 1 diabetes and MACRO/2, 7 wk periods with a 4-wk washout	0.8 g/kg/d soy protein (35% soy, 30% vegetable, 35% animal) or no soy (30% vegetable, 70% animal) (randomized crossover trial)	Soy vs no soy group: ↓ in proteinuria (P<0.001) and urinary urea nitrogen (P<0.001); NS differences in GFR
Meloni, 2004 (102)	n=24 patients with type 1 diabetes; 56 patients with type 2 diabetes/12 mo	LP (0.8 g protein/kg/d prescribed, actual 0.86 g/kg/d) vs control (unrestricted protein, 1.24 g/kg/d) (RCT, parallel)	LP vs control: change in AER 2,400→1,300 vs 2,600→2,400; NS change in GFR 43.9→38.9 vs 45→39.3; change in serum albumin (g/L) 4.7→ 3.7 vs 4.1→4.3
Robertson, 2007 (110)	12 studies with 585 participants/4.5 mo to 4 y	Usual protein (1-2 g/kg/d) vs LP (0.3-0.8 g/kg/d) (Cochrane review)	LP (actual protein intake 0.7-1.1 g/d/kg/d) vs usual protein: reducing protein may slow progression of renal failure but NS change in GFR; 1 study noted malnutrition in LP
Velázquez, 2008 (107)	n=60 patients with type 2 diabetes/4 mo (19 NORMO, 22 MICRO, 19 MACRO)/4 mo	LP (0.6-0.8 g/kg/d, actual 0.82 g/kg/d) vs control (1.0-1.2 g/kg/d, actual 1.2 g/kg/d) (RCT)	LP (patients with MACRO): ↓ AER (P<0.05 from baseline); ↑ GFR (P<0.05 from baseline); in NORMO and MICRO no change in AER or GFR from either diet
Azadbakht, 2008 (108)	n=41 patients with type 2 diabetes and MACRO/4 y	0.8 g/kg/d soy protein (35% soy, 30% veg, 35% animal) vs 0.8 g/kg/d no soy (30% veg, 70% animal) (RCT)	Soy vs no soy: ↓ urinary urea excretion (P=0.08), proteinuria (P=0.02), and urinary creatinine (P=0.01); ↓ total cholesterol, low-density lipoprotein cholesterol, and triglyceride (P=0.01)
Pan, 2008 (111)	8 studies with 519 participants/6 to 4 y	LP (actual 0.91 g/kg/d) vs control (1.27 g/kg/d) (meta-analysis)	LP vs control: GFR or creatinine clearance rate NS; HbA1c ↓ (P=0.005); LP not associated with improvement in renal function in either type 1 or 2 diabetes

[a]CKD=chronic kidney disease.
[b]GFR=glomerular filtration rate.
[c]LP=low protein.
[d]RCT=randomized controlled trial.
[e]AER=albumin excretion rate.
[f]NS=non-significant.
[g]NORMO=normoalbuminuria.
[h]MICRO=microalbuminuria.
[i]MACRO=macroalbuminuria.

sion to renal failure but is not statistically significant. They noted the variability of responses amongst patients and suggested "a pragmatic approach would be to reduce high protein intake to perhaps a maximum of 1 g/kg/day, or to 0.8 g/kg/day in those patients prepared to comply with that." Eight trials with a duration >6 months in patients with type 1 or type 2 diabetic renal disease were included in a meta-analysis to determine the effects of a low-protein diet on renal function (111). Five of the studies met ADA criteria and are included in Table 8 (98,99,102,103,106). The low-protein diets (prescribed 0.6 to 0.8 g/kg/day; actual average intake 0.9 g/kg/day) compared to the normal-protein diets (1.3 g/kg/day) were not significantly associated with change in GFR or creatinine clearance rate, but did result in a decline in urinary protein excretion. The authors expressed concern in regard to the potential for harm due to malnutrition from the low protein diets and concluded "low protein diets were not associated with a significant improvement in renal function in patients with either type 1 or 2 diabetic nephropathy."

Recommendations for Protein and Diabetic Nephropathy

In persons with diabetic nephropathy, a protein intake of <1.0 g/kg/day is recommended. Diets with <1.0 g/kg/day have been shown to improve albuminuria in persons with nephropathy; however, they have not been shown to have significant effects on GFR. For persons with late stage diabetic nephropathy (chronic kidney disease Stages 3 through 5), hypoalbuminemia and energy intake must be monitored and changes in protein and energy intake made to correct deficits and to prevent potential risk of malnutrition.

Limitations of Current Research and Additional Research Needed for Protein Intake and Diabetic Nephropathy

Studies in patients without diabetes have supported a reduced protein intake in the treatment of nephropathy (112). This has not been consistently duplicated in patients with diabetic nephropathy. Free-living patients in the diabetic nephropathy studies appear to have poor compliance with diets that recommend <1.0 g/kg/day of protein. Because of inconclusive findings, longer-term studies in larger representative groups of patients with both type 1 and type 2 diabetes investigating improvements in kidney function, role of soy and other vegetable proteins, quality of life, and cost-effectiveness vs concerns related to malnutrition from low-protein diets are needed.

PREVENTION AND TREATMENT OF CVD EVIDENCE AND RECOMMENDATIONS

Persons with diabetes are at a three- to fourfold increased risk for CVD, which is particularly evident in younger age groups and in women. Persons with diabetes have the equivalent CVD risk as persons with pre-existing CVD and no diabetes (113). Thus, it is essential that diabetes MNT interventions address this risk. A total of 12 studies (13 articles) (with duration of at least 1 year) that met predetermined criteria were evaluated to address increased CVD risk and nutrition interventions for the prevention of CVD in persons with diabetes (Table 9).

Primary goals of MNT for persons with CVD are to limit saturated and *trans*-fatty acids and cholesterol intake. Beneficial effects of fiber, phytostanols/phytosterols, n-3 fatty acids, a Mediterranean diet, and other plant-based food approaches are reported (89). Fewer studies examining these benefits have been conducted in persons with diabetes. However, since the two groups have equivalent CVD risks, the MNT recommendations for persons with diabetes are the same as for individuals with preexisting CVD. To determine the evidence supporting specific nutrition interventions in the treatment of CVD in people with diabetes, 20 studies meeting predetermined criteria were evaluated (Table 10).

Research Reviewed for Prevention of CVD

Diabetes is associated with an increased risk of complications related to CVD with diet often being a contributing factor (114-118). For example, in the analyzed dietary intake of 321 participants from the San Luis Valley Diabetes Study and 437 participants from the Insulin Resistance Atherosclerosis Study, a higher reported intake of total fat was related to significantly higher levels of LDL cholesterol ($P<0.05$) in both study groups and in the studies' subgroups (114).

Nutrition interventions with a duration of 1 year or longer, such as studies using the Mediterranean food patterns (119,120) and interventions that improve metabolic parameters, such as HbA1c (115,121-124), blood pressure (122-124), body weight (125), and lipid profile (122,123,125), all reduce risk for the development of CVD.

Research Published after Completion of the Initial Recommendations for Prevention of CVD

Patients receiving intensive diabetes therapy in the United Kingdom Prospective Study demonstrated an emergent risk reduction for myocardial infarction and death 10 years after the trial ended (126). One-year results of the Look AHEAD (Action For Health in Diabetes) study supported the role of weight loss and improved cardiovascular fitness in reducing CVD risk factors (127).

Two studies examined the benefits of a Mediterranean-style diet (128,129). The first, a substudy of a 4-year, multicenter, clinical trial, assessed the effects of the Mediterranean diet on the primary prevention of cardiovascular disease (Prevención con Dieta Mediterránea Study) (128). Persons with either type 2 diabetes or three or more CVD risk factors (ie, current smoking, hypertension, dyslipidemia, overweight or obesity, or a family history of premature CVD) were randomized to a Mediterranean diet with virgin olive oil or mixed nuts or a low-fat diet. After 3 months, the Mediterranean diet groups had lower mean plasma glucose levels, systolic blood pressure, and total cholesterol-high-density lipoprotein cholesterol ratios than the low-fat diet group. In the second study, between 1993 and 1999, 1,013 patients with diabetes from Greece were enrolled in the European Prospective Investigation into Cancer and Nutrition study (129). Two nutritional variables associated with mortality from diabetes were increased consumption

Table 9. Studies (1 y or longer) reporting on increased risk of cardiovascular disease in persons with diabetes and nutrition interventions for the prevention cardiovascular disease

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
DCCT[a] Research Group, 1993 (8) The DCCT/EDIC[b] Study Research Group, 2005 (121)	n=1,398 patients with type 1 diabetes/6.5-y and 17-y follow-up	Conventional therapy vs intensive therapy, monthly clinic visits, including registered dietitian visits) (RCT[c])	1993: Intensive diabetes therapy reduced the development of hypercholesterolemia by 34% ($P<0.02$); 2005: Intensive therapy ↓ risk of any CVD[d] event by 42% (95% CI[e]: 9%-63%; $P=0.02$) and nonfatal myocardial infarction, stroke or death by 57% (95% CI: 12%-79%; $P=0.02$)
Turner, 1998 (122)	n=7,108 patients with type 2 diabetes; complete data from 2,693 patients with no evidence of coronary artery disease/followed for 10 y	Nutrition therapy and medication in UKPDS[f] (RCT)	Stepwise ↑ risk coronary artery disease: ↑ LDL-C[g] ($P<0.0001$) and ↓ HDL-C[h] ($P=0.0001$); ↑ HbA1c[i] ($P=0.0022$); ↑ SBP[j] ($P=0.0065$); smoking ($P=0.056$)
Mayer-Davis, 1999 (114)	n=421 patients from San Luis Valley Diabetes Study and 437 patients from Insulin Resistance and Atherosclerosis Study/not applicable	Not applicable (cohort study, San Luis Valley Diabetes Study and Insulin Resistance and Atherosclerosis Study)	Higher intake of dietary fat related to higher LDL-C ($P<0.05$) in both studies and in all subgroups
Orchard, 2001 (116)	n=589 participants, mean duration of type 1 diabetes of 20.1 y/after 10 y	Not applicable (prospective cohort study)	Strong relationship between LDL-C and HDL-C, TG[k] and blood pressure and mortality (11% of participants) and CVD (17% of participants) (all $P<0.001$)
Mukamal, 2001 (115)	n=1935 participants from Determinants of Myocardial Infarction Onset Study interviewed after MI; 399 (21%) had diabetes/mean follow-up 3.7 y	Not applicable (prospective cohort study)	17% of cohort had died; 29% of patients with diabetes died; diabetes associated with higher mortality in unadjusted (hazard ratio=2.4; 95% CI: 1.9 to 3.0) and adjusted (hazard ratio=1.7; 95% CI: 1.3 to 2.1) analyses
Gaede, 2003 (123)	n=160 patients with type 2 diabetes and microalbuminuria/mean follow-up 7.8 y	Conventional therapy vs intensive therapy (<30% fat and <10% saturated fat, physical activity 3-5/wk, smoking cessation, and pharmacologic therapy (RCT)	Intensive therapy: ↓ HbA1c ($P<0.001$), SBP ($P<0.001$), DBP[l] ($P=0.006$), TC[m] ($P<0.001$), TG ($P=0.015$), urinary albumin excretion rate ($P=0.007$); ↓ risk of CVD (hazard ratio=0.47; 95% CI: 0.24 to 0.73)
Dhindsa, 2003 (125)	n=40 obese adults with type 2 diabetes/very-low-calorie diet for 8 wk, maintenance program for up to 1 y	Very-low-calorie diet (750 kcal/d) followed by standard diet and exercise advice every 2-3 mo (nonrandomized clinical trial)	8 wk: body weight ↓ 12 kg, TC ↓ 38.7 mg/dL, blood pressure ↓ 10/6 mm Hg, fructosamine ↓ 40 μmol/L; 1-y: body weight ↓ 10 kg ($P<0.001$) and fructosamine ↓ 15 μmol/L ($P<0.001$) from baseline, ↓ TC and ↓ blood pressure maintained.
Gill, 2003 (124)	n=500 patients with type 2 diabetes from the UKPDS/between audits in 1991 and 2001	UKPDS in 1991 intensified HbA1c targets (<7%) and blood pressure control (<140/85) (longitudinal study)	HbA1c: no change between audits; blood pressure: SBP ↓ 5 mm Hg ($P=0.001$), DPB ↓ 5 mm Hg ($P=0.0001$)
Ciccarone, 2003 (119)	n=144 patients with type 2 diabetes with peripheral arterial disease matched to 288 patients without complications/not applicable	Not applicable (cohort/case-control study)	A high-score Mediterranean dietary pattern associated with ↓ in perifpheral arterial disease, independent of diabetes duration and hypertension ($P<0.001$)
Selvin, 2004 (117)	n=17 prospective cohort studies; mean sample sizes 94 to 5,102/not applicable	No applicable (meta-analysis)	Patients with type 2 diabetes had a pooled relative risk for CVD of 1.18 (95% CI: 1.10 to 1.26); patients with type 1 diabetes had pooled relative risk of 1.15 (95% CI: 0.92 to 1.43)
Diakoumopoulou, 2005 (120)	n=126 patients with type 2 diabetes in a Mediterranean population/not applicable	Not applicable (cross-sectional study)	In participants with diabetes, age, consumption of fruits and vegetables, glomerular filtration rate were determinants of homocysteine (all $P=0.02$)
Faulkner, 2006 (118)	n=50 adolescents with type 1 diabetes, 14 with type 2 diabetes, 53 non-diabetic control/not applicable	Not applicable (cross-sectional study)	Lipid profiles and energy intake not different between groups; patients with type 1 diabetes had lowest homocysteine levels ($P<0.05$)
Estruch, 2006 (128)	n=772 patients with either type 2 diabetes or 3 or more CVD risk factors (Prevención con Dieta Mediterránea Study)/4 y	Mediterranean diet with virgin olive oil (1 L/wk) or mixed nuts (30 g/d) and nutrition education vs low-fat diet (RCT)	3 mo: Mediterranean diet vs low-fat diet ↓ SBP ($P<0.001$), blood glucose level ($P=0.017$), TC-HDL-C ratio ($P<0.001$), and ↑ HDL-C ($P<0.001$)
Trichopoulou, 2006 (129)	n=1,013 participants with diabetes from Greek arm of European Prospective Investigation into Cancer and Nutrition/4.5 y (range 2-114 mo)	Not applicable (cross-sectional study)	2 nutritional variables associated with diabetes mortality: ↑ daily intake eggs (hazard ration=1.31; 95% CI, 1.07 to 1.60) ($P=0.01$) and saturated fats (hazard ratio=1.82; 95% CI, 1.14 to 2.90) ($P=0.01$); physical activity inversely associated with mortality ($P=0.004$)
The Look AHEAD Research Group, 2007 (127)	n=5,145 (4,959) overweight/obese adults with type 2 diabetes/1-y results	Intensive lifestyle intervention (meal replacements or structured food plan, 175 min physical activity/wk, 3-4 weekly sessions/mo) vs control (diabetes support/education group, 4 sessions/y) (RCT)	Intensive lifestyle intervention vs control: weight ↓ 8.6% vs 0.7%; fitness ↑ 20.9% vs 5.8%; HbA1c ↓ 0.7% vs 0.1%; SBP ↓ 6.8 vs 2.8 mm Hg; DBP ↓ 3.0 vs 1.8 mm Hg; HDL-C ↑ 3.4 vs 1.4 mg/dL[n]; TG ↓ 30.3 vs 14.6 mg/dL[o] (all $P<0.001$); LDL-C ↓ 5.2 vs 5.7 mg/dL (NS[p])

(continued)

Table 9. Studies (1 y or longer) reporting on increased risk of cardiovascular disease in persons with diabetes and nutrition interventions for the prevention cardiovascular disease (continued)

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Holman, 2008 (126)	n=3,277 patients with type 2 diabetes enrolled in UKPDS/10-y follow-up of trial completion	After UKPDS results were published, all pts were advised to lower levels of blood glucose and blood pressure as much as possible (cross-sectional)	Intensive glucose control starting at diagnosis associated with ↓ risk of myocardial infarction (15%, $P=0.01$) and death from any cause (13%, $P=0.007$) as well continued reduction in microvascular complications (24%, $P=0.001$)

[a]DCCT=Diabetes Control and Complications Trial.
[b]EDIC=Epidemiology of Diabetes Interventions and Complications.
[c]RCT=randomized controlled trial.
[d]CVD=cardiovascular disease.
[e]CI=confidence interval.
[f]UKPDS=United Kingdom Prospective Diabetes Study.
[g]LDL-C=low-density lipoprotein cholesterol.
[h]HDL-C=high-density lipoprotein cholesterol.
[i]HbA1c=glycosylated hemoglobin.
[j]SBP=systolic blood pressure.
[k]TG=triglycerides.
[l]DBP=diastolic blood pressure.
[m]TC=total cholesterol.
[n]To convert mg/dL cholesterol to mmol/L, multiply mg/dL by 0.0259. To convert mmol/L cholesterol to mg/dL, multiply mmol/L by 38.7. Cholesterol of 193 mg/dL=5.0 mmol/L.
[o]To convert mg/dL triglycerides to mmol/L, multiply mg/dL by 0.0113. To convert mmol/L triglycerides to mg/dL, multiply mmol/L by 88.6. Triglycerides of 159 mg/dL=1.80 mmol/L.
[p]NS=non-significant.

of eggs and saturated fats. Increased physical activity by one quintile was associated with a 24% reduction of mortality from any cause.

Research Reviewed for Treatment of CVD

In people with diabetes and CVD, interventions based on low-fat diets and consumption of specific fatty acids (11,130-136), Mediterranean diets (137,138), reduced-sodium diets (139,140), currently generally accepted nutrition guidelines (141,142), and combination nutrition therapies and drugs (143,144) resulted in improved lipid profiles, reductions in blood pressure, and improved measures of endothelial health. In contrast, in persons with diabetes and a history of CVD, vitamin E supplements were found to have no beneficial effects on cardiovascular outcomes, microvascular complications, or on glycemic control (145). There is limited research on the effect of high -protein diets (92), low-GI diets (54), and phytosterol consumption (146) in the treatment of CVD.

Research Published after Completion of the Initial Recommendations for Treatment of CVD

Six additional studies examined nutrition-related interventions for CVD in persons with diabetes. In a 1-year clinical trial, a high-MUFA diet (45% carbohydrate, 40% fat [20% MUFA]) was compared to a high-carbohydrate, low-fat (60% carbohydrate, 25% fat) in 124 overweight/obese patients with type 2 diabetes (19). Energy intake was reduced in both diets by 200 to 300 kcal/d. Both diets resulted in beneficial effects on weight loss (−3.9 kg), blood pressure, high-density lipoprotein cholesterol, HbA1c, glucose, and insulin levels with no significant differences between diets. In a 1-month study, a Greek Mediterranean diet was compared to usual diet in patients with type 2 diabetes and a weight-matched control group without diabetes. The Greek Mediterranean diet was shown to reduce platelet aggregation in both groups compared to the previous usual diet (147).

Two studies using test meals reported benefit from olive and salmon oil compared to palm or safflower oil (148) and olive oil compared to butter (149). In two other studies, n-3 supplementation impact on blood lipid and glucose were evaluated. In one study, after 10 weeks, 2 g n-3 supplements improved triglyceride levels with no effect on other blood lipids, glucose, or insulin compared to the placebo (150). In the other study, a high intake of fish oil (~6 g/day n-3 fatty acids) increased glucose by 18 mg/dL (0.999 mmol/L) and decreased insulin sensitivity, but had no effect on blood lipids, including triglycerides, compared to corn oil (151). A 1-year study comparing a low-fat diet to a low-fat diet supplemented with 30 g walnuts per day reported favorable effects in all clinical parameters from both diets, although the walnut group experienced greater reductions in fasting insulin levels (152). This study confirmed that most of the effect of a nutrition intervention is seen in the first 3 to 6 months.

Recommendations for CVD

Cardioprotective nutrition interventions for the prevention and treatment of CVD should be implemented in the initial series of MNT encounters as both glycemic control

Table 10. Studies reporting on evidence supporting specific nutrition interventions in the treatment of cardiovascular disease

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Storm, 1997 (130)	n=15 adults with type 2 diabetes/3 wk on each diet	40% CHO[a], 44% fat (13% stearic acid) vs 40% CHO, 45% fat (16% palmitic acid) vs control (51% CHO, 19% fat) (randomized crossover trial)	TC[b] ↑ after palmitic diet compared to stearic acid or control diets (P=0.03); TG[c], LDL-C[d], HDL-C[e]:NS[f]
Osende, 2001 (143)	n=40 patients with type 2 diabetes; HbA1c[g] >7.5%/3 mo	Conservative (diet+placebo) vs intensive (diet+troglitazone) (RCT[h])	14 patients (intensive) and 10 patients (conservative) ↓ HbA1c; these patients had less thrombus formation vs those without improvement (r=0.47, P<0.01)
Parker, 2002 (92)	n=54 patients with type 2 diabetes/12 wk on each diet	HP[i] (28% protein) vs control (16% protein,); 8 wk energy restriction, 4 wk energy balance (RCT)	HP: ↓ TC and LDL-C[j] (13.5 mg/dL, P<0.01; 7.4 mg/dL, P<0.01, respectively); no difference in other lipid, insulin, or glycemic parameters
Houlihan, 2002 (139)	n=20 patients with type 2 diabetes, hypertension, and elevated albumin excretion rate/2 wks on each diet	Losartan vs placebo; each group randomly on a low sodium diet vs a regular sodium diet (diet: randomized crossover trial)	Losartan group+low sodium diet: ↓ blood pressure (SBP[k] 9.7 mm Hg; P=0.002; DBP[l] 5.5, P=0.002) and albumin excretion rate (−29%, P=0.002) vs other combinations
Lovejoy, 2002 (131)	Study 1: n=20 healthy adults; Study 2: n=34 adults with type 2 diabetes/4 wks on each diet	Study 1: 100 g almonds/d Study 2: 37% fat, 10% almonds vs 25% fat, 10% almonds vs control (25% fat, 10% MUFA[m]) (study 1: nonrandomized trial; study 2: randomized crossover trial)	Almonds: no effect on glycemia in patients with diabetes; almonds ↓ TC and LDL-C (P<0.05) in healthy adults and ↓ HDL-C (P=002) but no effect on LDL:HDL in both groups
Lonn, 2002 (145)	n=3,654 participants with diabetes from HOPE study and MICRO-HOPE substudy/4.5 y	400 IU vitamin E vs placebo and 10 mg ramipril vs placebo (RCT)	Daily vitamin E supplements had a neutral effect on cardiovascular outcomes and nephropathy (relative risk=1.03; 95% CI[n]: 0.88 to 1.21, P=0.70)
Krook, 2003 (141)	n=487 patients with type 2 diabetes who had repeated failure to achieve metabolic control; 415 (85%) returned for second visit/30 wk	Stays at a residential wellness center: 2 wk stay → 8 wk at home; 1 wk follow-up stay → 20 wk at home (time series)	Improved metabolic control after stays at residential wellness center: visit 2: ↓ HbA1c (P<0.0001), TC and LDL-C (P<0.001), blood pressure (P<0.0001), body mass index (P<0.0001); ↑ oxygen uptake (P<0.0001) and HDL-C (P<0.05)
Lee, 2003 (146)	n=85 patients with type 2 diabetes and LDL-C >140 mg/dL/12 wk	10 g low-fat spread vs 10 g phytosterol-enriched spread daily (RCT)	Modest and transient effect of phytosterol-enriched spread on TC and LDL-C (NS at 12 wks)
Perassolo, 2003 (142)	n=72 patients with type 2 diabetes (37 normonalbuminuric and 35 microalbuminuric/2 mo run-in followed by 4 wk diet intervention	Diet following American Diabetes Association guidelines; given corn oil for food preparation (case-control)	TC, HDL-C, LDL-C, TG (NS differences between groups)
Rizkalla, 2004 (54)	n=12 men with type 2 diabetes/4 wks on each diet	Low-Glycemic-Index (39) vs high-Glycemic-Index (71) diets (RCT)	Low-Glycemic-Index vs high-Glycemic-Index: ↓ TC and LDL-C (P<0.05), HbA1c (P<0.05) and fasting plasma glucose (P<0.05)
Rodriguez-Villar, 2004 (134)	n=22 patients with type 2 diabetes/6 wk on each diet	CHO diet (olive oil restricted to 10% kcal) vs MUFA diet (olive oil 25% kcal) (randomized crossover trial)	Weight, TC, LDL-C, HDL-C, TG similar after both diets; MUFA ↓ VLDL[o] by 35% (P=0.023) and VLDL-TG by 16% (P=0.016)
Neyestani, 2004 (132)	n=15 patients with type 2 diabetes for <1-y/8 wk dietary intervention	50%-60% CHO, 20%-30% fat, 35 g fiber; 3 meals and 2 snacks (nonrandomized trial)	FBG[p], HbA1c, and lipid peroxidation ↓ at 8-wk (P<0.05); TC, TG, LDL-C, HDL-C (NS)
Vedovato, 2004 (140)	n=41 patients with type 2 diabetes, 21 had microalbuminuria, normal BP/7 d	Low sodium diet (1,500 mg sodium chloride, 2,300 mg potassium, 800 mg calcium) vs high sodium diet (14,500 mg sodium chloride tablets added) (randomized crossover trial)	High sodium diet: patients with microalbuminuria blood pressure ↑ (P<0.001) and albuminuria ↑ (P<0.01) compared to those with normoalbuminuria
Mostad, 2004 (133)	n=19 patients with type 2 diabetes and TG ≥200 mg/dL/3 d	Usual diet vs low-fat diet intervention (24% fat, 51% CHO) (non-randomized trial)	3-d low-fat diet intervention: ↓ TC (P<0.005) and HDL-C (P<0.048); fasting blood glucose, fasting insulin (NS)
Gerhard, 2004 (11)	n=11 patients with type 2 diabetes/6 wk on each diet	Low-fat diet (20% fat, 65% CHO) vs high MUFA (25% MUFA, 45% CHO) (randomized crossover trial)	Low-fat vs MUFA diet: weight loss (1.53 kg; P<0.001); TC, LDL-C, HDL-C, TG, HbA1c (NS)
Didangelos, 2004 (144)	n=126 patients with type 2 diabetes and metabolic syndrome/6 mo	¾ treated with orlistat+hypocaloric diet vs ¼ on hypocaloric diet alone (RCT)	Orlistat+diet: ↓ weight (P=0.0001), HbA1c (P<0.0001), SBP (P=0.024), TC (P<0.0001), LDL-C (P=0.034); TG, HDL-C (NS)
Tapsell, 2004 (135)	n=58 patients with type 2 diabetes/6 mo	Control low-fat diet vs modified low-fat diet vs modified low-fat diet+30 g walnuts/d (RCT)	Walnut vs other 2 groups: ↑ polyunsaturated fatty acid → HDL-C ↑ (P=0.046) and LDL-C ↓ (P=0.032)
West, 2005 (136)	n=18 patients with type 2 diabetes/test meals	3 test meals: 47% MUFA vs 45% MUFA+3.3 g alpha-linoleic acids vs 44% MUFA+2.8 g eicosapentanaeoic acid+1.2 g docosahexanenoic acid +−.2 g alpha-linoleic acids (RCT)	In patients with elevated TG, meals containing 3-4 g n-3 fatty acids improved postprandial lipemia and endothelial function (P=0.052) vs only MUFA meal
Karantonis, 2006 (137)	n=45 adults with type 2 diabetes vs 22 weight-matched C/4 wk	22 control and 23 type 2 diabetes (38% fat, 50% CHO, Greek food) vs 22 type 2 diabetes (usual diet) (RCT)	Diet with Greek foods: lipids or glucose (NS) but did improve platelet aggregation (P<0.05)
Mantzoros, 2006 (138)	n=987 women with type 2 diabetes/not applicable	Diet given a "Mediterranean dietary pattern score" using a 9-point scale (cross-sectional)	Adherence to diet (alcohol, nuts, whole grains) was positively associated with adiponectin levels (P<0.01)

(continued)

Table 10. Studies reporting on evidence supporting specific nutrition interventions in the treatment of cardiovascular disease (continued)

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Antonopoulou, 2006 (147)	n=47 patients with type 2 diabetes and 22 weight-matched volunteers/1 mo	Two subgroups: Greek Mediterranean diet vs previous regular diet (RCT)	In both groups Greek Mediterranean diet reduced platelet aggregation ($P<0.05$) vs regular diet
Mostad, 2006 (141)	n=26 patients with type 2 diabetes with normal TG/9 wk	20 mL fish oil (~6 g/d n-3 fatty acids) vs 20 mL corn oil/d (8.5 g/d linoleic acid) added to usual diet (double-blind RCT)	Fish oil: ↑ glucose 18 mg/dL ($P=0.035$) and ↓ insulin sensitivity ($P=0.049$); TC, LDL-C and HDL-C, TG (NS)
Shah, 2007 (148)	n=11 patients with type 2 diabetes/test meals	1,000-kcal test meals: palmitic acid (palm oil) vs linoleic acid (safflower oil) vs oleic acid (olive oil) vs eicosapentaenoic acid and docosahexaenoic acid (salmon oil) (crossover study)	Oleic acids, eicosapentaenoic acid and docosahexaenoic acid meals lower insulin response vs plamitic acid or linoleic acid meals ($P<0.01$) without deteriorating glucose or TG response
Shidfar, 2008 (150)	n=50 patients with type 2 diabetes/10 wk	Supplementation with 2 g n-3 fatty acids vs placebo (RCT)	n-3 supplement vs placebo: ↓ TG ($P=0.01$); lipids, glucose, insulin, and HbA1c: NS
Tentolouris, 2008 (149)	n=33 patients with type 2 diabetes/test meals	2 isocaloric test meals: MUFA (33 g olive oil) vs saturated fatty acids (40 g butter) (crossover study)	Endothelial function measured by flow-mediated dilatation: MUFA did not change FMD, whereas saturated fatty acids ↓ flow-mediated dilatation ($P=0.01$)
Brehm, 2009 (19)	n=124 overweight/obese patients with type 2 diabetes/1 y	High-MUFA (45% CHO, 40% fat [20% MUFA]) diet vs high-CHO (60% CHO, 25% fat) diets with ↓ 200-300 kcal/d (RCT)	NS differences in beneficial effects on weight loss (−3.9 kg), blood pressure, HDL-C, HbA1c, glucose, and insulin between groups at 1 y
Tapsell, 2009 (152)	n=50 overweight adults with type 2 diabetes/ 1 y	Low-fat dietary advice +30 g/d walnuts vs control, both weight maintaining (RCT)	Weight loss and all clinical parameters improved, most effects seen in first 3 mo, NS between groups; walnut group ↓ fasting insulin levels ($P=0.046$)

[a]CHO=carbohydrate.
[b]TC=total cholesterol.
[c]TG=triglycerides.
[d]LDL-C=low-density lipoprotein.
[e]HDL-C=high-density lipoprotein.
[f]NS=non-significant.
[g]HbA1c=glycosylated hemoglobin.
[h]RCT=randomized controlled trial.
[i]HP=high protein.
[j]To convert mg/dL cholesterol to mmol/L, multiply mg/dL by 0.0259. To convert mmol/L cholesterol to mg/dL, multiply mmol/L by 38.7. Cholesterol of 193 mg/dL=5.0 mmol/L.
[k]SBP=systolic blood pressure.
[l]DBP=diastolic blood pressure.
[m]MUFA=monounsaturated fatty acid.
[n]CI=confidence interval.
[o]VLDL=very-low-density lipoprotein.
[p]FBG=fasting blood glucose.

and cardioprotective nutrition interventions improve the lipid profile. Cardioprotective nutrition interventions include reduction in saturated and *trans*-fatty acids and dietary cholesterol, and interventions to improve blood pressure. Studies in persons with diabetes using these interventions report a reduction in CVD risk and improved CVD outcomes.

Limitations of Current Research and Additional Research Needed for Prevention and Treatment of CVD

Although a number of nutrition interventions for prevention and treatment of CVD in persons with diabetes have been identified, additional research is needed to determine expected outcomes from identified interventions. Research is needed to assist in the prioritization of nutrition interventions and to further define macronutrient recommendations such as the role of specific fatty acids, including n-3 fatty acids. Although a Mediterranean diet is reported as being beneficial, a clearer understanding of the protective mechanisms from differing components of the diet and its role in the management of diabetes is needed.

WEIGHT MANAGEMENT EVIDENCE AND RECOMMENDATIONS

In individuals with type 2 diabetes and insulin resistance, weight loss generally improves glycemic outcomes and contributes to beneficial effects on blood pressure and blood lipids. However, as the disease progresses and insulin deficiency as compared to insulin resistance becomes more prominent, weight loss is less likely to be effective in improving glycemic outcomes. With insulin deficiency, additional anti-diabetes medications combined with MNT are necessary and prevention of weight gain becomes important. To determine the long-term effect (1 year or longer) of weight management on metabolic outcomes in persons with type 1 and type 2 diabetes, a total of 20 studies (21 articles) that met predetermined criteria were evaluated (Table 11). Bariatric surgery studies in patients with diabetes are not included in the analyses.

Research Reviewed

In randomized weight loss trials conducted between 2000 and 2006 of 1 year or longer duration implementing diet (and physical activity) interventions, approximately half of the diet intervention groups experienced improvement in HbA1c related to weight loss, whereas approximately half reported no improvement in HbA1c despite fairly similar weight losses. However, weight loss and weight maintenance contribute to improvements in lipid levels and blood pressure.

Eleven studies included a minimum of one diet intervention group and reported body weight loss and HbA1c values at 12 months (94,153-163). Diet intervention groups in five studies reported improvement in HbA1c ranging from −0.2% to −0.5% with body weight losses ranging from −1.0 to −3.4 kg (153-157). However, diet intervention groups in six studies reported no improvement in HbA1c despite fairly similar body weight losses ranging from −0.8 to −4.4 kg (94,158-163). Two studies did not report HbA1C values at 12 months (164,165). A nonrandomized clinical trial reported body weight loss correlated with improvements in HbA1c (166) as did a meta-analysis (167). One study in the meta-analysis met ADA criteria and is included in Table 11 (153).

One-year or longer studies using weight loss medications (orlistat and lifestyle, sibutramine) reported consistent improvement in HbA1c. Orlistat and lifestyle groups in six studies reported improvements in HbA1c ranging from −0.3% to −1.1% with weight losses ranging from −3.8 to −8.5 kg (154-158,168). Sibutramine groups in four studies reported improvements in HbA1c ranging from −0.3% to −0.6% with body weight losses ranging from −4.1 to −8.6 kg (159,160,169,170).

Twelve studies reported significant improvements in at least one blood lipid value, generally in triglycerides and high-density lipoprotein cholesterol from body weight loss either by diet alone or with weight loss medications (94,125,153-158,161,162,169,171). Eight studies reported improvement in blood pressure with weight loss (125,153,154,156,157,159, 168,171); however, one study using sibutramine reported no change in blood pressure (168) and one study reported an increase in blood pressure (169).

Research Published after Completion of the Initial Recommendations

Look AHEAD is a clinical trial being conducted in 16 centers around the United States to determine the effectiveness of intentional weight loss in reducing cardiovascular disease events in type 2 diabetes. Participants will be followed for up to 11.5 years; 1-year outcomes were published in 2007 (127). Participants randomized to the intensive lifestyle intervention consisting of meal replacements or structured food plans, 175 minutes of physical activity per week, and three to four education/counseling sessions per month, experienced an average body weight loss of 8.6%±6.9%, a 20.9%±29.1% improvement in cardiovascular fitness, and a 0.64%±0.02% decrease in HbA1c over Year 1. In comparison, participants in the diabetes support and education group experienced a body weight loss of 0.7%±4.8%, a 5.8%±22.0% increase in cardiovascular fitness, and a 0.1%4±0.02% decrease in HbA1c. Regular self-weighing, eating breakfast, and infrequent consumption of fast food were associated with a lower BMI in the study population (172).

Three studies compared low-carbohydrate diets to high-MUFA or low-fat diets for weight loss (19-21). In a retrospective follow-up study of 16 patients following a low-carbohydrate diet (20% of energy intake), at 44 months body weight loss and HbA1 levels were significantly improved with no sign of a negative cardiovascular effect (21). However, two larger 1-year randomized clinical trials reported no beneficial effects on body weight, HbA1c, LDL cholesterol, and blood pressure in participants following a low-carbohydrate diet compared to participants following a high-MUFA or low-fat diet (19,20).

A comparison of meal replacements to standard, self-selected diets (34 weeks intervention, 1 year maintenance) reported significant body weight loss in both groups but no significant differences between group difference (−5.6 vs −4.7 kg, respectively) (173). At 86 weeks HbA1c for both groups was not statistically different from baseline. In a retrospective cohort study, a weight-loss

pattern after new diagnosis of type 2 diabetes predicted improved glycemic and blood pressure control despite weight regain, supporting the importance of early weight loss interventions before advancing insulin deficiency (174).

Three studies reported on patients with type 2 diabetes who extended treatment with exenatide for 82 weeks (placebo-controlled trial ended at 30 weeks). Body weight decreased from baseline by −4.0 to −5.3 kg and HbA1c decreased 1.0% to 1.3% (175-177). Although weight loss continued over the entire time period, the amount of weight loss is comparable to weight loss reported at 6 months in most other weight loss studies. Rimonabant (20 mg/day), a selective cannabinoid type 1 receptor blocker, at 1 year resulted in weight loss and a decrease in HbA1c compared to a placebo (178). However, only two thirds of study participants completed 1 year of treatment, with more than half dropping out for reasons other than adverse events. Rimonabant was not approved by the Food and Drug Administration. In obese patients with type 2 diabetes, topiramate compared to placebo resulted in weight loss and improvement in HbA1C. However, the number of participants taking topiramate and completing the study was small; adverse effects on central nervous system and paresthesia caused a drop-out rate of 42% (179). A second study of topiramate also in obese patients with type 2 diabetes was ended early because of adverse events (180).

Recommendations for Weight Management

RDs should advise that glycemic control is the primary focus for diabetes management. Although decreasing energy intake may improve glycemic control, it is unclear whether weight loss alone will improve glycemic control. Sustained weight loss interventions using lifestyle interventions only and lasting 1 year or longer report inconsistent effects on HbA1c.

Studies support a reduced energy intake with reduced total and saturated fats, an increase in dietary fiber and whole grains, and a decrease in sodium. Physical activity should be strongly encouraged, especially for its contribution to weight maintenance after weight loss. A weight loss of 5% to 10% of body weight from lifestyle interventions is a realistic goal.

Limitations of Current Research and Additional Research Needed for Weight Management

In weight management studies it is difficult to account for potential bias based on selection of participants most likely to be successful. RDs need to be knowledgeable regarding successful interventions and be aware of potential barriers that may hinder weight loss in clinical weight management programs. For example, rarely can RDs be selective in the patients they enroll in weight management programs.

Attrition can be a problem in trials that are 1 year and longer, especially in lifestyle trials; this needs to be considered in translating research findings to clinical practice. Data on study completers has important value to practitioners because it clarifies what can be expected if participants complete a weight management intervention.

Future research needs to meet appropriate methodological standards such as rigorous application of good study design principles, minimization of attrition, and follow-up of dropouts. The Look AHEAD trial is designed to meet these standards.

PHYSICAL ACTIVITY EVIDENCE AND RECOMMENDATIONS

Studies in persons with type 2 diabetes have reported improvements in blood glucose control, reduced cardiovascular risk, assistance with weight management, and improved well-being from regular physical activity. Improvements in glycemia are reported to be independent of weight loss (181). In persons with type 1 diabetes, exercise may lower glucose levels, but also has potential negative effects related to hypo- and hyperglycemic excursions. To determine the effect of physical activity (3 months or longer) on metabolic outcomes in persons with type 2 diabetes, 12 studies that met predetermined criteria were evaluated (Table 12). Four studies (five articles) meeting predetermined criteria were evaluated related to the effects of physical activity in persons with type 1 diabetes (Table 13).

Research Reviewed

In persons with type 2 diabetes, five studies reported that 90 to 150 minutes of weekly physical activity (aerobic exercise and/or resistance/strength training) reduced HbA1c levels (182-186). Two studies reported improvements in HbA1c at 6 months (187,188), which were not maintained at 12 months (189,190). A meta-analysis of 14 studies conducted before 2001 with 504 participants concluded that HbA1c was significantly decreased by 0.66% in exercise groups (191). Improvements in insulin sensitivity were noted in two studies (184,192), and decreases in relative risk for all-cause mortality were reported in two studies (193,194). A technical review evaluating eight articles recommended 150 minutes per week of moderate-intensity physical activity (40% to 60% of maximal oxygen uptake or 50% to 70% of maximum heart rate) for improved glycemic control (181). Also noted was that to achieve long-term glycemic control, no more than 2 consecutive days should pass without physical activity.

In patients with type 1 diabetes, two studies reported that ongoing participation in physical activity generally does not improve glycemic control as it does in patients with type 2 diabetes (195,196). In a large crossover study, sedentary women had higher HbA1c levels than moderately active or active women, and physical activity was not associated with HbA1c in men (197). Risk of hypoglycemia as a result of exercise is an ongoing problem for persons with type 1 diabetes. The incidence of hypoglycemia during or after exercise appears to depend on pre-exercise blood glucose levels (198). After a 75-minute exercise session, in 83% of 46 patients with type 1 diabetes, glucose values dropped 25% from pre-exercise values and 30% of the patients became hypoglycemic (<60 mg/dL [3.33 mmol/L]) either during or after exercise which varied by baseline values (199). Treatment with 15 g glucose resulted in only a 20 mg/dL (1.11 mmol/L) rise in blood glucose, which in most patients did not increase blood glucose levels to 80 mg/dL (4.44 mmol/L).

Table 11. Studies (1 y or longer) reporting on the long-term effects of weight management on metabolic outcomes

First author, y, (reference)	Population, participants enrolled (completers)/duration	Intervention (type)	Major findings
Wing, 1987 (166)	n=124 (114) overweight patients with type 2 diabetes/1 y	Behavioral weight control program (nonrandomized clinical trial)	Weight loss correlated with ↓ HbA1c[a] (r=0.51); weight loss >6.9 kg or 5% ↓ HbA1c, less weight loss no improvement (P<0.001); TC[b], blood pressure: NS[c]
Manning, 1998 (163)	n=147 (1-y 132) (4-y 103) plus 58 control overweight patients with type 2 diabetes/4 y	Dietetic consultation vs with 30 mg/d dexfenfluramine vs home visits vs behavioural group therapy (RCT[d])	1-y: NS difference in weight loss (range −1.4 to −3.0 kg); control: +1.2 kg (P<0.01); no improvement in HbA1c in any group; 4-y: only dexfenfluramine weight loss (−2.5 kg) (P=0.025); HbA1c not decreased
Hollander, 1998 (158)	n=391 (254) obese patients with type 2 diabetes/52 wk	Hypocaloric diet (−500 kcal/d deficit) with orlistat (120 mg three times/d) or placebo (RCT)	Orlistat vs placebo: weight ↓ 6.2±0.5 vs 4.3±0.6 kg (P<0.001); HbA1c ↓ 0.28±0.09% vs ↑ 0.18±0.11% (P<0.001); ↓ TC and LDL-C[e] (both P<0.001) and TG[f] (P<0.05)
Metz, 2000 (153)	n=119 (92) patients with type 2 diabetes/1-y	Prepared meal plan vs usual care exchange-based diet plan (RCT)	Prepared meal plan vs usual care: weight loss ↓ 3.0±5.4 kg vs 1.0±3.8 kg (P<0.001); ↓ HbA1c, TC, LDL-C and HDL-C[g] and blood pressure (from baseline both groups P<0.001)
Paisey, 2002 (171)	n=30 (25) obese patients with type 2 diabetes/1 y and 5 y	Very-low-energy diet (650 kcal/d) for 6 wk vs intensive conventional diet (cohort study)	Weight loss slower in intensive conventional diet vs very-low-energy diet, but at 5-y better maintained (−8.9±4 kg vs −4.8±6 kg (P<0.05); intensive conventional diet: HDL-C ↑ and DBP[h] ↓ (from baseline P<0.05)
Hanefeld, 2002 (154)	n=492 (383) overweight adults with type 2 diabetes/1-y	Hypocaloric diet with orlistat (120 mg three timesd) or placebo (RCT)	Orlistat vs placebo: weight ↓ 5.5±5.1 kg vs 3.4±5.3 kg (P=0.006); HbA1c ↓ 0.9±1.3 vs 0.4±1.5% (P<0.001); TC ↓ (P<0.01), LDL-C ↓ (P<0.05); blood pressure ↓ in both groups (NS between groups)
Kelley, 2002 (155)	n=535 (265) overweight and obese patients with insulin-treated type 2 diabetes/1 y	Hypocaloric diet with orlistat (120 mg three times/d) or placebo (RCT)	Orlistat vs placebo: weight ↓ 3.9±0.3 kg vs 1.3±0.3 kg (P<0.001); ↓ HbA1c 0.62±0.1% vs 0.3±0.1% (P=0.02); TC (P=0.002), LDL-C (P=0.001); blood pressure, TG, HDL-C: no change in either group
Miles, 2002 (156)	n=516 (311) overweight and obese patients with metformin-treated type 2 diabetes/1 y	Hypocaloric diet with orlistat (120 mg three times/d) or placebo (RCT)	Orlistat vs placebo: weight ↓ 4.7±0.3 kg vs 1.8±0.3 kg (P<0.001); HbA1c ↓ 0.8±0.1% vs 0.4±0.1% (NS between groups); TC ↓ (P<0.05); LDL-C, HDL-C, TG: no change; SBP[i] and DBP ↓ (both groups P<0.05)
McNulty, 2003 (169)	n=194 (144) obese patients with metformin-treated type 2 diabetes/1 y	Sibutramine (15 mg/d) vs sibutramine (20 mg/d) vs placebo (dietetic advice) (RCT)	Sibutramine: 15 mg/d weight ↓ 5.5±0.6 kg and 20 mg/d weight ↓ 8.0±0.9 kg (P<0.001), placebo (NS); HbA1c, TC, and LDL-C: no change in either groups; SBP and DBP ↑ 3-4 mmHg with sibutramine
Ash, 2003 (164)	n=51 (27) overweight men with type 2 diabetes/18-mo	12-wk intermittent energy restriction vs pre-portioned meals vs self-selected meals, follow-up at 18 mo (RCT)	12 wk: weight loss ↓ 6.4±4.6 kg, HbA1c ↓ 1.0±1.4%, TG ↓ 26.6 mg/dL (NS between groups); 18 mo: all parameters returned to baseline levels
Redmon, 2003 (159) and 2005 (160)	n=48 obese patients with type 2 diabetes/1-y and 2-y follow-up	Usual care vs meal replacements (900-1,300 kcal) 7 d every 2 mo and 1 meal replacements/d between these wks and sibutramine (10-15 mg/d); after 1-y usual care crossed over to sibutramine therapy (RCT)	1-y: meal replacements and sibutramine, weight loss ↓ 7.3±1.3 kg vs 0.8±0.9 kg (P<0.001); HbA1C ↓ 0.6±0.03 vs no change (P<0.05); ↓ TC and LDL-C, SBP, DBP NS between groups; 2-y: meal replacements and sibutramine group, weight loss ↓ 4.6±1.2 kg (P<0.001), HbA1c ↓ 0.5±0.3% (P=0.08); UC 1-y and then meal replacements and sibutramine, 2 y: results similar to other group at 1 y
Dhindsa, 2003 (125)	n=44 (40) obese adults with type 2 diabetes/very-low-energy diet for 8 wk, maintenance program for up to 1 y	Very-low-energy diet (750 kcal/d) followed by standard diet and exercise advice every 2-3 mo (nonrandomized clinical trial)	1-y: body weight ↓ 10 kg (P<0.001); fructosamine ↓ 15 μmol/L (P<0.001); TC ↓ 38.7 mg/d (P<0.003); blood pressure ↓ average 8/3 mm Hg (P<0.001)
Derosa, 2004 (168)	n=144 (133) obese patients with type 2 diabetes/1 y	Hypocaloric diet+360 mg/d orlistat vs 10 g/d sibutramine (RCT)	12 mo: orlistat: body mass index ↓ 33.6±1.3 to 29.7±0.6, HbA1c ↓ 7.1±0.5% to 6.3±0.3%; sibutramine: body mass index ↓ 33.1±1.4 to 29.5±0.5 kg, HbA1c ↓ 7.0±0.6% to 6.3±0.2% (all P<0.01); blood pressure ↓ 3 mm Hg (P<0.05) in orlistat group but no change in sibutramine group
Sanchez-Reyes, 2004 (170)	n=86 (47) overweight and obese Hispanic adults with glibenclamide-treated type 2 diabetes/1 y	Sibutramine (10 mg/d) vs placebo (dietetic advice) (RCT)	Sibutramine vs placebo: weight ↓ 4.1 kg vs 1.4 kg (P<0.05); HbA1c ↓ 0.6% vs ↑ 0.1% (P<0.05) blood pressure ↓ in both groups (P<0.05)
Wolf, 2004 (161)	n=147 (118) obese patients with type 2 diabetes/1 y	Case management with registered dietitian vs usual treatment (educational material) (RCT)	Case management: weight ↓ 2.4 kg vs ↑ 0.6 kg (P<0.001); HbA1c (NS change in both groups); ↓ TC, LDL-C, HDL-C, TG (NS between groups)
Brinkworth, 2004 (94)	n=66 (38) obese patients with type 2 diabetes/64 wk	High protein (30% protein, 40% CHO) vs low protein (15% protein, 55% CHO) (RCT)	High protein vs low protein: weight ↓ 3.7±1.0 kg vs 2.2±1.1 kg (P<0.01 from baseline for both groups; no diet effect); HbA1c, TG, TC, blood pressure: NS compared to baseline in both groups
Mayer-Davis, 2004 (165)	n=187 (152) overweight patients with type 2 diabetes/1-y	Intensive lifestyle intervention vs reimbursable lifestyle intervention vs usual care (RCT)	Intensive lifestyle intervention: weight ↓ 2.2 kg (P<0.003) at 12 mo, no change in other groups; HbA1c, lipids, and blood pressure: NS differences, only 6-mo values reported

(continued)

Table 11. Studies (1 y or longer) reporting on the long-term effects of weight management on metabolic outcomes (continued)

First author, y, (reference)	Population, participants enrolled (completers)/duration	Intervention (type)	Major findings
Norris, 2004 (167)	22 RCT in adults with type 2 diabetes/follow-up 1 to 5 y	4,659 participants with weight loss interventions vs 585 with usual care (meta-analysis)	Pooled weight loss for any intervention vs usual care: ↓ 1.7 kg (95% confidence interval: 0.3 to 3.2 kg) or 3.1% of baseline weight ($P<0.05$); HbA1c generally corresponded to weight loss but NS between groups; TC ↓ 7.2 to ↑ 5.9 mg/dL and blood pressure ↓ 4 to ↑ 1 mm Hg between-group changes
Li, 2005 (162)	n=104 (77) obese patients with type 2 diabetes/1 y	Soy-based meal replacements vs individualized exchange-based diet plans (RCT)	Meal replacements: weight ↓ 4.4±5.3 vs 2.4±4.9 kg ($P=<0.05$); HbA1c; NS improvement in either group; Meal replacements: LDL-C[k] ↓ 6.10 mg/dL ($P=0.255$); TG both groups ↓ 28 mg/dL ($P=0.38$)
Berne, 2005 (157)	n=220 (190) obese patients with type 2 diabetes/1 y	Weight management program+orlistat (120 mg three times/d) vs placebo (RCT)	Orlistat vs placebo: weight ↓ 4.8±0.1 vs 1.7±0.01 kg ($P<0.0001$); HbA1c ↓ 1.1% vs 0.2% ($P<0.0001$); TC ↓ 9.3 vs ↑ 3.9 mg/dL; LDL-C ↓ 5.0 vs ↑ 8.5 mg/dL (both $P<0.001$); blood pressure ↓ 3.1/2.4 mm Hg vs ↓ 3.1/1.9 mm Hg (NS between groups)
Riddle, 2006 (175)	n=222 out of 401 patients with type 2 diabetes who completed treatment with exenatide/82 wk	Exenatide (10 μg twice/d) with sulphonylurea or metformin (cohort study)	Body weight from baseline to wk 30 ↓ 2.1±0.3 kg and at wk 82 to 4.0±0.3 kg (95% confidence interval: −4.6 to −3.4 kg); HbA1c at 30 wk ↓ 1.0±0.1% and maintained to wk 82 (95% confidence interval: −0.9 to −1.2%)
Ratner, 2006 (176)	n=92 out of 150 patients with type 2 diabetes who extended treatment with exenatide/82 wk	Exenatide with metformin (cohort study)	Body weight from baseline to wk 30 ↓ 3.0±0.6 kg and at wk 82 to 5.3±0.6 kg ($P<0.05$); HbA1c at 30 wk ↓ 1.0±0.1% and after 82 wks ↓ 1.3±0.1% ($P<0.05$); improvement in cardiovascular risk factors
Blonde, 2006 (176)	n=314 our of 551 patients with type 2 diabetes who extended treatment with exenatide/82 wk	Exenatide with sulphonylurea and/or metformin (RCT)	Body weight from baseline to wk 30 ↓ 2.1±0.2 kg and at wk 82 to 4.4±0.3 kg; HbA1c at 30 wk ↓ 0.9±0.1% and at wk 82 ↓ 1.1±0.1%; HDL-C ↑ 4.6 mg/dl; TG ↓36.6 mg/dL; DBP ↓ 2.7 mm Hg (significance not reported)
Scheen, 2006 (178)	n=1047 (692) overweight or obese patients with type 2 diabetes/1 y	Rimonabant (5 mg/d) vs rimonabant (20 mg/d) vs placebo; mild hypocaloric diet advice (RCT)	Placebo: weight ↓ 1.4±3.6 kg; 5 mg rimonabant: weight ↓ 2.3±4.2 kg ($P=0.01$ vs placebo); 20 mg rimonabant: weight ↓ 5.3±5.2 kg ($P<0.001$ vs placebo); 20 mg: HbA1c ↓ 0.6% vs 0.1 placebo ($P<0.001$), TG ↓, HDL ↑ (all $P<0.0001$), SBP ↓ ($P=0.02$)
Eliasson, 2007 (179)	n=38 (22) obese patients with diabetes/1 y	Topiramate (96 twice/d) vs placebo (double-blind RCT)	Topiramate vs placebo: weight ↓ 7.2±4.3 vs 1.5±1.5 kg ($P<0.001$); HbA1C ↓ 1.1±0.9% vs ↑ 0.3±0.8% ($P=0.0009$); lipids: NS in both groups; adverse effects on central nervous system and paresthesia caused drop-out rate of 42%
The Look AHEAD Research Group 2007 (127) and 2008 (172)	n=5,145 (4,959) overweight/obese adults with type 2 diabetes/1-y results	Intensive lifestyle intervention (meal replacements or structured food plan, 175 min physical activity/wk, 3-4 weekly sessions/mo) vs control (diabetes support/education group, 4 sessions/y) (RCT)	Intensive lifestyle intervention vs control: weight ↓ 8.6% vs 0.7%; fitness ↑ 20.9% vs 5.8%; HbA1c ↓ 0.7% vs 0.1%; SBP ↓ 6.8 vs 2.8 mm Hg; DBP ↓ 3.0 vs 1.8 mm Hg; HDL-C ↑ 3.4 vs 1.4 mg/dL; TG ↓ 30.3 vs 14.6 mg/dL (all $P<0.001$); LDL-C ↓ 5.2 vs 5.7 mg/dL: NS; regular self-weighing, eating breakfast, and infrequent consumption of fast food were related to lower body mass index in the study population.
Nielsen, 2008 (21)	n=31 patients with type 2 diabetes/44 mo	Low CHO diet (20%) vs higher CHO, low-fat diet (55%-60%, 15%, respectively (retrospective observational study)	Low CHO group: weight ↓ 100.6 kg to 93.1 kg; HbA1c ↓ 8.0% to 6.8%; both $P<0.001$; 7 of 15 controls switched to the low CHO diet at 6 mo. No sign of a negative cardiovascular effect in low-CHO group.
Cheskin, 2008 (173)	n=112 (24 at wk 86) overweight/obese patients with type 2 diabetes/86 wk	34 wk 25% kcal deficit diet from meal replacement vs standard, self-selected food diets, 1-y maintenance (RCT)	Meal replacement: weight ↓ 5.6±6.0 kg ($P=.006$) vs 4.7±7.3 kg ($P=0.09$): NS between groups; HbA1c: NS from baseline in both groups; TC, LDL-C, TG: NS changes in both groups; meal replacement: HDL-C ↑ 7.7±17.0 mg/dL ($P=0.007$); meal replacement: SBP ↓ −7.6 mm Hg ($P=0.48$); standard: DBP ↓ −9.7 mm Hg ($P=004$)
Feldstein, 2008 (174)	n=2,574 adults with newly diagnosed type 2 diabetes/3 y	High stable weight vs lower stable weight vs weight gain vs weight loss (retrospective cohort study)	Weight loss group ↓ 10.7 kg by 18 mo followed by regain to 36 mo; even with weight regain this group at 36 mo was less likely to have above goal HbA1c ($P<0.0001$) and above goal blood pressure ($P<0.0001$)
Brehm, 2009 (19)	n=124 overweight/obese patients with type 2 diabetes/1 y	High monounsaturated fatty acid (45% CHO, 40% fat [20% monounsaturated fatty acid]) diet vs high-CHO (60% CHO, 25% fat) diets with ↓ 200-300 kcal/d (RCT)	NS differences in beneficial effects on weight loss (−3.9 kg), blood pressure, HDL-C, HbA1c, glucose and insulin between groups at 1 y
Davis, 2009 (20)	n=105 overweight adults with type 2 diabetes/1 y	Low-CHO diet (modeled after Atkins diet) vs low fat diet (25%) (randomized clinical trial)	NS difference in weight loss (-3.1 kg), HbA1c, blood pressure, TC, TG, LDL-C between groups, all NS from baseline; HDL-C ↑ in low CHO group ($P=0.002$).

[a]HbA1c=glycosylated hemoglobin.
[b]TC=total cholesterol.
[c]NS=non-significant.
[d]RCT=randomized controlled trial.
[e]LDL-C=low-density lipoprotein cholesterol.
[f]TG=triglycerides.
[g]HDL-C=high-density lipoprotein cholesterol.
[h]DBP=diastolic blood pressure.
[i]SBP=systolic blood pressure.
[k]To convert mg/dL cholesterol to mmol/L, multiply mg/dL by 0.0259. To convert mmol/L cholesterol to mg/dL, multiply mmol/L by 38.7. Cholesterol of 193 mg/dL=5.0 mmol/L.

Table 12. Studies (3 mo or longer) reporting on the effects of physical activity on metabolic outcomes in persons with type 2 diabetes

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Mayer-Davis, 1998 (192)	n=1,467 African-Americans or non-Hispanic white adults with varying degrees of glucose tolerance/not applicable	Assessed: physical activity METS[a] by questionnaire, glucose tolerance, and insulin sensitivity (cross-sectional study)	Higher insulin sensitivity associated with ↑ participation in nonvigorous physical activity ($P<0.01$) and vigorous physical activity ($P<0.001$)
Wei, 2000 (193)	n=1,263 adult men with type 2 diabetes/11.8 y follow-up	Assessed: physical fitness by maximal exercise treadmill test (prospective cohort study)	Low fitness group: adjusted risk for all-cause mortality of 2.1 compared to fit men ($P<0.001$)
Boulé, 2001 (191)	n=504 adults from 14 articles/not applicable	Extracted: exercise interventions—type, frequency, duration, intensity, energy cost (meta-analysis)	Exercise: HbA1c[b] ↓ 0.66% ($P<0.001$); average weight change in exercise groups: −0.9 kg ($P=0.70$), in exercise and diet groups: −3.4 kg ($P=0.11$), in control +0.8 kg ($P=0.73$)
Castaneda, 2002 (182)	n=62 adults with type 2 diabetes/16 wk	Progressive resistance training 3 times/wk vs control (usual care) (RCT)	Resistance training vs control from baseline: HbA1c ↓ 1.1% vs 0.1% ($P=0.01$); SBP[c] ↓ 9.7 vs ↑ 7.7 mm Hg ($P=0.05$) TG[d,e] ↓ 18.6 vs ↑ 9.7 mg/dL ($P=0.08$)
Goldhaber-Fiebert, 2003 (183)	n=61 adults with type 2 diabetes/12 wk	Lifestyle intervention (walked 60 min 3 times/wk) vs control (diabetes education via lecture) (RCT)	Exercise group: HbA1c ↓ 1.8±2.3% vs 0.4±2.3% in control ($P<0.05$)
Church, 2004 (194)	n=2196 adult men with type 2 diabetes/1 to 26 y (average 14.6±7.1 y) follow-up	Assessed: physical fitness by maximal exercise treadmill test (prospective cohort study)	Fitness: inverse association with mortality, seen in all body mass index groups (P for trend <0.0001); no trend across body mass index categories for mortality after adjustment for fitness
Van Rooijen, 2004 (186)	n=149 women with type 2 diabetes/12 wk	Exercise group (45 min/d+45 min aerobics class every 2 wk) vs relaxation group (RCT)	HbA1c improved in both groups ($P<0.01$) but authors suggest due to study effect
Kirk, 2003 (188) and 2004 (190)	n=59 adults with type 2 diabetes/12 mo	Physical activity counseling vs control (weight loss diet plan) (RCT)	Physical activity counseling: HbA1c ↓ 0.31% at 6 mo (between group $P<0.05$); 12 mo: HbA1c, SBP, TC[f], weight: NS[g] between groups
Sigel, 2004 (181)	8 exercise articles (physical activity/exercise, type 2 diabetes)/not applicable	American Diabetes Association recommendations (technical review)	Recommend: 150 min/wk of moderate-intensity pysical activity (40-60% of VO_2[h] or 50%-70% maximum heart rate) to improve glycemic control; no more than 2 d without physical activity
Dunstan, 2002 (187) and 2005 (189)	n=33 sedentary adults with type 2 diabetes/12 mo	Resistance training (45 min high-intensity 3 d/wk) vs weight loss (flexible exercise every 2 wk); both groups given weight loss diet plan (RCT)	6 mo: resistance training HbA1c ↓ 1.2±1.0% vs 0.4±0.8% ($P<0.01$); 12 mo: HbA1c NS from baseline for either group; insulin sensitivity NS between groups
Di Loreto, 2005 (185)	n=182 adults with type 2 diabetes/2 y	Exercise (40%-60% heart rate) vs control (RCT)	11 to 20 METS energy expenditure/wk ↓ HbA1c, TC, TG, blood pressure (all $P<0.0001$); >20 METS energy expenditure/wk needed to ↓ weight, body mass index, low-density lipoprotein cholesterol and to ↑ high-density lipoprotein cholesterol
Cauza, 2005 (184)	n=43 adults with type 2 diabetes/4 mo	Strength training 3 times/wk vs endurance training 3 times/wk (RCT)	Strength training: improved HbA1c ($P=0.001$), insulin sensitivity ($P=0.04$), blood pressure ($P<0.001$); endurance training: improved blood pressure only ($P=0.002$)
Sigal, 2007 (200)	n=251 adults with type 2 diabetes/6 mo	Aerobic training vs resistance training vs combined exercise training (3 times/wk for all groups) vs sedentary control (RCT)	HbA1c: aerobic ↓ 0.43%, resistance training ↓ 0.30%, combined ↓ 0.90%, control ↑ 0.07% (combined groups total duration of exercise was longer); blood pressure and lipids: NS between groups
Kelley, 2007 (203)	n=7 studies with 220 adults with type 2 diabetes/studies 10-26 wk	Effects of aerobic exercise on lipids and HbA1c (meta-analysis)	Low-density lipoprotein cholesterol[i] ↓ 5% (mean −6.4 mg/dL; 95% confidence interval −11.8, −1.1; $P<0.05$); TC, high-density lipoprotein cholesterol, TG: NS reduction; HbA1c (trend for reduction)
Conn, 2007 (201)	n=103 studies with 10,455 participants with type 2 diabetes/not specified	Effects of diabetes self-management interventions that recommended increase exercise vs control (meta-analysis)	Exercise vs control: effect size consistent with a HbA1c difference ↓ 0.45
McAuley, 2007 (202)	n=831 patients with type 2 diabetes referred for exercise testing/mean follow-up 4.8±3.0 y	Patients classified by body mass index and exercise capacity (<5.0 or ≥5.0 maximal METS) (cohort study)	Each 1 MET ↑ =10% survival benefits (hazard ratio: 0.90, 95% confidence interval 0.82-0.98; $P=0.01$); body mass index: NS association with mortality
Wing, 2007 (204)	n=5,145 participants from Look AHEAD/baseline data	Association of cardiorespiratory fitness and obesity (cross-sectional study)	Body mass index average: 36±5.9; maximal average MET: 8.0±2.1 for men, 6.7±4.3 for women; body mass index and fitness highly associated ($P<0.0001$); heaviest least fit; HbA1c associated with fitness and SBP associated with body mass index; lipids not associated with either

[a]METS=metabolic equivalents; a unit of intensity equal to energy expenditure at rest.
[b]HbA1c=glycosylated hemoglobin.
[c]SBP=systolic blood pressure.
[d]TG=triglycerides.
[e]To convert mg/dL triglycerides to mmol/L, multiply mg/dL by 0.0113. To convert mmol/L triglycerides to mg/dL, multiply mmol/L by 88.6. Triglycerides of 159 mg/dL=1.80 mmol/L.
[f]TC=total cholesterol.
[g]NS=non-significant.
[h]VO_2=maximal oxygen uptake.
[i]To convert mg/dL cholesterol to mmol/L, multiply mg/dL by 0.0259. To convert mmol/L cholesterol to mg/dL, multiply mmol/L by 38.7. Cholesterol of 193 mg/dL=5.0 mmol/L.

Table 13. Studies reporting on the effects of physical activity in persons with type 1 diabetes

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Roberts, 2002 (195)	n=24 patients with type 1 diabetes/12 wk	Supervised vs unsupervised exercise training (RCT[a])	HbA1c[b]: no change in supervised training and remained stable during unsupervised ($P<0.05$)
Tsalikian, 2005 (198); Tansey, 2006 (199)	n=46 patients with type 1 diabetes/75 min exercise session	Blood tests done before, during and after an exercise session (randomized crossover trial)	In 83% patients, plasma glucose[c] ↓ at least 25% from baseline; 30% became hypoglycemic (<60 mg/dL) either during or after exercise; incidence of hypoglycemia varied by baseline glucose: 86% (<120) vs 13% (120-180) vs 6% (>180 mg/dL) ($P<0.001$); hypoglycemia developed overnight more often on exercise nights than on sedentary nights ($P=0.009$)
Waden, 2005 (197)	n=1,030 patients with type 1 diabetes/not applicable	Sedentary (n=247) vs moderately active (n=568) vs active (n=215) (cross-sectional study)	Sedentary women had higher HbA1c than moderately or active (8.8%±1.4% vs 8.3%±1.4%, $P=0.004$); physical activity did not correlate with HbA1c in men
Samblad, 2005 (196)	n=26 females with type 1 diabetes/7 d	Physical activity and energy intake assessed (prospective cohort study)	No association observed between physical activity, energy intake and HbA1c
Herbst, 2007 (205)	n=23,251 patients with type 1 diabetes/not applicable	Impact of regular physical activity on lipids and blood pressure (cross-sectional study)	HbA1c lower in pts with higher frequency of physical activity and with higher frequency of physical activity dyslipidemia ↓ from 41.2% to 34.4% (both $P<0.00001$); no difference in blood pressure
Guelfi, 2007 (206)	Not applicable	Managing risks of exercise in type 1 diabetes (review article)	Continuous moderate-intensity exercise increases risk of hypoglycemia both during and for up to 31 h after; sustained high-intensity exercise causes a progressive rise in blood glucose; intermittent high-intensity exercise (such as team sports) causes an attenuation of the decline in blood glucose
Rachmiel, 2007 (207)	Not applicable	Exercise recommendations for type 1 diabetes (review article)	Physiology and metabolic effects of exercise reviewed in persons without and with type 1 diabetes; exercise precautions and recommendations are listed

[a]RCT=randomized controlled trials.
[b]HbA1c=glycosylated hemoglobin.
[c]To convert mg/dL glucose to mmol/L, multiply mg/dL by 0.0555. To convert mmol/L glucose to mg/dL, multiply mmol/L by 18.0. Glucose of 108 mg/dL=6.0 mmol/L.

In addition, hypoglycemia developed in participants overnight more often on exercise nights than on sedentary nights.

Research Published after Completion of the Initial Recommendations

Sigal and colleagues (200) evaluated the effects on HbA1c in persons with type 2 diabetes from aerobic or resistance training alone or a combination of the two and concluded that both aerobic and resistance training alone improve glycemic control but improvements are greatest when the two are combined (although total duration of exercise was also longer). A meta-analysis of 103 research studies with 10,455 participants with type 2 diabetes assessed the effect of diabetes self-management interventions that included recommendations to increase exercise for benefit to metabolic outcomes and concluded that interventions that emphasize exercise are especially effective in improving metabolic control (201). The overall mean weighted effect size for exercise vs control group comparison was 0.29 (higher for treatment than control), an effect size that is consistent with a mean improvement in HbA1c of 0.45%. Another study documented the inverse association between exercise capacity and all-cause mortality, independent of BMI (202), which was also reported in two previous studies (193,194).

A meta-analysis by Kelley and colleagues (203) examined the effects of aerobic exercise on lipids and lipoproteins in adults with type 2 diabetes. They concluded that aerobic exercise lowers LDL cholesterol by about 5%, whereas, no statistically significant improvements were found in other blood lipid values. Wing and colleagues (204) examined the role of fitness and fatness on CVD risk in participants enrolled in the Look AHEAD study and reported that although fitness and fatness were highly associated with each other (heaviest participants were less fit), they appear to have a different affect on specific CVD risk factors. HbA1c was strongly inversely associated with fitness (more fit, lower HbA1c), whereas systolic blood pressure was strongly positively associated with BMI category (higher BMI, higher systolic blood pressure). Blood lipid levels were not consistently associated with either measurement.

In a cross-sectional study of patients with type 1 diabetes, increasing physical activity was associated with lower frequency of dyslipidemia and lower HbA1c levels (205). However, participation in exercise for individuals with type 1 diabetes also poses challenges. Two reviews summarized problems with hypoglycemia and hyperglycemia (206,207). Participation in continuous moderate-intensity exercise (aerobic activity between 40% and 59% of maximum oxygen uptake or 55% to 69% maximal heart rate) increases the risk of hypoglycemia, both during and for up to 31 hours of recovery time, whereas during sustained high-intensity exercise (approximately 15 minutes at >80% of maximum oxygen uptake) a progressive rise in blood glucose levels can occur. Combinations of the two referred to as intermittent high-intensity exercise (such as activity patterns of many team and field sports) are not as well studied.

In a review, Rachmiel and colleagues (207) suggested recommendations for insulin adjustments for exercise. With planned mild-to-moderate exercise, a reduction in

premeal insulin by 30% to 50% is recommended, according to the intensity and duration of the activity. With unplanned activity and when insulin has not been adjusted, an extra 15 to 30 g carbohydrate for every 60 minutes of moderate activity needs to be added and 15 to 30 g should be consumed after activity ends. Furthermore, pre-bedtime blood glucose should be >130 mg/dL (7.21 mmol/L) on days of afternoon or evening activity. With hyperglycemia caused by vigorous activity, an additional bolus of insulin should only be added after studying the individual's response to vigorous activity on several occasions.

Recommendations for Physical Activity

In persons with type 2 diabetes, 90 to 150 minutes of accumulated moderate-intensity aerobic physical activity per week as well as resistance/strength training three times per week is recommended. Both aerobic and resistance training improve glycemic control, independent of weight loss. Individuals who are already exercising at moderate intensity may be encouraged to consider increasing the intensity of their exercise to obtain additional benefits in both aerobic fitness and glycemic control. Physical activity also improves insulin sensitivity and decreases risk for CVD and all-cause mortality.

Individuals with type 1 diabetes should be encouraged to engage in regular physical activity. Although exercise is not reported to improve glycemic control in persons with type 1 diabetes, individuals may receive the same benefits from exercise as the general public—decreased risk of CVD and improved sense of well-being.

RDs should instruct individuals taking insulin or insulin secretagogues on safety guidelines to prevent hypoglycemia (eg, frequent blood glucose monitoring, possible adjustments in insulin dose or carbohydrate intake, and to carry carbohydrate food/beverages while exercising). Carbohydrate should be ingested if pre-exercise glucose levels are <100 mg/dL (5.55 mmol/L). Research indicates that the incidence of hypoglycemia during exercise may depend on baseline glucose levels.

Limitations of Current Research and Additional Research Needed for Physical Activity

Research in patients with type 2 diabetes has demonstrated the benefits of aerobic and resistance physical activities. However, research regarding the benefits and risks of physical activity in persons with type 1 diabetes is more limited. Individuals must learn to minimize risks by self-adjusting insulin doses or by intake of carbohydrate. Although some research has examined insulin adjustments, very little research has been done on type and amounts of carbohydrate to consume with exercise. This type of research is needed to help individuals and health professionals better understand how individuals with type 1 diabetes can safely participate in all types of physical activities.

GLUCOSE MONITORING EVIDENCE AND RECOMMENDATIONS

Before the 1980s, outside of laboratory blood glucose testing, urine was tested to indicate high blood glucose values. Since then, single point measurement of blood glucose and the laboratory value HbA1c have been used as measures of glycemic control in persons with diabetes. Although self-monitoring of blood glucose (SMBG) is recommended for persons using insulin, its usefulness in the management of type 2 diabetes is debated. Twenty studies that met predetermined criteria were reviewed to evaluate the relationship between SMBG and metabolic outcomes in persons with type 1 diabetes and type 2 diabetes (Table 14).

The next generation of glucose monitors is the continuous glucose monitoring devices, which measure glucose in interstitial fluid and provide readings every 5 to 10 minutes. They also have alarms for glucose highs and lows and the ability to download data and track trends over time. To determine the relationship between continuous glucose monitoring and metabolic outcomes, 14 studies meeting predetermined criteria were reviewed (Table 14).

Research Reviewed

Prospective intervention studies in patients with type 1 diabetes that included self-management training and adjustment of insulin doses based on SMBG showed significant improvement in glycemic control compared to study control groups (8,9). More frequent SMBG was also associated with better glycemic control, regardless of diabetes type or therapy (208).

In six studies in patients with type 2 diabetes, SMBG compared to non-SMBG was associated with greater improvement in HbA1c when it was a part of structured education programs and individuals used the information to make changes in the their management program (208-213). Evidence on optimum frequency and duration of SMBG, however, is inconclusive (208,214-221). Three studies reported greater reductions in HbA1c with SMBG ranging from one to three tests per day compared to no SMBG (211,213,217). In adults with type 2 diabetes treated with nutrition therapy and exercise, HbA1c decreased incrementally with each increase in SMBG frequency (208).

Six studies using continuous glucose monitoring reported improvements in glycemic control (222-227) and six studies reported improvements in hyper- and hypoglycemic ranges (225,227-233). Although data derived from continuous glucose monitoring can be used to modify food or insulin therapy, there is little research that examines whether use of this information will improve metabolic outcomes significantly more than use of information from SMBG. Two studies found that both methods improved HbA1c (226,230); however, one study reported only continuous glucose monitoring improved HbA1c (224), and one study reported that only continuous glucose monitoring reduced hyperglycemia (232). Three studies reported on normative glucose data and patterns from using continuous glucose monitoring (233-235).

Research Published after Completion of the Initial Recommendations

The question of whether to recommend SMBG among persons with type 2 diabetes who are not taking insulin continues to be debated. Although one study reported

Table 14. Studies reporting on the relationship between self-monitoring of blood glucose and continuous glucose monitoring and metabolic outcomes

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
DCCT[a] Research Group, 1993 (8)	n=1,398 patients with type 1 diabetes/6.5 y	Conventional vs intensive therapy (insulin pump or insulin >3/d, monthly clinic visits including registered dietitian visits) (RCT[b])	Intensive diabetes therapy reduced the overall risk for onset and progression of diabetic retinopathy, nephropathy, and neuropathy by ~50%
Karter, 2001 (208)	24,312 adults with type 1 or type 2 diabetes/data assessed over a 12-y period	Analysis of data from a questionnaire or telephone survey (cohort study)	More frequent SMBG[c] was associated with better glycemic control regardless of type or therapy; type 1 diabetes (P=0.0001), type 2 diabetes on insulin (P=0.0001), type 2 diabetes on oral agents (P=0.001)
DAFNE[d] Study Group, 2002 (9)	n=136 adults with type 1 diabetes/6 mo	5-d course taught by registered dietitians and nurse specialists; taught to adjust mealtime insulin based on planned CHO[e] intake vs control (fixed insulin doses) (RCT)	Treatment group vs control: HbA1c[f] ↓ 1.0%, 9.4%→8.4% (P<0.0001) and quality of life improved (P<0.01); no change in severe hypoglycemia, lipids, and weight
Allen, 1990 (209)	n=54 men with type 2 diabetes, no insulin use/6 mo	SMBG groups or urine (glucose) testing, monthly clinic visits, registered dietitian instructed all patients (RCT)	Change in HbA1c: NS[g] between groups; HbA1c ↓ in both groups (P<0.03-0.001)
Coster, 2000 (214)	6 RCT with 27-208 participants with type 2 diabetes/not applicable	Effectiveness of blood or urine self-monitoring (meta-analysis)	Estimated ↓ HbA1c with either was 0.25% (95% confidence interval −0.61% to −0.10%) vs no monitoring: NS difference between methods
Franciosi, 2001 (220)	n=2,855 patients with type 2 diabetes, all therapies/not applicable	Questionnaires at study entry, data collection from medical records (cross-sectional)	HbA1c lower when SMBG ≥1/day vs doing it less frequently (P=0.0001); improved HbA1c with higher frequency of SMBG in participants who adjusted their insulin (P<0.002)
Harris, 2001 (215)	n=1,480 adults with type 2 diabetes/not applicable	Completion of questionnaire and measurement of HbA1c (cross-sectional)	Frequency of SMBG not related to HbA1c within each diabetes therapy category (P≥0.5)
Meier, 2002 (216)	n=1,467 adults with type 2 diabetes, no insulin use/6 mo	Done to determine effect of reimbursing less SMBG strips (cohort study)	Decrease in SMBG utilization (P<0.001) without significant change in HbA1c
Schwedes, 2002 (211)	223 adults with type 2 diabetes not on insulin/6 mo+6 mo follow-up	SMBG (6 times/d, 2 d/wk) vs control (RCT)	SMBG vs control: HbA1c ↓ from baseline (P=0.0086) at 6 mo; 87% continued SMBG and glucose remained stable
Murata, 2003 (217)	n=201 adults with type 2 diabetes on insulin/8 wk, follow-up to wk 52	SMBG premeal and bedtime; compliance with SMBG assessed (cohort study)	At 8 wks, participants with highest HbA1c (>8.0%) and >75% compliance with SMBG ↓ HbA1c (P<0.001); maintained to wk 52 (P=0.001)
Jaworska, 2004 (218)	n=218 patients with type 2 diabetes/not applicable	Questionnaire completed; HbA1c from medical records (cross-sectional)	NS difference in HbA1c between participants performing SMBG at different frequencies
Wen, 2004 (219)	n=976 patients with type 2 diabetes on oral agents/3-y period	Review of clinic records and prescriptions of SMBG (cohort study)	NS association between duration of SMBG and glycemic control
Sarol, 2005 (213)	8 RCTs with 1,307 participants with type 2 diabetes/not applicable	SMBG vs no SMBG in participants not on insulin (meta-analysis)	SMBG ↓ HbA1c 0.39% (fixed effects model) and 0.42% (random effects model) vs no SMBG
Davidson, 2005 (212)	n=88 adults with type 2 diabetes, no insulin use at entry/6 mo	SMBG group vs control group, registered dietitian and nurse provided education (RCT)	Change in HbA1c NS between groups at study end (P=0.58)
Franciosi, 2005 (210)	n=1,896 patients with type 2 diabetes, no insulin use/3 y	Questionnaires at study entry and every 6 mo, documentation of SMBG and HbA1c (cohort study)	NS difference in HbA1c between subgroups with differing SMBG testing frequency (P=0.001)
Martin, 2006 (221)	n=3,268 adults with type 2 diabetes/8 yrs	Medical record data collection from time of diabetes diagnosis to nonfatal or fatal endpoint or study end (cohort study)	SMBG compared to non-SMBG associated with ↓ diabetes-related morbidity (hazard ratio 0.63) and all-cause mortality (hazard ratio 0.52)
Kaufman, 2001 (222)	n=40 adolescents with type 1 diabetes/3 mo	CGMS[h] vs SMBG to alter insulin regimen (time series)	CGMS found 4-7 times as many patterns as SMBG logs; HbA1c ↓ from baseline to 3 mo (P=0.03)
Schiaffini, 2002 (228)	n=27 adolescents with type 1 diabetes/6 wk	Study 1: CGMS (worn for 3 d) vs SMBG; Study 2: CGMS worn again at 6 wk, patterns used to adjust insulin (time series)	Study 1: glucose similar between CGMS and SMBG; however CGMS revealed higher number of hypoglycemic events (P<0.0001). Study 2. Incidence of hypoglycemia ↓ from baseline to 6 wk (P<0.05)
Schaepelynck-Belicar, 2003 (225)	n=12 patients with type 1 diabetes/6 mo	CGMS (baseline and at 2 mo) used to modify insulin therapy (time series)	HbA1c ↓ from 10.3% to 8.75% (P<0.05)
Ludvigsson, 2003 (224)	n=27 adolescents with type 1 diabetes/3 mo on each arm	Adjusting insulin: open arm using CGMS patterns vs blind arm using SMBG (crossover RCT)	HbA1c ↓ during open arm (P=0.013) but not during blind arm; hypoglycemia NS between arms
Chico, 2003 (223)	n=75 patients with type 1 diabetes and 30 with type 2 diabetes/3 mo	CGMS wore sensors for 3 d (therapy changes based on CGMS patterns) vs control did 3 d intensive SMBG (therapy changes based on SMBG patterns) (RCT)	HbA1c ↓ in both groups (P<0.01 for both groups); CGMS detected unrecognized hypoglycemia in 62% type 1 and 46.6% type 2 patients
Bode, 2004 (229)	n=71 adults with type 1 diabetes/two 72-hr periods	Alert group (real time sensors off first period and on second period) vs control group (sensors off both periods) (RCT)	Duration of hypoglycemia ↓ (64 to 34 min) in alert group and ↑ in control (64 to 70 min) (P=0.03 between groups)

(continued)

Table 14. Studies reporting on the relationship between self-monitoring of blood glucose and continuous glucose monitoring and metabolic outcomes (continued)

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Deiss, 2004 (226)	n=50 patients with type 1 diabetes/6 wks	CGMS used to compare glycemia before and after starting CSII[i] (time series)	HbA1c ↓ from baseline to end of study (P=0.0002); SMBG and CGMS both indicated similar improvement in 24-hr average glucose; no change in hypoglycemic events
Weintrob, 2004 (231)	n=21 adolescents with type 1 diabetes/3.5 mo multiple daily injections; 3.5 mo CSII	CSII (used insulin to carbohydrate ratios) vs multiple daily injections (fixed CHO) 3 d of CGMS at 2 wk and 3.5 mo used to adjust insulin in both groups (cross-over RCT)	HbA1c: NS between groups; CSII vs multiple daily injection ↓ total area under the glucose curve for nocturnal hypoglycemia (P=0.01) and postprandial total area under the glucose curve (P=0.05)
Garg, 2004 (230)	N=15 adults with type 1 diabetes/94 d	CGMS glucose measurements available to participants vs being blinded to measurements (nonrandomized clinical trial)	Unblinded participants spent 47% less time below 55 mg/dL[j] and 25% less time above 240 mg/dL vs blinded (P<0.05)
Tanenberg, 2004 (227)	n=109 with diabetes on insulin/3 mo	Therapy modified based on CGMS and SMBG at visits 3 and 5 vs therapy modified based on SMBG records (RCT)	HbA1c ↓ (9.1% to 8.3%) in both groups (P<0.001 for both groups); CGMS vs SMBG: hypoglycemia ↓ minutes/events (P=0.009)
Manuel-y-Keenoy, 2004 (233)	n=23 adults with type 1 diabetes/17 h	CGMS used to determine breakfast and lunch postprandial glucose (cross-sectional)	Lunch 2-h glucose and maximum glycemia less than breakfast postprandial glucose (P<0.0001 for both)
Streja, 2005 (235)	n=60 adults with type 1 diabetes/3 d	CGMS used to determine best predictors of hypoglycemia unawareness (cross-sectional)	Best predictor of hypoglycemia unawareness was maximal duration of hypoglycemia (P=0.001), followed by use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (P=0.003), and longer duration of diabetes (P=0.008)
Bode, 2005 (234)	n=60 patients with type 1 diabetes and 41 with type 2 diabetes/12 d	Participants wore CGMS to collect normative data (observational study)	Participants remained euglycemic ~63% of total day, were hypoglycemic ~8%, and were hyperglycemic 29%
Garg, 2006 (232)	n=75 adults with type 1 diabetes and 16 with type 2 diabetes on insulin/3 continuous 72-h periods	CGMS with hypo/hyperglycemic alarms vs SMBG only to self-adjust insulin (RCT)	CGMS vs SMBG: 21% less time as hypoglycemic and 23% less time as hyperglycemic and 26% more time in target range (all P<0.001); nocturnal hypoglycemia reduced (P<0.05)
Schütt, 2006 (236)	n=19,491 with type 1 diabetes, n=5,009 with type 2 diabetes/not applicable	Relationship between frequency of SMBG to long-term metabolic control (cross-sectional)	Patients with type 1 diabetes intensified therapy: more frequent SMBG associated with ↓ HbA1c (−0.32% for 1 additional SMBG/d); patients with type 2 diabetes on insulin therapy: (−0.16% for 1 additional SMBG/d); patients on oral agents or diet alone: no benefit
Jansen, 2006 (237)	13 studies with patients with type 2 diabetes/not applicable	3 types of studies compared: SMBG vs no self-monitoring, SMBG vs urine glucose, SMBG with regular feedback vs monitoring without feedback (meta-analysis)	SMBG vs no self-monitoring: HbA1c ↓ 0.4% (95% confidence interval 0.07 to 0.70%); regular feedback doubled the HbA1c ↓; self-monitoring of urine results similar to no monitoring (0.02% ↓ HbA1c)
Farmer, 2007 (238)	n=453 with type 2 diabetes not on insulin/12 mo	SMBG, alone, vs SMBG with instruction in use for self care vs usual care (RCT)	HbA1c: NS difference at 12 mo between 3 groups (P=0.12)
Bajkowska-Fiedziukiewicz, 2008 (239)	n=600 with type 2 diabetes/not applicable	Association between frequency of SMBG and HbA1c (cross-sectional)	No correlation between HbA1c levels and frequency of SMBG frequency
JDRF CGM[k] Study Group, 2008 (242)	n=322 adults and children with type 1 diabetes on intensive therapy/26 wk	CGMS vs C using SMBG; all patients stratified into 3 age groups (RCT)	Change in HbA1c varied by age group (P=0.003); in patients >25 y CGMS: average difference in change, −0.53% (P<0.001); NS differences in age 15-24 y or 8 to 14 y
Pearce, 2008 (245)	n=23 patients with type 2 diabetes/12 d	Composition of 4 diets: 40% CHO, 34% protein, 26% fat; carbohydrate evenly distributed, 70 g/meal vs carbohydrate loaded at breakfast, 125 mg vs carbohydrate loaded at lunch, 125 mg vs carbohydrate loaded at dinner, 125 mg; glucose measured by CGMS (crossover study)	Peak postprandial glucose ↑ after CHO loaded at breakfast with CHO evenly distributed at meals, CHO loaded at lunch, and CHO loaded at dinner having similar peaks (P=0.003); time spent >215 mg/dL lowest with CHO loaded at lunch followed by CHO loaded at dinner and CHO evenly distributed; total area under the curve NS difference between meals
Yoo, 2008 (244)	n=65 patients with type 2 diabetes and HbA1c between 8.0% and 10.0%/3 mo	CGM monthly (3 d at a time/3 mo) vs SMBG (RCT)	CGM vs SMBG: HbA1c ↓ (P=0.004); CGM group: ↓ in daily kcal (P=0.002), weight (P=0.014), PPG (P=0.034) and ↑ in exercise (P=0.02)
Chetty, 2008 (243)	7 studies with 335 patients with type 1 diabetes/12 to 24 wks	Difference in HbA1c from CGMS vs SMBG in RCT (systematic review)	CGMS vs SMBG: NS ↓ HbA1c (0.22%, P=0.055); some indication of ↑ detection of asymptomatic nocturnal hypoglycemia with CGMS
O'Kane, 2009 (241)	n=184 patients with newly diagnosed type 2 diabetes/1 y	SBGM vs control (no monitoring) (RCT)	HbA1c: NS differences between group (P=0.69), use of diabetes drugs, or incidence of hypoglycemia; monitoring ↑ score on depression subscale (P=0.01)

(continued)

Table 14. Studies reporting on the relationship between self-monitoring of blood glucose and continuous glucose monitoring and metabolic outcomes (continued)

First author, y, (reference)	Population/duration	Intervention (type)	Major findings
Welschen, 2005 (240)	n=6 RCT of SMBG in patients with type 2 diabetes not using insulin/not applicable	SMBG vs usual care and/or with urine glucose testing (review)	2 of 6 reported significant lowering effect of SMBG on HbA1c (however, 1 also had co-intervention with diet); methodological quality of studies was low

[a]DCCT=Diabetes Control and Complications Trial.
[b]RCT=randomized controlled trial.
[c]SMBG=self-monitoring blood glucose.
[d]DAFNE=dose adjustment for normal eating.
[e]CHO=carbohydrate.
[f]HbA1c=glycosylated hemoglobin.
[g]NS=non-significant.
[h]CGMS=continuous glucose monitoring sensors.
[i]CSII=continuous subcutaneous insulin infusion.
[j]To convert mg/dL glucose to mmol/L, multiply mg/dL by 0.0555. To convert mmol/L glucose to mg/dL, multiply mmol/L by 18.0. Glucose of 108 mg/dL=6.0 mmol/L.
[k]JDRF CGM=Juvenile Diabetes Research Foundation Continuous Glucose Monitoring.

improvement in HbA1c values in persons with type 1 diabetes or with type 2 diabetes on insulin (236), four studies reported no benefits on HbA1c from SMBG in persons with type 2 diabetes on oral agents or nutrition therapy alone (236-239). A Cochrane Review of six studies of SMBG in patients with type 2 diabetes not using insulin concluded that SMBG in these patients might be effective. However, because the methodological quality of these studies was low, the authors concluded that a large and well-designed trial is required to determine the role of SMBG in persons with type 2 diabetes (240).

Four studies compared continuous glucose monitoring with SMBG (241-244). One study reported that change in HbA1c varied by age group—continuous glucose monitoring benefiting adults (aged >25 years) with type 1 diabetes but not children and young adults aged 8 to 24 years (242). A systematic review of seven studies in persons with type 1 diabetes (five were in participants younger than age 18 years) reported no significant changes in HbA1c from continuous glucose monitoring compared to SBMG, but noted an indication that continuous glucose monitoring may increase detection of asymptomatic nocturnal hypoglycemia (243). A study in persons with type 2 diabetes reported improvement in HbA1c, daily energy intake, body weight, postprandial glucose, and exercise with continuous glucose monitoring compared to SMBG and suggested that continuous glucose monitoring may be useful in helping patients modify lifestyle habits that could lead to better glycemic control (244). Another study used continuous glucose monitoring to study the effect of carbohydrate distribution on postprandial glucose. Evenly distributed carbohydrate intake did not optimize glucose control as measured by postprandial peaks. Postprandial glucose values with an equal amount of carbohydrate were higher after breakfast compared to after lunch (245).

Recommendations for Glucose Monitoring

For persons with type 1 or type 2 diabetes on insulin therapy, at least three to eight glucose tests per day are recommended to determine the adequacy of the insulin dose(s) and to guide adjustments in insulin dose(s), food intake, and physical activity. Some insulin regimens require more testing to establish the best integrated therapy (ie, food, insulin, and activity). Once established, some insulin regimens will require less frequent SMBG. Intervention studies that include self-management training and adjustment of insulin doses based on SMBG report improved glycemic control.

For individuals receiving nutrition therapy alone or nutrition therapy in combination with glucose-lowering medications, SMBG can be recommended. Frequency and timing is dependent on diabetes management goals and therapies (ie, MNT, diabetes medications, and physical activity). When SMBG is incorporated into diabetes education programs and the information from SMBG is used to make changes in diabetes management, SMBG is associated with improved glycemic control.

Persons experiencing unexplained elevations in HbA1c or unexplained hypoglycemia and hyperglycemia may benefit from use of continuous glucose monitoring or more frequent SMBG. It is essential that persons with diabetes receive education as to how to use a continuous glucose

monitoring device and how to interpret and apply the results. Studies have proven the accuracy of continuous glucose monitoring and most show that using the trend/data pattern data from continuous glucose monitoring can result in less glucose variability and improved glucose control.

Limitations of Current Research and Additional Research Needed for Glucose Monitoring

Research on use of SMBG by persons with type 2 diabetes continues to be studied and debated. Additional research is needed to determine how best to assist individuals to use the information to improve glycemic control. Research in the use of continuous glucose monitoring will continue. Research on how foods and nutrients affect blood glucose responses and how to make adjustments in carbohydrate and insulin for exercise will be especially helpful. Continuous glucose monitoring is also the next step in the development of closed loop insulin therapy.

EFFECTIVENESS OF MNT FOR TYPE 1 AND TYPE 2 DIABETES IN ADULTS

Articles on the effectiveness of diabetes MNT interventions have been published in a supplement to the *Journal of the American Dietetic Association* (246). Twenty-one randomized controlled trials and observational studies are included in the review and summarize the evidence, both for MNT and for MNT in combination with diabetes self-management training. HbA1c is the clinical outcome reported because it is consistently reported across all studies. Some studies also reported improved lipid profiles, blood pressure, and weight management, adjustments in medications, and reduction in the risk for onset and progression of comorbidities.

The studies document decreases in HbA1c ranging from 0.5% to 2.6% (average of ~1% to 2%), similar to the effects of many glucose-lowering medications. Multiple individual or group sessions were employed initially and on a continued basis. Although MNT is effective at any time in the disease process, it appears to have its greatest affect in lowering HbA1c at initial diagnosis. Outcomes of the MNT interventions are evident by 6 weeks to 3 months and evaluation should be done at these times. At 3 months, if no clinical improvement in glycemic control is evident, an RD needs to recommend combining MNT with medication therapy or an adjustment in medication therapy. Type 2 diabetes is a progressive disease, and as β-cell function decreases, blood glucose lowering medication(s), including insulin, need to be combined with MNT to achieve glucose goals.

Attempts are often made to identify one approach to diabetes MNT; however, a single approach does not exist, just as there is no one medication or insulin regimen that applies to all persons with diabetes. A variety of interventions, such as reduced energy/fat intake, carbohydrate counting, simplified meal plans, healthy food choices, low-fat vegan diet, individualized meal-planning strategies, exchange lists, insulin-to-carbohydrate ratios, physical activity, and behavioral strategies were implemented in the reviewed studies. Furthermore, nutrition education and counseling must be sensitive to the personal needs and cultural preferences of the individual and their willingness and ability to make changes. This increases the complexity of developing an individualized nutrition intervention and the subsequent counseling needed for implementation. Research, however, documents the benefits of RDs addressing these challenges and improving outcomes in people with diabetes.

Based on the evidence, the ADA EBNPG recommends that individuals with diabetes be referred for MNT early after the diagnosis of diabetes. A series of MNT encounters that involve the Nutrition Care Process of nutrition assessment, nutrition diagnosis, nutrition interventions, and nutrition monitoring and evaluation are recommended. Ongoing MNT follow-up encounters are also important to support lifestyle changes, evaluate nutrition-related outcomes, and assess medication needs. Changes in MNT and/or medications are often necessary throughout an individual's life.

INTEGRATING RECOMMENDATIONS INTO THE NUTRITION CARE PROCESS

The EBNPG recommendations are integrated throughout the Nutrition Care Process. The following summarizes how the recommendations are applied throughout the Nutrition Care Process.

Implementation of MNT:

- An initial series of three to four encounters with an RD lasting from 45 to 90 minutes is recommended;
- this series, beginning at diagnosis of diabetes or at first referral to an RD for MNT for diabetes, should be completed within 3 to 6 months;
- an RD should determine whether additional MNT encounters are needed; and
- at least one follow-up encounter is recommended annually to reinforce lifestyle changes and to evaluate and monitor outcomes that indicate the need for changes in MNT or medication(s); an RD should determine whether additional MNT encounters are needed.

Nutrition assessment:

- An RD should assess food intake (focusing on carbohydrate), medication, metabolic control (eg, glycemia, lipids, and blood pressure), anthropometric measurements, and physical activity to serve as the basis for implementation of the nutrition prescription, goals and intervention;
- an RD should assess glycemic control and focus MNT to achieve and maintain blood glucose levels in the target range; and
- an RD should assess the relative importance of weight management for persons who are overweight or obese.

Nutrition interventions:

- An RD should implement MNT selecting from a variety of nutrition interventions that will assist patients/clients to achieve nutrition therapy goals;
- an RD should encourage consumption of macronutrients based on the Dietary Reference Intakes for healthy adults; and

- an RD should implement nutrition education and counseling with an emphasis on the recommendations from the major and contributing factors to nutrition therapy reviewed above.

Nutrition monitoring and evaluation:

- An RD should coordinate care with an interdisciplinary team;
- an RD should monitor and evaluate food intake, medication, metabolic control (eg, glycemia, lipids, and blood pressure), anthropometric measurements, and physical activity; and
- an RD should primarily use blood glucose monitoring results in evaluating the achievement of goals and effectiveness of MNT. Glucose monitoring results can be used to determine whether adjustments in foods and meals will be sufficient to achieve blood glucose goals or if medication additions or adjustments need to be combined with MNT.

CONCLUSIONS

The ADA has published EBNPGs for type 1 and type 2 diabetes in adults in the EAL. This review outlines the process for developing the guidelines, identified major and contributing factors for diabetes nutrition therapy, reviewed and summarized research, and stated the nutrition practice recommendations that are to be integrated into the Nutrition Care Process. The EBNPGs provide recommendations for assessing client/patient needs and for selecting interventions, monitoring, and evaluating outcomes. The evidence is strong that MNT provided by RDs is an effective and essential therapy in the management of diabetes. RDs are uniquely skilled in this process.

STATEMENT OF POTENTIAL CONFLICT OF INTEREST: No potential conflict of interest was reported by the authors.

ACKNOWLEDGEMENTS: The authors thank Kari Kren, MPH, RD; Deborah Cummins, PhD; Esther Meyers, PhD, RD; and lead analyst Erica Gradwell, MS, RD, for professional assistance. The authors also thank the following analysts: Eric Ciappio, MS, RD; Debby Demory-Luce, PhD, RD; Lori Greene, MS, RD; Carol Klitzke, MS, RD; Patti Landers, PhD, RD; Mamie Lausch, MS, RD, RN; Barbara Mark, PhD, RD; Linda Massey, PhD, RD; Melissa Reutimann, RD; Lee Wallace, MS, RD; Madelyn Wheeler, MS, RD; and Jane Ziegler, RD.

References

1. ADA diabetes type 1 and 2 evidence-based nutrition practice guideline for adults. American Dietetic Association Evidence Analysis Library Web site. http://www.adaevidencelibrary.com/topic.cfm?=3252. Accessed September 19, 2010.
2. American Diabetes Association. Nutrition recommendations and interventions for diabetes. A position statement of the American Diabetes Association. *Diabetes Care*. 2008;31(suppl 1):S61-S78.
3. American Dietetic Association. *Nutrition Practice Guidelines for Type 1 and Type 2 Diabetes Mellitus* [CD-ROM]. Chicago, IL: American Dietetic Association; 2001.
4. American Dietetic Association Scientific Affairs and Research. *American Dietetic Association Evidence Analysis Manual,* Edition IV. Chicago, IL: American Dietetic Association; 2003, updated 2005.
5. Wolever TMS, Hamad S, Chiasson JL, Josse RG, Leiter LA, Rodger NW, Ross SA, Ryan EA. Day-to-day consistency in amount and source of carbohydrate intake associated with improved glucose control in type 1 diabetes. *J Am Coll Nutr*. 1999;18:242-247.
6. Boden G, Sargrad K, Homko C, Mozzoli M, Stein TP. Effect of a low-carbohydrate diet on appetite, blood glucose levels, and insulin resistance in obese patients with type 2 diabetes. *Ann Intern Med*. 2005;142:403-411.
7. Nielsen JV, Jonsson E, Ivarsson A. A low-carbohydrate diet in type 1 diabetes: Clinical experience—A brief report. *Upsala J Med Sci*. 2005;110:267-273.
8. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329:977-986.
9. DAFNE Study Group. Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: Dose adjustment for normal eating (DAFNE) randomized controlled trial. *Br Med J*. 2002;325:746-751.
10. Garg A, Bantle JP, Henry RR, Coulston AM, Griver KA, Raatz SK, Brinkley L, Chen Y-D I, Grundy SM, Huet BA, Reaven GM. Effects of varying carbohydrate content of diet in patients with non-insulin diabetes mellitus. *JAMA*. 1994;271:1421-1428.
11. Gerhard GT, Ahmann A, Meeuws K, McMurry MP, Duell PB, Connor WE. Effects of a low-fat diet compared with those of a high-monounsaturated fat diet on body weight, plasma lipids and lipoproteins, and glycemic control in type 2 diabetes. *Am J Clin Nutr*. 2004;80:668-673.
12. Nielsen JV, Jonsson E, Nilsson AK. Lasting improvement of hyperglycemia and body weight: Low-carbohydrate diet in type 2 diabetes. A brief report. *Upsala J Med Sci*. 2005;109:179-184.
13. Komiyama N, Kaneko T, Sato A, Sato W, Asami K, Onaya T, Tawata M. The effect of high carbohydrate diet on glucose tolerance in patients with type 2 diabetes mellitus. *Diabetes Res Clin Pract*. 2002;57:163-170.
14. Lowe J, Linjawi S, Mensch M, James K, Attia J. Flexible eating and flexible insulin dosing in patients with diabetes: Results of an intensive self-management course. *Diabetes Res Clin Pract*. 2008;80:439-443.
15. Bergenstal RM, Johnson M, Powers MA, Wynn A, Vlajnic A, Hollander P, Rendell M. Adjust to target in type 2 diabetes: Comparison of a simple algorithm with carbohydrate counting for adjustment of mealtime insulin glulisine. *Diabetes Care*. 2008;31:1305-1310.
16. Barnard ND, Gloede L, Cohen J, Jenkins DJA, 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;109:263-272.
17. Turner-McGrievy G, Barnard ND, Cohen J, Jenkins DJA, Gloede L, Green AA. Changes in nutrient intake and dietary quality among participants with type 2 diabetes following a low-fat vegan diet or a conventional diabetes diet for 22 weeks. *J Am Diet Assoc*. 2008;108:1636-1645.
18. Wolever TMS, Gibbs AL, Mehling C, Chiasson J-L, Connelly PW, Josse RG, Leiter LA, Maheux P, Rabasa-Lhoret R, Rodger NW, Ryan EA. 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;87:114-125.
19. 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;32:215-220.
20. 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;32:1147-1152.
21. 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;5:14-19.
22. Xu J, Eilat-Adar S, Loria CM, Howard BV, Fabsitz RR, Begum M, Zephier EM, Lee ET. Macronutrient intake and glycemic control in a population-based samples of American Indians with diabetes: The Strong Heart Study. *Am J Clin Nutr*. 2007;86:480-487.
23. Delahanty LM, Nathan DM, Lachin JM, Hu FB, Cleary PA, Ziegler GA, Wylie-Rosett J, Wexler DJ for the Diabetes Control and Complications Trial/Epidemiology of Diabetes. *Am J Clin Nutr*. 2009;89:518-524.
24. Kirk JK, Graves DE, Craven TE, Lipkin EW, Austin M, Margolis KL.

Restricted-carbohydrate diet in patients with type 2 diabetes: A meta-analysis. *J Am Diet Assoc*. 2008;108:91-100.
25. Kodama S, Saito K, Tanaka S, Maki M, Yachi Y, Sato M, Sugawara A, Totsuka K, Shimano H, Ohashi Y, Yamada N, Sone H. Influence of fat and carbohydrate proportions on the metabolic profile in patients with type 2 diabetes: A meta-analysis. *Diabetes Care*. 2009; 32:959-965.
26. Vitolins MZ, Anderson AM, Delahanty L, Raynor H, Miller GD. Mobley C, Reeves R, Yamamoto M, Champagne C, Wing RR, Mayer-Davis E and the Look AHEAD Research Group. Action for Health in Diabetes (Look AHEAD) Trial: Baseline evaluation of selected nutrients and food group intake. *J Am Diet Assoc*. 2009;109:1367-1375.
27. Chantelau EA, Gosseringer G, Sonnenberg GE, Berger M. Moderate intake of sucrose does not impair metabolic control in pump-treated diabetic outpatients. *Diabetologia*. 1985;29:204-207.
28. Peterson DB, Lambert J, Gerring S, Darling P, Carter RD, Jelfs R, Mann JI. Sucrose in the diet of diabetic patients—Just another carbohydrate? *Diabetologia*. 1986;29:216-220.
29. Bantle JP, Laine DC, Thomas JW. Metabolic effects of dietary fructose and sucrose in Types I and II diabetic subjects. *JAMA*. 1986; 256:3241-3246.
30. Buysschaert M, Sory R, Mpoy M, Lambert AE. Effect of the addition of simple sugars to mixed meals on the glycemic control of insulin treated diabetic patients. *Diabetes Metab*. 1987;13:625-629.
31. Cooper PL, Wahlquist ML, Simpson RW. Sucrose versus saccharin as an added sweetener in non-insulin-dependent diabetes: Short- and medium-term metabolic effects. *Diabetic Med*. 1988;5:676-680.
32. Santacroce G, Forlani G, Giangiulio S, Galuppi V, Pagani M, Vannini P. Long-term effects of eating sucrose on metabolic control of type 1 (insulin-dependent) diabetic outpatients. *Acta Diabetol Lat*. 1990;27:365-370.
33. Loghmani E, Rickard K, Washburne L, Vandagriff J, Fineberg N, Golden M. Glycemic response to sucrose-containing mixed meals in diets of children with insulin-dependent diabetes mellitus. *J Pediatrics*. 1991;119:531-537.
34. Bantle JP, Swanson JE, Thomas W, Laine DC. Metabolic effects of dietary sucrose in type II diabetic subjects. *Diabetes Care*. 1993;16: 1301-1305.
35. Schwingshandl J, Rippel S, Unterluggauer M, Borkenstein M. Effect of the introduction of dietary sucrose on metabolic control in children and adolescents with type 1 diabetes. *Acta Diabetol*. 1994;31:205-209.
36. Malerbi DA, Duarter Al, Palva ESA, Wajchenberg BL. Metabolic effects of dietary sucrose and fructose in Type II diabetic subjects. *Diabetes Care*. 1996;19:1249-1256.
37. Nadeau J, Koski KG, Strychar I, Yale JF. Teaching subjects with type 2 diabetes how to incorporate sugar choices into their daily meal plan promotes dietary compliance and does not deteriorated metabolic profile. *Diabetes Care*. 2001;24:222-227.
38. Bantle JP, Laine DC, Castle GW, Thomas JW, Hoogwerf BJ, Goetz FC. Postprandial glucose and insulin responses to meals containing different carbohydrates in normal and diabetic subjects. *N Eng J Med*. 1983;309:7-12.
39. Rickard KA, Cleveland JL, Loghmani ES, Fineberg NS, Freidenberg GR. Similar glycemic responses to high versus moderate sucrose-containing foods in test meals for adolescents with type 1 diabetes and fasting euglycemia. *J Am Diet Assoc*. 2001;101:1202-1205.
40. Shimakawa T, Warram JH, Herrera-Acena MG, Krolewski AS. Usual dietary intake and hemoglobin A_1 level in patients with insulin-dependent diabetes. *J Am Diet Assoc*. 1993;93:1409-1412,1415.
41. Coulston AM, Hollenbeck CB, Donner CC, Williams R, Chiou YM, Reaven GM. Metabolic effects of added dietary sucrose in individuals with non-insulin-dependent diabetes mellitus (NIDDM). *Metabolism*. 1985;34:962-966.
42. Position of the American Dietetic Association: Use of nutritive and nonnutritive sweeteners. *J Am Diet Assoc*. 2004;104:255-275.
43. Mezitis NH, Maggio CA, Koch P, Quddoos A, Allison DB, Pi-Sunyear FX. Glycemic effect of a single high oral dose of the novel sweetener sucralose in patients with diabetes. *Diabetes Care*. 1996;19:1004-1005.
44. Grotz VL, Henry RR, McGill JB, Prince MJ, Shamoon H, Trout JR, Pi-Sunyer FX. Lack of effect of sucralose on glucose homeostasis in subjects with type 2 diabetes. *J Am Diet Assoc*. 2003;103:1607-1612.
45. Reyna N, Cano C, Bermudez VJ, Medina MT, Souki AJ, Ambard M, Nunez M, Ferrer MA, Inglett GE. Sweeteners and beta-glucans improve metabolic and anthropometrics variables in well controlled type 2 diabetic patients. *Am J Therapeutics*. 2003;10:438-443.
46. Mackenzie T, Brooks B, O'Connor G. Beverage intake, diabetes, and glucose control of adults in America. *Ann Epidemiol*. 2006;9:688-691.
47. Garnier-Sagne I, Lebland JC, Verger P. Calculation of the intake of three intense sweeteners in young insulin-dependent diabetics. *Food Chem Toxicol*. 2001;7:745-749.
48. Cullen M, Nolan J, Cullen M, Moloney M, Kearney J, Lambe J, Gibney MJ. Effect of high levels of intense sweetener intake in insulin dependent diabetics on the ratio of dietary sugar to fat: A case-controlled study. *Eur J Clin Nutr*. 2004;58:336-341.
49. Ilback NG, Alzin M, Jahri S, Enghardt-Barbien H, Busk L. Estimated intake of the artificial sweeteners ascesulfame-K, aspartame, cyclamate and saccharin in a group of Swedish diabetics. *Food Addit Contam*. 2003;2:99-114.
50. Barriocanal LA, Palacios M, Benitez G, Benitez S, Jimenez JT, Jimenez N, Rojas V. Apparent lack of pharmacological effect of steviol glycosides used as a sweeteners in humans. A pilot study of repeated exposures in some normotensive individuals with type 1 and type 2 diabetics. *Regul Toxicol Pharmacol*. 2008;51:37-41.
51. Maki KC, Curry LL, Reeves MS, Toth PD, McKenney JM, Farmer MV, Schwartz SL, Lubin BC, Boileau AC, Dicklin MR, Carakostas MC, Tarka SM. Chronic consumption of rebaudioside A, a steviol glycoside, in men and women with type 2 diabetes mellitus. *Food Chem Toxicol*. 2008;46(suppl 7):S47-S53.
52. Renwick AG. The intake of intense sweeteners—An update review. *Food Addit Contam*. 2006;23:327-338.
53. Frost G, Wilding J, Beecham J. Dietary advice based on the glycemic index improves dietary profile and metabolic control in type 2 diabetic patients. *Diabet Med*. 1994;11:397-401.
54. Rizkalla SW, Boillot J, Taghrid L, Rigoir A, Laromiguiere M, Elgrably F, Huet D, Slama G. Improved plasma glucose control, whole-body glucose utilization, and lipid profile on a low-glycemic index diet in type 2 diabetic men: A randomized controlled trial. *Diabetes Care*. 2004;27:1866-1872.
55. Wolever TMS, Jenkins DJA, Vuksan V, Jenkins AL, Buckley GC, Wong GS, Josse RG. Beneficial effect of a low glycemic index diet in type 2 diabetes. *Diabet Med*. 1992;9:451-458.
56. Buyken AE, Toeller M, Heitkamp G, Karamanos B, Rorriers R, Muggeo M, Fuller JH. Glycemic index in the diet of European outpatients with type 1 diabetes: Relations to glycated hemoglobin and serum lipids. *Am J Clin Nutr*. 2001;73:574-581.
57. Burani J, Longo P. Low glycemic index carbohydrates: An effective behavioral changes for glycemic control and weight management in patients with type 1 and type 2 diabetes. *The Diabetes Educator*. 2006;32:78-88.
58. Wolever TMS, Nguyen PM, Chiasson JL, Hunt JA, Josse RG, Palmason C, Rodger NW, Ross SA, Ryan EA, Tan JH. Determinants of diet glycemic index calculated retrospectively from diet records of 342 individuals with non-insulin-dependent diabetes mellitus. *Am J Clin Nutr*. 1994;59:1265-1269.
59. Brand-Miller J, Petocz P, Hayne S, Colagiuri S. Low-glycemic index diets in the management of diabetes: A meta-analysis of randomized controlled trials. *Diabetes Care*. 2003;26:2261-2267.
60. Wolever TMS, Jenkins DJA, Jenkins AL, Josse RG. The glycemic index: Methodology and clinical implications. *Am J Clin Nutr*. 1991; 54:846-854.
61. Gilbertson HR, Brand-Miller JC, Thorburn AW, Evans S, Chondros P, Werther GA. The effect of flexible low glycemic index dietary advice versus measured carbohydrate exchange diets on glycemic control in children with type 1 diabetes. *Diabetes Care*. 2001;24:1137-1143.
62. Gilbertson HR, Thorburn AW, Brand-Miller JC, Chondros P, Werther GA. Effect of low-glycemic-index dietary advice on dietary quality and food choices in children with type 1 diabetes. *Am J Clin Nutr*. 2003;77:83-90.
63. Heilbronn LK, Noakes M, Clifton PM. The effect of high- and low-glycemic index energy restricted diets on plasma lipid and glucose profiles in type 2 diabetic subjects with varying glycemic control. *J Am Coll Nutr*. 2002;21:120-127.
64. Jarvi AE, Karlstrom BE, Grandfeldt YE, Bjorck IE, Asp NGL, Vessby BOH. Improved glycemic control and lipid profile and normalized fibrinolytic activity on a low glycemic index diet in type 2 diabetic patients. *Diabetes Care*. 1999;22:10-18.
65. Fontvieille AM, Rizkalla SW, Penfornis A, Acosta M, Bornet FRJ, Slama G. The use of low glycemic index foods improves metabolic control of diabetic patients over five weeks. *Diabet Med*. 1992;9:444-450.
66. Kabir M, Oppert JM, Vidal H, Bruzzo F, Fiquet C, Wursch P, Slama G, Rizkalla SW. Four week low-glycemic index breakfast with a modest amount of soluble fibers in type 2 diabetic men. *Metabolism*. 2002;51:819-826.
67. Wolever TM, Mehling C, Chiasson JL, Josse RG, Leiter LA, Maheux P, Rabasa-Lhoret R, Rodger NW, Ryan EA. Low glycaemic index diet

and disposition index in type 2 diabetes (the Canadian Trial of Carbohydrates in Diabetes): A randomized controlled trial. *Diabetologia*. 2008;51:1607-1615.
68. Ma Y, Olendzki BC, Merriam PA, Chiriboga DE, Culver AL, Li W, Hebert 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.
69. Amano Y, Sugiyama J, Lee JS, Kawakubo K, Mori K, Tang AC, Akabayashi A. Glycemic index-based nutritional education improves blood glucose control in Japanese adults. *Diabetes Care*. 2007;30: 1874-1876.
70. Nansel TR, Bellar L, McGill A. Effect of varying glycemic index meals on blood glucose control assessed with continuous glucose monitoring in youth with type 1 diabetes on basal-bolus insulin regimens. *Diabetes Care*. 2008;31:695-697.
71. Rovner AJ, Nansel TR, Gellar L. The effect of a low-glycemic diet vs a standard diet on blood glucose levels and macronutrient intake in children with type 1 diabetes. *J Am Diet Assoc*. 2009;109:303-307.
72. Thomas D, Elliott EJ. Low glycaemic index, or low glycemic load, diets for diabetes mellitus. *Cochrane Database Syst Rev*. 2009;1: CD006296.
73. Pi-Sunyer FX. Glycemic index and disease. *Am J Clin Nutr*. 2002; 76(suppl):290S-298S.
74. Vega-Lopez S, Ausman LM, Griffith JL, Lichtenstein AH. Interindividual variability and intra-individual reproducibility of glycemic index values for commercial white bread. *Diabetes Care*. 2007;30: 1412-1417.
75. Chandalia M, Garg A, Lutjohann D, von Bergmann K, Grundy SM, Brinkley LJ. Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. *N Engl J Med*. 2000;342:1392-1398.
76. Hagander B, Asp N-G, Efendic S, Nilsson-Ehle P, Schersten B. Dietary fiber decreases fasting blood glucose levels and plasma LDL concentration in noninsulin-dependent diabetes mellitus patients. *Am J Clin Nutr*. 1988;47:852-858.
77. Giacco R, Parillo M, Rivellese AA, Lasorella G, Giacco A, D'Episcopo L, Riccardi G. Long-term dietary treatment with increased amounts of fiber-rich low-glycemic index natural foods improves blood glucose control and reduces the number of hypoglycemic events in type 1 diabetic patients. *Diabetes Care*. 2000;23:1461-1466.
78. Kinmonth A-L, Angus RM, Jenkins PA, Smith MA, Baum JD. Whole foods and increased dietary fibre improve blood glucose control in diabetic children. *Arch Dis Childhood*. 1982;57:187-194.
79. Del Toma E, Lintas C, Clementi A, Marcelli M. Soluble and insoluble dietary fiber in diabetic diets. *Eur J Clin Nutr*. 1988;42:313-319.
80. 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.
81. Anderson JW, Zeigler JA, Deakins DA, Floore TL, Dillon DW, Wood CL, Oeltgen PR, Whitley RJ. Metabolic effects of high-carbohydrate, high-fiber diets for insulin-dependent diabetic individuals. *Am J Clin Nutr*. 1991;54:936-943.
82. Stevens J, Burgess MB, Kaiser DL, Sheppa CM. Outpatient management of diabetes mellitus with patient education to increase dietary carbohydrate and fiber. *Diabetes Care*. 1985;8:359-366.
83. McCulloch DK, Mitchell RD, Ambler J, Tattersall RB. A prospective comparison of "conventional" and high carbohydrate/high fibre/low fat diets in adults with established type 1 (insulin-dependent) diabetes. *Diabetologia*. 1985;28:208-212.
84. Riccardi G, Rivellese A, Pacioni D, Genovese S, Mastranzo P, Mancini M. Separate influence of dietary carbohydrate and fibre on the metabolic control in diabetes. *Diabetologia*. 1984;26:116-121.
85. Story L, Anderson JW, Chen W-JL, Karounos D, Jefferson B. Adherence to high-carbohydrate, high fiber diets: Long-term studies of non-obese diabetic men. *J Am Diet Assoc*. 1985;85:1105-1110.
86. Lindsay AN, Hardy S, Jarrett L, Rallison ML. High-carbohydrate, high-fiber diet in children with type 1 diabetes mellitus. *Diabetes Care*. 1984;7:63-67.
87. Simpson RW, McDonald J, Wahlqvist ML, Balasz N, Sissons M, Atley L. Temporal study of metabolic change when poorly controlled noninsulin-dependent diabetics change from low to high carbohydrate and fiber diet. *J Clin Nutr*. 1988;48:104-109.
88. Buyken AE, Toeller M, Heitkamp G, Vitelli F, Stehle P, Scherbaum WA, Fuller JH and the EURODIAB IDDM Complications Study Group. Relation of fibre intake to HbA1c and the prevalence of severe ketoacidosis and severe hypoglycaemia. *Diabetologia*. 1998;41:882-890.
89. Van Horn L, McCoin M, Kris-Etherton PM, Burke F, Carson JA, Champagne CM, Karmally W, Sikand G. The evidence for dietary prevention and treatment of cardiovascular disease. *J Am Diet Assoc*. 2008;108:287-331.
90. Nordt TK, Besenthal I, Eggstein M, Jakober B. Influence of breakfasts with different nutrient contents on glucose, C peptide, insulin, glucagon, triglycerides, and GIP in non-insulin-dependent diabetes. *Am J Clin Nutr*. 1991;53:155-160.
91. Gannon MC, Nuttall JA, Damberg G, Gupta V, Nuttall FQ. Effect of protein ingestion on the glucose appearance rate in people with type 2 diabetes. *J Clin Endocrin Metab*. 2001;86:1040-1047.
92. Parker B, Noakes M, Luscombe N, Clifton P. Effect of a high-protein diet, high-monounsaturated fat weight loss diet on glycemic control and lipid levels in type 2 diabetes. *Diabetes Care*. 2002;25:425-430.
93. Luscombe ND, Clifton PM, Noakes M, Parker B, Wittert G. Effects of energy-restricted diets containing increased protein on weight loss, resting energy expenditure, and thermic effect of feeding in type 2 diabetes. *Diabetes Care*. 2002;25:652-657.
94. Brinkworth GD, Noakes M, Parker B, Foster P, Clifton PM. Long-term 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: 1-year follow-up of a randomized trial. *Diabetologia*. 2004; 47:1677-1686.
95. Nuttall FQ, Gannon MC, Saeed A, Jordan K, Hoover H. The metabolic response of subjects with type 2 diabetes to a high-protein, weight-maintenance diet. *J Clin Endocrinol Metab*. 2003;88: 3577-3583.
96. Gannon MC, Nuttall FQ, Saeed A, Jordan K, Hoover H. An increase in dietary protein improves the blood glucose response in persons with type 2 diabetes. *Am J Clin Nutr*. 2003;78:734-741.
97. Hansen HP, Christensen PK, Tauber-Lassen E, Klausen A, Jensen BR, Parving H. Low-protein diet and kidney function in insulin-dependent diabetic patients with diabetic nephropathy. *Kidney International*. 1999;55:621-628.
98. Raal FJ, Kalk WJ, Lawson M, Esser JD, Buys R, Fourie L, Panz VR. Effect of moderate protein restriction on the progression of overt diabetic nephropathy: A 6-month prospective study. *Am J Clin Nutr*. 1994;60:579-585.
99. Pijls LTJ, de Vries H, van Eijk JThM, Donker AJM. Protein restriction, glomerular filtration and albuminuria in patients with type 2 diabetes mellitus: A randomized trial. *Eur J Clin Nutr*. 2002;556: 1200-1207.
100. Pijls LTJ, de Vries H, Kriegsman DMW, Donker AJM, van Ejik JThM. Determinants of albuminuria in people with type 2 diabetes mellitus. *DiabetesRes Clin Pract*. 2001;52:133-143.
101. Meloni C, Morosetti M, Suraci C, Pennafina MG, Tozzo C, Taccone-Gallucci M, Casciani CU. Severe dietary protein restriction in overt diabetic nephropathy: Benefits or risks. *J Renal Nutr*. 2002;12:96-101.
102. Meloni C, Tatangelo P, Cipriani S, Rossi V, Suraci C, Tozzo C, Rossini B, Cecilia A, DiFranco D, Straccialano E, Casciani CU. Adequate protein dietary restriction in diabetic and nondiabetic patients with chronic renal failure. *J Renal Nutr*. 2004;14:208-213.
103. Hansen HP, Tauber-Lassen E, Jensen BR, Parving HH. Effect of dietary protein restriction on prognosis in patients with diabetic nephropathy. *Kidney Int*. 2002;61:220-228.
104. Stojceva-Taneva O, Polenakovic M, Grozdanovski R, Sikole A. Lipids, protein content and progression of diabetic nephropathy. *Neph Dial Transplant*. 2001;16(suppl 1):90-91.
105. Azadbakht L, Shakerhosseini R, Atabak S, Jamshidian M, Mehrabi Y, Esmaill-Zadeh A. Beneficiary effect of dietary soy protein on lowering plasma levels of lipid and improving kidney function in type II diabetes with nephropathy. *Eur J Clin Nutr*. 2003;57:1292-1294.
106. Dussol B, Iovanna C, Raccah D, Darmon P, Morange S, Vague P, Vialettes B, Oliver C, Loundoun A, Berland Y. A randomized trial of low-protein diet in type 1 and type 2 diabetes mellitus patients with incipient and overt nephropathy. *J Ren Nutr*. 2005;15:398-406.
107. Velázquez LL, Sil AMJ, Goycochea RMV, Torres TM, Castañeda LR. Effect of protein restriction diet on renal function and metabolic control in patients with type 2 diabetes: A randomized clinical trial. *Nutr Hosp*. 2008;23:141-147.
108. Azadbakht L, Atabak S, Esmaillzadeh A. Soy protein intake, cardiorenal indices, and C-reactive protein in type 2 diabetes with nephropathy. *Diabetes Care*. 2008;31:648-654.
109. Almeida JC, Zelmanovitz T, Vaz JS, Steemburgo T, Perassolo MS, Gross JL, Azevedo MJ. Sources of protein and polyunsaturated fatty acids of the diet and microalbuminuria in type 2 diabetes mellitus. *J Am Coll Nutr*. 2008;27:528-537.
110. Robertson L, Waugh N, Robertson A. Protein restriction for diabetic renal disease. *Cochrane Database Syst Rev*. 2007;4:CD002181.

111. Pan Y, Guo LL, Jin HM. Low-protein diet for diabetic nephropathy: A meta-analysis of randomized controlled trials. *Am J Clin Nutr*. 2008;88:660-666.
112. National Kidney Foundation. KDOQI clinical practice guidelines for nutrition in chronic renal failure. *Am J Kidney Dis*. 2000;35(suppl 2):S1-S140.
113. Buse JB, Ginsberg HN, Barkis GL, Clark NG, Costa F, Eckel R, Fonseca V, Gerstein HC, Grundy S, Nesto RW, Pignone MP, Plutzky J, Porte D, Redberg R, Stitzel KF, Stone NJ. Primary prevention of cardiovascular disease in people with diabetes mellitus: A scientific statement from the American Heart Association and the American Diabetes Association. *Diabetes Care*. 2007;30:162-172.
114. Mayer-Davis EJ, Levin S, Marshall JA. Heterogeneity in associations between macronutrient intake and lipoprotein profile in individuals with type 2 diabetes. *Diabetes Care*. 1999;22:1632-1639.
115. Mukarmal KJ, Nesto RW, Cohen MC, Muller JE, Maclure M, Sherwood JB, Mittleman MA. Impact of diabetes on long-term survival after acute myocardial infarction. Comparability of risk with prior myocardial infarction. *Diabetes Care*. 2001;24:1422-1427.
116. Orchard TJ, Forrest KY, Kuller LH, Becker DJ. Lipid and blood pressure treatment goals for type 1 diabetes: 10-year incidence data from the Pittsburgh Epidemiology of Diabetes Complications Study. *Diabetes Care*. 2001;24:1053-1059.
117. Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati FL, Powe NR, Goldren SH. Meta-analysis: Glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. *Ann Intern Med*. 2004;141: 421-431.
118. Faulkner MS, Chao W, Kamath SK, Quinn L, Fritschi C, Maggiore JA, Williams RH, Reynolds RD. Total homocystein, diet, and lipid profiles in type 1 and type 2 diabetic and nondiabetic adolescents. *J Cardiovasc Nurs*. 2006;21:47-55.
119. Ciccarone E, Di Casteinuovo A, Salcuni M, Siani M, Giacco A, Donati MB, De Gaetano G, Capani F, Iacoviello L, Gendiabe Investigators. A high-score Mediterranean dietary pattern is associated with a reduced risk of peripheral arterial disease in Italian patients with type 2 diabetes. *J Thromb Haemost*. 2003;1:1744-1752.
120. Diakoumopoulou E, Tentolouris N, Kirlaki E, Perrea D, Kitsou E, Psallas M, Doulgerakis D, Katsilambros N. Plasma homocystein levels in patients with type 2 diabetes in a Mediterranean population: Relation with nutritional and other factors. *Nutr Metab Cardiovasc Dis*. 2005;15:109-117.
121. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med*. 2005;353:2643-2653.
122. Turner RC, Millns H, Heil HAW, Stratton IM, Manley SE, Matthews DR, Holman RR. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS:23). *BMJ*. 1998;316:823-828.
123. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med*. 2003;348:383-393.
124. Gill GV, Woodward A, Pradhan S, Wallymahmed M, Groves T, English P, Wilding JP. Intensified treatment of type 2 diabetes—Positive effects on blood pressure, but not glycemic control. *Q J Med*. 2003;96:833-836.
125. Dhindsa P, Scott AR, Donnelly R. Metabolic and cardiovascular effects of very-low-calorie diet therapy in obese patients with type 2 diabetes in secondary failure: outcomes after 1 year. *Diabet Med*. 2003;20:319-324.
126. Holman RR, Paul SK, Bethel A, Matthews DR, Neil AW. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med*. 2008;359:1577-1589.
127. The Look AHEAD Research Group. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes. One-year results of the Look AHEAD trial. *Diabetes Care*. 2007;30: 1374-1383.
128. Estruch R, Martinez-González M, Corella D, Salas-Salvadó J, Ruiz-Gutiérrez, Covas MI, Fiol M, Gómez-Gracia E, López-Sabater MC, Vinyoles E, Arós F, Conde M, Lahoz C, Lapetra J. Sáez G, Ros E, for the PREDIMED Study Investigators. Effects of a Mediterranean-style diet on cardiovascular risk factors. *Ann Intern Med*. 2006;145: 1-11.
129. Trichopoulou A, Psaltopoulou T, Orfanos P, Trichopoulos D. Diet and physical activity in relation to overall mortality amongst adult diabetics in a general population cohort. *J Intern Med*. 2006;259:583-591.
130. Storm H, Thomsen C, Pedersen E, Rasmussen O, Christiansen C, Hermansen K. Comparison of a carbohydrate-rich diet and diets rich in stearic or palmitic acid in NIDDM patients. *Diabetes Care*. 1997;20:1807-1813.
131. Lovejoy JC, Most MM, Lefevre M, Greenway FL, Rood JC. Effect of diets enriched in almonds on insulin action and serum lipids in adults with normal glucose tolerance or type 2 diabetes. *Am J Clin Nutr*. 2002;76:1000-1006.
132. Neyestani TR, Alipour-Birgani R, Siassi F, Rajayi M, Djalali M, Hohamadi M. Glycemic optimization may reduce lipid peroxidation independent of weight and blood lipid changes in type 2 diabetes mellitus. *Diabetes Nutr Metab*. 2004;17:275-279.
133. Mostad IL, Qvigstad E, Bjerve KS, Grill VE. Effects of a 3-day low-fat diet on metabolic control, insulin sensitivity, lipids, and adipocyte hormones in Norwegian subjects with hypertriacylglycerolaemia and type 2 diabetes. *Scand J Clin Lab Invest*. 2004;17:275-279.
134. Rodriquez-Villar C, Perez-Heras A, Mercade I, Casals E, Ros E. Comparison of a high-carbohydrate diet 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;21:142-149.
135. Tapsell LC, Owen A, Gillen LJ, Bare M, Patch CS. Kennedy M, Betterham M. Including walnuts in a low-fat/modified-fat diet improves HDL cholesterol-to-cholesterol ratios in patients with type 2 diabetes. *Diabetes Care*. 2004;27:2777-2783.
136. West SG, Hecker KD, Mustad VA, Nicholson S, Schoemer SL, Wagner P, Hinderliter AL, Ulbrecht J, Ruey P, Kris-Etherton PM. Acute effects of monounsaturated fatty acids with and without omega-3 fatty acids on vascular reactivity in individuals with type 2 diabetes. *Diabetologia*. 2005;48:113-122.
137. Karantonis HC, Fragopoulou E, Antonopoulou S, Rementzis J, Phenekos C, Demopoulos CA. Effect of fast-food Mediterranean-type diet on type 2 diabetics and healthy human subjects' platelet aggregation. *Diabetes Res Clin Pract*. 2006;72:33-41.
138. Mantzoros CS, Williams CJ, Manson JE, Meigs JB, Hu FB. Adherence to the Mediterranean dietary pattern is positively associated with plasma adiponectin concentrations in diabetic women. *Am J Clin Nutr*. 2006;84:328-335.
139. Houlihan CA, Casley DJ, Allen TJ, Cooper ME, Bacter AL, Jerums G, Panangiotopoulos S. A low-sodium diet potentiates the effects of Losartan in type 2 diabetes. *Diabetes Care*. 2002;25:663-671.
140. Vedovato M, Lepore G, Coracina A, Dodesini AR, Jori E, Tiengo A, Del Prato S, Trevisan R. Effect of sodium intake on blood pressure and albuminuria in type 2 diabetic patients: The role of insulin resistance. *Diabetologia*. 2004;47:300-303.
141. Krook A, Holm I, Pettersson S, Wallberg-Henriksson H. Reduction of risk factors following lifestyle modification programme in subjects with type 2 (non-insulin dependent) diabetes mellitus. *Clin Physiol Funct Imaging*. 2003;23:21-30.
142. Perassolo MS, Moulin CC, Almeida JC, Camargo JL, Pra RL, Zelmanovitz T, Mello VD, Azevedo MJ, Mala AL, Gross JL. Fatty acid composition of serum lipid fractions in type 2 diabetic patients with microalbuminuria. *Diabetes Care*. 2003;26:613-618.
143. Osende JI, Badimon JJ, Fuster V, Herson P, Rabito P, Vidhum R, Zaman A, Rodriguez OJ, Lev EI, Rauch U, Hefit G, Fallon JT, Crandall JP. Blood thrombogenicity in type 2 diabetes mellitus patients is associated with glycemic control. *J Am Coll Cardiol*. 2001; 38:1307-1312.
144. Didangelos TP, Thanapoulou AK, Bousboulas SH, Sambanis CL, Athyros VG, Spanou EA, Dimitriou KC, Pappas SI, Karamanos BG, Karamitsos DT. The ORlistat and CArdiovascular risk profile in patients with metabolic syndrome and type 2 diabetes. (ORLICARDIA) study. *Curr Med Res Opin*. 2004;20:1393-1401.
145. Lonn E, Dagenais G, Yusuf S, Mann JFE, Hoogwerf B, Gerstein HC, Pogue J, Qilong Y, Zinman B, Bosch J. Effects of vitamin E on cardiovascular and microvascular outcomes in high-risk patients with diabetes: Results of the HOPE study and MICRO-HOPE substudy. *Diabetes Care*. 2002;25:1919-1927.
146. Lee YM, Haastert B, Scherbaum W, Hauner H. A phytosterol-enriched spread improves the lipid profile of subjects with type 2 diabetes. *Eur J Nutr*. 2003;42:111-117.
147. Antonopoulou S, Fragopoulou E, Karantonis HC, Mitsou E, Sitara M, Rementzis J, Mourelatos A, Ginis A, Phenekkos C. Effect of traditional Greek Mediterranean meals on platelet aggregation in normal subjects and in patients with type 2 diabetes mellitus. *J Med Food*. 2006;9:356-362.
148. Shah M, Adams-Huet B, Brinkley L, Grundy SM, Garg A. Lipid, glycemic, and insulin responses to meals rich in saturated, *cis-*

monounsaturated, and polyunsaturated (n–3 and n–6) fatty acids in subjects with type 2 diabetes. *Diabetes Care*. 2007;30:2993-2998.
149. Tentolouris N, Arapostathi C, Perrea D, Kyriaki D, Revenas C, Katsilambros N. Differential effects of two isoenergetic meals rich in saturated or monounsaturated fat on endothelial function in subjects with type 2 diabetes. *Diabetes Care*. 2008;31:2276-2278.
150. Shidfar F, Keshavarz A, Hosseyni S, Ameri A, Yarahmadi A. Effects of omega–3 fatty acid supplements on serum lipids, apolipoproteins and malondialehyde in type 2 diabetes patients. *East Mediterr Health J*. 2008;14:305-313.
151. Mostad IL, Bjerve KS, Bjorgaas MR, Lydersen S, Grill V. Effects of n–3 fatty acids in subjects with type 2 diabetes: Reduction of insulin sensitivity and time-dependent alteration from carbohydrate to fat oxidation. *Am J Clin Nutr*. 2006;84:540-550.
152. Tapsell LC, Batterham MJ, Teuss G, Tan S-Y, Dalton S, Quick CJ, Gillen IJ, Charlton KE. Long-term effects of increased dietary polyunsaturated fat from walnuts on metabolic parameters in type II diabetes. *Eur J Clin Nutr*. 2009;63:1008-1015.
153. Mertz JA, Stern JS, Kris-Etherton P, Reusser ME, Morris CD, Hatton DC, Oparil S, Haynes RB, Resnick LM, Pi-Sunyer FX, Clark S, Chester L, McMahon M, Snyder GW, McCarron DA. A randomized trial of improved weight loss with a prepared meal plan in overweight and obese patients: Impact on cardiovascular risk reduction. *Arch Intern Med*. 2000;160:2150-2158.
154. Hanefeld M, Sachse G. The effects of orlistat on body weight and glycaemic control in overweight patients with type 2 diabetes: A randomized, placebo-controlled trial. *Diabetes Obes Metab*. 2002;4: 415-423.
155. Kelley DE, Bray GA, Pi-Sunyer FX, Klein S, Hill J, Miles J, Holland P. Clinical efficacy of orlistat therapy in overweight and obese patients with insulin-treated type 2 diabetes: A 1-year randomized controlled trial. *Diabetes Care*. 2002;25:1033-1041.
156. Miles JM, Leiter L, Hollander P, Wadden T, Anderson JW, Doyle M, Foreyt J, Aronne L, Klein S. Effect of orlistat in overweight and obese patients with type 2 diabetes treated with metformin. *Diabetes Care*. 2002;25:1123-1128.
157. Berne C, for the Orlistat Swedish Type 2 Diabetes Study Group. A randomized study of orlistat in combination with a weight management programme in obese patients with type 2 diabetes treated with metformin. *Diabet Med*. 2005;22:612-618.
158. Hollander PA, Elbein SC, Hirsch IB, Kelley D, McGill J, Taylor T, Weiss SR, Crockett SE, Kaplan RA, Comstock J, Lucas CP, Lodewick PA, Canovatchel W, Chung J, Hauptman J. Role of orlistat in the treatment of obese patients with type 2 diabetes. *Diabetes Care*. 1998;21:1288-1294.
159. Redmon JB, Raatz SK, Reck KP, Swanson JE, Kwong CA, Fan Q, Thomas W, Bantle JP. One-year outcome of a combination of weight loss therapies for subjects with type 2 diabetes: A randomized trial. *Diabetes Care*. 2003;26:2505-2511.
160. Redmon JB, Reck KP, Raatz SK, Swanson JE, Kwong CA, Ji H, Thomas W, Bantle JP. Two-year outcomes of a combination of weight loss therapies for type 2 diabetes. *Diabetes Care*. 2005;28: 1311-1315.
161. Wolf AM, Conaway MR, Crowther JQ, Nadler JL, Oneida B, Bovbjerg VE. Translating lifestyle intervention to practice in obese patients with type 2 diabetes: Improving Control with Activity and Nutrition (ICAN) study. *Diabetes Care* 2004;27:1570-1576.
162. Li Z, Hong K, Saltsman P, DeShields S, Bellman M, Thames G, Liu Y, Wang H-J, Elashoff R, Heber D. Long-term efficacy of soy-based meal replacements vs an individualized diet plan in obese type II DM patients: Relative effects on weight loss, metabolic parameters, and C-reactive protein. *Eur J Clin Nutr*. 2005;59:411-418.
163. Manning RM, Jung RT, Leese GP, Newton RW. The comparison of four weight reduction strategies aimed at overweight patients with diabetes mellitus: Four-year follow-up. *Diabet Med*. 1998;15:497-502.
164. Ash S, Reeves MM, Yeo S, Morrison G, Carey D, Capra S. Effect of intensive interventions on weight and glycaemic control in overweight men with Type II diabetes: A randomized trial. *Int J Obesity*. 2003;27:797-802.
165. Mayer-Davis EJ, D'Antonio AM, Smith SM, Kirkner G, Martin SL, Parra-Medina D, Schultz R. Pounds Off with Empowerment (POWER): A clinical trial of weight management strategies for black and white adults with diabetes who live in medically underserved rural communities. *Am J Public Health*. 2004;94:1736-1742.
166. Wing RR, Koeske R, Epstein LH, Nowalk MP, Gooding W, Becker D. Long-term effects of modest weight-loss in type II diabetic patients. *Arch Intern Med*. 1987;147:1749-1753.
167. Norris Sl, Zhang X, Avenell A, Gregg E, Bowman B, Serdula M, Brown TJ, Schmid CH, Lau J. Long-term effectiveness of lifestyle and behavior weight loss interventions in adults with type 2 diabetes: A meta-analysis. *Am J Med*. 2004;117:762-774.
168. Derosa G, Cicero AF, Murdolo G, Ciccarelli L, Fogari R. Comparison of metabolic effects of orlistat and sibutramine treatment in type 2 diabetic obese patients. *Diabetes Nutr Metab*. 2004;17:222-229.
169. McNulty SJ, Ur E, Williams G, for the Multicenter Sibutramine Study Group. A randomized trial of sibutramine in the management of obese type 2 diabetic patients treated with metformin. *Diabetes Care*. 2003;26:125-131.
170. Sanchez-Reyes L, Fanghanel G, Yamamoto J, Martinez-Rivas L, Campos-Franco E, Berber A. Use of sibutramine in overweight adult Hispanic patients with type 2 diabetes mellitus: A 12-month, randomized, double-blind placebo-controlled clinical trial. *Clin Ther*. 2004;26:1427-1435.
171. Paisey RB, Frost J, Harvery P, Paisey A, Bower L, Paisey RM, Taylor P, Belka I. Five-year results of a prospective very-low calorie diet or conventional weight loss programme in type 2 diabetes: *J Hum Nutr Diet*. 2002;15:121-127.
172. Raynor HA, Jeffrey RW, Ruggiero AM, Clark JM, Delahanty LM, for the Look AHEAD (Action for Health for Diabetes) Research Group. Weight loss strategies associated with BMI in overweight adults with type 2 diabetes at entry into the Look AHEAD (Action for Health in Diabetes) Trial. *Diabetes Care*. 2008;31:1299-1304.
173. Cheskin LJ, Mitchell AM, Jhaveri AM, Mitola AH, Davis LM, Lewis RA, Yep MA, Lycan TW. Efficacy of a meal replacement versus a standard food-based diet for weight loss in type 2 diabetes. *Diabetes Educ*. 2008;3:118-127.
174. Feldstein AC, Nichols GA, Smith DH, Stevens VJ, Bachman K, Rosales AG, Perrin N. Weight change in diabetes and glycemic and blood pressure control. *Diabetes Care*. 2008;31:1960-1965.
175. Riddle MC, Henry RR, Poon TH, Zhang B, Mac SM, Holcombe JH, Kim DD, Maggs DG. Exenatide elicits sustained glycaemic control and progressive reduction in body weight in patients with type 2 diabetes inadequately controlled by sulphonylureas with or without metformin. *Diabetes Metab Res Rev*. 2006;22:483-491.
176. Ratner RW, Maggs D, Nielsen LL, Stonehouse AH, Poon T, Zhang B, Bicsak TA, Brodows RG, Kim DD. Long-term effects of exenatide therapy over 82 weeks on glycaemic control and weight in overweight metformin-treated patients with type 2 diabetes. *Diabetes Obes Metab*. 2006;8:419-428.
177. Blonde L, Klein EJ, Han J, Zhang B, Mac SM, Poon TH, Taylor KL, Trautmann ME, Kim DD, Kendall DM. Interim analysis of the effects of exenatide treatment on A2c, weight and cardiovascular risk factors over 82 weeks in 314 overweight patients with type 2 diabetes. *Diabetes Obes Metab*. 2006;8:436-447.
178. Scheen AJ, Finer N, Hollander P, Jensen MD, Van Gaal LF, for the RIO-Diabetes Study Group. Efficacy and tolerability of Rimonabant in overweight or obese patients with type 2 diabetes: A randomized controlled study. *Lancet*. 2006;368:1660-1672.
179. Eliasson B, Gudbjörnsdottir S, Cederholm J, Liang Y, Vercruysse F, Smith U. Weight loss and metabolic effects of topiramate in overweight and obese type 2 diabetic patients: Randomized double-blind placebo-controlled trial. *Int J Obes*. 2007;31:1140-1147.
180. Stenlöf L, Rössner S, Vercruysse F, Kumar A, Fitchet M, Sjöström, for the OBDM-003 Study Group. Topiramate in the treatment of obese subjects with drug-naïve type 2 diabetes. *Diabetes Obes Metab*. 2007;9:360-368.
181. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C. Physical activity/exercise and type 2 diabetes. *Diabetes Care*. 2004;27:2518–1539.
182. Castaneda C, Layne JE, Munoz-Orians L, Gordon PL, Walsmith J, Foldvari M, Roubenoff R, Tucker KL, Nelson ME. A randomized controlled trial of resistance exercise training to improve glycemic control in older adults with type 2 diabetes. *Diabetes Care*. 2002;25: 233-241.
183. Goldhaber-Fiebert JD, Goldhaber-Fiebert SN, Tristan ML, Nathan DM. Randomized controlled community-based nutrition and exercise intervention improves glycemia and cardiovascular risk factors in type 2 diabetic patients in rural Costa Rica. *Diabetes Care*. 2003; 26:24-29.
184. Cauza E, Hanusch-Enserer U, Strasser B, Ludvik B, Metz-Schimmerl S, Pacini G, Wagner O, Gerg P, Prager R, Kostner K, Dunky A, Haber P. The relative benefits of endurance and strength training on the metabolic factors and muscle function of people with type 2 diabetes mellitus. *Arch Phys Med Rehabil*. 2005;86:1527-1533.
185. Di Loreto C, Ranchelli A, Fanelli C, Fatone C, Lucidi P, Taglioni C, Murdolo G, Santeusanio F, De Cicco A, De Feo F, Parlanti N. Make

your diabetic patients walk: Long-term impact of different amounts of physical activity on type 2 diabetes. *Diabetes Care*. 2005;28:1295-1302.
186. Van Rooijen AJ, Rheeder P, Eales CH, Becker PJ. Effect of exercise versus relaxation on haemolglobin A1c in black females with type 2 diabetes. *QJ Med*. 2004;97:343-351.
187. Dunstan DW, De Courten M, Daly RM, Shaw J, Owen N, Zimmet P, Jolley D. High-intensity resistance training improves glycemic control in older patients with type 2 diabetes. *Diabetes Care*. 2002;25: 1729-1736.
188. Kirk A, MacIntyre P, Mutrie N, Fisher M. Increasing physical activity in people with type 2 diabetes. *Diabetes Care*. 2003;26:1186-1192.
189. Dunstan DW, Daly RM, Owen N, Jolley D, Vulikh E, Shaw J, Zimmet P. Home-based resistance training is not sufficient to maintain glycemic control following supervised training in older individuals with type 2 diabetes. *Diabetes Care*. 2005;28:3-9.
190. Kirk A, Mutrie N, MacIntyre P, Fisher M. Effects of a 12-month physical activity in people with type 2 diabetes. *Diabetologia*. 2004; 47:821-832.
191. Boule NG, Haddad E, Kenny GP, Wells GA, Sigal RJ. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus. A meta-analysis of controlled clinical trials. *JAMA*. 2001;286: 1218-1227.
192. Mayer-Davis EJ, D'Agostino R, Karter AJ, Haffner SM, Rewers MJ, Saad M, Bergman RN. Intensity and amount of physical activity in relation to insulin sensitivity. The Insulin Resistance and Atherosclerosis Study (IRAS). *JAMA*. 1998;279:660-674.
193. Wei M, Gibbons LW, Kampert JB, Nichaman MZ, Blair SN. Low cardiorespiratory fitness and physical inactivity in men with type 2 diabetes. *Ann Intern Med*. 2000;132:605-611.
194. Church TS, Cheng YJ, Earnest CP, Barlow CE, Gibbons LW, Priest WL, Blair SN. Exercise capacity and body composition as predictors of mortality among men with diabetes. *Diabetes Care*. 2004;27:83-88.
195. Roberts L, Jones TW, Fournier PA. Exercise training and glycemic control in adolescents with poorly controlled type 1 diabetes mellitus. *J Pediatr Endocrinol Metab*. 2002;15:621-627.
196. Sarnblad S, Ekelund U, Aman J. Physical activity and energy intake in adolescent girls with type 1 diabetes. *Diabet Med*. 2005;22:893-899.
197. Waden J, Tikkanen H, Forsblom C, Fagerudd J, Pettersson-Fernholm K, Lakka T, Riska M, Groop PH, FinnDiane Study Group. Leisure time physical activity is associated with poor glycemic control in type 1 diabetic women: The FinnDiane study. *Diabetes Care*. 2005;28:777-782.
198. Tsalikian E, Mauras N, Beck RW, Tamborlane WV, Janz KF, Chase HP, Wysocki T, Weinzimer SA, Buckingham BA, Kollman C, Xing D, Ruedy KJ; Diabetes Research in Children Network Direcnet Study Group. Impact of exercise on overnight glycemic control in children with type 1 diabetes mellitus. *J Pediatr*. 2005;147:528-534.
199. Tansey MJ, Tsalikian E, Beck RW, Mauras N, Buckingham BA, Weinzimer SA, Janz KF, Kollman C, Xing D, Ruedy KJ, Steffes MW, Borland TM, Singh RJ, Tamborlane WV, The Diabetes Research in Children Network (DirecNet) Study Group. The effects of aerobic exercise on glucose and counterregulatory hormone concentrations in children with type 1 diabetes. *Diabetes Care*. 2006;29:20-25.
200. Sigal RJ, Kenny GP, Boulé NG, Wells GA, Prud'homme D, Fortier M, Reid RD, Tulloch H, Coyle D, Phillips P, Jennings A, Jaffey J. Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes. A randomized trial. *Ann Intern Med*. 2007;147:357-369.
201. Conn VS, Hafdahl AR, Mehr DR, LeMaster JW, Brown SA, Nielsen PJ. Metabolic effects of interventions to increase exercise in adults with type 2 diabetes. *Diabetologia*. 2007;50:913-921.
202. McAuley PA, Myers JN, Abella JP, Tan SY, Froelicher VF. Exercise capacity and body mass index as predictors of mortality among male veterans with type 2 diabetes. *Diabetes Care*. 2007;30:1539-1543.
203. Kelley GA, Kelley KS. Effects of aerobic exercise on lipids and lipoproteins in adults with type 2 diabetes; a meta-analysis of randomized-controlled trials. *Public Health*. 2007;9:643-655.
204. Wing RR, Jakicic J, Neiberg R, Lang W, Blair SN, Cooper L, Hill JO. Fitness, fatness, and cardiovascular risk factors in type 2 diabetes: Look AHEAD. *Med Sci Sports Exerc*. 2007;39:2107-2116.
205. Herbst A, Kordonouri O, Schwab KO, Schmidt F, Holl RW, DPV Initiative of the German Working Group for Pediatric Diabetology Germany. Impact of physical activity on cardiovascular risk factors in children with type 1 diabetes: A multicenter study of 23,251 patients. *Diabetes Care*. 2007;30:2098-2100.
206. Guelfi KJ, Jones TW, Fournier PA. New insights into managing the risk of hypoglycaemia associated with intermittent high-intensity exercise in individuals with type 1 diabetes mellitus: Implications for existing guidelines. *Sports Med*. 2007;37:937-946.
207. Rachmiel M, Buccino J, Daneman D. Exercise and type 1 diabetes mellitus in youth: Review and recommendations. *Pediatr Endocrinol Rev*. 2007;5:656-665.
208. Karter AJ, Ackerson LM, Darbinian JA, D'Agostino RB Jr, Ferrara A, Liu J, Selby JV. Self-monitoring of blood glucose levels and glycemic control: The Northern California Permanente Diabetes registry. *Am J Med*. 2001;111:1-9.
209. Allen BT, DeLong ER, Feussner JR. Impact of glucose self-monitoring on non-insulin-treated patients with type II diabetes mellitus. Randomized controlled trial comparing blood and urine testing. *Diabetes Care*. 1990;13:1044-1050.
210. Franciosi M, Pellegrini F, DeBeradis G, Belfiglio M, DiNardo B, Greenfield S, Kaplan SH, Rossi MCE, Sacco M, Tognoni G, Valentini M, Nicolucci A, for The QuED Study Group—Quality of Care and Outcomes in Type 2 Diabetes. Self-monitoring of blood glucose in non-insulin-treated diabetic patients: A longitudinal evaluation of its impact on metabolic control. *Diabet Med*. 2005;22:900-906.
211. Schwedes U, Siebolds M, Mertes G, for the SMBG Study Group. Meal-related structured self-monitoring of blood glucose: Effect on diabetes control in non-insulin-treated type 2 diabetic patients. *Diabetes Care*. 2002;25:1928-1932.
212. Davidson MB, Bastellanos M, Kain D, Duran P. The effect of self-monitoring of blood glucose concentrations on glycated hemoglobin levels in diabetic patients not taking insulin: A blinded, randomized trial. *Am J Medicine*. 2005;118:422-425.
213. Sarol JN Jr, Nicodemus Jr NA, Tan KM, Grava MB. Self-monitoring of blood glucose as part of a multi-component therapy among non-insulin requiring type 2 diabetes patients: A meta-analysis (1966-2004). *Curr Med Res Opin*. 2005;21:173-184.
214. Coster S, Gulliford MC, Seed PT, Powrie JK, Swaminathan R. Self-monitoring of type 2 diabetes mellitus: A meta-analysis. *Diabet Med*. 2000;17:755-761.
215. Harris MI. Frequency of blood glucose monitoring in relation to glycemic control in patients with type 2 diabetes. *Diabetes Care*. 2001;24:979-982.
216. Meier JL, Swislocki ALM, Lopez JR, Noth RH, Bartlebaugh P, Siegel D. Reduction in self-monitoring of blood glucose in persons with type 2 diabetes results in cost savings and no change in glycemic control. *Am J Managed Care*. 2002;8:557-565.
217. Murata GH, Shah JH, Hoffman RM, Wendel CS, Adam KD, Solvas PA, Bokhari SU, Duckworth WC. Intensified blood glucose monitoring improves glycemic control in stable, insulin-treated veterans with type 2 diabetes: The Diabetes Outcomes in Veterans Study (DOVES). *Diabetes Care*. 2003;26:1759-1763.
218. Jaworska J, Dziemidok P, Kulik TB, Rudnicka-Drozak E. Frequency of self-monitoring and its effect on metabolic control in patients with type 2 diabetes. *Ann Univ Mariae Curie Sklodowska (Med)*. 2004; 59:310–216.
219. Wen L, Parchman ML, Linn WD, Lee S. Association between self-monitoring of blood glucose and glycemic control in patients with type 2 diabetes mellitus. *Am J Health Sys Pharm*. 2004;61:2401-2405.
220. Franciosi M, Pellegrini F, DeBerardis G, Belfiglio M, Cavaliere D, DiNardo B, Greenfield S, Kaplan SH, Sacco M, Tognoni G, Valentini M, Nicolucci A, for The QuED Study Group. The impact of blood glucose self-monitoring on metabolic control and quality of life in type 2 diabetic patients: An urgent need for better educational strategies. *Diabetes Care*. 2001;24:1870-1877.
221. Martin S, Schneider B, Heinemann L, Lodwig V, Kurth HJ, Kolb H, Scherbaum WA, for the ROSSO Study Group. Self-monitoring of blood glucose in type 2 diabetes and long-term outcome: An epidemiological cohort study. *Diabetologia*. 2006;49:271-278.
222. Kaufman FR, Gibson LLC, Halvorson M, Carpenter S, Fisher LK, Pitukcheewanont P. A pilot study of the continuous glucose monitoring system: Clinical decisions and glycemic control after its use in pediatric type 1 diabetic subjects. *Diabetes Care*. 2001;24:2030-2034.
223. Chico A, Vidal-Rios P, Subira M, Novials A. The continuous monitoring system is useful for detecting unrecognized hypoglycemias in patients with type 1 and type 2 diabetes but is not better than frequent capillary glucose measurements for improving metabolic control. *Diabetes Care*. 2003;26:1153-1157.
224. Ludvigsson J, Hanas R. Continuous subcutaneous glucose monitoring improved metabolic control in pediatric patients with type 1 diabetes: A controlled crossover study. *Pediatrics*. 2003;111:933-938.
225. Schaepelynck-Belicar P, Vague PH, Simonin G, Lassmann-Vague V. Improved metabolic control in diabetic adolescents using the contin-

uous glucose monitoring system (CGMS). *Diabetes Metab*. 2003;29:344-348.
226. Deiss D, Hartmann R, Hoeffe J, Kordonouri O. Assessment of glycemic control by continuous glucose monitoring system in 50 children with type 1 diabetes starting on insulin pump therapy. *Pediatric Diabetes*. 2004;5:117-121.
227. Tanenberg R, Bode B, Lane W, Levetan C, Mestman J, Harmel AP, Tobian J, Gross T, Mastrototaro J. Use of the continuous glucose monitoring system to guide therapy in patients with insulin-treated diabetes: A randomized controlled trial. *Mayo Clin Proc*. 2004;79: 1521-1526.
228. Schiaffini R, Ciampalini P, Fierabracci A, Spera S, Borrelli P, Bottazzo GF, Crino A. The continuous glucose monitoring system (CGMS) in type 1 diabetic children is the way to reduce hypoglycemic risk. *Diabetes Metab Res Rev*. 2002;18:324-329.
229. Bode B, Gross K, Rikalo N, Schwartz S, Wahl T, Page C, Gross T, Mastrototaro J. Alarms based on real-time sensor glucose values alert patients to hypo- and hyperglycemia: The Guardian Continuous Monitoring System. *Diabetes Technol Ther*. 2004;6:105-113.
230. Garg SK, Schwartz S, Edelman SV. Improved glucose excursions using an implantable real-time continuous glucose sensor in adults with type 1 diabetes. *Diabetes Care*. 2004;27:734-738.
231. Weintrob N, Schechter A, Benzaqwen H, Shalitin S, Lilos P, Galatzer A, Phillip M. Glycemic patterns detected by continuous subcutaneous glucose sensing in children and adolescents with type 1 diabetes mellitus treated by multiple daily injections vs continuous subcutaneous insulin infusion. *Arch Pediatr Adolesc Med*. 2004; 158:677-684.
232. Garg S, Zisser H, Schwartz S, Bailey T, Kaplan R, Ellis S, Jovanovic L. Improvement in glycemic excursions with a transcutaneous, real-time continuous glucose sensor: A randomized controlled trial. *Diabetes Care*. 2006;29:44-50.
233. Manuel-y-Keenoy B, Vertommen J, Abrams P, Van Gaal L, De Leeuw I, Messeri D, Poscia A. Postprandial glucose monitoring in type 1 diabetes: Use of continuous subcutaneous monitoring device. *Diabetes Metab Res Rev*. 2004;20(suppl 1):S24-S31.
234. Bode BW, Schwartz S, Stubbs HA, Block JE. Glycemic characteristics in continuously monitored patients with type 1 and type 2 diabetes. *Diabetes Care*. 2005;28:2361-2366.
235. Streja D. Can continuous glucose monitoring provide objective documentation of hypoglycemia unawareness? *Endocr Pract*. 2005;11: 83-90.
236. Schütt M, Kern W, Krause U, Busch P, Dapp A, Grziwotz R, Mayer I, Rosenbauer J, Wagner C, Simmermann A, Kerner W, Holl RW, DPV Initiative. Is the frequency of self-monitoring of blood glucose related to long-term metabolic control? Multicenter analysis including 24,500 patients from 191 centers in Germany and Austria. *Exp Clin Endocrinol Diabetes*. 2006;114:384-388.
237. Jansen JP. Self-monitoring of glucose in type 2 diabetes mellitus: A Bayesian meta-analysis of direct and indirect comparisons. *Curr Med Res Opin*. 2006;22:671-681.
238. Farmer A, Wade A, Goyder E, Yudkin P, French D, Craven A, Holman R, Kinmonth AL, Neil A. Impact of self monitoring of blood glucose in the management of patients with non-insulin treated diabetes: Open parallel group randomized trial. *BMJ*. 2007;335:132-139.
239. Bajkowska-Fiedziukiewicz A, Cypryk K, Kozdraj T, Mikotajczyk-Swatko A, Kosinski M, Jozefowska M. Self-monitoring of blood glucose and treatment of outcomes in type 2 diabetic patients. *Pol Arch Med Wewm*. 2008;118:267-272.
240. Welschen LM, Bloemendal E, Nijpels G, Dekker JM, Heine RJ, Stalman WA, Bouter LM. Self-monitoring of blood glucose in patients with type 2 diabetes who are not using insulin. *Cochrane Database Syst Rev*. 2005;2:CD005060.
241. O'Kane MJ, Bunting B, Copeland M, Coates VE, on behalf of the ESMON study group. Efficacy of self-monitoring of blood glucose in patients with newly diagnosed type 2 diabetes (ESMON study): Randomized controlled trial. *BMJ*. 2008;336:1174-1177.
242. The Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group. Continuous glucose monitoring and intensive treatment of type 1 diabetes. *N Engl J Med*. 2008;359:1464-1476.
243. Chetty VT, Almulla A, Odueyungbo A, Thabane L. The effects of continuous glucose monitoring (CGMS) versus intermittent whole blood finger-stick glucose monitoring (SBGM) on hemoglobin A1c (HBA1c) levels in type 1 diabetic patients: A systematic review. *Diabetes Res Clin Pract*. 2008;81:79-87.
244. Yoo HJ, An HG, Park SY, Ryu OH, Kim HY, Seo JA, Hong EG, Shin DH, Kim SG, Choi KM, Park IB, Yu JM, Balk SH. Use of real time continuous glucose monitoring system as a motivational device for poorly controlled type 2 diabetes. *Diabetes Res Clin Pract*. 2008;82: 73-79.
245. Pearce KL, Noakes M, Keogh J, Clifton PM. Effect of carbohydrate distribution on postprandial glucose peaks with the use of continuous glucose monitoring in type 2 diabetes. *Am J Clin Nutr*. 2008;87: 638-644.
246. Franz MJ, Boucher JL, Green-Pastors J, Powers MA. Evidence-based nutrition practice guidelines for diabetes and scope and standards of practice. *J Am Diet Assoc*. 2008;108(suppl 1):S52-S58.