Association of diet with glycated hemoglobin during intensive treatment of type 1 diabetes in the Diabetes Control and Complications Trial[1–3]

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ABSTRACT

Background: Persons with type 1 diabetes have received widely varying dietary advice based on putative effects on glycemic control.

Objective: The objective was to determine whether diet composition was associated with subsequent glycated hemoglobin (Hb A_{1c}) concentrations during intensive therapy for type 1 diabetes.

Design: We examined associations between quantiles of dietary intake and Hb A_{1c} adjusted for age and sex in 532 intensively treated participants in the Diabetes Control and Complications Trial (DCCT) who had complete dietary data through 5 y of follow-up. Multivariate macronutrient density linear regression models tested the association of Hb A_{1c} at year 5 with macronutrient composition and were adjusted for age, sex, exercise, triglyceride concentration, body mass index (BMI), baseline Hb A_{1c}, and concurrent insulin dose.

Results: Higher insulin dose, lower carbohydrate intake, and higher saturated, monounsaturated, and total fat intakes were associated with higher Hb A_{1c} concentrations at year 5. In age- and sex-adjusted multivariate macronutrient models, substitution of fat for carbohydrate was associated with higher Hb A_{1c} concentrations ($P = 0.01$); this relation remained significant after adjustment for exercise level, serum triglycerides, and BMI ($P = 0.02$) but was no longer significant ($P = 0.1$) after adjustment for baseline Hb A_{1c} and concurrent insulin dose.

Conclusion: Among intensively treated patients with type 1 diabetes, diets higher in fat and saturated fat and lower in carbohydrate are associated with worse glycemic control, independent of exercise and BMI. *Am J Clin Nutr* 2009;89:518–24.

INTRODUCTION

Persons with type 1 diabetes are subjected to widely varying dietary advice based in part on the putative effects of different foods on glycemic control. The 2006–2007 American Diabetes Association (ADA) nutrition recommendations suggest that people with type 1 diabetes adjust insulin doses to meal content, meal size, and activity levels to achieve near-normal glycemic control. Day-to-day carbohydrate consistency has been suggested to be especially important for individuals using fixed daily insulin doses (1–4).

The current ADA recommendations also suggest a flexible range of carbohydrate intake of between 45% and 65% of total calories, which is consistent with the Dietary Reference Intake (5) recommendations (1, 6). Despite this flexible range of carbohydrate intake, persons with type 1 and type 2 diabetes have consistently reported lower carbohydrate intakes of typically between 37% and 45% (7–11).

Studies evaluating the effect of differing percentages of dietary carbohydrate on glycemic control in persons with diabetes have been inconclusive. It is not clear whether a particular dietary macronutrient composition promotes improved glycemic control (12–16). Intensively treated participants in the Diabetes Control and Complications Trial (DCCT) received medical nutrition therapy that focused on carbohydrate consistency and adjustment of insulin doses for variations in dietary intake and activity.

Previous analyses of DCCT data showed that specific dietary composition, including diet consistency and adjustments of insulin dose for variations in food intake, were associated with lower glycated hemoglobin (Hb A_{1c}) concentrations in the intensively treated group (17). To date, no study has evaluated the role of diet in glycemic control in this well-characterized population. We sought to examine the association of diet composition with subsequent Hb A_{1c} concentrations in intensively treated participants with type 1 diabetes in the DCCT. Only participants in the intensive-treatment group were studied to avoid any possible obscuring of the putative association of diet composition by inadequate insulin therapy in the conventional-treatment group.

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SUBJECTS AND METHODS

The DCCT was described in detail previously (18). In brief, 1441 persons with type 1 diabetes aged 13–39 y were randomly assigned to intensive ($n = 711$) or conventional ($n = 730$) therapy. The goal of intensive treatment was to achieve Hb A_{1c} concentrations as close as safely possible to the nondiabetic range (<6.05%); these concentrations were achieved with either continuous subcutaneous insulin infusion or multiple daily injections of insulin, guided by frequent (>4 times/d) self-monitoring of blood glucose. The intensive-treatment group also received dietary, behavioral, and exercise counseling (18).

At the outset, the diet-composition goals for participants in the DCCT were 10–25% protein, 30–35% fat, 45–55% carbohydrate, a polyunsaturated:saturated fat ratio of 0.8:1.0, and <600 mg cholesterol (7). The study protocol was amended in 1988 in response to the National Cholesterol Education Program so that all participants received education on the Step I diet (≤30% fat, ≤10% saturated fat, and <300 mg cholesterol). Further counseling and advice were provided on the Step II diet, and cholesterol-lowering medications were administered to those who did not achieve target LDL concentrations. The importance of diet consistency and meal regularity was emphasized to all participants.

No particular meal-planning approach was mandated. Rather, a variety of meal-planning approaches were used to teach diet consistency, including the ADA exchange system, carbohydrate counting, total available glucose, and healthy food choices (19). Once participants established a framework for diet consistency, they were instructed on how to analyze the blood glucose response to food, insulin, and activity; to adjust insulin doses for expected changes in food intake or activity; and to respond to high blood glucose concentrations in a timely manner (7, 20). However, attaining glycemic goals took precedence over other dietary goals (7).

Participants were generally examined monthly in the DCCT clinics. Detailed anthropomorphic and laboratory data were collected as previously described (18).

Subjects

The 532 subjects in this study included all participants in the intensive-treatment group, other than those who died, who were enrolled in the study and who had been followed up for ≥5 y before the end of the study (75% of a total of 711 participants assigned to the intensive-treatment group).

DCCT dietary data

Trained dietitians collected a modified Burke-type diet history (21) at study entry, 2 and 5 y after randomization, and at the end of the study. Before the interview, DCCT participants or their family members completed a Food Pattern Questionnaire and a Food Preparation Questionnaire (Central Nutrition Coding Unit, University of Minnesota) that listed all foods consumed ≥2 times/mo. The person who usually prepared the meals was asked to participate to ensure completeness of diet history. Study dietitians recorded a description of each meal and snack eaten. Food variations, such as foods consumed on weekends, during different seasons of the year, and away from home, were noted. Fat or salt used in preparation or added topically was recorded. A validated set of 2-dimensional shapes was used to estimate portion sizes (22). Standardized NASCO 3-dimensional food models were used to estimate meat or fish intake. Amounts were documented in household units, eg, teaspoons, cups, and ounces. The diet history typically listed 120–160 food items for each participant. The reproducibility of the dietary history was validated at year 2 of the DCCT (23).

In the current analysis, the macronutrient composition of the diet included total carbohydrate, fat (total, saturated, polyunsaturated, and monounsaturated), protein, fiber (total, soluble, and insoluble), and total calorie intake. Available carbohydrate, defined as carbohydrate (g) minus total dietary fiber (g), was considered as nonfiber carbohydrate. The data did not include individual foods or food groups.

Dietary variables

The dietary history obtained at study entry represented the dietary composition before intervention (baseline, year 0). Diet during the intensive intervention in the DCCT was computed as the average of data obtained from the dietary histories at years 2 and 5 to provide a more stable estimate of dietary intake (24, 25). Dietary composition variables were calculated by dividing the average calories from each macronutrient assessed at years 2 and 5 by the average total calorie intake at years 2 and 5 of follow-up.

Covariates

Covariates included age at study entry, sex, baseline Hb A_{1c} concentration (after the run-in period but before initiation of intensive therapy), exercise level (mean of years 2 and 5), triglyceride concentration (mean of years 2 and 5), body mass index (BMI; in kg/m^2) at year 5, and insulin dose at year 5. Exercise levels were recorded at each annual visit and coded as follows: *1*) strenuous (physically strenuous occupation or ≥5 h of "very hard" exercise/wk), *2*) vigorous (occupation requiring some physical activity and ≥5 h of hard or very hard exercise or ≥8 h of hard or very hard exercise), *3*) moderate (occupation requiring some physical activity or ≥5 h of moderate exercise, or *4*) sedentary (sedentary occupation and ≤5 h exercise/wk). Fasting serum lipid concentrations were measured quarterly. Height and weight were used to calculate BMI. Insulin dose in units per kilogram per day was available yearly, but this value was missing for a few patients. Consequently, for 3 participants, insulin dose at year 4 was substituted for a missing value at year 5.

Glycated hemoglobin

Hb A_{1c} was measured at a central laboratory (18). For 6 subjects, the Hb A_{1c} value from the next available quarterly visit was substituted for a missing value from the year 5 visit. The primary outcome variable was Hb A_{1c} value at year 5. The mean Hb A_{1c} value in the intensive group at 5 y was 7.21 ± 1.17%, with a median of 7.10% and an interquartile range of 6.6%–7.7% (range: 4.7%–13.9%).

Statistics

Normal error linear models adjusted for age and sex were used to assess the association of covariates with the mean concentrations of Hb A_{1c}, with each modeled with quantiles and quantitative measures. To distinguish between the impact of macronutrient composition of the diet and the energy supplied by given macronutrients on the outcome, we used the method of multivariate nutrient density models as described by Willett (26) and Hu et al (27). We included the percentage of energy from protein and

carbohydrate in the model. Because dietary protein remains relatively stable, the models can be interpreted as showing the effect of substitution of carbohydrate for fat while holding the calorie intake constant. Multivariable linear regression macronutrient density models, adjusted for age and sex, were used to assess the relation of the macronutrient composition of diet to Hb A_{1c} at 5 y. We sequentially adjusted for potential confounders, including exercise level, serum triglyceride concentration, and BMI, and finally for concurrent insulin dose as a measure of adequate insulin and baseline Hb A_{1c} concentrations as an indicator of individual capability of achieving glycemic control or as a possible indicator of residual C-peptide production. We also used multivariable logistic regression models to assess the association of the covariates with the odds of an Hb $A_{1c} \leq 7\%$, but the results were consistent with the linear regression model (Table 3) and therefore are not presented. All analyses were conducted by using SAS (version 9.1; SAS Institute, Cary, NC).

RESULTS

At baseline in the DCCT, the 532 participants in the intensive-treatment group had a mean age of 27 ± 7 (range: 13–39) y, and 52% (274/531) were women. Hb A_{1c} concentrations decreased, as intended. There was minimal change in intakes as a percentage of energy from carbohydrate, protein, fiber, and total, saturated, polyunsaturated, and monounsaturated fat; however, a comparison of baseline and mean of intakes at years 2 and 5 showed a statistically significant change, with a slight increase in the percentage of energy from protein and a slight decrease in the percentage of energy from carbohydrate and fat (**Table 1**). During the DCCT, the mean carbohydrate intake was ≈45.5% of energy; total fat and saturated fat intakes contributed 36.8% and 12.7% of energy, respectively. The total calorie intake decreased, whereas BMI increased because of decreased catabolism with improved treatment of diabetes, as evidenced by an improvement of ≈2% in Hb A_{1c}.

Age- and sex- adjusted estimates of the mean concentrations of Hb A_{1c} within quantiles of the dietary variables (**Table 2**) showed that carbohydrate intake was inversely associated with Hb A_{1c} concentrations ($P = 0.01$). Conversely, saturated, monounsaturated, total fat intake and total insulin dose were directly associated with Hb A_{1c} ($P = 0.002$, 0.02, and 0.004, respectively; Table 2).

Multivariable linear regression macronutrient density models that controlled for age and sex showed that carbohydrate was inversely associated with Hb A_{1c} concentrations ($R^2 = 7\%$). The

TABLE 1
Metabolic profile, weight, dietary composition, and exercise in 532 subjects with type 1 diabetes assigned to intensive treatment at baseline and during the Diabetes Control and Complications Trial (DCCT)[1]

	Baseline		During the DCCT[2]		
Variable	Mean ± SD	Median (25th–75th percentile)	Mean ± SD	Median (25th–75th percentile)	*P* value for difference in means[3]
Age (y)	27.3 ± 7	28 (22–33)	—	—	—
Women [*n* (%)]	274 (52)	—	—	—	—
Hb A_{1c} at baseline (%)	9.12 ± 1.57	8.92 (7.95–10.05)	—	—	—
Hb A_{1c} at year 5 (%)	—	—	7.28 ± 1.17	7.10 (6.60–7.70)	0.6[4]
Total cholesterol (mg/dL)	177 ± 33	175 (154–197)	180 ± 29	179 (161–200)	0.002
LDL cholesterol (mg/dL)	110 ± 28	107 (91–127)	113 ± 26	111 (95–131)	0.001
HDL cholesterol (mg/dL)	50 ± 12	48 (42–58)	51 ± 13	50 (42–58)	0.0003
Triglycerides (mg/dL)	84 ± 46	71 (58–95)	78 ± 37	69 (55–90)	0.004
BMI at baseline (kg/m^2)	23.2 ± 2.7	23 (21–25)	—	—	—
BMI at year 5 (kg/m^2)	—	—	26.2 ± 3.7	26 (24–28)	<0.0001[4]
Baseline weight (kg)	68.4 ± 11.0	68.4 (60.5–75)	—	—	—
Absolute weight gain, years 0–5 (kg)	—	—	8.95 ± 7.93	8.0 (3.6–13.6)	<0.0001[4]
Total energy (kcal)	2496 ± 1036	2325 (1829–2938)	2144 ± 707	2010 (1632-2523)	<0.0001
Energy (kcal/kg)	36.9 ± 15.1	33.8 (27.4–42.5)	29 ± 9	27 (22–34)	<0.0001
Carbohydrate (% of energy)	45.7 ± 6.9	44.7 (39.7–49.1)	45.5 ± 6.4	45.5 (40.9–49.7)	0.01
Available carbohydrate (% of energy)[5]	40.4 ± 6.08	41.0 (36.4–44.4)	41.2 ± 5.6	41.2 (37.3–44.9)	0.004
Protein (% of energy)	17.8 ± 3.0	17.6 (15.8–19.5)	18.1 ± 2.4	18.0 (16.6–19.6)	0.02
Total fat (% of energy)	38.5 ± 6.6	38.7 (34.2–42.6)	36.8 ± 6.2	36.9 (32.7–41.3)	<0.0001
Saturated fat (% of energy)	13.5 ± 3.0	13.4 (11.5–15.6)	12.7 ± 2.7	12.7 (10.8–14.4)	<0.0001
Polyunsaturated fat (% of energy)	7.6 ± 2.4	7.3 (5.9–8.7)	7.5 ± 2.0	7.32 (6.2–8.5)	0.4
Monounsaturated fat (% of energy)	14.5 ± 3.0	14.5 (12.7–16.3)	13.9 ± 2.6	13.9 (12.1–15.7)	<0.0001
Fiber (g/1000 kcal)	10.7 ± 3.8	9.8 (8.0–12.7)	10.6 ± 3.4	10.0 (8.3–12.1)	0.6
Soluble fiber (g/1000 kcal)	3.2 ± 1.2	2.9 (2.3–3.8)	3.2 ± 1.2	3.0 (2.4–3.6)	0.7
Insoluble fiber (g/1000 kcal)	5.9 ± 2.7	5.4 (4.0–7.6)	5.8 ± 2.4	5.5 (4.1–7.0)	0.3
Exercise level[6]	2.8 ± 0.9	3 (3–3)	3.1 ± 0.7	3 (3–3.5)	<0.0001

[1] Hb A_{1c}, glycated hemoglobin.
[2] Values are the mean of those obtained at years 2 and 5, unless otherwise specified.
[3] *P* value for paired *t* test for difference in means between baseline and mean of years 2 and 5 unless otherwise specified.
[4] *P* value for change between baseline and year 5.
[5] Carbohydrate (g) minus total dietary fiber (g).
[6] Exercise level: 1 = strenuous, 2 = vigorous, 3 = moderate, and 4 = sedentary.

TABLE 2
Age- and sex-adjusted estimates of glycated hemoglobin (Hb A_{1c}) at year 5, by dietary quantile (Q) ($n = 532$)[1]

Variable	Q1	Q2	Q3	Q4	Q5	*P* value[2]
Energy (kcal/kg)[3]	18.0 (0.4)	23.3 (0.4)	27.1 (0.4)	32.3 (0.4)	43.3 (0.4)	—
Mean total energy intake (kcal)	1574 (33–35)	1831 (33–35)	2051 (33–35)	2298 (33–35)	2969	—
Hb A_{1c} (kcal/kg)	7.31 (0.11)	7.45 (0.11)	7.28 (0.11)	7.11 (0.11)	7.23 (0.11)	0.64
Daily dietary intake[3]						
Mean carbohydrate (g)	201 (6)	236 (6)	239 (6)	260 (6)	269 (6)	—
Total carbohydrate (% of energy)	37 (0.2)	42 (0.2)	45 (0.2)	49 (0.2)	56 (0.2)	—
Hb A_{1c} by carbohydrate intake quintile	7.47 (0.11)	7.29 (0.11)	7.42 (0.11)	7.12 (0.11)	7.08 (0.11)	0.01
Mean available carbohydrate (g)	181 (5)	215 (5)	216 (5)	236 (5)	246 (5)	—
Total available carbohydrate (% of energy)	34 (0.2)	38 (0.2)	41 (0.2)	44 (0.2)	49 (0.2)	—
Hb A_{1c} by available carbohydrate quintile	7.45 (0.11)	7.29 (0.11)	7.42 (0.11)	7.16 (0.11)	7.07 (0.11)	0.01
Mean protein (g)	89 (2)	96 (2)	95 (2)	98 (2)	102 (2)	—
Total protein (% of energy)	15 (0.1)	17 (0.1)	18 (0.1)	19 (0.1)	22 (0.1)	—
Hb A_{1c} by protein quintile	7.34 (0.11)	7.35 (0.11)	7.29 (0.11)	7.3 (0.11)	7.12 (0.11)	0.2
Mean total fat (g)	62 (2)	79 (2)	84 (2)	99 (2)	120 (2)	—
Total fat (% of energy)	28 (0.2)	34 (0.2)	37 (0.2)	40 (0.2)	45 (0.2)	—
Hb A_{1c} by total fat quintile	7.14 (0.11)	7.12 (0.11)	7.32 (0.11)	7.35 (0.11)	7.47 (0.11)	0.004
Mean saturated fat (g)	20.0 (1)	26 (1)	30 (1)	36 (1)	43 (1)	—
Total saturated fat (% of energy)	10 (0.01)	11 (0.01)	13 (0.01)	14 (0.01)	17 (0.01)	—
Hb A_{1c} by saturated fat quintile	7.05 (0.11)	7.23 (0.11)	7.40 (0.11)	7.30 (0.11)	7.41 (0.11)	0.002
Mean polyunsaturated fat (g)	12 (1)	15 (1)	18 (1)	20 (1)	25 (1)	—
Total polyunsaturated fat (% of energy)	5 (0.1)	6 (0.1)	7 (0.1)	8 (0.1)	10 (0.1)	—
Hb A_{1c} by polyunsaturated fat quintile	7.11 (0.11)	7.34 (0.11)	7.17 (0.11)	7.40 (0.11)	7.36 (0.11)	0.21
Mean monounsaturated fat (g)	22 (1)	29 (1)	33 (1)	38 (1)	46 (1)	—
Total monounsaturated fat (% of energy)	10 (0.1)	12.5 (0.1)	13.9 (0.1)	15.3 (0.1)	17.5 (0.1)	—
Hb A_{1c} by monounsaturated fat quintile	7.11 (0.11)	7.25 (0.11)	7.33 (0.11)	7.15 (0.11)	7.55 (0.11)	0.02
Fiber (g/1000 kcal)	7 (0.1)	9 (0.1)	10 (0.1)	12 (0.1)	16 (0.1)	—
Hb A_{1c} by fiber quintile	7.45 (0.11)	7.23 (0.11)	7.35 (0.11)	7.25 (0.11)	7.1 (0.11)	0.11
Exercise category[4]	2.0 (0.02)	3.0 (0.08)	3.5 (0.10)	4 (0.12)	—	—
Hb A_{1c} by exercise category	7.42 (0.11)	7.28 (0.11)	7.29 (0.11)	7.07 (0.11)	—	0.2
BMI at year 5	21.7 (0.13)	24.1 (0.13)	25.6 (0.13)	27.7 (0.13)	32.2 (0.13)	—
Hb A_{1c} by BMI quintile	7.11 (0.11)	7.21 (0.11)	7.01 (0.11)	7.45 (0.11)	7.6 (0.11)	0.0002
Insulin dose at year 5 ($U \cdot kg^{-1} \cdot d^{-1}$)	0.46 (0.01)	0.59 (0.01)	0.67 (0.01)	0.79 (0.01)	1.10 (0.01)	—
Hb A_{1c} by insulin dose at year 5 quintile	7.14 (0.11)	7.07 (0.11)	7.19 (0.11)	7.2 (0.11)	7.79 (0.11)	<0.0001
Carbohydrate (g)/insulin dose ($U \cdot kg^{-1} \cdot d^{-1}$)	192 (11)	275 (10)	340 (10)	417 (10)	628 (11)	—
Hb A_{1c} by carbohydrate:insulin ratio	7.75 (0.11)	7.22 (0.11)	7.1 (0.11)	7.16 (0.11)	7.17 (0.11)	0.01
Hypoglycemia category	0 (0.05)	1 (0.01)	2 (0.13)	>2, mean 5 (0.11)	—	—
Hb A_{1c} by hypoglycemia category	7.25 (0.06)	7.28 (0.11)	7.24 (0.18)	7.49 (0.15)	—	0.3

[1] Quintiles are presented for all variables except hypoglycemia, which had a high fraction of zero values (quantile 1 = 0), and exercise category, which is a 4-category variable. Dietary quantile and Hb A_{1c} estimates were calculated by using the general linear model procedure, and least-squares means were adjusted for age and sex. SEs are shown in parentheses.

[2] *P* value of coefficient of dietary variable in linear regression using Hb A_{1c} at year 5 as a quantitative variable, after age and sex were controlled for, by percentage of total energy intake quintile for dietary intake and by quantile for other variables.

[3] Calculated from the mean values at years 2 and 5.

[4] Exercise level: 1 = strenuous, 2 = vigorous, 3 = moderate, and 4 = sedentary.

inverse relation of carbohydrate intake to Hb A_{1c} was significant ($P = 0.01$) in a model that included age, sex, and dietary variables and after exercise level, triglycerides, and BMI were controlled for ($P = 0.02$); however, this relation became nonsignificant ($P = 0.2$) after baseline Hb A_{1c} and concurrent insulin dose were controlled for (**Table 3**). Further adjustment for rate of severe hypoglycemia did not affect the results (data not shown).

DISCUSSION

Although the DCCT was not designed to examine the effect of diet on glycemia, the current analyses suggest that in persons with type 1 diabetes pursuing intensive glycemic control, the substitution of fat for carbohydrate (ie, diets low in carbohydrate and high in fat and saturated fat) was associated with higher Hb A_{1c} concentrations independent of age, sex, exercise, triglyceride concentration, and BMI, although this relation was weakened after baseline Hb A_{1c} and insulin dose were controlled for. Considering the intensive nutrition counseling provided to the participants about maintaining a consistent carbohydrate intake in the DCCT, the powerful effect of timely and appropriate insulin adjustments in response to high blood glucose concentrations and in anticipation of variations in food intake and the previously shown effect of dietary consistency on glycemia, it is remarkable that any association of dietary composition on glycemia was detected. Notably, the dietary composition of subjects in this cohort is similar to that in other populations that have shown that persons with diabetes tend to have lower carbohydrate intakes and higher total and saturated fat intakes than recommended (8–11). These findings support recommendations that persons with type 1 diabetes restrict saturated fat

TABLE 3
Dietary and metabolic correlates of glycated hemoglobin (Hb A_{1c}) at year 5 in intensively treated patients in the Diabetes Control and Complications Trial (DCCT)[1]

	Model 1	*P* value	Model 2	*P* value	Model 3	*P* value
No. of subjects in model	532		528		528	
Model R^2	0.07		0.13		0.25	
Variables in model[2]						
Age	−0.03 ± 0.01	<0.0001	−0.03 ± 0.01	<0.0001	−0.02 ± 0.01	0.03
Sex	0.07 ± 0.13	0.6	0.14 ± 0.13	0.3	−0.009 ± 0.1	0.9
Percentage of energy from carbohydrate[3]	−0.02 ± 0.01	0.01	−0.02 ± 0.01	0.02	−0.01 ± 0.007	0.1
Percentage of energy from protein[3]	−0.02 ± 0.02	0.3	−0.03 ± 0.02	0.17	−0.01 ± 0.02	0.5
Total energy intake[3]	0.00005 ± 0.0001	0.6	0.00004 ± 0.0001	0.7	−0.00004 ± 0.0001	0.7
Mean exercise level[3,4]	—	—	−0.14 ± 0.07	0.05	−0.12 ± 0.06	0.08
Mean triglyceride[3]	—	—	0.005 ± 0.001	<0.0001	0.002 ± 0.001	0.07
BMI at year 5	—	—	0.04 ± 0.01	0.004	0.02 ± 0.01	0.2
Insulin dose at year 5 ($U \cdot kg^{-1} \cdot d^{-1}$)	—	—	—	—	0.8 ± 0.2	0.0002
Hb A_{1c} at baseline	—	—	—	—	0.25 ± 0.03	<0.0001

[1] Models are multivariable linear regression macronutrient density models in which adjustment for intake of total energy and of 2 of the 3 macronutrients allowed estimation of the substitution of specified macronutrients for the unspecified macronutrient (ie, fat). Hb A_{1c} at year 5 was modeled as the dependent variable.
[2] Parameter estimate.
[3] Calculated from the mean values at years 2 and 5.
[4] Exercise level: 1 = strenuous, 2 = vigorous, 3 = moderate, and 4 = sedentary.

consumption, which is in keeping with recommendations to follow a well-balanced diet.

The evidence to date has been inconclusive as to whether consuming a low-carbohydrate diet is beneficial to glycemic control in type 1 diabetes. The cross-sectional EURODIAB IDDM Complications Study found a modest tendency for Hb A_{1c} concentrations to increase with higher intakes of carbohydrate. The association was more pronounced in participants who received 1 or 2 insulin injections/d and was less pronounced in persons who received ≥3 injections/d. Moreover, these stratifications did not completely distinguish conventional therapy from intensive therapy in terms of self-management behaviors or glycemic outcomes (28). Nielson et al (16) found that a 20% carbohydrate diet (70–90 g carbohydrate/d) resulted in significant reductions in Hb A_{1c}, insulin requirements, and episodes of hypoglycemia. Studies that compared high-carbohydrate, high-fiber diets with low-carbohydrate diets have shown mixed results (29–31). Anderson et al (29) found no significant difference in glycemic control but significantly lower basal insulin requirements and lower total and HDL cholesterol concentrations with higher-carbohydrate, higher-fiber diets than with low-carbohydrate, low-fiber diets in a randomized crossover trial. Other studies have shown improved glycemic control with higher-carbohydrate, higher-fiber diets, but these studies were in persons with poorly controlled type 1 diabetes (30, 31). In patients consuming liquid diets with an adequate supply of endogenous or exogenous insulin, high-carbohydrate diets were associated with lower glucose concentrations, perhaps because the low content of free fatty acids in such diets improves insulin signaling (32, 33).

This factor suggests that the carbohydrate content is less critical than the fat content, to which it is usually inversely related. The higher Hb A_{1c} concentrations we observed in association with higher saturated fat intakes may also be related to an effect of saturated fat on absorption or insulin signaling. Savage et al (34) suggested that high-fat meals interfere with indexes of insulin signaling, which results in a transient increase in insulin resistance. A study by Rosenfalck et al (25) suggested that a lower-fat diet reduces basal free fatty acid concentrations and improves peripheral insulin sensitivity in type 1 diabetes. We found that, although fasting serum triglyceride concentrations (as a weak proxy for free fatty acid concentrations) were positively associated with Hb A_{1c} independently of dietary composition, this relation did not remain significant after insulin dose and baseline Hb A_{1c} concentration were controlled for, likely because an elevation in triglyceride concentrations is also correlated with insulin deficiency. The multivariate nutrient density model substitutes carbohydrate globally for fat. This model, along with the observation that diets that are lowest in saturated and total fat were associated with mean Hb A_{1c} concentrations of 7.05% and 7.14%, respectively, represents a clear signal that diets high in saturated fat are not associated with good glycemic control. The same, but less significant, trends with monounsaturated fats likely reflect the fact that common food choices, such as red meats, contain higher amounts of both saturated and monounsaturated fats. Notably, consumption of healthier polyunsaturated fats was not associated with worse glycemic control.

The relation of dietary composition to Hb A_{1c} became nonsignificant after baseline Hb A_{1c} and concurrent insulin dose were controlled for. This may be related to several factors. First, in the DCCT, participants in the intensive-treatment group who had more residual C-peptide had lower Hb A_{1c} concentrations at baseline and follow-up and a reduced risk of complications and hypoglycemia (35); it is possible that any degree of endogenous insulin secretion allows improved metabolism in a range of diets. In addition, subjects with better glycemic control at baseline may have been more motivated or had more advanced diabetes self-management skills throughout the study, which also would have obscured the association of dietary variation with glycemia. Unmeasured confounders that we were unable to capture elsewhere may have been captured here, because the epidemiologic analysis of dietary intake did not account for what is arguably the most

important factor in the relation of diet to glycemic control—the ability to adequately match the insulin dose to individual meals. The results of previous findings in the intensively treated DCCT cohort showed that consistency in health and diet behaviors was associated with a 1% improvement in Hb A_{1c} and that the adjustment of insulin doses for anticipated food intake was also associated with lower Hb A_{1c} (17). The DCCT was conducted before the availability of rapid-acting insulin analogs, which may improve the ability to match the insulin dose to individual meals. Because the relation of diet was no longer significant after baseline glycemia and global insulin dose were controlled for, however, we do not think the difference in availability of exogenous insulin analogs would have affected these findings.

Finally, several other findings deserve comment. More strenuous exercise or activity level at work was associated with worse glycemia. This may seem counterintuitive, because exercise lowers blood glucose. However, it is possible that subjects with strenuous jobs or exercise routines were tolerating higher mean blood glucose concentrations in an effort to prevent exertion-related hypoglycemia. In addition, weight gain with decreased calorie consumption was a striking finding over the 5 y of the study, which showed the effect of adequate insulin concentrations on reversing catabolism in uncontrolled diabetes. This weight gain was not without cost, as shown by the association between excess weight gain and elevated Hb A_{1c} concentrations in this study and as was shown by elevated inflammatory markers in association with weight gain in the DCCT cohort in another study (36). Further research is needed to determine the extent to which insulin resistance may explain the relation observed between high BMI and Hb A_{1c}.

In summary, this analysis of DCCT participants who were randomly assigned to intensive therapy found that diets higher in fat and saturated fat and lower in carbohydrate were associated with worse glycemic control, independently of exercise, triglyceride concentration, and BMI but not after the baseline degree of glycemic control or insulin dose were controlled for. Contrary to commonly reported dietary practices of persons with diabetes who may restrict carbohydrate intake, these results support current recommendations regarding the limitation of saturated fat intake while promoting the consumption of nutrient-dense carbohydrates, such as fruit, whole grains, and vegetables, with appropriate insulin doses as needed. Future research needs to explore whether persons with diabetes inadvertently increase their saturated fat intake in their efforts to control carbohydrate intake and glycemia.

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