Carbohydrate intake and biomarkers of glycemic control among US adults: the third National Health and Nutrition Examination Survey (NHANES III)[1–3]

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ABSTRACT

Background: Recommendations for preventing and treating type 2 diabetes include consuming carbohydrates, predominantly from whole grains, fruit, vegetables, and low-fat milk. However, the quantity and type of carbohydrates consumed may contribute to disorders of glycemic control.

Objective: We evaluated the association between carbohydrate intakes and biomarkers of glycemic control in a nationally representative sample of healthy US adults who participated in a cross-sectional study, the third National Health and Nutrition Examination Survey.

Design: The sample (5730 men and 6125 women aged ≥ 20 y) was divided into quintiles of carbohydrate intake (as a percentage of energy). Carbohydrate intakes were examined in relation to glycated hemoglobin (Hb A_{1c}), plasma glucose, serum C-peptide, and serum insulin concentrations by using logistic regression.

Results: Carbohydrate intakes were not associated with Hb A_{1c}, plasma glucose, or serum insulin concentrations in men or women after adjustment for confounding variables. Carbohydrate intakes were inversely associated with serum C-peptide concentrations in men and women. Odds ratios for elevated serum C-peptide concentrations for increasing quintiles of carbohydrate intake were 1.00, 0.88, 0.57, 0.39, and 0.75 (P for trend = 0.016) in men, and 1.00, 0.69, 0.57, 0.36, and 0.41 (P for trend = 0.007) in women. When carbohydrate intakes were further adjusted for intakes of total and added sugar, the association of serum C-peptide with carbohydrate intakes was strengthened in men.

Conclusions: Carbohydrate intakes were not associated with Hb A_{1c}, plasma glucose, or serum insulin concentrations but were inversely associated with the risk of elevated serum C-peptide; this supports current recommendations regarding carbohydrate intake in healthy adults. *Am J Clin Nutr* 2003;77:1426–33.

KEY WORDS Third National Health and Nutrition Examination Survey, NHANES III, carbohydrate intake, glycemic control, glycated hemoglobin, glucose, C-peptide, insulin

INTRODUCTION

Current nutrition recommendations for the prevention and treatment of type 2 diabetes and for the general public encourage consumption of foods containing carbohydrates, predominantly whole grains, fruit, vegetables, and low-fat milk (1). However, several authors have argued that total carbohydrates, or more specifically refined starches and sugars, contribute to insulin resistance or disorders of carbohydrate metabolism; other authors have argued against this (2–4). Liu et al (5) suggested that the high-carbohydrate, low-fat diet currently recommended in the United States may increase the risks of insulin resistance and glucose intolerance. However, Marshall et al (6) found that low-carbohydrate, high-fat diets were associated with the onset of type 2 diabetes when compared with high-carbohydrate diets, and that total fat intake was a better predictor of glucose tolerance than was carbohydrate intake. Meyer et al (7) and Salmeron et al (8, 9) reported no associations between intakes of total carbohydrate and risk for type 2 diabetes in cross-sectional studies. Clinical studies have reported that high-carbohydrate diets relative to high-fat diets had beneficial (10), detrimental (11), and neutral (12) effects on various measures of glycemia and insulin responses.

In addition to questions about the effects of total carbohydrate intake, there are long-standing questions regarding the effects of sugar intake, particularly sucrose intake, on risk of type 2 diabetes. Liu et al (13) reported that the sucrose content of the diet was positively associated with plasma concentrations of triacylglycerol (predominantly very-low-density-lipoprotein triacylglycerol) and fasting insulin. However, the results of the few epidemiologic studies about the relation between sugar intake and type 2 diabetes risk are inconsistent (1, 13, 14). The available evidence from clinical trials shows that dietary sucrose does not increase plasma glucose concentrations to a greater extent than do isoenergetic amounts of dietary starch (1). Consumption of fiber-containing foods is encouraged for people with type 2 diabetes and for the general public. It has been reported that dietary fiber improves the postprandial glycemic response and plasma insulin concentrations, most likely by slowing the digestion and absorption of food and by regulating several metabolic hormones (15). However, data on the relation

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between dietary fiber and type 2 diabetes from prospective and case-control studies have been inconsistent (8, 9, 16).

Many years before type 2 diabetes is diagnosed, the patient has identifiable risk factors, such as insulin resistance, hyperinsulinemia, and impaired glucose tolerance. Therefore, the purpose of this study was to examine the association between carbohydrate intake and biomarkers of glycemic control in healthy adults without prior diagnosis of diabetes in a nationally representative, free-living population. We evaluated the association between dietary intake of carbohydrates and biomarkers of glycemic control using data from the third National Health and Nutrition Examination Survey (NHANES III), which was conducted from 1988 to 1994.

SUBJECTS AND METHODS

Data set

NHANES III was conducted by the National Center for Health Statistics. Between 1988 and 1994, nationally representative information was obtained on the health and nutritional status of noninstitutionalized US civilians aged 2 mo and older. In NHANES III, a stratified, multistage probability design was used. The data were collected by using standardized questionnaires and physical examinations; in addition, blood samples were obtained and analyzed. Bilingual interviewers administered the questionnaires at participants' homes, and standardized medical examinations were conducted at the mobile examination centers by health examiners. Laboratory tests were performed on whole blood and serum. Of the 39 695 persons designated to participate, 86% completed the home questionnaire and 78% completed both the home questionnaire and the medical examination. A total of 33 998 persons were surveyed after being selected with the stratified, multistage probability sampling design. Additional details regarding the study design and sample selection were reported previously (17).

Subjects

The subjects included in this study were 5730 men and 6125 women, aged ≥ 20 y, who completed both the home questionnaire and the medical examination. The exclusion criteria were as follows: unreliable or incomplete dietary data as coded by the National Center for Health Statistics (n = 594), pregnancy (n = 230), lactation (n = 95), being told by a physician that they have diabetes (n = 1608), using hypoglycemic medications (insulin or diabetes pills) (n = 1207), not fasting for ≥ 10 h before the morning sample or ≥ 6 h before the afternoon or evening sample (n = 1848), having serum C-peptide or serum insulin concentrations that were extremely abnormal (n = 2), reporting that they changed their diet in the past year because of obesity or diabetes (n = 1194), having total daily energy intakes > 10 000 kcal or < 496 kcal (n = 144), and having intakes of total sugars that were greater than the total carbohydrate intake (n = 7).

Variables

Outcome variables

Carbohydrate intake as a percentage of energy was examined in relation to glycated hemoglobin (Hb A_{1c}), plasma glucose, serum C-peptide, and serum insulin concentrations. Because C-peptide is cosecreted by pancreatic b cells along with insulin and is not extracted by the liver (and thus has a constant peripheral clearance), an elevated fasting serum C-peptide concentration may be a marker for insulin resistance (18). In addition, it is important to note that the 24-h recall data represented food intake on the day before the blood was sampled, and thus the dietary intake data are temporally related to the biochemical data (19).

Dietary variables

Dietary intakes, including carbohydrates, total sugars, added sugars, total fiber, and total energy, were estimated from the 24-h dietary recall data. The primary source of food composition data for NHANES III is the US Department of Agriculture Survey Nutrient Database (20); this source was used in the present study. Total carbohydrates includes sugars and complex carbohydrates. The carbohydrate values for foods were measured by calculating the difference between 100% of the weight of the food and the sum of the weights of the protein, fat, ash, and water. Because total sugars includes the amounts of both naturally occurring and added sugars, whereas added sugars includes only the sugars added to foods, we examined intakes of total sugars and added sugars separately in our analyses. Intakes of total sugars were obtained by summing the intakes of individual sugars (ie, galactose, glucose, sucrose, maltose, fructose, and lactose). Intakes of added sugars were estimated by using the Food Guide Pyramid serving sizes database for NHANES III, which was developed by the National Cancer Institute (21). This database links NHANES III data to servings from each of the Food Guide Pyramid's food groups. Added sugars is a minor food group of the Food Guide Pyramid and includes all sugars used as ingredients in processed and prepared foods, such as breads, cakes, soft drinks, jam, and ice cream, and sugars eaten separately or added to foods at the table. Added sugars does not include naturally occurring sugars. Added sugars are defined by the US Department of Agriculture as white sugar, brown sugar, raw sugar, corn syrup, corn syrup solids, high fructose corn syrup, malt syrup, maple syrup, pancake syrup, fructose sweetener, liquid fructose, honey, molasses, anhydrous dextrose, crystal dextrose, saccharin, and aspartame, when eaten separately or used as ingredients in processed or prepared foods (22).

Other variables

Other variables that may have affected glycemic control were adjusted for in the statistical analyses to reduce residual variance in the outcomes and to control for potential confounding. These variables included age, ethnicity, education, income-to-poverty ratio, marital status, body mass index (BMI; in kg/m^2), cigarette smoking, alcohol consumption, exercise, time of blood collection, and total energy intake. The analyses were repeated controlling for total sugar intake (% of energy), added sugar intake (% of energy), and total fiber intake (g) to determine whether the relation of carbohydrate intake to glycemic control could be attributed to sugar intake (total or added) or fiber intake.

Statistical analyses

We used SAS, release 8.01 (SAS Institute Inc, Cary, NC) and SUDAAN, release 8.0 (Research Triangle Institute, Research Triangle Park, NC) software for all the analyses. SUDAAN was used because of its ability to estimate variances of statistics from a stratified, multistage probability survey design (23). SUDAAN is recommended for use in analyzing national survey data. Sample weights were applied to all analyses to account for the unequal probability of selection, noncoverage, and nonresponse bias resulting from oversampling of the elderly, blacks, and Mexican Americans. Estimates were calculated by the linearization (Taylor series) variance estimation method for population parameters with

TABLE 1
Subject characteristics and dietary intakes by quintile (Q) of carbohydrate intake as a percentage of energy in US adult men participating in the third National Health and Nutrition Examination Survey, 1988–1994[1]

	Q1 (≤39.6%)	Q2 (≤45.6%)	Q3 (≤51.3%)	Q4 (≤57.9%)	Q5 (>57.9%)
Age (y)[2]	42.4 ± 0.7[3]	42.7 ± 0.8	42.7 ± 0.8	44.48 ± 0.6	44.8 ± 0.6
Ethnicity (% white)[4]	77.0[5]	80.8	79.2	77.5	76.7
Education (% with >high school)[4]	43.9	46.2	45.3	41.2	47.6
Income (% not poor)[4,6]	79.4	82.4	80.4	79.3	79.1
Married (%)	72.4	73.4	70.4	75.5	70.0
Physical activity (% with a high level)	43.5	44.1	44.6	44.6	48.0
Current smoker (%)[4]	43.9	34.4	28.6	27.4	24.9
Alcohol use (% who never drink)[4]	20.6	25.6	34.7	36.6	43.8
Vitamin and mineral supplement use (%)	34.2	31.8	38.9	37.6	40.2
BMI (kg/m^2)	26.8 ± 0.3	26.5 ± 0.2	26.4 ± 0.2	26.3 ± 0.2	26.2 ± 0.3
Dietary intakes					
Energy (kJ)[2]	12 205 ± 234	11 912 ± 268	11 347 ± 268	10 970 ± 221	9929 ± 189
Carbohydrate (g)[2]	243.0 ± 4.1	303.5 ± 7.2	328.2 ± 7.7	356.7 ± 7.1	378.4 ± 7.1
Total sugars (g)[2]	95.9 ± 2.8	131.3 ± 4.8	157.3 ± 5.1	179.2 ± 5.4	197.6 ± 5.1
Added sugars (g)[2]	55.2 ± 1.8	84.8 ± 3.6	106.1 ± 4.0	121.4 ± 5.2	137.0 ± 4.4
Dietary fiber (g)[2]	17.2 ± 0.5	19.1 ± 0.5	19.9 ± 0.5	21.1 ± 0.6	21.2 ± 0.5
Total fat (g)[2]	132.0 ± 2.9	119.6 ± 2.7	107.5 ± 3.2	90.7 ± 2.1	65.9 ± 1.7
Energy from carbohydrate (%)[2]	33.2 ± 0.3	42.7 ± 0.1	48.5 ± 0.1	54.3 ± 0.1	64.3 ± 0.2
Energy from total sugars (%)[2]	13.0 ± 0.3	18.3 ± 0.3	22.8 ± 0.3	27.0 ± 0.5	33.2 ± 0.7
Energy from added sugars (%)[2]	7.3 ± 0.2	11.6 ± 0.3	15.1 ± 0.4	18.1 ± 0.5	22.4 ± 0.6
Energy from total fat (%)[2]	40.6 ± 0.4	38.0 ± 0.3	35.1 ± 0.3	31.1 ± 0.3	24.3 ± 0.3

[1] n = 5730.
[2] There was a significant difference between the quintiles, $P < 0.001$ (Wald F test).
[3] Weighted $\bar{x}$ ± SEM.
[4] There was a significant difference between the quintiles, $P < 0.05$ (chi-square test).
[5] Weighted percentage.
[6] Poverty index >1.3.

SUDAAN software. We used chi-square, Wald F test, and multiple logistic regression models for each sex separately. Although there were no significant interactions between sex and carbohydrate intake, we analyzed our data separately by sex because men have significantly different measurements from women for biomarkers of glycemic control and for many of the variables included in the statistical models (ie, intakes of carbohydrates, sugars, fiber, alcohol, and total energy; BMI; physical activity; smoking; and use of vitamin and mineral supplements).

Logistic regression analyses were performed to determine the extent to which carbohydrate intakes influence the likelihood of having abnormal values for biomarkers of glycemic control. Odds ratios (ORs) and 95% CIs for glycemic control variables were calculated by quintile-defined categories (Q1–Q5) of carbohydrate intake (% of energy) after multivariate adjustment for confounding factors. The glycemic control variables were divided into 2 groups (normal and abnormal). The criteria for normal were as follows: Hb A_{1c} <6.0%, fasting plasma glucose <6.16 mmol/L (110 mg/dL), serum insulin ≤17.2 pmol/L (24 microunits/mL), and serum C-peptide ≤1.6 nmol/L (18, 24). For computation of ORs, the first quintile-defined category (Q1) of carbohydrate intake was used as the reference group (OR = 1.0).

The covariates included age, ethnicity, education, income-to-poverty ratio, marital status, BMI, cigarette smoking, alcohol consumption, exercise, time of blood collection, and total energy intake. Age was divided into 6 categories (20–29 y, 30–39 y, 40–49 y, 50–59 y, 60–74 y, and ≥75 y). Ethnicity was divided into 4 categories (non-Hispanic white, non-Hispanic black, Mexican American, and other ethnic groups). Education was divided into 4 categories on the basis of years of school completed (less than high school, high school, some college, and college or more). Income level was divided into 3 categories on the basis of a poverty index (<1.3, 1.3–3.5, and >3.5). Marital status was divided into 2 categories (married and unmarried). BMI was divided into 4 categories (underweight, <20.0; desirable, 20.0–24.9; overweight, 25.0–29.9; and obese, ≥30). Cigarette smoking was divided into 4 categories (never smoked, former smoker, current smoker of <15 cigarettes/d, and current smoker of >15 cigarettes/d). Alcohol consumption was divided into 3 categories [nondrinker, moderate drinker (1–2 drinks/d), and heavy drinker (≥3 drinks/d)]. Physical activity, which was a composite measure of the frequency of exercise in the last month and the intensity rating (metabolic equivalent) of each activity, was divided into 3 categories (sedentary, <20th percentile; moderate activity, 20th to <60th percentile, and vigorous, ≥60th percentile). The time of blood collection was divided into 3 categories (morning sample, afternoon sample, and evening sample). Use of supplements (vitamins and minerals) was divided into 2 categories (yes or no). To understand the relation further, we adjusted for intakes of total sugars (% of energy), added sugars (% of energy), and total fiber (g) separately in additional multivariate models. Tests for trend were conducted by modeling the median value of each quintile-defined category as a continuous variable.

RESULTS

Descriptive statistics

In **Tables 1** and **2**, the distributions of subject characteristics and nutrient intakes according to quintile (Q) of carbohydrate intake as a percentage of energy are shown for men and women. Our data indicate that higher carbohydrate intakes were associated with

TABLE 2
Subject characteristics and dietary intakes by quintile (Q) of carbohydrate intake as a percentage of energy in US adult women participating in the third National Health and Nutrition Examination Survey, 1988–1994[1]

	Q1 (≤41.5%)	Q2 (≤47.7%)	Q3 (≤53.2%)	Q4 (≤60.1%)	Q5 (>60.1%)
Age (y)[2]	43.3 ± 0.8[3]	44.3 ± 0.8	46.0 ± 0.8	46.9 ± 0.8	48.6 ± 0.8
Ethnicity (% white)[4]	80.1[5]	80.1	77.3	74.2	77.3
Education (% with >high school)[4]	37.8	43.7	42.6	37.4	40.4
Income (% not poor)[4,6]	78.9	78.1	75.0	74.5	71.1
Married (%)	65.2	63.7	60.6	61.0	60.0
Physical activity (% with a high level)	33.2	32.5	35.9	36.9	40.5
Current smoker (%)[4]	31.8	25.7	23.1	20.1	19.2
Alcohol use (% who never drink)[4]	36.7	49.0	53.2	65.0	68.8
Vitamin and mineral supplement use (%)	47.8	44.9	47.2	44.4	51.7
BMI (kg/m^2)[2]	26.3 ± 0.2	26.4 ± 0.3	26.1 ± 0.4	25.9 ± 0.2	25.5 ± 0.2
Dietary intakes					
Energy (kJ)[2]	8260 ± 172	7780 ± 149	7870 ± 136	7156 ± 93	6596 ± 113
Carbohydrate (g)[2]	174.8 ± 3.4	207.2 ± 4.0	236.6 ± 4.0	241.2 ± 3.1	261.8 ± 4.4
Total sugars (g)[2]	73.1 ± 2.2	91.9 ± 1.9	113.2 ± 3.0	121.1 ± 2.3	136.5 ± 3.7
Added sugars (g)[2]	43.3 ± 1.7	58.6 ± 1.4	72.8 ± 2.6	79.1 ± 2.6	87.6 ± 3.5
Dietary fiber (g)[2]	12.6 ± 0.3	13.5 ± 0.3	14.6 ± 0.3	15.2 ± 0.4	16.2 ± 0.4
Total fat (g)[2]	91.9 ± 2.7	79.4 ± 1.6	73.5 ± 1.4	57.9 ± 0.9	40.5 ± 0.9
Energy from carbohydrate (%)[2]	35.6 ± 0.3	44.6 ± 0.1	50.4 ± 0.1	56.4 ± 0.1	66.8 ± 0.2
Energy from total sugars (%)[2]	14.7 ± 0.2	19.6 ± 0.3	23.6 ± 0.4	28.0 ± 0.3	34.4 ± 0.6
Energy from added sugars (%)[2]	8.5 ± 0.2	12.2 ± 0.3	14.7 ± 0.4	17.9 ± 0.5	21.5 ± 0.7
Energy from total fat (%)[2]	43.1 ± 0.4	44.0 ± 0.9	35.1 ± 0.3	31.1 ± 0.3	24.3 ± 0.3

[1] n = 6125.
[2] There was a significant difference between the quintiles, $P < 0.001$ (Wald F test).
[3] Weighted $\bar{x}$ ± SEM.
[4] There was a significant difference between the quintiles, $P < 0.05$ (chi-square test).
[5] Weighted percentage.
[6] Poverty index >1.3.

healthier lifestyles. Both men and women with higher carbohydrate intakes had lower prevalences of smoking and alcohol consumption. Higher carbohydrate intake was also associated with lower intakes of energy and fat, but higher intakes of total sugars, added sugars, and total fiber. In particular, intakes of total and added sugars in the highest carbohydrate intake quintiles (Q4 and Q5) were high, at ≈50% and 30% of total carbohydrate intake, respectively. This indicates that sugar intakes (both total and added sugars) contributed substantially to total carbohydrate intake for both men and women.

Inferential statistics

In **Tables 3** and **4**, we show medians, ranges, ORs, and 95% CIs for biomarkers of glycemic control (Hb A_{1c}, plasma glucose, serum C-peptide, and serum insulin concentrations) according to category of carbohydrate intake for men and women, respectively, after multivariate adjustment for potential confounding variables. On the basis of ORs and 95% CIs, carbohydrate intakes were not associated with Hb A_{1c} for men or women, regardless of adjustment for total sugars, added sugars, or total fiber intake. Carbohydrate intakes were not associated with abnormal plasma glucose or serum insulin concentrations for men or women in trend analyses.

Carbohydrate intakes were inversely associated with serum C-peptide concentrations for both men and women. ORs for high serum C-peptide concentrations from Q1 to Q5 of carbohydrate intake were 1.00, 0.88, 0.57, 0.39, and 0.59 (P for trend = 0.016) in men, and 1.00, 0.69, 0.57, 0.36, and 0.41 (P for trend = 0.007) in women. Men with carbohydrate intakes between 51.3% and 57.9% of energy (Q4) were ≈38% less likely to have high serum C-peptide concentrations than were men with carbohydrate intakes ≤39.6% of energy (Q1). In addition, women with carbohydrate intakes between 53.2% and 60.1% of energy (Q4) and >60.1% (Q5) were ≈64% and 59% less likely, respectively, to have high serum C-peptide concentrations than were women with carbohydrate intakes ≤41.5% of energy (Q1). When the relation was further adjusted for intakes of either total sugars or added sugars (% of energy), the association of serum C-peptide concentration with carbohydrate intake was strengthened in men. This suggests that intakes of sugars could play a role in the relation between carbohydrate intake and serum C-peptide concentration in men.

DISCUSSION

In the current study, carbohydrate intakes were not related to Hb A_{1c}, plasma glucose, or serum insulin concentrations in either men or women, after adjusting for demographic and lifestyle factors. However, consuming the lowest amount of carbohydrate (Q1) was associated with elevated concentrations of serum C-peptide, a measure of basal insulin secretion. This finding indicates an association between low-carbohydrate diets and increased basal insulin secretion in the present study. In other studies, low-carbohydrate, high-fat diets were shown to inadequately suppress postprandial mobilization of fatty acids (25), which might play an important role in leading to insulin resistance (26). In short- and long-term studies, increased circulating fatty acids were thought to cause insulin resistance by way of several metabolic defects, including increased basal insulin secretion (27). However, high carbohydrate intakes can raise

TABLE 3
Odds ratios (ORs) and 95% CIs for biomarkers of glycemic control by quintile (Q) of carbohydrate intake as a percentage of energy in US adult men participating in the third National Health and Nutrition Examination Survey, 1988–1994[1]

Biomarkers of glycemic control	Q1 ≤39.6%	Q2 ≤45.6%	Q3 ≤51.3%	Q4 ≤57.9%	Q5 >57.9%	*P* for trend
Hb A_{1c}						
Median (%)	5.19	5.19	5.16	5.21	5.19	
Range (%)	3.6–12.9	3.4–10.0	3.2–14.9	3.2–13.2	3.7–15.7	
Cases with values ≥6% (%)	6.9	8.0	6.9	8.4	6.6	
OR (95% CI)						
Multivariate adjusted[2]	1.00	1.24 (0.81, 1.91)	0.96 (0.71, 1.31)	1.16 (0.77, 1.77)	0.85 (0.52, 1.38)	0.40
Additional adjustment for total sugars	1.00	1.08 (0.69, 1.69)	0.79 (0.54, 1.16)	0.95 (0.61, 1.48)	0.72 (0.39, 1.35)	0.25
Additional adjustment for added sugars	1.00	1.27 (0.82, 1.99)	0.98 (0.72, 1.33)	1.17 (0.72, 1.91)	0.84 (0.47, 1.48)	0.44
Additional adjustment for fiber	1.00	1.33 (0.85, 2.08)	1.06 (0.75, 1.50)	1.33 (0.86, 2.05)	0.99 (0.60, 1.65)	0.94
Plasma glucose						
Median (mmol/L)	5.17	5.27	5.27	5.25	5.25	
Range (mmol/L)	3.0–22.0	3.1–14.0	2.9–24.5	3.7–19.4	3.6–29.2	
Cases with values ≥6.16 mmol/L (%)	9.4	8.8	6.8	8.5	7.8	
OR (95% CI)						
Multivariate adjusted[2]	1.00	0.81 (0.48, 1.37)	0.55 (0.35, 0.86)	0.72 (0.49, 1.05)	0.64 (0.37, 1.10)	0.07
Additional adjustment for total sugars	1.00	0.79 (0.46, 1.36)	0.53 (0.32, 0.88)	0.68 (0.41, 1.13)	0.59 (0.30, 1.17)	0.14
Additional adjustment for added sugars	1.00	0.89 (0.53, 1.47)	0.63 (0.40, 0.99)	0.82 (0.52, 1.30)	0.72 (0.38, 1.33)	0.30
Additional adjustment for fiber	1.00	0.83 (0.49, 1.42)	0.58 (0.37, 0.90)	0.75 (0.50, 1.13)	0.66 (0.38, 1.17)	0.12
Serum C-peptide						
Median (nmol/L)	0.56	0.57	0.58	0.57	0.59	
Range (nmol/L)	0.02–3.67	0.02–3.11	0.02–2.96	0.02–3.33	0.02–2.88	
Cases with values >1.6 nmol/L (%)	5.5	4.9	4.0	2.5	3.8	
OR (95% CI)						
Multivariate adjusted[2]	1.00	0.88 (0.45, 1.74)	0.57 (0.26, 1.22)	0.39 (0.19, 0.79)	0.59 (0.33, 1.04)	0.016
Additional adjustment for total sugars	1.00	0.79 (0.40, 1.55)	0.44 (0.19, 1.02)	0.27 (0.12, 0.60)	0.38 (0.19, 0.80)	0.006
Additional adjustment for added sugars	1.00	0.79 (0.39, 1.61)	0.48 (0.21, 1.14)	0.30 (0.15, 0.62)	0.42 (0.21, 0.86)	0.006
Additional adjustment for fiber	1.00	0.86 (0.44, 1.70)	0.56 (0.26, 1.24)	0.39 (0.18, 0.82)	0.58 (0.31, 1.09)	0.032
Serum insulin						
Median (pmol/L)	46.9	48.4	52.3	47.6	47.6	
Range (pmol/L)	10.6–494.8	10.6–435.1	10.6–385.4	10.6–611.2	10.6–549.7	
Cases with values >17.2 pmol/L (%)	4.5	3.4	3.1	3.2	3.6	
OR (95% CI)						
Multivariate adjusted[2]	1.00	0.64 (0.33, 1.26)	0.49 (0.21, 1.16)	0.63 (0.34, 1.16)	0.62 (0.31, 1.26)	0.26
Additional adjustment for total sugars	1.00	0.64 (0.31, 1.32)	0.46 (0.17, 1.22)	0.56 (0.25, 1.24)	0.53 (0.25, 1.12)	0.15
Additional adjustment for added sugars	1.00	0.64 (0.31, 1.30)	0.48 (0.19, 1.25)	0.60 (0.29, 1.24)	0.57 (0.28, 1.19)	0.20
Additional adjustment for fiber	1.00	0.61 (0.30, 1.24)	0.48 (0.19, 1.18)	0.61 (0.30, 1.23)	0.60 (0.28, 1.28)	0.29

[1] n = 5730. Hb A_{1c}, glycated hemoglobin.
[2] Adjusted for age, ethnicity, education, income, marital status, BMI, physical activity, smoking, alcohol intake, vitamin and mineral supplement use, timing of blood collection, and total energy intake.

plasma fasting triacylglycerol concentrations, primarily by enhancing hepatic synthesis of VLDL, and can also reduce HDL and induce insulin resistance in non-diabetic or diabetic persons (28–31).

Current trends in health promotion emphasize the importance of increasing carbohydrate intake and reducing fat intake, or at least saturated fat intake. High saturated fat intake was associated with increased risk of type 2 diabetes in various populations, such as Japanese Americans, Pima Indians, and Americans of Mexican descent (32). Diets high in complex carbohydrates were shown to protect against glucose intolerance and type 2 diabetes; this finding was thought to be primarily a result of the high fiber content of these diets (33). In the Potsdam cohort of the European Prospective Investigation into Cancer and Nutrition Study, high-energy and energy-adjusted saturated fat intakes were positively associated with Hb A_{1c} concentrations (34). The Nurses' Health Study, however, did not show an association between type 2 diabetes and saturated fat intake or total fat intake (35). A 12-y follow-up study of women in Sweden (36) and a 25-y follow-up of men in the Zutphen Study (37) found no significant associations between total dietary fat or specific types of fat and the risk of type 2 diabetes. Reducing dietary fat, which typically entails increasing dietary carbohydrate, can reduce body weight and improve glycemia in people with glucose intolerance (38). In the Health Professionals Follow-up Study, total fat and saturated fat intakes were associated with increased risk of type 2 diabetes, but this was not independent of BMI (39).

In a controlled feeding trial of hypertriacylglycerolemic subjects, high intakes of sugars, particularly sucrose, increased fasting insulin concentrations (13). However, the results of the few epidemiologic studies on the relation between sugar intakes and diabetes risk are inconsistent. Colditz et al (14) reported no association of sucrose intake with type 2 diabetes incidence in either lean or obese women. In another study, dietary sucrose was shown to have an adverse effect on insulin sensitivity, but this effect may occur only at high intakes (ie, >30% of total energy intake) (40). For carbohydrate-sensitive individuals (those with

TABLE 4
Odds ratios (ORs) and 95% CIs for biomarkers of glycemic control by quintile (Q) of carbohydrate intake as a percentage of energy in US adult women participating in the third National Health and Nutrition Examination Survey, 1988–1994[1]

Biomarkers of glycemic control	Q1 ≤41.5%	Q2 ≤47.7%	Q3 ≤53.2%	Q4 ≤60.1%	Q5 >60.1%	*P* for trend
Hb A_{1c}						
Median (%)	5.05	5.09	5.12	5.13	5.13	
Range (%)	3.4–11.7	3.3–11.6	3.6–14.0	3.3–14.3	3.3–13.0	
Cases with values ≥6% (%)	5.2	6.4	5.3	7.3	6.4	
OR (95% CI)						
Multivariate adjusted[2]	1.00	1.16 (0.64, 2.10)	0.81 (0.39, 1.67)	1.06 (0.58, 1.93)	0.87 (0.52, 1.47)	0.48
Additional adjustment for total sugars	1.00	1.22 (0.68, 2.17)	0.85 (0.42, 1.73)	1.16 (0.61, 2.18)	1.02 (0.56, 1.83)	0.98
Additional adjustment for added sugars	1.00	1.16 (0.66, 2.06)	0.82 (0.40, 1.66)	1.07 (0.59, 1.95)	0.89 (0.54, 1.47)	0.51
Additional adjustment for fiber	1.00	1.16 (0.64, 2.10)	0.81 (0.39, 1.69)	1.08 (0.58, 1.99)	0.91 (0.52, 1.57)	0.64
Plasma glucose						
Median (mmol/L)	4.97	5.01	5.01	5.07	5.08	
Range (mmol/L)	3.6–20.7	2.4–19.5	3.3–19.8	3.1–19.9	3.6–16.1	
Cases with values ≥6.16 mmol/L (%)	5.3	5.6	5.3	5.4	6.1	
OR (95% CI)						
Multivariate adjusted[2]	1.00	0.91 (0.58, 1.42)	0.88 (0.55, 1.40)	0.75 (0.43, 1.32)	0.79 (0.47, 1.33)	0.29
Additional adjustment for total sugars	1.00	1.04 (0.65, 1.65)	1.05 (0.58, 1.90)	0.93 (0.48, 1.77)	0.99 (0.55, 1.79)	0.87
Additional adjustment for added sugars	1.00	0.97 (0.62, 1.51)	0.98 (0.60, 1.57)	0.86 (0.49, 1.52)	0.92 (0.56, 1.51)	0.65
Additional adjustment for fiber	1.00	0.98 (0.62, 1.56)	0.88 (0.57, 1.37)	0.82 (0.46, 1.47)	0.91 (0.53, 1.55)	0.59
Serum C-peptide						
Median (nmol/L)	0.54	0.54	0.54	0.56	0.52	
Range (nmol/L)	0.02–3.31	0.04–4.70	0.03–3.44	0.02–4.01	0.02–3.34	
Cases with values >1.6 nmol/L (%)	4.5	3.8	3.1	2.3	2.0	
OR (95% CI)						
Multivariate adjusted[2]	1.00	0.69 (0.42, 1.12)	0.57 (0.28, 1.17)	0.36 (0.18, 0.73)	0.41 (0.19, 0.89)	0.007
Additional adjustment for total sugars	1.00	0.69 (0.40, 1.19)	0.58 (0.26, 1.30)	0.36 (0.17, 0.76)	0.36 (0.14, 0.92)	0.015
Additional adjustment for added sugars	1.00	0.69 (0.41, 1.14)	0.55 (0.27, 1.11)	0.33 (0.16, 0.66)	0.33 (0.15, 0.72)	0.001
Additional adjustment for fiber	1.00	0.71 (0.43, 1.16)	0.59 (0.29, 1.20)	0.39 (0.18, 0.84)	0.45 (0.20, 1.01)	0.024
Serum insulin						
Median (pmol/L)	45.4	47.2	44.8	47.9	46.2	
Range (pmol/L)	10.6–404.3	10.6–654.0	10.6–384.3	10.6–539.9	10.6–661.8	
Cases with values >17.2 pmol/L (%)	4.1	3.1	3.2	2.5	2.8	
OR (95% CI)						
Multivariate adjusted[2]	1.00	0.60 (0.37, 0.97)	0.74 (0.40, 1.37)	0.52 (0.31, 0.89)	0.75 (0.42, 1.31)	0.28
Additional adjustment for total sugars	1.00	0.68 (0.40, 1.16)	0.91 (0.47, 1.78)	0.67 (0.36, 1.24)	0.94 (0.52, 1.73)	0.81
Additional adjustment for added sugars	1.00	0.63 (0.37, 1.07)	0.80 (0.42, 1.52)	0.58 (0.33, 0.99)	0.80 (0.48, 1.32)	0.36
Additional adjustment for fiber	1.00	0.59 (0.36, 0.95)	0.72 (0.39, 1.32)	0.51 (0.30, 0.86)	0.74 (0.39, 1.40)	0.32

[1] n = 6125. Hb A_{1c}, glycated hemoglobin.
[2] Adjusted for age, ethnicity, education, income, marital status, BMI, physical activity, smoking, alcohol intake, vitamin and mineral supplement use, timing of blood collection, and total energy intake.

hypertriacylglycerolemia and hyperinsulinemia), diets that provide >30% of energy as sucrose may decrease insulin sensitivity and exacerbate hypertriacylglycerolemia (40). In our study, intakes of total sugars and added sugars (% of energy) did not have clear effects on the relation between carbohydrate intake and concentrations of Hb A_{1c}, plasma glucose, or serum insulin in either men or women. However, the association of serum C-peptide with carbohydrate intake (% of energy) was strengthened in men after further adjustment for intakes of total sugars and added sugars (% of energy). This suggests that intakes of total and added sugars (% of energy) may play a role in the relation between carbohydrate intake and serum C-peptide concentration in men.

The relation between dietary fiber intake and type 2 diabetes has received much attention. The Iowa Women's Health Study, a prospective study of postmenopausal women, suggested strong inverse associations between the incidence of type 2 diabetes and intakes of total grains, whole grains, dietary fiber, and cereal fiber (7). Salmeron et al (8, 9) reported that the ratio of high cereal-fiber intake to low glycemic load was associated with decreased risk of type 2 diabetes in the Nurses' Health Study (in women) and in the Health Professionals Follow-up Study (in men). In the European Prospective Investigation into Cancer and Nutrition Study, Boeing et al (34) observed no inverse association between total fiber intake and Hb A_{1c}. In our study, when the relation between carbohydrate intake and biomarkers of glycemic control was further adjusted for dietary fiber intake (g), the results did not change appreciably. However, note that fiber intakes in this nationally representative study sample were well below the commonly recommended amounts of 25–30 g/d.

Glucose tolerance was shown to improve with consumption of a high-carbohydrate diet compared with a high-fat diet, despite a lower response of insulin to an oral glucose load (41). An important factor in controlling the modifications of glucose tolerance and insulin sensitivity during high-carbohydrate diets may be whether hypertriacylglycerolemia is induced, because there is evidence that elevated plasma triacylglycerol concentrations may be

associated with the development of insulin resistance (40). A diet that is moderately high in carbohydrates (55% of energy, mainly complex carbohydrates) with 30% of energy from fat had favorable effects on both insulin sensitivity and the plasma lipid profile compared with a high-fat diet (40% carbohydrate and 45% fat) (5, 41).

Although it can be argued that biomarkers of glycemic control may be affected by dietary fat intake, we indirectly controlled for fat intake by conducting our analyses using percentage of energy from carbohydrate. This is because the percentage of energy derived from protein does not vary greatly; therefore, the percentage of energy from fat must increase as the percentage of energy from carbohydrate decreases (30). In addition, our study used cross-sectional data, and thus the data cannot be used to discriminate cause from effect. Nonetheless, important associations can be noted.

In conclusion, we found no evidence that high or low intakes of carbohydrates are associated with Hb A_{1c}, plasma glucose, or serum insulin concentrations. A low carbohydrate intake was, however, associated with elevated serum C-peptide concentrations, which indicates an association between low-carbohydrate diets and increased basal insulin secretion within the range of carbohydrate intakes in this nationally representative sample of healthy, free-living adults. When we further adjusted for intakes of total and added sugars, the inverse relation between carbohydrate intake and serum C-peptide concentration was strengthened in men, which suggests that the type of carbohydrate may play a role in the relation between total carbohydrate intake and glycemic control. Despite the fact that intakes of added sugars were above current recommendations (< 10% of total energy), our data support current recommendations regarding carbohydrate intake in healthy adults (21). Furthermore, if current recommendations for the intake of added sugars are followed, average serum C-peptide concentrations in the population may decrease, which would be desirable.

This study was designed collaboratively by JMK, YKP, DBA, and WOS using the national survey data accessible to the public. Extensive data analyses were carried out by EJY and JK. The manuscript was mainly written by EJY and JMK under the guidance of WOS and DBA. DBA is on the ILSI North America Board of Trustees. None of the other authors had any financial or personal interest in the organizations sponsoring the research, including advisory board affiliations.

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