The Journal of Nutrition
Nutritional Epidemiology

High Fiber and Low Starch Intakes Are Associated with Circulating Intermediate Biomarkers of Type 2 Diabetes among Women[1–3]

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Abstract

Background: Carbohydrate quality has been consistently related to the risk of type 2 diabetes (T2D). However, limited information is available about the effect of carbohydrate quality on biomarkers related to T2D.

Objective: We examined the associations of carbohydrate quality measures (CQMs) including carbohydrate intake; starch intake; glycemic index; glycemic load; total, cereal, fruit, and vegetable fiber intakes; and different combinations of these nutrients with plasma concentrations of adiponectin, C-reactive protein (CRP), and glycated hemoglobin (HbA1c).

Methods: This is a cross-sectional analysis of 2458 diabetes-free women, ages 43–70 y, in the Nurses Health Study. CQMs were estimated from food-frequency questionnaires, and averages from 1984, 1986, and 1990 were used. Plasma biomarkers were collected in 1990. Multiple linear regression models were used to assess the associations between CQMs and biomarkers.

Results: After age, body mass index, lifestyle, and dietary variables were adjusted, *1*) total fiber intake was positively associated with adiponectin (*P*-trend = 0.004); *2*) cereal fiber intake was positively associated with adiponectin and inversely associated with CRP, and fruit fiber intake was negatively associated with HbA1c concentrations (all *P*-trend < 0.03); *3*) starch intake was inversely associated with adiponectin (*P*-trend = 0.02); *4*) a higher glycemic index was associated with lower adiponectin and higher HbA1c (both *P*-trend < 0.05); *5*) a higher carbohydrate-to-total fiber intake ratio was associated with lower adiponectin (*P*-trend = 0.005); *6*) a higher starch-to-total fiber intake ratio was associated with lower adiponectin and higher HbA1c (both *P*-trend < 0.05); and *7*) a higher starch-to-cereal fiber intake ratio was associated with lower adiponectin (*P*-trend = 0.002).

Conclusions: A greater fiber intake and a lower starch-to-fiber intake ratio are favorably associated with adiponectin and HbA1c, but only cereal fiber intake was associated with CRP in women. Further research is warranted to understand the potential mechanism of these associations in early progression of T2D. *J Nutr* 2016;146:306–17.

Keywords: carbohydrate quality, biological markers/blood, diabetes mellitus, type 2, dietary fiber, starch, adiponectin, HbA1c, C-reactive protein, carbohydrate-to-fiber ratio

Introduction

In 2012, 24.1 million US adults were estimated to have diabetes, 90–95% of which is type 2 diabetes (T2D)[8], and an additional 26 million are estimated to have prediabetes (1). Certain adipocytokine, inflammatory, and glycemic control biomarkers, such as lower adiponectin and higher C-reactive protein (CRP) and glycated hemoglobin (HbA1c), have been identified as predictors of T2D risk and may help detect individuals who are at higher risk of progressing to T2D (2–4). Although it has been well documented that poor carbohydrate quality is positively associated with the risk of T2D (5–8), limited information is available on the association between carbohydrate quality and these intermediate biomarkers of T2D among individuals free of diabetes. Conventional measures of carbohydrate quality such

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[1] Supported by NIH grants UM1 CA186107, R01 CA49449, and U54CA155626.

[2] Author disclosures: HB AlEssa, SH Ley, B Rosner, VS Malik, WC Willett, H Campos, and FB Hu, no conflicts of interest.

[3] Supplemental Tables 1–6 are available from the ''Online Supporting Material'' link in the online posting of the article and from the same link in the online table of contents at http://jn.nutrition.org.

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[8] Abbreviations used: CQM, carbohydrate quality metric; CRP, C-reactive protein; GI, glycemic index; GL, glycemic load; HbA1c, glycated hemoglobin; MET, metabolic equivalent; NHS, Nurses' Health Study; T2D, type 2 diabetes.

Manuscript received July 13, 2015. Initial review completed August 29, 2015. Revision accepted December 8, 2015.

as total fiber, cereal fiber, whole grains, and low glycemic index (GI) and glycemic load (GL) intakes have been consistently associated with a lower risk of T2D (5–8). GL has been inversely associated with adiponectin concentrations among US men (9) and positively associated with HbA1c concentrations in Japanese adults (10). Total fiber intake has been inversely associated with CRP (11–13) concentrations in a nationally representative US study and in 2 other cohorts of US adults, but was not associated with CRP in a study among postmenopausal women (14).

A novel carbohydrate quality metric, the carbohydrate-to-fiber ratio (10:1), has been proposed by the American Heart Association to assess the quality of individual foods (15). A study comparing different carbohydrate selection criteria found that the 10:1 carbohydrate-to-fiber ratio identified more healthful whole grain products than the other criteria, such as the whole grains stamp and whole grains listed as the first ingredient (16). It would be of interest to use this ratio and different variations of it as measures of overall carbohydrate quality of the diet.

Because the effect of carbohydrate quality on the intermediate biomarkers of T2D is largely unknown, we examined the association of conventional measures of carbohydrate quality including GI and GL, carbohydrate intake, starch intake, and total, cereal, fruit, and vegetable fiber intakes and novel measures of carbohydrate quality, including carbohydrate-to-fiber and starch-to-fiber intake ratios, with plasma concentrations of adiponectin, CRP, and HbA1c in US women.

Methods

Study population. The Nurses' Health Study (NHS) was initiated in 1976, and 121,700 female registered nurses between the ages of 30 and 55 y were recruited from 11 US states. The participants were surveyed at baseline and every 2 y following that on their medical history, lifestyle, and incidence of chronic diseases by use of validated questionnaires. Between 1989 and 1990, blood samples were collected from 32,826 women. The current analysis included 2458 women who were previously selected as controls for nested-case control studies on T2D, myocardial infarction, and stroke. They were free of diabetes, cardiovascular disease, and cancer and consented to a blood draw for determination of adiponectin, CRP, and/or HbA1c. The sample sizes vary for the biomarkers because different combinations of biomarkers were previously measured in sub-studies by using a nested case-control design (adiponectin, $n = 2480$; CRP, $n = 1517$; HbA1c, $n = 2336$). The study was approved by the Human Research Committee of Brigham and Women's Hospital in Boston.

Assessment of diet. In 1984, diet was assessed using a 116-item semiquantitative FFQ. In 1986, the FFQ was expanded to 133 items and was mailed to participants every 4 y to update diet information. Participants were asked how often on average ("never" to "6 or more times per day") they consumed a specified common portion size or serving size of specific foods. The validity and reproducibility of the FFQ in measuring food intake has been previously demonstrated (17–20). In a previous validation study in a subsample of 173 nurses in the Boston area, FFQ assessment of total carbohydrate and total fiber intakes was moderately correlated with the average of four 1-wk diet records (total carbohydrate, $r = 0.64$; total fiber, $r = 0.56$) (17, 21). Carbohydrate-rich food items had similar correlation coefficients (cold breakfast cereal, $r = 0.79$; white bread, $r = 0.71$; dark bread, $r = 0.77$; pasta/rice, $r = 0.35$; potatoes, $r = 0.66$) (18).

The main exposure variables included grams of carbohydrate, starch, total fiber, cereal fiber, fruit fiber, and vegetable fiber; GI; GL; and the ratios of carbohydrate to total fiber, carbohydrate to cereal fiber, starch to total fiber, and starch to cereal fiber intakes. Nutrient intakes were calculated by multiplying the frequency of consumption by the nutrient content of the specified portion sizes of each food. Then, the nutrient content of all food items in a subject's diet was summed up to form the individual nutrient variables. The nutrient contents were determined using the USDA Food Composition tables and complemented with information from manufacturers (22). A detailed description of the methods used to assess the GI values of individual foods and mixed meals in the NHS as well as the GL is provided elsewhere (23–25). In brief, GL was calculated by multiplying the GI of each food by its carbohydrate content, then this value was multiplied by the frequency of consumption, and then these values of all foods were summed (25). The overall dietary GI was calculated by dividing the average daily GL by the average daily carbohydrate intake (25). All dietary variables were adjusted for total energy intake, using the residual method, to control for confounding and to remove extraneous variation due to differences in body size, metabolic efficiency, and physical activity (26).

Carbohydrates, starch, total fiber, cereal fiber, starch-to-total fiber ratio, starch-to-cereal fiber ratio, GI, and GL intakes at baseline were all significantly correlated with each other, except there was no significant correlation between starch-to-total fiber ratio and GL (P value = 0.20) (**Supplemental Table 1**). The correlation coefficients (r) ranged from −0.69 to 0.94. The weakest correlation was between GI and cereal fiber ($r = 0.10$), whereas the strongest correlation was between carbohydrates and GL ($r = 0.94$). The correlation between starch-to-total fiber ratio and carbohydrates and starch was −0.17 and 0.48, respectively, whereas the association between starch to cereal fiber ratio and carbohydrates and starch was −0.27 and −0.14, respectively.

Assessment of biomarkers. Participants who were willing to provide blood samples were sent a phlebotomy kit, as previously reported in detail (27). Blood samples were mailed on ice, overnight. Upon arrival at the laboratory, the samples were centrifuged (1200 × *g* for 15 min, at room temperature) to separate plasma, buffy coat, and erythrocytes, and all parts were immediately frozen in liquid nitrogen at a temperature no higher than −130°C until analysis (28). Of all samples mailed, 97% of them arrived within 26 h of phlebotomy (28). Quality-control samples were routinely frozen along with study samples to monitor for plasma changes due to long-term storage and to monitor assay variability.

All biomarkers were measured in the Clinical Chemistry Laboratory at the Children's Hospital in Boston. Plasma total adiponectin was measured by RIA (Linco Research, St. Charles, Missouri), which has a sensitivity of 2 μg/mL (29). The intra-assay CV for adiponectin was 8.9% based on blinded quality-control samples. Plasma high-sensitive CRP concentrations were measured by a latex-enhanced turbidimetric assay on a Hitachi 911 (Denka Seiken, Tokyo, Japan). Concentrations of HbA1c were based on turbidimetric immunoinhibition with hemolyzed whole blood or packed red cells. IL-6 was measured by a quantitative sandwich enzyme immunoassay technique (Quantikine HS Immunoassay kit). Plasma insulin was measured by using an RIA specific for insulin with 1% cross-reactivity between insulin and its precursors (Linco Research, St. Charles, Missouri). The interassay CV was 3.4–3.8% for CRP, <3% for HbA1c, and 5.8–8.2% for IL-6 and 9.5–14.7% for insulin.

Assessment of covariates. Anthropometric data and lifestyle behaviors were derived from the 1990 questionnaire, which was the closest to the timing of blood collection. Participants provided information on their age, weight, menopausal status, postmenopausal hormone use, smoking status, and multivitamin use. Height was reported on the 1976 questionnaire when the NHS was initiated. Self-reported weight was validated in a subsample of the NHS, among 184 women, and was highly correlated with measured weight ($r = 0.96$) (30). BMI was calculated (in kg/m^2). Family history of diabetes in first-degree relatives was reported in 1982 and 1988. Physical activity was assessed in 1988 as hours per week spent on common leisure-time physical activities expressed as metabolic equivalent (MET) hours per week. The correlations between physical activity reported on the questionnaires and that reported on recalls and diaries in 2 validation studies were high (0.79 and 0.62) in the NHS II (31).

TABLE 1 Age-adjusted characteristics of 2458 diabetes-free women from the NHS by quintiles of carbohydrate, starch, and fiber intakes, averaged from 1984 to 1990[1]

	Carbohydrates			Starch			Total Fiber			Cereal Fiber		
	Q1	Q3	Q5	Q1	Q3	Q5	Q1	Q3	Q5	Q1	Q3	Q5
n	576	506	538	567	552	494	514	529	587	468	573	616
Median, g/d	158	193	224	45.1	60.5	76.3	12.4	16.8	23.2	2.4	4.1	7.2
Plasma biomarker concentrations												
Adiponectin, μg/mL	12.2 ± 6.0	11.9 ± 5.7	12.8 ± 6.4	12.5 ± 6.1	11.7 ± 6.1	11.8 ± 5.9	11.4 ± 5.7	11.6 ± 5.9	13.3 ± 6.3	11.4 ± 5.9	12.3 ± 6.2	13.0 ± 6.1
CRP, mg/L	2.58 ± 2.6	2.46 ± 2.6	2.29 ± 2.3	2.44 ± 2.5	2.39 ± 2.7	2.11 ± 2.6	2.51 ± 2.4	2.61 ± 2.6	2.13 ± 2.3	2.52 ± 2.5	2.52 ± 2.6	2.09 ± 2.2
IL-6, pg/mL	1.87 ± 2.1	1.91 ± 2.1	1.75 ± 1.9	1.82 ± 2.0	1.77 ± 2.0	1.82 ± 1.9	1.90 ± 2.0	2.00 ± 2.1	1.69 ± 1.9	1.94 ± 2.1	1.87 ± 2.0	1.71 ± 2.0
HbA1c, %	5.41 ± 1.1	5.46 ± 1.1	5.40 ± 1.1	5.43 ± 1.1	5.44 ± 1.1	5.43 ± 1.1	5.45 ± 1.1	5.43 ± 1.1	5.43 ± 1.1	5.43 ± 1.1	5.45 ± 1.1	5.42 ± 1.1
Lifestyle and dietary characteristics												
Age, y	58 ± 7	58 ± 7	58 ± 7	58 ± 7	58 ± 7	58 ± 7	58 ± 7	58 ± 7	58 ± 7	58 ± 7	58 ± 7	58 ± 7
BMI, kg/m^2	26 ± 5	27 ± 5	25 ± 5	26 ± 5	26 ± 5	25 ± 5	26 ± 6	26 ± 5	25 ± 5	26 ± 6	26 ± 5	25 ± 4
Caucasian, %	99	98	97	98	99	97	99	98	98	98	98	100
Postmenopausal, %	73	75	75	71	76	74	72	73	74	72	73	76
Postmenopausal hormones (ever used), %	63	69	62	64	65	65	58	68	68	59	63	69
Family history of diabetes, %	18	19	19	17	19	22	18	19	20	19	17	19
History of hypertension, %	21	20	18	21	22	18	21	22	20	22	22	17
Hypercholesterolemia, %	7	8	12	8	10	11	8	8	11	9	9	9
Current smoker, %	28	13	10	20	15	12	32	12	6	28	14	8
Physical activity levels, MET-h/wk	14 ± 19	14 ± 16	18 ± 21	16 ± 19	17 ± 28	14 ± 18	10 ± 13	15 ± 16	21 ± 23	15 ± 19	15 ± 27	19 ± 21
Alcohol intake, g/d	14 ± 15	4 ± 7	2 ± 4	10 ± 15	6 ± 10	3 ± 5	10 ± 14	5 ± 10	4 ± 6	10 ± 14	4 ± 8	4 ± 6
Total energy, kcal/d	1739 ± 504	1817 ± 525	1721 ± 483	1747 ± 529	1798 ± 496	1711 ± 509	1693 ± 521	1786 ± 497	1759 ± 513	1739 ± 541	1820 ± 489	1715 ± 470
Carbohydrates, g/d	—	—	—	177 ± 30	192 ± 23	208 ± 24	172 ± 29	188 ± 20	212 ± 24	173 ± 29	191 ± 22	208 ± 23
Starch, g/d	52 ± 10	61 ± 11	66 ± 14	—	—	—	54 ± 12	61 ± 11	65 ± 14	48 ± 10	61 ± 10	69 ± 13
Fiber, g/d												
Total	14 ± 3	18 ± 3	21 ± 6	16 ± 5	18 ± 5	10 ± 5	—	—	—	15 ± 4	17 ± 4	21 ± 5
Cereal	3.4 ± 1.4	4.7 ± 1.8	5.9 ± 2.9	3.4 ± 1.8	4.7 ± 1.8	6.3 ± 2.4	3.2 ± 1.1	4.4 ± 1.4	6.7 ± 3.0	-	-	-
Fruit	2.6 ± 1.4	3.9 ± 1.6	5.4 ± 2.7	4.0 ± 2.3	4.0 ± 2.2	3.9 ± 2.1	2.1 ± 1.0	3.7 ± 1.2	6.1 ± 2.3	3.2 ± 2.0	4.0 ± 2.0	4.6 ± 2.2
Vegetable	5.9 ± 2.0	6.3 ± 2.0	7.3 ± 3.6	6.2 ± 2.2	6.5 ± 2.9	6.7 ± 3.0	4.4 ± 1.2	6.1 ± 1.5	8.9 ± 3.3	6.2 ± 2.3	6.4 ± 2.4	6.7 ± 2.9
Whole grains, g/d	11 ± 7	17 ± 10	24 ± 15	12 ± 8	17 ± 9	25 ± 16	8 ± 6	16 ± 9	27 ± 14	6 ± 4	14 ± 5	31 ± 12
Fruits and vegetables, servings/d	4.6 ± 1.8	5.7 ± 2.0	6.6 ± 2.8	5.6 ± 2.2	5.8 ± 2.4	5.4 ± 2.4	3.5 ± 1.4	5.4 ± 1.6	7.7 ± 2.5	5.2 ± 2.2	5.8 ± 2.4	5.8 ± 2.4
Glycemic load	79 ± 10	101 ± 6	122 ± 11	89 ± 17	101 ± 13	113 ± 14	90 ± 18	99 ± 13	110 ± 15	89 ± 18	100 ± 14	110 ± 14
Glycemic index	52 ± 3	53 ± 3	53 ± 3	50 ± 3	53 ± 2	55 ± 2	53 ± 3	53 ± 3	52 ± 3	52 ± 3	53 ± 3	53 ± 3

(Continued)

TABLE 1 *Continued*

	Carbohydrates			Starch			Total Fiber			Cereal Fiber		
	Q1	Q3	Q5	Q1	Q3	Q5	Q1	Q3	Q5	Q1	Q3	Q5
Sugar-sweetened beverages,[2] cups/d	0.9 ± 1.2	0.8 ± 0.9	0.9 ± 0.9	1.0 ± 1.1	0.8 ± 0.9	0.7 ± 0.8	1.0 ± 1.2	0.8 ± 0.9	0.8 ± 0.9	1.1 ± 1.2	0.8 ± 1.0	0.6 ± 0.8
Coffee,[2] cups/d	2.9 ± 1.9	2.7 ± 1.9	1.9 ± 1.8	2.6 ± 1.9	2.4 ± 1.8	2.3 ± 1.9	2.7 ± 1.8	2.5 ± 1.9	2.2 ± 1.8	2.6 ± 1.9	2.5 ± 1.8	2.3 ± 1.9
Polyunsaturated: saturated fat	0.5 ± 0.1	0.6 ± 0.1	0.6 ± 0.2	0.5 ± 0.1	0.6 ± 0.1	0.6 ± 0.2	0.5 ± 0.1	0.6 ± 0.1	0.6 ± 0.2	0.5 ± 0.1	0.6 ± 0.1	0.6 ± 0.2
Fat, % total energy												
Saturated	13 ± 2	12 ± 2	10 ± 2	12 ± 2	12 ± 2	11 ± 2	13 ± 2	12 ± 2	10 ± 2	13 ± 2	12 ± 2	11 ± 2
Polyunsaturated	7 ± 2	7 ± 1	6 ± 1	6 ± 2	6 ± 1	6 ± 1	6 ± 1	7 ± 1	6 ± 1	6 ± 2	6 ± 1	6 ± 1
trans	2 ± 1	2 ± 0	1 ± 0	2 ± 0	2 ± 1	2 ± 1	2 ± 1	2 ± 0	1 ± 0	2 ± 0	2 ± 1	2 ± 1
Magnesium, mg/d	283 ± 55	304 ± 59	321 ± 79	304 ± 71	300 ± 62	305 ± 67	260 ± 56	294 ± 48	359 ± 66	271 ± 61	295 ± 53	340 ± 66
Red meat intake, servings/d	1.3 ± 0.6	1.0 ± 0.5	0.7 ± 0.4	1.1 ± 0.6	1.1 ± 0.5	0.9 ± 0.5	1.2 ± 0.6	1.1 ± 0.5	0.7 ± 0.4	1.3 ± 0.6	1.0 ± 0.5	0.8 ± 0.5
Fish, servings/d	0.3 ± 0.2	0.3 ± 0.2	0.3 ± 0.2	0.3 ± 0.2	0.3 ± 0.2	0.3 ± 0.2	0.2 ± 0.2	0.3 ± 0.2	0.4 ± 0.2	0.2 ± 0.2	0.3 ± 0.2	0.3 ± 0.2
Dairy, servings/d	2.1 ± 1.2	2.2 ± 1.1	2.0 ± 1.0	2.4 ± 1.3	2.2 ± 1.1	1.7 ± 0.8	2.2 ± 1.3	2.1 ± 1.1	2.0 ± 1.0	2.1 ± 1.3	2.2 ± 1.2	2.0 ± 0.9

[1] Values are means ± SDs or percentages and are standardized to the age distribution of the study population, except for age. CRP, C-reactive protein; HbA1c, glycated hemoglobin; MET, metabolic equivalent task; NHS, Nurses' Health Study; Q, quintile.

[2] 1 cup = 237 mL.

Statistical analysis. Multiple linear regression was used to assess the association between intake measures of carbohydrate quality and the biomarkers. The biomarkers were logarithmically transformed to achieve a normal distribution. The means of the log-transformed biomarkers were calculated as geometric means along with their 95% CIs. Model 1 was age adjusted, and model 2 was adjusted for age, lifestyle, and other dietary factors. The potential confounding factors were age (continuous), total energy intake (in kilocalories per day; continuous), ethnicity (white/nonwhite), smoking status (current, past, never), alcohol consumption (0, 0.1–4.9, 5.0–9.9, 10.0–14.9, ≥15 g/d), physical activity (continuous), postmenopausal hormone use (yes/no), family history of diabetes (yes/no). Dietary covariates included intakes of polyunsaturated fat, saturated fat, *trans* fat (all in percent total energy), and cereal fiber (in grams per day) and were all assessed in quintiles. Because BMI may be on the causal pathway, including it in the model might be an overadjustment. Therefore, we presented the fully adjusted model without BMI in Model 2 and then additionally adjusted for BMI in Model 3.

Average dietary intakes were generated from available data from 1984, 1986, and 1990 FFQs to reduce within-subject variation and represent long-term diet (32). Participants were grouped into quintiles of energy-adjusted dietary exposure variables, with the lowest quintile being the reference group. This has the advantage of reducing the influence of outliers and does not assume linearity (21). Pearson correlation coefficients were used to evaluate associations between carbohydrates, starch, total fiber, cereal fiber, starch to total fiber, starch to cereal fiber, GI, and GL intakes in the study population in 1990.

The measure of biomarkers was standardized for batch effect as described by Rosner et al (33). β-Coefficients from a linear regression model of each biomarker, with a batch indicator variable, were averaged; for each specific batch, the difference between the corresponding β-coefficient from the model and the average coefficient was subtracted from the unadjusted biomarker value to create a continuous measurement that was standardized to the average batch (34). Tests for linear trends were conducted using quintiles of the dietary exposure variable as a continuous variable by assigning the median values of the quintiles to the variable. In our sensitivity analysis, we repeated our main analysis using dietary variables from the last available questionnaire, which was in 1990, instead of the averages.

We tested for potential effect modification of the association between the 4 ratios and the biomarkers by age (<60 and ≥60 y), BMI (<25, 25 to <30, ≥30 kg/m^2), and physical activity (<10 MET-h/week and ≥ 10 MET-h/week) by including a cross-product term in the fully adjusted models (Wald test, 1 df). We also tested for the joint effects of carbohydrate and total fiber, carbohydrate and cereal fiber, starch and total fiber, and starch and cereal fiber intake on the concentrations of the biomarkers. In addition, multiple logistic regression was used to evaluate the association between the main exposures, in quintiles, and dichotomous variables of impaired glucose tolerance (HbA1c <5.7% or ≥5.7 to <6.5%) and elevated CRP (<3 or ≥3 mg/L). All statistical tests were 2-sided, and a *P* value <0.05 was considered statistically significant. SAS version 9.3 for UNIX (SAS Institute Inc) was used for all statistical analysis.

Results

The age-adjusted characteristics of the study participants according to their energy-adjusted carbohydrate, starch, total, and cereal fiber intake are presented in **Table 1**. Women who had a diet higher in carbohydrate, starch, total, or cereal fiber, on average, had a lower alcohol intake and slightly lower BMI; higher physical activity levels (except across quintiles of starch intake); were more likely to have a history of hypercholesterolemia (except across quintiles of cereal fiber intake) or be postmenopausal; and were less likely to have a history of hypertension or to be current smokers. Across the quintiles of carbohydrate, starch, total, and cereal fiber intake, women with higher intakes of 1 also had higher intakes of the other 3. In addition, women who had a diet higher in carbohydrates, starch,

TABLE 2 Means (95% CIs) of total adiponectin (μg/mL) by quintiles of different CQMs in 2480 diabetes-free women from the NHS[1]

	Quintiles					
	1	2	3	4	5	*P*-trend[2]
Conventional CQMs						
GL						
n	544	499	520	454	463	
Median [range]	81 [44–88]	93 [88–97]	101 [97–105]	109 [105–114]	121 [114–171]	
Model 1	12.6 (12.1, 13.1)	11.9 (11.4, 12.5)	12.1 (11.6, 12.6)	11.9 (11.4, 12.5)	12.3 (11.7, 12.8)	0.31
Model 2	13.0 (12.3, 13.7)	12.2 (11.6, 12.9)	12.5 (12.0, 13.1)	12.4 (11.8, 13.1)	12.8 (12.1, 13.5)	0.85
Model 3	13.1 (12.4, 13.8)	12.4 (11.8, 13.0)	12.7 (12.1, 13.2)	12.3 (11.7, 12.9)	12.4 (11.7, 13.2)	0.24
GI						
n	556	520	510	485	409	
Median [range]	49 [37–50]	51 [51–52]	53 [52–54]	54 [54–55]	56 [55–64]	
Model 1	12.9 (12.4, 13.4)	12.6 (12.0, 13.1)	11.9 (11.4, 12.5)	11.6 (11.1, 12.1)	11.7 (11.2, 12.3)	<0.001
Model 2	13.0 (12.4, 13.6)	12.9 (12.3, 13.5)	12.2 (11.6, 12.8)	12.3 (11.7, 12.9)	12.5 (11.8, 13.2)	0.10
Model 3	13.3 (12.7, 13.8)	12.9 (12.3, 13.5)	12.1 (11.5, 12.7)	12.1 (11.5, 12.7)	12.5 (11.8, 13.1)	0.010
Carbohydrates						
n	522	533	455	482	488	
Median [range], g/d	158 [99–171]	180 [171–186]	193 [186–198]	205 [199–213]	224 [213–292]	
Model 1	12.4 (11.9, 12.9)	11.8 (11.3, 12.3)	11.9 (11.4, 12.5)	12.1 (11.6, 12.7)	12.6 (12.1, 13.1)	0.47
Model 2	12.6 (11.8, 13.4)	12.0 (11.4, 12.6)	12.5 (11.9, 13.1)	12.7 (12.0, 13.3)	13.3 (12.5, 14.0)	0.19
Model 3	12.8 (12.0, 13.6)	12.1 (11.5, 12.7)	12.7 (12.1, 13.3)	12.6 (12.0, 13.2)	12.8 (12.1, 13.6)	0.77
Starch						
n	520	530	494	489	447	
Median [range], g/d	45 [9–50]	54 [50–58]	61 [58–64]	67 [64–71]	76 [71–122]	
Model 1	12.4 (11.9, 12.9)	12.4 (11.9, 12.9)	11.8 (11.3, 12.3)	12.3 (11.8, 12.9)	11.9 (11.3, 12.4)	0.20
Model 2	13.0 (12.3, 13.6)	13.0 (12.5, 13.6)	12.2 (11.5, 12.8)	12.6 (12.0, 13.2)	12.1 (11.4, 12.8)	0.08
Model 3	13.1 (12.4, 13.7)	13.1 (12.5, 13.7)	12.1 (11.6, 12.7)	12.6 (12.0, 13.1)	12.0 (11.3, 12.7)	0.02
Total fiber						
n	457	468	474	543	538	
Median [range], g/d	12.4 [5.9–13.7]	14.8 [13.7–15.8]	16.8 [15.8–17.9]	19.1 [17.9–20.6]	23.2 [20.6–50.0]	
Model 1	11.6 (11.1, 12.2)	11.9 (11.4, 12.5)	11.7 (11.1, 12.2)	12.5 (12.0–13.0)	13.0 (12.5, 13.5)	<0.001
Model 2	12.0 (11.3, 12.7)	12.2 (11.6, 12.9)	12.0 (11.4, 12.7)	13.0 (12.4, 13.6)	13.4 (12.7, 14.0)	0.003
Model 3	11.9 (11.2, 12.6)	12.3 (11.6, 12.9)	12.1 (11.5, 12.7)	13.1 (12.5, 13.6)	13.2 (12.6, 13.8)	0.004
Cereal fiber						
n	425	479	504	509	563	
Median [range], g/d	2.4 [0.4–2.9]	3.3 [2.9–3.7]	4.1 [3.7–4.5]	5.2 [4.6–5.9]	7.2 [5.9–22.0]	
Model 1	11.5 (10.9, 12.1)	11.9 (11.4, 12.4)	12.3 (11.8, 12.8)	12.1 (11.5, 12.6)	12.9 (12.4, 13.4)	<0.001
Model 2	12.1 (11.3, 12.8)	12.2 (11.6, 12.9)	12.8 (12.2, 13.4)	12.3 (11.7, 12.8)	13.4 (12.8, 13.9)	0.006
Model 3	12.1 (11.4, 12.8)	12.3 (11.7, 12.9)	12.9 (12.3, 13.5)	12.3 (11.7, 12.9)	13.2 (12.6, 13.7)	0.026
Fruit fiber						
n	418	507	508	540	507	
Median [range], g/d	1.5 [0.1–2.1]	2.6 [2.1–3.0]	3.5 [3.1–4.1]	4.7 [4.1–5.4]	6.6 [5.5–21.0]	
Model 1	11.8 (11.3, 12.4)	11.8 (11.2, 12.3)	12.3 (11.8, 12.9)	12.2 (11.6, 12.7)	12.7 (12.2, 13.3)	0.014
Model 2	12.3 (11.5, 13.0)	12.3 (11.7, 13.0)	12.8 (12.2, 13.3)	12.5 (11.9, 13.1)	13.0 (12.4, 13.6)	0.17
Model 3	12.2 (11.4, 12.9)	12.3 (11.7, 13.0)	12.8 (12.3, 13.4)	12.4 (11.9, 13.0)	13.1 (12.5, 13.7)	0.10
Vegetable fiber						
n	468	486	534	488	504	
Median [range], g/d	3.8 [0.9–4.5]	5.1 [4.5–5.5]	6.0 [5.5–6.6]	7.2 [6.6–8.0]	9.3 [8.0–37.9]	
Model 1	12.3 (11.7, 12.8)	11.5 (11.0, 12.1)	11.9 (11.4, 12.4)	12.3 (11.7, 12.8)	12.9 (12.4, 13.4)	0.011
Model 2	13.2 (12.5, 13.8)	12.1 (11.5, 12.7)	12.5 (11.9, 13.1)	12.5 (12.0, 13.1)	12.7 (12.1, 13.4)	0.87
Model 3	12.8 (12.2, 13.5)	12.2 (11.6, 12.8)	12.4 (11.8, 13.0)	12.7 (12.1, 13.3)	12.9 (12.3, 13.5)	0.45
Novel CQMs						
Carbohydrates:total fiber						
n	537	561	499	468	415	
Median [range]	8.8 [5.0–9.6]	10.2 [9.6–10.8]	11.3 [10.8–11.9]	12.7 [11.9–13.6]	15.1 [13.6–32.7]	
Model 1	13.2 (12.7, 13.7)	12.2 (11.7, 12.7)	11.9 (11.3, 12.4)	12.1 (11.6, 12.6)	11.3 (10.7, 11.8)	<0.001
Model 2	13.2 (12.6, 13.7)	12.7 (12.1, 13.2)	12.5 (11.9, 13.1)	12.5 (11.9, 13.2)	11.9 (11.2, 12.7)	0.020
Model 3	13.2 (12.6, 13.7)	12.8 (12.2, 13.3)	12.5 (11.9, 13.1)	12.5 (11.9, 13.2)	11.7 (11.0, 12.4)	0.005

(Continued)

TABLE 2 *Continued*

	Quintiles					
	1	2	3	4	5	*P*-trend[2]
Carbohydrates:cereal fiber						
n	575	519	503	442	441	
Median [range]	31.2 [10.6–36.4]	41.3 [36.5–45.3]	49.9 [45.4–54.4]	59.5 [54.5–67.7]	80.4 [67.9–1246]	
Model 1	12.6 (12.1, 13.1)	12.2 (11.7, 12.8)	12.1 (11.6, 12.6)	12.4 (11.8, 12.9)	11.4 (10.9, 12.0)	0.005
Model 2	12.9 (12.3, 13.4)	12.6 (12.0, 13.2)	12.5 (11.9, 13.1)	13.0 (12.3, 13.6)	12.0 (11.3, 12.6)	0.09
Model 3	12.7 (12.2, 13.3)	12.6 (12.1, 13.2)	12.6 (12.0, 13.2)	12.9 (12.3, 13.6)	12.1 (11.4, 12.7)	0.19
Starch:total fiber						
n	532	566	492	491	399	
Median [range]	2.5 [0.6–2.9]	3.1 [2.9–3.4]	3.7 [3.4–3.9]	4.2 [3.9–4.5]	5.1 [4.6–11.4]	
Model 1	13.3 (12.8, 13.8)	12.3 (11.8, 12.8)	11.9 (11.4, 12.4)	11.6 (11.1, 12.1)	11.5 (10.9, 12.1)	<0.001
Model 2	13.3 (12.7, 13.9)	12.5 (12.0, 13.1)	12.4 (11.8, 13.0)	12.3 (11.7, 13.0)	12.2 (11.4, 12.9)	0.027
Model 3	13.4 (12.9, 14.0)	12.5 (12.0, 13.0)	12.4 (11.8, 13.0)	12.3 (11.6, 12.9)	12.1 (11.3, 12.8)	0.007
Starch:cereal fiber						
n	573	557	512	438	400	
Median [range]	9.9 [3.3–11.7]	13.1 [11.7–14.5]	15.7 [14.5–17.1]	18.4 [17.1–20.2]	22.6 [20.2–95.5]	
Model 1	13.0 12.5, 13.5)	12.7 (12.2, 13.2)	11.9 (11.4, 12.4)	11.4 (10.9, 12.0)	11.5 (10.9, 12.0)	<0.001
Model 2	13.3 (12.8, 13.8)	12.9 (12.4, 13.5)	12.3 (11.7, 12.9)	11.9 (11.3, 12.6)	12.0 (11.2, 12.7)	<0.001
Model 3	13.1 (12.6, 13.6)	13.0 (12.5, 13.5)	12.4 (11.9, 13.0)	12.0 (11.4, 12.7)	12.0 (11.3, 12.7)	0.002

[1] Model 1: Age-adjusted. Model 2: Adjusted for age (continuous), ethnicity (white/nonwhite), smoking status (never, past, current), alcohol intake (0, 0.1–4.9, 5.0–14.9, ≥15 g/d), postmenopausal hormone use (yes/no), family history of diabetes (yes/no), total energy (continuous), physical activity (continuous), polyunsaturated fat, saturated fat, and *trans* fat (all in quintiles). Models for GI, GL, total carbohydrate, and starch are additionally adjusted for cereal fiber (quintiles). Models for subtypes of fiber are mutually adjusted for the other 2 subtypes of fiber (quintiles). Model 3: Model 2 + additionally adjusted for BMI (continuous). CQM, carbohydrate quality metric; GI, glycemic index; GL, glycemic load; NHS, Nurses' Health Study.

[2] Test for trend based on variable containing median value for each quintile.

total, or cereal fiber, on average, also had higher intakes of whole grains, GL, magnesium, and fruits and vegetables (except across quintiles of starch intake) and had lower intakes of coffee, saturated fat, red meat intake, and sugar-sweetened beverages (except across quintiles of carbohydrate intake).

The age-adjusted characteristics of the study participants by their adiponectin, CRP, and HbA1c concentrations are shown in **Supplemental Table 2**. Participants with higher adiponectin concentrations and lower CRP and HbA1c concentrations had, on average, a lower BMI and total energy intake and higher physical activity levels and alcohol intake and were less likely to have a family history of diabetes, be hypertensive, or smoke. They also had, on average, higher intakes of total, cereal, fruit, and vegetable fiber; whole grains; and magnesium and lower intakes of sugar-sweetened beverages (except across quintiles of HbA1c) and saturated and *trans* fat.

The geometric means of total adiponectin by quintiles of different carbohydrate quality metrics are presented in **Table 2**. In the age-adjusted analysis, higher total, cereal, fruit, and vegetable fiber intakes were associated with higher plasma adiponectin concentrations (all *P*-trend <0.015), whereas the higher ratios of carbohydrate to total fiber, carbohydrate to cereal fiber, starch to total fiber, and starch to cereal fiber and GI were each associated with lower plasma adiponectin concentrations (all *P*-trend ≤0.005). After further adjustment for lifestyle and dietary variables, there were significant inverse associations between carbohydrate to total fiber, starch to total fiber, and starch to cereal fiber and plasma adiponectin and significant positive associations between total and cereal fiber intakes and plasma adiponectin (all *P*-trend <0.03). Further adjusting for BMI strengthened the significant associations between the carbohydrate-to-total fiber and starch-to-total fiber ratios of intake and adiponectin concentrations (all *P*-trend ≤0.007) but slightly weakened the significant results between total fiber, cereal fiber, and starch-to-cereal fiber ratio and adiponectin concentrations (all *P*-trend ≤0.026). In addition, further adjusting for BMI made the inverse associations between GI and starch intakes and plasma adiponectin concentrations statistically significant (all *P*-trend ≤0.021).

The associations between the different carbohydrate quality metrics and CRP concentrations are presented in **Table 3**. In the age-adjusted model, there was a significant trend of increasing CRP concentrations across quintiles of carbohydrate, carbohydrate to total fiber, carbohydrate to cereal fiber, starch to total fiber, and starch to cereal fiber intakes and decreasing CRP concentrations across quintiles of total, cereal, and fruit fiber intakes (all *P*-trend ≤0.042). After additionally adjusting for lifestyle and dietary variables, we found that cereal fiber intake was inversely associated with CRP concentrations, whereas the ratios of carbohydrate to cereal fiber and starch to cereal fiber intakes were positively associated with CRP (all *P*-trend ≤0.024). However, additionally adjusting for BMI attenuated these associations, and only the association between cereal fiber intake and CRP concentrations remained significant (*P*-trend = 0.020).

The geometric means of HbA1c (in percentage) by quintiles of the different carbohydrate quality metrics are presented in **Table 4**. In the age-adjusted models, there was a significant decreasing trend of HbA1c among quintiles of total, cereal, and fruit fiber intakes and a significant increasing trend among quintiles of GI and the ratios of carbohydrate to total fiber, starch to total fiber, and starch to cereal fiber intakes (all *P*-trend ≤0.017). After lifestyle and dietary factors were further adjusted, fruit fiber intake had a significant inverse association with HbA1c (*P*-trend = 0.027). Further adjustment for BMI slightly strengthened the associations, and we found a significant decreasing trend of HbA1c across quintiles of fruit fiber (*P*-trend = 0.020) and a marginally significant increasing trend of HbA1c across quintiles of GI and the ratio of starch to total fiber intake (all *P*-trend <0.05).

TABLE 3 Means (95% CIs) of CRP (mg/L) by quintiles of CQMs in 1517 diabetes-free women from the NHS[1]

	Quintiles					
	1	2	3	4	5	*P*-trend[2]
Conventional CQMs						
GL						
n	346	294	312	283	282	
Median [range]	81 [44–88]	93 [88–97]	101 [97–105]	109 [105–114]	121 [114–171]	
Model 1	2.50 (2.29, 2.72)	2.56 (2.34, 2.80)	2.39 (2.19, 2.60)	2.16 (1.97, 2.36)	2.34 (2.13, 2.57)	0.055
Model 2	2.62 (2.32, 2.96)	2.57 (2.31, 2.86)	2.43 (2.20, 2.69)	2.26 (2.02, 2.52)	2.54 (2.24, 2.88)	0.46
Model 3	2.53 (2.26, 2.83)	2.46 (2.22, 2.71)	2.39 (2.18, 2.63)	2.30 (2.08, 2.55)	2.76 (2.45, 3.10)	0.59
GI						
n	328	319	336	288	246	
Median [range]	49 [37–50]	51 [51–52]	53 [52–54]	54 [54–55]	56 [55–64]	
Model 1	2.27 (2.09, 2.47)	2.45 (2.25, 2.67)	2.31 (2.12, 2.53)	2.43 (2.22, 2.66)	2.54 (2.30, 2.80)	0.14
Model 2	2.45 (2.22, 2.69)	2.51 (2.27, 2.77)	2.47 (2.23, 2.73)	2.47 (2.22, 2.74)	2.55 (2.26, 2.88)	0.70
Model 3	2.37 (2.17, 2.59)	2.48 (2.27, 2.72)	2.46 (2.25, 2.70)	2.58 (2.34, 2.84)	2.58 (2.31, 2.89)	0.20
Carbohydrates						
n	327	315	283	297	295	
Median [range], g/d	158 [99–171]	180 [171–186]	193 [186–198]	205 [199–213]	224 [213–292]	
Model 1	2.61 (2.39, 2.85)	2.45 (2.25, 2.67)	2.45 (2.23, 2.70)	2.20 (2.02, 2.40)	2.25 (2.06, 2.47)	0.006
Model 2	2.83 (2.47, 3.25)	2.50 (2.25, 2.79)	2.43 (2.18, 2.71)	2.28 (2.05, 2.54)	2.42 (2.13, 2.75)	0.13
Model 3	2.71 (2.39, 3.08)	2.42 (2.19, 2.67)	2.37 (2.14, 2.61)	2.32 (2.11, 2.56)	2.62 (2.33, 2.95)	0.70
Starch						
n/quintile	320	327	314	293	263	
Median [range], g/d	45 [9–50]	54 [50–58]	61 [58–64]	67 [64–71]	76 [71–122]	
Model 1	2.43 (2.23, 2.65)	2.46 (2.26, 2.68)	2.40 (2.20, 2.62)	2.51 (2.29, 2.75)	2.12 (1.92, 2.34)	0.10
Model 2	2.45 (2.20, 2.73)	2.45 (2.22, 2.71)	2.53 (2.29, 2.80)	2.65 (2.38, 2.96)	2.31 (2.04, 2.63)	0.88
Model 3	2.44 (2.21, 2.70)	2.49 (2.27, 2.72)	2.43 (2.21, 2.67)	2.65 (2.40, 2.93)	2.41 (2.14, 2.70)	0.87
Total fiber						
n	278	283	303	309	344	
Median [range], g/d	12.4 [5.9–13.7]	14.8 [13.7–15.8]	16.8 [15.8–17.9]	19.1 [17.9–20.6]	23.2 [20.6–50.0]	
Model 1	2.57 (2.34, 2.82)	2.48 (2.26, 2.72)	2.61 (2.38, 2.86)	2.32 (2.13, 2.53)	2.08 (1.91, 2.27)	<0.001
Model 2	2.65 (2.34, 3.02)	2.45 (2.17, 2.75)	2.74 (2.46, 3.04)	2.37 (2.15, 2.61)	2.32 (2.08, 2.59)	0.10
Model 3	2.72 (2.42, 3.05)	2.46 (2.21, 2.74)	2.70 (2.45, 2.98)	2.32 (2.12, 2.54)	2.35 (2.12, 2.59)	0.06
Cereal fiber						
n	279	289	309	295	345	
Median [range], g/d	2.4 [0.4–2.9]	3.3 [2.9–3.7]	4.1 [3.7–4.5]	5.2 [4.6–5.9]	7.2 [5.9–22.0]	
Model 1	2.54 (2.31, 2.80)	2.71 (2.47, 2.97)	2.52 (2.31, 2.75)	2.24 (2.04, 2.44)	2.07 (1.90, 2.25)	<0.001
Model 2	2.59 (2.30, 2.93)	2.95 (2.64, 3.29)	2.57 (2.32, 2.85)	2.30 (2.08, 2.55)	2.19 (1.99, 2.42)	<0.001
Model 3	2.55 (2.28, 2.85)	2.85 (2.58, 3.16)	2.54 (2.32, 2.79)	2.27 (2.07, 2.49)	2.33 (2.12, 2.55)	0.020
Fruit fiber						
n	255	310	312	332	308	
Median [range], g/d	1.5 [0.1–2.1]	2.6 [2.1–3.0]	3.5 [3.1–4.1]	4.7 [4.1–5.4]	6.6 [5.5–21.0]	
Model 1	2.65 (2.41, 2.93)	2.33 (2.13, 2.54)	2.49 (2.27, 2.73)	2.40 (2.21, 2.62)	2.15 (1.96, 2.35)	0.008
Model 2	2.58 (2.26, 2.95)	2.45 (2.19, 2.73)	2.46 (2.22, 2.72)	2.47 (2.25, 2.71)	2.49 (2.24, 2.78)	0.91
Model 3	2.66 (2.36, 3.01)	2.49 (2.26, 2.76)	2.42 (2.21, 2.66)	2.48 (2.28, 2.71)	2.42 (2.19, 2.67)	0.40
Vegetable fiber						
n	281	296	320	307	313	
Median [range], g/d	3.8 [0.9–4.5]	5.1 [4.5–5.5]	6.0 [5.5–6.6]	7.2 [6.6–8.0]	9.3 [8.0–37.9]	
Model 1	2.37 (2.16, 2.59)	2.51 (2.29, 2.75)	2.43 (2.23, 2.65)	2.38 (2.17, 2.61)	2.27 (2.08, 2.48)	0.32
Model 2	2.39 (2.13, 2.68)	2.50 (2.24, 2.79)	2.52 (2.28, 2.79)	2.46 (2.22, 2.72)	2.54 (2.28, 2.82)	0.59
Model 3	2.56 (2.30, 2.84)	2.44 (2.20, 2.70)	2.55 (2.32, 2.79)	2.40 (2.19, 2.64)	2.48 (2.24, 2.73)	0.72
Novel CQMs						
Carbohydrates:total fiber						
n	337	330	326	284	240	
Median [range]	8.8 [5.0–9.6]	10.2 [9.6–10.8]	11.3 [10.8–11.9]	12.7 [11.9–13.6]	15.1 [13.6–32.7]	
Model 1	2.16 (1.98, 2.35)	2.44 (2.24, 2.65)	2.50 (2.29, 2.73)	2.33 (2.12, 2.55)	2.57 (2.33, 2.84)	0.036
Model 2	2.39 (2.16, 2.65)	2.58 (2.34, 2.83)	2.57 (2.32, 2.84)	2.28 (2.04, 2.54)	2.63 (2.32, 2.97)	0.65
Model 3	2.39 (2.18, 2.63)	2.49 (2.29, 2.72)	2.58 (2.35, 2.83)	2.28 (2.06, 2.53)	2.74 (2.45, 3.07)	0.24

(Continued)

TABLE 3 *Continued*

	Quintiles					
	1	2	3	4	5	*P*-trend[2]
Carbohydrates:cereal fiber						
n	339	321	311	273	273	
Median [range]	31.2 [10.6–36.4]	41.3 [36.5–45.3]	49.9 [45.4–54.4]	59.5 [54.5–67.7]	80.4 [67.9–1246]	
Model 1	2.16 (1.98, 2.34)	2.34 (2.14, 2.56)	2.52 (2.31, 2.76)	2.46 (2.23, 2.70)	2.56 (2.33, 2.81)	0.007
Model 2	2.24 (2.03, 2.47)	2.44 (2.21, 2.70)	2.58 (2.33, 2.85)	2.61 (2.33, 2.91)	2.65 (2.37, 2.96)	0.024
Model 3	2.33 (2.13, 2.55)	2.43 (2.22, 2.67)	2.54 (2.31, 2.78)	2.63 (2.38, 2.92)	2.55 (2.31, 2.83)	0.132
Starch:total fiber						
n	334	341	293	319	230	
Median [range]	2.5 [0.6–2.9]	3.1 [2.9–3.4]	3.7 [3.4–3.9]	4.2 [3.9–4.5]	5.1 [4.6–11.4]	
Model 1	2.35 (2.16, 2.57)	2.15 (1.97, 2.34)	2.48 (2.28, 2.71)	2.5 (2.28, 2.74)	2.56 (2.32, 2.84)	0.042
Model 2	2.62 (2.38, 2.90)	2.25 (2.05, 2.47)	2.49 (2.25, 2.76)	2.6 (2.33, 2.91)	2.52 (2.21, 2.88)	0.83
Model 3	2.53 (2.31, 2.78)	2.27 (2.08, 2.47)	2.54 (2.31, 2.79)	2.6 (2.35, 2.89)	2.57 (2.27, 2.90)	0.42
Starch:cereal fiber						
n	344	353	295	263	262	
Median [range]	9.9 [3.3–11.7]	13.1 [11.7–14.5]	15.7 [14.5–17.1]	18.4 [17.1–20.2]	22.6 [20.2–95.5]	
Model 1	2.06 (1.89, 2.24)	2.39 (2.20, 2.59)	2.40 (2.19, 2.62)	2.71 (2.45, 2.98)	2.59 (2.35, 2.85)	<0.001
Model 2	2.18 (1.99, 2.39)	2.54 (2.32, 2.79)	2.46 (2.22, 2.73)	2.78 (2.48, 3.13)	2.67 (2.36, 3.01)	0.005
Model 3	2.32 (2.13, 2.53)	2.51 (2.31, 2.74)	2.39 (2.17, 2.63)	2.72 (2.44, 3.03)	2.60 (2.33, 2.91)	0.07

[1] Model 1: Age-adjusted. Model 2: Adjusted for age (continuous), ethnicity (white/nonwhite), smoking status (never, past, current), alcohol intake (0, 0.1–4.9, 5.0–14.9, ≥15g/d), postmenopausal hormone use (yes/no), family history of diabetes (yes/no), total energy (continuous), physical activity (continuous), polyunsaturated fat, saturated fat, and *trans* fat (all in quintiles). Models for GI, GL, total carbohydrate, and starch are additionally adjusted for cereal fiber (quintiles). Models for subtypes of fiber are mutually adjusted for the other 2 subtypes of fiber (quintiles). Model 3: Model 2 + additionally adjusted for BMI (continuous). CQM, carbohydrate quality metric; CRP, C-reactive protein; GI, glycemic index; GL, glycemic load; NHS, Nurses' Health Study.

[2] Test for trend based on variable containing median value for each quintile.

The associations between the different carbohydrate quality metrics and both IL-6 and fasting insulin are presented in **Supplemental Tables 3** and **4**, respectively. There were no significant associations between any of the carbohydrate quality metrics and IL-6 or fasting insulin. In addition, we found no significant effect modification by age, BMI, or physical activity levels on the associations between any of the 4 ratios and plasma concentrations of adiponectin, CRP, or HbA1c. We also did not find any significant multiplicative interactions among carbohydrate and total fiber, carbohydrate and cereal fiber, starch and total fiber, and starch and cereal fiber intakes on any of the 3 biomarkers when we tested for joint effects (all *P*-interactions >0.05). In our sensitivity analysis using data from the 1990 questionnaire only, we found very similar, although slightly attenuated, results to our main analysis. In addition, using dichotomous variables of impaired glucose tolerance (HbA1c <5.7% or ≥5.7 to <6.5%) and elevated CRP (<3 or ≥3 mg/L), we found that none of the main exposures were associated with risk of prediabetes (HbA1c, 5.7 to <6.5%) (**Supplemental Table 5**) or elevated CRP concentrations (≥3 mg/L) (**Supplemental Table 6**), which is associated with higher risk of cardiovascular disease (35), after age, lifestyle, and dietary factors were adjusted.

Discussion

In diabetes-free women, higher starch-to-total fiber intake was associated with lower adiponectin concentrations and higher HbA1c concentrations, and higher starch-to-cereal fiber intake was associated with lower adiponectin. Higher starch intake was associated with lower adiponectin concentrations and higher CRP concentrations. Total fiber intake was positively associated with adiponectin concentrations, whereas cereal fiber intake was positively associated with adiponectin concentrations and inversely associated with CRP concentrations, and fruit fiber intake was inversely associated with HbA1c concentrations. GI, but not GL, was inversely associated with adiponectin and positively associated with HbA1c concentrations.

Although a meta-analysis of 13 prospective cohort studies found a 72% reduction in risk of T2D per 1-log μg/mL increment in adiponectin concentrations among diverse populations (2), the association between different measures of carbohydrate quality and plasma adiponectin concentrations is largely unknown. In our study population of healthy postmenopausal women, higher total and cereal fiber intakes and lower starch, starch-to-cereal fiber ratio, and GI intakes were associated with higher concentrations of adiponectin. In a 12-wk randomized controlled trial among obese T2D patients, a study population with different study characteristics than our study population, there was a 60% increase in plasma adiponectin concentrations in the fiber-supplemented group, whereas no significant change was observed in the control group (36). Among diabetic women from our same cohort, higher cereal fiber intake and lower GI and GL were also associated with higher plasma adiponectin, after age and lifestyle factors were adjusted (37). Although we did not find an association between GL intake and adiponectin concentrations, a study among men that had no cardiovascular disease, GL was modestly inversely associated with adiponectin concentrations where adiponectin concentrations lower by 1.3 μg/mL per 1 SD increase of GL (9).

HbA1c is a measure of glycemic control used to diagnose T2D (38). Most studies have investigated the associations between measures of carbohydrate quality and HbA1c among individuals with diabetes rather than healthy individuals. However, in this cross-sectional analysis of healthy postmenopausal women, higher cereal fiber intake and lower starch-to-cereal fiber and carbohydrate-to-cereal fiber intake were

TABLE 4 Means (95% CIs) of HbA1c (%) by quintiles of different CQMs in 2336 diabetes-free women from the NHS[1]

	Quintiles					
	1	2	3	4	5	*P*-trend[2]
Conventional CQMs						
GL						
n	515	465	485	442	429	
Median [range]	81 [44–88]	93 [88–97]	101 [97–105]	109 [105–114]	121 [114–171]	
Model 1	5.41 (5.38, 5.44)	5.46 (5.42, 5.49)	5.46 (5.42, 5.49)	5.46 (5.42, 5.49)	5.40 (5.37, 5.44)	0.98
Model 2	5.41 (5.36, 5.45)	5.46 (5.41, 5.50)	5.47 (5.44, 5.51)	5.49 (5.45, 5.53)	5.45 (5.40, 5.50)	0.22
Model 3	5.40 (5.36, 5.45)	5.44 (5.40, 5.48)	5.47 (5.43, 5.51)	5.50 (5.46, 5.54)	5.46 (5.41, 5.51)	0.054
GI						
n	524	495	487	445	385	
Median [range]	49 [37–50]	51 [51–52]	53 [52–54]	54 [54–55]	56 [55–64]	
Model 1	5.40 (5.37, 5.43)	5.44 (5.40, 5.47)	5.44 (5.40, 5.47)	5.46 (5.43, 5.50)	5.45 (5.41, 5.49)	0.014
Model 2	5.42 (5.38, 5.46)	5.46 (5.42, 5.50)	5.48 (5.44, 5.51)	5.46 (5.42, 5.50)	5.46 (5.41, 5.51)	0.16
Model 3	5.41 (5.38, 5.45)	5.45 (5.42, 5.49)	5.48 (5.44, 5.52)	5.47 (5.43, 5.51)	5.46 (5.41, 5.50)	0.048
Carbohydrates						
n	492	498	427	463	456	
Median [range], g/d	158 [99–171]	180 [171–186]	193 [186–198]	205 [199–213]	224 [213–292]	
Model 1	5.42 (5.39, 5.45)	5.46 (5.42, 5.49)	5.46 (5.43, 5.50)	5.46 (5.43, 5.50)	5.38 (5.35, 5.42)	0.24
Model 2	5.43 (5.37, 5.48)	5.45 (5.41, 5.49)	5.49 (5.45, 5.53)	5.49 (5.45, 5.53)	5.41 (5.36, 5.46)	0.97
Model 3	5.42 (5.37, 5.47)	5.45 (5.41, 5.49)	5.48 (5.44, 5.52)	5.49 (5.45, 5.54)	5.43 (5.38, 5.48)	0.47
Starch						
n	486	504	476	457	413	
Median [range], g/d	45 [9–50]	54 [50–58]	61 [58–64]	67 [64–71]	76 [71–122]	
Model 1	5.42 (5.39, 5.46)	5.43 (5.40, 5.47)	5.45 (5.41, 5.48)	5.44 (5.41, 5.48)	5.43 (5.40, 5.47)	0.61
Model 2	5.43 (5.39, 5.47)	5.44 (5.41, 5.48)	5.47 (5.43, 5.51)	5.48 (5.44, 5.52)	5.46 (5.41, 5.50)	0.25
Model 3	5.42 (5.38, 5.47)	5.44 (5.40, 5.48)	5.46 (5.43, 5.50)	5.48 (5.44, 5.52)	5.47 (5.42, 5.51)	0.10
Total fiber						
n	430	435	448	501	522	
Median [range], g/d	12.4 [5.9–13.7]	14.8 [13.7–15.8]	16.8 [15.8–17.9]	19.1 [17.9–20.6]	23.2 [20.6–50.0]	
Model 1	5.47 (5.44, 5.51)	5.44 (5.41, 5.48)	5.44 (5.40, 5.47)	5.44 (5.41, 5.47)	5.40 (5.37, 5.43)	0.006
Model 2	5.47 (5.42, 5.52)	5.46 (5.42, 5.51)	5.47 (5.43, 5.51)	5.46 (5.42, 5.49)	5.43 (5.38, 5.47)	0.15
Model 3	5.48 (5.43, 5.53)	5.46 (5.41, 5.50)	5.46 (5.42, 5.50)	5.45 (5.42, 5.49)	5.43 (5.39, 5.47)	0.19
Cereal fiber						
n	386	454	478	482	536	
Median [range], g/d	2.4 [0.4–2.9]	3.3 [2.9–3.7]	4.1 [3.7–4.5]	5.2 [4.6–5.9]	7.2 [5.9–22.0]	
Model 1	5.45 (5.41, 5.49)	5.45 (5.42, 5.49)	5.45 (5.42, 5.49)	5.44 (5.40, 5.47)	5.40 (5.37, 5.43)	0.017
Model 2	5.44 (5.39, 5.49)	5.47 (5.43, 5.52)	5.48 (5.44, 5.52)	5.45 (5.41, 5.49)	5.43 (5.04, 5.47)	0.30
Model 3	5.44 (5.39, 5.48)	5.47 (5.43, 5.51)	5.47 (5.44, 5.51)	5.45 (5.41, 5.48)	5.44 (5.41, 5.48)	0.57
Fruit fiber						
n	394	474	482	510	476	
Median [range], g/d	1.5 [0.1–2.1]	2.6 [2.1–3.0]	3.5 [3.1–4.1]	4.7 [4.1–5.4]	6.6 [5.5–21.0]	
Model 1	5.47 (5.43, 5.51)	5.43 (5.40, 5.47)	5.48 (5.44, 5.51)	5.42 (5.39, 5.45)	5.39 (5.36, 5.43)	0.003
Model 2	5.48 (5.43, 5.53)	5.44 (5.40, 5.49)	5.51 (5.47, 5.55)	5.43 (5.39, 5.47)	5.41 (5.37, 5.46)	0.027
Model 3	5.48 (5.44, 5.53)	5.45 (5.41, 5.49)	5.50 (5.47, 5.54)	5.43 (5.40, 5.47)	5.41 (5.37, 5.45)	0.020
Vegetable fiber						
n	441	449	487	465	494	
Median [range], g/d	3.8 [0.9–4.5]	5.1 [4.5–5.5]	6.0 [5.5–6.6]	7.2 [6.6–8.0]	9.3 [8.0–37.9]	
Model 1	5.48 (5.44, 5.51)	5.41 (5.37, 5.44)	5.43 (5.40, 5.47)	5.44 (5.40, 5.47)	5.43 (5.40, 5.46)	0.30
Model 2	5.47 (5.42, 5.51)	5.41 (5.37, 5.45)	5.46 (5.42, 5.50)	5.46 (5.42, 5.50)	5.47 (5.43, 5.51)	0.53
Model 3	5.49 (5.44, 5.53)	5.41 (5.37, 5.45)	5.46 (5.43, 5.50)	5.45 (5.41, 5.49)	5.46 (5.42, 5.50)	0.99
Novel CQMs						
Carbohydrates:total fiber						
n	530	511	475	438	382	
Median [range]	8.8 [5.0–9.6]	10.2 [9.6–10.8]	11.3 [10.8–11.9]	12.7 [11.9–13.6]	15.1 [13.6–32.7]	
Model 1	5.40 (5.37, 5.44)	5.44 (5.40, 5.47)	5.44 (5.40, 5.47)	5.43 (5.40, 5.47)	5.48 (5.44, 5.52)	0.007
Model 2	5.43 (5.39, 5.47)	5.45 (5.42, 5.49)	5.46 (5.42, 5.50)	5.46 (5.42, 5.50)	5.49 (5.44, 5.54)	0.10
Model 3	5.43 (5.40, 5.47)	5.45 (5.41, 5.48)	5.45 (5.42, 5.49)	5.46 (5.41, 5.50)	5.50 (5.45, 5.54)	0.056

(Continued)

TABLE 4 *Continued*

	Quintiles					
	1	2	3	4	5	*P*-trend[2]
Carbohydrates:cereal fiber						
n	543	47	484	419	403	
Median [range]	31.2 [10.6–36.4]	41.3 [36.5–45.3]	49.9 [45.4–54.4]	59.5 [54.5–67.7]	80.4 [67.9–1246]	
Model 1	5.41 (5.38, 5.44)	5.44 (5.40, 5.47)	5.44 (5.41, 5.48)	5.45 (5.41, 5.48)	5.46 (5.42, 5.50)	0.057
Model 2	5.44 (5.40, 5.47)	5.45 (5.41, 5.49)	5.48 (5.44, 5.52)	5.45 (5.41, 5.49)	5.46 (5.41, 5.50)	0.60
Model 3	5.44 (5.41, 5.48)	5.45 (5.41, 5.49)	5.47 (5.44, 5.51)	5.45 (5.41, 5.49)	5.45 (5.41, 5.49)	0.85
Starch:total fiber						
n	517	526	465	464	364	
Median [range]	2.5 [0.6–2.9]	3.1 [2.9–3.4]	3.7 [3.4–3.9]	4.2 [3.9–4.5]	5.1 [4.6–11.4]	
Model 1	5.41 (5.38, 5.44)	5.40 (5.37, 5.43)	5.46 (5.42, 5.49)	5.44 (5.40, 5.47)	5.49 (5.45, 5.53)	0.001
Model 2	5.44 (5.40, 5.47)	5.43 (5.40, 5.47)	5.47 (5.43, 5.51)	5.47 (5.43, 5.52)	5.48 (5.43, 5.53)	0.08
Model 3	5.43 (5.39, 5.47)	5.44 (5.40, 5.47)	5.47 (5.43, 5.50)	5.48 (5.44, 5.52)	5.48 (5.43, 5.53)	0.043
Starch:cereal fiber						
n	544	548	468	406	370	
Median [range]	9.9 [3.3–11.7]	13.1 [11.7–14.5]	15.7 [14.5–17.1]	18.4 [17.1–20.2]	22.6 [20.2–95.5]	
Model 1	5.40 (5.37, 5.43)	5.41 (5.38, 5.44)	5.47 (5.43, 5.50)	5.46 (5.43, 5.50)	5.46 (5.42, 5.50)	0.004
Model 2	5.44 (5.40, 5.47)	5.44 (5.41, 5.48)	5.49 (5.45, 5.53)	5.46 (5.41, 5.50)	5.45 (5.40, 5.50)	0.43
Model 3	5.45 (5.41, 5.48)	5.44 (5.40, 5.47)	5.48 (5.44, 5.52)	5.46 (5.42, 5.50)	5.45 (5.40, 5.50)	0.63

[1] Model 1: Age-adjusted. Model 2: Adjusted for age (continuous), ethnicity (white/nonwhite), smoking status (never, past, current), alcohol intake (0, 0.1–4.9, 5.0–14.9, ≥15g/d), postmenopausal hormone use (yes/no), family history of diabetes (yes/no), total energy (continuous), physical activity (continuous), polyunsaturated fat, saturated fat, and *trans* fat (all in quintiles). Models for GI, GL, total carbohydrate, and starch are additionally adjusted for cereal fiber (quintiles). Models for subtypes of fiber are mutually adjusted for the other 2 subtypes of fiber (quintiles). Model 3: Model 2 + additionally adjusted for BMI (continuous). CQM, carbohydrate quality metric; GI, glycemic index; GL, glycemic load; HbA1c, glycated hemoglobin; NHS, Nurses' Health Study.

[2] Test for trend based on variable containing median value for each quintile.

associated with lower concentrations of HbA1c. Among healthy adults, 2 cross-sectional studies found no association between whole grain intake and HbA1c concentrations, but 1 among obese Japanese adults found a positive association between GL (not GI) and HbA1c concentrations, which we did not observe in our study (10, 39, 40). Among adults with T2D, a meta-analysis of 10 randomized controlled trials of fiber supplementation lasting from 3 to 12 wk found that participants in the fiber intervention arm, overall, had a reduction in HbA1c of 0.26% more than the reduction in control participants (41).

CRP is an inflammatory marker and predictor of the development of T2D (27, 42, 43). Similar to our findings, other studies have found no association between dietary GI (44) and GL (44–46) and CRP concentrations. Although 1 study among postmenopausal women did not find an association between dietary fiber intake and CRP concentrations (14), which is similar to our findings, several cross-sectional and prospective studies have found inverse associations between dietary fiber intake and CRP concentrations after adjustment for age and lifestyle variables (11–13). This discrepancy could be due to several factors including further adjustment for dietary variables in our study, which may have attenuated the associations, or the possibility of different amounts of subtypes of fiber comprising total fiber intakes in previous studies. In our cohort we were able to study the associations between different subtypes of fiber and CRP concentrations and found that cereal fiber was the only subtype of fiber associated, inversely, with CRP concentrations.

In this analysis, carbohydrate quality, but not quantity, was associated with concentrations of adiponectin, CRP, or HbA1c, which was not unexpected because most observational studies found no association between total carbohydrate intake and risk of T2D (47–52). Starch and total fiber intakes were both individually associated with adiponectin concentrations, but not HbA1c, in our analysis. However, the starch-to-total fiber ratio was significantly associated with variation in both biomarkers. Intakes of starch and fiber, individually, are important measures of carbohydrate quality, but it seems that this ratio captures a broader representation of the overall carbohydrate quality of the diet. Carbohydrate quality is extremely complex, and thus far no individual nutrient or metric is able to summarize it or evaluate all aspects of it in the diet. However, the starch-to-total fiber intake ratio appears to be a promising potential carbohydrate quality metric of the overall diet in relation to diabetes and related diseases. Unlike the GI, which characterizes the response of blood to glucose, this ratio directly captures actual components or subtypes of carbohydrates. Diets higher in refined grains and lower in fiber, fruits, and vegetables will have a higher starch-to-fiber ratio, whereas diets rich in whole grains, legumes, fruits, and vegetables will have a lower ratio. Therefore, the starch-to-total fiber ratio may differentiate between diets of different carbohydrate quality.

The mechanism by which the starch-to-total fiber ratio affects adiponectin concentrations and glycemic control is not completely understood. In our analysis, some carbohydrate quality variables associated with adiponectin concentrations were also associated with HbA1c concentrations in the opposite direction. GI and the ratio of starch to total fiber intake were positively associated with HbA1c concentrations, a result of high plasma glucose levels, and in turn associated with lower plasma adiponectin concentrations (37). This is plausible because it has been proposed that dietary factors, such as low fiber and high GI and GL, decrease adiponectin concentrations by increasing blood glucose, which regulates adiponectin expression in adipocytes (37, 53). Adiponectin is associated with a lower risk of T2D by several proposed mechanisms, including increasing insulin sensitivity and anti-inflammatory effects (54). Furthermore, the role of dietary fiber, GI, or the ratio of starch to total fiber intake in inflammation has not been established. It has been proposed that postprandial hyperglycemia, which is associated with consuming a diet high in GI and GL and high in starch-to-fiber ratio, induces oxidative stress, which causes inflammation and is therefore associated with the risk of T2D (55).

There are several strengths to this study. A large sample size of healthy women with detailed diet and lifestyle information allowed us to finely adjust for potential confounding. Using the average intake from multiple FFQs reduced within-subject variability and better represented long-term diet (32). Having detailed information on medical history allowed us to reduce the degree of recall bias due to presence of other relevant chronic diseases by excluding participants with such conditions that may influence dietary modification. Limitations of our study include the cross-sectional nature of the study, which prevented inferring causality. The study was conducted among predominantly Caucasian female nurses, which increases internal validity but may decrease generalizability to other populations. In addition, some degree of measurement error in use of FFQs to collect dietary information and the single measure of biochemical markers is likely, and such nondifferential misclassification could have attenuated the results. However, the FFQ has been validated and the measures of carbohydrate foods are among the most accurately reported (17, 18), and the long-term stability of plasma biomarkers collected and stored under this protocol has been documented previously (56). Furthermore, carbohydrate-related variables are all naturally related in the diet, where diets rich in fiber tend to also be lower in GI and in starch-to-fiber ratios and higher in whole grains and micronutrients; therefore, separating the effect of 1 of these aspects from the rest is complicated.

In conclusion, we found that diets with higher fiber intake and lower starch-to-fiber intake ratio were significantly associated with higher concentrations of adiponectin and lower concentrations of HbA1c, but only cereal fiber intake was associated, inversely, with CRP concentrations in diabetes-free women. Additional research is warranted to understand the underlying mechanisms and causality of the associations.

Acknowledgments

HBA and FBH designed the analysis and had primary responsibility for final manuscript content; HBA conducted the analysis, interpreted the data, and wrote the manuscript; SHL, BR, VSM, WCW, HC, and FBH assisted in interpreting the data and edited the manuscript. All authors critically reviewed the manuscript for important intellectual content and read and approved the manuscript.

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