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Association of glycemic load with cardiovascular disease risk factors: the Women's Health Initiative Observational Study

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Abstract

Objective—Associations between dietary glycemic load (GL) and cardiovascular disease (CVD) risk factors, including plasma lipoprotein/lipid levels, blood pressure (BP), and glucose metabolism factors, in the Women's Health Initiative Observational Study were examined.

Methods—A random sample of 878 Observational Study participants (postmenopausal women age 50 to 79 years) with baseline blood measures (647 White, 104 Black, 127 Hispanic) was included. Dietary GL was estimated from baseline food frequency questionnaires, which assessed dietary intake over the previous three months. At the baseline visit, participants completed demographic and health habit questionnaires, fasting blood samples were collected, anthropometric measurements were completed, and BP was assessed.

Results—In all participants combined, GL was inversely associated with high-density lipoprotein (HDL) cholesterol (*P* for trend = 0.004) and positively associated with log10-transformed triglycerides (*P* = 0.008). While there were no statistically significant interactions of race/ethnicity

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with associations between GL and CVD risk factors, stratified results were suggestive, showing that GL was positively associated with total cholesterol ($P = 0.018$) and low-density lipoprotein (LDL) cholesterol ($P = 0.038$) in Hispanics. In Whites, there was a trend of reduced HDL cholesterol with higher GL ($P = 0.003$), while GL was positively associated with log10-transformed triglycerides ($P = 0.015$). Associations between GL and HDL cholesterol and GL and triglycerides also varied by BMI, although the interactions were not statistically significant.

Conclusions—Among these generally healthy postmenopausal women, GL was associated with HDL cholesterol and triglycerides. Suggestive effects of race/ethnicity and BMI on these associations need to be confirmed in larger studies.

Keywords

Glycemic load; Glycemic index; Carbohydrate; Cardiovascular disease; Women's Health Initiative

Introduction

The possible role of dietary carbohydrate in cardiovascular disease (CVD) risk has not been studied extensively. Diets with a high proportion of carbohydrate have been shown to raise fasting insulin levels compared to lower-carbohydrate diets [1]. Chronic hyperinsulinemia plays a critical role in the development of insulin resistance, manifested by chronic hyperinsulemia, along with hypertension and dyslipidemia, especially in the setting of excess energy intake and obesity [2]. Since recommendations to decrease fat intake for CVD prevention usually result in increased carbohydrate intake [3], it is important to investigate the association of measures of carbohydrate intake with CVD risk factors.

Carbohydrates elicit a wide spectrum of blood glucose and insulin responses within individuals, influenced by both the quantity and the quality of the carbohydrate. Glycemic index (GI) is a ranking of foods based on their postprandial blood glucose responses and is a measure of carbohydrate quality [4]. Glycemic load (GL) is a measure that incorporates both the quantity and quality of dietary carbohydrates and is considered by many investigators to be the biologically relevant exposure in epidemiologic studies of carbohydrate intake and disease risk [5,6].

There is mounting evidence that dietary GL influences blood lipoprotein and lipid levels. Observational studies consistently have shown positive associations between GL and triglyceride concentrations and inverse associations between GL and HDL cholesterol concentrations [7-10]. However, none of these studies investigated how these associations may vary by race/ethnicity. The possible effect of BMI on these associations also has not been studied extensively. In addition, there are few published studies on the possible influence of GL on other CVD risk factors, such as insulin resistance and blood pressure (BP), especially studies that presented results stratified by race/ethnicity and BMI.

The Women's Health Initiative (WHI) Observational Study provided an opportunity to investigate further the association between GL and CVD risk factors, including lipoprotein/lipid levels, BP, and glucose metabolism factors. The WHI included 17% non-white participants (primarily Black/African American and Hispanic/Latina), which allowed us to assess race/ethnicity-specific associations between GL and CVD risk factors as a secondary analysis. In addition, the Observational Study included women with BMIs ranging from normal to obese, also enabling us to assess these associations within strata of BMI.

Materials and methods

Subjects

The WHI is a large study of chronic diseases affecting postmenopausal women's health, including CVD, cancer, and osteoporosis. In addition to a set of randomized controlled Clinical Trials, the WHI included the Observational Study (N = 93,676), from which participants for the present study were drawn. Details of the study design and recruitment efforts for WHI participants have been published elsewhere [11,12]. Briefly, women learned of the WHI primarily from mailings sent by the 40 Clinical Centers and, if interested in participating, contacted the Clinical Centers to further determine interest and eligibility through a series of screening visits. Women uninterested or ineligible for participation in the WHI Clinical Trials component were invited to be enrolled in the Observational Study, as were those who were specifically recruited for the Observational Study. Women were eligible for participation in WHI if they were 50-79 years of age at screening and likely to live in close geographic proximity to one of the Clinical Centers for at least three years. Women were excluded for any medical condition associated with predicted survival of less than three years, conditions impacting retention (alcohol or drug dependence, mental illness, or dementia), or active participation in any intervention trial in which participants were individually randomized to an intervention or control group. The WHI protocol was approved by the institutional review boards at the Clinical Coordinating Center at the Fred Hutchinson Cancer Research Center (Seattle, WA) and at each of the 40 Clinical Centers. All participants provided written informed consent.

Dietary assessment

During screening, all Observational Study participants completed a standardized food frequency questionnaire (FFQ). The FFQ was developed for the WHI to estimate average daily nutrient intake over the previous three-month period and included 122 foods or food groups [13]. Originally, the dietary database for the WHI FFQ did not include GI and GL values; therefore, the database was modified to include these values. The methods for integrating GI and GL values into the existing WHI FFQ dietary database have been described in detail elsewhere [14]. Briefly, to add GI to the database, a spreadsheet was constructed that assigned GI values to each FFQ food item that contained at least five grams of carbohydrate. These data were then merged into the primary food and nutrient database so that GI became part of the nutrient string for each individual food. GI values of carbohydrate-containing foods on the WHI FFQ were obtained from published human experimental studies or imputed from foods with similar carbohydrate and fiber content [15]. After each eligible FFQ line item was assigned a GI value, a structured language server query was run to calculate the GL for both total carbohydrate and available carbohydrate (total carbohydrate minus total fiber) [6,16]. The GL values were then calculated for each FFQ line item, and the data were merged with the main nutrient database [14]. For these analyses, GL based on available carbohydrate was used.

Questionnaire and clinical data collection

WHI Observational Study participants provided data by completing standardized questionnaires, submitting to interviews, and attending clinic visits. Details of the data collection methods are published elsewhere [17]. Briefly, participants completed questionnaires at the baseline visit that inquired about age, race/ethnicity, health history, health habits, and behavioral and psychosocial characteristics. WHI-certified clinic staff measured height using a calibrated stadiometer and weight by a calibrated balance-beam or digital scale. BMI was calculated as kg/m^2. BP was measured using a mercury sphygmomanometer with appropriately sized BP cuffs, determined for each participant based on upper arm circumference. The first measurement was taken following a five-minute rest period. A second

measurement was taken following a 30-second rest. The mean of the two measurements was the BP reported for that visit.

Blood collection and analysis

Blood samples were collected from all Observational Study participants at baseline. Samples were obtained in a fasting state (at least 12 hours) and maintained at 4 °C for up to one hour until plasma or serum was separated from cells. Processed aliquots were placed in -70 °C freezers within two hours of collection. Aliquots of biospecimens were sent on dry ice to the central repository, where storage at -70 °C was maintained until samples were sent to labs for analysis.

Baseline blood samples were analyzed for a randomly selected 1% of the Observational Study participants (n = 1062) [18]; these samples were used for this investigation. All lipids and lipoprotein subfractions were analyzed from EDTA-treated plasma. Total cholesterol and triglycerides were measured enzymatically, HDL cholesterol was measured by manganese sulfate precipitation, and LDL cholesterol was calculated according to the method of Friedewald [19]. Additional details have been published [17] and described [20] elsewhere. Glucose and insulin were measured in serum; glucose by a hexokinase method and insulin by ELISA. Estimation of insulin resistance (IR) was assessed with fasting serum insulin and glucose concentrations using homeostasis model assessment (HOMA) according to the following formula [21]: fasting serum glucose (mmol/L) × fasting serum insulin (μU/mL)/22.5.

Statistical analysis

This was a cross-sectional analysis restricted to “not Hispanic White” (White), “not Hispanic Black” (Black), and Hispanic participants. To avoid confounding, analyses were restricted to participants who did not report having diabetes and had serum glucose <126 mg/dL at baseline, resulting in a final sample size of 878. Analyses began with descriptive statistics (mean, standard deviation) calculated for continuous covariates (age, BMI, physical activity), explanatory variables (energy, GL, GI, carbohydrate), and outcome measures (lipoprotein/lipid values, BP, glucose metabolism factors), overall and by self-reported race/ethnicity. For categorical covariates, proportions of individuals reporting current smoking and alcohol use (more than five alcoholic drinks per week) were calculated overall and by self reported race/ethnicity. To test for differences in covariates across racial/ethnic groups, analysis of variance models and chi-square analyses were used for continuous and categorical outcomes, respectively. For the continuous outcomes, logarithmic transformations (base 10) were employed when the normality assumption appeared to be violated. If the transformation approach failed to produce an adequate approximation to the normal distribution, the equivalent non-parametric method to ANOVA (Kruskal Wallis) was utilized. To examine associations of lipoproteins/lipids, BP, and glucose metabolism factors with the explanatory variables, ordinary least squares regression models were developed. Histograms and normal probability plots were used to check the normality assumptions for the regression models. When the normality assumption appeared to be violated (as was the case for triglycerides, glucose, and insulin), logarithmic transformations (base 10) were employed. To examine for collinearity among predictors, variance inflation factors were calculated for each predictor included in the regression models.

To test for linear trends in the CVD risk factors across the quartiles of GL, quartile ranks were included as a continuous predictor in the regression models. The primary associations assessed in this paper were tested using a standard variable added last test in regression. Specifically, the linear effect of the quartiles of GL was tested for significant association with the outcome after adjustment for the following baseline factors: age, BMI, energy intake, smoking, alcohol use, and physical activity (number of episodes of exercise per week). Similar models were

developed for the constituents of GL, GI and carbohydrate. To correct for multiple comparisons among ethnic groups, Bonferroni corrections were employed. All analyses were performed using SAS statistical software, version 9.1 (SAS Institute Inc., Cary, NC). All *P*-values reported in the text are tests for linear trend.

Given the stratified analysis by self-reported race/ethnicity of the relationship of GL with lipoproteins/lipids, glucose metabolism factors, and BP, careful consideration was given to the range of effect sizes detectable with 80% power for the sample. Assuming that the covariates age, BMI, energy intake, smoking, alcohol use, and physical activity could explain 5% of the variability of the outcome (as indicated by the data), 648 white participants would provide 80% power to detect an increase in r^2 of 1.1% by including one additional predictor. Under the same assumption, 104 Black participants would provide 80% power to detect an increase in r^2 of 6.7% by including one additional predictor, and 127 Hispanic participants would provide 80% power to detect an increase in r^2 of 5.6% by including one additional predictor. Based upon these power calculations, the white non-Hispanic strata has the greatest statistical power to detect small to medium associations between of GL with lipoproteins/lipids, glucose metabolism factors, and BP.

Stratified analyses were conducted to examine the relationship between GL and CVD risk factors by self-reported race/ethnicity and by BMI. Though formal tests of interaction were conducted to examine whether the associations between GL and the risk factors varied among the categories of race/ethnicity and BMI, the statistical power of these tests was low due to the small sample sizes within the strata. Therefore, we do present the stratified analyses as a set of descriptive secondary analyses despite the lack of statistically significant interactions in most cases.

Results

Baseline characteristics

Black participants, on average, had a higher BMI, were less physically active, and had a lower prevalence of alcohol use than White or Hispanic participants (Table 1). Blacks also reported significantly lower total daily energy intake than the other two groups. Mean dietary GL was significantly lower in Blacks compared to the other groups. This reflected primarily lower carbohydrate intake in Blacks, as mean GI was slightly higher in Blacks compared to Whites and Hispanics.

While total and LDL cholesterol concentrations were similar in all three groups, HDL cholesterol was significantly lower in Hispanics. Triglycerides were substantially lower in Blacks than in the other two groups. While systolic BP (SBP) did not differ significantly among the groups, diastolic BP (DBP) was higher in Blacks compared to Whites and Hispanics. Serum insulin concentration was lowest in Whites, as was HOMA-IR.

Compared to the Observational Study overall, the subsample means were similar for age and BMI among the racial/ethnic groups; rankings were similar for smoking status, self-reported energy intake, total cholesterol and lipoprotein cholesterol fractions, triglycerides, insulin, SBP, and DBP. Less similarity was seen for fasting glucose concentrations [11].

Overall associations of GL with CVD risk factors

GL was inversely associated with HDL cholesterol concentration in all participants combined (*P* for trend = 0.004) (Table 2). HDL cholesterol was approximately 10% lower in the highest quartile of GL compared to the lowest quartile. Neither component of GL (GI or carbohydrate) was significantly associated with HDL cholesterol, although the association with carbohydrate approached significance (*P* = 0.066; data not shown). GL was positively associated with log10-

transformed triglycerides ($P = 0.008$). Triglycerides were approximately 17% higher in the highest quartile of GL compared to the lowest quartile. The associations of GI and carbohydrate with triglycerides were each of borderline significance ($P = 0.062$ and 0.083, respectively). While there were higher total and LDL cholesterol concentrations with increasing GL in the entire sample, these trends were not statistically significant. There were no associations of GL with glucose metabolism factors or BP in all participants combined.

Associations of GL with lipoproteins/lipids by race/ethnicity

GL was positively associated with total cholesterol concentration in Hispanic participants ($P = 0.018$), with total cholesterol approximately 21% higher in the highest quartile of GL compared to the lowest (Table 3). This reflected a similar association between carbohydrate intake and total cholesterol in Hispanics ($P = 0.005$; data not shown); however, no association between GI and total cholesterol in Hispanics was observed. A positive association of GL with LDL cholesterol also was seen in Hispanic participants ($P = 0.038$), with LDL cholesterol approximately 34% higher in the highest quartile of GL compared to the lowest. Again, this reflected mainly an association between carbohydrate and LDL cholesterol ($P = 0.020$), but not between GI and LDL cholesterol in these participants. No associations were seen between GL and total or LDL cholesterol in Whites or Blacks. Tests of interaction, to examine whether the association between GL and total cholesterol or LDL cholesterol varied by race/ethnicity, were not statistically significant ($P = 0.431$ and 0.275, respectively).

There was a clear trend of decreasing plasma HDL cholesterol with increasing GL in Whites ($P = 0.003$). Mean HDL cholesterol concentration was approximately 12% lower in the highest quartile of GL compared to the lowest quartile in this group. Also in Whites, there was a significant inverse association of HDL cholesterol with carbohydrate intake ($P = 0.032$), but the association approached but did not reach significance for GI ($P = 0.086$). There were no significant associations between GL and HDL cholesterol in Blacks or Hispanics. A test of interaction of race/ethnicity with the association between GL and HDL cholesterol did not achieve statistical significance ($P = 0.540$).

GL was positively associated with log10-transformed plasma triglyceride concentration in Whites ($P = 0.015$), but not in Blacks or Hispanics. Triglycerides were approximately 17% higher in the highest quartile of GL compared to the lowest quartile in this group. Neither carbohydrate intake nor GI was separately associated with plasma triglycerides in Whites, although the association with GI approached significance ($P = 0.081$). There was no significant interaction of race/ethnicity with the association between GL and triglycerides ($P = 0.771$).

Associations of GL with glucose metabolism factors by race/ethnicity

No associations between GL (or its two component measures) and log10-transformed serum glucose, log10-transformed serum insulin, or HOMA-IR were evident in any of the racial/ethnic groups (Table 3).

Associations of GL with BP by race/ethnicity

SBP decreased with increasing GL in Whites ($P = 0.029$) (Table 3). SBP was inversely associated with carbohydrate intake in White participants ($P = 0.010$), but not with GI. An association between GL and SBP was not observed in Blacks or Hispanics. There was no significant interaction of race/ethnicity with the association between GL and SBP ($P = 0.858$). There were no associations between GL and DBP in any of the race/ethnicity groups.

Associations of GL with lipoproteins/lipids by BMI

GL was inversely associated with HDL cholesterol concentration in normal weight participants ($P = 0.036$), with HDL cholesterol approximately 11% lower in the highest quartile of GL compared to the lowest (Table 4). Neither GI nor carbohydrate was associated individually with HDL cholesterol in these participants (data not shown). No associations were seen between GL and HDL cholesterol in overweight or obese participants, although the inverse association approached statistical significance in overweight participants ($P = 0.067$). A positive association between GL and triglycerides was observed only in overweight participants ($P = 0.004$), with triglycerides approximately 38% higher in the highest quartile of GL compared to the lowest. This reflected primarily an association between carbohydrate and triglycerides ($P = 0.026$), but not between GI and triglycerides in these participants. No associations were seen between GL and triglycerides in normal weight or obese participants. Tests of interaction, to examine whether the association between GL and HDL cholesterol or GL and triglycerides varied by BMI, were not statistically significant ($P = 0.613$ and 0.752, respectively).

Associations of GL with glucose metabolism factors by BMI

No associations between GL (or its two component measures) and log10-transformed serum glucose, log10-transformed serum insulin, or HOMA-IR were evident in any of the BMI groups (Table 4).

Associations of GL with BP by BMI

No associations between GL (or its two component measures) and SBP or DBP were evident in any of the BMI groups (Table 4).

Discussion

This is one of the first studies to report on the associations of GL with CVD risk factors within race/ethnicity and BMI strata. While this study corroborated the results of previous studies confirming an association of GL with certain CVD risk factors (lipoproteins/lipids) and apparent lack of an association with others (glucose metabolism factors), previous studies either did not include race/ethnicity- and BMI-diverse samples or did not present their results by race/ethnicity or BMI strata.

In this sample of WHI Observational Study participants as a whole, we observed that GL was inversely associated with HDL cholesterol. This corroborates results from several observational studies, including the Nurses' Health Study [10], the Women's Health Study [22], the Whitehall II study [23], and the Third National Health and Nutrition Examination Survey (1988-1994) [8]. GL also was inversely associated with HDL cholesterol in studies of Japanese women [24], healthy adults [25], and healthy young males and females [9], but in men only in the Insulin Resistance Atherosclerosis Study (IRAS) [26]. We believe ours is the first study to extend these analyses by reporting the association between GL and HDL cholesterol by race/ethnicity and BMI.

We observed that GL was positively associated with triglycerides, again corroborating results from many previous observational studies. Dietary GL was positively associated with triglycerides in the Women's Health Study [22], the Nurses' Health Study [10], and IRAS [26]. In a study of Japanese women, the lowest concentration of triglycerides was observed in the lowest tertiles of both GL and GI [24]. However, dietary GI, but not GL, was positively associated with triglycerides in the Whitehall II study [23], and there was no association between GL and triglycerides in one study of healthy adults [25]. Again, our analyses go beyond those published previously by demonstrating that there were possible race/ethnicity and BMI

differences in the association between GL and triglycerides, although the test for interaction was not statistically significant. It is interesting to note that high-GI carbohydrates compared to low-GI carbohydrates have been shown to create a detrimental postprandial pattern in triglyceride-rich lipoproteins derived from both hepatic and intestinal sources in studies of obese, insulin-resistant persons [27]. However, the positive association between GL and triglycerides was not observed in obese participants in our study.

It may be tempting to attribute associations of GL with HDL cholesterol and triglycerides to effects of GL on circulating insulin concentrations and IR since hyperinsulinemia plays a critical role in the development of dyslipidemia [2]. However, in our study GL was not associated with glucose or insulin concentrations, or with IR, either overall or by specific race/ethnicity or BMI groups. Previous studies have produced equivocal results on these associations. GL was not associated with fasting glucose or insulin concentrations in a study of Japanese women [24]. However, lower fasting glucose concentrations were observed with increasing dietary GL, while fasting insulin was inversely related to GL in women in the Whitehall II study [23]. In female participants of the Health, Aging and Body Composition study, GL was not associated with either fasting glucose or insulin concentrations [28], while GL was positively associated with HOMA-IR in the Framingham Offspring Cohort [29]. GL was not associated with fasting glucose, fasting insulin, insulin sensitivity (assessed by frequently sampled intravenous glucose tolerance test [FSIVGTT]), or acute insulin response in IRAS [30,31], nor was GL associated with HOMA-IR in cross-sectional analyses within the Inter99 study [32].

The inverse association between GL and SBP in Whites in this study was somewhat unexpected. Very few observational studies have investigated the association between GL (or GI) and BP. In the British National Diet and Nutritional Survey, GI was not associated with SBP or DBP in participants over 65 years of age [33]. Intervention studies have produced equivocal results, with some showing no effect of reduced-GL/GI diets on BP [34] and others showing trends toward reductions in both SBP and DBP on such diets [35,36]. There was no effect of dietary GI on SBP in the Canadian Trial of Carbohydrates in Diabetes [37], a clinical trial utilizing low-GI carbohydrates.

The strengths of this study include the race/ethnicity- and BMI-diverse sample, the comprehensive data collection which took place within the WHI, and the availability of a comprehensive GI/GL database which was added to the existing WHI FFQ database. There were also potential limitations. In addition to the well-documented limitations associated with assessing diet with FFQs in general, there were further issues specific to this study which could have attenuated the results. While the addition of GI/GL values to the FFQ nutrient database was done in a systematic and well-documented manner [14], the structure of the FFQ itself was not optimal for assessment of GI and GL, and the FFQ has not been validated for this purpose. Further, energy underreporting has been noted among Black and Hispanic postmenopausal women compared to Whites, and among women with higher compared to lower BMI [38], which potentially dampens the ability to test for diet-metabolic effects among minority or heavier participants. WHI participants were postmenopausal women who were 50-79 years of age; thus, there is a potential limitation in generalizing our study results to other populations. The WHI Observational Study population may be healthier than US postmenopausal women in general [12], thus limiting the metabolic range of the study. Finally, the investigation was cross-sectional, leaving the potential for spurious correlations despite adjusting for relevant covariates.

Finally, we recognize that given the distribution of race/ethnicity within the subsample, power to detect linear trends was greatest for White participants. Nevertheless, the overall sample provided the opportunity to examine differences by race/ethnicity in the associations of GL

with the outcomes. Though formal tests of interaction were conducted to examine whether the associations between GL and the risk factors varied among the categories of race/ethnicity, the statistical power of these tests were low due to the small sample sizes within the strata. However, the stratified analyses were presented as a set of descriptive secondary analyses. These results should be interpreted with caution as exploratory and hypothesis generating. Further research is warranted to examine whether the differences in the degree of associations are observable in larger sample sizes for Blacks and Hispanics and, if so, to investigate factors contributing to these differences.

Conclusion

Among generally healthy postmenopausal women, GL was associated with HDL cholesterol and triglycerides. Higher dietary GL was associated with adverse lipoprotein/lipid concentrations among Whites (HDL cholesterol and triglycerides) and Hispanics (total cholesterol and LDL cholesterol). GL was associated with HDL cholesterol in normal-weight participants and with triglycerides in overweight participants. While provocative, there was no statistically significant interaction by race/ethnicity or BMI; therefore, these results require confirmation in larger studies.

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Table 1

Selected baseline descriptive, dietary intake, and metabolic/physiologic parameters in the random sample of WHI Observational Study participants with analyzed blood samples at baseline

Variables	All participants (n = 878)	Race/ethnicity			
		White (n = 647)	Black (n = 104)	Hispanic (n = 127)	*P* for difference*
Descriptive					
Age (y)	63.8 ± 7.3	64.4 ± 7.3	63.0 ± 7.4	61.6 ± 6.7	<0.001
BMI (kg/m^2)	26.9 ± 5.2	26.2 ± 4.7	29.9 ± 4.7	27.9 ± 5.7	<0.001
Physical activity‡ (episodes/wk)	5.2 ± 4.2	5.3 ± 4.3	4.3 ± 3.7	5.4 ± 4.5	0.050
Current smoking (%)	5.1	4.5	8.8	5.7	0.184
Current alcohol user (%)	39.1	44.0	18.6	31.0	<0.001
Dietary					
Energy (kcal/d)	1531 ± 672	1571 ± 635	1326 ± 766	1498 ± 743	0.002
Carbohydrate (g/d)	80.8 ± 75.9	184.5 ± 70.3	160.0 ± 84.2	179.1 ± 92.5	0.009
GI	52.3 ± 3.6	52.2 ± 3.4	53.3 ± 4.2	52.3 ± 3.8	0.011
GL	94.8 ± 41.0	96.5 ± 38.2	85.4 ± 46.0	93.5 ± 49.2	0.034
Metabolic/physiologic					
Total cholesterol (mg/dL)	218.1 ± 35.8	218.4 ± 35.6	216.5 ± 34.6	217.6 ± 38.1	0.866
LDL cholesterol (mg/dL)	125.5 ± 33.8	124.5 ± 33.6	129.8 ± 33.0	127.0 ± 35.1	0.287
HDL cholesterol (mg/dL)	64.3 ± 17.1	65.1 ± 17.1	64.6 ± 17.7	59.9 ± 16.3	0.007
Triglycerides (mg/dL)	141.9 ± 76.5	143.6 ± 73.9	112.3 ± 66.2	157.7 ± 90.6	<0.001§
Glucose (mg/dL)	91.2 ± 9.4	90.9 ± 8.9	93.3 ± 11.5	91.3 ± 9.9	0.355§
Insulin (μU/mL)	9.8 ± 5.1	9.2 ± 4.6	11.8 ± 6.1	11.3 ± 6.1	<0.001§
HOMA-IR	2.24 ± 1.27	2.09 ± 1.12	2.77 ± 1.53	2.60 ± 1.54	<0.001
Systolic BP (mm Hg)	127.2 ± 17.4	126.8 ± 17.4	129.8 ± 17.7	126.9 ± 17.4	0.268
Diastolic BP (mm Hg)	75.1 ± 9.0	74.6 ± 8.9	78.6 ± 9.1	74.6 ± 8.9	<0.001

BMI, body mass index; BP, blood pressure; GI, glycemic index; GL, glycemic load; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment-insulin resistance; LDL, low-density lipoprotein; WHI, Women's Health Initiative

*Analysis of variance.

† Values are means ± SDs, except where noted.

‡ Includes walking, mild, moderate, and strenuous physical activity.

§ Due to extreme skewness, tests were performed using the Kruskal Wallis test.

Table 2

Mean CVD risk factor values by quartile of GL; all participants*

Variables	Quartile of dietary GL				*P* for trend‡
	1 (50.4†) (n = 220)	2 (78.7) (n = 219)	3 (100.4) (n = 219)	4 (149.5) (n = 220)	
Total cholesterol (mg/dL)	215.4	216.7	216.8	224.0	0.171
LDL cholesterol (mg/dL)	121.9	124.2	124.8	130.2	0.140
HDL cholesterol (mg/dL)	67.1	66.0	63.9	60.5	0.004
Triglycerides (mg/dL)	123.0	120.2	128.8	144.5	0.008§
Glucose (mg/dL)	91.2	91.2	91.2	89.1	0.203§
Insulin (μU/mL)	8.91	8.91	8.91	8.91	0.422§
HOMA-IR	2.28	2.28	2.29	2.11	0.479
Systolic BP (mm Hg)	128.7	127.2	125.9	126.3	0.176
Diastolic BP (mm Hg)	75.4	75.4	74.5	75.4	0.678

BP, blood pressure; CVD, cardiovascular disease; GL, glycemic load; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment-insulin resistance; LDL, low-density lipoprotein

*Results adjusted for age, BMI, energy, smoking, alcohol, and physical activity.

†Mean value for quartile.

‡Variable added last test, linear regression.

§*P*-values based upon log-transformed outcomes. Values presented in the rows have been transformed back to original units.

Table 3

Mean CVD risk factor values by quartile of GL; stratified by race/ethnicity*

Variables	Race/Ethnicity	Quartile of dietary GL				*P* for trend‡
		1 (50.4†) (n = 220)	2 (78.7) (n = 219)	3 (100.4) (n = 219)	4 (149.5) (n = 220)	
Total cholesterol (mg/dL)	White	218.4	215.9	216.0	222.6	0.643
	Black	217.8	216.6	211.2	220.3	0.876
	Hispanic	200.0	216.8	222.1	242.0	0.018
LDL cholesterol (mg/dL)	White	122.8	123.3	122.8	127.6	0.545
	Black	124.5	132.1	129.0	137.8	0.534
	Hispanic	112.6	124.7	128.6	150.4	0.038
HDL cholesterol (mg/dL)	White	68.7	67.7	64.7	60.2	0.003
	Black	70.4	60.9	63.1	60.2	0.222
	Hispanic	57.2	60.2	62.7	60.8	0.414
Triglycerides (mg/dL)	White	125.9	114.8	128.8	147.9	0.015§
	Black	102.3	112.2	89.1	104.7	0.623§
	Hispanic	134.9	144.5	138.0	158.5	0.506§
Glucose (mg/dL)	White	91.2	91.2	91.2	89.1	0.859§
	Black	95.5	93.3	87.1	89.1	0.083§
	Hispanic	93.3	91.2	93.3	85.1	0.127§
Insulin (μU/mL)	White	7.9	8.5	8.5	7.8	0.983§
	Black	10.5	11.7	10.2	8.9	0.556§
	Hispanic	12.3	9.8	10.0	7.9	0.092§
HOMA-IR	White	2.03	2.13	2.20	1.95	0.972
	Black	2.78	3.15	2.64	2.48	0.595
	Hispanic	3.06	2.61	2.60	2.15	0.232
Systolic BP (mm Hg)	White	129.2	128.4	125.2	123.9	0.029
	Black	128.5	127.4	131.3	135.8	0.330
	Hispanic	125.9	120.0	128.3	131.7	0.346
Diastolic BP (mm Hg)	White	74.7	76.1	73.7	74.0	0.244

Variables	Race/Ethnicity	Quartile of dietary GL				*P* for trend‡
		1 (50.4†) (n = 220)	2 (78.7) (n = 219)	3 (100.4) (n = 219)	4 (149.5) (n = 220)	
	Black	77.8	75.8	79.0	83.2	0.256
	Hispanic	75.6	71.0	76.4	76.3	0.624

BP, blood pressure; CVD, cardiovascular disease; GL, glycemic load; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment-insulin resistance; LDL, low-density lipoprotein

*Results adjusted for age, BMI, energy, smoking, alcohol, and physical activity.

†Mean value for quartile.

‡Variable added last test, linear regression.

§*P*-values based upon log-transformed outcomes. Values presented in the rows have been transformed back to original units.

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Table 4

Mean CVD risk factor values by quartile of GL; stratified by BMI*

Variables	BMI	Quartile of dietary GL				*P* for trend‡
		1 (50.4†) (n = 220)	2 (78.7) (n = 219)	3 (100.4) (n = 219)	4 (149.5) (n = 220)	
Total cholesterol (mg/dL)	Normal§	219.7	212.2	216.6	219.6	0.926
	Overweight//	215.4	221.7	222.1	234.6	0.059
	Obese¶	205.9	223.3	216.1	226.0	0.147
LDL cholesterol (mg/dL)	Normal	122.9	120.1	124.4	125.3	0.654
	Overweight	126.9	131.9	131.5	139.5	0.214
	Obese	116.4	136.7	125.8	138.9	0.106
HDL cholesterol (mg/dL)	Normal	71.2	69.8	66.6	63.2	0.036
	Overweight	66.0	66.1	62.4	58.3	0.067
	Obese	61.5	57.1	60.0	56.2	0.422
Triglycerides (mg/dL)	Normal	113.2	103.8	112.6	133.6	0.172#
	Overweight	111.8	114.6	129.5	154.6	0.004#
	Obese	132.8	128.5	135.6	140.2	0.623#
Glucose (mg/dL)	Normal	87.9	88.4	89.0	88.4	0.664#
	Overweight	92.8	92.6	91.0	89.9	0.185#
	Obese	96.7	94.4	94.0	93.3	0.255#
Insulin (μU/mL)	Normal	7.5	7.6	8.0	7.6	0.637#
	Overweight	10.4	9.7	9.5	8.6	0.135#
	Obese	11.4	13.2	13.0	9.7	0.539#
HOMA-IR	Normal	1.88	1.97	2.11	2.04	0.391
	Overweight	2.67	2.57	2.44	2.21	0.130
	Obese	3.03	3.30	3.37	2.59	0.610
Systolic BP (mm Hg)	Normal	123.6	121.8	122.9	125.0	0.744
	Overweight	131.7	130.6	127.6	125.3	0.121
	Obese	134.1	132.5	132.3	130.0	0.441

Variables	BMI	Quartile of dietary GL				*P* for trend‡
		1 (50.4†) (n = 220)	2 (78.7) (n = 219)	3 (100.4) (n = 219)	4 (149.5) (n = 220)	
Diastolic BP (mm Hg)	Normal	73.8	74.7	73.4	74.5	0.961
	Overweight	76.8	76.5	75.2	75.1	0.350
	Obese	77.3	76.8	78.4	78.5	0.581

BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; GL, glycemic load; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment-insulin resistance; LDL, low-density lipoprotein

*Results adjusted for race/ethnicity, age, energy, smoking, alcohol, and physical activity.

†Mean value for quartile.

‡Variable added last test, linear regression.

§BMI <25.0 kg/m^2.

//BMI 25.0-29.9 kg/m^2.

¶BMI >29.9 kg/m^2.

#*P*-values based upon log-transformed outcomes. Values presented in the rows have been transformed back to original units.