

Carbohydrate nutrition, glycaemic load, and plasma lipids: the Insulin Resistance Atherosclerosis Study

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Aims We evaluated the relationship of carbohydrate nutrition and selected food groups with lipids using data from the Insulin Resistance Atherosclerosis Study (IRAS Exam I, 1992–1994).

Methods and results A total of 1026 middle-aged adults with normal or impaired glucose tolerance had complete data on fasting lipids and usual dietary intake from an interviewer-administered, validated food frequency questionnaire. Published glycaemic index (GI) values were assigned to food items and average dietary GI and glycaemic load (GL) were calculated per participant. Intake of carbohydrates differed by gender, men consuming more absolute digestible carbohydrates with higher GI and GL than women. In multivariate models adjusting for energy intake, in men, GL and carbohydrates were associated positively with total and LDL cholesterol, and inversely with HDL. In women, associations were limited to triglycerides. We estimated that a 100 g higher intake in GL or carbohydrates was associated with a 7–8 mg/dL higher total or LDL cholesterol level in men, and a 13–17 mg/dL higher triglyceride level in women. In the combined sample, GL and carbohydrates were consistently associated with all lipid levels and GI was inversely associated with HDL cholesterol.

Conclusion Our findings underscore the importance of carbohydrate nutrition for plasma lipids.

Introduction

Plasma lipid concentrations are strong predictors of atherosclerosis and risk of coronary heart disease, hence, identification of modifiable behavioural factors, such as dietary intake has long been of interest.¹ Previous work on the modification of dietary fat intake in favour of carbohydrates revealed an advantageous plasma cholesterol profile.^{2–5} Concurrently, evidence has emerged on the detrimental effect of some carbohydrates, in particular fructose, on triglyceride levels.⁶

Carbohydrate-containing foods differ systematically with respect to their effects on post-prandial glucose and insulin response, the differences in glucose response being quantified by the glycaemic index (GI).^{7,8} Opperman *et al.*⁹ recently conducted an extensive meta-analysis of clinical trials evaluating the impact of low compared with high GI diets on lipid levels. However, from a population perspective associations are less clear. Several observational studies have shown an association of GI and a derived concept, the glycaemic load (GL) with both HDL cholesterol and triglycerides.^{10–14} Less epidemiologic data exist on total

cholesterol or LDL cholesterol in relation to either measure.^{12–15}

The purpose of the present study was to examine the relationship of GI, GL, and intake of carbohydrates with plasma lipid levels in the Insulin Resistance Atherosclerosis Study (IRAS) population. Because specific food groups have been demonstrated to explain between 55 and 70% of variation in GI and GL in our population,¹⁶ we additionally explored the relation of these food groups to plasma lipid levels.

Research design and methods

Study population

The design and methods of IRAS have been described in detail.¹⁷ More than 1600 participants were recruited at four clinical centres (Los Angeles, CA, USA, Oakland, CA, USA, San Luis Valley, CO, USA, and San Antonio, TX, USA) between 1992 and 1994 for the baseline exam. The goal was to obtain nearly equal representation of participants across glucose tolerance status [normal, impaired glucose tolerance (IGT), non-insulin taking type 2 diabetes mellitus]; ethnicity [African American (AA), Hispanic (H), and non-Hispanic white (NHW)]; gender; and age (40–49, 50–59, and 60–69 years). Ethnicity was determined by self-report using 1990 U.S. census questions. At the Oakland and Los Angeles centres, NHW and AA subjects were recruited from Kaiser

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Permanente, a non-profit health maintenance organization. Centres in San Antonio and San Luis Valley recruited NHW and Hispanic-American (HA) subjects from two ongoing population-based studies (the San Antonio Heart Study and the San Luis Valley Diabetes Study). The final sample consisted of 1624 individuals. All participants provided written informed consent as approved by their respective field centre's institutional review board.

We limited our analysis to 1071 adults with normal (66%) or IGT (34%). Of them 36 individuals (3%) were excluded due to missing lipid values and an additional nine (1%) were excluded due to missing data on covariates. Data presented are based on 1026 IRAS participants.

Data collection

IRAS required a two-visit protocol, the first to determine glucose tolerance status and the second to measure insulin sensitivity. Participants were asked to fast for 12 h prior to each of the two visits, abstain from heavy exercise and alcohol for 24 h, and refrain from smoking the morning of the visit. A 2 h, 75 g oral glucose tolerance test (Orange-dex, Custom Laboratories, Baltimore, MD, USA) was performed during the first visit, and World Health Organization criteria¹⁸ were used to assign glucose tolerance status. Individuals currently taking oral hypoglycaemic medications were classified as having type 2 diabetes regardless of the results of the oral glucose tolerance test. Height and weight were measured in duplicate and recorded to the nearest 0.5 cm and 0.1 kg, respectively. Body mass index (BMI) was calculated as weight/height² (kg/m²).

Plasma lipid concentrations were determined from fasting plasma samples at the central IRAS laboratory (Medlantic Research Institute, Washington, DC, USA) using the Lipid Research Clinics methodology. Total cholesterol, LDL cholesterol, and HDL cholesterol were measured by the β -quantification method and triglycerides were measured by enzymatic methods with the use of glycerol-free assays on a Hitachi autoanalyser.

Usual intake of foods and nutrients was assessed by interview using a 1 year, semi-quantitative 114-item food frequency questionnaire (FFQ) interview modified from the National Cancer Institute Health History and Habits Questionnaire to include regional and ethnic food choices across the four clinical centres. Participants were asked to recall usual intake of foods and beverages over the past year. Both the frequency of intake and the serving size were ascertained. Interviewers were centrally trained and certified, and audiotapes of interviews were reviewed quarterly. The validity and reproducibility of the IRAS FFQ to measure nutrient intake including total carbohydrate intake and fractions of carbohydrates (fructose, starch) have been demonstrated in a subset of the IRAS population.¹⁹ Pearson correlation coefficients for FFQ carbohydrate estimates compared with eight 24 h recalls were moderate at $r = 0.39$ unadjusted ($r = 0.37$ adjusted for energy). A total of 33 food groups were created from the 114 line items of the FFQ based on similarities in food and nutrient composition as described previously.²⁰

Alcohol intake was evaluated separately using a frequency approach with additional questions about recent use and average lifetime use. Subjects were asked about their usual consumption of wine (red and white wine), beer, mixed drinks/mixers, and liquors. Frequency of consumption was expressed as servings per day standardized to a medium serving size.

Estimation of nutrients, GI, and GL

Daily nutrient and energy intake was estimated from the FFQ and the alcohol questionnaire using an expanded nutrient database (HHHQ-DIETSYS analysis software, version 3.0; NCI, Bethesda, MD, USA, 1993). All analyses of carbohydrates are based on digestible carbohydrates, which were calculated by subtracting fibre intake from total carbohydrate intake. We chose this approach to be in

line with the approach to testing of GI values of foods, where measurements are based only on the carbohydrates that are absorbable, i.e. the digestible fraction.^{7,21}

We assigned mean GI values based on the white bread standard from published data²¹ and other available resources (T.W., personal communication) to all 114 FFQ line items plus three items assessed in the interview on alcohol consumption (beer, wine, liquors) plus several additional foods (that were identified in open-ended questions as being consumed more than once per week on the FFQ). Details of the GI and GL estimation procedures in our study have been published.¹⁶

Average dietary GI was computed by summing the products of the digestible carbohydrate content per serving for each item multiplied by the average number of servings of that food per day, multiplied by its GI, and all divided by the total amount of digestible carbohydrate daily intake.²² The average dietary GL was computed like the GI but without dividing by the total digestible carbohydrate intake but by 100.

Statistical analysis

For descriptive purposes, the mean and standard deviation were computed for continuous variables and the distribution was computed for categorical variables under study. Following evaluation of the distribution of continuous variables, log transformations of all lipid variables were used in subsequent analyses.

To evaluate the relation of the dietary exposures with plasma lipid levels, we conducted linear regression analyses because all variables under study were continuous in nature and no threshold effects were observed in descriptive analyses. Results were presented as beta coefficients and *P*-values stratified by gender and also for the combined sample. We evaluated the impact of potential effect modifiers, including age groups, ethnicity, and glucose tolerance status by first conducting stratified analyses and comparing the size and direction of the effect estimates followed by formal test of interactions. None of the above mentioned variables appeared to modify the diet-lipids associations.

The associations of carbohydrate-related dietary exposures were first described at the unadjusted level and subsequently adjusted for confounders. The covariates contained in the models were age, ethnicity/clinic, smoking, total energy expenditure, family history of diabetes, hypertension, BMI, glucose tolerance status, lipid-lowering medication, and energy from non-carbohydrates. These covariates were selected based on previous work in our and other study populations suggesting that they would likely confound the associations under study. Assumptions of linear regression were assessed by visual inspection of normal probability plots and plots of the residuals vs. predicted values and evaluation of Durban-Watson *D* values (ranged from 1.7 to 2.2). Based on our multivariable models, we also estimated the predicted increase in lipid outcome levels associated with a 100 g increase in GL and carbohydrates. This increase corresponds to roughly the interquartile range in the distribution.

For energy adjustment, we chose the energy partition method, which controls for the non-carbohydrate contribution of correlated foods^{23,24} because it allowed us to parse out the contribution of carbohydrates from non-carbohydrate sources such as protein and fat. Subsequently, we repeated this analysis using the residuals method for energy-adjustment and our conclusions were unchanged.

We have previously identified 14 food groups explaining the majority of inter-individual variation in GI and GL in IRAS,¹⁶ from a total of 33 food groups. Detailed descriptions of these food groups have been published.²⁰ For the purposes of this manuscript, we extended these analyses to focus on digestible carbohydrates as well. Gender-specific stepwise linear regression modelling was used to detect the most predictive food groups explaining inter-individual variation in digestible carbohydrates adjusting for age and ethnicity/clinic. For these analyses, a constant value of 1 was

Table 1 Descriptive characteristics of the IRAS population (Exam 1, 1992–1994)

	Total (n = 1026) Mean (std)	Men (n = 445) Mean (std)	Women (n = 581) Mean (std)	P-value
<i>General characteristics</i>				
Age (years)	54.8 (8.5)	54.8 (8.6)	54.7 (8.3)	0.785*
Ethnicity ^a				0.074**
NHW	418 (40.7)	199 (44.7)	219 (37.7)	
H	340 (33.1)	136 (30.6)	204 (35.6)	
AA	268 (26.1)	110 (24.7)	158 (26.8)	
Glucose tolerance ^a				0.023**
Normal	687 (67.0)	315 (70.8)	372 (64.0)	
Impaired	339 (33.0)	130 (29.2)	209 (36.0)	
BMI (kg/m ²)	28.5 (5.7)	27.7 (4.7)	29.0 (6.4)	<0.001*
Current smoking ^a	168 (16.4)	85 (19.1)	83 (14.3)	0.039*
Hypertensive ^a	320 (31.2)	142 (31.9)	178 (30.6)	0.663**
Family history of diabetes ^a	413 (40.3)	169 (38.0)	244 (42.0)	0.193**
Total energy expenditure (kcal/kg/year)	14806 (2726)	15419 (3169)	14332 (2217)	<0.001*
<i>Outcome variables</i>				
Cholesterol (mg/dL)	212 (42)	211 (47)	213 (39)	0.288*
LDL-cholesterol (mg/dL)	142 (35)	142 (36)	141 (34)	0.981*
HDL-cholesterol (mg/dL)	47 (15)	42 (14)	51 (15)	<0.001*
Triglycerides (mg/dL)	134 (86)	147 (98)	124 (74)	<0.001*
<i>Dietary characteristics</i>				
GI ^b	83 (6)	85 (6)	82 (5)	<0.001*
GL (g/day)	183 (81)	208 (88)	163 (69)	<0.001*
Digestible carbohydrates (g/day)	220 (94)	246 (101)	200 (83)	<0.001*
Energy from carbohydrates (%)	46 (8)	46 (8)	47 (8)	0.011*
Total energy intake (kcal)	1962 (835)	2218 (888)	1765 (734)	<0.001*
<i>Food groups (served/day)</i>				
Regular soft drinks	0.2 (0.4)	0.2 (0.4)	0.2 (0.3)	0.175*
Beer	0.3 (0.9)	0.5 (1.3)	0.1 (0.3)	<0.001*
Dark bread/high-fibre cereal	0.8 (0.7)	0.8 (0.9)	0.8 (0.7)	0.506*
White bread/low-fibre cereal	1.3 (1.1)	1.4 (1.1)	1.2 (1.0)	0.059*
Pastry	0.3 (0.5)	0.4 (0.5)	0.3 (0.4)	0.025*
Rice/pasta	0.6 (0.5)	0.6 (0.5)	0.6 (0.5)	0.629*
Salty snacks	0.3 (0.4)	0.3 (0.4)	0.3 (0.3)	0.330*
Fruit juice	0.7 (0.8)	0.7 (0.8)	0.7 (0.8)	0.290*
Fruits	1.6 (1.4)	1.5 (1.4)	1.7 (1.3)	0.011*
Low-fat milk and products	0.2 (0.3)	0.2 (0.3)	0.3 (0.4)	0.012*
Dried beans	0.3 (0.4)	0.3 (0.4)	0.3 (0.3)	0.032*
Ice cream	0.2 (0.3)	0.2 (0.3)	0.2 (0.3)	0.753*
Sweets/sugar	0.6 (0.7)	0.7 (0.8)	0.6 (0.6)	0.017*
Fries/fried potatoes	0.1 (0.2)	0.2 (0.2)	0.1 (0.2)	<0.001*

P-value denotes significance level of gender difference.

^aFrequency (%).

^bWhite bread standard.

*t-statistic.

** χ^2 statistic.

added to the food group intakes in order to be able to transform these to their natural logarithms, as for some food groups the intake was zero. We focused only on food groups explaining at least 1% of variation in the exposure variable. In a second step, we evaluated the association of the pertinent food groups with lipid outcomes, again using multivariable regression modelling. Because the food groups selected for these analyses explained substantial variation in GL and carbohydrate intake, we similarly adjusted for basic demographic variables, lipid-lowering medication, hypertension, family history of diabetes, BMI, glucose tolerance status, total energy expenditure, current smoking, and total caloric intake; all relevant confounders. Results were presented as beta coefficients and P-values stratified by gender. All analyses

were performed using SAS version 8.2 (SAS Institute Inc., Cary, NC, USA).

Results

Descriptive characteristics of the study population are presented in *Table 1*. The population of middle-aged adults comprised 43% males and 57% females. Mean levels of total and LDL cholesterol were 212 and 142 mg/dL, respectively, and were similar between genders ($P = 0.288$ and 0.981 , respectively). Concentrations of HDL cholesterol and triglycerides differed by gender, women displaying a healthier lipid profile ($P < 0.001$ and $P < 0.001$, respectively).

Table 2 Association of GI, GL, and carbohydrate intake with lipid levels

	Total cholesterol		LDL		HDL		Triglycerides	
	β (SE)	P-value	β (SE)	P-value	β (SE)	P-value	β (SE)	P-value
Total sample								
GI	-0.0015 (0.0011)	0.201	-0.0024 (0.0016)	0.139	-0.0044 (0.0018)	0.017	0.0043 (0.0032)	0.176
GL	0.0003 (0.0001)	0.008	0.0004 (0.0002)	0.010	-0.0009 (0.0002)	<0.001	0.0014 (0.0003)	<0.001
Carbohydrates ^a	0.0003 (0.0001)	0.005	0.0004 (0.0001)	0.003	-0.0007 (0.0002)	<0.001	0.0010 (0.0003)	<0.001
Men								
GI	-0.0003 (0.0018)	0.883	-0.0027 (0.0026)	0.301	0.0023 (0.0027)	0.389	0.0032 (0.0051)	0.529
GL	0.0004 (0.0002)	0.041	0.0006 (0.0002)	0.028	-0.0008 (0.0003)	0.002	0.0007 (0.0005)	0.133
Carbohydrates ^a	0.0003 (0.0001)	0.035	0.0005 (0.0002)	0.011	-0.0007 (0.0002)	0.001	0.0005 (0.0004)	0.204
Women								
GI	-0.0012 (0.0016)	0.435	-0.0016 (0.0022)	0.460	-0.0011 (0.0024)	0.656	-0.0001 (0.0043)	0.990
GL	0.0003 (0.0002)	0.086	0.0003 (0.0002)	0.177	-0.0005 (0.0003)	0.051	0.0016 (0.0005)	0.001
Carbohydrates ^a	0.0003 (0.0001)	0.069	0.0003 (0.0002)	0.146	-0.0004 (0.0002)	0.067	0.0012 (0.0004)	0.001

β values are shown for $\ln(\text{total cholesterol})$, $\ln(\text{LDL-cholesterol})$, $\ln(\text{HDL-cholesterol})$, and $\ln(\text{triglycerides})$ for a one unit increase in GI, GL, and carbohydrates in a multivariate model adjusting for age, ethnicity/clinic, smoking, total energy expenditure, family history of diabetes, hypertension, BMI, glucose tolerance status, lipid-lowering medication, and energy from non-carbohydrates.

^aDigestible carbohydrates.

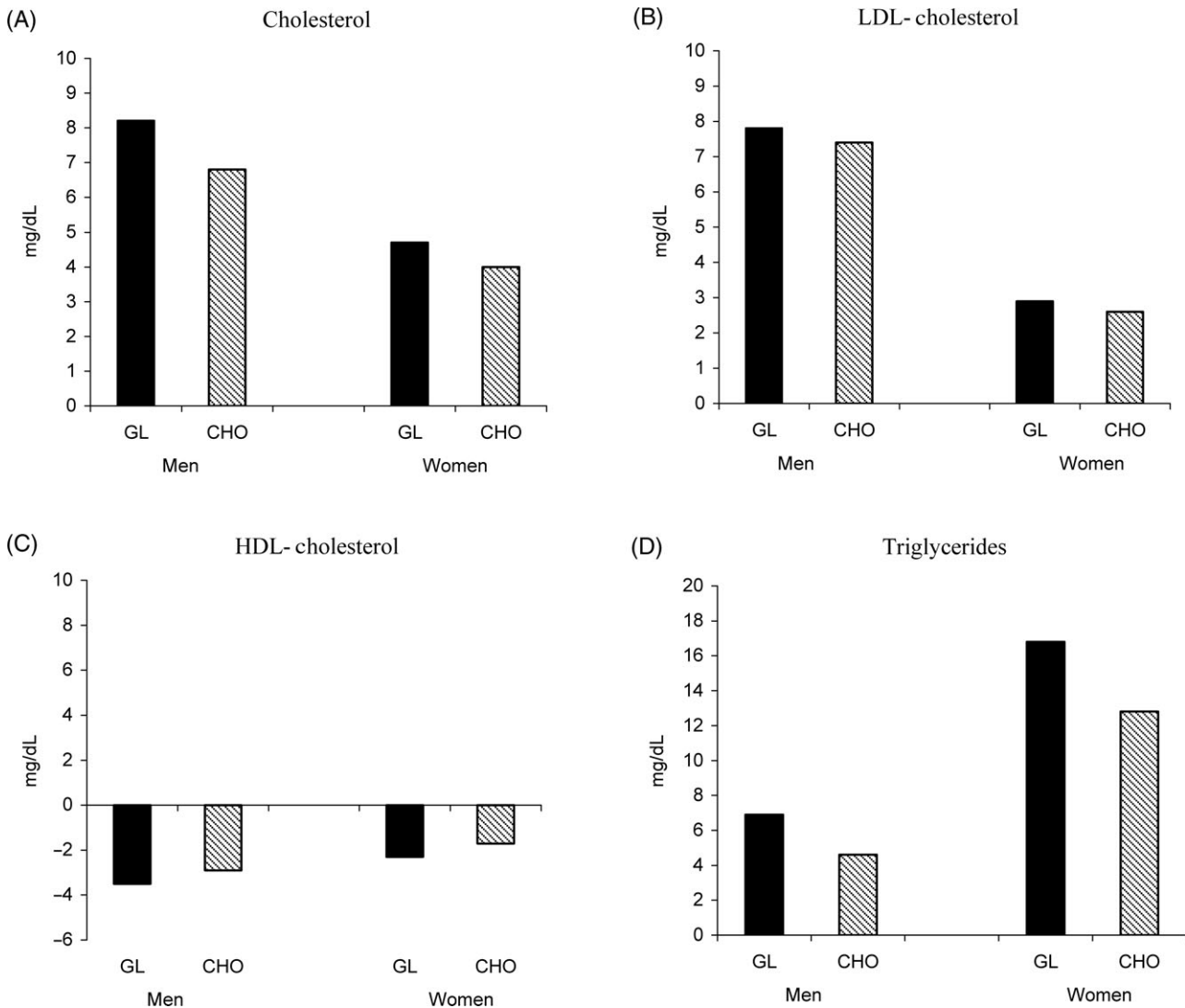


Figure 1 Predicted difference in (A) total cholesterol, (B) LDL-cholesterol, (C) HDL-cholesterol, and (D) triglycerides for a 100 g increase in GL and digestible carbohydrates (CHO) by gender.

Table 3 Correlation of food groups with GL and carbohydrates

	Partial R^{2a}	
	GL	Carbohydrates
Men	0.190 ^b	0.157 ^b
White bread/low-fibre cereal	0.297	0.265
Dark bread/high-fibre cereal	0.098	0.030
Regular soft drinks	0.078	0.114
Beer	0.044	0.022
Fruit	0.051	0.022
Sweets/sugar	0.045	0.062
Rice/pasta	0.026	0.043
Pastry	0.019	0.022
Fruit juice	0.015	0.022
Salty snacks	0.014	0.013
Dried beans	0.008	0.007
Fries/fried potatoes	0.005	0.003
Women	0.180 ^b	0.157 ^b
White bread/low-fibre cereal	0.272	0.228
Rice/pasta	0.113	0.137
Regular soft drinks	0.092	0.097
Dark bread/high-fibre cereal	0.071	0.028
Fruit juice	0.046	0.028
Fruit	0.031	0.087
Pastry	0.030	0.042
Fries/fried potatoes	0.018	0.015
Dried beans	0.013	0.012
Low-fat milk and products	0.010	0.048
Ice cream	0.008	0.011

Food group [$\log(\text{food group} + 1)$].

^aAdjusted for age and ethnicity/clinic.

^bExplained variation by demographic variables.

There were noteworthy gender differences in dietary GI and GL and in carbohydrate intake. Men consumed a diet higher in GI ($P < 0.001$) and GL ($P < 0.001$) than women. Digestible carbohydrate intake was roughly 45 g higher in men than in women ($P < 0.001$). With respect to food groups predictive of inter-individual variation in GL and carbohydrates, few gender differences were observed.

Table 2 displays the association of GI, GL, and carbohydrate intake with plasma lipid concentrations in the combined sample and in men and women. In the combined sample, GI was inversely related to HDL cholesterol. GL was significantly associated with total and LDL cholesterol and triglycerides and inversely with HDL cholesterol. Associations were of similar magnitude and direction for digestible carbohydrates.

GI was not associated with any of the lipids in men, neither in the crude (data not shown) nor in the adjusted analyses shown. In contrast, higher dietary GL was associated positively and significantly with total and LDL cholesterol and inversely with HDL cholesterol levels. The trend for GL to predict triglycerides in men was not significant ($P = 0.079$). The direction and magnitude of the association of digestible carbohydrates with total, LDL, and HDL cholesterol mirrored the associations observed for GL.

In women, no significant associations of GI with lipid concentrations were observed. Association of GL with total cholesterol and HDL cholesterol had the same direction as in men but did not reach statistical significance. Digestible carbohydrates were not associated with cholesterol levels in women. In women, the relationship of GL and HDL compared with carbohydrates and HDL appeared stronger and almost reached statistical significance. Both higher dietary GL and digestible carbohydrate intake were related to higher triglyceride levels both before and after multivariable adjustment.

Figure 1 visualizes the impact of increasing the average daily GL by 100 or digestible carbohydrate intake by 100 g based on predicted lipid outcome levels from our above referenced multivariable models. Compared with the mean intake level of GL or carbohydrates, we estimated that the 100 g increase was associated with a 7–8 mg/dL increase of total cholesterol in men, a 7–8 mg/dL increase of LDL cholesterol in men, a roughly 3 mg/dL decrease in HDL cholesterol levels in men, and a 13–17 mg/dL increase in triglyceride levels in women.

Table 3 displays the food groups contributing at least 1% of the inter-individual variation in dietary GL and digestible carbohydrates by gender along with the respective partial R^2 values. For both men and women, food groups predictive of carbohydrate intake and dietary GL were white bread/low-fibre cereal, dark bread/high-fibre cereal, rice/pasta, pastry, regular soft drinks, fruits, fruit juice, dried beans, and fries/fried potatoes. In men, salty snacks, beer, and sweets were additionally important. In women, low-fat milk and milk products and ice cream/frozen yogurt contributed also to variation in GL and digestible carbohydrates. Findings were very consistent for GL and carbohydrates. Findings for GI have been published previously.¹⁶

The results of the final analyses that evaluated the role of carbohydrate/GL-relevant food groups in relation to plasma lipid levels in multivariable models are presented in Table 4. In men, consumption of regular soft drinks (including lemonade and sweetened mineral water) was associated positively with total and LDL cholesterol and inversely with HDL cholesterol. HDL cholesterol levels in men were additionally associated inversely with fruit juice intake and pastry intake. Triglyceride levels were not significantly related to any carbohydrate-related food groups in men, but almost reached statistical significance with fruit juice intake. In women, a different pattern of food groups related to lipid levels emerged in the multivariable models. Rice and pasta intake was positively associated with total and LDL cholesterol. Pastry intake was also relevant for total cholesterol and marginally associated with LDL cholesterol. Triglyceride levels were positively related to fruit juice intake only. HDL cholesterol levels were unrelated to intake of carbohydrate-related food groups in women.

Discussion

In the IRAS population, a marked association of GL and carbohydrates with total, LDL, and HDL cholesterol was observed in men, and with triglyceride levels in women. In the combined sample these associations persisted. In addition, an inverse association of GI with HDL cholesterol emerged.

To our knowledge, only four larger epidemiologic studies of healthy adults have evaluated the effect of GL and GI on lipid levels.^{11,12,14,15} In addition, there are two smaller observational studies with less than 200 participants.^{10,13} Evaluating the current body of evidence is complicated by the fact that not all studies have evaluated a full range of lipid parameters, the focus having generally been on HDL cholesterol^{10,13,15} and occasionally on triglycerides.^{10,11} Furthermore, only a subset of studies evaluated GL and GI in parallel.^{10,11,13,14} Finally, some analyses were limited to only one gender group.^{10,13–15}

The most consistent observational findings to date are that decreased levels of HDL cholesterol have been associated with diets high in GL.^{10,11,13} Similarly in IRAS, we observed a significant inverse association of GL with HDL in the combined sample and in men, but not in women. In IRAS, an association of GI with HDL cholesterol was seen only in the combined sample, but not in the gender-stratified analyses. The exploration of the GI–HDL relation

Table 4 Association of carbohydrate-related food groups with lipid levels

Food group	Total Cholesterol		LDL		HDL		Triglycerides	
	β (SE)	P-value	β (SE)	P-value	β (SE)	P-value	β (SE)	P-value
<i>Men</i>								
Regular soft drinks	0.0611 (0.0290)	0.035	0.1173 (0.0417)	0.005	-0.1550 (0.0420)	< 0.001	0.1354 (0.0825)	0.102
Fruit juice	0.0101 (0.0136)	0.421	0.0142 (0.0196)	0.468	-0.0610 (0.0197)	0.002	0.0753 (0.0387)	0.053
Beer	-0.0101 (0.0094)	0.283	-0.0184 (0.0135)	0.174	0.0066 (0.0137)	0.629	-0.0091 (0.0268)	0.735
Salty snacks	0.0377 (0.0270)	0.164	0.0343 (0.0389)	0.379	-0.0756 (0.0392)	0.055	0.1471 (0.0771)	0.057
Pastry	0.0212 (0.0211)	0.316	0.0417 (0.0304)	0.171	-0.0648 (0.0306)	0.035	0.0332 (0.0602)	0.582
White bread/low-fibre Cereal	0.0079 (0.0133)	0.552	0.0140 (0.0192)	0.467	-0.0229 (0.0193)	0.237	0.0145 (0.0380)	0.702
Dark bread/high-fibre Cereal	-0.0112 (0.0139)	0.418	-0.0119 (0.0200)	0.551	-0.0324 (0.0201)	0.108	0.0149 (0.0395)	0.706
Fruit	0.0060 (0.0080)	0.454	0.0085 (0.0115)	0.464	0.0068 (0.0116)	0.560	-0.0187 (0.0228)	0.414
Sweets/sugar	-0.0121 (0.0138)	0.382	-0.0248 (0.0198)	0.211	-0.0377 (0.0200)	0.060	0.0345 (0.0392)	0.380
Rice/pasta	0.0078 (0.0241)	0.746	0.0088 (0.0348)	0.800	-0.0352 (0.0350)	0.316	-0.0149 (0.0688)	0.829
Dried beans	0.0407 (0.0334)	0.224	0.0058 (0.0482)	0.904	0.0679 (0.0485)	0.162	0.0673 (0.0953)	0.481
Fries/fried potatoes	-0.0503 (0.0480)	0.295	-0.0507 (0.0692)	0.464	-0.1291 (0.0697)	0.065	-0.0283 (0.1369)	0.837
<i>Women</i>								
Rice/pasta	0.0534 (0.0181)	0.003	0.0841 (0.0252)	0.001	-0.0330 (0.0271)	0.223	0.0068 (0.0492)	0.890
Pastry	0.0434 (0.0203)	0.033	0.0548 (0.0282)	0.052	0.0443 (0.0303)	0.144	-0.0122 (0.0550)	0.825
Regular soft drinks	0.0121 (0.0241)	0.615	0.0022 (0.0335)	0.947	-0.0521 (0.0360)	0.148	0.1214 (0.0653)	0.064
Dark bread/high-fibre cereal	-0.0110 (0.0117)	0.347	-0.0272 (0.0163)	0.095	0.0081 (0.0175)	0.643	0.0122 (0.0318)	0.701
Fruit juice	0.0148 (0.0107)	0.168	0.0153 (0.0149)	0.303	0.0031 (0.0160)	0.847	0.0581 (0.0291)	0.046
White bread/low-fibre cereal	-0.0130 (0.0113)	0.252	-0.0168 (0.0157)	0.285	-0.0170 (0.0169)	0.316	0.0063 (0.0307)	0.838
Fruit	-0.0001 (0.0066)	0.983	0.0045 (0.0091)	0.624	-0.0042 (0.0098)	0.671	0.0052 (0.0178)	0.771
Fries/fried potatoes	0.0176 (0.0503)	0.727	0.0562 (0.0698)	0.421	-0.1256 (0.0751)	0.095	0.1739 (0.1363)	0.203
Dried beans	0.0178 (0.0283)	0.530	0.0125 (0.0392)	0.750	-0.0013 (0.0422)	0.976	0.1353 (0.0766)	0.078
Low-fat milk and products	-0.0073 (0.0236)	0.757	-0.0218 (0.0328)	0.507	0.0240 (0.0353)	0.496	0.0526 (0.0640)	0.411
Ice cream	0.0269 (0.0263)	0.306	0.0368 (0.0364)	0.312	-0.0219 (0.0392)	0.576	0.1228 (0.0711)	0.085

β values are shown for ln (total cholesterol), ln (LDL-cholesterol), ln (HDL-cholesterol), and ln (triglycerides) for a one serving increase in food group intake in a multivariate model adjusting for age, ethnicity/clinic, smoking, total energy expenditure, family history of diabetes, hypertension, BMI, glucose tolerance status, lipid-lowering medication and total energy intake, and all other listed food groups.

in observational research has yielded somewhat more variable findings; the majority of studies showing a significant inverse association with HDL cholesterol,^{11–13} with others indicating a positive trend that lacked statistical significance.^{10,14} In addition, one study of elderly men found no evidence of an association of GI with total or HDL cholesterol.¹⁵

Previous epidemiologic work does not support an association of total or LDL cholesterol and GI,^{12–15} which we confirmed in IRAS in both men and women. Interestingly, strikingly few studies have focused on GL in this context. Two studies in women found no association.^{13,14} Similarly, in IRAS, we found no association of GL with total or LDL cholesterol in women. In contrast, however, a strong positive association was observed in men and in the combined sample. Of note, epidemiologic evidence here differs from the majority of intervention studies and meta-analyses thereof, which do support an association of GI with total cholesterol.²⁵ One reason for this discrepancy may lie in the fact that experimental studies achieve dietary GI values well below those present in observational studies of populations choosing more diets freely.

Finally, the relation of GI and GL to plasma triglycerides is of interest. In IRAS women (and in the combined sample), GL

and total carbohydrates were associated with increased levels of triglycerides. This finding confirms work conducted in women,^{10,13,14} though we did not observe the previously reported association of GI with triglycerides.¹⁴ In men, no association of GI or GL was present with triglycerides, similar to a study limited to men.¹⁵

In a previous study, we had identified specific food groups explaining a large proportion of variation in dietary GI and GL.¹⁶ We therefore included this new aspect of carbohydrate nutrition in the present study by evaluating carbohydrate-related food group intake associated with lipid levels. All 14 food groups were considered simultaneously in these analyses, which were additionally adjusted for total energy intake. In general, the carbohydrate-related food groups were associated with lipid levels in the predicted direction, i.e. higher intake was associated with a detrimental lipid profile. Gender-specific patterns emerged. In men, regular soft drinks exhibited the highest potential to affect total, LDL, and HDL cholesterol. Also in men, HDL cholesterol was found to be associated with a range of other food groups, including fruit juice and pastry intake. In women, we identified the food groups rice/pasta and pastries to be associated with

total and LDL cholesterol levels. Fruit-juice intake was positively and significantly associated with triglycerides in women in a similar order of magnitude as in men, though in the latter group this association did not reach statistical significance. In interpreting these findings, it is critical to recognize that only carbohydrate-containing food groups were considered given our focus on GI and GL, hence while we adjusted for total energy intake, larger dietary patterns might not have been considered here.

Our study differs from previous work in a number of ways. Because the GL is mathematically derived from both GI and the amount of carbohydrate intake,²⁶ it is informative to evaluate the concepts of GI and GL in parallel with carbohydrate intake. Only one previous study of lipid levels has also considered carbohydrate intake in addition to GI and GL.¹⁰ In IRAS, we found high levels of consistency in the magnitude, direction, and level of statistical significance of associations of both GL and carbohydrates with the respective lipids, independent of energy intake and a variety of confounders. Note that in previous IRAS work on measures of adiposity, insulin sensitivity, and insulin secretion, associations of GL and carbohydrates were explained entirely by confounding due to correlated energy intake.²⁷ In our data, we found less consistency between findings on GI and GL. This is in contrast to previous reports that had indicated agreement between GL and GI.^{10,11,13}

Several limitations apply to our study. The present study, similar to all other published observational studies on GI and GL in relation to lipid levels, was cross-sectional in nature. In addition, the IRAS FFQ, as most others, was not developed with GI or GL estimation in mind, thus no validation data for dietary GI estimation exist. The IRAS FFQ was validated in a multi-ethnic sub-sample of the IRAS population with respect to nutrients including total carbohydrate intake and fractions of carbohydrates (fructose, starch).¹⁹ Pearson correlation coefficients for FFQ carbohydrate estimates compared with eight 24 h recalls were moderate at $r = 0.39$ unadjusted ($r = 0.37$ adjusted for energy). However, validity differed substantially across ethnic group and centre, ranging from $r = 0.25$ in rural Hs, $r = 0.39$ in urban AAs, and $r = 0.64$ in urban NHWs. These findings are highly comparable to other work indicating lower levels of validity in minority populations.^{28,29} The results of our study need to be interpreted with caution in light of this limitation. Recognizing that subgroup analysis may not have had sufficient statistical power and therefore focusing exclusively on the magnitude and direction of the point estimates, it was reassuring to note that analyses stratified by ethnic group would not have changed our conclusions.

In conclusion, both dietary GL and carbohydrate intake were related to lipid levels in our combined study population. In addition, gender-specific relations were observed that were in part mirrored in associations with specific food groups. GI was inversely associated with HDL cholesterol in the overall population. In summary, this study underscores the importance of overall carbohydrate nutrition for plasma lipid levels.

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