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Associations between dietary macronutrient intake and plasma lipids demonstrate criterion performance of the Multi-Ethnic Study of Atherosclerosis (MESA) food-frequency questionnaire

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The validity of self-reported dietary intake is critical to the design and interpretation of diet–disease investigations. For many nutrients, there are no ideal methods to establish validity, given correlated error between reference and assessment tools, and constraints on time and resources available to perform such studies. Therefore, we quantified associations between macronutrient intakes and plasma HDL-cholesterol and TAG, relying on known associations between these factors to test the criterion validity of the FFQ used in the Multi-Ethnic Study of Atherosclerosis (MESA). Baseline dietary macronutrient intakes (derived from 120-item FFQ), and fasting plasma HDL and TAG were measured in 4510 MESA participants, aged 45–84 years. After adjusting for non-dietary factors known to affect plasma lipid concentrations, greater carbohydrate intake was associated with lower HDL and higher TAG (β per 5-unit change in percentage energy intake from carbohydrate = −5 (SE 1) mg/l ($P<0{\cdot}001$) for HDL and 15 (SE 6) mg/l ($P=0{\cdot}008$) for TAG), whereas higher energy intake from fat was associated with higher HDL and lower TAG (β per 5-unit change in percentage energy from fat = 3·7 (SE 2) mg/l ($P=0{\cdot}01$) for HDL and β = 19 (SE 7) mg/l ($P=0{\cdot}004$) for TAG). Associations of dietary carbohydrate and fat intakes with HDL and TAG concentrations were consistent with previous studies, demonstrating criterion validity of these dietary measures in the MESA.

FFQ: Criterion validity: Plasma lipids: Macronutrients

Knowing the quantitative accuracy of dietary assessment tools bolsters the validity of diet–disease findings, informs the design of appropriate research questions and allows for calibration of risk estimates correcting for known error[1]. FFQ are the most commonly used assessment tool in large epidemiological studies. Validity of data from FFQ can be assessed utilising a variety of study designs. Most often, a subset of the study population is selected to complete multiple food records or 24 h dietary recalls over a period of weeks or months as a reference for comparison with FFQ data. However, such reference measures are imperfect, given correlated errors between the FFQ and either diet recalls or records[2–4]. Opportunities for validation via dietary biomarkers are limited for most nutrients and/or food items and, in some cases, require special sample preparation[5,6]. Despite being objective (as opposed to self-reported), biomarkers themselves are imperfect markers; thus, non-dietary factors that affect circulating concentrations often need to be considered in the interpretation. Consequently, some large epidemiological studies[7–9] have taken advantage of the well-known associations of dietary carbohydrate and fat with plasma lipids (namely, TAG and HDL-cholesterol)[10–12].

The Multi-Ethnic Study of Atherosclerosis (MESA) is a cohort study including men and women from four different race/ethnic groups. The FFQ used in the MESA was based on an FFQ originally designed for the Insulin Resistance and Atherosclerosis Study (IRAS), the validity of which was previously studied in a sample of non-Hispanic whites, African-Americans and Hispanics[13,14]. Because Chinese-Americans were also included in the MESA study, modifications were made to the FFQ to accommodate their unique cuisine. Although the MESA FFQ, as changed from the IRAS FFQ, has not been formally validated through comparison with diet records, it performs well insofar as significant associations between various aspects of diet and disease risk factors[15–20] as well as incident type 2 diabetes[21] and CVD[22] have been

Abbreviations: IRAS, Insulin Resistance and Atherosclerosis Study; MESA, Multi-Ethnic Study of Atherosclerosis.

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reported in the MESA cohort. Since no single method of validation is capable of characterising the accuracy of all dietary constructs measured by FFQ, the utility of any FFQ must be evaluated on the basis of multiple complementary tests of its validity. In the context of predictive validity suggested by the published studies[15–22], further characterisation of the overall performance of the dietary data collected in the MESA in terms of known relationships of food and nutrients to biomarkers provides another lens through which to understand the performance of the FFQ. Furthermore, the MESA offers the opportunity to assess the race/ethnic-specific performance of dietary assessment by FFQ. Such data are valuable in terms of the long-standing concern regarding the reliability and accuracy of various diet assessment instruments in race/ethnic minorities, such as African-Americans[23–25].

Therefore, we evaluated the cross-sectional associations between reported macronutrient intakes and fasting plasma TAG and HDL in the full MESA cohort and in each race/ethnic group represented. Our hypotheses were as follows: (1) the percentage of total energy intake from dietary carbohydrate would be inversely associated with HDL but positively associated with TAG; (2) the percentage of total energy intake from fat would be positively associated with HDL but inversely associated with TAG; (3) the macronutrient–plasma lipid associations would be consistent across race/ethnic groups.

Methods

Participants

The MESA is a population-based study of 6814 non-Hispanic white, African-American, Hispanic and Asian-American (of Chinese descent) men and women, aged 45–84 years from six field centres in the USA: Baltimore City and County, MD; Chicago, IL; Forsyth County, NC; New York, NY; Los Angeles County, CA; St Paul, MN[26]. The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects and patients were approved by the affiliated institutional review boards affiliated with each of the participating academic centres. Written informed consent was obtained from all participants. The present cross-sectional investigation includes data from 4510 MESA participants (1868 non-Hispanic whites; 1111 African-Americans; 952 Hispanics; 579 Chinese-Americans), after excluding individuals who were missing fasting TAG or HDL measurements, who had TAG concentrations > 3990 mg/l, who provided insufficient or implausible dietary information (defined previously)[17], plus those with diabetes or who were taking cholesterol-lowering medications, since either of these conditions are likely to lead to dietary changes or otherwise alter diet–lipid relationships.

Diet assessment

At the baseline examination, usual dietary intake over the previous year was assessed with a modified Block-style 120-item FFQ[13,14]. Consumption frequency and serving size of each food or beverage were assessed. Characteristic of the Block FFQ design, serving sizes were quantified as small, medium or large, with corresponding weights (g) imputed according to National Health and Nutrition Examination Survey (NHANES) data[13]. Nutrients were calculated for each FFQ line item according to a weighted recipe using the Nutrition Data System for Research (NDS-R database; Nutrition Coordinating Center, Minneapolis, MN, USA). Additional input specified the type of milk on cold cereals, defined cold cereal as whole or refined, specified the type of fat used in refried beans, and incorporated information from responses to questions regarding low-fat food choices. To create the final MESA FFQ, several questions were added to the FFQ used in IRAS to help increase its validity with the range of ethnic groups. Specifically, to accommodate the unique cuisine of Chinese-Americans, the following questions were included: stir-fried vegetables; stir-fried vegetables with tofu; stir-fried vegetables with beef, chicken or pork; stir-fried vegetables with shrimp; fried rice; Chinese dumplings, spring rolls or dim sum; chow mein; oriental noodles with meat; desserts made with tofu; soya milk; miso soup. Although these questions were added to more accurately assess eating habits of the Chinese participants, others also consumed these items (mean servings/d of the sum of these items: non-Hispanic whites, 0·30 (SD 1·0); African-Americans, 0·38 (SD 0·93); Hispanics, 0·35 (SD 0·55); Chinese, 2·0 (SD 1·6)).

LDL, HDL and TAG measurements

Plasma HDL and TAG concentrations were measured directly with reagents from Roche Diagnostics (Indianapolis, IN, USA) (analytical CV were 2·9 and 4·0 %, respectively). LDL was calculated with the Friedewald equation for specimens having TAG concentrations < 4000 mg/l (4·52 mmol/l)[27]. All analytes were analysed at the Collaborative Studies Clinical Laboratory (Fairview-University Medical Center, Minneapolis, MN, USA).

Other measures

Information on demographics, education, medication use and smoking history was collected at baseline with a combination of self-administered and interviewer-administered questionnaires. BMI (kg/m^2) was calculated from measured weight and height. The frequency and time spent in various physical activities during a typical week in the previous month were assessed using the MESA Typical Week Physical Activity Survey, adapted from the Cross-Cultural Activity Participation Study[28].

Statistical analysis

Linear regression was used to examine baseline demographic, lifestyle, clinical and dietary characteristics of the study sample stratified by race/ethnic group. Comparisons among race/ethnic strata were tested by F test (continuous variables) or χ^2 (categorical variables). Relationships between macronutrient intakes and HDL and TAG (dependent variables) were expressed as β regression coefficients per 5 percentage points change in energy for carbohydrate and total fat or per 2 percentage points change in energy from each SFA, PUFA and MUFA. Nutrient–lipid associations were also depicted using a categorical nutrient variable (categories based on previous studies[7]. or distribution within the MESA dataset;

see Tables 4 and 5), with *P* trends calculated by modelling the categorical variable continuously.

Two multivariable models were used for these analyses. Model 1 adjusted for field centre, sex, age, energy intake, plus race/ethnicity in analyses of the race/ethnic pooled sample. Model 2 included the variables listed in model 1, plus physical activity level (two variables: active leisure included walking, sport and conditioning activities in metabolic equivalent-min/week; inactive leisure included television, reading and light sitting activities in metabolic equivalent-min/week), alcohol intake (drinks/week), smoking status, cigarette pack years and BMI. Results with additional adjustment for percentage energy from protein, dietary fibre or homeostasis model assessment of insulin resistance (HOMA-IR) did not differ from those of model 2 and, therefore, are not presented. Results are presented for the race/ethnic pooled sample and for each race/ethnic group separately. Interactions in prediction of the dependent variables between macronutrient intake and race/ethnicity, sex, BMI class ($<25\,kg/m^2$ *v.* $\geq 25\,kg/m^2$) and fasting glucose ($<1000\,mg/l$ *v.* $1000–1250\,mg/l$ ($1000\,mg/l$ glucose = 5·55 mmol/l glucose)) were tested by addition of a corresponding cross-product term to model 2.

All analyses were performed with SAS (version 9.1; SAS Institute, Inc., Cary, NC, USA). Due to skewed distribution, C-reactive protein was analysed on the log scale. After excluding participants with fasting TAG $\geq 4000\,mg/l$, TAG concentrations were close to being normally distributed and, thus, analysed without transformation. Plasma lipids were analysed in mg/l. To convert LDL from mg/l to mmol/l, multiply by 0·00259; to convert HDL from mg/l to mmol/l, multiply by 0·00259; to convert TAG from mg/l to mmol/l, multiply by 0·00113.

Results

Participant characteristics, macronutrient intakes and plasma lipid concentrations

Race/ethnic-specific demographic and lifestyle characteristics, intakes of dietary macronutrients and concentrations of plasma lipids are shown in Table 1. The highest prevalence of smoking was found in non-Hispanic whites. African-Americans reported the highest amount of leisure time spent in active pursuits (i.e. walking, conditioning and other sports activities) but also had the highest mean BMI among race/ethnic groups. BMI was lowest among the Chinese-Americans. Energy intake was highest in the Hispanic participants and lowest in Chinese-Americans. The energy contribution from macronutrients and crude plasma lipid concentrations also differed by race/ethnicity ($P<0·01$ for all; Table 1). For example, the Chinese-Americans had the highest protein and total fat, MUFA and PUFA intake, but the lowest SFA intake. The highest LDL and lowest HDL concentrations were observed in Hispanics; the highest C-reactive protein was observed in African-Americans; the highest TAG concentrations were observed in Chinese-Americans.

Associations between macronutrients and plasma HDL and TAG in all participants

In the pooled sample of all participants (men and women in all race/ethnic groups), statistically significant associations between macronutrients (as a percentage of total energy intake) and plasma concentrations of HDL and TAG were evident after adjustment for demographic characteristics and lifestyle factors, including physical activity and BMI (Table 2). Each 5-unit increase in the

Table 1. Daily energy and macronutrient intakes and plasma lipids of 4510 non-Hispanic white, African-American, Hispanic and Chinese-American men and women from the Multi-Ethnic Study of Atherosclerosis*

(Mean values with their standard errors or percentages)

	Non-Hispanic whites (*n* 1868)		African-Americans (*n* 1111)		Hispanics (*n* 952)		Chinese-Americans (*n* 579)	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Demographic and lifestyle factors								
Age (years)	61·9	0·2	61·3	0·3	60·0	0·3	61·1	0·4
Sex (% male)	46·7		43·3		48·9		48·7	
Smoking (% current)	43·6		36·4		31·9		18·3	
Active leisure (MET-min/week)	2693	71	2887	92	2133	99	1756	127
BMI (kg/m^2)	27·3	0·1	29·7	0·1	29·0	0·2	23·8	0·2
Dietary intake (daily values)								
Energy								
KJ	7192	75	7330	96	7644	105	5778	134
Kcal	1719	18	1752	23	1827	25	1381	32
Protein (% energy)	16·2	0·1	15·4	0·1	15·1	0·1	17·7	0·1
Carbohydrate (% energy)	49·3	0·2	51·2	0·2	50·7	0·3	48·9	0·3
Total fat (% energy)	33·5	0·2	34·2	0·2	34·9	0·2	35·7	0·3
SFA (% energy)	11·1	0·1	10·6	0·1	11·0	0·1	9·0	0·1
MUFA (% energy)	12·2	0·1	12·6	0·1	12·9	0·1	13·3	0·1
PUFA (% energy)	7·0	0·1	7·6	0·1	8·0	0·1	10·6	0·1
Plasma lipids†								
LDL-cholesterol (mg/l)	1204	7	1175	9	1222	10	1182	13
HDL-cholesterol (mg/l)	534	3	539	5	480	5	503	6
TAG (mg/l)	1230	14	921	18	1429	20	1321	25

MET, metabolic equivalents.

* $P<0·01$ for all, with the exception of sex (significance for difference among race groups: $P>0·05$).

† To convert LDL-cholesterol from mg/l to mmol/l, multiply by 0·00259; to convert HDL-cholesterol from mg/l to mmol/l, multiply by 0·00259; to convert TAG from mg/l to mmol/l, multiply by 0·00113.

Table 2. Regression coefficients reflecting expected change in plasma HDL-cholesterol or TAG concentration (mg/l) per 5-unit change in percentage of energy from dietary carbohydrate or total dietary fat and per 2-unit change in percentage energy from dietary saturated (SFA), monounsaturated (MUFA) or polyunsaturated fat (PUFA) in 4510 non-Hispanic white, African-American, Hispanic and Chinese-American men and women from the Multi-Ethnic Study of Atherosclerosis

(β Coefficients with their standard errors)

	Expected change in HDL-cholesterol (mg/l)†		Expected change in TAG (mg/l)†	
	β	SE	β	SE
Dietary carbohydrate				
Model 1‡	−6·3**	1	6·5	6
Model 2§	−5**	1	15**	6
Total dietary fat				
Model 1‡	−1·9	2	−7·4	7
Model 2§	3·7**	2	−19**	7
Dietary SFA				
Model 1‡	−0·8	1	−2·5	6
Model 2§	4·2**	1	−15*	6
Dietary PUFA				
Model 1‡	−2·2	2	−16*	7
Model 2§	0·3	2	−20**	7
Dietary MUFA				
Model 1‡	−1·3	1	−3·4	6
Model 2§	2·7*	1	−11	6

*$P < 0·05$, **$P < 0·01$.
† To convert HDL-cholesterol from mg/l to mmol/l, multiply by 0·00259; to convert TAG from mg/l to mmol/l, multiply by 0·00113.
‡ Adjusted for model 1 covariates: study centre, sex, race/ethnicity, age and energy intake.
§ Adjusted for model 2 covariates: above + education level, physical activity, smoking status, smoking pack years, alcoholic drinks per week and BMI.

percentage of energy intake contributed by dietary carbohydrate corresponded to a statistically significant 5 mg/l lower HDL concentration and 15 mg/l greater TAG concentration (β = −5 (SE 1) mg/l ($P<0·001$) for HDL; β = 15 (SE 6) mg/l ($P=0·008$) for TAG). Analogously, a 5-unit increase in the percentage of energy intake contributed by dietary fat corresponded to a statistically significant 3·7 mg/l greater HDL concentration and 19 mg/l lower TAG concentration (β = 3·7 (SE 2) mg/l ($P=0·01$) for HDL; β = 19 (SE 7) mg/l ($P=0·004$) for TAG). Similar associations with HDL and TAG were noted for SFA, PUFA and MUFA, although regression coefficients varied in magnitude and were not always statistically significant (Table 2).

Race/ethnic-specific associations between dietary macronutrients and plasma HDL and TAG

Although the magnitude and, in some instances, direction of macronutrient–plasma lipid associations did differ among race/ethnic groups, statistically significant interactions were observed only with dietary carbohydrate and with dietary SFA in prediction of HDL concentrations (Table 3). There were no statistically significant interactions between race/ethnicity and dietary macronutrient intake in prediction of TAG concentrations. In non-Hispanic whites, dietary carbohydrate, total fat, SFA and MUFA were significantly associated with plasma HDL concentrations, in directions consistent with those observed in the full sample. In Chinese-Americans, dietary carbohydrate, total fat and SFA were also significantly associated with plasma HDL concentrations, and regression coefficients representing these associations in the Chinese-Americans were very similar to those observed in the white participants. In contrast, the magnitudes of these associations

Table 3. Race/ethnic-specific regression coefficients reflecting expected change in plasma HDL-cholesterol or TAG concentrations (mg/l) per 5-unit change in percentage of energy from dietary carbohydrate or total dietary fat and per 2-unit change in percentage energy from dietary saturated (SFA), monounsaturated (MUFA) or polyunsaturated fat (PUFA) in 4510 non-Hispanic white, African-American, Hispanic and Chinese-American men and women from the Multi-Ethnic Study of Atherosclerosis

(β Coefficients with their standard errors)

	Non-Hispanic whites (*n* 1868)		African-Americans (*n* 1111)		Hispanics (*n* 952)		Chinese-Americans (*n* 579)		
	β	SE	β	SE	β	SE	β	SE	*P* for interaction between race/ethnicity and macronutrient intake
Predicted change in plasma HDL-cholesterol (mg/l)†‡									
Dietary carbohydrate	−8·9**	2	−1·4	3	−1·8	3	−6·6*	3	0·02
Total dietary fat	8·5**	2	0·4	3	0·1	3	8·5*	4	0·14
Dietary SFA	8·0**	2	−0·4	3	−1·1	3	12*	5	0·03
Dietary PUFA	4·9	3	4·7	4	−2·9	3	1	3	0·44
Dietary MUFA	6·9**	2	−0·7	3	2·3	3	4·8	3	0·14
Predicted change in plasma TAG (mg/l)†§									
Dietary carbohydrate	14	9	−0·9	8	14	15	57**	19	0·06
Dietary total fat	−18	11	−5·0	10	−13	17	−68**	21	0·16
Dietary SFA	−22*	9	14	10	−11	16	−28*	16	0·22
Dietary PUFA	−19	15	−29*	13	−0·3	15	−40**	15	0·10
Dietary MUFA	−4·7	10	−6·9	10	−14	16	−28	16	0·55

*$P<0·05$, **$P<0·01$.
† Adjusted for model 2 covariates: study centre, sex, race/ethnicity, age, energy intake, education level, physical activity, smoking status, smoking pack years, alcoholic drinks per week and BMI.
‡ To convert HDL-cholesterol from mg/l to mmol/l, multiply by 0·00259.
§ To convert TAG from mg/l to mmol/l, multiply by 0·00113.

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Table 4. HDL-cholesterol and TAG concentrations across categories of dietary carbohydrate intake in 4510 men and women from the Multi-Ethnic Study of Atherosclerosis*†

(Mean values with their standard errors)

	Dietary carbohydrate (% energy)												
	≤40·0		40·1–45·0		45·1–50·0		50·1–55·0		55·1–60·0		≥60·1		
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	P_{trend}
All participants (*n*)	442		781		1136		1016		630		505		
HDL-cholesterol (mg/l)	542	6	549	5	519	4	513	4	516	5	510	6	<0·001
TAG (mg/l)	1182	29	1182	21	1215	18	1218	19	1252	24	1265	27	0·04
Non-Hispanic whites (*n*)	222		328		464		418		261		175		
HDL-cholesterol (mg/l)	551	9	556	7	531	6	525	7	535	8	505	10	<0·001
TAG (mg/l)	1227	43	1180	34	1238	28	1197	30	1290	38	1294	47	0·09
African-Americans (*n*)	103		181		250		221		173		183		
HDL-cholesterol (mg/l)	563	14	543	11	541	9	523	9	531	11	546	11	0·31
TAG (mg/l)	945	46	963	35	959	29	1007	31	934	35	954	35	0·94
Hispanics (*n*)	61		156		248		244		137		106		
HDL-cholesterol (mg/l)	498	15	477	9	478	7	483	7	479	10	466	11	0·31
TAG (mg/l)	1463	85	1362	54	1438	42	1390	42	1461	57	1522	65	0·23
Chinese-Americans (*n*)	56		116		174		133		59		41		
HDL-cholesterol (mg/l)	535	16	505	11	509	9	491	10	479	15	502	18	0·04
TAG (mg/l)	1150	87	1290	58	1241	47	1425	54	1509	81	1379	100	0·002

* Adjusted for model 2 covariates: study centre, age, sex, race/ethnicity, total energy intake, education level, smoking status, smoking pack years, physical activity, alcoholic drinks per week and BMI.
† To convert HDL-cholesterol from mg/l to mmol/l, multiply by 0·00259; to convert TAG from mg/l to mmol/l, multiply by 0·00113.

were much smaller in the African-American and Hispanic participants and not statistically significant. Regression coefficients representing the associations between macronutrient intakes and plasma TAG were more comparable across race/ethnic groups, although they were larger in magnitude and formally significant only in the Chinese-American participants.

There were no interactions between macronutrient intake and sex or fasting glucose status (<1000 *v.* ≥1000 mg/l) in prediction of HDL or TAG concentrations (data not shown). When analyses were stratified by BMI class, the associations between percentage of energy intake from carbohydrate and HDL (inverse) and TAG (positive) were stronger in those participants with a BMI $< 25\,kg/m^2$ *v.* those with a BMI $\geq 25\,kg/m^2$ (for HDL, $\beta = -1{\cdot}5$ (SE 0·5) mg/l ($P<0{\cdot}01$) *v.* −0·6 (SE 0·3) mg/l ($P=0{\cdot}02$) ($P_{interaction} = 0{\cdot}009$); for TAG, $\beta = 4{\cdot}8$ (SE 2) mg/l ($P<0{\cdot}01$) *v.* 1·9 (SE 0·1) mg/l ($P = 0{\cdot}18$) ($P_{interaction} = 0{\cdot}01$)).

An alternative representation of these results with the percentage energy intake from carbohydrate and percentage energy intake from total dietary fat modelled categorically is given in Tables 4 and 5. These results mirrored those described above with dietary macronutrients modelled continuously.

Table 5. HDL-cholesterol and TAG concentrations across categories of dietary total fat intake in 4510 men and women from the Multi-Ethnic Study of Atherosclerosis*†

(Mean values with their standard errors)

	Total dietary fat (% energy)												
	≤25·0		25·1–30·0		30·1–33·0		33·1–37·0		37·1–40·0		≥40·1		
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	P_{trend}
All participants (*n*)	417		808		678		1051		700		856		
HDL-cholesterol (mg/l)	514	7	517	5	517	5	517	5	525	5	528	5	0·03
TAG (mg/l)	1211	30	1268	21	1213	23	1230	18	1209	23	1169	20	0·02
Non-Hispanic whites (*n*)	221		358		311		428		230		320		
HDL-cholesterol (mg/l)	517	9	526	7	539	8	527	6	547	9	554	8	0·002
TAG (mg/l)	1219	42	1300	32	1176	34	1266	29	1229	40	1162	35	0·12
African-Americans (*n*)	104		210		165		234		182		216		
HDL-cholesterol (mg/l)	551	14	543	10	524	11	530	9	535	10	556	10	0·65
TAG (mg/l)	920	45	962	32	964	36	1008	30	992	34	912	32	0·91
Hispanics (*n*)	66		155		130		239		177		185		
HDL-cholesterol (mg/l)	478	15	470	9	482	10	484	7	488	9	471	9	0·85
TAG (mg/l)	1455	84	1510	54	1440	58	1366	43	1400	50	1447	49	0·38
Chinese-Americans (*n*)	26		85		72		150		111		135		
HDL-cholesterol (mg/l)	471	22	500	12	481	13	508	9	513	11	509	10	0·07
TAG (mg/l)	1499	122	1353	68	1454	73	1337	51	1241	59	1245	54	0·01

* Adjusted for model 2 covariates: study centre, age, sex, race/ethnicity, total energy intake, education level, smoking status, smoking pack years, physical activity, alcoholic drinks per week and BMI.
† To convert HDL-cholesterol from mg/l to mmol/l, multiply by 0·00259; to convert TAG from mg/l to mmol/l, multiply by 0·00113.

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Discussion

This aim of the present cross-sectional study was to quantify the concordance of the MESA FFQ with known relationships between macronutrient intake and plasma lipid concentrations. Overall, the present results support our hypotheses, with positive associations between dietary fat and HDL and between dietary carbohydrate and TAG and negative associations between dietary fat and TAG and between dietary carbohydrate and HDL. Although there were possibly some differences among race/ethnic groups, race/ethnic interaction was at most marginally statistically significant and there could be metabolic differences among the race/ethnic groups.

Associations between macronutrient intakes and plasma lipid concentrations were statistically significant; however, the magnitudes of the predicted plasma lipid changes in association with macronutrient intake were small, clinically speaking[29], which is an important distinction between the present study and those aimed at quantifying disease risk incurred by dietary macronutrient intake[30]. The purpose of our exercise was not to determine how macronutrient intake might influence disease risk via lipid risk factors, but rather to test the criterion validity of the MESA FFQ, the validity of which otherwise rests on its affinity to the validated IRAS questionnaire and its predictive and correlational associations with risk factors and disease incidence. The use of plasma lipids as biomarkers for carbohydrate and fat intakes has precedent in other large epidemiological cohorts[7–9] and boasts the advantage of minimal participant burden, study expense, and uncorrelated error structure (unlike 24 h recalls or dietary records commonly used to calibrate FFQ[2–4]). Although plasma lipid concentrations are sensitive to macronutrient intake (particularly the relative contributions of total fat and carbohydrate[10,11]), concentrations are not specific to macronutrient intake. Other factors such as demographic characteristics, genetics, behavioural choices and adiposity also influence plasma lipid levels, most of which were included as covariates in our analyses.

Before inclusion of Chinese food items and administration at the MESA baseline examination, the validity of the parent FFQ was evaluated in a sample of non-Hispanic whites, African-Americans and Hispanics[13,14]. Given that Chinese-Americans were not included in that study and that subsequent FFQ modifications were specific to their cuisine, the associations between macronutrient intake and plasma HDL and TAG concentrations add to the evidence that the MESA FFQ is meaningful in the Chinese-American subgroup. The weaker associations of carbohydrate and fat in African-Americans and Hispanics could suggest lower validity in these two groups than in other race/ethnicities. For several reasons we do not weigh this finding heavily. Although race/ethnic interactions for associations of HDL with carbohydrate and total fat did have P values of 0·02 and 0·03, the interactions were not hypothesised and would not be judged to be statistically significant in the context of multiple testing. The possible race/ethnic interactions for TAG differed from those for HDL, with coefficients for African-Americans or Hispanics, in some cases, second largest, rather than smallest, as in the case of HDL. The observed differences among race/ethnic groups could be the result of residual confounding, for example, due to imperfectly measured or unmeasured demographic, genetic and lifestyle confounders. For example, differences in genotype frequencies for polymorphisms known to affect HDL and TAG metabolism[31–34] may have contributed to the inconsistencies in macronutrient–lipid associations among race/ethnic groups that we observed, especially if such genetic variation also translates into differences in the nature of macronutrient × genotype interactions[35]. Furthermore, the dietary patterns in each race/ethnic group (described previously)[17] were as expected based on external information. Other risk factor and longitudinal relationships with dietary patterns in the MESA cohort have not found weaker associations in African-American and Hispanic participants[15,17,21,36]. Considering the full context of work in the MESA, the findings of the present investigation, together with the results of previous MESA diet investigations, demonstrate that the performance of the MESA FFQ is comparable with that of FFQ utilised by other large epidemiological studies that do not face the challenge of accommodating an ethnically diverse population with correspondingly diverse dietary habits.

We observed significant interactions between BMI and percentage of energy intake from carbohydrate for both HDL and TAG, where stronger associations were noted in those with healthy BMI compared with those who were overweight or obese. Results from a similar analysis in the Health Professionals Follow-Up Study cohort suggested that macronutrient–plasma lipid associations were stronger in the overweight and obese men compared with the healthy-weight men, although the interaction was not statistically significant[7]. While biological differences may be responsible for the results in the Willett *et al.*[7] study (for example, metabolic differences in glucose handling), it may be that measurement error unique to the overweight/obese strata (particularly, under-reporting bias)[37] explains the weaker associations observed in the overweight/obese strata in the present study. However, it is important to note that despite the presence of statistical interaction due to differences in the magnitude of the relationships between percentage energy intake from carbohydrate and HDL and TAG concentrations, regression coefficients were statistically significant in each BMI strata and thus less likely to result in significant systematic bias.

Other limitations to our analysis deserve mention. Single plasma lipid measurements do not account for the intra-individual variation that is probably present. We did not adjust our regression estimates for measure of carbohydrate type or quality, such as glycaemic index or load[8]. However, we did adjust for fibre and found no material changes in regression coefficients, consistent with data from other epidemiological studies[9] and from controlled feeding studies utilising whole, high-fibre foods[38].

Associations of macronutrient intakes with HDL and TAG concentrations were statistically significant and in directions consistent with previous studies[7,9–11]. While in some instances the expected diet–lipid relationships were less consistent in MESA African-Americans and Hispanics, the race/ethnic interactions were not formally significant. Collectively, these data, together with previous MESA investigations showing that other dietary factors are associated with CVD risk factors[15–17,20] as well as predict incident diabetes[21] and clinical CVD events[22] consistently in all race/ethnic

groups, bolster our confidence in the accuracy of the dietary assessment tool used in the MESA. Ascertaining what individuals habitually eat is among the most difficult of epidemiological tasks. While no standard of perfection exists, the MESA FFQ appears to meet the needs of epidemiologists seeking to understand how diet influences multiple health outcomes in a multi-ethnic population.

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References

1. Willett WC (1998) *Nutritional Epidemiology*, 2nd ed. New York: Oxford University Press.
2. Prentice RL (1996) Measurement error and results from analytic epidemiology: dietary fat and breast cancer. *J Natl Cancer Inst* **88**, 1738–1747.
3. Plummer M & Clayton D (1993) Measurement error in dietary assessment: an investigation using covariance structure models. Part I. *Stat Med* **12**, 925–935.
4. Kipnis V, Carroll RJ, Freedman LS, *et al.* (1999) Implications of a new dietary measurement error model for estimation of relative risk: application to four calibration studies. *Am J Epidemiol* **150**, 642–651.
5. Potischman N (2003) Biologic and methodologic issues for nutritional biomarkers. *J Nutr* **133**, Suppl. 3, 875S–880S.
6. Arab L (2003) Biomarkers of fat and fatty acid intake. *J Nutr* **133**, Suppl. 3, 925S–932S.
7. Willett W, Stampfer M, Chu NF, *et al.* (2001) Assessment of questionnaire validity for measuring total fat intake using plasma lipid levels as criteria. *Am J Epidemiol* **154**, 1107–1112.
8. Liu S, Manson JE, Stampfer MJ, *et al.* (2001) Dietary glycemic load assessed by food-frequency questionnaire in relation to plasma high-density-lipoprotein cholesterol and fasting plasma triacylglycerols in postmenopausal women. *Am J Clin Nutr* **73**, 560–566.
9. Rock CL, Flatt SW, Thomson CA, *et al.* (2004) Plasma triacylglycerol and HDL cholesterol concentrations confirm self-reported changes in carbohydrate and fat intakes in women in a diet intervention trial. *J Nutr* **134**, 342–347.
10. Mensink RP & Katan MB (1992) Effect of dietary fatty acids on serum lipids and lipoproteins. A meta-analysis of 27 trials. *Arterioscler Thromb* **12**, 911–919.
11. Mensink RP, Zock PL, Kester AD, *et al.* (2003) Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr* **77**, 1146–1455.
12. Parks EJ & Hellerstein MK (2000) Carbohydrate-induced hypertriacylglycerolemia: historical perspective and review of biological mechanisms. *Am J Clin Nutr* **71**, 412–433.
13. Block G, Woods M, Potosky A, *et al.* (1990) Validation of a self-administered diet history questionnaire using multiple diet records. *J Clin Epidemiol* **43**, 1327–1335.
14. Mayer-Davis EJ, Vitolins MZ, Carmichael SL, *et al.* (1999) Validity and reproducibility of a food frequency interview in a Multi-Cultural Epidemiology Study. *Ann Epidemiol* **9**, 314–324.
15. Nettleton JA, Steffen LM, Palmas W, *et al.* (2008) Associations between microalbuminuria and animal foods, plant foods, and dietary patterns in the Multiethnic Study of Atherosclerosis. *Am J Clin Nutr* **87**, 1825–1836.
16. Nettleton JA, Schulze MB, Jiang R, *et al.* (2008) *A priori*-defined dietary patterns and markers of cardiovascular disease risk in the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Clin Nutr* **88**, 185–194.
17. Nettleton JA, Steffen LM, Mayer-Davis EJ, *et al.* (2006) Dietary patterns are associated with biochemical markers of inflammation and endothelial activation in the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Clin Nutr* **83**, 1369–1379.
18. Gao SK, Beresford SA, Frank LL, *et al.* (2008) Modifications to the Healthy Eating Index and its ability to predict obesity: the Multi-Ethnic Study of Atherosclerosis. *Am J Clin Nutr* **88**, 64–69.
19. Lutsey PL, Jacobs DR Jr, Kori S, *et al.* (2007) Whole grain intake and its cross-sectional association with obesity, insulin resistance, inflammation, diabetes and subclinical CVD: The MESA Study. *Br J Nutr* **98**, 397–405.
20. Jiang R, Jacobs DR Jr, Mayer-Davis E, *et al.* (2006) Nut and seed consumption and inflammatory markers in the Multi-Ethnic Study of Atherosclerosis. *Am J Epidemiol* **163**, 222–231.
21. Nettleton JA, Steffen LM, Ni H, *et al.* (2008) Dietary patterns and risk of incident type 2 diabetes in the Multi-Ethnic Study of Atherosclerosis (MESA). *Diabetes Care* **31**, 1777–1782.
22. Nettleton JA, Burke GL, Polak J, *et al.* (2009) Dietary patterns and risk of incident cardiovascular disease in the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Clin Nutr* (In the Press).
23. Lui KJ (1994) The performance of the O'Brien–Fleming multiple testing procedure in the presence of intraclass correlation. *Biometrics* **50**, 232–236.
24. Kristal AR, Feng Z, Coates RJ, *et al.* (1997) Associations of race/ethnicity, education, and dietary intervention with the validity and reliability of a food frequency questionnaire: the Women's Health Trial Feasibility Study in Minority Populations. *Am J Epidemiol* **146**, 856–869.
25. Coates RJ & Monteilh CP (1997) Assessments of food-frequency questionnaires in minority populations. *Am J Clin Nutr* **65**, Suppl. 4, 1108S–1115S.
26. Bild DE, Bluemke DA, Burke GL, *et al.* (2002) Multi-ethnic study of atherosclerosis: objectives and design. *Am J Epidemiol* **156**, 871–881.
27. Friedewald WT, Levy RI & Fredrickson DS (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* **18**, 499–502.
28. Ainsworth BE, Irwin ML, Addy CL, *et al.* (1999) Moderate physical activity patterns of minority women: the Cross-Cultural Activity Participation Study. *J Womens Health Gend Based Med* **8**, 805–813.
29. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (2002) Third Report of the National Cholesterol Education Program (NCEP) Expert

Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* **106**, 3143–3421.
30. Hu FB, Stampfer MJ, Manson JE, *et al.* (1997) Dietary fat intake and the risk of coronary heart disease in women. *N Engl J Med* **337**, 1491–1499.
31. Miljkovic-Gacic I, Bunker CH, Ferrell RE, *et al.* (2006) Lipoprotein subclass and particle size differences in Afro-Caribbeans, African Americans, and white Americans: associations with hepatic lipase gene variation. *Metabolism* **55**, 96–102.
32. Nie L, Niu S, Vega GL, *et al.* (1998) Three polymorphisms associated with low hepatic lipase activity are common in African Americans. *J Lipid Res* **39**, 1900–1903.
33. Vega GL, Clark LT, Tang A, *et al.* (1998) Hepatic lipase activity is lower in African American men than in white American men: effects of 5′ flanking polymorphism in the hepatic lipase gene (LIPC). *J Lipid Res* **39**, 228–232.
34. Carr MC, Brunzell JD & Deeb SS (2004) Ethnic differences in hepatic lipase and HDL in Japanese, black, and white Americans: role of central obesity and LIPC polymorphisms. *J Lipid Res* **45**, 466–473.
35. Nettleton JA, Steffen LM, Ballantyne CM, *et al.* (2007) Associations between HDL-cholesterol and polymorphisms in hepatic lipase and lipoprotein lipase genes are modified by dietary fat intake in African American and white adults. *Atherosclerosis* **194**, e131–e140.
36. Nettleton JA, Steffen LM, Schulze MB, *et al.* (2007) Associations between markers of subclinical atherosclerosis and dietary patterns derived by principal components analysis and reduced rank regression in the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Clin Nutr* **85**, 1615–1625.
37. Lissner L, Troiano RP, Midthune D, *et al.* (2007) OPEN about obesity: recovery biomarkers, dietary reporting errors and BMI. *Int J Obes (Lond)* **31**, 956–961.
38. Parks EJ, Krauss RM, Christiansen MP, *et al.* (1999) Effects of a low-fat, high-carbohydrate diet on VLDL-triglyceride assembly, production, and clearance. *J Clin Invest* **104**, 1087–1096.

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