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Plasma *trans*-Fatty Acid Concentrations Continue to Be Associated with Serum Lipid and Lipoprotein Concentrations among US Adults after Reductions in *trans*-Fatty Acid Intake[1–4]

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Abstract

Background: High intakes of *trans*-fatty acids (TFAs), especially industrially produced TFAs, can lead to unfavorable lipid and lipoprotein concentrations and an increased risk of cardiovascular disease. It is unknown how this relation might change in a population after significant reductions in TFA intake.

Objective: This study, which used a new analytical method for measuring plasma TFA concentrations, clarified the association between plasma TFA and serum lipid and lipoprotein concentrations before and after the US FDA enacted TFA food-labeling regulations in 2006.

Methods: Data were selected from the NHANES of 1999–2000 and 2009–2010. Findings on 1383 and 2155 adults, respectively, aged ≥20 y, were evaluated. Multivariable linear regressions were used to examine the associations between plasma TFA concentration and lipid and lipoprotein concentrations. The outcome measures were serum concentrations of total cholesterol (TC), LDL cholesterol, HDL cholesterol, and triglycerides and the ratio of TC to HDL cholesterol.

Results: The median plasma TFA concentration decreased from 80.6 μmol/L in 1999–2000 to 37.0 μmol/L in 2009–2010. Plasma TFA concentration continued to be associated with serum lipid and lipoprotein concentrations after significant reductions in TFA intake in the population. For example, by comparing the lowest with the highest quintiles of TFA concentration in 1999–2000, adjusted mean (95% CI) LDL-cholesterol concentrations increased from 118 mg/dL (112, 123 mg/dL) to 135 mg/dL (130, 141 mg/dL) (*P*-trend < 0.001). The corresponding values for 2009–2010 were 102 mg/dL (97.4, 107 mg/dL) and 129 mg/dL (125, 133 mg/dL) for LDL cholesterol

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

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(*P*-trend < 0.001). Differences between the highest and lowest quintiles were consistent across age groups, sexes, races/ethnicities, and other covariates.

Conclusions: Despite a 54% reduction in plasma TFA concentrations in US adults from 1999–2000 to 2009–2010, concentrations remained significantly associated with serum lipid and lipoprotein concentrations. There does not appear to be a threshold under which the association between plasma TFA concentration and lipid profiles might become undetectable.

Keywords

trans-fatty acids; total cholesterol; LDL cholesterol; HDL cholesterol; triglyceride; cardiovascular disease; public health

Introduction

trans-Fatty acids (TFAs)[7] are FAs that contain ≥1 double bond in the *trans* configuration (1). There are 2 predominant sources of dietary TFAs in the diets of US adults: naturally occurring TFAs found in ruminants and industrially produced, partially hydrogenated oils, which represent an important dietary source of TFAs in the United States (2, 3). Dietary TFA intake in US adults has been associated with an increased risk of cardiovascular disease (CVD) incidence and mortality (4–6). This increase in CVD risk might be attributed to the role that TFAs have in promoting systemic inflammation, endothelial dysfunction, disruption of glucose homeostasis, and, most importantly, in contributing to unfavorable lipid and lipoprotein concentrations (4, 5, 7–10). These unfavorable lipid profiles include having high concentrations of total cholesterol (TC) and LDL cholesterol and low concentrations of HDL cholesterol, which are major CVD risk factors (11–15).

Because of the negative health effects of TFAs, the US FDA has required that TFA concentrations be listed on the Nutrition Facts label for packaged foods since 2006 (16). Moreover, the FDA recently issued a regulation that will further reduce TFAs in foods sold in the United States by ending the use of partially hydrogenated oils by 2018 (17). Because of these activities, similar initiatives by state and local health departments, and industry changes in the United States, the amount of TFAs found in food products has declined significantly since the early 2000s (18–20). In 2012, a CDC study indicated that the mean plasma TFA concentration among adult non-Hispanic whites decreased by 58%, from 93.1 μmol/L in 2000 to 39.0 μmol/L in 2009 (21). A Danish study in healthy middle-aged men after a substantial reduction in dietary TFA intake suggested that the relation between dietary TFA intake and CVD risk factors, including unfavorable lipid profiles, might become undetectable at lower TFA intakes (22).

To our knowledge, no previous study has examined the association between plasma TFA concentration and lipid and lipoprotein concentrations before and after the FDA's regulation of TFA labeling in 2006. The present study, which used a highly specific analytical method to measure selected TFA concentrations in plasma, clarified the association between plasma TFA concentration and serum lipid and lipoprotein concentrations before and after a significant reduction in dietary TFA intake with the use of nationally representative samples of US adults in 1999–2000 and 2009–2010.

Methods

NHANES.

The NHANES is a series of cross-sectional, nationally representative surveys of the civilian, noninstitutionalized US population. For the present study, we used available data from NHANES 1999–2000 and 2009–2010, which included an ancillary assessment of serum in NHANES participants with the use of a new analytical method for measuring plasma TFA concentrations. Detailed descriptions of NHANES methodology have been previously published (23). For NHANES 1999–2000, of the 1613 adults aged ≥20 y with morning fasted blood samples and measured plasma TFA, we excluded 89 pregnant women, 24 participants with missing lipid measurements, and 117 with missing values on covariates, which left data on 1383 adults for analysis. For NHANES 2009–2010, of 2462 adults aged ≥20 y, we applied the same criteria and excluded 25 pregnant women, 22 with missing lipid measurements, and 260 with missing covariates, which left 2155 participants. The NHANES protocol was approved by the CDC's National Center for Health Statistics Ethics Review Board. Written informed consent was also obtained.

Measurements of plasma TFAs and lipid profiles.

TFA and all lipid analyses were conducted by using a morning fasted (≥8 to <24 h) venous sample collected according to a standardized protocol (24). In this study, plasma TFA represents the sum of 4 TFA subgroup concentrations [elaidic acid (18:1n–9t), vaccenic acid (18:1n–7t), linoelaidic acid (18:2n–6t,9t), and palmitelaidic acid (16:1n–7t)] analyzed in plasma by using GC and coupled with MS. This analytical method for measuring plasma TFA concentration has a high analytical specificity and represents 40–60% of the TFAs reported in human blood (21). (For further instrument details, see Supplemental Methods.)

Serum TC and TG concentrations were measured (Johns Hopkins University Lipoprotein Analytical Laboratory) by using enzymatic reactions in both 1999–2000 and 2009–2010; serum HDL cholesterol was measured by the direct immunoassay method in 2009–2010, whereas in 1999–2000, the heparin manganese precipitation method was used (25–27). Serum LDL cholesterol was calculated by using the following formula for participants with TG concentrations ≤400 mg/dL: LDL cholesterol = TC 2 [HDL cholesterol + (TGs/5)] (28). Participants with TG concentrations >400 mg/dL were included in analyses other than that for LDL cholesterol (n = 33 for NHANES 1999–2000 and n = 35 for NHANES 2009–2010). Standardization of serum lipid measurements was performed according to the criteria of the CDC's Lipid Standardization Program (29).

Covariates.

The covariates included the following: age; sex; race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, or other); education (<12, 12, or >12 y of education); smoking status (never, former, or current); alcohol consumption on the basis of self-report in the past 12 mo (0, >0 to <28, or ≥28 g ethanol/d for men and 0, >0 to <14, or ≥14 g ethanol/d for women); physical activity, classified at its most basic level (those reporting no activity compared with some activities because of substantial changes in questionnaires of physical activity from NHANES 1999–2000 to 2009–2010) (30); BMI (in kg/m^2; <25, 25

to <30, and ≥30); self-reported statin use (yes or no); diabetes status (yes or no); intakes of total calories, total PUFAs, total saturated fat, TC, and total dietary TFAs; and 2010 Healthy Eating Index (HEI-2010) score derived from the first-day 24-h dietary recall. We used the USDA National Nutrient Database for Standard Reference (release 16–1 for NHANES 1999–2000 and release 23 for NHANES 2009–2010) to estimate total dietary TFA intake (31, 32). We applied the HEI-2010 algorithm to both NHANES 1999–2000 and 2009–2010 participants; HEI-2010 scores range from 0 to 100, with a higher score indicating a healthier diet (33).

Statistical analysis.

We analyzed NHANES data from 1999–2000 and 2009–2010 separately and estimated the weighted prevalence and means of selected covariates by quintiles of plasma TFA concentration. We calculated the prevalence of different categories of serum lipid and lipoprotein concentrations on the basis of the Adult Treatment Panel III criteria by quintiles of plasma TFA concentration (34). For the abovementioned descriptive analysis, the polynomial statement in the SUDAAN Proc Descript (SUDAAN version 11, RTI) procedure was used to test for significance of linear trends across plasma TFA quintiles by using a *t* test with the appropriate degrees of freedom. We performed multivariable linear regression analysis to examine the association between plasma TFA concentration and TC, LDL-cholesterol, HDL-cholesterol, and TG concentrations and the TC-to-HDL-cholesterol ratio. For TGs, the distribution of regression residuals was not normal; therefore, we used the log transformation of TGs and present their geometric means. We present arithmetic means (95% CIs) for the remaining lipid measurements. For the multivariable linear regression analysis, we used the Wald *F* test for the difference across TFA quintiles. We estimated age, sex, race/ethnicity, and total calorie–adjusted mean lipid concentrations (model 1) and, in a fully adjusted model, we also included educational attainment, smoking status, alcohol consumption, statin use, physical activity, HEI-2010 score, diabetes status, BMI, total PUFAs, total saturated fat, total dietary TFAs, and total dietary cholesterol intake (model 2). We conducted stratified analyses to explore whether the associations between plasma TFA concentration and lipid profiles varied by age group (<60 compared with ≥60 y), sex, race/ethnicity, educational attainment (<12 compared with ≥12 y), physical activity (inactive compared with some activities), HEI-2010 [top 50% (score ≥44.4 or ≥47.7 for NHANES 1999–2000 and 2009–2010, respectively) compared with other], BMI (underweight or normal compared with overweight or obese), and use of statins (yes or no). Total dietary fat showed collinearity with total polyunsaturated and saturated fats as measured by a variance inflation factor (>20). After removing total dietary fat, no evidence of collinearity was identified among independent variables in the multivariate regression analyses. We tested for interactions between plasma TFA concentration and sex and race-ethnicity for each lipid outcome by evaluating the statistical significance of cross-product terms in the multivariable regression models on the basis of the Wald *F* test, and no sex-based or race/ethnicity-based differences were present (*P*-interaction > 0.05). We examined the dose-response associations between plasma TFA concentration and lipid profiles by using the restricted cubic spline with 5 knots (at the 10th, 25th, 50th, 75th, and 90th percentiles) in multivariable regression models (35). We used the fifth-percentile TFA concentration as the referent value (37.2 and 17.0 μmol/L for 1999–2000 and 2009–2010,

respectively) and tested for nonlinearity between TFA concentration and lipid profiles on the basis of the Wald *F* test (36). We pooled 2 NHANES data sets to test for the equality of slopes of TFA concentration on lipid profiles between 2 surveys by creating an indicator variable of the survey cycle and tested for significant interactions between plasma TFA concentration and this indicator variable in the multivariable regression models with the use of the Wald *F* test. For this test, we used the log-transformed TFA concentration to take into account the nonlinear relation between TFA concentration and TC, LDL-cholesterol, and TG concentrations.

We performed 2 sensitivity analyses: first, we examined the association between concentrations of each of 4 plasma TFAs and lipid profiles. Second, we used the TG concentration as a proxy for total FAs and presented TG adjusted (3 TG categories: <150, 150–199, and ≥200 mg/dL) associations between plasma TFA concentration and lipid profiles. All of the analyses were conducted with SAS (version 9.3) or SUDAAN (version 11) to account for the complex sampling design (37). All tests were 2-sided, and $P < 0.05$ was considered to be significant.

Results

The median plasma TFA concentration decreased by 54% from 1999–2000 to 2009–2010 ($P < 0.001$) (Table 1). In both NHANESs, the mean age increased with increasing plasma TFA quintiles and, in general, the percentage of non-Hispanic whites and BMI increased within the higher TFA quintiles. The HEI-2010 score decreased significantly with increasing plasma TFA quintiles (Table 1). Plasma vaccenic and elaidic acid concentrations accounted for >85% of plasma total TFA concentration, and the sum of these 2 TFAs decreased by 55% from 1999–2000 to 2009–2010. Palmitelaidic and linoelaidic acid concentrations accounted for <15% and their sum decreased by 44% from 1999–2000 to 2009–2010 (Table 1).

Plasma TFA concentrations were significantly associated with all lipids and lipoproteins in NHANES 1999–2000 and 2009–2010. In the fully adjusted model (model 2), the mean concentrations of TC, LDL cholesterol, and TGs and the TC-to-LDL-cholesterol ratio and HDL-cholesterol concentrations in the highest-TFA-quintile group were 18%, 14%, 130%, and 42% higher and 16% lower, respectively, than those in the lowest-TFA-quintile group for 1999–2000 (Table 2; *P*-trend < 0.001). The corresponding numbers for 2009–2010 were 24%, 27%, 136%, 53%, and 15% (Table 2; *P*-trend < 0.001). In both NHANESs, the prevalence of unfavorable lipid profiles increased significantly with increased plasma TFA concentrations (Table 3). The β-coefficients (slopes) of the log-transformed plasma TFA concentration associated with lipid and lipoprotein concentrations were not significantly different between NHANES 1999–2000 and NHANES 2009–2010 (Supplemental Table 1; *P*-interaction > 0.05). The associations between plasma TFA concentration and lipid and lipoprotein concentrations were consistent across age groups, sexes, races/ethnicities, educational levels, HEI-2010 categories, physical activity levels, BMI categories, and statin use in NHANES 1999–2000 and NHANES 2009–2010 (Figures 1–5).

The distribution of plasma TFA concentrations shifted substantially to the left from 1999–2000 to 2009–2010 (Figure 6, panel A compared with panel B). The association between plasma TFA concentration and lipid and lipoprotein concentrations was essentially linear for HDL cholesterol and the TC-to-HDL-cholesterol ratio (test for nonlinearity, $P = 0.09$) and nonlinear for TC ($P < 0.001$ for linearity), LDL cholesterol ($P < 0.001$), and TGs ($P = 0.002$) in NHANES 2009–2010 (Figure 6).

The pattern of association between each of the 4 plasma TFA subgroups and lipid and lipoprotein concentrations was consistent with that of the sum of the 4 plasma TFA subgroup concentrations (Supplemental Tables 2–5). The pattern of association remained largely unchanged after adjusting for TGs, but the magnitudes of association were noticeably attenuated for HDL cholesterol in NHANES 2009–2010 (Supplemental Table 6).

Discussion

With the use of data from 2 nationally representative samples, our study showed that plasma TFA concentrations in US adults declined significantly from 1999–2000 to 2009–2010, which is consistent with previous findings in non-Hispanic whites (21). Despite the substantial reduction, the present study clarified that plasma TFA concentrations remained significantly and independently associated with serum lipid and lipoprotein concentrations in the population. In 1999–2000 (2009–2010), a comparison of the participants in the highest to lowest plasma TFA concentration quintiles showed that TC increased by 18% (24%), LDL cholesterol by 14% (27%), TGs by 130% (136%), and the TC-to-HDL-cholesterol ratio by 42% (53%) and HDL cholesterol decreased by 16% (15%). These associations were consistent across age groups, sexes, races/ethnicities, and other covariates among NHANES 1999–2000 and 2009–2010 participants.

Many epidemiologic studies and randomized controlled trials (RCTs) have examined the association between dietary TFAs and adverse health outcomes, and a few have studied the effects with the use of circulating blood TFA concentrations measured with varying methodologies (4, 5, 7, 9, 10, 38–44). Although the results from RCTs and observational studies have shown a consistent relation between dietary TFA intake and lipid profiles (5, 7, 39, 42), the results from plasma TFA–related association studies have been inconsistent. Some studies showed significant associations between plasma TFA concentration and ≥1 of the lipid profile measurements (44–46); others suggested that the association between plasma TFA concentration and lipid profiles might be modified by age, sex, or the intake of other dietary fat (47, 48); and some showed no association (49). Differences in study designs, sample sizes, and measurement of biomarkers and inadequate control of potentially confounding factors, might partially explain these inconsistent findings. Our study attempts to overcome some of these previous limitations by being the first, to our knowledge, that uses a nationally representative sample to examine the association between plasma TFA concentrations, measured by using a highly specific analytical method, and lipid and lipoprotein concentrations. In addition, several meta-analyses and current observational studies have shown significant associations between TFAs and the risk of CVD, with many indicating a dose-response relation between TFAs and the risk of CVD (5, 8, 50, 51). However, findings with respect to the dose-response relation have been inconsistent. The

significant adverse effect of TFAs on lipid profiles represents one of the major mechanisms for an increased risk of CVD associated with TFAs (5). Our findings of dose-response relations between plasma TFAs and lipid profiles are consistent with the dose-response relations between TFAs and the risk of CVD.

In the United States, the estimated mean intake of industrially produced TFAs declined from ~4.6 to 1.3 g/d after the FDA food-labeling requirement was enacted in 2006 (2). A Danish study in healthy middle-aged men found no association between dietary TFAs, on the basis of a 7-d dietary recall, and lipid profiles at lower amounts of industrial TFA intake (estimated at 1.3 g total TFAs/d including 0.4 g industrially produced TFAs/d) (22). Although our study used plasma TFA intakes from 2 nationally representative samples and is not directly comparable to the findings of the Denmark study, the findings of our study do not support the hypothesis of a threshold under which the association between plasma TFA concentration and lipid profiles becomes undetectable. For example, a comparison of plasma TFA concentrations in quintile 2 (median TFA concentration: 29.5 μmol/L) with quintile 1 (median TFA concentration: 21.1 μmol/L) in 2009–2010 showed that TC increased by 6.3% and LDL cholesterol increased by 7.8%, respectively ($P < 0.05$). Our findings clarified that plasma TFA concentrations were significantly associated with unfavorable lipid profiles among US adults after significant reductions in TFA intake and are consistent with the 2015–2020 Dietary Guidelines for Americans, with the Institute of Medicine recommendations that intakes of TFAs should be as low as possible to eliminate their adverse effects on health, and with the FDA's regulation to remove industrially produced TFAs from foods in the United States by 2018 (17, 52, 53).

Studies have suggested that TFAs from various sources (i.e., industrially produced compared with naturally occurring) might have different effects on lipid profiles and the risk of developing CVD and diabetes, but the findings have been inconsistent (3, 50, 54–59). A recent meta-analysis concluded that all TFAs have the same detrimental effect on lipid profiles on a gram-to-gram basis (58). A recent RCT suggested that both vaccenic acid (TFAs from ruminant animals) and TFAs from partially hydrogenated oil adversely affect lipid profiles (59). However, another recent meta-analysis concluded that TFAs from natural sources, at the amount of intake and ≤4.2% of total energy, had no adverse effect on lipid profiles in healthy people (55). Other studies have suggested that increasing concentrations of *trans*-palmitoleate acid (16:1n–7), a naturally occurring TFA in dairy products, were associated with lower insulin resistance, a reduced risk of atherogenic dyslipidemia, and a lower risk of incident diabetes (56, 57). Although the current method for measuring plasma TFA concentrations could not distinguish between the naturally occurring and industrially produced TFAs, the subgroup of 4 TFAs in our study showed consistent negative effects on lipid profiles (Supplemental Tables 2–5). However, even after the FDA mandate to remove industrially produced TFAs from American diets by 2018, there will still be some exposure from naturally occurring TFAs in the population. Thus, further studies are needed on the specific effects of naturally occurring TFAs on health outcomes.

Our study has multiple strengths. First, we used plasma TFA concentrations collected by using established protocols with high standards of quality control among 2 nationally representative samples of US adults. Second, we used a new analytical method for

measuring plasma TFA concentration that has a high analytical specificity for the plasma TFAs investigated. Third, compared with the measurement of dietary TFA consumption, the measurement of circulating plasma TFAs is not subject to the recall bias and measurement error that is associated with dietary recall and might provide more reliable results for association studies than food-intake estimates. Finally, our study adjusted for a wide range of potentially confounding variables.

There are also several limitations to our study. First, plasma TFA concentraton does not distinguish between the industrially produced and naturally occurring TFAs. Our results show the relation between plasma TFAs (i.e., the sum of 4 TFA subgroups) and lipid profiles. Second, the analytical method represents 40–60% of TFAs reported in blood, and the observed association between plasma TFAs and lipid profiles might differ if all plasma TFAs could be measured. Third, although plasma TFA concentrations are free from dietary recall bias, studies showed moderate correlation between plasma TFAs and dietary intake of TFAs assessed by the validated FFQs (r = 0.20–0.37) (46, 60). However, the comparison between plasma and erythrocyte FA content as biomarkers of dietary FA intake supports the relative ability of biomarkers to reflect usual dietary FA intake, including dietary TFA intake (46). Fourth, we controlled for the HEI-2010, which included all major food groups based on 24-h dietary recall, in our analysis (33), but we cannot rule out that the observed association between plasma TFA concentration and lipid profiles might still be partly attributed to the long-term poor diets that are associated with unfavorable lipid profiles. In addition, because the more recent release of the National Nutrient Database for Standard Reference might contain improved data on dietary TFAs, the earlier dietary TFA intakes (NHANES 1999–2000) might be underestimated. Fifth, several studies of TFAs and lipid profiles used the percentage of TFAs as total FAs or adjusted for different classes of FAs in their analyses (45, 47, 48). However, total FA data are not available in NHANES, so we used TGs as a proxy. Although the pattern of association remained largely unchanged after adjusting for TGs, the magnitude of association changed noticeably for HDL cholesterol in NHANES 2009–2010, which might partly be due to the high correlation between plasma TFAs and TGs (r = 0.69 and 0.67 in NHANES 1999–2000 and 2009–2010, respectively). Sixth, the change in the method of measuring HDL cholesterol in NHANES 1999–2000 and 2009–2010 could have affected the HDL-cholesterol results. However, the values from both methods were standardized according to the CDC's Lipid Standardization Program to minimize the effects of a change in method. Finally, we observed a significant and consistent association between plasma TFA concentration and lipid profiles; however, it should not be interpreted as evidence of a causal relation between TFA concentration and lipid profiles, given the nature of observational studies.

In summary, plasma TFA concentrations among US adults declined by 54% from 1999–2000 to 2009–2010. The present study clarified that, despite significant reductions, plasma TFA concentrations were significantly and consistently associated with lipid and lipoprotein concentrations. There does not appear to be a threshold under which the association between plasma TFA concentration and lipid profiles might become undetectable.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations used:

CVD	cardiovascular disease
HEI-2010	2010 Healthy Eating Index
RCT	randomized controlled trial
TC	total cholesterol
TFA	*trans*-fatty acid

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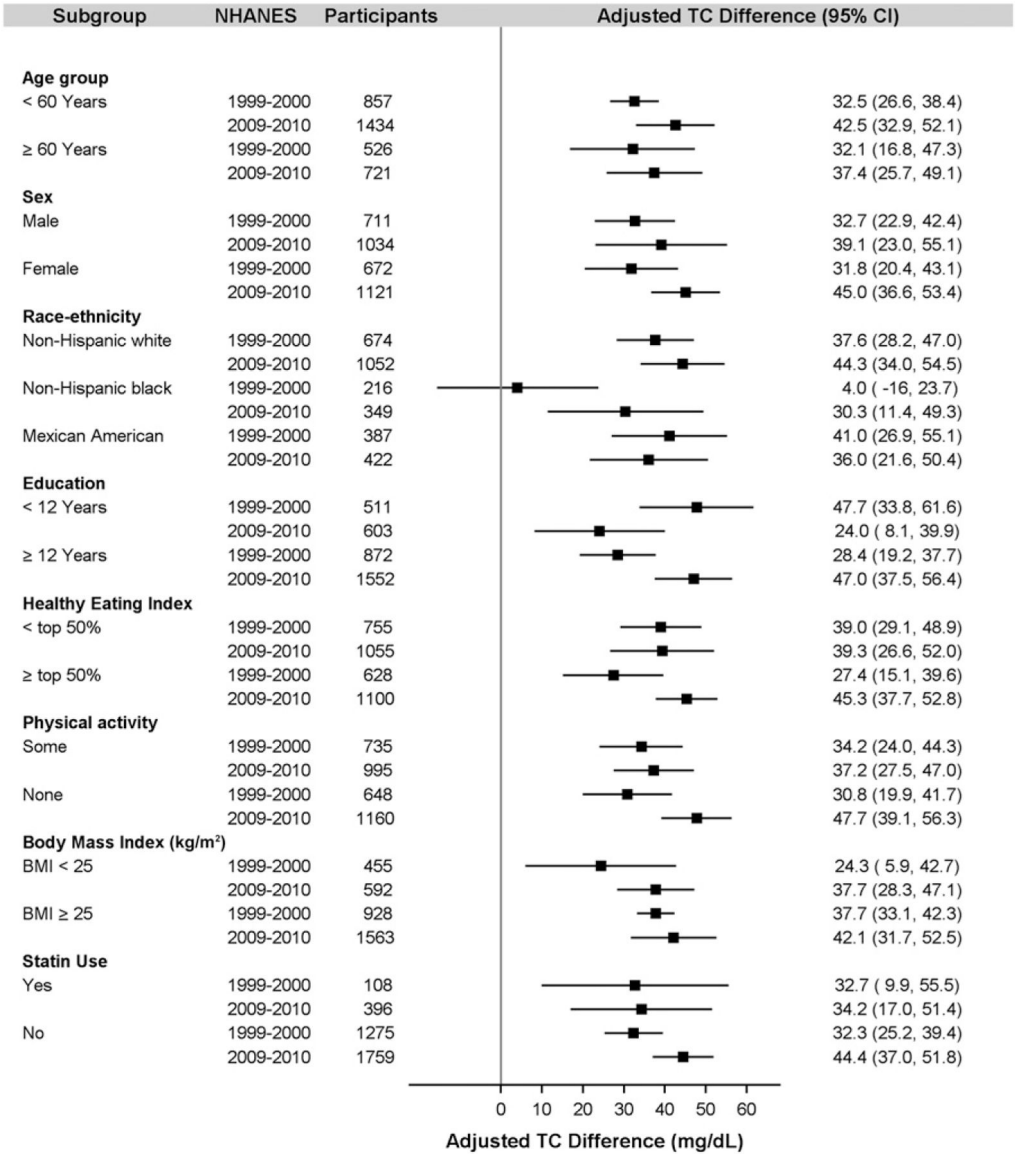

FIGURE 1.

Adjusted differences in mean (95% CI) serum TC concentrations between quintiles 1 and 5 of plasma TFA concentration: NHANES 1999–2000 and 2009–2010. TC, total cholesterol; TFA, *trans*-fatty acid.

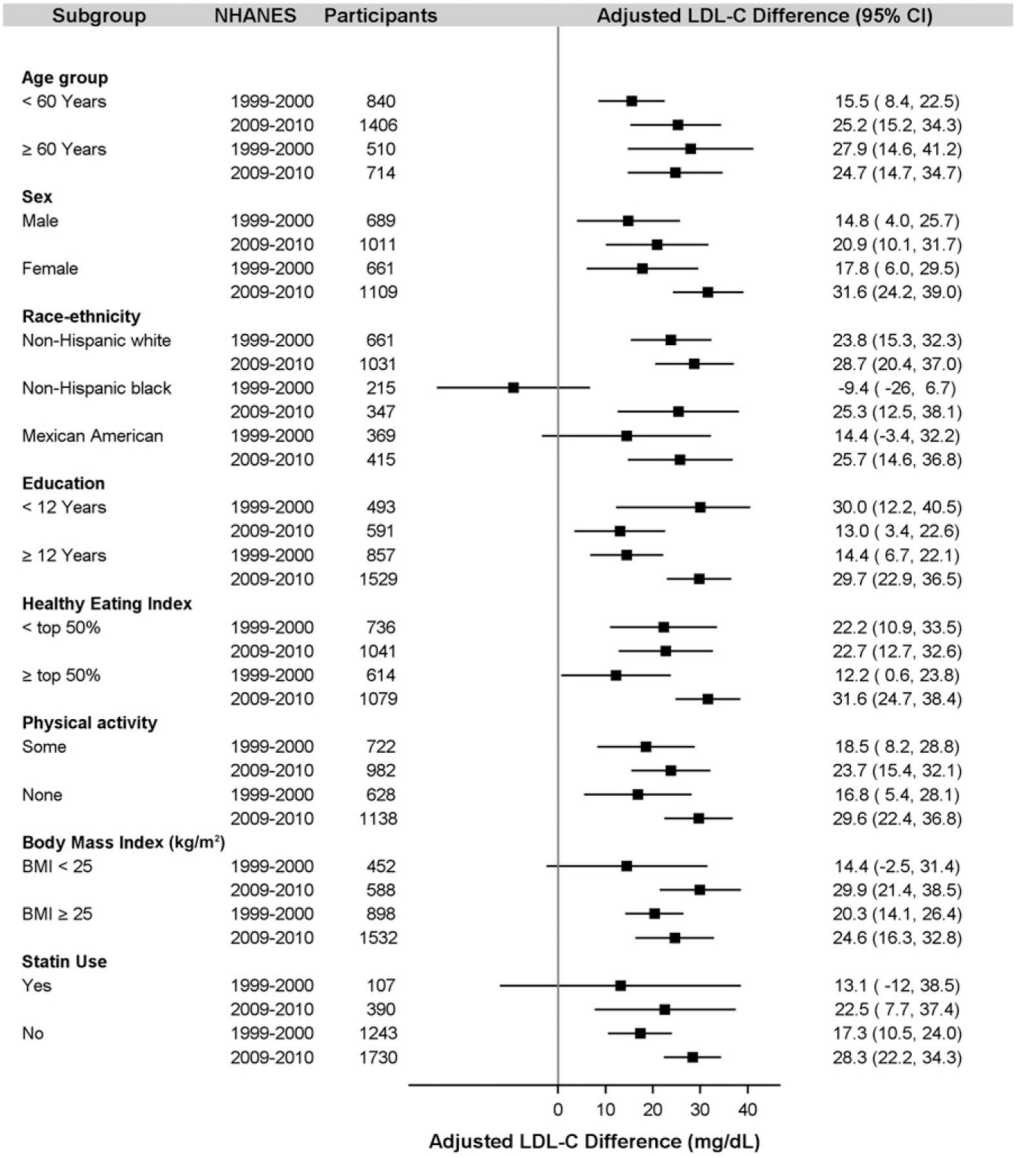

FIGURE 2.

Adjusted differences in mean (95% CI) serum LDL-C concentrations between quintiles 1 and 5 of plasma TFA concentration: NHANES 1999–2000 and 2009–2010 LDL-C, LDL cholesterol; TFA, *trans*-fatty acid.

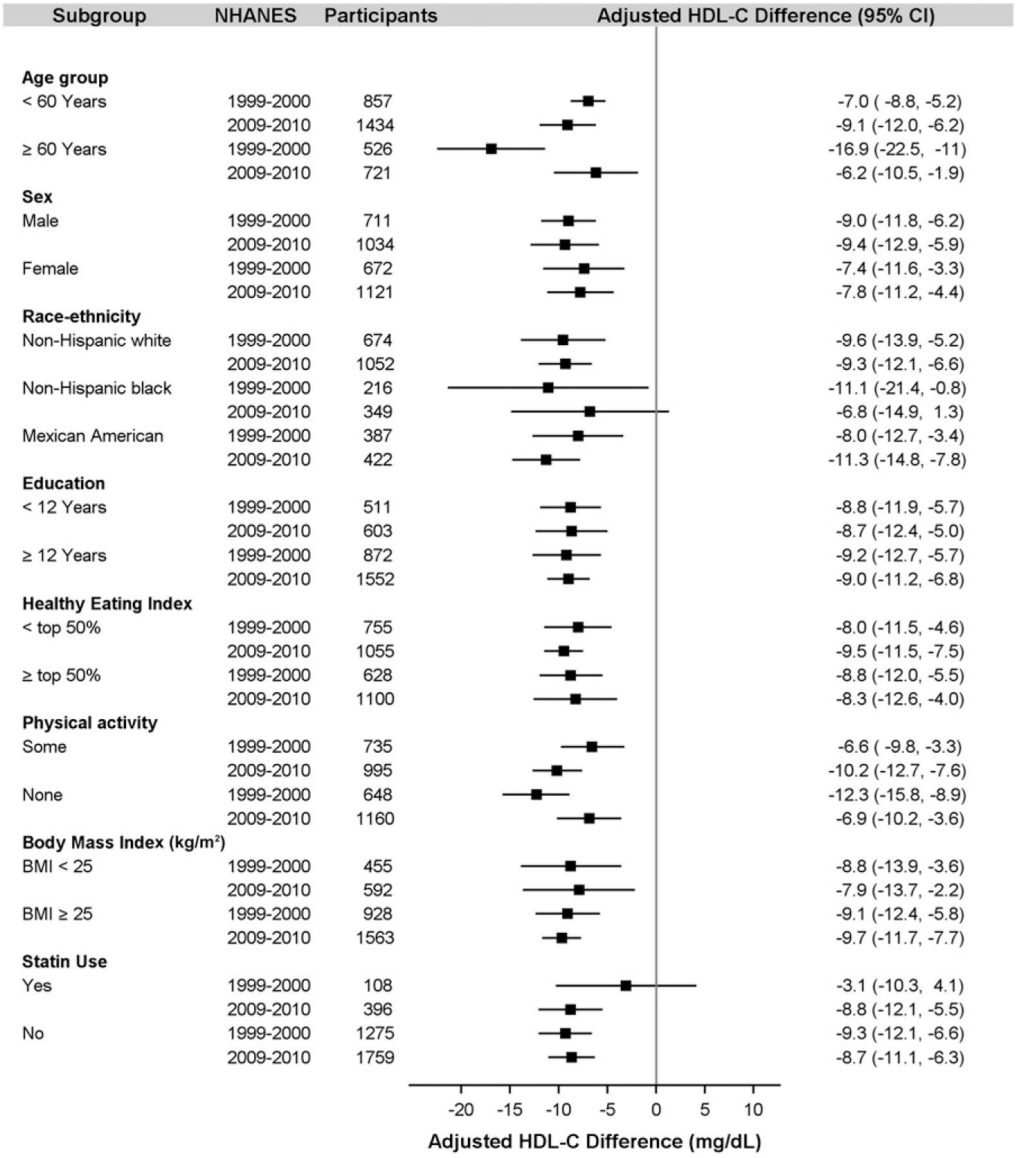

FIGURE 3.

Adjusted differences in mean (95% CI) serum HDL-C concentrations between quintiles 1 and 5 of plasma TFA concentration: NHANES 1999–2000 and 2009–2010 HDL-C, HDL cholesterol; TFA, *trans*-fatty acid.

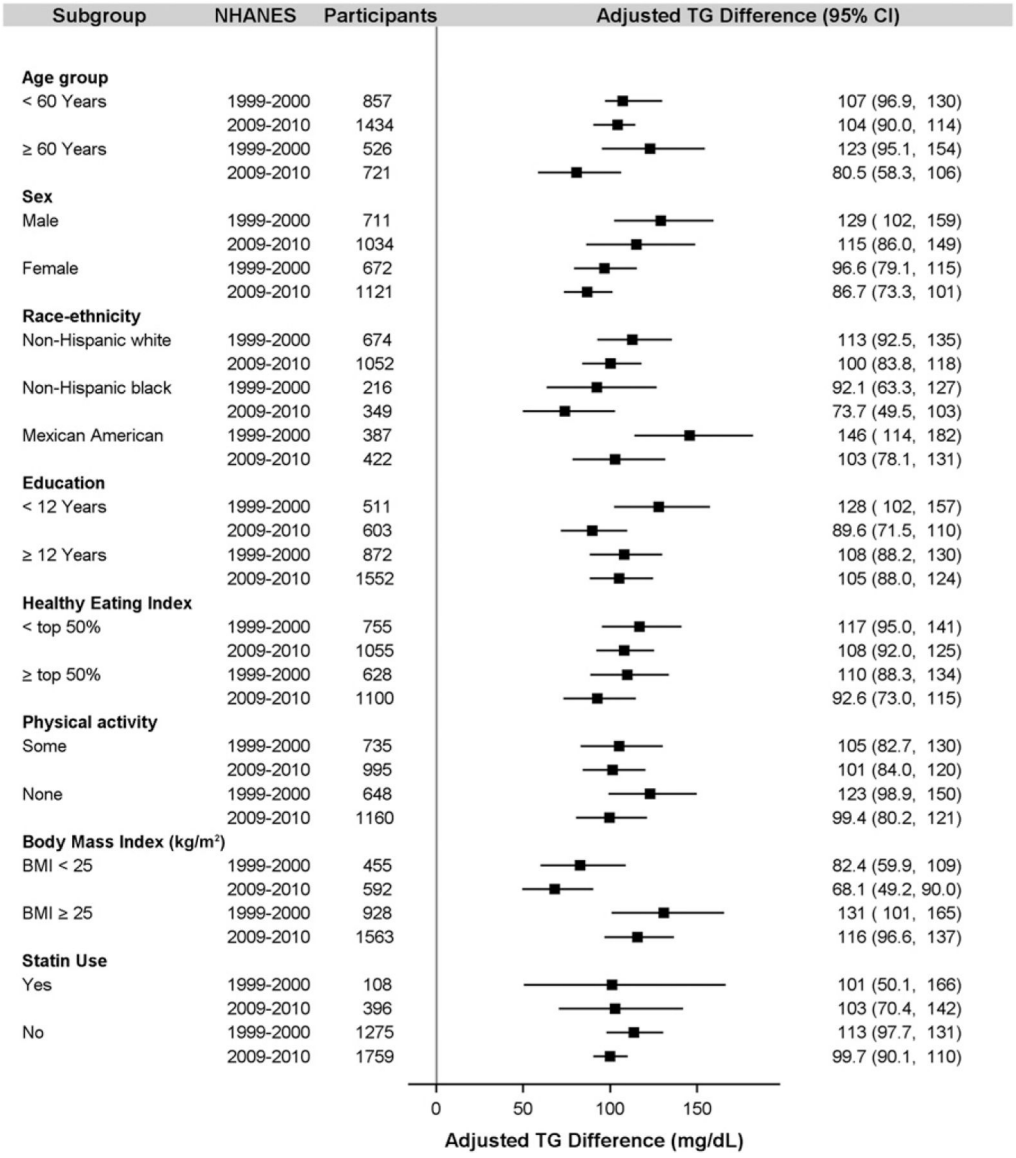

FIGURE 4.

Adjusted differences in mean (95% CI) serum TG concentration between quintiles 1 and 5 of plasma TFA concentration: NHANES 1999–2000 and 2009–2010. TFA, *trans*-fatty acid.

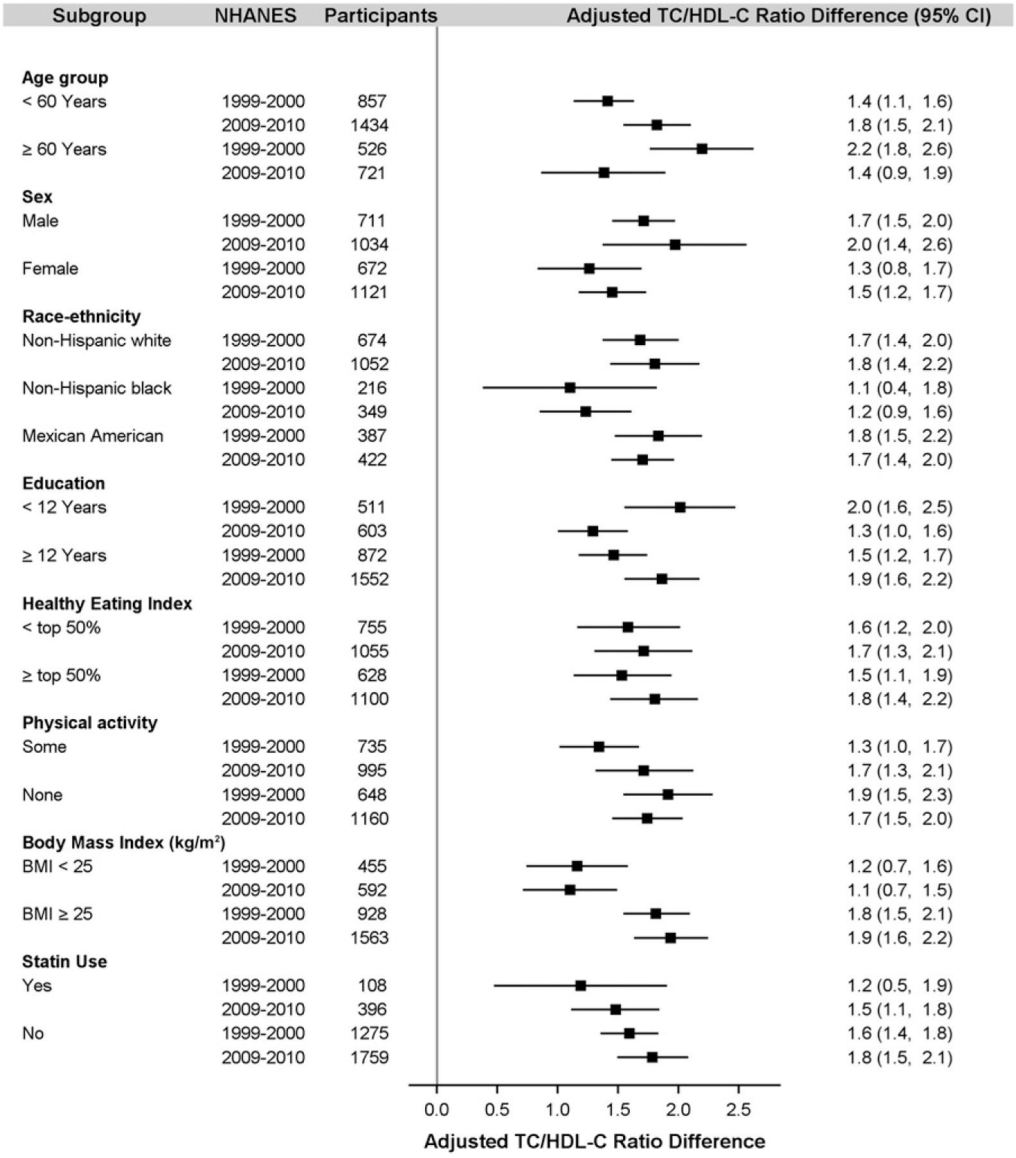

FIGURE 5.

Adjusted differences in mean (95% CI) TC/HDL-C ratio between quintiles 1 and 5 of plasma TFA concentration: NHANES 1999–2000 and 2009–2010. TC/HDL-C ratio, ratio of total cholesterol to HDL cholesterol; TFA, *trans*-fatty acid.

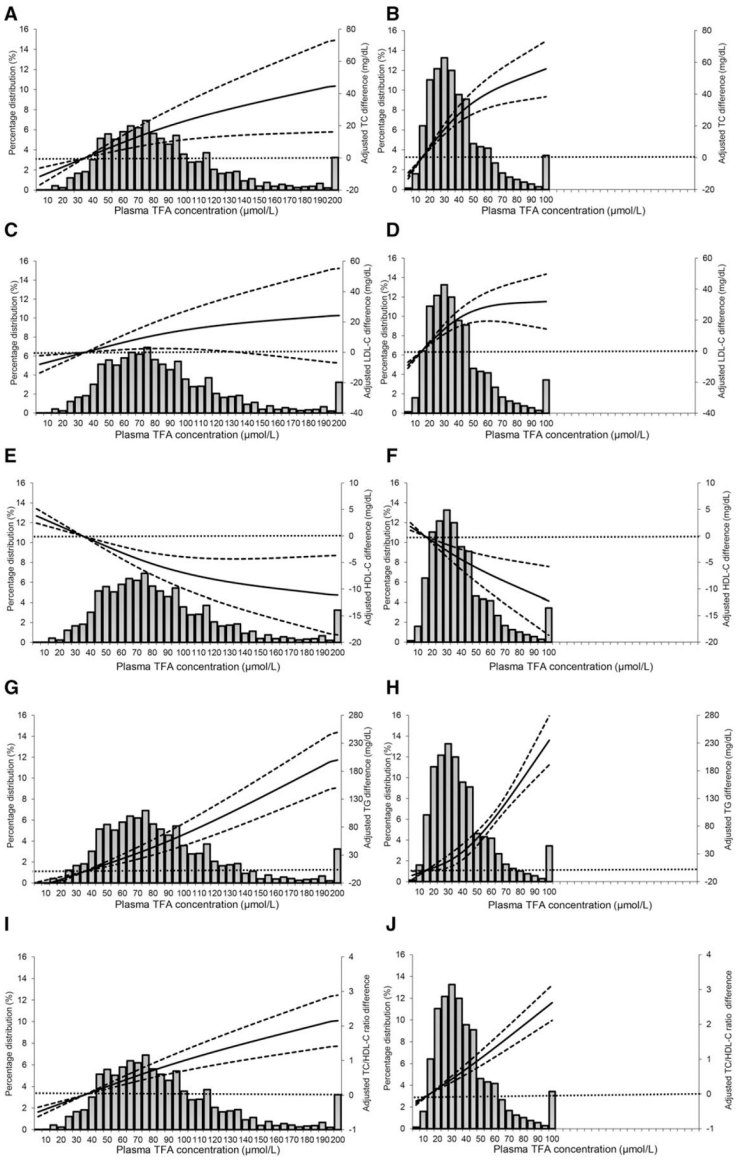

FIGURE 6.

A–J: Distributions of mean plasma TFA concentrations and adjusted differences in mean serum lipid and lipoprotein concentrations compared with the fifth-percentile plasma TFA concentration: NHANES 1999–2000 (left panels) and 2009–2010 (right panels). The lines show that the associations between the plasma TFA concentration and lipid profiles were not affected by the different upper limits of plasma TFA concentration used in NHANES 1999–2000 (n = 1383) and 2009–2010 (n = 2155). The solid line is the adjusted difference in the means of each variable compared with the fifth-percentile plasma TFA concentration (horizontal dotted line), and the dashed lines represent the 95% CIs. HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; TC, total cholesterol; TC/HDL-C ratio, ratio of total cholesterol to HDL cholesterol; TFA, *trans*-fatty acid.

TABLE 1

Characteristics of participants aged ≥20 y by quintiles of plasma TFA concentration: NHANES 1999–2000 and 2009–2010[1]

	Quintile of plasma TFA concentration											
	NHANES 1999–2000						NHANES 2009–2010					
Characteristics	**1 (*n* = 292)**	**2 (*n* = 295)**	**3 (*n* = 263)**	**4 (*n* = 260)**	**5 (*n* = 273)**	***P*-trend[2]**	**1 (*n* = 403)**	**2 (*n* = 428)**	**3 (*n* = 416)**	**4 (*n* = 450)**	**5 (*n* = 458)**	***P*-trend[2]**
Plasma TFAs, μmol/L	46.6 (11.0–55.6)	64.9 (55.7–72.6)	80.6 (72.7–89.9)	99.4 (90.0–117)	143 (117–596)		21.1 (7.3–25.4)	29.5 (25.5–33.3)	37.0 (33.4–41.2)	46.8 (41.3–55.1)	68.0 (55.2–307)	
Age, y	43.5 ± 1.05[3]	45.5 ± 0.94	43.7 ± 1.75	45.0 ± 1.73	47.9 ± 0.61	0.029	43.9 ± 0.95	45.0 ± 0.87	46.8 ± 0.90	48.3 6 0.77	52.7 ± 1.22	<0.001
Sex, %												
Male	61.7	49.3	43.6	42.9	52.5	0.17	53.5	47.6	50.2	48.0	47.8	0.20
Female	38.3	50.7	56.4	57.2	47.5	0.17	46.5	52.4	49.8	52.0	52.2	0.20
Race/ethnicity, %												
Non-Hispanic white	58.6	71.0	80.2	79.1	85.5	0.003	59.7	65.9	71.9	72.5	78.6	<0.001
Non-Hispanic black	12.6	9.2	8.9	6.7	4.7	0.042	14.6	12.9	11.8	9.4	5.4	<0.001
Mexican American	8.3	6.8	5.5	5.8	5.2	0.20	5.8	8.8	7.4	10.1	10.9	0.18
Other	20.6	13.1	5.5	8.5	4.6	0.043	19.9	12.4	8.9	8.0	5.1	0.002
Educational attainment, %												
0–11 y	24.5	28.4	15.5	22.7	19.8	0.17	14.8	15.5	14.4	21.1	26.7	<0.001
12 y	19.9	22.0	30.1	34.6	31.0	0.10	14.5	20.6	23.3	27.2	27.8	<0.001
>12 y	55.6	49.6	54.5	42.7	49.2	0.23	70.8	63.9	62.3	51.7	45.5	<0.001
Smoking status, %												
Current	25.9	23.5	26.1	23.4	27.1	0.86	16.5	16.8	20.4	22.0	20.4	0.27
Former	27.3	29.3	24.1	28.4	31.9	0.62	26.0	26.8	20.2	25.6	27.9	0.77
Never	46.8	47.2	49.9	48.2	40.9	0.56	57.6	56.4	59.5	52.4	51.8	0.11
BMI, kg/m^2	26.6 6 0.40	27.0 6 0.46	27.1 6 0.37	29.0 ± 0.36	29.3 ± 0.59	<0.001	26.7 ± 0.38	27.6 ± 0.44	29.5 ± 0.33	29.9 ± 0.49	30.5 ± 0.33	<0.001
HEI-2010 score	50.3 6 1.26	47.0 6 1.42	45.7 6 1.97	42.8 ± 1.41	42.0 ± 0.99	<0.001	55.1 ± 1.32	49.4 ± 0.73	47.3 ± 0.46	46.8 ± 0.62	46.1 ± 0.86	<0.001
Subgroup of plasma TFAs, μmol/L												

Characteristics	Quintile of plasma TFA concentration											
	NHANES 1999–2000						NHANES 2009–2010					
	1 (*n* = 292)	2 (*n* = 295)	3 (*n* = 263)	4 (*n* = 260)	5 (*n* = 273)	*P*-trend[2]	1 (*n* = 403)	2 (*n* = 428)	3 (*n* = 416)	4 (*n* = 450)	5 (*n* = 458)	*P*-trend[2]
Vaccenic (18:1n–7t)	21.1 (4.5–26.0)	30.6 (26.1–34.1)	38.2 (34.2–42.0)	46.6 (42.1–53.4)	64.2 (53.5–313)		9.5 (2.9–12.1)	14.3 (12.2–16.0)	17.8 (16.1–20.0)	23.0 (20.1–26.5)	33.5 (26.6–161)	
Elaidic (18:1n–9t)	18.0 (4.5–21.7)	25.4 (21.8–28.3)	32.3 (28.4–36.9)	41.5 (37.0–48.3)	59.8 (48.4–238)		6.9 (2.7–8.5)	10.1 (8.6–11.4)	13.0 (11.5–15.0)	17.2 (15.1–20.5)	26.8 (20.6–127)	
Palmitelaidic (16:1n–7t)	3.9 (1.1–4.7)	5.5 (4.8–6.0)	6.7 (6.1–7.4)	8.4 (7.5–9.6)	11.7 (9.7–33.1)		2.2 (0.9–2.6)	3.1 (2.7–3.4)	3.8 (3.5–4.2)	4.9 (4.3–5.4)	6.7 (5.5–33.1)	
Linoelaidic (18:2n–6t,9t)	1.5 (0.6–1.8)	2.2 (1.9–2.3)	2.7 (2.4–3.0)	3.6 (3.1–3.9)	5.1 (4.0–13.1)		0.9 (0.4–1.0)	1.2 (1.1–1.3)	1.5 (1.4–1.6)	2.0 (1.8–2.2)	2.8 (2.3–15.1)	

[1] Values are medians (ranges) unless otherwise indicated. HEI-2010, 2010 Healthy Eating Index; TFA, *trans*-fatty acid.

[2] *P* values are presented for the linear difference across quintiles of plasma TFA concentration. All tests were 2-tailed and based on a *t* test.

[3] Mean ± SE (all such values).

TABLE 2

Serum lipid and lipoprotein concentrations among participants aged ≥20 y by quintiles of plasma TFA concentration: NHANES 1999–2000 and 2009–2010[1]

	Quintile of plasma TFA concentration							
	NHANES 1999–2000				NHANES 2009–2010			
Lipid profiles	**1 (*n* = 292)**	**3 (*n* = 263)**	**5 (*n* = 273)**	***P*-trend[2]**	**1 (*n* = 403)**	**3 (*n* = 416)**	**5 (*n* = 458)**	***P*-trend[2]**
Plasma TFAs, μmol/L	46.6 (11.0–55.6)	80.6 (72.7–89.9)	143 (117–596)		21.1 (7.3–25.4)	37.0 (33.4–41.2)	68.0 (55.2–307)	
TC, mg/dL								
Model 1[3]	191 (186, 197)	200 (197, 203)	222 (215, 229)	<0.001	175 (170, 180)	198 (193, 204)	215 (208, 221)	<0.001
Model 2[4]	189 (184, 195)	200 (197, 202)	223 (215, 230)	<0.001	174.7 (170, 180)	198 (194, 202)	217 (212, 222)	<0.001
LDL-C, mg/dL								
Model 1[3]	117 (112, 123)	125 (122, 128)	136 (131, 141)	<0.001	100 (96, 105)	120 (116, 125)	129 (123, 134)	<0.001
Model 2[4]	118 (112, 123)	125 (122, 128)	135 (130, 141)	<0.001	102 (97, 107)	119 (116, 123)	129 (125, 133)	<0.001
HDL-C, mg/dL								
Model 1[3]	55.4 (53.4, 57.4)	49.8 (49.8, 51.4)	42.9 (41.1, 44.4)	<0.001	59.2 (57.7, 60.8)	54.1 (51.9, 56.3)	44.9 (43.6, 46.2)	<0.001
Model 2[4]	53.5 (51.4, 55.6)	49.2 (47.7, 50.8)	44.7 (43.1, 46.3)	<0.001	56.7 (54.8, 58.4)	54.4 (52.8, 56.0)	48.0 (46.4, 49.6)	<0.001
TGs,[5] mg/dL								
Model 1[3]	85.9 (82.9, 89.0)	114 (110, 118)	201 (185, 216)	<0.001	73.6 (69.8, 77.0)	107 (102, 111)	180 (173, 189)	<0.001
Model 2[4]	85.5 (83.0, 88.0)	117 (112, 123)	198 (185, 212)	<0.001	74.2 (70.4, 78.3)	108 (103, 113)	175 (168, 183)	<0.001
TC:HDL-C								
Model 1[3]	3.7 (3.5, 3.8)	4.3 (4.2, 4.4)	5.5 (5.3, 5.7)	<0.001	3.1 (3.0, 3.2)	4.0 (3.8, 4.1)	5.2 (5.0, 5.3)	<0.001
Model 2[4]	3.8 (3.7, 3.9)	4.3 (4.2, 4.5)	5.4 (5.2, 5.6)	<0.001	3.3 (3.1, 3.5)	3.9 (3.8, 4.1)	5.0 (4.8, 5.2)	<0.001

[1] Values are medians (ranges) for plasma TFA concentration or adjusted means (95% CIs). HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; TC, total cholesterol; TFA, *trans*-fatty acid.

[2] *P* values are presented for the linear difference across quintiles of plasma TFA concentration. All tests were 2-tailed and based on the Wald *F* test.

[3] Model 1 adjusted for age, sex, race/ethnicity, and total calorie intake.

[4] Model 2 adjusted for variables as in model 1 and additionally adjusted for educational attainment, smoking status, alcohol consumption, physical activity level, statin use, diabetes status, Healthy Eating Index-2010, BMI, total PUFAs, total saturated fat, total dietary TFAs, and TC intakes.

[5] TG concentrations were log transformed and are presented as geometric means.

TABLE 3

Prevalence of different categories of serum lipid and lipoprotein concentrations among participants aged >20 y by quintiles of plasma TFA concentration: NHANES 1999–2000 and 2009–2010[1]

	Quintile of plasma TFA concentration									
	NHANES 1999–2000					NHANES 2009–2010				
Lipid profiles	**Participants, *n***	**1**	**3**	**5**	***P*-trend[2]**	**Participants, *n***	**1**	**3**	**5**	***P*-trend[2]**
Plasma TFAs, μmol/L		46.6 (11.0–55.6)	80.6 (72.7–89.9)	143 (117–596)			21.1 (7.3–25.4)	37.0 (33.4–41.2)	68.0 (55.2–307)	
TC, mg/dL										
<200	651	62.0	54.4	30.4	<0.001	1223	78.7	55.6	39.6	<0.001
200–239	496	27.6	34.5	39.4	0.10	646	18.1	30.1	32.0	<0.001
≥240	241	10.4	11.2	30.2	0.001	301	3.2	14.3	28.3	<0.001
LDL-C, mg/dL										
<100	291	32.3	17.3	20.4	0.011	729	54.8	29.8	24.9	<0.001
100–129	476	35.0	44.0	22.7	0.06	698	29.0	35.7	27.0	<0.001
130–159	369	21.4	26.7	31.3	0.32	468	12.8	24.8	27.1	<0.001
160–189	162	7.5	10.2	18.9	<0.001	179	2.0	7.9	15.9	
≥190	56	3.9	1.8	6.7	0.56	59	1.4	2.4	5.2	<0.001
HDL-C, mg/dL										
<40	352	19.9	23.1	42.9	<0.001	423	10.0	20.7	35.8	<0.001
40–59	723	48.1	52.4	44.2	0.44	1065	47.3	47.6	50.0	
≥60	313	32.1	24.5	12.9	<0.001	682	42.6	31.7	14.2	<0.001
TGs, mg/dL										
<150	900	88.5	72.2	25.2	<0.001	1576	94.7	80.9	38.0	<0.001
150–199	226	7.2	19.5	26.0	<0.001	296	3.8	12.7	23.0	
200–400	262	4.3	8.3	48.7	<0.001	298	1.5	6.4	39.1	<0.001

[1] Values are medians (ranges) for plasma TFA concentration or prevalences (%) unless otherwise indicated. HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; TC, total cholesterol; TFA, *trans*-fatty acid.

[2] *P* values are presented for the difference across quintiles of plasma TFA concentration. All tests were 2-tailed and based on a *t* test.