The Relation between *Trans* Fatty Acid Levels and Increased Risk of Myocardial Infarction Does Not Hold at Lower Levels of *Trans* Fatty Acids in the Costa Rican Food Supply[1]

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Abstract

Data on the effects of recent industrial modifications that reduced the *trans* fatty acid (TFA) content in food supplies are scarce. In this study, incident cases ($n = 1797$) of a first nonfatal myocardial infarction (MI) were matched with population controls ($n = 1797$) for age, sex, and area of residence in Costa Rica. Odds ratio (OR) and 95% CI were calculated from conditional logistic regressions before and after a reduction of TFA in Costa Rican foods. Initially, the median quintiles of total adipose tissue TFA were 1.85, 2.47, 2.99, 3.58, and 4.40 g/100 g; total TFA was positively associated with increased MI risk after adjusting for established risk factors (OR by quintiles of total TFA: 1.00, 1.37, 1.91, 1.86, 3.28; P for trend $<$ 0.001). This association was mostly due to 18:2 *trans.* In contrast, after industrial modification, median quintiles of total adipose tissue TFA were 1.84, 2.26, 2.57, 2.88, and 3.42 g/100 g; the association with MI was no longer significant (OR by quintiles of total TFA: 1.00, 0.78, 1.03, 0.88, and 1.03; P for trend $= 0.65$). Adipose tissue 18:1 *trans* fatty acids were not associated with risk of MI before or after the modification. Although to date there are no TFA regulations in Costa Rica, it appears that indirect international influence has led to a TFA reduction in the food supply and, consequently, to a reduction in the risk of nonfatal MI. The public health sector of Costa Rica should regulate food labeling and content to ensure very low levels of TFA intake. J. Nutr. 136: 2887–2892, 2006.

Introduction

Intake of *trans* fatty acids (TFA) elevates LDL cholesterol, decreases levels of HDL cholesterol (1–3), and is suspected to play a role in various other cardiovascular risk factors, such as elevation of lipoprotein(a), activation of coagulant factor VI, activation of cholesterol ester transfer protein, and increase in plasma triglycerides, among others (4–9). Epidemiologic evidence shows consistent positive associations between total *trans* fat intake and myocardial infarction (MI) (10–15). These results have led to recommendations to decrease or eliminate TFA intake (16–18) and to the release of the U.S. Food and Drug Administration's mandatory TFA label in January 2006 (19).

In many developed countries, the industry has acted either voluntarily or by government decree upon these recommendations; as a result, the TFA content of foods has decreased (17,20–23). However, data are lacking on the effects that modifications of TFA content in the food supply may have had on cardiovascular outcomes. Only 1 published study has examined the effect of the elimination of TFA, specifically from margarines, in Australia (22). Previously, we showed that between the years 1998 and 2000 there was a reduction in the TFA content of most food products in Costa Rica but particularly in soybean oil (24). The current study uses case-control data to examine the risk of nonfatal acute MI before and after the TFA reduction in the food supply in Costa Rica.

Materials and Methods

Study population. The catchment area of the entire study consisted of the metropolitan area of Costa Rica, and covered a full range of socioeconomic levels, as well as urban and rural lifestyles. Eligible cases were men and women who were diagnosed as survivors of a first acute MI by 2 independent cardiologists. All cases met the World Health Organization's criteria for MI (25). The details of the case-control study were published elsewhere (26,27). Briefly, controls were randomly selected for each case, and matched for age (± 5 y), sex, and area of residence using the information available at the National Census and Statistics Bureau of Costa Rica. Because of the comprehensive social services provided in Costa Rica, all persons living in the catchment area had access to medical care without regard to income. Therefore, control subjects came from the source population that gave rise to the cases and were unlikely to have undiagnosed cardiovascular disease as the result of poor access to medical care. Field-workers also carried out daily visits to the 6 hospitals for recruitment of cases to achieve 100% ascertainment.

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Cases were ineligible if they *1*) died during hospitalization, *2*) were older than 75 y of age on the day of their first MI, *3*) were physically or mentally unable to answer the questionnaire, and *4*) had a previous hospital admission related to cardiovascular disease.

Control subjects were ineligible if they had ever had a MI or if they were physically or mentally unable to answer the questionnaires. All subjects were visited at their homes for the collection of dietary and health information, anthropometric measurements, and biological specimens between the years of 1994 and 2004. All subjects gave informed consent on documents approved by the Human Subjects Committee of the Harvard School of Public Health and the University of Costa Rica. The study was approved by the Ethics Committee of each institution. Participation was 97% for cases and 88% for controls.

Data collection. Trained personnel visited the subjects at their homes for data collection. Subjects provided information on socioeconomic, demographic, and health characteristics during an interview. A subcutaneous adipose tissue biopsy was collected from the upper buttock, and fatty acid samples and analyses were carried out using gas-liquid chromatography as described elsewhere (27,28). Self-reported diabetes and hypertension were validated using the recommended definitions by the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus and the Third Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (29,30).

Anthropometric measures were taken during home visits. Subjects were also asked about the mean frequency and time spent on several occupational and leisure-time activities during the last year. Energy expenditure was calculated for each activity as the product of frequency (times per week), duration (hours per occasion), and intensity (METS, or metabolic equivalents). Validation studies and details are published elsewhere (31).

Dietary-intake data were collected using a food frequency questionnaire (FFQ) that was developed and validated specifically to assess fatty acid intake among the Costa Rican population (32–33). The instrument also inquired about type of fat most frequently used for home cooking or frying, which was confirmed by visual identification at the subject's home. The fatty acid composition of all foods and oils commonly consumed in Costa Rica was assessed using the same methodology for biological samples (24). These analyses were incorporated into the nutrient database for the assessment of fatty acid intake.

Statistical analysis. Statistical Analysis Systems software, version 8.00 (SAS) was used for analyses. Variables were checked for outliers and normality and, where necessary, transformed using natural logarithm or square-root transformation. Individuals with missing values for physical activity, cigarette smoking, self-reported history of hypertension and diabetes, and subcutaneous adipose tissue values, were deleted. Of 3770 subjects that were recruited between 1994 and 2004, the final sample size consisted of 1797 case-control pairs, of which 26% were female.

Nutrient intakes were adjusted for total energy intake using regression methods (34). The significance of differences in the distribution of categorical variables by case-control status was tested using McNemar's test for changes in prevalence; continuous variables were tested by the paired two-tailed *t* test, if normally distributed, or by the Wilcoxon's Signed Rank test if not normally distributed. The *trans* fatty acids in the models were defined as: 18:1 = 18:1 (n-7*t*) + 18:1 (n-9*t*) + 18:1 (n-12*t*); 18:2 = 18:2 (n-6*tt*) + 18:2 (n-6*ct*) + 18:2 (n-6*tc*). Subjects were divided into quintiles and the median value for each quintile was assigned. Tests for trends were performed across quintiles using the median value for each of the quintiles modeled as a continuous variable. Odds ratios (OR) and 95% CI of the top quintiles relative to the lowest quintile of total or each adipose tissue TFA were estimated using conditional logistic regression adjusting for matching factors (age, gender, and area of residence) and other potential confounders (adipose tissue α-linolenic acid, vitamin E intake, saturated fat intake, alcohol intake, total energy intake, physical activity, cigarette smoking, history of hypertension and diabetes, and income). We performed stratified analyses by 2-y periods: *1*) before the industrial modification that decreased TFA content (1994–1999), and *2*) after industrial modification (2000–2003). Tests for a trend in soybean oil users vs. nonusers were also performed across year categories using the median value in adipose tissue *trans* for each year as a continuous variable (Fig. 1). Differences were considered significant at $P < 0.05$.

Results

Cases had a larger waist-to-hip ratio ($P < 0.05$) and a higher prevalence of diabetes, hypertension, and smoking ($P < 0.05$) than controls between both 1994–1999 and 2000–2003 (**Table 1**).

The distribution of potential confounders by quintiles of total adipose tissue *trans* fat is shown in **Table 2**, before and after the industrial modification of TFA. Positive associations were found for α-linolenic acid, linoleic acid, income, multivitamin use, and intake of vitamin E. Waist-to-hip ratio, physical activity, intake of alcohol, saturated fat and fiber, total energy intake, smoking status, and history of diabetes were negatively associated.

The median values for quintiles of total *trans* (**Table 3**) 18:1 (**Table 4**) and 18:2 (**Table 5**) *trans*-fatty acids in adipose tissue were higher in the years before 2000 than the period between 2000 and 2003. In the earlier years, before the industrial modification, total TFA content in adipose tissue was associated with increased risk of MI after adjusting for age, residence, sex, income, history of diabetes, history of hypertension, physical activity, smoking, alcohol intake, adipose tissue α-linolenic acid, intake of vitamin E, saturated fat, and energy. However, in the second-year period (2000–2003) this association was no longer significant.

Adipose tissue 18:1 *trans* fatty acid was not associated with risk of MI in the years before or after 2000 (Table 4). Adjustment for confounders, including adipose tissue α-linolenic acid, intake of vitamin E, saturated fat, and total energy, did not render this association significant.

Adipose tissue 18:2 *trans* fatty acid was associated with risk of MI ($P < 0.001$). Adjusting for dietary variables strengthened this association, mainly due to controlling for adipose tissue α-linolenic acid. However, the association between 18:2 *trans* fatty acid and MI was not significant during the time period between 2000 and 2003, even after adjusting for important confounding variables. For example, in the years before 2000, subjects in the highest quintile showed a higher risk of MI than subjects in the lowest quintile (median of highest quintile before 2000 was 2.02 g/100 g; OR of 4.76; 95% CI: 2.24, 10.11), but the risk of MI for subjects in the highest quintile during the years 2000 and 2003 was reduced and not significant (median of highest quintile for 2000–2003 was 1.40 g/100 g; OR of 1.15; 95% CI: 0.80, 1.64) (Table 5).

The reduction of the TFA content in the food supply was reflected in a decrease of total adipose tissue TFA among soybean

TABLE 1 General characteristics of Costa Rican adult survivors of myocardial infarction and population-based matched controls[1]

	1994–1999		2000–2003	
	Controls, $n = 477$	Cases, $n = 477$	Controls, $n = 1320$	Cases, $n = 1320$
Age, *y*	57 ± 11	57 ± 10	59 ± 11	59 ± 11
Gender, *% women*	26	26	27	27
Waist-to-hip ratio	0.93 ± 0.07	0.95 ± 0.07*	0.95 ± 0.07	0.97 ± 0.07*
Physical activity, *METS*	1.48 ± 0.77	1.42 ± 0.73	1.57 ± 0.60	1.53 ± 0.65
Income, *$/mo*	572 ± 487	464 ± 438*	580 ± 398	521 ± 375*
Diabetes, *%*	12	24*	16	25*
Hypertension, *%*	27	44*	31	38*
Current smokers,[2] *%*	27	43*	19	38*
Multivitamin users,[3] *%*	10.7	7.9*	10.0	8.2

[1] Values are means ± SD or percentages. *Different from controls, $P < 0.05$.
[2] Smokes more than 1 cigarette/d.
[3] Includes vitamin E supplement users.

TABLE 2 Distribution of dietary and personal characteristics of Costa Rican population-based controls by adipose tissue *trans* fatty acids[1]

	Quintiles 1, 3, and 5 of total *trans* fat in adipose tissue, *median, g/100 g*					
	1994–1999, $n = 477$			2000–2003, $n = 1320$		
	1 (1.85)	3 (2.99)	5 (4.40)	1 (1.84)	3 (2.57)	5 (3.42)
Adipose tissue fatty acid, *g/100 g*						
18:1 *Trans* fatty acids	0.94	1.67	2.55*	0.86	1.32	2.00†
18:2 *Trans* fatty acids	0.79	1.23	1.94*	0.78	1.07	1.35†
α-Linolenic acid	0.43	0.50	0.66*	0.57	0.72	0.74†
Linoleic acid	10.9	12.4	15.9*	14.2	17.0	17.0†
Total long chain (n-3)	0.42	0.41	0.40	0.37	0.36	0.34†
Waist-to-hip ratio	0.95	0.93	0.91*	0.97	0.96	0.94†
Income, *\$/mo*	396	623	688*	485	609	599†
Physical activity, *METS*	1.65	1.42	1.33*	1.59	1.60	1.51
Age, *y*	58	56	55	58	58	58
Diabetes, %	12.0	9.6	6.1	19.3	18.6	12.6†
Hypertension, %	39	27	23	31	29	27
Current smokers, %	32	19	23	27	17	14†
Multivitamin users,[2]%	2.1	7.5	9.1	3.0	5.8	9.4†
Daily Intake						
Total energy, *kJ/d*	2393	2476	2327	2511	2391	2347†
Saturated fat, % *energy*	13	12	11*	12	11	12
Alcohol, *g/d*	11.1	5.5	5.2*	9.3	4.2	3.1†
Vitamin E, *mg/d*	10.5	16.2	20.8*	10.9	16.8	20.1†
Folate, *μg/d*	326	343	338	473	470	462
Fiber, *g/d*	23.7	23.8	23.7	25.2	24.4	23.9†

[1] Values are means or percentages. Some of the characteristics that can potentially bias the results were controlled for statistically in subsequent analyses. *P for trend < 0.05, 1994–1999. †P for trend < 0.05, 2000–2003.
[2] Includes vitamin E supplement users.

oil users over time (P for trend < 0.001) (**Fig. 1**). The adipose tissue TFA level was stable over time among soybean oil nonusers. In contrast, the level of α-linolenic acid in adipose tissue increased among soybean oil users over time, from 0.59 ± 0.15 to 0.88 ± 0.23 g/100 g fat (P for trend < 0.001, data not shown). Adjustment for other dietary variables such as fiber, folate, dietary cholesterol, protein, fish, dairy or margarine intake, and other potential confounders, such as education, weight, height, waist-to-hip ratio, and other fatty acids in adipose tissue did not change results.

Discussion

This study assessed the risk of acute nonfatal MI in Costa Rican adults in 2 consecutive time periods: before and after an industrial modification that reduced TFA in the food supply of Costa Rica. Intakes and adipose tissue levels of total, 18:2, and 18:1 TFA decreased for the entire study population; a significant trend was apparent among soybean oil users. Between 1994 and 1999, high levels of 18:2 TFA in adipose tissue were highly associated with an increased risk of MI; however, in the

TABLE 3 Odds ratios (OR) and 95% CI of myocardial infarction by quintiles of adipose tissue total *trans* fatty acid levels in the entire population[1]

	Quintiles of adipose tissue total *trans* fatty acid (median, g/100 g)					
OR	1 (1.85)	2 (2.47)	3 (2.99)	4 (3.58)	5 (4.40)	*P*-value
1994–1999, $n = 954$						
Age-, sex-, and residence-adjusted	1.00	0.97 (0.64, 1.47)	1.01 (0.66, 1.53)	0.99 (0.66, 1.52)	0.90 (0.59, 1.39)	0.70
Multivariate[2]	1.00	1.26 (0.76, 2.08)	1.70 (1.01, 2.85)	1.34 (0.81, 2.24)	1.65 (0.95, 2.87)	0.10
Multivariate[3]	1.00	1.37 (0.80, 2.35)	1.91 (1.08, 3.37)	1.86 (1.04, 3.32)	3.28 (1.68, 6.42)	<0.001
	Quintiles of adipose tissue total *trans* fatty acid (median, g/100 g)					
	1 (1.84)	2 (2.26)	3 (2.57)	4 (2.88)	5 (3.42)	
2000–2003, $n = 2638$						
Age-, sex-, and residence-adjusted	1.00	0.71 (0.55, 0.92)	0.81 (0.63, 1.03)	0.70 (0.55, 0.90)	0.69 (0.53, 0.89)	<0.001
Multivariate[2]	1.00	0.73 (0.56, 0.97)	0.95 (0.72, 1.36)	0.78 (0.59, 1.04)	0.89 (0.67, 1.20)	0.59
Multivariate[3]	1.00	0.78 (0.58, 1.04)	1.03 (0.80, 1.43)	0.88 (0.65, 1.18)	1.03 (0.75, 1.42)	0.65

[1] Values are OR and 95% CI from conditional logistic regression models.
[2] Adjusted for income, history of diabetes, history of hypertension, physical activity, smoking status, and alcohol intake.
[3] Further adjusted for adipose tissue α-linolenic acid, intake of vitamin E, saturated fat, and total energy.

TABLE 4 Odds ratios (OR) and 95% CI of myocardial infarction by quintiles of adipose tissue 18:1 *trans* fatty acid levels in the entire population[1]

OR	Quintiles of adipose tissue 18:1 *trans* fatty acid (median, g/100 g)					
	1 (0.93)	2 (1.30)	3 (1.61)	4 (1.96)	5 (2.54)	*P*-value
1994–1999, $n = 954$						
Age-, sex-, and residence-adjusted	1.00	1.25 (0.82, 1.90)	1.14 (0.74, 1.77)	1.05 (0.69, 1.59)	0.93 (0.61, 1.42)	0.43
Multivariate[2]	1.00	1.53 (0.94, 2.52)	1.55 (0.92, 2.64)	1.74 (1.03, 2.92)	1.23 (0.72, 2.10)	0.60
Multivariate[3]	1.00	1.84 (1.09, 3.11)	1.54 (0.87, 2.71)	2.13 (1.21, 3.74)	1.75 (0.97, 3.15)	0.12
	Quintiles of adipose tissue 18:1 *trans* fatty acid (median, g/100 g)					
	1 (0.85)	2 (1.10)	3 (1.29)	4 (1.52)	5 (1.94)	
2000–2003, $n = 2638$						
Age-, sex-, and residence-adjusted	1.00	0.87 (0.68, 1.11)	0.81 (0.63, 1.03)	0.78 (0.61, 0.99)	0.79 (0.61, 1.02)	0.06
Multivariate[2]	1.00	0.90 (0.69, 1.17)	0.86 (0.66, 1.14)	0.90 (0.68, 1.20)	0.95 (0.71, 1.27)	0.83
Multivariate[3]	1.00	0.94 (0.71, 1.24)	0.92 (0.69, 1.23)	0.97 (0.72, 1.30)	1.02 (0.75, 1.37)	0.80

[1] Values are OR and 95% CI from conditional logistic regression models.
[2] Adjusted for income, history of diabetes, history of hypertension, physical activity, smoking status, and alcohol intake.
[3] Further adjusted for adipose tissue α-linolenic acid, intake of vitamin E, saturated fat, and total energy.

following years this association was no longer significant at any level of total, 18:2, or 18:1 TFA.

Previously, we showed an association between increased levels of 18:2 TFA in adipose tissue and an increased risk of MI (27). Our current findings for the period of 1994–1999 are consistent with the previous study. Prospective studies that have examined the association between cardiovascular disease and TFA intake have also found a positive association between high TFA intake and risk of MI (10–15), where mean intakes range from 1.3 g/d to 1.69 g/d in the lowest quintile, to 5.6 g/d to 6.51 g/d in the highest quintiles (15,35). Comparatively, in our current study, the general median intake of total TFA between 1994 and 1999 was 4.1 g/d.

Some studies examining the association between serum lipids and TFA intake, specifically 18:1 *trans* isomer, failed to find a positive association (1,36,37). Interestingly, these studies also reported relatively low intakes (~2 g/d) of TFA in their population (1,38), compared with the studies in Costa Rica and to other studies in the U.S. (~4 g/d) (28,39,40). The decrease in total TFA intake in the later years (to 2.9 g/d, and even lower, to 2.4 g/d among nonsoybean oil users) and the subsequent lower levels of *trans* in adipose tissue, may offer some insight to these apparent discrepancies. Consistent with data of the before-mentioned European studies, we found no association with MI at these lower levels.

The unexpected reduction in TFA content in the food supply of Costa Rica (24) is consistent with our findings of lower TFA intake, particularly among soybean oil consumers, and lower adipose tissue total *trans*, as well as 18:2, and 18:1 TFA. Even though our findings reveal dramatic reductions of TFA among soybean oil users, the benefits of this reduction are likely to be reflected in the general Costa Rican population, because, apart from home cooking, soybean oil is also used in the elaboration of other goods such as canned tuna, mayonnaise, some margarines, and baked and fried prepackaged snacks, among others (24).

The controversy about the differential effects of TFA persists. In Costa Rica, we found an association with 18:2, but not 18:1, *trans* isomer. Interestingly, in Costa Rica before the industrial modification, levels of 18:2 TFA in adipose tissue were higher than in other European countries and the U.S., whereas levels of the 18:1 *trans* isomer remained relatively lower (27). The fact that adipose tissue reflected the low intake of 18:1 TFA in the Costa Rican population may have been why we failed to find an association of MI with 18:1 TFA. The major sources of 18:1 *trans* in Costa Rica are a mixture of vegetable oils and animal fats, whereas 18:2 *trans* are concentrated mainly in partially

TABLE 5 Odds ratios (OR) and 95% CI of myocardial infarction by quintiles of adipose tissue 18:2 *trans* fatty acid levels in the entire population[1]

OR	Quintiles of adipose tissue 18:2 *trans* fatty acid (median, g/100 g)					
	1 (0.75)	2 (0.98)	3 (1.20)	4 (1.50)	5 (2.02)	*P*-value
1994–1999, $n = 954$						
Age-, sex-, and residence-adjusted	1.00	0.92 (0.61, 1.41)	1.02 (0.66, 1.60)	1.03 (0.67, 1.58)	0.90 (0.59, 1.39)	0.76
Multivariate[2]	1.00	0.95 (0.57, 1.57)	1.41 (0.8, 2.38)	1.50 (0.89, 2.53)	1.40 (0.81, 2.41)	0.10
Multivariate[3]	1.00	1.04 (0.60, 1.80)	2.16 (1.18, 3.96)	2.86 (1.50, 5.45)	4.76 (2.24, 10.11)	<0.001
	Quintiles of adipose tissue 18:2 *trans* fatty acid (median, g/100 g)					
	1 (0.74)	2 (0.91)	3 (1.05)	4 (1.19)	5 (1.40)	
2000–2003, $n = 2638$						
Age-, sex-, and residence-adjusted	1.00	0.82 (0.64, 1.04)	0.77 (0.60, 0.98)	0.76 (0.60, 0.98)	0.66 (0.51, 0.85)	0.002
Multivariate[2]	1.00	0.97 (0.74, 1.27)	0.95 (0.72, 1.24)	0.89 (0.67, 1.18)	0.85 (0.64, 1.14)	0.23
Multivariate[3]	1.00	1.09 (0.81, 1.46)	1.10 (0.81, 1.50)	1.05 (0.75, 1.46)	1.15 (0.80, 1.64)	0.56

[1] Values are OR and 95% CI from conditional logistic regression models.
[2] Adjusted for income, history of diabetes, history of hypertension, physical activity, smoking status, and alcohol intake.
[3] Further adjusted for adipose tissue α-linolenic acid, intake of vitamin E, saturated fat, and total energy.

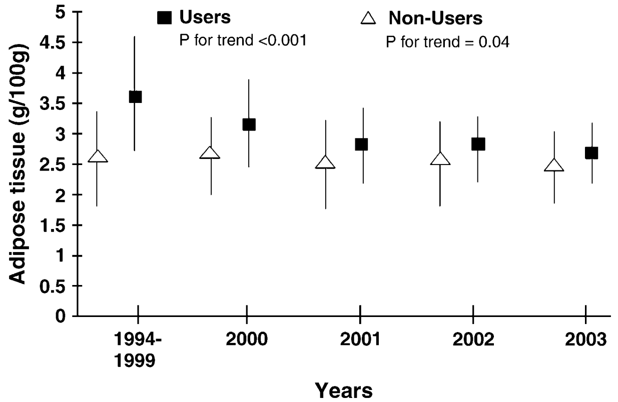

Figure 1 Adipose tissue total TFA concentrations in soybean oil users ($n = 918$) and nonusers ($n = 879$) in population-based controls. Values are means ± SD.

hydrogenated soybean oil (24), which is used by >50% of the population for cooking (41,42) and are higher in adipose tissue from Costa Ricans than in tissue from Europeans or U.S. citizens. The trends in nutrition transition in Costa Rica and Central America (43–45) and the results from the current study suggest that 18:2 TFA play a more important role in these regions than in Western countries, and that a better understanding of these *trans* fatty acids is warranted.

It is also important to note the important role of α-linolenic acid as a confounder of the relation of TFA intake and MI (15,26,41,46). In our study, the content of α-linolenic acid in adipose tissue of soybean oil users increased significantly after the reduction of TFA in soybean oil (24). In addition, our models show how, without adjustment for α-linolenic acid, TFA gives the impression of being somewhat protective against MI; after adjustment for α-linolenic acid this apparent relation disappeared and, particularly in the years before 2000, it became a significant risk factor. This suggests that the levels of α-linolenic acid in our study may compensate for the harmful effects of TFA. Moreover, Kabagambe et al. (41) previously showed that there was no significant difference between the effects of high *trans* soybean oil and highly saturated palm oil on MI; conversely, they found a protective effect of low *trans* soybean oil against MI compared with palm oil, possibly due to the beneficial effects of the increased levels of α-linolenic acid after a reduction in partial hydrogenation (41).

Our findings should be carefully interpreted so that they do not lead to assumptions of a safe recommendation for TFA daily intake. First, our findings of no association with MI and relatively lower levels of TFA are based on adipose tissue levels. The dose-response and metabolic lifetime between daily intake of TFA and accumulated *trans* in adipose tissue is not clear. The turnover of adipose tissue fatty acids is over 2 y; therefore, the lower levels observed in TFA in adipose tissue in the highest quintiles for the period 2000–2003 may be higher than expected, given the large decrease in *trans* in the food supply. Second, studies of the effects of differential TFA isomers on plasma lipids are scarce. Third, studies have not examined exhaustively the mechanisms through which different TFA isomers increase the risk of MI. We recommend that total TFA intake should be kept as close to zero as possible.

In summary, changes in the TFA content of the food supply were associated with decreased *trans* fatty acid intake and adipose tissue *trans* fatty acid levels among the Costa Rican population. At these lower levels of intake, *trans* fatty acids were not associated with MI risk.

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