Maternal *trans* fatty acid intake and fetal growth[1–3]

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ABSTRACT

Background: It is unclear from previous studies whether total or common subtypes of *trans* fatty acids are associated with fetal growth.

Objective: We examined associations of maternal *trans* fatty acid intake during pregnancy with fetal growth.

Design: We studied 1369 mother-child pairs participating in Project Viva—a prospective cohort study of pregnant women and their offspring. We assessed *trans* fatty acid consumption by using a validated semiquantitative food-frequency questionnaire in each of the first and second trimesters of pregnancy. We estimated fetal growth as the birth-weight-for-gestational-age (BW/GA) *z* value in infants born at term.

Results: We observed no associations of first-trimester *trans* fatty acid consumption with fetal growth. In the second trimester, the estimated mean (±SD) total *trans* fatty acid intake was 2.35 ± 1.07 g/d, of which 0.11 g was 16:1(n−7*t*), 1.78 g was 18:1 (n−9*t*), 0.13 g was 18:2(n−6*tt*), 0.33 g was 18:2(n−6*tc*), and 0.12 g was 18:2(n−6*ct*). The mean (±SD) BW/GA was 0.24 ± 0.95 *z* score units. Total *trans* fatty acid consumption during the second trimester was positively associated with the fetal growth *z* score (0.29 units; 95% CI: 0.07, 0.51 units) for each 1% increment in energy from *trans* fatty acids as a replacement for carbohydrates. The associations were limited to the *trans* fatty acids 16:1*t* (0.12 units; 95% CI: 0.02, 0.22 units) and 18:2*tc* (0.53 units; 95% CI: 0.09, 0.96 units).

Conclusion: A higher maternal intake of *trans* fatty acids, especially 16:1*t* and 18:2*tc,* during the second trimester of pregnancy was associated with greater fetal growth. *Am J Clin Nutr* 2011;94:1241–7.

INTRODUCTION

Both higher and lower fetal growth, estimated as birth weight adjusted for length of gestation, are associated with adverse metabolism, diabetes, and cardiovascular disease in adulthood (1–4). Maternal nutrition affects fetal development, and one important dietary determinant of fetal growth may be TFAs[4].

TFAs occur naturally in ruminant sources (ie, milk and meat) and from the industrial partial hydrogenation of vegetable oils. Naturally occurring TFAs usually account for ~5% of the fat content of milk or meat (5). Whereas a reduction in industrial TFAs has occurred in North America, many foods still contain TFAs, which can account for up to 30% of the fats in frying oils and shortenings (6, 7). Bakery goods and fast foods are the predominant sources of TFAs in the diets of pregnant women (8).

TFAs are transferred to the fetus through the placenta (9, 10). Studies examining umbilical cord plasma cholesterol esters and circulating lipids in newborns have found an inverse association of TFAs with DHA and arachidonic acid—2 PUFAs that may influence fetal growth (9, 10). TFAs may block the transfer of PUFAs to the fetus or interfere with PUFA metabolism (9, 10). TFAs may also prevent the desaturation of α-linolenic acid to DHA and of linoleic acid to arachidonic acid, thereby influencing fetal growth (11).

Despite the possible effects of TFAs on fetal growth, few studies have examined this association. One study of 84 Canadian pregnant women found that naturally occurring and industrially produced TFAs were inversely associated with length of gestation (11). This study did not find an association with birth weight, but the analysis may have been underpowered. Fetal growth, which takes into account the length of gestation, was not examined. A study of 782 mother-infant pairs from a Dutch birth cohort that included adjustment for gestational age found no association of the TFA isomer 18:1*t* in maternal plasma phospholipids with birth weight (12). In the same cohort, concentrations of 18:1*t* in the umbilical cord erythrocyte phospholipids were inversely associated with birth weight after adjustment for confounders (13). However, the authors found no associations between birth weight and other umbilical cord measurements (13). Last, a study in the Netherlands (n = 4389) found that, after full-adjustment, intake of 18:1(n−9*t*) was not significantly associated with fetal growth but concluded that the intake of 18:1(n−9*t*) may have been too low to find a meaningful association (14). It is therefore unclear whether intake of total TFAs or of individual isomers is associated with fetal growth. The purpose of this analysis was to examine the association between TFA consumption during pregnancy and fetal growth among infants born at term.

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[4] Abbreviations used: BW/GA, birth-weight-for-gestational age; FFQ, food-frequency questionnaire; LGA, large-for-gestational age; SGA, small-for-gestational age; TFA, *trans* fatty acid.

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SUBJECTS AND METHODS

Subjects

Participants were enrolled in Project Viva, a prospective observational cohort study of gestational diet, pregnancy outcomes, and maternal and child health. From 1999 to 2002, we recruited women in the Boston area attending their first prenatal visit at one of 8 urban and suburban obstetrical offices in a multispecialty group medical practice. Women were eligible to participate if they were able to complete interviews and study forms in English, attended an initial clinical visit before 22 wk of gestation, had a singleton pregnancy, and did not plan to move out of the study area before delivery. Detailed recruitment and retention information was reported previously (15, 16). Institutional review boards of participating institutions approved the study, and all participants provided written informed consent. All procedures were in accordance with ethical standards for human experimentation.

Of the 2128 women who delivered a live infant, 1543 (73%) completed an FFQ in both the first and second trimesters. For the current analysis, we excluded 86 women with a history of type 1 or type 2 diabetes or gestational diabetes and 88 women who gave birth to infants with a gestational age of <37 wk, which left 1369 participants available for inclusion. Modest differences in race-ethnicity, education, income, and BMI were observed between the 1369 women included in this study and the 759 women excluded from the Viva cohort for the analyses. The participants in this analysis had a higher proportion of white race-ethnicity (76% compared with 49%), college or graduate education (73% compared with 50%), annual household income >$70,000 (66% compared with 51%), and lower mean maternal prepregnancy BMI (in kg/m^2; 24.3 compared with 26.0) than did the Viva participants who were excluded.

Dietary assessment

The participants completed a self-administered semiquantitative FFQ during the first and second trimesters of pregnancy. The validity of the FFQ was previously assessed for TFAs in large cohort studies and within our pregnant population (17–19). A previous study in this cohort also found moderate correlations (r = 0.30) between total TFAs in maternal erythrocyte phospholipids and intake assessed by FFQ (20).

At the first prenatal visit, the FFQ assessed the woman's average frequency of consumption "during this pregnancy" (ie, since the last menstrual period) of ~140 specified foods. The FFQ also included questions regarding beverages and preparation methods, such as the types of fats or oils used for cooking or consumed as a spread or condiment. During the second-trimester visit (26–28 wk of gestation), participants filled out a similar FFQ that assessed diet "during the past 3 months." We used the Harvard nutrient composition database to calculate the intake of nutrients, which obtains information from USDA publications (National Nutrient Database for Standard Reference, release 16) as well as other current published sources and personal communications from manufacturers and laboratories (21). Values for TFAs are also updated every 4 y based on laboratory analyses of current brands of foods, conducted at the Harvard School of Public Health. To further refine the database, the Department of Nutrition at the Harvard School of Public Health performed additional biochemical analyses to determine the TFAs contents of foods commonly used in the local area.

Measurement of fetal growth

We collected data on infant birth weight (in g) from hospital medical records and determined the length of gestation (in d) by subtracting the date of the last menstrual period from the day that the infant was delivered. If the second-trimester ultrasound estimate differed by >10 d, the ultrasound was used to determine the gestational age. We then calculated the BW/GA z value (fetal growth) using US national reference data (22). We defined SGA and LGA infants as those below the 10th percentile and those equal to or greater than the 90th percentile, respectively.

Statistical analysis

We first performed bivariate analyses of maternal characteristics that were previously associated with fetal growth or birth weight in the medical literature. To calculate unadjusted P-trend values across quartiles, we used the Mantel-Haenszel chi-square test for categorical characteristics and linear regression for continuous characteristics.

We used multivariable linear regression to examine the association between TFA intake and fetal growth. We calculated all estimates as isocaloric replacement of carbohydrates for TFAs using nutrient-density models, which express energy from a macronutrient as a percentage of total energy intake (23). The coefficients in the models represent the substitution of TFAs for an equal amount of energy from carbohydrates, represented as a percentage of energy. Whereas food manufacturers typically replace TFAs with unsaturated fats, there is not one fat type commonly used for substitution (7); by selecting carbohydrates for the substitution models, the estimates were not dependent on the replacement fat type. Carbohydrates were also the most stable variable because they are typically the greatest source of energy in the diets of pregnant women (24–26).

We first examined TFA intake in quartiles and then as a continuous variable. We abbreviated the TFAs in the models as follows: 16:1t = 16:1(n−7t), 18:1 = 18:1(n−9t), 18:2tt = 18:2(n−6tt), 18:2ct = 18:2(n−6ct), 18:2tc = 18:2(n−6tc), and total TFAs = 16:1t + 18:1 + 18:2. We used multinomial logistic regression to calculate associations of TFA consumption with SGA and LGA, with appropriate for gestational age as the comparison. In secondary analyses we also examined the associations between fetal growth and the TFA subtypes in maternal erythrocyte phospholipids and with conjugated linoleic acids.

In our multivariable models, we adjusted for variables that were associated with either the outcome or the exposure in our data or that were found to be important confounders from the previous literature (16, 26–28). These variables included maternal age, race-ethnicity, education, household income, parity, prepregnancy BMI, smoking status during pregnancy, physical activity during the pregnancy, television viewing during the pregnancy, and intakes of fish and total energy. Whereas alcohol has been inversely associated with TFA intake in previous studies, we did not find alcohol to confound the relation of TFA intake with fetal growth, possibly because of the small percentage of women in the study consuming alcohol (13%) and the small quantity of alcohol consumed (mean: 0.94 servings/wk in consumers) (29, 30). Similarly, we did not find that fiber, linoleic

acid, and cholesterol intakes—previously associated with TFA consumption—were confounders in our study; therefore, we did not include them in the final models (29–31).

We analyzed the first and second trimester diets separately. Inclusion of maternal weight gain during pregnancy did not appreciably change the estimates of the association between TFA intake and fetal growth; thus, this covariate was not included in the final model. We performed all the analyses using SAS version 9.2 (SAS Institute Inc).

RESULTS

The characteristics of the 1369 pregnant women included in this study are shown in **Table 1**. Approximately 24% identified themselves as racial-ethnic minorities. The mean (±SD) age at enrollment was 32.4 ± 4.7 y, and prepregnancy BMI was 24.3 ± 5.0. Of the infants born at term, the mean (±SD) birth weight was 3559 ± 476 g, and the mean (±SD) length of gestation was 39.9 ± 1.2 wk; 4.9% of the infants were SGA and 14.2% were LGA. The mean (±SD) daily total TFA intakes were similar during the first and second trimesters of pregnancy: 2.19 ± 1.03 and 2.35 ± 1.07 g/d.

Total TFA intake was associated with some factors that are themselves associated with fetal growth; women with higher intakes of TFAs tended to be less educated, to have higher prepregnancy BMIs, and to watch more television (**Table 2**). The TFA intake was not associated with maternal age, parity, or income.

The unadjusted and adjusted associations of TFA intake, expressed as quartiles and as continuous variables, with fetal growth are shown in **Table 3**. In the unadjusted analyses, replacement of 1% of energy from carbohydrates with TFAs during the second trimester was associated with an increase in fetal growth of 0.31 z score units (95% CI: 0.09, 0.53). After adjustment for the covariates associated with fetal growth, the association was not materially changed (β = 0.29; 95% CI: 0.07, 0.51). Because of the small number of infants born LGA and SGA, there was insufficient power to detect a significantly decreased risk of SGA or increased risk of LGA (SGA OR: 0.47; 95% CI: 0.14, 1.54; LGA OR: 1.38; 95% CI: 0.67, 2.85). The first trimester total TFA intake was not associated with fetal growth after adjustment for covariates (β = 0.02; 95% CI: −0.20, 0.25).

In secondary analyses, we explored fetal growth by type of TFA intake during the second trimester (**Table 4**). The consumption of 16:1*t* TFAs from ruminant fats and 18:2*tc* TFAs from partially hydrogenated vegetables was directly associated with fetal growth. Adjustment for covariates associated with fetal growth strengthened these associations. For each additional 1% of energy from carbohydrates replaced with 16.1 TFA, the fetal growth *z* value was 0.12 units higher (95% CI: 0.02, 0.22). For each 0.1% of energy from carbohydrates replaced with 18:2*tc* TFA, the fetal growth *z* value was 0.53 units higher (95% CI: 0.09, 0.96). We also examined fetal growth by conjugated linoleic acid intake and by TFA subtypes in maternal erythrocyte phospholipids during the second trimester, and no significant associations were found (data not shown).

A major dietary source of 16:1*t* is dairy products. Previous investigators have found maternal prenatal milk intake to be directly associated with greater birth weight for gestational age and an increased risk of LGA (32). When we included a term for intake of dairy products, which contributed ~35% of the 16:1*t* TFA in the participants' diets, in the multivariate model, the association between 16:1*t* and fetal growth remained unchanged (0.13; 95% CI: 0.03, 0.23). The other main dietary contributors to 16:1*t* in the participants' diets were meat products, especially beef. The main food sources of 18:2*tc* in the participants' diets were baked goods and fried foods.

TABLE 1
Characteristics of 1369 participating mother-infant pairs in Project Viva[1]

Characteristic	Value
Mothers	
Age at enrollment [*n* (%)]	
15–24 y	85 (6.2)
25–29 y	278 (20.3)
30–34 y	602 (44.0)
35–39 y	353 (25.8)
40–44 y	51 (3.7)
Race-ethnicity [*n* (%)]	
White	1039 (75.9)
Black or African American	144 (10.5)
Hispanic or Latina	66 (4.8)
Other/more than one race	120 (8.8)
Education [*n* (%)]	
No college degree	376 (27.5)
College or graduate degree	993 (72.5)
Annual household income [*n* (%)]	
<$40,000	141 (10.3)
$40,000–$70,000	303 (22.1)
>$70,000	849 (62.0)
Missing/don't know	76 (5.6)
Marital status [*n* (%)]	
Married or cohabitating	1289 (94.2)
Divorced, separated, never married, other	79 (5.8)
Number of previous pregnancies [*n* (%)]	
0	679 (49.6)
≥1	690 (50.4)
Prepregnancy BMI (kg/m^2)	24.3 ± 5.0[2]
Second-trimester total energy (kcal)	2136 ± 628
Second-trimester fish intake (servings/wk)	1.58 ± 1.40
Second-trimester physical activity (h/wk)	7.1 ± 7.0
Second-trimester television viewing (h/wk)	11.3 ± 8.4
Children	
Birth weight (g)	3559 ± 476
Gestational age at birth (wk)	39.9 ± 1.2
Fetal growth *z* score	0.24 ± 0.95
BW/GA percentile [*n* (%)]	
SGA (<10th)	67 (4.9)
AGA (10th to <90th)	1108 (80.9)
LGA (≥90th)	194 (14.2)

[1] AGA, appropriate-for-gestational age; BW/GA, birth-weight-for-gestational age; LGA, large-for-gestational age; SGA, small-for-gestational age.
[2] Mean ± SD (all such values).

DISCUSSION

In this prospective study, we found that higher consumption of TFAs during the second trimester was associated with greater fetal growth. Adjustment for potential confounders resulted in no appreciable change in the strength of the association. We saw no evidence that TFA consumption during the first trimester was associated with fetal growth.

TABLE 2
Characteristics of 1369 mother-infant pairs in Project Viva according to maternal intake of total TFAs in the second trimester[1]

		Quartile of total TFA intake				
	Overall	1	2	3	4	*P*-trend[2]
Total TFA (g/d)	2.35 ± 1.07[3]	1.19 ± 0.30	1.91 ± 0.17	2.53 ± 0.19	3.76 ± 0.93	<0.0001
16:1*t*	0.11 ± 0.05	0.06 ± 0.02	0.09 ± 0.03	0.12 ± 0.03	0.15 ± 0.05	<0.0001
18:1	1.78 ± 0.82	0.89 ± 0.23	1.44 ± 0.14	1.91 ± 0.16	2.85 ± 0.74	<0.0001
18:2*tt*	0.13 ± 0.07	0.06 ± 0.02	0.104 ± 0.02	0.14 ± 0.02	0.22 ± 0.06	<0.0001
18:2*tc*	0.33 ± 0.15	0.17 ± 0.05	0.26 ± 0.04	0.35 ± 0.05	0.51 ± 0.13	<0.0001
18:2*ct*	0.12 ± 0.06	0.07 ± 0.03	0.10 ± 0.03	0.13 ± 0.033	0.18 ± 0.06	<0.0001
Age (y)	32.4 ± 4.7	32.6 ± 4.6	32.2 ± 4.4	32.4 ± 4.4	32.2 ± 5.2	0.45
Prepregnancy BMI (kg/m^2)	24.3 ± 5.0	23.6 ± 4.4	24.0 ± 4.9	24.4 ± 5.1	25.2 ± 5.4	<0.0001
Television viewing (h/wk)	11.3 ± 8.4	9.2 ± 7.2	11.2 ± 8.1	11.5 ± 7.0	13.2 ± 10.3	<0.0001
BW/GA *z* value[4]	0.24 ± 0.95	0.05 ± 0.89	0.25 ± 0.92	0.28 ± 0.93	0.36 ± 1.02	0.0001
≥College graduate (%)	72.5	74.5	77.2	74.7	63.7	0.001
White race-ethnicity (%)	75.9	65.7	78.7	82.6	76.6	0.0004

[1] BW/GA, birth-weight-for-gestational age; TFA, *trans* fatty acid.
[2] Based on Mantel-Haenszel chi-square test for categorical variables and linear regression for continuous variables.
[3] Mean ± SD (all such values).
[4] Calculated by using US national reference data (22).

The analyses examined the substitution of TFAs with carbohydrates; in a secondary analysis examining models substituting TFAs for MUFAs, PUFAs, or SFAs, the results did not change appreciably. Because the mean TFA intakes in the 2 trimesters were similar, differences in intake do not explain why the association is limited to the second trimester. It is possible that consumption of TFAs later in pregnancy has a greater effect on fetal growth. The placenta plays a more important role in transferring essential fatty acids from the mother to the fetus after 10 wk of gestation (33). Quantities of these fatty acids typically increase as the pregnancy progresses and, in particular, concentrations of DHA increase as the fetus develops (33, 34). Therefore, the trimester-specific role observed for TFAs in fetal development may be the result of interfering with DHA metabolism.

Intake of 2 TFAs, 16:1(n−7*t*) and 18:2(n−6*tc*), were directly associated with fetal growth. Dairy product consumption, a large source of 16:1*t* in the diet, did not appear to explain the association. Our findings agree with those of 2 studies in the Netherlands, which found no relation between 18:1*t* and fetal growth (12, 14), although one of the studies found reductions in fetal growth in the unadjusted analyses (14). Whereas another study using a Dutch birth cohort found an inverse association between birth weight and 18:1*t* in umbilical cord erythrocyte phospholipids, the study found no associations between birth weight and neonatal 18:1*t*

TABLE 3
Associations of total TFA intake, presented by quartile and as a continuous variable, with fetal growth (BW/GA *z* score), SGA, and LGA by trimester of intake in 1369 pregnant women participating in Project Viva[1]

	BW/GA *z* value[2]			SGA[3]			LGA[3]		
	n	Unadjusted	Adjusted[4]	*n*	Unadjusted	Adjusted[4]	*n*	Unadjusted	Adjusted[4]
First trimester									
Q1	342	0.0 (ref)	0.0 (ref)	14	1.0 (ref)	1.0 (ref)	36	1.0 (ref)	1.0 (ref)
Q2	342	−0.01 (−0.17, 0.14)	−0.03 (−0.18, 0.12)	20	1.73 (0.82, 3.64)	1.70 (0.77, 3.78)	52	1.44 (0.89, 2.33)	1.35 (0.81, 2.25)
Q3	343	0.10 (−0.06, 0.27)	0.07 (−0.09, 0.24)	16	1.46 (0.63, 3.37)	1.49 (0.61, 3.65)	56	1.51 (0.90, 2.53)	1.37 (0.79, 2.38)
Q4	342	0.06 (−0.12, 0.24)	0.01 (−0.18, 0.20)	17	1.50 (0.60, 3.74)	1.74 (0.65, 4.65)	50	1.30 (0.72, 2.33)	1.05 (0.55, 1.99)
Continuous	1369	0.06 (−0.15, 0.28)	0.02 (−0.20, 0.25)	67	1.28 (0.46, 3.55)	1.23 (0.41, 3.72)	194	1.65 (0.85, 3.18)	1.30 (0.62, 2.71)
Second trimester									
Q1	342	0.0 (ref)	0.0 (ref)	20	1.0 (ref)	1.0 (ref)	31	1.0 (ref)	1.0 (ref)
Q2	342	0.20 (0.05, 0.35)	0.17 (0.02, 0.32)	15	0.77 (0.37, 1.60)	0.79 (0.36, 1.75)	56	1.86 (1.13, 3.07)	1.70 (1.00, 2.87)
Q3	343	0.18 (0.01, 0.35)	0.10 (−0.07, 0.27)	19	0.99 (0.46, 2.14)	1.13 (0.49, 2.61)	62	2.08 (1.22, 3.57)	1.75 (0.99, 3.10)
Q4	342	0.27 (0.08, 0.45)	0.25 (0.06, 0.43)	13	0.58 (0.23, 1.44)	0.45 (0.16, 1.27)	45	1.36 (0.73, 2.52)	1.27 (0.66, 2.45)
Continuous	1369	0.31 (0.09, 0.53)	0.29 (0.07, 0.51)	67	0.53 (0.17, 1.62)	0.47 (0.14, 1.54)	194	1.47 (0.76, 2.85)	1.38 (0.67, 2.85)

[1] BW/GA, birth-weight-for-gestational age; LGA, large-for-gestational age; Q, quartile; ref, reference; SGA, small-for-gestational age; TFA, *trans* fatty acid. Values are based on ANOVA (Q) and linear regression (continuous variables) by using nutrient-density substitution models in which 1% of energy from carbohydrate was replaced with total TFAs. The nutrients were adjusted for total energy intake.
[2] Values are βs; 95% CIs in parentheses.
[3] Values are ORs; 95% CIs in parentheses.
[4] Adjusted for total energy intake, race, income, parity, education, smoking status, age, prepregnancy BMI, physical activity, television viewing, and fish consumption.

TABLE 4
Associations of second-trimester intake of TFA subtypes, by quartile and as a continuous variable, with fetal growth (BW/GA *z* score), SGA, and LGA in 1369 pregnant women participating in Project Viva[1]

	BW/GA *z* score[2]			SGA (n = 67)[3]			LGA (n = 194)[3]		
Nutrient quartile	n	Unadjusted	Adjusted[4]	n	Unadjusted	Adjusted[4]	n	Unadjusted	Adjusted[4]
16:1*t*[5]									
Q1	342	0.0 (ref)	0.0 (ref)	20	1.0 (ref)	1.0 (ref)	38	1.0 (ref)	1.0 (ref)
Q2	342	0.07 (−0.10, 0.23)	0.07 (−0.10, 0.24)	22	1.04 (0.48, 2.24)	0.93 (0.41, 2.12)	45	1.13 (0.66, 1.94)	1.14 (0.64, 2.03)
Q3	343	0.18 (−0.03, 0.38)	0.20 (−0.01, 0.40)	12	0.54 (0.20, 1.52)	0.43 (0.14, 1.29)	57	1.41 (0.74, 2.65)	1.53 (0.77, 3.02)
Q4	342	0.27 (0.00, 0.55)	0.34 (0.06, 0.61)	13	0.46 (0.11, 1.86)	0.32 (0.07, 1.48)	54	1.37 (0.58, 3.25)	1.68 (0.66, 4.24)
Continuous	1369	0.12 (0.02, 0.22)	0.12 (0.02, 0.22)	67	0.86 (0.53, 1.39)	0.85 (0.50, 1.44)	194	1.10 (0.81, 1.49)	1.11 (0.78, 1.56)
18:1[6]									
Q1	342	0.0 (ref)	0.0 (ref)	19	1.0 (ref)	1.0 (ref)	31	1.0 (ref)	1.0 (ref)
Q2	342	0.12 (−0.04, 0.29)	0.09 (−0.07, 0.26)	16	0.81 (0.37, 1.79)	0.77 (0.32, 1.85)	54	1.59 (0.94, 2.71)	1.48 (0.84, 2.60)
Q3	343	0.17 (−0.02, 0.37)	0.09 (−0.11, 0.30)	18	0.87 (0.33, 2.27)	0.89 (0.31, 2.58)	63	1.77 (0.96, 3.27)	1.43 (0.73, 2.78)
Q4	342	0.22 (−0.06, 0.50)	0.18 (−0.12, 0.47)	14	0.53 (0.13, 2.22)	0.36 (0.07, 1.92)	46	1.02 (0.42, 2.46)	0.88 (0.33, 2.34)
Continuous	1369	0.08 (0.01, 0.15)	0.01 (−0.06, 0.09)	67	0.66 (0.45, 0.96)	0.67 (0.44, 1.01)	194	1.06 (0.86, 1.32)	0.90 (0.71, 1.14)
18:2*tt*[5]									
Q1	342	0.0 (ref)	0.0 (ref)	16	1.0 (ref)	1.0 (ref)	34	1.0 (ref)	1.0 (ref)
Q2	342	−0.02 (−0.19, 0.15)	0.00 (−0.17, 0.18)	16	1.79 (0.72, 4.46)	1.51 (0.58, 3.94)	54	1.29 (0.76, 2.19)	1.45 (0.81, 2.58)
Q3	343	−0.10 (−0.30, 0.11)	−0.03 (−0.24, 0.18)	19	3.20 (1.03, 9.98)	2.53 (0.76, 8.36)	61	1.24 (0.67, 2.31)	1.44 (0.72, 2.90)
Q4	342	−0.24 (−0.53, 0.05)	−0.09 (−0.40, 0.22)	16	4.25 (0.85,21.26)	2.12 (0.36,12.38)	45	0.57 (0.23, 1.40)	0.76 (0.27, 2.12)
Continuous	1369	−0.18 (−0.28, −0.09)	−0.07 (−0.17, 0.03)	67	1.64 (0.99, 2.72)	1.32 (0.75, 2.31)	194	0.71 (0.53, 0.95)	0.88 (0.63, 1.23)
18:2*tc*[6]									
Q1	342	0.0 (ref)	0.0 (ref)	22	1.0 (ref)	1.0 (ref)	28	1.0 (ref)	1.0 (ref)
Q2	342	0.18 (0.01, 0.35)	0.19 (0.03, 0.36)	14	0.70 (0.32, 1.57)	0.70 (0.29, 1.71)	51	2.02 (1.14, 3.56)	2.10 (1.15, 3.85)
Q3	343	0.28 (0.07, 0.48)	0.31 (0.09, 0.52)	15	0.80 (0.30, 2.11)	0.76 (0.25, 2.33)	64	2.90 (1.45, 5.82)	3.07 (1.46, 6.42)
Q4	342	0.33 (0.04, 0.62)	0.40 (0.09, 0.70)	16	0.75 (0.20, 2.86)	0.58 (0.11, 3.04)	51	2.65 (1.01, 6.99)	3.01 (1.06, 8.56)
Continuous	1369	0.63 (0.21, 1.05)	0.53 (0.09, 0.96)	67	0.39 (0.05, 3.30)	0.73 (0.08, 6.89)	194	3.71 (1.01, 13.64)	3.69 (0.87,15.71)
18:2*ct*[5]									
Q1	342	0.0 (ref)	0.0 (ref)	17	1.0 (ref)	1.0 (ref)	33	1.0 (ref)	1.0 (ref)
Q2	342	0.12 (−0.04, 0.27)	0.06 (−0.09, 0.21)	21	1.51 (0.74, 3.10)	1.63 (0.73, 3.65)	52	1.71 (1.04, 2.82)	1.59 (0.93, 2.73)
Q3	343	0.15 (−0.01, 0.32)	0.06 (−0.11, 0.23)	12	0.83 (0.35, 2.00)	1.08 (0.42, 2.81)	55	1.89 (1.11, 3.23)	1.63 (0.90, 2.96)
Q4	342	0.23 (0.02, 0.43)	0.11 (−0.10, 0.32)	17	1.23 (0.45, 3.38)	1.58 (0.52, 4.81)	54	2.11 (1.11, 4.02)	1.83 (0.90, 3.71)
Continuous	1369	0.02 (−0.02, 0.07)	0.00 (−0.05, 0.04)	67	1.14 (0.94, 1.40)	1.25 (1.01, 1.56)	194	1.14 (1.00, 1.30)	1.11 (0.96, 1.28)

[1] BW/GA, birth-weight-for-gestational age; LGA, large-for-gestational age; Q, quartile; ref, reference; SGA, small-for-gestational age; TFA, *trans* fatty acid; 16:1*t*, 16:1(n−7*t*); 18:1, 18:1(n−9*t*); 18:2*tt*, 18:2(n−6*tt*); 18:2*ct*; 18:2(n−6*ct*); 18:2*tc*, 18:2(n−6*tc*). Values are based on ANOVA (Q) and linear regression (continuous variables) by using nutrient-density substitution models in which carbohydrate was replaced with TFA subtypes. The nutrients were adjusted for total energy intake.

[2] Values are βs; 95% CIs in parentheses.

[3] Values are ORs; 95% CIs in parentheses.

[4] Adjusted for race, income, parity, education, smoking status, age, prepregnancy BMI, physical activity, television viewing, and fish consumption.

[5] A 1% increase in energy from TFA subtype.

[6] A 0.1% increase in energy from TFA subtype.

concentrations in other umbilical cord domains (13). Although in a secondary analysis we did not observe significant associations between fetal growth and TFA subtypes in maternal erythrocyte phospholipids, this biomarker may be more likely to reflect short term intake compared with adipose tissue, which was not available for this cohort (35).

Our observations are also consistent with the hypothesis that TFAs may block the placental transfer of omega-3 (n−3) fatty acids to the fetus or disrupt their metabolism; a previous Project Viva analysis found that omega-3 fatty acids were inversely associated with fetal growth, although this relation was not seen in the Dutch birth-cohort studies (12, 13, 16). If TFAs are blocking the omega-3 transfer, consuming TFAs should lead to increased fetal growth, as we observed.

Our study had several potential limitations. The relatively high socioeconomic status of the participants may limit the generalizability of the data to other populations. However, the data were collected before the general decline in *trans* fats available in foods in the United States; thus, the broad range in *trans* fat intakes in this population represents an important biological range for many populations worldwide. Our study was also strengthened by prospective data collection, a relatively large sample size, and information on many maternal factors previously shown to be associated with fetal growth. We obtained detailed dietary information for both the first and second trimesters using a validated FFQ. Nevertheless, some misclassification of intake of TFAs is possible because foods can vary greatly in their TFA content, especially industrially produced TFAs. This misclassification, however, would most likely bias results toward the null.

In conclusion, we found that higher second-trimester TFA consumption, particularly 16:1*t*, which occurs naturally in animal foods, and 18:2*tc,* a result of industrial hydrogenation, was associated with greater fetal growth. Whereas macrosomia is associated with an increased risk of adverse health outcomes later in life, including overweight and diabetes, the extent to which the TFA-associated increased fetal growth is likely to be harmful or beneficial is unknown (3, 4). However, because no apparent benefits are associated with the consumption of industrially hydrogenated TFAs, and because higher TFA intakes in nonpregnant adults are associated with health risks, pregnant women should consider avoiding this ingredient (36–41). Our findings provide additional support for the effort to ban artificial TFAs in restaurants and to reduce TFAs in the general food supply (42). Additional research is warranted before recommendations are made about the naturally occurring TFA 16:1*t*, because its sources—primarily dairy products and meats—may confer some benefits to pregnant women, such as the promotion of bone health and the prevention of anemia (43, 44).

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