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Intake of Different Types of Fatty Acids in Infancy Is Not Associated with Growth, Adiposity, or Cardiometabolic Health up to 6 Years of Age[1–3]

Wendy Stroobant,[4,8] Kim VE Braun,[4,8] Jessica C Kiefte-de Jong,[4,6] Henriëtte A Moll,[5] Vincent WV Jaddoe,[4,5] Ingeborg A Brouwer,[7] Oscar H Franco,[4] and Trudy Voortman[4]*

Departments of [4]Epidemiology and [5]Pediatrics, Erasmus Medical Center, University Medical Center, Rotterdam, Netherlands; [6]Leiden University College, The Hague, Netherlands; and [7]Department of Health Sciences, Vrije Universiteit, Amsterdam, Netherlands

Abstract

Background: Studies in adults indicate that a lower saturated and higher unsaturated fat intake is associated with a lower risk of metabolic syndrome and cardiovascular diseases. However, studies on fat intake in relation to cardiometabolic health during childhood are scarce.

Objective: We examined associations between dietary intake of fatty acids (FAs) at age 1 y and measures of growth, adiposity, and cardiometabolic health up to age 6 y.

Methods: This study was conducted in 2927 children participating in the Generation R Study, a multiethnic, prospective, population-based cohort in the Netherlands. We measured children's total fat intake and intakes of saturated FAs (SFAs), monounsaturated FAs (MUFAs), and polyunsaturated FAs (PUFAs) at a median age of 12.9 mo (95% range: 12.2, 18.9 mo) with a food-frequency questionnaire. We repeatedly measured their height and weight up to age 6 y. At 6 y of age, we measured body fat percentage, diastolic and systolic blood pressure, and serum insulin, triacylglycerol, and HDL cholesterol. These outcomes were combined into a cardiometabolic risk factor score. We examined associations of FA intake with repeated measures of height, weight, and body mass index by using linear mixed models and with cardiometabolic outcomes by using linear regression models, adjusting for sociodemographic and lifestyle factors and taking into account macronutrient substitution effects.

Results: In multivariable models, we observed no associations of a higher intake of total fat or SFAs, MUFAs, or PUFAs with growth, adiposity, or cardiometabolic health when fat was consumed at the expense of carbohydrates. In subsequent models, there were also no associations observed for higher MUFA or PUFA intakes at the expense of SFAs with any of the outcomes. Results did not differ by sex, ethnicity, age, or birth weight.

Conclusion: The results of this study did not support our hypothesis that intake of different types of FAs was associated with adiposity or cardiometabolic health among children. *J Nutr* 2017;147:413–20.

Keywords: fatty acids, fat intake, infants, children, obesity, cardiometabolic health, cohort

Introduction

Cardiometabolic diseases, such as cardiovascular disease and type 2 diabetes, are highly prevalent. Risk factors for these diseases include obesity, dyslipidemia, elevated blood pressure (BP)[9], and insulin resistance; and a clustering of these risk factors is often referred to as the metabolic syndrome (1). Several studies have suggested that the development of cardiometabolic risk factors already begins in early life and that these risk factors track during the lifetime (2–4). Therefore, gaining knowledge about factors that may influence cardiometabolic health among children is highly relevant for the early prevention of later cardiovascular disease and type 2 diabetes.

Several studies in adults report associations for different types of dietary fat intakes with cardiometabolic risk factors. Overall, these studies suggest that a lower SFA intake, when replaced by a higher PUFA or MUFA intake, may reduce coronary heart disease risk and provide cardiometabolic benefits (5–7). Suggested underlying mechanisms include, for example, differences in inflammatory responses, changes in endothelial function, or changes in lipid metabolism in response to different FAs (8). On the basis of these studies, dietary guidelines generally advise lowering SFA intake and increasing PUFA intake (9).

In contrast to these dietary recommendations for adults, to our knowledge no specific guidelines are available with regard to fat intake for young children. Nutritional requirements in this period may be different; however, evidence on the

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cardiometabolic health effects of FA intake in early life is scarce (10). A few studies in school-aged children indicated that the intake of different types of FAs may be associated with certain cardiometabolic risk factors (11–13), but studies on fat intake in early childhood are lacking (14) and early life may be an important period for programming for long-term health (15). Considering the divergent effects of different types of FAs on cardiometabolic outcomes in previous studies, we hypothesized that the intake of SFAs is negatively associated with cardiometabolic health and that the intake of MUFAs and PUFAs is positively associated with cardiometabolic health. Therefore, the objective of this study was to examine the association between the intake of different types of FAs in early childhood and body composition and cardiometabolic health at 6 y of age in a prospective cohort study.

Methods

Study design and subjects. This study was embedded in the Generation R Study, a prospective cohort from fetal life onward in Rotterdam, Netherlands (16). All pregnant women living in the urban area of Rotterdam and with an expected delivery date between April 2002 and January 2006 were invited to participate. Response at baseline was 61% (n = 9778 women). After birth, 7893 children were available for follow-up studies. The study was approved by the Medical Ethical Committee of Erasmus Medical Center in Rotterdam, and parents of all children provided written informed consent. To determine their child's dietary intake, mothers of 5088 children received an FFQ. After excluding children whose parents did not return the FFQ and children whose FFQ was not completely filled out, complete and valid food-intake data were available for 3629 (72%) children (17, 18). Of these children, 2967 visited the research center around the age of 6 y and had data available on ≥1 cardiometabolic outcome (**Figure 1**).

Dietary intake assessment. Food intake was assessed between 2003 and 2006 when the children had a median age of 12.9 mo (95% range: 12.2, 18.9) by using a semiquantitative FFQ. This questionnaire was completed by the parents or caregivers of the children. The FFQ was specifically designed for this age group and contained 211 food items (17). The FFQ was validated against three 24-h recalls in 32 children aged 14 mo living in Rotterdam, and interclass correlation coefficients for nutrient intakes ranged from 0.4 to 0.7 (17, 18). With the Dutch Food-Composition Database (2006), we calculated intakes of total energy, total fat, SFAs, MUFAs, PUFAs, n–3 PUFAs, and n–6 PUFAs (19). Intakes of different types of fat were calculated as a percentage of total energy intake. Information on the content of *trans* fat was unfortunately not available, but was assumed to be low (20, 21). To be able to apply macronutrient substitution models, we also calculated intakes of other protein and carbohydrates, and we calculated energy from total fat minus that from SFAs, MUFAs, and PUFAs [i.e., from glycerol, *trans* FAs, sterols, and phospholipids (22)], which amounted to ~4% of total energy intake in our study population.

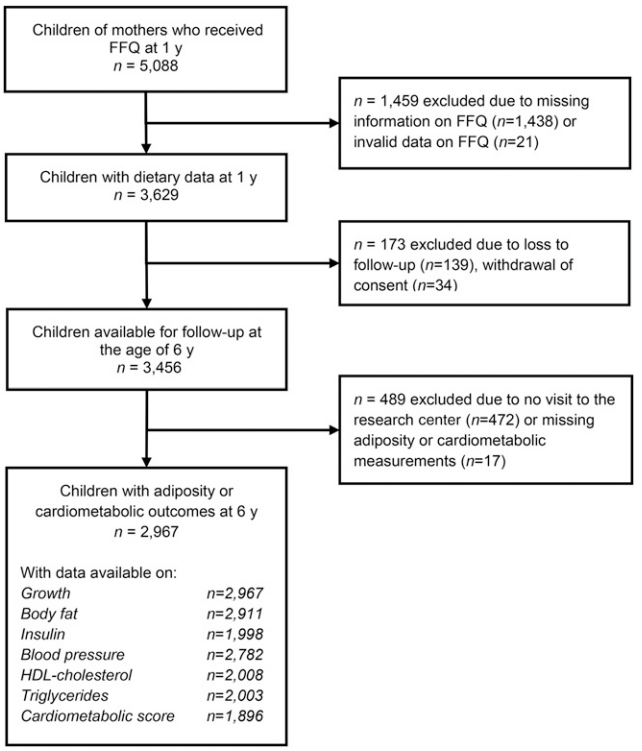

FIGURE 1 Flowchart of participants included for analysis.

Assessment of anthropometric measures, adiposity, and cardiometabolic health. Data on height, weight, and BMI were collected at 8 different time points between the ages of 1 and 6 y. Children's height and weight up to the age of 4 y were measured during routine visits to Child Health Centers at the median (95% range) ages of 11 (10, 13), 14 (13, 16), 19 (17, 21), 24 (23, 28), 30 (29, 34), 36 (35, 40), and 45 (44, 48) mo. At the median age of 6.0 y (95% range: 5.7, 6.6 y), we measured children's height, weight, body composition, and cardiometabolic health factors in our research center at the Erasmus Medical Center (16). Height was determined in the standing position to the nearest millimeter with a Harpenden stadiometer (Holtain Limited). Weight was measured by using a mechanical personal scale (Seca) to the nearest 0.1 kg. For each time point, BMI was calculated as total body weight (kg) divided by height squared (m^2). Overweight was determined according to the Cole et al. (23) criteria.

Body fat mass was measured with a DXA scanner (iDXA; Lunar, 2008; GE Healthcare) and was analyzed with Encore software (version 13.6) (24). Body fat percentage (BF%) was calculated by expressing total fat mass as a percentage of total body weight; fat mass index was calculated as fat mass (kg) divided by height squared (m^2) and fat-free mass index as fat-free mass (kg) divided by height squared (m^2). BP was measured 4 times at the right brachial artery by using a validated automatic sphygmomanometer (Accutorr Plus; Datascope Corp.). The mean of the last 3 measurements was calculated and used for analyses. Nonfasting blood samples were obtained, and concentrations of insulin, TGs, total cholesterol, HDL cholesterol, LDL cholesterol, and C-peptide were determined with enzymatic methods (by using a Cobas 8000 analyzer; Roche) (16). Quality-control samples showed intra- and interassay CVs ranging from 0.77% to 1.69%. For all body-composition and cardiometabolic outcomes, age- and sex-specific SD scores were calculated on the basis of our study population.

[1] The general design of the Generation R Study was made possible by financial support from Erasmus Medical Center, Rotterdam; Erasmus University, Rotterdam; the Dutch Ministry of Health, Welfare, and Sport; and the Netherlands Organization for Health Research and Development (ZonMw). VWVJ received an additional grant from the Netherlands Organization for Health Research and Development (ZonMw VIDI: 016.136.361).
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[3] Supplemental Tables 1–3 are available from the ''Online Supporting Material'' link in the online posting of the article and from the same link in the online table of contents at http://jn.nutrition.org.
[8] These authors contributed equally to this work.
*To whom correspondence should be addressed. E-mail: trudy.voortman@erasmusmc.nl.
[9] Abbreviations used: BF%, body fat percentage; BP, blood pressure; E%, percentage of energy; STRIP, Special Turku Coronary Risk Factor Intervention Project.

We applied a cardiometabolic risk factor score, modeled following metabolic syndrome-like definitions used in adults and adapted for use in the pediatric population (25, 26). As described in more detail elsewhere, this score consisted of the sum of SD scores from BF%, systolic BP, diastolic BP, insulin concentrations, TG concentrations, and the inverse of HDL-cholesterol concentrations (26), with a higher cardiometabolic risk factor score reflecting a higher cardiometabolic risk. For our analyses, we chose the cardiometabolic risk factor score and its components as primary outcomes of interest, but we additionally examined the other cardiometabolic outcomes that were available in our study (i.e., total cholesterol, LDL-cholesterol, and C-peptide concentrations).

Covariates. Information on maternal age, parental educational level, net household income, folic acid supplement use during pregnancy, and maternal parity was collected via self-administered questionnaires at enrollment in the study. Parental highest finished educational levels were classified into no or primary education, middle school or <4 y of high school, or higher education. Net household income was categorized into <€1400, €1400–2200, or >€2200/mo. Parity was categorized into 0, 1, or ≥2. Information on smoking and alcohol consumption during pregnancy was obtained through questionnaires in each trimester, and both variables were categorized into never, until pregnancy was known, or continued during pregnancy. Maternal food intake during first trimester was assessed with an FFQ, and overall diet quality was assessed with a predefined quality score (27).

Information on children's sex, birth weight, and gestational age was available from obstetric records (16). Sex- and gestational age–specific *z* scores for birth weight were determined according to reference data (28). Children's ethnic background was defined as Dutch or non-Dutch on the basis of the country of birth of the parents (18). Information on breastfeeding was available from postnatal questionnaires and was categorized into never, partially, or exclusively for ≥4 mo. Information on the timing of introduction of solid foods was available from a questionnaire. A previously developed diet score was applied to assess overall diet quality of the children at the age of 1 y on the basis of adherence to dietary guidelines for preschool children. Briefly, the ratio of reported and recommended intakes for 10 food groups was calculated, each truncated at 1. The scores of the 10 diet score components were summed, resulting in an overall score ranging from 0 to 10 on a continuous scale, with a higher score representing a better diet quality (18). Screen time (watching television or using a computer; hours per day) and participation in sports (yes or no) were assessed with questionnaires when the children were 6 y old.

Statistical analysis. Associations between the intake of FAs and repeated measures of height, weight, and BMI were analyzed with linear mixed models. Associations of dietary FA intakes with adiposity and cardiometabolic outcomes at the age of 6 y were analyzed with linear regression analyses. To test whether exposure variables showed a linear relation with the outcomes, we applied natural cubic splines with 3 df (29). We found indications for a nonlinear association only for the relation between PUFA intake and the cardiometabolic risk score ($P < 0.05$). Therefore, we also examined the associations of quartiles of PUFA intake with cardiometabolic health.

To account for the effect of energy intake and substitution effects of macronutrients in the diet, 2 different multivariable nutrient density substitution models were used (30). We chose to enter all of the nutrients in the model per 5% of energy (E%), which is in line with previous studies (6, 31). First, we examined the association of fat intake at the expense of carbohydrates with cardiometabolic outcomes. To study this, we included the intake of total energy, protein, and total fat or the intake of total energy, protein, SFAs, MUFAs, and PUFAs in the same model. Because total carbohydrate intake is the only macronutrient left out of this model, coefficients for fat intake can be interpreted as a 5E% higher intake of fat at the expense of carbohydrate. We then examined the association of MUFA and PUFA intakes at the expense of SFAs with cardiometabolic health. In these models, total energy intake and energy from carbohydrate, protein, total fat minus FAs, MUFAs, and PUFAs were included in 1 model (i.e., all energy sources except for SFAs).

In addition to the nutrients, we included child's sex, ethnicity, and age at dietary assessment in our basic models. In this model, sex, ethnicity, age at completion of the FFQ, and birth weight were also tested as possible effect modifiers, but none of the interaction terms were significant (all $P > 0.05$).

TABLE 1 Characteristics of the mothers and children included in the analyses[1]

	Value
Maternal characteristics	
Maternal age, y	31.5 ± 4.5
Maternal BMI at intake, kg/m^2	23.5 (18.8, 35.3)
Nulliparous, %	60.5
Educational level, %	
None or primary education	5.5
Middle school or <4 y of high school	36.0
Higher education	58.6
Monthly household income, %	
<€1400	13.9
€1400–€2200	19.4
>€2200	66.6
Smoking during pregnancy, %	
Never	77.3
Until pregnancy was known	10.7
Continued	11.9
Alcohol consumption during pregnancy, %	
Never	37.7
Until pregnancy was known	16.4
Continued	45.9
Infant characteristics	
Sex, % boys	48.7
Dutch ethnic background, %	68.6
Gestational age at birth, wk	40.1 (35.6, 42.3)
Birth weight, g	3452 ± 569
Breastfeeding, %	
Exclusive ≥4 mo	29.8
Partial ≥4 mo	59.9
Never	10.3
Child characteristics at dietary assessment	
Age at FFQ, mo	12.9 (12.2, 18.9)
Total energy intake, kcal	1310 ± 388
Total protein intake, E%	12.9 ± 2.4
Total carbohydrate intake, E%	58.4 ± 5.9
Total fat intake, E%	28.5 ± 5.6
SFA intake	11.5 ± 3.6
MUFA intake	9.8 ± 3.1
PUFA intake	5.5 ± 1.5
Child characteristics at follow-up visit	
Age, y	6.0 (5.7, 6.6)
Height, cm	118 ± 5
Weight, kg	21.8 (17.4, 30.4)
BMI, kg/m^2	16.0 ± 1.6
Screen time, h/d	1.25 (0.25, 4.71)
Participation in sports, %	44.9
Body fat percentage (n = 2911)	24.2 ± 5.0
Systolic blood pressure (n = 2843), mm Hg	102 ± 8
Diastolic blood pressure (n = 2843), mm Hg	60 ± 7
HDL cholesterol (n = 2008), mmol/L	1.34 ± 0.31
Insulin (n = 1998), pmol/L	115 (18, 397)
TGs (n = 2003), mmol/L	0.97 (0.40, 2.36)

[1] Values are means ± SDs when continuous variables were normally distributed, medians (95% range) for continuous variables with a skewed distribution, and percentages for categorical variables; n = 2967 unless otherwise indicated. E%, percentage of energy.

Covariates were selected on the basis of theory and previous studies and were included in the multivariable model when adding them to the basic model resulted in changes in effect estimates >10%. On the basis of this criterion, multivariable models were additionally adjusted for the following variables: maternal BMI, age, alcohol consumption during pregnancy, smoking during pregnancy, education, parity, household income, birth-weight *z* score, breastfeeding, and children's screen time and playing sports. The following covariates were considered but not included because they did not meet the 10%-change criterion: folic acid supplement use during pregnancy, maternal diet quality score, paternal educational level, timing of introduction of solid foods, and child's diet quality score. As a sensitivity analysis, we repeated our models among children with a Dutch ethnic background only, because the FFQ was originally designed for Dutch children. Furthermore, we performed sensitivity analyses in which we replaced protein intake by carbohydrate intake in the models in order to examine fat intake at the expense of protein. Finally, to assess if potential associations with the cardiometabolic risk factor score were driven by a single cardiometabolic risk factor, we performed sensitivity analyses in which we excluded each cardiometabolic outcome from the cardiometabolic score 1 by 1.

To increase statistical power and to reduce bias due to missing data, missing values of covariates (ranging from 0% to 19%) were multiply imputed (10 imputations) according to the Fully Conditional Specification method with the use of predictive mean matching (32). We report the pooled regression coefficients after the multiple imputation procedure. Statistical analyses were performed by using SPSS version 21.0 (IBM Corporation) and R version 3.1.2 (R Foundation for Statistical Computing).

Results

Subject characteristics. Maternal and child characteristics, dietary intakes, and cardiometabolic outcomes are presented in **Table 1**. Most of the children had a Dutch ethnic background (68.8%) and had mothers with a high educational level (59.4%). Children's mean ± SD total energy intake was 1310 ± 388 kcal/d and 28.5% ± 5.6 E% was derived from fat. The mean intakes of SFAs, MUFAs, and PUFAs in our population were 11.5 ± 3.6, 9.8 ± 3.1, and 5.5 ± 1.5 E%, respectively. The main food sources contributing to SFA intake in our study population were sauces, solid cooking fats, and cakes and pastry. Main food sources of MUFA intake were sauces and cooking fats and oils; and main sources of PUFA intake were margarines, liquid cooking fats and oils, and mayonnaise. At the age of 6 y, 404 (13.6%) of the children in this study population were overweight or obese. In nonresponse analyses, we observed that children without FFQ data were slightly taller and heavier at follow-up than children with FFQ data (33).

Associations of fat intake with growth, adiposity, and cardiometabolic health. The covariate-adjusted associations for the carbohydrate substitution models are presented in **Tables 2** and **3**. A higher total fat intake at the expense of a lower carbohydrate intake in early childhood was not associated with any of the anthropometric or cardiometabolic outcomes at the ages of 6 y. Similarly, higher intakes of SFAs, MUFAs, or PUFAs at the expense of carbohydrates were not associated with growth (Table 2) or cardiometabolic health (Table 3). For analyses with PUFA intake in quartiles, there were also no significant associations or clear nonlinear trends observed (data not shown).

Substitution models in which we examined the substitution of SFAs by unsaturated fat showed similar results as were observed for carbohydrate substitution models: neither MUFA nor PUFA intakes were associated with any of the anthropometric (data not shown) or cardiometabolic (**Table 4**) outcomes when consumed at the expense of SFAs.

Associations with cardiometabolic health unadjusted for confounders are shown in **Supplemental Table 1**. In these models, a higher SFA intake was associated with a higher systolic BP and lower insulin concentrations and a higher MUFA intake was associated with higher insulin concentrations when consumed at the expense of carbohydrates. Other results were similar to those of the adjusted model.

Additional analyses. Sensitivity analyses restricted to children with a Dutch ethnic background showed similar associations between fat intakes, either at the expense of carbohydrates or of SFAs, with cardiometabolic health as were observed for the whole study population (**Supplemental Table 2**). The intake of FAs was also not associated with other measures of adiposity (fat mass index or fat-free mass index) or other cardiometabolic health outcomes that were not included in the cardiometabolic score (i.e., total cholesterol, LDL-cholesterol, or C-peptide concentrations; **Supplemental Table 3**).

When we explored the substitution of protein instead of carbohydrates we found that higher total fat, PUFA, or MUFA intakes at the expense of protein were associated with a lower BF% but not with any of the other outcomes (data not shown). This is in line with results for protein intake, either at the expense of fat or carbohydrates, which we described previously (26, 34). Finally, in line with the main analysis, in sensitivity analyses in which we excluded each component from the cardiometabolic score 1 by 1, no significant associations were observed.

Discussion

The aim of this study was to examine the associations between intakes of total, saturated, monounsaturated, and polyunsaturated

TABLE 2 Associations between fat intake at the expense of carbohydrates at age 1 y and growth between the ages of 1 and 6 y[1]

	SDS		
Intake	Height (*n* = 2967)	Weight (*n* = 2967)	BMI (*n* = 2967)
Total fat, 5E%	−0.023 (−0.056, 0.010)	−0.027 (−0.059, 0.007)	−0.003 (−0.030, 0.024)
SFAs	0.088 (−0.049, 0.225)	0.074 (−0.062, 0.211)	0.049 (−0.062, 0.159)
MUFAs	−0.139 (−0.314, 0.035)	−0.102 (−0.275, 0.072)	−0.016 (−0.157, 0.125)
PUFAs	−0.006 (−0.163, 0.151)	−0.082 (−0.238, 0.074)	−0.094 (−0.221, 0.033)

[1] Values are based on multivariable linear mixed models and reflect differences (95% CIs) of the whole trajectory of the anthropometric outcome between the ages of 1 and 6 y (age- and sex-adjusted SDSs) per a 5E% higher intake of a specific fat intake at the expense of carbohydrates. Models were adjusted for intakes of total energy and energy from protein and all types of fats (i.e., all energy sources except for carbohydrates) to examine macronutrient substitution effects. Models were additionally adjusted for age at FFQ, sex, ethnicity, maternal education, household income, parity, maternal BMI, maternal age, smoking during pregnancy, alcohol consumption during pregnancy, breastfeeding, birth weight, and screen time and playing sports at 6 y of age. SDS, SD score; 5E%, 5% of energy.

TABLE 3 Associations between fat intake at the expense of carbohydrates at age 1 y and cardiometabolic health at age 6 y[1]

	SDS						
Intake	BF% (n = 2911)	SBP (n = 2843)	DBP (n = 2843)	HDL cholesterol (n = 2008)	Insulin (n = 1998)	TGs (n = 2003)	Cardiometabolic risk factor score (n = 1896)
Total fat, 5E%	−0.014 (−0.043, 0.014)	0.020 (−0.014, 0.055)	−0.006 (−0.040, 0.028)	0.025 (−0.017, 0.066)	−0.009 (−0.051, 0.032)	−0.024 (−0.066, 0.018)	−0.076 (−0.181, 0.030)
SFAs	−0.028 (−0.142, 0.086)	0.074 (−0.065, 0.214)	0.073 (−0.063, 0.209)	0.043 (−0.119, 0.205)	−0.158 (−0.321, 0.005)	−0.073 (−0.236, 0.089)	−0.213 (−0.624, 0.199)
MUFAs	0.020 (−0.125, 0.164)	−0.065 (−0.241, 0.110)	−0.132 (−0.303, 0.039)	−0.010 (−0.217, 0.197)	0.163 (−0.045, 0.371)	0.028 (−0.179, 0.235)	0.040 (−0.483, 0.564)
PUFAs	−0.079 (−0.213, 0.054)	0.109 (−0.053, 0.272)	0.121 (−0.037, 0.272)	0.053 (−0.138, 0.245)	−0.065 (−0.258, 0.127)	−0.038 (−0.230, 0.154)	−0.017 (−0.503, 0.470)

[1] Values are based on multivariable linear regression models and reflect differences (95% CIs) in cardiometabolic outcomes (age- and sex-adjusted SDSs) and cardiometabolic risk factor score per a 5E% higher intake of a specific fat at the expense of carbohydrates. Models were adjusted for intakes of total energy, energy from protein, and energy from all types of fats (i.e., all energy sources except for carbohydrates) to examine macronutrient substitution effects. Models were additionally adjusted for age at FFQ, sex, ethnicity, maternal education, household income, parity, maternal BMI, maternal age, smoking during pregnancy, alcohol consumption during pregnancy, breastfeeding, birth weight, and screen time and playing sports at 6 y of age. BF%, body fat percentage; DBP, diastolic blood pressure; SBP, systolic blood pressure; SDS, SD score; 5E%, 5% of energy.

fat in children in early childhood and their growth and cardiometabolic health up to the age of 6 y. Overall, our results showed no consistent associations between intakes of total fat or different types of FAs, at the expense of either carbohydrates or saturated fat, with growth or cardiometabolic outcomes.

One large intervention study in children focused on outcome variables similar to those in our study. This Special Turku Coronary Risk Factor Intervention Project (STRIP) study investigated the influence of low-saturated-fat counseling compared with no dietary counseling on cardiometabolic health in >1000 children from ≥7 mo of age in Finland. Outcomes that were examined included metabolic syndrome, BP, insulin sensitivity, and cholesterol concentrations; and in several follow-up studies in later childhood or adolescence, a beneficial effect of the intervention was observed for many of these cardiometabolic outcomes (13, 35–37). In contrast to the findings of the STRIP study, in our study we did not find associations between lower SFA intake and better cardiometabolic health. However, because the intervention in the STRIP study consisted of dietary counseling, it is not certain whether the effects were caused by a low-saturated-fat diet or other effects of the long-term lifestyle advice. For example, in one of the analyses in the STRIP study, it was shown that the intervention group had a lower HOMA-IR, but that actual SFA intake was not significantly associated with HOMA-IR in multivariable analyses (37). In addition, dietary counseling in the STRIP study remained until 20 y of age and the observed effects may therefore also be caused by dietary changes in later childhood rather than in early childhood.

A few observational studies focused on dietary fat intake in young children in relation to their weight or BMI. In previous analyses in our study population, Heppe et al. (38) observed that a higher PUFA intake at the age of 1 y was associated with a lower BMI at 4 y of age, which is an earlier follow-up measurement than in our cohort. Considering that we did not find this association with BMI up to the age of 6 y might suggest that the potential effects of fat intake weaken after a longer follow-up period. Another possible explanation for our null findings with BF% may be that the adiposity rebound, which occurs around the age of 6 y (39), obscured a possible inverse association between PUFA intake and body fat at this age specifically. In line with our results, Williams and Strobino (40), who performed a prospective study in 519 children, did not find any significant associations between SFA or MUFA intake at 3–4 y of age and BMI at 7–10 y of age. In addition, Agostoni et al. (41), who measured dietary intake at 1 and 5 y and BMI at 5 y in 147 children, observed that intakes of total fat, SFAs, MUFAs, or PUFAs at 1 or 5 y were not associated with BMI at 5 y of age. Also in line with our findings, PUFA supplementation in infancy has been shown not to influence growth (42). No previous studies were identified that examined fat intake in relation to measures of body fat in young children.

Two previous studies investigated the association between FA intake with cholesterol and TG concentrations in children. Contrary to our findings, Cowin and Emmett (43) observed that a higher intake of PUFAs or SFAs at the age of 18 mo was associated with a lower HDL-cholesterol concentration at the age of 31 mo. However, this association was only present among girls and not among boys. Moreover, among boys, but not girls, a higher total fat intake or SFA intake was associated with a higher total cholesterol concentration (43). In our population, we found no significant interaction between child sex and FA intake on cardiometabolic health. In line with our results, the study of Williams and Strobino (40) did not find any association between SFA or MUFA intakes at 3–4 y of age and

TABLE 4 Associations for unsaturated fat intake at the expense of saturated fat at age 1 y and cardiometabolic health at age 6 y[1]

	SDS						Cardiometabolic risk factor score
Intake	BF% (n = 2911)	SBP (n = 2843)	DBP (n = 2843)	HDL cholesterol (n = 2008)	Insulin (n = 1998)	TGs (n = 2003)	(n = 1896)
MUFAs, 5E%	0.048 (−0.202, 0.298)	−0.139 (−0.443, 0.164)	−0.205 (−0.501, 0.091)	−0.053 (−0.408, 0.302)	0.321 (−0.036, 0.678)	0.102 (−0.253, 0.457)	0.253 (−0.647, 1.153)
PUFAs, 5E%	−0.051 (−0.182, 0.079)	0.035 (−0.124, 0.194)	0.048 (−0.107, 0.203)	0.010 (−0.178, 0.197)	0.093 (−0.096, 0.281)	0.035 (−0.152, 0.223)	0.196 (−0.283, 0.675)

[1] Values are based on multivariable linear regression models and reflect differences (95% CIs) in cardiometabolic outcomes (age- and sex-adjusted SDSs) and cardiometabolic risk factor score per 5E% or per 1E% increase in MUFA and PUFA intakes at the expense of SFAs. Models were adjusted for intakes of total energy and energy from protein, energy carbohydrates, and energy from all fats except for SFAs to examine macronutrient substitution effects. Models were additionally adjusted for age, sex, ethnicity, maternal education, household income, parity, maternal BMI, maternal age, smoking during pregnancy, alcohol consumption during pregnancy, breastfeeding, birth weight, and screen time and playing sports at 6 y of age. BF%, body fat percentage; DBP, diastolic blood pressure; E%, percentage of energy; SBP, systolic blood pressure; SDS, SD score; 1E%, 1% of energy; 5E%, 5% of energy.

total cholesterol, HDL-cholesterol, and TG concentrations at 7–10 y of age. However, cross-sectional data from the same study population showed that intakes of MUFAs, but not SFAs, in later childhood were inversely associated with total cholesterol and TG concentrations (40).

In contrast to our hypothesis, no associations were found in our study for lower SFA intake and higher MUFA and PUFA intakes and better cardiometabolic health. This is in line with a review and meta-analysis of studies in adults by Chowdhury et al. (44), who also reported no consistent effects of dietary or circulating SFAs, MUFAs, or PUFAs on cardiovascular disease. A possible explanation for the fact that we did not find associations might be that different individual FAs within the subgroups of SFAs, MUFAs, and PUFA may have different effects on cardiometabolic health. Unfortunately, we could not reliably calculate the intake of specific FAs from our FFQ data. We also did not have information available on *trans* FAs, but intake was assumed to be <1% of total energy intake on the basis of national food-consumption data in the years of our dietary assessment (20, 21). Although many food items were included in the FFQ, including many detailed subtypes of oils and margarines, the intraclass correlation coefficient for total fat intake in a validation study was only 0.4. This indicates measurement errors in our assessment of fat intake in early childhood. However, dietary fat intake remains difficult to estimate and our reference method with 24-h recalls is also not an optimal way to measure this variable (45). Therefore, it is difficult to judge the quality of the estimates of fat intake in our study and whether our exposure measurement was specific enough to detect a potential association of FA intake with growth or cardiometabolic health. Future studies should use more detailed measurements of fat intake, such as weighed food records or repeated 24-h recalls, or should combine dietary intake data with FA concentrations in, for example, blood or adipose tissue. In particular, serum or erythrocyte concentrations of certain n–3 or n–6 PUFAs may provide good estimates for the dietary intake of FAs (46, 47).

An important strength compared with other studies is that we accounted for the effect of energy intake and macronutrient substitution by using a multivariable nutrient density substitution model. By using different substitution models, we could examine the effects of replacing different macronutrients by FAs. Finally, a strength of our study is the large number of variables measured in this cohort, which made it possible to examine many potential confounders and effect modifiers. A limitation, however, was that no information was available on the children's cardiometabolic health earlier in childhood or their dietary intake at the age of 6 y. Therefore, it was not possible to perform longitudinal analyses or to examine whether FA intake at the age of 6 y was associated with cardiometabolic health or diluted a potential effect of fat intake in early childhood.

In conclusion, results from this prospective cohort study showed no consistent associations between intakes of total, saturated, monounsaturated, or polyunsaturated fat in early childhood with growth or cardiometabolic health outcomes at school age. Because the number of studies that examined these associations is low, future studies are needed to further investigate the associations between intakes of different types of fat in early childhood and adiposity and cardiometabolic health, preferably with the use of more detailed dietary assessment methods and combined with FA biomarkers.

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WS, KVEB, and TV designed the research project, conducted the analyses, and wrote the manuscript; HAM, VWVJ, and

OHF were involved in the design and planning of the study and data collection; JCK-dJ, IAB, and OHF provided consultation regarding the analyses and interpretation of the data; and TV had primary responsibility for the final content. All authors critically reviewed and approved the final manuscript.

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