

REGULAR ARTICLE

Maternal dietary fat and fatty acid intake during lactation and the risk of asthma in the offspring

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ABSTRACT

Aim: To explore the association between maternal dietary fat and fatty acid (FA) intake during lactation, and the risk of asthma in the offspring by the age of 5 years.

Methods: The subjects comprised 1798 mother–child pairs from the Type 1 Diabetes Prediction and Prevention (DIPP) Nutrition Study. Dietary intake was assessed by a validated 181-item food frequency questionnaire, which covered the third month of lactation. The cumulative incidence of asthma was assessed at the age of 5 years with a questionnaire modified from the International Study of Asthma and Allergies in Childhood (ISAAC). Cox proportional hazards regression was used for statistical analysis.

Results: The maternal use of margarines during lactation was associated with a marginally increased risk of asthma [hazard ratio (HR) for user vs. nonuser 1.96, 95% confidence interval (CI) 1.01–3.82, $p = 0.047$] after adjusting for putative confounders. The maternal intakes of n-3 polyunsaturated FA (PUFA) and fish during lactation were not associated with the risk of asthma.

Conclusion: Maternal use of margarines during lactation was weakly associated with an increased risk of asthma in the offspring at the age of 5 years. Other fats or FAs during lactation were not associated with the risk of asthma. However, the nonadherence to dietary recommendations regarding especially fats of our study population may restrict the generalizability of our results.

INTRODUCTION

Prenatal nutrition and early infant nutrition have been implicated as modulators of the immune system and also playing a role in the development of IgE-mediated allergic diseases and asthma (1). It has been suggested that exposure to n-3 polyunsaturated fatty acids (PUFA) during the critical

stages may protect the infant against the development of allergic diseases and asthma (2). The foetus receives n-6 and n-3 PUFA via the placenta, while breast milk is an important source of them postnatally (3,4). The placental transport processes favour n-3 fatty acids (FA) over n-6 FA (3,4).

Abbreviations

ALA, α -linolenic acid; ARA, arachidonic acid; DGLA, dihomogammalinolenic acid; DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; FA, fatty acid; GLA, gamma-linolenic acid; LA, linoleic acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid; total n-3 PUFA, ALA, EPA, DPA and DHA; total n-6 PUFA, LA, ARA, GLA and DGLA.

Key notes

- Maternal use of margarines during lactation was weakly associated with an increased risk of asthma in the offspring by the age of 5 years. Other fats or FAs failed to show any associations.
- The nonadherence to dietary recommendations regarding especially fats of our study population may restrict the generalizability of our results.

The FA composition of breast milk is modulated by both maternal diet and maternal FA stores.

Only a few studies on the associations between maternal dietary FA composition during lactation and the risk of asthma in the offspring are available. By contrast, the relationship between the duration of breastfeeding, maternal allergen avoidance during breastfeeding, the FA composition of breast milk and atopic diseases in childhood has been investigated extensively (5,6).

We previously reported that high maternal intake of total n-3 PUFA, especially α -linolenic acid (18:3n-3), and total saturated fatty acids (SAFA), in particular palmitic acid (16:0), during pregnancy was associated with a decreased risk of asthma in the offspring, while high intake of arachidonic acid (20:4n-6) was associated with an increased risk (7). The aim here was to assess the associations between maternal dietary fat intake during lactation and the risk of asthma in the offspring by the age of 5 years.

SUBJECTS AND METHODS

The Type 1 Diabetes Prediction and Prevention (DIPP) Project is a birth cohort study, where all newborn infants in Turku, Tampere and Oulu University Hospitals were screened for human leucocyte antigen (HLA)-conferred susceptibility (HLA-DQB1) to type 1 diabetes mellitus with the use of cord blood samples. All children with a high or moderate genetic risk (HLA-DQB1*02/0302 heterozygotes and DQB1*0302/x-positive subjects; x stands for homozygosity or a neutral allele) of type 1 diabetes were invited to participate in the DIPP Study (15% of those screened) (8).

The DIPP Nutrition Study was started in 1996 (9). The pregnancy study started among mothers of children born late in 1997 (totally 7238 children invited). The lactation study started among mothers of children born in 1998 (6360 children invited). Mothers of 4943 children participated in the pregnancy study and 2943 in the lactation study. The children still participating in the dietary follow-up at the age of 5 years were invited to the DIPP Allergy Study. Here, we analyse children born between 1998 and 2004 in Tampere and Oulu. Of children with data on maternal lactation diet available ($n = 2943$), 1798 also had information on asthma. Only mothers still breastfeeding at 3 months of child age were invited to the lactation study.

Dietary intake during lactation was assessed by a validated, self-administered, semi-quantitative 181-item food frequency questionnaire (FFQ) (10) during the third month of lactation (10,11). The FFQ was designed to assess the maternal total diet (intake of foods and nutrients) during lactation, over a period of 1 month. The diet during the third month of lactation was queried by an FFQ given to the mothers at the child's 3-month visit to the study centre and returned at the child's 6-month visit. The frequency of food consumption was asked as common serving sizes. The use of dietary supplements during the whole lactation was asked separately: the name, the manufacturer and the dosage (per day, per week or per month) of the supplement. The used supplements were entered into the database and

calculated and converted into a mean daily intake. Information on the fats used in cooking and baking and oils used for salad dressing was requested and included in the nutrient calculations. The mothers were asked to circle the right picture of the amount of margarine on one slice of bread they used. The consumption frequency was also asked. The use of margarines was classified depending on their fat content: margarines containing 70–80% or 30–60% fat, and brand names were given. The questionnaire was specifically designed to reflect the food consumption of Finnish women.

A trained nutritionist checked the returned FFQ forms and rejected those with 10 or more food items with missing data. Food consumption data were analysed using a special version of the Finnish Food Composition Database (<http://www.fineli.fi>), software program developed at the National Institute for Health and Welfare. To reflect changes in the diet, the recipe compositions are continuously updated, and Fineli includes, for example, every margarine used in Finland at a certain time period with the nutrient values. This information was combined with that from the FFQ form, converted into a daily food diary, from which mean daily intakes of foods, food groups, ingredients and nutrients were calculated and analysed. Dietary intake during pregnancy was determined at the eighth month of pregnancy with the same questionnaire (7).

When the child was 5 years old, the parents completed an ISAAC-based (12) questionnaire to inform on the child's history of allergic diseases. The questionnaire was validated against the antiasthmatic medication reimbursement data of the Finnish Social Insurance Institution (13) and is an acceptable tool for defining the prevalence of parental-reported childhood asthma in epidemiological studies. We defined asthma as doctor-diagnosed asthma plus any wheezing symptom or the use of asthma medication during the previous 12 months preceding the completion of the questionnaire. To define persistent asthma, the age of 5 years was chosen to exclude viral wheeze common in young children. We did not perform any allergy tests.

Child's sex, mother's age at child's birth and parental vocational education were elicited from parents with a structured questionnaire after delivery. Information on the duration of gestation, number of earlier deliveries, mode of delivery (vaginal delivery or caesarean section), birth weight, place of birth and maternal smoking during pregnancy were obtained from the Medical Birth Registers of Tampere and Oulu. Information on exposure to farming, contacts with a cow shed, pets at home during the first year of life and atopic eczema by the age of 6 months, as well as parental asthma and allergic rhinitis, was requested from the parents in the allergy questionnaire.

Statistical methods

Mean nutrient intakes during pregnancy and lactation were calculated in relation to energy intake to compare the intakes between pregnancy and lactation. Paired-samples *t*-test was used to compare the intakes. The nutrient variables were calculated as a percentage of energy to better

describe the quality of the diet, not depending on the amounts consumed.

Cox proportional hazards regression was used to estimate associations between maternal intake of FA and dietary fats during lactation, and the risk of asthma in the offspring by the age of 5 years. The dietary intake of FA was energy-adjusted using Willet's residual method (14). When analysing the food variables, energy was included in the model. Dietary variables were divided into quarters. The lowest and highest quarters were compared with the combined mid-half as the reference category. Some food variables were dichotomized (user/nonuser) because of high proportion (>25%) of nonusers. The statistical significance of the dietary variables in Cox proportional hazards models was tested with the Wald's chi-square test. Selection of confounding variables was based on their relations with the exposure and the outcome in this study and according to earlier findings. The following covariates were used as putative confounders: sex, area of birth, duration of gestation, maternal age, maternal vocational education, maternal smoking during pregnancy, number of previous deliveries, maternal asthma or allergic rhinitis, paternal asthma or allergic rhinitis, atopic eczema by the age of 6 months, birth weight, mode of delivery, duration of breastfeeding, pets at home, farming, and contacts to cow shed during the first year of life. The results were also adjusted with the corresponding FA or fat intake during pregnancy. The associations between maternal intake of FA during lactation and the risk of asthma in the offspring were also analysed separately in allergic and nonallergic mothers as well as in children with exclusive breastfeeding for <3 months vs. for 3 months or longer. All analyses were carried out using the SAS statistical package (version 9.1; SAS Institute, Cary, NC, USA).

Ethics

The study was reviewed by the ethics committees of the respective hospitals, and a written informed consent was obtained from the parent(s).

RESULTS

At the age of 5 years, altogether 96 of 1798 (5.3%) children had asthma, diagnosed at a median (range) age of 2.5 (0.3–4.9) years. The mean (SD) duration of exclusive breastfeeding was 2.3 (1.8) months, while that of total breastfeeding was 9.2 (4.7) months. The mean (SD) age of the mothers at the time of delivery was 30.1 (4.9) years, and the gestational age was 39.8 (1.5) weeks. The mothers had had on average 0.9 (1.2) previous deliveries.

The use of margarines was associated with a marginally increased risk of asthma [hazard ratio (HR) for user vs. non-user 1.96 (95% confidence interval (CI) 1.01–3.82), $p = 0.047$] after adjusting for putative confounders (Fig. 1). There was no evidence of the association of intake of n-3 PUFA and fish with the risk of asthma (Figs 1 and 2). The results remained the same when the analyses were carried out separately for children who were exclusively breastfed

for <3 months and for 3 months or longer as well as for allergic and nonallergic mothers (data not shown). The ratio of n-6 to n-3 PUFA was not associated with the risk of asthma (Fig. 1). There was no evidence of association between trans fatty acids (TFA) and asthma (data not shown).

High intake of 20:4n-6 was associated with an increased risk of asthma in the unadjusted model [HR for highest quarter vs. mid-half 1.66 (95% CI 1.06–2.61), $p = 0.009$] (Fig. 2). Significance disappeared after adjusting for putative confounders.

Maternal consumption of oils, margarines, butter and butter-spreads and meat and meat products in relation to energy intake was greater during lactation, while that of milk and milk products was greater during pregnancy (Table S1). The energy intake from carbohydrate was higher during pregnancy (Table S1). The reverse was true for protein, total fat, SAFA, monounsaturated fat (MUFA), total PUFA, n-6 PUFA, 20:5n-3 and 22:6n-3 (Table S1). The energy intake from n-3 PUFA or the consumption of fish per energy during pregnancy and lactation showed no difference. The nutrient variables were calculated as percentage of energy to better describe the quality of the diet, not depending on the amounts consumed (Table S1).

DISCUSSION

The present results show only minor associations between maternal dietary fat or FA intake during lactation and the development of asthma in the offspring: taking all potential available confounding factors into account, only maternal use of margarine was weakly associated with an increased risk of asthma in the offspring.

A German birth cohort study reported predominant use of margarine over predominant use of butter in children to be associated with an increased risk of allergic sensitization and atopic eczema in 2-year-olds (15). In an Italian cohort study, intake of neither butter nor margarine during pregnancy was associated with the risk of allergies in the offspring (16). Previous DIPP Nutrition Study results indicated that maternal intake of margarines during lactation may decrease the risk of sensitization to wheat allergen in the offspring (17). Maternal margarine intake during pregnancy has not been associated with respiratory allergies or atopic eczema in the offspring (18), nor with asthma in children (19,20) or young adults (21). Differing compositions of margarines may hinder comparing results between countries. Margarines are rich in n-6 PUFA. In Finland, <50% of margarines contain TFA (only minute amounts of 0.3–0.5%), whereas elsewhere in Europe, TFA is more common and used in greater amounts. Trans fatty acids was not associated with the risk of asthma in the present study.

Previously, pregnancy intakes of 18:3n-3, total n-3 PUFA and 16:0 were associated with a decreased risk of developing asthma and high intake of 20:4n-6 with an increased risk of asthma in the offspring (7). Interestingly, these associations were not observed during lactation even when adjusting for those during pregnancy. Of note, the present

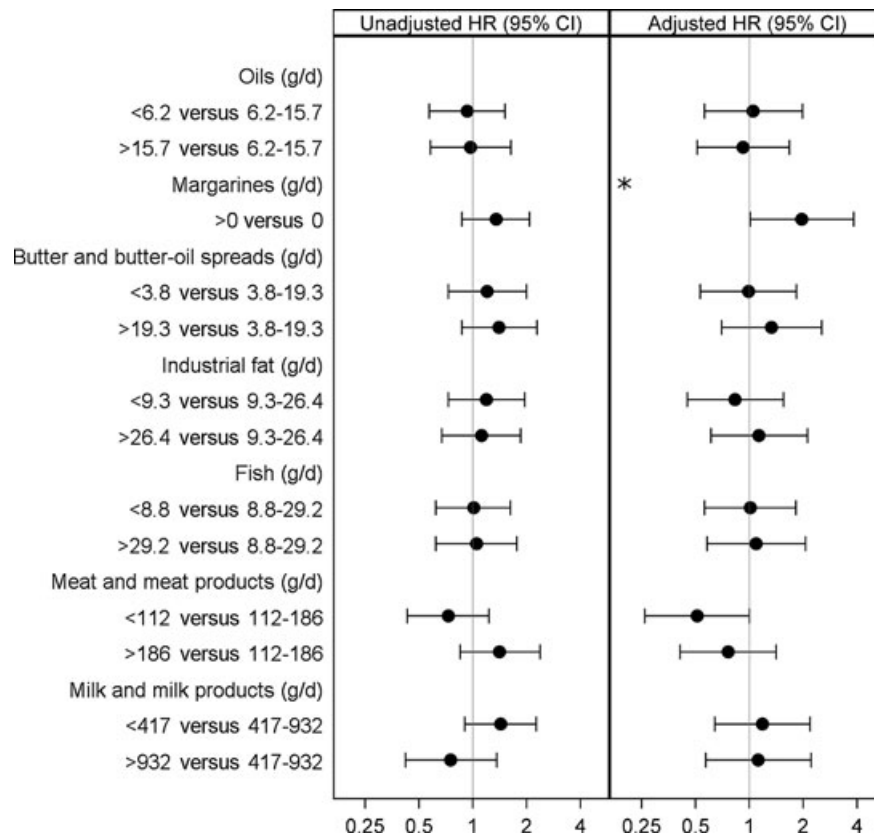


Figure 1 The risk of asthma in the offspring [hazard ratios (HR) and 95% confidence interval (CI)] associated with maternal dietary fat consumption during lactation (n = 1798). Energy intake was included in the model. Adjusted model included sex, area of birth, duration of gestation, maternal age, maternal vocational education, maternal smoking during pregnancy, number of previous deliveries, maternal asthma or allergic rhinitis, paternal asthma or allergic rhinitis, birth weight, mode of delivery, duration of breastfeeding, pets at home, farming, contacts to cow shed during the first year of life, atopic eczema at the age of 6 months, and the corresponding fatty acid consumption during pregnancy. Significant p-values (<0.05) are indicated with a star (*). Industrial fat, industrial fat-mixes and animal fats.

cohort of mothers did not comply with dietary recommendations very well: SAFA intake exceeded, while PUFA, margarine and oil intakes were below the recommended levels. About 46–47% of the fat was saturated, while the recommendation is <33%. This is a potential explanation of our limited findings, while the role of prenatal exposures in the modulation of the immune system may be speculated (22). Diet during pregnancy influences maternal fat FA composition and thus also affects breast milk FA composition after birth (4).

The present results suggest no association between maternal fish or n-3 PUFA intake during lactation and childhood asthma. The food database used in the present study is lacking accuracy regarding the FA content of fish species, possibly affecting the results, which are, however, in accordance with an earlier Finnish study (23). A systematic review concluded that n-3 PUFA supplementation (2.7 g fish oil per day) during lactation does not affect the incidence of allergic disorders (24). A shift in the ratio of n-6 to n-3 PUFA has been suggested to lead to the development of asthma, for which we found no evidence, failing to show any association between the ratio of n-6 to n-3 PUFA and the risk of asthma.

The strengths of this study include assessing maternal dietary intake and the asthma endpoint in the offspring with validated questionnaires. The collection of dietary data prior to the development of asthma allowed us to study the temporal relation between maternal diet and development of asthma in the offspring. It is possible that the retrospective report of maternal dietary intake could introduce some level of recall bias. The FFQ does overestimate the intake of foods and nutrients and thus energy (10), which we ameliorated by energy-adjusting the FA variables and including energy in the model when analysing food variables. Not selecting subjects based on their asthma or allergic status minimized the potential for selection bias regarding the endpoint. Five years was selected as the age of diagnosis of asthma to exclude children with viral wheeze, while no allergic testing was performed.

The birth cohort is based on genetic risk of type 1 diabetes (approximately 15% of all newborn infants in Finland), which may limit the applicability of results to the general population (8). However, evidence on the interaction between type 1 diabetes and allergic diseases remains controversial (25–27). In Russian Karelia, where the incidence of allergic diseases and type 1 diabetes is low and the

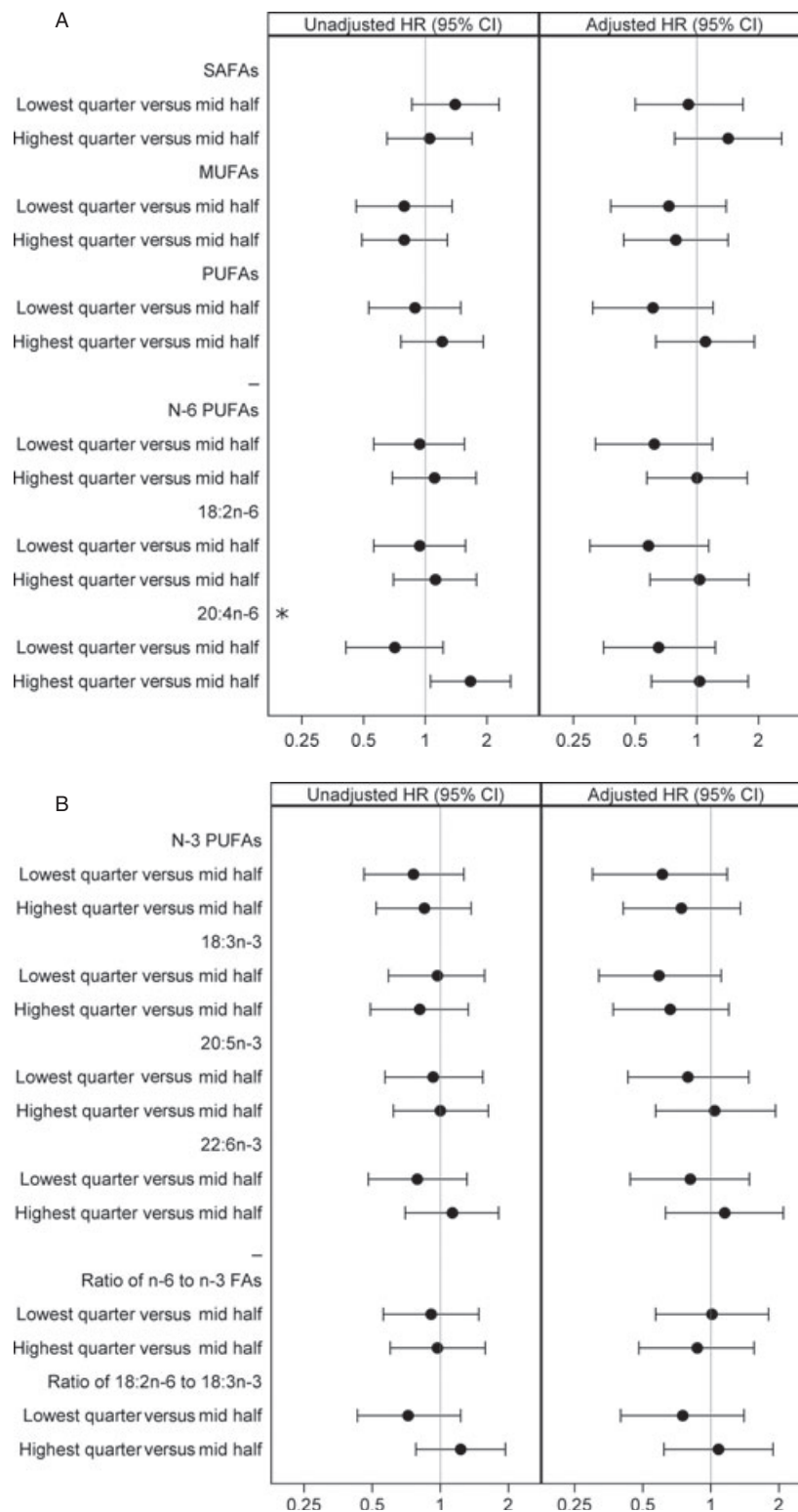


Figure 2 (a, b) The risk of asthma [hazard ratios (HR) and 95% confidence interval (CI)] associated with maternal fatty acid intake during lactation (n = 1798). Adjusted model included sex, area of birth, duration of gestation, maternal age, maternal vocational education, maternal smoking during pregnancy, number of previous deliveries, maternal asthma or allergic rhinitis, paternal asthma or allergic rhinitis, birth weight, mode of delivery, duration of breastfeeding, pets at home, farming, contacts to cow shed during the first year of life, atopic eczema at the age of 6 months, and the corresponding fatty acid consumption during pregnancy. Significant p-values (<0.05) are indicated with a star (*). FA, fatty acid; SAFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; LA, linoleic acid; ALA, α -linolenic acid.

incidence of infectious diseases is high, allergic sensitization of those with type 1 diabetes is more common than that in the general population (28). This was not found in Finland where the incidence of allergic diseases, type 1 diabetes and infectious diseases is reversed (28). The present cumulative incidence of asthma (5.3%) is comparable to previous findings in Finland (29).

Mothers not breastfeeding or not breastfeeding during the month prior to the data collection (third month) were excluded, resulting in a smaller sample compared with the previous pregnancy study. Moreover, as a prospective cohort, participation is voluntary at each stage. Background factors of mothers who did or did not return the pregnancy FFQ have been analysed previously in the DIPP Nutrition Study: those not participating differed in age, parity, region, education and degree of urbanization (11,30). Possibly, nutrient intakes differ between participants and nonparticipants.

In conclusion, maternal use of margarines during lactation was weakly associated with an increased risk of asthma in the offspring at the age of 5 years. Other fats or FAs were not associated with the risk of asthma. However, the nonadherence to dietary recommendations regarding especially fats of our study population may restrict the generalizability of our results.

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DISCLOSURE OF POTENTIAL CONFLICT OF INTEREST

The authors have declared that they have no conflict of interest.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1 Maternal mean (SD) daily consumption of selected food groups (g/day) and mean (SD) daily intakes of energy-yielding nutrients and fatty acids (E%) expressed in relation to energy intake (E%/MJ) during pregnancy (n = 2865) and lactation (n = 2943).

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Table S1 Maternal mean (SD) daily consumption of selected food groups (g/d) and mean (SD) daily intakes of energy-yielding nutrients and fatty acids (E%) expressed in relation to energy intake (E%/MJ) during pregnancy (n=2865) and lactation (n=2943).

	<i>Pregnancy</i>		<i>Lactation</i>		<i>p-value*</i>
	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	
Oils (g/d)	13.2	8.4	11.9	7.6	0.017
Margarines (g/d)	9.4	12.9	8.6	11.9	0.007
Butter and butter-oil spreads (g/d)	14.6	14.3	13.9	14.2	<0.0001
Industrial fat (g/d)	22.6	15.9	20.3	15.5	0.012
Fish (g/d)	25.0	20.6	21.7	18.4	0.464
Meat and meat products (g/d)	164.8	70.2	154.3	68.5	<0.0001
Milk and milk products (g/d)	853.1	406.6	692.4	355.9	<0.0001
Energy (MJ/d)	11.4	3.2	9.9	2.8	<0.0001
Protein (E%)	16.6	2.2	16.7	2.3	<0.0001
Carbohydrate (E%)	49.7	5.1	48.5	5.6	<0.0001
Fat (E%)	33.6	4.7	34.5	5.0	<0.0001
SAFA (E%)	14.3	2.9	14.5	3.1	<0.0001
MUFA (E%)	11.7	2.0	12.1	2.1	<0.0001
PUFA (E%)	4.7	1.1	4.8	1.1	<0.0001
Palmitic acid 16:0 (E%)	6.6	1.2	6.7	1.3	0.003
N-6 PUFA (E%)**	3.5	0.8	3.6	0.9	<0.0001
Linoleic acid (LA) 18:2n-6 (E%)	3.4	0.8	3.5	0.9	<0.0001
Conjugated linoleic acid (E%)	0.06	0.01	0.1	0.02	0.252
Arachidonic acid (ARA) 20:4n-6 (E%)	0.03	0.01	0.03	0.01	<0.0001
N-3 PUFA (E%)***	1.0	0.3	1.0	0.3	0.217
α -linolenic acid (ALA) 18:3n-3 (E%)	0.9	0.3	0.9	0.3	0.769
Eicosapentaenoic acid (EPA) 20:5n-3 (E%)	0.03	0.03	0.03	0.03	0.001
Docosahexaenoic acid (DHA) 22:6n-3 (E%)	0.09	0.07	0.1	0.1	0.025

* The difference between pregnancy and lactation tested with paired samples t-test

SAFA=saturated fatty acid, MUFA=monounsaturated fatty acid, PUFA=polyunsaturated fatty acid

**n-6 PUFA=LA, ARA, GLA and DGLA

***n-3 PUFA=ALA, EPA, DPA and DHA, total n-6 PUFA=LA, ARA, GLA and DGLA