Maternal intake of fatty acids during pregnancy and allergies in the offspring

Citation for published version:

Digital Object Identifier (DOI):
10.1017/S0007114511005940

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Publisher's PDF, also known as Version of record

Published in:
British Journal of Nutrition

Publisher Rights Statement:
Copyright The Authors 2011

General rights
Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

Download date: 23. Dec. 2018
Maternal intake of fatty acids during pregnancy and allergies in the offspring

Bright I. Nwaru1*, Maijaliisa Erkkola2, Mirka Lumia3, Carina Kronberg-Kippilä3, Suvi Ahonen1,4, Minna Kaila5, Jorma Ilonen6,7, Olli Simell8, Mikael Knip5,9,10, Riitta Veijola11 and Suvi M. Virtanen1,3,4,5

1School of Health Sciences, University of Tampere, Tampere FIN-33014, Finland
2Department of Food and Environmental Sciences, Division of Nutrition, University of Helsinki, Helsinki, Finland
3Nutrition Unit, Department of Lifestyle and Participation, National Institute of Health and Welfare, Helsinki, Finland
4The Science Center of Pirkanmaa Hospital District, Tampere, Finland
5Department of Pediatrics, Tampere University Hospital, Tampere, Finland
6Immunogenetics Laboratory, University of Turku, Turku, Finland
7Department of Clinical Microbiology, University of Eastern Finland, Kuopio, Finland
8Department of Pediatrics, University of Turku, Turku, Finland
9Children’s Hospital, University of Helsinki, Helsinki University Central Hospital, Helsinki, Finland
10Folkhälsan Research Center, Helsinki, Finland
11Department of Pediatrics, University of Oulu, Oulu, Finland

(Submitted 15 April 2011 – Final revision received 4 October 2011 – Accepted 5 October 2011 – First published online 9 November 2011)

Abstract

Fatty acids (FA) are known to have a number of immunological effects and, accordingly, may play a role in the development of allergic diseases. We investigated the effect of maternal intake of FA during pregnancy on the risk of allergic rhinitis, wheeze and atopic eczema in children aged 5 years. The present study analysed data from the Finnish Type 1 Diabetes Prediction and Prevention Nutrition Study, a population-based birth cohort study with a 5-year follow-up. Complete information on maternal diet (assessed by a validated FFQ) and International Study of Asthma and Allergies in Childhood-based allergic outcomes was available for 2441 children. Cox proportional regression and logistic regression were used for the analyses. After adjusting for potential confounding variables, high maternal consumption of butter and butter spreads (hazard ratio (HR) 1·33; 95 % CI 1·03, 1·71) and higher ratio of \( n-6 : n-3 \) FA (HR 1·37; 95 % CI 1·07, 1·77) during pregnancy were associated with an increased risk of allergic rhinitis in the offspring by 5 years of age. High maternal intakes of total PUFA (HR 0·71; 95 % CI 0·52, 0·96) and \( \alpha \)-linolenic FA (HR 0·73; 95 % CI 0·54, 0·98) were associated with a decreased risk of allergic rhinitis. However, these results lost their significance after adjustment for multiple comparisons. Overall, our data suggest that maternal consumption of butter, the ratio of \( n-6 : n-3 \) FA and intake of PUFA and \( \alpha \)-linolenic FA during pregnancy may be potential determinants of allergic rhinitis in the offspring.

Key words: Allergic rhinitis; Atopic eczema; Children; Fatty acids; Maternal diet; Pregnancy; Wheeze

The increasing prevalence of allergic diseases in Western countries has partly been linked to changes in the modern diet(1), particularly changes in the intake of dietary fats(2). Over the past few decades, consumption of foods rich in \( n-6 \) PUFA has increased, whereas that of \( n-3 \) PUFA has decreased. Arachidonic acid (AA), which is an \( n-6 \) PUFA, is a precursor for pro-inflammatory eicosanoids, while \( n-3 \) EPA, is a precursor for anti-inflammatory eicosanoids(3). Changes in fatty acid consumption may shift the T-helper balance from type 1 to type 2, which, consequently, may increase the incidence of IgE-mediated allergic diseases(3,4).

The results of studies on the association between dietary intake of fats and fatty acids (FA) during pregnancy and allergic diseases in the offspring are inconsistent. A recent Japanese cohort study has linked maternal intake of \( \alpha \)-linolenic acid and DHA during pregnancy to a reduced risk of wheezing in 2-year-old children, while intake of \( n-6 \) PUFA and linoleic acid was associated with an increased risk of eczema(5). Maternal consumption of butter and margarine was not associated with atopy in the offspring in an Italian cohort study(6). Maternal fish consumption decreased the risk of allergic diseases in the offspring(6–10). In contrast, maternal

Abbreviations: AA, arachidonic acid; DIPP, Diabetes Prediction and Prevention; FA, fatty acids.

* Corresponding author: B. I. Nwaru, fax +358 403901665, email bright.nwaru@uta.fi
fish consumption was not associated with asthma or asthma symptoms in the offspring in a Dutch follow-up study (11). Further research is required in this area to elucidate the putative role of dietary fats during pregnancy and early life in the development of allergies. In the present large cohort with a relatively long follow-up, we aimed at examining the effects of maternal intake of dietary fats and a wide range of FA during pregnancy on the development of allergic rhinitis, wheeze and atopic eczema in the offspring by the age of 5 years.

Materials and methods

Subjects

In 1994, the Finnish Type 1 Diabetes Prediction and Prevention (DIPP) study was started. It is a multidisciplinary population-based prospective cohort study that examines potential means to predict and prevent type 1 diabetes (12). Newborn infants with human leucocyte antigen (HLA)-conferring susceptibility to type 1 diabetes are recruited from three university hospitals in Finland (Turku, Oulu and Tampere) and monitored at 3–12-month intervals for diabetes-associated antibodies, growth and environmental exposures. The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the ethics committees of the Universities of Oulu and Tampere. Written informed consent was obtained from the parents.

In September 1996 and October 1997, the DIPP Nutrition Study was started within the framework of the DIPP study in Oulu (Northern Finland) and Tampere (Southern Finland), respectively (13), examining the relationship of maternal diet during pregnancy and lactation, and the child's diet during infancy to the development of type 1 diabetes, allergic diseases and asthma in childhood. At the age of 5 years, 3523 children who were still participating in the dietary follow-up (born between 20 October 1997 and 29 February 2004) were invited to take part in the allergy study by completing a questionnaire on the child's history of allergic symptoms (16,17). Allergic rhinitis was defined as sneezing, nasal congestion or rhinitis other than with respiratory infections, accompanied by itching of the eye and tearing during the previous 12 months. Wheezing was defined as parental ‘yes’ answer on whether the child has had any of the following during the last 12 months: wheezy sound in respiration; wheezy sound in respiration in connection with physical activity; difficulties in respiration in the morning on waking up; wheezy respiration without having the sniffles or respiratory infection; dry cough at nights not associated with common colds or respiratory infections. Age of the onset of rhinitis and wheeze was indicated by the date of the doctor-made diagnosis. Atopic eczema was defined with a positive answer to the question: ‘Has your child ever had atopic eczema?’

Sociodemographic and perinatal characteristics

Information on the child’s sex, maternal age, maternal educational level and the number of siblings was recorded in a structured questionnaire completed by the parents after the delivery. Information on duration of gestation, birth weight and height, and maternal smoking during pregnancy was received from the Medical Birth Registries of Oulu and Tampere University Hospitals.

Statistical analysis

The distribution of maternal intake of n-3 and n-6 PUFA in the study population was analysed using the t test and ANOVA. Cox proportional hazards regression was used to estimate the risk of the onset of allergic rhinitis and wheeze (because we had the follow-up times for these outcomes), while logistic regression was used to estimate the prevalence of atopic eczema. The FA were energy adjusted by the residual method (18) while total energy intake was included in the models containing the dietary fats. The dietary
variables were categorised in quarters, and the two middle quarters were combined and used as the reference category. *A priori*, we judge that the two middle quarters constitute those with average diet intake in the study population, thus using them as the reference category and comparing the other two extreme quarters seems logical. Selection of confounding covariates was based on their relationships with the exposure and/or the outcome and, in respect of nutrients, on earlier findings. In the adjusted models, the following covariates were included and categorised as shown in Table 1: sex of child, hospital of birth, duration of gestation, maternal age at delivery, maternal basic education, maternal smoking during pregnancy, mode of delivery, number of siblings at the time of the child’s birth, parental asthma, parental allergic rhinitis, pets at home by 1 year of age. A second adjusted model was computed for the FA in which potentially confounding nutrients, vitamin C, Zn, Se, vitamin D and vitamin E were included as additional covariates. Correction for multiple comparisons was performed using the Bonferroni adjustments. All analyses were computed using SPSS version 15.0 (SPSS, Inc., IL, USA).

**Results**

Participants in the allergy study were generally not systematically different from non-participants regarding the

<table>
<thead>
<tr>
<th>Table 1. Distribution of maternal intake of n-3 and n-6 PUFA by the characteristics of the participating children (Mean values with their standard errors, n 2441)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristics</strong></td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Boys</td>
</tr>
<tr>
<td>Girls</td>
</tr>
<tr>
<td>Delivery hospital</td>
</tr>
<tr>
<td>Oulu (Northern Finland)</td>
</tr>
<tr>
<td>Tampere (Southern Finland)</td>
</tr>
<tr>
<td>Duration of gestation</td>
</tr>
<tr>
<td>Quarter: 38–90 weeks</td>
</tr>
<tr>
<td>Quarter: 39–40 weeks</td>
</tr>
<tr>
<td>Quarter: &gt;40 weeks</td>
</tr>
<tr>
<td>Maternal age</td>
</tr>
<tr>
<td>&lt;25 years</td>
</tr>
<tr>
<td>25–29 years</td>
</tr>
<tr>
<td>30–34 years</td>
</tr>
<tr>
<td>≥35 years</td>
</tr>
<tr>
<td>Maternal basic education</td>
</tr>
<tr>
<td>Less than high school</td>
</tr>
<tr>
<td>High school graduate</td>
</tr>
<tr>
<td>Maternal smoking during pregnancy</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No information</td>
</tr>
<tr>
<td>Mode of delivery</td>
</tr>
<tr>
<td>Vaginal delivery</td>
</tr>
<tr>
<td>Forceps or suction</td>
</tr>
<tr>
<td>Caesarean section</td>
</tr>
<tr>
<td>Number of siblings</td>
</tr>
<tr>
<td>None</td>
</tr>
<tr>
<td>One</td>
</tr>
<tr>
<td>Two or more</td>
</tr>
<tr>
<td>Parental asthma</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No information</td>
</tr>
<tr>
<td>Parental allergic rhinitis</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No information</td>
</tr>
<tr>
<td>Atopic eczema by 6 months of age</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>Pets at home during the first year</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
</tr>
</tbody>
</table>

* Based on the t test or ANOVA.
As a prospective study, the determination of dietary intake before the emergence of the outcomes ensured minimising bias related to the selection of the subjects. The FFQ used in the present study was validated and is suitable for the assessment of dietary intake among childbearing Finnish women. The rationale for the dietary assessment was to get a general picture of the diet of the mothers during the first 8 months of pregnancy. We assumed that by assessing the maternal diet during the month preceding the maternity leave (i.e. the 8th month of pregnancy), we obtained a more appropriate overall picture of the maternal diet during pregnancy than by assessing it over the period of the last month before delivery (the 9th month) when most of the mothers did not work outside the home any longer. Dietary measurement error is most consequential if a proportion of subjects are misclassified according to the exposure. There are three recommended validity estimates for nutrients of interest in epidemiological studies: Spearman's correlation coefficients should be above 0.5; more than 50% of subjects should be correctly classified; less than 10% of subjects should be grossly misclassified into thirds. In terms of dietary fats, the greatest misclassifications were found for MUFA (9% of the subjects grossly misclassified). Although biomarker assessments represent a precise estimate of the FA, they are limited by being unable to assess the long-term nutrient status. In this case, the FFQ is beneficial, since long-term and habitual intake can be measured. By assessing maternal dietary intake during the 8th month of pregnancy, we aimed at estimating the overall picture of maternal diet during the first 8 months of pregnancy. Although some seasonal variations have been observed in maternal diet during pregnancy as a result of fluctuations in nutrient intakes, it has been suggested that such changes may be difficult to accurately detect with the rather imprecise dietary assessment methods currently available. Consequently, our generalisation of maternal dietary intake during the 8th month to the whole pregnancy period may remain only a rough approximation. In order to improve the classification of dietary fats, the grouping and brand names of spreads in our FFQ are continuously checked and updated. Most importantly, the overall quintile notation was acceptable for all FA.

There is considerable heterogeneity in respiratory symptoms among children. Consequently, we found associations between FA and rhinitis but not with eczema and wheeze. We lack the knowledge on the mechanisms and the optimal timing of exposure to lower or higher FA levels to influence the development of the different allergic diseases. To exclude younger children having transient respiratory symptoms related to viral infections, the endpoints in the present study were measured in subjects aged 5 years. Because of the lack of data, the child's fat and/or fatty acid intake was not included into our models as a possible confounding factor; thus, we cannot totally rule out that the present results might not have been influenced by dietary intake during infancy. Previous findings have suggested that processes leading to allergic diseases can be initiated very early in the immune development. The complex relationship between early nutrition and allergic outcomes emphasises background characteristics of the study population either in absolute or relative terms, except for the place of birth: those from Southern Finland were slightly more likely not to take part in the study (10%) than those from Northern Finland (4%; \( P<0.001 \)). The mean total daily intake of energy for participating mothers was 11,386 (SD 3148) kJ. Protein accounted for 16% (mean intake 110 g; SD 31), fat for 35% (105 g; SD 34) and total carbohydrates for 49% (325 g; SD 95) of the total energy intake. The mean total daily intake of SFA was 45 (SD 17) g, MUFA 37 (SD 12) g, n-3 PUFA 3-2 (SD 1-3) g and n-6 PUFA 10-8 (SD 4-0) g. None of the women was taking fatty acid supplements during pregnancy.

Significantly higher mean daily intake of n-3 PUFA was seen among women over 35 years of age, women with high school degree, children with one sibling and children without parental asthma (Table 1). A higher intake of n-6 PUFA was seen among those from Southern Finland, women with high school degree, women who smoked during pregnancy and among children with one sibling. Duration of gestation for more than 40 weeks and having a pet at home during the first year of the child were associated with a decreased risk of atopic eczema, whereas children with parental asthma and rhinitis were at increased risk of atopic eczema. A decreased risk of allergic rhinitis was seen among girls, while children with parental asthma, those with parental rhinitis and those who had atopic eczema by 6 months of age appeared to have an increased risk of rhinitis. Increasing maternal age was associated with decreased risk, whereas increasing number of siblings increased the risk of wheeze (Table 2).

After adjusting for potential confounders, none of the dietary fats or FA was significantly associated with atopic eczema and wheeze. For allergic rhinitis, high maternal consumption of butter and butter spreads was associated with an increased risk of the emergence of allergic rhinitis in the offspring by the age of 5 years (Table 3). A higher ratio of n-6:n-3 FA during pregnancy was associated with an increased risk of allergic rhinitis (Table 4). On the other hand, a decreased risk of allergic rhinitis was observed with high intakes of total PUFA and α-linolenic FA (Table 4). These results did not change in the models adjusted additionally for the effect of vitamin C, Zn, Se, vitamin D and vitamin E (Table 5). However, after a Bonferroni correction for multiple comparisons, these results lost their statistical significance.

**Discussion**

The results from the present study show that high maternal consumption of butter and higher ratio of n-6:n-3 FA during pregnancy were associated with an increased risk of allergic rhinitis in the offspring by the age of 5 years. Conversely, high maternal intake of total PUFA and α-linolenic FA was associated with a decreased risk of rhinitis in the offspring. Adjustment for the effects of vitamin C, Zn, Se, vitamin D and vitamin E did not alter these results, but the results were no longer significant after correction for multiple comparisons.
Table 2. Relationship of characteristics of the participating children (n 2441) to the incidence of atopic eczema, allergic rhinitis and wheeze by 5 years of age
(Number of participants, percentages, odds ratios, hazard ratios and 95 % confidence intervals)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency (all)</th>
<th>Atopic eczema endpoints</th>
<th>Atopic eczema</th>
<th>Allergic rhinitis endpoints</th>
<th>Allergic rhinitis</th>
<th>Wheeze endpoints</th>
<th>Wheeze</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>OR 95 % CI</td>
<td>n</td>
<td>%</td>
<td>Hazard ratio 95 % CI</td>
<td>n</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>1272</td>
<td>52</td>
<td>480 38</td>
<td>1</td>
<td>212 17</td>
<td>1</td>
<td>338</td>
</tr>
<tr>
<td>Girls</td>
<td>1169</td>
<td>48</td>
<td>446 38</td>
<td>1-02</td>
<td>0-86, 1-20</td>
<td>147 13</td>
<td>292</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P=0-857</td>
<td></td>
<td></td>
<td>P=0-004</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Delivery hospital</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oulu (Northern Finland)</td>
<td>855</td>
<td>35</td>
<td>341 40</td>
<td>1</td>
<td>119 14</td>
<td>1</td>
<td>212</td>
</tr>
<tr>
<td>Tampere (Southern Finland)</td>
<td>1586</td>
<td>65</td>
<td>585 37</td>
<td>0-88</td>
<td>0-74, 1-05</td>
<td>240 15</td>
<td>438</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P=0-450</td>
<td></td>
<td></td>
<td>P=0-027</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration of gestation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quarter: &lt;38-90 weeks</td>
<td>597</td>
<td>25</td>
<td>235 39</td>
<td>1</td>
<td>79 13</td>
<td>1</td>
<td>171</td>
</tr>
<tr>
<td>Quarter: 39-00-39-90 weeks</td>
<td>565</td>
<td>23</td>
<td>205 36</td>
<td>0-86</td>
<td>0-68, 1-09</td>
<td>85 15</td>
<td>153</td>
</tr>
<tr>
<td>Quarter: 40-00-40-70 weeks</td>
<td>614</td>
<td>25</td>
<td>265 43</td>
<td>1-16</td>
<td>0-92, 1-46</td>
<td>99 16</td>
<td>152</td>
</tr>
<tr>
<td>Quarter: &gt;40-70 weeks</td>
<td>646</td>
<td>27</td>
<td>216 33</td>
<td>0-78</td>
<td>0-61, 0-98</td>
<td>95 15</td>
<td>179</td>
</tr>
<tr>
<td><strong>Maternal age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25 years</td>
<td>361</td>
<td>15</td>
<td>131 36</td>
<td>1</td>
<td>57 16</td>
<td>1</td>
<td>117</td>
</tr>
<tr>
<td>25–29 years</td>
<td>871</td>
<td>36</td>
<td>352 40</td>
<td>1-20</td>
<td>0-93, 1-55</td>
<td>127 15</td>
<td>227</td>
</tr>
<tr>
<td>30–34 years</td>
<td>751</td>
<td>31</td>
<td>289 38</td>
<td>1-10</td>
<td>0-84, 1-42</td>
<td>114 15</td>
<td>179</td>
</tr>
<tr>
<td>≥35 years</td>
<td>458</td>
<td>19</td>
<td>154 33</td>
<td>0-89</td>
<td>0-67, 1-19</td>
<td>61 13</td>
<td>127</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P=0-326</td>
<td></td>
<td></td>
<td>P=0-124</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Maternal basic education</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>834</td>
<td>34</td>
<td>315 38</td>
<td>1</td>
<td>132 16</td>
<td>1</td>
<td>219</td>
</tr>
<tr>
<td>High school graduate</td>
<td>1558</td>
<td>64</td>
<td>594 38</td>
<td>1-01</td>
<td>0-85, 1-20</td>
<td>220 14</td>
<td>414</td>
</tr>
<tr>
<td>Missing</td>
<td>49</td>
<td>2</td>
<td>17 35</td>
<td>1</td>
<td>7 12</td>
<td></td>
<td>17</td>
</tr>
<tr>
<td><strong>Maternal smoking during pregnancy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2177</td>
<td>89</td>
<td>830 38</td>
<td>1</td>
<td>325 15</td>
<td>1</td>
<td>581</td>
</tr>
<tr>
<td>Yes</td>
<td>29</td>
<td>1</td>
<td>80 28</td>
<td>0-61</td>
<td>0-27, 1-38</td>
<td>6 21</td>
<td>4 26</td>
</tr>
<tr>
<td>No information</td>
<td>194</td>
<td>8</td>
<td>77 40</td>
<td>1-06</td>
<td>0-78, 1-43</td>
<td>24 12</td>
<td>49</td>
</tr>
<tr>
<td>Missing</td>
<td>41</td>
<td>2</td>
<td>11 27</td>
<td>1</td>
<td>4 10</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td><strong>Mode of delivery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>1959</td>
<td>80</td>
<td>759 39</td>
<td>1</td>
<td>279 14</td>
<td>1</td>
<td>508</td>
</tr>
<tr>
<td>Forceps or suction</td>
<td>158</td>
<td>6</td>
<td>57 36</td>
<td>0-89</td>
<td>0-63, 1-25</td>
<td>33 21</td>
<td>46</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>309</td>
<td>13</td>
<td>107 35</td>
<td>0-84</td>
<td>0-65, 1-08</td>
<td>47 15</td>
<td>94</td>
</tr>
<tr>
<td>Missing</td>
<td>15</td>
<td>1</td>
<td>4 27</td>
<td>0</td>
<td>0 0</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td><strong>Number of siblings</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1122</td>
<td>46</td>
<td>427 38</td>
<td>1</td>
<td>177 16</td>
<td>1</td>
<td>314</td>
</tr>
<tr>
<td>One</td>
<td>750</td>
<td>31</td>
<td>296 39</td>
<td>1-08</td>
<td>0-89, 1-30</td>
<td>101 14</td>
<td>181</td>
</tr>
<tr>
<td>Two or more</td>
<td>546</td>
<td>22</td>
<td>197 36</td>
<td>0-93</td>
<td>0-75, 1-15</td>
<td>79 16</td>
<td>150</td>
</tr>
<tr>
<td>Missing</td>
<td>23</td>
<td>1</td>
<td>6 26</td>
<td>2</td>
<td>2 9</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td><strong>Parental asthma</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2004</td>
<td>82</td>
<td>716 36</td>
<td>1</td>
<td>269 13</td>
<td>1</td>
<td>486</td>
</tr>
<tr>
<td>Yes</td>
<td>381</td>
<td>16</td>
<td>185 49</td>
<td>1-70</td>
<td>1-36, 2-12</td>
<td>81 21</td>
<td>149</td>
</tr>
<tr>
<td>No information</td>
<td>33</td>
<td>1</td>
<td>15 45</td>
<td>1-56</td>
<td>0-78, 3-15</td>
<td>5 15</td>
<td>8</td>
</tr>
<tr>
<td>Missing</td>
<td>23</td>
<td>1</td>
<td>10 43</td>
<td>1</td>
<td>4 17</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td><strong>Parental allergic rhinitis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>797</td>
<td>33</td>
<td>227 28</td>
<td>1</td>
<td>61 8</td>
<td>1</td>
<td>150</td>
</tr>
<tr>
<td>Yes</td>
<td>1512</td>
<td>62</td>
<td>650 43</td>
<td>1-92</td>
<td>1-59, 2-31</td>
<td>280 19</td>
<td>462</td>
</tr>
<tr>
<td>No information</td>
<td>109</td>
<td>4</td>
<td>43 39</td>
<td>1-68</td>
<td>1-11, 2-54</td>
<td>16 15</td>
<td>35</td>
</tr>
<tr>
<td>Missing</td>
<td>23</td>
<td>1</td>
<td>6 26</td>
<td>2</td>
<td>9</td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>
the need for consistent and thorough assessment of maternal
diets throughout the duration of pregnancy and the child's
diet throughout early years. However, duration of exclusive
and total breast-feeding has not been related to allergic out-
comes in our cohort.

After adjusting for multiple comparisons, the results no
longer achieved statistical significance. Therefore, we suggest
cautions in the interpretation of the present findings. However,
we note that the hypotheses linking each of the FA and
allergies are mixed, and the precise mechanisms of the role
of fatty acids on the occurrence of allergies are not clearly
elucidated. Consequently, we believe that each of the associ-
ations between the studied FA and the allergic outcomes
should be judged on its own merit. Furthermore, the limited
and conflicting reports in this area of research signify that
reproducibility of these results in further studies would be
crucial to rule out any chance finding.

The genetic susceptibility to type 1 diabetes of our study
subjects may constrain the generalisability of the present
results. Type 1 diabetes is associated with T helper cell 1
(Th1) immune responses, while allergic diseases are related
to T helper cell 2 (Th2)-type responses (24). In addition to the
complexities surrounding the components of the immune
system that relate to the generation of Th1 and Th2 responses,
it is inconclusive how type 1 diabetes and allergies may be
associated (25). However, the cumulative incidence of allergies
in the present study paralleled that observed in the general
Finnish population (17,26). Furthermore, our subjects were
unselected in terms of history of allergy, thus minimising
bias towards more selection of children with a positive history
for allergic diseases. Participants in the present allergy
study were generally not systematically different from non-
participating women regarding the background characteristics,
suggesting that differential loss to follow-up was minimised
in the present study.

The immunological properties of FA have been elabo-
rated (3,27), particularly that of the n-3 and n-6 families,
which represent the most widely studied FA. While
n-6 PUFA may possess pro-inflammatory properties, n-3 PUFA
are thought to act as anti-inflammatory mediators (27,28).
These effects may be prominent during fetal and early life,
emphasising the consequences of maternal intake of FA
during pregnancy (29,30). In the present study, while both n-6
and n-3 PUFA were not appreciably related to the outcomes,
total PUFA and α-linolenic FA, however, were associated
with a decreased risk of rhinitis. In addition to our present
findings, our earlier report has shown an unclear association
between maternal intake of PUFA during pregnancy and aller-
gen-specific IgE sensitisation in the offspring in a different
subject series of this cohort (31). In a Japanese study, maternal
intake of α-linolenic acid during pregnancy was associated
with a reduced risk of wheezing in 2-year-old children (32).
Also, consistent with the present findings, no association
was seen between any of the FA and suspected eczema
in the Japanese children at the age of 3–4 months (33).
The younger age of children in the Japanese cohort makes it likely that their wheezing symptoms may be a
result of viral infections, which are usually unrelated to

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Wheeze endpoints</th>
<th>Allergic rhinitis endpoints</th>
<th>Atopic eczema by 6 months of age</th>
<th>Pets at home during the first year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2441</td>
<td>100</td>
<td>926</td>
<td>100</td>
</tr>
<tr>
<td>Frequency (all)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atopic eczema by 6 months of age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2007</td>
<td>82%</td>
<td>384</td>
<td>384</td>
</tr>
<tr>
<td>Yes</td>
<td>1034</td>
<td>25%</td>
<td>514</td>
<td>514</td>
</tr>
<tr>
<td>%</td>
<td>35%</td>
<td></td>
<td>35%</td>
<td></td>
</tr>
<tr>
<td>Pets at home during the first year</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1547</td>
<td>60%</td>
<td>384</td>
<td>384</td>
</tr>
<tr>
<td>Yes</td>
<td>894</td>
<td>40%</td>
<td>514</td>
<td>514</td>
</tr>
<tr>
<td>%</td>
<td>40%</td>
<td></td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>0-12 months of age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1547</td>
<td>60%</td>
<td>384</td>
<td>384</td>
</tr>
<tr>
<td>Yes</td>
<td>894</td>
<td>40%</td>
<td>514</td>
<td>514</td>
</tr>
<tr>
<td>%</td>
<td>40%</td>
<td></td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>13-24 months of age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1224</td>
<td>60%</td>
<td>312</td>
<td>312</td>
</tr>
<tr>
<td>Yes</td>
<td>824</td>
<td>40%</td>
<td>504</td>
<td>504</td>
</tr>
<tr>
<td>%</td>
<td>40%</td>
<td></td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>0-12 months of age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1547</td>
<td>60%</td>
<td>384</td>
<td>384</td>
</tr>
<tr>
<td>Yes</td>
<td>894</td>
<td>40%</td>
<td>514</td>
<td>514</td>
</tr>
<tr>
<td>%</td>
<td>40%</td>
<td></td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>13-24 months of age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1224</td>
<td>60%</td>
<td>312</td>
<td>312</td>
</tr>
<tr>
<td>Yes</td>
<td>824</td>
<td>40%</td>
<td>504</td>
<td>504</td>
</tr>
<tr>
<td>%</td>
<td>40%</td>
<td></td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2441</td>
<td>100</td>
<td>926</td>
<td>100</td>
</tr>
<tr>
<td>Frequency (all)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>100%</td>
<td></td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Atopic eczema at 6 months of age</td>
<td>0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazard ratio</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.13</td>
<td></td>
<td>1.13</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.15</td>
<td></td>
<td>1.15</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>100%</td>
<td></td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Pets at home during the first year</td>
<td>0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazard ratio</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.13</td>
<td></td>
<td>1.13</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.15</td>
<td></td>
<td>1.15</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>100%</td>
<td></td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>
Table 3. Association between maternal consumption of dietary fats during pregnancy and prevalence of atopic eczema and incidence of allergic rhinitis and wheeze in 5-year-old children

(Hazard ratios (HR), odds ratios and 95% confidence intervals)

<table>
<thead>
<tr>
<th>Food variables</th>
<th>Atopic eczema</th>
<th>Allergic rhinitis</th>
<th>Wheeze</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted†</td>
<td>Adjusted‡</td>
<td>Unadjusted†</td>
</tr>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
<td>HR</td>
</tr>
<tr>
<td>Butter and butter spreads</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 4·72 g/d)</td>
<td>0·91</td>
<td>0·74, 1·11</td>
<td>1·10</td>
</tr>
<tr>
<td>Second and third quarters (4·7–19·82 g/d)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fourth quarter (19·83–128·38 g/d)</td>
<td>1·09</td>
<td>0·89, 1·34</td>
<td>1·42*</td>
</tr>
<tr>
<td>Industrial fats§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 4·84 g/d)</td>
<td>0·96</td>
<td>0·78, 1·17</td>
<td>0·81</td>
</tr>
<tr>
<td>Second and third quarters (4·85–10·85 g/d)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fourth quarter (10·86–115·93 g/d)</td>
<td>0·94</td>
<td>0·75, 1·17</td>
<td>0·91</td>
</tr>
<tr>
<td>Margarines</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-consumers</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Consumers (0·06–120 g/d)</td>
<td>0·92</td>
<td>0·78, 1·09</td>
<td>0·88</td>
</tr>
<tr>
<td>Oils</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 7·25 g/d)</td>
<td>0·98</td>
<td>0·80, 1·20</td>
<td>0·92</td>
</tr>
<tr>
<td>Second and third quarters (7·25–16·37 g/d)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fourth quarter (16·38–145·00 g/d)</td>
<td>0·97</td>
<td>0·80, 1·19</td>
<td>0·79</td>
</tr>
</tbody>
</table>

* P < 0·05.
† Total energy included in the model.
‡ Adjusted for total energy, sex of child, hospital of birth, duration of gestation, maternal age at delivery, maternal basic education, maternal smoking during pregnancy, mode of delivery, number of siblings at the time of the child’s birth, parental asthma, parental allergic rhinitis, pets at home by 1 year of age.
§ Industrial fats: industrial fat mixes and animal fats (grease, suet, lard).
### Table 4. Association between maternal fatty acid intake during pregnancy and prevalence of atopic eczema and incidence of allergic rhinitis and wheeze in 5-year-old children

(Hazard ratios (HR), odds ratios and 95% confidence intervals)

<table>
<thead>
<tr>
<th>Fatty acids</th>
<th>OR (Unadjusted)</th>
<th>95% CI</th>
<th>OR (Adjusted model †)</th>
<th>OR (Adjusted model †)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atopic eczema</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total fatty acids</td>
<td>0.89</td>
<td>0.72, 1.09</td>
<td>0.84</td>
<td>0.68, 1.04</td>
</tr>
<tr>
<td>First quarter (&lt; 196.85 g/d)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second and third quarters (196.85–280.83 g/d)</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fourth quarter (280.84–299.25 g/d)</td>
<td>1.03</td>
<td>0.85, 1.26</td>
<td>1.04</td>
<td>0.84, 1.28</td>
</tr>
<tr>
<td>SFA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 82.24 g/d)</td>
<td>1.01</td>
<td>0.83, 1.24</td>
<td>0.99</td>
<td>0.80, 1.23</td>
</tr>
<tr>
<td>Second and third quarters (82.24–118.56 g/d)</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fourth quarter (118.57–145.84 g/d)</td>
<td>1.04</td>
<td>0.85, 1.27</td>
<td>1.03</td>
<td>0.84, 1.27</td>
</tr>
<tr>
<td>Trans-fatty acids</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 3.10 g/d)</td>
<td>0.95</td>
<td>0.78, 1.16</td>
<td>0.84</td>
<td>0.68, 1.04</td>
</tr>
<tr>
<td>Second and third quarters (3.10–4.18 g/d)</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fourth quarter (4.19–7.73 g/d)</td>
<td>0.78*</td>
<td>0.62, 0.99</td>
<td>1.08</td>
<td>0.88, 1.33</td>
</tr>
<tr>
<td>MUFAs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 78.05 g/d)</td>
<td>0.94</td>
<td>0.77, 1.15</td>
<td>0.90</td>
<td>0.73, 1.11</td>
</tr>
<tr>
<td>Second and third quarters (78.05–93.52 g/d)</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fourth quarter (93.53–104.16 g/d)</td>
<td>0.98</td>
<td>0.81, 1.20</td>
<td>0.98</td>
<td>0.80, 1.21</td>
</tr>
<tr>
<td>PUFA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 22.90 g/d)</td>
<td>1.02</td>
<td>0.83, 1.25</td>
<td>0.94</td>
<td>0.76, 1.17</td>
</tr>
<tr>
<td>Second and third quarters (22.90–32.46 g/d)</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fourth quarter (32.47–59.37 g/d)</td>
<td>1.00</td>
<td>0.82, 1.22</td>
<td>1.03</td>
<td>0.83, 1.27</td>
</tr>
<tr>
<td>Ratio of n-6 to n-3 PUFA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter</td>
<td>0.97</td>
<td>0.80, 1.19</td>
<td>0.99</td>
<td>0.80, 1.22</td>
</tr>
<tr>
<td>Second and third quarters (3.10–4.18 g/d)</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fourth quarter (4.19–7.73 g/d)</td>
<td>0.78*</td>
<td>0.62, 0.99</td>
<td>1.08</td>
<td>0.88, 1.33</td>
</tr>
<tr>
<td>n-6 PUFA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 19.32 g/d)</td>
<td>1.03</td>
<td>0.85, 1.26</td>
<td>0.97</td>
<td>0.78, 1.20</td>
</tr>
<tr>
<td>Second and third quarters (19.32–24.50 g/d)</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fourth quarter (24.51–49.23 g/d)</td>
<td>1.10</td>
<td>0.90, 1.35</td>
<td>1.15</td>
<td>0.93, 1.43</td>
</tr>
<tr>
<td>Linoleic fatty acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 18.64 g/d)</td>
<td>1.05</td>
<td>0.86, 1.28</td>
<td>0.98</td>
<td>0.79, 1.21</td>
</tr>
<tr>
<td>Second and third quarters (18.64–23.87 g/d)</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fourth quarter (23.87–47.75 g/d)</td>
<td>1.14</td>
<td>0.93, 1.39</td>
<td>1.17</td>
<td>0.95, 1.45</td>
</tr>
<tr>
<td>Linoleic fatty acid, conjugated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 0.38 g/d)</td>
<td>0.96</td>
<td>0.79, 1.18</td>
<td>0.93</td>
<td>0.75, 1.15</td>
</tr>
<tr>
<td>Second and third quarters (0.38–0.54 g/d)</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fourth quarter (0.54–0.75 g/d)</td>
<td>1.01</td>
<td>0.83, 1.23</td>
<td>1.01</td>
<td>0.82, 1.24</td>
</tr>
<tr>
<td>Arachidonic fatty acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 0.14 g/d)</td>
<td>1.03</td>
<td>0.85, 1.27</td>
<td>1.02</td>
<td>0.82, 1.26</td>
</tr>
<tr>
<td>Second and third quarters (0.14–0.20 g/d)</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fourth quarter (0.20–0.44 g/d)</td>
<td>1.04</td>
<td>0.86, 1.27</td>
<td>1.02</td>
<td>0.83, 1.25</td>
</tr>
<tr>
<td>n-3 PUFA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 5.55 g/d)</td>
<td>1.08</td>
<td>0.88, 1.32</td>
<td>1.03</td>
<td>0.84, 1.27</td>
</tr>
<tr>
<td>Second and third quarters (5.55–7.34 g/d)</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

--

*Significant at the 0.05 level.
**Table 4. Continued**

<table>
<thead>
<tr>
<th>Fatty acids</th>
<th>( \text{OR} )</th>
<th>95 % CI</th>
<th>( \text{OR} )</th>
<th>95 % CI</th>
<th>( \text{HR} )</th>
<th>95 % CI</th>
<th>( \text{HR} )</th>
<th>95 % CI</th>
<th>( \text{HR} )</th>
<th>95 % CI</th>
<th>( \text{HR} )</th>
<th>95 % CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atopic eczema</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fourth quarter (7·35–11·28 g/d)</td>
<td>0·94</td>
<td>0·77, 1·15</td>
<td>0·93</td>
<td>0·75, 1·14</td>
<td>0·78</td>
<td>0·60, 1·02</td>
<td>0·82</td>
<td>0·63, 1·08</td>
<td>0·95</td>
<td>0·75, 1·21</td>
<td>1·11</td>
<td>0·85, 1·43</td>
</tr>
<tr>
<td>n-3 PUFA from fish‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt;0·38 g/d)</td>
<td>1·16</td>
<td>0·95, 1·42</td>
<td>1·16</td>
<td>0·93, 1·43</td>
<td>0·99</td>
<td>0·77, 1·30</td>
<td>0·99</td>
<td>0·76, 1·30</td>
<td>1·15</td>
<td>0·92, 1·45</td>
<td>1·08</td>
<td>0·85, 1·38</td>
</tr>
<tr>
<td>Second and third quarters (0·38–0·98 g/d)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fourth quarter (0·99–5·50 g/d)</td>
<td>0·96</td>
<td>0·79, 1·18</td>
<td>0·97</td>
<td>0·79, 1·20</td>
<td>0·91</td>
<td>0·71, 1·17</td>
<td>0·94</td>
<td>0·72, 1·22</td>
<td>0·95</td>
<td>0·75, 1·20</td>
<td>0·95</td>
<td>0·74, 1·22</td>
</tr>
<tr>
<td>n-3 PUFA from plants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt;4·79 g/d)</td>
<td>1·02</td>
<td>0·83, 1·24</td>
<td>0·97</td>
<td>0·78, 1·19</td>
<td>1·02</td>
<td>0·80, 1·30</td>
<td>0·97</td>
<td>0·75, 1·25</td>
<td>0·86</td>
<td>0·69, 1·08</td>
<td>0·94</td>
<td>0·74, 1·19</td>
</tr>
<tr>
<td>Second and third quarters (4·79–6·27 g/d)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fourth quarter (6·28–8·97 g/d)</td>
<td>0·93</td>
<td>0·76, 1·14</td>
<td>0·92</td>
<td>0·74, 1·14</td>
<td>0·80</td>
<td>0·61, 1·04</td>
<td>0·79</td>
<td>0·60, 1·05</td>
<td>0·88</td>
<td>0·69, 1·11</td>
<td>0·94</td>
<td>0·73, 1·21</td>
</tr>
<tr>
<td>α-Linolenic fatty acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt;4·45 g/d)</td>
<td>1·08</td>
<td>0·89, 1·32</td>
<td>1·05</td>
<td>0·86, 1·30</td>
<td>1·06</td>
<td>0·83, 1·35</td>
<td>1·01</td>
<td>0·79, 1·29</td>
<td>0·79</td>
<td>0·63, 0·99</td>
<td>0·87</td>
<td>0·69, 1·11</td>
</tr>
<tr>
<td>Second and third quarters (4·45–6·40 g/d)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fourth quarter (6·40–8·90 g/d)</td>
<td>1·01</td>
<td>0·83, 1·23</td>
<td>0·99</td>
<td>0·80, 1·23</td>
<td>0·74*</td>
<td>0·56, 0·97</td>
<td>0·74*</td>
<td>0·56, 0·99</td>
<td>0·87</td>
<td>0·69, 1·08</td>
<td>0·95</td>
<td>0·74, 1·22</td>
</tr>
<tr>
<td>EPA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt;0·07 g/d)</td>
<td>1·09</td>
<td>0·89, 1·34</td>
<td>1·07</td>
<td>0·86, 1·33</td>
<td>1·02</td>
<td>0·79, 1·32</td>
<td>0·99</td>
<td>0·76, 1·30</td>
<td>1·05</td>
<td>0·83, 1·29</td>
<td>1·01</td>
<td>0·79, 1·29</td>
</tr>
<tr>
<td>Second and third quarters (0·07–0·23 g/d)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fourth quarter (0·23–1·25 g/d)</td>
<td>0·96</td>
<td>0·78, 1·17</td>
<td>0·94</td>
<td>0·76, 1·16</td>
<td>1·00</td>
<td>0·78, 1·29</td>
<td>0·99</td>
<td>0·76, 1·28</td>
<td>0·97</td>
<td>0·77, 1·23</td>
<td>0·98</td>
<td>0·76, 1·26</td>
</tr>
<tr>
<td>DHA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt;0·19 g/d)</td>
<td>1·21</td>
<td>0·99, 1·48</td>
<td>1·18</td>
<td>0·95, 1·46</td>
<td>1·00</td>
<td>0·78, 1·29</td>
<td>0·94</td>
<td>0·72, 1·22</td>
<td>1·10</td>
<td>0·87, 1·38</td>
<td>1·06</td>
<td>0·83, 1·36</td>
</tr>
<tr>
<td>Second and third quarters (0·19–0·60 g/d)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fourth quarter (0·60–3·5 g/d)</td>
<td>0·98</td>
<td>0·81, 1·20</td>
<td>0·98</td>
<td>0·79, 1·20</td>
<td>0·94</td>
<td>0·73, 1·21</td>
<td>0·93</td>
<td>0·72, 1·21</td>
<td>0·94</td>
<td>0·74, 1·19</td>
<td>0·93</td>
<td>0·73, 1·20</td>
</tr>
</tbody>
</table>

* \( P<0·05. \)

† Adjusted for sex of child, hospital of birth, duration of gestation, maternal age at delivery, maternal basic education, maternal smoking during pregnancy, mode of delivery, number of siblings at the time of the child’s birth, parental asthma, parental allergic rhinitis, pets at home by 1 year of age.

‡ n-3 PUFA from fish is a summary variable including all n-3 fatty acids from fish and fish products.
Table 5. Association between maternal fatty acid intake during pregnancy and prevalence of atopic eczema and incidence of allergic rhinitis and wheeze in 5-year-old children

<table>
<thead>
<tr>
<th>Fatty acids</th>
<th>Atopic eczema</th>
<th>Allergic rhinitis</th>
<th>Wheeze</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted model II†</td>
<td>Adjusted model II†</td>
<td>Adjusted model II†</td>
</tr>
<tr>
<td></td>
<td>OR 95 % CI</td>
<td>HR 95 % CI</td>
<td>OR 95 % CI</td>
</tr>
<tr>
<td>Total fatty acids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 196-85 g/d)</td>
<td>0·84</td>
<td>0·94</td>
<td>1·09</td>
</tr>
<tr>
<td>Second and third quarters (196-85—280-83 g/d)</td>
<td>1·03</td>
<td>0·96</td>
<td>0·93</td>
</tr>
<tr>
<td>Fourth quarter (280-84—299-25 g/d)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SFA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 82-24 g/d)</td>
<td>1·00</td>
<td>1·08</td>
<td>1·0</td>
</tr>
<tr>
<td>Second and third quarters (82-24—118-56 g/d)</td>
<td>1·0</td>
<td></td>
<td>1·0</td>
</tr>
<tr>
<td>Fourth quarter (118-57—145-84 g/d)</td>
<td>1·00</td>
<td>0·76</td>
<td>0·77</td>
</tr>
<tr>
<td>Trans-fatty acids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 3-10 g/d)</td>
<td>0·84</td>
<td>0·98</td>
<td>1·08</td>
</tr>
<tr>
<td>Second and third quarters (3-10—4-18 g/d)</td>
<td>1·07</td>
<td></td>
<td>0·80</td>
</tr>
<tr>
<td>Fourth quarter (4-19—7-73 g/d)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MUFA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 78-05 g/d)</td>
<td>0·90</td>
<td>0·90</td>
<td>1·02</td>
</tr>
<tr>
<td>Second and third quarters (78-05—93-52 g/d)</td>
<td>1·0</td>
<td></td>
<td>0·79</td>
</tr>
<tr>
<td>Fourth quarter (93-53—104-16 g/d)</td>
<td>0·97</td>
<td>0·73</td>
<td>1·08</td>
</tr>
<tr>
<td>PUFAs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 22-90 g/d)</td>
<td>0·92</td>
<td>0·81</td>
<td>0·92</td>
</tr>
<tr>
<td>Second and third quarters (22-90—32-46 g/d)</td>
<td>1·0</td>
<td></td>
<td>0·70</td>
</tr>
<tr>
<td>Fourth quarter (32-47—59-37 g/d)</td>
<td>0·71*</td>
<td>0·52</td>
<td>1·09</td>
</tr>
<tr>
<td>Ratio of n-6 to n-3 PUFAs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter</td>
<td>1·00</td>
<td>1·0</td>
<td>0·86</td>
</tr>
<tr>
<td>Second and third quarters</td>
<td>1·0</td>
<td></td>
<td>0·66</td>
</tr>
<tr>
<td>Fourth quarter</td>
<td>1·01</td>
<td>1·37*</td>
<td>0·84</td>
</tr>
<tr>
<td>n-6 PUFAs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 19-32 g/d)</td>
<td>0·92</td>
<td>0·82</td>
<td>1·0</td>
</tr>
<tr>
<td>Second and third quarters (19-32—24-50 g/d)</td>
<td>1·0</td>
<td></td>
<td>0·76</td>
</tr>
<tr>
<td>Fourth quarter (24-51—49-23 g/d)</td>
<td>0·83</td>
<td>0·62</td>
<td>1·17</td>
</tr>
<tr>
<td>Linoleic fatty acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 18-64 g/d)</td>
<td>0·94</td>
<td>0·85</td>
<td>1·0</td>
</tr>
<tr>
<td>Second and third quarters (18-64—23-87 g/d)</td>
<td>1·21</td>
<td></td>
<td>0·76</td>
</tr>
<tr>
<td>Fourth quarter (23-87—47-75 g/d)</td>
<td>0·81</td>
<td>0·60</td>
<td>1·05</td>
</tr>
<tr>
<td>Linoleic fatty acid, conjugated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 0-38 g/d)</td>
<td>0·94</td>
<td>1·00</td>
<td>0·97</td>
</tr>
<tr>
<td>Second and third quarters (0-38—0-54 g/d)</td>
<td>1·0</td>
<td></td>
<td>0·97</td>
</tr>
<tr>
<td>Fourth quarter (0-54—0-75 g/d)</td>
<td>0·91</td>
<td>0·70</td>
<td>0·84</td>
</tr>
<tr>
<td>n-Linolenic fatty acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 0-11 g/d)</td>
<td>0·91</td>
<td>0·82</td>
<td>1·22</td>
</tr>
<tr>
<td>Second and third quarters (0-11—0-16 g/d)</td>
<td>1·06</td>
<td></td>
<td>0·95</td>
</tr>
<tr>
<td>Fourth quarter (0-16—0-98 g/d)</td>
<td>0·80</td>
<td>0·60</td>
<td>0·97</td>
</tr>
<tr>
<td>Arachidonic fatty acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 0-14 g/d)</td>
<td>0·98</td>
<td>0·80</td>
<td>0·98</td>
</tr>
<tr>
<td>Second and third quarters (0-14—0-20 g/d)</td>
<td>1·06</td>
<td></td>
<td>0·74</td>
</tr>
<tr>
<td>Fourth quarter (0-20—0-44 g/d)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n-3 PUFAs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 5-55 g/d)</td>
<td>1·03</td>
<td>0·84</td>
<td>0·97</td>
</tr>
<tr>
<td>Second and third quarters (5-55—7-34 g/d)</td>
<td>1·0</td>
<td></td>
<td>0·75</td>
</tr>
<tr>
<td>Fourth quarter (7-35—11-28 g/d)</td>
<td>0·91</td>
<td>0·64</td>
<td>1·14</td>
</tr>
<tr>
<td>n-3 PUFAs from fish</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 0-38 g/d)</td>
<td>1·13</td>
<td>0·91</td>
<td>1·08</td>
</tr>
<tr>
<td>Second and third quarters (0-38—0-98 g/d)</td>
<td>1·01</td>
<td></td>
<td>0·84</td>
</tr>
<tr>
<td>Fourth quarter (0-99—5-50 g/d)</td>
<td>1·00</td>
<td>0·80</td>
<td>0·97</td>
</tr>
<tr>
<td>n-3 PUFAs from plants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 4-79 g/d)</td>
<td>0·96</td>
<td>0·95</td>
<td>0·95</td>
</tr>
<tr>
<td>Second and third quarters (4-79—6-27 g/d)</td>
<td>1·0</td>
<td></td>
<td>0·74</td>
</tr>
<tr>
<td>Fourth quarter (6-28—8-97 g/d)</td>
<td>0·90</td>
<td>0·78</td>
<td>0·93</td>
</tr>
<tr>
<td>α-Linolenic fatty acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 4-45 g/d)</td>
<td>1·05</td>
<td>0·78</td>
<td>0·87</td>
</tr>
<tr>
<td>Second and third quarters (4-45—6-40 g/d)</td>
<td>1·0</td>
<td></td>
<td>0·67</td>
</tr>
<tr>
<td>Fourth quarter (6-40—8-90 g/d)</td>
<td>0·98</td>
<td>0·54</td>
<td>0·95</td>
</tr>
<tr>
<td>EPA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (&lt; 0-07 g/d)</td>
<td>1·04</td>
<td>0·90</td>
<td>1·0</td>
</tr>
<tr>
<td>Second and third quarters (0-07—0-23 g/d)</td>
<td>1·0</td>
<td></td>
<td>0·77</td>
</tr>
<tr>
<td>Fourth quarter (0-23—1-25 g/d)</td>
<td>0·97</td>
<td>0·84</td>
<td>1·03</td>
</tr>
</tbody>
</table>
actual allergic manifestations. The role of supplementation with n-3 and n-6 PUFA for primary prevention of allergic outcomes has provided inconclusive evidence\(^{33–37}\).

Recently, it has been suggested that the ratio of n-6:n-3 FA, rather than the intake of their absolute amount, may represent a more important indicator of optimum health\(^{38,39}\). Although previous studies have been inconsistent\(^{4,39}\), the results from the present study, however, show that a higher ratio of n-6:n-3 FA was associated with an increased risk of rhinitis in the offspring by the age of 5 years. While this finding is in line with the results of an Australian study reporting an enhanced risk of asthma in children aged 8 years with a higher ratio of n-6:n-3 FA during pregnancy\(^{59}\), it is at odds with that of a recent Japanese study reporting no association\(^{52}\). In a previous US cohort, cord blood ratios of AA:EPA and linoleic acid:α-linolenic acid were positively associated with eczema and wheeze, respectively, while the ratio of α-linolenic acid:n-3 PUFA was inversely associated with wheeze in 30- to 42-month-old toddlers\(^{60}\). In another US study, higher n-3 EPA, n-6 AA and a reduced ratio of AA:EPA were associated with reduced allergen-stimulated interferon-γ levels in neonates\(^{41}\).

We found an increased risk of rhinitis with high maternal consumption of butter. It has been hypothesised that margarines may increase the risk of allergies, whereas butter may decrease the risk\(^{42}\). The present results of no association between consumption of margarines and the risks of allergies did not support this proposition. In addition, our data on butter are in contrast to the hypothesised role of butter in the development of allergies, and also contradictory to the present observation on the effect of the ratio of n-6:n-3 FA on the risk of rhinitis, considering that n-6 FA are particularly derived from margarines. We lack the explanation for these disparities, but as earlier noted, it may highlight the complex mechanisms relating FA to the development of allergies, especially during early life. In a German cohort, maternal consumption of margarine but not butter during pregnancy was associated with an increased risk of allergies in the offspring\(^{42}\), whereas an Italian retrospective cohort study found no association between either maternal consumption of butter or margarine and atopy in the offspring\(^{61}\). Oily fish is a major source of n-3 PUFA, and its consumption during pregnancy has been related to a reduced risk of asthma\(^{7}\), eczema\(^{9,10}\), house dust mite, wheeze\(^{59}\) and allergic sensitisation\(^{6,8}\) in the offspring. In contrast, in an 8-year longitudinal follow-up study from The Netherlands, maternal fish consumption during pregnancy was not associated with asthma or any asthma symptom in the offspring\(^{11}\). We did not have a measure of oily fish in the present study; therefore, we were unable to assess its association with the endpoints.

**Conclusion**

The present data indicate that maternal consumption of butter, the ratio of n-6:n-3 PUFA, and intake of PUFA and α-linolenic during pregnancy may be potential determinants of the development of allergic rhinitis in the offspring. In the light of discordant reports, more evidence is needed to confirm and further define the putative role of dietary butter and FA in the current increasing prevalence of allergic diseases.

**Acknowledgements**

This study was supported by the following: the Academy of Finland (grants 44105, 48724, 80846, 201988, 126813, 129492); the Finnish Pediatric Research Foundation; Doctoral Programs in Public Health; the Juho Vainio Foundation; the Yrjö Jahnsson Foundation; Medical Research Funds, Turku; Oulu and Tampere University Hospitals; Juvenile Diabetes Research Foundation; Novo Nordisk Foundation; the University of Tampere Foundation; and EU Biomed 2 Program (BMH4-CT98-3314). The authors are grateful to the DIPP doctors, research nurses, nutritionists and laboratory staff for their continuous collaboration through the years. The authors also express their gratitude to Sirpa Pohjola and Ilona Kalliomäki for their expert technical assistance. The authors declare that they have no financial relationship or conflict of interest related to this manuscript to disclose. The authors’ contributions were as follows: B. I. N. and M. E. designed, analysed and prepared the present paper under the supervision of S. M. V. and M. K. S. M. V. designed and was responsible for the DIPP Nutrition and Allergy studies. S. M. V. and M. K. planned the allergy study questionnaire.

**Table 5. Continued**

<table>
<thead>
<tr>
<th></th>
<th>Atopic eczema Adjusted model II†</th>
<th>Allergic rhinitis Adjusted model II†</th>
<th>Wheeze Adjusted model II†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR 95 % CI</td>
<td>HR 95 % CI</td>
<td>OR 95 % CI</td>
</tr>
<tr>
<td>DHA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First quarter (0·19–0·60 g/d)</td>
<td>1·15 0·92, 1·45</td>
<td>0·85 0·64, 1·12</td>
<td>1·04 0·80, 1·34</td>
</tr>
<tr>
<td>Second and third quarters (0·60–3·5 g/d)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fourth quarter (0·60–3·5 g/d)</td>
<td>1·00 0·80, 1·26</td>
<td>1·05 0·79, 1·39</td>
<td>0·95 0·72, 1·26</td>
</tr>
</tbody>
</table>

* P<0.05.
† In addition to the covariates in model I, adjusted for energy-adjusted maternal intake of vitamin C, Zn, Se, vitamin D and vitamin E.
‡ n-3 PUFA from fish is a summary variable including all n-3 fatty acids from fish and fish products.
for 5-year-olds. M. L. participated in the data analysis, interpretation, preparation and review of the manuscript and revising it critically for important intellectual content. S. A. and C. K.-K. were responsible for the data acquisition and preparation, interpretation of the results and critically reviewing the manuscript. R. V., J. I., O. S. and M. K. were responsible for data collection in the clinics and for paediatric expertise in this study, and review of the manuscript and revising it critically for important intellectual content.

References
36. Almqvist C, Garden F, Xuan W, et al. (2007) Omega-3 and omega-6 fatty acid exposure from early life does not affect


