Fish Consumption in Infancy and Asthma-like Symptoms at Preschool Age

WHAT’S KNOWN ON THIS SUBJECT: Several studies have reported inverse associations between fish consumption during pregnancy or later childhood and asthma prevalence. However, because fish can also be highly allergenic, the optimal timing of introduction of fish and the adequate amount in infancy remains unclear.

WHAT THIS STUDY ADDS: Introduction of fish between 6 and 12 months but not fish consumption afterward is associated with a lower risk of wheezing whereas no introduction of fish or introduction between 0 and 6 months of life increases the risk of wheezing.

OBJECTIVE: To assess whether timing of introduction of fish and the amount of fish consumption in infancy were associated with asthma-like symptoms at preschool age.

METHODS: This study was embedded in the Generation R study (a population-based birth cohort in Rotterdam, Netherlands). At the age of 12 and 14 months, timing of introduction of fish into the infant’s diet was assessed. The amount of fish consumption at 14 months was assessed by a semiquantitative food frequency questionnaire. Presence of asthma-like symptoms in the past year was assessed at the child’s age of 36 and 48 months.

RESULTS: Relative to no introduction in the first year of life, introduction between age 6 and 12 months was significantly associated with a lower risk of wheezing at 48 months (odds ratio [OR]: 0.64; 95% CI: 0.43–0.94). When compared with introduction between 6 and 12 months, no introduction in the first year and introduction between 0 and 6 months were associated with an increased risk of wheezing at 48 months (OR: 1.57; 95% CI: 1.07–2.31 and OR: 1.53, 95% CI: 1.07–2.19, respectively). The amount of fish at age 14 months was not associated with asthma-like symptoms (P > .15).

CONCLUSIONS: Introduction of fish between 6 and 12 months but not fish consumption afterward is associated with a lower prevalence of wheezing. A window of exposure between the age of 6 and 12 months might exist in which fish might be associated with a reduced risk of asthma. *Pediatrics* 2012;130:1060–1068

AUTHORS: Jessica C. Kiefte-de Jong, RD, PhD,a,b Jeanne H. de Vries, PhD,c Oscar H. Franco, MD, PhD,d Vincent W.V. Jaddoe, MD, PhD,a,b-c Albert Hofman, MD, PhD,d Hein Raat, MD, PhD,a Johan C. de Jongste, MD, PhD,f and Henriette A. Moll, MD, PhDg

aThe Generation R Study Group, and Departments of bPediatrics, cEpidemiology, dPublic Health, and ePediatrics/Respiratory Medicine, Erasmus Medical Center, Rotterdam, Netherlands; and fDepartment of Human Nutrition, Wageningen, Netherlands

KEY WORDS: fish, wheezing, shortness of breath, complementary feeding, asthma

ABBREVIATIONS: CI—confidence interval, DHA—docosahexaenoic acid, EPA—eicosapentaenoic acid, FFQ—Food Frequency Questionnaire, n-3 PUFA—N-3 polyunsaturated fatty acids, OR—odds ratio, PCBs—polychlorinated biphenyls

Dr Jessica C. Kiefte-de Jong analyzed the data, wrote the first draft of the manuscript, had full access to all the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis. She fulfills the criteria as described by the International Committee of Medical Journal Editors (ICMJE) as follows: (1) substantial contributions to conception and design, acquisition of data, and analysis and interpretation of the data; (2) drafting the article; and (3) final approval of the version to be published. Dr de Vries has participated in the acquisition and data analysis of nutritional data. She fulfills the criteria as described by the ICMJE as follows: (1) substantial contributions to acquisition of data, and analysis of the data; (2) critical revision of the paper for important intellectual content; and (3) final approval of the version to be published. Drs Franco, Jaddoe, Raat, Hofman, and de Jongste fulfill the criteria as described by the ICMJE as follows: (1) substantial contribution to interpretation of the data; (2) critical revision of the paper for important intellectual content; and (3) final approval of the version to be published. Dr Moll supervised the study. She fulfills the criteria as described by the ICMJE as follows: (1) substantial contributions to conception and design, acquisition of data, and interpretation of the data; (2) critical revisions of the paper for important intellectual content; and (3) final approval of the version to be published.

(Continued on last page)
The prevalence of asthma in Westernized countries is increasing.\(^1\) It has been suggested that adoption of a Westernized diet can be one of the reasons related to the increase of asthma.\(^2\) Indeed, we have previously found that a “Western-like” dietary pattern in toddlers was associated with asthmalike symptoms at preschool age.\(^3\) In contrast, we did not find any association with a dietary pattern characterized by high intake of fish, vegetables, and fruit\(^3\) whereas adherence to this diet during pregnancy or at school age has been noted to protect against asthma in previous studies.\(^4\)–\(^8\) Because we did not find a clear association between a dietary pattern including fish and asthmalike symptoms,\(^5\) we hypothesized that any potential beneficial effect of fish consumption in toddlers may be diluted in our previous study as a result of the dietary pattern approach and therefore deserves additional study. Various studies have suggested that early life exposure of n-3 polyunsaturated fatty acids (n-3 PUFA), a major component in fatty fish, protects against the development of asthma.\(^2,9,10\) In line with this, a recent study reported a beneficial effect of introduction of fish before age 9 months on the development of wheezing at age 4.5 years,\(^11\) whereas another study reported no association between introduction of fish and asthma.\(^12\) However, because fish can also be highly allergenic,\(^13\) the optimal timing of introduction of fish in the infant’s diet and the adequate amount remains unclear. We aimed in this study to assess whether timing of introduction of fish in the first year of life and fish consumption afterward were associated with the development of asthmalike symptoms at preschool age.

**METHODS**

The current study was performed within the Generation R Study, a population-based multiethnic prospective birth cohort in Rotterdam, Netherlands.\(^14\) The cohort includes 7210 children born between April 2002 and January 2006 whose parents provided postnatal consent (Supplemental Fig 2). The Medical Ethical Committee of the Erasmus Medical Centre, Rotterdam, approved the study (MEC 198.782/2001/31). Written informed consent was obtained from all participants.

**Timing of the Introduction of Fish and Amount of Fish Consumption in Infancy**

From 2003 onward, nutritional data of the child was collected at age 14 months (mean ± SD: 14 ± 2 months) by using a semiquantitative food frequently questionnaire (FFQ), which was validated in Dutch children and has been described in detail previously.\(^15\) Questions from the FFQ on the consumption fish are found in Supplemental Table 6. We divided the fish products into 2 groups on the basis of their fat content: (1) fatty fish defined as >10 g fat per 100 g: herring, mackerel, eel, and salmon; (2) other fish defined as 0 to 10 g fat per 100 g: white fish, fish fingers, squid, flounder, cod, pollack, haddock, tilapia, sole, tuna, whiting, trout, gurnard, perch, plaice, wolf fish, and swordfish.\(^16\) Consumption of fish was categorized as follows: “No consumption,” “Less than a half serving per week,” and “At least a half serving per week.” In addition, intake of 120 g raw fish was counted as one serving of fish.\(^17\) Both at the child’s age of 12 and 14 months, parents were asked the following question: “Please indicate how old your child was when you gave him or her fish for the first time.” The observed agreement between measurement at 12 and 14 months was 85% with a Cohen’s \(\kappa\) of .31. Answers categories included “never given in first year of life,” “0 to 3 months,” “3 to 6 months,” “after 6 months and thereafter.” Because of the small number in the group of introduction between 0 and 3 months \((n = 7)\), this was combined with the group “3 to 6 months” into a new category: 0 to 6 months.

**Asthmaligne symptoms**

Information regarding the presence of wheezing and shortness of breath in the past year was obtained by using an age-adapted version of the validated “International Study of Asthma and Allergies in Childhood”\(^18\) questionnaire at the ages of 36 months and 48 months. The observed agreement for wheezing and shortness of breath between measurement by questionnaire and by physician interview in our cohort was 75% (Cohen’s \(\kappa = .30\)) and 81% (Cohen’s \(\kappa = .39\)), respectively.\(^19\) To establish potential reverse causality, sensitivity analyses were performed with and without exclusion of any asthmalike symptoms at the age of 12 and 24 months. However, because effect estimates were similar, final analyses were performed in all children.

**Covariates**

Variables possibly related to food consumption and wheezing were considered potential confounders in this study and selected based on previous knowledge and literature.\(^15,20\) Infant’s gender, gestational age and birth weight were obtained from obstetric records assessed in midwife practices and hospital registries.\(^14\) Information about maternal age, maternal BMI, parity, educational level, ethnicity, marital status, household income, and any family history of asthma, eczema, allergy to house dust, or hay fever was obtained by questionnaire at enrollment. Maternal smoking and alcohol habits were assessed by questionnaire in each trimester of pregnancy. We assessed maternal dietary fish intake at enrollment using a modified version of the validated semiquantitative FFQ described previously.\(^21,22\) Mother’s intake of folic acid was assessed by...
questionnaire at enrollment of the study as described earlier.\textsuperscript{25} Data on breastfeeding was collected by a combination of delivery reports and postnatal questionnaires at ages 2, 6, and 12 months. Breastfeeding was defined in this study as follows: (1) never, (2) partially through 4 months, (3) exclusively through 4 months.\textsuperscript{24} Postnatal questionnaires completed by the mother at age 6 and 12 months included information on any day-care attendance (yes versus no), any vitamin D supplementation (yes versus no), and any history of doctor-attended food allergy and eczema. Weight and height were measured at the child health centers during routine visits around age 48 months. The definition of overweight was established according to international cutoff points for children.\textsuperscript{25}

**Statistical Analysis**

Univariate associations between maternal and child characteristics and timing of introduction of fish were performed with 1-way analysis of variance (continuous variables) and \( \chi^2 \) test (categorical variables). Logistic regression analyses were used to assess the association between timing of introduction of fish and amount fish consumption and asthmalike symptoms. A crude model was computed followed by a multivariate model adjusting for potential confounders. All analyses on the amount of fish consumption at 14 months were adjusted for total energy intake.\textsuperscript{26} To assess whether the association between fish and asthmalike symptoms was different by strata of, for example, ethnicity, history of food allergy, and parental history of atopy, stratified analyses were performed by these groups and statistical interaction was tested by adding the product term of the fish variable multiplied by the stratum (eg, fish consumption \( \times \) food allergy) as an independent variable to the crude models.

A multiple imputation procedure (\( n = 5 \) imputations) was performed on all variables to reduce potential bias associated with missing data (Supplemental Fig 2, Supplemental Table 7).\textsuperscript{27} Analyses were then performed in each of the 5 imputed data sets separately, and the final results were pooled and presented as odds ratios (ORs) and 95% confidence intervals (CIs). Statistical analyses were performed with PASW Statistics 17.0.

**RESULTS**

Characteristics of the study population and prevalence of wheezing according to timing of introduction of fish are shown in Tables 1 and 2. A fish-free dietary regimen at age 14 months was reported in only 0.1% of the children. Fish consumption of the children at age 14 months was higher in children introduced to fish in the first year of life relative to those without fish introduction in the first year of life (Fig 1).

Timing of introduction of fish showed no similarities with timing of introduction of other foods in the first year of life (Cohen’s \( \kappa \leq .15 \), Supplemental Table 9).

**Timing of Introduction of Fish and Asthmalike Symptoms**

Children who were introduced to fish between 6 and 12 months had a significantly lower prevalence of wheezing at 48 months than children who were not introduced to fish in the first year of life (Table 3). Symptoms of shortness of breath were less prevalent in children introduced to fish between 6 and 12 months, but this was not statistically significant (Supplemental Table 10). Relative to introduction between 6 and 12 months, both fish introduction between 0 and 6 months and no introduction in the first year of life were associated with an increased prevalence of wheezing and shortness of breath at 48 months (Table 4, Supplemental Table 11). The associations between timing of introduction of fish and asthmalike symptoms were not different within strata of ethnicity, family history of allergic disease, maternal fish consumption during pregnancy, any history of food allergy, eczema, breastfeeding duration, and type of fish consumption at age 14 months (\( P_{\text{interaction}} > .15 \) for all comparisons).

**Amount of Fish Servings and Wheezing and Shortness of Breath**

No association was found between the amount of fish servings and wheezing and shortness of breath at 36 and 48 months (Table 5, Supplemental Table 7). Fatty fish consumption of less than \( \frac{1}{2} \) serving per week was significantly associated with wheezing at 48 months but this association was mainly explained by confounding factors (Table 5).

Results did not differ within strata of ethnicity, maternal fish consumption during pregnancy, any family history of allergic disease, any history of food allergy, eczema, and breast-feeding duration (\( P_{\text{interaction}} > .20 \) for all comparisons).

**DISCUSSION**

This study showed that introduction of fish between 6 and 12 months, but not the amount of fish servings afterward, was associated with a lower prevalence of wheezing in preschool children. However, no introduction in the first year of life or introduction between 0 and 6 months was associated with an increased prevalence of asthmalike symptoms.

Most studies on fish intake and asthma have assessed maternal fish intake during pregnancy and asthma in the offspring. Both epidemiologic studies and randomized controlled trials showed protective effects of fish and fish fatty acids during pregnancy and asthma in children.\textsuperscript{28,29} However, evidence from epidemiologic studies
assessing the effects of fish intake in young children and asthma is scarce and contradictory. Nafstad et al found no significant association between introduction of fish in the first year and any asthma diagnosis. Hesselmar et al found a tendency between early fish introduction of fish and asthma (between group-difference of fish introduction: 9 vs 13 months). Another study by Kull et al showed that consumption of fish more than once a week in the first year of life was associated with a lower prevalence of asthma. Arvaniti et al and Tabak et al showed that fish intake was associated with a lower prevalence of asthma in older children (>8 years). In contrast, Willers et al showed no association between the amount of fish consumption at age 2 to 3 years and 7 to 8 years and asthma diagnosis at 8 years. Age differences and variation in measuring fish consumption make it difficult to compare our results with previous studies but there seems to be a tendency for a beneficial effect on asthma when fish exposure occurs in the first year of life. Our study suggests that appropriate timing of introduction of fish rather than the amount of fish servings after 12 months is important in the association with wheezing. Underlying mechanisms why fish may protect against asthma are speculative. Fish is a great source of n-3 PUFAs such as decosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). Several studies suggest that DHA and EPA have immunoregulatory and/or antiinflammatory properties. Lower levels of n-3 fatty acids have been found in asthmatics relative to control subjects, but others found no association between levels of n-3 fatty acids and asthma in schoolchildren aged 8 to 13 years. In addition, the optimal intake of n-3 fatty acids in young children remains controversial. In 2002, the US Institute of Medicine concluded that there is insufficient evidence to provide clear recommendation on n-3 PUFA intake in children, whereas the Technical Committee on Dietary Lipids of the International Life Sciences Institute of North America stated in 2009 that a daily EPA and DHA intake between 250 and 500 mg per day reduces the risk of coronary head disease later in life. The European Food Safety Authority Panel on Dietetic Products, Nutrition and Allergies concluded in 2009 that in older infants, DHA intake of 50 to
100 mg per day can improve visual function but evidence does not permit to define an age specific dietary recommendation for EPA and DHA from 2 years onward.39 None of the recommendations on EPA and DHA were related to influence on asthma. In line with this, the European Society for Pediatric Gastroenterology Hepatology and Nutrition commented in 2011 on supplementation of n-3 fatty acids to diet of children from 2 years and possible benefits on clinical outcomes.40 The committee concluded that there is no convincing evidence that supplementation with n-3

TABLE 2 Prevalence Rates of Wheezing According to Weekly Intake of Fish and Timing of Introduction of Fish in the Infant’s Diet

<table>
<thead>
<tr>
<th>Fatty fish consumption at 14 mo</th>
<th>Children With Wheezing at 36 mo, N = 2480, n (%)</th>
<th>Children With Wheezing at 36 mo, N = 2439, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No fatty fish consumption</td>
<td>4831 (68)</td>
<td>1736 (35)</td>
</tr>
<tr>
<td>Less than ½ serving a week</td>
<td>1910 (27)</td>
<td>622 (33)</td>
</tr>
<tr>
<td>At least ½ serving a week</td>
<td>356 (5)</td>
<td>121 (33)</td>
</tr>
<tr>
<td>Other fish consumption at 14 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No other fish consumption</td>
<td>2182 (30)</td>
<td>745 (34)</td>
</tr>
<tr>
<td>Less than ½ serving a week</td>
<td>2965 (41)</td>
<td>980 (33)</td>
</tr>
<tr>
<td>At least ½ serving a week</td>
<td>2063 (29)</td>
<td>755 (37)</td>
</tr>
<tr>
<td>Timing of introduction of fish in first year of life</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never in first year</td>
<td>431 (6)</td>
<td>173 (40)</td>
</tr>
<tr>
<td>0–6 mo</td>
<td>1281 (18)</td>
<td>667 (32)</td>
</tr>
<tr>
<td>6–12 mo</td>
<td>5498 (76)</td>
<td>1639 (30)</td>
</tr>
</tbody>
</table>

Table represents the pooled results after the multiple imputation procedure.

FIGURE 1

A, Fish consumption at 14 months according to timing of introduction of fish in first year of life (*P < .05 compared with never given in first year of life). B, Type of fish consumption at 14 months according to timing of introduction of fish in first year of life (*P < .05 compared with never given in first year of life). ♦, Fatty fish consumption; ▲, other fish consumption. IQ, interquartile.
fatty acids has beneficial effects on asthma in children. If n-3 fatty acids are the components in fish that may protect against asthmalike symptoms, one would expect that not only timing of introduction but also the amount of fish consumption and fatty fish in particular determines the effect. This was not the case in our study, which may be explained in several ways. First, timing of introduction of fish may act as a proxy of other lifestyle factors and behaviors; for instance, it may be associated with intake of other foods that may have an influence on asthmalike symptoms. Nonetheless, we have previously demonstrated that timing of introduction of food allergens and a dietary pattern including fish, vegetables, and fruit at age 14 months were not significantly associated with asthmalike symptoms in our cohort. Also, the timing of introduction of fish showed no similarities with timing of introduction of other foods. This raises questions as to whether confounding by other diet factors plays a role. Furthermore, to our knowledge, not many studies have assessed the amount of fish consumption at such a young age and its effect on asthmalike symptoms. Most studies have been carried out in older children or assessed the timing of introduction of fish in the infant’s diet rather than the amount of fish consumption afterward. However, Goksor et al showed that early fish introduction, but not the frequency of fish consumption at 12 months, was associated with recurrent wheeze, which is in line with our results. Similar results were also found in the Prevention of Allergy Among Children in Trondheim study. Assessing nutrient intake at very young age is challenging because variation in certain foods can be limited and the diet can be subject to major changes at this age. The lack of significant results on the amount of fish consumption in infancy may be due to the relatively low fish consumption in this age group. Therefore, additional studies on the effect of fish consumption at preschool age are necessary. Third, contamination of fish by, for example, mercury and polychlorinated biphenyls (PCBs) might be an explanation for negative results on fish consumption. Although studies suggest that exposure to these components may have immunologic effects early in life, the effect on the development of asthma is indistinct. Fish is the major contributor of mercury consumption, and no association between mercury exposure and wheezing symptoms have been found in preschool children. In addition, a report by the Dutch Institute for Food Safety showed that high mercury intake is not a major problem in Dutch infants. Another study showed that PCBs exposure may both increase and decrease the risk of allergic disease in children. Nonetheless, intake of PCBs and dioxins is due to contributions of many food items; fish contributes 16% to 26% to the total intake of dioxins and PCBs in the Dutch population. Because particularly the intake of fish is relatively low in this population of infants, we think it is unlikely that the intake of mercury, PCBs, and dioxins from fish may have markedly influenced our results. Finally, given the results related to timing of introduction rather than to quantity of fish intake, there might be a specific window of exposure between

<table>
<thead>
<tr>
<th>Timing of Introduction of Fish</th>
<th>Univariate Model, OR (95% CI)</th>
<th>P Value</th>
<th>Multivariate Model, OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheezing age 36 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never in first year</td>
<td>Reference</td>
<td>.33</td>
<td>Reference</td>
<td>.48</td>
</tr>
<tr>
<td>0–6 mo</td>
<td>1.58 (0.53–4.75)</td>
<td>.33</td>
<td>1.31 (0.53–3.29)</td>
<td>.48</td>
</tr>
<tr>
<td>6–12 mo</td>
<td>0.05 (0.40–1.07)</td>
<td>.08</td>
<td>0.72 (0.51–1.03)</td>
<td>.07</td>
</tr>
<tr>
<td>Wheezing age 48 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never in first year</td>
<td>Reference</td>
<td>.44</td>
<td>Reference</td>
<td>.92</td>
</tr>
<tr>
<td>0–6 mo</td>
<td>1.25 (0.65–2.41)</td>
<td>.44</td>
<td>0.98 (0.60–1.59)</td>
<td>.92</td>
</tr>
<tr>
<td>6–12 mo</td>
<td>0.58 (0.33–1.02)</td>
<td>.06</td>
<td>0.64 (0.43–0.94)</td>
<td>.03</td>
</tr>
</tbody>
</table>

ORs relative to “never wheezing in the past year” derived from logistic regression with “never given in first year of life” as reference category after the multiple imputation procedure.

* Adjusted for maternal age, maternal BMI, maternal alcohol and smoking during pregnancy, household income, maternal educational background, family history of asthma, eczema, hay fever or allergy to house dust, maternal fish consumption during pregnancy, folic acid supplementation during pregnancy, parity, birth weight, gestational age, infant’s gender, infant’s ethnicity, breastfeeding duration, early day-care attendance, any vitamin D supplementation in first year of life.

TABLE 4 Association Between Timing of Introduction of Fish and Wheezing Symptoms When Compared With Introduction Between Age 6 and 12 Months

<table>
<thead>
<tr>
<th>Timing of Introduction of Fish</th>
<th>Univariate Model, OR (95% CI)</th>
<th>P Value</th>
<th>Multivariate Model, OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheezing age 36 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never in first year</td>
<td>Reference</td>
<td>.8</td>
<td>Reference</td>
<td>.07</td>
</tr>
<tr>
<td>0–6 mo</td>
<td>1.53 (0.93–2.53)</td>
<td>.2</td>
<td>1.38 (0.87–1.97)</td>
<td>.07</td>
</tr>
<tr>
<td>6–12 mo</td>
<td>2.45 (1.28–4.60)</td>
<td>.02</td>
<td>1.82 (1.00–3.32)</td>
<td>.05</td>
</tr>
<tr>
<td>Wheezing age 48 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never in first year</td>
<td>Reference</td>
<td>.06</td>
<td>Reference</td>
<td>.03</td>
</tr>
<tr>
<td>0–6 mo</td>
<td>1.72 (0.98–3.03)</td>
<td>.06</td>
<td>1.57 (1.07–2.31)</td>
<td>.03</td>
</tr>
<tr>
<td>6–12 mo</td>
<td>2.16 (1.04–4.48)</td>
<td>.04</td>
<td>1.53 (1.07–2.19)</td>
<td>.03</td>
</tr>
</tbody>
</table>

ORs relative to “never wheezing in the past year” derived from logistic regression with “never given in first year of life” as reference category after the multiple imputation procedure.

* Adjusted for maternal age, maternal BMI, maternal alcohol and smoking during pregnancy, household income, maternal educational background, family history of asthma, eczema, hay fever or allergy to house dust, maternal fish consumption during pregnancy, folic acid supplementation during pregnancy, parity, birth weight, gestational age, infant’s gender, infant’s ethnicity, breastfeeding duration, early day-care attendance, any vitamin D supplementation in first year of life.
in combination might be associated with a decreased risk of asthma and asthmalike symptoms. A limitation of this work is the lack of objective measurement on asthma. The main outcomes in this study were parental-reported asthmalike symptoms. In preschool children, a diagnosis of asthma is based on symptoms of wheezing or shortness of breath because it is complicated to perform lung function measurements in young children. Moreover, the diagnosis of asthma as proposed by current guidelines relies on symptoms rather than measurements.

Although a reasonable level of agreement was seen between timing of introduction of fish assessed at 12 months and at 14 months, misclassification on the timing of fish may occur. If this misclassification is also related to asthmalike symptoms, this would have influenced our results, but this seems unlikely. Also, we did not have data on type of the amount of fish consumed at the moment of introduction. Nevertheless, nutritional assessment can be subject to measurement error, and therefore, repeated measures of n-3 fatty acids in blood during infancy can be useful to shed light on the association between fish consumption and asthma development and whether any potential beneficial effect of the timing of the introduction of fish can be attributed to n-3 fatty acids.

This is an epidemiologic study and thus does not permit final conclusions with respect to the causality of the described associations because residual confounding by other lifestyle factors may exist.

**CONCLUSIONS**

Introduction of fish between the age of 6 and 12 months but not dietary fish intake at 14 months was associated with a lower prevalence of wheezing at preschool age. A specific window of opportunity between the age of 6 and 12 months might exist in which fish may protect against asthma.

**ACKNOWLEDGMENTS**

The Generation R Study is conducted by the Erasmus Medical Center in close collaboration with the School of Law and Faculty of Social Sciences of the Erasmus University Rotterdam; the Municipal Health Service, Rotterdam Metropolitan Area; the Rotterdam Homecare Foundation; and the Stichting Trombosefond en Artsenlaboratorium Rijnmond. We acknowledge the contributions of children and parents, general practitioners, hospitals, and midwives in Rotterdam. Also, we thank Saskia Meyboom, Corine Perenboom, and Els Siebelink of the Department of Human Nutrition, Wageningen University, Netherlands for their contribution in processing the food consumption data.
REFERENCES


17. Donders-Engelen M, Heijden van der L, Hulshof KF. Maten, gewichten en code-nummers. Wageningen, the Netherlands: Human Nutrition of TNO and Wageningen University; 2003


29. Clemens CM, Berman DN, Mozukewich EL. The effect of perinatal omega-3 fatty acid supplementation on inflammatory markers and allergic diseases: a systematic review. BMJ. 2011;118(8):916–925


36. Rodríguez-Rodríguez E, Pereira JM, Jiménez AI, Rodríguez-Rodríguez P, López-Sobaler AM, Ortega RM. Fat intake and asthma in Spanish schoolchildren. Eur J Clin Nutr. 2010;64(10):1065–1071


1067

Downloaded from by guest on May 2, 2017

39. EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA). Scientific opinion on dietary reference values for fats, including saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, trans fatty acids, and cholesterol. *EFS J*. 2010;8:1461


47. van Asselt ED, de Mul A, Traag WA, van Klaveren JD. Inname aan zware metalen en nitraat door jonge kinderen (Consumption of heavy metals and nitrate in young children). Wageningen: Wageningen Universiteit en Researchcentrum, Instituut voor Voedselzekerheid; 2008


(Continued from first page)
Fish Consumption in Infancy and Asthma-like Symptoms at Preschool Age
Jessica C. Kiefte-de Jong, Jeanne H. de Vries, Oscar H. Franco, Vincent W.V. Jaddoe, Albert Hofman, Hein Raat, Johan C. de Jongste and Henriette A. Moll
Pediatrics 2012;130;1060; originally published online November 12, 2012; DOI: 10.1542/peds.2012-0875

Updated Information & Services
including high resolution figures, can be found at:
/content/130/6/1060.full.html

Supplementary Material
Supplementary material can be found at:
/content/suppl/2012/11/06/peds.2012-0875.DCSupplemental.html

References
This article cites 47 articles, 12 of which can be accessed free at:
/content/130/6/1060.full.html#ref-list-1

Citations
This article has been cited by 1 HighWire-hosted articles:
/content/130/6/1060.full.html#related-urls

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Pulmonology
/cgi/collection/pulmonology_sub
Respiratory Tract
/cgi/collection/respiratory_tract_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
/site/misc/reprints.xhtml
Fish Consumption in Infancy and Asthma-like Symptoms at Preschool Age
Jessica C. Kiefte-de Jong, Jeanne H. de Vries, Oscar H. Franco, Vincent W.V. Jaddoe, Albert Hofman, Hein Raat, Johan C. de Jongste and Henriette A. Moll
Pediatrics 2012;130;1060; originally published online November 12, 2012; DOI: 10.1542/peds.2012-0875

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/130/6/1060.full.html