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Maternal food consumption during pregnancy and asthma, respiratory and atopic symptoms in 5-year-old children

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ABSTRACT (word count 251)

Background We have previously reported associations between maternal vitamin E, vitamin D and zinc intakes during pregnancy and asthma, wheeze and eczema in 5-year-old children. In this report we investigate whether maternal intake of specific foods during pregnancy is associated with asthma, and allergic outcomes in the same children.

Methods A longitudinal birth cohort study was conducted among 1924 children born to women recruited during pregnancy. Maternal diet during pregnancy was assessed by food frequency questionnaire (FFQ). Cohort children were followed up at 5 years by symptom questionnaire and FFQ. Food groups of interest were fruit, vegetables, fruit juice, whole grain products, fish, dairy products and fat spreads. Trends across outcome groups defined by level of food intake are presented.

Results 1253 children participated at 5 years, maternal FFQ data were available for 1212. No consistent associations were found between childhood outcomes and maternal intake of the analysed foods, except for apples and fish. Maternal apple intake was beneficially associated with ever wheeze (OR highest vs lowest tertile 0.63; 95% CI 0.42-0.95), ever asthma (OR 0.54; 0.32-0.92) and doctor-confirmed asthma (OR 0.47; 0.27-0.82) in the children. Maternal fish consumption was beneficially associated with doctor-confirmed eczema (OR ≥1/week vs never 0.57; 0.35-0.92).

Conclusion There was no evidence for associations between maternal intake of most foods during pregnancy, and asthma, respiratory and allergic outcomes in 5-year-old children, except for apples and fish. Consumption of apples and fish during pregnancy may have a protective effect against the development of childhood asthma and allergic disease.

INTRODUCTION

Can mothers protect their children from developing asthma or atopic disease through what they eat during pregnancy? The answer to this question is important because of the potential for intervention to prevent childhood asthma and atopic disease. There is some evidence that lifestyle and dietary habits can influence the development of childhood asthma and allergy *in utero*.[1-3] We have established a birth cohort to investigate whether maternal diet during pregnancy is associated with childhood asthma and atopic disease. We have reported associations between maternal vitamin E intake during pregnancy and cord blood mononuclear cell (CBMC) responses at birth, wheezing in the second year of life and wheeze, asthma, ventilatory function, and exhaled nitric oxide at age 5 years.[2-4] We have also reported associations between maternal intakes of vitamin D and zinc and wheeze, asthma, and eczema outcomes in the same children.[5]

To date, nearly all reports relating maternal diet during pregnancy to childhood asthma and atopy have focused on individual nutrients,[2, 4-7] little data exists relating maternal intake of specific foods during pregnancy and the subsequent development of childhood asthma and atopic disease. Our birth cohort provides an opportunity to examine associations between childhood respiratory/atopic outcomes and maternal intake of individual foods during pregnancy, particularly those foods (fruit, vegetables, whole grain products, and fish) that are rich sources of the nutrients (vitamin E, vitamin D, and zinc) that we have previously reported to be associated with childhood outcomes.[2-5] A second group of foods of particular interest are those that have previously been reported to be associated with asthma or atopic disease in adults and children (citrus fruit, apples, fruit juices, vegetables, fish, oily fish, dairy products, and whole grain products). Beneficial associations in children have been reported for fruit,[8-10] fruit juice,[11] vegetables,[8] fish,[9,12] oily fish,[12] full fat dairy products,[13] and whole grain products,[13,14] while harmful associations have been reported for margarine and salt.[15,16]

Advantages of looking at foods are that they contain a mixture of micronutrients that may contribute more than the sum of their parts, and that it examines associations with micronutrients that may be currently unrecognised or not easily quantifiable. In addition, an evaluation of the associations with nutrients and foods will guide any future intervention study that could be the basis for public health intervention to prevent asthma and atopic disease by dietary intervention.

METHODS

Study population and study design

Details of the study design have been published previously.[2- 4] Briefly, 2000 healthy pregnant women were recruited between October 1997 and April 1999 irrespective of their asthma/atopic status, while attending antenatal clinics at Aberdeen Maternity Hospital at a median gestational age of 12 weeks. Apart from expected slight biases the recruited women were representative of the local obstetric population.[4] At enrolment, the women completed an interviewer-administered questionnaire and atopic status was ascertained by skin prick testing (ALK-UK, Hungerford, UK). Although the ensuing cohort of singleton children was followed up at 1, 2 and 5 years, this report is limited to the 5-year follow up.

Child's health outcomes

At 5-years a questionnaire based on the ISAAC core questions on symptoms of asthma, allergic rhinitis and atopic eczema was sent to all participating families, with up to two reminders.[2, 4, 17] The main questionnaire-derived outcomes of interest were 'Has your child ever wheezed' (with supplementary questions about wheeze in the last year), 'Has your child ever suffered from asthma', 'Has this been confirmed by a doctor', and 'Has your child received treatment for asthma in the past 12 months'. Similar questions enquired about eczema and hay-fever. Current asthma was defined as asthma and wheeze in the previous year.

Responding parents were also invited to complete a food frequency questionnaire (FFQ) pertaining to the study child's current diet and to bring the child to the hospital for an assessment including spirometry, skin prick testing, and measurement of exhaled nitric oxide (FE_{NO}). Originally, measurement of bronchodilator response and FE_{NO} were not included in the study protocol but introduced for the last 510 and 262 children respectively.[2] Details of the hospital assessment have been published previously.[2] Spirometry was measured using a pneumotachograph (Spirotrac IV version 4.22, Vitalograph, Maids Moreton, UK). Bronchodilator response was expressed as percentage change in FEV_1, 15 minutes after inhalation of 400 μg salbutamol. Atopy was defined as at least one positive skin prick test response to the allergens: cat, timothy grass, egg, and house dust mite (ALK-UK, Hungerford, UK). A positive response was defined as a mean wheal diameter of 3 mm or greater than the negative control. A NIOX® analyser (Aerocrine-AB, Solna, Sweden) was used to measure FE_{NO}. Parents gave their written consent and the Grampian Research Ethics Committee approved the study.

Assessment of maternal diet during pregnancy

Maternal diet during pregnancy was assessed by a semi-quantitative FFQ (version 5.4 of the Scottish Collaborative Group FFQ) mailed at 32 weeks gestation.[18] This FFQ consisted of 150 items, divided into 20 food groups. Mothers were asked to describe how much of each food on the list they had eaten in the previous 2-3 months. Categories for the frequency of the foods eaten were 'R' for rarely or never, 'M' for once or twice a month, and the categories 1 to 7 days per week. Further to this categorisation the amount of each food consumed ranged from 1 to 5+ measures per day. For each food a measure was specified, which was usually a small unit (e.g. slice), or household measure (e.g. tablespoon), rather than a typical portion. In order to convert to a numerical scale the frequency value 'R' was replaced by 0 and the value 'M' by 0.375. The number of measures per day was multiplied by the number of days per week to obtain the total measures per week. The food groups of interest in this study were total fruit, citrus/kiwi fruit, apples, total vegetables, green leafy vegetables, pure fruit juice, whole grain products, total fish, total oily fish, total fat from dairy products, and exclusive butter versus margarine/low fat spread used as spread. The individual foods included in the food groups are described in table 1.

Table 1. Constituent foods of the food groups used for analyses

Food group	Constituent foods
Total fresh fruit	Apples, bananas, oranges, pears, peaches and nectarines, kiwi fruit, all other fruit (grapes, strawberries, melon, plums etc.)
Citrus/kiwi fruit	Oranges, kiwi fruit
Total vegetables	Peas and green beans, carrots, cabbage and swede, broccoli, spinach and spring greens, leeks and courgettes, sweetcorn, onions, tomatoes, sweet peppers, other cooked vegetables (cauliflower, sprouts etc.) other salad vegetables (lettuce, cucumber etc.)
Green leafy vegetables	Broccoli, spinach and spring greens, leeks and courgettes, and other cooked vegetables (cauliflower, sprouts)
Pure fruit juice	Pure fruit juices (orange, apple etc.)
Whole grains products	Whole meal bread, bran flakes/sultana bran/all bran, shredded wheat/weetabix, muesli, porridge, brown rice
Total fish	Fish fingers, fried white fish (cod, haddock, plaice etc.), grilled steamed or baked white fish, fried oily fish (salmon, herrings, mackerel), grilled steamed or baked oily fish, smoked fish (haddock, mackerel, kippers etc.), tinned sardines, tinned tuna
Oily fish	Fried oily fish (salmon, herrings, mackerel), grilled steamed or baked oily fish, smoked fish (haddock, mackerel, kippers etc.)
Dairy products	Milk, low fat yoghurt, full fat yoghurt, low calorie yoghurt, fromage frais, cream, full fat cheddar-type cheese, medium fat cheese, full fat cream cheese, low fat cream cheese, cottage cheese, butter

The total number of measures per week was divided into tertiles for total fruit, citrus/kiwi fruit, apples, total vegetables, green leafy vegetables, pure fruit juice, whole grain products and into the categories never, less than once a week, and once or more a week for total fish and total oily fish. To facilitate extrapolation to the general population, subdivision of food intakes into tertiles were derived from all of the women completing the FFQ and not merely those responding at 5 years.

Assessment of childhood diet at age 5

Parents were invited to complete an FFQ to assess the study child's dietary intake over the previous 3 months. Version C1 of the Scottish Collaborative Group FFQ was used, this is a 121 item semi-quantitative instrument based on the questionnaire used for the mothers in pregnancy, but has been modified for use in pre-school children aged 3-5 years by simplifying the response choices, and changing the food list and portion sizes to be appropriate for pre-school children. Validity for specific nutrients in this age group has been reported.[19]

Statistical analyses

All analyses were carried out using SPSS version 13.0 (SPSS Inc., Chicago, USA). Mantel-Haenszel odds ratios were used to assess the univariate associations between childhood outcomes and food groups, while ordinary least squared multiple logistic regression analysis using forced choice selection to adjust for covariates was used for the multivariate analyses. Covariates in the multivariate model were: maternal age, paternal social class, maternal age of leaving full time education, maternal smoking during pregnancy, maternal asthma (for wheeze, asthma, and hay-fever outcomes), maternal atopy, child's birth weight, child's gender, presence of older siblings, breast feeding, and smoking in the child's home at 5 years.

RESULTS

Study population and prevalence of respiratory and allergic symptoms

Two thousand pregnant women were recruited, of whom 1751 completed the FFQ. There were 1924 live singleton births. Symptom questionnaire data at age 5 were obtained for 1253 children and maternal FFQ data were available for 1212 of these. FFQ, spirometry, bronchodilator response, skin prick test, and FE_{NO} results were available for 1120, 639, 238, 700, and 167 children respectively. Maternal intake of the food groups during pregnancy and for those responding at 5 years is shown in table 2.

Table 2. Maternal and dietary characteristics of the mothers responding to the 5-year questionnaire

Maternal dietary intake	**Mothers completing FFQ during pregnancy** n = 1751	**Respondent mothers at age 5** n = 1212	**p***
Energy intake (KJ/day) (geometric mean, 95% CI)	10,137 (9987-10,290)	9981 (9815-10149)	0.006
Total fruit intake (servings/day) (mean, 95% CI)	2.22 (2.16-2.27)	2.27 (2.20-2.34)	0.008
Apple intake (measures/week) (mean, 95% CI)	3.58 (3.41-3.76)	3.59 (3.39-3.80)	0.697
Citrus/kiwi fruit intake (measures/week) (median, 25^{th}-75^{th} percentiles)	1.38 (0.38-4.00)	1.38 (0.38-4.00)	0.040#
Total vegetable intake (servings/day) (mean, 95% CI)	1.93 (1.88-1.98)	1.95 (1.89-2.01)	0.385#
Green leafy vegetable intake (measures/week) (median, 25^{th}-75^{th} percentiles)	4.38 (1.5-9.00)	4.50 (1.75-9.00)	0.013#
Fruit juice intake (measures/week) (median, 25^{th}-75^{th} percentiles)	5.00 (1.00-10.00)	5.00 (1.00-10.00)	0.146#
Whole grain product intake (portions/week) (median, 25^{th}-75^{th} percentiles)	3.73 (0.38-8.18)	4.13 (0.38-8.67)	< 0.001#
Total fish intake (portions/week) (median, 25^{th}-75^{th} percentiles)	1.58 (0.67-3.00)	1.67 (0.75-3.08)	0.054#
Oily fish intake (portions/week) (median, 25^{th}-75^{th} percentiles)	0.00 (0.00-0.50)	0.00 (0.00-0.50)	0.002#
Fat from dairy products intake (g/week) (mean, 95% CI)	154 (149-159)	151 (145-157)	0.070
Exclusively butter vs margarine/low fat spread	20.5% vs 79.5%	21.6% vs 78.4%	0.148

p* value: responders at 5 vs non-responders
#: non-parametric test

Although the mothers responding to the 5-year questionnaire were more likely to eat fruit, citrus/kiwi fruit, green leafy vegetables, whole grain products, and oily fish during pregnancy than non-responding mothers, the magnitude of the differences was small (<10%). Responding mothers also had significantly lower energy intake and a lower intake of fat from dairy products. The characteristics of the mothers and children who did or did not attend the hospital for assessment has been published previously.[2] Briefly, the mothers and children who attended for hospital assessment were broadly representative of those responding to the questionnaire, with any significant differences being of small magnitude.[2] The characteristics of the mothers and their children and the prevalence of asthma and atopic symptoms in both are shown in table 3.

Table 3. Maternal and children's characteristics and prevalence of respiratory and atopic symptoms

Maternal characteristics	n = 1253	**Children's characteristics**	n = 1253
Age at recruitment (mean, 95%CI)	29.9 (29.6-30.2)	Male (%)	630 (50.3%)
Partner's social class % nonmanual	767 (61.2%)	Birth weight (g) (mean, 95%CI)	3458 (3426-3489)
Age left full time education (median, IQR)	18.5 (16.0-21.0)	Ever breast fed	74.3%
FFQ returned	1212 (96.7%)		
Smoking during pregnancy	288 (23.0%)		
Prevalence of respiratory and allergic symptoms			
Ever wheezed	415 (33.1%)	Wheeze in last 12 months	162 (12.9%)
Current asthma	125 (10.0%)	Wheeze in absence of cold in last 12 months	84 (6.7%)
Ever had asthma	189 (15.1%)	Ever wheezed	253 (20.2%)
Asthma medication	123 (9.8%)	Asthma and wheeze in the last 12 months	107 (8.5%)
Ever had hay-fever	313 (25.0%)	Doctor confirmed asthma	145 (11.6%)
Ever had eczema	213 (17.0%)	Ever had asthma	156 (12.5%)
Atopic sensitisation	448 (35.8%)	Doctor confirmed eczema	380 (30.4%)
		Current eczema treatment	191 (15.3%)
		Ever had eczema	406 (32.4%)
		Doctor confirmed hay-fever	68 (5.4%)
		Current hay-fever medication	44 (3.5%)
		Ever had hay-fever	111 (8.9%)
		Atopic sensitisation	149/699 (21.3%)

Associations between maternal diet during pregnancy and respiratory and allergic symptoms in children aged 5 years

Recruitment data were available for all 1253 mother-child pairs, however because of incomplete ascertainment at the ensuing data collection points the number of mother-child pairs with complete datasets included in the final multivariate analyses was less than the total number of respondents at age 5 (1253). For the 1253 mother-child pairs FFQ data at 32 weeks gestation were available for 1212, birth weight data were available for 1200 and breast feeding and maternal age of leaving full time education data collected at 1 year were available for 1176 and 1113 respectively. Incomplete mother-child pairs appeared to be random and those with complete datasets did not differ significantly from those with incomplete datasets for all the variables included in the multivariate analyses.

No consistent linear associations were found between maternal intake of total fruit, citrus/kiwi fruit, total vegetables, green leafy vegetables, fruit juice, whole grain products, fat from dairy products, or butter versus margarine/low fat spread use and respiratory or atopic outcomes in the 5-year-old children.

There were no consistent associations between maternal intake of food groups and spirometry, atopic sensitisation, bronchodilator response, or exhaled nitric oxide in the 5-year-old children.

There were beneficial associations between maternal apple intake and the childhood outcomes of ever wheezed, ever had asthma and doctor confirmed asthma, at age 5, with significant linear trends (table 4).

Table 4. Associations between maternal apple consumption and childhood wheeze and asthma at age 5 years

		Maternal apple consumption			
		T1 (0-1/week) n =398	T2 (1-4/week) n = 427	T3 (>4/week) n = 384	(n-1209)
Childhood outcome n (%)	**N**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**p-trend**
Wheeze in last 12 months 162 (12.9%)					
Univariate	1003	1	1.09 (0.69-1.67)	0.61 (0.37-1.01)	0.066
Multivariate#	1003	1	1.08 (0.68-1.71)	0.67 (0.40-1.13)	0.156
Wheeze without cold in last 12 months 84 (6.7%)					
Univariate	1003	1	1.32 (0.72-2.43)	0.64 (0.31-1.35)	0.286
Multivariate#	1003	1	1.27 (0.67-2.43)	0.70 (0.32-1.51)	0.411
Ever wheezed 253 (20.2%)					
Univariate	999	1	0.86 (0.60-1.23)	0.59 (0.40-0.88)	0.009
Multivariate#	999	1	0.85 (0.58-1.24)	0.63 (0.42-0.95)	0.029
Asthma and wheeze in last 12 months 107 (8.5%)					
Univariate	998	1	1.02 (0.60-1.73)	0.55 (0.29-1.03)	0.072
Multivariate#	998	1	1.03 (0.59-1.80)	0.60 (0.31-1.16)	0.148
Doctor confirmed asthma 145 (11.6%)					
Univariate	998	1	0.87 (0.56-1.36)	0.46 (0.27-0.78)	0.005
Multivariate#	998	1	0.83 (0.52-1.32)	0.47 (0.27-0.82)	0.008
Ever had asthma 156 (12.5%)					
Univariate	998	1	0.90 (0.58-1.38)	0.52 (0.31-0.86)	0.013
Multivariate#	998	1	0.86 (0.54-1.36)	0.54 (0.32-0.92)	0.026

#: Adjusted for maternal age of leaving full time education, paternal social class, maternal age, maternal smoking during pregnancy, smoking in the home during childhood, energy intake, maternal asthma, maternal atopy, birth weight, presence of older siblings, child's gender and breastfeeding

Maternal apple intake was not associated with childhood eczema and hay-fever or atopic sensitisation. However, beneficial associations were found between maternal total fish intake and doctor confirmed eczema and currently treated eczema (table 5), and between maternal oily fish intake and doctor confirmed hay-fever (table 6).

Table 5. Associations between maternal total fish consumption and childhood eczema at age 5 years

		Maternal total fish consumption			
		Never n = 107	< 1/week n = 255	≥ 1/week n = 831	(n=1193)
Childhood outcome n (%)	**N**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**p-trend**
Doctor confirmed eczema 380 (30.4%)					
Univariate	979	1	0.77 (0.46-1.28)	0.60 (0.38-0.96)	0.016
Multivariate#	979	1	0.79 (0.47-1.32)	0.57 (0.35-0.92)	0.008
Current eczema medication 191 (15.3%)					
Univariate	982	1	0.85 (0.45-1.61)	0.67 (0.38-1.19)	0.111
Multivariate#	982	1	0.88 (0.46-1.67)	0.58 (0.32-1.06)	0.028
Ever had eczema 406 (32.4%)					
Univariate	983	1	0.88 (0.53-1.47)	0.73 (0.47-1.16)	0.111
Multivariate#	983	1	0.91 (0.54-1.53)	0.68 (0.43-1.10)	0.050

#: Adjusted for maternal age of leaving full time education, paternal social class, maternal age, maternal smoking during pregnancy, smoking in the home during childhood, energy intake, maternal atopy, birth weight, presence of older siblings, child's gender and breastfeeding

Table 6. Associations between maternal oily fish consumption and childhood hay-fever at age 5 years

		Maternal oily fish consumption			
		Never n = 629	< 1/week n = 414	≥ 1/week n = 161	(n=1204)
Childhood outcome n (%)	**N**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**p-trend**
Doctor confirmed hay-fever 68 (5.4%)					
Univariate	990	1	0.57 (0.31-1.08)	0.20 (0.05-0.85)	0.006
Multivariate#	990	1	0.66 (0.34-1.28)	0.28 (0.06-1.19)	0.043
Current hay-fever medication 44 (3.5%)					
Univariate	988	1	1.08 (0.53-2.22)	0.20 (0.03-1.53)	0.226
Multivariate#	988	1	1.02 (0.48-2.20)	0.19 (0.02-1.48)	0.194
Ever had hay-fever 111 (8.9%)					
Univariate	988	1	1.11 (0.70-1.75)	0.38 (0.15-0.98)	0.155
Multivariate#	988	1	1.11 (0.68-1.82)	0.37 (0.14-0.98)	0.159

#: Adjusted for maternal age of leaving full time education, paternal social class, maternal age, maternal smoking during pregnancy, smoking in the home during childhood, energy intake, maternal asthma, maternal atopy, birth weight, presence of older siblings, child's gender and breastfeeding

There was a significant beneficial association between higher maternal oily fish intake (≥1 portion a week) and ever having hay-fever, but the association did not show a significant linear trend (p=0.159) (table 6).

Inclusion of maternal supplement use during pregnancy did not alter the magnitude or significance of the associations between maternal food intake and outcomes in 5-year-old children.

Association between the children's diet and respiratory and allergic symptoms at age 5 years
Maternal diet during pregnancy and the child's diet at age 5 were weakly but significantly positively correlated. Kendall's tau-b statistics were 0.21 (p<0.001) for the child's and maternal total fruit consumption, 0.15 (p<0.001) apple consumption, and 0.20 (p<0.001) and 0.26 (p<0.001) for total fish and oily fish consumption respectively.

Despite this, we found no consistent associations between the children's apple, total fish, or oily fish intake and the respiratory or allergic symptoms at age 5 years.

DISCUSSION

This study investigated associations between maternal intake of different food groups during pregnancy and symptoms of asthma and atopy in children. There was no evidence of associations between asthma, respiratory or atopic outcomes in 5-year-old children and maternal intakes of total fruit, citrus/kiwi fruit, total vegetables, green leafy vegetables, fruit juice, whole grain products, fat from dairy products, or butter versus margarine/low fat spread use. However, we have demonstrated beneficial associations between maternal apple intake and childhood wheeze, and asthma, and between maternal fish intake and childhood eczema and hay-fever. There are some reports of beneficial effects of maternal fish consumption and maternal fish oil supplementation during pregnancy on childhood asthma and neonatal CBMC responses,[20, 21] but to our knowledge our finding of the protective effects of maternal apple consumption during pregnancy on childhood wheeze and asthma is a novelty.

In this cohort, we have reported beneficial associations between maternal vitamin E intake during pregnancy and CBMC responses at birth,[3] wheeze at age 2,[4] and wheeze and asthma at age 5 years.[2] We have also demonstrated beneficial associations between maternal zinc intake during pregnancy and asthma and eczema in children at the age of 5, and between maternal vitamin D intake and wheeze in children at age 5.[2, 5] One of the aims of this study was to investigate whether these associations with maternal nutrient intakes could be a consequence of associations with individual foods rich in one or several of these nutrients, with obvious implications for a potential dietary intervention during pregnancy. It would seem that the associations reported here with maternal intake of apples and fish are insufficient to account for the associations with vitamin E, vitamin D, and zinc because in the UK apples and fish provide less than 10% of dietary vitamin E, and zinc intakes in women of this age group. In addition the pattern of associations between vitamin E, vitamin D, zinc and childhood respiratory and allergic outcomes differed from those in the present study. In the UK there is no single major dietary source of vitamin E in women aged 25-49, with intake being evenly distributed between fat spreads (15%), cereals/cereal products (10%), potatoes/potato snacks (12-14%), vegetables (16-17%) and meat/meat products (10%).[22] In the present study, the absence of any association between the usual dietary sources of vitamin E and respiratory outcomes, suggests that the associations with vitamin E in a previous report [2] were unlikely to represent associations with other nutrients commonly found in vitamin E containing foods.

The present study suggests beneficial associations between maternal apple intake during pregnancy and wheeze and asthma at age 5 years. The evidence from other observational studies on children's diet and respiratory and atopic symptoms is relatively consistent, showing beneficial effects of fruit and vegetable intake on indicators of asthma.[8-11] However, it is not clear whether these effects can be attributed to specific nutrients or that a high intake of fruit and vegetables is an indicator of a healthier lifestyle. The specific association found with apples in this study, and not with total fruit, citrus, fruit juice or vegetable consumption, suggests an apple specific effect, possibly because of its phytochemical content, such as flavonoids. Flavonoids are polyphenolic compounds with powerful antioxidant capacities and are associated with reduced risks of several diseases, including asthma and COPD.[23-25] Intake of apples as a significant source of flavonoids and other polyphenols has been beneficially associated with asthma, bronchial hypersensitivity, and lung function in adults.[24, 26-28] These effects are usually ascribed to the strong antioxidant capacities of apples, although there is also evidence that some polyphenolic compounds can influence cytokine gene expression by Th-cells, promoting the secretion of the Th1 cytokine interferon-γ and inhibiting secretion of the Th2 cytokine interleukin-4.[29] However, there is a lack of epidemiological evidence on the relation between the intake of flavonoids or specific flavonoid-rich foods and asthma or allergy in children. Although the consumption of total fresh fruit has increased in recent years, UK apple consumption fell from 207 g/person/day in 1974 to 173 g/person/day in 2004/5.[30] It has also been suggested that the mineral content of fruit and vegetables declined between 1940 and 1991.[31] This could be the consequence of changes in cultivation, the use of fertilizers and the choice of fruit species that can be more easily harvested or stored.

The observation of beneficial associations between maternal total and oily fish consumption and current eczema and ever hay-fever at age 5 respectively, is consistent with earlier observations.[20, 21] Dunstan et al. examined the effect of fish oil supplementation during pregnancy on early developing immune responses and clinical outcomes in infants predisposed to allergic disease. Neonates born to the mothers supplemented with fish oil tended to have lower CBMC cytokine responses to allergens, and at 1 year of age significantly less severe disease if they had atopic dermatitis.[21] Salam et al. studied the association between maternal fish consumption during pregnancy and childhood asthma. They found that maternal oily fish consumption at least monthly was significantly protective for persistent asthma in the 5-year-old children.[20] Other epidemiological evidence on the effect of fish intake or fish oil supplementation on asthma or allergic diseases provided by observational and intervention studies in children is inconsistent.[32, 33] Therefore it is more likely that the time window for n-3 polyunsaturated fatty acids to have an effect on immune regulation and subsequent asthma and atopic disease is indeed in fetal life, and that effects are limited once allergic immune responses are established.[21]

Originally, the study population of 2000 pregnant women was demographically very similar to the local obstetric population.[4] In this study, there was some evidence of response bias due to the loss to follow up with time. Participating mothers were of higher socio-economic status, and had slightly higher consumption of fruit, green leafy vegetables, whole grain products, and fish, and had less respiratory symptoms.[2] An analysis of the wheezing symptoms of the children whose mothers responded at 2 years but not at 5 years indicated that the children with no data at 5 years were more likely to have wheezed at 2 years (not presented). This type of response bias often plays a role in cohort studies because it is known that subjects with poorer social economic status and life-style (lower educational level, poorer diet, smoking etc.) are more difficult to trace, and that people who suffer poor health during the follow-up period are prone to attrition.[34] However, due to this type of bias, it is more likely that the observed associations in this study are underestimated than overestimated, for instance improved ascertainment at 5 years would have resulted in a larger proportion of wheezy children with low maternal apple consumption, this would make the observed associations between maternal apple consumption and childhood asthma/wheezing symptoms stronger (in this case odds ratios closer to zero). A limitation of FFQ derived estimates is that they are susceptible to dietary misreporting, which leads to dietary misclassification of intake and/or portion sizes. Usually this misclassification is random and it also rather weakens than augments the associations. To avoid multiple hypothesis testing we chose a restricted number of food groups based on our previous findings in this cohort and earlier reported associations,[13, 14, 27] the lipid hypothesis,[35] and antioxidant hypothesis.[36] It is possible that the associations reported could be a consequence of the number of analyses performed. However, we consider this is unlikely because some of the associations were highly significant and the associations were clustered with food groups that have been previously associated with similar outcomes in children and adults.

The predominance of associations between maternal food intakes and doctor-diagnosed outcomes raises the possibility of ascertainment bias, whereby mothers more conscious of health issues were both more likely to follow dietary advice to eat healthily and more likely to take their unwell children to the doctor to receive a formal diagnosis. Such ascertainment bias seems unlikely because it predicts that maternal apple consumption should be adversely associated with childhood doctor diagnosed conditions; the opposite of what we report.

The observed associations with maternal food intake during pregnancy were independent of the childhood diet because inclusion of children's apple and fish consumption in the models did not change the results despite maternal and childhood diet being weakly correlated.

Published cross-sectional surveys of children have reported associations between the dietary intake of citrus, kiwi, fruit and vegetables and indicators of asthma, [8-10] however the present study failed to demonstrate any consistent associations between the food intake of children aged 5 and respiratory and atopic symptoms. The children in the present study were younger than the children participating in previous studies (6-11 years) and this may account for disparity between this and previous studies. In the present study it would appear that until at least the age of 5 years maternal diet during pregnancy is more influential on respiratory health than childhood diet. Further follow-up of this birth cohort will be required to determine whether the associations with maternal diet decline in older children and if maternal and childhood diets interact in older children.

The associations between maternal apple consumption and asthma and symptoms could represent effects on airway and immune development, while the associations between maternal (oily) fish consumption and eczema and hay-fever suggest effects on Th-cell differentiation,[37] yet, no associations were found with lung function measures, FE_{NO} and atopic sensitisation. This could reflect a loss of power due to the smaller number of children who had spirometry or skin prick tests.

The results of this cohort study indicate that there were no consistent linear associations between maternal intake of total fruit, citrus/kiwi fruit, total vegetables, green leafy vegetables, fruit juice, whole grain products, fat from dairy products, or butter versus margarine/low fat spread use during pregnancy and asthma, respiratory and atopic outcomes in 5-year-old children. Yet, we did find some evidence for protective effects of maternal apple and fish consumption. Thus in addition to maternal intake of vitamin E, vitamin D, and zinc during pregnancy,[2-5] maternal consumption of apples and fish during pregnancy may reduce the risk of children developing asthma or atopic disease. If these results are confirmed, recommendations on dietary modification during pregnancy may help to prevent childhood asthma and allergy.

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COMPETING INTERESTS

The authors declare to have no competing interests.

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