



# Effect of diet and maternal education on allergies among preschool children: A case-control study



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## ABSTRACT

**Introduction:** The prevalence of asthma and allergy has increased among children. This increase in prevalence might be related to dietary patterns.

**Aims:** The present epidemiological study investigated the relationship between the consumption of fruit, vegetables, nuts, meat and fish, and the prevalence of wheeze, asthma, and eczema among preschool children.

**Methods:** This nested case-control study included 1489 children aged 4–6 years and residing in Kaunas city, Lithuania. The subjects were recruited to the KANC newborn cohort study during 2007–2009. Parents' responses to questionnaires were used to collect information on allergic diseases, diet, and other variables. The association between dietary patterns and children's allergic diseases were tested by using logistic regressions, after adjustment for maternal education level, smoking during pregnancy, parental asthma, children's sex, parity, and antibiotic usage during the first year of life.

**Results:** In this study, 83.3% of all children consumed fresh fruit and/or vegetables at least three times per week. A significantly lower adjusted odds ratio (aOR) of wheeze was found among children who ate fruit than among those who did not (aOR: 0.48; 95% CI: 0.22–0.96). The consumption of nuts was also associated with a lower 61% risk of eczema among 4–6 years old children.

**Conclusion:** The results indicated a beneficial effect of a frequent consumption of fresh fruit and nuts on the prevalence of allergies among children. These results might have important implications for children's health.

## 1. Introduction

Childhood asthma causes a large public health burden because of its high prevalence and increasing morbidity. Over the past few decades, the prevalence of asthma has markedly increased worldwide, and this increase is largely caused by environmental factors, changes of lifestyle behaviors, and dietary patterns (Lv et al., 2014). Previous studies suggested that the avoidable environmental hazards, such as tobacco smoke, poor housing conditions, and diets with a high caloric content and a low content of antioxidants may be considered to be potential risk factors for childhood asthma (Burke et al., 2012; Eder et al., 2006). Nutrition could contribute to the development of asthma and allergic diseases, although the epidemiological evidence to date is still unclear (Devereux and Seaton, 2005; Romieu and Trenga, 2001; Tricon et al., 2006).

A growing body of evidence suggests that environmental factors, particularly adverse nutritional family habits in the prenatal and early life, significantly contribute to the development of chronic childhood diseases such as obesity and asthma (Julia et al., 2015; Symonds et al.,

2009). The children's dietary patterns often depend on their parents' socioeconomic status, family status, or health behavior. Exposures that confer risk for incident childhood asthma and allergy include early-life stressors and infections, allergens, outdoor pollutants, and tobacco smoke (Chan-Yeung et al., 2008). Pre-natal exposure to tobacco smoke adversely affects postnatal lung function and increases the risk of developing asthma and asthma symptoms later in life (Cook et al., 1998; Gilliland et al., 2000). The mechanisms of the development asthma and allergies are unclear but there is growing evidence indicating that early-life environmental and socioeconomic disadvantage may be associated with higher pro-inflammatory cytokine levels later in life, whereas associations with markers of lipid and glucose metabolism are less consistent (Danese et al., 2009; Entringer et al., 2008; Slopen et al., 2015).

Several epidemiological studies on children have demonstrated a reduced risk of allergic diseases in relation to a high fruit intake. Epidemiological studies have shown a beneficial effect of increased fruit and vegetable consumption on asthma and allergy in children (Farchi et al., 2003; Forastiere et al., 2000). This effect is associated with increased intake antioxidants, which play a positive role in decreasing the

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risk of allergic diseases throughout childhood and adulthood (Chatzi et al., 2007; Maynard et al., 2003). A higher intake of fruit and vegetables has also been associated with lower blood pressure and a lower risk of stroke in adulthood (Moore et al., 2005; Ness et al., 2005). Previous studies have reported that the quality of the diet is socially oriented, and is associated with parental occupation, education, and income levels (Groth et al., 2001; Krieger et al., 1997; Petrauskienė et al., 2015; Turrell et al., 2003). Less healthy diets are more prevalent among people of lower social classes (Galobardes et al., 2001). Most of the studies on the associations between children's dietary patterns and asthma were cross-sectional and reported inconsistent findings and different levels of associations, while few studies were cohort studies (Romieu et al., 2009; Tromp et al., 2012). A recently published systematic review based on a meta-analysis concluded that the Mediterranean diet in children might prevent current wheeze and asthma during any period of life (Garcia-Marcos et al., 2013).

Meanwhile, a study conducted in Japan found a beneficial effect of maternal “Western” dietary pattern (also called the Standard American Diet, or the meat-sweet diet), characterized by a high intake of sea food and fish and a high intake of processed meat, eggs, and animal fats (Hu, 2002) on wheeze (OR: 0.59; 95% CI: 0.35–0.98;  $p = 0.02$ ) in infants aged 16–24 months (Miyake et al., 2011). In Japan, the “Western” dietary pattern was improved by ingredients associated with a high intake of  $\alpha$ -linolenic acid, vitamin E, and  $\beta$ -carotene, which have a beneficial effect on asthma and wheezing (Allan and Devereux, 2011; Nurmatov et al., 2011; Varraso, 2012). Therefore, we can expect that dietary patterns are region-specific and population-specific, and that socio-environmental factors should be taken into account when studying the effects of dietary patterns on children's allergies in diverse populations.

This study seeks to analyze the associations between children's dietary habits (the data were obtained from standardized food frequency questionnaires (FFQ)) and health outcomes, at the individual level controlling for the impact of the covariates associated with asthma. The aim of the present study was to investigate the relationship between the consumption of fruit, vegetables, nuts, meat and fish and the prevalence of wheezing, physician-diagnosed asthma, and eczema among preschool children.

## 2. Materials and methods

### 2.1. Study population and data collection

In this study, we used primary data of women residing in Kaunas city who were recruited to the pregnant women's cohort study during 2007–2009. In 2012–2013, we invited 3294 mothers and their 4–6 year-old children to participate in the asthma study. A detailed description of the study has been provided previously (Andrusaityte et al., 2016; Grazuleviciene et al., 2014). Responses to postal questionnaires were received from 1489 mothers. The participants of this research were children whose parents or guardians filled out the questionnaires and agreed to participate in the study. The study was approved by the Lithuanian Bioethics Committee, and parental informed consent was obtained from all participants. Questionnaire responses by parents or guardians were used to categorize children's basic information, medical history, family history, medical history of asthma and allergic rhinitis in the family, personal habits, and housing and environmental conditions, tobacco exposure, and including diet.

Outcome variables were defined as providing positive answers to the following questions of the standardized International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire: for physician-diagnosed asthma - ‘Has your child ever had physician-diagnosed asthma?’; for wheeze - ‘Has your child ever had wheezing or whistling in the chest?’; and for atopic eczema - ‘Has your child ever had eczema?’. Dietary information was collected using a food frequency questionnaire (FFQ), asking about the diet and nutrition of the children.

Information was also collected about the weekly frequency of the consumption of each food group – vegetables (broccoli or cauliflower, carrot, tomato, potatoes, courgettes, lettuce, avocado, cladodes, green beans, and chili or chili sauce) and fruit and nuts (orange, grape, apple, banana, peach, watermelon, pineapple, papaya, pear, kiwi, mango, strawberry, prickly pears, plums, orange juice, grapefruit juice, almonds, walnuts, hazelnuts, and peanuts); meat and fish. In the present study, we considered “fruit and vegetables” to be any fresh, frozen, dried, or canned fruit and vegetables. Questions about the intake frequency of fruit, vegetables, nuts, meat and fish were asked separately. The answer alternatives were: ‘never’; ‘1–2 times per week’; and ‘3 and more times per week’. In analysis to compare the results with previous studies, foods intake were dichotomized into a ‘yes intake category’ if a child eating at least one and more times per week of foods and a ‘no intake category’ if a child do not eat of fruit, vegetables, nuts, meat or fish.

The evaluation of sedentary behavior (physical inactivity) was based on answers to questions on the duration of television watching and computer use. The following questions were asked “How many hours per day does your child watch television on weekdays?” and “How many hours per day does your child spend at the computer on weekdays?” The responses were recorded as the mean number of hours of sedentary behavior per day. According to the recommendation of the American Academy of Pediatrics, the average preschool children screen time should be limited to 3 h per day (American Academy of Pediatrics, 2001).

### 2.2. Statistical analysis

We used the chi-squared univariate logistic regression analysis to compare the values and the frequencies of baseline characteristics to the allergy status of the children, and to evaluate the associations among the covariates that are known to be related to an increased risk of allergies. Predictor variables whose univariate test showed a statistically significant association ( $p < 0.05$ ) to the outcome or that changed the adjusted odds ratios (aOR) by 10% or more were retained for inclusion in the multivariate logistic regression analysis.

Multivariate logistic regressions were used to assess the relationship between weekly consumption of vegetables, fruit, nuts, meat and fish, and asthma, wheeze, and eczema among children, adjusting for maternal education, active and passive smoking, parental history of asthma, the child's sex, and antibiotic use during the first year of life. Additionally we also adjusted for consumed foods. The group of children who did not consume vegetables, fruit, nuts, meat or fish was used as the reference group. The association between diet and children's allergic diseases was estimated as unadjusted (crude) and adjusted odds ratios with 95% confidence intervals (CI). All statistical analyses were performed using SPSS version 18.0.

## 3. Results

The demographic variables of those women who did not respond to the questionnaire (non-participants) were not statistically significantly different from the participants with regard to the age, education level, other characteristics, and birth outcomes (see [Supplementary materials Table S1](#)). The characteristics of the children who participated in the study are shown in [Table 1](#). The prevalence of wheeze, atopic eczema, and physician-diagnosed asthma were 11.3%, 6.8%, and 7.5%, respectively. The women who participated in the study were highly educated – 60.8% of them had university degree. The majority of the studied children (83.3% of all participants) ate fresh fruit/vegetables; among them 62.7% consumed vegetables, and 6.2% - nuts at least three times per week. Even 73.3% of children three and more times per week consumed processed meat, while 47.4% of them did not ate fish.

[Table 2](#) shows the distribution of the variables according to the maternal educational level. In general, some characteristics were

**Table 1**  
Characteristics of the study population (N = 1489).

| Characteristic                     | N (%)       |
|------------------------------------|-------------|
| Physician-diagnosed asthma         | 112 (7.5)   |
| Wheeze (during any period of life) | 168 (11.3)  |
| Eczema                             | 101 (6.8)   |
| Nuts allergy                       | 13 (0.9)    |
| Weekly fruits consumption          |             |
| Never                              | 41 (2.8)    |
| 1–2 times                          | 208 (14.0)  |
| 3 and more times                   | 1240 (83.3) |
| Weekly vegetable consumption       |             |
| Never                              | 134 (9.0)   |
| 1–2 times                          | 421 (28.3)  |
| 3 and more times                   | 934 (62.7)  |
| Weekly nuts consumption            |             |
| No                                 | 831 (55.8)  |
| Yes                                | 658 (44.2)  |
| Weekly meat consumption            |             |
| Never                              | 26 (1.7)    |
| 1–2 times                          | 372 (25.0)  |
| 3 and more times                   | 1091 (73.3) |
| Weekly fish consumption            |             |
| Never                              | 706 (47.4)  |
| 1–2 times                          | 738 (49.6)  |
| 3 and more times                   | 45 (3.0)    |
| <b>Covariates</b>                  |             |
| Maternal age at childbirth, years  |             |
| 30 and less                        | 995 (66.8)  |
| More than 30                       | 494 (33.2)  |
| Maternal educational level         |             |
| Low (10 or fewer years)            | 307 (20.6)  |
| Medium                             | 277 (18.6)  |
| High                               | 905 (60.8)  |
| Maternal smoking during pregnancy  |             |
| Non-smokers                        | 1376 (92.4) |
| Smokers                            | 113 (7.6)   |
| Maternal passive smoking           |             |
| No                                 | 956 (64.2)  |
| Yes                                | 533 (35.8)  |
| Parity                             |             |
| No                                 | 822 (55.2)  |
| Yes                                | 667 (44.8)  |
| Child's sex                        |             |
| Girl                               | 751 (50.4)  |
| Boy                                | 738 (49.6)  |

unequally distributed between the maternal educational level groups ( $p < 0.05$ ): maternal family status, maternal active and passive smoking, parity, child's birth weight, antibiotic use during the first year of life, sedentary behavior, children's allergies, and frequent consumption of fruit, vegetable, and weekly meat consumption. In the group with low education level, physician-diagnosed asthma was found in 10.7% of families, while in high educational level group the prevalence of physician-diagnosed asthma was 5.7% ( $p < 0.05$ ). The prevalence of eczema among mothers with high educational level was 8.5% while among mothers with medium and low educational level – 5.4% and 2.9%, accordingly.

Table 3 presents the crude and adjusted associations of wheeze, asthma, and eczema with the weekly consumption of fruit, vegetables, nuts, meat and fish. The consumption of fruit was found to have a statistically significant beneficial effect on wheeze in univariate analysis, and remain robust after adjusting for potential confounders (aOR: 0.48; 95% CI: 0.22–0.96;  $p < 0.05$ ) to compare with no fruit consumption. Crude and adjusted odds ratio of asthma were lower for children who ate fruit, vegetables, nuts and meat, however, the result was not statistically significant. The consumption of nuts was statistically significant associated with a lower risk of eczema (aOR: 0.61; 95% CI: 0.39–0.95). The intake of fish had a tendency to increase crude and adjusted odds ratios for asthma and wheeze and decrease for eczema odds ratios. These associations were robust after additional controlling

**Table 2**  
Comparison of participants' characteristics by maternal educational level.

| Characteristics                              | Low educational level, N (%) | Medium educational level, N (%) | High educational level, N (%) | p-value     |
|----------------------------------------------|------------------------------|---------------------------------|-------------------------------|-------------|
| Family status                                |                              |                                 |                               | $p = 0.000$ |
| Both parents                                 | 239 (77.9)                   | 236 (85.2)                      | 831 (91.8)                    |             |
| Single                                       | 68 (22.1)                    | 41 (14.8)                       | 74 (8.2)                      |             |
| Eczema                                       |                              |                                 |                               | $p = 0.002$ |
| No                                           | 298 (97.1)                   | 262 (94.6)                      | 828 (91.5)                    |             |
| Yes                                          | 9 (2.9)                      | 15 (5.4)                        | 77 (8.5)                      |             |
| Asthma                                       |                              |                                 |                               | $p = 0.005$ |
| No                                           | 274 (89.3)                   | 250 (90.3)                      | 853 (94.3)                    |             |
| Yes                                          | 33 (10.7)                    | 27 (9.7)                        | 52 (5.7)                      |             |
| Wheeze (during any period of life)           |                              |                                 |                               | $p = 0.006$ |
| No                                           | 244 (79.5)                   | 228 (82.3)                      | 785 (86.7)                    |             |
| Yes                                          | 63 (20.5)                    | 49 (17.7)                       | 120 (13.3)                    |             |
| Active smoking during pregnancy              |                              |                                 |                               | $p = 0.000$ |
| No                                           | 249 (81.1)                   | 260 (93.9)                      | 867 (95.8)                    |             |
| Yes                                          | 58 (18.9)                    | 17 (6.1)                        | 38 (4.2)                      |             |
| Passive smoking                              |                              |                                 |                               | $p = 0.000$ |
| No                                           | 122 (39.7)                   | 172 (62.1)                      | 662 (73.1)                    |             |
| Yes                                          | 185 (60.3)                   | 105 (37.9)                      | 243 (26.9)                    |             |
| Maternal age at childbirth                   |                              |                                 |                               | $p = 0.898$ |
| ≤ 30 years                                   | 207 (67.4)                   | 182 (65.7)                      | 606 (67.0)                    |             |
| > 30 years                                   | 100 (32.6)                   | 95 (34.3)                       | 299 (33.0)                    |             |
| Child's birth weight                         |                              |                                 |                               | $p = 0.032$ |
| ≤ 2500 g                                     | 27 (8.8)                     | 10 (3.6)                        | 54 (6.0)                      |             |
| > 2500 g                                     | 280 (91.2)                   | 267 (96.4)                      | 851 (94.0)                    |             |
| Child's sex                                  |                              |                                 |                               | $p = 0.632$ |
| Male                                         | 145 (47.2)                   | 141 (50.9)                      | 452 (49.9)                    |             |
| Female                                       | 162 (52.8)                   | 136 (49.1)                      | 453 (50.1)                    |             |
| Sedentary behavior (h per day)               |                              |                                 |                               | $p = 0.000$ |
| ≤ 3                                          | 221 (72.0)                   | 210 (75.8)                      | 761 (84.1)                    |             |
| > 3                                          | 86 (28.0)                    | 67 (24.2)                       | 144 (15.9)                    |             |
| Child's BMI                                  |                              |                                 |                               | $p = 0.005$ |
| < 18                                         | 271 (88.3)                   | 262 (94.6)                      | 845 (93.4)                    |             |
| ≥ 18                                         | 36 (11.7)                    | 15 (5.4)                        | 60 (6.6)                      |             |
| Parity                                       |                              |                                 |                               | $p = 0.014$ |
| No                                           | 151 (49.2)                   | 145 (52.3)                      | 526 (58.1)                    |             |
| Yes                                          | 156 (50.8)                   | 132 (47.7)                      | 379 (41.9)                    |             |
| Antibiotic use during the first year of life |                              |                                 |                               | $p = 0.020$ |
| No                                           | 195 (63.5)                   | 164 (59.2)                      | 615 (68.0)                    |             |
| Yes                                          | 112 (36.5)                   | 113 (40.8)                      | 290 (32.0)                    |             |
| Weekly fruit consumption                     |                              |                                 |                               | $p = 0.028$ |
| Never                                        | 14 (4.6)                     | 8 (2.9)                         | 19 (2.1)                      |             |
| 1–2 times                                    | 52 (16.9)                    | 44 (15.9)                       | 112 (12.4)                    |             |
| 3 and more times                             | 241 (78.5)                   | 225 (81.2)                      | 774 (85.5)                    |             |
| Weekly vegetable consumption                 |                              |                                 |                               | $p = 0.000$ |
| Never                                        | 39 (12.7)                    | 28 (10.1)                       | 67 (7.4)                      |             |
| 1–2 times                                    | 108 (35.2)                   | 75 (27.1)                       | 238 (26.3)                    |             |
| 3 and more times                             | 160 (52.1)                   | 174 (62.8)                      | 600 (66.3)                    |             |
| Weekly nut consumption                       |                              |                                 |                               | $p = 0.053$ |

(continued on next page)

Table 2 (continued)

| Characteristics         | Low educational level, N (%) | Medium educational level, N (%) | High educational level, N (%) | p-value   |
|-------------------------|------------------------------|---------------------------------|-------------------------------|-----------|
| Never                   | 165 (53.7)                   | 149 (53.8)                      | 517 (57.1)                    |           |
| 1–2 times               | 113 (36.8)                   | 16 (41.9)                       | 337 (37.2)                    |           |
| 3 and more times        | 29 (9.4)                     | 12 (4.3)                        | 51 (5.6)                      |           |
| Weekly meat consumption |                              |                                 |                               | p = 0.000 |
| Never                   | 7 (2.3)                      | 7 (2.5)                         | 12 (1.3)                      |           |
| 1–2 times               | 106 (34.5)                   | 76 (27.4)                       | 190 (21.0)                    |           |
| 3 and more times        | 194 (63.2)                   | 194 (70.0)                      | 703 (77.7)                    |           |
| Weekly fish consumption |                              |                                 |                               | p = 0.070 |
| Never                   | 161 (52.4)                   | 130 (46.9)                      | 415 (45.9)                    |           |
| 1–2 times               | 132 (43.0)                   | 139 (50.2)                      | 467 (51.6)                    |           |
| 3 and more times        | 14 (4.6)                     | 8 (2.9)                         | 23 (2.5)                      |           |

for impact of each studied food, as presented in Table 3 footnote.

#### 4. Discussion

In this nested case-control study, we found a statistically significantly higher prevalence of asthma and wheeze among 4–6 year-old children whose mothers had low educational level. This study revealed a positive effect of vegetable and fruit consumption on allergy in children. Weekly consumption of vegetables and fruit was higher among children of higher-educated mothers. Our results are in accordance with the findings of a cross-sectional study in Norway, where families with a lower socioeconomic status reported lower intake of fruit and vegetables (Fismen et al., 2014). A cohort study found that fruit consumption increased with the family's material wealth and higher parental occupational status (Vereecken et al., 2005). Socioeconomic status influenced food preferences and eating behavior in children (Cullen et al., 2002) and families (Janssen et al., 2006). A lower education level, poorer knowledge about nutrition, and lower affordability of healthy food has been shown to contribute to unhealthy eating behavior in families with low socioeconomic status (Evans et al., 2006). A recent French EDEN mother-child cohort study also concluded that diets in

developed countries are socially differentiated with a positive correlation between the quality of dietary intake and the socioeconomic position (Camara et al., 2015).

Concerning the associations between the participants' characteristics and childhood allergy, this study confirmed the predictors of allergies in such children: lower maternal education level, maternal active smoking during pregnancy and passive smoking, and antibiotic usage during the first year of life. We found higher prevalence of eczema among 4–6 year-old children whose mothers were higher educated. The results of our study are in accordance with those from other study (Shaw et al., 2011) regarding the association between maternal educational level and children eczema. This study inferences are accordant with the findings of previous studies indicating that maternal smoking during pregnancy is associated with the children's wheezing (Csonka et al., 2000; Grazuleviciene et al., 2014) and may affect the development of the immune system in the fetus (Mund et al., 2013). Moreover, there is evidence that tobacco smoke damages the antioxidant system, produces changes in DNA methylation (Breton et al., 2009; Koshy et al., 2011), and mediates eating behavior (Danford et al., 2015). Studies of mechanisms in humans have provided insight into novel metabolite signatures associated with dietary exposures, such as fish, red meat, and vegetable consumption (Beckman, 2013; Guertin et al., 2014). DNA methylation may alter metabolic pathways involved in the etiology of chronic diseases, such as obesity and asthma (Acevedo et al., 2015; Dick et al., 2014). There is evidence that antibiotic use in early life impairs postnatal maturation of the immune system that protects against the development of atopy (Holt and Strickland, 2010). Similarly to this study, a cohort study in the US confirmed the association between early antibiotic exposure and an increased risk of asthma (aOR: 1.52; 95% CI: 1.07–2.16) (Risnes et al., 2011), while diversity of the microflora in infants has been associated with the development of the infants' immunity and possibly an increased risk of allergic diseases in later childhood (Ly et al., 2011).

Several epidemiological studies of adults have demonstrated a reduced risk of asthma associated with a high fruit intake (Garcia et al., 2005; Patel et al., 2006; Romieu et al., 2006; Shaheen et al., 2001) but findings in children have been inconsistent (Antova et al., 2003; Hijazi et al., 2000). This study findings are in line with other studies reporting on positive role of fruit on wheeze in children. The PIAMA birth cohort

Table 3

Association (crude and adjusted odds ratios and 95% confidence interval) of wheeze, asthma, and eczema with weekly consumption of fruit, vegetables, nuts, meat and fish among children of Kaunas city.

| Food groups                            | Asthma            |                  | Wheeze                        |                               | Eczema                        |                               |
|----------------------------------------|-------------------|------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
|                                        | Crude OR (95% CI) | aOR (95% CI)     | Crude OR (95% CI)             | aOR (95% CI)                  | Crude OR (95% CI)             | aOR (95% CI)                  |
| <b>Fruit intake<sup>a,b</sup></b>      |                   |                  |                               |                               |                               |                               |
| No                                     | Reference         | Reference        | Reference                     | Reference                     | Reference                     | Reference                     |
| Yes                                    | 0.46 (0.19–1.12)  | 0.68 (0.24–1.96) | 0.43 <sup>c</sup> (0.22–0.86) | 0.48 <sup>c</sup> (0.22–0.96) | 0.66 (0.23–1.90)              | 0.49 (0.16–1.55)              |
| <b>Vegetables intake<sup>a,c</sup></b> |                   |                  |                               |                               |                               |                               |
| No                                     | Reference         | Reference        | Reference                     | Reference                     | Reference                     | Reference                     |
| Yes                                    | 0.67 (0.37–1.21)  | 0.82 (0.42–1.62) | 0.88 (0.55–1.41)              | 1.14 (0.66–1.96)              | 1.16 (0.55–2.46)              | 1.23 (0.55–2.75)              |
| <b>Nuts intake<sup>a,d</sup></b>       |                   |                  |                               |                               |                               |                               |
| No                                     | Reference         | Reference        | Reference                     | Reference                     | Reference                     | Reference                     |
| Yes                                    | 0.71 (0.48–1.06)  | 0.71 (0.47–1.09) | 0.93 (0.70–1.23)              | 0.93 (0.69–1.26)              | 0.57 <sup>e</sup> (0.37–0.87) | 0.61 <sup>e</sup> (0.39–0.95) |
| <b>Meat intake<sup>a,e</sup></b>       |                   |                  |                               |                               |                               |                               |
| No                                     | Reference         | Reference        | Reference                     | Reference                     | Reference                     | Reference                     |
| Yes                                    | 0.62 (0.18–2.09)  | 0.53 (0.62–2.34) | 0.77 (0.29–2.07)              | 0.68 (0.23–2.03)              | –                             | –                             |
| <b>Fish intake<sup>a,f</sup></b>       |                   |                  |                               |                               |                               |                               |
| No                                     | Reference         | Reference        | Reference                     | Reference                     | Reference                     | Reference                     |
| Yes                                    | 1.17 (0.80–1.73)  | 1.24 (0.82–1.87) | 1.23 (0.93–1.63)              | 1.23 (0.90–1.66)              | 0.74 (0.49–1.11)              | 0.75 (0.49–1.14)              |

\* p < 0.05.

<sup>a</sup> Adjusted for: maternal active and passive smoking, education status, parental asthma, antibiotic use during the first year of life, the child's sex, nuts allergy, and parity.

<sup>b</sup> Adjusted for: vegetables intake, nuts intake, meat intake, fish intake.

<sup>c</sup> Adjusted for: fruits intake, nuts intake, meat intake, fish intake.

<sup>d</sup> Adjusted for: fruit intake, vegetables intake, meat intake, fish intake.

<sup>e</sup> Adjusted for: fruit intake, vegetables intake, nuts intake, fish intake.

<sup>f</sup> Adjusted for: fruit intake, vegetables intake, nuts intake, meat intake.

data revealed that school age children, who ate continuously high amount of fruits since infancy, had less asthma risk than children who did not ate (Willers et al., 2011). A cross sectional study among 6–7 year-old children in Italy found an association between abundant consumption of fresh fruit and a highly significant protective effect against wheeze in the last 12 months (Forastiere et al., 2000). An ecological study has shown a decrease in the symptoms of wheezing and other allergic diseases associated with an increased consumption of vegetables and nuts (Ellwood et al., 2001). The meta-analysis of the results showed that the Mediterranean diet was negatively associated with current wheeze (OR: 0.79; 95% CI: 0.66–0.94) in Mediterranean regions, and with asthma during any period of life (OR: 0.86; 95% CI: 0.75–0.98;  $p = 0.027$ ) in non-Mediterranean regions (Lv et al., 2014).

It is difficult to compare this study results with other children populations in Europe because of different methods use for estimation of dietary patterns. The International Study on Allergies and Asthma in Childhood (ISAAC) that assessed the dietary data of children in 20 countries concluded that countries outside the Mediterranean region, for example, Sweden, can have higher adherence levels to a Mediterranean-like dietary pattern than in Southern European countries, for example, Cyprus (Nagel et al., 2010). Findings from recent study (Tognon et al., 2014) revealed a low prevalence of high consumers of vegetables and legumes (36.2%) between Italian children, the highest prevalence of fish consumers in Spain (25.8%), also a low prevalence of high consumers of meat (30.9%) in Sweden. In Portugal most children frequently ate fresh fruits (93%) and vegetables (99%) daily (Pereira-da-Silva et al., 2016), however, even 48% of school-children in Spain never or occasionally ate vegetables and fruit – 9.5%, nuts 56.6% and meat 2.3% (Castro-Rodriguez et al., 2008). Our findings showed similar frequency of never ate meat (1.7%) and nuts (55.8%) and lower frequency of fish consumption.

Dietary intake of vegetables and fruit is associated with antioxidant vitamins – especially vitamins A, C, and E and carotenoids – as well as with other antioxidants such as selenium and flavonoids that may have beneficial effects on asthma, wheezing symptoms, and the respiratory function (Devereux and Seaton, 2005; McKeever and Britton, 2004; Romieu and Trenga, 2001). Apart from the most widely known antioxidants found in fruit and vegetables, other compounds such as oleuropein, hydroxytyrosol, and other polyphenols present in olive oil are characterized by marked antioxidant activity and other advantageous biological properties (Fito et al., 2005; Pitsavos et al., 2005). Vitamin C is the major antioxidant present in the airway surface liquid of the lung, and it may protect against various allergens, tobacco smoke, and environmental hazards (Hatch, 1995). There is some evidence that asthmatic people have low plasma concentration of vitamin C and an increased oxidative stress (Rahman and MacNee, 1996). A cohort study in Mexico found that the higher vitamin E intake was associated with higher levels of vitamin C in the body, and this combination is positively related to lung function (Moreno-Macías et al., 2014). On the other hand, a cross-sectional study in Istanbul did not find any association between the consumption of antioxidant-containing food such as fruit or vegetables and atopic diseases (Tamay et al., 2014).

#### 4.1. Strengths and limitations

This study has advantages over previous similar studies because of its case-control design, a large sample size, the possibility to study the associations between children's dietary intakes evaluated using the standardized FFQ and health outcomes, at the individual level controlling for the impact of the covariates associated with childhood asthma.

The limitations of this study include its possible random measurement errors because the assessments of children's food consumption were based on the parents' responses to questions, and thus recall biases cannot be excluded. In addition, the estimations of the associations may

be skewed by unmeasured variables, which could have resulted in the misclassification of health outcomes and might have attenuated the strengths of the observed associations. However, these errors are assumed to be random.

## 5. Conclusion

The findings of this study indicated a beneficial effect of the frequent consumption of fresh fruit and nuts on children's allergies. Maternal education level affected the frequency of their children's fruit, vegetable and meat consumption. These results might have important implications for children's health, focusing future interventions on specific early-life diets for allergy prevention.

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## Ethics review

All participants provided written informed consent, and the study was approved by the Ethics Committee of Lithuania on April 30, 2012, No. 6B-12-147.

## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.envres.2017.08.020>.

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## Supplemental materials

**Table S1: Distribution of variables according to wheeze among children**

| <b>Variables</b>                               | <b>Wheeze yes<br/>N (%) (N=168)</b> | <b>Wheeze no<br/>N (%) (N=1321)</b> |
|------------------------------------------------|-------------------------------------|-------------------------------------|
| Mother's age at childbirth (years)             |                                     |                                     |
| <30                                            | 110 (11.1%)                         | 885 (88.9%)                         |
| 31 and more                                    | 58 (11.7%)                          | 436 (88.3%)                         |
| Maternal education level*                      |                                     |                                     |
| Low (10 or less years)                         | 52 (16.9%)                          | 255 (83.1%)                         |
| Medium, high (>10 years)                       | 116 (9.8%)                          | 1066 (90.2%)                        |
| Maternal smoking during pregnancy              |                                     |                                     |
| No                                             | 150 (10.9%)                         | 1226 (89.1%)                        |
| Yes                                            | 18 (15.9%)                          | 95 (84.1%)                          |
| Maternal secondhand smoking                    |                                     |                                     |
| No                                             | 98 (10.3%)                          | 858 (89.7%)                         |
| Yes                                            | 70 (13.1%)                          | 463 (86.9%)                         |
| Gas cooking                                    |                                     |                                     |
| No                                             | 52 (9.7%)                           | 483 (90.3%)                         |
| Yes                                            | 116 (12.2%)                         | 838 (87.8%)                         |
| Children's sex*                                |                                     |                                     |
| Male                                           | 103 (14.0%)                         | 635 (86.0%)                         |
| Female                                         | 65 (8.7%)                           | 686 (91.3%)                         |
| Children parity*                               |                                     |                                     |
| 1                                              | 79 (9.6%)                           | 743 (90.4%)                         |
| 2 and more                                     | 89 (13.3%)                          | 578 (86.7%)                         |
| Birth weight                                   |                                     |                                     |
| <2500 g                                        | 14 (15.4%)                          | 77 (84.6%)                          |
| 2501 g and more                                | 154 (11.0%)                         | 1244 (89.0%)                        |
| Breastfeeding                                  |                                     |                                     |
| No                                             | 16 (16.2%)                          | 83 (83.8%)                          |
| Yes                                            | 152 (10.9%)                         | 1238 (89.1%)                        |
| Paracetamol use during the first year of life  |                                     |                                     |
| No                                             | 41 (9.1%)                           | 412 (90.9%)                         |
| Yes                                            | 127 (12.3%)                         | 909 (87.7%)                         |
| Antibiotic use during the first year of life * |                                     |                                     |
| No                                             | 75 (7.7%)                           | 899 (92.3%)                         |
| Yes                                            | 93 (18.1%)                          | 422 (81.9%)                         |
| Asthma in parents*                             |                                     |                                     |
| No                                             | 140 (10.1%)                         | 1251 (89.9%)                        |
| Yes                                            | 28 (28.6%)                          | 70 (71.4%)                          |

\*p<0.05.

**Table S2: Distribution of variables according to children's asthma status**

| <b>Variables</b>                              | <b>Asthma yes<br/>N (%) (N=112)</b> | <b>Asthma no<br/>N (%) (N=1377)</b> |
|-----------------------------------------------|-------------------------------------|-------------------------------------|
| Mother's age at childbirth                    |                                     |                                     |
| ≤30                                           | 71 (7.14)                           | 923 (92.86)                         |
| 31 and more                                   | 41 (8.28)                           | 454 (91.72)                         |
| Maternal education status*                    |                                     |                                     |
| Low (10 or fewer years)                       | 33 (10.75)                          | 274 (89.25)                         |
| Medium and high (>10 years)                   | 79 (6.68)                           | 1103 (93.32)                        |
| Maternal smoking during pregnancy             |                                     |                                     |
| No                                            | 98 (7.12)                           | 1278 (92.88)                        |
| Yes                                           | 14 (12.39)                          | 99 (87.61)                          |
| Maternal passive smoking                      |                                     |                                     |
| No                                            | 66 (6.90)                           | 890 (93.10)                         |
| Yes                                           | 46 (8.63)                           | 487 (91.37)                         |
| Gas cooking                                   |                                     |                                     |
| No                                            | 34 (6.36)                           | 501 (93.64)                         |
| Yes                                           | 78 (8.18)                           | 876 (91.82)                         |
| Living in a flat                              |                                     |                                     |
| No                                            | 41 (6.73)                           | 568 (93.27)                         |
| Yes                                           | 71 (8.07)                           | 809 (91.93)                         |
| Sex                                           |                                     |                                     |
| Male                                          | 63 (8.54)                           | 675 (91.46)                         |
| Female                                        | 49 (6.52)                           | 702 (93.48)                         |
| Birth order                                   |                                     |                                     |
| 1                                             | 56 (6.81)                           | 766 (93.19)                         |
| 2 and more                                    | 56 (8.40)                           | 611 (91.60)                         |
| Breastfeeding                                 |                                     |                                     |
| No                                            | 11 (11.11)                          | 88 (88.89)                          |
| Yes                                           | 101 (7.27)                          | 1289 (93.73)                        |
| Paracetamol use during the first year of life |                                     |                                     |
| No                                            | 27 (5.96)                           | 426 (94.04)                         |
| Yes                                           | 85 (8.20)                           | 951 (91.80)                         |
| Antibiotic use during the first year of life* |                                     |                                     |
| No                                            | 50 (5.13)                           | 924 (94.87)                         |
| Yes                                           | 62 (12.04)                          | 453 (87.96)                         |
| Asthma in parents                             |                                     |                                     |
| No                                            | 91 (6.54)                           | 1300 (93.46)                        |
| Yes                                           | 21 (21.43)                          | 77 (78.57)                          |

\* p&lt;0.05.

**Table S3. Distribution of variables according to children's eczema status**

| <b>Variables</b>                              | <b>Eczema yes<br/>N (%) (N=112)</b> | <b>Eczema no<br/>N (%) (N=1377)</b> |
|-----------------------------------------------|-------------------------------------|-------------------------------------|
| Mother's age at childbirth                    |                                     |                                     |
| ≤30                                           | 67 (6.7)                            | 928 (93.3)                          |
| 31 and more                                   | 34 (6.9)                            | 460 (93.1)                          |
| Maternal education status*                    |                                     |                                     |
| Low (10 or fewer years)                       | 9 (2.9)                             | 298 (97.1)                          |
| Medium and high (>10 years)                   | 92 (7.8)                            | 1090 (92.2)                         |
| Maternal smoking during pregnancy*            |                                     |                                     |
| No                                            | 98 (7.1)                            | 1278 (92.9)                         |
| Yes                                           | 3 (2.7)                             | 110 (97.3)                          |
| Maternal passive smoking                      |                                     |                                     |
| No                                            | 68 (7.1)                            | 888 (92.9)                          |
| Yes                                           | 33 (6.2)                            | 500 (93.8)                          |
| Gas cooking                                   |                                     |                                     |
| No                                            | 34 (6.4)                            | 501 (93.6)                          |
| Yes                                           | 67 (7.0)                            | 887 (93.0)                          |
| Living in a flat                              |                                     |                                     |
| No                                            | 39 (6.4)                            | 570 (93.6)                          |
| Yes                                           | 62 (7.0)                            | 818 (93.0)                          |
| Sex                                           |                                     |                                     |
| Male                                          | 55 (7.5)                            | 683 (92.5)                          |
| Female                                        | 46 (6.1)                            | 705 (93.9)                          |
| Birth order                                   |                                     |                                     |
| 1                                             | 51 (6.2)                            | 771 (93.8)                          |
| 2 and more                                    | 50 (7.5)                            | 617 (92.5)                          |
| Breastfeeding                                 |                                     |                                     |
| No                                            | 4 (4.1)                             | 93 (95.6)                           |
| Yes                                           | 97 (7.0)                            | 1295 (93.0)                         |
| Paracetamol use during the first year of life |                                     |                                     |
| No                                            | 25 (5.5)                            | 428 (94.5)                          |
| Yes                                           | 76 (7.3)                            | 960 (92.7)                          |
| Antibiotic use during the first year of life  |                                     |                                     |
| No                                            | 60 (6.2)                            | 914 (93.8)                          |
| Yes                                           | 41 (8.0)                            | 474 (92.0)                          |

\* p&lt;0.05.

**Table S4: Distribution of the main characteristics study participants and non-participants.**

| <b>Characteristic</b>              | <b>Participants<br/>% (N=1489)</b> | <b>Non-participants<br/>% (N=1805)</b> | <b>p-value</b> |
|------------------------------------|------------------------------------|----------------------------------------|----------------|
| Maternal age at childbirth         |                                    |                                        |                |
| ≤ 30 year                          | 56.6                               | 59.5                                   | p=0.21         |
| >30 year                           | 43.4                               | 40.5                                   |                |
| Marital status                     |                                    |                                        |                |
| Married                            | 87.5                               | 84.9                                   | p=0.11         |
| Not married                        | 12.5                               | 15.1                                   |                |
| Socio-economic status              |                                    |                                        |                |
| Low                                | 30.3                               | 32.2                                   | p=0.61         |
| Medium                             | 54.9                               | 52.6                                   |                |
| High                               | 14.8                               | 15.2                                   |                |
| Maternal smoking during pregnancy  |                                    |                                        |                |
| No                                 | 95.3                               | 95.7                                   | p=0.68         |
| Yes                                | 4.7                                | 4.3                                    |                |
| Maternal passive smoking           |                                    |                                        |                |
| No                                 | 56.4                               | 52.1                                   | p=0.06         |
| Yes                                | 43.6                               | 47.9                                   |                |
| Low birth weight newborn (<2500 g) |                                    |                                        |                |
| No                                 | 95.3                               | 95.5                                   | p=0.82         |
| Yes                                | 4.7                                | 4.5                                    |                |
| Preterm birth (<37 weeks)          |                                    |                                        |                |
| No                                 | 94.9                               | 94.2                                   | p=0.55         |
| Yes                                | 5.1                                | 5.8                                    |                |
| Distance to city park (m)          |                                    |                                        |                |
| ≤ 300                              | 26.6                               | 25.0                                   | p=0.74         |
| 300-999                            | 60.2                               | 61.4                                   |                |
| ≥1000                              | 13.2                               | 13.6                                   |                |