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## Peanut, milk, and wheat intake during pregnancy is associated with reduced allergy and asthma in children

Supinda Bunyavanich, MD, MPH<sup>1,2,3,\*</sup>, Sheryl L. Rifas-Shiman, MPH<sup>4,5</sup>, Thomas A. Platts-Mills, MD<sup>6</sup>, Lisa Workman<sup>6</sup>, Joanne E. Sordillo, ScD<sup>5,7</sup>, Carlos A. Camargo Jr., MD, Dr. PH<sup>5,7,8</sup>, Matthew W. Gillman, MD, SM<sup>4,5</sup>, Diane R. Gold, MD, MPH<sup>5,7,9</sup>, and Augusto A. Litonjua, MD, MPH<sup>5,7,9</sup>

<sup>1</sup>Division of Pediatric Allergy and Immunology, Department of Pediatrics, Icahn School of Medicine at Mount Sinai, New York, New York, USA

<sup>2</sup>Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, New York, USA

<sup>3</sup>Mindich Child Health and Development Institute, Icahn School of Medicine at Mount Sinai, New York, New York, USA

<sup>4</sup>Department of Population Medicine, Harvard Pilgrim Health Care Institute, Boston, Massachusetts, USA

<sup>5</sup>Harvard Medical School, Boston, Massachusetts, USA

<sup>6</sup>Asthma and Allergic Diseases Center, University of Virginia Health System, Charlottesville, Virginia, USA

<sup>7</sup>Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA

<sup>8</sup>Department of Emergency Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA

<sup>9</sup>Division of Pulmonary and Critical Care Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA

### Abstract

**Background**—Maternal diet during pregnancy may influence childhood allergy and asthma.

**Objective**—To examine the associations between maternal intake of common childhood food allergens during early pregnancy and childhood allergy and asthma.

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\*Address correspondence to Supinda Bunyavanich, MD, MPH, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place #1198, New York, NY 10029, USA, Tel. +1 212 241 6188, Fax +1 212 426 1902, supinda@post.harvard.edu.

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**Methods**—We studied 1277 mother-child pairs from a United States pre-birth cohort unselected for any disease. Using food frequency questionnaires administered during the first and second trimesters, we assessed maternal intake of common childhood food allergens during pregnancy. In mid-childhood (mean age 7.9 years), we assessed food allergy, asthma, allergic rhinitis, and atopic dermatitis by questionnaire and serum specific IgE levels. We examined the associations between maternal diet during pregnancy and childhood allergy and asthma. We also examined the cross-sectional associations between specific food allergies, asthma, and atopic conditions in mid-childhood.

**Results**—Food allergy was common (5.6%) in mid-childhood, as was sensitization to at least one food allergen (28.0%). Higher maternal peanut intake (each additional z-score) during the first trimester was associated with 47% reduced odds of peanut allergic reaction (OR 0.53, 95%CI 0.30–0.94). Higher milk intake during the first trimester was associated with reduced asthma (OR 0.83, 95%CI 0.69–0.99) and allergic rhinitis (OR 0.85, 95%CI 0.74–0.97). Higher maternal wheat intake during the second trimester was associated with reduced atopic dermatitis (OR 0.64, 95%CI 0.46–0.90). Peanut, wheat, and soy allergy were each cross-sectionally associated with increased childhood asthma, atopic dermatitis, and allergic rhinitis (ORs 3.6 to 8.1).

**Conclusion**—Higher maternal intake of peanut, milk, and wheat during early pregnancy was associated with reduced odds of mid-childhood allergy and asthma.

### Keywords

maternal diet; pregnancy; food allergy; sensitization; asthma; allergic rhinitis; peanut; milk; wheat; childhood

### Introduction

Allergy and asthma are growing as clinical and public health problems in the United States.<sup>1, 2</sup> Recent data suggest that approximately 5% of the US population has food allergy,<sup>1</sup> and 8.4% has asthma.<sup>2</sup> Intra-uterine exposures may play a role in the development of childhood allergy and asthma, as the immune system takes form during the fetal period.<sup>3, 4</sup> Research on the effects of early-life exposures—such as maternal diet during pregnancy-- on childhood allergy and asthma development could inform primary prevention.

The American Academy of Pediatrics previously advised that “no maternal dietary restrictions during pregnancy are necessary with the possible exception of excluding peanuts.”<sup>5</sup> Subsequent systematic reviews of the literature concluded that the current evidence is inadequate to support any dietary restrictions during pregnancy.<sup>6–9</sup> The majority of studies on this topic have been conducted in populations selected for allergic propensity,<sup>10–14</sup> rendering inference to the general population challenging. Further, previous studies of the potential impact of maternal diet during pregnancy have examined only the last month or trimester of pregnancy<sup>10–18</sup> and analyzed outcomes only in the first year(s) of life.<sup>10–13, 16–18</sup> Because many cells thought to be involved in the pathogenesis of allergy and asthma are formed during early pregnancy<sup>19, 20</sup>, an examination of exposures during the first and second trimesters could be worthwhile. Further, studying the potential effects of such exposures beyond early-childhood could help with clinical counseling.

In this article, we characterize the association between maternal diet during early pregnancy and risk of childhood allergy and asthma in mid-childhood in a US pre-birth cohort unselected for any disease. In particular, we focused on maternal intake of foods containing common childhood food allergens (peanut, milk, wheat, egg, and soy) during early pregnancy. As data on food allergen sensitization in US populations unselected for any disease are limited to a few childhood food allergens,<sup>21, 22</sup> we also present our cross-sectional findings on food allergen sensitization and associations between specific food allergies, asthma, and atopic conditions.

## Methods

### Study design and subjects

Participants of the Project Viva pre-birth cohort were recruited from a large multispecialty practice in Massachusetts. The goal of this longitudinal epidemiologic cohort was to study dietary factors that could influence health in early life. Health was broadly defined to encompass diverse areas. Participants were not selected for any disease. Study details have been previously described.<sup>23</sup>

Enrollment occurred between 1999 and 2002 for women with singleton pregnancy. In-person interviews and questionnaires were administered after the initial prenatal visit, at an average of 10 weeks of gestation, and at 26–28 weeks of gestation. Interviews and questionnaires on child health were administered at 6 months, 1 year, and annually thereafter. We collected outcome data for this study at the mid-childhood in-person visit (mean age 7.9 years). Study protocols were approved by the institutional review boards of participating institutions. Of the 2128 children delivered in Project Viva, we included 1277 mother-child pairs who presented for an in-person interview at mid-childhood.

### Maternal dietary assessment during pregnancy

Maternal dietary assessments at the first and second trimester visits were based on a validated 166-item semi-quantitative food frequency questionnaire (FFQ) modified for pregnancy<sup>24</sup> and have been previously described (see Online Supplement for additional details).<sup>23, 25, 26</sup> The total servings per day of each major food allergen (peanut, milk, wheat, egg, soy) were calculated by summing the servings per day of the foods on the FFQ containing these respective food allergens. We derived z scores for the servings per day of each major food allergen that were standardized to a mean of 0 and standard deviation of 1. We chose to use z-scores to (1) allow readers to more easily compare results across different food allergens, which had varying distributions for servings/day, and (2) to aid with interpretation of food allergens with mean servings/day < 1.

### Childhood outcomes

Questions for asthma, allergic rhinitis and atopic dermatitis were from the International Study of Asthma and Childhood.<sup>27</sup> Current asthma was defined as positive if a mother reported at the mid-childhood visit that her child had ever doctor-diagnosed asthma plus either use of asthma medication or wheezing in the past 12 months. Current allergic rhinitis was defined as positive if a mother reported that her child had a runny nose or sneezing apart

from colds in the past 12 months. Current atopic dermatitis was defined as positive if a mother reported at the mid-childhood visit that her child had ever doctor-diagnosed eczema plus an itchy rash in the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears, or eyes in the past 12 months that did not go completely away for at least 6 months. Ever asthma, ever allergic rhinitis, and ever atopic dermatitis were defined as positive if a mother reported a doctor's diagnosis of each respective condition in the child in any questionnaire since birth. Maternal and paternal asthma, allergic rhinitis, and atopic dermatitis were each considered positive if a mother reported at week 10 of gestation that she or the child's biological father had a history of the respective condition. Maternal asthma and allergy (henceforth "maternal atopy") was considered positive if maternal asthma, allergic rhinitis, or atopic dermatitis was positive; the analogous was used to define paternal atopy. Parental atopy was considered positive if maternal or paternal atopy was positive.

Of the 1277 children who presented for an in-person interview at mid-childhood, 702 (55.0%) agreed to have blood drawn and 616 (87.7% of those with blood samples) children had sufficient sample to measure allergen specific IgE (spIgE) levels by Phadia ImmunoCAP. Sensitization to a food allergen was considered positive if the respective allergen spIgE level was  $\geq 0.35$  kU/L. Prescription of an epinephrine auto-injector was assessed with the question, "Has a health care professional, such as a doctor, physician assistant or nurse practitioner, ever prescribed an EpiPen for your child?" A child was considered to have food allergy to peanut, milk, wheat, egg, and/or soy if (s)he had a spIgE level  $\geq 0.35$  kU/L to the particular food *and* EpiPen prescribed. For further details, please see the Online Supplement. We additionally assessed peanut allergy specifically given rising prevalence of peanut allergy at the inception of this cohort study<sup>28</sup>; a child was considered to have had a peanut allergic reaction if his/her mother answered yes to, "Has your child ever had an allergic reaction to peanuts," *and* yes to at least one of the following categories of allergic reaction symptoms with peanut ingestion: "Skin related (e.g. hives, swelling)," "Respiratory (e.g., shortness of breath, wheezing, cough)," "Cardiovascular (e.g. low blood pressure, dizziness or fainting)," "Gastrointestinal (e.g. vomiting, diarrhea)," or "Anaphylaxis (severe, multi-system allergic reaction)." Assessment of food allergy based on report of convincing IgE-mediated reaction symptoms such those covered by our questions has been shown to be effective, with only a 7% false positive rate.<sup>29</sup>

### Statistical analyses

To assess the associations between maternal diet during the first and second trimesters of pregnancy and allergy and asthma outcomes, we created multivariable logistic regression models using food allergen z-score as the unit for maternal dietary intake. Models with food sensitization or food allergy as the outcome were constrained to the 616 subjects with spIgE levels. Because the associations between specific childhood food allergies, asthma, and atopic conditions have not been well characterized, we additionally used multivariable logistic regression to assess the cross-sectional associations between food allergy and current asthma, current allergic rhinitis, and current atopic dermatitis. Given the known associations between food allergy and sex<sup>30</sup>, age<sup>30</sup>, family history of allergy,<sup>30, 31</sup> maternal education<sup>32</sup>, and breastfeeding<sup>32</sup>, we adjusted all models for these variables (Model 1). We

created secondary models additionally adjusted for race/ethnicity (Model 2). Although we anticipated power limitations, we also created secondary models stratified by parental atopy. We performed all analyses using SAS 9.3 (SAS Institute, Cary, NC).

## Results

### Study population

The baseline characteristics of the participants are shown in Table 1. Compared to the 851 participants excluded, the 1277 participants included showed higher proportions of maternal white race (69% vs. 62%), college or graduate education (69% vs. 58%), annual household income exceeding \$70,000 (63% vs. 58%), and parental atopy (59% vs. 56%). Compared to the general US population,<sup>33</sup> there was a higher proportion of blacks and lower proportion of Hispanics among participants. The majority of mothers were college-educated and most households were not low income. Rates of parental asthma, allergic rhinitis, and atopic dermatitis were consistent with those for the general US population.<sup>34–36</sup> Consistent with previous observations demonstrating underdiagnosis of allergic rhinitis by physicians,<sup>37</sup> the prevalence of current allergic rhinitis (definition based on current symptoms) was higher than the prevalence of ever allergic rhinitis (defined based on physician's diagnosis).

### Association between maternal intake during pregnancy and current outcomes at mid-childhood

Distributions of maternal intake of each food allergen during pregnancy are in Table 1. For additional FFQ results, see Tables E1 and E2. Each additional z-score of maternal peanut intake during the first trimester was associated with a 47% reduced odds of peanut allergic reaction in childhood (OR 0.53, 95% CI 0.30–0.94) (Figure 1; Table E3). We focus on the results of Model 1 because child's race/ethnicity was highly collinear with maternal education in our sample ( $\chi^2$  187.9, P value < 0.0001), and models containing collinear terms (i.e. Model 2) yield inaccurate results for individual predictors.<sup>38</sup> We did not observe associations between first trimester peanut intake and current asthma or other atopic outcomes, nor between second trimester peanut intake and current outcomes (Figure 2; Table E4). Each additional z-score of maternal milk intake during the first trimester was associated with reduced odds of current asthma (OR 0.83, 95% CI 0.69–0.99) and current allergic rhinitis (OR 0.85, 95% CI 0.74–0.97) (Figure 1; Table E3). We did not detect these associations with second trimester milk intake (Figure 2; Table E4). Maternal wheat intake during the second trimester was associated with reduced odds of current atopic dermatitis (OR 0.64, 95% CI 0.46–0.90) (Figure 2; Table E4). Results of the models stratified by parental atopy are shown in Table E5 and E6. Of note, maternal intakes of peanut, milk, wheat, egg, and soy during pregnancy did not differ in families with and without parental atopy (Table E7).

### Sensitization, allergy, and asthma

The 616 participants with specific IgE levels measured at mid-childhood had similar characteristics to the 1277 study sample (Table 1). The most prevalent food allergen sensitization among them was to milk (15.9%) followed by peanut (13.8%) (Table 1). The most prevalent food allergy was to peanut (4.9%). 27 (4.6%) specifically reported a peanut

allergic reaction (i.e. convincing IgE-mediated symptoms following peanut intake, specified as cutaneous, respiratory, cardiovascular, gastrointestinal, and/or anaphylactic symptoms).

Figure 3A shows the distribution of food allergen sIgE levels among study participants. The range for peanut sIgE levels was wide, spanning <0.35 to 423 kU/L.

Sensitization to multiple food allergens was more prevalent than monosensitization. Figure 4 summarizes the prevalences of combination food allergen sensitizations. 77 children (13% of subjects with specific IgE levels) were sensitized to 1 food allergen only, 26 (4.4%) were sensitized to 2 food allergens, 32 (5.4%) to 3 food allergens, 16 (2.7%) to 4 food allergens, and 12 (2.0%) to all 5 food allergens. 29 (19%) of the 155 children sensitized to at least one food allergen also had food allergy (Figure 3B).

### **Association between food allergy, asthma, and atopic conditions**

In mid-childhood, peanut, wheat, and soy allergy were each cross-sectionally associated with increased odds of current atopic dermatitis (ORs 5.8 to 8.1), current asthma (ORs 6.4 to 7.0), and current allergic rhinitis (ORs 3.6 to 4.4) (Figure 5; Table E8). Milk allergy was associated with increased odds of asthma (OR 5.4, 95% CI 1.3–23.1).

## **Discussion**

In this prospective pre-birth cohort study of participants unselected for atopic propensity, higher maternal intakes of allergenic foods during early pregnancy were associated with lower risks of allergy and asthma in mid-childhood. Maternal peanut intake during the first trimester was associated with a 47% reduction in the odds of childhood peanut allergic reaction, maternal milk intake during the first trimester was associated with reduced odds of childhood asthma and allergic rhinitis, and maternal intake of wheat during the second trimester was associated with reduced childhood atopic dermatitis. We did not detect associations between maternal egg or soy intakes and childhood outcomes. We also observed that allergies to these five foods in childhood were associated with concurrent asthma and atopic disease.

Our results support the hypothesis that maternal diet during early pregnancy affects allergy and asthma outcomes in mid-childhood. Our study is distinct from previous work for several reasons. Most prior studies on this topic were conducted in European populations,<sup>10–12, 15–18, 39–41</sup> which have different trends in atopy<sup>42</sup> and different lifestyles.<sup>43</sup> US-based studies addressing this issue selected subjects from atopic families,<sup>13, 31</sup> or relied on distant recall of pregnancy diet after food allergy status was known.<sup>13</sup> Overall, most studies examining the role of maternal diet on child atopy selected subjects from atopic families,<sup>10–14</sup> or recruited subjects with the aim of examining asthma and allergy.<sup>15, 17, 18, 44</sup> The topic has been examined in general birth cohort studies, but with limitations; a UK-based general birth cohort study relied on distant recall of pregnancy diet after study enrollment,<sup>39</sup> and a Danish general birth cohort study did not assess maternal diet before the 25<sup>th</sup> week of pregnancy.<sup>40</sup> In that study, Maslova et al. found that midpregnancy nut intake was associated with decreased odds of asthma and allergic rhinitis, although they did not examine other foods or outcomes other than asthma and allergic rhinitis.<sup>40</sup> We found

no other studies that examined maternal diet before 25 weeks, with most assessing diet for the last month or last trimester of pregnancy only,<sup>10–16, 18</sup> and most relying on distant recall of diet after the child's birth and after study enrollment.<sup>13, 16, 39</sup> Thus, a strength of our study is the prospective collection of dietary information at two time points during pregnancy. Additionally, to assess the potential longer term effects of such exposures, we examined outcomes in mid-childhood. The majority of previous studies examined outcomes in the initial year(s) of life only, assessing for allergy and asthma in infancy,<sup>12, 13</sup> at 18 months,<sup>10</sup> 2 years,<sup>17</sup> 3 years,<sup>18</sup> and 5 years.<sup>11, 16</sup>

The first trimester is a formative period of fetal immune system development.<sup>3</sup> Cells with dendritic/macrophage structure are present at 4–6 weeks.<sup>45</sup> Positive and negative selection in T cell development occur during this time, such that by 15 weeks, human thymocytes express a complete set of T cell receptors,<sup>19</sup> and the variable domains of TCR beta chains are expressed.<sup>46</sup> B cells with sIgM+ isotypes are detectable by 9 weeks, and sIgA, sIgG, and sIgD isotypes appear by 10 weeks.<sup>20</sup> IgE is made by 11 weeks.<sup>47</sup> Thus, early forms of many cells involved in allergy are formed during the first trimester. Early encounter with food allergens via maternal diet during this critical period of immune system formation could lead to tolerance rather than sensitization. Maternal dietary antigens are known to cross the placenta.<sup>48</sup> Maternal diet may influence Th cell differentiation as well as fetal airway differentiation.<sup>4</sup> For example, some studies report associations between maternal intake of antioxidants and wheezing, asthma, allergen sensitization, lung function, and exhaled nitric oxide.<sup>26, 49, 50</sup> Our observation of a 47% reduced odds of peanut allergic reaction with each z-score of peanut intake in the maternal first trimester diet, and a 15% reduced odds of asthma and allergic rhinitis with each z-score of milk intake in the maternal first trimester diet, are consistent with these developmental principles. Such effects may be food-specific due to distinct nutrients in each food. For example, peanut contains high linoleic acid, an essential fatty acid that has been associated with T-cell signaling, MHCII expression, and the production of arachidonic acid and prostaglandins.<sup>51</sup> Milk is the main food source for vitamin D, and maternal vitamin D intake has been associated with decreased childhood wheezing in this cohort.<sup>25</sup> Although many prior studies found no association between maternal diet during pregnancy and childhood outcomes,<sup>6, 8–12, 18, 39</sup> their null results could be because maternal diet before 25 weeks of pregnancy was not assessed. Consistent with this hypothesis, we observed strongest associations with our first trimester data.

In contrast to our findings, some studies observed a positive association between high peanut intake during pregnancy and child atopic outcomes.<sup>13–16, 44</sup> For example, a Dutch birth cohort study of asthma and dust mite allergy reported increased asthma in children whose mothers had daily versus rare intake of nut products during the last month of pregnancy.<sup>15</sup> Sicherer et al. observed that maternal recall of frequent third trimester peanut ingestion was associated with peanut sensitization in children with existing egg or milk allergy.<sup>13</sup> Frank et al. reported increased peanut allergy, atopic dermatitis, and other food sensitization in children from atopic families whose mothers recalled frequent peanut intake during pregnancy.<sup>44</sup> Our findings may differ from these earlier findings because: (1) we targeted maternal diet during early rather than late pregnancy, (2) we administered FFQs during pregnancy, reducing recall bias, and/or (3) our participants were unselected for atopic propensity.

The 5.6% prevalence of mid-childhood food allergy in our study population is consistent with data from the National Health Interview Survey (NHIS) showing increasing rates of food allergy in the United States from 3.4% in 1997–1999 to 5.1% in 2009–2011.<sup>1</sup> The 2005–2006 National Health and Nutrition Examination Survey (NHANES) estimated food allergy prevalence to be 3.8% among those 6–19 years old.<sup>22</sup> Gupta et al. reported a higher rate of overall food allergy (8.0%).<sup>52</sup> These differences likely reflect methodology,<sup>53</sup> as NHIS defined food allergy using parental report,<sup>1</sup> NHANES relied on sIgE level,<sup>22</sup> and Gupta et al. used subject-reported history.<sup>52</sup> Because food allergy is not accurately reported by patients, the NIAID-sponsored expert panel recommends that objective measurements are used to establish a true diagnosis of food allergy.<sup>7</sup> We required both elevated food-sIgE level and prescribed EpiPen to define a food allergy, and we had specific questions targeting convincing symptoms of peanut allergic reaction.

We recognize that the rates of specific food allergies that we report are higher (e.g. peanut 4.9%) than those previously reported.<sup>22, 52</sup> We believe our results are valid for several reasons. First, the prevalence of peanut allergic reaction (i.e. convincing IgE-mediated symptoms following peanut ingestion) was 4.6% in our study, which is similar to our peanut allergy prevalence. Assessment of food allergy based on report of convincing IgE-mediated reaction symptoms such those covered by our questions has been previously shown to have a low false positive rate.<sup>29</sup> Therefore, our similar rates of peanut allergy and peanut allergic reaction support our strategy of using elevated sIgE and prescribed EpiPen for defining a specific food allergy. Second, the odds of food allergy are higher in the Northeast<sup>54</sup> and in urban areas<sup>55</sup>; our subjects came from mostly urban eastern Massachusetts. Third, the estimated prevalence of clinical allergy to peanut, milk, and egg were lower among 6–19 year olds in NHANES (e.g. peanut allergy 2.7%). While the 6–19 year-old category overlaps with the mean age of our cohort (7.9 years), it includes many older individuals, and the prevalence of food allergy is generally lower in older age groups.<sup>22</sup> Fourth, selection bias may have caused children with allergies and other pediatric diseases to present for the mid-childhood visit, as compared to healthy children. Finally, food allergy is increasingly prevalent, and our results could be consistent with this trend.<sup>1</sup>

Apart from NHANES,<sup>21, 22</sup> limited data are available on food sensitization in the general US population.<sup>22</sup> Sensitization to multiple food allergens (14.5%) was more prevalent than monosensitization (13%) in our cohort. This was not observed in NHANES,<sup>22</sup> but NHANES did not examine sensitization to soy and wheat, common childhood food allergens that we studied in addition to peanut, milk, and egg. Our study reports rates of combination cosensitizations to the common childhood food allergens in a US population unselected for atopy or any disease, which we have not seen reported. Consistent with prior observations, many sensitized subjects were not also clinically allergic to the relevant food allergen.<sup>21, 22</sup>

Food allergy, asthma, allergic rhinitis, and atopic dermatitis commonly occur in combination, which we observed and quantified. Previous studies have demonstrated concurrence of asthma and food allergy overall, suggesting a relationship due to shared mechanisms, or perhaps a causal link.<sup>21</sup> We sought to characterize the association between *specific* food allergies and current atopic outcomes, choosing to do so in the same cohort to minimize variation between studies. We observed that peanut, wheat, and soy allergy were



all consistently associated with higher odds of prevalent asthma, allergic rhinitis, and atopic dermatitis. The associations were not uniformly consistent for milk and egg allergies, perhaps due to their lower prevalence among our participants. Our results reinforce that clinicians treating school-age children with peanut, wheat, and soy allergy in particular should screen for comorbid asthma and allergy.

We recognize limitations to our study. While imperfect, our definition of food allergy based on both spIgE levels *and* EpiPen prescription status should reflect food allergy better than either parameter alone, as sensitization alone overestimates clinical food allergy,<sup>21, 22</sup> while epinephrine is underprescribed among those with convincing symptoms of IgE-mediated food allergy.<sup>29</sup> Although 95% predictive spIgE values for clinical food allergy have been described,<sup>56</sup> these were derived from highly atopic patients referred to allergists for food allergy concerns. Because our study sample had markedly different baseline characteristics, the application of such predictive values to define food allergy in our cohort was deemed unwise, as it would likely lead to misclassification. Our implemented definition requiring diagnostic evaluation and EpiPen prescription following healthcare provider evaluation may in fact represent more rigor than real-world practice, where 30% of reported food allergy is not diagnosed by a physician, and 23% is not evaluated by diagnostic testing.<sup>57</sup> We recognize the limitation that subjects sensitized to >1 food allergen and prescribed EpiPen may have been classified as having >1 food allergy when they may have had only one. While we could corroborate our definition for peanut allergy with our specific questions targeting convincing IgE-mediated symptoms that would characterize a peanut allergic reaction, we did not have analogous questions targeting reaction symptoms to milk, wheat, egg, and soy. Our results for non-peanut allergies should therefore be interpreted with caution. We plan to ask questions targeting reaction symptoms to non-peanut foods going forward as we follow this pre-birth cohort into adolescence. Another limitation is the number of children with IgE measurements. While there were no differences in the characteristics of these children with the bigger sample, we cannot fully rule out selection bias in the analysis. Additionally, we did not administer FFQs during the third trimester, although theoretically and empirically, early pregnancy is likely to be a more sensitive period for development of atopic predisposition. Our study examined multiple outcomes and we performed multiple tests, so our findings should be cautiously interpreted in this light. Finally, our results are from an observational longitudinal pre-birth cohort study; further study using a randomized, controlled interventional design will be more conclusive.

While many clinicians and researchers believed that maternal dietary restrictions during pregnancy and lactation and delayed introduction of allergenic foods to infants could prevent atopic disease,<sup>5</sup> systematic reviews do not support these interventions.<sup>6, 8</sup> Recent guidelines acknowledge that there are insufficient data to support such restrictions.<sup>6-9, 58</sup> In fact, evidence is accumulating that early introduction of peanut, egg, wheat, milk, and fish to the infant diet—rather than delay or avoidance-- may be helpful in inducing tolerance rather than allergy.<sup>58-63</sup> Our findings suggest potential benefits to including peanut, milk, and wheat in the maternal diet during pregnancy.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations

<b>CI</b>	confidence interval
<b>FFQ</b>	food frequency questionnaire
<b>MHCII</b>	major histocompatibility complex II
<b>NHIS</b>	National Health Interview Survey
<b>NHANES</b>	National Health and Nutrition Examination Survey
<b>NIAID</b>	National Institute of Allergy and Infectious Disease
<b>OR</b>	odds ratio
<b>SD</b>	standard deviation
<b>spIgE</b>	specific IgE
<b>US</b>	United States

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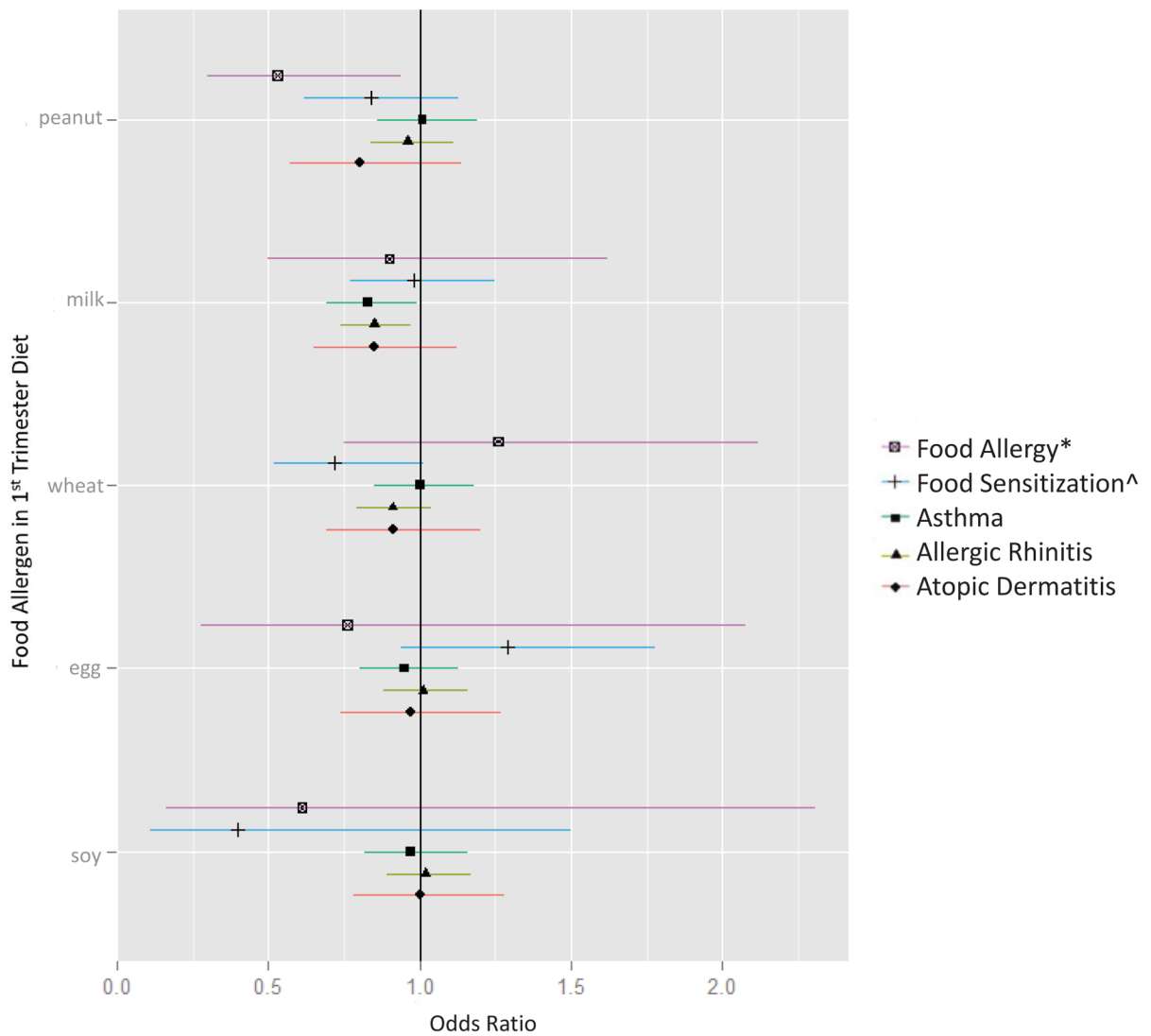
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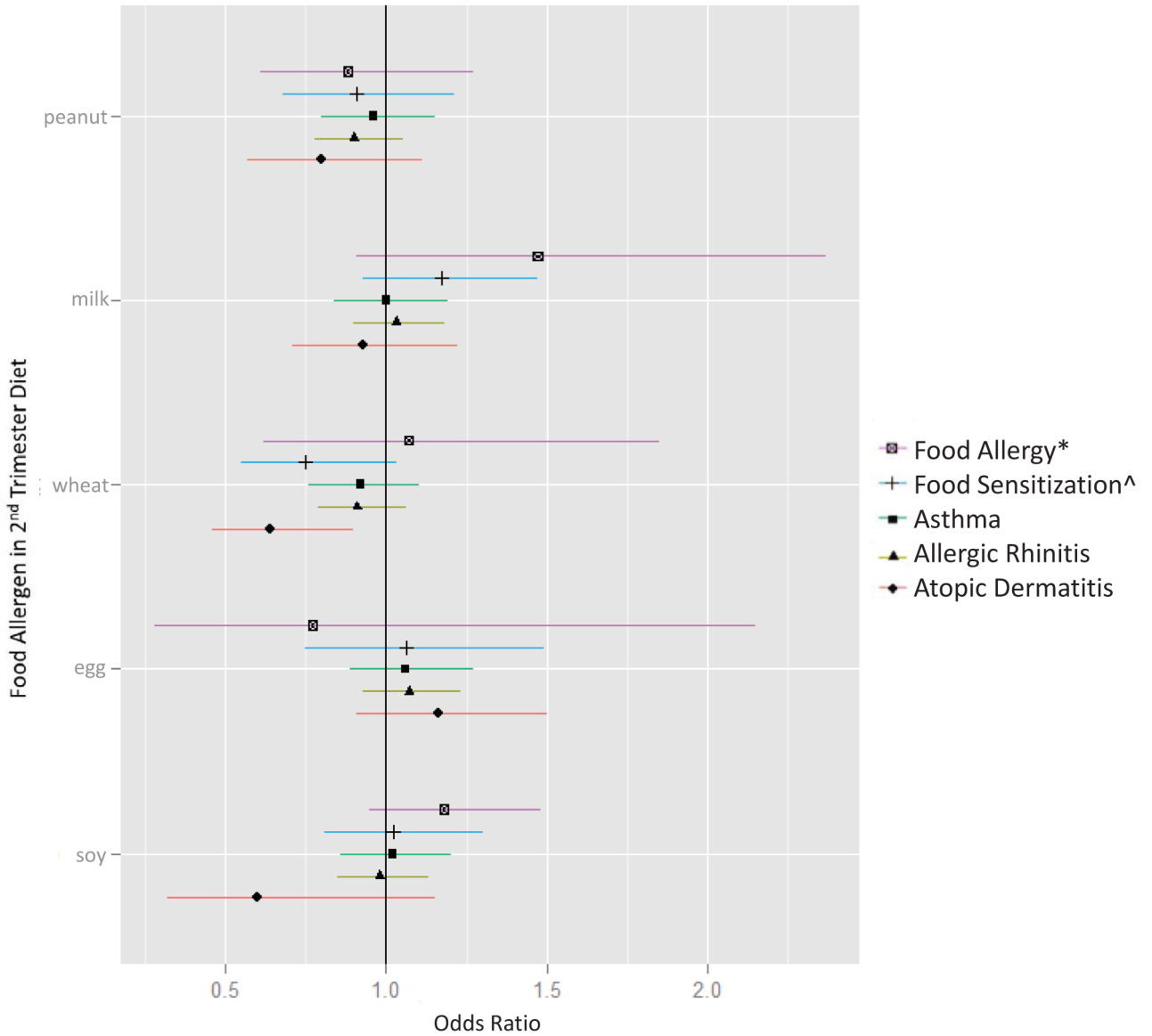
**Key messages**

- The relationship between maternal diet and childhood allergy and asthma is controversial
- In a US pre-birth cohort unselected for any disease, higher maternal intake of peanut, milk, and wheat during early pregnancy was associated with reduced odds of mid-childhood allergy and asthma
- Our findings do not support avoidance of specific foods during pregnancy to prevent allergy and asthma in children. Inclusion of these foods could be beneficial for allergy and asthma prevention



**Figure 1. Associations between maternal intake of food allergens during the first trimester and current allergy and asthma outcomes at mid-childhood**

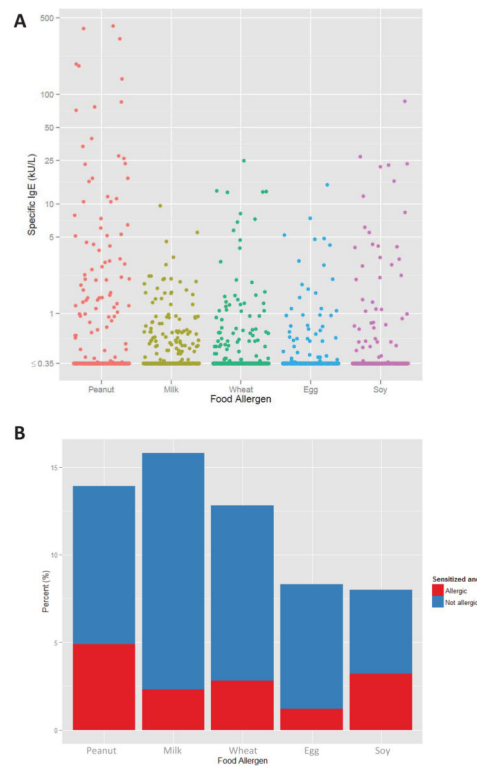
Models were adjusted for child age, sex, breastfeeding history, parental atopy, and maternal education. \*Food allergy defined as sensitization to the respective food AND EpiPen prescribed, except for peanut allergy, which was more specifically defined by convincing symptoms of a peanut allergic reaction (history of peanut allergy AND a cutaneous, respiratory, cardiovascular, gastrointestinal and/or anaphylactic symptom following peanut ingestion). ^Food sensitization defined as spIgE  $\geq$  0.35 kU/L to the respective food.



**Figure 2. Associations between maternal intake of food allergens during the second trimester and current allergy and asthma outcomes at mid-childhood**

Models were adjusted for child age, sex, breastfeeding history, parental atopy, and maternal education. \*Food allergy defined as sensitization to the respective food AND EpiPen prescribed, except for peanut allergy, which was more specifically defined by convincing symptoms of a peanut allergic reaction (history of peanut allergy AND a cutaneous, respiratory, cardiovascular, gastrointestinal and/or anaphylactic symptom following peanut ingestion). ^Food sensitization defined as spIgE ≥ 0.35 kU/L to the respective food.

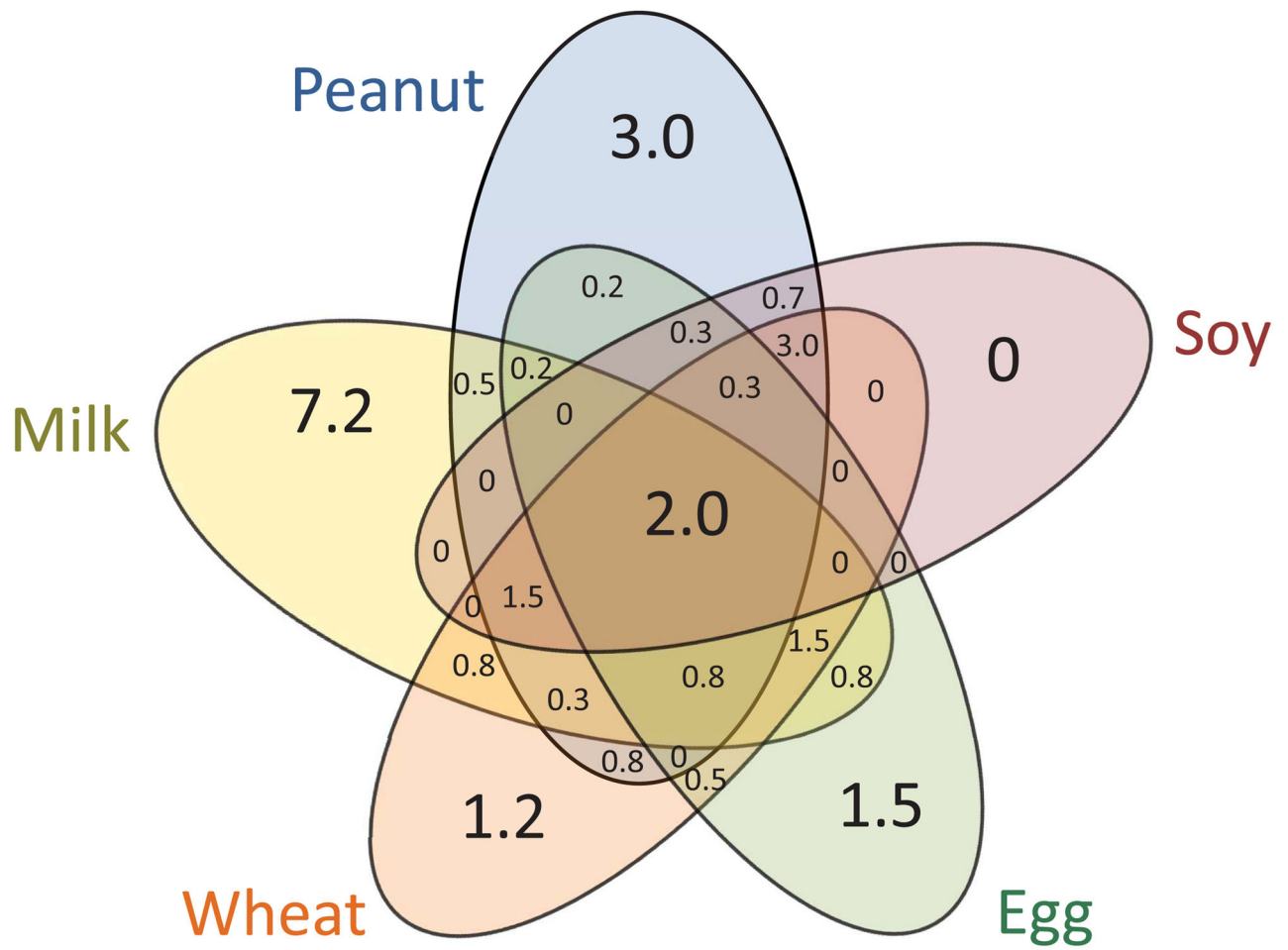




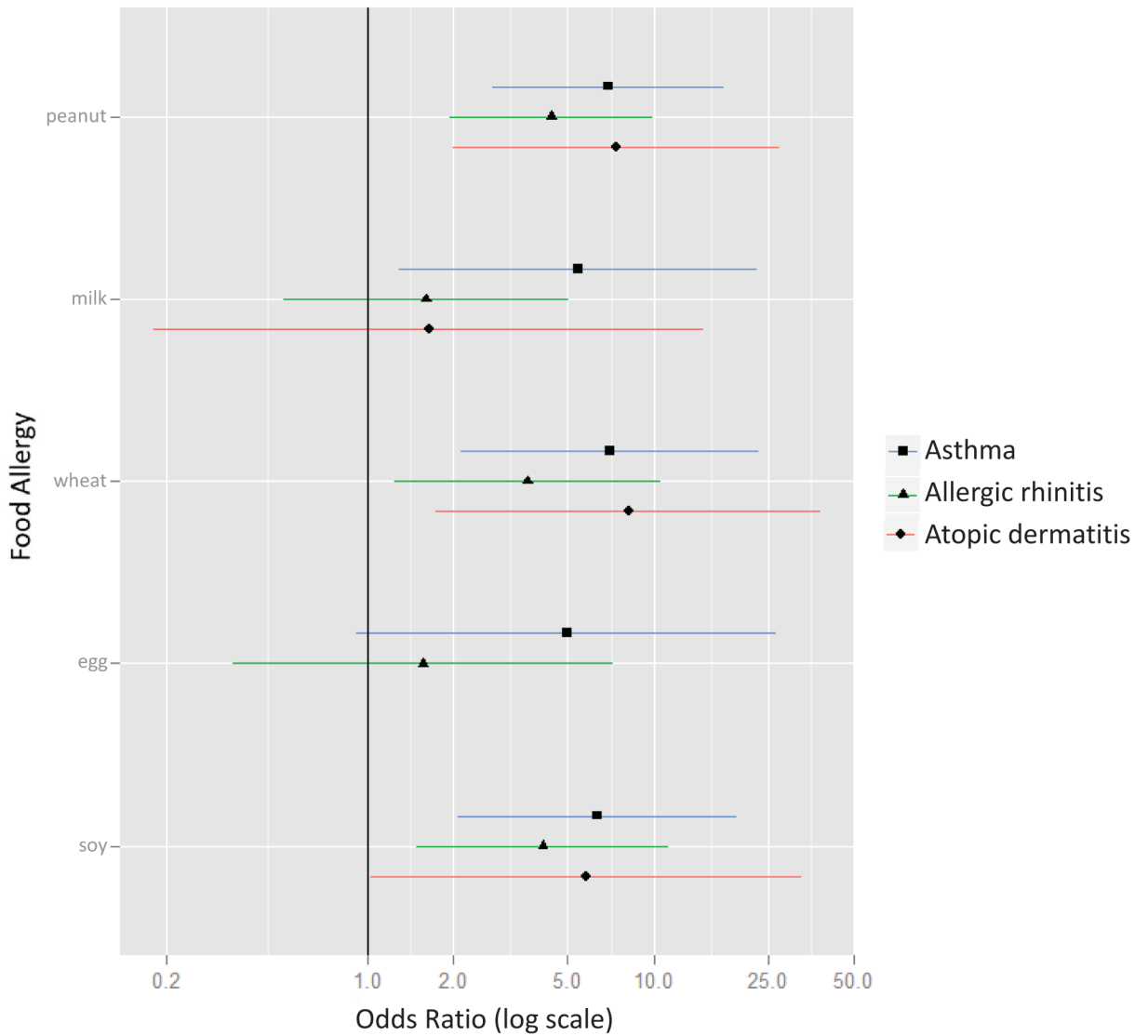
**Figure 3. Food allergen sensitization and food allergy among participants of the Project Viva birth cohort**

**A:** Distribution of food allergen specific IgE levels among the 616 participants for whom sIgE levels were measured.

**B:** Percent of study population sensitized with and without allergy. The total height of each bar represents the prevalence of sensitization to each food allergen among the 616 participants for whom sIgE levels were measured. Each bar is then divided into two parts—the red part representing the proportion sensitized to the food allergen and food allergic, and the blue part representing the proportion sensitized to the food allergen and not food allergic.



**Figure 4. Prevalences of single and multiple food allergen sensitization**  
 Numbers are percent of study sample with mid-childhood data and spIgE levels (N = 616).



**Figure 5. Cross-sectional associations between food allergy and current asthma, current allergic rhinitis, and current atopic dermatitis at mid-childhood**

Models were adjusted for child age, sex, breastfeeding history, parental atopy, and maternal education. Association for egg allergy and atopic dermatitis not shown given 0 subjects with both conditions at mid-childhood.

**Table 1**

Parental and child characteristics among participants from the Project Viva pre-birth cohort

Characteristic	Participants with mid-childhood data (N = 1277)	Participants with mid-childhood data AND spIgE levels measured (N = 616)
<b>Parental Characteristics</b>		
Maternal education college graduate	881 (69.3%)	407 (66.5%)
Household income \$70,000	733 (63.0%)	359 (64.2%)
Maternal atopy	510 (40.1%)	241 (39.4%)
Maternal asthma	161 (12.7%)	84 (13.7%)
Maternal allergic rhinitis	376 (29.6%)	167 (27.3%)
Maternal atopic dermatitis	167 (13.1%)	72 (11.8%)
Paternal atopy	433 (34.6%)	200 (33.2%)
Paternal asthma	146 (11.8%)	71 (12.0%)
Paternal allergic rhinitis	324 (26.7%)	154 (26.5%)
Paternal atopic dermatitis	76 (6.1%)	29 (4.9%)
<b>Maternal intake during pregnancy (servings/day)</b>		
First trimester		
Peanut	0.34 (0.44)	0.34 (0.48)
Milk	1.16 (1.04)	1.17 (1.07)
Wheat	2.65 (1.48)	2.64 (1.44)
Egg	0.32 (0.30)	0.32 (0.28)
Soy	0.08 (0.27)	0.08 (0.29)
Second trimester		
Peanut	0.36 (0.43)	0.35 (0.42)
Milk	1.50 (1.82)	1.52 (1.85)
Wheat	2.69 (1.44)	2.66 (1.41)
Egg	0.33 (0.30)	0.33 (0.29)
Soy	0.08 (0.28)	0.09 (0.34)
<b>Child characteristics</b>		
Sex- female	632 (49.5%)	302 (49.0%)
Age - years	7.93 (0.82)	7.82 (0.71)
Race		
White	831 (65.2%)	383 (62.4%)
Black	199 (15.6%)	121 (19.7%)
Hispanic	53 (4.2%)	30 (4.9%)
Asian	43 (3.4%)	13 (2.1%)
>1 race or other	149 (11.7%)	67 (10.9%)
Breastfed 6 months	662 (55.6%)	319 (55.5%)
<b>Child food sensitization and food allergy</b>		
Food allergen sensitization		168 (28.0%)

Characteristic	Participants with mid-childhood data (N = 1277)	Participants with mid-childhood data AND spIgE levels measured (N = 616)
Peanut		85 (13.8%)
Milk		96 (15.9%)
Wheat		77 (12.9%)
Egg		50 (8.3%)
Soy		47 (7.9%)
Food allergy		32 (5.6%)
Peanut		29 (4.9%)
Milk		13 (2.3%)
Wheat		16 (2.8%)
Egg		7 (1.2%)
Soy		18 (3.2%)
EpiPen prescribed		45 (7.6%)
Peanut allergic reaction		27 (4.6%)
<b>Child asthma and atopy</b>		
Asthma- ever	277 (22.3%)	137 (22.5%)
Asthma- current	219 (19.6%)	105 (19.2%)
Allergic rhinitis- ever	291 (23.5%)	145 (23.8%)
Allergic rhinitis - current	389 (33.6%)	199 (34.1%)
Atopic dermatitis- ever	306 (24.7%)	149 (24.4%)
Atopic dermatitis - current	75 (7.4%)	42 (8.3%)

Values are number (%) or mean (SD)