

## Original Investigation

# Prospective Study of Peripregnancy Consumption of Peanuts or Tree Nuts by Mothers and the Risk of Peanut or Tree Nut Allergy in Their Offspring

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**IMPORTANCE** The etiology of the increasing childhood prevalence of peanut or tree nut (P/TN) allergy is unknown.

**OBJECTIVE** To examine the association between peripregnancy consumption of P/TN by mothers and the risk of P/TN allergy in their offspring.

**DESIGN, SETTING, AND PARTICIPANTS** Prospective cohort study. The 10 907 participants in the Growing Up Today Study 2, born between January 1, 1990, and December 31, 1994, are the offspring of women who previously reported their diet during, or shortly before or after, their pregnancy with this child as part of the ongoing Nurses' Health Study II. In 2006, the offspring reported physician-diagnosed food allergy. Mothers were asked to confirm the diagnosis and to provide available medical records and allergy test results. Two board-certified pediatricians, including a board-certified allergist/immunologist, independently reviewed each potential case and assigned a confirmation code (eg, likely food allergy) to each case. Unadjusted and multivariable logistic regression analyses were used to evaluate associations between peripregnancy consumption of P/TN by mothers and incident P/TN allergy in their offspring.

**EXPOSURE** Peripregnancy consumption of P/TN.

**MAIN OUTCOMES AND MEASURES** Physician-diagnosed P/TN allergy in offspring.

**RESULTS** Among 8205 children, we identified 308 cases of food allergy (any food), including 140 cases of P/TN allergy. The incidence of P/TN allergy in the offspring was significantly lower among children of the 8059 nonallergic mothers who consumed more P/TN in their peripregnancy diet ( $\geq 5$  times vs  $< 1$  time per month: odds ratio = 0.31; 95% CI, 0.13-0.75;  $P_{\text{trend}} = .004$ ). By contrast, a nonsignificant positive association was observed between maternal peripregnancy P/TN consumption and risk of P/TN allergy in the offspring of 146 P/TN-allergic mothers ( $P_{\text{trend}} = .12$ ). The interaction between maternal peripregnancy P/TN consumption and maternal P/TN allergy status was statistically significant ( $P_{\text{interaction}} = .004$ ).

**CONCLUSIONS AND RELEVANCE** Among mothers without P/TN allergy, higher peripregnancy consumption of P/TN was associated with lower risk of P/TN allergy in their offspring. Our study supports the hypothesis that early allergen exposure increases tolerance and lowers risk of childhood food allergy.

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**P**eanut allergy affects 1% to 2% of the population in most Western countries,<sup>1-3</sup> and in the United States, the prevalence of childhood peanut allergy has more than tripled, from 0.4% in 1997 to 1.4% in 2010.<sup>4</sup> Typically, the onset of peanut allergy is in early childhood; 70% of reactions occur during the first known exposure.<sup>5</sup> These IgE-mediated hypersensitivity reactions require prior allergen exposure and sensitization, implying that prior exposure to peanut had already occurred in utero or through unknown exposures in the diet or environment, such as through skin or respiratory routes.<sup>6</sup> Because of frequent overlap between peanut allergy and tree nut allergy and their similar natural history, with 80% to 90% persistence of the food allergy into adulthood,<sup>7</sup> these 2 allergies are often considered together as peanut or tree nut (P/TN) allergy.

For many years, pediatric guidelines have recommended the avoidance of P/TN for at least the first 3 years of life, with some experts also recommending that P/TN be avoided during pregnancy.<sup>8</sup> These recommendations were rescinded recently when literature reviews showed little support for them.<sup>9,10</sup> For decades, many investigators have posited that modifications of the maternal diet during pregnancy might prevent food allergies.<sup>11-14</sup> However, some studies on maternal avoidance of peanut during pregnancy actually demonstrated an increase in peanut sensitization in the child,<sup>15-17</sup> while other studies found no association.<sup>5,14,18,19</sup> In related research, early exposure to allergenic foods in infant diets may decrease sensitization and increase oral tolerance to those foods.<sup>20-24</sup>

Given the lack of clarity in the current literature, an important quandary exists: should the pregnant mother include or exclude P/TN in her diet? The goal of our investigation was to clarify the association between peripregnancy consumption of P/TN by mothers and the subsequent development of P/TN allergy in their offspring.

## Methods

### Study Populations

The Nurses' Health Study II (NHSII) began in 1989 when 116 430 female nurses, aged 24 to 44 years, answered a detailed questionnaire including items on lifestyle and medical history.<sup>25</sup> Dietary data were first collected in 1991 using a semiquantitative food frequency questionnaire; this information is updated every 4 years. Women reported their usual intake of peanuts, other nuts, and peanut butter using 9 categories ranging from never to 6 or more times per day. Response rates have been greater than 90% for each 2-year cycle.

The Growing Up Today Study 2 (GUTS2) began in 2004 when the baseline questionnaire was mailed to all offspring of participants in the NHSII who were between the ages of 10 and 14 years ( $n = 17\,563$ ) (<http://www.gutsweb.org/>). Approximately 67% of girls ( $n = 6002$ ) and 57% of boys ( $n = 4905$ ) answered this baseline questionnaire, and these 10 907 participants constitute the GUTS2 cohort. The cohort has provided detailed information on lifestyle and medical history on subsequent biennial questionnaires. The study was approved by

the institutional review boards at Harvard School of Public Health and Brigham and Women's Hospital. Return of the questionnaire was considered written informed consent.

### Peripregnancy Diet

Children in the GUTS2 cohort were born between January 1, 1990, and December 31, 1994; their mothers reported their diet on the NHSII questionnaire in 1991 and 1995. Using the return date of the NHSII questionnaire, we selected the questionnaire closest to the birthday of each child. Overall, 45% of diet reports were provided during the time that the mother would have been pregnant with the child; 76% were within 1 year of the pregnancy. Because not all diets recorded by the mothers did occur during pregnancy, we examined how the consumption of nuts changed from the diet that was recorded during a pregnancy to the same individual's diet when not pregnant. Among the women, 72% report either no change or an increase or decrease of less than one-quarter serving per day of nuts when pregnant, indicating that nut consumption is relatively stable and independent of pregnancy.

### Identification of Food Allergy Cases

In 2009, a food allergy questionnaire was sent to the mother of every child in the original 2004 GUTS2 cohort ( $n = 10\,907$ ) asking whether her child had a food allergy and, if yes, to which food he or she was allergic, including peanuts, tree nuts, shellfish, milk, eggs, or other. Tree nuts were defined as walnut, almond, pistachio, cashew, pecan, hazelnut, macadamia, and Brazil nut. The questionnaire also included questions about exposures that have been linked to food allergy, including the mother's personal history of food allergy. Mothers are registered nurses and long-time participants in the NHSII. The response rate to the mother's questionnaire was 83%.

If the child had already reported on the 2006 GUTS2 survey that he or she had a food allergy ( $n = 523$ ), the mother also was sent a supplementary questionnaire asking the mother to report the dermatologic, respiratory, cardiovascular, and/or gastrointestinal symptoms associated with her child's food allergy as well as results of diagnostic testing (skin tests, specific IgE, oral challenges). Actual copies of the test results were requested if the mother had them in her possession. Permission was also requested to contact the child's treating physician(s) to obtain medical records for the confirmation process; 89% of these mothers ( $n = 466$ ) returned the supplementary questionnaire.

If the child had not returned the 2006 GUTS2 survey or had not reported a food allergy on the 2006 GUTS2 survey but the mother reported that her child had a food allergy on the 2009 mother's questionnaire, we then sent the mother the supplementary questionnaire as outlined earlier. An additional 325 cases of food allergy were reported that had not been reported on the 2006 GUTS2 survey; 82% of these mothers ( $n = 267$ ) completed the supplementary questionnaire.

### Confirmation of Food Allergy Cases

Among the 733 GUTS2 participants whose mothers returned the supplementary questionnaire used to confirm diagnosis, 233 mothers disagreed with their child's report of food al-

lergy. The most common reason (45%) for discordance between the mother's and child's reports was a child's report of milk allergy and the nurse mother's report of lactose intolerance. The remaining 500 children had supplementary information supplied by their mothers on their diagnosis, treatment, and sequelae of food allergy. All of the questionnaires and medical records were reviewed independently by 2 board-certified pediatricians (A.L.F. and M.C.Y.), one of whom is a board-certified allergist/immunologist (M.C.Y.). This physician review resulted in disconfirmation of food allergy in 192 children (38%). (Among the 142 children who reported P/TN allergy, only 1 case [ $<1\%$ ] was disconfirmed during physician review.) Permission was granted by 279 of the 308 remaining cases (90%) to request medical records from a treating physician or hospital; 228 records (82%) were obtained.

The potential food allergy cases then were divided into 7 levels of confirmation, ranging from likely to possible, based on the data provided (eTable 1 in Supplement). Criteria for level of confirmation included maternal confirmation of food allergy diagnosis, review of physical copies of laboratory results of testing (skin tests, specific IgE, oral challenges), and confirmation in writing from the child's treating physician of food allergy. For the current analysis, children were not included if their mothers did not return the mother's survey ( $n = 1825$ ) or if the mother did not have pregnancy diet data from either the 1991 or 1995 survey ( $n = 216$ ). We also excluded children who had a non-P/TN food allergy only ( $n = 166$ ). Taken together, these exclusions resulted in an analysis data set of 8205 children (75% of the baseline 2004 GUTS2 cohort), including 140 cases of P/TN allergy.

### Statistical Analysis

Unadjusted analyses were conducted to evaluate the associations between peripregnancy maternal P/TN consumption and other possible risk factors for P/TN allergy, including child age, sex, race, season at birth, age at which the child first ate P/TN, child's history of other atopic diseases (asthma, eczema, rhinitis), maternal nut or food allergy, mother's history of atopic diseases, age of the mother at the child's birth, race of the mother, maternal smoking during pregnancy, household income, peripregnancy maternal intake of fruits and vegetables, and maternal exposure to secondhand smoke during pregnancy. In multivariable analyses, we selected those variables that were either statistically significant in the univariate analysis but not on the same causal pathway (variables included in the multivariable model are continuous maternal age, maternal history of non-nut food allergy, maternal allergic rhinitis, eczema, or asthma, and season at child's birth [spring or summer vs fall or winter]). We used generalized estimating equations to adjust for the nonindependence of sibling clusters to estimate in multivariable analysis the odds ratio (OR) of incident P/TN allergy among the offspring, adjusting for those factors significantly associated with the diagnosis.<sup>26</sup> All ORs are reported with 95% confidence intervals.

To test for a linear trend in risk of P/TN allergy with increasing consumption of nuts by the mother during pregnancy, we included in the model a continuous variable with values corresponding to the median value for each exposure

category; the statistical significance of the coefficient for that variable was evaluated using the Wald test. Sensitivity analyses were conducted comparing results with all confirmed cases vs analyses restricted only to the most likely cases (ie, confirmation probable).

## Results

For the 140 cases of P/TN allergy, we compared the results of the confirmation code assigned by the physician reviewers with the mothers' answers about allergy symptoms and medical interventions. This exercise addressed the internal validity of the codes assigned by the 2 pediatrician reviewers. As expected, the likelihood of food allergy was associated with frequency of clinical outcomes (eTable 1 in Supplement).

We next examined the association of maternal P/TN consumption with other sociodemographic and clinical characteristics (Table 1). Women who reported the highest consumption of P/TN in their peripregnancy diet were more likely to also report the highest consumption of fruits and vegetables and that they had introduced P/TN into their child's diet at a younger age. These associations differed by the P/TN allergy status of the mother. The P/TN-allergic mothers were more likely to report a higher consumption of vegetables than non-P/TN-allergic mothers (34% vs 26% reported  $\geq 4$  vegetable servings per day, respectively) and more likely to introduce P/TN after the child was aged 2 years (45% vs 40%, respectively). Some mothers who were allergic to P/TN did report consumption of nuts, but when this was investigated in more detail, generally the nut consumption of mothers who were allergic to peanuts was entirely tree nuts and vice versa. Otherwise, all other tested variables (including child sex, maternal age at child's birth, household income, season at the child's birth, and maternal smoking during pregnancy) were not associated with maternal peripregnancy P/TN consumption.

In multivariable analysis of the odds of P/TN allergy in the offspring (Table 2), offspring whose mothers reported the highest consumption of P/TN in the peripregnancy period had the lowest risk of P/TN allergy (OR = 0.58; 95% CI, 0.34-0.99;  $P_{\text{trend}} = .04$ ). In the stratified analysis, we observed that this risk reduction was limited to children whose mothers did not have a P/TN allergy. Increasing maternal consumption of nuts lowered the risk of P/TN allergy in children across all categories ( $P_{\text{trend}} = .004$ ). Children whose nonallergic mothers were in the highest quartile of P/TN consumption ( $\geq 5$  times a week) had the lowest risk of P/TN allergy (OR = 0.31; 95% CI, 0.13-0.75;  $P_{\text{trend}} = .004$ ). This lower risk of P/TN allergy was not observed among the offspring of mothers who had a P/TN allergy themselves ( $n = 146$ ); on the contrary, the association, although not statistically significant, was in the opposite direction (OR for P/TN consumption  $\geq 5$  times per week = 2.62; 95% CI, 0.74-9.27;  $P_{\text{trend}} = .12$ ). The interaction between maternal peripregnancy P/TN consumption and maternal P/TN allergy status was significant ( $P_{\text{interaction}} = .004$ ). In sensitivity analyses, these results did not materially differ when either maternal vegetable intake or age at first introduction of nuts to the child's diet were added to the model (eTable 2 in Supple-

Table 1. Demographic Characteristics of the Cohort According to Peripregnancy Peanut or Tree Nut Consumption by 8205 Mothers

| Characteristic                                         | Peripregnancy Maternal P/TN Consumption <sup>a</sup> |                               |                               |                              |
|--------------------------------------------------------|------------------------------------------------------|-------------------------------|-------------------------------|------------------------------|
|                                                        | <1 Serving/mo<br>(n = 2747)                          | 1-3 Servings/mo<br>(n = 1201) | 1-4 Servings/wk<br>(n = 2891) | ≥5 Servings/wk<br>(n = 1366) |
| <b>Children</b>                                        |                                                      |                               |                               |                              |
| Age at baseline, mean, y                               | 11.7                                                 | 13.7                          | 13.7                          | 13.6                         |
| Female, %                                              | 54                                                   | 56                            | 55                            | 55                           |
| White, %                                               | 95                                                   | 96                            | 96                            | 96                           |
| Born in spring or summer, %                            | 54                                                   | 54                            | 53                            | 53                           |
| Age at first consumption of nuts, %                    |                                                      |                               |                               |                              |
| <6 mo                                                  | 1                                                    | 0                             | 0                             | 1                            |
| 6-11 mo                                                | 9                                                    | 12                            | 11                            | 15                           |
| 1 y                                                    | 45                                                   | 41                            | 48                            | 47                           |
| 2 y                                                    | 29                                                   | 33                            | 29                            | 26                           |
| ≥3 y                                                   | 13                                                   | 10                            | 9                             | 8                            |
| <b>Mothers</b>                                         |                                                      |                               |                               |                              |
| Allergies, %                                           |                                                      |                               |                               |                              |
| Nut                                                    | 2                                                    | 2                             | 2                             | 2                            |
| Food other than nut                                    | 4                                                    | 5                             | 5                             | 4                            |
| Allergic rhinitis, eczema, asthma                      | 34                                                   | 35                            | 34                            | 33                           |
| Age at child's birth, median, y                        | 33                                                   | 32                            | 31                            | 32                           |
| White, %                                               | 97                                                   | 97                            | 98                            | 98                           |
| Smoking during pregnancy, %                            | 4                                                    | 5                             | 5                             | 5                            |
| Household income, %                                    |                                                      |                               |                               |                              |
| <\$50 000                                              | 9                                                    | 10                            | 10                            | 13                           |
| \$50 000 to <\$150 000                                 | 62                                                   | 58                            | 61                            | 56                           |
| ≥\$150 000                                             | 13                                                   | 16                            | 14                            | 14                           |
| Missing                                                | 15                                                   | 15                            | 14                            | 17                           |
| Servings/d of fruit and vegetables during pregnancy, % |                                                      |                               |                               |                              |
| ≤3                                                     | 30                                                   | 23                            | 16                            | 11                           |
| >3 to 4                                                | 18                                                   | 15                            | 14                            | 11                           |
| >4 to 6                                                | 29                                                   | 31                            | 34                            | 27                           |
| >6 to 8                                                | 13                                                   | 17                            | 20                            | 24                           |
| >8                                                     | 9                                                    | 13                            | 17                            | 27                           |

Abbreviation: P/TN, peanut or tree nut.

<sup>a</sup> Column percentages may not sum to 100% due to rounding.

ment) or when P/TN cases were restricted to the 58 participants whose confirmation code was probable (eTable 3 in Supplement).

## Discussion

In a large national cohort of mothers and their offspring, with extensive efforts taken to validate all cases of physician-diagnosed food allergy, we found that frequent peripregnancy consumption of P/TN by mothers was associated with a decreased risk of P/TN allergy in their offspring. The inverse association was driven by the large majority of mothers without P/TN allergy. Among mothers with P/TN allergy, a non-significant positive association was found, and the statistical interaction of maternal peripregnancy P/TN consumption and maternal P/TN allergy status was statistically significant ( $P_{\text{interaction}} = .004$ ). Although animal studies have suggested a benefit from frequent exposure to dietary antigens during pregnancy and lactation, prior human studies have important meth-

odological limitations and have shown either no risk or increased risk of P/TN allergy in offspring; to our knowledge, no prior study in humans has shown that maternal peripregnancy exposure to P/TN is associated with a reduced risk of P/TN allergy in their offspring. We review the prior studies here.

Animal studies consistently demonstrate a protective effect of maternal exposure to dietary antigens during pregnancy and lactation.<sup>27-30</sup> However, most animal models use egg albumin and bovine serum albumin as the allergen; only 1 animal model has examined peanut allergy using peanut-sensitized mice.<sup>30</sup> In this mouse study, the offspring of mothers fed peanut were protected from peanut sensitization; maximum protection occurred in offspring of mothers fed peanut with the adjuvant.

Human studies examining the impact of antenatal and perinatal maternal diets on peanut allergy show less consistent results. A prospective US study<sup>13,31</sup> showed no benefit of maternal and early childhood avoidance of milk, egg, or peanut in children up to age 7 years in preventing food allergies. Likewise, 2 population-based UK studies<sup>18,19</sup> showed that mater-

**Table 2. Odds of Peanut or Tree Nut Allergy in Offspring According to Peripregnancy Peanut or Tree Nut Consumption by 8205 Mothers, Overall and Stratified by Maternal Peanut or Tree Nut Allergy Status**

| Model <sup>a</sup>                | Maternal Peripregnancy P/TN Consumption |                  |                  |                  | <i>P</i> <sub>trend</sub> <sup>b</sup> | <i>P</i> <sub>interaction</sub> <sup>c</sup> |
|-----------------------------------|-----------------------------------------|------------------|------------------|------------------|----------------------------------------|----------------------------------------------|
|                                   | <1 Serving/mo                           | 1-3 Servings/mo  | 1-4 Servings/wk  | ≥5 Servings/wk   |                                        |                                              |
| All mothers                       |                                         |                  |                  |                  |                                        |                                              |
| Child P/TN allergy, No./Total No. | 60/2747                                 | 23/1201          | 40/2891          | 17/1366          |                                        |                                              |
| OR (95% CI)                       |                                         |                  |                  |                  |                                        |                                              |
| Unadjusted                        | 1 [Reference]                           | 0.87 (0.54-1.42) | 0.63 (0.42-0.94) | 0.56 (0.33-0.97) | .03                                    | .009                                         |
| Multivariable <sup>d</sup>        | 1 [Reference]                           | 0.90 (0.55-1.48) | 0.65 (0.43-0.97) | 0.58 (0.34-0.99) | .04                                    | .002                                         |
| Mothers without P/TN allergy      |                                         |                  |                  |                  |                                        |                                              |
| Child P/TN allergy, No./Total No. | 39/2692                                 | 15/1179          | 22/2844          | 6/1344           |                                        |                                              |
| OR (95% CI)                       |                                         |                  |                  |                  |                                        |                                              |
| Unadjusted                        | 1 [Reference]                           | 0.88 (0.48-1.60) | 0.53 (0.31-0.90) | 0.31 (0.13-0.72) | .003                                   |                                              |
| Multivariable <sup>d</sup>        | 1 [Reference]                           | 0.94 (0.51-1.74) | 0.56 (0.33-0.95) | 0.31 (0.13-0.75) | .004                                   |                                              |
| Mothers with P/TN allergy         |                                         |                  |                  |                  |                                        |                                              |
| Child P/TN allergy, No./Total No. | 21/55                                   | 8/22             | 18/47            | 11/22            |                                        |                                              |
| OR (95% CI)                       |                                         |                  |                  |                  |                                        |                                              |
| Unadjusted                        | 1 [Reference]                           | 0.93 (0.32-2.67) | 1.00 (0.45-2.25) | 1.62 (0.55-4.75) | .31                                    |                                              |
| Multivariable <sup>d</sup>        | 1 [Reference]                           | 1.28 (0.39-4.17) | 1.03 (0.42-2.56) | 2.62 (0.74-9.27) | .12                                    |                                              |

Abbreviations: OR, odds ratio; P/TN, peanut or tree nut.

<sup>a</sup> Generalized estimating equation regression models controlling for siblings.<sup>b</sup> *P*<sub>trend</sub> is for maternal P/TN consumption during pregnancy using category medians as a continuous variable.<sup>c</sup> The interaction term between maternal peripregnancy P/TN consumption and

maternal P/TN allergy status.

<sup>d</sup> Multivariable models control for continuous maternal age, maternal history of non-nut food allergy, maternal allergic rhinitis, eczema, or asthma, and season at child's birth (spring or summer vs fall or winter).

nal peanut consumption during pregnancy and lactation was not associated with risk of peanut allergy in offspring. In contrast, a Dutch birth cohort study<sup>14</sup> found that frequent maternal P/TN consumption during pregnancy increased the diagnosis of asthma but not the diagnosis of peanut allergy in the offspring at age 8 years. A questionnaire-based UK study by Fox et al<sup>6</sup> showed no association between maternal peanut consumption during pregnancy or lactation and the development of peanut allergy in the offspring. A 2010 meta-analysis<sup>5</sup> of 6 human studies<sup>10,15,18,32-34</sup> found no evidence that mothers' avoidance or exposure to peanut during the antenatal or perinatal period had an impact on sensitization or allergy to peanut in their offspring.

In contrast, other studies suggest an increased risk of peanut allergy with maternal peanut consumption during pregnancy and the perinatal period. A retrospective UK study by Hourihane et al<sup>16</sup> evaluated 622 subjects with peanut allergy by questionnaire and found that subjects younger than 6 years were more likely to have mothers who ate peanuts during the pregnancy or lactation period. In South Africa, Frank et al<sup>15</sup> conducted a retrospective case-control study examining 25 children with peanut allergy and found an association with maternal peanut ingestion during pregnancy, but statistical significance was not reached. In the United States, Sicherer et al<sup>17</sup> performed a retrospective study examining 503 infants with eczema, milk allergy, or egg allergy who were at high risk for developing peanut allergy. They found a dose-dependent association between reported maternal peanut ingestion during the third trimester of pregnancy and peanut sensitization. A retrospective case-control study from Montreal of 403 infants with history of clinical reactions to peanut and posi-

tive peanut-specific IgE also found that mothers reported greater maternal consumption of peanut during pregnancy and lactation.<sup>35</sup> All these retrospective studies are limited by likely recall bias. Accordingly, the issue of maternal dietary modification during pregnancy and its effect on development of P/TN allergy in offspring remains controversial. Our novel finding of reduced P/TN allergy with increased maternal P/TN consumption in the peripregnancy period supports more recent studies showing that early food allergen exposure promotes food allergen tolerance and reduced risk of food allergy.<sup>20-24</sup>

Our study has several strengths. The maternal history of P/TN consumption was obtained during or within 6 months of the pregnancy, giving more accurate quantitative results than other studies that collected dietary histories retrospectively many years after pregnancy. Recruitment of subjects was not based on atopic history or on a genetically high-risk population, so generalizability is enhanced. We reviewed all self-reported cases of physician-diagnosed P/TN allergy by having 2 pediatricians independently examine the medical records, allergy skin test results, and specific IgE data and assign confirmation codes based on the strength of evidence. Using this approach, many potentially false-positive cases of food allergy were removed (eg, children with lactose intolerance). Our conclusions are derived from the cases with the highest likelihood of being a true food allergy as opposed to food sensitization. Our results did not change when we restricted the analysis to only P/TN cases with the highest level of confirmation (eTable 3 in Supplement).

Our study also has potential limitations. The dietary questionnaires were not specific for the actual dates of the pregnancy but were chosen as the one completed closest to

the child's date of birth. Consequently, only 45% of the dietary questionnaires were completed during the pregnancy; 76% were within 1 year of the pregnancy. Because the dietary assessment was completed long before the start of this food allergy study, the data are less subject to recall bias. Lastly, our study only examined maternal history, so any paternal influences on the development of P/TN allergy were not investigated.

Another potential limitation of our study is confounding by other dietary and behavioral differences among mothers with frequent P/TN consumption. For example, these mothers also were more likely to consume fruits and vegetables, which are high in antioxidants and may lower the risks of allergic sensitization and asthma.<sup>36,37</sup> Likewise, they were more likely to introduce P/TN into the child's diet at a younger age, which may promote oral tolerance.<sup>23,24</sup> Thus, there was a theoretical possibility that higher in utero antioxidant exposure (not higher P/TN exposure) was responsible for incident food al-

lergy in offspring. To address this possibility, we controlled for these factors and they had no material effect on our results (eTable 2 in Supplement).

## Conclusions

We found a strong inverse association between peripregnancy P/TN consumption by mothers and risk of P/TN allergy in their offspring. The more P/TN the mother consumed, the lower the risk was of her child developing physician-diagnosed P/TN allergy. Our study supports the hypothesis that early allergen exposure increases the likelihood of tolerance and thereby lowers the risk of childhood food allergy. Additional prospective studies are needed to replicate this finding. In the meantime, our data support the recent decisions to rescind recommendations that all mothers avoid P/TN during pregnancy and breastfeeding.<sup>9,10</sup>

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**Author Contributions:** Dr Frazier had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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**Analysis and interpretation of data:** All authors.

**Drafting of the manuscript:** Frazier, Young.

**Critical revision of the manuscript for important intellectual content:** All authors.

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