

# Food Allergy: A Comprehensive Population-Based Cohort Study



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## Abstract

**Objective:** To determine the incidence and temporal trends of food allergies.

**Patients and Methods:** We performed a historical cohort study to describe the epidemiology of food allergies among residents of all ages in Olmsted County, Minnesota, during a 10-year period from January 2, 2002, through December 31, 2011, using the Rochester Epidemiology Project database. Overall incidence and trends in biannual incidence rates over time were evaluated.

**Results:** During the 10-year study period, 578 new cases of food allergies were diagnosed. The average annual incidence rate was significantly higher among males compared with females (4.1 [95% CI, 3.6-4.5] vs 3.0 [95% CI, 2.7-3.4];  $P < .001$ ; per 10,000 person-years; 3.6 per 10,000 person-years overall). The pediatric incidence rate of food allergy increased from 7.0 (95% CI, 6.2-8.9) to 13.3 (95% CI, 10.9-15.7) per 10,000 person-years between the 2002-2003 and 2006-2007 calendar periods and then stabilized at 12.5 and 12.1 per 10,000 person-years in the last 2 calendar periods. Milk, peanut, and seafood were the most common allergen in infancy, in children between ages 1 and 4 years, and in the adult population, respectively.

**Conclusion:** This is one of the first population-based studies to examine the temporal trends of food allergies. The incidence of food allergies increased markedly between 2002 and 2009, with stabilization afterward. Additional longitudinal studies are warranted to assess for epidemiological evidence of changes in food allergy incidence with changing recommendations for allergenic food introduction.

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Food allergy is a growing public health concern that has received increased attention in recent years.<sup>1</sup> Food allergy is a major social stressor for families and causes substantial impairment in quality of life for families of children with food allergies.<sup>2</sup> There is also a considerable economic burden on affected families, with increased health care cost (averaging nearly \$4184 per year per child with food allergy), expenses incurred during doctor's visits, emergency medical treatment, hospitalizations, and loss of productivity.<sup>3</sup>

Estimates of food allergy indicate that more than 2%, but less than 10%, of the population have a food allergy,<sup>4</sup> and rates tend to be higher in children (3%-4% vs 1%-2% adults) and are presumed to be increasing over the past few decades. A large telephone-based survey found increasing rates of peanut or tree nut allergy in children

from 0.6% in 1997 to 1.2% in 2002 and finally 2.1% in 2007.<sup>5</sup> However, self-reporting or parental reporting of food allergy likely overestimates the prevalence of the disease. Other studies have focused on one or a few food allergies, and longitudinal studies are also lacking. Despite these attempts to better understand and define food allergy epidemiology, the difficulties in performing quality studies have led some to question whether food allergy prevalence is truly increasing.

Additionally, the underlying cause of this potential increase in food allergy prevalence remains unclear. The numerous hypotheses to explain this trend include an increase in associated atopic conditions (such as atopic dermatitis, which is thought to be a risk factor for development of food allergy)<sup>6</sup> and previous recommendations to delay introduction of allergenic foods.



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In 2000, the American Academy of Pediatrics (AAP) committee on nutrition published guidelines recommending delay in introduction of allergenic foods including milk (until 12 months), egg (until 24 months), peanut, and shellfish.<sup>7</sup> In the years following these recommendations, food allergy experts became concerned about rising trends in food allergy among young children. In 2008, the AAP updated the recommendation, citing inadequate evidence to support delayed introduction of allergenic foods.<sup>8</sup> By 2013, the concept of primary prevention and using early introduction to help prevent food allergy came to the forefront,<sup>9</sup> and with publication of the Learning Early About Peanut Allergy<sup>10</sup> (LEAP) study 2 years later, the protective effects of early introduction of certain allergenic foods were further appreciated. Since publication of the LEAP and LEAP-On (Persistence of Oral Tolerance to Peanut) trials,<sup>11</sup> addendum guidelines for the early introduction of peanut have been published that reverse the previous recommendation to delay introduction of allergenic foods.<sup>12</sup> Whether these changing recommendations have contributed to changes in food allergy incidence are yet unknown.

Using the unique medical records linkage system of the Rochester Epidemiology Project,<sup>13</sup> we examined temporal trends in the incidence of all types of food allergy in Olmsted County, Minnesota, residents over a 10-year period from January 2, 2002, through December 31, 2011.

## PATIENTS AND METHODS

We performed a retrospective medical record review of food allergies in Olmsted County utilizing the data resources of the Rochester Epidemiology Project (REP). The REP provides the infrastructure for medical research on the approximately 148,000 citizens of Olmsted County as the result of a unique medical records linkage system in Rochester, Minnesota.<sup>14</sup> Census information indicates that the age, sex, and racial/ethnic characteristics of people living in Olmsted County are comparable to those of people residing in the rest of the state of Minnesota and in the midwestern United States, but overall, the population is less ethnically diverse than the rest of the United States.<sup>15</sup>

All Olmsted County residents with an incident diagnosis of a food allergy by an REP-affiliated clinician between January 2, 2002, and December 31, 2011, who had approved access to their medical records for research purposes were identified using REP resources. The diagnosis codes used to identify the patients are provided in the [Supplemental Table](#) (available online at <http://www.mayoclinicproceedings.org>). The medical records of all 2734 patients with a potential food allergy were reviewed by the first author (E.W.) to confirm accurate diagnosis of food allergy. Patients were included in the study only if they met the following criteria: (1) clinical history consistent with food allergy and (2) confirmatory IgE-specific blood testing ( $>0.35$  kU/L), positive results on skin prick testing ( $>3$  mm), or positive findings on open food challenge. Demographic data, specific food allergen, type of reaction, and other comorbid atopic conditions were recorded. When available, data on type of birth (vaginal vs cesarean section) and comorbid atopic conditions was also collected.

The data were analyzed using SAS statistical software, version 9.4 (SAS Institute). Age- and sex-specific incidence rates in Olmsted County during 2002-2011 were calculated; the numerator was the number of persons with a food allergy, and the denominator was obtained from the REP census.<sup>13</sup> Rates were age- and sex-adjusted to the total population structure of the United States in 2010. The 95% CIs for the rates were calculated assuming a Poisson error distribution. Incidence rates were compared between males and females or between biannual calendar periods by fitting generalized linear regression models assuming a Poisson error structure. The observations used for the regression analysis were the crude incidence counts for the subgroups, which were offset by the natural logarithm of the number of person-years.

## RESULTS

### Patient Characteristics and Incidence Rates

A total of 578 incident cases of food allergy were identified (242 females [41.9%] and 336 males [58.1%]). Patient characteristics are summarized in [Table 1](#); nearly three-

fourths of the patients were white. The median age at the time of the diagnosis was 2.1 years (interquartile range, 1.2-9.2). Other conditions present at the time of the abstraction were recorded; 324 patients (56.1%) had coexistent atopic dermatitis, 218 (37.7%) had asthma, 30 (5.2%) had penicillin/amoxicillin allergy, and 28 (4.8%) had other drug allergies. The incidence rates are summarized in Table 2. Overall, the average annual age- and sex-adjusted incidence was 3.6 (95% CI, 3.3-3.9) per 10,000 person-years, and the age-adjusted incidence was significantly higher among males compared with females (4.1 [95% CI, 3.6-4.5] vs 3.0 [95% CI, 2.7-3.4] per 10,000 person-years;  $P < .001$ ). Among females, the incidence was highest among children younger than 5 years, with an incidence of 26.9 (95% CI, 18.3-38.1) per 10,000 person-years among females less than 1 year of age and 25.8 (95% CI, 21.3-31.1) per 10,000 person-years among females between 1 and 4 years of age. Among males, the incidence rate was highest at 44.6 (95% CI, 38.7-51.1) per 10,000 person-years among children between the ages of 1 and 4 years, followed by an incidence rate of 31.3 (95% CI, 22.1-42.9) per 10,000 person-years among children younger than 1 year. The incidence rate in the 1- to 4-year age group was significantly higher among males compared with females ( $P < .001$ ); however, none of the other age-specific incidence rates were significantly different between males and females ( $P > .05$ ). The pediatric incidence rates of food allergy increased from 7.0% (95% CI, 6.2-8.9) to 13.3% (95% CI, 10.9-15.7) per 10,000 person-years between 2002-2003 and 2006-2007 calendar periods and then stabilized at 12.5 and 12.1 per 10,000 person-years in the last 2 calendar periods.

Table 3 summarizes the type of food allergies. Overall, the most common food allergy was a peanut allergy in 268 of the 578 patients (46.4%), followed by a tree nut allergy in 195 (33.7%) and an egg allergy in 139 (24.0%). A third of the patients were allergic to more than one food category. Among the 69 patients first diagnosed before 1 year of age, the 3 most common food allergies were milk (35 patients [50.7%]), egg (31 [44.9%]), and peanut (26 [37.7%]),

**TABLE 1. Characteristics of Food Allergy Incident Cases, Stratified by Sex<sup>a,b,c</sup>**

Characteristic	Female (n=242)	Male (n=336)	Total (N=578)
Race/ethnicity			
White	184 (76.0)	246 (73.2)	430 (74.4)
Black	13 (5.4)	15 (4.5)	28 (4.8)
Asian	23 (9.5)	31 (9.2)	54 (9.3)
Hawaiian/Pacific Islander	1 (0.4)	1 (0.3)	2 (0.3)
American Indian	0 (0.0)	1 (0.3)	1 (0.2)
Other/mixed	17 (7.0)	32 (9.5)	49 (8.5)
Not disclosed	4 (1.7)	10 (3.0)	14 (2.4)
Hispanic ethnicity			
No	226 (93.4)	315 (93.8)	541 (93.6)
Yes	12 (5.0)	11 (3.3)	23 (4.0)
Not disclosed	4 (1.7)	10 (3.0)	14 (2.4)
Age at diagnosis (y)			
Median (IQR)	2.9 (1.2-17.0)	2.0 (1.1-5.6)	2.1 (1.2-9.2)
Range	0.4-89.6	0.3-76.0	0.3-89.6
Family history of food allergy			
Sibling			
None	189 (78.1)	284 (84.5)	473 (81.8)
Yes	13 (5.4)	24 (7.1)	37 (6.4)
Unknown	40 (16.5)	28 (8.3)	68 (11.8)
Parent			
No	183 (75.6)	274 (81.5)	457 (79.1)
Yes	20 (8.3)	34 (10.1)	54 (9.3)
Unknown	39 (16.1)	28 (8.3)	67 (11.6)
Other conditions (ever)			
Asthma	82 (33.9)	136 (40.5)	218 (37.7)
Atopic dermatitis	119 (49.2)	205 (61.0)	324 (56.1)
Penicillin/amoxicillin allergy	15 (6.2)	15 (4.5)	30 (5.2)
Other drug allergy	16 (6.6)	12 (3.6)	28 (4.8)

<sup>a</sup>IQR = interquartile range.

<sup>b</sup>Data are presented as No. (percentage) of patients unless indicated otherwise. Percentages may not total 100 because of rounding.

<sup>c</sup>The total for other conditions is greater than the cohort as 22 patients had more than one associated other condition.

whereas among the 319 patients first diagnosed in the 1- to 4-year age group, the most common allergy was peanut (195 [61.1%]). Among the 93 children first diagnosed between ages 5 and 18 years, the most common allergy was tree nut (55 [59.1%]), followed by peanut (37 [39.8%]). The most common allergy among the 97 patients first diagnosed in adulthood (age 19 years or older) was seafood (47 [48.5%]).

Among the 388 patients first diagnosed at less than five years of age, the mode of delivery was available for 364 patients. The types of food allergies were similar between those delivered by cesarean section vs vaginally (Table 4).

TABLE 2. Incidence of Food Allergy in Olmsted County, Minnesota, per 10,000 Person-Years, Stratified by Age and Sex

Age group (y)	Female (n=242)		Male (n=336)		Total (N=578)	
	No. of patients	Incidence (95% CI)	No. of patients	Incidence (95% CI)	No. of patients	Incidence (95% CI)
<1	31	26.9 (18.3-38.1)	38	31.3 (22.1-42.9)	69	29.1 (22.7-36.9)
1-4	113	25.8 (21.3-31.1)	206	44.6 (38.7-51.1)	319	35.5 (31.7-39.6)
5-9	21	4.3 (2.7-6.6)	32	6.3 (4.3-8.9)	53	5.3 (4.0-7.0)
10-18	20	2.1 (1.4-3.6)	20	2.2 (1.4-3.4)	40	2.3 (1.6-3.1)
19-90	57	1.1 (0.8-1.3)	40	0.8 (0.6-1.1)	97	0.9 (0.8-1.1)
Overall, age- and sex-adjusted <sup>a</sup>						
0-18	185	8.9 (7.6-10.2)	296	13.5 (11.9-15.0)	481	11.3 (10.2-12.3)
0-90	242	3.0 (2.7-3.4)	336	4.1 (3.6-4.5)	578	3.6 (3.3-3.9)

<sup>a</sup>Adjusted to the population structure of the US total population in 2010.

### Temporal Trends in the Incidence of Any Food Allergy and Peanut Allergy

Figure 1 illustrates the age- and sex-adjusted biannual incidence of any food allergy and specifically peanut allergy for all ages combined. Figure 2 presents the annual incidence rate in children aged 0 to 4 years and in those aged 0 to 18 years. Although there has been a statistically significant increase in the incidence during the first 3 calendar periods ( $P < .001$ ), the overall incidence in the most recent calendar period remains low at 4.1 (95% CI, 3.4-4.8) per 100,000 person-years for any food allergy. The incidence of any food allergy has stabilized after 2007, and the incidence of peanut allergy

has attenuated after 2007. The age- and sex-adjusted biannual incidence rates among children are depicted in Figure 3. Similar to the trend observed for all ages, the incidence of any food allergy, as well as peanut allergy, has increased among children during first 3 calendar periods ( $P < .05$ ). Among children first diagnosed before age 1 year, the differences in the incidence rates across the time periods were not significantly different for either any food allergy or peanut allergy (both  $P > .05$ ). However, among children in the 1- to 4-year age group, the incidence in the last 2 calendar periods appears to be on the decline compared with the peak in 2006-2007.

TABLE 3. Type of Food Allergy, Stratified by Age at Diagnosis<sup>a</sup>

Variable	Age at diagnosis (y)					Total (N=578)
	<1 (n=69)	1-4 (n=319)	5-9 (n=53)	10-18 (n=40)	19-90 (n=97)	
Food category <sup>b</sup>						
Milk	35 (50.7)	45 (14.1)	1 (1.9)	0 (0.0)	1 (1.0)	82 (14.2)
Egg	31 (44.9)	98 (30.7)	6 (11.3)	1 (2.5)	3 (3.1)	139 (24.0)
Soy	4 (5.8)	6 (1.9)	1 (1.9)	2 (5.0)	4 (4.1)	17 (2.9)
Peanut	26 (37.7)	195 (61.1)	25 (47.2)	12 (30.0)	10 (10.3)	268 (46.4)
Tree nut	14 (20.3)	93 (29.2)	30 (56.6)	25 (62.5)	33 (34.0)	195 (33.7)
Seafood	3 (4.3)	18 (5.6)	9 (17.0)	8 (20.0)	47 (48.5)	85 (14.7)
Other	6 (8.7)	23 (7.2)	8 (15.1)	4 (10.0)	19 (19.6)	60 (10.4)
No. of categories						
Only 1 food	35 (50.7)	210 (65.8)	34 (64.2)	31 (77.5)	80 (82.5)	390 (67.5)
>1 food	34 (49.3)	109 (34.2)	19 (35.8)	9 (22.5)	17 (17.5)	188 (32.5)

<sup>a</sup>Data are presented as No. (percentage) of patients.

<sup>b</sup>Some patients had allergies to more than one food.

## DISCUSSION

This is the first comprehensive population-based study on food allergies in the United States. Such data provide a more accurate estimate of the temporal trends in the incidence of food allergy at a population level (outpatients and inpatients combined) as compared with hospital-based case series or patient self-reported surveys, which are distorted by referral bias and ascertainment bias.<sup>16</sup> Consistent with findings from a previous study of this population,<sup>17</sup> this retrospective review found an increase in incident cases of all food allergies in Olmsted County, Minnesota, over a 10-year period from 2002-2011. Males had a higher incidence of food allergy, and other coexistent atopic diseases were common. In particular, 324 of the 578 patients (56.1%) with food allergy also had atopic dermatitis, consistent with findings of previous studies. The types of food allergies were similar between those delivered by cesarean section vs vaginally. In this cohort, 30 patients (5.2%) had associated penicillin/amoxicillin allergy. This is an area that is often overlooked and underaddressed by clinicians and may need further attention to address the potential role of antibiotic allergies in this population<sup>18,19</sup> and vice versa.

Our population-based study is unique because it was not based on registry data, which may underestimate or overestimate the true incidence of food allergies based on reporting bias. In addition, the availability of 10 years of data has made it possible for us to examine changes in the incidence of food allergies over time with changing recommendations from the AAP.

Interestingly, despite changes in AAP recommendations regarding the uncertainty surrounding the introduction of allergenic foods in 2008, food allergy incidence remained high in the subsequent years. This issue may be due to the delay in overall implementation of new recommendations by primary care practices or difficulties in changing established practices, especially when concrete evidence was lacking. Our study is strengthened by the unique REP medical records linkage system,<sup>20</sup> which allowed for accurate ascertainment of cases. This system

**TABLE 4. Food Allergies Among 388 Patients First Diagnosed With a Food Allergy at Less Than 5 Years of Age, Stratified by Mode of Delivery<sup>a</sup>**

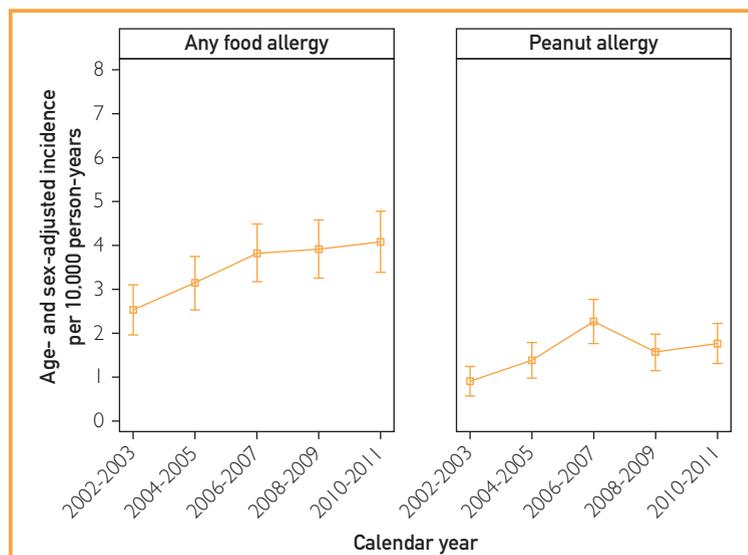
Variable	Mode of delivery		
	Cesarean section (N=111)	Vaginal (N=253)	Not documented (N=24)
Food category <sup>b</sup>			
Milk	22 (19.8)	49 (19.4)	9 (37.5)
Egg	44 (39.6)	80 (31.6)	5 (20.8)
Soy	3 (2.7)	5 (2.0)	2 (8.3)
Peanut	60 (54.1)	146 (57.7)	15 (62.5)
Tree nut	27 (24.3)	73 (28.9)	7 (29.2)
Seafood	4 (3.6)	15 (5.9)	2 (8.3)
Other	8 (7.2)	19 (7.5)	2 (8.3)
No. of categories			
Only 1 category	72 (64.9)	158 (62.5)	15 (62.5)
>1 category	39 (35.1)	95 (37.5)	9 (37.5)

<sup>a</sup>Data are presented as No. (percentage) of patients.

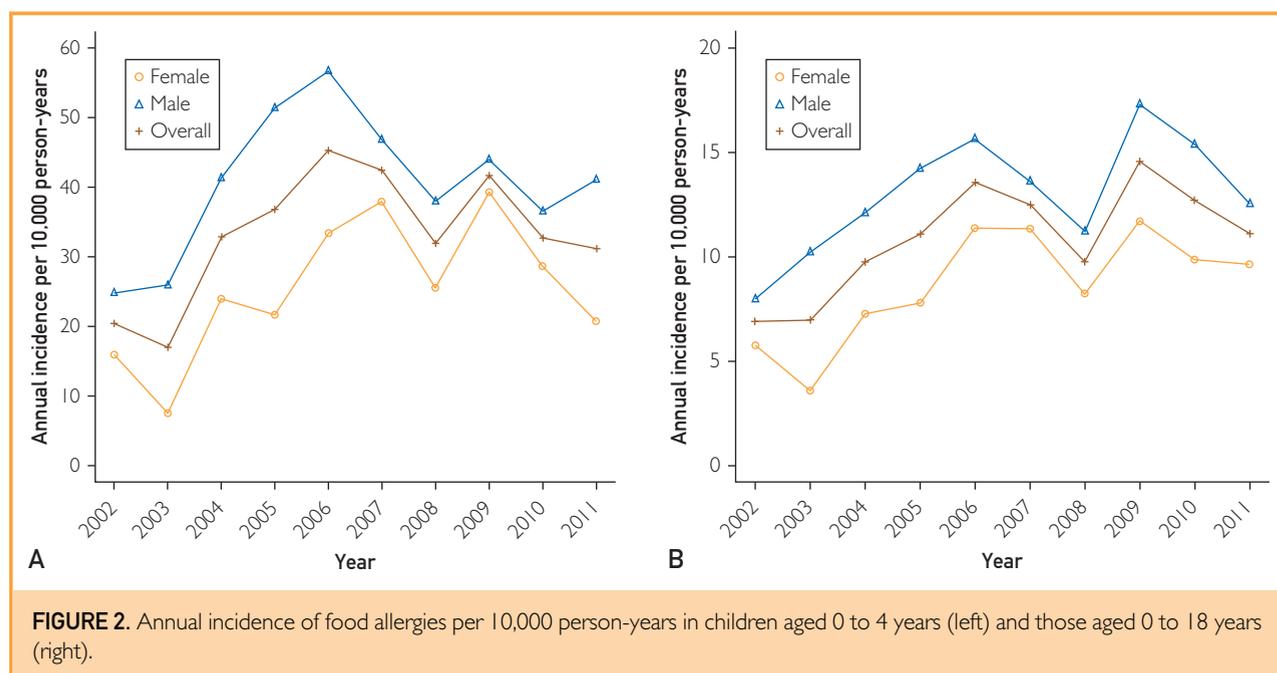
<sup>b</sup>Some patients had allergies to more than one food.

helped minimize ascertainment and misclassification bias.

Our study has several limitations. We included only cases that were clinically diagnosed as food allergy because we were reliant on diagnosed cases. The number of undiagnosed cases is unknown because no



**FIGURE 1.** Age- and sex-adjusted biannual incidence of any food allergy (left) and peanut allergy (right) per 10,000 person-years for all ages (0-90 years) in Olmsted County, Minnesota, 2002-2011. Error bars represent 95% CIs.



**FIGURE 2.** Annual incidence of food allergies per 10,000 person-years in children aged 0 to 4 years (left) and those aged 0 to 18 years (right).

population-based screen is available. With the severe, usually life-threatening clinical manifestations of food allergies, it is unlikely that these cases would not have come to medical attention; hence, the possibility of missing cases was relatively low.

In addition, the generalizability of the study findings is limited largely to white people because the Olmsted County population is mainly white (~90%-95% during the study period). However, studies comparing various chronic diseases in Olmsted County with those in other communities in the United States indicate that data from this population can be extrapolated to a large part of the population of the country.<sup>14</sup> Finally, the use of a retrospective study design is subject to several biases, including reviewer bias. A reliability study was conducted in a smaller sample (25 patients) of the study patients. There was complete agreement between the 2 investigators (E.K.W. and A.Y.J.).

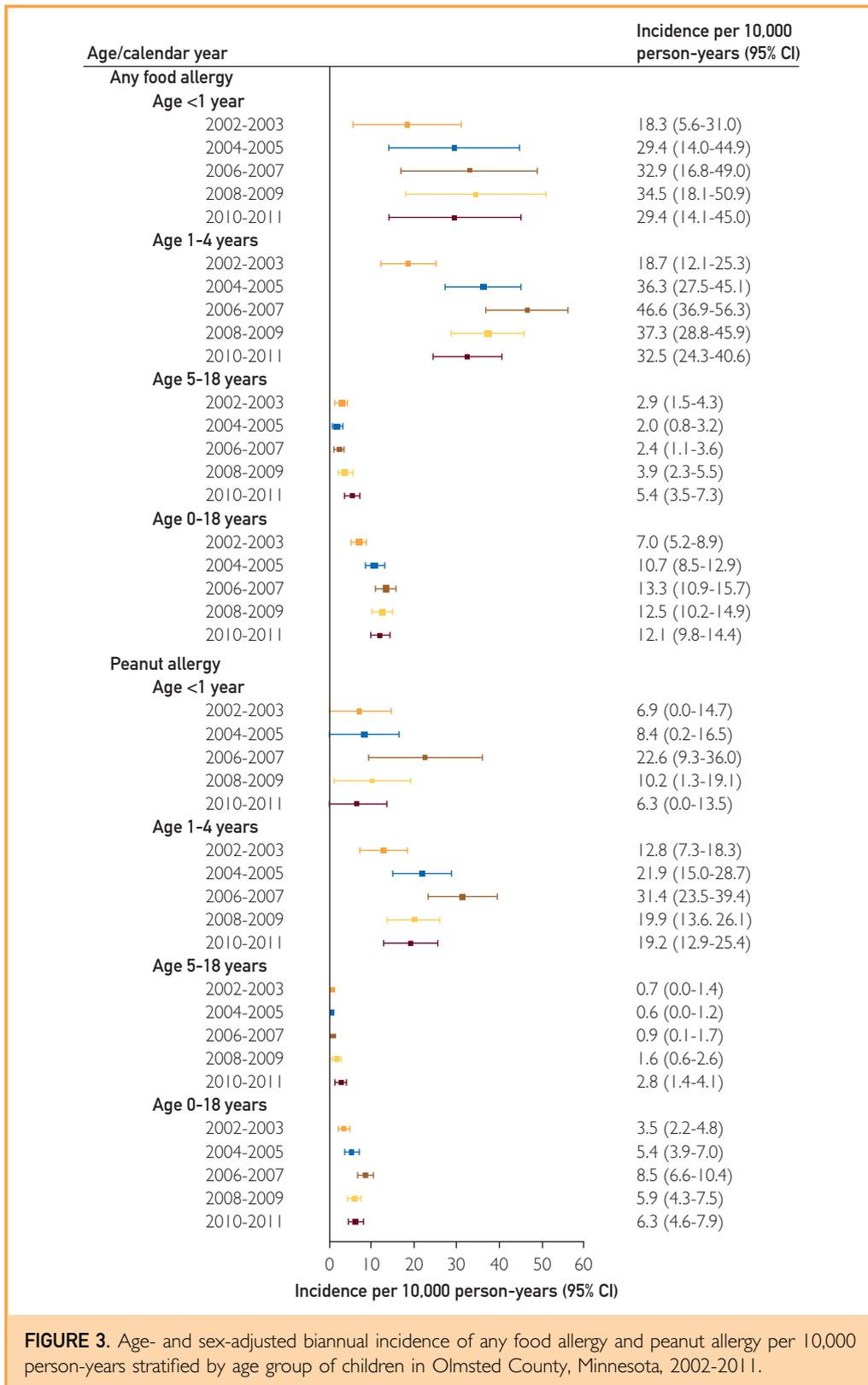
The incidence and prevalence of food allergy will remain a topic of interest as recommendations for the introduction of allergenic foods evolves. Although current recommendations for early introduction include only peanut, this situation may change in the future as we learn more about the etiology of milk

and egg sensitization. We hope that with this population-based study, our understanding of food allergies will improve, which in turn will help guide avenues for primary and secondary prevention of food allergies.

## CONCLUSION

In this first-ever, as far as we know, population-based study on the incidence of food allergies, we found that the incidence of food allergies peaked in 2006-2008 and has stabilized since 2009.

We also found that there is a higher incidence in males, milk is the most common allergen in infancy, and peanut allergy is more common in children between the ages of 1 and 5 years. Seafood allergy is the most common allergy in the adult population. Such epidemiological data are crucial if we are to raise the awareness of the medical community about food allergies. With changing guidelines about introduction of allergenic food, we need epidemiological data to support the cost-effectiveness and the public health benefits of early introduction to prevent the occurrence and persistence of food allergies. We plan to undertake future studies to assess for changes in incidence after 2011, which may enhance our understanding of whether



**FIGURE 3.** Age- and sex-adjusted biannual incidence of any food allergy and peanut allergy per 10,000 person-years stratified by age group of children in Olmsted County, Minnesota, 2002-2011.

the changing dietary recommendations have impacted incidence rates.

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### SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at <http://www.mayoclinicproceedings.org>. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

**Abbreviations and Acronyms:** AAP = American Academy of Pediatrics; REP = Rochester Epidemiology Project

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