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Characteristics of Peanut Allergy Diagnosis in a US Healthcare Claims Database (2011-2017)

Todd A. Mahr, MD, Jay A. Lieberman, MD, Tmirah Haselkorn, PhD, Varsha Damle, MS, Yasser Ali, MBA, Arul Chidambaram, BE, Noelle M. Griffin, PhD, J. Wesley Sublett, MD, MPH

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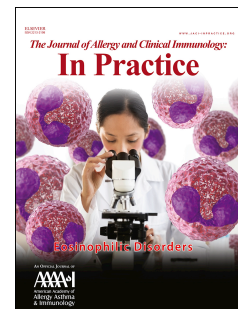
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Todd A. Mahr, MD,^a Jay A. Lieberman, MD,^b Tmirah Haselkorn, PhD,^c Varsha Damle, MS,^d Yasser Ali, MBA,^d Arul Chidambaram, BE,^e Noelle M. Griffin, PhD,^d J. Wesley Sublett, MD, MPH^f

^aDivision of Allergy, Asthma, and Immunology, Gundersen Health System, La Crosse, WI;

^bDepartment of Pediatrics, Division of Pulmonology, Allergy, & Immunology, The University of Tennessee Health Science Center, Memphis, TN; ^cEpiMetrix, Inc, Los Altos, CA; ^dAimmune Therapeutics, a Nestle Health Science company, Brisbane, CA; ^e159 Solutions, Inc, San Mateo, CA; ^fFamily Allergy & Asthma, Louisville, KY

Corresponding author: Todd A. Mahr, MD, Allergy/Asthma/Immunology, Gundersen Health System, 1900 South Avenue, H03-003, La Crosse, WI 54601; phone: 608-775-2161; fax: 608-775-6692; email: tamahr@gundersenhealth.org

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TH and **AC** are consultants to Aimmune Therapeutics.

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ABSTRACT

Background: Peanut allergy is the most common food allergy among children. Studies assessing the burden of peanut allergy in a real-world setting are limited.

Objective: To estimate annual incidence and prevalence of peanut allergy cases among children aged 4-17-years and assess severe reaction and associated healthcare utilization rates.

Methods: Patient longitudinal data between 1/2011-12/2017 from a geographically and payor-type representative US healthcare claims database were utilized. Peanut allergy cases were identified using diagnostic codes and/or services indicating peanut-allergy-associated severe reactions/anaphylaxis. Estimated annual incidence was defined as peanut-allergic births as a proportion of all 1-year-olds and adjusted for <100% dataset capture, undercoding, patient underpresenting rates, and spontaneous outgrowth. Prevalence was calculated based on incidence. To assess rates of severe reactions to peanut and associated healthcare utilization, the cohort of 720,490 peanut allergy cases identified in 2011 was evaluated over a 6-year period from 2011-2017.

Results: Annual incidence increased from 1.7% to 5.2% between 2001-2017. Estimated prevalence in 4-17-year-olds was 1.25 million (2.2%) in 2017. Atopic comorbidities (asthma, 60.8%; atopic dermatitis, 61.7%) and other food allergies (35.3%) were common. Severe reactions (≥ 1) were observed in over half ($n=399,806$) of patients, and 37.9% were triggered by an accidental exposure. One in five patients ($n=144,883$) visited the emergency department due to peanut exposure.

Conclusion: Claims data suggest that the incidence and prevalence of peanut allergy in the US may be increasing. Estimated severe reaction rates and healthcare utilization were high, suggesting that the burden of peanut allergy may be considerable.

71

72 **Highlights box:**

73 What is already known about this topic?

74 Although peanut allergy is a serious, potentially life-threatening condition that substantially
75 impairs quality of life among patients and their caregivers, the epidemiology and disease burden
76 is not well-defined.

77 What does this article add to our knowledge?

78 This large, nationally representative, longitudinal claims analysis suggests that the incidence and
79 prevalence of peanut allergy in the United States may be increasing and characterized by a high
80 comorbidity burden and severe reaction rate.

81 How does this study impact current management guidelines?

82 Peanut allergy management using avoidance measures alone may be insufficient.

83 Implementation of effective tools to manage peanut allergy is needed to avoid severe reactions
84 and reduce impact on healthcare burden and patient quality of life.

85

86 **Key words:** (10; up to 10) Peanut allergy; anaphylaxis; atopic dermatitis; asthma; poly-food-
87 allergy; quality of life; healthcare utilization; epinephrine; severe reaction; accidental exposure

88

89 **Abbreviations used:** ED: emergency department; *ICD-9: International Classification of*
90 *Diseases, Ninth Revision; ICD-10: International Classification of Diseases, Tenth Revision; IgE:*
91 *immunoglobulin E; LEAP: Learning Early About Peanut [allergy]; NIH: National Institutes of*
92 *Health; psIgE: peanut-specific immunoglobulin E.*

93

INTRODUCTION

Peanut allergy is a serious and sometimes fatal¹⁻³ condition that negatively impacts both the individual and their family's quality of life.⁴⁻⁶ The reasons for this poorer quality of life are multifaceted, including dietary restrictions, activity limitations, the fear of exposure (in spite of avoidance measures), and bullying because of peanut allergy.⁷⁻¹¹ Further, comorbid atopic conditions are common in patients with peanut allergy: a recent characterization of a pediatric peanut-allergic cohort revealed that all subjects reported at least 1 comorbid atopic allergy or other food allergy, and approximately 40% of subjects reported more than 1 comorbid allergy or other food allergy.¹² The epidemiology of peanut allergy is not well-defined, with estimates of its prevalence varying from 0.6% to 8.6% in the United States,¹³⁻¹⁸ and variances attributed to differences in diagnosis, methodology, age of study population, and geographic area. The most recent national survey of self-reported food allergies completed between 2015 and 2016 estimated the prevalence of peanut allergy to be 2.2%.¹⁴ National population-based estimates of the incidence of peanut allergy are lacking; however, a historical cohort study from Olmsted County, Minnesota suggests it may be increasing.^{19, 20}

Peanut allergy may be more severe than other food allergies^{13, 14} and is associated with a greater number of food-related anaphylactic events leading to emergency and hospital care.^{21, 22} Recent studies show that between one-half and two-thirds of peanut-allergic children reported at least 1 severe reaction.^{13, 14, 23} A recent national survey of food-allergic children found that approximately 1 in 5 peanut-allergic children will visit an emergency department (ED) within 1 year, with 50% of peanut-allergic children visiting the ED due to peanut allergy at least once in their lifetimes.¹⁴ However, the severity of reactions to peanut cannot be accurately predicted by

the degree of severity of past reactions, measured levels of immunoglobulin E (IgE), or skin tests.

The primary management strategy for peanut allergy is strict allergen avoidance and symptomatic treatment of allergic reactions with emergency medications, including epinephrine autoinjectors.^{24, 25} Among children with food allergies, peanut-allergic children are most likely to have a current epinephrine prescription,¹⁴ emphasizing the significant risk of accidental exposures in these children. A study investigating the economic burden of childhood food allergy found direct medical costs in 2011 (eg, of prevention, diagnosis, and treating reactions to allergen exposures) to be \$4.3 billion annually, increasing to \$24.8 billion annually when indirect costs in 2011 (such as for travel, special diets, lost labor productivity, and lost opportunities) were considered.²⁶

Despite the substantial disease and economic burden of peanut allergy, large, population-based studies of patients with peanut allergy are lacking. The primary objective of this study was to assess the incidence and prevalence of peanut allergy in the United States using a large, nationally representative longitudinal claims database. The secondary objectives were: 1) to describe comorbid atopic conditions and poly-food-allergies in patients with peanut allergy, and 2) to assess rates of severe reactions and related healthcare utilization in these patients.

METHODS

Data source

PatientSourceTM (Symphony Health, a PRA Health Sciences company, Phoenix, AZ) is a proprietary, patient–physician longitudinal de-identified claims database, which represents 270 million active patients in the United States, including prescription, physician, and hospital healthcare claims. Age, sex, and regional patient distributions in the dataset are similar to US census distributions.²⁷ The database also includes point-of-sale prescription purchase information detailing the patient’s out-of-pocket liability (after application of coupons or copay assistance) and final claim payment status (paid or reversed claim). This unique combination of patients across insurance segments with detailed prescription life-cycle data is typically not available in traditional insurance claims datasets (eg, Medicare claims). To allow for longitudinal tracking, claims for each patient are linked across data sources (eg, pharmacy, hospital) and de-identified, using unique encrypted identifiers in compliance with the Health Insurance Portability and Accountability Act. The database has been used in numerous prior studies in oncology^{28, 29} and other disease areas.³⁰⁻³³ For this analysis, claims from January 2011 to December 2017 were included. This time frame was used to ensure the recency of data and sufficient claims volume and were balanced with data purchasing costs.

Study population

Patients aged 4-17 years with a claim for peanut allergy diagnosis or peanut-related anaphylaxis were identified using the *International Classification of Diseases, Ninth Revision (ICD-9)* and *Tenth Revision (ICD-10)* codes (Table E1). For each patient, the observation period began on the

date of the first documented claim related to peanut allergy in 2011, ending in 2017 exactly 6 years after the first documented claim.

Estimated annual incidence and cumulative prevalence of peanut allergy

Annual incidence and cumulative prevalence were extrapolated using adjustments to account for potential undercoding of peanut allergy, <100% claim capture rates, underpresenting to healthcare providers, development of peanut allergy in early childhood, and spontaneous resolution of peanut allergy over time (Figure 1, Table I). Each factor is described in detail below.

Undercoding rates

Studies in the literature suggest that a diagnosis code for peanut allergy (as opposed to anaphylaxis) may not be documented by healthcare professionals, which may result in undercoding of the allergy. For this analysis, undercoding rates were estimated using psIgE levels in the literature to establish thresholds for diagnosis of peanut allergy (Figure 2).³⁴ Peanut-allergic individuals with psIgE levels ≥ 14 kU_A/L were assumed to have a 95% probability of reacting to a food challenge. In addition, it was assumed that the probability of reacting to a food challenge decreased, but did not diminish at psIgE <14 kU_A/L.

Using these assumptions, potential undercoding for peanut allergy diagnosis was accounted for by matching patient claims to an additional available dataset containing psIgE lab results from a leading provider of lab testing in the United States (January 2014 to December 2016). Among 80,000 patients with a medical claim and a laboratory test, a weighted average of 42% of patients

were expected to have a documented peanut allergy diagnosis (Figure 2). However, 38% of these patients who were expected to have a corresponding medical claim documenting the peanut allergy diagnosis did not have a peanut allergy diagnosis. This undercoding rate was consistent across the 7 specific IgE subgroups for peanut allergy diagnosis, suggesting that undercoding was more evident in the dataset than overcoding (Figure E1, Table E1). The authors also considered micro-survey data (data not published) based on a sample of allergists fielded by an external research company, which was specifically designed to understand the undercoding rate using physicians' response. The undercoding rate was estimated to be about 20% to 25% using the survey data. Thus, the applied PA undercoding rate for this analysis was 30%, which was believed to be reflective and appropriate based on both the primary and secondary research data points.

Capture rates

The estimates of capture rates were based on total number of patients captured in patient medical claims database compared against the general population, which was later confirmed by Symphony Health. Coverage rates of peanut allergy-related claims varied based on place of service and were adjusted by applying projection factors, with 40% of claims filed through medical offices (non-hospital settings; 2.5× multiplier) and 25% filed through hospitals (4× multiplier). Symphony Health confirmed that the patient capture in the medical claims database remained consistent across the years of consideration for this analysis.

Underpresenting rates

The estimated underpresenting rate for each age was calculated as the difference between the estimated persistence of peanut allergy in patients over time as reported in the literature³⁵ versus what was identified in the claims database (Table I). Studies have shown that underpresenting typically begins at adolescence, with rates varying from 3-24% by age, or approximately 15% on average.³⁵

Aging patients back to birth

Peanut-allergic patients in this analysis were aged back to birth, with the assumption that peanut-allergic children develop the disease early in childhood.¹² This approach allows for the true capture of historical peanut allergy incidence and prevalence rates.

Spontaneous resolution rates

A previous 12-year longitudinal study of 202 patients estimated that 27% of patients naturally outgrow their peanut allergy by age 12.³⁵ This estimate was utilized for calculating annual peanut allergy incidence. This is considered a conservative estimate based on other studies evaluating the natural resolution of peanut allergy (Table E2).³⁶⁻⁴⁰

Analysis

Estimated annual incidence of peanut allergy was calculated as the proportion of peanut-allergy births versus all 1-year-olds.⁴¹⁻⁴³ Actual incidence was calculated from 2001 to 2006 by aging the peanut-allergic individuals from the 2011-to-2017 dataset to birth. Estimated incidence was calculated from 2007 to 2023 accounting for trends and assumptions from historical data. As

shown in Figure 3, incidence data for the index year of 2005 was derived from raw patient counts for clinic, hospital, and ED claims diagnosis data (anaphylaxis, nonanaphylaxis) with projection multipliers applied to account for under-counting and less than 100% capture rates. The resulting totals were further adjusted by patient/year in comparison with projected totals of actual peanut allergy incidence to account for projected under-presenting of cases. These totals were then adjusted for projected spontaneous resolution by patient age/year to derive a final estimate of births with peanut allergy in 2005. To summarize, incidence was calculated as (unadjusted patient count + % under presenting) + (% who outgrew peanut allergy); prevalence was calculated as incidence – % spontaneously outgrowing peanut allergy = projected number of patients with peanut allergy by cohort year.

Prevalence of peanut allergy at birth was estimated based on the described data adjustments and on incidence estimates calculated in this report. An example of these calculations is available in Figure 3, which delineates the projections used to arrive at the number of peanut allergy births for the year 2005 (Table I, Figure 3). To derive an estimate of peanut allergy prevalence for the year 2017, the estimated incidence total derived for 2005 (see above description) and projected estimates for each subsequent year until 2014 were adjusted by the projected percent of spontaneous resolution (or outgrowth) of PA by patient age/year, resulting in totals for each year, and allowing for a projection of 2017 prevalence (Figure 3).

Results from the Learning Early About Peanut [allergy] (LEAP) trial demonstrated that early introduction of peanut significantly decreased the risk of developing peanut allergy.⁴⁴ Subsequently, the National Institutes of Health (NIH) issued updated guidelines for preventing

peanut allergy,⁴⁵ resulting in an assumed slowing of peanut allergy incidence that is reflected in the projected data in Figure 4.

Comorbid atopic conditions

ICD diagnoses and prescription records were used to identify comorbid conditions. Peanut-allergic patients were considered to have asthma and/or atopic dermatitis if they had claims in the following categories: documented diagnosis of asthma (Table E3) or atopic dermatitis (Table E4); utilization of drugs primarily used to treat asthma; at least 6 (for asthma; Table E5) or 3 (for atopic dermatitis; Table E6) prescription refills within a 365-day period. Peanut-allergic patients with other food allergies (tree nut, seafood, dairy, and egg) were identified through related claims (Table E7). Undercoding was assumed to occur for reports of other food allergies, but was not adjusted for when calculating the proportion of peanut-allergic individuals with other food allergies in this analysis.

Definition of severe reaction to peanut

To identify peanut-allergic individuals who experienced a severe reaction, previously outlined criteria defining anaphylaxis were extrapolated to relevant *ICD* codes.⁴⁶ Confirmed peanut-allergic patients with claims in any of the following 5 categories were considered to have experienced a severe reaction (Table II).

After applying all definitions, a resulting 37% had a coded anaphylaxis due to peanut *or* anaphylaxis due to unspecified food with an allergy to peanuts *ICD* code; 12% had an ED visit with allergy to peanuts *ICD* code; 6% had symptoms from 2+ organ systems (these were

recorded for an allergy to peanuts diagnosis at some point in time, not necessarily concomitantly with the 2+ symptoms); 45% had an allergy to peanuts *ICD* code only.

Estimated rates of severe reactions and healthcare utilization

The number of severe reactions per observed patient and associated healthcare utilization between the years 2011 and 2017 were examined, including the number of ED visits and epinephrine prescription filling rates. Rates of severe reactions, stratified by atopic comorbidities and allergies other than peanut, were also calculated. Accidental exposures to peanut, defined as patients with a prior diagnosis of peanut allergy and experiencing a subsequent severe reaction due to peanut, were also calculated.

RESULTS

Annual incidence of peanut allergy

The estimated annual incidence of peanut allergy in 1-year-olds steadily increased between 2001 and 2017, with an estimated 1.7% (66,736 peanut allergy cases) in 2001 and 5.2% (210,056) in 2017 (Figure 4). Based on data from the LEAP trial and the updated NIH guidelines,^{44, 45} a decrease in incidence is expected after peaking in 2020.

Prevalence of peanut allergy

After all adjustments to the raw data (Table I, Figure 3), the estimated prevalence of peanut allergy cases among 4-17-year-olds in the United States was 1,247,838 patients in 2017 (2.2% of 58 million children in this age group) (Figure 5). About two-thirds (63.6%) of this cohort were children aged 4-11 years and the majority were diagnosed and treated by an allergist (Table III). Comorbid atopic conditions were common in this cohort of peanut allergy cases, including approximately 41% with both asthma and atopic dermatitis. Additionally, multiple food allergies were reported in 440,720 (35.3%) of the overall cohort.

Severe reaction rates and healthcare utilization

In 2011, 720,490 peanut allergy cases were identified via the claims database and observed over a 6-year observation period (2011-2017). Over half had at least 1 severe reaction (55.5%, n=399,806), 32.2% had multiple severe reactions (n=232,123), with 7.2% having on average 1 severe reaction per year (n=52,170) (Figure 6). The estimated accidental exposure rate was 37.9% (n=272,845).

When examining the study population of peanut allergy cases by comorbid atopic conditions or other food allergies, the rates of severe reactions over the mean 6-year observation period increased with increasing number of atopic comorbidities (Figure 7A) and with increasing poly-food-allergies (Figure 7B).

Over the 6-year observation period, 20.1% of peanut allergy cases aged 4-17-years-old visited the ED due to a severe reaction to peanut exposure (n=144,883); of these cases, 45,259 visited the ED more than 1 time during the observation period (31.2%; 6.3% overall). Total annualized ED visits due to peanut exposure were 38,319 per year.

Over the same 6-year period, 672,353 (93.3%) of peanut allergy cases aged 4-17-years-old filled a 2-pack epinephrine prescription. On average, 223,377 (33.2% overall) patients filled <1 epinephrine prescription per year; 355,580 (52.9% overall) filled 1 to 2 epinephrine prescriptions per year; and 93,396 (13.9% overall) filled >2 epinephrine prescriptions per year. Total annualized fills of 2-pack epinephrine autoinjector prescriptions were 878,772 per year.

DISCUSSION

Data from this large population-based, real-world study provide estimated incidence and prevalence of peanut allergy cases among 4-17-year-olds in the United States, and the estimated associated disease burden as described by associated atopic comorbidities, rates of severe reactions, and healthcare utilization. Findings suggest that the impact of peanut allergy may be greater than previously reported, with an increase in the annual incidence of peanut allergy over the last ~15 years, and approximately 1.25 million children and adolescents in the United States (2.2%) with the condition.⁴⁷⁻⁵¹ Most of these patients also suffer from comorbid atopic conditions, including asthma, atopic dermatitis, and other food allergies, that require additional care and treatment. Young patients with peanut allergy appear to exhibit high rates of severe reactions, with over half experiencing at least 1 severe reaction, of whom 1 in 3 experienced a severe reaction despite a prior peanut allergy diagnosis within the 6-year observation period. A high rate of healthcare utilization was also described, with about 1 in 5 children visiting the ED for a severe reaction triggered by peanut.

Despite varied methodologies across studies, prevalence estimates for peanut allergy in this report are consistent with those from other studies, which vary from 0.6% to 2.2%.¹³⁻¹⁷ In a recent survey-based study estimating the prevalence of confirmed, physician-diagnosed peanut allergy in patients aged 4-17 years in the United States, the prevalence was approximately 1.2 million patients;¹³ an update to this study published in 2018 estimated the prevalence among 0-17 year-olds at 1.6 million patients, or 2.2%. Indeed, although previous studies conducted surveys at different time points, prevalence estimates (and thereby incidence) have increased over the past 15 years.^{13, 14, 17} The findings of increasing peanut allergy incidence in this study

are generally consistent with historical, population-based incidence estimates of children aged 17 years or less from Olmsted County, Minnesota, which suggests a 3-fold increase in peanut allergy diagnoses from 2.05 per 10,000 children in 1999 to 6.88 per 10,000 children in 2007.¹⁹ While an overall increase in food allergies in patients of all ages between 2002-2009 was observed, with stabilization between 2009-2011, the incidence of peanut allergy in the 5-18-year-old age group increased between 2002 and 2011 (0.7 per 10,000 person-years in 2002 to 2.8 per 10,000 person-years in 2011).²⁰ Future studies calculating prevalence and incidence of peanut allergy will determine the effect of the recent LEAP trial and subsequent changes to the NIH guidelines on prevention of peanut allergy.^{44, 45}

Estimates of severe reactions in young peanut-allergic patients in the current study were consistent with other reports^{13, 14} and suggest a high healthcare burden in patients with peanut allergy. The recent Food Allergy Research and Education dataset estimated 203,000 annual ED visits for all food allergies across all ages in the United States;⁵² results from the current analysis, although estimated based on several assumptions, suggest that peanut allergy alone accounts for nearly one-fifth of these ED visits. Similarly, a national survey of food-allergic children found that 1 in 5 peanut-allergic children reported ED visits due to peanut exposure in the previous year.¹⁴ We corroborate the data previously reported, with 1 in 5 children and adolescents aged 4-17 years visiting the ED due to accidental exposure to peanut. Related to a high rate of accidental exposure and subsequent severe reactions, we observed that the majority of peanut-allergic patients had filled an epinephrine prescription, which is similar to the recent finding based on survey data that peanut allergy increased the odds of having a current epinephrine prescription.¹⁴

It is important to note that 30% of patients in the database were not diagnosed or treated by an allergist. Future analyses should describe the peanut allergy management strategies for this group versus the group diagnosed and managed by allergists. However, data from the current analysis together with recent supportive survey data suggest that management strategies for allergen avoidance and emergency intervention with rescue medication upon exposure are not sufficient to prevent reactions in peanut-allergic patients. Indeed, analysis of reactions during oral food challenges has shown that very small amounts of peanut protein (as little as 1 mg) may induce a reaction in peanut-allergic children.⁵³ In real-world settings, larger amounts of peanut are consumed accidentally in a short period of time before a reaction occurs and an individual realizes they were exposed to the allergen. A recent study estimated that a median 125 mg of peanut protein (Q1, Q3: 34 mg, 177 mg) was ingested during an accidental exposure.¹² In a 5-year longitudinal study of peanut-allergic children, nearly 30% had a potentially life-threatening first reaction (defined as involving respiratory system, being hypotensive, or losing consciousness); 71% had a potentially life-threatening reaction during at least 1 subsequent exposure.⁵⁴ In addition, 44% of the observed patients experienced a potentially life-threatening allergic reaction after a non-life-threatening first reaction (including skin reactions, gastrointestinal symptoms, or non-life-threatening respiratory symptoms). Risk and uncertainty are common among peanut-allergic children and adolescents, subsequently affecting all family members and requiring both knowledge and understanding of the risks involved.^{4, 55, 56} As the current recommended management strategy is avoidance, patients and caregivers must practice constant vigilance and alter eating habits and social engagements that may negatively impact quality of life.⁵⁷

While these findings are consistent with previous reports,^{14, 19, 20} several limitations should be considered. First, this analysis included a number of vital adjustments that required the application of assumptions to the dataset for generating the national estimates of incidence and prevalence. In estimating overcoding, we performed a sensitivity analysis examining psIgE levels in a sample of the patient population and extrapolated these values based on available literature. We recognize that this is a poor surrogate to attempt to capture missed claims in our dataset; however, we attempted to use as conservative estimates as possible. Estimating underpresenting rates required assumptions for the spontaneous resolution of peanut allergy and the frequency of peanut allergy-related claims. The higher rates of underpresenting observed during adolescence may reflect adolescents' improved ability to manage their allergy, with a concomitant reduction in peanut allergy-related healthcare encounters.

Potential overcoding was not applied in this analysis, which could occur in the following instances: when a reported peanut-allergy history is recorded in a patient, but subsequent testing is nonconfirmatory or rules out the diagnosis; or when incomplete evaluation or improper interpretation of psIgE testing occurs. However, our observed diagnosis rates never exceeded those suggested by the literature, indicating that undercoding was more evident than overcoding in the dataset. Another assumption was the impact of the National Institute of Allergy and Infectious Diseases guidelines on peanut allergy incidence, but was based on a reduction in incidence 60 months after the publication of LEAP.⁴⁴

A sensitivity analysis of the raw incidence data with and without these additional adjustments was conducted by updating the adjusted model to remove all projections, with the exception of

aging of patients back to when they were 0-1 years of age. Across both projected and raw patient counts, we see a comparable growth in incidence rate for years from 2002 to 2007 (Table E8), suggesting that the observed increased incidence rate is not a result of applying adjustments to account for capture rate, undercoding, underpresenting, and spontaneous resolution.

Other limitations were encountered when determining the prevalence of comorbid asthma by applying a threshold of at least 6 asthma medications in the claims database, which could have resulted in an underestimation. However, our estimate was similar to other studies of peanut-allergic children and adolescents.¹² It should also be noted that peanut-allergic patients who have not yet been diagnosed were not represented in the database. Therefore, children diagnosed with peanut allergy after 2016 could not be included in incidence and prevalence estimates.

Additionally, the actual severity of anaphylaxis within a claims database could not be ascertained, given the reliance on *ICD* coding, which do not provide this differentiation. It was also not possible to identify whether patients with severe reactions were receiving peanut oral immunotherapy. We do not expect that differences in *ICD-9* and *ICD-10* should have resulted in differences in coding, as the only difference between them was the implementation of the sequencing of the reaction, whether it was a first-time reaction or a repeating reaction. The change from *ICD-9* to *ICD-10* should not impact the number of patients diagnosed with the disease on average, but rather, help define more precisely the diagnosis description and type. The change in the number of new patients might be possible, however, in cases where the *ICD-9* codes had been more general in nature and were assigned to specific codes in the *ICD-10* coding schema. For all assumptions applied to the analysis, the most conservative approaches were used, which should mitigate potential inflated incidence rates.

435 This study represents real-world, nationwide estimates of the burden of peanut allergy on
436 affected patients and on the healthcare system in the United States, utilizing a large, longitudinal
437 dataset. Such findings suggest that management of peanut allergy using avoidance measures
438 alone may not be sufficient and can lead to frequent accidental severe reactions and healthcare
439 utilization. Implementation of effective tools to manage peanut allergy are needed to avoid
440 severe reactions and reduce impact on healthcare burden and patient quality of life.

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588 **Table I. Projection inputs for extrapolating incidence and prevalence of PA**

Input	Variable	Multiplier
Undercoding, by diagnosis*	Anaphylaxis diagnosis	0
	Nonanaphylaxis diagnosis	1.428571
Capture <100%, site [†]	Clinic	2.5
	Hospital	4.0
Underpresenting, age, y	% Underpresenting	
	1–10	0
	11	1
	12	3
	13	5
	14	8
	15	11
	16	14
	17	18
	18–80	20
Spontaneous resolution, age, y	% Outgrown	
	1	0
	2	4
	3	7
	4	10
	5	14
	6	18
	7	20
	8	22
	9	24
	10	26
	≥11	27

589 PA=peanut allergy.

590 *Based on an assumed undercoding rate of 30% for diagnoses other than anaphylaxis.

591 [†]Based on assumed capture rates of 25% for claims filed through hospitals and 40% for claims filed through non-
 592 hospital settings

593

594 **Table II. ICD-9 and ICD-10 Codes for Identifying Severe Reactions to Peanut^a**

Category	ICD-9 or -10 Code	ICD Description
Severe Reaction Category 1: Severe reaction - anaphylaxis due to peanut	995.61	ANAPHYLACTIC REACTION TO PEANUTS
	T78.01XA	ANAPHYLACTIC REACTION TO PEANUT, INITIAL ENCOUNTER
	T78.01XD	ANAPHYLACTIC REACTION TO PEANUT, SUBSEQUENT
	T78.01XS	ANAPHYLACTIC SHOCK TO PEANUT, SEQUELA
Severe Reaction Category 2: Severe reaction - unspecified food	995.6	ANAPHYLACTIC REACTION DUE TO UNSPECIFIED FOOD
	T78.00XA	ANAPHYLACTIC REACTION DUE TO UNSPECIFIED FOOD, INITIAL ENCOUNTER
	T78.00XD	ANAPHYLACTIC REACTION DUE TO UNSPECIFIED FOOD, SUBSEQUENT ENCOUNTER
	T78.00XS	ANAPHYLACTIC REACTION DUE TO UNSPECIFIED FOOD, SEQUELA
Severe Reaction Category 3: CPT codes - emergency department	99281	EMERGENCY DEPARTMENT VISIT LIMITED/MINOR PROB
	99282	EMERGENCY DEPARTMENT VISIT LOW/MODER SEVERITY
	99283	EMERGENCY DEPARTMENT VISIT MODERATE SEVERITY
	99284	EMERGENCY DEPARTMENT VISIT HIGH/URGENT SEVERITY
	99285	EMERGENCY DEPT VISIT HIGH SEVERITY&THREAT FUNC
	99288	PHYS/QHP DIRECTION EMERGENCY MEDICAL SYSTEMS
Severe Reaction Category 4: Severe reaction - symptoms/severe reactions	J38.4	EDEMA OF LARYNX
	K14X	DISEASE OF TONGUE
	K13.79	OTHER LESIONS OF ORAL MUCOSA
	J96.0	ACUTE RESPIRATORY FAILURE
	J95.X	HYPOTENSION
	R23.0	CYANOSIS
	R41.0	DISORIENTATION
	R55	SYNCOPE AND COLLAPSE
	N39.X	INCONTINENCE
Severe Reaction Category 5: Severe Reaction - Hypersensitivity in ≥2 organ systems	L29.9	CUTANEOUS - GENERALIZED PRURITIS
	L50.1	CUTANEOUS - IDIOPATHIC URTICARIA
	T78.3XX	CUTANEOUS - ANGIONEUROTIC EDEMA
	R23.2	CUTANEOUS - FLUSHING
	J45.991	LOWER OR UPPER RESPIRATORY - COUGH VARIANT ASTHMA
	R06.2	LOWER OR UPPER RESPIRATORY - WHEEZING
	J45.XX	LOWER OR UPPER RESPIRATORY - ASTHMA
	R06.02	LOWER OR UPPER RESPIRATORY - SHORTNESS OF BREATH
	R06.0	LOWER OR UPPER RESPIRATORY - DYSPNEA
	J30.5	LOWER OR UPPER RESPIRATORY - ALLERGIC RHINITIS DUE TO FOOD
	R06.7	LOWER OR UPPER RESPIRATORY - SNEEZING
	R09.81	LOWER OR UPPER RESPIRATORY - NASAL CONGESTION
	J34.89	LOWER OR UPPER RESPIRATORY - OTHER SPECIFIED DISORDERS OF NOSE AND NASAL SINUSES

	R07.0	LOWER OR UPPER RESPIRATORY - PAIN IN THROAT
	R13.1X	LOWER OR UPPER RESPIRATORY - DYSPHAGIA
	R06.1	LOWER OR UPPER RESPIRATORY - STRIDOR
	H11.4XX	CONJUNCTIVAL - CONJUNCTIVAL HYPEREMIA
	H04.2XX	CONJUNCTIVAL - EPIPHORA
	R10.XX	GASTROINTESTINAL - ABDOMINAL AND PELVIC PAIN
	R11.1X	GASTROINTESTINAL - VOMITING
	R11.0	GASTROINTESTINAL - NAUSEA
	K59.1	GASTROINTESTINAL - DIARRHEA

^aSevere reaction to peanut is defined as when a **confirmed peanut allergy patient** has any of the following documented: 1) anaphylactic reaction to peanut, or to unspecified food (when the closest claim is for a peanut allergy diagnosis); 2) an ED visit coded for peanut allergy (without regard for subsequent HCP visits); 3) any severe reaction as identified in Category 4; 4) any hypersensitivity symptoms in 2+ organ systems as identified in Category 5.

CPT, Current Procedural Terminology; ED, emergency department; HCP, healthcare provider; ICD-9, *International Classification of Diseases, Ninth Revision*; ICD-10, *International Classification of Diseases, Tenth Revision*.

Table III. Demographic and clinical characteristics of N=1,247,838 peanut-allergic patients, 2017

Characteristic		% of Patients
Age group	4-11 years	63.6
	12-17 years	36.4
Sex	Male	60.2
	Female	39.8
Insurance type	Commercial	63.2
	Managed Medicaid	24.5
	Medicaid	6.1
	Assistance programs	3.9
	Cash	2.0
	Medicare	0.3
Physician specialty	Diagnosed/treated by allergist	42.0
	Diagnosed by pediatrician/treated by allergist	28.0
	Diagnosed/treated outside of allergist	30.0
Comorbidity ^a	None	18.5
	Asthma	60.8
	Atopic dermatitis	61.7
	Asthma and atopic dermatitis	40.9

^aCategories are not mutually exclusive.

Figure Legends

FIG 1. Adjustments applied for calculation of incidence and prevalence of peanut allergy.

HCP, healthcare provider; ICD, *International Classification of Diseases*; PA, peanut allergy.

FIG 2. Calculating undercoding rates: triangulating medical literature, documented peanut allergy diagnosis, and laboratory test results.

For each psIgE group, expected prevalence of PA (represented by the sum of the orange and green bars in Fig 2) was estimated based on psIgE levels reported in the literature.³⁴ The proportions of documented and undocumented peanut allergy cases were then calculated. The overall undercoding rate was calculated based on the 80,000 cases in which a laboratory test and medical claim were available from the dataset (bar on right).

FIG 3. (A) Extrapolations used to calculate the number births with peanut allergy in 2005 (incidence),* and (B) prevalence calculation for 2017 after identification of cohorts aged ≤1 y for each year.

*Model shows data for a single cohort of patients that would have been ≤1 year old in 2005 (patients aged 7 in 2011 to those aged 12 in 2016) since these would all have been age ≤1 year old in 2005.

†Projection multiplier=undercoding multiplier x capture multiplier (see Table E2).

Differences in prevalence estimates between the manuscript text and the figure representation are due to rounding.

ER=emergency room; PA=peanut allergy; SH=Symphony Health Solutions database.

FIG 4. Annual incidence of peanut allergy in the United States, 2001-2023.

Annual incidence (represented by red line in Fig 3) was calculated using the number of peanut-allergic patients identified via ICD-9 and ICD-10 claims aged back to Age 1 (dark- and light-green bars), divided by the total number of births in the United States (“US Births”) for that year. Total number of births was based on data from the United States Census Bureau, with actual births reported in the 2010 census data and projected births from models based on historical data.⁴¹⁻⁴³

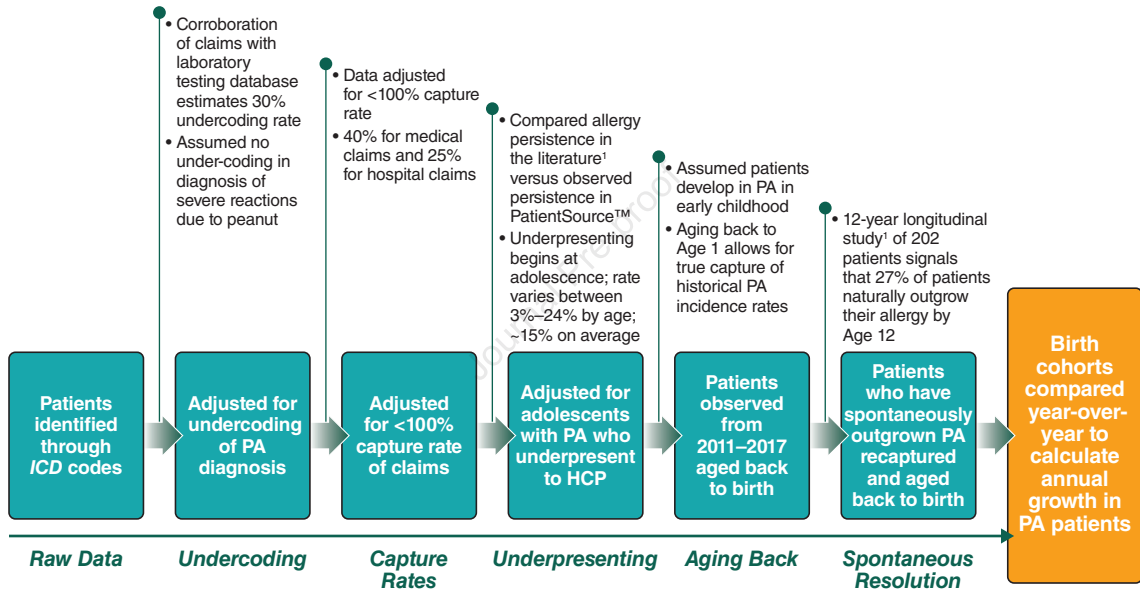
FIG 5. Prevalence of peanut allergy in 4-17-year-olds, 2017

ICD, International Classification of Diseases; PA, peanut allergy.

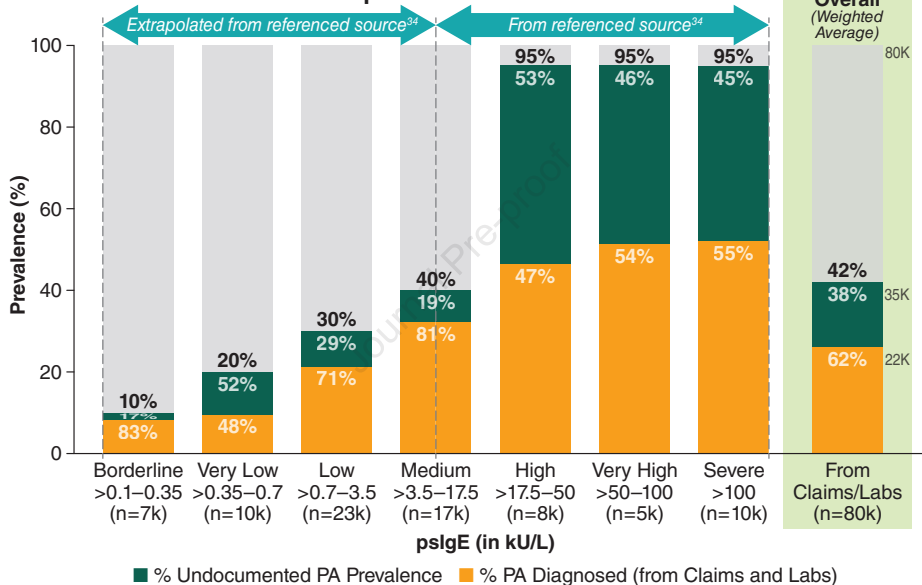
FIG 6. Rates of severe reactions in patients diagnosed with peanut allergy, 2011-2017.

FIG 7. Severe reaction rates in peanut-allergic patients with atopic comorbidities (A) and additional food allergies (B), 2011-2017.

Additional food allergies were not adjusted for undercoding rates, although estimates for peanut allergy were adjusted for undercoding rates. FA, food allergy; PA, peanut allergy.



Expected Prevalence of PA



Step 1: Account for Under-Coding and <100% Capture

Age / Index Year	Diagnosis Setting	PA Diagnosis	Patient Count (SH)	×	Projection Multiplier [†]	=	Projected Patient Count 1
7 / 2011	Clinic	Anaphylaxis	1,909		2.50		4,773
	Clinic	Non-Anaphylaxis	1,800		3.57		6,429
	ER	Anaphylaxis	309		4.00		1,236
	Hospital	Anaphylaxis	96		4.00		384
	Hospital	Non-Anaphylaxis	387		5.71		2,211
8 / 2012	Clinic	Anaphylaxis	1,239		2.50		3,098
	Clinic	Non-Anaphylaxis	1,118		3.57		3,993
	ER	Anaphylaxis	304		4.00		1,216
	Hospital	Anaphylaxis	64		4.00		256
	Hospital	Non-Anaphylaxis	300		5.71		1,714
9 / 2013	Clinic	Anaphylaxis	987		2.50		2,468
	Clinic	Non-Anaphylaxis	1,289		3.57		4,604
	ER	Anaphylaxis	304		4.00		1,216
	Hospital	Anaphylaxis	58		4.00		232
	Hospital	Non-Anaphylaxis	279		5.71		1,594
10 / 2014	Clinic	Anaphylaxis	851		2.50		2,128
	Clinic	Non-Anaphylaxis	1,407		3.57		5,025
	ER	Anaphylaxis	320		4.00		1,280
	Hospital	Anaphylaxis	53		4.00		212
	Hospital	Non-Anaphylaxis	277		5.71		1,583
11 / 2015	Clinic	Anaphylaxis	796		2.50		1,990
	Clinic	Non-Anaphylaxis	1,460		3.57		5,214
	ER	Anaphylaxis	285		4.00		1,140
	Hospital	Anaphylaxis	42		4.00		168
	Hospital	Non-Anaphylaxis	241		5.71		1,377
12 / 2016	Clinic	Anaphylaxis	895		2.50		2,238
	Clinic	Non-Anaphylaxis	1,825		3.57		6,518
	ER	Anaphylaxis	271		4.00		1,084
	Hospital	Anaphylaxis	49		4.00		196
	Hospital	Non-Anaphylaxis	202		5.71		1,154

66,729

Step 2: Account for Under-Presenting

Index Year	Age as of Index Year	Projected Patient Count 1	+	% Under-Presenting	=	Projected Patient Count 2
2011	7	15,033		0%		15,033
2012	8	10,277		0%		10,277
2013	9	10,113		0%		10,113
2014	10	10,227		0%		10,227
2015	11	9,889		1%		9,977
2016	12	11,190		3%		11,512

67,139

Step 3: Account for Spontaneous Resolution

Index Year	Age as of Index Year	Projected Patient Count 2	+	% Who Outgrew PA	=	Projected Patient Count 3
2011	7	15,033		20%		18,791
2012	8	10,277		22%		13,175
2013	9	10,113		24%		13,307
2014	10	10,227		26%		13,821
2015	11	9,977		27%		13,574
2016	12	11,512		27%		15,770

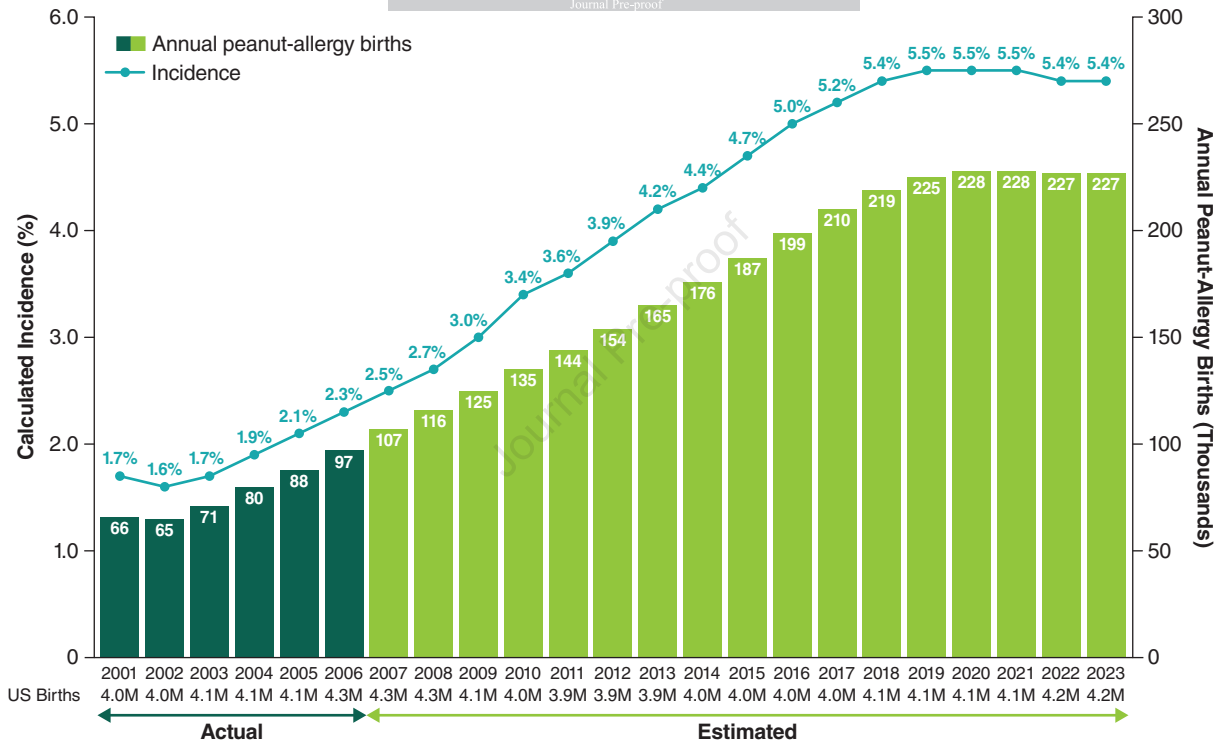
Estimated births with peanut allergy in 2005

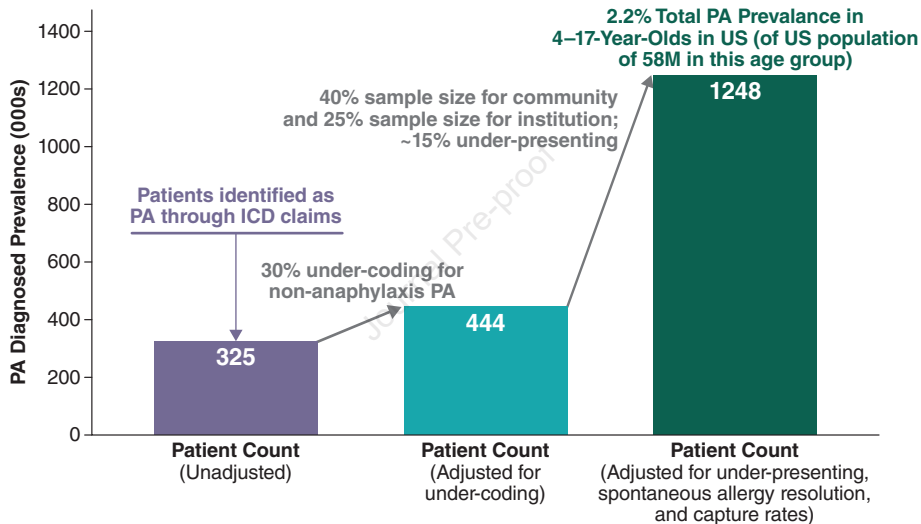
88,438

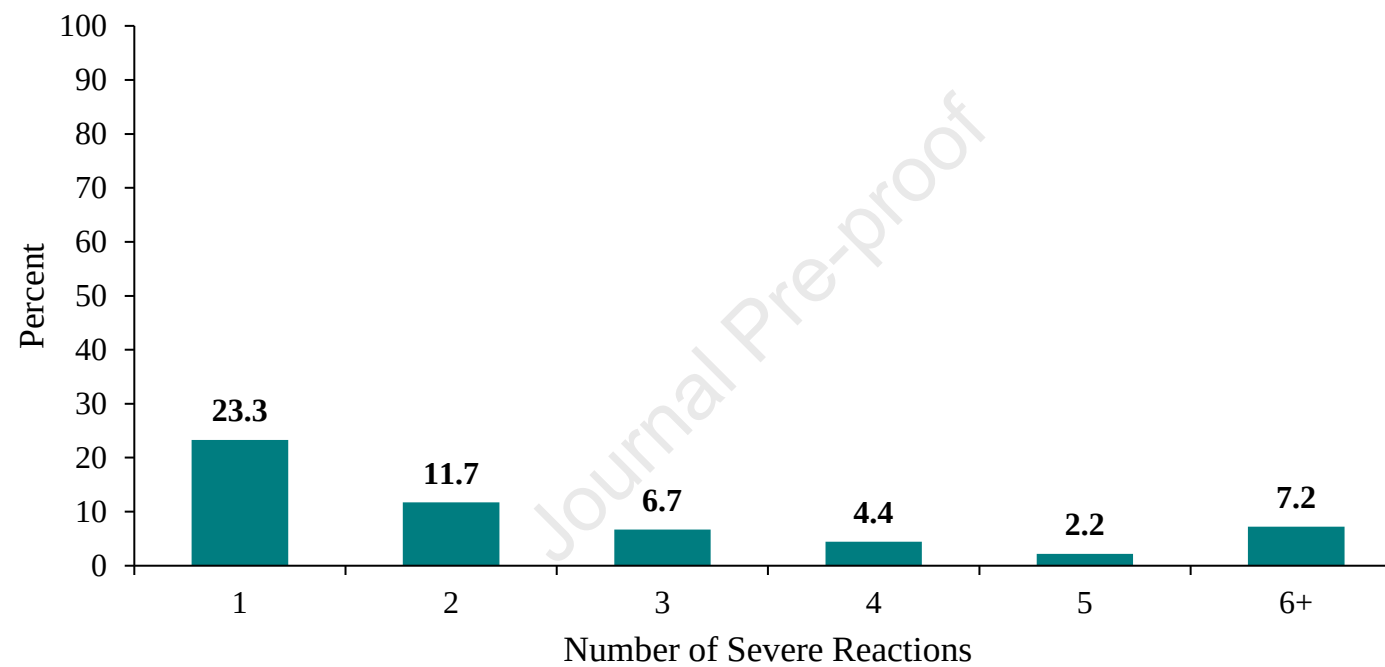
Step 4: Apply spontaneous resolution rate for cohort as of 2017

Cohort year	Patients aged ≤1 year	Age in 2017	% spontaneously outgrew PA by 2017	% with PA in 2017	Projected PA Patients
2001	66,376	17	27	73	48,455
2002	64,650	16	27	73	47,195
2003	71,484	15	27	73	52,184
2004	79,811	14	27	73	58,262
2005	88,438	13	27	73	64,559
2006	97,500	12	27	73	71,175
2007	106,558	11	27	74	78,320
2008	115,616	10	26	74	85,555
2009	124,958	9	24	76	94,967
2010	134,551	8	22	78	104,950
2011	144,389	7	20	80	115,511
2012	154,497	6	18	82	126,687
2013	164,931	5	14	86	141,840
2014	175,741	4	10	90	158,167

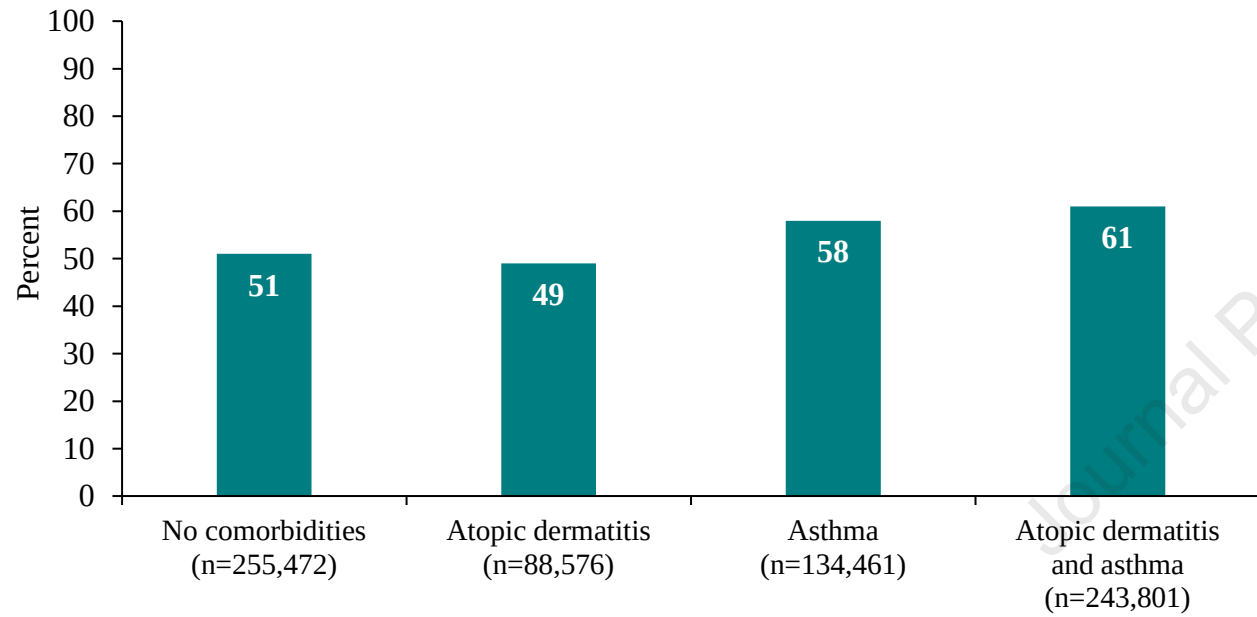
Total 4 to 17 year olds with PA in 2017 (Prevalence)**1,247,829.09**







A



B

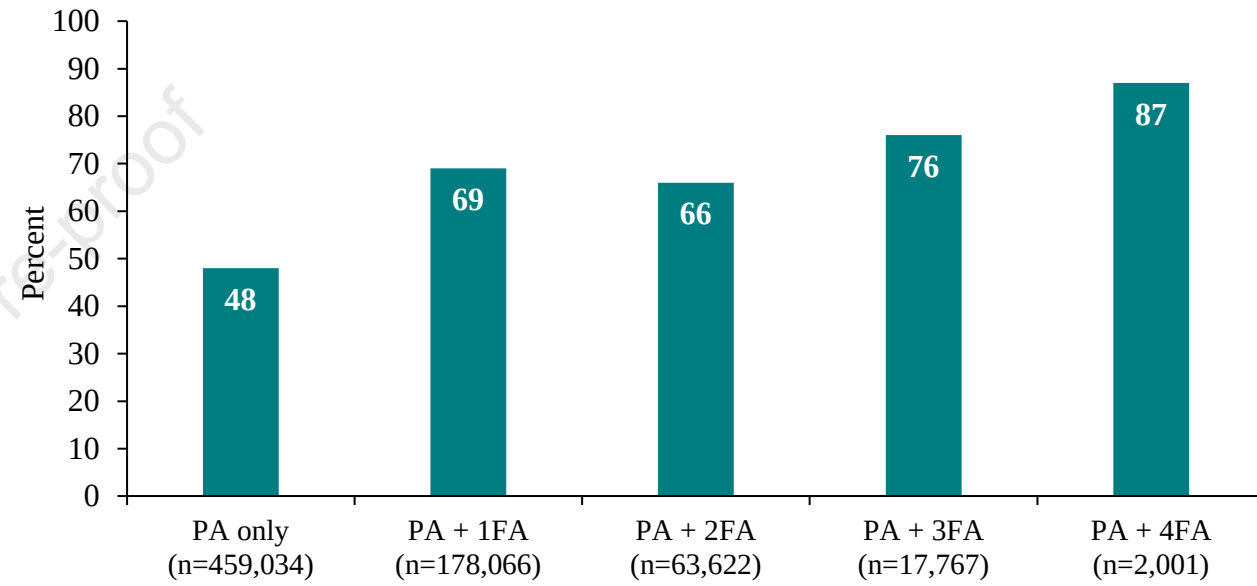


Figure Legend

Figure E1: Literature review results: Expected peanut allergy prevalence based on specific IgE levels.