

Health-care resource utilization associated with peanut allergy management under allergen avoidance among commercially insured individuals

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ABSTRACT

Background: Until recently, the standard approach to care for individuals with peanut allergy (PA) was limited to allergen avoidance and treatment of reactions with emergency medicines.

Objectives: To assess health-care resource utilization (HRU) and costs associated with PA management under allergen avoidance and to identify risk factors associated with peanut reactions that resulted in inpatient (IP) and/or emergency department (ED) visits.

Methods: Privately insured individuals with PA diagnosis codes were identified from a large U.S. administrative claims data base (January 1, 1999, to March 31, 2017). PA-related HRU, indicated by a PA diagnosis and/or diagnostic procedure codes and by epinephrine autoinjectors (EAI) prescription fills in medical and pharmacy claims, respectively, and all-cause costs were described per patient-year (PPY). Risk factors associated with peanut reactions in an IP and/or ED setting were identified by using a multivariable logistic regression model.

Results: A total of 86,483 patient-years from 14,136 individuals with PA were included. At the patient-year level, 28.1% were ages 0–3 years, 43.6% were ages 4–11 years, 13.7% were ages 12–17 years, and 14.5% were ages ≥ 18 years; 35.6% had PA-related outpatient visits; 50.6% had EAI fills; and 2.4% had PA-related IP and/or ED visits PPY. Younger individuals had more PA-related outpatient visits and EAI fills, with peak intensive use at ages 4–11 years. The proportion of individuals with PA-related IP and/or ED visits was highest among those aged ≥ 18 years. Mean all-cause costs were \$3084 PPY; individuals with PA-related IP and/or ED visits incurred \$8902 PPY (\$17,451 for those with one or more IP visits). Risk factors associated with peanut reactions that resulted in IP and/or ED visits included young adults (odds ratio [OR] 3.19 [95% confidence interval {CI}, 2.66–3.83]), previous peanut reaction(s) (OR 1.66 [95% CI, 1.23–2.24]), asthma (OR 1.33 [95% CI, 1.18–1.51]), and male sex (OR 1.14 [95% CI, 1.01–1.28]).

Conclusion: Individuals with PA and under allergen avoidance had significant HRU that varied across all age groups, with more PA-related outpatient visits during preschool and/or school age and PA-related urgent care among adults. Individuals with previous peanut reaction(s), asthma, and males had a higher risk of peanut reactions that resulted in IP and/or ED visits.

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Peanut allergy (PA) is the most common childhood food allergy in the United States, and its prevalence has been steadily rising,^{1,2} with most cases persisting into adulthood.^{3,4} PA is the leading cause of food-related anaphylaxis and hospitalizations, and account for 37% of food allergy anaphylaxis cases and 35% of hospital admissions due to anaphylaxis.⁵ This large disease burden is worsened by the existence of many comorbidities, including asthma, other food allergies, and allergic rhinitis.^{6–8} When evaluating a patient for PA, common diagnostic procedures may include skin-prick tests, immunoglobulin E (IgE) tests, and ingestion challenge tests, the latter of which is the criterion standard and is the most specific test for diagnosing PA and other food allergies.^{3,9,10} After the initial diagnostic evaluation, individuals with PA may undergo additional follow-up visits and testing related to PA management, which results in additional costs.

Treatment guidelines for the clinical management of food allergy recommend allergen avoidance as a

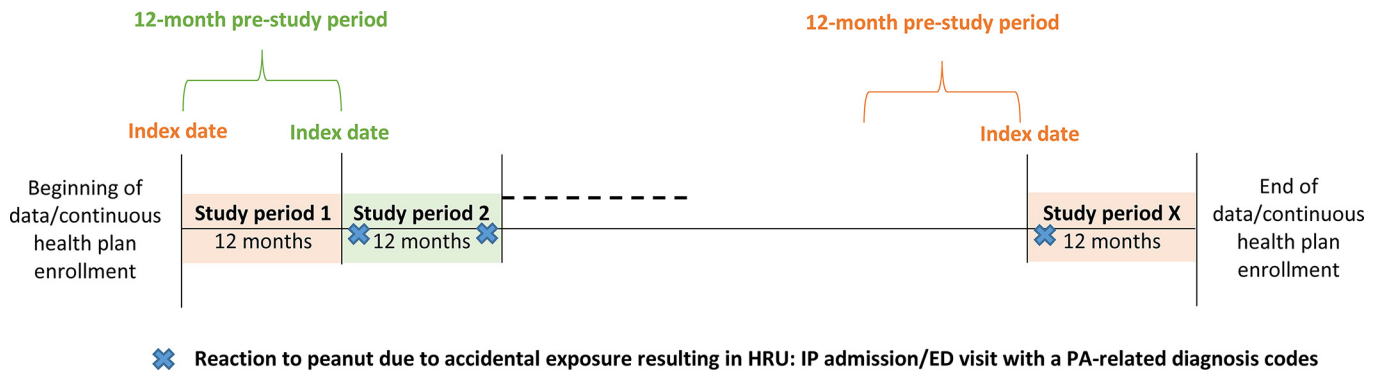


Figure 1. Study design. ED = Emergency department; HRU = health-care resource utilization; IP = inpatient; PA = peanut allergy.

preventative strategy once PA has been diagnosed.^{3,9} In the event of accidental exposure, current treatment options for management of allergic reactions include epinephrine autoinjectors (EAI) and a visit to the emergency department (ED); antihistamines, corticosteroids, and bronchodilators are sometimes used as adjunctive treatments.³ In addition to these emergency management treatments, the U.S. Food and Drug Administration (FDA) recently approved the Peanut (*Arachis hypogaea*) Allergen Powder-dnfp (previously known as AR101), on January 31, 2020, an oral immunotherapy indicated for the mitigation of allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanut when used in conjunction with a peanut-avoidant diet.¹¹

Although the economic burden of food allergy in general is known to be substantial,^{12–16} there is a paucity of real-world data that assessed the health-care resource utilization (HRU) and costs associated with PA management in the United States despite peanut avoidance practice. Due to the highly variable nature of PA, the unreliability of allergen avoidance practice,^{17,18} the risk of accidental exposure to peanut,^{17,18} and the lack of effective preventative treatment options at the time the study was conducted, PA-related HRU is likely to vary substantially across individuals with PA. In addition, there is evidence that the risk and severity of food allergic reactions may vary according to age and other factors, *e.g.*, existing comorbidities,¹⁹ which may also affect HRU and costs.

The current study aimed to assess the HRU associated with PA management practice and direct health-care costs observed in commercial claims data from a period of 18 years, when the only preventative treatment option was allergen avoidance. In parallel, the study aimed to identify risk factors associated with reactions to peanut after accidental exposure that resulted in inpatient (IP) admissions or ED visits. These analyses were focused on the privately insured population to inform private payers and physicians, and to facilitate future treatment decision-making.

METHODS

Data Source

Patient data obtained from the Optum Health Care Solutions, Inc., Eden Prairie, MN, from January 1, 1999, to March 31, 2017, a large U.S. administrative claims data base, was used. This data base includes claims for individuals covered by self-insured companies across all areas of the United States. Data elements include detailed information on health plan enrollment, demographics, diagnoses, procedures, and claims for medical care received across all settings as well as pharmacy services. Data were de-identified and complied with the Health Insurance Portability and Accountability Act; therefore, no reviews by an institutional review board were required.

Study Design and Sample Selection

A retrospective cohort design with annual cross-sections from 1999 to 2017 was used (Fig. 1). Individuals with two or more medical claims with a PA diagnosis on distinct dates and a period of ≥ 12 months of continuous health plan enrollment (medical and pharmacy) were identified by using medical claims with diagnosis codes related to PA (*i.e.*, *International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] codes (<https://www.cms.gov/Medicare/Coding/ICD9ProviderDiagnosticCodes/codes>): V15.01 allergy to peanuts and 995.61 anaphylactic shock due to peanuts; *International Classification of Diseases, Tenth Revision, Clinical Modification* [ICD-10-CM] codes (<https://www.cms.gov/medicare/icd-10/2021-icd-10-cm>): Z91.010 allergy to peanuts and T78.01XA, T78.01XD, and T78.01XS anaphylactic reaction due to peanuts). Due to the inherent limitations of claims data, including the possibility of coding errors and the use of diagnosis codes for testing procedures, a minimum of a second PA diagnosis in medical claims was required to support the presence of PA. The duration of the study period varied by patient and spanned from the beginning until the end of data or continuous health plan enrollment, whichever occurred first, to use all available data. Continuous health plan enrollment was split into episodes of 12-month study periods (*i.e.*, patient-years).

Outcomes and Statistical Analysis

Study outcomes included PA-related HRU, all-cause health-care costs, and risk factors associated with reactions to peanut in an IP and/or ED setting, which were measured during each study period of 12 months (*i.e.*, each patient-year). PA-related HRU was reported on an annual basis (per patient-year [PPY]) and included the number of outpatient (OP) visits with a PA-related diagnosis code, the number of OP visits with PA-related diagnostic procedures (including ingestion food challenge tests, peanut-specific IgE tests, and skin-prick tests), prescription fills for EAIs (two-pack carton per prescription dispensed; *i.e.*, two EAIs per prescription dispensed), and the number of IP admissions and ED visits with a PA-related diagnosis code. Direct all-cause health-care costs, including medical and pharmacy costs, were reported on an annual basis (PPY) in 2019 U.S. dollars (USD) from a payer's perspective.

Risk factors associated with reactions to peanut that resulted in an IP admission or an ED visit were identified by using a multivariable logistic regression model with random effects based on a report of a diagnosis code related to PA in medical claims in an IP or ED setting during a 12-month study period. Of note, the events identified represented a subgroup of potential reactions to peanut experienced by these individuals with PA because they did not include those managed outside of the IP or ED setting. This analysis was conducted among a subgroup of individuals with ≥ 36 months of continuous enrollment to identify potential risk factors presented before the 12-month study period when IP or ED visits occurred.

Potential factors were selected by using bidirectional stepwise selection from an *a priori* list of characteristics observed in claims for individuals with PA, with univariate regression models conducted for each potential factor before inclusion in the multivariable regression model (Supplemental Table S1). The model included factors such as demographic characteristics (age, sex), comorbidity profile, and HRU. HRU included prescription fills for EAIs, observed reaction(s) to peanut in an IP or ED setting, and diagnostic procedures for PA during the 12 months before the study period (*i.e.*, the previous year). Comorbidities included conditions frequently associated with PA (*i.e.*, asthma, atopic dermatitis and/or eczema, other food allergies, and allergic rhinitis)^{6–8} and were identified by using diagnosis codes in medical claims observed anytime during the health plan enrollment. Odds ratios (OR) and 95% confidence intervals (CI) were reported for the risk factors identified. All analyses were stratified and adjusted for age at the beginning of the 12-month study period; age groups were based on developmental stages and were stratified as 0–3 years (infant/toddler), 4–11 years (preschool/school age), 12–17 years (adolescents), and ≥ 18 years (adults).

RESULTS

Patient Characteristics

A total of 14,136 individuals with PA, which represented 86,483 patient-years, were included in the analysis. At the patient-year level, 28.1% were ages 0–3 years, 43.6% were ages 4–11 years, 13.7% were ages 12–17 years, and 14.5% were ages ≥ 18 years (Table 1). In addition, 42% of the individuals were female.

PA-Related HRU

After review of all the patient-years, 22.4% of the individuals with PA had one or more OP visits with a PA-related diagnosis PPY, and, among these, 5.4% had three or more such visits PPY. Younger individuals were observed to have more OP visits with a PA-related diagnosis PPY, particularly those aged 4–5 years, and the proportion of individuals with these visits seemed to decline with increasing age (Fig. 2). The proportion of individuals with three or more OP visits with a PA-related diagnosis PPY was observed to be the highest among individuals aged 4–7 years.

In addition, 28.8% of individuals with PA had one or more OP visits with PA-related diagnostic procedures PPY, and, among these, 6.8% had three or more such visits PPY. Younger individuals were observed to have had more OP visits with PA-related diagnostic procedures, particularly those aged 0–3 years, and the proportion of individuals with these visits seemed to decline with increasing age (Fig. 2). Among individuals who had one or more OP visits with PA-related diagnostic procedures, the most prevalent PA-related diagnostic procedures were skin-prick tests (68.9%), followed by IgE tests (48.6%) and ingestion challenge tests (9.3%; individuals may have had one or more PA-related diagnostic procedures in a given year).

With regard to EAI prescriptions, 50.6% of the individuals with PA had two or more EAIs PPY (one or more prescription fills) and, among these, 10.7% had six or more EAIs PPY (three or more prescription fills) (Fig. 3). Younger individuals were observed to have more prescriptions filled for EAIs, particularly those aged 4–11 years, with a peak at ages 6–7 years, followed by a decline, with the lowest levels among those aged ≥ 18 years. The proportion of individuals with six or more EAIs PPY (three or more prescription fills) was also observed to be the highest among individuals aged 4–7 years. Furthermore, 26.9% of the individuals with PA had two or more EAIs PPY and one or more OP visits with a PA-related diagnosis or diagnostic procedure during the same year.

At the patient-year level, 2.4% of the individuals with PA had one or more IP or ED visits with a PA-related diagnosis PPY (Fig. 3). The proportion of individuals with one or more IP or ED visits with a PA-related diagnosis was observed to be the lowest among

Table 1 Characteristics of individuals with PA

	Overall Patients (N = 14,136)	Overall Patient- Years (N = 86,483)
Age, mean $\pm$ SD (median), y	6.75 $\pm$ 11.37 (3)	11.36 $\pm$ 13.38 (7)
0–3, n (%)	8358 (59.1)	24,342 (28.1)
4–11, n (%)	3682 (26.0)	37,732 (43.6)
4–5	1360 (9.6)	11,667 (13.5)
6–7	1010 (7.1)	10,416 (12.0)
8–11	1312 (9.3)	15,649 (18.1)
12–17, n (%)	734 (5.2)	11,866 (13.7)
≥ 18 , n (%)	1362 (9.6)	12,543 (14.5)
18–30	519 (3.7)	4831 (5.6)
≥ 31	843 (6.0)	7712 (8.9)
Males, n (%)	8263 (58.5)	50,049 (57.9)
Region of residence, n (%)		
Northeast	4693 (33.2)	29,040 (33.6)
Midwest	2900 (20.5)	17,678 (20.4)
South	3492 (24.7)	22,293 (25.8)
West	2562 (18.1)	13,976 (16.2)
Health plan type with > 10% prevalence, n (%)		
HMO	1804 (12.8)	10,180 (11.8)
PPO	7633 (54.0)	50,077 (57.9)
POS	2702 (19.1)	15,213 (17.6)
Comorbidities frequently associated with PA, n (%)		
Asthma	6919 (48.9)	47,702 (55.2)
Atopic dermatitis and/or eczema	7884 (55.8)	51,016 (59.0)
≥ 1 specified food allergy (other than peanut)	6007 (42.5)	37,439 (43.3)
≥ 2 specified food allergy (other than peanut)	1131 (8.0)	6873 (7.9)
Allergic rhinitis	8954 (63.3)	62,529 (72.3)
Depression	1726 (12.2)	14,806 (17.1)
Anxiety	1410 (10.0)	11,840 (13.7)
No. comorbidities associated with PA, mean $\pm$ SD (median)	2.33 $\pm$ 1.30 (2)	2.61 $\pm$ 1.32 (3)
No. comorbidities associated with PA (excluding depression and anxiety), mean $\pm$ SD (median)	2.11 $\pm$ 1.15 (2)	2.30 $\pm$ 1.14 (2)

PA = Peanut allergy; SD = standard deviation; HMO = health maintenance organization; PPO = preferred provider organization; POS = point of service.

individuals aged 4–11 years and highest among those aged ≥ 18 years. Furthermore, 42.5% of individuals with one or more IP and/or ED visits also had OP visits related to PA management during the same year, and 70.0% of these individuals with one or more IP and/or ED visits also had prescriptions filled for EAIs during the year.

Direct Health-Care Costs

Individuals with PA incurred mean $\pm$ standard deviation (SD) direct all-cause health-care costs of \$3084 $\pm$ \$14,435 PPY during the study period (Table 2). After stratifying for high PA-related HRU on an annual basis, individuals with two or more OP visits and those with three or more OP visits with a PA-related diagnosis incurred mean $\pm$ SD costs of \$3349 $\pm$ \$10,051 and \$3849 $\pm$ \$8902

PPY, respectively. Individuals with one or more OP visits with PA-related diagnostic procedures incurred mean $\pm$ SD costs of \$3633 $\pm$ \$13,296 PPY; whereas those with four or more EAIs and those with six or more EAIs (two or more or three or more prescription fills, respectively) had mean $\pm$ SD costs of \$3175 $\pm$ \$10,677 and \$3408 $\pm$ \$10,688 PPY, respectively. Also, individuals with one or more IP and/or ED visits with a PA-related diagnosis incurred mean $\pm$ SD costs of \$8902 $\pm$ \$40,590 PPY, driven by those with one or more IP admissions, at \$17,451 $\pm$ \$38,242 PPY.

Risk Factors for Reactions to Peanut that Result in IP and/or ED Visits

A subgroup of 10,959 individuals with PA, which represented 55,193 patient-years, were included in the

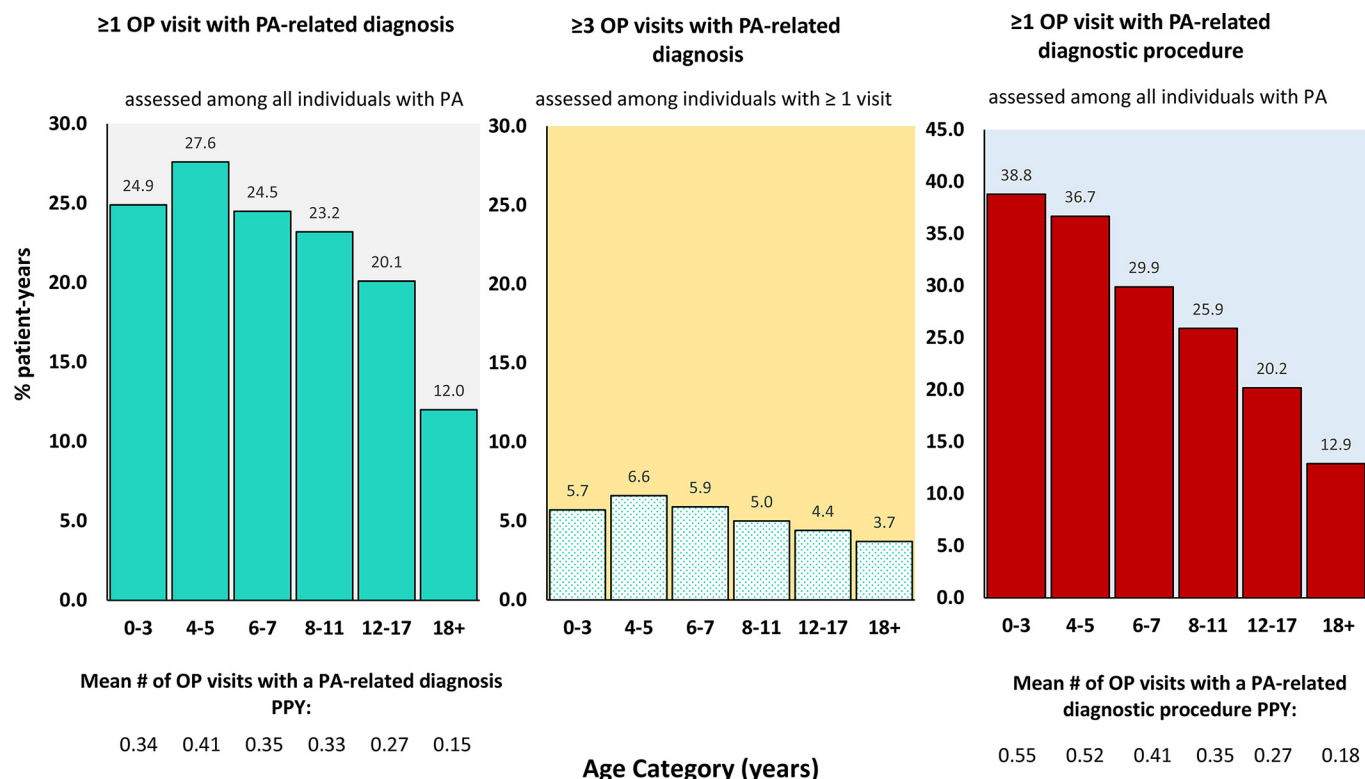


Figure 2. PA-related HRU in an OP setting PPY stratified by age group (note: The proportion of individuals with one or more visits was assessed among all the individuals with PA; the proportion of the individuals with three or more visits was assessed among the individuals with one or more visits). PA = Peanut allergy; HRU = health-care resource utilization; OP = outpatient; PPY = per patient-year.

analysis to identify risk factors associated with reactions to peanut that resulted in IP and/or ED visits. Among these individuals, patient characteristics were similar to those reported for the overall sample of individuals with PA (Supplemental Table S2), and a total of 1243 reactions to peanut were observed in an IP and/or ED setting. Risk factors associated with increased odds of reacting to peanut included age (adults, particularly young adults aged 18–30 years [OR 3.19 {95% CI, 2.66–3.83}]; adolescents aged 12–17 years [OR 1.65 {95% CI, 1.41–1.93}]; toddlers aged 2–3 years [OR 1.68 {95% CI, 1.42–1.98}]; reference, ages 4–11 years), reaction(s) to peanut observed during the previous year (OR 1.66 [95% CI, 1.23–2.24]; reference, no such reaction), asthma (OR 1.33 [95% CI, 1.18–1.51]; reference, no asthma), and male sex (OR 1.14 [95% CI, 1.01–1.28]; reference, female) (all $p < 0.05$) (Table 3). Having a diagnostic procedure for PA during the previous year was associated with decreased odds of reacting to peanut (OR 0.82 [95% CI, 0.71–0.95]; reference, no diagnostic procedure) ($p = 0.008$) (Table 3).

DISCUSSION

This retrospective claims-based study demonstrated the significant HRU associated with PA across all age groups (0–3, 4–11, 12–17, and ≥ 18 years). The highest

HRU was observed among individuals aged 4–11 years, with a peak at ages 4–7 years, a period when children are being integrated into school and are developing the knowledge and skills needed to reduce their exposure risk without the supervision of their caregivers. Up to 18% of children have experienced a food allergic reaction in the school setting.^{18,20} Although individuals with PA had IP admissions and ED visits related to PA in the present study, medical service utilization was mainly driven by frequent OP visits. This high resource use in an OP setting at a younger age may suggest that caregivers are seeking management for PA in preparation for transition into the school setting, such as the development of a personalized emergency action plan with health-care professionals (e.g., pediatrician, allergist) in case of accidental allergen exposure at school.²⁰

The high HRU reported in the current study translated to mean direct all-cause health-care costs of \$3084 PPY during the study period. Two recent studies also evaluated HRU and direct health-care costs associated with PA^{21,22}; however, differences in study design and patient selection prevent direct comparisons with the current analysis. In a study of commercially insured patients with PA diagnoses, Shaker *et al.*²² reported annual direct costs of \$6436 (2016 USD). These higher costs may be due to their study period, which was

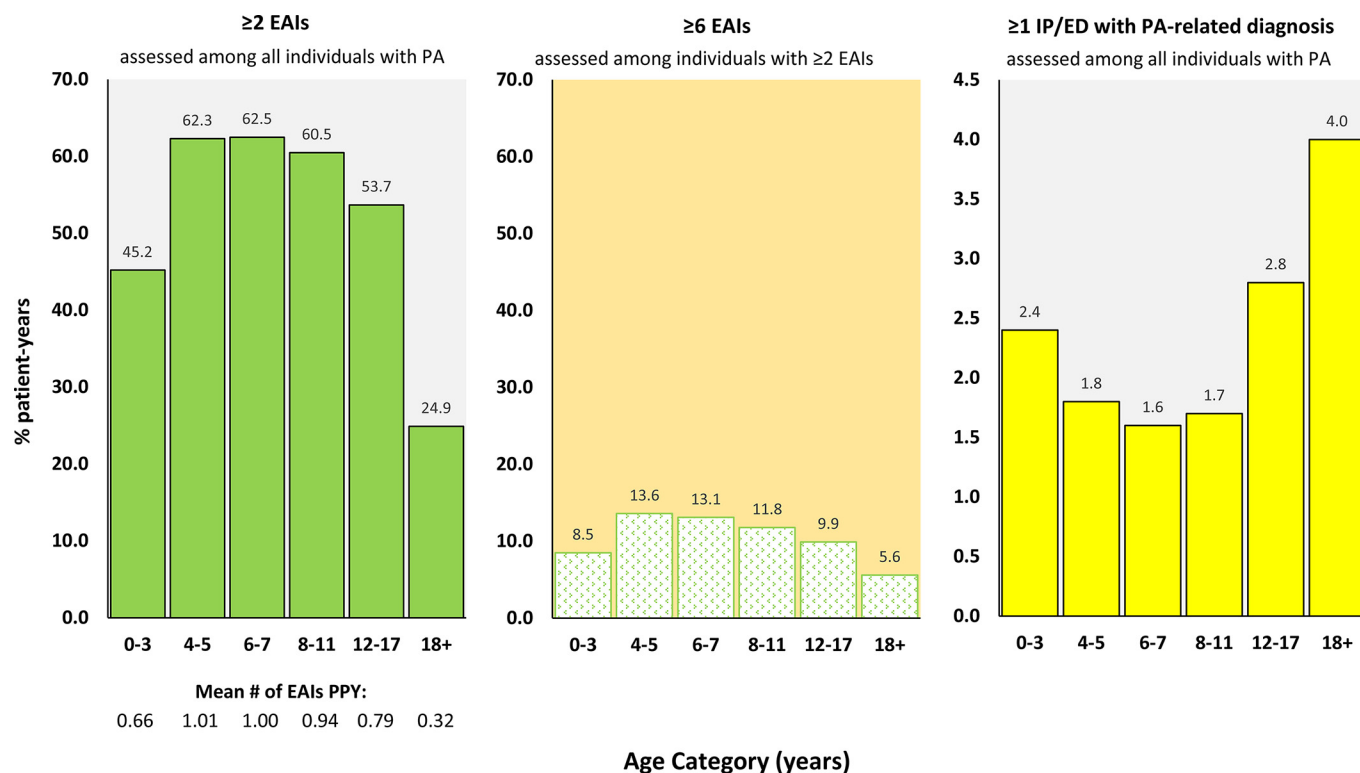


Figure 3. HRU related to management of reactions to peanut PPY stratified by age group (note: An EAI prescription fill is supplied in a two-pack carton. The proportion of individuals with two or more EAIs was assessed among all individuals with PA; the proportion of individuals with six or more EAIs was assessed among individuals with two or more EAIs). HRU = Health-care resource utilization; PPY = per patient-year; EAI = epinephrine autoinjector; PA = peanut allergy; ED = emergency department; OP = outpatient.

restricted to the first year after first observed medical claims with a diagnosis code of PA or PA-related anaphylactic reactions, and their inclusion of patient out-of-pocket costs. Similarly, Blaiss *et al.*²¹ estimated the costs of pediatric patients with evidence of reactions to peanut in the commercially insured and Medicaid-insured pediatric population at \$4336 PPY and \$6239 PPY (2017 USD), respectively. These estimated costs were also higher than those of the current study, likely because patients included in the study by Blaiss *et al.*²¹ were required to have evidence of reactions to peanut (*i.e.*, with potentially more severe PA). Of note, the variability in costs reported in the literature reflects the highly heterogeneous levels of HRU among individuals with PA, further corroborated by the different rates of OP, IP, and ED visits observed in the current study. Nevertheless, both Shaker *et al.*²² and Blaiss *et al.*²¹ support the current findings that management of PA was associated with substantial direct health-care costs.

In the literature, the rate of ED visits for food-related anaphylaxis has been shown to be increasing,^{23,24} and the true frequency may be underestimated.²⁵ The current study likely underestimated the proportion of events PPY, with a total of 2043 reactions (2.4% PPY) observed during IP and/or ED visits. Underreporting of these allergic reactions may be due to the selection

of other causes of respiratory failure or hypotension by physicians as opposed to selecting diagnosis codes for anaphylactic reaction due to peanuts in the ED setting^{26,27} or that the trigger was unidentified at the time of the reaction.^{24,27} In addition, caregivers may not recognize the allergic reaction because children, particularly infants, may not be able to verbalize the associated symptoms, such as rash, vomiting, diarrhea, or abdominal pain.^{24,28,29} Moreover, it is strongly advised that individuals who experience an anaphylactic reaction are monitored in the ED until symptoms have fully resolved.^{26,30,31} In this study, we may have captured more severe reactions (*e.g.*, those with upper airway obstruction) because milder reactions may have resolved shortly after allergen exposure, with or without treatment, and these individuals may not have received ED monitoring.^{28,31} Despite the potential underestimation of ED visits, individuals with one or more reactions that result in an IP or ED visit had the highest direct all-cause health-care costs in the present study, with a mean of \$8902 PPY. This finding was consistent with the literature, with IP admissions and ED visits previously identified as major components of medical costs associated with food allergy.^{14,32}

Reactions to peanut that result in hospitalization may be precipitated by certain risk factors.¹⁹ The

Table 2 Direct annual all-cause health-care costs of individuals with PA (N = 86,483 patient-years)

	Total Costs (2019 U.S. dollars), PPY	
	Mean $\pm$ SD	Median
Overall (patient-years)	\$3084 $\pm$ \$14,435	\$896
Age as of patient-year start		
0–3 y	\$3692 $\pm$ \$17,349	\$1400
4–11 y	\$1968 $\pm$ \$8,082	\$657
12–17 y	\$2850 $\pm$ \$13,109	\$811
≥ 18 y	\$5485 $\pm$ \$21,982	\$1223
OP visits with a PA-related diagnosis		
0–1	\$3070 $\pm$ \$14,634	\$865
≥ 2	\$3349 $\pm$ \$10,051	\$1447
≥ 3	\$3849 $\pm$ \$8,902	\$1821
OP visits with PA-related diagnostic procedures		
0	\$2862 $\pm$ \$14,865	\$681
≥ 1	\$3633 $\pm$ \$13,296	\$1447
≥ 2	\$4312 $\pm$ \$10,768	\$1932
EAI filled		
0	\$3241 $\pm$ \$16,698	\$731
≥ 2	\$2931 $\pm$ \$11,810	\$1036
≥ 4	\$3175 $\pm$ \$10,677	\$1176
≥ 6	\$3408 $\pm$ \$10,688	\$1291
IP and/or ED visit with a PA-related diagnosis		
0 IP and/or ED visit	\$2944 $\pm$ \$13,142	\$867
≥ 1 IP and/or ED visit	\$8902 $\pm$ \$40,590	\$3202
≥ 1 IP admission	\$17,451 $\pm$ \$38,242	\$7812

PA = Peanut allergy; PPY = per patient-year; SD = standard deviation; OP = outpatient; EAI = epinephrine autoinjector; IP = inpatient; ED = emergency department.

present study identified age ≥ 18 years as the most significant risk factor for the development of reactions to peanut that result in IP and/or ED visits, particularly among young adults aged 18–30 years. This finding may be related to lower rates of EAI prescription fills and PA-related OP visits among this age group, potentially interpreted as evidence of less active and routine PA management. Adolescence and young adult age have previously been identified as a risk factor for food allergic reactions in general because of decreased parental oversight and increased independence associated with older age.^{19,33,34} Adolescents and young adults may be more willing to engage in risk-taking behavior, such as purposefully ingesting potentially unsafe food or not carrying an EAI at all times.³⁴ In addition, adults tend to have more severe symptoms than children during allergic reactions, such as hypotension and respiratory distress.³⁵ Accordingly, up to 90% of anaphylactic deaths occur in adolescents and adults.^{33,36} The current findings supported the need for more patient education about preventative strategies as early as in childhood to mitigate these negative outcomes in adolescence and adulthood.

In addition to age, reaction(s) to peanut observed in the previous year and comorbid asthma were also identified as risk factors for reactions to peanut that result in IP and/or ED visits. The latter finding was consistent with the literature, with 85–96% of fatal food anaphylaxis events occurring in people with asthma.^{19,37} Of note, male sex was also found to increase the odds of IP and/or ED visits for reaction to peanut, which may be explained by the tendency for men to use less preventative health-care services,^{38,39} e.g., OP visits, to actively manage PA and/or obtain an EAI prescription fill. Indeed, active management, including periodic diagnostic testing for PA when appropriate, may be more beneficial in preventing the occurrence of anaphylaxis, as evidenced by the reduced odds of IP and/or ED visits for reaction to peanut observed in the current study. Taken together, these factors should be considered during the treatment decision-making process, especially for individuals with severe reactions who may be high users of costly health-care services. With the new availability of prophylactic treatment for PA, it is now more important than ever for patients to participate in shared

Table 3 Risk factors associated with reactions to peanut that resulted in IP and/or ED visits (N = 55,193 patient-years)

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p
Demographic characteristics			
Age as of patient-year start			
2–3 y	1.653 (1.40–1.95)*	1.676 (1.42–1.98)	<0.001*
4–11 y (reference)	—	—	—
12–17 y	1.731 (1.48–2.03)	1.648 (1.41–1.93)	<0.001*
18–30 y	3.454 (2.81–4.24)*	3.190 (2.66–3.83)	<0.001*
≥31 y	1.826 (1.51–2.22)*	1.815 (1.49–2.21)	<0.001*
Male vs female (reference, female)	1.072 (0.95–1.21)	1.135 (1.01–1.28)	0.032*
Region of residence			
Northeast (reference)	—	—	—
Midwest	1.021 (0.86–1.21)	1.000 (0.84–1.18)	0.999
South	1.195 (1.03–1.39)*	1.231 (1.06–1.43)	0.007*
West	1.334 (1.12–1.58)*	1.339 (1.13–1.59)	<0.001*
No U.S. census region	1.092 (0.82–1.46)	1.081 (0.81–1.44)	0.592
Health plan type			
PPO (reference)	—	—	—
HMO	0.629 (0.51–0.78)*	0.650 (0.53–0.80)	<0.001*
POS	0.753 (0.63–0.89)*	0.762 (0.64–0.90)	0.002*
Other	0.897 (0.75–1.07)	0.836 (0.70–0.99)	0.047*
Patients who experienced comorbidities frequently associated with PA			
Asthma (anytime) vs not	1.168 (1.04–1.32)*	1.331 (1.18–1.51)	<0.001*
Atopic dermatitis and/or eczema (anytime) vs not	0.915 (0.81–1.03)	1.063 (0.94–1.20)	0.319
≥2 specified food allergy other than peanut (anytime) vs not	0.671 (0.52–0.86)*	0.755 (0.59–0.97)	0.028*
Allergic rhinitis (anytime) vs not	0.702 (0.62–0.80)*	0.674 (0.59–0.77)	<0.001*
Had historic event during the previous year	1.908 (1.32–2.75)*	1.657 (1.23–2.24)	<0.001*
Diagnostic procedure for PA during the previous year	0.756 (0.66–0.87)*	0.820 (0.71–0.95)	0.008*
EAI during the previous year	0.938 (0.88–1.00)	1.026 (0.96–1.09)	0.424

IP = Inpatient; ED = emergency department; OR = odds ratio; CI = confidence interval; PPO = preferred provider organization; HMO = health maintenance organization; POS = point of service; PA = peanut allergy; EAI = epinephrine autoinjector. *p < 0.05.

decision-making with physicians with regard to their treatment options, especially when considering the presence of any risk factors and patients' comorbidity profiles.

Notably, filling of a previous prescription for EAI did not have a statistical impact on the occurrence of reactions observed in an IP or ED setting. This seemingly contradictory finding may suggest that the number of prescribed EAI reflected something other than an increased risk of anaphylaxis, such as shared parenting in multiple households or parental insistence. Therefore, an additional prescription filled for EAI may not reduce costly HRU that results from reactions to peanut. In addition, having a diagnosis for allergic rhinitis or a specified food allergy other than peanut in medical claims was also associated with counterintuitive findings of decreased risk of reaction. This

observation may be explained by real-world coding practices, in which health-care providers may prioritize the reporting of the PA-related diagnosis in claim forms instead of consistently reporting these associated conditions when providing medical services in any setting to patients with PA-related comorbidities, thus not coding the comorbid conditions during medical visits for PA.

Limitations

There are limitations associated with this study. Because the study sample only included privately insured individuals, generalizability to the overall U.S. population may be limited. For instance, Medicaid beneficiaries or uninsured individuals were not included in this study; therefore, the analysis was specific to those with a commercial health plan. Practice of strict

peanut avoidance by individuals was assumed when considering that there were no FDA-approved preventative treatment options available at the time the study was conducted. Indicators of PA management were identified based on HRU with PA-related codes in the claims data. Because claims data bases contain diagnosis and procedure codes that are recorded for reimbursement purposes, the data may be subject to coding errors or data omissions. However, the HRU and direct health-care costs of individuals with PA can only be comprehensively quantified by using claims data bases. For example, ICD-9-CM code V15.01 and ICD-10-CM code Z91.010, both for allergy to peanut, observed in the claims data base were used to identify patients with PA and PA-related HRU throughout the time frame of the study to capture cases and events that might otherwise be missed. In addition, a filled prescription does not necessarily indicate its use, and most prescriptions filled for EAIIs to maintain the recommended stock are likely unused and discarded after their expiration.⁴⁰ Individuals with PA may also have other food allergies, and laboratory test results from diagnostic tests were not available. However, peanut is the most prevalent food allergy, which thereby likely represents the majority of medical service use for PA. Also, indirect costs associated with PA were not evaluated in this study.

CONCLUSION

Until recently, strict allergen avoidance alone was considered the only FDA-approved option available for the mitigation of allergic reactions for individuals with PA. The current study demonstrated that this approach was associated with significant HRU across all age groups examined in this study. However, PA-related HRU varied among the commercially insured population in the United States, with a subset of younger individuals seeking more frequent services in an OP setting and a peak of PA-related OP utilization observed at preschool and school age. Adults required more services in an IP or ED setting, particularly during young adulthood. Those with intensive HRU, particularly IP admissions, accrued substantial health-care costs related to evidence of PA management in HRU. Accordingly, there are significant unmet treatment needs particularly related to PA management in HRU for individuals with PA. Indeed, practice of peanut avoidance alone is not sufficient to prevent reactions to peanut. Individuals with previous reaction(s) to peanut or comorbid asthma, as well as male individuals, were observed to have a higher risk of reactions to peanut that resulted in IP and/or ED visits in this study. These factors should be considered in the management of PA and eventually in the treatment decision-making process by health-care professionals.

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