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Commercial Claims Costs Related to Healthcare Resource Use Associated With a Diagnosis of Peanut Allergy

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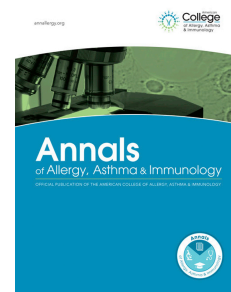
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Commercial Claims Costs Related to Healthcare Resource Use Associated With a Diagnosis of Peanut Allergy

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[footnote]

Anna Vlahiotis was an employee of IBM Watson Health at the time of the study.

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Conflict of Interest

MS is a member of the Joint Taskforce on Allergy Practice Parameters and a member of the Editorial Boards of the *Annals of Allergy, Asthma, & Immunology* and the *Journal of Food Allergy*; has a family member who is CEO of Altrix Medical. JMC, TK, and TDG are employed by DBV Technologies. OT is and AV was employed by IBM Watson Health as consultants and received funding from DBV Technologies to conduct this study (AV is no longer employed at IBM Watson Health). HS is a paid consultant of DBV Technologies. MG is supported by grant #5K08HS024599-02 from the Agency for Healthcare Research and Quality; is an expert panel and coordinating committee member of the NIAID-sponsored Guidelines for Peanut Allergy Prevention; has served as a consultant for the Canadian Transportation Agency, Thermo Fisher, Intrommune, and Aimmune Therapeutics; is a member of physician/medical advisory boards for Aimmune Therapeutics, DBV Technologies, Sanofi/Genzyme, Glaxo Smith Kline, Genentech, Nutricia, Kaléo Pharmaceutical, Nestlé, Acquestive, Allergy Therapeutics, Allergenics, Aravax, Prota, and Monsanto; is a member of the scientific advisory council for the National Peanut Board; has received honorarium for lectures from Thermo Fisher, Aimmune Therapeutics, DBV Technologies, Before Brands, multiple state allergy societies, the American College of Allergy Asthma and Immunology, the European Academy of Allergy and Clinical Immunology; is an

associate editor for the *Annals of Allergy, Asthma & Immunology*; and is a member of the Joint Taskforce on Allergy Practice Parameters. This research was presented in part at ISPOR 2019 in New Orleans, LA, and the ACAAI 2019 in Houston, TX.

Keywords: Peanut allergy; anaphylaxis; healthcare resource utilization; healthcare costs; treatment patterns; allergic comorbidity; hospitalization; emergency department

List of abbreviations/acronyms: CM, Clinical Modification; ED, emergency department; HCRU, healthcare resource utilization; HIPAA, Health Insurance Portability and Accountability Act; HRQOL, health-related quality of life; ICD, International Classification of Diseases; IM, intramuscular; IV, intravenous; PA, peanut allergy; SD, standard deviation.

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Author Contributions:

Oth Tran, MA and Anna Vlahiotis, MA were responsible for the data acquisition from the IBM MarketScan Commercial Claims and Encounters Database and statistical analysis of the primary data. All authors (1) made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; (2) drafted the article or reviewed it critically for important intellectual content; (3) have given final approval of the version to be published; and (4) agree to be accountable for all aspects of the work related to its accuracy or integrity.

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Background: Peanut allergy (PA) affects ~1.6 million US children. The current standard of care is strict avoidance and prompt reaction treatment. PA healthcare costs and healthcare resource utilization (HCRU) are poorly understood.

Objective: To estimate PA healthcare costs and HCRU using a nationally representative commercial payer database.

Methods: The IBM MarketScan[®] Commercial Claims and Encounters Database was examined for PA diagnosis/reaction codes between January 2011 and October 2015 in patients ≤64 years, with age cohort-matched controls. Outcomes were measured 12 months before and after the first claim date. Healthcare costs and HCRU were compared using Student's t-tests and chi-square tests.

Results: Patients with a PA-related diagnostic code (n=41,675) incurred almost double all-cause healthcare costs versus controls (\$6436 vs \$3493, $P < 0.001$), mainly from inpatient and outpatient medical costs (\$5002 vs \$2832, $P < 0.001$). Over 1/3 of the PA group patients (36%) had a code indicative of an anaphylactic reaction during follow-up. Mean PA or reaction-related code costs per visit totaled \$7921 for hospitalizations and \$1115 for emergency department (ED) visits. Costs were 30% lower in patients with asthma codes without PA codes versus those with both codes (\$5678 vs \$8112, $P < 0.001$); all-cause ED costs were more than double in patients with atopic dermatitis codes with PA codes versus those without PA codes (\$654 vs \$308, $P < 0.001$).

Conclusion: National commercial payer claims data indicate a significant healthcare burden associated with a PA-related code, including over \$6400/patient in annual allcause costs and increased healthcare utilization.

1 Introduction

2 Peanut allergy (PA) is a common pediatric food allergy, with an estimated US prevalence
3 between 1.4% and 4.6%, depending on the methodology used for assessment.^{1,2} This estimated
4 prevalence has increased more than 4-fold since 1997.^{2,3} PA is often a lifelong allergy, outgrown
5 in only approximately 22%–31% of children,⁴ and due to this persistence, at least 1.8% of US
6 adults report having PA.⁵ Food allergy is a leading cause of anaphylaxis among both children
7 and adults.^{6,7} PA, in particular, is a source of significant morbidity, with reaction severity poorly
8 predicted.⁸⁻¹⁰ Recent estimates indicate that 42% of children and ~51% of adults with food
9 allergy report suffering at least one severe reaction in their lifetime, leading to significant
10 emergency and advance care costs and utilization.^{5,9,10} While food allergy-related fatality is rare
11 (1–2 cases per million person-years), the available data suggest that PA is a leading cause of
12 food allergy-related fatality among teenagers and young adults.^{7,11,12} In addition, PA is associated
13 with reduced health-related quality of life (HRQOL), high anxiety, poor self-efficacy, and poor
14 coping/adaptation among both affected individuals and their caregivers.¹³⁻¹⁵

15 New paradigms of food introduction are expected to prevent many (but not all) cases of PA
16 through the early introduction of peanut in the first year of life.¹⁶⁻²¹ In addition, novel
17 immunotherapies may increase reaction thresholds or eliciting doses in patients with PA by
18 gradual desensitization,^{22,23} which can potentially augment the current standard of care of strict
19 peanut avoidance.²⁴⁻²⁷ However, while treatment options are emerging, these are limited by the
20 lack of long-term safety and efficacy data to understand the long-term effects such treatment
21 options may have, as well as how treatment may impact future healthcare resource utilization
22 (HCRU).^{26,27}

There are limited data available that detail the health and economic burdens that food allergy may place on the healthcare system, including costs of HCRU.²⁸⁻³⁰ One large study from 2013 estimated food allergy had a societal cost of \$24.8 billion (\$4184/affected individual), most of which stemmed from indirect as opposed to direct medical costs, and indicated that these cost burdens were not experienced equally along racial/ethnic and socioeconomic demographics.²⁹ This analysis did not partition costs for individual allergens. However, a more recent white paper analysis by FAIR Health, Inc. explored private insurer claims data for all food allergens, noting significant increases in food allergy-related claims (including claims for anaphylaxis from foods), but this analysis was largely descriptive of the increasing trends, contained minimal data on costs and disposition of costs, and did not focus on cost differentials for any particular allergy type related to specific patterns of HCRU.²⁸

A contemporary understanding of the HCRU burden of PA is needed to clarify areas where future prevention and treatment options could be of maximal benefit. While recent cost-effectiveness analyses have created a better understanding of critical levers to optimize health and economic benefits of both PA prevention through early introduction and treatment through peanut immunotherapies, evidence suggests that the burden of PA will remain significant from a societal perspective.^{26,27} This study was therefore undertaken to examine baseline patterns of HCRU in PA, including determination of the overall burden of illness, treatment patterns, and incremental healthcare costs among patients with PA across different ages, using a nationally representative commercial payer database.

Methods

Data source

This is an observational retrospective cohort analysis using de-identified US administrative claims data for the period from January 1, 2010, through October 31, 2016, obtained from the IBM MarketScan Commercial Claims and Encounters Database.³¹ This claims database contains the inpatient, outpatient, and outpatient prescription drug experience of approximately 135 million employees and their dependents, covered under a variety of fee-for-service and managed care health plans, including exclusive provider organizations, preferred provider organizations, point of service plans, indemnity plans, and health maintenance organizations, including approximately 24.4 million lives in 2016. The database also provides detailed cost (paid amounts, not just payment claims), utilization, and outcomes data for healthcare services performed in both inpatient and outpatient settings. The medical claims are linked to outpatient prescription drug claims and person-level enrollment data using unique enrollee identifiers. All study data were obtained using International Classification of Diseases, 9th and 10th Revisions, Clinical Modification (ICD-9-CM and ICD-10-CM) codes, Current Procedural Terminology, 4th edition codes, Healthcare Common Procedure Coding System codes, and National Drug Codes.

Patient selection and cohort assignment

Cases: Individuals with ≥ 1 inpatient (in the primary position) or outpatient (in any position) medical claim with a diagnosis of PA or PA-related anaphylactic reaction (ICD-9-CM codes: V15.01 and 995.61; ICD-10-CM codes: Z91.010, T78.01XA, T78.01XD, and T78.01XS) were eligible for inclusion in the PA cohort (herein referred to as the PA group, specifically referencing someone with a diagnostic code for PA). The date of the first eligible claim was defined as the index date. Patients in the PA group were stratified into four age groups: 0–3 years

old (infant), 4–11 years old (child), 12–18 years old (adolescent/teen), and 19–64 years old (adult).

Controls: Individuals in the MarketScan database without a diagnosis code for PA or a PA-related anaphylactic reaction between January 1, 2010 and September 30, 2016 were eligible for inclusion in the control cohort. Index dates for controls were randomly assigned based on the index date distribution of the PA cases. Control patients were randomly selected from the subset of the eligible population (N=16,044,824) to assemble a population that was direct matched 1:1 to the PA group patients based on age group, gender, geographic region, index year, and insurance plan type.

Exclusion Criteria: All PA group and control patients were required to be ≤ 64 years old on the index date and be continuously enrolled in the MarketScan database with medical and pharmacy benefits for 12 months before (baseline) and 12 months after (follow-up) the index date. The presence or absence of additional food allergy, asthma, or other allergy diagnosis was not an exclusion criterion for the PA group.

Outcomes

Demographic characteristics, including age, sex, index year, geographic region, and insurance plan type were captured on the index date. Geographic regions were classified as Northeast, North Central, South, West, and unreported. Baseline clinical characteristics, including the number of unique medications and the number of unique diagnosis codes, were recorded for the baseline period. PA code-related treatment patterns were evaluated for the follow-up period and included physician office visits by specialty (eg, allergist, pediatrician, general practitioner) and services/medications (eg, epinephrine autoinjector, intramuscular (IM) and intravenous (IV))

corticosteroids, and use of a nebulizer). All-cause and PA code-related HCRU and costs, including inpatient, outpatient (ED visits, ambulance services, urgent care facility visits, physician office visits, and other outpatient services), and outpatient pharmacy services, were documented for the 12-month follow-up period. All-cause utilization included any inpatient admission, ED visit, office visit, other outpatient services, and outpatient prescriptions. PA code-related costs and utilizations were specifically defined as a PA or PA-reaction diagnosis in a primary position for inpatient claims and any position for outpatient claims and office administered medications, including epinephrine or injectable (IM and IV) steroids for outpatient claims. Pharmacy claims accompanying a PA diagnostic code included antihistamines, corticosteroids, mast cell stabilizers, leukotriene receptor inhibitors, nasal anticholinergics, decongestants, and immunomodulators.

Costs represent the paid amounts of fully adjudicated claims, including insurer and health plan payments as well as patient cost-sharing in the form of copayment, deductible, and coinsurance. All costs are reported as per-person per-year and were adjusted to 2016 US dollars using the medical care component of the Consumer Price Index.³²

Analyses

Mean and standard deviation (SD) were reported for continuous variables, and statistical significance was determined using paired t-tests. Frequencies and percentages were reported for categorical variables, and statistical significance was determined using McNemar's test. Trends were explored across prespecified age stratifications for sensitivity analyses. In the matched cohort analysis, standardized differences were reported to examine the balance among the matched factors, with a difference of <0.1 considered acceptable. The alpha level for all

statistical tests was 0.05. All data analyses were conducted using SAS version 9.4 (SAS Inc., Cary, NC).

Approval

All study data were accessed with protocols compliant with US patient confidentiality requirements, including the Health Insurance Portability and Accountability Act of 1996 regulations (HIPAA). Because all databases used in the study were fully de-identified before analysis and HIPAA compliant, and because the study did not involve the collection, use, or transmittal of individually identifiable data, this study was not considered as human subjects research and did not require institutional review board review and approval.

Results

Demographics

Of the 109,596 patients in the MarketScan Commercial database between January 1, 2010 and September 30, 2016 with a diagnostic code for PA (e.g., the PA group, as described in the methods), there were 41,744 patients who met all the inclusion criteria (Figure 1). The index event for 69% of patients (n=28,787) was a specific claim of PA diagnosis, while the index event for the remaining 31% of patients (n=12,957) was a diagnosis claim of an anaphylactic reaction to peanut. There were 16,044,824 patients meeting all inclusion criteria for the control group, from which 1,222,108 patients were randomly selected to be matched 1:1 to the PA group for a final enrollment of 41,675 control patients. Patients with a PA code who could not be directly matched to a control (n=69) were excluded from the analysis, for a total of 41,675 patients in the PA group.

The mean age of all patients in the PA group was 10.5 years old, the largest proportion between ages 4 and 11 years (44%), 57.9% were male, and 31% were from the South geographic region. Table 1 details the baseline differences between groups along year of index claim, insurance type, claim numbers, and total costs. Individuals in the PA group had a significantly higher frequency of multiple atopic comorbidities, including asthma (35.6% vs 0.2%, $P<0.001$), atopic dermatitis (16% vs 0.4%, $P<0.001$), and allergic rhinitis (43.1% vs 6%, $P<0.001$). PA group patients had a higher mean number of 3-digit ICD9/10 code diagnoses than matched controls (7.9 vs 6.2 codes, $P<0.001$).

Utilization

Routine and Emergency Services

During the 12-month follow-up period, 58.5% of the PA group versus 6.5% of controls ($P<0.001$) had ≥ 1 allergist visit (Table 2). The mean number of unique days in a year with an allergist visit in the PA group was 2.1. Similarly, a significantly higher proportion of children up to age 18 years in the PA group had a pediatrician visit, and there was a significantly higher mean number of pediatrician visits compared with matched controls (Table 2). Additionally, significantly more individuals in the PA group had more all-cause physician office visits (98.8% vs 89.4%, $P<0.001$), ED visits (32.8% vs 19.6%, $P<0.001$), ambulance services (7.6% vs 3.7%, $P<0.001$), urgent care visits (7.7% vs 6.2%, $P<0.001$), and inpatient admissions (4.7% vs 2.1%, $P<0.001$) than the matched controls (Table 3, eFigure 1). As a marker of the potential severity of the underlying PA among those in the PA group, during the 12-month follow-up period, 36.0% of all PA group patients had a claim for an anaphylactic reaction, and 14.3% had an ED visit related to PA (Figure 2).

Medications

PA group patients filled a mean 5.0 unique medications (vs 3.4 in controls) and had 7.9 unique medical diagnoses (vs 6.2 in controls) during the baseline period when evaluated by National Drug Code (NDC) (Table 1). During the 12-month period, 4.5% vs 2.8% of PA group used a nebulizer ($P<0.001$) and 6.3% vs 2.6% ($P<0.001$) had ≥ 1 claim for an injectable steroid medication compared with controls, although these are related to all-cause claims and not specifically to PA. On average, PA group patients who utilized epinephrine had claims for 1.5 epinephrine autoinjector products during the follow-up period (Table 2). Notably, 34.8% of the PA group patients did not fill an autoinjector prescription.

Healthcare costs

Total mean per-patient annual all-cause healthcare costs among the PA group were \$6436 compared with \$3493 in controls ($P<0.001$) (Table 3, eFigure 1). This was driven by medical costs (\$5002 in the PA group vs \$2832 in controls, $P<0.001$). The mean costs of a PA-related hospitalization and ED visit in the PA group patients were \$7921 and \$1115. Among patients with ≥ 1 claim, the mean cost of a PA-related ambulance service, urgent care service, or physician office visit was \$784, \$78 or \$134, respectively. Total mean, annual direct PA-related healthcare costs (including inpatient, outpatient, and pharmacy) for the PA group were \$1490 per patient. Control patients spent an average of \$159 annually on outpatient pharmaceuticals, including epinephrine, antihistamines, corticosteroids, mast cell stabilizers, leukotriene inhibitors, nasal anticholinergics, decongestants, and immunomodulators. By comparison, PA group patients spent \$806 on pharmaceuticals, including an average of \$608 attributable to the cost of branded epinephrine devices.

Cost Variation

Costs were subject to variation based on selected subgroups. Patients with diagnostic codes for asthma in the PA group had significantly higher all-cause costs than PA group patients without asthma codes (\$8112 vs \$5678, $P<0.001$). Similarly, patients in the PA group who also had diagnostic codes for atopic dermatitis had significantly higher all-cause ED costs compared with controls (\$654 vs \$308, $P<0.001$). When specifically looking at costs among children ages 4–11 years and 12–18 years, similar trends were shown with significant cost differences noted between the PA and control groups (Table 3).

Discussion

Commercial claims data from a large national database suggest significant financial and HCRU burden associated with a diagnostic code for PA compared with matched controls without a PA diagnosis. These costs are significantly higher for inpatient services, outpatient services, emergency medical services (including transportation), and pharmacy services. As well, the overall visit frequency and proportion of subjects utilizing specific healthcare services are significantly greater among those in the PA group versus matched controls without PA codes. PA is differentiated from other food allergies because it is responsible for a larger proportion of food anaphylaxis and persistent adult food allergy. Therefore, understanding the unique patterns of services and costs potentially associated with PA is important in light of emerging PA treatment options, given peanut is the first allergen to be prioritized for FDA-approved treatments.^{27,33,34} Such therapies have been shown to have potential pathways to cost-effectiveness, so a better understanding of the specific PA health economics apart from other foods can enhance and underscore the health and economic impact of PA therapies.²⁷

It has been previously suggested in multiple large food allergy epidemiologic studies that a disproportionate percentage of individuals with PA have suffered a severe reaction, and our data highlight a similarly high occurrence of coding for severe reactions.^{9,35} However, our data also demonstrate a high service utilization rate for acute medical services, and denote the actual average cost per patient of such services associated with a PA diagnostic code compared with matched controls without a PA diagnostic code. These are novel data in that respect. On average in the 12-month analysis period, in a sample where approximately 36% experienced an anaphylactic reaction related to a PA code, having a PA diagnostic code was associated with costs of \$7921 per unique inpatient hospitalization, \$784 per unique ambulance services, and \$1115 per unique emergency department visit. Altogether, patients in the PA group had annual all-cause healthcare costs \$2943 higher than controls (45% of which was directly attributable to a PA diagnostic code). All these trends held constant across different ages, reflecting that PA diagnostic code is associated with higher costs.

Prior economic analysis has confirmed similar high direct and indirect medical costs associated with food allergies, but these are the first data to uniquely focus on actual commercial claims payments associated with PA codes specifically, and our findings are somewhat unique. While many similar trends are noted in comparison to prior data from Patel et al and Gupta et al, there are some surprising differences.^{29,30} Both Gupta et al and Patel et al, despite looking across all food allergens and not just PA, noted lower inpatient, office, ED, and ambulance related costs to our reported costs, comparatively. Of note, the Patel et al costs are approximately 12 years older than ours, and reflect a different payer subset. The Gupta et al data resulted from a nationally representative self-report survey where caregiver participants reported their estimated frequency of events comprising total direct and indirect (including opportunity) care related to food allergy,

which was then multiplied by the Patel et al cost basis and Medicare cost data (with post-stratification survey weights applied). These are also pre-2010 costs like Patel et al. Nonetheless, our data describe a unique and higher than expected (compared with the prior published data) cost-of-care estimate related to having a diagnosis of PA, and such data can greatly inform PA-specific cost-benefit modeling.

There have been limited previous data to help understand the yearly HCRU of a PA individual. While it is known that food-allergic patients commonly have other atopic comorbidities such as asthma, allergic rhinitis, and multiple food allergies, these data show a financial disparity between those with a PA diagnostic code and matched controls without PA in terms of basic service utilization such as pediatric and pediatric subspecialist care visits and outpatient pharmacy costs, with branded epinephrine device costs making up a large proportion of the cost difference between groups, even though 34.8% of patients in this study did not fill an autoinjector prescription, and 41.5% did not visit an allergy specialist during follow-up. Sensitivity analyses noted that these trends held when explored within age strata.

Our findings demonstrate that a significant minority of patients with a PA-related code do not fill prescriptions for epinephrine autoinjectors. This is consistent with a previous claims analysis, which found that 30.4% of patients did not fill an epinephrine autoinjector prescription and 60.2% did not visit an allergy specialist within a year of a food allergy-related ED visit for anaphylaxis.³⁶ Our study continues to highlight the urgent need to improve epinephrine autoinjector access (in this case, filling a prescription), echoing prior research that has clearly identified the need for improved self-injectable epinephrine carriage rates in food-allergic individuals.³⁷⁻⁵¹ It also implies that the total direct cost burden may be underestimated by patients not adhering to care recommendations.

There may be some already published solutions to help reduce some of the cost burden specifically related to PA care that this study identifies. Previous work has suggested that epinephrine pricing significantly exceeds a value-based threshold based on an outcome of reducing fatal anaphylaxis from peanut, that epinephrine has support to exist as a shared public resource, that fewer devices could be prescribed to individuals to stock schools in light of a universal stock epinephrine strategy at the school level (which could provide superior value for PA reactions), and that immediate emergency medical service activation upon use of epinephrine for a reaction to peanut is not cost-effective for patients with promptly resolved anaphylaxis.⁵²⁻⁵⁷

Limitations

The limitations of the study are like other retrospective studies using claims databases. First, claims data are subject to underreporting, data coding limitations, and data entry error. Second, this study was limited to individuals with commercial health coverage. Therefore, the results of this analysis may not be generalizable to patients with other insurance or without health insurance coverage, although commercial payers capture approximately 70% of the US population. Third, this analysis was limited to patients with 24 months of continuous enrollment, and the results may not be applicable to patients with less stable health insurance coverage. Fourth, while these data reflect actual costs (as opposed to claims, a significant strength) related to ICD9/10 codes for PA, this does not necessarily imply that every patient captured with these codes has a valid PA, and there is potential for misclassification where a peanut tolerant individual has been misdiagnosed as peanut allergic and is living a peanut-allergic lifestyle. This, however, is the major limitation related to any analysis of claims. Fifth, the costs being captured are not necessarily directly attributable to PA-related care, but rather are occurring in individuals with this coding in selected positions in the encounters. This is important because PA may

involve additional food allergies, asthma, and allergic comorbidities that could be directly attributable to some of these costs, although this is being compared with a matched control group without a PA diagnostic code to control for this possibility. Of note, these limitations were all encountered in the previous published economic analyses of the cost of food allergy care by Patel et al and Gupta et al and this situation with coding is not unique to food allergy.^{20,21} Sixth and lastly, while we comprehensively evaluated direct costs associated with a PA diagnosis, our analysis did not investigate indirect costs borne by patients and families living with PA.

While previous data have noted a significant healthcare service and cost of care related to food allergy, to our knowledge this is the first study to explore payments specifically associated with a PA diagnostic code using a large, robust commercial claims source as opposed to federal data. Patients with an ICD9/10 diagnostic code related to PA experience a significant burden of disease compared with age-matched controls without such a diagnostic code for inpatient, outpatient, emergency medical, and pharmacy costs. At over \$6400 per patient, the all-cause annual costs associated with a PA-related diagnostic code are nearly double those incurred by individuals without a PA-related diagnostic code. These costs of direct medical care exceed previously published estimates that were generic to all types of food allergy. As novel approaches to PA prevention and treatment become incorporated into standard practice, further research evaluating temporal trends in PA costs and utilization will be valuable to better understand future societal impacts and individual burdens of PA.

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Figure Legends

Figure 1. Patient Selection.

¹From a subset of 1,222,108 randomly selected eligible individuals without peanut allergy (PA), controls were matched 1:1 to patients with PA on age, sex, index year, geographic region, and insurance plan type.

Figure 2. Percentage of Peanut Allergy Patients With Peanut Allergy-Specific HCRU.

ED, emergency department; HCRU, healthcare resource utilization.

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1 **Table 1** Baseline Patient Characteristics

	Peanut Allergy		Control		
	N=41,675		N=41,675		
	N/Mean	%/SD	N/Mean	%/SD	Std. Diff.
Age (mean, SD)¹	10.5	11.6	10.5	11.6	0.00
Age (N,%)					
0–3	10,774	25.9%	10,774	25.9%	0.00
4–11	18,517	44.4%	18,517	44.4%	0.00
12–18	6992	16.8%	6992	16.8%	0.00
19–64	5392	12.9%	5392	12.9%	0.00
Sex (N, %)¹					
Male	24,149	57.9%	24,149	57.9%	0.00
Female	17,526	42.1%	17,526	42.1%	0.00
Geographic region (N, %)¹					
Northeast	11,306	27.1%	11,306	27.1%	0.00
North Central	8298	19.9%	8298	19.9%	0.00
South	12,837	30.8%	13,087	31.4%	1.30
West	8587	20.6%	8587	20.6%	0.00
Unknown	647	1.6%	397	1.0%	5.40
Insurance plan type (N, %)¹					
Comprehensive	391	0.9%	391	0.9%	0.00
PPO/EPO	24,769	59.4%	24,769	59.4%	0.00
POS with or without capitation	3016	7.2%	3016	7.2%	0.00
HMO	5613	13.5%	5613	13.5%	0.00
CDHP/HDHP	6558	15.7%	6558	15.7%	0.00

Other/Unknown	1328	3.2%	1328	3.2%	0.00
Index year (N, %)¹					
2011	9677	23.2%	9677	23.2%	0.00
2012	7118	17.1%	7118	17.1%	0.00
2013	7810	18.7%	7810	18.7%	0.00
2014	9357	22.5%	9357	22.5%	0.00
2015	7713	18.5%	7713	18.5%	0.00
Unique NDCs (mean, SD)	5.0	4.7	3.4	4.2	36.05
Unique 3-digit ICD-9/10-CM codes (mean, SD)	7.9	5.7	6.2	5.1	32.02
Total healthcare costs (mean, SD)	\$5165	\$23,357	\$3714	\$23,409	6.20

CDHP, consumer-driven health plan; EPO, exclusive provider organization; HDHP, high-deductible health plan; HMO, health maintenance organization; ICD-9/10-CM, International Classification of Diseases, Ninth or Tenth Revision, Clinical Modification; NDC, national drug code; POS, point of service; PPO, preferred provider organization; SD, standard deviation; Std. Diff., standardized difference.

¹Demographic and clinical characteristics used in direct matching 1:1 between peanut allergy and control patients.

9 **Table 2** Treatment Patterns

	Peanut Allergy		Control		
	N=41,675		N=41,675		
	N/Mean	%/SD	N/Mean	%/SD	P-value
Office visits by physician specialty					
Patients with ≥ 1 office visit (N, %)					
Allergy specialist	24,385	58.5%	2701	6.5%	<0.001
Pediatrician ¹					
Aged 0–3 years, N=10,774	9203	85.4%	8510	79.0%	<0.001
Aged 4–11 years, N=18,517	14,649	79.1%	12,673	68.4%	<0.001
Aged 12–18 years, N=6992	4496	64.3%	3498	50.0%	<0.001
General practitioner	15,263	36.6%	14,101	33.8%	<0.001
Other physician type	34,279	82.3%	27,200	65.3%	<0.001
Count of visits² (mean, SD)					
Allergy specialist	2.1	5.9	0.4	2.8	<0.001
Pediatrician					
Aged 0–3 years, N=10,774	4.8	4.4	3.8	3.9	<0.001
Aged 4–11 years, N=18,517	3.0	3.5	2.4	2.9	<0.001
Aged 12–18 years, N=6992	2.1	3.1	1.6	2.6	<0.001
General practitioner	1.4	4.3	1.1	3.5	<0.001
Other physician type	5.9	12.5	4.3	10.7	<0.001
Procedures of interest					

Patients with ≥ 1 claim (N, %)					
Nebulizer utilization	1889	4.5%	1168	2.8%	<0.001
Injectable steroid medications	2624	6.3%	1088	2.6%	<0.001
Epinephrine autoinjector products	27,179	65.2%	1329	3.2%	<0.001
Count of services³ (mean, SD)					
Nebulizer utilization	2.6	2.3	2.7	2.8	0.54
Injectable steroid medications	1.4	1.1	1.5	1.1	0.384
Epinephrine autoinjector products	1.5	0.9	1.3	0.7	<0.001
Costs³ (mean, SD)					
Nebulizer utilization	\$87	\$121	\$96	\$196	0.113
Injectable steroid medications	\$22	\$50	\$14	\$27	<0.001
Epinephrine autoinjector products	\$608	\$502	\$526	\$416	<0.001

SD, standard deviation.

¹Among patients in the age subgroup.

²Number of unique days with office visits.

³Counts and costs among patients with ≥ 1 claim of that type.

Table 3 All-Cause and Peanut Allergy-Related Healthcare Utilization and Costs in the Follow-Up Period by Age Group

	All Ages				Aged 4–11 Years				Aged 12–18 Years		
	Peanut Allergy N=41,675	Control N=41,675	P-value		Peanut Allergy N=18,517	Control N=18,517	P-value		Peanut Allergy N=6992	Control N=6992	P-value
All-cause											
Patients	% (N)	% (N)			% (N)	% (N)			% (N)	% (N)	
Inpatient (IP)	4.7% (1962)	2.1% (888)	<0.001		3.1% (574)	1.3% (235)	<0.001		5.0% (352)	2.1% (146)	<0.001
Outpatient (OP)	100% ¹ (41,667)	92.7% (38,627)	<0.001		100% (18,517)	92.5% (17,125)	<0.001		100% (6989)	89.9% (6285)	<0.001
ED visit	32.8% (13,690)	19.6% (8166)	<0.001		27.3% (5052)	17.3% (3196)	<0.001		35.8% (2505)	20.0% (1400)	<0.001
Ambulance services	7.6% (3175)	3.7% (1542)	<0.001		4.9% (911)	2.4% (444)	<0.001		9.6% (668)	4.0% (279)	<0.001
Urgent care facility visit	7.7% (3218)	6.2% (2603)	<0.001		7.3% (1355)	6.3% (1163)	<0.001		7.3% (510)	5.6% (393)	<0.001
Physician office visit	98.8% (41,185)	89.4% (37,262)	<0.001		99.2% (18,373)	88.7% (16,433)	<0.001		98.1% (6862)	85.6% (5988)	<0.001
Other OP	97.6% (40,675)	85.5% (35,613)	<0.001		97.4% (18,039)	84.0% (15,558)	<0.001		96.5% (6749)	82.2% (5745)	<0.001
Pharmacy	94.3% (39,283)	73.3% (30,559)	<0.001		94.4% (17,489)	71.0% (13,140)	<0.001		93.0% (6504)	72.3% (5053)	<0.001
Cost per event	Mean	Mean			Mean	Mean			Mean	Mean	

Inpatient (IP)	\$19,484	\$26,751			\$15,610	\$22,495			\$27,554	\$22,142	
ED visit	\$928	\$801			\$846	\$757			\$997	\$850	
Ambulance services	\$684	\$712			\$672	\$685			\$659	\$647	
Urgent care facility visit	\$79	\$80			\$81	\$80			\$73	\$74	
Physician office visit	\$116	\$106			\$115	\$105			\$117	\$108	
Costs²	Mean	Mean			Mean	Mean			Mean	Mean	
	(SD)	(SD)			(SD)	(SD)			(SD)	(SD)	
Total	\$6436	\$3493	<0.001		\$4818	\$2540	<0.001		\$8138	\$3798	<0.001
(IP+OP+pharmacy)	(\$25,165)	(\$23,217)			(\$14,184)	(\$18,383)			(\$40,321)	(\$18,839)	
Medical	\$5002	\$2832			\$3448	\$2048			\$6343	\$2890	
(IP+OP)	(\$24,160)	(\$22,132)	<0.001		(\$12,986)	(\$17,600)	<0.001		(\$38,783)	(\$17,187)	<0.001
IP	\$1219	\$721			\$602	\$414			\$2053	\$684	
	(\$19,040)	(\$18,158)	<0.001		(\$6,972)	(\$13,182)	<0.001		(\$32,876)	(\$14,171)	<0.001
OP	\$3783	\$2111	<0.001		\$2847	\$1634	<0.001		\$4290	\$2206	<0.001
	(\$10,281)	(\$8508)			(\$9,054)	(\$8810)			(\$11,096)	(\$6902)	
Pharmacy	\$1434	\$661	<0.001		\$1370	\$492	<0.001		\$1795	\$907	<0.001
	(\$4248)	(\$4900)			(\$4078)	(\$2407)			(\$5740)	(\$5836)	
PA-related											
Number of patients	%	%			%	%			%	%	
	(N)	(N)			(N)	(N)			(N)	(N)	
IP ³	0.3%	0.0%	<0.001		0.2%	0.0%	<0.001		0.4%	0.0%	<0.001
	(143)	(0)			(36)	(0)			(28)	(0)	
OP ³	98.5%	2.6%	<0.001		98.9%	1.1%	<0.001		98.3%	3.0%	<0.001
	(41,070)	(1094)			(18,318)	(211)			(6871)	(210)	
ED visit	14.3%	0.0%	<0.001		10.7%	0.0%	<0.001		18.4%	0.0%	<0.001
	(5954)	(0)			(1,978)	(0)			(1289)	(0)	

Ambulance services	0.4% (159)	0.0% (3)	<0.001	0.3% (52)	0.0% (2)	<0.001	0.5% (34)	0.0% (0)	<0.001
Urgent care facility visit	0.9% (367)	0.1% (62)	<0.001	0.7% (137)	0.1% (13)	<0.001	1.0% (68)	0.2% (15)	<0.001
Physician office visit	79.1% (32,967)	0.0% (0)	<0.001	83.3% (15,418)	0.0% (0)	<0.001	74.4% (5199)	0.0% (0)	<0.001
Other outpatient	68.1% (28,401)	2.5% (1037)	<0.001	67.9% (12,569)	1.1% (196)	<0.001	65.7% (4596)	2.8% (196)	<0.001
Pharmacy ⁴	82.1% (34,214)	27.5% (11,468)	<0.001	86.2% (15,960)	28.6% (5298)	<0.001	79.4% (5550)	25.6% (1,789)	<0.001
Cost per event	Mean	Mean		Mean	Mean		Mean	Mean	
Inpatient (IP)	\$7921	-		\$6186	-		\$9130	-	
ED visit	\$1115	-		\$1071	-		\$1149	-	
Ambulance services	\$784	\$6		\$665	\$8		\$547	-	
Urgent care facility visit	\$78	\$10		\$89	\$13		\$84	\$12	
Physician office visit	\$134	-		\$129	-		\$131	-	
Costs²	Mean	Mean		Mean	Mean		Mean	Mean	
	(SD)	(SD)		(SD)	(SD)		(SD)	(SD)	
Total	\$1490	\$159	<0.001	\$1453	\$154	<0.001	\$1626	\$152	<0.001
(IP+OP+pharmacy)	(\$2701)	(\$1282)		(\$1891)	(\$1138)		(\$4232)	(\$1265)	
Medical	\$684	\$0	<0.001	\$579	\$0	<0.001	\$804	\$0	<0.001
(IP+OP)	(\$1763)	(\$5)		(\$1278)	(\$2)		(\$2497)	(\$4)	
IP	\$27	\$0	<0.001	\$12	\$0	<0.001	\$37	\$0	<0.001
	(\$576)	(\$0)		(\$317)	(\$0)		(\$700)	(\$0)	
OP	\$657	\$0	<0.001	\$567	\$0	<0.001	\$768	\$0	<0.001
	(\$1657)	(\$5)		(\$1239)	(\$2)		(\$2363)	(\$4)	

Pharmacy	\$806 (\$1995)	\$159 (\$1282)	<0.001		\$873 (\$1351)	\$154 (\$1138)	<0.001		\$821 (\$3297)	\$152 (\$1265)	<0.001
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17 ED, emergency department; PA, peanut allergy; SD, standard deviation.

18 ¹The actual percentage is 99.98% (rounded to 100%), representing 41,667 individuals out of a total of
19 41,675 individuals in the PA group.

20 ²Costs represent the paid amounts of fully adjudicated claims, including insurer and health plan payments
21 as well as patient cost-sharing in the form of copayment, deductible, and coinsurance.

22 ³Peanut allergy- or reaction-related utilization and costs included peanut allergy or reaction diagnosis in a
23 primary position for inpatient claims and any position for outpatient claims, and office-administered
24 medications (Healthcare Common Procedure Coding System), including epinephrine and injectable
25 steroids for outpatient claims.

26 ⁴Peanut allergy- or diagnosis-associated pharmacy costs were captured with new drug codes for
27 epinephrine, antihistamines, corticosteroids, mast cell stabilizers, leukotriene inhibitors, nasal
28 anticholinergics, decongestants, and immunomodulators.

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Figure 1

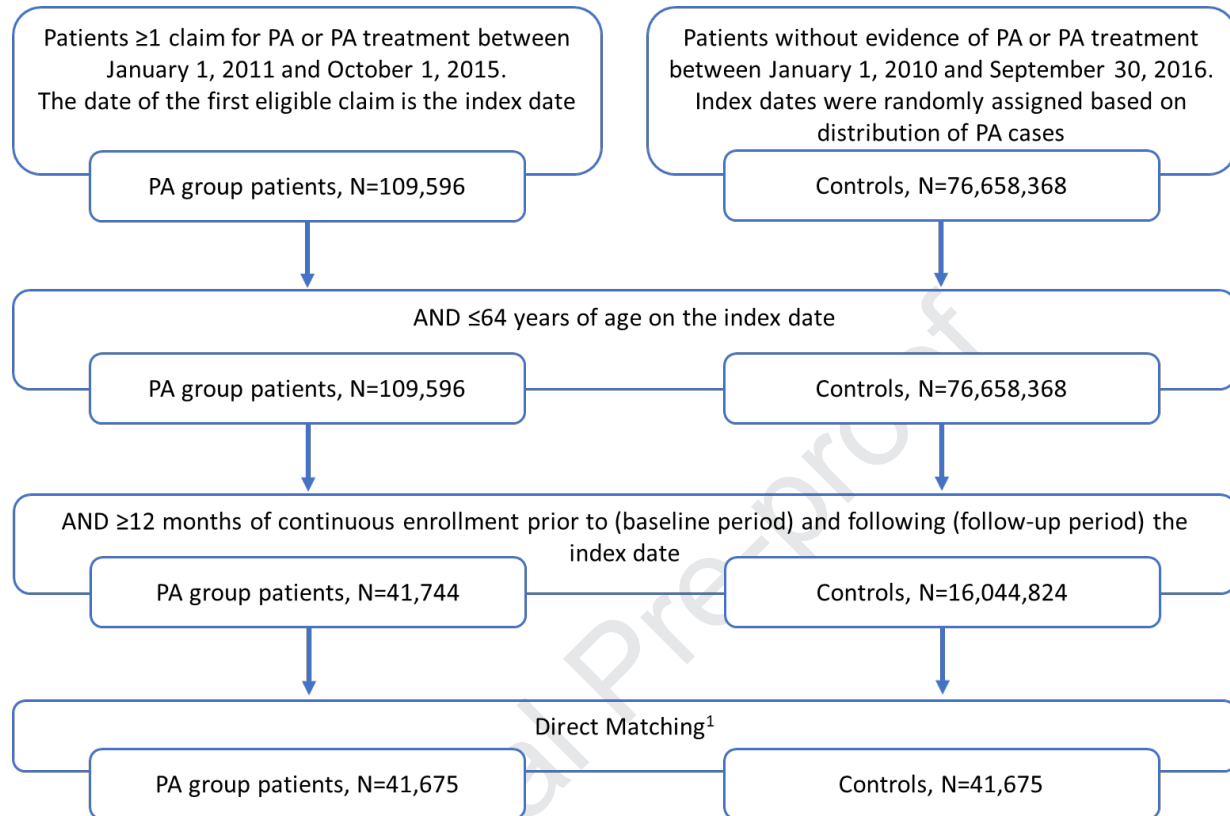
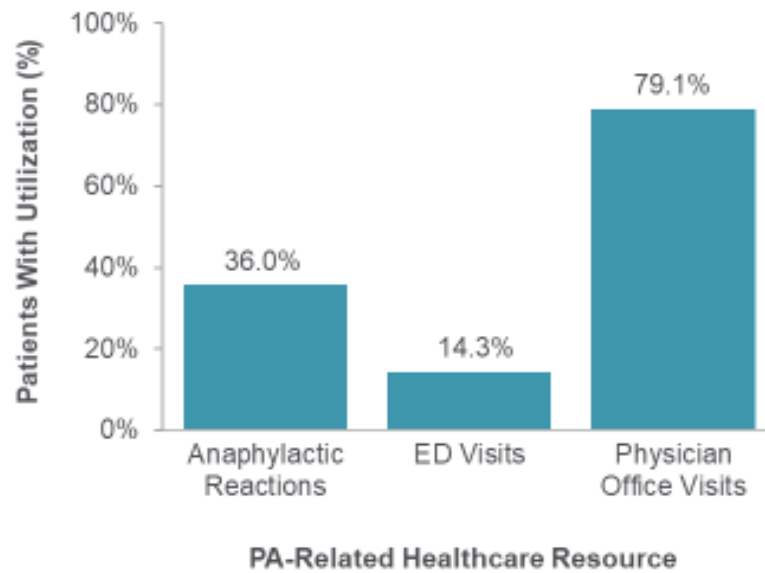


Figure 2



eFigure 1: All-Cause Healthcare Cost and Resource Utilization

